THE DISPENSATORY

OF

THE UNITED STATES OF AMERICA

TWENTIETH EDITION

THOROUGHLY REVISED, LARGELY REWRITTEN, AND BASED UPON THE NINTH REVISION OF THE UNITED STATES PHARMACOPŒIA AND THE BRITISH PHARMACOPŒIA 1914

BY

JOSEPH P. REMINGTON, PH.M., F.C.S.

LATE PROFESSOR OF THEORY AND PRACTICE OF PHARMACY IN THE PHILADELPHIA COLLEGE OF PHARMACY; LATE CHAIRMAN OF THE COMMITTEE OF REVISION OF THE PHARMACOPŒIA OF THE UNITED STATES OF AMERICA

HORATIO C. WOOD, JR., M.D.

PROFESSOR OF PHARMACOLOGY AND THERAPEUTICS IN THE UNIVERSITY OF PENNSYLVANIA; VICE-CHAIRMAN OF THE COMMITTEE OF REVISION OF THE PHARMACOPŒIA OF THE UNITED STATES OF AMERICA

SAMUEL P. SADTLER, PH.D., LL.D.

FORMER PROFESSOR OF CHEMISTRY IN THE PHILADELPHIA COLLEGE OF PHARMACY; MEMBER OF THE COMMITTEE OF REVISION OF THE PHARMACOPŒIA OF THE UNITED STATES OF AMERICA

CHARLES H. LAWALL, PH.M.

PROFESSOR OF THEORY AND PRACTICE OF PHARMACY IN THE PHILADELPHIA COLLEGE OF PHARMACY; CHAIRMAN OF THE COMMITTEE OF REVISION OF THE PHARMACOPŒIA OF THE UNITED STATES OF AMERICA

HENRY KRAEMER, PH.G., PH.D.

PROFESSOR OF BOTANY AND PHARMACOGNOSY IN THE UNIVERSITY OF MICHIGAN; MEMBER OF THE COMMITTEE OF REVISION OF THE PHARMACOPŒIA OF THE UNITED STATES OF AMERICA

JOHN F. ANDERSON, M.D.

DIRECTOR OF THE RESEARCH AND BIOLOGICAL LABORATORIES OF E. R. SQUIBB AND SONS; MEMBER OF THE COMMITTEE OF REVISION OF THE PHARMACOPŒIA OF THE UNITED STATES OF AMERICA

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EXPLANATORY NOTES

The "Em" is the printer's measure. Technically it is "a square of the height of the face of the type upon which it is calculated." As used here it represents the actual amount of printed matter in various editions of the U. S. Dispensatory from 1833 to 1917, showing that although the number of pages has been only a little more than doubled, the amount of matter has been nearly quadrupled by increasing the size of the page and decreasing that of the type.

On the title-page of the 14th edition occur the words "completely revised by George B. Wood, assisted by H. C Wood." The facts are that George B. Wood, when he was nearly 80 years of age, insisted on revising the book himself until after he had accomplished about one-half his task further effort became impossible, whereupon he asked his nephew, Horatio C Wood, to take the whole responsibility upon himself.

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PREFACE TO THE TWENTIETH EDITION.

AMERICAN pharmacy has suffered an inestimable loss in the death of Joseph P. Remington, since 1880 one of the editors of this work, who passed away while this edition was on the presses. Professor Remington, feeling strongly the need of the pharmacists for the U. S. Dispensatory, forced himself, regardless of his failing strength, to strenuous endeavor to hasten the work of revision. He was able by the effort of his will to keep at his work until the manuscript was completed. Already stricken with the fatal malady, when the last page of copy had been placed in the hands of the printer, even his indomitable courage could go no further and the task of seeing the book through the press was taken over by the other editors.

Since the appearance of the 19th edition of the United States Dispensatory there have been such extraordinary advances in the pharmaceutical and medical sciences that a most extensive revision of this work has been required. While the general form of the previous edition, which has proven so acceptable, has been retained, the subject-matter has been thoroughly revised, so much so that the book has been *almost entirely* rewritten. In order that this task should be more thoroughly performed, and the work should have the authority of eminent specialists in each of the various branches of drug knowledge, it has been deemed advisable to increase the staff of editors. The men who have been called to this work are so well known to both the professions of Pharmacy and Medicine that any extended introduction seems unnecessary. Their names will be found on the title-page.

Within the last three years new revisions of all of the standards upon which this work especially comments—the U. S. Pharmacopœia, the British Pharmacopœia, and the National Formulary—have been published. The change in the character of the National Formulary, from a collection of recipes for the convenience of the apothecary to a legal authority of purity, seems to demand for it more extended recognition than formerly. Therefore, all of the crude drugs standardized by that work have been considered in considerable detail. While the editors have thought it wise to retain these drugs—except such as are also recognized by the British Pharmacopœia—in Part II, to indicate their lesser importance, each such substance has been indicated by the letters N. F. The galenical preparations of the National Formulary are, as heretofore, given in abstract in a separate place. Recognition of the list of Approved "New and Non-official Remedies," published by the American Medical Association, has also been extended, such drugs being marked N. N. R. 1917.

Among the valuable features of the 19th edition which have been retained in the 20th, may be mentioned the list of synonyms, the insertion of alternative quantities in the formulæ of the official preparations, the use of diacritical marks as a guide to pronunciation, and the list of official preparations at the close of the description of each official crude drug. Attention may be called also to the fact that the dose of each drug is given at the end of the description of its therapeutic uses: this uniformity of situation enables the reader, who usually wishes such information in a hurry, to find it at once. The quantities inserted, it may be mentioned in passing, are not intended to indicate either the minimum or maximum doses, but merely to serve as a guide to the amounts usually employed.

Greater prominence has been given to the subject of chemical incompatibilities. A summary of the incompatibilities of each of the more important drugs has been placed immediately before the description of its therapeutic uses.

The extensive use of bacterial products as therapeutic agents has led to the addition of articles on the so-called Vaccines as well as to enlargement of those on the various serums.

Attention may also be called to the summary of the Food Inspection decisions under the Food and Drugs Act of 1906, given in the preliminary matter. The importance of a knowledge of these regulations to both wholesale and retail pharmacists, and the difficulty of obtaining it, we believe makes this a valuable convenience. By referring to the special index of these decisions the reader can at once find an abstract of all the decisions touching any especial point in which he may be interested. The Harrison Antinarcotic Law and the regulations of the Internal Revenue office in connection with it are also given in full.

The editors desire to express their thanks to Prof. E. Fullerton Cook, whose assistance in many directions, especially in the correcting of proof and in the preparation of the Index, has been of material value; and to Dr. H. S. Zulick, who has prepared the Index of Diseases.

PREFACE TO THE FIRST EDITION.

THE objects of a Dispensatory are to present an account of medicinal substances in the state in which they are brought into the shops, and to teach the modes in which they are prepared for use. The importance of these objects, and the general value and even necessity of a work of this nature, will not be disputed. It may, however, be a question, how far the wants of the medical and pharmaceutical community in this country are supplied by the Dispensatories already in circulation; and whether such a deficiency exists as to justify the offer of a new one to the public attention. The great merits of the works severally entitled "The Edinburgh New Dispensatory" and "The London Dispensatory," the former edited by the late Andrew Duncan, M.D., the latter by Anthony Todd Thomson, M.D., are well known wherever the English language is spoken. Founded, as they both are, upon the excellent basis laid by Lewis, they are nevertheless entitled, from the great addition of valuable materials, and the distinctive character exhibited in the arrangement of these materials, to be considered as original works; while the style in which they have been executed speaks strongly in favor of the skill and industry of their authors. But they were calculated especially for the sphere of Great Britain, and are too deficient in all that relates exclusively to this country, to admit of being received as standards here. In the history of our commerce in drugs, and of the nature, growth, and collection of our indigenous medical plants; in the chemical operations of our extensive laboratories; and in the modes of preparing, dispensing, and applying medicines, which have gradually grown into use among us; there is much that is peculiar, a knowledge of which is not to be gained from foreign books, and is yet necessary to the character of an accomplished American pharmaceutist. We have, moreover, a National Pharmacopœia, which requires an explanatory commentary, in order that its precepts may be fully appreciated, and advantageously put into practice. On these accounts, it is desirable that there should be a Dispensatory of the United States, which, while it embraces whatever is useful in European pharmacy, may accurately represent the art as it exists in this country, and give instruction adapted to our peculiar wants. It appears due to our national character that such a work should be in good faith an American work, newly prepared in all its parts, and not a mere edition of one of the European Dispensatories, with here and there additions and alterations, which, though they may be useful in themselves, cannot be made to harmonize with the other materials so as to give to the whole an appearance of unity, and certainly would not justify the assumption of a new national title for the book. Whether, in the Dispensatories which have been published in the United States, these requisites have been satisfactorily fulfilled, it rests with the public to determine. That valuable treatises on Materia Medica and Pharmacy have been issued in this country, no candid person, acquainted with our medical literature, will be disposed to deny. In offering a new work to the medical and pharmaceutical professions, the authors do not wish to be considered as undervaluing the labors of their predecessors. They simply conceive that the field has not been so fully occupied as to exclude all competition. The Pharmacy of continental Europe is ground which has been almost untouched; and much information in relation to the natural history, commerce, and management of our own drugs, has lain ungathered in the possession of individuals, or scattered in separate treatises and periodicals not generally known and read. Since the publication of the last edition of our National Pharmacopœia, no general explanation of its processes has appeared, though required in justice both to that work and to the public. The hope of being able to supply these deficiencies may, perhaps, be considered a sufficient justification for the present undertaking.

The Pharmacopœia of the United States has been adopted as the basis of this Dispensatory. It is followed both in its general division of medicines, and in its alphabetical arrangement of them under each division. Precedence is, in every instance, given to the names it recognizes, while the explanations by which it fixes the significance of these names are inserted in immediate connection with the titles to which they severally belong. Every article which it designates is more or less fully described; and all its processes, after being literally copied, are commented on and explained wherever comment and explanation appeared necessary. Nothing, in fine, has been omitted, which, in the estimation of the authors, could serve to illustrate its meaning, or promote the ends which it was intended to subserve. This course of proceeding appeared to be due to the national character of the Pharmacopœia, and to the important object of establishing, as far as possible, throughout the United States, uniformity, both in the nomenclature and preparation of medicines. In one particular, convenience required that the plan of the Pharmacopœia should be departed from. The medicines belonging to the department of MATERIA MEDICA, instead of being arranged in two divisions corresponding with the *Primary and Secondary Catalogues* of that work, have been treated of indiscriminately in alphabetical succession; and the place which they respectively hold in the Pharmacopœia is indicated by the employment of the term *Secondary*, in connection with the name of each of the medicines included in the latter catalogue.

But, though precedence has thus been given to the Pharmacopœia of the United States, those of Great Britain have not been neglected. The nomenclature adopted by the different British Colleges, and their formulas for the preparation of medicines, have been so extensively followed throughout the United States, that a work intended to represent the present state of pharmacy in this country would be imperfect without them; and the fact that the writings of British physicians and surgeons, in which their own official terms and preparations are exclusively employed and referred to, have an extensive circulation among us, renders some commentary necessary in order to prevent serious mistakes. The Pharmacopœias of London, Edinburgh, and Dublin have, therefore, been incorporated, in all their essential parts, into the present work. Their official titles are uniformly given, always in subordination to those of the United States Pharmacopœia, when they express the same object; but in chief, when, as often happens, no corresponding medicine or preparation is recognized by our national standard. In the latter case, if different names are applied by different British Colleges to the same object, that one is generally preferred which is most in accordance with our own system of nomenclature, and the others are given as synonymes. The medicines directed by the British Colleges are all described, and their processes either copied at length, or so far explained as to be intelligible in all essential particulars.

Besides the medicinal substances recognized as official by the Pharmacopœias alluded to, some others have been described, which, either from the lingering remains of former reputation, from recent reports in their favor, or from their important relation to medicines in general use, appear to have claims upon the attention of the physician and apothecary. Opportunity has, moreover, been taken to introduce incidentally brief accounts of substances used in other countries or in former times, and occasionally noticed in medical books; and, that the reader may be able to refer to them when desirous of information, their names have been placed with those of the standard remedies in the Index.

In the description of each medicine, if derived immediately from the animal, vegetable, or mineral kingdom, the attention of the authors has been directed to its natural history, the place of its growth or production, the method of collecting and preparing it for market, its commercial history, the state in which it reaches us, its sensible properties, its chemical composition and relations, the changes which it undergoes by time and exposure, its accidental or fraudulent adulterations, its medical properties and application, its economical uses, and the pharmaceutical treatment to which it is subjected. If a

chemical preparation, the mode and principles of its manufacture are indicated in addition to the other particulars. If a poison, and likely to be accidentally taken, or purposely employed as such, its peculiar toxicological effects, together with the mode of counteracting them, are indicated; and the best means of detecting its presence by reagents are explained.

The authors have followed the example of Dr. A. T. Thomson, in giving botanical descriptions of the plants from which the medicines treated of are derived. In relation to all indigenous medicinal plants, and those naturalized or cultivated in this country, the advantages of such descriptions are obvious. The physician may often be placed in situations in which it may be highly important that he should be able to recognize the vegetable which yields a particular medicine; and the apothecary is constantly liable to imposition from the collectors of herbs, unless possessed of the means of distinguishing, by infallible marks, the various products presented to him. A knowledge of foreign medicinal plants, though of less importance, will be found useful in various ways, independently of the gratification afforded by the indulgence of a liberal curiosity in relation to objects so closely connected with our daily pursuits. The introduction of these botanical notices into a Dispensatory appears to be peculiarly appropriate; as they are to be considered rather as objects for occasional reference than for regular study or continuous perusal, and therefore coincide with the general design of the work, which is to collect into a convenient form for consultation all that is practically important in relation to medicines. The authors have endeavored to preserve a due proportion between the minuteness of the descriptions, and their value as means of information to the student; and, in pursuance of this plan, have generally dwelt more at length upon our native plants than upon those of foreign growth; but, in all instances in which they have deemed a botanical description necessary, they have taken care to include in it the essential scientific character of the genus and species, with a reference to the position of the plant in the artificial and natural systems of classification; so that a person acquainted with the elements of botany may be able to recognize it when it comes under his observation.

In preparing the Dispensatory, the authors have consulted, in addition to many of the older works of authority, the greater number of the treatises and dissertations which have recently appeared upon the various subjects connected with Pharmacy, and especially those of the French writers, who stand at present at the head of this department of medical science. They have also endeavored to collect such detached facts, scattered through the various scientific, medical, and pharmaceutical journals, as they conceive to be important in themselves, and applicable to the subjects under consideration; and have had frequent recourse to the reports of travellers in relation to the natural and commercial history of foreign drugs. The occasional references in the body of the work will indicate the sources from which they have most largely drawn, and the authorities upon which they have most relied. In relation to our own commerce in drugs, and to the operations of our chemical laboratories, they are indebted for information chiefly to the kindness of gentlemen engaged in these branches of business, who have always evinced, in answering their numerous inquiries, a promptitude and politeness which merit their warm thanks, and which they are pleased to have this opportunity of acknowledging.[1]

It has not been deemed necessary to follow the example of the British Dispensatories, by inserting into the work a treatise upon chemistry, under the name of Elements of

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[1] The authors deem it proper to state that they are peculiarly indebted for assistance to Mr. Daniel B. Smith, president of the Philadelphia College of Pharmacy, to whom, besides much important information in relation to the various branches of the apothecary's business, they owe the prefatory remarks on Pharmacy, which are placed at the commencement of the second part of the work, and the several articles, in the Materia Medica, upon *Leeches*, *Carbonate of Magnesia*, and *Sulphate of Magnesia*.

Pharmacy. Such a treatise must necessarily be very meagre and imperfect, and, as systems of chemistry are in the hands of every physician and apothecary, would uselessly occupy the place of valuable matter of less easy access.

The authors may, perhaps, be permitted to observe, in relation to themselves, that they have expended much time and labor in the preparation of the work; have sought diligently for facts from every readily accessible source; have endeavored, by a comparison of authorities, and a close scrutiny of evidence, to ascertain the truth whenever practicable; and have exerted themselves to the extent of their abilities to render the Dispensatory worthy of public approbation, both for the quality and quantity of its contents, and the general accuracy of its statements. They are conscious, nevertheless, that in so great a multiplicity of details, numerous errors and deficiencies may exist, and that the faults of undue brevity in some cases, and prolixity in others, may not have been entirely avoided; but they venture to hope that a candid public will make all due allowances; and they take the liberty to invite, from all those who may feel interested in the diffusion of sound pharmaceutical knowledge, the communication of friendly suggestions or criticisms in relation to the objects and execution of the work.

PHILADELPHIA, January, 1833.

ABBREVIATIONS.

Ait.—W. Aiton.
Arab.—Arabic.
Aubl.—Aublet.
B.—Baumé's Hydrometer.
B. et H.—Bentham and Hooker.
B. & T.—Bentley & Trimen's Medicinal Plants.
Baill.—Baillon.
Bart.—Barton.
Benth.—Bentham.
Bl.—Blume.
Boehm.—Boehmer.
Boiss.—Boissier.
Br.—The British Pharmacopœia, 1914.
Br. Add.—Indian and Colonial Addendum (1900) to the British Pharmacopœia (1898).
Britt.—Britton.
Brot.—Brotero.
C. et S.—Chamisso and Schlechtendal.
Carr.—Carriere.
Cav.—Cavaniles.
Cc.—Cubic centimeter (see Mil).
Cerv.—Cervantes.
Cham.—Chamisso.
Chois.—Choisey.
Cm.—Centimeter.
Cod.—Codex Medicamentarius. The French Pharmacopœia, 1908.
Coult.—Coulter.
Coult. et R.—Coulter and Rose.
DC.—De Candolle.
Desf.—Desfontaines.
Desr.—Desroussaux.
Dry.—Dryander.
Duh.—Duhamel.
E. et P.—Engler and Prantl.
Ell.—Elliott.
Engl.—Engler.
F. Müll.—Ferdinand von Müller.
Fam.—Family.
Fisch.—Fischer.
Fr.—French.
Fr. Cod.—The French Pharmacopœia, 1908.
Froel.—Froelich.
G.—German.
Gaert.—Gaertner.
Gm.—Gramme.
Griseb.—Grisebach.
H. B. K.—Humboldt, Bonpland, and Kunth.
Hassk.—Hasskarl.
Hook.—W. J. Hooker.
Hook. f.—J. D. Hooker.
Houtt.—Houttyn.
It.—Italian.
Jacq.—Jacquin.
Juss.—Jussieu.
Kze.—Kunze.
Labil.—Labillardière.
Lam.—Lamarck.
Lindl.—Lindley.
Linn.—Linnæus (Linné).
Michx.—Michaux.
Mil.—Milliliter, Cubic Centimeter, Cc.
Miq.—Miquel.
Mm.—Millimeter.
Moench.—Moenchausen.
Mol.—Molecule.
N. F.—National Formulary IV.
Nat. Ord.—Natural Order
Nutt.—Nuttall.
Off. Prep.—Official Preparations.
P. G.—The German Pharmacopœia. Arzneibuch für das Deutsche Reich (1910).
Pav.—Pavon.
Port.—Portuguese.
Raf.—Rafinesque.
Roxb.—Roxburgh.
Schlecht.—Schlechtendal.
Sonn.—Sonnerat.
Sp.—Spanish.
Sp. Gr.—Specific Gravity.
Sw.—Swartz.
T. et G.—Torrey and Gray.
Thunb.—Thunberg.
Tul.—Tulasne.
U. S.—The Pharmacopœia of the United States, IX. Older editions have date attached thus: *U. S.* (1890).
Vaill.—Vaillant.
Var.—Variety.
Willd. Sp. Plant.—Willdenow's edition of the Species Plantarum of Linnæus.
Woodv. Med. Bot.—Woodville's Medical Botany. 2d edition.

TABLE OF ABBREVIATED TITLES OF JOURNALS AND BOOKS REFERRED TO IN THIS WORK.

A. de P.—Archives de Physiologie normale et pathologique.
A. de S.—Académie des Sciences.
A. E. P. P.—Archiv für Experimentelle Pathologie und Pharmakologie.
A. G. M.—Archives générales de Médecine.
A. G. P.—Archiv der gesammte Physiologie.
A. I. B.—Archives Italiennes de Biologie.
A. I. P.—Archives internationales de Pharmacodynamique.
A. In. M.—Archives of Internal Medicine.
A. J. P.—American Journal of Pharmacy.
A. Klin. Chir.—Archiv für Klinische Chirurgie.
A. M. S. J.—Atlanta Medical and Surgical Journal.
A. Pharm.—Archiv der Pharmacie.
A. Phys.—Archiv für Anatomie und Physiologie, physiologisches Abteilung.
Aerzt. Rund.—Aerztliche Rundschau.
All. M. C. Z.—Allgemeine medicinische Central Zeitung.
All. W. M. Z.—Allgemeine Wiener medicinische Zeitung.
Am. Chem. J.—American Chemical Journal.
Am. Drug.—American Druggist and Pharmaceutical Record.

Am. J. M. S.—American Journal of Medical Sciences.
Am. J. Sci.—American Journal of Science (and Arts).
Am. Med.—American Medicine.
Am. Pract. and News.—American Practitioner and News.
An.—The Analyst.
Ann. Ch. Ph.—Annalen der Chemie und Pharmacie.
Ann. Ch. Phys.—Annales de Chimie et de Physique.
Ann. Pharm.—Annalen der Pharmacie.
Ann. Thér.—Annuaire de Thérapeutique.
Ap. Ztg.—Apotheker Zeitung.
Apoth.—Apothecary.
Arch. I. C. M.—Archivio Italiano di Clinica Medica.
Arch. Pharm.—Archiv der Pharmazie.
Ber. d. pharm. Ges.—Berichte der deutschen pharmazeutischen Gesellschaft.
B. A. M.—Bulletin de l'Académie de Médecine de Paris.
B. A. R. B.—Bulletin de l'Académie Royale de Belge.
B. C. D.—British and Colonial Druggist.
B. D. A. J.—Bulletin Department of Agriculture, Jamaica.
B. F. M. R.—British and Foreign Medical Review.
B. G. T.—Bulletin général de Thérapeutique, médicale et chirurgicale.
B. Hôp. Par.—Bulletin de la Société Médicale des Hôpitaux de Paris.
B. K. Ch.—Beitrage zur Klinische Chirurgie.
B. K. W.—Berliner klinische Wochenschrift.
B. M.—Le Bulletin Médicale.
B. M. J.—British Medical Journal.
B. M. N.—Bulletin Médicale du Nord.
B. M. S. J.—Boston Medical and Surgical Journal.
B. P. G.—Berichte der Deutschen Pharmaceutischen Gesellschaft.
B. S. Ph. Br.—Bulletin de la Société Royale de Pharmacie de Bruxelles.
B. Sc. Pharm.—Bulletin de la Société Pharmacologique.
B. Thier. W.—Berliner Thierärztliche Wochenschrift.
Ber. d. Chem. Ges.—Berichte der Deutschen Chemischen Gesellschaft.
Biochem. J.—Biochemical Journal.
Biochem. Zeit.—Biochemische Zeitschrift.
Boston J. Chem.—Boston Journal of Chemistry.
Br.—British Pharmacopœia (1914).
Br. Add.—British Pharmacopœia, Indian and Colonial Addendum.
Bull. Pharm.—Bulletin of Pharmacy.
Bull. Soc. Chim.—Bulletin de la Société Chimique de Paris.
C. D.—Chemist and Druggist.
C. R. A. S.—Comptes-rendus de l'Académie de Science de Paris.
C. R. S. B.—Comptes-rendus de la Société de Biologie de Paris.
Can. Drug.—Canadian Druggist.
Can. Pharm. Journ.—Canadian Pharmaceutical Journal.
Cb. B.—Centralblatt für Bacteriologie.
Cb. Chir.—Centralblatt für Chirurgie.
Cb. G. T.—Centralblatt für die gesammte Therapie.
Cb. Gyn.—Centralblatt für Gynekologie.
Cb. I. M.—Centralblatt für Innere Medicin.
Cb. M. W.—Centralblatt für medicinische Wissenschaften.
Cb. Path.—Centralblatt für Allgemeine Pathologie und Pathologisches Anatomie.
Cb. Phys.—Centralblatt für Physiologie.
Ch. Ph.—Chicago Pharmacist.
Chem. Cb.—Chemisches Centralblatt.
Chem. Gaz.—Chemical Gazette.
Chem. News.—Chemical News.
Chem. Ztg.—Chemiker Zeitung.
D. A. K. M.—Deutsches Archiv für Klinische Medicin.
D. C.—Druggists Circular.
D. M. W.—Deutsche medicinische Wochenschrift.
D. M. Ztg.—Deutsche medicinische Zeitung.
D. Z. Chir.—Deutsche Zeitschrift für Chirurgie.
Derm. Cb.—Dermatologisches Centralblatt.
Derm. Zeit.—Dermatologische Zeitschrift.
Dublin Q. J.—Dublin Quarterly Journal of Medical Science.
Ed. M. J.—Edinburgh Medical Journal.
Ephem.—Ephemeris (Squibb).
F. Th.—Folia Therapeutica.
F. I. D.—Food Inspection Decisions.
Fort. Med.—Fortschritte der Medicin.
France Méd.—La France Médicale.
G. H. M. C.—Gazette Hebdomadaire de Médecine et de Chirurgie.
G. M. P.—Gazette Médicale de Paris.
G. Osp.—Gazetta degli Ospedale e delle Cliniche.
Hyg. Rund.—Hygienische Rundschau.
In. Dis.—Inaugural Dissertation.
Ind. Ann. Med. Sci.—Indian Annals of Medical Science.
Ind. L.—Indian Lancet.
Ind. Med. Jour.—Indiana Medical Journal.
Int. M. J.—Intercolonial Medical Journal.
J. A. C.—Journal of Applied Chemistry.
J. A. M. A.—Journal American Medical Association.
J. A. P.—Journal of Anatomy and Physiology
J. A. Ph. A.—Journal of American Pharmaceutical Association.
J. Am. C. S.—Journal of the American Chemical Society.
J. Bi. Chem.—Journal of Biological Chemistry.
J. Chem. S.—Journal of the Chemical Society of London.
J. Ex. M.—Journal of Experimental Medicine.
J. F. I.—Journal of the Franklin Institute.
J. H. H. B.—Johns Hopkins Hospital Bulletin.
J. I. and E. C.—Journal of Industrial and Engineering Chemistry.
J. M. S.—Journal of Mental Science.
J. P.—Journal of Physiology.
J. P. A.—Journal de Pharmacie d'Anvers.
J. P. C.—Journal de Pharmacie et de Chimie (Paris).
J. P. Ex. T.—Journal of Pharmacology and Experimental Therapeutics.
J. P. L.—Journal de Pharmacie de Liège.
J. P. P.—Journal de Physiologie et de Pathologie Generalé.
J. Pr. Chem.—Journal für Praktische Chemie.
J. Pract.—Journal des Practiciens.
J. Soc. Chem. Ind.—Journal of the Society of Chemical Industry.
Jahresb.—Jahresberichte (Dragendorff's).
K. S. A.—Korrespondenzblatt für Schweizer Arzte.

K. T. W.—Klinisch-therapeutische Wochenschrift.
L. L.—The London Lancet.
L. M. R.—London Medical Recorder.
London Med. Gaz.—London Medical Gazette.
Lyons Méd.—Lyons Médicale.
M. A.—Merck's Archives.
M. B. D.—Meyer Brothers' Druggist.
M. Bull.—Merck's Bulletin.
M. Chem.—Monatshefte für Chemie.
M. H. S. A.—Monatsschrift der Harn und Sexual-Apparat.
M. M.—Medicinische Monatsschrift.
M. M. J.—Maryland Medical Journal.
M. M. W.—Münchner medicinische Wochenschrift.
M. News.—Medical News.
M. R.—Merck's Market Report and Pharmaceutical Journal.
M. S. Rep.—Medical and Surgical Reporter.
M. T. G.—Medical Times and Gazette.
Med. Chron.—Medical Chronicle.
Med. Klin.—Medicinsches Klinik.
Med. Mod.—La Médicine Moderne.
Med. Rec.—Medical Record.
Mit. Greuz. M. C.—Mittenlingen aus der Greuzgebeit der Medicin und Chirurgie.
Mont. Pharm. Jour.—Montreal Pharmaceutical Journal.
N. A. R. D. J.—Journal of National Association of Retail Druggists.
N. I.—New Idea.
N. J. Med. Rep.—New Jersey Medical Reporter.
N. O. M. S. J.—New Orleans Medical and Surgical Journal.
N. P.—New Preparations.
N. R.—New Remedies.
N. R. Pharm.—Neues Repertorium für Pharmacie.
N. Y. M. J.—New York Medical Journal.
N. Y. M. R.—New York Medical Record.
Nat. Drug.—National Druggist.
Nouv. Rem.—Les Nouveaux Remèdes.
O. Z.—Oesterreichische Zeitschrift, 1903.
P. G.—German Pharmacopœia.
P. J.—Pharmaceutical Journal, London.
P. M. T.—Philadelphia Medical Times.
Pac. Drug.—Pacific Druggist.
Ph. Archiv.—Pharmaceutical Archives.
Ph. Cb.—Pharmaceutisches Centralblatt.
Ph. Centralh.—Pharmaceutische Centralhalle.
Ph. Era.—Pharmaceutical Era.
Ph. Post.—Pharmaceutische Post.
Ph. Rec.—Pharmaceutical Record.
Ph. Rev.—Pharmaceutical Review.
Ph. Rund.—Pharmaceutisches Rundschau.
Ph. Z. R.—Pharmaceutische Zeitschrift für Russland.
Ph. Ztg.—Pharmaceutische Zeitung.
Pharm.—The Pharmacist.
Philos. Mag.—Philosophical Magazine.
Philos. Trans.—Philosophical Transactions of the Royal Society of London.
Pr. M. W.—Präger medicinische Wochenschrift.
Pract.—Practitioner.
Pract. Drug.—Practical Druggist.
Press. Méd.—La Presse Médicale.
Proc. A. Ph. A.—Proceedings of the American Pharmaceutical Association.
Proc. Am. Med. Ass.—Proceedings of American Medical Association.
Proc. Chem. Soc.—Proceedings of the Chemical Society.
Proc. N. J. Ph. A.—Proceedings of the New Jersey Pharmaceutical Association.
Proc. P. Ph. A.—Proceedings of Pennsylvania Pharmaceutical Association.
Proc. Roy. Soc. N. S. W.—Proceedings of the Royal Society of New South Wales.
Prog. M.—Le Progrès Médicale.
R. C. C.—Revue des Cultures Coloniale.
R. M. Est.—Revue Médicale de l'Est.
R. M. S. R.—Revue Médicale de la Suisse Romande.
R. T.—Revue de Thérapeutique Médicale et Chirurgicale.
Rif. M.—La Riforma Medica.
S. Jb.—Schmidt's Jahrbücher der in- und auslandischen gesammten Medicin.
S. M.—La Semaine Médicale.
S. W. P.—Schweizerische Wochenschrift für Pharmacie.
Schim. Rep.—Schimmel & Co.'s Semi-annual Report.
St. L. M. S. J.—St. Louis Medical and Surgical Journal.
St. P. M. W.—St. Petersburger medicinische Wochenschrift.
T. G.—Therapeutic Gazette.
T. Mod.—Terapia Moderna.
Th. M.—Therapeutische Monatshefte.
Ther. Geg.—Die Therapie der Gegenwart.
Ther. Prog.—Therapeutic Progress.
Ther. Woch.—Therapeutische Wochenschrift.
Tr. Am. Asso. Phys.—Transaction of the American Association of Physicians.
Tr. Chem. Soc.—Transactions Chemical Society of London.
Tr. Col. State Med. Soc.—Transactions of the Colorado State Medical Society.
Tr. Linn. Soc.—Transactions of the Linnæan Society.
Ungar. Med. Presse.—Ungarische medicinische Presse.
Union Méd.—L'Union Médicale.
U. P. M. B.—University of Pennsylvania Medical Bulletin.
U. S.—United States Pharmacopœia.
V. A. P. A.—Virchow's Archiv für Pathologische Anatomie und Physiologie.
W. J. M. S.—Western Journal of Medicine and Surgery.
W. K. R.—Wiener klinische Rundschau.
W. K. W.—Wiener klinische Wochenschrift.
W. M. Bl.—Wiener medicinische Blätter.
W. M. P.—Wiener medicinische Presse.
West. Drug.—The Western Druggist.
Y. B. P.—Year-book of Pharmacy and Transactions of British Pharmaceutical Conference.
Z. B.—Zeitschrift für Biologie.
Zeit. An. Chem.—Zeitschrift für Analytische Chemie.
Zeit. Angew. Chem.—Zeitschrift für Angewandte Chemie.
Zeit. Anorg. Chem.—Zeitschrift für anorganischen Chemie.
Zeit. E. P. T.—Zeitschrift für Experimentelle Pathologie und Therapie.
Zeit. Hyg.—Zeitschrift für Hygiene und Infektions krankheiten.
Zeit. K. M.—Zeitschrift für Klinische Medicin.
Zeit. Oest. Apoth. Ver.—Zeitschrift des Allgemeinen Oesterreichischen Apotheker-Vereines.
Zeit. P. C.—Zeitschrift für Physiologische Chemie.
Zeit. T. M.—Zeitschrift für thierische Medicin.

EXPLANATORY KEY TO THE PRONUNCIATION.

The introduction of diacritical marks to indicate the pronunciation of the official titles in this work requires the insertion of a key to make them intelligible.

ā..long, as in fāte.
ä..broad, as in fär, cärbon.
ă..short, as in făt, călcium.
ạ..obscure, as in ạbide, cạlumbạ.
â..closed, as in fâll, mâltum.

ē..long, as in bē, lobēlia.
ĕ..short, as in bĕt, sĕnna.
ẹ..obscure, as in hẹr, glycẹrin.

ī..long, as in pīne, kīno.
ĭ..short, as in pĭt, lĭthĭum.
į..obscure, as in fįrm, composįtus.
î..like ē, as in polîce, morphîna.

ç..soft, like s.
ȼ..hard, like k.

ō..long, as in gō, ōpium.
ŏ..short, as in gŏt, ŏxidum.
ȯ..broad, as in ȯr, fȯrmaldehyde.
ọ..obscure, as in harbọr, carbọn.

ū..long, as in fūse, būchū.
ŭ..short, as in bŭt, sŭlphŭr.
û..long and close, as in rûle, prûnum
ụ..obscure, as in bụsh, sụppositoria.

ȳ..long, as in tȳpe, hȳdrastis.
ў..short, as in lўmph, glўcerin.
y..obscure, as in myrrh.
ŷ..like ī.

ģ..like j.
ș..like z.

GLOSSARY.

In the following Glossary will be found short definitions of many of the terms employed in the Dispensatory to designate the medical properties of the remedies; most of the words are commonly employed as nouns, and sometimes as adjectives.

Absorbents.—Drugs used to produce absorption of exudates or diseased tissues.
Abstergents.—Detergents.
Alteratives.—Medicines used to so modify nutrition as to overcome morbid processes.
Anæsthetics.—Medicines used to produce anæsthesia or unconsciousness.
Analeptics.—Restorative medicines, or food.
Analgesics.—Medicines used to allay pain.
Anaphrodisiacs.—Medicines used to allay sexual feeling.
Anodynes.—Medicines used to allay pain.
Antacids.—Medicines used to neutralize acid in the stomach and intestines.
Anthelmintics.—Medicines used to destroy intestinal worms.
Antiarthritics.—Medicines used for the relief of gout.
Antihydropics.—Medicines used for the relief of dropsy.
Antilithics.—Medicines used for the relief of calculous affections.
Antiperiodics.—Medicines used for the relief of malarial fevers.
Antipyretics.—Medicines used for the reduction of bodily temperature in fevers.
Antiseptics.—Substances which have the power of preventing putrefaction.
Antispasmodics.—Medicines used for the relief of nervous irritability and minor spasms.
Antisyphilitics.—Medicines used for the relief of syphilis.
Antizymotics.—Substances which have the power of killing disease-germs.
Aperients.—Mild purgatives.
Aphrodisiacs.—Substances used to increase sexual power or excitement.
Aromatics.—Medicines characterized by a fragrant or spicy taste and odor, and stimulant to the gastro-intestinal mucous membrane.
Aromatic Bitters.—Medicines which unite the properties of the aromatics and the simple bitters.
Astringents.—Medicines having the power of influencing vital contractility, thereby condensing tissues.
Bitters—Simple.—Medicines which have a bitter taste and have the power of stimulating the gastro-intestinal mucous membrane, without affecting the general system.
Blisters.—Medicines which when locally applied cause inflammatory exudation of serum from the skin, and are used as revulsants.
Calefacients.—Medicines used externally to cause a sense of warmth.
Cardiac Depressants.—Medicines used to lower the heart's action.
Cardiac Stimulants.—Medicines used to increase the heart's action.
Carminatives.—Medicines containing a volatile oil used to excite intestinal peristalsis and provoke an expulsion of flatus.
Cathartics.—Purgatives.
Caustics.—Medicines used to destroy living tissues.
Cholagogues.—Medicines which provoke a flow of bile.
Constringents.—Astringents.
Convulsants.—Medicines which cause convulsions.
Correctives.—Medicines used to correct or render more pleasant the action of other remedies, especially purgatives.
Corrigents.—Correctives.
Demulcents.—Mucilaginous principles which are used in solution to soothe and protect irritated mucous membranes or other tissues.
Deobstruents.—(Term obsolete and not very definite.) Medicines which overcome obstruction; aperients.
Deodorants.—Substances which destroy or hide foul odors.
Depilatories.—Substances used to remove hair.
Depressants.—Sedatives.
Depresso-Motors.—Medicines which lessen motor activity.
Depurants.—Medicines which act upon the emunctories so as to cause excretion and thereby purify the system.

Detergents.—Medicines which cleanse wounds, ulcers, etc.
Diaphoretics.—Medicines which produce sweating.
Digestants.—Ferments and acids which have the power of aiding in the solution of food.
Diluents.—Medicines which dilute secretions and excretions.
Disinfectants.—Substances which have the power of destroying disease-germs or the noxious properties of decaying organic matter.
Diuretics.—Medicines which increase the secretion of urine.
Drastics.—Purgatives which cause much irritation.
Ecbolics.—Medicines which produce abortion.
Ecœoprotics, or Ectoprotics.—Laxatives.
Emetics.—Medicines which cause vomiting.
Emmenagogues.—Medicines which stimulate menstruation.
Emollients.—Substances used to mechanically soften and protect tissues.
Epispastics.—Blisters.
Errhines.—Medicines which increase the nasal secretions.
Escharotics.—Caustics.
Evacuants.—Medicines which evacuate: chiefly applied to purgatives.
Excitants.—Stimulants.
Excito-Motors.—Medicines which increase motor activity.
Expectorants.—Medicines which act upon the pulmonic mucous membrane and increase or alter its secretions.
Febrifuges.—Medicines which dissipate fever.
Galactagogues.—Medicines which increase the secretion of milk.
Hæmostatics.—Medicines which arrest hemorrhages.
Hydragogues.—Purgatives which cause large watery discharges.
Hypnotics.—Medicines which cause sleep.
Laxatives.—Mild purgatives.
Local Anæsthetics.—Medicines which when applied locally destroy sensation.
Mydriatics.—Medicines which cause *mydriasis*, or dilatation of the pupil.
Myotics.—Medicines which cause *myosis*, or contraction of the pupil.
Narcotics.—Powerful anodyne hypnotics.
Neurotics.—Medicines which act upon the nervous system.
Nutriants.—Medicines which modify the nutritive processes.
Nutrients.—Substances which nourish.
Oxytocics.—Medicines which stimulate uterine contractions.
Peristaltics.—Medicines which increase peristalsis.
Prophylactics.—Medicines which prevent the taking or development of disease.
Protectives.—Medicines which protect a part when applied to it.
Ptyalagogues.—Sialagogues.
Purgatives.—Medicines which produce copious discharges from the bowels.
Refrigerants.—Medicines which lessen the bodily temperature.
Revulsants.—Medicines which by causing irritation draw nervous force and blood from a distant diseased part.
Rubefacients.—Medicines which cause irritation and redness, and are used as revulsants.
Sedatives.—Medicines which lower functional activity.
Sialagogues.—Medicines which excite the salivary glands to secretion.
Somnifacients.—Soporifics.
Soporifics.—Medicines which cause sleep.
Sorbefacients.—Medicines which cause absorption.
Specifics.—Medicines which have a direct curative influence on certain individual diseases.
Stimulants.—Medicines which increase functional activity.
Stomachics.—Stimulants to the stomach.
Styptics.—Hæmostatics.
Sudorifics.—Medicines which produce sweating.
Tænicides.—Medicines which kill the tapeworm.
Tonics.—Medicines which permanently increase the systemic tone by stimulating nutrition.
Vermicides.—Medicines which kill intestinal worms.
Vermifuges.—Medicines which cause the expulsion of intestinal worms.
Vesicatories.—Blisters.

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Wounds.
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THE FOOD AND DRUGS ACT.

In force and effect from and after January 1, 1907.

THE Food and Drugs Act, passed by the Congress of the United States, June 30th, 1906, and amended August 23rd, 1912, is of such vital importance to the readers of the United States Dispensatory that it is reproduced here, in order that every manufacturer, wholesale jobbing, or retail druggist, dealer, or other interested party, may have in permanent form, a copy of the Act, together with the official regulations for the enforcement of the same, as published by the United States Department of Agriculture in their official circular. It is as follows:

AN ACT For preventing the manufacture, sale, or transportation of adulterated or misbranded or poisonous or deleterious foods, drugs, medicines, and liquors, and for regulating traffic therein, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That it shall be unlawful for any person to manufacture within any Territory or the District of Columbia any article of food or drug which is adulterated or misbranded, within the meaning of this Act; and any person who shall violate any of the provisions of this section shall be guilty of a misdemeanor, and for each offense shall, upon conviction thereof, be fined not to exceed five hundred dollars or shall be sentenced to one year's imprisonment, or both such fine and imprisonment, in the discretion of the court, and for each subsequent offense and conviction thereof shall be fined not less than one thousand dollars or sentenced to one year's imprisonment, or both such fine and imprisonment in the discretion of the court.

SEC. 2. That the introduction into any State or Territory or the District of Columbia from any other State or Territory or the District of Columbia, or from any foreign country, or shipment to any foreign country of any article of food or drugs which is adulterated or misbranded, within the meaning of this Act, is hereby prohibited; and any person who shall ship or deliver for shipment from any State or Territory or the District of Columbia to any other State or Territory or the District of Columbia, or to a foreign country, or who shall receive in any State or Territory or the District of Columbia from any other State or Territory or the District of Columbia, or foreign country, and having so received, shall deliver, in original unbroken packages, for pay or otherwise, or offer to deliver to any other person, any such article so adulterated or misbranded within the meaning of this Act, or any person who shall sell or offer for sale in the District of Columbia or the Territories of the United States any such adulterated or misbranded foods or drugs, or export or offer to export the same to any foreign country, shall be guilty of a misdemeanor, and for such offense be fined not exceeding two hundred dollars for the first offense, and upon conviction for each subsequent offense not exceeding three hundred dollars or be imprisoned not exceeding one year, or both, in the discretion of the court: *Provided,* That no article shall be deemed misbranded or adulterated within the provisions of this Act when intended for export to any foreign country and prepared or packed according to the specifications or directions of the foreign purchaser when no substance is used in the preparation or packing thereof in conflict with the laws of the foreign country to which

said article is intended to be shipped; but if said article shall be in fact sold or offered for sale for domestic use or consumption, then this proviso shall not exempt said article from the operation of any of the other provisions of this Act.

SEC. 3. That the Secretary of the Treasury, the Secretary of Agriculture, and the Secretary of Commerce and Labor shall make uniform rules and regulations for carrying out the provisions of this Act, including the collection and examination of specimens of foods and drugs manufactured or offered for sale in the District of Columbia, or in any Territory of the United States, or which shall be offered for sale in unbroken packages in any State other than that in which they shall have been respectively manufactured or produced, or which shall be received from any foreign country, or intended for shipment to any foreign country, or which may be submitted for examination by the chief health, food, or drug officer of any State, Territory, or the District of Columbia, or at any domestic or foreign port through which such product is offered for interstate commerce, or for export or import between the United States and any foreign port or country.

SEC. 4. That the examinations of specimens of foods and drugs shall be made in the Bureau of Chemistry of the Department of Agriculture, or under the direction and supervision of such Bureau, for the purpose of determining from such examinations whether such articles are adulterated or misbranded within the meaning of this Act; and if it shall appear from any such examination that any of such specimens is adulterated or misbranded within the meaning of this Act, the Secretary of Agriculture shall cause notice thereof to be given to the party from whom such sample was obtained. Any party so notified shall be given an opportunity to be heard, under such rules and regulations as may be prescribed as aforesaid, and if it appears that any of the provisions of this Act have been violated by such party, then the Secretary of Agriculture shall at once certify the facts to the proper United States district attorney, with a copy of the results of the analysis or the examination of such article duly authenticated by the analyst or officer making such examination, under the oath of such officer. After judgment of the court, notice shall be given by publication in such manner as may be prescribed by the rules and regulations aforesaid.

SEC. 5. That it shall be the duty of each district attorney to whom the Secretary of Agriculture shall report any violation of this Act, or to whom any health or food or drug officer or agent of any State, Territory, or the District of Columbia shall present satisfactory evidence of any such violation, to cause appropriate proceedings to be commenced and prosecuted in the proper courts of the United States, without delay, for the enforcement of the penalties as in such case herein provided.

SEC. 6. That the term "drug," as used in this Act, shall include all medicines and preparations recognized in the United States Pharmacopœia or National Formulary for internal or external use, and any substance or mixture of substances intended to be used for the cure, mitigation, or prevention of disease of either man or other animals. The term "food," as used herein, shall include all articles used for food, drink, confectionery, or condiment by man or other animals, whether simple, mixed, or compound.

SEC. 7. That for the purposes of this Act an article shall be deemed to be adulterated:

In case of drugs:

First. If, when a drug is sold under or by a name recognized in the United States Pharmacopœia or National Formulary, it differs from the standard of strength, quality, or purity, as determined by the test laid down in the United States Pharmacopœia or National Formulary official at the time of investigation: *Provided*, That no drug defined in the United States Pharmacopœia or National Formulary shall be deemed to be adulterated under this provision if the standard of strength, quality, or purity be plainly stated upon the bottle, box, or other container thereof although the standard may differ

from that determined by the test laid down in the United States Pharmacopœia or National Formulary.

Second. If its strength or purity fall below the professed standard or quality under which it is sold.

In the case of confectionery:

If it contain terra alba, barytes, talc, chrome yellow, or other mineral substance or poisonous color or flavor, or other ingredient deleterious or detrimental to health, or any vinous, malt, or spirituous liquor or compound or narcotic drug.

In the case of food: First. If any substance has been mixed and packed with it so as to reduce or lower or injuriously affect its quality or strength.

Second. If any substance has been substituted wholly or in part for the article.

Third. If any valuable constituent of the article has been wholly or in part abstracted.

Fourth. If it be mixed, colored, powdered, coated, or stained in a manner whereby damage or inferiority is concealed.

Fifth. If it contain any added poisonous or other added deleterious ingredient which may render such article injurious to health: *Provided,* That when in the preparation of food products for shipment they are preserved by any external application applied in such manner that the preservative is necessarily removed mechanically, or by maceration in water, or otherwise, and directions for the removal of said preservative shall be printed on the covering or the package, the provisions of this Act shall be construed as applying only when said products are ready for consumption.

Sixth. If it consists in whole or in part of a filthy, decomposed, or putrid animal or vegetable substance, or any portion of an animal unfit for food, whether manufactured or not, or if it is the product of a diseased animal, or one that has died otherwise than by slaughter.

SEC. 8. That the term "misbranded," as used herein, shall apply to all drugs, or articles of food, or articles which enter into the composition of food, the package or label of which shall bear any statement, design, or device regarding such article, or the ingredients or substances contained therein which shall be false or misleading in any particular, and to any food or drug product which is falsely branded as to the State, Territory, or country in which it is manufactured or produced.

That for the purposes of this Act an article shall also be deemed to be misbranded:

In case of drugs:

First. If it be an imitation of or offered for sale under the name of another article.

Second. If the contents of the package as originally put up shall have been removed, in whole or in part, and other contents shall have been placed in such package, or if the package fail to bear a statement on the label of the quantity or proportion of any alcohol, morphine, opium, cocaine, heroin, alpha or beta eucaine, chloroform, cannabis indica, chloral hydrate, or acetanilide, or any derivative or preparation of any of such substances contained therein.

Third. If its package or label shall bear or contain any statement, design, or device regarding the curative or therapeutic effect of such article or any of the ingredients or substances contained therein, which is false and fraudulent.

In the case of food: First. If it be an imitation of or offered for sale under the distinctive name of another article.

Second. If it be labeled or branded so as to deceive or mislead the purchaser, or purport to be a foreign product when not so, or if the contents of the package as originally put up shall have been removed in whole or in part and other contents shall have been placed in such package, or if it fail to bear a statement on the label of the quantity or proportion of any morphine, opium, cocaine, heroin, alpha or beta eucaine, chloroform,

cannabis indica, chloral hydrate, or acetanilide, or any derivative or preparation of any such substances contained therein.

Third. If in package form, and the contents are stated in terms of weight or measure, they are not plainly and correctly stated on the outside of the package.

Fourth. If the package containing it or its label shall bear any statement, design, or device regarding the ingredients or the substances contained therein, which statement, design, or device shall be false or misleading in any particular: *Provided*, That an article of food which does not contain any added poisonous or deleterious ingredients shall not be deemed to be adulterated or misbranded in the following cases:

First. In the case of mixtures or compounds which may be now or from time to time hereafter known as articles of food, under their own distinctive names, and not an imitation of or offered for sale under the distinctive name of another article, if the name be accompanied on the same label or brand with a statement of the place where said article has been manufactured or produced.

Second. In the case of articles labeled, branded, or tagged so as to plainly indicate that they are compounds, imitations, or blends, and the word "compound," "imitation," or "blend," as the case may be, is plainly stated on the package in which it is offered for sale: *Provided*, That the term blend as used herein shall be construed to mean a mixture of like substances, not excluding harmless coloring or flavoring ingredients used for the purpose of coloring and flavoring only: *And provided further*, That nothing in this Act shall be construed as requiring or compelling proprietors or manufacturers of proprietary foods which contain no unwholesome added ingredient to disclose their trade formulas, except in so far as the provisions of this Act may require to secure freedom from adulteration or misbranding.

SEC. 9. That no dealer shall be prosecuted under the provisions of this Act when he can establish a guaranty signed by the wholesaler, jobber, manufacturer, or other party residing in the United States, from whom he purchases such articles, to the effect that the same is not adulterated or misbranded within the meaning of this Act, designating it. Said guaranty, to afford protection, shall contain the name and address of the party or parties making the sale of such articles to such dealer, and in such case said party or parties shall be amenable to the prosecutions, fines, and other penalties which would attach, in due course, to the dealer under the provisions of this Act.

SEC. 10. That any article of food, drug, or liquor that is adulterated or misbranded within the meaning of this Act, and is being transported from one State, Territory, District, or insular possession to another for sale, or, having been transported, remains unloaded, unsold, or in original unbroken packages, or if it be sold or offered for sale in the District of Columbia or the Territories, or insular possessions of the United States, or if it be imported from a foreign country for sale, or if it is intended for export to a foreign country, shall be liable to be proceeded against in any district court of the United States within the district where the same is found, and seized for confiscation by a process of libel for condemnation. And if such article is condemned as being adulterated or misbranded, or of a poisonous or deleterious character, within the meaning of this Act, the same shall be disposed of by destruction or sale, as the said court may direct, and the proceeds thereof, if sold, less the legal costs and charges, shall be paid into the Treasury of the United States, but such goods shall not be sold in any jurisdiction contrary to the provisions of this Act or the laws of that jurisdiction: *Provided, however*, That upon the payment of the costs of such libel proceedings and the execution and delivery of a good and sufficient bond to the effect that such articles shall not be sold or otherwise disposed of contrary to the provisions of this Act, or the laws of any State, Territory, District, or insular possession, the court may by order direct that such articles be delivered to the

owner thereof. The proceedings of such libel cases shall conform, as near as may be, to the proceedings in admiralty, except that either party may demand trial by jury of any issue of fact joined in any such case, and all such proceedings shall be at the suit of and in the name of the United States.

SEC. 11. The Secretary of the Treasury shall deliver to the Secretary of Agriculture, upon his request from time to time, samples of foods and drugs which are being imported into the United States or offered for import, giving notice thereof to the owner or consignee, who may appear before the Secretary of Agriculture, and have the right to introduce testimony, and if it appear from the examination of such samples that any article of food or drug offered to be imported into the United States is adulterated or misbranded within the meaning of this Act, or is otherwise dangerous to the health of the people of the United States, or is of a kind forbidden entry into, or forbidden to be sold or restricted in sale in the country in which it is made or from which it is exported, or is otherwise falsely labeled in any respect, the said article shall be refused admission, and the Secretary of the Treasury shall refuse delivery to the consignee and shall cause the destruction of any goods refused delivery which shall not be exported by the consignee within three months from the date of notice of such refusal under such regulations as the Secretary of the Treasury may prescribe: *Provided,* That the Secretary of the Treasury may deliver to the consignee such goods pending examination and decision in the matter on execution of a penal bond for the amount of the full invoice value of such goods, together with the duty thereon, and on refusal to return such goods for any cause to the custody of the Secretary of the Treasury, when demanded, for the purpose of excluding them from the country, or for any other purpose, said consignee shall forfeit the full amount of the bond: *And provided further,* That all changes for storage, cartage, and labor on goods which are refused admission or delivery shall be paid by the owner or consignee, and in default of such payment shall constitute a lien against any future importation made by such owner or consignee.

SEC. 12. That the term "Territory" as used in this Act shall include the insular possessions of the United States. The word "person" as used in this Act shall be construed to import both the plural and the singular, as the case demands, and shall include corporations, companies, societies and associations. When construing and enforcing the provisions of this Act, the act, omission, or failure of any officer, agent, or other person acting for or employed by any corporation, company, society, or association, within the scope of his employment or office, shall in every case be also deemed to be the act, omission, or failure of such corporation, company, society, or association as well as that of the person.

SEC. 13. That this Act shall be in force and effect from and after the first day of January, nineteen hundred and seven.

Approved, June 30, 1906.

RULES AND REGULATIONS FOR THE ENFORCEMENT OF THE FOOD AND DRUGS ACT.

INTRODUCTION.

Under date of October 17, 1906, forty rules and regulations for the enforcement of the food and drugs act, June 30, 1906, were adopted by the three Secretaries. Since that date eight regulations, Nos. 3, 5, 9, 15, 17, 19, 28, and 34, have been amended, the first named by F. I. D. 79, "Collection of Samples," approved by Secretary Wilson of the Department of Agriculture, Secretary Cortelyou of the Treasury Department, and Secretary Straus of the Department of Commerce and Labor, No. 5 by F. I. D. 130, "Amendment to

Regulation 5, Hearings," No. 9 by F. I. D. 99, "Change in Form of Guaranty Legend," No. 15 to accord with F. I. D. 104 on Benzoate of Soda and Nos. 135, 138, and 142 on Saccharin, Nos. 17 and 19 by F. I. D. 84, "Label" and "Character of Name," No. 28 by F. I. D. 112, on "Labeling of Derivatives," and No. 34 by F. I. D. 93, "Denaturing," all over the signatures of the Secretaries of Agriculture, the Treasury, and Commerce and Labor, with the exception of F. I. D. 142, from which the Secretary of the Treasury dissented.

Regulation 2, Original Unbroken Package, has been interpreted by F. I. D. 86, and Regulation 9, Form of Guaranty, by F. I. D. 83, the latter an opinion rendered by the Attorney General on the issue of a guaranty based upon a guaranty.

In accordance with Regulation 15, Wholesomeness of Colors and Preservatives, F. I. D. 76, on Dyes, Chemicals, and Preservatives in Foods, F. I. D. 89, Relating to the Use in Foods of Benzoate of Soda and Sulphur Dioxid, F. I. D. 92, on the Use of Copper Salts, and F. I. D. 102, amending F. I. D. 92, have been issued over the signatures of the three Secretaries, constituting decisions on these points pending the completion of investigations and the issuance of final regulations governing the use of such substances. F. I. D. 104 constitutes the final decision on the use of benzoate of soda in foods, and allows such use; F. I. D. 135, 138, and 142 constitute the final decision on the use of saccharin in food and prohibit such use after April 1, 1912.

With the exception of these amendments and amplifications the regulations as originally issued remain unchanged, and no additional rules have been adopted, the revision issued under this date incorporating the changes enumerated, together with the amendments to section 8 of the food and drugs act.

D. F. Houston, *Secretary of Agriculture.*

Washington, D. C., *March* 21, 1913.

GENERAL.

Regulation 1. Short Title of the Act.

The act, "For preventing the manufacture, sale, or transportation of adulterated or misbranded or poisonous or deleterious foods, drugs, medicines, and liquors, and for regulating traffic therein, and for other purposes," approved June 30, 1906, shall be known and referred to as "The Food and Drugs Act, June 30, 1906."

Regulation 2. Original Unbroken Package.

[See also F. I. D. 86 (see page lxxi) for interpretation of this regulation.]
(Section 2, page li.)

The term "original unbroken package" as used in this act is the original package, carton, case, can, box, barrel, bottle, phial, or other receptacle put up by the manufacturer, to which the label is attached, or which may be suitable for the attachment of a label, making one complete package of the food or drug article. The original package contemplated includes both the wholesale and the retail package.

Regulation 3. Collection of Samples.

[As amended by F. I. D. 79, October 8, 1907, to take effect November 1, 1907.]
(Section 4, page lii.)

Samples of unbroken packages shall be collected only by authorized agents of the Department of Agriculture, or by the health, food, or drug officer of any State, Territory, or the District of Columbia, when commissioned by the Secretary of Agriculture for this purpose.

Samples may be purchased in the open market, and, if in bulk, the marks, brands, or tags upon the package, carton, container, wrapper, or accompanying printed or written matter shall be noted. The collector shall also note the names of the vendor and agent through whom the sale was actually made, together with the date of the purchase. The collectors shall purchase representative samples.

A sample taken from bulk goods shall be divided into three parts, and each shall be labeled with the identifying marks.

If a package be less than four pounds, or in volume less than two quarts, three packages shall be purchased, when practicable, and the marks and tags upon each noted as above. When three samples are purchased, one sample shall be delivered to the Bureau of Chemistry or to such chemist or examiner as may be designated by the Secretary of Agriculture; the second and third samples shall be held under seal by the Secretary of Agriculture, who, upon request, shall deliver one of such samples to the party from whom purchased or to the party guaranteeing such merchandise.

When it is impracticable to collect three samples, or to divide the sample or samples, the order of delivery outlined above shall obtain, and in case there is a second sample the Secretary of Agriculture may, at his discretion, deliver such sample to parties interested.

All samples shall be sealed by the collector with a seal provided for the purpose.

Regulation 4. Methods of Analysis.

(Section 4, page lii.)

Unless otherwise directed by the Secretary of Agriculture, the methods of analysis employed shall be those prescribed by the Association of Official Agricultural Chemists and the United States Pharmacopœia.

Regulation 5. Hearings.

[As amended by F. I. D. 130, January 18, 1911.]
(Section 4, page lii.)

(*a*) When the examination or analysis shows that samples are adulterated or misbranded within the meaning of this act notice of that fact shall be given in every case to the party or parties against whom prosecution lies under this act for the shipment or manufacture or sale of the particular product and such other interested parties as the Secretary of Agriculture may direct, and a date shall be fixed at which such party or parties may be heard before the Secretary of Agriculture or such other person as he may direct. The hearings shall be had at places designated by the Secretary of Agriculture most convenient for all parties concerned. These hearings shall be private and confined to questions of fact. The parties interested therein may appear in person or by attorney and may submit oral or written evidence to show any fault or error in the findings of the analyst or examiner. Interested parties may present proper interrogatories to analysts, to be submitted to and propounded by the Secretary of Agriculture or the officer conducting the hearing. Such privilege, however, shall not include the right of cross-examination. The Secretary of Agriculture may order a re-examination of the sample or have new samples drawn for further examination.

(*b*) If, after hearings held, it appears that a violation of the act has been committed, the Secretary of Agriculture shall give notice to the proper United States attorney.

(*c*) Any health, food, or drug officer or agent of any State, Territory, or the District of Columbia who shall obtain satisfactory evidence of any violation of the Food and Drugs Act, June 30, 1906, as provided by section 5 thereof, shall first submit the same to the Secretary of Agriculture in order that he may give notice and fix dates for hearings to the proper parties.

Regulation 6. Publication.

(Section 4, page lii.)

(*a*) When a judgment of the court shall have been rendered there may be a publication of the findings of the examiner or analyst, together with the findings of the court.

(*b*) This publication may be made in the form of circulars, notices, or bulletins, as the Secretary of Agriculture may direct, not less than thirty days after judgment.

(*c*) If an appeal be taken from the judgment of the court before such publication, notice of the appeal shall accompany the publication.

Regulation 7. Standards for Drugs.

(Section 7, page lii.)

(*a*) A drug bearing a name recognized in the United States Pharmacopœia or National Formulary, without any further statement respecting its character, shall be required to conform in strength, quality, and purity to the standards prescribed or indicated for a drug of the same name recognized in the United States Pharmacopœia or National Formulary, official at the time.

(*b*) A drug bearing a name recognized in the United States Pharmacopœia or National Formulary, and branded to show a different standard of strength, quality, or purity, shall not be regarded as adulterated if it conforms to its declared standard.

Regulation 8. Formulas—Proprietary Foods.

(Section 8, pages liii-lix.)

(*a*) Manufacturers of proprietary foods are only required to state upon the label the names and percentages of the materials used, in so far as the Secretary of Agriculture may find this to be necessary to secure freedom from adulteration and misbranding.

(*b*) The factories in which proprietary foods are made shall be open at all reasonable times to the inspection provided for in Regulation 16.

Regulation 9. Guaranty.

[As amended by F. I. D. 83, 96 and 153—see also F. I. D. 99.]

(Section 9, page liv.)

(*a*) It having been determined that the legends "Guaranteed under the Food and Drugs Act, June 30, 1906," and "Guaranteed by (name of guarantor), under the Food and Drugs Act, June 30, 1906," borne on the labels or packages of food and drugs, accompanied by serial numbers given by the Secretary of Agriculture, are each misleading and deceptive, in that the public is induced by such legends and serial numbers to believe that the articles to which they relate have been examined and approved by the Government and that the Government guarantees that they comply with the law, the use of either legend, or any similar legend, on labels or packages should be discontinued. Inasmuch as the acceptance by the Secretary of Agriculture for filing of the guaranties of manufacturers and dealers and the giving by him of serial numbers thereto contribute to the deceptive character of legends on labels and packages, no guaranty in any form shall hereafter be filed with and no serial number shall hereafter be given to any guaranty by the Secretary of Agriculture. All guaranties now on file with the Secretary of Agriculture shall be stricken from the files, and the serial numbers assigned to such guaranties shall be canceled.

(*b*) The use on the label or package of any food or drug of any serial number required to be canceled by paragraph (*a*) of this regulation is prohibited.

(*c*) Any wholesaler, manufacturer, jobber, or other party residing in the United States may furnish to any dealer to whom he sells any article of food or drug a guaranty that such article is not adulterated or misbranded within the meaning of the Food and Drugs Act, June 30, 1906, as amended.

(*d*) Each guaranty to afford protection shall be signed by, and shall contain the name and address of, the wholesaler, manufacturer, jobber, dealer, or other party residing in the United States making the sale of the article or articles covered by it to the dealer, and shall be to the effect that such article or articles are not adulterated or misbranded within the meaning of the Federal Food and Drugs Act.

(*e*) Each guaranty in respect to any article or articles should be incorporated in or attached to the bill of sale, invoice, bill of lading, or other schedule, giving the names and quantities of the article or articles sold, and should not appear on the labels or packages.

(*f*) No dealer in food or drug products will be liable to prosecution if he can establish that the articles were sold under a guaranty given in compliance with this regulation.

ADULTERATION.

Regulation 10. Confectionery.

(Section 7, page liii.)

(*a*) Mineral substances of all kinds (except as provided in Regulation 15) are specifically forbidden in confectionery whether they be poisonous or not.

(*b*) Only harmless colors or flavors shall be added to confectionery.

(*c*) The term "narcotic drugs" includes all the drugs mentioned in section 8, food and drugs act, June 30, 1906, relating to foods, their derivatives and preparations, and all other drugs of a narcotic nature.

Regulation 11. Substances Mixed and Packed with Foods.

(Section 7, under "Foods," page liii.)

No substance may be mixed or packed with a food product which will reduce or lower its quality or strength. Not excluded under this provision are substances properly used in the preparation of food products for clarification or refining, and eliminated in the further process of manufacture.

Regulation 12. Coloring, Powdering, Coating, and Staining.

(Section 7, under "Foods," page liii.)

(*a*) Only harmless colors may be used in food products.

(*b*) The reduction of a substance to a powder to conceal inferiority in character is prohibited.

(*c*) The term "powdered" means the application of any powdered substance to the exterior portion of articles of food, or the reduction of a substance to a powder.

(*d*) The term "coated" means the application of any substance to the exterior portion of a food product.

(*e*) The term "stain" includes any change produced by the addition of any substance to the exterior portion of foods which in any way alters their natural tint.

Regulation 13. Natural Poisonous or Deleterious Ingredients.

(Section 7, paragraph 5, under "Foods," page liii.)

Any food product which contains naturally a poisonous or deleterious ingredient does not come within the provisions of the food and drugs act, June 30, 1906, except when the presence of such ingredient is due to filth, putrescence, or decomposition.

Regulation 14. External Application of Preservatives.

(Section 7, paragraph 5, under "Foods," proviso, page liii.)

(*a*) Poisonous or deleterious preservatives shall only be applied externally, and they and the food products shall be of a character which shall not permit the permeation of any of the preservative to the interior, or any portion of the interior, of the product.

(*b*) When these products are ready for consumption, if any portion of the added preservative shall have penetrated the food product, then the proviso of section 7, paragraph 5, under "Foods," shall not obtain, and such food products shall then be subject to the regulations for food products in general.

(*c*) The preservative applied must be of such a character that, until removed, the food products are inedible.

Regulation 15. Wholesomeness of Colors and Preservatives.

[As amended 1912 by addition of (*c*) and (*d*).]

(Section 7, paragraph 5, under "Foods," page liii.)

(*a*) Respecting the wholesomeness of colors, preservatives, and other substances which are added to foods, the Secretary of Agriculture shall determine from chemical or other examination, under the authority of the agricultural appropriation act, Public 382, approved June 30, 1906, the names of those substances which are permitted or inhibited in food products; and such findings, when approved by the Secretary of the Treasury and the Secretary of Commerce and Labor, shall become a part of these regulations.

(*b*) The Secretary of Agriculture shall determine from time to time, in accordance with the authority conferred by the agricultural appropriation act, Public 382, approved June 30, 1906, the principles which shall guide the use of colors, preservatives, and other substances added to foods; and when concurred in by the Secretary of the Treasury and the Secretary of Commerce and Labor, the principles so established shall become a part of these regulations.

(*c*) It having been determined that benzoate of soda mixed with food is not deleterious or poisonous and is not injurious to health, no objection will be raised under the food and drugs act to the use in food of benzoate of soda, provided that each container or package of such food is plainly labeled to show the presence and amount of benzoate of soda. Food Inspection Decisions 76 and 89 are amended accordingly.

(*d*) It having been determined that saccharin mixed with food is an added poisonous and deleterious ingredient such as is contemplated by the act, and also that the substitution of saccharin for sugar in foods reduces and lowers their quality, the Secretary of Agriculture will regard as adulterated under the food and drugs act foods containing saccharin which, on or after April 1, 1912, are manufactured or offered for sale in the District of Columbia or Territories or shipped in interstate or foreign commerce, or offered for importation into the United States. (F. I. D. 135, 138, and 142, dated April 26 and June 20, 1911, and March 1, 1912, respectively.)

Regulation 16. Character of the Raw Materials.

(Section 7, paragraph 1, under "Drugs," page lii; paragraph 6, under "Foods," page liii.)

(*a*) The Secretary of Agriculture, when he deems it necessary, shall examine the raw materials used in the manufacture of food and drug products, and determine whether any filthy, decomposed, or putrid substance is used in their preparation.

(*b*) The Secretary of Agriculture shall make such inspections as often as he may deem necessary.

MISBRANDING.

Regulation 17. Label.

[As amended by F. I. D. 84 (see page lxxi), January 31, 1908, taking effect February 10, 1908.]

(Section 8, page liii.)

(*a*) The term "label" applies to any printed, pictorial, or other matter upon or attached to any package of a food or drug product, or any container thereof subject to the provisions of this act.

(*b*) The principal label shall consist, first, of all information which the food and drugs act, June 30,

1906, specifically requires, to wit, the name of the place of manufacture in the case of food compounds or mixtures sold under a distinctive name; statements which show that the articles are compounds, mixtures, or blends; the words "compound," "mixture," or "blend," and words designating substances or their derivatives and proportions required to be named in the case of foods and drugs. All this information shall appear upon the principal label, and should have no intervening descriptive or explanatory reading matter. Second, if the name of the manufacturer and place of manufacture are given, they should also appear upon the principal label. Third, preferably upon the principal label, in conjunction with the name of the substance, such phrases as "artificially colored," "colored with sulphate of copper," or any other such descriptive phrases necessary to be announced should be conspicuously displayed. Fourth, elsewhere upon the principal label other matter may appear in the discretion of the manufacturer. If the contents are stated in terms of weight or measure, such statement should appear upon the principal label and must be couched in plain terms, as required by Regulation 29.

(*c*) If the principal label is in a foreign language, all information required by law and such other information as indicated above in (*b*) shall appear upon it in English. Besides the principal label in the language of the country of production, there may be also one or more other labels, if desired, in other languages, but none of them more prominent than the principal label, and these other labels must bear the information required by law, but not necessarily in English. The size of the type used to declare the information required by the act shall not be smaller than 8-point (Brevier) capitals: *Provided*, That in case the size of the package will not permit the use of 8-point type, the size of the type may be reduced proportionately.

(*d*) Descriptive matter upon the label shall be free from any statement, design, or device regarding the article or the ingredients or substances contained therein, or quality thereof, or place of origin, which is false or misleading in any particular. The term "design" or "device" applies to pictorial matter of every description, and to abbreviations, characters, or signs for weights, measures, or names of substances.

(*e*) An article containing more than one food product or active medicinal agent is misbranded if named after a single constituent.

In the case of drugs the nomenclature employed by the United States Pharmacopœia and the National Formulary shall obtain.

(*f*) The use of any false or misleading statement, design, or device appearing on any part of the label, shall not be justified by any statement given as the opinion of an expert or other person, nor by any descriptive matter explaining the use of the false or misleading statement, design, or device.

Regulation 18. Name and Address of Manufacturer.

(Section 8, page liii.)

(*a*) The name of the manufacturer or producer, or the place where manufactured, except in case of mixtures and compounds having a distinctive name, need not be given upon the label, but if given, must be the true name and the true place. The words "packed for ————," "distributed by ————," or some equivalent phrase, shall be added to the label in case the name which appears upon the label is not that of the actual manufacturer or producer, or the name of the place not the actual place of manufacture or production.

(*b*) When a person, firm, or corporation actually manufactures or produces an article of food or drug in two or more places, the actual place of manufacture or production of each particular package need not be stated on the label except when in the opinion of the Secretary of Agriculture the mention of any such place, to the exclusion of the others, misleads the public.

Regulation 19. Character of Name.

[As amended by F. I. D. 84 (see page lxxi), January 31, 1908, taking effect February 10, 1908.]
(Section 8, page liii.)

(*a*) A simple or unmixed food or drug product not bearing a distinctive name should be designated by its common name in the English language, or, if a drug, by any name recognized in the United States Pharmacopœia or National Formulary. No further description of the components or qualities is required, except as to content of alcohol, morphine, etc.

(*b*) The use of a geographical name shall not be permitted in connection with a food or drug product not manufactured or produced in that place, when such name indicates that the article was manufactured or produced in that place.

(*c*) The use of a geographical name in connection with a food or drug product will not be deemed a

misbranding when by reason of long usage it has come to represent a generic term and is used to indicate a style, type, or brand; but in all such cases the State or Territory where any such article is manufactured or produced shall be stated upon the principal label.

(*d*) A foreign name which is recognized as distinctive of a product of a foreign country shall not be used upon an article of domestic origin except as an indication of the type or style of quality or manufacture, and then only when so qualified that it can not be offered for sale under the name of a foreign article.

Regulation 20. Distinctive Name.

(Section 8, page liii.)

(*a*) A "distinctive name" is a trade, arbitrary, or fancy name which clearly distinguishes a food product, mixture, or compound from any other food product, mixture, or compound.

(*b*) A distinctive name shall not be one representing any single constituent of a mixture or compound.

(*c*) A distinctive name shall not misrepresent any property or quality of a mixture or compound.

(*d*) A distinctive name shall give no false indication of origin, character, or place of manufacture, nor lead the purchaser to suppose that it is any other food or drug product.

Regulation 21. Compounds, Imitations, or Blends Without Distinctive Name.

(Section 8, page liv.)

(*a*) The term "blend" applies to a mixture of like substances, not excluding harmless coloring or flavoring ingredients used for the purpose of coloring and flavoring only.

(*b*) If any age is stated, it shall not be that of a single one of its constituents, but shall be the average of all constituents in their respective proportions.

(*c*) Coloring and flavoring can not be used for increasing the weight or bulk of a blend.

(*d*) In order that colors or flavors may not increase the volume or weight of a blend, they are not to be used in quantities exceeding 1 pound to 800 pounds of the blend.

(*e*) A color or flavor can not be employed to imitate any natural product or any other product of recognized name and quality.

(*f*) The term "imitation" applies to any mixture or compound which is a counterfeit or fraudulent simulation of any article of food or drug.

Regulation 22. Articles Without a Label.

(Section 8, paragraph 1, under "Drugs," paragraph 1, under "Foods," page liii.)

It is prohibited to sell or offer for sale a food or drug product bearing no label upon the package or no descriptive matter whatever connected with it, either by design, device, or otherwise, if said product be an imitation of or offered for sale under the name of another article.

Regulation 23. Proper Branding not a Complete Guaranty.

Packages which are correctly branded as to character of contents, place of manufacture, name of manufacturer, or otherwise, may be adulterated and hence not entitled to enter into interstate commerce.

Regulation 24. Incompleteness of Branding.

A compound shall be deemed misbranded if the label be incomplete as to the names of the required ingredients. A simple product does not require any further statement than the name or distinctive name thereof, except as provided in Regulations 19 (*a*) and 28.

Regulation 25. Substitution.

(Sections 7, page liii, and 8, page liii.)

(*a*) When a substance of a recognized quality commonly used in the preparation of a food or drug product is replaced by another substance not injurious or deleterious to health, the name of the substituted substance shall appear upon the label.

(*b*) When any substance which does not reduce, lower, or injuriously affect its quality or strength, is added to a food or drug product, other than that necessary to its manufacture or refining, the label shall bear a statement to that effect.

Regulation 26. Waste Materials.

(Section 8, page liii.)

When an article is made up of refuse materials, fragments, or trimmings, the use of the name of the substance from which they are derived, unless accompanied by a statement to that effect, shall be deemed a misbranding. Packages of such materials may be labeled "pieces," "stems," "trimmings," or with some similar appellation.

Regulation 27. Mixtures or Compounds with Distinctive Names.

(Section 8. First proviso under "Foods," paragraph 1, page liii.)

(*a*) The terms "mixtures" and "compounds" are interchangeable and indicate the results of putting together two or more food products.

(*b*) These mixtures or compounds shall not be imitations of other articles, whether simple, mixed or compound, or offered for sale under the name of other articles. They shall bear a distinctive name and the name of the place where the mixture or compound has been manufactured or produced.

(*c*) If the name of the place be one which is found in different States, Territories, or countries, the name of the State, Territory, or country, as well as the name of the place, must be stated.

Regulation 28. Substances Named in Drugs or Foods.

(Section 8. Second under "Drugs," second under "Foods," page liii.)

(*a*) The term "alcohol" is defined to mean common or ethyl alcohol. No other kind of alcohol is permissible in the manufacture of drugs except as specified in the United States Pharmacopœia or National Formulary.

(*b*) The words alcohol, morphine, opium, etc., and the quantities and proportions thereof, shall be printed in letters corresponding in size with those prescribed in Regulation 17, paragraph (*c*), page lx.

(*c*) A drug, or food product except in respect of alcohol, is misbranded in case it fails to bear a statement on the label of the quantity or proportion of any alcohol, morphine, opium, heroin, cocaine, alpha or beta eucaine, chloroform, cannabis indica, chloral hydrate, or acetanilide, or any derivative or preparation of any such substances contained therein.

(*d*) A statement of the maximum quantity or proportion of any such substances present will meet the requirements, provided the maximum stated does not vary materially from the average quantity or proportion.

(*e*) In case the actual quantity or proportion is stated it shall be the average quantity or proportion with the variations noted in Regulation 29.

(*f*) The following are the principal derivatives and preparations made from the articles which are required to be named upon the label:

ALCOHOL, ETHYL: (*Cologne spirits, Grain alcohol, Rectified spirits, Spirits, and Spirits of wine.*)

Derivatives—

Aldehyde, Ether, Ethyl acetate, Ethyl nitrite, and Paraldehyde.

Preparations containing alcohol—

Bitters, Brandies, Cordials, Elixirs, Essences, Fluidextracts, Spirits, Sirups, Tinctures, Tonics, Whiskies, and Wines.

MORPHINE, ALKALOID:

Derivatives—

Apomorphine, Dionine, Peronine, Morphine Acetate, Hydrochloride, Sulphate, and other salts of morphine.

Preparations containing morphine or derivatives of morphine—

Bougies, Catarrh Snuff, Chlorodyne, Compound powder of morphine, Crayons, Elixirs, Granules, Pills, Solutions, Sirups, Suppositories, Tablets, Triturates, and Troches.

OPIUM, GUM:

Preparations of opium—

Extracts, Denarcotized opium, Granulated opium, and Powdered opium, Bougies, Brown mixture, Carminative mixtures, Crayons, Dover's powder, Elixirs, Liniments, Ointments, Paregoric, Pills, Plasters, Sirups, Suppositories, Tablets, Tinctures, Troches, Vinegars, and Wines.

Derivatives—

Codeine Alkaloid, Hydrochloride, Phosphate, Sulphate, and other salts of codeine.

Preparations containing codeine or its salts—

Elixirs, Pills, Sirups, and Tablets.

COCAINE, ALKALOID:

Derivatives—

Cocaine Hydrochloride, Oleate, and other salts.

Preparations containing cocaine or salts of cocaine—

Coca leaves, Catarrh powders, Elixirs, Extracts, Infusion of coca, Ointments, Paste pencils, Pills, Solutions, Sirups, Tablets, Tinctures, Troches, and Wines.

HEROIN:

Preparations containing heroin—

Sirups, Elixirs, Pills, and Tablets.

ALPHA AND BETA EUCAINE:

Preparations—

Mixtures, Ointments, Powders, and Solutions.

CHLOROFORM:

Preparations containing chloroform—

Chloranodyne, Elixirs, Emulsions, Liniments, Mixtures, Spirits, and Sirups.

CANNABIS INDICA:

Preparations of cannabis indica—

Corn remedies, Extracts, Mixtures, Pills, Powders, Tablets, and Tinctures.

CHLORAL HYDRATE (*Chloral*, U. S. Pharmacopœia, 1890):

Derivatives—

Chloral acetophenonoxim, Chloral alcoholate, Chloralamide, Chloralimide, Chloral orthoform, Chloralose, Dormiol, Hypnal, and Uraline.

Preparations containing chloral hydrate or its derivatives—

Chloral camphorate, Elixirs, Liniments, Mixtures, Ointments, Suppositories, Sirups, and Tablets.

ACETANILIDE (*Antifebrine, Phenylacetamide*):

Derivatives—

Acetphenetidine, Citrophen, Diacetanilide, Lactophenin, Methoxy-acctanilide, Methylacetanilide, Para-Iodoacetanilide, and Phenacetine.

Preparations containing acetanilide or derivatives—

Analgesics, Antineuralgics, Antirheumatics, Cachets, Capsules, Cold remedies, Elixirs, Granular effervescing salts, Headache powders, Mixtures, Pain remedies, Pills, and Tablets.

(*g*) In declaring the quantity or proportion of any of the specified substances the names by which they are designated in the act shall be used, and in declaring the quantity or proportion of derivatives of any of the specified substances, in addition to the trade name of the derivative, the name of the specified substance shall also be stated, so as to indicate clearly that the product is a derivative of the particular specified substance.

Regulation 29. Statement of Weight, Measure, or Count.

(Section 8, paragraph 3, under "Food," as amended by act of March 3, 1913, page liv.)

(*a*) Except as otherwise provided by this regulation, the quantity of the contents, in all cases of food, if in package form, must be plainly and conspicuously marked, in terms of weight, measure, or numerical count, on the outside of the covering or container usually delivered to consumers.

(*b*) The quantity of the contents so marked shall be the amount of food in the package.

(*c*) The statement of the quantity of the contents shall be plain and conspicuous, shall not be a part of or obscured by any legend or design, and shall be so placed and in such characters as to be readily seen and clearly legible when the size of the package and the circumstances under which it is ordinarily examined by purchasers or consumers are taken into consideration.

(*d*) If the quantity of the contents be stated by weight or measure, it shall be marked in terms of the largest unit contained in the package, except that, in the case of an article with respect to which there exists a definite trade custom for marking the quantity of the article in terms of fractional parts of larger units, it may be so marked in accordance with the custom. Common fractions shall be reduced to their lowest terms; decimal fractions shall be preceded by zero and shall be carried out to not more than two places.

(*e*) Statements of weight shall be in terms of avoirdupois pounds and ounces; statements of liquid measure shall be in terms of the United States gallon of 231 cubic inches and its customary subdivisions, *i.e.*, in gallons, quarts, pints, or fluid ounces, and shall express the volume of the liquid at 68° F. (20° C.); and statements of dry measure shall be in terms of the United States standard bushel of 2,150.42 cubic inches and its customary subdivisions, *i.e.*, in bushels, pecks, quarts, or pints, or, in the case of articles in barrels, in terms of the United States standard barrel and its lawful subdivisions, *i.e.*, third, half, or three-

quarters barrel, as fixed by the act of March 4, 1915 (38 Stat., 1186): *Provided*, That statements of quantity may be in terms of metric weight or measure. Statements of metric weight should be in terms of kilograms or grams. Statements of metric measure should be in terms of liters or centiliters. Other terms of metric weight or measure may be used if it appears that a definite trade custom exists for marking articles with such other terms and the articles are marked in accordance with the custom.

(*f*) The quantity of solids shall be stated in terms of weight and of liquids in terms of measure, except that in case of an article in respect to which there exists a definite trade custom otherwise, the statement may be in terms of weight or measure in accordance with such custom. The quantity of viscous or semi-solid foods, or of mixtures of solids and liquids, may be stated either by weight or measure, but the statement shall be definite and shall indicate whether the quantity is expressed in terms of weight or measure, as, for example, "Weight 12 oz.," or "12 oz. avoirdupois"; "Volume 12 ounces," or "12 fluid ounces."

(*g*) The quantity of the contents shall be stated in terms of weight or measure unless the package be marked by numerical count and such numerical count gives accurate information as to the quantity of the food in the package.

(*h*) The quantity of the contents may be stated in terms of minimum weight, minimum measure, or minimum count, for example, "minimum weight 10 oz.," "minimum volume 1 gallon," or "not less than 4 oz."; but in such case, the statement must approximate the actual quantity and there shall be no tolerance below the stated minimum.

(*i*) The following tolerances and variations from the quantity of the contents marked on the package shall be allowed:

(1) Discrepancies due exclusively to errors in weighing, measuring, or counting which occur in packing conducted in compliance with good commercial practice.

(2) Discrepancies due exclusively to differences in the capacity of bottles and similar containers resulting solely from unavoidable difficulties in manufacturing such bottles or containers so as to be of uniform capacity: *Provided*, That no greater tolerance shall be allowed in case of bottles or similar containers which, because of their design, can not be made of approximate uniform capacity than is allowed in case of bottles or similar containers which can be manufactured so as to be of approximate uniform capacity.

(3) Discrepancies in weight or measure, due exclusively to differences in atmospheric conditions in various places, and which unavoidably result from the ordinary and customary exposure of the packages to evaporation or to the absorption of water.

Discrepancies under classes (1) and (2) of this paragraph shall be as often above as below the marked quantity. The reasonableness of discrepancies under class (3) of this paragraph will be determined on the facts in each case.

(*j*) A package containing two avoirdupois ounces of food or less is "small" and shall be exempt from marking in terms of weight.

(*k*) A package containing one fluid ounce of food or less is "small" and shall be exempt from marking in terms of measure.

(*l*) When a package is not required by paragraph (*g*) to be marked in terms of either weight or measure, and the units of food therein are six or less, it shall, for the purpose of this regulation, be deemed "small" and shall be exempt from marking in terms of numerical count.

Regulation 30. Method of Stating Quantity or Proportion.

(Section 8, page liv.)

In the case of alcohol the expression "quantity" or "proportion" shall mean the average percentage by volume in the finished product. In the case of the other ingredients required to be named upon the label, the expression "quantity" or "proportion" shall mean grains or minims per ounce or fluidounce, and also, if desired, the metric equivalents therefor, or milligrams per gram or per cubic centimeter, or grams or cubic centimeters per kilogram or per liter; provided that these articles shall not be deemed misbranded if the maximum of quantity or proportion be stated, as required in Regulation 28 (*d*).

EXPORTS AND IMPORTS OF FOODS AND DRUGS.

Regulation 31. Preparation of Food Products for Export.

(Section 2, page li.)

(*a*) Food products intended for export may contain added substances not permitted in foods intended for interstate commerce, when the addition of such substances does not conflict with the laws of the countries to which the food products are to be exported and when such substances are added in accordance with the directions of the foreign purchaser or his agent.

(*b*) The exporter is not required to furnish evidence that goods have been prepared or packed in compliance with the laws of the foreign country to which said goods are intended to be shipped, but such shipment is made at his own risk.

(*c*) Food products for export under this regulation shall be kept separate and labeled to indicate that they are for export.

(*d*) If the products are not exported they shall not be allowed to enter interstate commerce.

Regulation 32. Imported Food and Drug Products.

(Section 11, page lv.)

(*a*) Meat and meat food products imported into the United States shall be accompanied by a certificate of official inspection of a character to satisfy the Secretary of Agriculture that they are not dangerous to health, and each package of such articles shall bear a label which shall identify it as covered by the certificate, which certificate shall accompany or be attached to the invoice on which entry is made.

(*b*) The certificate shall set forth the official position of the inspector and the character of the inspection.

(*c*) Meat and meat food products as well as all other food and drug products of a kind forbidden entry into or forbidden to be sold or restricted in sale in the country in which made or from which exported, will be refused admission.

(*d*) Meat and meat food products which have been inspected and passed through the customs may, if identity is retained, be transported in interstate commerce.

Regulation 33. Declaration.

(Section 11, page lv.)

(*a*) All invoices of food or drug products shipped to the United States shall have attached to them a declaration of the shipper, made before a United States consular officer, as follows:

I, the undersigned, do solemnly and truly declare that I am the ———— (Manufacturer, agent, or shipper.) of the merchandise herein mentioned and described, and that it consists of food or drug products which contain no added substances injurious to health.

These products were grown in ——— (Country.) and manufactured in ——— (Country.) by ———— (Name of manufacturer.) during the year ——— and are exported from ——— (City.) and consigned to ——— (City.) The products bear no false labels or marks, contain $\frac{\text{no}}{\text{some}}$ added coloring matter or preservative ———— (Name of added color or preservative.), and are not of a character to cause prohibition or restriction in the country where made or from which exported.

Dated at —— this —— day of ——, 19—. (Signed) ————

(*b*) In the case of importations to be entered at New York, Boston, Philadelphia, Chicago, San Francisco, and New Orleans, and other ports where food and drug inspection laboratories shall be established, this declaration shall be attached to the invoice on which entry is made. In other cases, the declaration shall be attached to the copy of the invoice sent to the Bureau of Chemistry.

Regulation 34. Denaturing.

[As amended by F. I. D. 93, May 12, 1908.]
(Section 11, page lv.)

Unless otherwise declared on the invoice all substances ordinarily used as food products will be treated as such. Shipments of substances ordinarily used as food products intended for technical purposes should be accompanied by a declaration stating that fact. Such products should be denatured before entry, but denaturing may be allowed under customs supervision with the consent of the Secretary of the Treasury, or the Secretary of the Treasury may release such products without denaturing, under such conditions as may preclude the possibility of their use as food products.

Regulation 35. Bond, Imported Foods, and Drugs.

(Section 11, page lv.)

Unexamined packages of food and drug products may be delivered to the consignee prior to the completion of the examination to determine whether the same are adulterated or misbranded, upon the execution of a penal bond by the consignee, in the sum of the invoice value of such goods with the duty added, for the return of the goods to customs custody.

Regulation 36. Notification of Violation of the Law.

(Section 11, page lv.)

If the sample on analysis or examination be found not to comply with the law, the importer shall be notified of the nature of the violation, the time and place at which final action will be taken upon the question of the exclusion of the shipment, and that he may be present, and submit evidence (Form No. 5), which evidence, with a sample of the article, shall be forwarded to the Bureau of Chemistry at Washington, accompanied by the appropriate report card.

Regulation 37. Appeal to the Secretary of Agriculture and Remuneration.

(Section 11, page lv.)

All applications for relief from decisions arising under the execution of the law should be addressed to the Secretary of Agriculture, and all vouchers or accounts for remuneration for samples shall be filed with the chief of the inspection laboratory, who shall forward the same, with his recommendation, to the Department of Agriculture for action.

Regulation 38. Shipment beyond the Jurisdiction of the United States.

(Section 11, page lv.)

The time allowed the importer for representations regarding the shipment may be extended at his request to permit him to secure such evidence as he desires, provided that this extension of time does not entail any expense to the Department of Agriculture. If at the expiration of this time, in view of the data secured in inspecting the sample and such evidence as may have been submitted by the manufacturers or importers, it appears that the shipment can not be legally imported into the United States, the Secretary of Agriculture shall request the Secretary of the Treasury to refuse to deliver the shipment in question to the consignee, and to require its reshipment beyond the jurisdiction of the United States.

Regulation 39. Application of Regulations.

These regulations shall not apply to domestic meat and meat food products which are prepared, transported, or sold in interstate or foreign commerce under the meat-inspection law and the regulations of the Secretary of Agriculture made thereunder.

This regulation was revoked June 16, 1913.

Regulation 40. Alteration and Amendment of Regulations.

These regulations may be altered or amended at any time, without previous notice, with the concurrence of the Secretary of the Treasury, the Secretary of Agriculture, and the Secretary of Commerce and Labor.

The above rules and regulations are hereby adopted.

WASHINGTON, D. C., *October* 17, 1906.

ABSTRACT OF
FOOD INSPECTION DECISIONS.

[Note: These summaries of Food Inspection Decisions are given for reference purposes. The full text of any desired Decision can be obtained by communicating with the Secretary of Agriculture.]

F. I. D. 40.

Filing Guaranty.

It contains information relative to the method of filing the guaranty.

F. I. D. 41.

Approval of Labels.

The Department refuses to pass upon labels sent in by individuals.

F. I. D. 42.
Mixing Flours.

Suggestions concerning the proper labeling of mixtures of different kinds of flours and specific cases are cited as examples.

F. I. D. 43.
Relabeling of Goods on Hand.

Advice is given as to the proper method of labeling goods on hand.

F. I. D. 44.
Scope and Purpose of Food-Inspection Decisions.

In this opinion it is made clear that the views expressed in the form of F. I. D.'s are intended to be explanatory as regards the law and regulations and are for the guidance of the trade in general. They need not be considered as mandatory, but the Department is prepared to uphold the opinions in cases which may come up for trial.

F. I. D. 45.
Blended Whiskies.

An opinion is given as to what may properly be considered a "blend" of whiskies. This decision was superseded by F. I. D. 113 and 127.

F. I. D. 46 [as amended].
Fictitious Firm Names.

Fictitious firm names should not be used in such a manner as to imply they were the manufacturers. Example of properly labeling a specific brand is given.

F. I. D. 47.
Flavoring Extracts.

Declaration of percentage of alcohol in flavoring extracts is not required unless they are used for medicinal purposes. Imitation flavors must be labeled in unambiguous language as imitation or "substitute." Specific examples are given.

F. I. D. 48.
Substances Used in the Preparation of Foods.

Any article used in the preparation of foods, even though it be not a food itself, comes within the comprehension of the act.

F. I. D. 49.
Time Required to Reach Decisions on Different Problems Connected with the Food and Drugs Act, June 30, 1906.

Explanation is made of the delay in answering the many individual questions which have arisen.

F. I. D. 50.
Imitation Coffee.

The use of the word cereal-coffee for an article containing no coffee whatever is held to be improper and it is stated that such a product should be properly labeled "imitation coffee."

F. I. D. 51.
Coloring of Butter and Cheese.

The coloring of butter and of cheese being specifically permitted under a former law, it will not be held to be illegal if the coloring matter used be not harmful.

F. I. D. 52.

Form of Label.

Specific details are given as to the form and arrangement of the subject matter of labels of various types, together with facsimile examples.

F. I. D. 53.

Formula on the Label of Drugs.

It is not required that the formula of medicinal preparations be given, but, if it does appear upon the label or package, it must be correct in every detail.

F. I. D. 54.

Declaration of the Quantity or Proportion of Alcohol Present in Drug Products.

There are no exceptions to the requirement that the alcohol content of medicinal preparations shall be declared even though they be official articles of the U. S. P. and N. F. and not patent medicines.

F. I. D. 55.

Method of Stating Quantity or Proportion of Preparations (Containing Opium, Morphine, etc.) Used in Manufacturing Other Preparations.

Information is given as to the details of the method of stating amounts of narcotic drugs where the primary drugs themselves are not used but are represented by preparations such as tinctures or extracts.

F. I. D. 56.

Names to be Employed in Declaring the Amount of the Ingredients as Required By the Law.

Specific advice is given as to the form of declaration of ingredients necessary to be declared upon the label. The names used to designate these substances in the act are the ones which are required to be used upon the label and no use of chemical formulas, synonyms or obsolete names will be tolerated to any extent whatever.

F. I. D. 57.

Physicians' Prescriptions.

Physicians' prescriptions are interpreted as coming within the law if shipped, sent or transported in interstate commerce.

F. I. D. 58.

The Labeling of Products Used as Foods and Drugs as Well as for Technical and Other Purposes.

Articles not intended for medicinal or food purposes should be plainly and specifically labeled to that effect or be labeled "for technical purposes only."

F. I. D. 59.

National Formulary III, Appendix.

The articles in the N. F. III, appendix, are not to be considered as official articles, but are subject to the law as is the case with other articles not recognized by the U. S. P. or N. F.

F. I. D. 60.

Minor Border Importations.

Certain minor importations such as the bringing of butter, farm produce, etc., over the border from adjacent foreign countries are permitted without the declaration required by Regulation No. 33.

F. I. D. 61.
Cocoa Butter Substitutes.

Where fats other than cacao fat are used in so-called chocolate confectionery, it will be necessary to declare the nature of the substituting substance.

F. I. D. 62.
Guaranty on Imported Products.

Although imported articles are subject to food inspection and approval before being permitted entry into the United States, this in no wise eliminates the necessity of the guaranty by the importer or distributor.

F. I. D. 63.
Use of the Word "Compound" in Names of Drug Products.

Specific details are given as to the nomenclature of mixtures of two or more ingredients and the propriety of the use of the word "compound" in certain cases.

F. I. D. 64.
Labeling of Sardines.

Technical details are given as to the propriety of labeling sardines of differing geographical origins.

F. I. D. 65.
The Labeling of Whisky, Blends, Compounds, and Imitations Thereof.

This decision supplements F. I. D. 45 as to the interpretation of the law regarding the labeling of whiskies. A six-page opinion of the Attorney General is appended, based upon a trade hearing and the collection of information from various sources. [This has been amended in F. I. D. 95, 98, 113, 118, and 127.]

F. I. D. 66.
The Use of Sugar in Canned Foods.

When sugar is used as in canned foods, fruit juices, etc., its presence must be declared.

F. I. D. 67.
Polishing and Coating Rice.

Detailed information is given as to the declaration necessary in the case of rice which has been first decorticated and subsequently polished and coated with glucose and talc.

F. I. D. 68.
Labeling of Food and Drug Products "Manufactured for," "Prepared for," "Distributed by," etc.

Specific information is given as to the procedure to be followed by those who have goods packed under their label by other firms. It is held necessary in such cases to use the phrases, "Prepared for," "Manufactured for," or "Distributed by," and it is stated that the phrase "Sold by," is not satisfactory. The phrase must appear in type not smaller than eight-point (brevier) caps.

F. I. D. 69.
Inspection of Food and Drugs and Identification of Inspectors.

Information is given to the trade as to the details of proposed inspection of establishments where foods are prepared and handled and forms of inspectors identification credentials are given.

F. I. D. 70.
Abuse of Guaranty for Advertising Purposes.

Attention is called to abuses of the guaranty clause which by some manufacturers is made to appear as though the article were guaranteed by the U. S. Government. Warning is given that such practices are unwarranted, and must be discontinued.

F. I. D. 71.
Labeling of Succotash.

Succotash is a term only applicable to fresh corn and fresh lima beans and where the dried and soaked products are used the fact must be declared.

F. I. D. 72.
Use of Guaranties and Serial Numbers Thereof.

Explanatory details regarding the use of the guaranty legend and serial number. (See Regulation 9, page lviii.)

F. I. D. 73.
Interstate Transportation of Imported Meats and Meat-Food Products.

An interpretation is given of the proper use of the statement, "Inspected under the Food and Drugs Act, June 30, 1906," as applied to meat products.

F. I. D. 74.
Certificates for Imported Meats and Meat-Food Products of Cattle, Sheep, Swine and Goats.

Provision is made for certification of imported meat products in lieu of domestic inspection regulations.

F. I. D. 75.
The Labeling of Mixtures of Cane and Maple Sirups.

Details are given as to the proper methods of labeling mixtures of cane sirup and maple syrup.

F. I. D. 76.
Dyes, Chemicals, and Preservatives in Foods.

Specific regulations are promulgated as to the presence of coloring matters and chemical preservatives, common salt, sugar, wood smoke, potable distilled liquors, saltpetre, vinegar and condiments, which may be used as preservatives, pending further investigation.

Sulphur dioxide is permitted in the preparation of such food products as contain acetaldehyde, sugars, etc., in an amount not exceeding 350 milligrams of SO_2 per kilogram of food product. Sodium benzoate may be used in amounts not exceeding one tenth of one per cent. (See also F. I. D. 89.)

The use of any dye, harmless or otherwise, to conceal inferiority is prohibited.

Where proper declaration is made and no inferiority is concealed, harmless animal or vegetable colors may be used as may also a selected list of coal tar colors. [See F. I. D. 164.]

These colors must be true to name and free from harmful impurities arising from their manufacture.

Copper compounds are permitted in vegetables if not used in excessive amount. [The use of copper is at present forbidden under F. I. D. 148.]

Detailed analytical data in support of the above decisions are appended. This decision has been variously amended (see F. I. D. 89, 92, 102, 104, 106, 117, and 164).

F. I. D. 77.
Certificate and Control of Dyes Permissible for Use in Coloring Foods and Foodstuffs.

The forms of certification as applied to colors permitted in F. I. D. 76 are herewith given in full together with complete details as to the certification of mixtures of such colors. [This was amended in F. I. D. 159.]

F. I. D. 78.
The Use of Labels after October 1, 1907.

Certain misapprehensions and misunderstandings as to labels after October 1, 1907 are corrected and it is specifically stated that any label which is not false or deceptive in any particular will be tolerated even if the results are obtained by the use of stickers or erasures. Contradictory statements, however, will not be permitted.

F. I. D. 79.
Collection of Samples.

Detailed information is given as to the method of taking samples and dividing them for subsequent investigation and reference.

F. I. D. 80.
Glazed Coffee.

Coffee may not be glazed to conceal inferiority and any foreign substances used for purely protective purposes must be declared in detail as to character.

F. I. D. 81.
Labeling of Caramels.

The terms, "milk caramels," "peaches and cream caramels" and "whipped cream caramels" are held to be illegal unless the constituents named are used in the manufacture of the caramels.

F. I. D. 82.
Labeling of Coffee Produced in the Dutch East Indies.

Detailed advice is given as to the proper labeling of coffees of certain geographical origins.

F. I. D. 83.
The Issue of a Guaranty Based upon a Former Guaranty.

A four-page opinion of the Attorney General of the United States is given upon this subject in which the original guarantor is held to be liable under the law.

F. I. D. 84.
Amendments to Regulations 17 and 19.

(See pages lix and lx.)

Certain amendments of Regulations 17 and 19 are given, which have been incorporated under these specific regulations (see pages lix and lx).

F. I. D. 85.
Labeling of Bitters.

The question of classification of "bitters" is taken up and discussed at some length. It is held that the final classification will altogether depend upon the claims appearing upon the label of the article in question.

F. I. D. 86.
Original Packages: Interpretation of Regulation 2 of Rules and Regulations for the Enforcement of the Food and Drugs Act.

A nine-page discussion of the question as to what is an original package contains all existing data upon which to base an opinion in any particular case.

F. I. D. 87.
Labeling of Corn Sirup.

Permission is given to use the phrase "Corn Sirup" as applied to glucose either alone or in mixtures with refiners' sirup.

F. I. D. 88.
Private Importations.

Private importations of articles not intended for resale will be held to the same requirements as ordinary imports.

F. I. D. 89.
Amendment to Food Inspection Decision 76, Relating to the Use in Foods of Benzoate of Soda and Sulphur Dioxid.

F. I. D. 76 is amended to permit the use of sodium benzoate in amounts not exceeding one-tenth of one per cent. in such foodstuffs in which it has been heretofore used.

Sulphur dioxide may be used in ordinary quantities, if its presence is plainly stated upon the label and if it be not used in excessive amount, for the purpose of marketing an article of abnormal moisture content. [This F. I. D. has been amended, see Regulation 15, page lix.]

F. I. D. 90.
The Labeling of Foods and Medicinal Mixtures for Stock and Poultry.

It is advised that a clear differentiation must be made between cattle and poultry foods and cattle and poultry remedies.

F. I. D. 91.
The Labeling of Mocha Coffee.

Detailed information is given as to the proper method of labeling Mocha coffee. It is not proper to apply the title "Mocha Coffee" to the Abyssinian variety, even if the latter is shipped from Arabian ports.

F. I. D. 92.
The Use of Copper Salts in the Greening of Foods.

The permission given in F. I. D. 76 to employ copper salts in the greening of vegetables is hereby unqualifiedly rescinded.

F. I. D. 93.
Amendment to Regulation 34.

In further explanation of Regulation 34, it is stated that "unless otherwise declared upon the invoice, all substances ordinarily used as food products will be treated as such."

F. I. D. 94.
The Labeling of Medicinal and Table Waters.

The following detailed advice is given for guidance in the labeling of medicinal and table waters:

All waters which, though natural in the beginning, have anything added to them or abstracted from them after they come from source, should either be labeled as "artificial" or should be so labeled as to indicate that certain constituents have been added to or extracted from them. It is suggested that the word "artificial" or the above explanation, as the case may be, should appear in as large type as the name of the water in question and on a uniform background.

The following examples are explanatory of the above principles. If lithia be added to a natural water, the water should either be labeled as "artificial lithia water," as "water artificially lithiated," or as "water treated with lithia." Again, if carbon dioxid be added to a natural water, whether the carbon dioxid be of the manufactured variety or collected from the spring itself, the water should either be labeled as "artificially carbonated water," "water artificially carbonated," "water treated with carbon dioxid," or "contains added carbon dioxid."

No water should be labeled as a natural water unless it be in the same condition as at source, without additions or abstractions of any substance or substances.

No water should be labeled as "medicinal water" unless it contains one or more constituents in suf-

ficient amounts to have a therapeutic effect from these constituents when a reasonable quantity of the water is consumed. No water should be named after a single constituent unless it contains such constituent in sufficient amounts to have a therapeutic effect when a reasonable amount of the water is consumed.

No manufactured water should bear upon the label any design or device that would lead the consumer to believe that the water is a natural one. Among such designs may be mentioned pictures of springs, fountains, woodland streams, etc.

No water should be characterized by a geographical name which gives a false or misleading idea in regard to the composition of said water. For example, it would not be correct to designate a water as "Lithia water" merely because the water came from Lithia, Fla., or Lithia, Mass.

Manufactured water may be named after a natural water in case the words "imitation" or "artificial" are used, but such manufactured waters must clearly resemble in chemical composition the natural waters after which they are named.

In accordance with Regulation 19 (*c*) and (*d*), no natural American spring water should be named after a foreign spring, unless the name of the foreign spring has become generic and indicative of the character of the water, except to indicate a type or style, and then only when so qualified that it could not be offered for sale under the name of the foreign spring. In these cases, the State or Territory where the spring is situated should be stated on the principal label.

Inasmuch as mineral waters are largely purchased because of their supposed freedom from contamination, any showing such contamination will be considered as adulterated and therefore in violation of the Food and Drugs Act.

F. I. D. 95.

The Use of Neutral Spirits Distilled from Beet Sugar Molasses in the Preparation of Whisky Compounds and Imitation Whiskies.

The labeling of whisky compounds and imitation whiskies, in the preparation of which neutral spirit distilled from beet sugar molasses has been used, will be governed by the opinion of the Attorney-General, dated May 11, 1908.

F. I. D. 96.

Serial Number Guaranty.

Additional details are given as regards the proper use of the serial number and guaranty legend.

F. I. D. 97.

"Soaked Curd" Cheese.

Cheese which has been manufactured by the process of soaking the curd in cold water is not to be considered as pure cheese and must be specifically designated as "soaked curd cheese."

F. I. D. 98.

The Labeling of Whisky Compounds.

In interpreting the word "Whisky compound" used in F. I. D. 65, the Attorney-General will not advise a prosecution if the amount of whisky exceeds one-third of the spirituous content.

F. I. D. 99.

Change in Form of Guaranty Legend.

(Amending Section *b* of Regulation 9. See page lviii.)

In consequence of the wide-spread misuse of the guaranty legend to create the impression that the United States Government is responsible for the purity of the article so designated, certain radical changes in the form and use of the statement are promulgated, as follows:

"Section *b* of Regulation 9 is hereby amended to read as follows:

"(*b*) A general guaranty may be filed with the Secretary of Agriculture by the manufacturer or dealer and be given a serial number, which number shall appear on each and every package of goods sold under such guaranty with the words 'Guaranteed by [insert name of guarantor] under the food and drugs act, June 30, 1906.'"

F. I. D. 100.

Bleached Flour.

Flour bleached by the use of nitrogen peroxide is declared to be an adulterated article.

F. I. D. 101.
Benzoate of Soda.

This is a reaffirmation of the statements in F. I. D. 89.

F. I. D. 102.
Entry of Vegetables Greened with Copper Salts.

The importation of vegetables greened with copper salts is again permitted if the copper compounds be not present in excessive amount. [Rescinded by F. I. D. 148.]

F. I. D. 103.
The Labeling of Turpentine.

Specific instructions are given as to the proper labeling of varieties of turpentine other than those intended for medicinal use.

F. I. D. 104.
Amendment to Food Inspection Decisions No. 76 and No. 89, Relating to the Use in Foods of Benzoate of Soda.

The regulations regarding the use of sodium benzoate are so changed as to permit the use of any amount of the preservative in any kind of food product, provided a statement of its presence is made on the label.

F. I. D. 105.
The Labeling of Canned Salmon and White Fish.

Specific details are given as to the proper labeling of various kinds of canned fish commonly known in the trade as canned salmon or white fish.

F. I. D. 106.
Amendment to F. I. D. 77.

This is a further elucidation of the subject of certification of coal tar colors.

F. I. D. 107.
Decision of the Attorney-General in Regard to the Legality of the Referee Board.

The question of the legality of the payment of the members of the referee board for services rendered, out of the funds appropriated for the enforcement of the Food and Drugs Act, having arisen, the matter was submitted to the Attorney-General, who gave as his opinion that such payment was legal.

F. I. D. 108.
Importation of Coffee.

Coffee which has been damaged by water during shipment and immature coffee berries known as Quakers, are forbidden to be sold. The screenings of whole coffee when ground for sale must be labeled as to its origin.

F. I. D. 109.
The Labeling of Wines.

No beverage is entitled to the unqualified designation "wine" unless it be made from the juice of sound, ripe grapes without addition or abstraction either prior or subsequent to fermentation. Wines made from the marc or pomace should be labeled "Imitation wine." [See also 120 and F. I. D. 156.]

F. I. D. 110.
Shellfish.

It is unlawful to ship shellfish taken from insanitary or polluted beds, or packed in unclean receptacles, or shellfish which have been subjected to "floating" or "drinking" in brackish water or water containing less salt than that in which they were grown. [Amended by F. I. D. 121.] Shucked oysters may not have either water or ice added to them.

F. I. D. 111.
The Labeling of Yeast.

Compressed yeast without qualification means distillers yeast without admixture of starch. Where starch is used in the mixture its presence should be declared. It is not permitted to sell decomposed yeast under any label.

F. I. D. 112.
Amendment to Regulation 28 (Labeling of Derivatives).

This amendment has been incorporated in the regulation as previously given.

F. I. D. 113.
The Labeling of Whisky, Mixtures and Imitations Thereof, Under the Food and Drugs Act of June 30, 1906.

This is a supplementary decision revoking and superseding F. I. D.'s 45, 65, 95 and 98 upon the same subject. [See also F. I. D. 127.]

F. I. D. 114.
The Labeling of "Caracas Cocoa."

The term caracas cocoa is understood to mean a grade of Venezuelan cocoa rather than to designate specifically its geographical origin.

F. I. D. 115.
In the Use of Geographical Names.

Further interpretation is given of the problems and questions arising from the use of geographical names, some of which have come to possess a generic rather than a specific meaning.

F. I. D. 116.
Amendment to F. I. D. 74.

This has reference to the necessity of requiring a certificate with importations of stearin to show its freedom from disease germs.

F. I. D. 117.
The Use of Certified Colors.

Further information is given in amplification of F. I. D.'s 76 and 77, with reference to the use of colors in foods.

F. I. D. 118.
Labeling of Whisky Compounds Under F. I. D. 113.

This is a reaffirmation in positive terms of the principles stated in F. I. D. 113.

F. I. D. 119.
The Use of Shellac and Other Gums for Coating Chocolates and Other Confections.

The opinion is given that the coating of confectionery with shellac and other resinous glazes is not a proper proceeding.

F. I. D. 120.
Labeling of Ohio and Missouri Wines.

Permission is given to use sugar in the juice of grapes used in the manufacture of wines in Ohio and in Missouri in recognition of an ancient trade practice and necessity. [See also F. I. D. 156.]

F. I. D. 121.
The Floating of Shellfish.

Oysters may be brought to maturity or floated in water of a less saline content than that in which they are grown, if they be subsequently clearly and legibly labelled "Floated Oysters." Care must be taken as to the freedom of the water, in which the oysters are floated, from pollution or contamination of any kind.

F. I. D. 122.

The Labeling of Port and Sherry Wines Produced in the United States.

The terms Port and Sherry, without qualification, are held to be properly applied only to the respective products from Portugal or Spain, but domestic wines of these types are held not to be misbranded if the names are qualified by the name of the state where the wine is produced.

F. I. D. 123.

Labeling of Rices.

An elucidation is afforded of the proper labeling of different geographical varieties of rice when grown in localities other than those from which they were originally derived.

F. I. D. 124.

Labeling of Stock Feed.

An interpretation of the proper method of labeling stock feed as to the content of various proximate constituents is herewith given.

F. I. D. 125.

The Labeling of Cordials.

Detailed information is given as to the proper labeling of cordials which are sweetened alcoholic liquors of an aromatic flavor.

F. I. D. 126.

Salts of Tin in Food.

Canned goods are not permitted to contain more than 300 milligrams to the kilogram of salts of tin.

F. I. D. 127.

Decision of the Attorney-General in Regard to the Labeling of Whiskies Sold Under Distinctive Names.

A six page opinion by the attorney-general throws further light upon this much debated question of whiskey labeling. A whiskey sold under a distinctive name, as "Canadian Club," need not be declared as "a blend of whiskies."

F. I. D. 128.

Sago and Tapioca.

These names are held to be specifically descriptive as to the origins of the respective products, and products made in imitation thereof from other starches must be correctly designated as to the source.

F. I. D. 129.

The Certification of Straight Dyes and Mixtures Under Secondary Certificates.

This is an amendment to F. I. D. 77, giving further information relative to the certification of the approved coal tar colors. [See also F. I. D. 164.]

F. I. D. 130.

Amendment to Regulation 5.

This amendment has been incorporated in the appropriate regulation.

F. I. D. 131.

The Composition of Evaporated Milk.

The following standards were adopted for evaporated milk:

(1) It should be prepared by evaporating the fresh, pure, whole milk of healthy cows, obtained by complete milking and excluding all milkings within 15 days before calving and 7 days after calving, provided at the end of this 7-day period the animals are in a perfectly normal condition.

(2) It should contain such percentages of total solids and of fat that the sum of the two shall be not less than 34.3 and the percentage of fat shall be not less than 7.8 per cent. This allows a small reduction in total solids with increasing richness of the milk in fat. [See also F. I. D. 158 and 170.]

(3) It should contain no added butter or butter oil incorporated either with whole milk or skimmed milk or with the evaporated milk at any stage of manufacture.

F. I. D. 132.

The Use of Homogenized Butter and Skimmed Milk in the Manufacture of Ice Cream.

A product made from homogenized butter and skimmed milk cannot be properly called ice cream.

F. I. D. 133.

The Coloring of Green Citrus Fruits.

It is held to be illegal to develop the color of citrus fruits by holding in a warm atmosphere after removal from the tree, because no corresponding change occurs in the sugar or acid content and the fruit is made to look ripe while yet immature.

F. I. D. 134.

The Labeling of New Orleans Molasses.

The term "New Orleans Molasses" is restricted to the product coming from Louisiana and in addition should bear the designation of its grade; namely, "open kettle," "first centrifugal," "second centrifugal," "black strap," etc.

F. I. D. 135.

Saccharin in Food.

Saccharin is prohibited in foods shipped in interstate or foreign commerce or offered for importation into the United States.

F. I. D. 136.

Labeling of Chocolate and Cocoa.

(See also F. I. D. 165.)

The following standards were adopted for these products:

The names "chocolate," "plain chocolate," "bitter chocolate," "chocolate liquor," and "bitter chocolate coatings," are applied to the solid or plastic mass obtained by grinding cocoa nibs without the removal of fat or other constituents except the germ, containing not more than three (3) per cent. of ash insoluble in water, three and fifty hundredths (3.50) per cent. of crude fiber, and nine (9) per cent. of starch, and not less than forty-five (45) per cent. of cocoa fat.

"Sweet chocolate" and "sweet chocolate coatings" are terms applied to chocolate mixed with sugar (sucrose), with or without the addition of cocoa butter, spices, or other flavoring materials, and contain in the sugar and fat-free residue no higher percentage of either ash, fiber, or starch than is found in the sugar and fat-free residue of chocolate.

Cocoa, and powdered cocoa, are terms applied to cocoa nibs, with or without the germ, deprived of a portion of its fat and finely pulverized, and contain percentages of ash, crude fiber, and starch corresponding to those in chocolate after correction for fat removed.

Sweet cocoa, and sweetened cocoa, are terms applied to cocoa mixed with sugar (sucrose), and contain not more than sixty (60) per cent. of sugar (sucrose), and in the sugar and fat-free residue no higher percentage of either ash, crude fiber, or starch than is found in the sugar and fat-free residue of chocolate.

Cocoa nibs, and cracked cocoa, are the roasted broken seeds of the cacao tree freed from shell or husk.

Milk chocolate and milk cocoa, in the opinion of the Board, should contain not less than 12 per cent. of milk solids, and the so-called nut chocolates should contain substantial quantities of nuts. If sugar is added, for example, to milk chocolate, it should be labeled "sweet milk chocolate," "sweet nut chocolate," etc.

When cocoa is treated with an alkali or an alkaline salt, as in the so-called Dutch process, and the finished cocoa contains increased mineral matter as the result of this treatment, but no alkali as such is present, the label should bear a statement to the effect that the cocoa contains added mineral ingredients, stating the amount. Cocoas and chocolates containing an appreciable amount of free alkali are adulterated. In the opinion of the Board, cocoa not treated with alkali is not soluble in the ordinary acceptance of the term. Cocoa before and after treatment with alkali shows essentially the same lack of solubility. To designate the alkali-treated cocoa as "soluble" cocoa is misleading and deceptive.

F. I. D. 137.

The Use of Charlock as a Substitute for Mustard.

The seed of charlock (*Brassica arvensis*) when present in either white or black mustard must be declared upon the label.

F. I. D. 138.

Saccharin in Food.

The time for prohibition of saccharin is extended to January 1, 1912.

F. I. D. 139.

The Use of the Term Sweet Oil.

It is held that any oil other than olive oil is misbranded when sold under the name sweet oil.

F. I. D. 140.

Labeling of Vinegars.

Various kinds of vinegars are specifically defined. These include cider or apple vinegar, wine or grape vinegar, malt vinegar, sugar vinegar, glucose vinegar, spirit vinegar. The question of second pressings, vinegar from dried apple products, added water, addition of boiled cider or coloring matter and the proper labeling of mixtures of vinegars are also discussed.

F. I. D. 141.

The Labeling of Maraschino and Maraschino Cherries.

It is held that unless true maraschino liqueur or cordial is used in the preparation of cocktail cherries, they must be labeled "imitation."

F. I. D. 142.

Saccharin in Food.

The prohibition of saccharin covered in F. I. D.'s 135 and 138 is affirmed; an exception being made where it is used in sweetening foods especially prepared for diabetic sufferers.

F. I. D. 143.

The Labeling of Candied Citron.

The term "Candied citron" is specifically reserved for the candied peel of the fruit of *Citrus medica*, and when the rind of *Citrullus vulgaris*, the citron melon, is similarly prepared, it must be properly and unmistakably designated.

F. I. D. 144.

Canned Foods: Use of Water, Brine, Syrup, Sauce, and Similar Substances in the Preparation Thereof.

Canned food will be deemed to be adulterated if they are found to contain any of the above accessories in excess of the amount necessary for their proper preparation and sterilization.

F. I. D. 145.

Bleached Oats and Barley.

Every package of grains which has been bleached with sulphur fumes to remove weather or soil staining must be labeled so as to clearly show the fact that the contents have been treated with sulphur dioxide.

F. I. D. 146.

On the Use of Saccharin in Foods.

This is a reaffirmation of the permissibility of the sale of foods containing saccharine when they are used in the cure and mitigation of disease. See F. I. D. 142.

F. I. D. 147.

Absinth.

This announces a complete prohibition of importation or sale in interstate commerce of the beverage or liqueur commonly known as absinth.

F. I. D. 148.

Use of Copper Salts in the Greening of Foods.

Copper salts as used in the artificial greening of foods are again, and finally, prohibited as being injurious.

F. I. D. 149.

Use of Copper Salts in the Greening of Foods.

An extension of time is granted in connection with the prohibition of copper greened foods to January 1, 1913, as to importations, and May 1, 1913, as regards interstate commerce.

F. I. D. 150.

Frozen Citrus Fruit.

Citrus fruit will be deemed adulterated within the meaning of the Food and Drugs Act if the contents of any package found in interstate commerce contain 15 per cent. or more of citrus fruit which, on a transverse section through the center, shows a marked drying in 20 per cent. or more of the exposed pulp.

F. I. D. 151.

Application of Regulations.

This is a revocation of Regulation 39, and a notation has been made of the fact under the regulation named.

F. I. D. 152.

Brandy.

The Board of Food and Drug Inspection is of the opinion that brandy is the alcoholic distillate obtained solely from the fermented juice of fruit, distilled under such conditions that the characteristic bouquet, or volatile flavoring and aromatic principles, is retained in the distillate.

Grape brandy is the distillate obtained from grape wine under these conditions.

Apple, peach, and other fruit brandies are similarly prepared from the fermented juices of the respective fruits.

The board is of the further opinion that so-called brandy prepared from grain, potato, or other form of industrial alcohol, or from alcohol obtained from the by-products of wine manufacture, mixed with more or less true brandy or other flavoring material, is adulterated and misbranded unless labeled to indicate its true composition.

F. I. D. 153.

Amendment to Regulation 9, Relating to Guaranties by Wholesalers, Jobbers, Manufacturers, and Other Parties Residing in the United States to Protect Dealers from Prosecution.

This amendment has been inserted in its appropriate place in Regulation 9.

F. I. D. 154.

Regulation of Marking the Quantity of Food in Package Form.

This is an amendment of Regulation 29, and is inserted in the appropriate place.

F. I. D. 155.

Changing Effective Date of Food Inspection Decision No. 153, Which Amends Regulation 9, Relating to Guaranties by Wholesalers, Jobbers, Manufacturers, and Other Parties Residing in the United States, to Protect Dealers from Prosecution.

The effective date of Food Inspection Decision No. 153, issued May 5, 1914, is hereby postponed until May 1, 1916: *Provided:* That as to products packed and labeled prior to May 1, 1916, in accordance with law and with the regulations in force prior to May 5, 1914, it shall become effective November 1, 1916; *And provided further*, That compliance with the terms of Regulation 9 of the Rules and Regulations for the enforcement of the Food and Drugs Act as amended by Food Inspection Decision No. 153 will be permitted at any time after the date of this decision. [Amended by F. I. D. 167.]

F. I. D. 156.
Wine.

Food Inspection Decisions 109 and 120 are abrogated and wine is defined to be the product of the normal alcoholic fermentation of the juice of fresh, sound, ripe grapes, with the usual cellar treatment.

To correct the natural defects, the following additions to musts or wines are permitted:

In the case of excessive acidity, neutralizing agents which do not render wine injurious to health, such as neutral potassium tartrate or calcium carbonate;

In the case of deficient acidity, tartaric acid;

In the case of deficiency in saccharine matter, condensed grape must or a pure dry sugar.

The foregoing definition does not apply to sweet wines made in accordance with the Sweet Wine Fortification Act of June 7, 1906 (34 Stat., 215).

A product made from pomace, by the addition of water, with or without sugar or any other material whatsoever, is not entitled to be called wine. It is not permissible to designate such a product as "pomace wine," nor otherwise than as "imitation wine."

F. I. D. 157.
Amending Regulation 29, Which Relates to Marking the Quantity of Food in Package Form.

This is an amendment of Regulation 29, section *h*, which has been inserted in its proper place.

F. I. D. 158.
Condensed Milk, Evaporated Milk, Concentrated Milk.

The above terms may only be applied to a product containing not less than 25.5 per cent. of total solids and not less than 7.8 per cent. of milk fat. This supersedes F. I. D. 131, which is hereby revoked. [See also F. I. D's. 131 and 170.]

F. I. D. 159.
Certification of Mixtures Containing Coal-Tar Colors. (Amending Food Inspection Decisions 77, 106, and 129.)

Hereafter, no mixture containing one or more certified coal-tar dyes, in combination with other components, constituents, or ingredients not coal-tar dyes, will be certified unless the manufacturer shall make and deposit with the Secretary of Agriculture a declaration that each and every package in which any of such mixture shall be sold or offered for sale shall have, plainly and conspicuously declared upon the label or container, a statement of the quantity or proportion of the certified dye or dyes present in the mixture.

F. I. D.'s 77, 106, and 129 are amended accordingly.

F. I. D. 160.
Gluten Products and "Diabetic" Food.

The following definitions and standards for gluten products and "diabetic" food were adopted by the Joint Committee on Definitions and Standards April 9, 1915, and were approved by the Association of American Dairy, Food, and Drug Officials August 3, 1915, and by the Association of Official Agricultural Chemists November 17, 1915:

Ground gluten is the clean, sound product made from wheat flour by the almost complete removal of starch and contains not more than ten per cent. (10%) of moisture, and, calculated on the water-free basis, not less than fourteen and two-tenths per cent. (14.2%) of nitrogen, not more than fifteen per cent. (15%) of nitrogen-free extract (using the protein factor 5.7), and not more than five and five-tenths per cent. (5.5%) of starch (as determined by the diastase method).

Gluten flour is the clean, sound product made from wheat flour by the removal of a large part of the starch and contains not more than ten per cent. (10%) of moisture, and, calculated on the water-free basis, not less than seven and one-tenth per cent. (7.1%) of nitrogen, not more than fifty-six per cent. (56%) of nitrogen-free extract (using the protein factor 5.7), and not more than forty-four per cent. (44%) of starch (as determined by the diastase method).

Gluten flour, self-raising, is a gluten flour containing not more than ten per cent. (10%) of moisture, and leavening agents with or without salt.

"Diabetic" food. Although most foods may be suitable under certain conditions for the use of persons suffering from diabetes, the term "diabetic" as applied to food indicates a considerable lessening of the

carbohydrates found in ordinary products of the same class, and this belief is fostered by many manufacturers on their labels and in their advertising literature.

A "diabetic" food contains not more than half as much glycogenic carbohydrates as the normal food of the same class. Any statement on the label which gives the impression that any single food in unlimited quantity is suitable for the diabetic patient is false and misleading.

F. I. D. 161.

Maple Products.

The following definitions and standards for maple products were adopted by the Joint Committee on Definitions and Standards June 4, 1915, and were approved by the Association of American Dairy, Food, and Drug Officials August 3, 1915, and by the Association of Official Agricultural Chemists November 17, 1915:

Maple sugar, maple concrete, is the solid product resulting from the evaporation of maple sap or maple sirup.

Maple sirup is sirup made by the evaporation of maple sap or by the solution of maple concrete, and contains not more than thirty-five per cent. (35%) of water and weighs not less than eleven (11) pounds to the gallon (231 cu. in.).

F. I. D. 162.

Egg Noodles and Plain Noodles.

The following definitions and standards for egg noodles and plain noodles were adopted by the Joint Committee on Definitions and Standards June 4, 1915, and were approved by the Association of American Dairy, Food, and Drug Officials August 3, 1915, and by the Association of Official Agricultural Chemists November 17, 1915:

Noodles, egg noodles, are dried alimentary pastes made from wheat flour and egg. They contain not less than five per cent. (5%) by weight of the solids of whole, sound egg exclusive of the shell.

Plain noodles, water noodles, are dried alimentary pastes made from wheat flour without egg, or with less than five per cent. (5%) by weight of the solids of whole, sound egg exclusive of the shell.

F. I. D. 163.

Amending Regulation 29, Which Relates to Marking the Quantity of Food in Package Form.

This amendment to Regulation 29 has been inserted in its proper place.

F. I. D. 164.

Colors in Food.

(Amendment to F. I. D.'s 76, 117, and 129.)

F. I. D.'s 76 is hereby amended by striking out of the list of permitted dyes contained therein, the words:

Yellow shade:

4. Naphthol yellow S.

and substituting therefor the words:

Yellow shades:

4. Naphthol yellow S.
94. Tartrazine.

F. I. D.'s 117 and 129 are also amended so that, hereafter, the coal-tar dyes which may be used in food, subject to the provisions of F. I. D.'s 76, 117 and 129, shall be the following:

Red shades:

107. Amaranth.
56. Ponceau 3 R.
517. Erythrosine.

Orange shade:

85. Orange I.

Yellow shades:

4. Naphthol yellow S.
94. Tartrazine.

Green shade:

435. Light green S. F. yellowish.

Blue shade:

692. Indigo disulfoacid.

F. I. D. 165.

Cacao Products.

The following definitions and standards for cacao products were adopted by the Joint Committee on Definitions and Standards June 4, 1915, and were approved by the Association of American Dairy, Food, and Drug Officials August 3, 1915, and by the Association of Official Agricultural Chemists November 17, 1915:

Cacao beans, cocoa beans, are the seeds of the cacao tree, *Theobroma cacao* L.

Cacao nibs, cocoa nibs, cracked cocoa, is the roasted, broken cacao bean freed from its shell or husk.

Chocolate, plain chocolate, bitter chocolate, chocolate liquor, chocolate paste, bitter chocolate coatings, is the solid or plastic mass obtained by grinding cacao nibs without the removal of fat or other constituents except the germ.

Chocolate, plain chocolate, bitter chocolate, chocolate liquor, chocolate paste, bitter chocolate coatings, contains not more than three per cent. (3%) of ash insoluble in water, three and fifty hundredths per cent. (3.50%) of crude fiber, nine per cent. (9%) of cacao starch, and not less than forty-five per cent. (45%) of cacao fat.

Sweet chocolate, sweet chocolate coatings, is chocolate mixed with sugar (sucrose), with or without the addition of cocoa butter, spices, or other flavoring materials.

Sweet chocolate, sweet chocolate coatings, contains in the sugar- and fat-free residue no higher percentage of ash, fiber or starch than is found in the sugar- and fat-free residue of chocolate.

Cocoa, powdered cocoa, is cacao nibs, with or without the germ, deprived of a portion of its fat and finely pulverized.

Cocoa, powdered cocoa, contains percentages of ash, crude fiber and starch corresponding to those in chocolate after correction for fat removed.

Sweet cocoa, sweetened cocoa, is cocoa mixed with not more than sixty per cent. (60%) of sugar (sucrose).

Sweet cocoa, sweetened cocoa, contains in the sugar- and fat-free residue no higher percentage of ash, crude fiber or starch than is found in the sugar- and fat-free residue of chocolate.

Milk chocolate, milk cocoa, sweet milk chocolate or sweet milk cocoa, respectively, is chocolate, cocoa, sweet chocolate or sweet cocoa which contains not less than twelve per cent. (12%) of whole milk solids in the finished product.

F. I. D. 166.

Rocky Ford Melons.

This is a further explanation of the labeling of melons grown from Rocky Ford type seed.

F. I. D. 167.

(Amending F. I. D.'s 153 and 155.)

Use of Guaranty Legends and Serial Numbers on Labels and Containers Printed or Marked Prior to May 5, 1914.

Owing to the fact that many dealers had on hand a great many labels and containers printed or marked prior to the date of F. I. D. 153 (May 5, 1914), and great financial loss will result to such dealers, through their inability to use these labels and containers, if Regulation 9, as amended by F. I. D.'s 153 and 155, be enforced beginning on May 1, 1916, "proceedings under the Food and Drugs Act, based on the shipment in interstate or foreign commerce, or the sale in the District of Columbia or the Territories, prior to May 1, 1918, of any article of food or drugs, will not be instituted solely on account of the fact that the label thereon or the container thereof bears the legend 'Guaranteed by (name of guarantor) under the Food and Drugs Act, June 30, 1906,' or a serial number issued by the United States Department of Agriculture, or both, upon it being established that such label or container was so printed or marked prior to May 5, 1914."

F. I. D. 168.

Amending Paragraph (E) of Regulation 29, Which Relates to Marking the Quantity of Food in Package Form.

This amendment has been inserted in its proper place in Regulation 29.

F. I. D. 169.

Edible Vegetable Fats and Oils.

The following definitions and standards for edible vegetable fats and oils were adopted by the Joint Committee on Definitions and Standards August 7, 1916, and were approved by the Association of American

Dairy, Food, and Drug Officials August 10, 1916, and by the Association of Official Agricultural Chemists November 22, 1916:

Edible fats and edible oils are such glycerids of the fatty acids as are recognized to be wholesome foods. They are dry and sweet in flavor and odor.

Cacao butter, cocoa butter, is the edible fat obtained from sound cacao beans (*Theobroma cacao* L.) either before or after roasting.

Coconut oil, copra oil, is the edible oil obtained from the kernels of the coconut (*Cocos nucifera* L. or *Cocos butyracea* L.).

Cochin oil is coconut oil prepared in Cochin (Malabar).

Ceylon oil is coconut oil prepared in Ceylon.

Corn oil, maize oil, is the edible oil obtained from the germ of Indian corn, maize (*Zea mays* L.).

Cottonseed oil is the edible oil obtained from the seed of the cotton plant (*Gossypium herbaceum*, L.), or from the seed of other species of Gossypium.

Olive oil, sweet oil, is the edible oil obtained from the sound, mature fruit of the olive tree (*Olea europæa* L.)

Palm kernel oil is the edible oil obtained from the kernels of the fruit of the palm tree (*Elaeis guineensis* L. or *Elaeis melanococca* Gärt.).

Peanut oil, arachis oil, earthnut oil, is the edible oil obtained from the peanut (*Arachis hypogæa* L.).

Poppy seed oil is the edible oil obtained from the seeds of the poppy (*Papaver somniferum* L.).

Rape seed oil, rape oil, colza oil, is the edible oil obtained from the seed of the rape plant (*Brassica napus* L.), or from the seed of closely related Brassica species, which yields oils similar in composition and character to the oil obtained from the seed of *Brassica napus* L.

Soy bean oil, soy oil, soja oil, is the edible oil obtained from the seed of the soy bean plant (*Glycine soja* L.; *Soja hispida*, Sieb et Zucc.; *Soja max.* (L.) Piper).

Sesame oil, gingili oil, teel oil, benne oil, is the edible oil obtained from the seed of the sesame plant (*Sesamum indicum*, De Candolle; *Sesamum radiatum*, Schum and Thonn; *Sesamum orientale* L.).

Sunflower oil is the edible oil obtained from the seed of the sunflower (*Helianthus annuus* L.).

F. I. D. 170.

Sweetened Condensed Milk, Condensed Skimmed Milk, Sweetened Condensed Skimmed Milk, Dried Milk, Dried Skimmed Milk, and Malted Milk.

The following definitions and standards for sweetened condensed milk, condensed skimmed milk, sweetened condensed skimmed milk, dried milk, dried skimmed milk, and malted milk were adopted by the Joint Committee on Definitions and Standards, August 7, 1916, and were approved by the Association of American Dairy, Food, and Drug Officials August 10, 1916, and by the Association of Official Agricultural Chemists November 22, 1916:

Sweetened condensed milk, sweetened evaporated milk, sweetened concentrated milk, is the product resulting from the evaporation of a considerable portion of the water from the whole, fresh, clean, lacteal secretion obtained by the complete milking of one or more healthy cows, properly fed and kept, excluding that obtained within fifteen days before and ten days after calving, to which sugar (sucrose) has been added. It contains, all tolerances being allowed for, not less than twenty-eight per cent. (28.0%) of total milk solids, and not less than eight per cent. (8.0%) of milk fat.

Condensed skimmed milk, evaporated skimmed milk, concentrated skimmed milk, is the product resulting from the evaporation of a considerable portion of the water from skimmed milk, and contains, all tolerances being allowed for, not less than twenty per cent. (20.0%) of milk solids.

Sweetened condensed skimmed milk, sweetened evaporated skimmed milk, sweetened concentrated skimmed milk, is the product resulting from the evaporation of a considerable portion of the water from skimmed milk to which sugar (sucrose) has been added. It contains, all tolerances being allowed for, not less than twenty-eight per cent. (28.0%) of milk solids.

Dried milk is the product resulting from the removal of water from milk, and contains, all tolerances being allowed for, not less than twenty-six per cent. (26.0%) of milk fat, and not more than five per cent. (5.0%) of moisture.

Dried skimmed milk is the product resulting from the removal of water from skimmed milk and contains, all tolerances being allowed for, not more than five per cent. (5.0%) of moisture.

Malted milk is the product made by combining whole milk with the liquid separated from a mash of ground barley malt and wheat flour, with or without the addition of sodium chlorid, sodium bicarbonate, and potassium bicarbonate in such a manner as to secure the full enzymic action of the malt extract and by removing water. The resulting product contains not less than seven and one-half per cent. (7.5%) of butter fat and not more than three and one-half per cent. (3.5%) of moisture.

Circular No. 19.
Standards of Purity for Food Products.

Superseding Circulars Nos. 13 and 17.

SUPPLEMENTAL PROCLAMATION.

Referring to Circular No. 13 of this Office, dated December 20, 1904, and to Circular No. 17 of this Office, dated March 8, 1906, the following food standards are hereby established as superseding and supplemental to those proclaimed on the dates above named.

JAMES WILSON,
Secretary of Agriculture.

WASHINGTON, D. C., *June* 26, 1906.

LETTER OF SUBMITTAL.

The Honorable the SECRETARY OF AGRICULTURE.

SIR: The undersigned, representing the Association of Official Agricultural Chemists of the United States, and the Interstate Food Commission, and commissioned by you, under authority given by the act of Congress approved March 3, 1903, to collaborate with you "to establish standards of purity for food products and to determine what are regarded as adulterations therein," respectfully report that they have carefully reviewed, in the light of recent investigations and correspondence, the standards earlier recommended by them and have prepared a set of amended schedules, in which certain changes have been introduced for the purpose of securing increased accuracy of expression and a more perfect correspondence of the chemical limits to the normal materials designated, and from which standards previously proclaimed for several manufactured articles have been omitted because of the unsatisfactory condition of trade nomenclature as applied thereto; and also additional schedules of standards for ice creams, vegetables and vegetable products, tea and coffee. They respectfully recommend that the standards herewith submitted be approved and proclaimed as the established standards, superseding and supplementing those established on December 20, 1904, and March 8, 1906.

The principles that have guided us in the formulation of these standards are appended hereto.

The several schedules of additional standards recommended have been submitted, in a tentative form, to the manufacturing firms, and the trade immediately interested, and also to the State food-control officials for criticism.

Respectfully,

WILLIAM FREAR,
EDWARD H. JENKINS,
M. A. SCOVELL,
H. A. WEBER,
H. W. WILEY,
Committee on Food Standards,
Association of Official Agricultural Chemists.
RICHARD FISCHER.
Representing the Interstate Food Commission.

PRINCIPLES ON WHICH THE STANDARDS ARE BASED.

"The general considerations which have guided the committee in preparing the standards for food products are the following:

"1. The standards are expressed in the form of definitions, with or without accompanying specifications of limit in composition.

"2. The main classes of food articles are defined before the subordinate classes are considered.

"3. The definitions are so framed as to exclude from the articles defined, substances not included in the definitions.

"4. The definitions include, where possible, those qualities which make the articles described wholesome for human food.

"5. A term defined in any of the several schedules has the same meaning wherever else it is used in this report.

"6. The names of food products herein defined usually agree with existing American trade or manufacturing usage; but where such usage is not clearly established or where trade names confuse two or more articles for which specific designations are desirable, preference is given to one of the several trade names applied.

"7. Standards are based upon data representing materials produced under American conditions and manufactured by American processes or representing such varieties of foreign articles as are chiefly imported for American use.

"8. The standards fixed are such that a departure of the articles to which they apply, above the maximum or below the minimum limit prescribed, is evidencethat such articles are of inferior or abnormal quality.

"9. The limits fixed as standards are not necessarily the extremes authentically recorded for the article in question, because such extremes are commonly due to abnormal conditions of production and are usually accompanied by marks of inferiority or abnormality readily perceived by the producer or manufacturer."

Food Standards.

I. ANIMAL PRODUCTS.

A. Meats and the Principal Meat Products.

a. MEATS.

1. *Meat, flesh,* is any clean, sound, dressed, and properly prepared edible part of animals in good health at the time of slaughter, and if it bears a name descriptive of its kind, composition, or origin, it corresponds thereto. The term "animal," as herein used, includes not only mammals, but fish, fowl, crustaceans, mollusks, and all other animals used as food.

2. *Fresh meat* is meat from animals recently slaughtered and properly cooled until delivered to the consumer.

3. *Cold storage meat* is meat from animals recently slaughtered and preserved by refrigeration until delivered to the consumer.[1]

4. *Salted, pickled,* and *smoked meats* are unmixed meats preserved by salt, sugar, vinegar, spices, or smoke, singly or in combination, whether in bulk or in suitable containers.[2]

b. MANUFACTURED MEATS.

1. *Manufactured meats* are meats not included in paragraphs 2, 3, and 4, whether simple or mixed, whole or comminuted, in bulk, or in suitable containers,[2] with or without the addition of salt, sugar, vinegar, spices, smoke, oils, or rendered fat. If they bear names descriptive of kind, composition, or origin, they correspond thereto, and when bearing such descriptive names, if force or flavoring meats are used, the kind and quantity thereof are made known.

c. MEAT EXTRACTS, MEAT PEPTONES, ETC.

(Schedule in preparation.)

d. LARD.

1. *Lard* is the rendered fresh fat from hogs in good health at the time of slaughter, is clean, free from rancidity, and contains, necessarily, incorporated in the process of rendering, not more than one (1) per cent. of substances other than fatty acids and fat.

2. *Leaf lard* is lard rendered at moderately high temperatures from the internal fat of the abdomen of the hog, excluding that adherent to the intestines, and has an iodin number not greater than sixty (60).

3. *Neutral lard* is lard rendered at low temperatures.

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[1] The establishment of proper periods of time for cold storage is reserved for future consideration when the investigations of this subject, authorized by Congress, are completed.

[2] Suitable containers for keeping moist food products, such as sirups, honey, condensed milk, soups, meat extracts, meats, manufactured meats, and undried fruits and vegetables, and wrappers in contact with food products, contain on their surfaces, in contact with the food products, no lead, antimony, arsenic, zinc, or copper or any compounds thereof or any other poisonous or injurious substance. If the containers are made of tin plate, they are outside-soldered and the plate in no place contains less than one hundred and thirteen (113) milligrams of tin on a piece of five (5) centimeters square or one and eight-tenths (1.8) grains on a piece two (2) inches square.

The inner coating of the containers is free from pin holes, blisters, and cracks.

If the tin plate is lacquered, the lacquer completely covers the tinned surface within the container and yields to the contents of the container no lead, antimony, arsenic, zinc or copper or any compounds thereof, or any other poisonous or injurious substance.

B. Milk and Its Products.

a. MILKS.

1. *Milk* is the fresh, clean, lacteal secretion obtained by the complete milking of one or more healthy cows, properly fed and kept, excluding that obtained within fifteen days before and ten days after calving, and contains not less than eight and one-half (8.5) per cent. of solids not fat, and not less than three and one-quarter (3.25) per cent. of milk fat.

2. *Blended milk* is milk modified in its composition so as to have a definite and stated percentage of one or more of its constituents.

3. *Skim milk* is milk from which a part or all of the cream has been removed and contains not less than nine and one-quarter (9.25) per cent. of milk solids.

4. *Pasteurized milk* is milk that has been heated below boiling but sufficiently to kill most of the active organisms present and immediately cooled to 50° Fahr. or lower.

5. *Sterilized milk* is milk that has been heated at the temperature of boiling water or higher for a length of time sufficient to kill all organisms present.

6. *Condensed milk, evaporated milk*, is milk from which a considerable portion of water has been evaporated and contains not less than twenty-eight (28) per cent. of milk solids, of which not less than twenty-seven and five-tenths (27.5) per cent. is milk fat. [See also F. I. D. 158.]

7. *Sweetened condensed milk* is milk from which a considerable portion of water has been evaporated and to which sugar (sucrose) has been added, and contains not less than twenty-eight (28) per cent. of milk solids, of which not less than twenty-seven and five-tenths (27.5) per cent. is milk fat. [See also F. I. D. 170.]

8. *Condensed skim milk* is skim milk from which a considerable portion of water has been evaporated.

9. *Buttermilk* is the product that remains when butter is removed from milk or cream in the process of churning.

10. *Goat's milk, ewe's milk, et cetera*, are the fresh, clean, lacteal secretions, free from colostrum, obtained by the complete milking of healthy animals other than cows, properly fed and kept, and conform in name to the species of animal from which they are obtained.

b. CREAM.

1. *Cream* is that portion of milk, rich in milk fat, which rises to the surface of milk on standing, or is separated from it by centrifugal force, is fresh and clean, and contains not less than eighteen (18) per cent. of milk fat.

2. *Evaporated cream, clotted cream*, is cream from which a considerable portion of water has been evaporated.

c. MILK FAT OR BUTTER FAT.

1. *Milk fat, butter fat*, is the fat of milk and has a Reichert-Meissl number not less than twenty-four (24) and a specific gravity not less than 0.905 $\left(\frac{40°C.}{40°C.}\right)$.

d. BUTTER.

1. *Butter* is the clean, non-rancid product made by gathering in any manner the fat of fresh or ripened milk or cream into a mass, which also contains a small portion of the other milk constituents, with or without salt, and contains not less than eighty-two and five-tenths (82.5) per cent. of milk fat. By acts of Congress approved August 2, 1886, and May 9, 1902, butter may also contain added coloring matter.

2. *Renovated butter, process butter*, is the product made by melting butter and reworking, without the addition or use of chemicals or any substances except milk, cream, or salt, and contains not more than sixteen (16) per cent. of water and at least eighty-two and five-tenths (82.5) per cent. of milk fat.

e. CHEESE.

1. *Cheese* is the sound, solid, and ripened product made from milk or cream by coagulating the casein thereof with rennet or lactic acid, with or without the addition of ripening ferments and seasoning, and contains, in the water-free substance, not less than fifty (50) per cent. of milk fat. By act of Congress, approved June 6, 1896, cheese may also contain added coloring matter.

2. *Skim milk cheese* is the sound, solid, and ripened product, made from skim milk by coagulating the casein thereof with rennet or lactic acid, with or without the addition of ripening ferments and seasoning.

3. *Goat's milk cheese, ewe's milk cheese, et cetera*, are the sound, ripened products made from the milks of the animals specified, by coagulating the casein thereof with rennet or lactic acid, with or without the addition of ripening ferments and seasoning.

f. ICE CREAMS.

1. *Ice cream* is a frozen product made from cream and sugar, with or without a natural flavoring, and contains not less than fourteen (14) per cent. of milk fat.

2. *Fruit ice cream* is a frozen product made from cream, sugar, and sound, clean, mature fruits, and contains not less than twelve (12) per cent. of milk fat.

3. *Nut ice cream* is a frozen product made from cream, sugar, and sound, nonrancid nuts, and contains not less than twelve (12) per cent. of milk fat.

g. MISCELLANEOUS MILK PRODUCTS.

1. *Whey* is the product remaining after the removal of fat and casein from milk in the process of cheese-making.

2. *Kumiss* is the product made by the alcoholic fermentation of mare's or cow's milk.

II. VEGETABLE PRODUCTS.

A. GRAIN PRODUCTS.

a. GRAINS AND MEALS.

1. *Grain* is the fully matured, clean, sound, air-dry seed of wheat, maize, rice, oats, rye, buckwheat, barley, sorghum, millet, or spelt.

2. *Meal* is the clean, sound product made by grinding grain.

3. *Flour* is the fine, clean, sound product made by bolting wheat meal and contains not more than thirteen and one-half (13.5) per cent. of moisture, not less than one and twenty-five hundredths (1.25) per cent. of nitrogen, not more than one (1) per cent. of ash, and not more than fifty hundredths (0.50) per cent. of fiber.

4. *Graham flour* is unbolted wheat meal.

5. *Gluten flour* is the clean, sound product made from flour by the removal of starch and contains not less than five and six-tenths (5.6) per cent. of nitrogen and not more than ten (10) per cent. of moisture.

6. *Maize meal, corn meal, Indian corn meal,* is meal made from sound maize grain and contains not more than fourteen (14) per cent. of moisture, not less than one and twelve-hundredths (1.12) per cent. of nitrogen, and not more than one and six-tenths (1.6) per cent. of ash.

7. *Rice* is the hulled, or hulled and polished grain of *Oryza sativa.*

8. *Oatmeal* is meal made from hulled oats and contains not more than twelve (12) per cent. of moisture, not more than one and five-tenths (1.5) per cent. of crude fiber, not less than two and twenty-four hundredths (2.24) per cent. of nitrogen, and not more than two and two-tenths (2.2) per cent. of ash.

9. *Rye flour* is the fine, clean, sound product made by bolting rye meal, and contains not more than thirteen and one-half (13.5) per cent. of moisture, not less than one and thirty-six hundredths (1.36) per cent. of nitrogen, and not more than one and twenty-five hundredths (1.25) per cent. of ash.

10. *Buckwheat flour* is bolted buckwheat meal and contains not more than twelve (12) per cent. of moisture, not less than one and twenty-eight hundredths (1.28) per cent. of nitrogen, and not more than one and seventy-five hundredths (1.75) per cent. of ash.

B. FRUIT AND VEGETABLES.

a. FRUIT AND FRUIT PRODUCTS.

(Except fruit juices, fresh, sweet, and fermented, and vinegars.)

1. *Fruits* are the clean, sound, edible, fleshy fructifications of plants, distinguished by their sweet, acid, and ethereal flavors.

2. *Dried fruit*[1] is the clean, sound product made by drying mature, properly prepared, fresh fruit, in such a way as to take up no harmful substance, and conforms in name to the fruit used in its preparation; *sun-dried fruit* is dried fruit made by drying without the use of artificial means; *evaporated fruit* is dried fruit made by drying with the use of artificial means.

3. *Evaporated apples* are evaporated fruit made from peeled and cored apples, and contain not more than twenty-seven (27) per cent. of moisture determined by the usual commercial method of drying for four (4) hours at the temperature of boiling water.

(Standards for other dried fruits are in preparation.)

[1] The subject of sulphurous acid in dried fruits is reserved for consideration in connection with the schedule "Preservatives and Coloring Matters." See F. I. D. 76, pages lxx and lxxii.

4. *Canned fruit* is the sound product made by sterilizing clean, sound, properly matured and prepared fresh fruit, by heating with or without sugar (sucrose) and spices, and keeping in suitable, clean, hermetically sealed containers, and conforms in name to the fruit used in its preparation.

5. *Preserve*[1] is the sound product made from clean, sound, properly matured and prepared fresh fruit and sugar (sucrose) sirup, with or without spices or vinegar, and conforms in name to that of the fruit used, and in its preparation not less than forty-five (45) pounds of fruit are used to each fifty-five (55) pounds of sugar.

6. *Honey preserve*[1] is preserve in which honey is used in place of sugar (sucrose) sirup.

7. *Glucose preserve*[1] is preserve in which a glucose product is used in place of sugar (sucrose) sirup.

8. *Jam, marmalade,*[1] is the sound product made from clean, sound, properly matured and prepared fresh fruit and sugar (sucrose), with or without spices or vinegar, by boiling to a pulpy or semisolid consistence, and conforms in name to the fruit used, and in its preparation not less than forty-five (45) pounds of fruit are used to each fifty-five (55) pounds of sugar.

9. *Glucose jam, glucose marmalade,*[1] is jam in which a glucose product is used in place of sugar (sucrose).

10. *Fruit butter*[1] is the sound product made from fruit juice and clean, sound, properly matured and prepared fruit, evaporated to a semisolid mass of homogeneous consistence, with or without the addition of sugar and spices or vinegar, and conforms in name to the fruit used in its preparation.

11. *Glucose fruit butter*[1] is fruit butter in which a glucose product is used in place of sugar (sucrose).

12. *Jelly*[1] is the sound, semisolid, gelatinous product made by boiling clean, sound, properly matured and prepared fresh fruit with water, concentrating the expressed and strained juice, to which sugar (sucrose) is added, and conforms in name to the fruit used in its preparation.

13. *Glucose jelly*[1] is jelly in which a glucose product is used in place of sugar (sucrose).

b. VEGETABLES AND VEGETABLE PRODUCTS.

1. *Vegetables* are the succulent, clean, sound, edible parts of herbaceous plants used for culinary purposes.

2. *Dried vegetables* are the clean, sound products made by drying properly matured and prepared vegetables in such a way as to take up no harmful substance, and conform in name to the vegetables used in their preparation; *sun-dried vegetables* are dried vegetables made by drying without the use of artificial means; *evaporated vegetables* are dried vegetables made by drying with the use of artificial means.

3. *Canned vegetables* are sound, properly matured and prepared fresh vegetables, with or without salt, sterilized by heat, with or without previous cooking in vessels from which they take up no metallic substance, kept in suitable, clean, hermetically sealed containers, are sound and conform in name to the vegetables used in their preparation.

4. *Pickles* are clean, sound, immature cucumbers, properly prepared, without taking up any metallic compound other than salt, and preserved in any kind of vinegar, with or without spices; *pickled onions, pickled beets, pickled beans,* and other pickled vegetables are vegetables prepared as described above, and conform in name to the vegetables used.

5. *Salt pickles* are clean, sound, immature cucumbers, preserved in a solution of common salt, with or without spices.

6. *Sweet pickles* are pickled cucumbers or other vegetables in the preparation of which sugar (sucrose) is used.

7. *Sauerkraut* is clean, sound, properly prepared cabbage, mixed with salt, and subjected to fermentation.

8. *Catchup* (*ketchup, catsup*) is the clean, sound product made from the properly prepared pulp of clean, sound, fresh, ripe tomatoes, with spices and with or without sugar and vinegar; *mushroom catchup, walnut catchup, et cetera,* are catchups made as above described, and conform in name to the substances used in their preparation.

C. SUGARS AND RELATED SUBSTANCES.

a. SUGAR AND SUGAR PRODUCTS.

SUGARS.

1. *Sugar* is the product chemically known as sucrose (saccharose) chiefly obtained from sugar cane, sugar beets, sorghum, maple, and palm.

2. *Granulated, loaf, cut, milled,* and *powdered sugars* are different forms of sugar and contain at least ninety-nine and five-tenths (99.5) per cent. of sucrose.

3. *Maple sugar* is the solid product resulting from the evaporation of maple sap, and contains, in the water-free substance, not less than sixty-five one-hundredths (0.65) per cent. of maple sugar ash.

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[1] Products made with mixtures of sugar, glucose, and honey, or any two thereof, are reserved for future consideration.

4. *Massecuite, melada, mush sugar,* and *concrete* are products made by evaporating the purified juice of a sugar-producing plant, or a solution of sugar, to a solid or semisolid consistence, and in which the sugar chiefly exists in a crystalline state.

MOLASSES AND REFINER'S SIRUP

1. *Molasses* is the product left after separating the sugar from massecuite, melada, mush sugar, or concrete, and contains not more than twenty-five (25) per cent. of water and not more than five (5) per cent. of ash. [See also F. I. D. 161.]

2. *Refiner's sirup, treacle,* is the residual liquid product obtained in the process of refining raw sugars and contains not more than twenty-five (25) per cent. of water and not more than eight (8) per cent. of ash.

SIRUPS

1. *Sirup* is the sound product made by purifying and evaporating the juice of a sugar-producing plant without removing any of the sugar.

2. *Sugar-cane sirup* is sirup made by the evaporation of the juice of the sugar-cane or by the solution of sugar-cane concrete, and contains not more than thirty (30) per cent. of water and not more than two and five-tenths (2.5) per cent. of ash.

3. *Sorghum sirup* is sirup made by the evaporation of sorghum juice or by the solution of sorghum concrete, and contains not more than thirty (30) per cent. of water and not more than two and five-tenths (2.5) per cent. of ash.

4. *Maple sirup* is sirup made by the evaporation of maple sap or by the solution of maple concrete, and contains not more than thirty-two (32) per cent. of water and not less than forty-five hundredths (0.45) per cent. of maple sirup ash. [See also F. I. D. 161.]

5. *Sugar sirup* is the product made by dissolving sugar to the consistence of a sirup and contains not more than thirty-five (35) per cent. of water.

b. GLUCOSE PRODUCTS.

1. *Starch sugar* is the solid product made by hydrolyzing starch or a starch-containing substance until the greater part of the starch is converted into dextrose. Starch sugar appears in commerce in two forms, anhydrous starch sugar and hydrous starch sugar. The former, crystallized, without water of crystallization, contains not less than ninety-five (95) per cent. of dextrose and not more than eight-tenths (0.8) per cent. of ash. The latter, crystallized with water of crystallization, is of two varieties—70 sugar, also known as brewers' sugar, contains not less than seventy (70) per cent. of dextrose and not more than eight-tenths (0.8) per cent. of ash; 80 sugar, climax or acme sugar, contains not less than eighty (80) per cent. of dextrose and not more than one and one-half (1.5) per cent. of ash.

The ash of all these products consists almost entirely of chlorids and sulphates.

2. *Glucose, mixing glucose, confectioner's glucose,* is a thick, sirupy, colorless product made by incompletely hydrolyzing starch, or a starch-containing substance, and decolorizing and evaporating the product. It varies in density from forty-one (41) to forty-five (45) degrees Baumé at a temperature of 100° Fahr. (37.7° C.), and conforms in density, within these limits, to the degree Baumé it is claimed to show, and for a density of forty-one (41) degrees Baumé contains not more than twenty-one (21) per cent. and for a density of forty-five (45) degrees not more than fourteen (14) per cent. of water. It contains on a basis of forty-one (41) degrees Baumé not more than one (1) per cent. of ash, consisting chiefly of chlorids and sulphates.

c. CANDY.

1. *Candy* is a product made from a saccharine substance or substances with or without the addition of harmless coloring, flavoring, or filling materials, and contains no terra alba, barytes, talc, chrome yellow, or other mineral substances, or poisonous colors or flavors, or other ingredients deleterious or detrimental to health, or any vinous, malt, or spirituous liquor or compound, or narcotic drug.

d. HONEY.

1. *Honey* is the nectar and saccharine exudations of plants gathered, modified, and stored in the comb by honey bees (*Apis mellifica* and *A. dorsata*); is lævo-rotatory, contains not more than twenty-five (25) per cent. of water, not more than twenty-five hundredths (0.25) per cent. of ash, and not more than eight (8) per cent. of sucrose.

2. *Comb honey* is honey contained in the cells of comb.

3. *Extracted honey* is honey which has been separated from the uncrushed comb by centrifugal force or gravity.

4. *Strained honey* is honey removed from the crushed comb by straining or other means.

D. Condiments (except Vinegar and Salt).

a. spices.

1. *Spices* are aromatic vegetable substances used for the seasoning of food and from which no portion of any volatile oil or other flavoring principle has been removed and which are clean, sound, and true to name.

2. *Allspice, pimento,* is the dried fruit of the *Pimenta pimenta* (L.) Karst., and contains not less than eight (8) per cent. of quercitannic acid[1]; not more than six (6) per cent. of total ash, not more than five-tenths (0.5) per cent. of ash insoluble in hydrochloric acid, and not more than twenty-five (25) per cent. of crude fiber.

3. *Anise* is the fruit of the *Pimpinella anisum* L.

4. *Bay leaf* is the dried leaf of *Laurus nobilis* L.

5. *Capers* are the flower buds of *Capparis spinosa* L.

6. *Caraway* is the fruit of *Carum carvi* L.

cayenne and red pepper.

7. *Red pepper* is the red, dried, ripe fruit of any species of *Capsicum.*

8. *Cayenne pepper, cayenne,* is the dried ripe fruit of *Capsicum frutescens* L., *Capsicum baccatum* L., or some other small-fruited species of *Capsicum,* and contains not less than fifteen (15) per cent. of nonvolatile ether extract; not more than six and five-tenths (6.5) per cent. of total ash; not more than five-tenths (0.5) per cent. of ash insoluble in hydrochloric acid; not more than one and five-tenths (1.5) per cent. of starch, and not more than twenty-eight (28) per cent. of crude fiber.

9. *Paprika* is the dried ripe fruit of *Capsicum annuum* L., or some other large-fruited species of *Capsicum,* excluding seeds and stems.

10. *Celery seed* is the dried fruit of *Apium graveolens* L.

11. *Cinnamon* is the dried bark of any species of the genus *Cinnamomum,* from which the outer layers may or may not have been removed.

12. *True cinnamon* is the dried inner bark of *Cinnamomum zeylanicum* Breyne.

13. *Cassia* is the dried bark of various species of *Cinnamomum,* other than *Cinnamomum zeylanicum,* from which the outer layers may or may not have been removed.

14. *Cassia buds* are the dried immature fruit of species of *Cinnamomum.*

15. *Ground cinnamon, ground cassia,* is a powder consisting of cinnamon, cassia, or cassia buds, or a mixture of these spices, and contains not more than six (6) per cent. of total ash and not more than two (2) per cent. of sand.

16. *Cloves* are the dried flower buds of *Caryophyllus aromaticus* L., which contain not more than five (5) per cent. of clove stems; not less than ten (10) per cent. of volatile ether extract; not less than twelve (12) per cent. of quercitannic acid[1]; not more than eight (8) per cent. of total ash; not more than five-tenths (0.5) per cent. of ash insoluble in hydrochloric acid, and not more than ten (10) per cent. of crude fiber.

17. *Coriander* is the dried fruit of *Coriandrum sativum* L.

18. *Cumin seed* is the fruit of *Cuminum cyminum* L.

19. *Dill seed* is the fruit of *Anethum graveolens* L.

20. *Fennel* is the fruit of *Foeniculum foeniculum* (L.) Karst.

21. *Ginger* is the washed and dried or decorticated and dried rhizome of *Zinziber zingiber* (L.) Karst., and contains not less than forty-two (42) per cent. of starch; not more than eight (8) per cent. of crude fiber, not more than (6) per cent. of total ash, not more than one (1) per cent. of lime, and not more than three (3) per cent. of ash insoluble in hydrochloric acid.

22. *Limed ginger, bleached ginger,* is whole ginger coated with carbonate of lime and contains not more than ten (10) per cent. of ash, not more than four (4) per cent. of carbonate of lime, and conforms in other respects to the standard for ginger.

23. *Horse-radish* is the root of *Roripa armoracia* (L.) Hitchcock, either by itself or ground and mixed with vinegar.

24. *Mace* is the dried arillus of *Myristica fragrans* Houttuyn, and contains not less than twenty (20) nor more than thirty (30) per cent. of nonvolatile ether extract, not more than three (3) per cent. of total

[1] Calculated from the total oxygen absorbed by the aqueous extract.

ash, and not more than five-tenths (0.5) per cent. of ash insoluble in hydrochloric acid, and not more than ten (10) per cent. of crude fiber.

25. *Macassar mace, Papua mace,* is the dried arillus of *Myristica argentea* Warb.

26. *Bombay mace* is the dried arillus of *Myristica malabarica* Lamarck.

27. *Marjoram* is the leaf, flower and branch of *Majorana majorana* (L.) Karst.

28. *Mustard seed* is the seed of *Sinapis alba* L. (white mustard), *Brassica nigra* (L.) Koch (black mustard), or *Brassica juncea* (L.) Cosson (black or brown mustard).

29. *Ground mustard* is a powder made from mustard seed, with or without the removal of the hulls and a portion of the fixed oil, and contains not more than two and five-tenths (2.5) per cent. of starch and not more than eight (8) per cent. of total ash.

30. *Prepared mustard, German mustard, French mustard, mustard paste,* is a paste composed of a mixture of ground mustard seed or mustard flour with salt, spices and vinegar, and, calculated free from water, fat and salt, contains not more than twenty-four (24) per cent. of carbohydrates, calculated as starch, determined according to the official methods, not more than twelve (12) per cent. of crude fiber nor less than thirty-five (35) per cent. of protein, derived solely from the materials named.

31. *Nutmeg* is the dried seed of the *Myristica fragrans* Houttuyn, deprived of its testa, with or without a thin coating of lime, and contains not less than twenty-five (25) per cent. of nonvolatile ether extract, not more than five (5) per cent. of total ash, not more than five-tenths (0.5) per cent. of ash insoluble in hydrochloric acid, and not more than ten (10) per cent. of crude fiber.

32. *Macassar nutmeg, Papua nutmeg, male nutmeg, long nutmeg,* is the dried seed of *Myristica argentea* Warb. deprived of its testa.

PEPPER.

33. *Black pepper* is the dried immature berry of *Piper nigrum* L., and contains not less than six (6) per cent. of nonvolatile ether extract, not less than twenty-five (25) per cent. of starch, not more than seven (7) per cent. of total ash, not more than two (2) per cent. of ash insoluble in hydrochloric acid, and not more than fifteen (15) per cent. of crude fiber. One hundred parts of the nonvolatile ether extract contain not less than three and one-quarter (3.25) parts of nitrogen. *Ground black pepper* is the product made by grinding the entire berry and contains the several parts of the berry in their normal porportions.

34. *Long pepper* is the dried fruit of *Piper longum* L.

35. *White pepper* is the dried mature berry of *Piper nigrum* L. from which the outer coating or the outer and inner coatings have been removed, and contains not less than six (6) per cent. of nonvolatile ether extract, not less than fifty (50) per cent. of starch, not more than four (4) per cent. of total ash, not more than five-tenths (0.5) per cent. of ash insoluble in hydrochloric acid, and not more than five (5) per cent. of crude fiber. One hundred parts of the nonvolatile ether extract contain not less than four (4) parts of nitrogen.

36. *Saffron* is the dried stigma of *Crocus sativus* L.

37. *Sage* is the leaf of *Salvia officinalis* L.

38. *Savory, summer savory,* is the leaf, blossom, and branch of *Satureja hortensis* L.

39. *Thyme* is the leaf and tip of blooming branches of *Thymus vulgaris* L.

b. FLAVORING EXTRACTS.

1. *A flavoring extract*[1] is a solution in ethyl alcohol of proper strength of the sapid and odorous principles derived from an aromatic plant, or parts of the plant, with or without its coloring matter, and conforms in name to the plant used in its preparation.

2. *Almond extract* is the flavoring extract prepared from oil of bitter almonds, free from hydrocyanic acid, and contains not less than one (1) per cent. by volume of oil of bitter almonds.

2a. *Oil of bitter almonds,* commercial, is the volatile oil obtained from the seed of the bitter almond (*Amygdalus communis* L.), the apricot (*Prunus armeniaca* L.), or the peach (*Amygdalus persica* L.).

3. *Anise extract* is the flavoring extract prepared from oil of anise, and contains not less than three (3) per cent. by volume of oil of anise.

3a. *Oil of anise* is the volatile oil obtained from the anise seed.

4. *Celery seed extract* is the flavoring extract prepared from celery seed or the oil of celery seed, or both, and contains not less than three-tenths (0.3) per cent. by volume of oil of celery seed.

4a. *Oil of celery seed* is the volatile oil obtained from celery seed.

5. *Cassia extract* is the flavoring extract prepared from oil of cassia and contains not less than two (2) per cent. by volume of oil of cassia.

[1] The flavoring extracts herein described are intended solely for food purposes and are not to be confounded with similar preparations described in the Pharmacopœia for medicinal purposes.

5*a*. *Oil of cassia* is the lead-free volatile oil obtained from the leaves or bark of *Cinnamomum cassia* Bl., and contains not less than seventy-five (75) per cent. by weight of cinnamic aldehyde.

6. *Cinnamon extract* is the flavoring extract prepared from oil of cinnamon, and contains not less than two (2) per cent. by volume of oil of cinnamon.

6*a*. *Oil of cinnamon* is the lead-free volatile oil obtained from the bark of the Ceylon cinnamon (*Cinnamomum zeylanicum* Breyne), and contains not less than sixty-five (65) per cent. by weight of cinnamic aldehyde and not more than ten (10) per cent. by weight of eugenol.

7. *Clove extract* is the flavoring extract prepared from oil of cloves, and contains not less than two (2) per cent. by volume of oil of cloves.

7*a*. *Oil of cloves* is the lead-free, volatile oil obtained from cloves.

8. *Ginger extract* is the flavoring extract prepared from ginger and contains in each one hundred (100) cubic centimeters, the alcohol-soluble matters from not less than twenty (20) grams of ginger.

9. *Lemon extract* is the flavoring extract prepared from oil of lemon, or from lemon peel, or both, and contains not less than five (5) per cent. by volume of oil of lemon.

9*a*. *Oil of lemon* is the volatile oil obtained, by expression or alcoholic solution, from the fresh peel of the lemon (*Citrus limonum* L.), has an optical rotation (25° C.) of not less than +60° in a 100-millimeter tube, and contains not less than four (4) per cent. by weight of citral.

10. *Terpeneless extract of lemon* is the flavoring extract prepared by shaking oil of lemon with dilute alcohol, or by dissolving terpeneless oil of lemon in dilute alcohol, and contains not less than two-tenths (0.2) per cent. by weight of citral derived from oil of lemon.

10*a*. *Terpeneless oil of lemon* is oil of lemon from which all or nearly all of the terpenes have been removed.

11. *Nutmeg extract* is the flavoring extract prepared from oil of nutmeg, and contains not less than two (2) per cent. by volume of oil of nutmeg.

11*a*. *Oil of nutmeg* is the volatile oil obtained from nutmegs.

12. *Orange extract* is the flavoring extract prepared from oil of orange, or from orange peel, or both, and contains not less than five (5) per cent. by volume of oil of orange.

12*a*. *Oil of orange* is the volatile oil obtained, by expression or alcoholic solution, from the fresh peel of the orange (*Citrus aurantium* L.) and has an optical rotation (25° C.) of not less than + 95° in a 100-millimeter tube.

13. *Terpeneless extract of orange* is the flavoring extract prepared by shaking oil of orange with dilute alcohol, or by dissolving terpeneless oil of orange in dilute alcohol, and corresponds in flavoring strength to orange extract.

13*a*. *Terpeneless oil of orange* is oil of orange from which all or nearly all of the terpenes have been removed.

14. *Peppermint extract* is the flavoring extract prepared from oil of peppermint, or from peppermint, or both, and contains not less than three (3) per cent. by volume of oil of peppermint.

14*a*. *Peppermint* is the leaves and flowering tops of *Mentha piperita* L.

14*b*. *Oil of peppermint* is the volatile oil obtained from peppermint and contains not less than fifty (50) per cent. by weight of menthol.

15. *Rose extract* is the flavoring extract prepared from otto of roses, with or without red rose petals, and contains not less than four-tenths (0.4) per cent. by volume of otto of roses.

15*a*. *Otto of roses* is the volatile oil obtained from the petals of *Rosa damascena* Mill., *R. centifolia* L., or *R. moschata* Herrm.

16. *Savory extract* is the flavoring extract prepared from oil of savory, or from savory, or both, and contains not less than thirty-five hundredths (0.35) per cent. by volume of oil of savory.

16*a*. *Oil of savory* is the volatile oil obtained from savory.

17. *Spearmint extract* is the flavoring extract prepared from oil of spearmint, or from spearmint, or both, and contains not less than three (3) per cent. by volume of oil of spearmint.

17*a*. *Spearmint* is the leaves and flowering tops of *Mentha spicata* L.

17*b*. *Oil of spearmint* is the volatile oil obtained from spearmint.

18. *Star anise extract* is the flavoring extract prepared from oil of star anise, and contains not less than three (3) per cent. by volume of oil of star anise.

18*a*. *Oil of star anise* is the volatile oil distilled from the fruit of the star anise (*Illicium verum* Hook.).

19. *Sweet basil extract* is the flavoring extract prepared from oil of sweet basil, or from sweet basil, or both, and contains not less than one-tenth (0.1) per cent. by volume of oil of sweet basil.

19*a*. *Sweet basil, basil,* is the leaves and tops of *Ocymum basilicum* L.

19*b*. *Oil of sweet basil* is the volatile oil obtained from basil.

20. *Sweet marjoram extract, marjoram extract,* is the flavoring extract prepared from the oil of marjoram, or from marjoram, or both, and contains not less than one (1) per cent. by volume of oil of marjoram.

20*a*. *Oil of marjoram* is the volatile oil obtained from marjoram.

21. *Thyme extract* is the flavoring extract prepared from oil of thyme, or from thyme, or both, and contains not less than two-tenths (0.2) per cent. by volume of oil of thyme.

21*a*. *Oil of thyme* is the volatile oil obtained from thyme.

22. *Tonka extract* is the flavoring extract prepared from tonka bean, with or without sugar or glycerin, and contains not less than one-tenth (0.1) per cent. by weight of coumarin extracted from the tonka bean, together with a corresponding proportion of the other soluble matters thereof.

22*a*. *Tonka bean* is the seed of *Coumarouna odorata* Aublet (*Dipteryx odorata* (Aubl.) Willd.).

23. *Vanilla extract* is the flavoring extract prepared from vanilla bean, with or without sugar or glycerin, and contains in one hundred (100) cubic centimeters the soluble matters from not less than ten (10) grams of the vanilla bean.

23*a*. *Vanilla bean* is the dried, cured fruit of *Vanilla planifolia* Andrews.

24. *Wintergreen extract* is the flavoring extract prepared from oil of wintergreen, and contains not less than three (3) per cent. by volume of oil of wintergreen.

24*a*. *Oil of wintergreen* is the volatile oil distilled from the leaves of the *Gaultheria procumbens* L.

C. EDIBLE VEGETABLE OILS AND FATS.

1. *Olive oil* is the oil obtained from the sound, mature fruit of the cultivated olive tree (*Olea europæa* L.) and subjected to the usual refining processes; is free from rancidity; has a refractive index (25° C.) not less than one and forty-six hundred and sixty ten-thousandths (1.4660) and not exceeding one and forty-six hundred and eighty ten-thousandths (1.4680); and an iodin number not less than seventy-nine (79) and not exceeding ninety (90).

2. *Virgin olive oil* is olive oil obtained from the first pressing of carefully selected, hand-picked olives.

3. *Cotton-seed oil* is the oil obtained from the seeds of cotton plants (*Gossypium hirsutum* L., *G. barbadense* L., or *G. herbaceum* L.) and subjected to the usual refining processes; is free from rancidity, has a refractive index (25° C.) not less than one and forty-seven hundred ten-thousandths (1.4700) and not exceeding one and forty-seven hundred and twenty-five ten-thousandths (1.4725); and an iodin number not less than one hundred and four (104) and not exceeding one hundred and ten (110).

4. *"Winter-yellow" cotton-seed oil* is expressed cotton-seed oil from which a portion of the stearin has been separated by chilling and pressure, and has an iodin number not less than one hundred and ten (110) and not exceeding one hundred and sixteen (116).

5. *Peanut oil, arachis oil, earthnut oil,* is the oil obtained from the peanut (*Arachis hypogæa* L.) and subjected to the usual refining processes; is free from rancidity; has a refractive index (25° C.) not less than one and forty-six hundred and ninety ten-thousandths (1.4690) and not exceeding one and forty-seven hundred and seven ten-thousandths (1.4707); and an iodin number not less than eighty-seven (87) and not exceeding one hundred (100).

6. *"Cold-drawn" peanut oil*[1] is peanut oil obtained by pressure without heating.

7. *Sesame oil, gingili oil, teel oil,* is the oil obtained from the seeds of the sesame plants (*Sesamum orientale* L. and *S. radiatum* Schum. and Thonn.) and subjected to the usual refining processes; is free from rancidity; has a refractive index (25° C.) not less than one and forty-seven hundred and four ten-thousandths (1.4704) and not exceeding one and forty-seven hundred and seventeen ten-thousandths (1.4717); and an iodin number not less than one hundred and three (103) and not exceeding one hundred and twelve (112).

8. *"Cold-drawn" sesame oil*[1] is sesame oil obtained by pressure without heating.

9. *Poppy-seed oil*[1] is the oil obtained from the seed of the poppy (*Papaver somniferum* L.) subjected to the usual refining processes and free from rancidity.

10. *White poppy-seed oil, "cold-drawn" poppy-seed oil,*[1] is poppy-seed oil of the first pressing without heating.

11. *Coconut oil*[1] is the oil obtained from the kernels of the coconut (*Cocos nucifera* F.) and subjected to the usual refining processes and free from rancidity.

12. *Cochin oil* is coconut oil prepared in Cochin (Malabar).

13. *Ceylon oil* is coconut oil prepared in Ceylon.

14. *Copra oil* is coconut oil prepared from copra, the dried kernels of the coconut.

15. *Rape-seed oil, colza oil,*[1] is the oil obtained from the seeds of the rape plant (*Brassica napus* L.) and subjected to the usual refining processes and free from rancidity.

16. *"Cold-drawn" rape-seed oil*[1] is rape-seed oil obtained by the first pressing without heating.

17. *Sunflower oil*[1] is the oil obtained from the seeds of the sunflower (*Helianthus annuus* L.) and subjected to the usual refining processes and free from rancidity.

18. *"Cold-drawn" sunflower oil*[1] is sunflower oil obtained by the first pressing without heating.

[1] The fixing of limits for chemical and physical properties is reserved for future consideration.

19. *Maize oil, corn oil,*[1] is the oil obtained from the germ of the maize (*Zea mays* L.) and subjected to the usual refining processes and free from rancidity.

20. *Cocoa butter, cacao butter,* is the fat obtained from roasted, sound cocoa beans, and subjected to the usual refining processes; is free from rancidity; has a refractive index (40° C.) not less than one and forty-five hundred and sixty-six ten-thousandths (1.4566) and not exceeding one and forty-five hundred and ninety-eight ten-thousandths (1.4598); an iodin number not less than thirty-three (33) and not exceeding thirty-eight (38); and a melting point not lower than 30° C. nor higher than 35° C.

21. *Cotton-seed oil stearin* is the solid product made by chilling cotton-seed oil and separating the solid portion by filtration, with or without pressure, and having an iodin number not less than eighty-five (85) and not more than one hundred (100).

E. Tea, Coffee, and Cocoa Products.

a. TEA.

1. *Tea* is the leaves and leaf buds of different species of *Thea*, prepared by the usual trade processes of fermenting, drying, and firing; meets the provisions of the act of Congress approved March 2, 1897, and the regulations made in conformity therewith (Treasury Department Circular 16, February 6, 1905); conforms in variety and place of production to the name it bears; and contains not less than four (4) nor more than seven (7) per cent. of ash.

b. COFFEE.

1. *Coffee* is the seed of *Coffea arabica* L. or *Coffea liberica* Bull., freed from all but a small portion of its spermoderm, and conforms in variety and place of production to the name it bears.

2. *Roasted coffee* is coffee which by the action of heat has become brown and developed its characteristic aroma, and contains not less than ten (10) per cent. of fat and not less than three (3) per cent. of ash.

c. COCOA AND COCOA PRODUCTS.

1. *Cocoa beans* are the seeds of the cacao tree, *Theobroma cacao* L.

2. *Cocoa nibs, cracked cocoa*, is the roasted, broken cocoa bean freed from its shell or husk.

3. *Chocolate, plain chocolate, bitter chocolate, chocolate liquor, bitter chocolate coatings*, is the solid or plastic mass obtained by grinding cocoa nibs without the removal of fat or other constituents except the germ, and contains not more than three (3) per cent. of ash insoluble in water, three and fifty hundredths (3.50) per cent. of crude fiber, and nine (9) per cent. of starch, and not less than forty-five (45) per cent. of cocoa fat.

4. *Sweet chocolate, sweet chocolate coatings*, is chocolate mixed with sugar (sucrose), with or without the addition of cocoa butter, spices, or other flavoring materials, and contains in the sugar- and fat-free residue no higher percentage of either ash, fiber, or starch than is found in the sugar- and fat-free residue of chocolate.

5. *Cocoa, powdered cocoa*, is cocoa nibs, with or without the germ, deprived of a portion of its fat and finely pulverized, and contains percentages of ash, crude fiber, and starch corresponding to those in chocolate after correction for fat removed.

6. *Sweet cocoa, sweetened cocoa*, is cocoa mixed with sugar (sucrose), and contains not more than sixty (60) per cent. of sugar (sucrose), and in the sugar- and fat-free residue no higher percentage of either ash, crude fiber, or starch than is found in the sugar- and fat-free residue of chocolate.

F. Beverages.

a. FRUIT JUICES—FRESH, SWEET, AND FERMENTED.

1. FRESH AND 2. SWEET.

(Schedules in preparation.)

3. FERMENTED FRUIT JUICES.

1. *Wine* is the product made by the normal alcoholic fermentation of the juice of sound, ripe grapes, and the usual cellar treatment,[2] and contains not less than seven (7) nor more than sixteen (16) per cent. of alcohol, by volume, and, in one hundred (100) cubic centimeters (20° C.), not more than one-tenth (0.1)

[1] The fixing of limits for chemical and physical properties is reserved for future consideration.

[2] The subject of sulphurous acid in wine is reserved for consideration in connection with the schedule, "Preservatives and Coloring Matters."

gram of sodium chlorid nor more than two-tenths (0.2) gram of potassium sulphate; and for red wine not more than fourteen hundredths (0.14) gram, and for white wine not more than twelve hundredths (0.12) gram of volatile acids produced by fermentation and calculated as acetic acid. *Red wine* is wine containing the red coloring matter of the skins of grapes. *White wine* is wine made from white grapes or the expressed fresh juice of other grapes.

2. *Dry wine* is wine in which the fermentation of the sugars is practically complete and which contains, in one hundred (100) cubic centimeters (20°C.), less than one (1) gram of sugars and for dry red wine not less than sixteen hundredths (0.16) gram of grape ash and not less than one and six-tenths (1.6) grams of sugar-free grape solids, and for dry white wine not less than thirteen hundredths (0.13) gram of grape ash and not less than one and four-tenths (1.4) grams of sugar-free grape solids.

3. *Fortified dry wine* is dry wine to which brandy has been added but which conforms in all other particulars to the standard of dry wine.

4. *Sweet wine* is wine in which the alcoholic fermentation has been arrested, and which contains in one hundred (100) cubic centimeters (20° C.), not less than one (1) gram of sugars, and for sweet red wine not less than sixteen hundredths (0.16) gram of grape ash, and for sweet white wine not less than thirteen hundredths (0.13) gram of grape ash.

5. *Fortified sweet wine* is sweet wine to which wine spirits have been added. By act of Congress, "sweet wine" used for making fortified sweet wine and "wine spirits" used for such fortification are defined as follows (sec. 43, Act of October 1, 1890, 26 Stat., 567, as amended by section 68, Act of August 27, 1894, 28 Stat., 509, and further amended by Act of Congress approved June 7, 1906): "That the wine spirits mentioned in section 42 of this act is the product resulting from the distillation of fermented grape juice to which water may have been added prior to, during, or after fermentation, for the sole purpose of facilitating the fermentation and economical distillation thereof, and shall be held to include the products from grapes or their residues, commonly known as grape brandy; and the pure sweet wine, which may be fortified free of tax, as provided in said section, is fermented grape juice only, and shall contain no other substance whatever introduced before, at the time of, or after fermentation, except as herein expressly provided and such sweet wine shall contain not less than four per centum of saccharine matter, which saccharine strength may be determined by testing, with Balling's saccharometer or must scale, such sweet wine, after the evaporation of the spirits contained therein, and restoring the sample tested to original volume by addition of water: *Provided*, That the addition of pure boiled or condensed grape must or pure crystallized cane or beet sugar or pure anhydrous sugar to the pure grape juice aforesaid, or the fermented product of such grape juice prior to the fortification provided by this Act for the sole purpose of perfecting sweet wine according to commercial standard, or the addition of water in such quantities only as may be necessary in the mechanical operation of grape conveyers, crushers, and pipes leading to fermenting tanks, shall not be excluded by the definition of pure sweet wine aforesaid: *Provided, however*, That the cane or beet sugar, or pure anhydrous sugar, or water, so used shall not in either case be in excess of ten (10) per centum of the weight of the wine to be fortified under this Act: *And provided further*, That the addition of water herein authorized shall be under such regulations and limitations as the Commissioner of Internal Revenue, with the approval of the Secretary of the Treasury, may from time to time prescribe; but in no case shall such wines to which water has been added be eligible for fortification under the provisions of this Act where the same, after fermentation and before fortification, have an alcoholic strength of less than five per centum of their volume."

6. *Sparkling wine* is wine in which the after part of the fermentation is completed in the bottle, the sediment being disgorged and its place supplied by wine or sugar liquor, and which contains, in one hundred (100) cubic centimeters (20° C.), not less than twelve hundredths (0.12) gram of grape ash.

7. *Modified wine, ameliorated wine, corrected wine*, is the product made by the alcoholic-fermentation, with the usual cellar treatment, of a mixture of the juice of sound, ripe grapes with sugar (sucrose), or a sirup containing not less than sixty-five (65) per cent. of sugar (sucrose), and in quantity not more than enough to raise the alcoholic strength after fermentation, to eleven (11) per cent. by volume.

8. *Raisin wine* is the product made by the alcoholic fermentation of an infusion of dried or evaporated grapes, or of a mixture of such infusion or of raisins with grape juice.

b. MEAD, ROOT BEER, ETC.

(Schedule in preparation.)

c. MALT LIQUORS.

(Schedule in preparation.)

d. SPIRITUOUS LIQUORS.

(Schedule in preparation, see F. I. D. 113.)

e. CARBONATED WATERS, ETC.

(Schedule in preparation, see F. I. D. 94.)

G. VINEGAR.

1. *Vinegar, cider vinegar, apple vinegar*, is the product made by the alcoholic and subsequent acetous fermentations of the juice of apples, is lævo-rotatory, and contains not less than four (4) grams of acetic acid, not less than one and six-tenths (1.6) grams of apple solids, of which not more than fifty (50) per cent. are reducing sugars, and not less than twenty-five hundredths (0.25) gram of apple ash in one hundred (100) cubic centimeters (20° C.); and the water-soluble ash from one hundred (100) cubic centimeters (20° C.) of the vinegar contains not less than ten (10) milligrams of phosphoric acid (P_2O_5), and requires not less than thirty (30) cubic centimeters of decinormal acid to neutralize its alkalinity.

2. *Wine vinegar, grape vinegar*, is the product made by the alcoholic and subsequent acetous fermentations of the juice of grapes and contains, in one hundred (100) cubic centimeters (20° C.), not less than four (4) grams of acetic acid, not less than one (1.0) gram of grape solids, and not less than thirteen hundredths (0.13) gram of grape ash.

3. *Malt vinegar* is the product made by the alcoholic and subsequent acetous fermentations, without distillation, of an infusion of barley malt or cereals whose starch has been converted by malt, is dextro-rotatory, and contains, in one hundred (100) cubic centimeters (20° C.), not less than four (4) grams of acetic acid, not less than two (2) grams of solids, and not less than two-tenths (0.2) gram of ash; and the water-soluble ash from one hundred (100) cubic centimeters (20° C.) of the vinegar contains not less than nine (9) milligrams of phosphoric acid (P_2O_5), and requires not less than four (4) cubic centimeters of decinormal acid to neutralize its alkalinity.

4. *Sugar vinegar* is the product made by the alcoholic and subsequent acetous fermentations of solutions of sugar, sirup, molasses, or refiners' sirup, and contains, in one hundred (100) cubic centimeters (20° C.), not less than four (4) grams of acetic acid.

5. *Glucose vinegar* is the product made by the alcoholic and subsequent acetous fermentations of solutions of starch sugar or glucose, is dextro-rotatory, and contains, in one hundred (100) cubic centimeters (20° C.), not less than four (4) grams of acetic acid.

6. *Spirit vinegar, distilled vinegar, grain vinegar*, is the product made by the acetous fermentation of dilute distilled alcohol, and contains, in one hundred (100) cubic centimeters (20° C.), not less than four (4) grams of acetic acid.

III. SALT.

1. *Table salt, dairy salt*, is fine-grained crystalline salt containing, on a water-free basis, not more than one and four-tenths (1.4) per cent. of calcium sulphate ($CaSO_4$), nor more than five-tenths (0.5) per cent. of calcium and magnesium chlorids ($CaCl_2$ and $MgCl_2$), nor more than one-tenth (0.1) per cent. of matters insoluble in water.

IV. PRESERVATIVES AND COLORING MATTERS.

(Schedules in preparation.)

See Food and Drugs Index (page cvii) for decisions upon preservatives and coloring matters.

Notices of Judgment, Food and Drugs Act.

The United States Department of Agriculture has published a series of pamphlets entitled "Notice of Judgment, Food and Drugs Act"; these now number approximately five thousand. Indexes of titles or any pamphlet may be obtained by writing to the Department of Agriculture at Washington.

HARRISON NARCOTIC ACT.

Because of the importance of the Harrison Narcotic Act of December 17, 1914, an Internal Revenue regulation governing the production, importation, manufacture, compounding, sale, dispensing, or giving away of opium or coca leaves, their salts, derivatives, or preparations within the jurisdiction of the United States, and because it should be readily available to doctors and druggists, it is here inserted in full, with the regulations issued by the Treasury Department up to April 10, 1917.

INTERNAL REVENUE REGULATIONS NO. 35, REVISED MAY, 1916.

LAW AND REGULATIONS

RELATING TO THE

Production, Importation, Manufacture, Compounding, Sale, Dispensing, or Giving Away of Opium or Coca Leaves, their Salts, Derivatives, or Preparations.

THE LAW.

By an act of Congress approved December 17, 1914, it is provided:

Persons who are required to register.

That on and after the first day of March, nineteen hundred and fifteen, every person who produces, imports, manufactures, compounds, deals in, dispenses, sells, distributes, or gives away opium or coca leaves or any compound, manufacture, salt, derivative, or preparation thereof, shall register with the collector of internal revenue of the district his name or style, place of business, and place or places where such business is to be carried on: *Provided*, That the office, or if none, then the residence of any person shall be considered for the purpose of this Act to be his place of business. At the time of such registry and on or before the first day of July, annually thereafter, every person who produces, imports, manufactures, compounds, deals in, dispenses, sells, distributes, or gives away any of the aforesaid drugs shall pay to the said collector a special tax at the rate of $1 per annum: *Provided*, That no employee of any person who produces, imports, manufactures, compounds, deals in, dispenses, sells, distributes, or gives away any of the aforesaid drugs, acting within the scope of his employment, shall be required to register or to pay the special tax provided by this section: *Provided further*, That the person who employs him shall have registered and paid the special tax as required by this section: *Provided further*, That officers of the United States Government who are lawfully engaged in making purchases of the above-named drugs for the various departments of the Army and Navy, the Public Health Service, and for Government hospitals and prisons, and officers of any State government, or of any county or municipality therein, who are lawfully engaged in making purchases of the above-named drugs for State, county, or municipal hospitals or prisons, and officials of any Territory or insular possession or the District of Columbia or of the United States who are lawfully engaged in making purchases of the above-named drugs for hospitals or prisons therein shall not be required to register and pay the special tax as herein required.

Special tax to be paid.

Exemption—Drugs purchased for U. S., etc.

Failure to register and to pay special tax.

It shall be unlawful for any person required to register under the terms of this Act to produce, import, manufacture, compound, deal in, dispense, sell, distribute, or give away any of the aforesaid drugs without having registered and paid the special tax provided for in this section.

Word "person" to include partnership, etc.

That the word "person" as used in this Act shall be construed to mean and include a partnership, association, company, or corporation, as well as a natural person; and all provisions of existing law relating to special taxes, so far as applicable, including the provisions of section thirty-two hundred and forty of the Revised Statutes of the United States are hereby extended to the special tax herein imposed.

Regulations to be prescribed.

That the Commissioner of Internal Revenue, with the approval of the Secretary of the Treasury, shall make all needful rules and regulations for carrying the provisions of this Act into effect.

Purchase orders required.

SECTION 2. That it shall be unlawful for any person to sell, barter, exchange, or give away any of the aforesaid drugs except in pursuance of a written order of the person to whom such article is sold, bartered, exchanged, or given, on a form to be issued in blank for that purpose by the Com-

missioner of Internal Revenue. Every person who shall accept any such order, and in pursuance thereof shall sell, barter, exchange, or give away any of the aforesaid drugs, shall preserve such order for a period of two years in such a way as to be readily accessible to inspection by any officer, agent, or employee of the Treasury Department duly authorized for that purpose, and the State, Territorial, District, municipal, and insular officials named in section five of this Act. Every person who shall give an order as herein provided to any other person for any of the aforesaid drugs shall, at or before the time of giving such order, make or cause to be made a duplicate thereof on a form to be issued in blank for that purpose by the Commissioner of Internal Revenue, and in case of the acceptance of such order, shall preserve such duplicate for said period of two years in such a way as to be readily accessible to inspection by the officers, agents, employees, and officials hereinbefore mentioned. Nothing contained in this section shall apply—

Orders to be preserved for 2 years. Inspection of same by officers, agents, etc.

Duplicate orders to be retained by purchaser.

Exemptions—Drugs dispensed to patient, in certain cases.

(*a*) To the dispensing or distribution of any of the aforesaid drugs to a patient by a physician, dentist, or veterinary surgeon registered under this Act in the course of his professional practice only: *Provided:* That such physician, dentist, or veterinary surgeon shall keep a record of all such drugs dispensed or distributed, showing the amount dispensed or distributed, the date, and the name and address of the patient to whom such drugs are dispensed or distributed, except such as may be dispensed or distributed to a patient upon whom such physician, dentist or veterinary surgeon shall personally attend; and such record shall be kept for a period of two years from the date of dispensing or distributing such drugs, subject to inspection, as provided in this Act.

Prescriptions—how to be issued and signed.

(*b*) To the sale, dispensing, or distribution of any of the aforesaid drugs by a dealer to a consumer under and in pursuance of a written prescription issued by a physician, dentist, or veterinary surgeon registered under this Act: *Provided, however*, That such prescription shall be dated as of the day on which signed and shall be signed by the physician, dentist, or veterinary surgeon who shall have issued the same: *And provided, further*, That such dealer shall preserve such prescription for a period of two years from the day on which such prescription is filled in such a way as to be readily accessible to inspection by the officers, agents, employees, and officials hereinbefore mentioned.

Prescriptions to be preserved for 2 years.

Exemption—drugs shipped to a foreign country.

(*c*) To the sale, exportation, shipment or delivery of any of the aforesaid drugs by any person within the United States or any Territory or the District of Columbia or any of the insular possessions of the United States to any person in any foreign country, regulating their entry in accordance with such regulations for importation thereof into such foreign country as are prescribed by said country, such regulations to be promulgated from time to time by the Secretary of State of the United States.

Sales, etc., to Department of Army, Navy, etc.

(*d*) To the sale, barter, exchange, or giving away of any of the aforesaid drugs to any officer of the United States Government or of any State, territorial, district, county, or municipal or insular government lawfully engaged in making purchases thereof for the various departments of the Army and Navy, the Public Health Service, and for Government, State, territorial district, county, or municipal or insular hospitals or prisons.

Blank forms to be provided

The Commissioner of Internal Revenue, with the approval of the Secretary of the Treasury, shall cause suitable forms to be prepared for the purposes above mentioned, and shall cause the same to be distributed to collectors of internal revenue for sale by them to those persons who shall have registered and paid the special tax as required by section one of this Act in their districts, respectively; and no collector shall sell any of such forms to any persons other than a person who has registered and paid the special tax as required by section one of this Act in his district. The price at which such forms shall be sold by said collectors shall be fixed by the Commissioner of Internal Revenue, with the approval of the Secretary of the Treasury, but shall not exceed the sum of $1 per hundred. Every collector shall keep an account of the number of such forms sold by him, the names of the purchasers, and the number of such forms sold to each of such purchasers. Whenever any collector shall sell any of such forms, he shall cause the name of the purchaser thereof to be plainly written or stamped thereon before delivering the same, and no person other than such purchaser shall use any of said forms bearing the name of such purchaser for the purpose of procuring any of the aforesaid drugs, or furnish any of the forms bearing the name of such purchaser to any person with intent thereby to procure the shipment or delivery of any of the aforesaid drugs. It shall be unlawful for any person to obtain by means of said order forms any of the aforesaid drugs for any purpose other than the use, sale, or distribution thereof by him in the conduct of a lawful business in said drugs or in the legitimate practice of his profession.

Sale of same.

Collector to keep account of sales.

Blanks to be sold only to persons who have registered.

Unlawful use of forms

The provisions of this Act shall apply to the United States, the District of Columbia, the Territory

of Alaska, the Territory of Hawaii, the insular possessions of the United States, and the Canal Zone. In Porto Rico and the Philippine Islands the administration of this Act, the collection of the said special tax, and the issuance of the order forms specified in section two shall be performed by the appropriate internal-revenue officers of those governments, and all revenues collected hereunder in Porto Rico and the Philippine Islands shall accrue intact to the general governments thereof, respectively. The courts of first instance in the Philippine Islands shall possess and exercise jurisdiction in all cases arising under this Act in said islands. The President is authorized and directed to issue such Executive orders as will carry into effect in the Canal Zone the intent and purpose of this Act by providing for the registration and the imposition of a special tax upon all persons in the Canal Zone who produce, import, compound, deal in, dispense, sell, distribute, or give away opium or coca leaves, their salts, derivatives, or preparations.

Porto Rico and Philippine Islands.

Canal Zone.

SECTION 3. That any person who shall be registered in any internal-revenue district under the provisions of section one of this Act, shall whenever required so to do by the collector of the district, render to the said collector a true and correct statement or return, verified by affidavit, setting forth the quantity of the aforesaid drugs received by him in said internal-revenue district during such period immediately preceding the demand of the collector, not exceeding three months, as the said collector may fix and determine; the names of the persons from whom the said drugs were received; the quantity in each instance received from each of such persons, and the date when received.

Collector may require sworn statement as to drugs received.

SECTION 4. That it shall be unlawful for any person who shall not have registered and paid the special tax as required by section one of this Act to send, ship, carry or deliver any of the aforesaid drugs from any State or Territory or the District of Columbia, or any insular possession of the United States, to any person in any other State or Territory or the District of Columbia or any insular possession of the United States: *Provided*, That nothing contained in this section shall apply to common carriers engaged in transporting the aforesaid drugs, or to any employee acting within the scope of his employment, of any person who shall have registered and paid the special tax as required by section one of this Act, or to any person who shall deliver any such drug which has been prescribed or dispensed by a physician, dentist, or veterinarian required to register under the terms of this Act, who has been employed to prescribe for the particular patient receiving such drug, or to any United States, State, county, municipal, District, Territorial, or insular officer or official acting within the scope of his official duties.

Shipment of drugs unlawful, except—

Common carriers and employees exempt.

SECTION 5. That the duplicate-order forms and the prescriptions required to be preserved under the provisions of section two of this Act, and the statements or returns filed in the office of the collector of the district, under the provisions of section three of this Act, shall be open to inspection by officers, agents, and employees of the Treasury Department duly authorized for that purpose; and such officials of any State or Territory, or of any organized municipality therein, or of the District of Columbia, or any insular possession of the United States, as shall be charged with the enforcement of any law or municipal ordinance regulating the sale, prescribing, dispensing, dealing in, or distribution of the aforesaid drugs. Each collector of internal revenue is hereby authorized to furnish, upon written request, certified copies of any of the said statements or returns filed in his office to any of such officials of any State or Territory or organized municipality therein, or the District of Columbia, or any insular possession of the United States, as shall be entitled to inspect the said statements or returns filed in the office of the said collector, upon the payment of a fee of $1 for each one hundred words or fraction thereof in the copy or copies so requested. Any person who shall disclose the information contained in the said statements or returns or in the said duplicate-order forms, except as herein expressly provided, and except for the purpose of enforcing the provisions of this Act, or for the purpose of enforcing any law of any State or Territory or the District of Columbia, or any insular possession of the United States, or ordinance of any organized municipality therein, regulating the sale, prescribing, dispensing, dealing in, or distribution of the aforesaid drugs, shall, on conviction, be fined or imprisoned as provided by section nine of this Act. And collectors of internal revenue are hereby authorized to furnish upon written request, to any person, a certified copy of the names of any or all persons who may be listed in their respective collection districts as special tax payers under the provisions of this Act, upon payment of a fee of $1 for each one hundred names or fraction thereof in the copy so requested.

Order forms, prescriptions, and statements filed to be open to inspection of officers.

Certified copies of statements and returns to be furnished by collectors.

Fees.

Penalty for disclosing information, except—

Certified list of names may be furnished.

SECTION 6. That the provisions of this Act shall not be construed to apply to the sale, distribution, giving away, dispensing, or possession of preparations and remedies which do not contain more than two grains of opium, or more than one-fourth of a grain of morphine, or more than one-eighth of a grain of heroin, or more than one grain of codeine, or any salt or derivative of any of them in one fluid ounce, or, if a solid or semisolid preparation, in one avoirdupois ounce; or

Act not to apply to certain preparations, etc.

to liniments, ointments, or other preparations which are prepared for external use only, except liniments, ointments, and other preparations which contain cocaine or any of its salts or alpha or beta eucaine or any of their salts or any synthetic substitute for them: *Provided*, That such remedies and preparations are sold, distributed, given away, dispensed, or possessed as medicines and not for the purpose of evading the intentions and provisions of this Act. The provisions of this Act shall not apply to decocainized coca leaves or preparations made therefrom, or to other preparations of coca leaves which do not contain cocaine.

Conditions imposed.

Decocainized coca leaves.

Certain revenue laws made applicable.

SECTION 7. That all laws relating to the assessment, collection, remission, and refund of internal-revenue taxes including section thirty-two hundred and twenty-nine of the Revised Statutes of the United States, so far as applicable to and not inconsistent with the provisions of this Act, are hereby extended and made applicable to the special taxes imposed by this Act.

Possession of drugs prohibited, except—

SECTION 8. That it shall be unlawful for any person not registered under the provisions of this Act, and who has not paid the special tax provided for by this Act, to have in his possession or under his control any of the aforesaid drugs; and such possession or control shall be presumptive evidence of a violation of this section, and also of a violation of the provisions of section one of this Act: *Provided*, That this section shall not apply to any employee of a registered person, or to a nurse under the supervision of a physician, dentist, or veterinary surgeon registered under this Act, having such possession or control by virtue of his employment or occupation and not on his own account; or to the possession of any of the aforesaid drugs which has or have been prescribed in good faith by a physician, dentist, or veterinary surgeon registered under this Act; or to any United States, State, county, municipal, District, Territorial, or insular officer or official who has possession of any said drugs, by reason of his official duties, or to a warehouseman holding possession for a person registered and who has paid the taxes under this Act; or to common carriers engaged in transporting such drugs: *Provided further*, That it shall not be necessary to negative any of the aforesaid exemptions in any complaint, information, indictment, or other writ or proceeding laid or brought under this Act; and the burden of proof of any such exemption shall be upon the defendant.

Certain persons exempt.

Burden of proof on defendant.

Penalties.

SECTION 9. That any person who violates or fails to comply with any of the requirements of this Act, shall, on conviction, be fined not more than $2,000 or be imprisoned not more than five years, or both, in the discretion of the court.

Appointment of agents, deputy collectors, etc.

SECTION 10. That the Commissioner of Internal Revenue, with the approval of the Secretary of the Treasury, is authorized to appoint such agents, deputy collectors, inspectors, chemists, assistant chemists, clerks, and messengers in the field and in the Bureau of Internal Revenue in the District of Columbia as may be necessary to enforce the provisions of this Act.

Appropriation.

SECTION 11. That the sum of $150,000, or so much thereof as may be necessary, be, and hereby is, appropriated, out of any moneys in the Treasury not otherwise appropriated, for the purpose of carrying into effect the provisions of this Act.

Act not to be construed as impairing or repealing certain acts.

SECTION 12. That nothing contained in this Act shall be construed to impair, alter, amend, or repeal any of the provisions of the Act of Congress approved June thirtieth, nineteen hundred and six, entitled "An Act for preventing the manufacture, sale, or transportation of adulterated or misbranded, or poisonous, or deleterious foods, drugs, medicines, and liquors, and for regulating traffic therein, and for other purposes," and any amendment thereof, or of the Act approved February ninth, nineteen hundred and nine, entitled "An Act to prohibit the importation and use of opium for other than medicinal purposes," and any amendment thereof.

REGULATIONS.

TREASURY DEPARTMENT,
OFFICE OF COMMISSIONER OF INTERNAL REVENUE,
Washington, D. C., May 4, 1916.

Under the authority conferred by section 1 of the act of December 17, 1914, the following regulations are issued, effective on and after June 1, 1916. All regulations and decisions in conflict herewith are hereby revoked to take effect on said date.

Registry and Payment of Special Tax.

ARTICLE 1. As required by section 1 of said act, every person, partnership, association, company, or corporation therein described, and not specifically exempt, must, on or before the first day of July, annually, register with the collector of the district, and at the time of such registration, and on or before the first day of July in each year, pay to such collector a special tax at the rate of $1 per annum.

Application for registration must be made and special tax paid for each separate place of business or branch where any of the drugs coming within the purview of the law are made, stored, dispensed, or distributed, and records of the distribution made of such drugs must be kept on file at each location. Every person conducting more than one class or place of business, or practicing more than one profession, or at more than one place, in which the narcotic drugs are sold, dispensed, or given away, must register and pay special tax for each profession and business separately, even though conducted at the same address, and separate records must be kept under each registration. Physicians, dentists, or veterinary surgeons prescribing any of the narcotic drugs described, or synthetic substitutes for cocaine[1] must register and pay special tax, even though having none of the drugs in their possession, as all narcotic prescriptions, except when calling for an exempt preparation or remedy, must bear the registry number of the person writing the prescription. Under section 2 of the act, any official of the Federal Government, or of a State, county, or municipal government using or prescribing in his official capacity, any of the drugs within the scope of the law, is exempt, officially, from registration and payment of special tax. Where such official is engaged in a private business or practice of a profession in which the drugs are sold, dispensed, given away, or prescribed, registration is required.

Only those persons lawfully entitled to deal in narcotic drugs, or holding a license issued by the State authorizing them to administer, dispense, or prescribe drugs, including narcotics, in the practice of their profession are eligible for registration. Failure to register and pay special tax on or before July 1, annually, or at the time of commencing a business in which narcotic drugs are dealt in, or in the practice of medicine, dentistry, or veterinary medicine or surgery, renders such person liable to a 50 per cent. penalty in addition to the special tax, and the penalties imposed by section 9 of the Act.

Application for registration and special tax stamp must be made for a partnership, a firm, or a corporation, and each individual member thereof who also is separately engaged in private business or a profession in which narcotic drugs are sold, dispensed, given away, distributed, or otherwise disposed of.

ARTICLE 2. Application for registry and special tax stamp must be made on or before commencement of business, and on or before July 1, annually, thereafter during continuance of such buisness, on a special form furnished by collectors upon request. (For list of collection districts and addresses of collectors, see Appendix.) These forms must bear the written signature of the person making application and in the case of a firm or corporation must be signed by a member or an officer duly authorized to so act. Collectors will refuse to issue a registration number and special tax stamp unless the application form is properly executed, with affidavit that the applicant is authorized by law to engage in the business or the profession specified, and for which registration is desired.

ARTICLE 3. Applications for registration will be carefully scrutinized by collectors to see that the requirements of articles 1 and 2 have been complied with. When in proper form, a registration number, commencing with No. 1 in each district for the first application and continuing in numerical order with subsequent applications, will be stamped or imprinted on the form. Collectors will refuse a registry number and special tax stamp until the application complies with the requirements of articles 1 and 2.

The registry number thus given is a permanent number for all renewal applications and will be entered on all blank orders issued to the applicant upon receipt of proper requisition therefor, as indicated in article 8. All applications for registration will, after issuance of registry number and payment of the special tax, be recorded alphabetically by classes in special record 10A, and filed according to registry numbers.

ARTICLE 4. Appropriate coupon stamps, denoting payment of the special tax under the act named, will be furnished collectors on requisition, and will be charged to them and accounted for as in the case of other special tax stamps.

Collectors, when issuing such stamps, will distinctly imprint thereon the registry number of the applicant to avoid the error being made of using the serial number of the stamp. A special tax stamp, when received by a person registered under this act, must immediately be conspicuously posted in his place of business or office. A special tax stamp can not be transferred from one collection district to another without first being submitted to the collector of internal revenue who issued same. Transfers must be made in accordance with instructions contained in T. D. 1637.

Sale and Disposal of Drugs.

ARTICLE 5. Where any of the drugs coming within the purview of the Act are to be sold or otherwise disposed of, the purchaser or receiver (unless specifically exempt under section 2 of the Act, see articles 1 and 10) will, prior to such purchase or receipt, prepare his order therefor in duplicate on forms furnished by collectors upon proper requisition, and forward the original to the registered person who will furnish the drugs, and retain the duplicate, both original and duplicate to be kept on file for a period of two years from

[1] A ruling of the Treasury Department of April 10, 1917 (see p. cvi) revokes the requirement that synthetic substitutes for cocaine are subject to the provisions of this Act.

the date of acceptance in such a manner as to be easily accessible to inspection by internal-revenue officers.

Court officers, in making sales of narcotic drugs and preparations under judicial proceedings, must prepare a complete inventory of such drugs and preparations, and require the purchaser, who must be registered, to make out a Government order form to the insolvent concern, the duplicate of this order to be retained by the purchaser. (See T. D. 2299.)

Section 2 of the Act provides: "It shall be unlawful for any person to obtain by means of said order forms any of the aforesaid drugs for any purpose other than the use, sale, or distribution thereof by him in the conduct of a lawful business in said drugs or in the legitimate practice of his profession." Every registered person should use precaution in furnishing an individual with such drugs to avoid violating the above-quoted section, and for his own protection a druggist should refuse to fill a prescription calling for an amount greater than would be prescribed in the course of legitimate practice only, to meet the immediate needs of the patient, or when the druggist has reason to believe or knows the drugs so obtained are to be used for other than medicinal purposes.

ARTICLE 6. Blanks of such order forms are printed on distinctive paper and are issued in tablets of ten blanks each, a charge of ten cents for each tablet (including originals and duplicates) being made therefor, as authorized by section 2 of the Act. The sales of these orders must be accounted for by collectors to whom furnished.

Blank orders can only be secured from the collector of the district by a registered person having legitimate use for same, and a requisition will not be accepted by the collector from any other person.

In addition to the special record 10A., provided for in article 3, collectors will keep an account of the number of order forms sold each registered person by filing all requisitions made on form 679, according to the registry numbers, stamping or writing thereon the date when filled.

ARTICLE 7. Requisitions accompanied by proper remittance for order blanks must be made on forms 679, which are only supplied to registered persons upon request made on the collector. The registry number imprinted on the special-tax stamp must be placed by the registered person on every requisition in the space provided therefor in the upper right-hand corner.

ARTICLE 8. Upon receipt of a requisition by the collector, the signature thereon must be compared with the one appearing on the application for registry, or if signed by an agent, with the power of attorney already on file (see article 9), before the blank orders are issued.

ARTICLE 9. The order forms must be prepared in duplicate and the duplicate must be retained by the maker. If accepted, the law requires all such orders (both the original and duplicate) to be retained on file for a period of two years, in such a manner as to be readily accessible to an inspecting officer. If an order form is not accepted, it should be returned to the maker with a letter of explanation. When received by the maker, the unaccepted order form and letter of explanation must be attached to the duplicate order. Where it is not possible for the official signing the application for registry to sign order forms, the signature of another person is permissible, provided a proper power of attorney granting such authority is filed with the collector. The firm, corporate, or business name alone will not be accepted, but the signature of the individual responsible for the issuance of the order forms must also appear thereon. In filling out order forms, the name of the preparation, the quantity in ounces if in liquid or solid form, or if in tablet, pill, ampule, or suppository form, the units or total thereof, and the name of the particular narcotic drug contained in such preparations, tablets, pills, ampules, or suppositories must be indicated thereon. Such forms must be used only to obtain narcotic drugs or preparations coming within the law. The forms are arranged to permit the preparation of the original and duplicate at one operation by use of a carbon sheet attached to each tablet of ten blanks, and an original order must not leave the possession of a person registered before a duplicate (carbon copy) is made. Failure to make a duplicate and keep it on file is a violation of section 2 of the law. When order forms are lost or destroyed through accident, a sworn statement to that effect must be filed with the collector. Improperly written or mutilated order forms are not to be destroyed, but must be kept on file (both the original and duplicate) with other records. Unused order forms are void at the expiration of the registry period and unless reregistration is granted, must be forwarded to the collector who issued same to be marked "canceled" and returned to the owner to be kept on file for two years. In case of change of ownership of a business the successor, if duly registered, may use order forms of predecessor after same have been returned to the collector and overprinted by him with the registry number of the successor.

Wholesale dealers or jobbers when unable to fill orders received from retail dealers must send their own purchase order on an official blank to the manufacturer with request that such drugs be shipped direct to the retail dealers. Such an order must give the name of the retail dealer and his registry number, and the number of his purchase order. Narcotic drugs may be invoiced to a wholesale dealer or jobber upon the request of a retail dealer in ordering directly from a wholesale dealer or jobber.

Where exempt officials and institutions order narcotic drugs from a wholesale dealer or jobber on their

official stationery, and the wholesale dealer or jobber, not having the goods in stock, directs a manufacturer to make the delivery direct to the exempt official or institution, it is necessary for the wholesale dealer or jobber to send to the manufacturer his own official narcotic order blank before the manufacturer executes for the account of the wholesale dealer or jobber the order from the exempt official or institution.

Dispensing of Drugs by Physicians, Dentists, Veterinary Surgeons, Hospitals, and Similar Institutions.

ARTICLE 10. Under the exempting provisions of section 2 of the act, no *written order* is required for the "dispensing or distribution of any of the aforesaid drugs to a patient by a physician, dentist, or veterinary surgeon, registered under this Act, in the course of his professional practice only." A record, however, is required to be kept of all such drugs dispensed, distributed or administered in his office and of all such drugs left with any person or patient to be taken in his absence. Only such drugs as are personally administered by a physician, dentist, or veterinary surgeon, when away from his office, are exempt from record. The record must show, first, the date when such drugs are dispensed or distributed; second, the kind and quantity dispensed or distributed in each case; and, third, the name and address of the patient to whom such drug was dispensed or distributed. (For method of preparing prescriptions, see article 12.)

Those persons engaged in a lawful profession who administer in their office practice minute quantities of narcotics in the form of solutions, pastes, or ointments, such as dentists, oculists, aurists, and other specialists, may keep a record of the date when a stock solution is made and the date when such stock solution is exhausted, and where pastes or ointments are used, a record of the date when the container is first opened and the date when its contents are exhausted, without keeping a record of the name and address of each patient. From the express language of the Act, a physician, dentist, or veterinary surgeon can register and dispense the narcotic drugs embraced therein in the course of his professional practice only. He can prescribe such drugs only when he has been employed to prescribe for the particular patient receiving such drugs, and upon whom he shall personally attend in the course of his professional practice only. A physician, dentist, or veterinary surgeon may not engage in the business of selling narcotic drugs unless he is a registered dealer, authorized by the State laws to engage in such business. Additional registration is not required, however, when narcotic drugs are sold to a patient upon whom a physician, dentist, or veterinary surgeon is in personal attendance. Under section 2, relating to prescriptions, and section 8, concerning unlawful possession, prescriptions are exempted, provided they are written in good faith by a physician, dentist or veterinary surgeon for a patient upon whom they are in personal attendance and the drugs are prescribed for medicinal purposes and not to evade the intentions and purposes of this Act. Prescriptions written upon request of any person calling for the narcotic drugs for any purpose other than medicinal use, or written for a person upon receipt, through the mails, of a symptom blank or descriptive sheet, are held not to come within the exemptions above noted.

Nurses are not permitted to register and pay special tax under the provisions of the law and can only have narcotic drugs in their possession or control when under the immediate direction of a physician, dentist, or veterinary surgeon, and then only by virtue of their employment, or occupation, and not on their own account. When nurses are discharged from a case and are no longer under the direction of a registered physician, dentist, or veterinary surgeon, the narcotic drugs coming into their possession through prescriptions written for the patient or left with nurses by a physician, dentist, or veterinary surgeon while in personal attendance upon the patient, should be surrendered to the physician, dentist, or veterinary surgeon, who will make proper entry on his records as to the kind and quantity received.

A veterinary surgeon, whose practice is limited by law to the use of narcotic drugs in the treatment of animals, can not, under the registration provided by this act, dispense, administer to, or prescribe for human beings any of the narcotic drugs under the limitation imposed upon the practice of his profession. Physicians who are authorized by law to dispense, administer, or prescribe narcotic drugs for the treatment of domestic animals are not required to register as veterinary surgeons. If, however, a physician or veterinary surgeon is licensed to practice both professions, he should register for each, and keep separate records covering the narcotic drugs in the practice of the respective professions.

Hospitals and similar institutions are required to register and pay special tax and keep accurate records of all narcotic drugs used therein. No special form of record is required, but it must enable an inspecting officer to quickly ascertain the quantity and kind of narcotic drugs used and show the names and addresses of patients to whom administered, and indicate the authority for such administration. The initials of a physician giving directions for the administration of a narcotic should appear on the chart of the patient, or separate prescriptions should be required by the pharmacist in charge of the drug room before the narcotics leave his possession. The record of narcotic drugs dispensed in a hospital or similar institution must balance approximately with the quantities received as indicated by the official order forms on file.

Prescriptions.

ARTICLE 11. Drugs dispensed or distributed under and in pursuance of a written prescription issued by a physician, dentist, or veterinary surgeon duly registered under the act must show the name and address of the patient, the date, the name and address of the physician, and his registry number. All prescriptions for such drugs not specifically exempt under section 6 of the Act, as defined in Treasury Decision 2309, must be dated and signed on the day when issued; must be preserved for a period of two years from the date indicated thereon; and must be readily accessible to the inspecting officer above referred to. A separate file of all such prescriptions must be kept by each dealer lawfully authorized to fill prescriptions. The refilling of a narcotic prescription is prohibited, except where such prescription calls for an exempt preparation or remedy prepared in accordance with the "U. S. P.," "N. F.," or other recognized or established formula usually carried in stock by a dealer and sold without a prescription (see T. D. 2309). Prescriptions can not be filled upon telephone orders. Prescriptions must be filled entirely at the time of presentation. Partial filling will not be permitted.

Drugs Dispensed by Dealers.

ARTICLE 12. Under the authority conferred by section 1 of the Act named, for the issuing of regulations necessary for carrying its provisions into effect, physicians, dentists, and veterinary surgeons writing any such prescriptions are required to sign their names in full on the same; to state therein their registry number and the location of their office, and the name and address of the person to whom such prescriptions are written, and the date. Druggists must refuse to fill any such prescription unless signed as herein required, nor should prescriptions for narcotic drugs be filled by any dealer, lawfully authorized to fill prescriptions, if he has reason to suspect that they were fraudulently issued or obtained. The dispensing or distribution of such drugs by lawfully authorized dealers, except on physician's original prescriptions or on original orders issued by persons who have duly registered, is in violation of the Act.

Refilling of prescriptions is prohibited unless such prescriptions call for exempted preparations or remedies, referred to in article 11. An accurate record of narcotic drugs entering into the composition of exempted preparations and remedies must be kept by all registered dealers and manufacturers, and must show:

1. The name of the preparation made;
2. The amount of narcotic used;
3. The date of manufacture; and
4. The amount of finished product,

and must be accessible to inspection by internal-revenue officers.

Supplying Narcotic Drugs and Preparations for Ocean-Bound Vessels and Vessels Engaged in Trade Between Points in the United States, Where No Registered Physician or Surgeon is Employed on Board Same.

As authorized by the Commissioner of Internal Revenue, with the approval of the Secretary of the Treasury, opium or coca leaves, their salts, derivatives, or preparations, coming within the scope of the act of Congress, may be purchased for stocking medicine chests and dispensaries maintained on board both ocean-bound vessels and vessels engaged in trade between ports of the United States (provided there is no registered physician employed on board the same) and vessels belonging to the various departments of the Government, upon the approval of commissioned medical officers and acting assistant surgeons of the United States Public Health Service. If a physician registered under the provisions of this act is employed on board a vessel, said medical supplies may be purchased only upon his order.

Such purchases can only be made on special order forms issued for that purpose, which may be procured from commissioned medical officers and acting assistant surgeons of the United States Public Health Service. The forms, both original and duplicate, must be kept on file with regular order forms for a period of two years from the date of filling.

Opium, coca leaves, or any compound, manufacture, salt, derivative, or preparation thereof, required by exempted officers in the discharge of their official duties, should be ordered on the official stationery of the department, bureau, or municipality under which such officers are employed, and these orders should be signed with the full name of the official, followed by his title and the department of the Federal, State, county, or municipal government under authority of which he acts.

When an exempt official prescribes, in his official capacity, any narcotic drugs covered by the law, his prescription should be written on an official prescription blank, if such blanks are provided by the department of which he is an official, and the name and address of the patient, and the name and title of the official as above indicated, inserted therein.

Dealers who supply narcotic drugs to exempt officials should require that such orders and prescriptions, be written on their official stationery, and that the title of the persons signing same is shown as indicated. Such orders and prescriptions should be filed with the regular narcotic orders and prescriptions required under the law.

ARTICLE 13. Every person, firm, or corporation making application for registration must, at the time of applying for such registration, prepare in duplicate an inventory of all narcotic drugs and preparations (other than those preparations and remedies specifically exempt under the provisions of section 6 of the Act, as defined in T. D. 2309) on hand at the date of application for registration. Where, however, a registered person, at some fixed date annually, takes a stock inventory, either at the close of the business fiscal year or of the calendar year, such inventory in duplicate, showing the quantity and names of the narcotic drugs and preparations on hand on the date next preceding the date of application for registration, may be filed in lieu of the annual inventory required at time of registration. The original inventory must be kept on file with previous inventories by the maker and the duplicate forwarded to the collector of internal revenue. No special form of inventory is required, but it must clearly set forth the name and quantity of each kind of narcotic drug, preparation, or remedy, and be verified by oath or affirmation executed in conformity with law. Collectors will refuse a registration number and special tax stamp to an applicant who fails to furnish annually, at or before the date of registration, a duplicate of such inventory. Narcotic drugs and preparations must at all times be segregated from the general stock of drugs and medicines, and should be kept under lock and key to prevent theft. Where losses by theft or in transit are reported, a sworn statement of the facts, a list of the lost narcotic drugs and preparations, and, in the case of theft, evidence that the local authorities were notified, must be filed immediately with the collector.

ARTICLE 14. Section 3 of the Act provides:

"That any person who shall register in any internal-revenue district under the provisions of section 1 of this act shall, whenever required to do so by the collector of the district, render to the said collector a true and correct statement or return, verified by affidavit, setting forth the quantity of the aforesaid drugs received by him in said internal-revenue district during such period immediately preceding the demand of the collector, not exceeding three months, as the said collector may fix and determine."

Under this authority a collector will require a sworn statement in any case where, from the number of order blanks obtained, or from the character of the business carried on, he has reason to suspect that any narcotic drugs are being procured, compounded, or disposed of by any person for illegal purposes, and in any other case in which he thinks it advisable to secure such information.

ARTICLE 15. The statements to be furnished in such cases must be made on a form supplied by the collector of internal revenue, and such statements must be sworn to.

ARTICLE 16. It will be the duty of collectors, deputy collectors, agents, and other officers to visit the premises of all persons, firms, or companies registered under the Act, or where they have reason to believe drugs of the character defined in the Act are stored, and to see that all requirements of the law and the regulations issued under authority thereof are strictly complied with. Under authority of sections 2 and 5, they will, when necessary, inspect and check such records, orders, prescriptions, statements, or returns made or received, and at once report to the Commissioner of Internal Revenue any violation of the law discovered by them. Where suspected narcotic drugs or preparations are found in the possession of unregistered persons, samples of same should be immediately procured, and, after being properly labeled and identified as required by Treasury Decision 1587, forwarded to the Chemistry Division, office of Commissioner of Internal Revenue, for analysis.

ARTICLE 17. Officers will conduct their investigations in such manner as to not annoy or interfere unnecessarily with the business of persons preparing or handling the aforementioned drugs. Officers must observe this requirement, but they should make their inspection thorough that the law and regulations may be strictly enforced; and it is the duty of every registered person to produce all records required under the law and afford necessary facilities for investigation upon demand of inspecting officers.

W. H. OSBORN,
Commissioner of Internal Revenue.

Approved May 4, 1916.

BYRON R. NEWTON,
Acting Secretary.

TREASURY DEPARTMENT,
OFFICE OF COMMISSIONER OF INTERNAL REVENUE,
Washington, D. C., April 10, 1917.

To collectors of internal revenue and others concerned:

The ruling contained in T. D. 2194 of April 26, 1915, holding synthetic substitutes subject to the provisions of the act of December 17, 1914, and requiring manufacturers of, dealers in, and physicians prescribing any such substitutes as therein defined to register and otherwise conform to the Harrison Narcotic Law and the regulations issued thereunder is hereby revoked, to take effect this date.

W. H. OSBORN,
Commissioner of Internal Revenue.

Approved:
W. G. MCADOO,
Secretary of the Treasury.

All persons exempt from registration under the above decision are requested to notify this office so that the name may be stricken from the records.

INDEX

Food and Drugs Act and Harrison Narcotic Act

The following index covers the Food and Drugs Act, Rules and Regulations for enforcing it, Circulars 19 and 21, Office of the Secretary of Agriculture, and abstracts of Food Inspection Decisions to and including decision No. 170; also the Harrison Narcotic Act and its Regulations. Cir. means Circular, Office of the Secretary; F. I. D. means Food Inspection Decision. It should be remembered that Food Inspection Decisions 1 to 39, inclusive, were adopted for the regulation of imported foods before the passage of the Food and Drugs Act.

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THE DISPENSATORY

OF

THE UNITED STATES

PART I

THE United States Dispensatory may very properly be considered as a commentary upon the United States and British Pharmacopœias, while such preparations of the German Pharmacopœia and French Codex as are used generally in the United States are also commented upon. Part I of the present volume contains the discussion of all the remedies recognized by either of the two Pharmacopœias used by English speaking people. In Part II the National Formulary and non-official drugs are treated, as heretofore, by themselves; the type is smaller than that used for Pharmacopœial substances, it being deemed judicious to adhere to a plan which has given so much satisfaction in the previous editions. In Part III are considered the Tests and Test Solutions of the two Pharmacopœias, Weights and Measures, the Art of Prescribing Medicines, an abstract of the National Formulary IV, and cognate miscellaneous matters.

There can be no question as to the superiority of the alphabetical arrangement of drugs in a book of reference of an encyclopedic character. Their scientific classification belongs to works which treat of them rather in their relations than their essential properties; and different systems have been adopted, according to the set of relations towards which the mind of the author has been especially directed. Thus, the naturalist classifies them according to the affinities of the several objects in nature from which they are derived; the chemist, according to their composition; the practitioner of medicine, according to their effects upon the system in a state of health and disease.

ACACIA. U. S. (Br.)

ACACIA Acac. [Gum Arabic]

(ą-cā'cĭ-ą)

"The dried gummy exudation of *Acacia Senegal* Willdenow, and of other African species of *Acacia* (Fam. *Leguminosæ*)." *U. S.* "A gummy exudation from the stem and branches of Acacia Senegal, *Willd.*, and of other species of Acacia, *Willd.*" *Br.*

Acaciæ Gummi, *Br.*; Gummi Africanum; Gummi Mimosæ; Gum Acacia; Galam Gum; Gomme Arabique Vraie, *Fr.*; Gummi Arabicum, *P. G.*; Arabisches Gummi, *G.*; Gomma Arabica, Gomma del Cordofan, *It.*; Goma Arabiga, *Sp.*; Samagh Arabee, *Arab.*

The name *Acacia* was employed by the ancient Greeks to designate the gum tree of Egypt, and has been appropriately applied to the genus in which that plant is included.

The most important of the gum-yielding Acacias is the official *A. Senegal* Willd. This is a small tree rarely exceeding a height of 6 m., with a grayish bark, the inner layers of which are strongly fibrous, bipinnate leaves, dense spikes of small yellow flowers longer than the leaves, and broad pods containing 5 or 6 seeds. It forms large forests in Western Africa, north of the river Senegal, and is abundant in Eastern Africa, Kordofan, and Southern Nubia. It is known by the natives of Senegambia as *Verek* and of Kordofan as *Hashab*.

Nearly all species of Acacia growing in Africa yield a gum. The commercial *Somali gum*, which is usually of fair quality, is yielded by *A. glaucophylla* Steud. and *A. abyssinica* Hochst., shrubs growing in Abyssinia and the Somali country. The following species yield a gum having a brownish or reddish color (called *Amrad Gums*), and hence are less valuable, viz., *A. arabica* Willd., *A. stenocarpa* Hochst., *A. Seyal* Del. and *A. Ehrenbergiana* Hayne. Inferior gums are also yielded by the following: *A. horrida* Willd., which furnishes the so-called *Cape gum* and is distinguished by being very brittle and yielding a less adhesive mucilage. *Talca* or *Sennarr gum* is derived from *A. Fistula* Schweinf. This gum has a greenish tinge and yields a ropy mucilage. Australian

gum has a reddish color, said to be due to the presence of tannin. This gum is also spoken of as *Wattle gum* or *Australian gum,* and is derived from the *Golden Wattle* (*A. pycnantha* Benth.), a shrub growing in New South Wales, Victoria and Southern Australia. For commercial history of the several varieties of gum arabic, see *U. S. D.,* 19th edition, p. 2. For further information in regard to gum bearing trees of Northern Africa, see *P. J.,* Aug., 1873; *C. R. A. S.,* t. lxxix, p. 1175; *Toxicologie Africaine,* vol. ii.

The bark and unripe fruit of the acacia contain both tannic and gallic acids. The dried juice of the pod was used by the ancient Greeks; and an extract is still sold in the bazaars of India under the name of *Akakia.* This extract is heavy, hard, of an agreeable odor, varying in color from greenish to dark-reddish, or, when seen in bulk, blackish. It has a sweet, astringent taste, and yields a mucilaginous infusion. A similar preparation, *acacia nostras,* has been prepared in Europe by expression and inspissation from the unripe fruit of *Prunus spinosa,* or wild plum tree.

The gum of the acacias exudes spontaneously from the bark, and hardens on exposure; but incisions are sometimes made in order to facilitate the exudation. The gum is said also to be found immediately under the bark, where it is sometimes collected in regular cavities. It is formed within the plant by metamorphosis of the cells of the inner bark. The tissues involved are chiefly those of the sieve and the cambiform cells. While to some extent it is a natural change, yet it is usually looked upon as being in part a pathological production, as gummosus develops more largely upon the wounding of the trees. The attack of the Acacia plants by various parasites is held by some to account for the enormous production of gums in these plants. The investigations of Smith tends to show that all vegetable gums are of bacterial origin and that the differences in the several gums are due to the differences in the nature of the bacteria producing them. (*Proc. Linn. Soc. N. S. Wales,* 1904, p. 217.) For further discussion on the origin of acacia gum see Tschirch, "*Handbuch der Pharmakognosie.*"

The trees are not tapped for gum until they are about six years old. The annual yield varies very greatly, being from 188 to 2856 Gm. in young trees and from 379 to 6754 Gm. in large trees. The average annual yield of gum from young trees is about 900 Gm. and from old trees over 2 kilos. (Edie, 4th Report of the *Wellcome Tropical Research Laboratory.*)

It is stated by Jackson that, in Morocco, the greatest product is obtained in the driest and hottest weather, and from the most sickly trees. An elevated temperature appears to be essential, for in cooler climates, though the tree may flourish, it yields no gum. It is probable that some species of acacia yield finer gum than others, but it is also certain that the same tree will often yield some gum of the finest quality in regular tears or globular masses, and some irregular shaped, dark colored fragments of inferior value. Thus, from the same tree it will exude frothy or thick, and clear or dark colored, and will assume, upon hardening, different shapes and sizes; so that the pieces, when collected, require to be assorted before being delivered into commerce. This sorting is usually done on its arrival in European ports and only the selected or picked gum corresponding to the U. S. P. description should be used.

Commercial History and Varieties.—There are two principal commercial varieties of gum arabic: 1. The *Khordofan, Turkey* or *Arabian* Gum and 2. The *Senegal* or *West African* Gum, both of these being derived from *A. Senegal.* The former of these has the finer commercial qualities, being nearly white or faint yellowish-white and yielding a more or less transparent viscid mucilage.

KHORDOFAN, TURKEY, OR ARABIAN GUM.—This variety was formerly the only kind designated as gum arabic and entered commerce almost exclusively through Egypt, being collected in Upper Egypt, Nubia, Khordofan, Darfur, and other regions of the Upper Nile, and carried to Alexandria, from whence it passed directly into the world's commerce or entered the latter through Smyrna, Trieste, or some other Mediterranean entrepôt. At one time the more or less colored varieties were known as *gum gedda,* while the white and fine drug was known as *gum turic,* names derived from Jiddah and Tor, Red Sea ports, through which the varieties were supposed to be respectively exported. Three chief commercial varieties are recognized. (*a*) *Hashabi* or *Khordofan gum,* the finest of these varieties, was collected in the country westward of the White Nile; formerly it constituted the bulk of the superior gum arabic of commerce. (*b*) *Sennari gum* was an inferior variety, yielding a mucilage which turned sour more quickly than that produced by Khordofan gum. It was collected in a country eastward of the White Nile, and in the region of the Blue Nile. (*c*) *Ghezzirah* or *Gezireh gum* is obtained from Ghezzirah and neighboring countries and sent to Trieste. It has much of the same appearance as the official Khordofan gum.

Formerly, Khordofan gum was collected in all parts of the Soudan and Upper Egypt, and forwarded on the backs of camels to Assouan, at the head of the Nile navigation, often being many months en route. The closure of the Soudan by the Mahdi caused Egyptian gum almost to disappear from commerce, but the reopening of the region by the British government has resulted in large quantities of the gum being brought by rail to Assouan, whence after being sorted into three varieties it is put in palm-leaf sacks and sent down the Nile. The finest Egyptian gum consists of large roundish or smaller more or less irregular fragments, transparent but usually rendered opaque upon

the surface by innumerable minute fissures. The inferior gum varies from yellow to dark-reddish as the quality deteriorates, and often contains impurities. H. C. Wood found that the gum arabic comes into Assouan in sacks or mats which are simply piled in rectangular roofless spaces surrounded by walls about ten feet high, made of dry mud. He was informed by the traders that the gum is gathered during the months of January, February and March by collectors having vested rights in a certain portion of the forests. Long incisions are made vertically through the bark and the exuding gum allowed to harden, the trees not being injured by the process, the collections going on from year to year. *Gedda gum,* sometimes spoken of as an Egyptian gum, enters commerce through Geddah, or Jiddah, on the Arabian side of the Red Sea. It seems to be the same as *Mecca* or *El Wisch* or *Aden gums,* which are sometimes spoken of as Egyptian gums, but are probably produced in the triangular peninsula which forms the eastern extremity of Africa.

Suakin gum, Talca or *Talha gum,* from *A. stenocarpa* and *A. Seyal,* is exceedingly brittle, and usually semi-pulverulent. It is a mixture of nearly colorless and brownish gums, is exported at Alexandria, and is sometimes termed *gum savakin.*

SENEGAL OR WEST AFRICAN GUM.—This variety is sometimes incorrectly referred to as synonymous with the official gum. It is derived from *A. Senegal* and other species of *Acacia* growing in the Soudan and Senegal. It yields a good adhesive mucilage and is valuable for technical purposes. Some of the best qualities of Senegal gum are also adapted for certain pharmaceutical uses. There are a number of different commercial varieties named from their geographical sources. It was introduced into Europe by the Dutch. The French afterwards planted a colony on the western coast of Africa, and took possession of the trade. St. Louis, at the mouth of the Senegal, and Portendic, considerably farther north, are the ports in which the commerce in gum chiefly centers. Immense forests exist in the interior, containing many species of the genus *Acacia,* all of which are said to yield gum, as is affirmed do also various trees belonging to other genera. The chief harvest begins in October and ends in December, although gum is also collected in March. The dry winds, which prevail after the rainy season, cause the bark to crack; the juice flows out and hardens in masses, which are often as large as a pigeon's egg, and sometimes as that of an ostrich. It is affirmed that the exudation is also largely caused by a parasitic plant, *Loranthus Acaciæ* Zucc., the gummy exudation freely oozing out at the point where the parasite penetrates the bark. (*Ph. Centralh.,* Aug., 1895.) Senegal gum is usually in roundish or oval unbroken pieces, or in straight or curled cylindrical pieces of various sizes, in the finest grades whitish or colorless, but generally yellowish, reddish, or brownish red. The pieces are larger than those of Turkey gum, less brittle and pulverizable, and breaking with a more conchoidal fracture. In recent years the commercial supply of gum Senegal has been a variable one. In 1911 the gum was extremely scarce, there was practically none on the market, owing to a failure of the crop.

INDIA GUM.—*Persian gum,* which is said to be sent from Persia to Assouan to be packed as genuine gum arabic, can be distinguished from the latter, which it closely resembles, by its not dissolving in water. Sickenberger thinks that it is the product of *Prunus bokharensis* or of *P. puddum. India gum* is not produced in India, but reaches Bombay from Aden and the Red Sea ports, and is almost certainly the product of the Soudan, being therefore identical with Egyptian gum. It occurs in India in two forms, "*Maklai,*" in large round tears or vermicular pieces, white, yellow or reddish, and much fissured; and "*Maswai,*" in fragments and vermicular pieces similar in color and fissuring to the other variety. It is often crudely adulterated before reaching Europe, especially with *Bassora gum,* distinguished by its insolubility in water. Of recent years various India gums have come into commerce in increasing quantities as substitutes for true gum arabic. India gum is brought to this country partly from Calcutta or Bombay, and partly by way of England. It usually comes in large cases. We have seen a parcel said to have come directly from the Red Sea, enclosed in large sacks made of a kind of matting, and bearing a close resemblance to the gum from Calcutta, except that it was more impure, and contained numerous large, irregular, very brittle masses, not much less than the fist in size. The term India gum should not be confused with *India gum Tragacanth,* which is called simply by the name India gum in the confectionery and ice cream trades where it is used as a filler and to give bulk and firmness; nor with *Indian gum.* (See *Gummi Indicum.*)

SUBSTITUTES FOR GUM ARABIC.—According to A. Mander, the East India gums appearing in the London market are:

Amrad, Amra or *Oomra Gum.*—A name applied to various East Indian gums having a reddish color and being in more or less irregular stalactitic pieces. (See *U. S. D.,* 19th ed., p. 4.)

Ghatti Gum.—A pale gum consisting of rounded or vermiform pieces varying in size, clear internally, but dull and roughened on the surface, apparently caused by shrinkage in drying; from brownish-yellow to perfectly colorless and transparent. According to the *Pharmacographia Indica,* this gum is readily distinguished from all others by its dull white, roughened surface and glassy fracture free from cracks; it possesses about double the viscosity of gum arabic.

Ghatti gum is said to be obtained from *Anogeissus latifolia* Wallich in enormous quantities,

to be much used in India, and to be exported from Bombay in the pure state.

Small quantities of gum are produced in India by a large number of trees often having no botanical relations with the Acacias. For an account of these gums see *Pharmacographia Indica,* vol. i.

Under the names of *Brazilian gum, Para gum,* and *gum angico,* large quantities of a gum occurring in large dark-amber or dark-brown glossy drops, soluble in water, are occasionally found in commerce. It is said to be the product of *Acacia angico.* Its mucilage is very adhesive, but usually too dark in color for pharmaceutical purposes. It must be distinguished from the gum resin often known as *Brazilian gum,* which is said to be obtained from *Hymenæa courbaril,* and is used in making varnishes.

Chagual or *Maguey gum* of Chili occurs in hollow cylindrical pieces from 0.2 to 1.5 cm. in thickness, occasionally having the form of stalactites or irregular tubers. On their inner surface they are longitudinally streaked, while their outer surface is usually numerously fissured, the fissures penetrating deeply toward the interior. In the absence of these, the pieces are of glassy brightness, transparent, and of very dense structure internally. The color varies from colorless, through yellowish and brownish to a tolerably deep brown, isolated pieces being almost black. According to the experiments made by Guehm, the commercial drug is scarcely fitted for technical use as a gum, but the clear pieces when made into a concentrated mucilage by prolonged heating answer the purposes of the calico printer well. *Puya chilensis, P. lanuginosa,* and *P. lanata* are commonly said to be the sources of the gum, though the researches of Hartwich make this uncertain. The exudation is asserted to be the result of the bite of a caterpillar, *Kastina elegans.* (*Zeit. Oest. Apoth. Ver.,* Aug. 1, 1896.)

Specimens of gum arabic are sometimes found in commerce, which are soluble in water with difficulty. According to Köchlin, if ten parts of such gum, fifty parts of water, and three parts of a 12 per cent. solution of hydrogen dioxide be heated together for two or three hours, the gum is rendered easily soluble. (*Nat. Drug.,* 1894, 176.) Related to the acacia gums are *wood gum,* from the wood of foliage trees, yielding xylose on hydrolysis; *cherry gum,* the gum of cherry and almond trees, yielding β-arabinose on hydrolysis; *peach gum,* from the peach tree, yielding arabinose and galactose on hydrolysis; *barley gum,* obtained in the nitrogen-free extractive material of cereals, yielding galactose and xylose. Martina examined twenty-seven varieties of gum, and the composition of some of the principal ones is given in the table below.

Thos. Maben gives the following method of testing mucilage obtained from various gums sold for gum arabic as the best that he has been able to devise after much experimentation. Two or three drops of the mucilage prepared from the gum are placed on a glass or porcelain slab, and one or two drops of the following reagents added; these are then stirred together with a glass rod and the results compared. In the case of borax, acacia mucilage at once agglutinates or hardens into a gummy mass, similarly with basic lead acetate and ferric chloride, while it gelatinizes or forms a softer mass with potassium silicate. Similar reactions are given by the Senegal gums, the Indian Amrad gums, white Barbary, white and brown Cape, and Geddah gums. Barbary brown and Amrad give a jelly only with borax, otherwise they react as acacia. Australian gum agglutinates with borax, but only gelatinizes with basic lead acetate, and has no reaction with ferric chloride and potassium silicate. Brazilian gum has no reaction with potassium silicate, but gelatinizes with borax and ferric chloride and slightly with basic lead acetate. Ghatti gum gelatinizes with all four reagents, but in a slight degree only with potassium silicate. Oomra gum reacts similarly to acacia, except that it is entirely unaffected by basic lead acetate, and forms a softer jelly with ferric chloride. There are, of course, shades of difference in the various reactions which cannot be indicated by these terms, but, generally speaking, a fair idea is given of the nature of the gum. (*P. J.,* March 1, 1890, 717.)

Origin.	Source.	Ash.	Lime.	Mucic Acid.	Galactose.	Furfurol.	Penta-glucose.	Total Glucoses.
Gum Arabic	Arabia	3.60	1.84	22.98	30.66	13.57	27.14	58.3
	Senegal	3.25	0.90	19.72	26.29	12.97	25.94	57.58
	Gezireh	2.75	0.94	12.42	17.89	19.32	36.62	60.66
	Aden	3.70	1.33	18.68	24.90	15.26	30.52	56.90
	Mogador	3.50	0.78	18.10	24.13	13.90	27.80	50.31
	N. Holland	0.50	....	45.82	61.09	10.85	21.70	43.75
	Indies	4.16	0.97	14.75	19.66	17.98	35.96	56.52
Mimosa nilotica	Egypt	2.80	1.36	5.91	7.88	21.44	42.88	49.13
Acacia dealbata	Van Diémen	0.65	....	39.09	52.12	8.89	17.68	73.93
Acacia angico	Brazil	2.89	....	1.23	1.63	40.35	80.70	74.22
Gum of Apricot	.....	4.20	1.85	9.16	12.21	17.27	34.52	43.48
Gum of Plum	.....	2.15	1.07	5.19	6.92	31.03	62.06	66.47
Gum of Cherry	.....	2.50	1.00	6.13	8.17	23.07	46.14	56.38

General Properties.—Gum arabic is "In ovoid, more or less spheroidal tears, or in broken, angular fragments from 2 to 30 mm. in diameter, varying from white or yellowish-white to light amber-colored; translucent; very

brittle; fractured surface glass-like, sometimes iridescent; nearly inodorous; taste insipid, mucilaginous. Insoluble in alcohol; slowly and almost completely soluble in twice its weight of water, forming a mucilaginous liquid, which has a slight, characteristic odor and is acid to litmus. When either 0.1 mil of basic lead acetate T.S., or 0.1 mil of a concentrated solution of sodium borate, or 0.1 mil of ferric chloride T.S. is added to 10 mils of a 10 per cent. aqueous solution of Acacia, a gelatinous precipitate is produced. The precipitate produced with ferric chloride T.S. is neither black nor brownish-black (*tannin*). The powder is whitish, with few or no starch grains or fragments of vegetable tissues. Not more than 1 per cent. of powdered Acacia is insoluble in water (*plant tissues, sand, or dirt*). Acacia yields not more than 4 per cent. of ash, and the powder contains not more than 15 per cent. of moisture." *U. S.*

"When dissolved in an equal weight of *water*, the solution is not glairy, and after admixture with more *water*, yields no gummy deposit on standing. An aqueous solution (1 in 10) exhibits slight lævorotation (absence of dextrin, certain sugars, etc.). 10 millilitres of the same solution are not precipitated by *solution of lead acetate;* are not, after previous boiling and cooling, colored blue or brown by 0.1 millilitre of *N/10 solution of iodine* (absence of starch and dextrin), or bluish-black by *T. Sol. of ferric chloride* (absence of tannin). Ash not more than 4 per cent." *Br.*

The commercial gum arabic contains 17 per cent. of water and 3 per cent. of ash, consisting almost entirely of calcium, potassium and magnesium carbonates.

The gum dissolves slowly, at ordinary temperature, in twice its weight of water, forming a thick glutinous liquid of distinctly acid reaction. It is insoluble in alcohol, ether, and the oils. One hundred parts of 22 per cent. alcohol, by volume, dissolve 57 parts of gum, diluted alcohol containing 40 per cent. alcohol takes up 10 parts, and 50 per cent. alcohol only 4 parts (Flückiger). On adding hydrochloric acid to the aqueous solution and precipitating with alcohol, a colorless amorphous substance is obtained. This is *arabic acid.* On hydrolysis, it yields *galactose, arabinose,* and a pentabiose named *arabinon.* The *arabin* (or arabic acid) may also be prepared by placing a solution of gum, acidulated with hydrochloric acid, on a dialyzer, when calcium chloride will diffuse out, leaving behind solution of arabin.

Arabic acid dried at 100° C. (212° F.) has the composition $2C_5H_{10}O_5 + H_2O$; the water separates when it unites with bases. It has a decided tendency to form acid salts. Concentrated nitric acid forms with it nitro-compounds; diluted nitric acid, on the other hand, gives rise to mucic and saccharic acids, together with oxalic and a little tartaric acid. Diluted sulphuric acid on prolonged boiling gives rise to *arabinose,* or *arabin sugar* (*pectinose,* or *pectin sugar*), $C_5H_{10}O_5$, which reduces alkaline copper solution and turns the plane of polarization 121° to the right. Kiliani (*Ber. d. Chem. Ges.,* 1887, 339) first established the formula as given above, and it is now recognized as belonging to the class of *pentoses.* They are not fermentable, and, on prolonged boiling with diluted hydrochloric acid, lose the elements of water and yield *furfurol,* $C_5H_4O_2$. Neutral lead acetate does not precipitate an aqueous solution of gum arabic, but the basic acetate forms, even in a very diluted solution, a precipitate.

Prolonged heating of the dry gum causes it to change readily into *metarabic* (*metagummic*) *acid,* which is identical with the *cerasin* found in the beet and in cherry gum. Sulphuric acid will also change arabic into metarabic acid. 25 Gm. pure gum arabic are covered with 50 mils strong alcohol, 10 mils water, and 5 mils sulphuric acid, and allowed to stand twenty-four hours. On pouring off the fluid, and washing the residue with alcohol and with water, metarabic acid remains behind as a voluminous mass, which dries to a white, tasteless, and odorless powder of acid reaction. (Graeger, *Jahresbericht der Chem.,* 1872, 781.) The *metapectic acid* which is prepared by Scheibler from the sugar beet is identical with metarabic acid.

The principle separated by cold water from the soluble arabin proves to be the same as metarabic (metagummic) acid prepared direct from the pure gum arabic by heating, or by the action of sulphuric acid. It is also identical with gum extracted from the sugar beet by Scheibler. In the normal and sound beet this gum is insoluble in water, and merely swells up like metarabic acid, while in altered beets there is found a portion (arabin) soluble in water. (Scheibler, *Ber. d. Chem. Ges.,* 1873, p. 612.)

The similarity of the reactions and composition of *arabinose* and *galactose* (from sugar of milk by inversion) led Kiliani to assert the identity of these two varieties of sugar, but later studies by himself, Claesson, and Scheibler have shown that they are distinct. Thus, galactose is fermentable, while arabinose is not; galactose yields mucic acid when oxidized with nitric acid, and dulcite when reduced with sodium amalgam, while arabinose does not yield either; the fusing point of the crystallized galactose is given at 142° to 144° C. (287.6°-291.2° F.), while that of arabinose is 160° C. (320° F.); galactose yields with phenylhydrazin a light yellow compound, fusing at 170° to 171° C. (338°–339.8° F.), while arabinose forms a brownish-yellow compound, fusing at 157° to 158° C. (314.6°–316.4° F.). (Scheibler, *Ber. d. Chem. Ges.,* 17, 1731.) Arabinose is said to be obtainable only from those varieties of gum arabic that yield no mucic acid when treated with nitric acid. (Claesson, *Ber. d. Chem. Ges.,* 14, 1271.)

Gum arabic undergoes no change by age, when kept in a dry place. Its concentrated aqueous solution remains for a considerable time unaltered, but ultimately becomes sour,

from the production of acetic acid. The disposition to sour is increased by employing hot water in making the solution. The tendency of a weak solution to become moldy is said to be obviated by adding a few drops of sulphuric acid, and decanting from the calcium sulphate deposited. (*A. J. P.*, 1872, 353.) Solution of gum arabic does not ferment upon the addition of yeast, saliva, or gastric juice; the addition of chalk and cheese, however, starts a fermentation which gives rise to lactic acid and alcohol, but not to mannite or glycerin. The addition of a solution of gum to an acidified albumin solution causes a precipitate, which disappears on further addition of gum, but the solution will then curdle and become flocculent on application of heat. Gum may be distinguished from dextrin by the following tests: 1. Gum contains no dextroglucose, which, however, is present in dextrin, and may be recognized by the copper test. (See *Alkaline Cupric Tartrate Volumetric Solution*, Part III.) 2. Gum contains a lime compound; hence its solution is rendered milky by oxalic acid, while a solution of dextrin remains almost clear. 3. Gum gives a slimy, yellow deposit when its solution is mixed with a neutral ferric salt.

J. Henry Schroeder examined twelve specimens of powdered acacia, and states that dextrin is not frequently used as an adulterant, and that if in using the alkaline cupric tartrate test the heat be prolonged during twenty minutes, a well defined reduction was produced even when pure Senegal gum was used. (*A. J. P.*, 1897, 195.) R. G. Shoults (*A. J. P.*, 1900, 267) supplemented the conclusions of Schroeder and proposed to use the difference in rotatory power of acacia and dextrin as a test. He found a solution of pure acacia to have a lævorotatory power of $-18°$, while one of dextrin was dextrorotatory varying to the extent of from $+120°$ to $+138°$. This method of testing the presence of dextrin may be replaced by the simpler one with the microscope. (See also Kebler's paper, *Am. Drug.*, 1901, 343.) The following test is given in the *Ph. Post*, 1894, 563. Add 3 mils of a solution consisting of 15 drops of solution of ferric chloride, 15 drops of a saturated solution of potassium ferrocyanide, 5 drops of HCl (1–125), and 60 mils of water to a 20 per cent. solution of the gum. If the gum arabic is pure, it will remain a clear yellow for from eight to ten hours. If there is dextrin present, the color changes to blue.

The properties above enumerated belong to gum arabic generally. There are, however, varieties with differences which deserve notice. 1. *Gum that is transparent and readily soluble.* This constitutes by far the greater portion of the commercial varieties distinguished by the names of Turkey and Senegal gum. It is characterized by its transparency, ready solubility, and the comparatively slight degree of thickness and viscidity of its solution. Under this head may be included the *gomme blanche fendillée* of Guibourt. It is distinguished by the whiteness and deficient transparency of the pieces, attributable to the minute cracks or fissures with which they abound, and which render them very brittle and easily pulverizable. This peculiar structure is generally ascribed to the influence of solar heat and light, but is conjectured by Hayne to arise from the exudation of the juice in the frothy state noticed by Ehrenberg. Though the unbroken pieces are somewhat opaque, each minute fragment is perfectly transparent and homogeneous. This variety, in consequence of its prompt and entire solubility, is usually preferred for medicinal use and for most purposes in pharmacy. 2. *Gum less transparent and less soluble.* Guibourt has proposed for portions of this gum the name of *gomme pelliculée*, from the circumstance that the masses are always apparently covered, on some part of their surface, by a yellowish opaque pellicle. Other portions of it have a mammillary appearance on the surface. It is less transparent than the former variety, is less freely and completely dissolved by water, and forms a more viscid solution. It dissolves with difficulty in the mouth, and adheres tenaciously to the teeth. It is found in all the commercial varieties of gum, but least in that from Egypt. Its peculiarities have been ascribed to variable proportions of *bassorin* or *cerasin* associated with the soluble *arabin*. Between these two varieties there are insensible gradations, so that it is not always easy to classify specimens.

E. Bourquelot (*J. P. C.*, 1904 [6], 19, 473, 474) states that acacia contains an active oxidizing ferment which renders it unsuitable for use in many pharmaceutical preparations, and that, notwithstanding the wide use of acacia as an excipient, it is possible that certain active ingredients may become altered in its presence. Nor is acacia the only gum which contains a ferment; myrrh, frankincense and bdellium also contain an oxydase. Among the substances stated as being incompatible with acacia are pyrogallol, morphine, vanillin, ordinary phenol, cresylol, ortho- and meta-xylol, thymol, carvol, *a*- and *b*-naphthol, pyrocatechol, guaiacol, phenols, lysol, cresols, acetylguaiacol, veratrol, creosol, eugenol, acetyleugenol, methylaniline, ethylaniline, paratoluidine, crude aniline, xylidine, *a*-naphthylamine, pyramidon apomorphine, eserine, adrenaline, isobarbaloin, caffeotannic acid, gallic acid and tannin. Paraxylenol, hydroquinone, resorcinol, anisol and phenetol do not appear to be affected. Nor is the action confined to chemical substances; acacia is incompatible with the opium and Calabar bean products, suprarenal extract, aloetic preparations, and all substances flavored with vanillin, tannin-containing extracts, such as those of rhatany, catechu, and rhubarb; fluidextract of viburnum prunifolium, and kola preparations. Obviously, in cases where mucilage of acacia is concerned, this oxidizing action may be eliminated by heating the liquid to 100° C. (212° F.), and thus destroying the ferment.

Impurities and Adulterations. — As gum

arabic is usually collected in huge piles at Khartoum before being shipped to Port Soudan the sand and impurities are likely to sift to the bottom. As a consequence the first orders are likely to be filled with the cleaner article while the latter containing the siftings may run as high as 4 per cent. of ash. The inferior grades are often mixed with, or substituted for, the better kinds, especially in powder. Very occasionally flour or foreign starch is fraudulently added to the powder, but may be easily detected by the use of the microscope and the blue color which it produces with tincture of iodine. In consequence of the impurities and difference in quality, gum arabic should generally be garbled. In fact, it is surprising what a good effect the removal of 1 or 2 per cent. of objectionable matter has upon the remainder of the drug. It has been proposed to change the arabinic acid of the sugar beet, by the method of Scheibler, into metarabinic acid, as the foundation of a true artificial gum arabic, but the *artificial* gums of the market have no such close chemical relation with the natural gum; many of them are mixtures of various substances, others are produced from starch by the action of sulphuric acid or by other means. *Universal gum,* a patented product obtained from potato starch, has been highly commended for the permanency and adhesiveness of its mucilage, but is said not to act well as an emulsifier. A substitute has also been made from Irish moss. (See *Chondrus.*) Gelatin is sometimes added to acacia as an adulterant; formaldehyde has been recommended by Trillet (*Ph. Post,* 1899, 629) as an agent for its detection. (See also *Proc. A. Ph. A.,* 1900, 643.)

Uses.—Acacia is used in medicine chiefly as a demulcent. Hence it is advantageously employed in catarrhal affections and irritation of the fauces, by being held in the mouth and allowed to dissolve slowly. It has been used as a food, but has very little if any nutritive value. In pharmacy, gum arabic is extensively used for the suspension of insoluble substances in water, and for the formation of pills and troches. Two kinds of powdered gum arabic are used, one a coarse powder called *granulated,* the other *finely dusted.* The granulated dissolves more readily in water, according to Hager, because it has lost during desiccation only two per cent. of moisture, while in preparing the "finely dusted" powder the high heat necessarily used to thoroughly dry it drives off ten per cent. of water. Its easy solubility and absence of tendency to form "lumps" cause the coarse powder to be preferred for solutions, emulsions, etc.

Acacia is incompatible with strongly alcoholic solutions, solutions of ferric chloride and lead subacetate, and strong solutions of sodium borate.

Off. Prep.—Mucilago Acaciæ, *U. S., Br.;* Pulvis Cretæ Compositus, *U. S.;* Syrupus Acaciæ, *U. S.;* Syrupus Morphinæ et Acaciæ (from Syrup of Acacia), *N. F.*

ACACIÆ CORTEX. Br.

ACACIA BARK

(ą-cā'cĭ-ą cōr'tĕx)

"Acacia Bark is the dried bark of Acacia arabica, *Willd.,* and also the dried bark of Acacia decurrens, *Willd.;* obtained from wild or cultivated trees not less than seven years old, and, after being dried, kept for one year before use." *Br.*

Wattle Bark; Black Wattle; Babul Bark; Neb-neb.

The Acacias are known not only for their gums, but a number of them contain large quantities of tannin and hence are used in tanning. Among the latter are the so-called wattle barks of Australia, and also catechu. The chief of the Australian trees is the black wattle (*A. decurrens*), the bark of which yields from 24 to 42 per cent. of tannin, and is employed as an astringent. More recently *A. arabica* has been similarly used in East Africa.

Characters.—"Bark of *A. arabica* hard and woody, rusty brown, and tending to divide into several layers. Outer surface of the older pieces covered with thick blackish periderm, rugged, fissured longitudinally and transversely. Inner surface red, longitudinally striated and fibrous. Taste astringent and mucilaginous."

"Bark of *A. decurrens* usually in curved or channelled pieces, 1.5 to 3 mm. thick. External surface greyish-brown, darkening with age; often with irregular longitudinal ridges, and, sometimes, transverse cracks. Inner surface reddish-brown, longitudinally striated; fracture irregular and coarsely fibrous, freshly fractured surface pale. Slight tan-like odor; taste astringent." *Br.*

Acacia bark owes its medicinal properties to the tannin it contains. It is used as an astringent in *diarrheas,* being usually employed in the form of a decoction (1 : 16), in *doses* of one-half to two fluidounces (15–60 mils).

ACETANILIDUM. U. S., Br.

ACETANILID Acetanil. [Acetanilide Antifebrin]

(ăc-ę-tăn-ĭ-lĭ'dŭm)

"The monoacetyl derivative [C_6H_5ON or $C_6H_5NH.CH_3CO = 135.08$] of aniline." *U. S.* "Acetanilide, C_8H_9NO, may be obtained by the interaction of glacial acetic acid and aniline." *Br.*

Acetylamidobenzene, Phenylacetamide; Acétanilide, *Fr. Cod.;* Acetanilidum, *P. G.;* Antifebbrina, *It.;* Acetanilida, *Sp.*

Acetanilid was introduced into the Pharmacopœia of 1890, and its very extensive use caused it to be retained in succeeding editions. The process for its manufacture is not patented.

Preparation.—Acetanilid is made, according to Yvon, as follows: 372 grammes of pure aniline and 240 grammes of glacial acetic acid are heated for four hours, to the boiling point, in a flask provided with a reversed condenser;

the excess of both ingredients is then distilled off on a sand bath, this being completed when the temperature reaches 260° C. (500° F.). The cooled, congealed residue is crude acetanilid, which may be purified by sublimation or, better, by repeated crystallization from water. The yield is about 400 Gm. It may also be prepared by acting on aniline with acetyl chloride (Gerhardt), or by heating aniline with acetamide (Kolbe). The sublimed salt is whiter and lighter than that obtained by crystallization from water, which has the appearance of boric acid. For Walters' method of preparing acetanilid, on a small scale, see *Bull. Pharm.*, 1899, 53.

Properties.—Acetanilid is in "colorless, shining, micaceous, crystalline laminæ, or as a crystalline powder; odorless, having a slightly burning taste; permanent in the air. One Gm. of Acetanilid dissolves in 190 mils of water, 3.4 mils of alcohol, 3.7 mils of chloroform, 17 mils of ether, 47 mils of benzene, and in about 5 mils of glycerin at 25° C. (77° F.), also in 20 mils of boiling water and in 0.6 mil of boiling alcohol. Its saturated aqueous solution is neutral to litmus. Acetanilid melts between 112° and 114° C. (233.6°–237.2° F.). Boil about 0.1 Gm. of Acetanilid with 5 mils of potassium hydroxide T.S., the characteristic odor of aniline becomes noticeable. Now add 1 mil of chloroform, and again heat the mixture; the disagreeable odor of phenylisocyanide (a poisonous substance) is evolved. Boil about 0.1 Gm. of Acetanilid for several minutes with 2 mils of hydrochloric acid; a clear solution results, which, when mixed with 3 mils of an aqueous solution of phenol (1 in 20) and afterwards with 5 mils of a filtered, saturated solution of chlorinated lime, acquires a brownish-red color, which becomes deep blue upon supersaturation with ammonia water. Bromine T.S. produces a white, crystalline precipitate in an aqueous solution of Acetanilid. Incinerate about 2 Gm. of Acetanilid; not more than 0.05 per cent. of ash remains. The solution of about 0.5 Gm. of Acetanilid in 5 mils of colorless sulphuric acid is not more than faintly yellow (*readily carbonizable impurities*). Add 5 drops of ferric chloride T.S. to 5 mils of a cold, saturated aqueous solution of Acetanilid; the color does not differ from that produced by adding 5 drops of ferric chloride T.S. to 5 mils of distilled water (*aniline salts or other allied substances*)." *U. S.*

"Colorless, glistening lamellar crystals; inodorous; taste slightly pungent. Melting point 113° C. (235.4° F.). Soluble in 210 parts of *water*, and in 4.2 parts of *alcohol* (90 per cent.); soluble in *ether*, and in *chloroform*. Heated with *solution of sodium hydroxide* the odor of aniline is given off, and if the liquid is then warmed with a few drops of *chloroform* the unpleasant odor of phenyl isocyanide is developed. An aqueous solution mixed with *solution of bromine* gives a yellowish-white precipitate (distinction from phenacetin). Forms a colorless solution with cold *sulphuric acid* or with cold *nitric acid*. A cold saturated aqueous solution does not affect *solution of litmus* (absence of free acid), and is not affected by *T. Sol. of ferric chloride* (absence of phenazone, and salts of aniline). Ash not more than 0.1 per cent." *Br.*

Ritsert (*Ph. Ztg.*, 1890, 306) believes that the difference in melting point of acetanilid given by various writers is due to the almost constant presence of toluidine in aniline, and the production of acettoluids which have the following melting points: *ortho*, 170° C. (224.6° F.); *meta*, 65.5° C. (149.9° F.); and *para*, 147° C. (296.6° F.). A very important reaction, by which the presence of acettoluid may be detected in acetanilid, is in the use of a boiling solution of potassium permanganate. If the acetanilid be pure, it is not altered, and does not reduce the permanganate, but acettoluid, if it be present, is oxidized to acetamidobenzoic acid with reduction of the permanganate. Of a number of samples of acetanilid examined, in only one was the reduction slight, while all the others showed a decided reduction.

Uses.—Acetanilid is one of a numerous group of compounds which yield in the system paramido-phenol. Since these drugs owe their therapeutic virtues to the formation of this body the action of all of them is essentially the same. They differ, however, in the brusqueness of their effects according to the rapidity with which the paramido-phenol is formed from them.

The most striking actions of acetanilid are upon the heat regulating mechanism and the pain perception. The maintenance of the body temperature at a constant level is due to a delicate balance between the amount of heat generated in the system and that which is thrown off. The source of the bodily heat is chiefly from the oxidation of hydrocarbons in the organism; the dissipation of heat is accomplished partly by direct radiation from the skin and partly through the evaporation of the sweat. It is evident that the body temperature can be lowered either by diminishing oxidative processes or by increasing the rapidity in the dissipation of heat. There has been a great deal of experimental research to determine which of these functions acetanilid and the other antipyretics affected, but the present evidence indicates strongly that this group of drugs does not act directly upon either, but through an effect upon a center whose function it is to maintain the proper balance between them. It would seem that there is produced in the body in certain infections some poison which irritates the thermoregulator center and leads to a higher level of body temperature; the tendency of the system to maintain the temperature at a constant level is not lost but the level is higher than in health. It seems probable that acetanilid, perhaps by some sort of narcotic effect, lessens the irritability of the heat-regulating mechanism so that it does not respond to the irritation produced by poisons circulating in the

blood. It is worthy of note that these drugs do not affect the body temperature in healthy persons unless given in poisonous quantities. Of the manner in which acetanilid lessens the sensibility towards pain, we are entirely ignorant.

In ordinary dose acetanilid has no demonstrable action upon the respiration or circulation in the lower animals, although in very large quantities it acts as a depressant to the heart. (Hale, *J. P. Ex. T.*, 1909, i, p. 185.) It appears also to be feebly depressant to the motor centers in the cord. When used continuously or given in toxic quantity, it acts upon the hemoglobin of the blood producing a new compound known as methemoglobin, which does not yield its oxygen to the tissues with sufficient readiness to maintain their function.

Locally acetanilid is mildly antiseptic and to some degree anesthetic.

Acetanilid is used in medicine chiefly as an analgesic or as an antipyretic. As a pain relieving drug its greatest value is in cases of *neuralgia* whether of the head or other portions of the body. It is, however, an agent of much usefulness even in those pains in which there are actual anatomical lesions in the nervous system, such as *neuritis* or crises in *locomotor ataxia*. When, however, the pain is due to conditions outside of the nervous system, although it may enhance the potency of the opiates, by itself it is of little service.

There has been a great deal of difference of opinion as to the advisability as to the use of antipyretic drugs for the purpose of lowering *fever* temperature. One of their great disadvantages is a liability to overaction; at times they produce such a sudden or excessive change in body temperature as to lead to a condition of collapse.

Locally acetanilid has been used as a dusting powder in various types of *ulcers*, but its use is not free from danger and it does not appear to have any great advantage over a number of other safer remedies for this purpose.

Toxicology.—Two distinct types of acetanilid poisoning must be recognized, one in which the symptoms are caused by single large dose, and the other by repeated use of the drug over long periods of time. Under ordinary circumstances acetanilid is a relatively safe remedy, but there are not a few persons who possess an idiosyncrasy towards the drug and are liable to show toxic symptoms after doses which cannot be regarded as excessive. In poisoning from single doses of acetanilid there is marked fall of the body temperature with the symptoms of collapse, rapid feeble pulse, cold, clammy skin, more or less drowsiness or even coma, sometimes tinnitus aurium, or mydriasis; there is frequently a peculiar eruption of the skin resembling that of measles; sometimes there is cyanosis, although this is less common than in the more chronic types of intoxication.

The frequency with which the laity employ various mixtures containing acetanilid for the relief of the minor discomforts of life is a serious danger to the welfare of the community. In the first place, acetanilid is to be ranked among the habit-forming drugs; there are a number of well authenticated instances on record of acetanilid habit. In the second place the prolonged use of the drug leads to chemical changes in the blood, as has been pointed out above. When acetanilid is taken regularly and frequently these changes in the blood are frequently manifest, even to the casual observer, by a peculiar dusky cyanotic color of the skin and especially of the lips. Probably because of the diminished oxygen carrying power of the blood there is a tendency towards degenerative changes in various organs, especially the heart muscle, and sudden death from slight over-exertion is liable to occur.

Acetanilid is incompatible with alkalies (which liberate aniline) and when it is triturated with phenol, thymol, and some other similar organic drugs it liquefies.

Dose, three to eight grains (0.2–0.5 Gm.).

Off. Prep.—Pulvis Acetanilidi Compositus, *N. F.*

ACETONUM. U. S., Br.

ACETONE Aceton. [Dimethyl-ketone]

(ăç-ẹ-tō'nŭm)

"A liquid containing not less than 99 per cent. by weight of C_3H_6O or $CH_3.CO.CH_3$ (58.05). Preserve it in well-closed containers, in a cool place, remote from fire," *U. S.* "Acetone, or dimethyl-ketone, C_3H_6O, may be obtained by the dry distillation of calcium acetate, or barium acetate." *Br.*

Pyroacetic Spirit; Acétone, Ether (Esprit) pyroacétique, *Fr.*; Acetone, Essiggeist, Mesitalkohol, *G.*; Acetone, Chetone, Metilacetone, *It.*

Preparation.—Acetone is found in small amount in normal urine, in blood, etc., and in larger amount in certain pathological conditions. Acetone is produced by the dry distillation of sugar, gum, cellulose, etc., and therefore is always contained in crude wood-naphtha.

E. R. Squibb has also prepared it on a large scale by passing acetic acid vapor through a rotating iron cylinder heated to from 500° to 600° C. (932°–1112° F.), and containing pumice stone with precipitated barium carbonate. (*J. Am. C. S.*, 1895, 197.) Prepared commercially by the dry distillation of calcium acetate at a temperature not exceeding 300° C. (572° F.). The crude acetone thus obtained is purified by digestion with quicklime and again distilled from sodium hydroxide. Acetone of even higher purity is obtained by a subsequent distillation from sodium sulphite. It boils at 56° C. (132.8° F.), and has a peculiar ethereal odor and sharp, burning taste.

Properties.—The official description is as follows: "A transparent, colorless, mobile and volatile liquid of a characteristic ethereal odor and a pungent, sweetish taste. Specific gravity:

about 0.790 at 25° C. (77° F.). Miscible without cloudiness with water, alcohol, ether, chloroform, and with most volatile oils. It volatilizes even at low temperatures and boils between 56° and 58° C. (132.8° and 136.4° F.). It is inflammable and burns with a luminous, non-sooty flame. Acetone does not affect the color of blue or red litmus paper previously moistened with water. Evaporate 25 mils of Acetone in a platinum or porcelain dish on a water bath; not more than 0.002 Gm. of residue remains. Mix 20 mils of Acetone in a clean, glass-stoppered bottle, with 0.1 mil of tenth-normal potassium permanganate V.S.; the pink tint so produced does not wholly disappear in less than fifteen minutes (*empyreumatic substances*)." *U. S.*

"A colorless, transparent, mobile and volatile liquid. Characteristic odor; taste pungent and sweetish. Forms clear mixtures with *water, alcohol* (90 per cent.), *ether,* and *chloroform* in all proportions. Specific gravity 0.795 to 0.798. Not less than 95 per cent. distils between 55° and 57° C. (131° and 134.6° F.). Leaves no residue when evaporated on a water-bath. 10 millilitres, to which a few drops of *solution of phenolphthalein* have been added, require not more than 1 drop of *N/1 solution of sodium hydroxide* to produce a permanent pink coloration. 20 millilitres do not completely decolorise 0.1 millilitre of *N/10 solution of potassium permanganate* within fifteen minutes (limit of readily oxidisable impurities). Yields a clear mixture with an equal volume of *petroleum spirit* (limit of water)." *Br.*

Distilled with water and chlorinated lime, it yields nearly 200 per cent. of its weight in chloroform, and hence largely used in the manufacture of this substance, both in this country and in Germany. In the presence of an alkali, iodine converts it into iodoform, so that a trace of acetone in methyl alcohol can be detected by iodoform formation. This reaction is taken advantage of in the quantitative determination of acetone. It may also be determined by Strache's phenyl-hydrazine method. (*Zeit. An. Chem.,* 1892, p. 573.) (Kraemer's test.)

Schlagdenhauffen asserts that commercial acetone contains an alkaloidal substance. (*P. J.,* 1884, 163.) Reagents for detecting acetone in the urine are described under *Diagnostic Reagents,* Part III.

Acetone oil, largely a mixture of higher ketones, obtained as a by-product in the manufacture of acetone and suggested by Lang as an addition to alcohol and spirits to denaturize them, cannot be used on a large scale as pointed out by Klar, as the commercial supply would probably be insufficient. (*Chem. News,* 1899, 205.)

Assay.—"Pour about 1 mil of Acetone into a tared weighing-bottle having a stopper, partly fill it with distilled water and weigh accurately. Transfer the contents of the bottle, washing the bottle well with distilled water, to a 1000 mil graduated flask, fill to the mark with distilled water, and mix the contents thoroughly. Place 25 mils of normal potassium hydroxide V.S. in a 250 mil glass-stoppered flask, add exactly 25 mils of Acetone solution (representing one-fortieth of the weight of Acetone taken), then, with constant agitation of the flask, add 35 mils of tenth-normal iodine V.S., and allow the mixture to stand for fifteen minutes. Now add 26 mils of normal hydrochloric acid V.S. and at once titrate the residual iodine with tenth-normal sodium thiosulphate V.S., with the addition of starch T.S. as indicator when the liquid is nearly decolorized. Conduct a blank test with the same quantities of the reagents and subtract the quantity of tenth-normal iodine V.S. consumed in this blank test from that consumed in the assay.

"Each mil of this difference, which represents the iodine consumed by the reaction with the Acetone, corresponds to 0.0009675 Gm. of C_3H_6O. Each gramme of Acetone corresponds to not less than 1023 mils of tenth-normal iodine V.S." *U. S.*

Uses.—Acetone is used chiefly as a solvent for fats, resins, and camphors, and was used as a menstruum for extracting oleoresins in the U. S. P. VIII. As a solvent it is particularly valuable in that it possesses the fat dissolving power of the immiscible solvents and the miscibility with water which makes it similar to alcohol. As a drug it has been employed locally to a certain extent in inoperable *carcinomata of the uterus* for the purpose of relieving hemorrhage and discharge. (Gellhorn, *Cb. Gyn.,* 1911, 1240.)

Off. Prep.—Collodium Cantharidatum, *U. S.;* Petroxolinum Iodoformi, *N. F.*

ACETPHENETIDINUM. U. S. (Br.)

ACETPHENETIDIN Acetphen. [Phenacetin]

(ăc-ĕt-phĕn-ĕt-ĭd'nŭm)

"The monoacetyl derivative [$C_{10}H_{13}O_2N$ or $C_6H_4(OC_2H_5).NH.CH_3CO$ 1:4 = 179.11] of para-amidophenetol." *U. S.* "Phenacetin or para-acet-phenetidin, $C_{10}H_{13}NO_2$, may be obtained by the interaction of glacial acetic acid and paraphenetidin." *Br.*

Phenacetinum, *Br., P. G.;* Para-acetphenetidin, Para-ethoxyacetanilide; Phenacetin; Acet-Phénétidine, *Fr. Cod.;* Phénacetine, Para-acétophénétidine, Amide Acétique de l'amido-phénétol, *Fr.;* Fenacetina, *It., Sp.*

The chemical relationship of this body to phenol is seen by an examination of its formula and the formulas of the intermediate compounds obtained as stages in its preparation.

Phenol, $C_6H_5.OH$, is converted into *nitrophenol,* $C_6H_4(NO_2)OH$. Only the paranitrophenol is available, and this is separated by distilling off the ortho-nitrophenol by steam distillation. The residual *paranitrophenol,* in the form of the sodium compound, is treated with ethyl bromide, when ethyl paranitrophenol or *paranitrophenetol,* $C_6H_4(NO_2)OC_2H_5$, is produced. This is now reduced by the action of hydrochloric acid and iron turnings to *para-*

phenetidin, $C_6H_4(NH_2)OC_2H_5$. Glacial acetic acid then serves to introduce the acetyl group, and *para-acetamidophenetol* (phenacetin), $C_6H_4(NHC_2H_3O)OC_2H_5$, is obtained.

Properties.—Acetphenetidin occurs in "white, glistening, crystalline scales or as a fine crystalline powder; odorless, having a slightly bitter taste and producing a faint numbing effect on the tongue; permanent in the air. One Gm. of Acetphenetidin dissolves in 1310 mils of water, 15 mils of alcohol, 14 mils of chloroform, and in 90 mils of ether at 25° C. (77° F.); also in 82 mils of boiling water and 2.8 mils of boiling alcohol. Its saturated aqueous solution is neutral to litmus. Acetphenetidin melts between 133° and 135° C. (271.4° and 275° F.). Boil about 0.1 Gm. of Acetphenetidin for one minute with 1 mil of hydrochloric acid, dilute the mixture with 10 mils of distilled water, cool, and filter it; a drop of potassium dichromate T.S. added to the filtrate produces a ruby-red color. Incinerate about 2 Gm. of Acetphenetidin; not more than 0.05 per cent. of ash remains. A mixture of about 0.005 Gm. of Acetphenetidin and 1 mil of nitric acid is colored yellow, the color becoming darker on standing. The solution of about 0.5 Gm. of Acetphenetidin in 5 mils of colorless sulphuric acid is not more than faintly yellow (*readily carbonizable impurities*). Boil about 0.1 Gm. of Acetphenetidin with 10 mils of distilled water until dissolved, cool the solution, filter it, and add bromine T.S. to the filtrate, drop by drop, with agitation after each addition, until the solution remains permanently yellow; neither turbidity nor precipitation is produced (*acetanilid*). A mixture of about 0.3 Gm. of Acetphenetidin with 1 mil of alcohol and 1 drop of tenth-normal iodine V.S. does not acquire a red tint when diluted with three times its volume of distilled water and boiled (*para-phenetidin*)." *U. S.*

The British Pharmacopœia gives the following tests for phenacetin. "Small, colorless, glistening, scaly crystals. Inodorous; tasteless. Melting point 135° C. (275° F.). Very sparingly soluble in cold *water,* more freely in boiling *water;* soluble in 21 parts of *alcohol* (90 per cent.), the solution being neutral to *litmus.* 0.1 gramme boiled with 2 millilitres of *hydrochloric acid* for half a minute yields a liquid which, diluted with 10 times its volume of *water,* cooled and filtered, assumes a deep-red color on the addition of *solution of chromic acid. Sulphuric acid* dissolves Phenacetin without coloration. A cold saturated aqueous solution does not become turbid on the addition of *solution of bromine* (absence of acetanilide). A mixture of 0.3 gramme of Phenacetin with 1 millilitre of *alcohol* (90 per cent.) does not acquire a red tint when diluted with 3 times its volume of *water,* and boiled with 1 drop of *N/10 solution of iodine* (absence of paraphenetidin). No appreciable ash." *Br.*

The test with chromic acid will serve to distinguish it from acetanilid and exalgin; that with bromine water will indicate the absence of phenol and acetanilid, both of which will show a white turbidity, owing to the formation of difficultly soluble bromine derivatives. The presence of unchanged paraphenetidin may be detected by melting 2.5 Gm. of hydrated chloral in a test tube and adding 0.5 Gm. of the acetphenetidin to be tested. If pure, it will remain colorless; if paraphenetidin be present, it will become violet or reddish-blue in tint. For further information see a paper in *Proc. A. Ph. A.,* 1903, 180, on an examination of samples of commercial phenacetin by G. M. Beringer, and *Proc. A. Ph. A.,* 1903, 365, for a paper by L. F. Kebler on its history, methods of manufacture, and chemical constitution.

Uses.—Acetphenetidin, like acetanilid, yields in the body paramido-phenol and its physiological action and therapeutic effects are therefore essentially the same as those of acetanilid (see p. 8). Its action, however, is more gradual and more prolonged and it is less likely to give rise to undesirable symptoms. Enormous quantities of it can be administered to the lower animals without disturbances of the vital functions: H. C. Wood, Jr. (*U. M. M.,* July, 1900), found that 0.5 Gm. per kilo could be injected intravenously into the dog before the occurrence of serious disturbances of either respiration or circulation. In large quantities it is mildly depressant to the spinal cord. The relative safety of acetphenetidin as shown both by animal experimentation and clinical experience, is probably dependent upon the slowness with which it undergoes chemical change in the blood and consequent gradual formation of the active phenylamine. It is, however, capable of causing serious poisoning; we are cognizant of a case in which five powders of 2 grains each taken over an interval of ten hours, produced death in a baby one year old, and Hollopeter reports serious collapse from 22½ grains in a woman. Acetphenetidin is useful as an antipyretic and analgesic in the same group of cases in which acetanilid is of service (see p. 9). It requires, however, somewhat larger doses to produce the same degree of action.

Acetphenetidin is incompatible with strong acids and alkalies, and also with oxidizing agents, such as chlorine, bromine, and iodine. It becomes liquid when rubbed with chloral, phenol, etc. It conceals the fluorescence of dilute quinine sulphate solutions.

Dose, five to fifteen grains (0.32–1.0 Gm.).

ACETUM CANTHARIDINI. Br.

Vinegar of Cantharidin

(ą-cē'tŭm cąn-thăr'ĭ-dĭn-i)

Vinaigre cantharidé, *Fr.;* Canthariden-Essig, *G*

"Cantharidin, 1 gramme; Glacial Acetic Acid, 200 millilitres; Acetic Acid sufficient to produce 2000 millilitres. Dissolve the Cantharidin in the Glacial Acetic Acid with the aid of a water-bath; cool, and add sufficient Acetic Acid to produce the required volume." *Br.*

This preparation contains approximately the same proportion of Cantharidin as the Acetum Cantharidis of the British Pharmacopœia, 1898."

This preparation which was formerly made by macerating and then percolating bruised cantharides with diluted glacial acetic acid is now made by dissolving cantharidin, the crystalline active principle in acetic acid. This is an improvement, as the process is simpler and a saving in time and labor is effected.

Procter found that, by digestion at a temperature of 100° C. (212° F.), the active principle of the flies is readily taken up by official acetic acid, though a portion of the cantharidin is deposited upon cooling. (*A. J. P.*, xxiv, 299.) It would seem, therefore, that the vinegar of Spanish flies would be best prepared with the aid of heat; and, to a certain extent, this advantage is enjoyed in the present process. Greenish and Wilson (*P. J.*, 1898, 259) proposed to make this preparation directly from the active principle, by dissolving 1 Gm. of cantharidin in 200 mils of glacial acetic acid and adding sufficient diluted acetic acid to make 2000 mils. The official British vinegar is based upon this proposition.

Uses.—This preparation is intended exclusively for external use, as a speedy epispastic. It is said, when lightly applied by a brush, to act as a rubefacient; and, when rubbed freely upon the skin for three minutes, to be followed in two or three hours by full vesication. The pain produced by the application, though more severe, is also more transient than that occasioned by the blistering cerate.

ACETUM SCILLÆ. U. S., Br.

VINEGAR OF SQUILL Acet. Scill.

(ą-cē'tŭm sçĭl'læ)

Aceticum scilliticum; Meerzwiebel-Essig, *G.*; Vinaigre de scille, *Fr. Cod.*; Vinaigre scillitique, *Fr.*; Aceto scillitico, *It.*; Vinagre de escila, *Sp.*

• "Squill, in No. 20 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Diluted Acetic Acid, *a sufficient quantity*, to make *one thousand millilitres* [or 33 fl. oz., 6½ fluidrachms]. Macerate the squill with *nine hundred mils* [or 30 fluidounces] of diluted acetic acid during seven days with frequent agitation; then strain the mixture, and wash the mass on the strainer with enough diluted acetic acid to make the strained liquid measure nearly *one thousand mils* [or 33 fl. oz., 6½ fluidrachms]. Heat this liquid to boiling, filter while hot, and when cold add sufficient diluted acetic acid to make the product measure *one thousand mils* [or 33 fl. oz., 6½ fluidrachms]." *U. S.*

"Squill, bruised, 1000 grammes; Acetic Acid, 1000 millilitres; Distilled Water, 3200 millilitres. Macerate for seven days; press and filter.

"*Tests.*—Specific gravity 1.070. 10 millilitres require for neutralisation not less than 10.8 millilitres of *N/1 solution of sodium hydroxide.*" *Br.*

The British preparation is of approximately twice the strength of the Acetum Scillæ of the British Pharmacopœia 1898 or of the U. S. P. IX.

Vinegar of Squill may also be prepared by percolating the Squill with the Diluted Acetic Acid after previous maceration with an equal bulk of the Diluted Acetic Acid (this precaution being necessary in order to satisfy thoroughly its tendency to swell) and filtering through paper.

The process now official differs from that of the U. S. Pharm. of 1890 in directing the heating of the strained liquid to coagulate albuminous matter and filtering, so that when the vinegar is mixed with sugar and water, in making syrup of squill, a transparent syrup may be secured.

Vinegar of Squill was formerly official in the Lond., Ed. and Dub. Colleges, but was omitted as a distinct preparation in the first British Pharmacopœia, reintroduced in 1874 and since retained. As vinegar of squill is apt to be injured by keeping, it should be prepared in small quantities, as wanted for use. The British preparation is now stronger than that of the U. S. P. IX (U. S. P. 1 in 10. Br. 1 in 4.2). As shown by E. Gregory (*Can. Pharm. Journ.*, Oct., 1875), the spirit added to it in the former British formula was of no use as a preservative. In the German Pharmacopœia 5 parts of squill are macerated in a mixture of 9 parts of acetic acid (30 per cent.), 36 parts of water, and 5 parts of alcohol, for three days, with frequent shaking, strained without forcible expression, allowed to stand twenty-four hours, and then filtered. In the Codex, 12 parts of white vinegar are used to macerate 1 part of squill for eight days. Vinegar of squill is employed chiefly in preparing the syrup.

Uses.—Vinegar of squill is certainly inferior to the alcoholic preparations of this drug in its effects upon the heart and kidneys. It is used solely for making syrup of squill.

Dose, of the U. S. preparation, from fifteen minims to a fluidrachm (0.9–3.75 mils), but the latter quantity would be apt to nauseate; of the Br., five to fifteen minims (0.3–0.9 mil).

Off. Prep.—Syrupus Scillæ, *U. S., Br.*; Oxymel Scillæ, *N. F.*

ACETUM URGINEÆ. Br.

VINEGAR OF URGINEA Vinegar of Indian Squill

(ą-cē'tŭm ür-gĭn'ē-æ)

"Urginea, bruised, 1000 grammes; Acetic Acid, 1000 millilitres; Distilled Water, 3200 millilitres. Macerate for seven days; press and filter.

"*Tests.*—Specific gravity 1.070. 10 millilitres require for neutralisation not less than 10.8 millilitres of *N/1 solution of sodium hydroxide.*" *Br.*

Vinegar of Urginea was admitted to the Indian and Colonial Addendum of the British Pharmacopœia in 1900, but the strength was

doubled approximately in the Br. Pharm., 1914. It is used to make syrup of urginea in the same way that vinegar of squill is used by the addition of sugar. It is to be regretted that the end product was not definitely stated in the above process, as some loss during expression cannot be avoided. Under these circumstances the requirement that the specific gravity shall be exactly 1.070 cannot always be met satisfactorily.

Dose, five to fifteen minims (0.3–0.9 mil).

ACIDUM ACETICUM. U. S., Br.

ACETIC ACID Acid. Acet.

(ăç'ĭ-dŭm ą-cēt'ĭ-cŭm)

"An aqueous solution containing not less than 36 per cent. nor more than 37 per cent. of $C_2H_4O_2$ or $CH_3.COOH$ (60.03)." *U. S.* "Acetic Acid may be obtained by the destructive distillation of wood, and contains 33 per cent. by weight of hydrogen acetate, $HC_2H_3O_2$, and 67 per cent. by weight of water." *Br.*

Acetum Concentratum; Ethanoic Acid; Acide acétique, *Fr. Cod.*; Acidum Aceticum Dilutum, *P. G.*; Essigsäure, *G.*; Acido acetico, *It., Sp.*

ACIDUM ACETICUM DILUTUM. U. S., Br.

DILUTED ACETIC ACID Acid. Acet. Dil.

(ăç'ĭ-dŭm ą-cēt'ĭ-cŭm dĭ-lū'tŭm)

"An aqueous solution containing not less than 5.7 nor more than 6.3 per cent. of $C_2H_4O_2$ or $CH_3.COOH$ (60.03)." *U. S.* "Diluted Acetic Acid contains 5 per cent. by weight of hydrogen acetate, $HC_2H_3O_2$." *Br.*

Acetum Destillatum; Acide acétique dilué, *Fr.*; Acetum, *P. G.*; Reiner Essig, Verdünnte Essigsäure, *G.*

ACIDUM ACETICUM GLACIALE. U. S., Br.

GLACIAL ACETIC ACID Acid. Acet. Glac.

(ăç'ĭ-dŭm ą-cēt'ĭ-cŭm glā-cĭ-ā'lē)

"A liquid containing not less than 99 per cent. of $C_2H_4O_2$ or $CH_3.COOH$ (60.03). Preserve it in glass-stoppered bottles." *U. S.* "Glacial Acetic Acid contains not less than 98.9 per cent. by weight of hydrogen acetate, $HC_2H_3O_2$." *Br.*

Acidum Aceticum Concentratum; Acidum Aceticum, *P. G.*; Acide acétique crystallisable, *Fr. Cod.*; Acide acétique concentré, Vinaigre glacial, Esprit de vinaigre, *Fr.*; Essigsäure, Eisessig, *G.*; Acido acetico concentrato, *It.*

Three strengths of acetic acid are now official in the U. S. and Br. Pharmacopœias. These are *Acidum Aceticum Glaciale,* of sp. gr. 1.047 to 1.050 at 25° C. (77° F.), *U. S.*; *Acidum Aceticum,* of sp. gr. 1.045, *U. S.*, at 25° C. (77° F.), and 1.044, *Br.*, at 15.5° C. (59.9° F.), and *Acidum Aceticum Dilutum,* sp. gr. 1.008, *U. S.*, at 25° C. (77° F.), and 1.007, *Br.*, at 15.5° C. (59.9° F.).

We shall consider these grades separately, in the order of their strength.

Acidum Aceticum Glaciale.—A process for this preparation was given in the British Pharmacopœia of 1864, which consisted in first heating sodium acetate so as to drive off all its water of crystallization, then, after cooling, distilling it with concentrated sulphuric acid, and, finally, if the resulting acetic acid, upon being tested with a mixture of solution of potassium iodate and a little mucilage of starch, was found to contain sulphurous acid, agitating the distilled acid with perfectly dry black manganese oxide, and again distilling. The object of the process was to furnish an acid of the maximum strength. But, on trial, it was not found to be satisfactory, as the resulting acid was not truly glacial, and always contained sulphurous acid. (C. H. Wood, *P. J.*, 1867, 17.) The following modification of the process does, however, yield a pure product. After the crystallized salt has been fused in an iron dish in its own water of crystallization, and has dried out, it is again brought to fusion by increased heat, whereby, if the heat applied be not too strong, no acid is decomposed or vaporized. The anhydrous salt is then treated with half a molecule of sulphuric acid (for 82 parts anhydrous acetate 49 parts of strongest sulphuric acid), which, according to Mohr and Buchner, suffices, instead of twice the amount, usually employed. No sulphurous acid is liberated in this case. A process to be followed on a large scale, practically the counterpart of this, is given in a footnote, page 18, 14th ed., U. S. Dispensatory.

Acetic acid of maximum strength may also be obtained by distilling dried potassium acetate at a heat between 199° C. (390.2° F.) and 299° C. (570.2° F.). One molecule of monohydrated acetic acid distils over, and neutral potassium acetate is left. The acid acetate may be formed by evaporating a mixture of the neutral acetate with an excess of aqueous acetic acid. In this process, the same potassium acetate serves repeatedly for conversion into acid acetate, and subsequent decomposition. This process is said to be employed by manufacturers on a large scale in some parts of the continent of Europe. It originated with Melsens. It is customary in the preparation of the very pure acid to construct the head of the still and the entire condensing system of pure silver.

Properties. *Glacial Acetic Acid.*—This acid, sometimes called *radical vinegar,* is "a clear, colorless liquid with a strong, vinegar-like odor, and a very pungent, acid taste. It is miscible with water or alcohol. Specific gravity: from 1.047 to 1.050 at 25° C. (77° F.). It boils between 117° and 118° C. (242.6° and 244.4° F.). Congealing point: not below 14.5° C. (58.1° F.).

"Glacial Acetic Acid responds to the tests for identity and purity under *Acidum Aceticum* when diluted to that strength, but the tint produced by the addition of 0.1 mil of tenth-normal potassium permanganate V.S. to 2 mils of Glacial Acetic Acid, diluted with 10 mils of

distilled water and contained in a glass-stoppered bottle, is not changed to brown within two hours." *U. S.*

"At summer temperatures [about 15° to 20° C. (59°–68° F.)] it is a clear, colorless liquid with a very pungent odor. Yields, when neutralised, the *reactions* characteristic of acetates. Crystallizes when sufficiently cooled, and does not entirely re-melt until the temperature rises above 14.7° C. (58.46° F.). 1 gramme diluted with 50 millilitres of *water* requires for neutralisation not less than 32.9 millilitres of *N/2 solution of sodium hydroxide.* Leaves no residue on evaporation, and yields no characteristic *reactions* for lead, copper, arsenic, chlorides, nitrates, sulphates, or sulphites. Does not immediately darken in color when neutralised with *solution of ammonia* and warmed with *solution of silver nitrate* (absence of formates). 2 millilitres of Glacial Acetic Acid do not completely decolorize a mixture of three drops of *solution of potassium permanganate* and 10 millilitres of *water* within half a minute (limit of empyreumatic matter)." *Br.* The anhydride was first isolated by C. Gerhardt, who found it to be a limpid liquid, heavier than water, and having the constant boiling point of 138° C. (280.4° F.). Glacial acetic acid should be kept in carefully stoppered glass containers, as it otherwise loses strength.

The U. S. and Br. acids are identical in strength (99 per cent.) but the temperature at which the sp. gr. is taken is 25° C. (77° F.) in the U. S. and 15° C. (59° F.) in the Br. It possesses the property of dissolving a number of substances, such as volatile and fixed oils (*P. J.*, Sept. 11, 1875), camphor, resins and gum resins, fibrin, albumin, etc. As it attracts humidity from the atmosphere, it should be preserved in well-stoppered bottles. Its combinations with salifiable bases are called acetates.

"**Assay.**—Pour about 2.5 mils of Glacial Acetic Acid into a tared flask containing 10 mils of distilled water, stopper and weigh accurately, dilute with 40 mils of distilled water, and titrate this solution with normal potassium hydroxide V.S., using phenolphthalein T.S. as indicator. It shows not less than 99 per cent. of $C_2H_4O_2$.

"Each mil of normal potassium hydroxide V.S. used corresponds to 0.06003 Gm. of $C_2H_4O_2$. Each gramme of Glacial Acetic Acid corresponds to not less than 16.5 mils of normal potassium hydroxide V.S." *U. S.*

ACIDUM ACETICUM. *U. S., Br.* (sp. gr. 1.045, *U. S.*, 1.044, *Br.*). *Acetic Acid.*—This is the acid resulting from the purification of the crude acetic acid obtained by the destructive distillation of wood. It is the acid most useful to the apothecary, and is employed in making numerous pharmaceutical preparations. As this grade of acid has its source in the impure acetic acid it will be proper to premise some account of the crude acid, called *pyroligneous acid.*

Wood, when charred, yields many volatile products, among which are an acid liquor, an empyreumatic oil, and tar containing creosote and some other proximate principles. When the carbonization is performed in closed vessels, these products, which are lost in the ordinary process of charring, may be collected, and, at the same time, a large amount of charcoal be obtained.

Senff has furnished some comparative results in respect to the dry distillation of wood. The points worked out are a comparison of the products of distillation under similar conditions yielded by wood from various parts of the same trees, and from the same wood in a healthy and in an unsound state; also a comparison of the products from one and the same wood distilled slowly or rapidly. It has been found that when similarly distilled the yield by weight of crude acid, tar, charcoal, and gas from the most diverse species of wood does not essentially differ, but that the percentage of real acid in the crude acid obtained varies considerably, and in this respect the wood from ordinary foliage trees compares favorably with that from needle-leaved trees; also that stem-wood yields more acid than branch-wood, that wood yields more acid than bark, and that sound wood yields more acid than unsound wood. (*Ber. d. Chem. Ges.*, xviii, p. 60; *P. J.*, 1885, p. 696.)

Crude pyroligneous acid, sometimes called *pyroligneous vinegar*, or *wood vinegar*, is a dark brown liquid, having a strong smoky odor, and consists of acetic acid, diluted with more or less water, and holding in solution some creosote and empyreumatic oil, with methyl alcohol. It is from this crude acid that the U. S. and British acetic acid, corresponding to the acetic acid of commerce, is obtained. The purification is effected as follows: The acid is saturated with milk of lime, whereby calcium acetate is formed in solution, and thus most of the tarry matter is precipitated. The solution of calcium acetate is then mixed with a concentrated solution of sodium sulphate, and, by double decomposition, sodium acetate is formed in solution, and calcium sulphate precipitated. The solution of sodium acetate is next subjected to evaporation, during which further impurities that separate on the surface are skimmed off. The solution, being duly concentrated, is set aside to crystallize, and the impure salt thus obtained, after having been partially purified by solution and recrystallization, is fused in an iron vessel, stirred until it dries, and, the heat being carefully raised, subjected to incipient carbonization, whereby remaining empyreumatic matters are carbonized, with little damage to the salt. The mass is then dissolved in water, and the solution, being strained and recrystallized, furnishes pure sodium acetate. (See *Sodii Acetas.*) Finally, this salt, distilled with from 34 to 35 per cent. of its weight of sulphuric acid, yields the acetic acid of commerce, the residue being sodium sulphate, which is reserved for decomposing fresh portions of calcium acetate. The acid has still an empyreumatic flavor, which is removed by filtering it through animal charcoal

Acetic Acid

Per cent. $HC_2H_3O_2$	Sp. gr. app. 25° C. / 25° C.	Sp. gr. app. 15° C. / 15° C.	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal KOH mils	Per cent. = 0.01 mil normal KOH.
‡0	1.0000	1.0000	0.00018	0.0714	0.000	0.0599
1	1.0014	1.0015	0.00019	0.0714	0.167	0.0602
2	1.0028	1.0030	0.00020	0.0714	0.333	0.0595
3	1.0042	1.0045	0.00022	0.0714	0.501	0.0599
4	1.0056	1.0060	0.00023	0.0714	0.668	0.0595
5	1.0070	1.0075	0.00024	0.0769	0.836	0.0592
6	1.0083	1.0090	0.00025	0.0714	1.005	0.0592
7	1.0097	1.0105	0.00026	0.0714	1.174	0.0588
8	1.0111	1.0120	0.00028	0.0769	1.344	0.0588
9	1.0124	1.0135	0.00029	0.0714	1.514	0.0588
10	1.0138	1.0150	0.00030	0.0769	1.684	0.0585
11	1.0151	1.0165	0.00031	0.0714	1.855	0.0585
12	1.0165	1.0179	0.00033	0.0769	2.026	0.0581
13	1.0178	1.0193	0.00034	0.0769	2.198	0.0581
14	1.0191	1.0208	0.00036	0.0769	2.370	0.0581
15	1.0204	1.0222	0.00037	0.0769	2.542	0.0578
16	1.0217	1.0236	0.00038	0.0833	2.715	0.0578
17	1.0229	1.0251	0.00040	0.0769	2.888	0.0575
18	1.0242	1.0265	0.00041	0.0833	3.062	0.0575
19	1.0254	1.0279	0.00043	0.0833	3.236	0.0571
20	1.0266	1.0293	0.00044	0.0769	3.411	0.0571
21	1.0279	1.0307	0.00045	0.0833	3.586	0.0571
22	1.0291	1.0320	0.00046	0.0833	3.761	0.0571
23	1.0303	1.0333	0.00048	0.0833	3.936	0.0568
24	1.0315	1.0346	0.00049	0.0833	4.112	0.0568
25	1.0327	1.0359	0.00050	0.0909	4.288	0.0565
26	1.0338	1.0372	0.00051	0.0833	4.465	0.0565
27	1.0350	1.0384	0.00053	0.0909	4.642	0.0565
28	1.0361	1.0397	0.00054	0.0909	4.819	0.0565
29	1.0372	1.0409	0.00055	0.0909	4.996	0.0562
30	1.0383	1.0421	0.00056	0.0909	5.174	0.0562
31	1.0394	1.0433	0.00057	0.1000	5.352	0.0562
32	1.0404	1.0445	0.00059	0.0909	5.530	0.0559
33	1.0415	1.0456	0.00060	0.1000	5.709	0.0559
34	1.0425	1.0468	0.00062	0.1000	5.888	0.0559
35	1.0435	1.0479	0.00063	0.1000	6.067	0.0559
36	1.0445	1.0490	0.00064	0.1000	6.246	0.0559
37	1.0455	1.0501	0.00065	0.1111	6.425	0.0559
38	1.0464	1.0511	0.00066	0.1000	6.604	0.0556
39	1.0474	1.0522	0.00067	0.1111	6.784	0.0556
40	1.0483	1.0532	0.00068	0.1111	6.964	0.0556
41	1.0492	1.0542	0.00069	0.1111	7.144	0.0552
42	1.0501	1.0552	0.00070	0.1111	7.325	0.0552
43	1.0510	1.0561	0.00070	0.1250	7.506	0.0552
44	1.0518	1.0571	0.00071	0.1111	7.687	0.0552
45	1.0527	1.0580	0.00072	0.1250	7.868	0.0549
46	1.0535	1.0589	0.00073	0.1250	8.050	0.0552
47	1.0543	1.0598	0.00074	0.1250	8.231	0.0552
48	1.0551	1.0607	0.00075	0.1429	8.412	0.0552
49	1.0558	1.0616	0.00076	0.1250	8.593	0.0549
50	1.0566	1.0624	0.00077	0.1429	8.775	0.0552

* Add if the temperature is above, subtract if it is below the standard.
† Corresponding with a difference in specific gravity of 0.0001.
‡ The figures on this line across the page are for fractional percentages below 1.

Acetic Acid—Continued

Per cent. $HC_2H_3O_2$	Sp. gr. app. 25° C. / 25° C.	Sp. gr. app. 15° C. / 15° C.	Correction of specific gravity for 1° C.	Fractional per cent.	Normality. 1 mil requires normal KOH mils	Per cent. = 0.01 mil normal KOH.
51	1.0573	1.0632	0.00077	0.1429	8.956	0.0549
52	1.0580	1.0640	0.00078	0.1429	9.138	0.0552
53	1.0587	1.0647	0.00079	0.1667	9.319	0.0549
54	1.0593	1.0655	0.00079	0.1429	9.501	0.0549
55	1.0600	1.0662	0.00080	0.1667	9.683	0.0549
56	1.0606	1.0669	0.00081	0.1667	9.865	0.0549
57	1.0612	1.0675	0.00081	0.1667	10.047	0.0549
58	1.0618	1.0682	0.00082	0.1667	10.229	0.0549
59	1.0624	1.0688	0.00083	0.2000	10.411	0.0549
60	1.0629	1.0694	0.00084	0.2000	10.593	0.0549
61	1.0634	1.0700	0.00084	0.2000	10.775	0.0549
62	1.0639	1.0706	0.00085	0.2000	10.957	0.0552
63	1.0644	1.0711	0.00086	0.2500	11.138	0.0549
64	1.0648	1.0716	0.00086	0.2500	11.320	0.0552
65	1.0652	1.0721	0.00087	0.2500	11.501	0.0552
66	1.0656	1.0726	0.00087	0.2500	11.682	0.0549
67	1.0660	1.0730	0.00088	0.2500	11.864	0.0552
68	1.0664	1.0734	0.00089	0.2500	12.045	0.0552
69	1.0668	1.0738	0.00089	0.3333	12.226	0.0552
70	1.0671	1.0742	0.00090	0.3333	12.407	0.0556
71	1.0674	1.0746	0.00090	0.5000	12.587	0.0556
72	1.0676	1.0749	0.00091	0.5000	12.767	0.0559
73	1.0678	1.0751	0.00092	1.0000	12.946	0.0559
74	1.0679	1.0753	0.00092	1.0000	13.125	0.0559
75	1.0680	1.0755	0.00093	1.0000	13.304	0.0562
76	1.0681	1.0756	0.00093	.....	13.482	0.0562
77	1.0681	1.0757	0.00094	.....	13.660	0.0562
78	1.0681	1.0757	0.00094	.....	13.838	0.0565
79	1.0681*	1.0757	0.00095	1.0000	14.015	0.0565
80	1.0680	1.0757	0.00096	0.5000	14.192	0.0571
81	1.0678	1.0756	0.00096	0.5000	14.367	0.0571
82	1.0676	1.0755	0.00097	0.5000	14.542	0.0575
83	1.0674	1.0753	0.00097	0.3333	14.716	0.0578
84	1.0671	1.0751	0.00098	0.2500	14.889	0.0581
85	1.0667	1.0748	0.00099	0.2500	15.061	0.0585
86	1.0663	1.0745	0.00099	0.2000	15.232	0.0592
87	1.0658	1.0740	0.00100	0.1667	15.401	0.0592
88	1.0652	1.0735	0.00101	0.1667	15.570	0.0599
89	1.0646	1.0729	0.00102	0.1250	15.737	0.0602
90	1.0638	1.0722	0.00103	0.1111	15.903	0.0610
91	1.0629	1.0714	0.00103	0.1111	16.067	0.0617
92	1.0620	1.0705	0.00103	0.0833	16.229	0.0629
93	1.0608	1.0695	0.00104	0.0833	16.388	0.0637
94	1.0596	1.0683	0.00104	0.0714	16.545	0.0654
95	1.0582	1.0669	0.00105	0.0588	16.698	0.0676
96	1.0565	1.0653	0.00106	0.0526	16.846	0.0694
97	1.0546	1.0634	0.00106	0.0455	16.990	0.0709
98	1.0524	1.0613	0.00107	0.0400	17.131	0.0746
99	1.0499	1.0589	0.00108	0.0357	17.265	0.0781
100	1.0471	1.0562	0.00109	.....	17.393	.....

* Below this point the specific gravity diminishes as the strength of the acid increases.

NOTE: If the specific gravity of the acid is greater than 1.045, mix some of the acid with an equal weight of water and take the specific gravity of the mixture, then multiply the corresponding percentage taken from the table by two. It is better, however, to determine the strength of any sample of acetic acid by its normality.

To find the volume per cent. of official Acetic Acid (36 per cent.) multiply the "normality" by 16.01. For the volume per cent. of Acetic Acid ($HC_2H_3O_2$), multiply the "normality" by 5.751. For the volume per cent. of official Diluted Acetic Acid (6 per cent.), multiply the "normality" by 99.5.

or rectifying with potassium dichromate. The odor is due to *furfurol*, $C_5H_4O_2$, which, as Victor Meyer has shown, can be detected even in glacial acetic acid by the red coloration it gives with aniline. It may be removed from pyroligneous acid by agitating the liquid with 2 or 3 per cent. of benzene. The aqueous layer, after separation from the benzene, is stated to give, by a single distillation, a palatable table vinegar.

Acetic acid, according to E. R. Squibb, improves very much by age, and a sample examined for odor when freshly distilled would not be recognized as the same three months afterward.

An excellent quality of acetic acid was made by E. R. Squibb by an improvement on the process of Schwartz, the principal feature being the careful regulation of the heat, whereby the excessive charring of the wood is prevented and the formation of the tarry substances so reduced as to leave the acetic acid almost entirely free from empyreuma. The retorts, which are rectangular in shape, are supported by wheels secured to shafts, rotating in bearings connected with the sides, and are run upon car tracks into the ovens, after they have been loaded with some billets of oak wood from the transfer car, in an ingenious and simple manner. In the construction of the ovens, care is taken to economize the fuel and to secure control of the temperature by the use of corrugated bottoms to the retorts and dampers in the flues; when necessary, the vapors are condensed in earthenware air condensers. Experience has shown that the production and liberation of acetic acid take place at a considerably lower temperature than that sufficient to convert the wood into charcoal, Squibb having proved that wood begins to char at 218.3° C. (425° F.); indeed, the wood which is removed from the retorts after the operation is over is sold as kindling wood, and has the color of black walnut. The crude acetic acid does not require the tedious method of purification usually employed, but is treated with soda ash, forming sodium acetate, which is decomposed by sulphuric acid, and the acetic acid recovered in a purified condition by distillation.

The sp. gr. of the different acetic acids increases with their strength up to the density of 1.0679 at $\frac{25°C.}{25°C.}$ (maximum), after which it decreases until it reaches 1.0472 at $\frac{25°C.}{25°C.}$, the density of the strongest acid (*glacial acid*).

It will be noticed, however, upon an examination of the official table (pp. 15–16) that the specific gravities of the glacial (100 per cent.) and the 39 per cent. acid are practically the same, and this applies also to the 74 and 81 per cent.; the 76, 77, and 78 per cent. acids have exactly the same density, the variations between 71 and 83 per cent. being very slight. It will thus be seen that specific gravity cannot be relied upon as a criterion for strength. The glacial acid may, however, be distinguished from the 39 per cent. acid by adding 10 per cent. of water, when, if the density increases, the specimen is the stronger acid.

Properties.—*Acetic acid* of the U. S. P. is described as "a clear, colorless liquid, having a strong, characteristic, vinegar-like odor, a sharply acid taste, and a strongly acid reaction. Acetic Acid is miscible with water or alcohol. Specific gravity: about 1.045 at 25° C. (77° F.). Add sufficient ammonia water to Acetic Acid to neutralize it or to leave the Acid in slight excess, and then add ferric chloride T.S.; a blood-red color develops which is discharged by strongly acidulating the liquid with sulphuric acid. Evaporate 20 mils of Acetic Acid to dryness on a water bath; not more than 0.002 Gm. of residue remains. Acetic Acid diluted with 20 volumes of distilled water does not respond to the Test for heavy metals (see Part III, Test No. 3). Separate portions of 1 mil each of Acetic Acid, diluted with 10 volumes of distilled water, show no turbidity on the addition of a few drops of barium chloride T.S. (*sulphuric acid*) nor any opalescence with a few drops of silver nitrate T. S. (*hydrochloric acid*). Supersaturate 5 mils of the Acid with 10 mils of ammonia water, add 5 mils of tenth-normal silver nitrate V.S. and boil the solution for one or two minutes; no dark deposit is produced (*formic or sulphurous acid*). Dilute 4 mils of the Acid, in a glass-stoppered bottle, with 20 mils of distilled water and add 0.5 mil of tenth-normal potassium permanganate V.S. The pink tint is not changed to brown at once, and does not become entirely brown or free from pinkish brown in less than half a minute (*empyreumatic substances*)." *U. S.*

ACIDUM ACETICUM DILUTUM. *U. S., Br. Diluted Acetic Acid.*—* "Acetic Acid, *one hundred and twenty grammes* [or 4 ounces av., 102 grains]; Distilled Water, *six hundred and ten grammes* [or 21 ounces av., 226 grains]; to make *seven hundred and thirty grammes* [or 25 ounces av., 328 grains]. Mix them." *U. S.*

"Acetic Acid, 152.6 grammes; Distilled Water, sufficient to produce 1000.0 millilitres. Mix." *Br.*

Properties. *Diluted Acetic Acid.*—"Specific gravity, about 1.008 at 25° C. (77° F.). It should respond to the tests of purity given under *Acidum Aceticum*. "It is miscible with water or alcohol. Diluted Acetic Acid responds to the tests for identity and purity under *Acidum Aceticum*, allowance being made for the difference in strength." *U. S.*

"Specific gravity 1.007. 20 millilitres require for neutralisation 16.7 millilitres of *N/1 solution of sodium hydroxide*. Free from the impurities indicated under 'Acidum Aceticum.'" *Br.*

"**Assay.**—Pour about 25 mils of Diluted Acetic Acid into a tared flask, weigh accurately, and titrate with normal potassium hydroxide V.S., using phenolphthalein T.S. as indicator. It shows not less than 5.8 nor more than 6.3 per cent. or $C_2H_4O_2$.

"Each mil of normal potassium hydroxide

V.S. used corresponds to 0.06003 Gm. of $C_2H_4O_2$. Each gramme of Diluted Acetic Acid corresponds to not less than 0.95 mil nor more than 1.05 mils of normal potassium hydroxide V.S." *U. S.*

The British Pharmacopœia requires that acetic acid shall be "a clear, colorless liquid with pungent odor, yielding, when neutralised with an alkali, the *reactions* characteristic of acetates. Specific gravity 1.044. Yields no residue on evaporation, and no characteristic *reactions* for copper, chlorides, nitrates, sulphates, or sulphites. Does not immediately darken in color when exactly neutralised with *solution of ammonia* and warmed with *solution of silver nitrate* (absence of formates). 5 millilitres require for neutralisation 28.7 millilitres of *N/1 solution of sodium hydroxide.* 2 millilitres do not completely decolorise a mixture of one drop of *solution of potassium permanganate* and 10 millilitres of *water* within half a minute (limit of empyreumatic matter). When tested for lead according to the quantitative method described in Appendix V, using 10 grammes in each Nessler glass, no difference in color is observed on the addition of the *solution of sodium sulphide* to one of the solutions (absence of lead). *Arsenic limit* 2 parts per million." *Br.*

Of the British acid (sp. gr. 1.044) the strength in hydrogen acetate is 33 per cent. The U. S. official acid is somewhat stronger than the British. In the arts *Acetic Acid No. 8* (sp. gr. 1.040) has long been used; it derives its name from the fact that one part added to sufficient water to make eight parts, by measure, constitutes so-called distilled vinegar, used in pickling; the latter is not equal to the official diluted acetic acid in strength (one-fifth weaker).

Calcium phosphate has been frequently detected in acetic acid sold as pure and was copiously precipitated by ammonia added in excess. (Bruchner, *A. J. P.*, Sept., 1870, p. 389.) Victor Meyer has met with glacial acetic acid contaminated with 0.108 Gm. furfurol in a liter. (*Ber. d. Chem. Ges.*, 1878, p. 1870.)

Charles F. Squibb has made numerous experiments proving the value of many strengths of acetic acid as menstrua for exhausting the valuable organic principles of drugs by percolation; he found even diluted acetic acid a reliable menstruum. J. P. Remington preferred a 10 per cent. acetic acid, and suggested a class of preparations termed "*acetracts*" to replace solid extracts. Acetic acid is a powerful solvent and can frequently be made to take the place of the more expensive alcoholic menstrua. (*A. J. P.*, 1897, p. 121.)

"**Assay.**—Pour about 6 mils of Acetic Acid into a tared flask, stopper and weigh accurately, dilute with 50 mils of distilled water, and titrate with normal potassium hydroxide V.S., using phenolphthalein T.S. as indicator. It shows not less than 36 per cent. nor more than 37 per cent. of $C_2H_4O_2$.

"Each mil of normal potassium hydroxide V.S. used corresponds to 0.06003 Gm. of $C_2H_4O_2$. Each gramme of Acetic Acid corresponds to not less than 6.00 mils nor more than 6.16 mils of normal potassium hydroxide V.S." *U. S.*

Uses. *Crude Pyroligneous Acid.*—This acid having been incidentally described as the source of the acetic acid of commerce, it may be proper in this place to notice its uses. It is an active disinfectant and stimulant, the former property being mainly due to the presence of creosote. It has been used as a local application to *gangrene* and ill-conditioned *ulcers.* Kolipinski recommends it internally in doses of one to two teaspoonfuls (3.75–7.5 mils) three times a day in the treatment of *arthritis deformans.* (*Trans. American Therap. Soc.*, 1907.) It has also been suggested for the preservation of food-stuffs, especially meat and fish. Its use, however, is specifically prohibited by the food laws of most states.

Glacial Acetic Acid.—Glacial acetic acid has been employed externally as a vesicant and as a caustic. For the former purpose it may be applied by means of a blotting paper moistened with the acid. It requires, however, considerable carefulness in its use and is generally inferior to cantharides. As an escharotic it is useful for the destruction of *warts* and *corns,* but has been largely replaced by the trichloracetic acid (see p. 82).

Strong acetic acid is also a useful agent for detecting small quantities of albumin and is widely used in the examination of urine, especially in conjunction with potassium ferrocyanide.

Diluted Acetic Acid.—The object of making diluted acetic acid official is to possess a weak solution of *pure* acetic acid which may be substituted for distilled vinegar in all formulas in which accuracy is required. For a long period diluted acetic acid has been made by mixing one part of acetic acid with seven parts of water by measure. *Acetic Acid No. 8* is the commercial designation of an acid of 30 per cent. strength. The official diluted acid was made considerably stronger in the U. S. P., 1880, and the strength has not been altered in the subsequent revisions. Distilled vinegar contains a little organic matter, which is always darkened or precipitated when its acid is saturated with an alkali, a change which does not take place when diluted acetic acid is employed.

Either in the form of the official diluted acetic acid or in the form of vinegar, acetic acid is useful as a refrigerant drink in febrile conditions. As it is entirely oxidized in the system, escaping through the breath as carbonic acid, it does not tend to increase the acidity of the urine. It is also of service as an astringent and styptic. As an emergency remedy it may prove life-saving in *hemorrhage* from the stomach or uterus. For the former condition the diluted acetic acid should be further weakened by the addition of one or two parts of water, and this mixture taken in doses of a tablespoonful every few

minutes. Owing to its volatility and pungency the vapor of acetic acid is frequently applied to the nostrils as an excitant in *syncope* or *headache* as a substitute for smelling salts. Used in this manner it has been recommended for the purpose of quieting post-anesthetic *nausea.*

Acetic acid is incompatible with carbonates, free chlorine, and ferric salts, the latter producing a deep red color which is destroyed by excess of mineral acids.

Dose, of diluted acetic acid, twenty to sixty minims (1.3–3.9 mils).

Off. Prep.—From *Acetic Acid,* Acidum Aceticum Dilutum, *U. S.;* Acetum Aromaticum, *N. F.;* Linimentum Terebinthinæ Aceticum, *N. F.* From *Glacial Acetic Acid,* Linimentum Terebinthinæ Aceticum, *Br.*

ACIDUM ACETYLSALICYLICUM. Br.

ACETYLSALICYLIC ACID

(ăc'ĭ-dŭm ă-cē'tyl-să-lĭ-cĭl'ĭ-cŭm)

"Acetylsalicylic Acid, $C_9H_8O_4$, may be obtained by the action of acetic anhydride or of acetyl chloride on salicylic acid." *Br.*

Aspirin; Acidum Acetylosalicylicum.

This acid was not introduced into the U. S. P. IX under the name of *Aspirin,* as this name is the property of the Farbenfabriken Company, of Leverkusen, Germany. The patent expired in 1917. It is made by heating together 50 parts of salicylic acid and 75 parts of anhydrous acetic acid at about 150° C. (302° F.). It is then purified by recrystallization. The British Pharmacopœia described acetylsalicylic acid as follows: "A white, crystalline powder; taste slightly acid. Sparingly soluble in *water;* soluble in 5 parts of *alcohol* (90 per cent.); soluble in *ether.* Melting point from 133° to 135° C. (271.4°–275° F.). When 0.5 gramme is boiled for two or three minutes with 10 millilitres of *solution of sodium hydroxide* and to the cooled solution excess of *diluted sulphuric acid* is added, a crystalline precipitate is produced which, after washing and drying, responds to the tests described under 'Acidum Salicylicum,' and the filtrate, after neutralisation, yields the *reactions* characteristic of acetates. When 0.5 gramme is shaken with 20 millilitres of *water* and 1 drop of *T. Sol. of ferric chloride* is added, no violet coloration is produced (absence of salicylic acid). *Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million. No appreciable ash." *Br.*

Uses.—Although it has been shown that salicylic acid occurs in the urine within from twenty minutes to half an hour after the ingestion of acetylsalicylic acid, there is strong reason to believe that the drug circulates in the blood in large part unbroken; in other words, the action is not purely that of salicylic acid but there is also a different effect of acetylsalicylic acid. In the first place Christone and Lapresa (*P. J.,* lxxxv) have found that it requires forty minutes for the decomposition of acetylsalicylic acid by the gastric juice and that its toxicity is three times as great as that of sodium salicylate. Moreover, there have been reported a very considerable number of cases of acetylsalicylic acid poisoning in human beings with symptoms very different from those caused by the salicylates and in many of these cases of poisoning the dosage has been so small as to practically exclude salicylic acid poisoning; in a case reported by Graham (*J. A. M. A.,* 1911), after two doses of five grains each there occurred marked cardiac weakness with pulse rate of 136 and edematous swelling of the face and mucous membranes with eversion of the lids and lips from the swelling. In the third place, clinical experience has demonstrated that the range of therapeutic usefulness of acetylsalicylic acid is not the same as that of the salicylates.

Acetylsalicylic acid has been used in medicine (1) as an antirheumatic, (2) as an analgesic, (3) as an antipyretic, (4) locally.

In *inflammatory rheumatism,* while often of service, it is generally of less value than ammonium or sodium salicylate. On the other hand, in those *myalgias* or *neuralgias* of dubious origin commonly diagnosed as *chronic rheumatism,* acetylsalicylic acid is often of great usefulness. In a general way it may be said that the more nearly these types of pain approach to true rheumatism the more likely it is that sodium salicylate will be a superior drug to acetylsalicylic acid. As an analgesic acetylsalicylic acid comes in competition with acetanilid and other coal tars for the relief of *headaches, neuritis,* and similar painful conditions. As an antipyretic, as has been shown by Chambers (*B. M. J.,* 1912), Bondi (*Th. M.,* 1911, p. 179) and others, it far exceeds the salicylates in power. It has been used for the reduction of the temperature in *typhoid fever* and *rheumatic fever* but in some cases it is liable to produce serious collapse. Locally it has been recommended by Fetterolf (*T. G.,* November, 1908) in *acute tonsillitis* and has also been employed to a lesser extent in *eczema* and other *skin diseases.*

Overdoses of acetylsalicylic acid commonly produce ringing in the ears as do the inorganic salicylates. Frequently, however, even in quantities not excessive it produces a very different type of intoxication. Among the most common symptoms are profuse sweating, cold extremities, either with or without a fall in body temperature, rapid or irregular pulse and occasionally albuminuria. In many reported cases there has been marked facial edema involving not only the skin but the mucous membrane of the mouth and throat.

Acetylsalicylic acid is incompatible with alkalies which convert it into sodium salicylate. It is said to produce the poisonous substance *quinotoxin* when combined with quinine compounds under certain conditions which are not clearly understood.

The *dose* of acetylsalicylic acid is from five to fifteen grains (0.32–1.0 Gm.).

ACIDUM BENZOICUM. U. S., Br.

BENZOIC ACID Acid. Benz.

(ăc'ĭ-dŭm bĕn-zō'ĭ-cŭm)

"An organic acid obtained from benzoin, or prepared synthetically. It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99.5 per cent. of $C_7H_6O_2$ or $C_6H_5.COOH$ (122.05). Preserve it in well-closed containers, in a cool place, protected from light." *U. S.*

"Benzoic Acid, $HC_7H_5O_2$, may be obtained from benzoin, or prepared synthetically." *Br.*

Acidum Benzoicum Sublimatum, Flores Benzoes; Flowers of Benzoin; Flowers of Benjamin; Acide benzoïque; Fleurs de Benjoin, *Fr.*; Acidum Benzoïcum, *P. G.*; Benzoesäure, Benzoeblümen, *G.*; Acido benzoico, *It., Sp.*

Both the U. S. and Br. Pharmacopœias have omitted processes for the preparation of benzoic acid.

Formerly the benzoin before sublimation was mixed with sand; but this is now usually omitted, as not only useless, but probably injurious by favoring the production of empyreumatic substances. The acid, which exists in the benzoin combined with resin, is volatilized by the heat, and condensed in the upper part of the apparatus. Unless the temperature be very carefully regulated, a portion of the resin is decomposed, and an oily substance generated, which rises with the acid, and gives it a brown color, from which it cannot be entirely freed by bibulous paper; and this result, even with the greatest caution, sometimes takes place. The process for subliming benzoic acid may be conducted in a glazed earthenware vessel, capped by a cone of paper, or by another vessel with a small opening at the top, and a band of paper pasted round the place of junction. After the heat has been applied for an hour, the process should be suspended until the sublimed acid is removed from the upper vessel or paper cone, when it may be renewed, and the acid again removed, and thus alternately until colored vapors rise. Mohr, after experimenting, recommended the following plan as unobjectionable. In a round cast iron vessel, eight or nine inches in diameter and two inches deep, a pound or less of coarsely powdered benzoin is placed, and uniformly strewed over the bottom. The top of the vessel is closed by a sheet of bibulous paper, which is secured to the sides by paste. A cylinder of thick paper in the form of a hat, just large enough to fit closely around the sides of the pot, is then placed over it, and in like manner secured by paste. A moderate heat is now applied by means of a sand bath, and continued for three or four hours. The vapors pass through the bibulous paper, which absorbs the empyreumatic oil, and are condensed within the hat in brilliant white flowers, having an agreeable odor of benzoin. (*Ann. Pharm.*, xxix, 178.) The process official in U. S. P. 1870 was based upon Mohr's, but it frequently happens that the sublimed crystals, after they have formed in the cap, and while the sublimation is still going on, fall upon the bibulous paper, and if this paper should happen to be heated to only 120° C. (248° F.) the crystals will melt, and soon stop up the pores of the paper. If coarse muslin be substituted for the bibulous paper, it serves the purpose of retaining any empyreumatic substances, and yet permitting the vapors to pass through without becoming glazed by a deposit of melted acid. Strips of paper passed at irregular intervals across the cap prevent the falling back of crystals. The remaining acid of the benzoin may be extracted, if deemed advisable, by treating the residue of the benzoin with lime or sodium carbonate. From the mode of preparing benzoic acid by sublimation, it was formerly called *flowers of benzoin* or flowers of Benjamin.

Another mode of separating the acid from benzoin is by combining it with a salifiable base and precipitating with an acid. Such is the process of Scheele. It consists in boiling the powdered benzoin with calcium hydroxide and water, filtering the solution of calcium benzoate thus obtained, and precipitating the benzoic acid with hydrochloric acid. In order to get the benzoic acid in the ordinary form, it has been proposed to sublime the acid after its precipitation.

Several other modes of extracting the acid have been recommended. The following is the process of Stolze. One part of the benzoin is dissolved in three parts of alcohol, the solution filtered and introduced into a retort, and the acid saturated by sodium carbonate dissolved in a mixture of eight parts of water and three of alcohol. The alcohol is distilled off and the sodium benzoate contained in the residuary liquid is decomposed by sulphuric acid, which precipitates the benzoic acid. This is purified by solution in boiling water, which lets fall the acid when it cools. By this process Stolze obtained 18 per cent. of acid from benzoin containing 19.425 per cent. By the process of Scheele he obtained 13.5 per cent.; by the agency of sodium carbonate, 12 per cent.; by sublimation, only 7.6 per cent. Scharling prepared benzoic acid by means of heated steam, and obtained 8 per cent. (*A. J. P.*, xxiv, 236.)

The acid is manufactured very cheaply by synthetic methods. The two processes most commonly employed both start with *toluene*, $C_6H_5CH_3$. In the first method the toluene is changed to benzotrichloride, $C_6H_5.CCl_3$, and this, heated with water to 150° C. (302° F.) in closed vessels, generates benzoic acid according to the reaction:

$$C_6H_5.CCl_3 + 2H_2O = C_6H_5.COOH + 3HCl$$

In the second method the benzoic acid is obtained as a by-product in making benzaldehyde from toluene (see *Benzaldehydum*, p. 223); in the process of manufacturing much of the benzaldehyde is converted into benzoyl alcohol and calcium benzoate by the excess of lime used. This latter salt is then treated with hydrochloric

acid, and the benzoic acid thus set free. This acid is frequently resublimed in contact with benzoin, in order to give it the vanilla-like odor of the acid sublimed from the gum. A method of making benzoic acid from tannin or gallic acid is described in *Ph. Era*, 1892, 172. P. Schulze produced benzoic acid by heating benzal chloride or benzotrichloride in the presence of ferric benzoate or metallic iron. The process is patented. (*Ph. Centralh.*, 1896, 221.)

Under the name of *German benzoic acid*, there was at one time imported into the United States benzoic acid prepared from the urine of cattle and horses by treating it with milk of lime and boiling the calcium hippurate with hydrochloric acid. By boiling the hippuric acid thus separated, with hydrochloric acid, it is split into benzoic acid and glycocoll, according to the reaction:

$$C_9H_9NO_3 + H_2O = C_2H_5NO_2 + C_7H_6O_2$$

It is white, has a fine luster, and is said to be very pure, but sometimes has a slight urinous odor indicative of its origin. (*A. J. P.*, xxvii, 23; *P. J.*, July, 1875.) Owing to the scarcity in the market of benzoin yielding paying quantities of benzoic acid, it was asserted that the English manufacturers used certain varieties of Botany Bay gum (see *Gum acroides*, Part II), and obtained a larger yield of an acid which was at one time regarded as cinnamic, but has been shown to be benzoic acid. (*N. R.*, Feb., 1879.) The name *German Benzoic Acid* is the present commercial designation for the synthetic acid from coal tar, while the name *English Benzoic Acid* is applied exclusively to the acid of natural origin.

Properties.—Sublimed benzoic acid is in "lustrous scales or friable needles. The synthetic Acid is white, odorless, or with a slight odor of benzaldehyde; the natural Acid is white or yellowish, acquires a darker color on exposure to light, and has a slight odor of benzoin. Benzoic Acid has a pungent taste, is somewhat volatile at moderately warm temperatures and freely volatile with steam. One Gm. of Benzoic Acid dissolves in 275 mils of water, 2.3 mils of alcohol, 4.5 mils of chloroform, 3 mils of ether, in 10 mils of benzene and in 23 mils of oil of turpentine at 25° C. (77° F.); also in 18 mils of boiling water, 1.5 mils of boiling alcohol, and in fixed or volatile oils. A saturated aqueous solution of Benzoic Acid is acid to litmus. It melts between 120° and 122° C. (248° and 251.6° F.). Benzoic Acid is freely dissolved by solutions of the alkali hydroxides; neutralize such a solution carefully and add ferric chloride T.S., previously diluted with 2 volumes of distilled water and neutralize, if necessary, with ammonia water; a pink precipitate of ferric benzoate is produced. Incinerate about 2 Gm. of Benzoic Acid; not more than 0.05 per cent. of the ash remains. A solution of about 0.1 Gm. of the synthetic Acid in 2 mils of sulphuric acid does not become darker than light yellow, when warmed for five minutes at 50° C. (122° F.). The color produced by the Acid from benzoin tested in the same manner, does not become darker than light brown (*readily carbonizable impurities*). Mix 0.5 Gm. of the Acid and about 1 Gm. of calcium carbonate (free from chloride) with a little distilled water in a crucible, dry the mixture and incinerate it at a low red heat. Dissolve the residue in 25 mils of diluted nitric acid (free from chloride) and filter. If the synthetic Acid is being tested, the addition of 0.5 mil of silver nitrate T.S. to the filtrate does not produce a greater turbidity than is produced by the same quantity of the reagent in a mixture of 25 mils of distilled water and 0.1 mil of tenth-normal hydrochloric acid V.S. If the Acid from benzoin is being tested, the turbidity is not greater than that produced by the same quantity of reagent in a mixture of 25 mils of distilled water and 0.05 mil of tenth-normal hydrochloric acid V.S. (*chlorine*). Warm 0.5 Gm. of the Acid with 5 mils of distilled water and 0.5 Gm. of potassium permanganate in a loosely-stoppered test tube, and place it in a water bath, heated to about 45° C. (113° F.), for ten minutes. Stopper the test tube tightly and allow it to cool. On removing the stopper, no odor of benzaldehyde is perceptible (*cinnamic acid*)." *U. S.*

"**Assay.**—Dissolve about 0.5 Gm. of Benzoic Acid, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed, in 25 mils of diluted alcohol which has been previously neutralized with tenth-normal potassium hydroxide V.S., phenolphthalein T.S. being used as indicator. Titrate this solution with tenth-normal barium hydroxide V.S., using phenolphthalein T.S. as indicator. It shows, in the dried acid, not less than 99.5 per cent. of $C_7H_6O_2$.

"Each mil of tenth-normal barium hydroxide V.S. used corresponds to 0.012205 Gm. of $C_7H_6O_2$. Each gramme of Benzoic Acid, previously dried, corresponds to not less than 81.5 mils of tenth-normal barium hydroxide V.S." *U. S.*

"Soluble in 450 parts of *water*, in 3 of *alcohol* (90 per cent.), in 2.5 of *ether*, and in 7 of *chloroform*. Melting point 121.5° C. (250.7° F.), but if sublimed from benzoin about 120° C. (248° F.). Heated in a dry test-tube it melts and sublimes leaving only a slight residue. Volatilises in the vapor of *water*. The solution obtained by gently warming 0.2 gramme with 20 millilitres of *water* and 1 millilitre of *N/1 solution of sodium hydroxide* and filtering yields a pale reddish precipitate with *T. Sol. of ferric chloride*. When 0.5 gramme is heated in a closed crucible with twice its weight of *calcium carbonate*, the mass dissolved in *diluted nitric acid*, and *solution of silver nitrate added*, not more than the slightest cloudiness results (absence of chlorobenzoic acid). Yields no characteristic *reactions* for oxalates. Does not develop the odor of benzaldehyde when warmed with its own weight of *potassium permanganate* and ten times its own

weight of *diluted sulphuric acid* (absence of cinnamic acid). *Arsenic limit* 2 parts per million." *Br.*

It is entirely soluble in solutions of potassium, sodium, or ammonium hydroxides, from which it is precipitated by hydrochloric acid. On carefully neutralizing any of these solutions and adding solution of ferric sulphate previously diluted with water, a flesh-colored precipitate is produced. Its solution reddens litmus paper, and with salifiable bases it forms salts called benzoates.

Benzoic acid is a characteristic constituent of the balsams, and has been found in vegetable and animal products. When heated, it should sublime without residue; but the Br. Pharm. allows a slight residue for impurities.

Potassium permanganate has been depended upon more than any other reagent to distinguish between benzoic acids as obtained from different sources. Schacht proposes the following test: If 3 grains of benzoic acid be dissolved in 96 minims of solution of potassium hydroxide, sp. gr. 1.777, diluted with 96 minims of distilled water, and 10 drops of a solution made by dissolving 1 grain of potassium permanganate in 200 grains of water be added to it and the whole heated to boiling, dark green liquids (in which brown precipitates gradually appear) are produced if the benzoic acid be obtained from urine, from toluene, or from commercial benzoin, while if the benzoic acid be from Siam benzoin (sublimed or made by wet process) decoloration of the liquids and brown precipitates are produced, due to the presence of cinnamic acid. (*Ph. Centralh.*, 1881, 565.) The odor of bitter almonds confirms the presence of cinnamic acid. Essell (*Ph. Ztg.*, 1904, 272) modifies this test to secure greater accuracy as follows: 0.2 Gm. of the *finely* powdered benzoic acid and 5 mils of tenth-normal permanganate solution are mixed in a test tube of wide diameter and securely corked. When the red color is discharged (usually after a few minutes) 5 mils more of tenth-normal permanganate solution are added, and the tube is set aside from fifteen to thirty minutes, with frequent shaking. If then the cork be removed the odor of benzaldehyde will be strongly perceptible in the presence of 5 per cent. of cinnamic acid, and distinctly recognizable if only 1 per cent. is present. It is claimed that benzoic acid from benzoin can be distinguished from that from other sources by adding resorcinol and sulphuric acid to the alcoholic solution of the acid; the benzoin-benzoic acid gives a beautiful red color, due probably to a trace of vanillin or other aldehyde in the natural product. (Göldner, *Ph. Ztg.*, 1892, 697.)

Uses.—When benzoic acid is taken into the system it appears in the urine chiefly as hippuric acid. This conversion would appear to take place in the kidneys, since, after the exhibition of large doses, benzoic and not hippuric acid can be detected in the blood, while even small amounts of hippuric acid injected into the blood produce violent poisoning. Moreover, Bunge and Schmiedeberg have succeeded in converting benzoic acid into hippuric acid by passing blood containing benzoic acid slowly through the kidneys immediately after their removal from the body. In rare cases, according to Meissner and Shepard, the benzoic acid is converted into succinic instead of hippuric acid. When it is given very freely a portion of the benzoic acid escapes unchanged. Where the nitrogen necessary for the conversion of the benzoic into hippuric acid comes from, is at present unknown. A priori it would seem probable that the source of this nitrogen was the urea, but the testimony as to the effect of benzoic acid upon the urea and uric acid excretion is contradictory. The most recent investigations indicate that benzoic acid has practically no effect on the elimination of either urea or uric acid, although Denis (*J. P. Ex. T.*, 1915, vii, 601) finds that in large doses the output of uric acid is increased.

The only advantageous uses of benzoic acid as a remedy are connected with its antibacterial properties. As small quantities as one part in a thousand have a distinctly inhibiting action on the growth of many micro-organisms, and in somewhat stronger solution it is actively germicidal. It is a popular ingredient in many of the supposedly antiseptic mouth washes. It has also been used internally as a urinary antiseptic but because of its irritant action upon the stomach is much better administered for such purpose in the form of one of its salts. For a discussion of the use of benzoic acid as a food preservative, see *Sodii Benzoas.*

Benzoic acid is incompatible with salts of iron, silver, lead, and mercury. It precipitates a solution of quinine sulphate and is decomposed by hydrogen dioxide in the presence of inorganic acids with the production of salicylic acid.

Dose, ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Tinctura Opii Ammoniata, *Br.;* Tinctura Opii Camphorata, *U. S.* (*Br.*); Trochiscus Acidi Benzoici, *Br.;* Nebula Aromatica, *N. F.*

ACIDUM BORICUM. U. S., Br.

BORIC ACID Acid. Bor. [Boracic Acid]

(ăç'ĭ-dŭm bō'rĭ-cŭm)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99.5 per cent. of H_3BO_3 (62.02)." *U. S.* "Boric Acid may be obtained by the interaction of sulphuric acid and borax, and contains not less than 99.5 per cent. of orthoboric acid, H_3BO_3." *Br.*

Hydrogen Borate; Acidum Boracicum; Boracic Acid, Acide Borique Cristallisé, *Fr. Cod.;* Acidum Boricum. *P. G.;* Borsäure, *G.;* Acido borico, *It., Sp.*

Boric acid occurs in small amount, most probably in combination as a magnesium salt, in sea water and in certain mineral waters, as the hot springs of Wiesbaden, Aix-la-Chapelle, and Vichy; in certain mineral substances, such as the *borocalcite* which occurs in considerable quantities in the niter beds of Chili; in the

natural borax or *tincal*, first found in the basins of dried-up lagoons in Central Asia, and afterwards in large amount in Clear Lake, California; in *ulexite* (sodium and calcium borate) and *colemanite* (calcium borate). The last of these minerals yields by far the largest amount of the boric acid now obtained on the Pacific coast. It is found in a large vein deposit in San Bernardino County, California, where it is mined and shipped to the works of the Borax Consolidated Co. (Limited), at Alameda, California. Boric acid itself is extracted, under the name of *sassolin*, from the lagoons of the volcanic districts of Tuscany, and from the crater of Vulcano, one of the Lipari Islands.

Preparation.—In the neighborhood of Monte Rotondo, Lago Zolforeo, Sasso, and Larderello are found numerous hillocks and fissures, the latter of which emit hot aqueous vapor containing boric acid and certain gases. Around one or several of these fissures, called *suffioni*, a circular basin of masonry is built, which is filled with water and called a lagoon. By the jets of vapor constantly breaking through it, the water becomes gradually impregnated with boric acid and heated. A series of such lagoons are made to communicate with each other on the declivity of a hill, and the lowest to discharge itself into a reservoir, where the solution is allowed to rest and deposit mechanical impurities. From this reservoir the solution is made to pass into leaden evaporating pans, heated by the natural vapor, where it is sufficiently concentrated to fit it for being conducted into wooden tubs, where it is allowed to cool and crystallize. The crude acid thus obtained contains from 74 to 84 per cent. of boric acid, the impurities consisting chiefly of alum, the double ammonium and magnesium sulphate, and calcium sulphate. The production of Tuscan boric acid for the year 1913 was stated to be 2763 metric tons, while that for 1914 amounted to 2410 metric tons.

Considerable amounts of a calcium borate known as *pandermite* are produced in Turkey, but the chief foreign producer at present is Chile, from which country 43,356 metric tons were obtained in 1913.

The native borax minerals of California supply, at present, the entire American demand for boric acid. Boric acid is obtained from borax by acidulating a hot saturated solution of borax with hydrochloric or sulphuric acid. Upon cooling the mixture, crystals of boric acid separate from the more soluble sodium chloride or sulphate. The crystals thus obtained may be purified by recrystallization from water and if a small amount of albuminous matter be added before crystallizing, large, light, shining crystalline scales of the acid may be obtained. The American production of refined borax including boric acid for the year 1915 was 67,004 tons of 2000 lbs. each. The production of boric acid in the United States for the year 1914 was 8,590,310 lbs.

Properties.—"Boric Acid occurs in transparent, colorless scales, of a somewhat pearly luster, as six-sided, triclinic crystals, or as a white, bulky powder, slightly unctuous to the touch; odorless, having a faintly bitter taste; permanent in the air. One Gm. of Boric Acid dissolves in 18 mils of water, 18 mils of alcohol, and in 4 mils of glycerin at 25° C. (77° F.); also in 4 mils of water and 10 mils of boiling alcohol. When heated to 100° C. (212° F.), Boric Acid loses water, forming metaboric acid (hydrogen metaborate, HBO_2), which slowly volatilizes at that temperature. Heated to about 160° C. (320° F.), Boric Acid fuses to a glassy mass of tetraboric or pyroboric acid (hydrogen tetraborate, $H_2B_4O_7$); at a higher temperature the fused mass swells, loses all of its water, and becomes boron trioxide (B_2O_3), which fuses into a transparent, non-volatile, hygroscopic mass. Boric Acid volatilizes from a boiling aqueous or alcoholic solution. Its solution in alcohol or glycerin, when ignited, burns with a flame enveloped by a green mantle. An aqueous solution of Boric Acid (1 in 50) is slightly acid to litmus. Turmeric paper moistened with such a solution, to which a little hydrochloric acid T.S. has been added, becomes reddish-brown on drying, this color being changed to greenish-black by ammonia water. One Gm. of Boric Acid dissolves completely in 10 mils of boiling alcohol. An aqueous solution of the Acid does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of Boric Acid meets the requirements of the Test for arsenic (see Part III, Test No. 1)." *U. S.*

"Soluble in 25 parts of *water*, in 4 of *glycerin*, and in 30 of *alcohol* (90 per cent.), the solutions being clear. *Turmeric paper* moistened with an aqueous solution slightly acidified with *hydrochloric acid* becomes brownish-red on gently drying, and this color changes to a greenish-black on the addition of *solution of potassium hydroxide*. The alcoholic solution burns with a flame tinged with green. 1 gramme dissolved in a mixture of 25 millilitres of *water* and 20 millilitres of *glycerin* requires for neutralisation not less than 16.0 millilitres of *N/1 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator. Yields no characteristic *reactions* for copper, and not more than the slightest *reactions* for iron, calcium, magnesium, chlorides, or sulphates. *Lead limit* 25 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Boric acid has a sp. gr. of 1.434, dissolves in three parts of boiling water and in volatile oils, but is insoluble in ether. On evaporation of the alcoholic solution, the boric acid volatilizes even more readily than from the aqueous solution. Glycerin, when heated, dissolves a very large quantity of boric acid. (See *Glyceritum Boroglycerini*, U. S.; also *Boroglyceride*, Part II.) Its aqueous solution tastes somewhat acid, colors litmus paper a wine red, and changes turmeric paper to a brown color, analogous to that pro-

duced by alkalies, even when hydrochloric acid is present. On moistening the paper so browned and then dried with caustic alkali solution, it turns first blue and then a dirty gray color. Cassol and Gerraus (*Chem. News,* 1903, 27) use *curcumin* with oxalic acid for determining the presence of boric acid when used as a preservative for foods.

Boric acid is a weak acid, or may even act as a base. Thus, with sulphuric and phosphoric acids it forms compounds which may be considered as salts. Its compounds with bases, when in solution, are readily decomposed by other acids, but at red heat boric oxide will displace many of the stronger but more volatile acids.

Boric acid requires 18 parts of cold water to dissolve it, and this fact has led to many attempts to increase its solubility without interfering with its usefulness. The use of glycerin has been officially sanctioned. Scholz and Mansier recommended the use of magnesium carbonate (11 per cent.), but such an addition is not always permissible. When equal parts of boric acid and borax are dissolved in boiling water a crystalline mass separates on cooling, which has been termed *boro-borax.* Its advantages are increased solubility and neutral reaction. The remarkable volatility of boric acid when in alcoholic solution has been observed by Schneider and the fact utilized in its quantitative determination. (*Zeit. Oest. Apoth. Ver.,* 1896, 791.)

"**Assay.**—Dissolve about 2.5 Gm. of Boric Acid, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed, in 50 mils of distilled water and 50 mils of glycerin and titrate with normal sodium hydroxide V.S., phenolphthalein T.S. being used as indicator. It shows, in the dried acid, not less than 99.5 per cent. of H_3BO_3.

"Each mil of normal sodium hydroxide V.S. used corresponds to 0.06202 Gm. of H_3BO_3. Each gramme of Boric Acid, previously dried, corresponds to not less than 16.04 mils of normal sodium hydroxide V.S." *U. S.*

Uses.—Boric acid in single dose is about as near physiologically inert as a substance can be, indeed, the assertion has been made on reputable authority that, in the frog, at least, it is less poisonous than sodium chloride. In very large doses, however, it has some depressant action upon the spinal centers. When taken by the mouth it is absorbed, somewhat slowly but completely, and eliminated unchanged through the kidney. According to Rost (*A. I. P. T.,* xv, p. 291) it may be detected in the urine for some days after a single dose and when taken repeatedly tends to accumulate in the system.

Although it has been abundantly shown that boric acid has no germicidal effect, in concentrated solutions it is distinctly antiseptic. Because of freedom from toxic properties or local irritant influence its solution is widely used as a detergent wash in inflammations of mucous membranes, such as *rhinitis, conjunctivitis,* and *stomatitis.* It is also useful as an internal antiseptic in *fermentative cystitis.* It differs from most urinary antiseptics in that it is almost as efficacious in alkaline as in acid urine and has the further advantage that it tends to restore the acidity. As a surgical antiseptic it is too feeble to be of any use. Internally it has from time to time been recommended in the treatment of *epilepsy* but is probably without value.

Boric acid and the borates have been used to a considerable extent as food preservatives and there has waged an acrimonious dispute as to their harmfulness when used for this purpose. Although as mentioned above their toxicity is very low, yet there have been reported a few cases in which death was apparently induced from washing out internal cavities with solutions of boric acid. These instances, however, are so rare and the dose of boron ingested probably so large as to have little bearing on the harmfulness of the boric acid food preservatives. A considerable number of cases of skin eruptions have been reported from the continued use of the boron derivatives over long periods of time. It must be acknowledged, however, that even in these cases the quantity ingested has been larger than would be at all probable from the use of any food containing it. The question of whether or not its use in smaller quantities over long periods of time is injurious can scarcely be considered as definitely settled, but in the elaborate investigation of the U. S. Department of Agriculture under H. A. Wiley, it was found that quantities of less than 0.5 Gm. daily, if continued over long periods of time, caused disturbances of digestion and assimilation. The question, however, is not merely whether it is theoretically possible for boric acid used in the preservation of food to have an injurious action upon the system, but whether the danger from this preservative is any greater than from other agents which are used for the same purpose. Certainly if it is possible to obtain undecomposed food free from preservatives they are preferable, but we do not believe that boric acid is any more injurious to the system than, for instance, is saltpeter.

For the detection of boric acid in food products, see *Chem. News,* 1903, 27; *A. Pharm.,* 1904, 194; *J. Am. C. S.,* 1904, 91.

The tendency of the crystals of boric acid to slip from under the pestle renders the process of pulverization very tedious. It is essential that the acid be in an impalpable powder when it is desired to make an ointment. The gradual addition of ether to the acid has been suggested as a valuable aid to trituration. Manufacturers at the present time supply boric acid made by precipitation in an impalpable powder. Boric acid ointment (Lister's) is made from one part each of boric acid and white wax, and two parts each of oil of sweet almond and paraffin.

The only important incompatibility of boric acid is the fact that in combination with salicylic acid it sometimes acts as an alkaloidal

precipitant. A solution containing two and one-half grains of boric acid and one-fourth grain of salicylic acid to the fluidounce will precipitate quinine, strychnine, and other alkaloids.

Dose, of boric acid, five to twenty grains (0.32–1.2 Gm.).

Off. Prep.—Glyceritum Boroglycerini, *U. S.* (*Br.*); Liquor Antisepticus, *N. F.;* Unguentum Acidi Borici, *U. S., Br.;* Cataplasma Kaolini, *N. F.;* Liquor Antisepticus, *N. F.;* Pulvis Antisepticus, *N. F.;* Pulvis Talci Compositus, *N. F.*

ACIDUM CITRICUM. U. S., Br.

CITRIC ACID Acid. Cit.

(ăç'ĭ-dŭm cĭt'rĭ-cŭm)

"A tribasic organic acid usually obtained from the juice of limes or lemons. It contains not less than 99.5 per cent. of $C_6H_8O_7 + H_2O$ or $C_3H_4(OH)(COOH)_3 + H_2O$ (210.08). Preserve it in well-closed containers." *U. S.* "Citric Acid may be obtained from the juice of the fruit of various species of Citrus, and contains not less than 99.5 per cent. of hydrogen citrate, $H_3C_6H_5O_7,H_2O$." *Br.*

Acidum Citri, s. Limonis, s. Limonum, s. Limonorum; Acide citrique, *Fr. Cod.;* Acide du Citron, *Fr.;* Acidum citricum, *P. G.;* Citronensäure, Citronsäure, *G.;* Acido citrico, *It., Sp.*

Citric acid is the peculiar acid to which limes and lemons owe their sourness. It is present also in the juice of other fruits, such as the cranberry, the red whortleberry, the berry of the bittersweet, the red gooseberry, the currant, the strawberry, the raspberry, the tamarind, and the red elderberry (fruit of *Sambucus pubens*). The latter berry contains citric acid so abundantly that it has been proposed as a source of the acid by Thibierge, of Versailles. It is contained also largely in the fruit of *Cyphomandra betacea,* a solanaceous plant, indigenous in Mexico, Peru, and other parts of South America, where it is called *tomato de la paz.* Citric acid is now known to be a normal constituent of fresh, whole cows' milk; the amount present is about 0.19 Gm. per 100 mils, and it may be estimated by a method given in *Arch. Chem. Micros.,* 1915, viii, 120. The commercial source of citric acid is lime, lemon, and bergamot juice; large quantities of *lime juice* are made in Sicily, concentrated, and exported to England and the United States. Citric acid, which was formerly imported in large quantities from Great Britain, is now made extensively in the United States.

The acid is extracted from lemon or lime juice by a very simple process, for which we are indebted to Scheele; it is one requiring some careful manipulation. The boiling juice is first completely saturated with calcium carbonate (chalk or whiting) in fine powder, and the calcium citrate thus formed is allowed to subside. This is then washed repeatedly with water, and decomposed by diluted sulphuric acid. An insoluble calcium sulphate is precipitated, and the disengaged citric acid remains in solution. This is carefully concentrated in leaden boilers, until a pellicle begins to form, when it is transferred to other vessels to cool and crystallize.

The commercial lemon juices contain free citric acid; free acids other than citric; citrates, salts of organic acids other than citric; salts of inorganic acids; and albuminous, mucilaginous, saccharine, and other indifferent bodies. Spirit is frequently added as a preservative, and mineral acids are not uncommonly employed as adulterants, although sulphur dioxide is more commonly used for this purpose and its presence is usually declared upon the label. Verjuice has also been used for the purpose (Allen). See *Limonis Succus,* also *Montserrat lime juice, P. J.,* 1883, p. 606, and notes on manufacture, *N. R.,* 1883, 47.

Preparation.—In the U. S. Pharmacopœia, very properly, no process is given for making citric acid, as it is always purchased from the manufacturing chemist. The former British Pharmacopœia gave the following process for preparing it:

"Take of Lemon Juice *four pints* [Imperial measure]; Prepared Chalk *four ounces and a half* [avoirdupois]; Sulphuric Acid *two fluidounces and a half;* Distilled Water, *a sufficiency.* Heat the Lemon Juice to its boiling point, and add the Chalk by degrees till there is no more effervescence. Collect the deposit on a calico filter, and wash it with hot water till the filtered liquor passes from it colorless. Mix the deposit with a pint [Imp. meas.] of Distilled Water, and gradually add the Sulphuric Acid previously diluted with a pint and a half [Imp. meas.] of Distilled Water. Boil gently for half an hour, keeping the mixture constantly stirred. Separate the acid solution by filtration, wash the insoluble matter with a little Distilled Water, and add the washings to the solution. Concentrate this solution to the density of 1.21, then allow it to cool, and after twenty-four hours decant the liquor from the crystals of sulphate of calcium which will have formed; further concentrate the liquor until a film forms on its surface, and set it aside to cool and crystallize. Purify the crystals, if necessary, by recrystallization." *Br.,* 1867.

On the large scale the juice is placed in a wooden vat, closed at top, and is saturated with whiting (calcium carbonate). Carbonic acid gas is thus evolved, which passes out by an exit pipe, and may be used in the manufacture of sodium bicarbonate, while calcium citrate precipitates. The supernatant liquor, containing much extractive matter, is drawn off, and the calcium citrate is decomposed by diluted sulphuric acid, liberating the citric acid, and precipitating the lime as a sulphate. The mixture of citric acid and calcium sulphate is run off into a wooden filter-back, lined with lead, furnished with a perforated false bottom, and lined throughout with stout twilled flannel. The solution of citric acid passes off through a pipe leading from the bottom of the back to suitable reservoirs.

The sulphate is washed until it becomes tasteless, and the washings are run off into the same reservoirs. The filtered acid solution is then concentrated by evaporation in wooden vessels lined with lead, through which steam is made to pass by means of coiled lead pipes. As citric acid is liable to decomposition if subjected to a very high temperature, the use of the vacuum pan is highly advantageous in concentrating the solution. When the liquor is sufficiently concentrated, it is transferred to cylindrical sheet-lead vessels, placed in a warm situation, to crystallize. The crystals at first obtained are colored. In order to purify them, they are redissolved in a small quantity of water, with the assistance of heat, and the solution is digested with purified animal charcoal, filtered, evaporated, and the crystals, after having been washed and drained, are dried on wooden trays lined with sheet-lead, in a room heated by steam.

The calcium citrate of the above process should be decomposed without any delay; for, if kept, it will undergo fermentation, with the effect of destroying the citric acid. According to Personne, the products of this fermentation are acetic and butyric acids, carbon dioxide and hydrogen being evolved. It is desirable to have a slight excess of sulphuric acid, as this rather favors than otherwise the crystallization of the citric acid. It is found necessary, also, to add occasionally a small proportion of sulphuric acid to the citric acid liquor, during the progress of its concentration. According to J. Carter Bell (*N. R.*, 1880, p. 2274), the concentrated juice contains from sixty-four to ninety-six ounces of citric acid to the imperial gallon. The more recent the juice the better the quality. That which is stale will sometimes be quite sour, without containing any citric acid, in consequence of having undergone the acetous fermentation.

Citric acid by fermentation of carbohydrates is claimed by German patent No. 72,957 of 1893, and species of citromyces (*Citromyces pfefferienus* and *C. glaber*) are especially mentioned as bringing about this fermentation. This patent was supplemented by a German patent 91,891 of 1897, based upon the discovery that the same result may be obtained by means of *Mucor pyroformis*. The latter fungus is found on putrefying fruit, especially on pears and apples; its spore carriers grow only in a moist atmosphere and form long white filaments, terminated by brownish-black heads. It can be readily obtained in pure culture by sowing the spores in a suitable medium, such as sugar solutions, beer wort, steamed rice, starch paste, etc., the ordinary room temperature being favorable for its growth. The solution becomes acid from the formation of citric acid. (*J. Soc. Chem. Ind.*, June 30, 1897; see also *P. J.*, 1893, 182; 1894, 893; 1902, 551; *A. J. P.*, 1916, p. 337.)

Ohley (*Ph. Era*, 1901, 706) has devised a process which consists in diluting fresh concentrated lemon juice with twice its volume of water, filtering after standing over night to remove albumen, then adding a calculated quantity of calcium chloride, followed by solution of sodium hydroxide, gradually added, until the solution is exactly neutral, when, upon stirring, a magma of calcium citrate is quickly deposited. From this the sodium chloride formed is readily removed by hot water, and the calcium citrate is then decomposed by the calculated quantity of sulphuric acid. The main advantages of the new process are: convenience, a yield approximating to theoretical figures, and decidedly superior purity of product. In the manufacture of citric acid, the quantity of alkaline salt added to the juice must be sufficient to combine with all of the citric acid, and the amount of sulphuric acid added should thoroughly decompose the calcium citrate and not be in excess to avoid contaminating the crystals with sulphuric acid.

Properties.—" Colorless, translucent, right-rhombic prisms, or as a white powder; odorless and having an acid taste; efflorescent in warm air. One Gm. of Citric Acid dissolves in 0.5 mil of water, 1.8 mils of alcohol, and in about 30 mils of ether at 25° C. (77° F.); also in 0.5 mil of boiling water. An aqueous solution of Citric Acid (1 in 20) is acid to litmus. Add 1 mil of an aqueous solution of the Acid (1 in 10) to 50 mils of calcium hydroxide T.S. (or sufficient of the latter to render the mixture alkaline); the liquid remains clear. When boiled for about one minute, the solution becomes opaque through the precipitation of calcium citrate. When slowly ignited, Citric Acid is gradually decomposed without emitting an odor resembling burning sugar (difference from *tartaric acid*). Incinerate about 2 Gm. of Citric Acid; not more than 0.05 per cent. of ash remains. An aqueous solution of Citric Acid (1 in 10), which has been nearly neutralized with ammonia water, remains clear on the addition of calcium sulphate T.S. (*oxalic acid*). Heat about 5 Gm. of powdered Citric Acid for fifteen minutes on a water bath with 5 mils of sulphuric acid in a porcelain dish, which has previously been rinsed with sulphuric acid, keeping the mixture protected from dust; no darker color than yellow develops (*tartaric acid*). Ten mils of an aqueous solution of the Acid (1 in 50) mixed with 0.5 mil of hydrochloric acid does not respond to the Test for heavy metals (see Part III, Test No. 3). The addition of 1 mil of barium chloride T.S. to 10 mils of an aqueous solution of the Acid (1 in 100), to which have previously been added a few drops of hydrochloric acid, produces no turbidity (*sulphuric acid*). Dissolve 10 Gm. of Citric Acid in 20 mils of distilled water, add 2 mils of sulphurous acid and boil the mixture until the odor of sulphur dioxide is barely perceptible. Cool the solution, mix it with 1 mil of sodium cyanide T.S. and follow this immediately with stronger ammonia water until the solution possesses a slight odor of ammonia. When cold, transfer the solution to a glass-stoppered cylinder graduated at 50 mils, dilute

it with sufficient distilled water to measure 50 mils, and add 3 drops of sodium sulphide T.S. After mixing well, the color produced in the solution, if any, when viewed downward against a white surface, is not greater than the color of a control solution prepared as follows: Dissolve 2 Gm. of ammonium chloride (see Reagents, Part III) in 20 mils of distilled water, add 4 mils of a solution containing 0.08 Gm. of lead nitrate in 1000 mils of distilled water, and then 1 mil of diluted hydrochloric acid. Treat this solution with the same quantity of sulphurous acid, sodium cyanide T.S. and stronger ammonia water, as directed above, transfer to another 50 mil glass-stoppered cylinder, then dilute it with sufficient distilled water to make 50 mils and add 3 drops of sodium sulphide T.S. (before adding the sodium sulphide T.S., the liquid must possess a distinct odor of ammonia, and the two cylinders used must be matched, be of practically colorless glass, and have the same internal diameter) (*lead*).

Assay.—" Dissolve about 3 Gm. of the Acid, accurately weighed, in 50 mils of distilled water and titrate the solution with normal potassium hydroxide V.S., using phenolphthalein T.S. as indicator. It shows not less than 99.5 per cent. of $C_6H_8O_7 + H_2O$.

" Each mil of normal potassium hydroxide V.S. used corresponds to 0.07003 Gm. of $C_6H_8O_7 + H_2O$. Each gramme of Citric Acid corresponds to not less than 14.2 mils of normal potassium hydroxide V.S." *U. S.*

It is nearly insoluble in chloroform, benzene and petroleum benzin. A weak solution of it has an agreeable taste, but cannot be kept, as it undergoes spontaneous decomposition. It is incompatible with alkalies, converting them into citrates; also with the earthy and metallic carbonates, most acetates, the alkaline sulphides, and soaps. It possesses the valuable property of lessening or entirely removing the incompatibilities of iron salts with tannin, alkalies, etc. It is characterized by its taste, by the shape of its crystals, and by forming an insoluble salt with lime water when heated, and a deliquescent one with potassium hydroxide. If sulphuric acid be present the acid will be hygroscopic, and the precipitate by lead acetate will not be entirely soluble in nitric acid, the insoluble portion being lead sulphate.

Sometimes crystals of tartaric acid are substituted for or mixed with the citric, or the two acids may be mixed in powder, a fraud which is detected by adding a solution of potassium acetate to that of the suspected acids, when, if tartaric acid be present, a crystalline precipitate of potassium bitartrate will be formed. Pusch's method of determining the presence of tartaric acid in citric acid is as follows: 1 Gm. of powdered citric acid is added to 10 Gm. of strong, pure, colorless, sulphuric acid in a dry test tube, and the tube is then immersed in boiling water for an hour. The citric acid dissolves with frothing and evolution of gas, and a lemon-colored liquid is formed, which undergoes no change within half an hour if the sample be pure; but if as much as one-half per cent. of tartaric acid be present, the color is brownish and reddish-brown an hour afterward. (*A. Pharm.*, xxii, 316.) Another method of detecting tartaric acid is to digest the suspected acid with ferric hydroxide in a test tube, afterwards to raise the heat slowly to the boiling point, and, having allowed the excess of hydroxide to subside, to decant the clear liquid, and evaporate it to a syrupy consistence. If the acid be pure, the liquid remains limpid, and of a fine red color; if contaminated with tartaric acid, even to the extent of only one per cent., it becomes cloudy, and deposits tartrate. Another test is potassium permanganate, of which an alkaline solution is without action on citric acid, while under the influence of tartaric acid the manganese peroxide is deposited.

" Soluble in about 0.5 part of *water*, somewhat less soluble in *alcohol* (90 per cent.), and slightly soluble in *ether*. Yields, when neutralised, the *reactions* characteristic of citrates. 1 gramme dissolved in *water* requires for neutralisation 14.2 millilitres of *N/1 solution of sodium hydroxide*. Yields no characteristic *reactions* for copper or iron, and not more than very slight *reactions* for calcium or sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 1.4 parts per million. 1 gramme of powdered Citric Acid mixed with 10 millilitres of *sulphuric acid* in a test-tube previously rinsed with *sulphuric acid* acquires not more than a pale yellow color when kept at a temperature of 90° C. (194° F.) for one hour (absence of tartaric acid). Ash not more than 0.05 per cent." *Br.*

Lead is often found in the metallic state in citric acid in small quantity, and this arises from small portions being rubbed off in breaking off the crystals from the crystallizing vats. The presence of lead or copper may be detected as above, or by igniting in a porcelain crucible a small quantity of the acid, dissolving the ash in a few drops of nitric acid, diluting largely, and passing hydrogen sulphide through it, a black precipitate indicating the impurity. A most delicate test for lead is that of the U. S. P. IX given above. Some interesting observations in relation to the presence of lead in citric acid and citrates are recorded by Haussmann in *A. J. P.*, 1894, 173.

Composition.—The formula of the anhydrous acid is $C_6H_8O_7H_3$. It is a tribasic acid, and may therefore yield three classes of citrates according as one, two, or three atoms of hydrogen are replaced by metal, the first two classes being acid citrates, and the third class neutral citrates. When crystallized from its solution by cooling, it contains one molecule of water. Crystals of the formula $(C_6H_8O_7)_2 + H_2O$ have also been formed. (Flückiger, *Pharm. Chem.*, 1879, p. 157.) Witter (*Ph. Centralh.*, 1892, 1003) has obtained anhydrous citric acid, in crystals melting at 153° C. (307.4° F.), by heating aqueous solutions of the hydrated acid to 130° C. (266° F.). If citric acid be heated until all its water

of crystallization has been driven off, there will be produced *aconitic acid* ($H_3C_6H_3O_6$), which is found naturally in aconite, larkspur, black hellebore, equisetum, yarrow, and other plants. According to Hentschel, aconitic acid is best obtained by boiling for six hours 100 Gm. of citric acid with 50 Gm. of water mixed with 100 Gm. of pure sulphuric acid in a flask provided with a reverse condenser. Upon cooling the flask a solid cake of aconitic acid is formed, which may be purified by mixing with strong hydrochloric acid, and washing until free from sulphuric acid; colorless, shining crystals are obtained. (*A. Pharm.*, 1887, p. 357.)

Uses.—Except for its local irritant action citric acid is almost without effect upon the system. In any ordinary quantity it is entirely oxidized in the body and eliminated through the lungs as carbonic acid. For this reason the citrates of sodium and potassium, although neutral salts in themselves, tend to alkalize the system, appearing in the urine as carbonates. This change probably occurs in nearly all the tissues of the body so that after the ingestion of a citrate, carbonates can be found in the blood. According to Bence Jones, however, when sufficiently large quantities are given some of the citric acid appears in the urine unchanged.

Citric acid is mildly astringent and is popularly used to a large extent in various inflamed conditions of the skin, such as *sunburn*. It is, however, inferior in this regard to acetic acid. Although it has been suggested as a substitute for lemon juice in *scurvy*, it is entirely without value.

A substitute for lemonade may be made by dissolving from two to four parts of the acid, mixed with sugar and a little oil of lemon, in nine hundred parts of water; or twenty grains of the acid may be dissolved in a pint of water, and sweetened with sugar which has been rubbed on fresh lemon-peel. Citric acid is used as one of the ingredients in the effervescent salts on account of the presence of the water of crystallization which is an essential factor in the process. In the experiments of Strong, one-half to one per cent. of citric acid was found to be so poisonous to the cholera germ as to make impure water to which it was added probably a safe drink. It was further found that a large Philippine lemon, containing 40 mils of juice, was the equivalent of 2.74 grammes of citric acid. (*Report Government Laboratories, Philippine Islands*, Sept. 1, 1903.)

Dose, of the acid, from five to thirty grains (0.32–2.0 Gm.).

Off. Prep.—Syrupus Acidi Citrici, *U. S.*

ACIDUM GALLICUM. U. S.

GALLIC ACID Acid. Gallic.

(ăç'ĭ-dŭm găl'lĭ-cŭm)

"An organic acid [$C_7H_6O_5 + H_2O$ or $C_6H_2(OH)_3.COOH$ 1:3:4:5 + H_2O = 188.06]." *U. S.*

Trioxybenzoic Acid, Dioxysalicylic Acid, Trihydroxybenzoic Acid; Acide gallique, *Fr. Cod.*; Gallussäure, *G.*' Acido gallico, *It.*; Acido agallico, *Sp.*

Gallic acid was not introduced into the Br., 1914; the former British Pharmacopœia (1885) process for making gallic acid is as follows: "Boil one part of coarsely powdered galls with four fluid parts of diluted sulphuric acid for half an hour, then strain through calico while hot; collect the crystals that are deposited on cooling, and purify these with animal charcoal and repeated crystallization."

The process based on sulphuric acid's influence in favoring the change of tannic into gallic acid, requires less time than former processes.

The U. S., 1870, process was founded upon the fact that when galls in infusion, or in the state of moistened powder, are exposed to the air, their tannic acid is gradually converted into gallic acid. The gallic acid, being freely soluble in boiling but very sparingly in cold water, is extracted from the altered galls by decoction, and is deposited as the water cools. A repetition of the solution and deposition renders the acid more pure; but it cannot be obtained wholly colorless unless by the aid of animal charcoal. There are few processes in which it is more necessary that the animal charcoal should be purified. The presence of the slightest quantity of ferric salt will color the acid; and it is even advisable to examine the filtering paper, lest it may contain sufficient of this substance to vitiate the results of the process. The first crop of crystals in the process retains a very large proportion of water; and it will be found convenient to subject them to strong expression between folds of bibulous paper.

The elder Robiquet first suggested that galls contained a principle capable of converting tannic into gallic acid, with the presence of water, and in the absence of atmospheric air. Laroque proved that this principle acts as a ferment, and that the change referred to is the result of a *gallic acid fermentation* in the galls. E. Robiquet showed that galls contain *pectose* and *pectase*, the former of which, according to the experiments of Frémy, is the principle out of which pectin is formed in plants, and the latter a peculiar ferment which effects the transformation. He believed that in galls the pectase, aided by a proper temperature and the presence of water, changed not only pectose into pectin, but also tannic into gallic acid. Strecker previously advanced the opinion that tannic acid was a combination of gallic acid and sugar, the latter of which is destroyed in the process for procuring gallic acid, which is thus simply set free from the combination. E. Robiquet admitted the occasional transformation of tannic acid into gallic acid and sugar, but did not believe that the sugar pre-existed as such in the tannin. (*J. P. C.*, 3e sér., xxiii, 241.) Wittstein, in endeavoring to obtain gallic acid from *Chinese galls* by forming them into a paste with water, found that but a very small propor-

tion of the acid was generated at the end of six weeks. Thinking that this might have resulted from the want of the ferment in the Chinese galls, he added to these one-eighth of their weight of common galls, and at the end of three weeks obtained an amount of gallic acid nearly equal to one-half the weight of the galls employed. The same result, though more slowly, followed the addition of yeast to the Chinese galls. Wittstein obtained both carbonic acid and alcohol as products of this operation, thus favoring the views of Strecker as to the constitution of tannic acid; and the idea that tannin was a glucoside convertible through exposure of galls to the air, or more rapidly by sulphuric acid, into glucose and gallic acid, was accepted without qualification, until Schiff (*Ber. d. Chem. Ges.*, iv, 231, 967) proved that although crude tannic acid contains glucose, it is possible to separate a large quantity of the glucose without destroying the tannic acid. He proposed that *pure tannic acid* be called *digallic acid*, and that the term *tannin* be applied to natural tannin, *i.e.*, the *glucoside* of digallic or pure tannic acid, for when natural tannin is boiled with diluted mineral acids or subjected to the influence of a nitrogenous ferment it splits into gallic acid and glucose:

$$C_{34}H_{28}O_{22} + 4H_2O = 4C_7H_6O_5 + C_6H_{12}O_6$$

Digallic acid is the first anhydride of gallic acid:

$$C_{14}H_{10}O_9 + H_2O = 2C_7H_6O_5$$

Gallic acid is a *phenol acid*, or combination of these two classes of organic compounds; its formula is $C_6H_2(OH)_3.COOH$. It may be termed, therefore, a *trioxybenzoic acid* or, more properly speaking, 3 : 4 : 5 *trihydroxybenzenecarboxylic acid*. It is monobasic. Unlike tannin it does not precipitate alkaloids from their solutions.

Properties.—Gallic acid is in "white, or pale fawn-colored, silky, interlaced needles, or triclinic prisms; odorless; having an astringent and slightly acidulous taste; permanent in the air. One Gm. of Gallic Acid dissolves in 87 mils of water, 4.6 mils of alcohol, 10 mils of glycerin, and in about 100 mils of ether at 25° C. (77° F.); also in about 3 mils of boiling water; almost insoluble in chloroform. A saturated aqueous solution of Gallic Acid is acid to litmus. Add 6 drops of sodium hydroxide T.S. to 5 mils of a cold, saturated aqueous solution of the Acid; a deep green color gradually develops, which is changed to reddish or brownish-red by acids. Gallic Acid neither colors nor precipitates solutions of pure ferrous salts, but it forms a bluish-black precipitate with ferric salts. When dried to constant weight at 100° C. (212° F.), the Acid loses not more than 12 per cent. of its weight. Incinerate about 1 Gm. of Gallic Acid; not more than 0.1 per cent. of ash remains. A cold, saturated aqueous solution of Gallic Acid yields no precipitate with gelatin T.S. or starch T.S. (*tannic acid*)." *U. S.*

It produces a deep bluish-black color with solutions of ferric salts, which disappears when the solution is heated, a result which Mahla has shown to depend on the conversion of the gallic into *pyrogallic* or *metagallic acid* (pyrogallol) by the loss of carbon dioxide. Gallic acid does not precipitate gelatin, or a solution of ferrous sulphate.

By the action of arsenic it is converted almost entirely into tannic acid without the production of arsenous acid. (Schiff, *Chem. News*, xxix, 73.) Young's test, potassium cyanide, gives a reddish color with gallic acid and none with tannic acid. A mixture of ammonium chloride and ammonia produces a red coloration, but no precipitate, in gallic acid solution; while in tannic acid solution it produces a whitish precipitate rapidly turning reddish-brown. (*A. J. P.*, April, 1889.) A test proposed by Flückiger consists in adding to the solution of gallic acid a diluted (1 to 100) solution of pure ferrous sulphate. To the colorless solution a little sodium acetate is to be added, when a deep violet color will appear, due to the formation of ferrous gallate. Heated to 216° C. (420.8° F.), gallic acid gives off carbon dioxide, and is changed into *pyrogallic acid*.

Uses.—Gallic acid differs essentially from tannic acid in that it does not coagulate albumen. It is readily absorbed from the intestinal tract and eliminated through the kidneys. Its presence in the urine can be demonstrated by the addition of a soluble ferric salt after acidulation of the urine with hydrochloric acid. The older writers attributed astringent properties to gallic acid, although less active than those of tannic acid, but as the modern conception of the action of astringent drugs is that their effects depend upon the precipitation of albuminous matters this view must be regarded with doubt. Nevertheless, there is considerable clinical evidence of its utility as an internal styptic, for example, in *hematuria* or *hemoptysis*. It is also asserted that it will lessen the quantity of albumen in the urine in cases of *nephritis*. Gallic acid is incompatible with solutions of alkali hydroxides and carbonates with which it combines to produce colors ranging from green to yellow, red, and brown. With lime water it gives even more marked color changes and produces a blue precipitate. With ferrous salts no change occurs, but as soon as oxidation begins or with ferric salts direct, an inky color is produced. It acts as a reducing agent with salts of silver and gold, and with iodine, arsenates, permanganates, etc. With lead salts and some other metallic salts it produces precipitates.

Dose, five to twenty grains (0.32–1.3 Gm.).

ACIDUM HYDRIODICUM DILUTUM.
U. S., Br.

DILUTED HYDRIODIC ACID Acid. Hydriod. Dil.

(ăç'ĭ-dŭm hȳ-drĭ-ŏd'ĭ-cŭm dī-lū'tŭm)

"An aqueous solution containing not less than 9.5 per cent. nor more than 10.5 per cent. of HI (127.93). Preserve it in amber-colored,

glass-stoppered bottles, protected from light, and do not dispense it if it contains free iodine." *U. S.* "Diluted Hydriodic Acid is an aqueous liquid containing, when freshly prepared, 10 per cent. by weight of hydrogen iodide, HI, and 1 per cent. by weight of hydrogen hypophosphite, HPH_2O_2. It may be obtained by the action of hydrogen sulphide on a solution of iodine, with the subsequent addition of hydrogen hypophosphite." *Br.*

Acide hydroiodique dilué, *Fr.*; Verdünnte Jodwasserstoffsäure, *G.*

* "Potassium Iodide, *one hundred and thirty-five grammes* [or 4 ounces av., 333 grains]; Potassium Hypophosphite, *ten grammes* [or 154 grains]; Tartaric Acid, *one hundred and thirty-six and five-tenths grammes* [or 4 ounces av., 356 grains]; Distilled Water, Diluted Alcohol, each, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains].

"Dissolve the Potassium Salts in *two hundred and fifty mils* [or 8 fluidounces, 217 minims] of Distilled Water with the aid of heat, and the Tartaric Acid in *four hundred mils* [or 13 fluidounces, 252 minims] of Diluted Alcohol. Having poured the solution of Tartaric Acid into a bottle of about one thousand mils capacity, add the solution of the Potassium Salts and shake the mixture briskly. Cool the mixture to about 5° C. (41° F.) for several hours and, having inserted a pledget of purified cotton tightly in the throat of a funnel, transfer the contents of the bottle to the funnel. When all the liquid has passed through, wash the bottle and crystalline precipitate with Diluted Alcohol in successive small portions until the filtrate weighs *one thousand grammes* [or 35 ounces av., 120 grains]. Evaporate the liquid at a moderate temperature, on a water-bath, until all of the Alcohol has evaporated, and add sufficient Distilled Water to make the product weigh *one thousand grammes* [or 35 ounces av., 120 grains]." *U. S.*

The official description is as follows: "Diluted Hydriodic Acid is a colorless or not more than pale yellow, odorless liquid; it has a strongly acid taste and is strongly acid to litmus. Specific gravity: about 1.100 at 25° C. (77° F.). Add a few drops of ferric chloride T.S. or chlorine water to Diluted Hydriodic Acid, diluted with twice its volume of distilled water; iodine is liberated and imparts to the solution a reddish-brown color. On agitating this mixture with a few drops of chloroform, the latter acquires a violet color. No blue color is produced on adding a few drops of starch T.S. to 5 mils of the Acid (*free iodine*). Five mils of Diluted Hydriodic Acid, when evaporated to dryness on a water bath and the residue ignited, leaves not more than 0.165 Gm. of residue. The addition of 1 mil of barium chloride T.S. to 10 mils of Diluted Hydriodic Acid produces not more than a slight cloudiness (*sulphuric acid*); the addition of 1 mil of potassium sulphate T.S. to 10 mils of the Acid causes no turbidity (*barium*). Mix 0.5 mil of Diluted Hydriodic Acid with 10 mils of distilled water, add 8 mils of silver nitrate T.S. and 6 mils of ammonium carbonate T.S., digest the mixture for ten minutes on a water bath, cool, and filter. The filtrate upon supersaturating with nitric acid does not become more than slightly opalescent (*chloride*). Ten mils of Diluted Hydriodic Acid, without further acidulation, does not respond to the Test for heavy metals (see Part III, Test No. 3). Mix 5 mils of Diluted Hydriodic Acid with 1 mil of nitric acid and evaporate the liquid to dryness on a water bath; the residue meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"**Assay.**—Pour about 5 mils of Diluted Hydriodic Acid into a tared flask, weigh accurately, dilute with 20 mils of distilled water, add 50 mils of tenth-normal silver nitrate V.S. and shake the mixture well. Now add 5 mils of nitric acid, heat the mixture on a water bath until the precipitate has a bright yellow color, cool and add 2 mils of ferric ammonium sulphate T.S. The residual titration with tenth-normal potassium sulphocyanate V.S. shows not less than 9.5 per cent. nor more than 10.5 per cent. of HI.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.012793 Gm. of HI. Each gramme of Diluted Hydriodic Acid corresponds to not less than 7.4 mils nor more than 8.2 mils of tenth-normal silver nitrate V.S." *U. S.*

"A clear, colorless liquid. Yields, when neutralised, the *reactions* characteristic of iodides. Yields no characteristic *reactions* for barium, calcium, potassium, sulphates, or sulphides. When to 5 grammes of the Acid, diluted with a little *water,* 45 millilitres of *N/10 solution of silver nitrate,* 5 millilitres of *nitric acid,* and 0.5 millilitre of *solution of ferric sulphate* are added, not less than 5 or more than 7 millilitres of *N/10 solution of ammonium thiocyanate* are required to produce a permanent pink coloration. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Diluted hydriodic acid was introduced into the U. S. Pharmacopœia 1860; it was dismissed in the revision of 1870, and was again recognized in the 8th and 9th Revisions. The old process consisted in passing hydrogen sulphide into a bottle containing iodine and water until the iodine disappeared and the liquid was colorless, it was then filtered to separate the precipitated sulphur and the filtrate heated to drive off the excess of hydrogen sulphide. The reaction is as follows:

$$2H_2S + 2I_2 = 4HI + S_2$$

Various processes have been proposed for making hydriodic acid. Buchanan used an extemporaneous formula, which consisted in dissolving 330 grains of potassium iodide and 264 of tartaric acid, each in one and a half fluidounces of water, mixing the solutions, filtering to separate the potassium bitartrate formed, and

finally adding sufficient distilled water to make the solution measure fifty fluidrachms. Each fluidrachm of this preparation represents five grains of iodine. Dunn's modification of Buchanan's process is as follows: Take of potassium iodide 209¾ grains; tartaric acid, in crystals, 190¼ grains. Dissolve the iodide in three fluidrachms of distilled water, and the acid in the same quantity, and filter if necessary; mix the solutions, set the mixture in ice-cold water, and allow it to stand for one hour; then filter, and make up the measure to two fluidounces. Each fluidrachm represents 10 grains of iodine. (*A. J. P.*, 1869, 41.) H. Kolbe (*J. Pr. Chem.*, 1879, 172, and *A. J. P.*, June, 1877) adds phosphorus to iodine in a retort filled with carbon dioxide. Heat is applied, and water added; on application of moderate heat, hydriodic acid gas free from iodine is produced. C. Winckler (*A. J. P.*, May, 1880) dissolves iodine in carbon disulphide, adds sufficient water to form a layer on top of the solution of iodine, and passes a stream of hydrogen sulphide through the mixture; when this has acquired a yellow color, the layers are separated, the aqueous hydriodic acid is boiled a few minutes to expel hydrogen sulphide, and it is then supposed to be chemically pure.

The present U. S. process is based on Buchanan's method, but directs in addition to potassium iodide and tartaric acid, potassium hypophosphite and diluted alcohol. The hypophosphite is added in order to provide a small quantity of hypophosphorous acid which acts as a preservative, while the diluted alcohol aids in the precipitation of the potassium bitartrate because of the insolubility of the latter in alcohol. The cooling of the mixture is also used to assist in the separation of the potassium bitartrate.

$$KI + 2H_2C_4H_4O_6 + KPH_2O_2 = HI + 2KHC_4H_4O_6 + HPH_2O_2$$

Uses.—Diluted hydriodic acid is used in the preparation of syrup of hydriodic acid by adding 125 mils to 300 mils of distilled water and 575 mils of syrup; as now prepared the acid is reasonably permanent, but it should not be used or dispensed if discolored by the presence of free iodine. Diluted hydriodic acid was introduced into use as a medicine by Andrew Buchanan, of Glasgow. The acid official in 1860 contained ten grains of iodine in each fluidrachm, and was therefore twice as strong as Buchanan's solution. There can be little doubt that hydriodic acid is capable of producing the alterative effects of iodine, and it may be given in all cases to which that medicine is applicable. When the solution becomes discolored it may be irritant through the liberated iodine, and should not be dispensed. Diluted hydriodic acid is incompatible with oxidizing agents in general, such as chlorates, nitrates, permanganates, hydrogen dioxide, etc., which liberate iodine. It is also incompatible with salts of mercury, bismuth, and cupric and ferric salts.

Dose, ten minims (0.6 mil) three times a day, well diluted.

Off. Prep.—Syrupus Acidi Hydriodici, *U. S.; Br.*

ACIDUM HYDROBROMICUM DILUTUM.
U. S., Br.

DILUTED HYDROBROMIC ACID **Acid. Hydrobrom. Dil.**

(ăç'ĭ-dŭm hȳ-drǫ-brō'mĭ-cŭm dī-lū'tŭm)

"An aqueous solution containing not less than 9.5 per cent. nor more than 10.5 per cent. of HBr (80.93). Preserve it in amber-colored, glass-stoppered bottles, protected from light." *U. S.* "Diluted Hydrobromic Acid is an aqueous liquid containing 10 per cent. by weight of hydrogen bromide, HBr. It may be obtained by the interaction of bromine and sulphurous acid, and subsequent distillation." *Br.*

Acidum Bromhydricum Dilutum, Acidum Bromohydricum; Acide Bromhydrique dissous, *Fr. Cod.*; Acide hydrobromique dilué, *Fr.*; Acidum hydrobromicum, *P. G.*; Verdünnte Hydrobromsäure, *v.* Bromwasserstoffsäure, *G.*

The U. S. and Br. Pharmacopœias do not give processes for this acid. Both acids are identical in strength. Dr. E. R. Squibb published a process (*A. J. P.*, 1878, 116) for making this acid which was based on the decomposition of potassium bromide with sulphuric acid. (See *U. S. D.*, 19th ed., p. 32.)

The most convenient process is undoubtedly that of Dewitt C. Wade (*Peninsular Medical Journal*, Feb., 1875), modelled after Buchanan's method of making hydriodic acid, which directs that 120 grains of potassium bromide be dissolved in one fluidounce of water, and 153 grains of tartaric acid be added to the solution; acid potassium tartrate is produced, the greater part of which crystallizes out on standing twelve hours at a low temperature, and a solution of hydrobromic acid is formed, sp. gr. 1.228, containing about 80 grains pure hydrobromic acid to the fluidounce, equivalent to nearly 15 per cent. Fothergill's acid, although based upon Wade's formula, is weaker, the quantity of potassium bromide being 81¼ grains and that of tartaric acid 99 grains to the fluidounce, the manipulation being the same; each fluidounce of Fothergill's acid contains about 55 grains of pure hydrobromic acid, or about 10 per cent. Diluted hydrobromic acid made in this way is open to the objection of containing cream of tartar, and probably some undecomposed potassium bromide in solution, and thus is not strictly pure. To lessen this, Charles Rice proposed the addition of a double quantity of alcohol to facilitate the precipitation, recovering the alcohol by distillation subsequently. (*N. R.*, 1877, p. 107.) Other processes have been suggested for the preparation of hydrobromic acid. Edward Goebel (*N. R.*, Sept., 1880) proposed a method based on Glover's process, which is to decompose 148 grains of barium bromide dissolved in

half an ounce of water, with 50.6 grains of sulphuric acid, diluted with two drachms of distilled water; the precipitated barium sulphate is washed with distilled water until the filtrate weighs 810 grains to make the 10 per cent. acid solution. The processes of Balard, Millon, and Loewig are commented upon by John M. Maisch (*Proc. A. Ph. A.*, 1860), who proposed some useful modifications. Markoe (*Ibid.*, 1875, p. 686) recommends an economical process, which, however, must be followed with care, and is better adapted for making the acid on a large scale. He pours a pint of water into a gallon stoneware jar, and then adds one pound or more of phosphorus, distributing it over the bottom; ice is now added until the jar is half full, a gallon glass funnel is inserted in the throat of the jar, and a funnel tube adjusted, so that the end will be a short distance above the surface of the phosphorus; the funnel is about one-third filled with broken ice, and the jar placed in a larger vessel, and broken ice packed between. Three or four pounds of bromine, after being chilled, are *slowly* added, in order that the fumes of hydrobromic acid and bromine that may arise may be fully condensed by the ice in the funnel, and an accumulation of bromine avoided, which might produce an explosion from too sudden reaction. The excess of phosphorus is removed after all the bromine has been added, the liquid distilled, hydrobromic acid condensed, and the strength adjusted, while to the residue in the retort water may be added to make diluted phosphoric acid. A convenient method for obtaining a small amount of hydrobromic acid gas or solution was described by L. H. Friedburg, in a communication before the New York Section of the American Chemical Society (May, 1905). Bromine is allowed to trickle into paraffin which is kept in a melted condition by placing the flask containing it in a shallow steam bath. The bromine vapors, which will pass over with the hydrobromic acid, are partly absorbed by a second flask containing paraffin, joined to the first flask and standing with it in the steam bath. (See also Gassman's process, *S. W. P.*, 1893, 107.) Marshall proposed a method which depends on the easy solubility of bromine in hydrobromic acid, the conversion of the bromine into sulphur bromide by the addition of sulphur, and the ready decomposition of sulphur bromide when shaken with water, thus:

$$3Br_2 + S + 4H_2O = 6HBr + H_2SO_4$$

Properties.—"Diluted Hydrobromic Acid is a colorless, odorless liquid having a strongly acid taste; it is strongly acid to litmus. Specific gravity: about 1.076 at 25° C. (77° F.). On distilling it, weak acid passes over first; when the temperature of 126° C. (258.8° F.) is reached, an acid of 48 per cent. remains, which may be distilled unchanged." *U. S.*

Although of a pungent and irritating odor, and fuming when in contact with the atmosphere when concentrated, in its diluted state it is odorless. On adding chlorine or nitric acid to diluted hydrobromic acid, there is liberated bromine, which is soluble in chloroform or carbon disulphide, imparting to these liquids a yellow color.

Tests.—"Silver nitrate T.S. produces a yellowish-white precipitate, which is insoluble in diluted nitric acid, slowly soluble in an excess of stronger ammonia water, but readily soluble in a 10 per cent. solution of sodium thiosulphate. Evaporate 25 mils of Diluted Hydrobromic Acid from a platinum or porcelain dish and afterwards dry it at 110° C. (230° F.); not more than 0.0025 Gm. of residue remains. The addition of 1 mil of barium chloride T.S. to 10 mils of the Acid produces not more than a slight cloudiness (*sulphuric acid*); the addition of 1 mil of potassium sulphate T.S. to 10 mils of the Acid causes no turbidity (*barium*). Shake 10 mils of the Acid with 2 mils of chloroform; no color is imparted to the latter (*free bromine*). Now add 5 drops of ferric chloride T.S. and shake the mixture; the chloroform does not acquire a violet tint (*iodine*). Ten mils of Diluted Hydrobromic Acid, without further acidulation, does not respond to the Test for heavy metals (see Part III, Test No. 3). Mix 5 mils of Diluted Hydrobromic Acid with 1 mil of nitric acid and evaporate the liquid to dryness on a water bath; the residue meets the requirements of the Test for arsenic (see Part III, Test No. 1). Mix 0.5 mil of Diluted Hydrobromic Acid with 10 mils of distilled water, add 8 mils of silver nitrate T.S., and 6 mils of ammonium carbonate T.S., digest the mixture for ten minutes on a water bath, cool and filter. The filtrate, on supersaturating with nitric acid, does not at once become more than slightly turbid (*chloride*).

"**Assay.**—Pour about 20 mils of Diluted Hydrobromic Acid into a tared flask, weigh accurately, dilute with 30 mils of distilled water, and titrate the liquid with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 9.5 per cent. nor more than 10.5 per cent. of HBr.

"Each mil of normal potassium hydroxide V.S. used corresponds to 0.08093 Gm. of HBr. Each gramme of Diluted Hydrobromic Acid corresponds to not less than 1.17 mils nor more than 1.30 mils of normal potassium hydroxide V.S." *U. S.*

"Yields, when neutralised, the *reactions* characteristic of bromides. Specific gravity 1.077. 10 millilitres require for neutralisation 13.3 millilitres of *N/1 solution of sodium hydroxide.* 2 millilitres require for complete precipitation 26.6 millilitres of *N/10 solution of silver nitrate.* Yields no characteristic *reactions* for barium, chlorides, phosphates, or sulphites, and only a slight *reaction* for sulphates. *Lead limit* 5 parts per million. *Arsenic limit* 5 parts per million. Leaves not more than 0.01 per cent. of residue on evaporation." *Br.*

Concentrated hydrobromic acid has been furnished by manufacturing chemists contain-

ing from 20 to 50 per cent. of absolute hydrobromic acid; C. T. Tyrer states that the stronger acids are prone to show discoloration in a few days after being made, but that even the highly colored acids, when diluted to the official strength, become colorless; the concentrated acid attacks glass rapidly and the silica is not thrown out on dilution; he recommends acid of the sp. gr. 1.250 as having the most suitable limit of concentration for pharmaceutical purposes. (*Y. B. P.*, 1896, 296.)

The following table by Biel will be found useful in showing from the specific gravities of solutions the percentage of absolute hydrobromic acid.

Biel's Table of Percentage and Specific Gravity of Hydrobromic Acid

Per cent. HBr.	Specific Gravity at 15° C. (59° F.)	Per cent. HBr.	Specific Gravity at 15° C. (59° F.)
1	1.0082	26	1.219
2	1.0155	27	1.229
3	1.0230	28	1.239
4	1.0305	29	1.249
5	1.038	30	1.260
6	1.046	31	1.270
7	1.053	32	1.281
8	1.061	33	1.292
9	1.069	34	1.303
10	1.077	35	1.314
11	1.085	36	1.326
12	1.093	37	1.338
13	1.102	38	1.350
14	1.110	39	1.362
15	1.119	40	1.375
16	1.127	41	1.388
17	1.136	42	1.401
18	1.145	43	1.415
19	1.154	44	1.429
20	1.163	45	1.444
21	1.172	46	1.459
22	1.181	47	1.474
23	1.190	48	1.490
24	1.200	49	1.496
25	1.209	50	1.513

Uses.—The action of hydrobromic acid upon the system is practically identical with that of the alkaline bromides, but is too irritant to the stomach to be used freely. Two fluidrachms contain about 12 grains of bromine, equivalent in this to 18 grains of potassium bromide, and may be given at once, well diluted with water or syrup. The addition of a trace of spirit of lemon to the mixture will impart a flavor to this dose closely similar to lemonade.

Diluted Hydrobromic Acid is incompatible with many oxidizing agents, as is hydriodic acid; it is also incompatible with salts of lead, silver, mercury, and bismuth.

Dose, from one-half to two fluidrachms (1.8 to 7.5 mils).

Off. Prep.—Elixir Calcii Bromidi. *N. F.*

ACIDUM HYDROCHLORICUM. U. S., Br.

HYDROCHLORIC ACID Acid. Hydrochl.

(ăç'ĭ-dŭm hȳ-drọ-ċhlō'rĭ-cŭm)

"An aqueous solution containing not less than 31 per cent. nor more than 33 per cent. of HCl (36.47). Preserve it in glass-stoppered bottles." *U. S.* "Hydrochloric Acid is a liquid containing 31.79 per cent. by weight of hydrogen chloride, HCl, and 68.21 per cent. by weight of water. It may be obtained by dissolving in water the gas produced by the interaction of sulphuric acid and sodium chloride." *Br.*

Acidum Muriaticum, *U. S.*, 1870; Acidum Hydrochloratum, s. Chlorhydricum; Spirit of Sea Salt, Marine Acid, Muriatic Acid, Chlorhydric Acid; Acide chlorhydrique officinal, *Fr. Cod.*; Acide hydrochlorique, Acide chlorhydrique ou muriatique, *Fr.*; Acidum hydrochloricum, *P. G.*; Salzsäure, Chlorwasserstoffsäure, *G.*; Acido cloridrico concentrato, Acido muriatico, *It.*; Acido clorhidrico, Acido muriatico, *Sp.*

Preparation.—Hydrochloric acid is obtained mainly by the action of sulphuric acid on sodium chloride or common salt. In England it is produced in enormous quantities during the decomposition of common salt for the purpose of making sodium sulphate, from which soda ash and sodium carbonate are afterwards manufactured in immense quantities. The decomposition of the sea salt is performed in semi-cylindrical vessels, the curved part, next the fire, being made of iron, and the upper or flat surface, of stone. The acid gas is conveyed by a pipe to a double-necked stoneware receiver, half filled with water, and connected with a row of similar receivers, likewise containing water. As carried out on a larger scale, the decomposition of the salt takes place in hemispherical iron pans, 9 feet in diameter, covered by a brick-work dome; upon the mass of salt the requisite quantity of sulphuric acid is allowed to run from a leaden cistern placed above the decomposing pan. Torrents of hydrochloric acid gas are evolved, which collect in the space between the pan and the brick-work dome, whence they pass by a brick-work or earthenware flue into upright towers or condensers. These towers are filled with bricks or coke, down which a small stream of water is allowed to trickle. The gas, passing upward, meets the water and is dissolved by it, and as the acid liquor approaches the bottom, it becomes more and more nearly saturated with gas.

The development of this process and indeed of the increased use of hydrochloric acid was the outcome of legislation against the manufacturing plants for sodium sulphate, which permitted the acid vapors to escape into the air to the detriment of surrounding vegetation and property.

Next in importance is the Hargreaves and Robinson process which has recently been made successful in a mechanical way. It depends upon the following reaction:

$$2NaCl + SO_2 + H_2O + O = Na_2SO_4 + 2HCl.$$

It is carried out as a continuous process, the temperature of the reaction being from 400° to 500° C. (752°–932° F.).

Under former industrial conditions chlorine was largely manufactured from hydrochloric acid. These conditions are now occasionally reversed, owing to the immense amount of chlorine which is obtained as a by-product in the manufacture of caustic soda by electrolysis. The subsequent conversion of chlorine into hydrochloric acid takes place when chlorine and

steam are heated to 1000° C. (1832° F.) in the presence of an excess of carbon, and is according to the following reaction: $Cl_2 + H_2O + C = 2HCl + CO$. (*Ch. Ztg.*, 1912, p. 54.)

An electrolytic process is now being operated at Niagara Falls by the Roberts Chemical Company, who electrolyze potassium chloride and obtain as products potassium hydroxide and hydrochloric acid. This is done by burning the chlorine direct with the hydrogen set free at the cathode.

The acid, when required to be pure, is generally prepared by saturating distilled water with the gas in Woulff's apparatus. A quantity of pure fused sodium chloride is introduced into a retort or flask, placed on a sand bath. The vessel is then furnished with an S-tube, and connected with a series of bottles, each two-thirds full of water. A quantity of sulphuric acid is then gradually added, equal in weight to the common salt employed, and diluted with one-third of its weight of water. The materials ought not to occupy more than half the body of the retort. When the evolution of the gas slackens, heat is applied, and gradually increased until the water in the bottles refuses to absorb any more, or until no more gas is found to come over. As soon as the process is completed, boiling water should be added to the contents of the retort or flask, in order to facilitate the removal of the residue. During the progress of the saturation, the water in the several bottles increases in temperature, which lessens its power of absorption. It is, therefore, expedient, in order to obtain a strong acid, to keep the bottles cool by means of water or ice. The connecting tubes need not plunge deeply into the acid.

In the process for hydrochloric acid, theory calls for a little less than 90 parts of liquid sulphuric acid to 100 of common salt. A moderate excess of the former may be useful to insure the complete decomposition of the salt. The reaction for its formation is:

$$NaCl + H_2SO_4 = HCl + HNaSO_4$$

If only half the amount of sulphuric acid be used, the reaction is:

$$2NaCl + H_2SO_4 = 2HCl + Na_2SO_4$$

In the first of these reactions, as only one molecule of salt is taken, it is obvious that there is not enough sodium furnished to neutralize the sulphuric acid completely and make the normal sulphate, Na_2SO_4, so the result is the acid sulphate, $HNaSO_4$. On the other hand, in the second reaction, the two molecules of salt furnish just the sodium necessary to neutralize the one molecule of sulphuric acid and make the neutral sulphate, Na_2SO_4.

As hydrochloric acid, prepared in the ordinary mode, often contains arsenic, so as to obscure its indications when employed in testing for that poison, it is of interest to the practical toxicologist to know that it may be obtained free from that impurity by distilling sodium or potassium chloride with oxalic acid in equivalent proportions.

The following method of freeing hydrochloric acid from arsenic trioxide is recommended by Engel as easy and entirely efficacious. It is founded on the fact that arsenic trioxide is reduced to arsenic by hypophosphorous acid. Into a liter (about 2 pints) of arsenical hydrochloric acid introduce 4 to 5 grammes (about 60 or 70 grains) of potassium hypophosphite, dissolved in a little water. At the end of an hour or two, the liquid becomes yellow and then brown; and a precipitate soon forms, more or less copious according to the amount of impurity. After the liquid becomes clear, which usually happens in forty-five minutes, decant the hydrochloric acid and distil it. The acid thus obtained is entirely free from arsenic. This process should be conducted in a place where the direct rays of the sun may fall on the vessels; or, where this is impossible, the vessels should be subjected, by means of a water bath, from four to six hours, to a heat little short of the boiling point of the acid. (*J. P. C.*, 1873, p. 10.) Traces of arsenic may also be removed by adding solution of stannous chloride, and after the precipitate of impure arsenic has settled, the clear liquid is redistilled. (Bettendorf, *Zeit. An. Chem.* [2], v, p. 492.) The best results in the removal of arsenic seem to be obtained by the process of Meister Lucius and Bruning of Hoechst (1905), in which cheap vanadious salts are employed which may be regenerated and recovered electrolytically.

Properties.—Official hydrochloric acid is a "colorless, fuming liquid, having a pungent odor, and an intensely acid taste; the fumes and odor disappear on diluting the Acid with 2 volumes of water; it is strongly acid to litmus, even when highly diluted. Specific gravity: about 1.155 at 25° C. On distilling it at normal barometric pressure, a stronger acid passes over first, until, at 110° C., an acid of about 20 per cent. remains, which distills unchanged. When heated with manganese dioxide, it evolves chlorine. It conforms to the tests for identity and purity under *Acidum Hydrochloricum Dilutum* when diluted to that strength.

"**Assay.**—Pour about 3 mils of Hydrochloric Acid into a tared bottle containing about 10 mils of distilled water, stopper, weigh accurately, dilute with 50 mils of distilled water and titrate the liquid with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 31 per cent. nor more than 33 per cent. of HCl.

"Each mil of normal potassium hydroxide V.S. used corresponds to 0.03647 Gm. of HCl. Each gramme of Hydrochloric Acid corresponds to not less than 8.50 mils nor more than 9.05 mils of normal potassium hydroxide V.S." *U. S.*

"Yields, when neutralised, the *reactions* characteristic of chlorides. Specific gravity 1.160. 5 millilitres, diluted with *water*, require for neutralisation 50.6 millilitres of *N/1 solution of sodium hydroxide*. When diluted with *water* yields no characteristic *reactions* for bromides,

iodides, sulphates, or sulphites, and only slight *reactions* for iron. Diluted with *water* and *solution of potassium iodide* added, no blue color is produced on the addition of *mucilage of starch* (absence of free chlorine). *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million. Leaves not more than 0.01 per cent. by weight of residue on evaporation." *Br.*

Exposed to the air it emits white fumes, owing to the escape of the acid gas and its union with the moisture of the atmosphere. When concentrated, it blackens organic substances, as does sulphuric acid. Its sp. gr. varies with its strength. When as highly concentrated as possible, its density is 1.21. The U. S. acid has the specific gravity of 1.158 at

Table of Percentage and Specific Gravity of Hydrochloric Acid.
U. S. P. IX.

Per cent. HCl	Sp. gr. app. 25° C. / 25° C.	Sp. gr. app. 15° C. / 15° C.	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal KOH mils.	Per cent. = 0.01 mil normal KOH.
‡0	1.0000	1.0000	0.00018	0.0203	0.000	0.0362
1	1.0049	1.0050	0.00018	0.0204	0.276	0.0360
2	1.0098	1.0099	0.00019	0.0204	0.554	0.0357
3	1.0147	1.0149	0.00020	0.0205	0.834	0.0355
4	1.0196	1.0198	0.00020	0.0206	1.116	0.0352
5	1.0245	1.0247	0.00021	0.0207	1.400	0.0345
6	1.0293	1.0296	0.00022	0.0207	1.690	0.0344
7	1.0341	1.0346	0.00023	0.0208	1.981	0.0341
8	1.0389	1.0395	0.00024	0.0209	2.274	0.0339
9	1.0437	1.0444	0.00025	0.0210	2.569	0.0336
10	1.0485	1.0493	0.00027	0.0210	2.867	0.0332
11	1.0532	1.0542	0.00029	0.0211	3.168	0.0329
12	1.0580	1.0591	0.00030	0.0211	3.472	0.0327
13	1.0627	1.0640	0.00032	0.0212	3.778	0.0325
14	1.0674	1.0689	0.00034	0.0211	4.086	0.0322
15	1.0722	1.0738	0.00036	0.0211	4.397	0.0318
16	1.0769	1.0788	0.00038	0.0210	4.711	0.0316
17	1.0817	1.0837	0.00039	0.0209	5.027	0.0313
18	1.0865	1.0886	0.00041	0.0209	5.346	0.0311
19	1.0912	1.0936	0.00043	0.0209	5.668	0.0308
20	1.0960	1.0986	0.00045	0.0207	5.993	0.0306
21	1.1009	1.1036	0.00047	0.0205	6.320	0.0303
22	1.1057	1.1086	0.00049	0.0203	6.650	0.0300
23	1.1107	1.1137	0.00051	0.0202	6.983	0.0298
24	1.1156	1.1189	0.00053	0.0200	7.319	0.0295
25	1.1206	1.1241	0.00055	0.0201	7.658	0.0292
26	1.1256	1.1293	0.00057	0.0202	8.000	0.0290
27	1.1305	1.1344	0.00059	0.0203	8.345	0.0288
28	1.1355	1.1395	0.00061	0.0203	8.692	0.0287
29	1.1404	1.1446	0.00062	0.0203	9.041	0.0284
30	1.1453	1.1497	0.00064	0.0202	9.393	0.0281
31	1.1503	1.1548	0.00066	0.0203	9.749	0.0280
32	1.1532	1.1599	0.00068	0.0203	10.106	0.0278
33	1.1601	1.1650	0.00069	0.0203	10.466	0.0275
34	1.1651	1.1700	0.00070	0.0203	10.829	0.0274
35	1.1700	1.1751	0.00072	0.0209	11.194	0.0272
36	1.1748	1.1800	0.00073	0.0212	11.561	0.0271
37	1.1795	1.1848	0.00074	0.0216	11.930	0.0270
38	1.1841	1.1895	0.00075	0.0220	12.301	0.0267
39	1.1886	1.1941	0.00076	0.0221	12.675	0.0266
40	1.1931	1.1986	0.00077	.....	13.051	.....

* Add if the temperature is above, subtract if it is below, the standard.
† Corresponding with a difference in specific gravity of 0.0001.
‡ The figures on this line across the page are for fractional percentages below 1.
NOTE: To find the per cent. of chlorine, multiply the per cent. of Hydrochloric Acid by 0.9724.
For the volume per cent. of official Hydrochloric Acid (32 per cent.), multiply the "normality" by 9.895. For the volume per cent. of official Diluted Hydrochloric Acid (10 per cent.), multiply the "normality" by 34.88.

25° C. (77° F.), which is practically equivalent to the figure given in the British Pharmacopœia, which is 1.160 at 15.5° C. (59.9° F.). When exposed to heat, it continues to give off hydrochloric acid gas, with the appearance of ebullition, until its sp. gr. falls to 1.094, when it properly boils, and may be distilled unchanged, or entirely volatilized.

Hydrochloric acid is characterized by forming, on the addition of silver nitrate, a white precipitate (silver chloride), insoluble in nitric acid, but readily soluble in ammonia. It is incompatible with alkalies, with metallic oxides and their carbonates, and with potassium sulphide, potassium tartrate, tartar emetic, iron and potassium tartrates, silver nitrate, and solution of lead subacetate.

Ammonia in excess, if it produces no precipitate, shows the absence of iron.

If a small portion of the diluted acid be treated with test zinc, the evolved gas should not blacken paper wet with silver nitrate test solution (arsenous or sulphurous acid). Free chlorine or nitric acid may be discovered by its having the power to dissolve gold leaf. Any minute portion of the leaf which may be dissolved is detected by adding a solution of stannous chloride, which will give rise to a purplish tint. The free chlorine is derived from the reaction of nitric or nitrous acid on a small portion of the hydrochloric acid, which is thus deprived of its hydrogen. Hence it is that, when free chlorine is present, nitrous acid or some other oxide of nitrogen is also present as an impurity. The nitric and nitrous acids are derived from nitrates found as impurities in the common salt and from nitrous acid in the commercial sulphuric acid employed in the preparation of the hydrochloric acid.

It is very often desirable to know, in chemical and pharmaceutical operations, the quantity of absolute acid contained in samples of acid of different densities. (See table, p. 35.)

Hydrochloric Acid of Commerce. Muriatic Acid.—So-called by Priestley, from *murum*, the old name of chlorine, which in turn was derived from the Latin *murias*, brine. This acid has the general properties of the pure aqueous acid. It has a yellowish color owing to the presence of ferric chloride, or of a minute proportion of organic matter, such as cork, wood, etc. It usually contains sulphuric acid, and sometimes free chlorine and nitrous acid. Sulphurous Acid was formerly a frequent impurity (for methods for its detection see *U. S. D.*, 19th ed., p. 37), but is not at present an important adulterant.

Arsenic, derived from sulphuric acid, used in its manufacture, and lead, from the vessels used, were also often present. The official tests will exclude these impurities. (For other tests see *U. S. D.*, 19th ed., p. 38.) A small proportion of thallium has been detected in commercial hydrochloric acid by Wm. Crookes, being derived from sulphuric acid, in the manufacture of which pyrites was employed. Selenium has been found in French hydrochloric acid, causing the acid to have a bad odor.

Properties of Hydrochloric Acid Gas.—Hydrochloric acid gas is colorless and elastic, possessing a very pungent odor, and the property of irritating the organs of respiration. It destroys life and extinguishes flame. It reddens litmus powerfully, and has the other properties of a strong acid. Its sp. gr. is 1.278 (Gay-Lussac and Biot). Subjected to a pressure of 40 atmospheres, at the temperature of 10° C. (50° F.), it is condensed into a transparent liquid, to which alone the name of *liquid hydrochloric acid* properly belongs. Water absorbs this gas with the greatest avidity.

It consists of one volume of chlorine and one of hydrogen, united without condensation.

Toxicological Properties.—Hydrochloric acid, when swallowed, is highly irritating and corrosive, but less so than sulphuric or nitric acid. It produces hiccough, violent efforts to vomit, and agonizing pain in the stomach. There is much thirst, with great restlessness, a dry and burning skin, and a small concentrated pulse. If the acid has been recently swallowed, white vapors of a pungent odor will be emitted from the mouth. The best antidote is magnesia, but soap or sufficiently diluted alkaline solutions are almost equally efficient. In the course of the treatment, bland and mucilaginous drinks must be freely given. When inflammation supervenes, it must be treated on general principles.

Uses.—Stronger hydrochloric acid is rarely used in medicine. For a discussion of the therapeutic properties, incompatibilities, etc., see *Acidum Hydrochloricum Dilutum*, p. 37.

Dose, five to ten minims (0.3–0.6 mil) well diluted.

Off. Prep.—Acidum Hydrochloricum Dilutum, *U. S., Br.;* Acidum Nitrohydrochloricum, *U. S.;* Acidum Nitrohydrochloricum Dilutum, *U. S., Br.*

ACIDUM HYDROCHLORICUM DILUTUM.

U. S., Br.

DILUTED HYDROCHLORIC ACID **Acid. Hydrochl. Dil.**

(ăç'ĭ-dŭm hȳ-drǫ-ȼhlō'rĭ-cŭm dī-lū'tŭm)

"An aqueous solution containing not less than 9.5 per cent. nor more than 10.5 per cent. of HCl (36.47). Preserve it in glass-stoppered bottles." *U. S.* "Diluted Hydrochloric Acid contains 10 per cent. by weight of hydrogen chloride, HCl." *Br.*

Acidum Muriaticum Dilutum, *U. S.*, 1870; Diluted Muriatic Acid; Acide chlorhydrique dilué, *Fr.;* Acidum hydrochloricum dilutum, *P. G.;* Verdünnte Salzsäure, *G.;* Acido cloridrico diluito, *It.*

* "Hydrochloric Acid, *one hundred grammes* [or 3 ounces av., 231 grains]; Distilled Water, *two hundred and twenty grammes* [or 7 ounces av., 333 grains], to make *three hundred and twenty grammes* [or 11 ounces av., 126 grains]. Mix them." *U. S.*

"Hydrochloric Acid, 330 grammes; Distilled Water sufficient to produce 1000 millilitres. Mix." *Br.*

The official description is as follows: "Diluted Hydrochloric Acid is a colorless, odorless liquid; it has a strongly acid taste and is strongly acid to litmus. Specific gravity: about 1.049 at 25° C. (77° F.). With silver nitrate T.S., it yields a white, curdy precipitate, insoluble in nitric acid, but readily soluble in ammonia water. Evaporate 25 mils of Diluted Hydrochloric Acid from a platinum or porcelain dish and dry at 110° C. (230° F.); not more than 0.003 Gm. of residue remains. Add 1 mil of chloroform to 10 mils of Diluted Hydrochloric Acid and then cautiously introduce chlorine water, which has been diluted with an equal volume of distilled water, a drop at a time, with constant agitation; the chloroform remains free from any yellow, orange or violet color (*bromide or iodide*). Add 1 mil of potassium iodide T.S. and 1 mil of chloroform to 10 mils of Diluted Hydrochloric Acid and agitate the mixture; the chloroform remains free from any violet coloration (*free chlorine or bromine*). Two mils of Diluted Hydrochloric Acid, diluted with seven volumes of distilled water, does not respond to the Test for heavy metals (see Part III, Test No. 3). Five mils of Diluted Hydrochloric Acid diluted with 12 mils of distilled water (without the treatment with sulphuric and sulphurous acids) meets the requirements of the Test for arsenic (see Part III, Test No. 1). Add 5 drops of barium chloride T.S. to a mixture of 3 mils of Diluted Hydrochloric Acid and 5 mils of distilled water; neither turbidity nor precipitation appears within one hour (*sulphuric acid or sulphates*). At the end of this period, the further addition to the liquid of 2 drops of tenth-normal iodine V.S. produces neither turbidity nor decoloration of the iodine (*sulphurous acid*).

"**Assay.**—Pour about 10 mils of Diluted Hydrochloric Acid into a tared flask, weigh accurately, dilute with 30 mils of distilled water and titrate the liquid with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 9.5 per cent. nor more than 10.5 per cent. of HCl.

"Each mil of normal potassium hydroxide V.S. used corresponds to 0.03647 Gm. of HCl. Each gramme of Diluted Hydrochloric Acid corresponds to not less than 2.6 mils nor more than 2.9 mils of normal potassium hydroxide V.S." *U. S.*

"Yields, when neutralised, the *reactions* characteristic of chlorides. Specific gravity 1.048. 10 millilitres require for neutralisation 28.7 millilitres of *N/1 solution of sodium hydroxide.* Free from the impurities indicated under 'Acidum Hydrochloricum.'" *Br.*

The British diluted acid is now of the same strength as the U. S. preparation.

Uses.—As is well known, hydrochloric acid is secreted by the glands of the stomach and is essential in gastric digestion for the purpose of activating pepsinogen. It probably also plays an important part in the digestive processes by determining the rapidity of the discharge of the gastric contents in the duodenum. Cannon has shown that free acid in the gastric pyloric portion of the stomach leads to a relaxation of the pylorus and that when the duodenal contents have become acid through the discharge of the gastric contents there is a closing of this orifice. Moreover, hydrochloric acid forms with the duodenal mucous membrane a hormone known as *secretin* which stimulates the pancreas. In a large proportion of cases of gastric indigestion, and probably also in many cases of intestinal indigestion, the cause of the disturbance is a diminution in the amount of hydrochloric acid secreted. The most important use of hydrochloric acid in medicine is for the purpose of replacing at least in part the lack of the natural acid in the treatment of *fermentative gastritis, nervous dyspepsia,* and similar conditions. For the same reason it is often of service to improve the digestion, and thereby the nutrition, in various *low fevers, phthisis,* and other forms of *malnutrition.* The doses which are sometimes employed are absurdly small. When we remember that the normal acidity of the stomach during gastric digestion ranges from 0.2 to 0.3 per cent. of hydrochloric acid—which would necessitate nearly two grammes of absolute hydrochloric acid for an ordinary meal—the futility of administering five to ten drops of a 10 per cent. solution of this acid is evident. Hydrochloric acid has also been highly recommended in *pernicious anemia* by Beebe and by Croftan (*J. A. M. A.*, August, 1910, p. 593), and in the treatment of *gout* by Falkenstein and others. Its value in these cases is probably due to improvement of the patient's nutrition.

Hydrochloric Acid and diluted hydrochloric acid are incompatible with lead, silver, and mercury salts; with antimony and potassium tartrate solution, a precipitate of basic chloride of antimony is produced. In bismuth and ammonium citrate, bismuth citrate is precipitated. The strong acid decomposes chlorates, nitrates, etc., with the evolution of chlorine, and other irritating gases.

Dose, ten to sixty minims (0.6–3.75 mils) well diluted.

ACIDUM HYDROCYANICUM DILUTUM. U. S., Br.

DILUTED HYDROCYANIC ACID **Acid. Hydrocyan. Dil.** **[Diluted Prussic Acid Acidum hydrocyanicum dilutum P. I.]**

(ăç'ĭ-dŭm hī-drō-cī-ăn'ĭ-cŭm dī-lū'tŭm)

"An aqueous solution containing not less than 1.9 per cent. nor more than 2.1 per cent. of HCN (27.02) and not more than 0.1 per cent. of HCl. Preserve it in small, dark amber-colored, well-stoppered vials." *U. S.* "Diluted Hydrocyanic Acid is an aqueous solution containing 2 per cent. by weight of hydrogen cyanide, HCN. It may be obtained by the interaction of diluted sulphuric acid and potassium ferrocyanide, and subsequent distillation. Should be stored in a dark place, in

small, inverted stoppered bottles of amber-coloured glass." *Br.*

Cyanhydric Acid; Acidum Hydrocyanatum, s. Borussicum; Acide cyanhydrique dissous, *Fr. Cod.*; Acide cyanhydrique, ou hydrocyanique, *Fr.*; Cyanwasserstoffsäure, Blausäure, *G.*; Acido cianhidrico, *Sp.*

The United States Pharmacopœia IX does not give a process for making Diluted Hydrocyanic Acid. The U. S. P. VIII gave the following extemporaneous process: "Silver Cyanide, *six grammes* [or 92.5 grains]; Diluted Hydrochloric Acid, *fifteen and fifty-four hundredths mils* [or 4 fluidrachms, 12 minims]; Distilled Water, *forty-four and one-tenth mils* [or 1 fluidounce, 3 fluidrachms, 56 minims]. Mix the Diluted Hydrochloric Acid with the Distilled Water, add the Silver Cyanide, and shake the whole together in a glass-stoppered bottle. When the precipitate has subsided, pour off the clear liquid." *U. S. VIII.*

The U. S. P., 1890, process, which may be used on a larger scale, is as follows: "Potassium Ferrocyanide, in coarse powder, *twenty grammes* [or 308.6 grains]; Sulphuric Acid, *eight mils* [or 2 fluidrachms, 10 minims]; Water, *sixty-five mils* [or 2 fluidounces, 95 minims]; Distilled Water, *a sufficient quantity.* Place the Potassium Ferrocyanide in a tubulated retort, and add to it *forty mils* [or 1 fluidounce, 3 fluidrachms] of water. Connect the neck of the retort (which is to be directed upward), by means of a bent tube, with a well-cooled condenser, the delivery tube of which terminates in a receiver surrounded with ice-cold water, and containing *sixty-five mils* [or 2 fluidounces, 95 minims] of Distilled Water. All the joints of the apparatus, except the neck of the receiver, having been made air-tight by means of well-fitting corks, pour into the retort, through the tubulure, the Sulphuric Acid, previously diluted with *twenty-five mils* [or 6 fluidrachms, 46 minims] of Water. Gently mix the contents of the retort, and then heat it, in a sand-bath, so as to keep the liquid in brisk ebullition, until about one-half of its volume has passed over into the receiver. Detach the receiver, and assay a small portion of the contents by the method given below. Then add to the remainder so much Distilled Water as may be required to bring the product to the strength of *two per cent.*, by weight, of absolute Hydrocyanic Acid."

When potassium ferrocyanide is decomposed by sulphuric acid, the residue in the retort is potassium sulphate, mixed with an insoluble compound of iron cyanide and potassium cyanide (*Everitt's Salt*). The reaction is expressed by the following equation:

$$2K_4FeC_6N_6 + 3H_2SO_4 = 3K_2SO_4 + 2KFeC_3N_3 + 6HCN$$

Half of the cyanogen present in the potassium ferrocyanide goes to form the hydrocyanic acid, while the other half remains in the white residue. Everitt's salt, so named from its discoverer, is a yellowish-white powder. Like potassium ferrocyanide, it is a double salt (iron and potassium cyanide), but of different molecular ratio. As it appears in practice, it is apt to be greenish, owing probably to the presence of a little Prussian blue.

Investigations have shown that potassium ferrocyanide is decomposable not only by the weakest acids but also by numerous non-acid organic substances, hydrocyanic acid being liberated; thus the diluted mineral acids (containing even less than 0.1 per cent.), formic, acetic, butyric, lactic, tartaric, benzoic acids, even carbon dioxide and hydrogen sulphide, phenols, peptones, casein, etc., will decompose potassium ferrocyanide more or less quickly at temperatures below 100° C. (212° F.), liberating a portion of the hydrocyanic acid. (*A. J. P.*, 1893, p. 283.)

In the U. S. VIII process for obtaining hydrocyanic acid extemporaneously, the reacting materials are single molecules respectively of silver cyanide and hydrochloric acid. These, by double decomposition, generate hydrocyanic acid, which dissolves in the water, and silver chloride, which subsides, and from which the acid is poured off when clear. (See *Argenti Cyanidum.*) The extemporaneous process is useful to country practitioners, because the acid will not keep indefinitely. It is doubtful, however, whether all of the silver cyanide will be decomposed, except under much more careful treatment than the process is likely to receive.

The change which was made in the process of the Pharmacopœia of 1880, in the substitution of diluted alcohol for the distilled water formerly used as the solvent for the hydrocyanic acid, was in accordance with the views of Gault and others, who asserted that greater stability was thus secured. It was not of sufficient value to be retained in the U. S. P., 1890, and the use of diluted alcohol was abandoned. (F. T. Drake, *Proc. A. Ph. A.*, 1891, p. 147.)

The processes thus far given are intended to furnish a *diluted* hydrocyanic acid for medicinal purposes. For processes for making the *anhydrous* acid, see U. S. Dispensatory, 19th ed., p. 40.

Berthelot has made hydrocyanic acid synthetically. He first prepared, by a direct synthesis of its elements, *acetylene* (C_2H_2). He then mixed this gas with pure nitrogen, passed a series of electric discharges from a Ruhmkorff coil through the mixture, and, when the odor of prussic acid was perceptible, agitated with a solution of potassium hydroxide to get the fixed cyanide. It has also been made by heating chloroform with ammonia and potassium hydroxide solution. (Hofmann.)

Properties of the Diluted Acid.—Diluted hydrocyanic acid, of the proper medicinal strength, is officially described as "a colorless liquid, of a characteristic odor resembling that of bitter almond; it is acid to litmus. On account of its poisonous character *it must be handled with great caution.* Render 1 mil of

the Acid alkaline with potassium hydroxide T.S., add a few drops of ferrous sulphate T.S., boil the mixture, and then acidulate with hydrochloric acid; a blue precipitate is formed. Not more than 0.002 Gm. of residue remains on evaporating 10 mils of Diluted Hydrocyanic Acid to dryness on a water bath. Pour 5 mils of Diluted Hydrocyanic Acid into a tared 100 mil glass-stoppered flask containing 25 mils of distilled water, accurately determine the weight of the Acid added and then add 50 mils of tenth-normal silver nitrate V.S. and enough distilled water to make 100 mils. Agitate it well and filter through a dry filter, rejecting the first 10 mils of the filtrate. In 50 mils of the clear filtrate determine the excess of silver nitrate by titration with tenth-normal potassium sulphocyanate V.S., previously adding 2 mils of nitric acid and 2 mils of ferric ammonium sulphate T.S. From the number of mils of tenth-normal silver nitrate V.S. consumed in this assay subtract twice the number of mils of tenth-normal silver nitrate V.S. consumed in the assay of the same quantity of Diluted Hydrocyanic Acid as ascertained below. The difference when calculated to free hydrogen chloride, using the factor 0.003647, does not amount to more than one-tenth of 1 per cent. of the weight of Diluted Hydrocyanic Acid originally taken for the determination (*hydrogen chloride*)." *U. S.*

Tests.—The Br. Pharm. requires that "5 millilitres, mixed with 50 millilitres of *water*, 5 millilitres of *solution of ammonia*, and 3 drops of *solution of potassium iodide*, require the addition of not less than 18.4 and not more than 19 millilitres of *N/10 solution of silver nitrate* before a permanent precipitate begins to form. 5 millilitres evaporated in a platinum dish leave no appreciable residue. Yields not more than the slightest characteristic *reactions* for sulphates or chlorides." *Br.*

It imparts a slight and evanescent red color to litmus. If it reddens litmus strongly and permanently, some acid impurity is present. It loses strength rapidly in open vessels. It is not reddened by potassium and mercury iodocyanide. The non-action of this test shows the absence of contaminating acids, which, if present, would react upon the iodocyanide and produce mercuric iodide. The red color produced when ammonium picrate is added to a solution of an alkaline cyanide and heated has been proposed as a test for prussic acid. (Guyot, *N. R.*, May, 1877.) It is liable to undergo decomposition if exposed to the light, but it may be kept for a longer time in a bottle covered with black paint or black paper. From experiments carefully conducted by Bussy and Buignet, it appears that, when the alteration in the acid under the influence of light has begun, it will afterwards go on very rapidly in the dark; and that after exposure for a certain time to the light, though no alteration may be apparent, an influence has nevertheless been exerted which disposes to change, and promotes decomposition even in the absence of light. Hence the necessity of immediately enclosing the acid in bottles from which the light is excluded. (*J. P. C.*, 1863, p. 475.) Experience has shown that it is best preserved in cork-stoppered bottles of amber glass; when glass and rubber stoppers were used, decomposition frequently took place rapidly. The U. S. P. IX permits the presence of 0.1 per cent. of hydrochloric acid, which acts as a preservative and it also directs the use of amber-colored vials. Sulphuric acid is sometimes found in diluted hydrocyanic acid, it may be detected by barium chloride, which will produce a precipitate of barium sulphate. John Williams has found in a series of experiments that the addition of 20 per cent. of glycerin has a very pronounced influence in preventing deterioration of the acid. (*P. J.*, Sept., 1874; Sept., 1875.)

"**Assay.**—Pour about 5 mils of Diluted Hydrocyanic Acid into a 100 mil flask containing 25 mils of distilled water and 5 mils of potassium hydroxide T.S., the whole having been previously tared, and weigh the Acid accurately. Then add 3 drops of potassium iodide T.S. and titrate with tenth-normal silver nitrate V.S. to the production of a slight, permanent precipitate. It shows not less than 1.9 per cent. nor more than 2.1 per cent. of HCN.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.005404 Gm. of HCN. Each gramme of Diluted Hydrocyanic Acid corresponds to not less than 3.5 mils nor more than 3.9 mils of tenth-normal silver nitrate V.S." *U. S.*

Formerly the medicinal acid was of different strengths, as ordered by the different pharmaceutical authorities, but happily the U. S. and Br. Pharmacopœias conform in this important point. At one time its strength was indicated by its specific gravity, which is lower in proportion as it is stronger; but this inaccurate method is not now relied on, and, though the British Pharmacopœia gives the sp. gr. of its diluted acid at 0.997, both Pharmacopœias give quantitative tests as indices of the strength. The International Protocol also adopted the strength of 2 per cent.

In connection with the determination of the minute amounts of hydrocyanic acid encountered in work on cyanogenetic plants, Viehoever and Johns have published a method in *J. Am. C. S.*, 1915, based upon a colorimetric comparison with a standard suspension of Prussian blue.

Scheele's medicinal hydrocyanic acid contains about 5 per cent. of anhydrous acid, and therefore two minims of it are equal to five of the U. S. acid. The use of Scheele's acid should be discouraged as unnecessary and very dangerous.

Properties of the Anhydrous Acid.—Hydrocyanic acid, perfectly free from water, is a colorless, transparent, inflammable liquid, of extreme volatility, boiling at 27° C. (80.6° F.), and congealing at −15° C. (5° F.). Its sp. gr. as a liquid is 0.6969, at the temperature of 18° C. (64.4° F.); and as a vapor 0.9423. Its taste is

at first cooling, then burning, with an after-taste in the throat like that of bitter almonds; but, from its extremely poisonous nature, it must be tasted with the utmost caution. Its odor is so strong as to produce immediate headache and giddiness, and its vapor so deleterious that the smallest portion of it cannot be inhaled without the greatest danger. Both water and alcohol dissolve it readily. It is much more prone to undergo decomposition than the diluted acid. In the course of a few hours it sometimes begins to assume a reddish-brown color, which becomes gradually deeper, till at length the acid is converted into a black liquid, which exhales a strong odor of ammonia. It is a very weak acid in its chemical relations, and reddens litmus but slightly. It does not form solid compounds with metallic oxides, but cyanides of metals, the elements of water being eliminated. According to Sobero, hydrocyanic acid is generated, in sensible quantities, by the action of weak nitric acid on the volatile oils and resins. Wöhler affirmed in 1828 that picric acid when treated with baryta water yields it; and Julius Post and H. Hübner have found that nitrobenzene and dinitrobenzene do also when treated, the former with fused potassium hydroxide, the latter with boiling diluted solution of potassium hydroxide. Though a product of art, it exists in some plants, and is generated by reaction between the constituents of many vegetable products upon contact with water. These principles are usually amygdalin and emulsin, but according to Peckholt the root of *Manihot utilissima* (Pohl) copiously generates hydrocyanic acid with water, although he was unable in 15 analyses to find amygdalin in it. (*A. J. P.*, Oct., 1872.) (See *Amygdala Amara.*)

Composition.—Hydrocyanic acid consists of one atom each of cyanogen and hydrogen; or, in volumes, of one volume of cyanogen and one of hydrogen without condensation, its formula being HCN or HCy. *Cyanogen,* $(CN)_2$, is a colorless gas, of a strong and penetrating odor, inflammable, and burning with a beautiful bluish-purple flame. Its sp. gr. is 1.8157. It was discovered in 1815 by Gay-Lussac, who viewed it as a compound radical which when combined with hydrogen becomes hydrocyanic acid. Hydrocyanic acid, in a diluted state, was discovered in 1780 by Scheele, who correctly stated its elements to be carbon, nitrogen, and hydrogen; but the peculiar way in which they are combined was first pointed out by Gay-Lussac, by whom also the anhydrous acid was first obtained.

Uses.—Diluted hydrocyanic acid has been much used in respiratory diseases and to quiet *cough,* but its action is so fugacious that it has really very little medicinal value except as a local remedy in sick stomach of nervous origin and in *gastrodynia.* Externally, it may be of occasional service in *pruritus,* but should be used circumspectly, as its vapors are poisonous.

It should be administered with the greatest caution, on account of its minute dose and its variable strength as usually found. The proper plan, therefore, is to begin with a small dose, two drops, for example, and gradually to increase the quantity until some obvious impression is produced. On account of the rapidity and uncertainty of its action, it should be given at intervals of not more than two hours; indeed, it is very improbable that the largest therapeutic dose of the substance exerts any influence whatever upon the system one hour after its ingestion. If giddiness, weight at the top of the head, sense of tightness at the stomach, or faintness come on, its use should be discontinued. In all cases in which a fresh portion of medicine is used, the dose should be lowered to the minimum quantity, lest the new sample should prove stronger than that previously employed. As a lotion it may be diluted with from eight to fifteen parts of water.

Diluted Hydrocyanic Acid is incompatible with the strong mineral acids which decompose it to formic acid and a salt of ammonium. It is also incompatible with salts of silver, lead and mercury. Oxidizing agents destroy it with the formation of a number of compounds.

Toxicology.—Hydrocyanic acid is an exceedingly powerful poison acting with great rapidity. After large doses death may take place in from two to ten minutes, but from minimal fatal quantities may be delayed as long as two or three hours. The smallest fatal quantity upon record seems to be that reported by Garstang (*L. L.*, 1888, ii, p. 15), in which 2 drachms of the 2 per cent. solution proved fatal. The ordinarily fatal dose is about 1 to 1½ grains of the pure acid. Of potassium cyanide the ordinarily fatal dose is about five grains.

After large doses the progress of the poison is so rapid that one can scarcely speak of symptoms; the patient gives a cry and falls down insensible and respirations which are at first hurried become in a few seconds slow and gasping and death may occur in a few minutes either with or without preceding convulsions. In the majority of cases, however, the poison progresses somewhat more slowly and the symptoms will be as follows: Immediately after swallowing the poison there is a sense of constriction in the throat followed by salivation and nausea with vertigo and headache. The respirations are at first rapid and then become slow and irregular, with expiration often being greatly prolonged. The pulse is slow and at first bounding, the pupils dilated and insensible to light, the eyes wide open and staring, the skin cold and cyanotic, and violent convulsions with foaming of the mouth are not uncommon. This stage is followed by one of weakness, the patient becoming unconscious, the temperature falling, the pulse growing feeble, the respirations very slow and gasping in character. Death is the result of asphyxia and the symptoms are those in general characteristic of interference with oxygenation. Post mortem the blood may be either of a uniform arterial hue in both

veins and arteries or the dark blood of cyanosis, according as to whether death has taken place rapidly or slowly.

The treatment of prussic acid poisoning to be of any avail must be undertaken with great promptness. The stomach should be immediately emptied with the pump, as emetics often fail to produce the desired effect. Among the chemical antidotes which have been suggested the most useful are the ferric salts suggested by T. and H. Smith. Martin and O'Brien (*Proceedings of the Soc. for Chemical Industry*, Victoria, i, p. 119) recommend that in mines, etc., where accidental poisoning is likely to occur, there should be kept on hand one ounce each of a 23 per cent. solution of ferrous sulphate, of a 5 per cent. solution of potassium hydroxide, and 30 grains of magnesium oxide. These are to be mixed in a half pint of water before being used. Cobaltous nitrate has been recommended, but, although an efficient antidote, it is so poisonous that its use in the human subject seems hardly justifiable. Kobert and Krohl (*Arb. d. Pharm. Inst. z. Dorpat*, 1891, vii; *Ph. Centralh.*, 1891) have found that in the lower animals good results may be achieved in the poisoning by the conversion in the system of the prussic acid into oxamide by means of peroxide of hydrogen. The oxamide is itself somewhat poisonous, and after its production it is essential to give large draughts of water to wash it out of the system. It is affirmed that in various mining and extracting establishments, and in certain chemical works, where the cyanides are used in enormous quantities, Kobert's method is practically employed, and Merck furnishes what is known as an "antidote-box," containing the necessary apparatus and the supply of hydrogen peroxide. (See *M. A.*, ii, p. 94.) When the cyanide has been taken into the system the peroxide must be introduced by means of a stomach tube into the stomach itself, and the latter should then be washed out. Before or immediately after the administration by the mouth the salts should be given hypodermically. In cases of poisoning by inhalation the antidote should be used subcutaneously. The poison's action is, however, so rapid that there is rarely time for any antidote to be of value. Atropine, which has been suggested as physiologically antagonistic to hydrocyanic acid, has no antidotal value.

Dose, of diluted hydrocyanic acid, one to four minims (0.06–0.25 mil).

Off. Prep.—Tinctura Chloroformi et Morphinæ Composita, *Br.*

ACIDUM HYPOPHOSPHOROSUM. U. S.

HYPOPHOSPHOROUS ACID Acid. Hypophos.

(ăç′ĭ-dŭm hȳ-pǫ-phŏs-phǫ-rō′sŭm)

"An aqueous solution containing not less than 30 per cent. nor more than 32 per cent. of HPH_2O_2 (66.06). Preserve it in glass-stoppered bottles." *U. S.*

Acide hypophosphoreux, *Fr.*; Unterphosphorigesäure, *G.*

This acid was introduced into the U. S. P. VIII to have a permanent concentrated solution of hypophosphorous acid which could be conveniently reduced in strength by adding water, as in making the official diluted acid.

Properties.—It is officially described as "a colorless or slightly yellow, odorless liquid; it has an intensely acid taste, and is acid to litmus, even when highly diluted. Specific gravity: about 1.130 at 25° C. (77° F.). When the Acid is heated in a suitable dish, water evaporates and it becomes more concentrated. On further heating between 130° and 140° C. (266° and 284° F.), it decomposes, forming hydrogen phosphide, which ignites, and phosphorous acid; the latter between 160° and 170° C. (320° and 338° F.) decomposes into hydrogen phosphide and phosphoric acid; the pasty residue finally reddens, ignites, and the last portions of unoxidized phosphorus burn out at a higher temperature. Hypophosphorous Acid conforms to the tests for identity and purity under *Acidum Hypophosphorosum Dilutum* when diluted to that strength.

"**Assay.**—Pour about 7 mils of Hypophosphorous Acid into a tared and stoppered flask, weigh accurately, dilute with 50 mils of distilled water and titrate with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 30 per cent. nor more than 32 per cent of HPH_2O_2.

"Each mil of normal potassium hydroxide V.S. used corresponds to 0.06606 Gm. of HPH_2O_2. Each gramme of Hypophosphorous Acid corresponds to not less than 4.54 mils nor more than 4.84 mils of normal potassium hydroxide V.S." *U. S.*

A new method of assay for hypophosphorous acid and the hypophosphites has been proposed by T. T. Cocking and J. T. Kettel (*Tr. Br. Ph. Conf.*, 1913, 518), which is more accurate and expeditious than any hitherto proposed. It is as follows: Two and one half Gm. of the hypophosphite (or the acid) are dissolved in 40 mils of water and an excess of lead acetate solution (10 per cent.) added to precipitate phosphites (5 mils is usually sufficient) and the solution is made up to 50 mils, well shaken and allowed to stand until the supernatant liquid is clear. Then 10 mils, representing 0.5 Gm. of the material taken, is carefully pipetted off, 50 mils of normal potassium dichromate and 10 mils of sulphuric acid added and the mixture heated on a water bath. After one hour the solution is cooled and diluted with distilled water to 250 mils. The excess of dichromate is then determined in 50 mils of the solution by titration with tenth normal sodium thiosulphate V.S., after adding potassium iodide. The reaction upon which calculations are based is as follows:

$$R'.PH_2O_2 + O_2 = R'H_2PO_4.$$

The authors gave the method a thorough trial

with a number of samples of hypophosphites obtained in the market.

Uses.—This acid is not used for medicinal purposes; in pharmacy it is employed in making the diluted acid or other preparations.

Off. Prep.—Acidum Hypophosphorosum Dilutum, *U. S.*

ACIDUM HYPOPHOSPHOROSUM DILUTUM. U. S.

DILUTED HYPOPHOSPHOROUS ACID Acid. Hypophos. Dil.

(ăç'ĭ-dŭm hȳ-pŏ-phŏs-phŏ-rō'sŭm dī-lū'tŭm)

"An aqueous solution containing not less than 9.5 per cent. nor more than 10.5 per cent. of HPH_2O_2 (66.06). Preserve it in well-stoppered bottles." *U. S.*

Acide Hypophosphoreux dilué, *Fr.*; Verdünnte Unterphosphorigesäure, *G.*

* "Hypophosphorous Acid, *one hundred grammes* [or 3 ounces av., 231 grains]; Distilled Water, *two hundred and ten grammes* [or 7 ounces av., 178 grains], to make *three hundred and ten grammes* [or 10 ounces av., 409 grains]. Mix them. Keep the product in well-stoppered bottles." *U. S.*

This acid was introduced into the U. S. Pharmacopœia of 1890, and retained in the 8th and 9th Revisions mainly because of its value as an addition, as a reducing agent, to pharmaceutical preparations containing iodides, which are liable to decomposition through exposure to light and air. Diluted hypophosphorous acid has proved to be the most satisfactory preservative to these easily decomposed salts. It may be added directly, or, as in the case of diluted hydriodic acid, a hypophosphite can be employed, and the salt decomposed by an acid during the manipulation. It may be made on a large scale, however, by boiling phosphorus with milk of lime and subsequently decomposing the calcium hypophosphite with a strong acid, oxalic acid being frequently used for this purpose. The following process of Procter's (*A. J. P.*, 1858, p. 121) is based on this principle. Take of calcium hypophosphite 480 grains, crystallized oxalic acid 350 grains, distilled water 9 fluidounces. Dissolve the hypophosphite in 6 fluidounces of the water, and the acid in the remainder with the aid of heat; mix the solutions, pour the mixture on a white paper filter, and when the liquid has passed add distilled water carefully till it measures 10 fluidounces; evaporate this to 8½ fluidounces. Charles T. Tyrer prefers to make this acid by decomposing barium hypophosphite carefully with diluted sulphuric acid and subsequently concentrating the acid under reduced pressure. By this method it can be obtained in a syrupy form which sometimes crystallizes in white scales having a melting point of 17° C. (62.6° F.). Hypophosphorous acid is frequently made to contain 30 per cent. of absolute acid; such an acid has the sp. gr. of 1.137 at 15.6° C. (60° F.), and does not deposit on long standing. (See preceding article.)

Properties.—Diluted hypophosphorous acid is "a colorless, odorless liquid; it has a strongly acid taste and is strongly acid to litmus. Specific gravity; about 1.042 at 25° C. (77° F.). When heated in a porcelain dish, water evaporates with the evolution of hydrogen phosphide, and further decomposition takes place as described under *Acidum Hypophosphorosum*. With silver nitrate T.S. it yields a black precipitate of silver, and with mercuric chloride T.S., a white precipitate of mercurous chloride. Neutralize 30 mils of Diluted Hypophosphorous Acid with ammonia water; not more than a slight precipitate results, and, after filtering, a portion of the filtrate, slightly acidulated with hydrochloric acid, does not become turbid upon the addition of potassium sulphate T.S. (*barium*); another portion of the filtrate shows no turbidity with calcium chloride T.S. (*oxalic acid*). One mil of Diluted Hypophosphorous Acid mixed with 9 mils of distilled water does not respond to the Test for heavy metals (see Part III, Test No. 3). Mix 5 mils of Diluted Hypophosphorous Acid with 3 mils of nitric acid and 10 mils of distilled water, and evaporate the liquid to dryness on a water bath; the residue meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"**Assay.**—Pour about 25 mils of Diluted Hypophosphorous Acid into a tared flask, weigh accurately, add 25 mils of distilled water and titrate with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 9.5 per cent. nor more than 10.5 per cent. of HPH_2O_2.

"Each mil of normal potassium hydroxide V.S. used corresponds to 0.06606 Gm. of HPH_2O_2. Each gramme of Diluted Hypophosphorous Acid corresponds to not less than 1.44 mils nor more than 1.6 mils of normal potassium hydroxide V.S." *U. S.*

Uses.—This acid is believed by many clinicians to have tonic properties, but is very rarely, if ever, used for medicinal purposes except in combinations with strychnine, quinine, or iron, which are thought by many practitioners to be especially valuable in *nervous debility*.

Diluted Hypophosphorous Acid is incompatible with many substances on account of its powerful reducing properties, and in exercising these effects it is oxidized to phosphoric acid and thus loses its own identity. It reduces bismuth, mercuric, and mercurous compounds to the metallic state. Ferric and cupric compounds are reduced to ferrous and cuprous. Permanganates are changed to manganous compounds; arsenates are reduced to arsenites and sometimes to metallic arsenic. With some oxidizing agents like potassium chlorate, it must not be triturated for fear of causing an explosion.

Dose, from five to twenty minims (0.3–1.3 mils).

ACIDUM LACTICUM. U. S., Br.

LACTIC ACID Acid. Lact.

(ăç'ĭ-dŭm lăc'tĭ-cŭm)

"A liquid containing lactic acid [optically inactive alphahydroxypropionic acid, $C_3H_6O_3$ or $CH_3.CHOH.COOH = 90.05$] and lactic anhydrides, equivalent to a total of not less than 85 per cent. nor more than 90 per cent. of $C_3H_6O_3$." *U. S.* "Lactic Acid is an aqueous solution containing not less than 75 per cent. by weight of hydrogen lactate, $HC_3H_5O_3$, and not less than 10 per cent. by weight of lactide, $C_6H_8O_4$. It may be obtained by the fermentation of lactose." *Br.*

Alphahydroxypropionic Acid, Oxypropionic Acid, Ethylidenelactic Acid, Isolactic Acid; Acide lactique, *Fr. Cod.*; Acidum lacticum, *P. G.*; Milchsäure, *G.*; Acido lactico, *Sp.*

The strength of lactic acid in the U. S. IX was changed from that of the U. S. VIII which contained 75 per cent. by weight of absolute lactic acid. The U. S. IX requires a total of 85 to 90 per cent. of $C_3H_6O_3$, including lactic anhydrides. The British Pharmacopœia requires not less than 75 per cent. of $C_3H_6O_3$, and not less than 10 per cent. of lactide, $C_6H_8O_4$.

Lactic acid was discovered in 1780 by Scheele. It exists in sour milk, and is a product of the viscous or lactic fermentation of rice water, or of the juices of the beet, turnip, and carrot, and is a normal constituent of sauer kraut and of ensilage. Indeed, it is formed whenever sugar in solution, of whatever kind, is placed in contact with an alkaline or earthy carbonate in presence of a special ferment. Pasteur demonstrated that the lactic acid fermentation, like the vinous, is caused by a peculiar microscopic plant or mycoderm. It is attended with the production not only of lactic acid, but of other substances also, and among them a peculiar gum-like substance, in abundance, which, first noticed by Kirchof, has been isolated in a pure state by Brüning. Though similar to arabin and dextrin, with the formula $C_6H_{10}O_5$, it is not exactly identical with either. The lactic acid of fermentation is one of four isomeric acids possessing the formula $C_3H_6O_3$. The *first* of these is the official lactic acid, and is inactive optically. The *second* is identical chemically with this, but physically different, being dextrorotatory, and is found in the juice of flesh. It is called *paralactic acid.* The *third,* or *ethylene lactic acid,* is found mixed with the second in the so-called "*sarcolactic*" acid extracted from meat. The *fourth* acid has only been obtained synthetically, and is known as *hydracrylic acid.*

Preparation.—Lactic acid may be obtained by the following process, which was recommended by Louradour as the first step in preparing ferrous lactate: Ferment whey by keeping it at a temperature between 21.1° C. (70° F.) and 26.6 C. (80° F.), whereby it becomes charged with a considerable quantity of lactic acid. Evaporate the liquor to one-third of its bulk, decant and filter, and then saturate with milk of lime. This converts the lactic acid into calcium lactate, which remains in solution, and a precipitate is thrown down, consisting principally of calcium phosphate. The liquor is filtered again, and precipitated by oxalic acid, which throws down the lime as calcium oxalate, and sets free the lactic acid. By a third filtration a solution of lactic acid is obtained, containing lactose (sugar of milk) and certain salts. From these it may be purified by concentrating it to a syrupy consistence and treating it with alcohol, which dissolves the acid, and precipitates the lactose and foreign salts. The solution is filtered, and the lactic acid is obtained pure by distilling off the alcohol. Wackenroder's method is to mix 10 parts of skimmed milk, 2.5 of milk sugar, 2 of chalk, and 20 of water, to digest at about 23.8° C. (75° F.) for a month, or till the chalk is dissolved, then to express, clarify, and evaporate so as to crystallize the calcium lactate, and, after recrystallization, to decompose it with sulphuric or oxalic acid in exact saturating proportions.

Alan A. Claflin thus describes the manufacture of lactic acid as carried out on a large scale under the patent of Charles E. Avery (*J. Soc. Chem. Ind.,* June 30, 1897). A saccharine solution varying in density from 1.05 to 1.075 is taken. This will contain from 7.5 to 11 per cent. of saccharine matter. It is advantageous to have from 10 to 15 per cent. of this, cane sugar, the rest being grape sugar. The saccharine solution, having been made up and boiled for an hour to insure sterilization, is conveyed into the fermentation tank and cooled to from 55° to 45° C. (131°–113° F.), and then impregnated with nitrogenous matter (such as is extracted from bran by the action of boiling water and diluted acid) in amount equal to about 8 per cent. of the saccharine matter, and the *Bacillus acidi lactici.* In continuous manufacture the ferment solutions are impregnated from a preceding ferment liquor in which a lively fermentation is in progress; 20 per cent. of such impregnating liquor may be added. The impregnation having taken place at 45° C. (113° F.) or over, the temperature is allowed to decrease somewhat as the fermentation proceeds. The glucose is practically all decomposed, and the yield of lactic acid is over 98 per cent. As the fermentation progresses the solution must be neutralized with milk of lime, as the limits of acidity in which lactic acid bacteria are healthy are rigidly confined between 0.02 and 0.5 per cent. If the fermenting solution is overneutralized, the butyric ferment will immediately begin to act, and once active is difficult to control. The lactic fermentation is best completed in from three to six days, and when the fermentation is ended, the liquor must be heated sharply to kill all bacteria and spores and prevent subsequent fermentation. The solution is now filtered and evaporated, when calcium lactate may be crystallized out; or if commercial syrupy acid only

is required, the solution may be at once decomposed by sulphuric acid. Chemically pure lactic acid is obtained by converting calcium lactate into zinc lactate with zinc carbonate, precipitating the zinc with H_2S, passing through animal charcoal and evaporating *in vacuo*.

Kiliani (*Ber. d. Chem. Ges.*, xv, 136 and 699) has found that lactic acid may be readily prepared by the action of potassium or, preferably, sodium hydroxide upon either grape sugar or invert sugar (*i.e.*, cane sugar after treatment with diluted acids). He found that invert sugar gave a better yield than ordinary glucose.

His method for the preparation of lactic acid is as follows: 500 grammes of cane sugar are placed with 150 grammes of water and 10 mils of the sulphuric acid, in a stoppered flask of 2 liters' capacity and heated for 3 hours to about 50° C. (122° F.). The solution of invert sugar so obtained is colorless, or at most faintly yellow. After cooling there is to be added to it in portions of 50 mils at a time 400 mils of a caustic soda solution made by dissolving 1 part of caustic soda in 1 part of water. The strong alkali settles at first as a slimy mass on the bottom, and a new portion is only to be added when the mixture has become perfectly homogeneous by shaking. The flask should also be cooled with water while the alkali is being added. The mixture nevertheless becomes colored and greatly heated. Finally the mixture is heated to 60° or 70° C. (140° to 158° F.) until a portion heated over a boiling water bath does not separate cuprous oxide from Fehling's solution, but gives it only a slight greenish tinge. Into the cooled mixture the calculated amount of sulphuric acid (made by mixing 3 parts of sulphuric acid with 4 of water) is then run. As soon as the acid liquid has cooled to the temperature of the room, a crystal of Glauber's salt is dropped in and the flask dipped in cold water until a thin crystalline crust forms on the sides, which is removed by a rapid shaking of the flask. Cooling and shaking are continued until a crust no longer forms, when the mixture is allowed to stand at rest for twelve to twenty-four hours. At the end of this time the contents of the flask appear to consist of a crystalline cake soaked with a reddish liquid. There is then added alcohol of 93 per cent., and the whole is shaken up until on further addition no precipitate separates out. The separated Glauber's salt is freed from the alcoholic solution by a vacuum filter, and can be washed with relatively very little alcohol. The half of the alcoholic solution is neutralized over the water bath with zinc carbonate, filtered boiling hot, and united with the other half. The crystallization begins immediately upon cooling, and is complete after standing 36 hours. The zinc lactate so obtained can be pressed free from mother liquor and crystallized once, when it is perfectly pure. The weight of this first crystallization amounts to from 30 to 40 per cent. of the sugar used. The concentrated mother liquor yields yet another portion of nearly pure, although slightly yellowish, crystals. The zinc lactate may then be treated with hydrogen sulphide to remove the zinc. Lactic acid is also made from the liquid cheese residues. For a method of making lactic acid from corn meal, see *N. R.*, 1882, p. 235.

George Jacquemin adds the pure lactic ferment, prepared by Pasteur's method, with a quantity of pure sterilized calcium carbonate, to a wort at 45° C. (113° F.). Fermentation is conducted at that temperature, care being taken to exclude dust, to admit filtered air at the bottom of the vessel, and to allow the carbon dioxide to escape. Fermentation is complete in five or six days, and the solution of calcium lactate is freed from nitrogenous matters by the addition of tannic acid. The calcium lactate crystallizes out on evaporation of the filtrate. This may be decomposed with an exact quantity of sulphuric or oxalic acid. (*Chem. News*, 1891, lxiv, 62.) Beckers (*Ap. Ztg.*, 1899, 400) patented a process for making lactic acid from the liquors obtained in the manufacture of "sauer kraut" which were formerly wasted. The liquor is neutralized with lime, filtered, evaporated and set aside to crystallize; the calcium lactate is purified, if necessary, by washing or recrystallization and then dissolved in cold water and the solution treated with sufficient sulphuric acid to set free the lactic acid.

Properties.—"Lactic Acid is a colorless, or slightly yellow, syrupy liquid, nearly odorless, having an acid taste, and absorbing moisture on exposure to air. It is miscible with water, alcohol or ether; insoluble in chloroform, petroleum benzin, or carbon disulphide. Lactic Acid is strongly acid to litmus. Specific gravity: about 1.206 at 25° C. (77° F.). Lactic Acid is not vaporized at a temperature below 160° C. (320° F.); at a higher temperature it emits inflammable vapors. Add about 0.1 Gm. of potassium permanganate to 2 mils of a mixture of equal volumes of Lactic and sulphuric acids, and heat it gently; the odor of aldehyde becomes perceptible. Not more than 0.006 Gm. of ash remains on incinerating 5 mils of Lactic Acid. Ten mils of a solution of the Acid in distilled water (1 in 100) is not rendered opalescent by 1 mil of silver nitrate T.S. (*chloride*). Separate portions of 10 mils each of an aqueous solution of the Acid (1 in 20) remain unaffected by the addition of 1 mil of barium chloride T.S. (*sulphate*), or by 1 mil of copper sulphate T.S. (*sarcolactic acid*). An aqueous solution of the Acid does not respond to the Test for heavy metals (see Part III, Test No. 3). Add a few drops of Lactic Acid to 10 mils of hot alkaline cupric tartrate V.S.; no red precipitate is produced (*sugars*). Add 1 mil of Lactic Acid, in drops, to 5 mils of ether, shaking it after each addition; the ether solution does not become even transiently turbid (*glycerin*). Pour Lactic Acid carefully upon an equal volume of colorless, concentrated sulphuric acid contained in a clean test tube, and keep the temperature at 15° C. (59° F.); no dark

colored zone develops at the line of contact upon standing for fifteen minutes (*organic impurities*). No turbidity is produced on heating the Acid with an excess of lime water (*phosphoric, tartaric, citric, or oxalic acid*)." *U. S.*

"Specific gravity about 1.21. Warmed with one-tenth of its weight of *potassium permanganate* it yields the odor of aldehyde. 1 gramme diluted with 10 millilitres of *water* requires for neutralisation not less than 8.3 millilitres of *N/1 solution of sodium hydroxide.* After the further addition of 10 millilitres of the alkaline solution and boiling for fifteen minutes, not more than 8.6 millilitres of *N/1 solution of sulphuric* acid are required to neutralise the excess of alkali. Yields no characteristic *reactions* for copper, iron, chlorides, citrates, oxalates, phosphates, sulphates, or tartrates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million. Diluted with *water* gives no precipitate with *solution of copper sulphate* (absence of sarco-lactic acid), and none, or only the slightest traces, with excess of *solution of potassio-cupric tartrate,* even after prolonged boiling (absence of more than traces of various sugars). The mixture obtained by heating Lactic Acid with excess of *zinc carbonate* and evaporating to dryness, when exhausted with *absolute alcohol* and the latter evaporated, does not leave any sweet residue (absence of glycerin). Yields no rancid odor when gently warmed (absence of fatty acids). When carefully poured upon an equal volume of *sulphuric acid* contained in a clean test-tube, little or no darkening in color occurs (absence of organic impurities). No turbidity, whether permanent or transient, is produced when the Acid is added drop by drop to twice its volume of *ether* (absence of gum, sugars, mannite, calcium phosphate). Yields no precipitate with *solution of lead subacetate* (absence of malic acid and sulphuric acid)." *Br.*

Exposed to a temperature of 150° C. (302° F.), it is for the most part converted into a new body, which is called concrete lactic acid or *lactide,* an anhydride having the formula $C_3H_6O_4$. It coagulates albumin and dissolves a large quantity of freshly precipitated calcium phosphate, a property which doubtless renders it important in the animal economy.

"Assay.—Pour about 2.5 mils of Lactic Acid into a tared and stoppered 250 mil flask, weigh accurately, add 50 mils of normal potassium hydroxide V.S. and boil the liquid for twenty minutes. The residual titration of the boiling solution with normal sulphuric acid V.S., using phenolphthalein T.S. as indicator, shows not less than 85 per cent. nor more than 90 per cent. of $C_3H_6O_3$.

"Each mil of normal potassium hydroxide V.S. used corresponds to 0.09005 Gm. of $C_3H_6O_3$ or lactic anhydrides calculated as $C_3H_6O_3$. Each gramme of Lactic Acid corresponds to not less than 9.44 mils nor more than 10.0 mils of normal potassium hydroxide V.S." *U. S.*

Uses.—Lactic acid has been used in *dyspepsia;* for the removal of *phosphatic deposits* in the urine; also used in *tuberculous diarrhea,* and in the *green diarrhea of children.* The remedy should be taken at the time of meals, in solution sweetened with sugar, prepared like lemonade. Cantani, of Naples, was induced by theoretical considerations to employ lactic acid in *diabetes,* and reported very remarkable success. (*Ed. M. J.,* 1871, p. 533.) The use of this remedy, however, has not met with the success anticipated.

Hypnotic properties have also been ascribed to lactic acid, but the claim has not been verified. In concentrated form lactic acid is an active caustic; when diluted it is stimulant and germicidal. The 50 to 80 per cent. solution has been used as a caustic antiseptic in *infected wounds, ozena, otitis, endometritis,* etc.; the 20 per cent. solution has been used for the destruction of false membrane in *diphtheria;* the three per cent. solution has been strongly recommended by Sneguirewa for irrigation in foul *leucorrheas.* (For consideration of the therapeutic uses of the lactic acid forming bacteria see under *Kephir,* Part II.)

Lactic acid has the incompatibilities of the organic acids in general, but it is also incompatible with oxidizing agents which convert it into aldehyde, oxalic acid, etc. Hydriodic acid decomposes lactic acid with the production of propionic acid.

Dose, twenty to thirty minims (1.3–1.8 mils).

ACIDUM NITRICUM. U. S., Br.

NITRIC ACID Acid. Nitric.

(ăç'ĭ-dŭm nī'trĭ-cŭm)

"An aqueous solution containing not less than 67 per cent. nor more than 69 per cent. of HNO_3 (63.02). Preserve it in dark amber-colored, glass-stoppered bottles, and protect it from light." *U. S.* "Nitric Acid contains 70 per cent. by weight of hydrogen nitrate, HNO_3, and 30 per cent. by weight of water. It may be obtained by the interaction of sulphuric acid and sodium nitrate." *Br.*

Acidum Nitri, s. Azoticum, Spiritus Nitri Acidus; Spirit of Nitre; Aqua Fortis; Acide azotique officinal, *Fr. Cod.;* Acide nitrique, *Fr.;* Acidum nitricum, *P. G.;* Salpetersäure, *G.;* Acido nitrico concentrato, *It.;* Acido nitrico, *Sp.;* Zaltpeterzuur, Sterkwater, *Dutch;* Shedwater, *Sw.*

Nitric oxide is one of the five compounds formed by nitrogen and oxygen. These are, nitrogen monoxide or hyponitrous oxide (laughing gas), N_2O; nitrogen dioxide, N_2O_2, or NO; nitrous oxide, N_2O_3; nitrogen tetroxide or peroxide, N_2O_4; and nitric oxide, N_2O_5. From this latter by the addition of water is formed nitric acid:

$$N_2O_5 + H_2O = 2HNO_3$$

Nitric acid is now official in the U. S. IX in two forms—the strong acid of the sp. gr. 1.403 at 25° C. (77° F.) and the diluted. The nitric acid of the British Pharmacopœia is slightly stronger, containing 70 per cent. of HNO_3.

Preparation.—The usual practice adopted in the laboratory for obtaining nitric acid is to add to sodium nitrate in coarse powder contained in a retort, an equal weight of strong sulphuric acid, poured in by means of a tube or funnel, so as not to soil the neck. The materials should not occupy more than two-thirds of the capacity of the retort. A receiver being adapted, heat is applied by means of a sand bath, moderately at first, but afterwards more strongly when the materials begin to thicken, in order to bring the whole into a state of perfect fusion. Red vapors will at first arise and afterwards disappear in the course of the distillation. Towards its close they will be reproduced, and their reappearance will indicate that the process is completed.

The proportion of equal weights, as above given, corresponding nearly to one molecule of sodium nitrate and one of sulphuric acid, is the best for operations on a small scale in the laboratory.

A practical disadvantage in this method of obtaining very strong nitric acid is that, owing to the high heat and the presence of the crystals, the retort is frequently fractured. Henry Trimble recommended adding one part of commercial nitric acid to two parts of strong sulphuric acid in a retort and distilling slowly until the nitric acid is all collected.

The industrial manufacture of nitric acid is now accomplished by the use of sodium nitrate instead of the more expensive potassium nitrate which was used formerly. The sodium nitrate has two important advantages over potassium nitrate. In the first place it is less than half as expensive, even in times of normal supply, and in the second place the yield is twenty per cent. higher on account of the lower molecular weight of the sodium salt.

The reaction is as follows:

$$NaNO_3 + H_2SO_4 = NaHSO_4 + HNO_3.$$

This reaction takes place below 200° C. (392° F.).

At higher temperatures the sodium acid sulphate may be made to react with another molecule of sodium nitrate and normal sodium sulphate, Na_2SO_4, is produced, but in practice the reaction is rarely forced up to the second phase on account of some practical disadvantages connected with the removal of the by-product from the still.

The by-product, acid sodium sulphate, has found but a limited use and is practically given away free of charge to get rid of it. Formerly it was the custom to use glass retorts in the manufacture of nitric acid, but they have been abandoned in favor of cast iron retorts, the vapors being condensed in stoneware vessels. These condensers are so arranged that the various gases produced as variants or by-products of the reaction, such as N_2O_3, HCl, NOCl, O, and the halogens, if present, are collected and obtained separately, so that instead of the first distillation producing a very impure nitric acid which required subsequent redistillation and purification, a pure nitric acid is obtained directly.

During recent years nitric acid has been manufactured from atmospheric nitrogen by causing it to combine directly with oxygen through the heat of an electric arc. This forms nitric oxide which, as the temperature falls, is converted into nitrogen peroxide. This latter gas is led into granite towers filled with broken quartz where it meets with falling water, with the elements of which it unites to form a dilute nitric acid. (See Strong, *A. J. P.*, 1915, p. 39.) Another method of utilization of atmospheric nitrogen is by burning carbon monoxide in the presence of air in closed chambers, under pressure, and by rapidly cooling the flame against a cold surface. Still another method is by transforming ammonia into nitric acid by mixing it with air and passing it over spongy platinum heated to 300° C. (572° F.). Nitric acid has also been prepared industrially from synthetic calcium nitrate which is one of the modern products of the electric furnace.

Lunge and Rey obtained pure, colorless, concentrated nitric acid by the following method: A quantity of nitric acid, prepared and deprived of coloring impurities in the usual manner, and containing 98.7 per cent. of absolute nitric acid, was put into a retort together with twice its volume of absolute sulphuric acid (H_2SO_4), and distilled *in vacuo*, the pressure being reduced to 20 mm. by means of a water-jet pump. This was found to be the only way to prevent the acid from becoming yellow. The connection between the neck of the retort and the receiver was effected by wrapping with asbestos paper and an external coat of moulder's clay. Great care was taken to insure the absence of organic matter. The distillation takes place at a temperature of 35° C. (95° F.), and the distillate was completely colorless. It contained 99.7 per cent. of HNO_3. (*Am. Drug.*, June 1, 1891, 170; from *Zeit. An. Chem.*)

Monohydrated Nitric Acid. Hydrogen Nitrate.—This is the strongest liquid nitric acid that can be procured, and may be obtained by distilling one molecule of pure and dry sodium nitrate with one molecule of monohydrated sulphuric acid. One molecule of monohydrated nitric acid distils over, and one molecule of sodium bisulphate remains behind:

$$NaNO_3 + H_2SO_4 = HNO_3 + HNaSO_4$$

Acid of this strength is very difficult to make, and requires for its preparation the most elaborate attention to separate the superabundant water. According to Arthur Smith, of London, acid dehydrated as far as possible is perfectly colorless, boils at 84° C. (183.2° F.), and has the sp. gr. 1.517 at 15.4° C. (59.7° F.), and nearly approaches, in composition, to a monohydrate. Acid of this strength, even at the boiling temperature, has not the slightest action on tin or iron. According to Kolb (*Ann. Ch. Phys.* [4], x, 140), the true HNO_3 has a sp. gr. at 15° C. (59° F.) as high as 1.530.

The acid of a former Br. Pharmacopœia,

Table showing percentage of HNO_3 in Nitric Acid of different densities. U. S. IX

Per cent. HNO_3	Sp. gr. app. 25° C. / 25° C.	Sp. gr. app. 15° C. / 15° C.	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal KOH mils.	Per cent.= 0.01 mil normal KOH.
‡0	1.0000	1.0000	0.000180	0.0182	0.000	0.0629
1	1.0055	1.0056	0.000191	0.0185	0.159	0.0621
2	1.0109	1.0111	0.000201	0.0185	0.320	0.0617
3	1.0163	1.0165	0.000210	0.0185	0.482	0.0606
4	1.0217	1.0221	0.000215	0.0182	0.647	0.0602
5	1.0272	1.0277	0.000228	0.0182	0.813	0.0595
6	1.0327	1.0334	0.000255	0.0179	0.981	0.0588
7	1.0383	1.0392	0.000278	0.0175	1.151	0.0585
8	1.0440	1.0451	0.000299	0.0175	1.322	0.0575
9	1.0497	1.0510	0.000319	0.0172	1.496	0.0568
10	1.0555	1.0570	0.000335	0.0172	1.672	0.0568
11	1.0613	1.0630	0.000355	0.0169	1.848	0.0559
12	1.0672	1.0690	0.000374	0.0169	2.027	0.0556
13	1.0731	1.0751	0.000393	0.0169	2.207	0.0546
14	1.0790	1.0812	0.000415	0.0167	2.390	0.0543
15	1.0850	1.0874	0.000436	0.0167	2.574	0.0532
16	1.0910	1.0937	0.000455	0.0161	2.762	0.0529
17	1.0972	1.1000	0.000474	0.0161	2.951	0.0524
18	1.1034	1.1064	0.000492	0.0159	3.142	0.0518
19	1.1097	1.1128	0.000512	0.0161	3.335	0.0510
20	1.1159	1.1192	0.000530	0.0161	3.531	0.0508
21	1.1221	1.1256	0.000550	0.0159	3.728	0.0503
22	1.1284	1.1321	0.000569	0.0161	3.927	0.0495
23	1.1346	1.1385	0.000588	0.0159	4.129	0.0493
24	1.1409	1.1449	0.000604	0.0156	4.332	0.0488
25	1.1473	1.1514	0.000618	0.0156	4.537	0.0478
26	1.1537	1.1580	0.000635	0.0154	4.746	0.0476
27	1.1602	1.1647	0.000651	0.0156	4.956	0.0472
28	1.1668	1.1714	0.000666	0.0154	5.168	0.0465
29	1.1734	1.1781	0.000682	0.0154	5.383	0.0461
30	1.1800	1.1848	0.000696	0.0154	5.600	0.0459
31	1.1866	1.1916	0.000714	0.0149	5.818	0.0450
32	1.1933	1.1985	0.000727	0.0147	6.040	0.0448
33	1.2001	1.2054	0.000742	0.0149	6.263	0.0441
34	1.2068	1.2123	0.000763	0.0147	6.490	0.0439
35	1.2135	1.2191	0.000786	0.0152	6.718	0.0435
36	1.2201	1.2260	0.000810	0.0152	6.948	0.0431
37	1.2267	1.2329	0.000830	0.0149	7.180	0.0427
38	1.2334	1.2397	0.000849	0.0152	7.414	0.0424
39	1.2400	1.2464	0.000865	0.0152	7.650	0.0420
40	1.2466	1.2531	0.000879	0.0154	7.888	0.0418
41	1.2531	1.2598	0.000895	0.0154	8.127	0.0415
42	1.2596	1.2665	0.000915	0.0156	8.368	0.0412
43	1.2660	1.2731	0.000932	0.0156	8.611	0.0408
44	1.2724	1.2797	0.000952	0.0156	8.856	0.0405
45	1.2788	1.2862	0.000973	0.0159	9.103	0.0403
46	1.2851	1.2927	0.000992	0.0161	9.351	0.0402
47	1.2913	1.2991	0.001011	0.0161	9.600	0.0397
48	1.2975	1.3055	0.001032	0.0161	9.852	0.0395
49	1.3037	1.3119	0.001053	0.0164	10.105	0.0394
50	1.3098	1.3182	0.001076	0.0169	10.359	0.0392
51	1.3157	1.3243	0.001085	0.0169	10.614	0.0389
52	1.3216	1.3304	0.001115	0.0175	10.871	0.0389
53	1.3273	1.3363	0.001134	0.0179	11.128	0.0389
54	1.3329	1.3421	0.001154	0.0182	11.385	0.0389
55	1.3384	1.3477	0.001173	0.0185	11.643	0.0386

* Add if the temperature is above, subtract if it is below, the standard.
† Corresponding with a difference in specific gravity of 0.0001.
‡ The figures on this line across the page are for fractional percentages below 1.

Table showing percentage of HNO_3 in Nitric Acid of different densities (Continued).

Per cent. HNO_3	Sp. gr. app. 25° C. / 25° C.	Sp. gr. app. 15° C. / 15° C.	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal KOH mils.	Per cent. = 0.01 mil normal KOH.
56	1.3438	1.3533	0.001191	0.0192	11.902	0.0385
57	1.3490	1.3587	0.001211	0.0196	12.162	0.0385
58	1.3541	1.3640	0.001229	0.0200	12.422	0.0383
59	1.3591	1.3692	0.001250	0.0204	12.683	0.0383
60	1.3640	1.3742	0.001269	0.0208	12.944	0.0383
61	1.3688	1.3792	0.001287	0.0213	13.205	0.0382
62	1.3735	1.3841	0.001305	0.0213	13.467	0.0377
63	1.3782	1.3890	0.001321	0.0213	13.732	0.0376
64	1.3829	1.3938	0.001338	0.0213	13.998	0.0373
65	1.3876	1.3987	0.001352	0.0208	14.266	0.0372
66	1.3924	1.4035	0.001365	0.0213	14.535	0.0369
67	1.3971	1.4083	0.001372	0.0213	14.806	0.0369
68	1.4018	1.4131	0.001382	0.0213	15.077	0.0366
69	1.4065	1.4179	0.001389	0.0213	15.350	0.0365
70	1.4112	1.4226	0.001397	0.0213	15.624	0.0362
71	1.4159	1.4273	0.001404	0.0217	15.900	0.0361
72	1.4205	1.4320	0.001412	0.0222	16.177	0.0360
73	1.4250	1.4366	0.001419	0.0227	16.455	0.0361
74	1.4294	1.4411	0.001427	0.0233	16.732	0.0365
75	1.4336	1.4454	0.001439	0.0278	17.006	0.0372
76	1.4372	1.4491	0.001442	0.0286	17.275	0.0372
77	1.4407	1.4527	0.001454	0.0303	17.544	0.0373
78	1.4440	1.4561	0.001469	0.0323	17.812	0.0372
79	1.4471	1.4595	0.001491	0.0333	18.081	0.0373
80	1.4501	1.4627	0.001515	0.0333	18.349	0.0372
81	1.4531	1.4659	0.001542	0.0333	18.618	0.0373
82	1.4561	1.4691	0.001564	0.0345	18.886	0.0372
83	1.4590	1.4721	0.001577	0.0345	19.155	0.0372
84	1.4619	1.4751	0.001583	0.0345	19.424	0.0372
85	1.4648	1.4780	0.001580	0.0345	19.693	0.0369
86	1.4677	1.4809	0.001578	0.0333	19.964	0.0366
87	1.4707	1.4838	0.001573	0.0345	20.237	0.0362
88	1.4736	1.4867	0.001569	0.0345	20.513	0.0364
89	1.4765	1.4895	0.001562	0.0333	20.788	0.0368
90	1.4795	1.4924	0.001553	0.0400	21.060	0.0377
91	1.4819	1.4949	0.001564	0.0435	21.325	0.0377
92	1.4842	1.4973	0.001575	0.0500	21.590	0.0377
93	1.4862	1.4994	0.001586	0.0526	21.855	0.0377
94	1.4881	1.5015	0.001597	0.0556	22.120	0.0377
95	1.4899	1.5033	0.001608	0.0588	22.385	0.0350
96	1.4916	1.5053	0.001631	0.0357	22.671	0.0344
97	1.4944	1.5083	0.001658	0.0270	22.962	0.0340
98	1.4981	1.5123	0.001683	0.0217	23.256	0.0336
99	1.5027	1.5171	0.001708	0.0175	23.554	0.0330
100	1.5084	1.5230	0.001732	.....	23.857	.....

NOTE: To find the per cent. of N_2O_5, multiply the per cent. of HNO_3 by 0.85703. To find the per cent. of NO_3, multiply the per cent. of HNO_3 by 0.98397. To find the volume per cent. of official Nitric Acid (68 per cent.), multiply the "normality" by 6.633. For the volume per cent. of official Diluted Nitric Acid (10 per cent.), multiply the "normality" by 59.81.

(See reference on page 49.)

having the sp. gr. 1.5, is of a yellowish color, and strongly corrosive. Strictly speaking, it is hydrogen nitrate diluted with half a molecule of water. An acid of this strength is inconveniently strong, is constantly undergoing decomposition under the influence of light. Besides, acid of this density was not necessary for any process of the Pharmacopœia. These considerations led to a reduction in the strength of both the U. S. and British Pharmacopœias to their present strengths. In the U. S. Pharmacopœia of 1890 the strength was again very slightly reduced from 1.42 to 1.414 at 15° C. (59° F.), since it has been shown that 68 per cent. acid has this specific gravity, the acid of U. S. P., 1880, of the specific gravity of 1.42, having an inconvenient fraction in its percentage (69.4 per cent.). The specific gravity 1.403 given in the U. S. Pharmacopœia (8th and 9th Revisions) is practically equivalent to that given in the U. S. Pharmacopœia of 1890 (1.414), the temperature used in the U. S. Pharmacopœia (8th and 9th Revisions) for specific gravity being 25° C. (77° F.) instead of the lower one of 15.6° C. (60° F.). (See official table pp. 47 and 48.) It is officially described as follows:

Properties.—"Nitric Acid is a fuming liquid, very caustic and corrosive; it has a peculiar, somewhat suffocating odor, and is strongly acid to litmus, even when highly diluted. Specific gravity: about 1.403 at 25° C. (77° F.). It is volatilized at 110° C. (230° F.). Nitric Acid dissolves copper, mercury, silver, and many other metals with the evolution of brownish-red fumes, and stains woollen fabrics and animal tissues a bright yellow. Evaporate 20 mils of Nitric Acid from a platinum or porcelain dish and dry at 110° C. (230° F.); not more than 0.003 Gm. of residue remains (*non-volatile impurities*). Shake 2.5 mils of Nitric Acid, diluted with 7.5 mils of distilled water, with 2 mils of chloroform; the latter remains colorless (*iodine or bromine*) even after the introduction of a small piece of metallic tin (*iodic or bromic acid*). Nitric Acid diluted with 25 volumes of distilled water and neutralized with ammonia water does not respond to the Test for heavy metals (see Part III, Test No. 3). Evaporate 0.5 mil of Nitric Acid to dryness on a water bath; the residue meets the requirements of the Test for arsenic (see Part III, Test No. 1). Separate portions of Nitric Acid, diluted with 10 volumes of distilled water, do not yield a precipitate upon the addition of barium chloride T.S. (*sulphuric acid*), or of silver nitrate T.S. (*hydrochloric acid*)." *U. S.*

"A clear, colorless, or almost colorless liquid emitting corrosive fumes. Yields, when neutralised, the *reactions* characteristic of nitrates. Specific gravity 1.42. 1 gramme diluted with *water* requires for neutralisation 11.1 millilitres of *N/1 solution of sodium hydroxide*. When diluted with *water* yields no characteristic *reactions* for copper, iron, chlorides, bromates, iodates, or sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million. Leaves not more than 0.05 per cent. by weight of residue on evaporation." *Br.*

Acid of the density 1.42 at 15° C. (59° F.) is the most stable of the hydrated compounds of nitric acid, and boils at 121° C. (249.8 F.), the official acid boiling at 120.5° C. (248.9° F.). When either stronger or weaker than this, it distils over at a lower temperature, and, by losing more acid than water in the first case, and more water than acid in the second, constantly approaches to the sp. gr. 1.42, when its boiling point becomes stationary. Dalton first observed these facts in relation to nitric acid of this strength, which have been confirmed by Arthur Smith, of London. This acid may be assumed to have the composition $HNO_3 + 1\frac{1}{2} H_2O$.

The reddish acid called *aqua fortis* or *nitrous acid* is nitric acid containing more or less nitrogen tetroxide (N_2O_4). The same acid may be formed by impregnating, to a limited extent, nitric acid with nitrogen dioxide (N_2O_2). If the saturation be complete, every two molecules of nitric oxide become three molecules of nitrogen tetroxide by the aid of one molecule of nitrogen dioxide ($2N_2O_5 + N_2O_2 = 3N_2O_4$). More commonly it is obtained by distilling a mixture of 4 parts of starch and 100 parts of potassium nitrate with 100 parts of sulphuric acid. In this way the nitrogen tetroxide produced is at once taken up in the concentrated nitric acid and an acid of sp. gr. 1.50 is obtainable. This acid is sometimes sold under the name of *fuming nitric acid.*

The ordinary commercial acid has a specific gravity of from 1.30 to 1.41, and is usually prepared by means of chamber (sulphuric) acid; but if a more concentrated acid is required, a stronger sulphuric acid must be employed. The strongest nitric acid occurring in commerce has a sp. gr. of 1.43, and this is obtained by distilling well dried Chili saltpetre with sulphuric acid having a specific gravity of 1.85.

Nitric acid, so called from nitre, is an extremely sour and corrosive liquid. It was discovered by Raymond Lully, in the thirteenth century, and its constituents by Cavendish, in 1784. When perfectly pure it is colorless; but, as usually obtained, it has a straw color, owing to the presence of hyponitric acid. The concentrated acid, when exposed to the air, emits white fumes, possessing a disagreeable odor. By the action of light it undergoes a slight decomposition, and becomes yellow. It acts powerfully on animal matter, causing its decomposition. On the living fiber it operates as a strong caustic. It stains the skin and most animal substances an indelible yellow color. The compound produced being a nitrogen derivative of protein called *xanthoproteic acid.* On vegetable fiber it acts peculiarly, abstracting hydrogen or water, and oxidizing the remaining elements. When diluted, nitric acid converts most animal and vegetable substances into oxalic, malic, and carbonic acids. The general character of its action is to impart oxygen to

other bodies, which it is enabled to do, as oxygen in the nascent state is liberated in its decomposition. If this liberation takes place while in contact with bodies capable of oxidation, the oxygen goes to effect this oxidation. Free nitric acid, however, will evolve oxygen at a red heat, according to the following reaction:

$$4HNO_3 = 2N_2O_4 + O_2 + 2H_2O$$

It oxidizes sulphur and phosphorus, giving rise to sulphuric and phosphoric acids, and all the metals, except chromium, tungsten, columbium, cerium, titanium, osmium, rhodium, gold, platinum, and iridium. It combines with salifiable bases and forms nitrates. When mixed with hydrochloric acid, mutual decomposition takes place, according to the reaction

$$HNO_3 + 3HCl = NOCl + Cl_2 + 2H_2O$$

and nitrohydrochloric acid is formed.

Great care must be used in transporting nitric acid, for if the strong acid comes in contact in quantity with vegetable substances like hay, tow, excelsior, paper, etc., fire will be apt to occur. The cause of such accidents was proved by the official inquiry of R. Hass. (*Ber. d. Chem. Ges.*, 1881, 597.)

Composition.—Nitric oxide or anhydride consists of two atoms of nitrogen and five atoms of oxygen; or, in volumes, of two volumes of nitrogen and five volumes of oxygen, supposed to be condensed into two volumes to form nitric oxide vapor. In 1849 the interesting discovery was made by Deville of Besançon, of the means of isolating nitric acid oxide or anhydride. The method pursued was to pass perfectly dry chlorine over silver nitrate. The oxide is in the form of colorless brilliant limpid crystals which melt at 29.5° C. (85.1° F.) and boil at 45° C. (113° F.). In contact with water they form a colorless solution with evolution of heat, without the disengagement of gas. (*J. P. C.*, 1849, p. 207.)

"Assay.—Pour about 2 mils of Nitric Acid into a tared flask containing 10 mils of distilled water, stopper, weigh accurately, dilute with 50 mils of distilled water and titrate with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 67 per cent. nor more than 69 per cent. of HNO_3.

"Each mil of normal potassium hydroxide V.S. used corresponds to 0.06302 Gm. of HNO_3. Each gramme of Nitric Acid corresponds to not less than 10.63 mils nor more than 10.95 mils of normal potassium hydroxide V.S." *U. S.*

Uses.—Nitric acid is capable of replacing the hydrochloric acid in the activation of the peptic enzyme and may therefore be used in the treatment of those types of *indigestion* in which hydrochloric acid is of service. It differs from hydrochloric acid in being astringent and is therefore often preferred where there is looseness of the bowels associated with digestive failure. In the past it has also been employed in the treatment of *syphilis*, but the only influence it can exert in this condition is general improvement of nutrition through its digestant action. It has also been found of service in chronic *hepatitis*, but is probably inferior to the nitro-hydrochloric acid. For internal use it should be well diluted and taken through a glass tube to avoid injury to the teeth.

Externally, diluted solutions of nitric acid in the proportion of about 12 minims of the stronger acid to a pint of water have been employed as astringent and antiseptic applications to *ulcers*. The most important external use of this acid, however, is as an escharotic. It has been especially employed as combining both caustic and disinfectant properties to *venereal ulcers* and poisoned *wounds*, especially the *bites* of rabid animals. It is also of service for destruction of small tumors, such as *warts;* for this purpose one or two drops of the official nitric acid may be applied by means of a glass rod, repeating in two or three days if necessary. Too deep caustic action may be prevented by washing the part in an alkaline solution as soon as the proper degree of effect has been obtained. In *cancrum oris*, concentrated nitric acid, freely applied, is one of the best local remedies that can be employed for arresting the phagedænic ulceration and disposing the sore to heal, but great care must be exercised to protect the teeth.

Toxicology.—The swallowing of concentrated nitric acid is immediately followed by burning heat in the mouth, esophagus, and stomach, acute pain, disengagement of gas, abundant eructations, nausea, and hiccough. These effects are soon followed by repeated and excessive vomiting of matter having a peculiar odor and taste, tumefaction of the abdomen with exquisite tenderness, a feeling of coldness on the surface, horripilation, icy coldness of the extremities, small depressed pulse, great anxiety, continual tossings and contortions, and extreme thirst. The cases are almost always fatal. Sometimes the collapse has been immediate and has masked all the other symptoms. The best remedies are repeated large doses of alkaline solutions, soap, magnesia, and chalk, as antidotes, mucilaginous drinks, olive or almond oil in large doses, emollient fomentations, etc.

Nitric acid is an energetic oxidizing agent and its incompatibilities are usually shown along that line. It decomposes most organic principles when brought in contact with them, sometimes with the production of dangerous explosive compounds, as with the volatile oils, glycerin, etc.

Dose, three to eight minims (0.2–0.5 mil), largely diluted.

Off. Prep.—Acidum Nitricum Dilutum, *U. S., Br.;* Acidum Nitrohydrochloricum, *U. S.;* Acidum Nitrohydrochloricum Dilutum, *U. S., Br.*

ACIDUM NITRICUM DILUTUM. Br.

DILUTED NITRIC ACID

(ăç'ĭ-dŭm nĭ'trĭ-cŭm dī-lū'tŭm)

"Diluted Nitric Acid contains 10 per cent. by weight of hydrogen nitrate, HNO_3." *Br.*

Acide azotique dilué, *Fr.*; Verdünnte Salpetersäure, *G.*; Acido nitrico diluito, *It.*

"Nitric Acid, 151 grammes; Distilled Water, sufficient to produce 1000 millilitres. Mix." *Br.*

Diluted Nitric Acid was not introduced into the U. S. IX, excepting among the reagents, but was retained in the British Pharmacopœia (1914) with its strength reduced from 17.44 per cent. to 10 per cent. The latter strength corresponds with that of the U. S. VIII.

The U. S. VIII acid did not vary appreciably from that formerly official. "Specific gravity: about 1.054 at 25° C. (77° F.). It should respond to the reactions and tests given under *Acidum Nitricum.* To neutralize 6.26 Gm. (6.257 Gm.) of Diluted Nitric Acid should require 10 mils of normal potassium hydroxide V.S. (each mil corresponding to 1 per cent. of absolute Nitric Acid), methyl-orange T.S. being used as indicator." *U. S. VIII.*

The British diluted acid is now 10 per cent. "Specific gravity 1.057. 10 millilitres require for neutralisation 16.8 millilitres of *N/1 solution of sodium hydroxide.*" *Br.* This Diluted Acid is of approximately three-fifths the strength of the corresponding preparation of the British Pharmacopœia, 1898.

The medicinal properties of the diluted acid are the same as those of the strong acid, and the incompatibilities are the same, but in a less marked degree. (See *Acidum Nitricum.*)

Dose, from five to thirty minims (0.3–1.9 mils), properly diluted.

ACIDUM NITROHYDROCHLORICUM. U. S.

NITROHYDROCHLORIC ACID Acid. Nitrohydrochl. [Nitromuriatic Acid]

(ăç'ĭ-dŭm nī-trō-hȳ-drō-ĉhlō'rĭ-cŭm)

"A strong aqueous solution containing hydrochloric acid, nitric acid, nitrosyl chloride, and chlorine." *U. S.*

Acidum Nitromuriaticum, U. S. P. 1870; Aqua regia, Aqua-regis; Acide chlorazotique, Eau régale, *Fr.*; Acidum Chloronitrosum; Salpetersalzsäure, Königswasser, *G.*

* "Nitric Acid, *eighteen milliliters* [or 4 fluidrachms, 52 minims]; Hydrochloric Acid, *eighty-two milliliters* [or 2 fluidounces, 371 minims]; to make about *one hundred milliliters* [or 3 fluidounces, 183 minims]. Mix the acids in a capacious glass vessel, and when effervescence has ceased, pour the product into dark amber-colored, glass-stoppered bottles, which must not be more than half filled, and must be kept in a cool place.

"Note—Do not dispense Nitrohydrochloric Acid which does not immediately liberate iodine when one drop of the Acid is added to 1 mil of an aqueous solution of potassium iodide (1 in 5)." *U. S.*

Nitrohydrochloric acid is the *aqua regia* of the earlier chemists, so called from its property of dissolving gold. Nitric and hydrochloric acids, when mixed together, are mutually decomposed. According to the researches of Gay-Lussac, the reaction gives rise to two compounds, NO_2Cl (nitroxyl chloride) and NOCl (nitrosyl chloride), mixed with free chlorine. Later researches seem, however, to show that the latter of the two chlorides exclusively is produced, the reaction for the decomposition of nitrohydrochloric acid being:

$$HNO_3 + 3HCl = NOCl + Cl_2 + 2H_2O$$

For an apparatus for making nitrohydrochloric acid upon a large scale, see *P. J.*, xi, 422.

The power of nitrohydrochloric acid to dissolve gold and similar metals having a weak affinity for oxygen, is owing exclusively to the free chlorine present, and is in no wise dependent on the compound above referred to, which remains entirely passive during the solution of the metal. When nitrohydrochloric acid is made from strong acids, there is always a loss of the nitrosyl chloride and of free chlorine by effervescence, in consequence of the acids not containing sufficient water to hold the gaseous products in solution.

Properties.—"Nitrohydrochloric Acid is a golden-yellow, fuming, and very corrosive liquid; it has a strong odor of chlorine and is intensely acid to litmus, afterwards bleaching it. It readily dissolves gold leaf. Not more than 0.0035 Gm. of residue remains on evaporating 10 mils of the Acid in a glass or porcelain dish and drying at 110° C. (230° F.)." *U. S.*

Nitrohydrochloric acid has an orange color, soon changing to a golden yellow, and the odor of chlorine. It should be kept in a cool dark place, on account of its liability to lose chlorine by heat, and to have its chlorine converted into hydrochloric acid by the action of light and the decomposition of water. On account of its tendency to decomposition, it should not be made in large quantities, nor be kept very long by the apothecary; and care should be taken not to transfer it to the bottle in which it is to be dispensed, until effervescence has ceased, lest the pressure within should drive out the stopper.

Uses.—Nitrohydrochloric acid was brought to the notice of the profession in consequence of the favorable report of its efficacy as an external remedy in *hepatitis,* made by Scott, formerly of Bombay. When thus employed, it produces a tingling sensation of the skin, thirst, a peculiar taste in the mouth, and occasional soreness of the gums and plentiful ptyalism, and at the same time stimulates the liver, as is evinced by an increased flow of bile. It is used either by sponging or in the form of a local or general bath. When applied by sponging, the acid is first diluted so as to have the sourness of strong vinegar. When used as a foot bath, three gallons of water, contained in a deep narrow wooden tub, may be acidulated with six fluidounces of the acid. In this the feet and legs are to be immersed for twenty minutes or half an hour. The bath may be employed at first daily, and afterwards twice or thrice a week; and the sponging may be used at the

same time. The bath is said to be effective in promoting the passage of *biliary calculi*. The solution, prepared for a bath as above mentioned, may be used for a week, adding to it daily a pint of water acidulated with two fluidrachms of the acid, to make up for the waste by evaporation. The bath should have a temperature of about 36.1° C. (97° F.), which may be attained by heating part of the acid solution in a non-metallic container and throwing it back into the remainder.

Nitrohydrochloric acid is much used internally and it is an excellent remedy in chronic *hepatic affections*, in *oxaluria*, and in *dyspepsia* with a tendency to constipation. It is sometimes given also in *syphilitic diseases*. The freshly prepared strong acid is preferable to the diluted, and should be given well diluted, after meals, care being exercised to prevent its injuring the teeth. It should never be prescribed in combination with strong alcoholic liquids undiluted, as gases may be generated in sufficient volume to cause explosion. (See *A. J. P.*, 1878, 67.) Its incompatibilities are the same as strong nitric acid and strong hydrochloric acid with the added factor of the free chlorine.

Dose, three to six minims (0.2–0.4 mil).

ACIDUM NITROHYDROCHLORICUM DILUTUM. U. S., Br.

DILUTED NITROHYDROCHLORIC ACID Acid. Nitrohydrochl. Dil. [Diluted Nitromuriatic Acid]

(ăç′ĭ-dŭm nī-trō-hī-drō-klō′rĭ-cŭm dī-lū′tŭm)

"A diluted aqueous solution containing hydrochloric acid, nitric acid, nitrosyl chloride, and chlorine." *U. S.*

Acidum Nitromuriaticum Dilutum, U. S. P. 1870; Acide chlorazotique dilué, *Fr.*; Verdünnte Salpetersalzsäure, *G.*

* "Nitric Acid, *ten milliliters* [or 162 minims]; Hydrochloric Acid, *forty-five and five-tenths milliliters* [or 1 fluidounce, 258 minims]; Distilled Water, *one hundred and ninety-four and five-tenths millilitres* [or 6 fluidounces, 277 minims]; to make about *two hundred and fifty milliliters* [or 8 fluidounces, 218 minims]. Mix the acids in a capacious glass vessel, and, when effervescence has ceased, add the distilled water; pour it into dark amber-colored, glass-stoppered bottles and keep it in a cool place.

"Note.—Do not dispense Diluted Nitrohydrochloric Acid which does not immediately liberate iodine when five drops of the Acid are added to 1 mil of an aqueous solution of potassium iodide (1 in 5)." *U. S.*

"Nitric Acid, 60 millilitres; Hydrochloric Acid, 80 millilitres; Distilled Water, 500 millilitres. Mix the Acids with the Distilled Water, and keep the mixture in a glass-stoppered bottle for fourteen days before use." *Br.*

The strength of this acid of the British Pharmacopœia is greater than that of the U. S. IX, the difference being as follows: U. S. Nitric Acid, 1; Hydrochloric Acid, 4.55; Water, to 25. British Nitric Acid, 3; Hydrochloric Acid, 4; Water, 25.

"Diluted Nitrohydrochloric Acid is a colorless or pale yellow liquid; it has a faint odor of chlorine, a very acid taste and is strongly acid to litmus, afterwards bleaching it. Not more than 0.0015 Gm. of residue remains on evaporating 20 mils of the Acid in a glass or porcelain dish and drying at 110° C. (230° F.)." *U. S.*

"Specific gravity 1.07. 10 millilitres require for neutralisation about 26.6 millilitres of *N/1 solution of sodium hydroxide*." *Br.*

Between diluted nitric and hydrochloric acids no reaction occurs, and therefore the U. S. Pharmacopœia directs that the acids shall be mixed before dilution. The incompatibilities of diluted nitrohydrochloric acid are the same as the other diluted acids and it is also incompatible with bromides and iodides from which it liberates the halogen elements.

Dose, from ten to twenty minims (0.6–1.3 mils).

ACIDUM OLEICUM. U. S., Br.

OLEIC ACID Acid. Oleic.

(ăç′ĭ-dŭm ō-lē′ĭ-cŭm)

"An acid obtained from fats, consisting chiefly of $C_{18}H_{34}O_2$ or $C_{17}H_{33}.COOH$ (282.27). Preserve it in well-closed glass or stoneware containers, in a cool place." *U. S.* "Oleic Acid may be obtained by the saponifying action of alkalies and subsequent action of acids, or by the action of superheated steam upon commercial oleins." *Br.*

Acidum oleinicum, Acidum elainicum; Elaic acid; Acide oléique, *Fr.*; Oleinsäure, Elainsäure, Oelsäure, *G.*

This acid, although known for many years, was not used medicinally until 1872 (*L. L.*, 1872, 709), when John Marshall introduced the oleates to the profession as substitutes for some of the older ointments, stating that they are not only cleaner and more elegant, but also much more efficacious. (See *Oleata*.)

Preparation.—The difficulty in preparing oleates of good quality arises usually from the use of the commercial oleic acid, which, being obtained as a by-product in the manufacture of glycerin and candles, has a reddish-brown color and a disagreeable fatty odor. It is almost always contaminated with stearic and palmitic acids, with undecomposed glycerides when obtained by the autoclave process, and hydrocarbons when obtained by the distillation of the fat acids. Various processes have been suggested for the purification of oleic acid. Charles Rice (*A. J. P.*, xlv, 2) exposes the commercial acid to a temperature of 4° C. (39.2° F.), and expresses the liquid portion, which is oleic acid deprived of the greater part of the contaminating substances. The odorous and coloring principles are not removed by this process. A writer in *A. J. P.* (xlv, 97) prepares oleic acid for making oleates by saponifying almond oil with potassium hydroxide;

decomposing by tartaric acid, separating the precipitated bitartrate, heating for several hours on a water bath with half its weight of finely powdered lead oxide; after cooling, mixing with three times its volume of ether, settling, decanting, and treating the residue with ether as before; agitating the mixed ethereal solutions with diluted hydrochloric acid; skimming off the ethereal solution of oleic acid, washing it with water, reskimming, and recovering the ether by distillation. Wolff (*A. J. P.*, 1879) saponifies oil of sweet almond with lead oxide, agitates the lead soap in petroleum benzin, which retains lead oleate in solution, the lead palmitate being deposited. The benzin solution of lead oleate is shaken repeatedly with diluted hydrochloric acid (1 to 7), when lead chloride separates, and a benzin solution of purified oleic acid is left; finally the benzin is driven off by evaporation. The objection to this process is the difficulty of freeing the oleic acid from traces of a disagreeable benzin odor. Saunders (*N. R.*, June, 1880) makes a solution of 5 pounds of white castile soap in 20 pounds of boiling water, adds 10 ounces of sulphuric acid, and boils with stirring, until two clear layers are formed. The upper layer is decanted, shaken with 5 pounds of hot water, and the oily layer again decanted; 4 ounces of lead oxide are dissolved in it with a gentle heat, and while hot, 5 pounds of alcohol, previously heated to 65.5° C. (149.9° F.), are added. It is filtered after standing 24 hours, and 1 ounce of hydrochloric acid shaken with the filtrate; 10 pounds of water are added, the acid decanted, again washed with 10 pounds of water, and finally recovered; the yield is about 2½ pounds. See also process by Charles T. George (*A. J. P.*, 1881, p. 379). Low grade oleic acids, obtained by the distillation of wool-grease, etc., may contain cholesterin and other unsaponifiable materials from this source (Allen). Commercial oleic acid is often adulterated with linoleic acid. Hazura claims to be able to show the presence of one per cent. of this by saponifying the mixture and then adding potassium permanganate. (For details see *A. J. P.*, 1889, p. 356.) Grandval and Valser (*Chem. News*, 1890, p. 85) give the following tests for linoleic acid: If a thin layer of the fraudulent oleic acid be placed upon a slip of lead scraped quite clean, and some pure oleic acid be put upon a similar slip of lead for comparison, the next day the impure acid will be more or less resinified, while the pure acid will be scarcely altered. If some drops of oleic acid adulterated with linoleic acid be mixed with an equal volume of soda lye, an intense yellow color will be produced; pure oleic acid, if similarly treated, will merely take a grayish tint. Commercially, oleic acid is now obtainable by the process of decomposition of fatty oils by the action of enzymes. For this purpose, the ferment of the castor oil bean has proven most efficient. Connstein has described the technical application of this process in a paper read at the *International Congress of Applied Chemistry*, held at Berlin in 1903. (Vol. ii, p. 537.) For a paper on the esterification of oleic acid in the presence of a pancreatic ferment, by H. Pottevin, see *P. J.*, 1904, 492.

Properties.—"A yellowish or brownish-yellow, oily liquid, having a peculiar, lard-like odor and taste; becoming darker and absorbing oxygen on exposure to air. It is practically insoluble in water; slightly soluble in 60 per cent. alcohol (by volume), the solubility very rapidly increasing in stronger alcohol; it is completely miscible with about 85 per cent. alcohol (by volume); it is also soluble in chloroform, benzene, petroleum benzin, or in fixed or volatile oils. Specific gravity: about 0.895 at 25° C. (77° F.). When gradually cooled, Oleic Acid does not become semi-solid above 9° C. (48.2° F.); on further cooling, it congeals to a whitish, solid mass at about 4° C. (39.2° F.). When heated to a temperature of about 95° C. (203° F.), decomposition commences and acrid vapors are produced. Incinerate 5 mils of Oleic Acid; not more than 0.005 Gm. of ash remains. Shake Oleic Acid with an equal volume of distilled water; the separated water after filtration is not reddened by the addition of a drop of methyl orange T.S. (*mineral acids*). Boil about 1 Gm. of Oleic Acid and about 0.5 Gm. of monohydrated sodium carbonate with 30 mils of distilled water in a capacious flask; the resulting solution while hot is clear or at most opalescent (*undecomposed fat or mineral oil*)." *U. S.*

According to Dieterich, pure oleic acid has the iodine figure 89.8 to 90.05 and commercial oleic acid 65.03 to 86.18.

"A straw-colored liquid, occasionally with a faintly rancid odor. Insoluble in *water*, but readily soluble in *alcohol* (90 per cent.), in *chloroform*, or in *ether*. When cooled it does not become semi-solid until the temperature has fallen below 9° C. (48.2° F.). Specific gravity 0.890 to 0.910." *Br.*

Chemical Constitution.—Oleic acid, $C_{18}H_{34}O_2$, does not belong to the "fatty acid" series, but differs from the corresponding acid of that series, stearic acid, $C_{18}H_{36}O_2$, by having two atoms less of hydrogen. It belongs to a series derived by oxidation from alcohols which, like allyl alcohol, C_3H_5OH, have two atoms of hydrogen less than the normal monatomic alcohols, like propyl alcohol, C_3H_7OH. The alcohol from which oleic acid is in theory derivable is not, however, known. Oleic acid is monobasic, as shown in the formula $HC_{18}H_{33}O_2$.

Uses.—Oleic acid is used chiefly in preparing the oleates and in ointments. It has, however, been administered in capsules taken on first rising in the morning as a substitute for olive oil in the treatment for *gallstones*. (*R. T.*, 1901.)

Its chief importance is for the preparation of the so-called "oleates," and in certain ointment bases.

Oleic acid is incompatible with alkalies with which it forms soaps, and with oxidizing agents which effect its decomposition.

Dose, seven to fifteen grains (0.45–1 Gm.).

ACIDUM PHENYLCINCHONINICUM. U. S.

PHENYLCINCHONINIC ACID Acid. Phenylcinch.

[Phenyl-quinoline-carboxylic Acid]

(ăç'ĭ-dŭm phē'nȳl-cĭn-chō-nĭn'ĭ-cŭm)

"An organic acid, 2-phenyl-quinoline-4-carboxylic acid [$C_{16}H_{11}O_2N$ or $C_6H_5.C_9H_5N.CO\,OH = 249.10$]." *U. S.*

Phenylcinchoninic acid or *atophan,* was admitted to the U. S. IX, the manufacturers and owners of the patent rights giving permission to the Committee of Revision for its insertion. It is officially described as follows: "It occurs in small, colorless needles, or as a white or yellowish-white micro-crystalline powder; odorless or having a slight odor resembling benzoic acid, and a bitter taste. It is permanent in the air. Insoluble in cold water; slightly soluble in cold alcohol, hot water or ether; readily soluble in hot alcohol. It melts at about 210° C. (410° F.) with partial decomposition. A saturated solution of Phenylcinchoninic Acid in hot diluted hydrochloric acid yields a precipitate of reddish-brown crystals with platinic chloride T.S. Dissolve about 1 Gm. of Phenylcinchoninic Acid in an excess of ammonia water, evaporate the solution to dryness on a water bath, or until free from the odor of ammonia, then dilute to 20 mils with distilled water, and filter. Separate portions of this filtrate yield a white, flocculent precipitate with silver nitrate T.S.; a yellowish, flocculent precipitate with lead acetate T.S.; and a green, flocculent precipitate with copper sulphate T.S. No weighable ash remains on incinerating about 0.5 Gm. of Phenylcinchoninic Acid." *U. S.*

Paratophan is methyl-phenyl-quinoline-carboxylic acid or *methyl-atophan. Novatophan* is the ethyl ester of paratophan. *Isatophan* is methoxy-phenyl-quinoline carboxylic acid or *methoxy-atophan.*

Uses.—In 1908 Nicolaier and Dohrn (*D. K. M.,* 1908, xciii) showed that phenylcinchoninic acid caused an extraordinary increase in the excretion of uric acid; as this excretion was increased in persons upon a purin-free diet, they believed that it was due to increased output of the endogenous uric acid. That it produces a marked increase in the quantity of uric acid eliminated through the kidneys—in some cases amounting to as much as 100 or 200 per cent.—without a corresponding increase in the quantity or urea, seems to be established beyond question. Starkenstein (*A. E. P. P.,* 1911, lxv, p. 177) believes, however, that the increase in the uric acid is due to a diminished ability to oxidize the purin foods, but Folin and Lyman (*J. P. Ex. T.,* 1913, iv, p. 539) have shown that the increased elimination is accompanied by the diminution in the quantity of uric acid in the blood. It is probable, therefore, that the effects produced are due to an increased capacity of the kidneys to excrete uric acid. It appears also to have some analgesic action.

Phenylcinchoninic acid is a valuable remedy in the treatment of both acute and chronic *gout* and in those allied disorders generally spoken of as the *lithemic diathesis.* The improvement in these conditions is due probably in chief part to the increased output of the purin substances through the kidney, but in part, perhaps, also to its anodyne properties. Weintraud recommends that when using atophan in gouty disorders alkalies should be administered simultaneously in order to prevent the precipitation of uric acid in the kidney or bladder. While there is some clinical evidence that the drug is of service in *acute articular rheumatism,* in chronic rheumatism it has not proven of value.

The *dose* of phenylcinchoninic acid is from eight to fifteen grains (0.5–1.0 Gm.) three times a day. It is preferably administered in the form of a powder which may be stirred up in a tablespoonful of water at the time of taking.

ACIDUM PHOSPHORICUM. U. S. (Br.)

PHOSPHORIC ACID Acid. Phos.

(ăç'ĭ-dŭm phŏs-phŏr'ĭ-cŭm)

"A liquid containing not less than 85 per cent. nor more than 88 per cent. of H_3PO_4 (98.06). Preserve it in glass-stoppered bottles." *U. S.* "Concentrated Phosphoric Acid is a liquid containing 66.3 per cent. by weight of hydrogen orthophosphate, H_3PO_4, and 33.7 per cent. by weight of water. It may be obtained by the oxidation of phosphorus." *Br.*

Acidum Phosphoricum Concentratum, *Br.;* Concentrated Phosphoric Acid; Orthophosphoric Acid; Acide Phosphorique, *Fr.;* Acidum phosphoricum, *P. G.;* Phosphorsäure, *G.;* Acido fosforico, *It., Sp.*

The U. S. P. has very properly abandoned the former official process for this acid; it is more profitably and conveniently made on a large scale, and with such precautions and safeguards as cannot be easily used by the apothecary; the U. S. P. 1880 process, however, will be found upon page 77, U. S. D., 18th edition.

This preparation is recommended on account of its small bulk and its great convenience to the apothecary for preparing the diluted acid. The glacial phosphoric acid is no longer official, it having been shown that it is practically impossible to obtain it of sufficient purity to be reliable. (See *Proc. A. Ph. A.,* 1875, pp. 666, 672.) The present syrupy acid is a great improvement in every way, as it can be obtained of undoubted purity and strength, and by the addition of water, diluted phosphoric acid of any desired strength can easily be produced from it. The process for its preparation is the well-known one of oxidizing phosphorus by the use of nitric acid, the former British method not differing materially from that of the U. S.

Pharmacopœia of 1880, except in the absence of the use of hydrogen sulphide for precipitating the arsenical compounds usually found in phosphorus, and in the greater strength of the finished product. The U. S. IX retained this strong acid termed "85 per cent. phosphoric acid" and the British Pharmacopœia (1914) also retained their 66.3 per cent. acid, so that the U. S. acid is about 20 per cent. stronger than that of the British and that of the German Pharmacopœia is only 25 per cent. Phosphorus is oxidized at the expense of the nitric acid, any excess of nitric acid and all the lower oxides of nitrogen being driven off by heat. Strong nitric acid acts too energetically on phosphorus, producing explosion and rapid combustion, but when diluted, as in the processes above referred to, it parts with its oxygen slowly, and it is even desirable to aid the operation with a gentle heat. Along with the nitrous fumes, a portion of the undecomposed nitric acid also rises in vapor, which, in the former British process, to prevent loss, is collected by means of a distillatory apparatus and returned to the retort. In the U. S. process of 1870 the same result was effected by placing over the liquid in the capsule a glass funnel, upon the inner surface of which the acid was condensed, and returned of itself into the capsule so as considerably to simplify the operation. C. L. Diehl found, in using this process that the glass funnel covering the capsule almost always breaks through the violence of the reaction, thus causing loss of phosphorus, besides annoyance. He therefore prefers using a French tubulated glass retort, which was adopted in the process for Phosphoric Acid (U. S. P. 1880). (*A. J. P.*, 1867. p. 138.)

Markoe (*Proc. A. Ph. A.*, 1875, p. 677) proposed a method for making phosphoric acid which is particularly adapted for making large quantities, yet works well in a smaller way. Into a flask (or stone jar) having double the capacity of the materials used, 12 troyounces of water, 2 troyounces of phosphorus, and 10 grains of iodine are placed, then 40 grains of bromine are cautiously dropped in; when the reaction has ceased, 12 troyounces of nitric acid are added; a glass funnel is adjusted in the neck of the flask, and a smaller inverted funnel set inside of it; the apparatus is placed in a stoneware dish, and surrounded with cold water or ice; the reaction takes place slowly and regularly. In about 24 hours, if all the phosphorus be not acted upon, heat may be applied until it disappears, and the excess of bromine, iodine, and nitric acid is driven off. The acid may then be diluted to the desired specific gravity. J. U. Lloyd (*N. R.*, July, 1880) suggests the use of pure alcohol to unite with the nitric acid to form nitrous ether, which is more volatile and more easily driven off. Markoe added a small quantity of pure oxalic acid, and heated the mixture to 148.8° C. (300° F.); at this temperature it is asserted that all the oxalic acid splits into carbon monoxide and carbon dioxide.

Much dissatisfaction has been caused among pharmacists by the fact that diluted phosphoric acid frequently produces a white precipitate in solutions of ferric salts. An examination proved that this occurred when the glacial acid is used, or when high heat had been employed in the concentration. Experiments conducted by Louis Dohme and Remington indicated that the precipitation resulted from the presence of pyrophosphoric acid. (*Proc. A. Ph. A.*, 1874, 431, 511; 1875, 663, 670, 667.) Considerable difficulty was experienced in driving off all the nitric acid, and in the attempt to do so the temperature became so elevated as to reconvert some of the tribasic acid to the bibasic form. This occurred slightly at 148.8° C. (300° F.), but to a much greater extent between 176.6° C. (350° F.) and 204.4° C. (400° F.). The diluted acid, made from phosphorus, can be brought to the boiling point of 232.2° C. (450° F.), and will then only produce a slight cloud with tincture of ferric chloride, but if diluted, when cool, with about half its bulk of cold water, which causes considerable elevation of temperature, it forms a clear solution. The same acid evaporated, heated to redness, allowed to congeal, and then dissolved in water, precipitated the iron solution. The addition of twenty per cent. of sodium pyrophosphate to the same diluted acid made a preparation which in all respects resembled that made from the glacial acid, thus giving evidence that the presence of this contamination was the cause of the difference in the two preparations.

It has been suggested that red phosphorus might be substituted for common phosphorus, as producing the same results, with less danger of explosion; but the former official process, when carefully followed in reference to due dilution and a moderate heat, is not dangerous.

Properties.—"A colorless, odorless liquid of a syrupy consistence; it has a strongly acid taste and is strongly acid to litmus, even when highly diluted. Specific gravity: about 1.72 at 25° C. (77° F.). When heated, the liquid loses water; at 200° C. (392° F.) it gradually begins to change to pyrophosphoric acid. At a still higher temperature, it is converted into metaphosphoric acid, which volatilizes in dense fumes, or which forms, on cooling, a transparent mass of glacial metaphosphoric acid. Phosphoric Acid conforms to the tests for identity and purity given under *Acidum Phosphoricum Dilutum* when diluted to that strength.

"Assay.—Pour about 1 Gm. of Phosphoric Acid into a tared flask, stopper, and weigh accurately, transfer it to a 100 mil graduated flask and make it up to 100 mils with distilled water. Transfer 10 mils of this solution to a 100 mil graduated flask, add a drop of phenolphthalein T.S. and neutralize it with special potassium hydroxide T.S. (see *Reagents*, Part III). Add 50 mils of tenth-normal silver nitrate V.S. and agitate it, gradually adding zinc oxide

Lyons' Table of Percentage and Specific Gravity of Phosphoric Acid. U. S. IX

Per cent. phosphoric acid.	Specific Gravity. 25° C. / 25° C.	Specific Gravity. 15° C. / 15° C.	Correction of specific gravity for 1° C.[1]	Fractional per cent.[2]	Normality. 1 mil requires normal KOH mil	Per cent. = 0.01 mil normal KOH.
1	1.0056	1.0056	0.00017	0.018	0.21	0.048
2	1.0113	1.0113	0.00017	0.018	0.42	0.048
3	1.0169	1.0170	0.00018	0.018	0.63	0.048
4	1.0225	1.0226	0.00019	0.018	0.84	0.048
5	1.0281	1.0283	0.00020	0.018	1.05	0.045
6	1.0338	1.0340	0.00020	0.018	1.27	0.045
7	1.0395	1.0398	0.00021	0.017	1.49	0.045
8	1.0453	1.0457	0.00022	0.017	1.71	0.043
9	1.0512	1.0517	0.00022	0.017	1.94	0.043
10	**1.0572**	**1.0577**	**0.00023**	**0.017**	**2.17**	**0.043**
11	1.0632	1.0637	0.00024	0.017	2.40	0.043
12	1.0692	1.0698	0.00025	0.016	2.63	0.043
13	1.0753	1.0759	0.00025	0.016	2.86	0.042
14	1.0814	1.0821	0.00026	0.016	3.10	0.042
15	1.0875	1.0883	0.00027	0.016	3.34	0.042
16	1.0937	1.0945	0.00028	0.016	3.58	0.040
17	1.0999	1.1008	0.00029	0.016	3.83	0.040
18	1.1062	1.1072	0.00030	0.016	4.08	0.040
19	1.1125	1.1136	0.00031	0.016	4.33	0.038
20	1.1189	1.1201	0.00032	0.015	4.59	0.040
21	1.1254	1.1266	0.00033	0.015	4.84	0.038
22	1.1319	1.1332	0.00034	0.015	5.10	0.037
23	1.1385	1.1399	0.00034	0.015	5.37	0.038
24	1.1452	1.1467	0.00035	0.015	5.63	0.037
25	1.1519	1.1535	0.00036	0.014	5.90	0.037
26	1.1588	1.1604	0.00037	0.014	6.17	0.036
27	1.1657	1.1674	0.00037	0.014	6.45	0.036
28	1.1727	1.1745	0.00038	0.014	6.73	0.036
29	1.1799	1.1817	0.00039	0.014	7.01	0.034
30	1.1871	1.1889	0.00040	0.014	7.30	0.034
31	1.1943	1.1962	0.00040	0.014	7.59	0.034
32	1.2015	1.2035	0.00041	0.014	7.88	0.033
33	1.2088	1.2109	0.00042	0.014	8.18	0.033
34	1.2162	1.2184	0.00042	0.013	8.48	0.033
35	1.2237	1.2260	0.00043	0.013	8.78	0.033
36	1.2313	1.2336	0.00044	0.013	9.08	0.032
37	1.2389	1.2412	0.00044	0.013	9.39	0.031
38	1.2465	1.2489	0.00045	0.013	9.71	0.032
39	1.2542	1.2567	0.00046	0.013	10.02	0.032
40	1.2620	1.2645	0.00047	0.013	10.34	0.030
41	1.2698	1.2724	0.00047	0.013	10.67	0.030
42	1.2778	1.2804	0.00048	0.013	11.00	0.030
43	1.2858	1.2885	0.00049	0.012	11.33	0.029
44	1.2940	1.2967	0.00049	0.012	11.67	0.029
45	1.3023	1.3050	0.00050	0.012	12.01	0.029
46	1.3106	1.3134	0.00051	0.012	12.35	0.029
47	1.3190	1.3219	0.00052	0.012	12.70	0.028
48	1.3276	1.3305	0.00052	0.012	13.06	0.028
49	1.3362	1.3392	0.00053	0.011	13.42	0.028
50	1.3449	1.3479	0.00054	0.011	13.78	0.027
51	1.3537	1.3568	0.00055	0.011	14.15	0.027
52	1.3626	1.3658	0.00055	0.011	14.52	0.026
53	1.3716	1.3748	0.00056	0.011	14.90	0.026
54	1.3807	1.3840	0.00057	0.011	15.28	0.026
55	1.3898	1.3932	0.00058	0.011	15.66	0.025

Table of Percentage and Specific Gravity of Phosphoric Acid. U. S. IX. (Continued).

Per cent. phosphoric acid.	Specific Gravity. 25° C. / 25° C.	Specific Gravity. 15° C. / 15° C.	Correction of specific gravity for 1° C.[1]	Fractional per cent.[2]	Normality. 1 mil requires normal KOH mil	Per cent. = 0.01 mil normal KOH.
56	1.3991	1.4026	0.00058	0.011	16.06	0.026
57	1.4085	1.4120	0.00059	0.011	16.45	0.025
58	1.4180	1.4215	0.00060	0.010	16.85	0.024
59	1.4276	1.4312	0.00060	0.010	17.26	0.024
60	1.4373	1.4409	0.00061	0.010	17.67	0.024
61	1.4471	1.4508	0.00062	0.010	18.09	0.024
62	1.4570	1.4607	0.00063	0.010	18.51	0.023
63	1.4669	1.4706	0.00064	0.010	18.94	0.023
64	1.4768	1.4807	0.00065	0.010	19.37	0.023
65	1.4868	1.4908	0.00066	0.010	19.80	0.023
66	1.4970	1.5010	0.00067	0.010	20.24	0.022
67	1.5072	1.5113	0.00067	0.010	20.69	0.022
68	1.5175	1.5217	0.00068	0.010	21.14	0.022
69	1.5280	1.5322	0.00069	0.009	21.60	0.021
70	1.5386	1.5429	0.00070	0.009	22.07	0.021
71	1.5493	1.5536	0.00071	0.009	22.54	0.021
72	1.5600	1.5644	0.00072	0.009	23.01	0.021
73	1.5708	1.5753	0.00072	0.009	23.49	0.020
74	1.5817	1.5862	0100073	0.009	23.98	0.020
75	1.5927	1.5972	0.00074	0.009	24.47	0.020
76	1.6038	1.6083	0.00073	0.009	24.97	0.020
77	1.6149	1.6193	0.00072	0.009	25.48	0.020
78	1.6261	1.6304	0.00072	0.009	25.99	0.020
79	1.6374	1.6416	0.00071	0.009	26.50	0.019
80	1.6488	1.6529	0.00070	0.009	27.02	0.019
81	1.6602	1.6642	0.00070	0.009	27.55	0.019
82	1.6717	1.6756	0.00069	0.009	28.09	0.019
83	1.6832	1.6871	0.00069	0.009	28.63	0.019
84	1.6948	1.6986	0.00068	0.009	29.17	0.018
85	1.7065	1.7102	0.00068	.....	29.72	.....

[1] Add if the temperature is above, subtract if below, 25° C.

[2] Corresponding with a difference in specific gravity of 0.0001.

NOTE.—To find the per cent. of P_2O_5, multiply the per cent. of H_3PO_4 by 0.7243. To find the per cent. of PO_4, multiply the per cent. of H_3PO_4 by 0.96916.

To find the weight in grammes of H_3PO_4 in 100 mils, multiply the specific gravity by the per cent. of H_3PO_4.

To find the volume per cent. of official Phosphoric Acid, multiply the "normality" by 3.365. For the volume per cent. of official Diluted Phosphoric Acid, multiply the "normality" by 46.08.

(see page 554) in small portions until the liquid is neutral to litmus paper. Now add distilled water to make the liquid measure 100 mils, agitate it thoroughly, filter through a dry filter, collect 50 mils of the filtrate, add 2 mils of nitric acid and 2 mils of ferric ammonium sulphate T.S. and determine the excess of silver nitrate by titration with tenth-normal potassium sulphocyanate V.S., to the production of a permanent red color. When calculated to the amount of Phosphoric Acid originally taken, it shows not less than 85 per cent. nor more than 88 per cent. of H_3PO_4.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.0032687 Gm. of H_3PO_4. Each gramme of Phosphoric Acid corresponds to not less than 260.0 mils nor more than 269.2 mils of tenth-normal silver nitrate V.S." *U. S.*

"A colorless, syrupy liquid with an acid taste and reaction. Leaves, on evaporation, a residue which melts at a low red heat, and when cold forms a glass-like mass. Yields, when neutralised, the *reactions* characteristic of phosphates. Specific gravity 1.5. 1 gramme mixed with a solution of 5 grammes of *sodium chloride* in 20 millilitres of *water* requires for neutralisation 13.5 millilitres of *N/1 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator. Yields when diluted with *water* no characteristic *reactions* for copper, calcium, chlorides, or nitrates, and not more than slight *reactions* for iron or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Uses.—This acid is used in making phosphates and lactophosphates. It has the same medicinal properties and uses as the diluted Phosphoric Acid (see p. 60).

Dose, two to five minims (0.12–0.3 mil).

Off. Prep.—Acidum Phosphoricum Dilutum, *U. S., Br.;* Liquor Phosphatum Acidus, *N. F.;* Liquor Phosphatum Compositus, *N. F.*

Acidum Phosphoricum Glaciale.—(*Glacial Phosphoric Acid; Metaphosphoric Acid; Monobasic Phosphoric Acid; Monohydrated Phosphoric Acid; Acide phosphorique glaciale,* Fr.; *Glasige Phosphorsaure,* G.) Formula HPO_3; mol. wt. 79.41.—Phosphoric oxide consists of two atoms of phosphorus and five atoms of oxygen, P_2O_5, and can be obtained only by the direct union of its constituents, which takes place when phosphorus is burned in perfectly dry oxygen gas. Thus procured, it is in the form of a white amorphous powder, extremely deliquescent, volatilizable at a red heat, and assuming, when it cools after fusion, a vitreous appearance. The classic researches of Graham first established clearly the character of the several varieties of phosphoric acid, which may be considered as derived from this oxide.

When amorphous phosphorus is boiled with nitric acid, or when phosphoric oxide is boiled with water, the oxide takes up three molecules of water, and yields tribasic or *ordinary phosphoric* acid according to the reaction:

$$P_2O_5 + 3H_2O = H_6P_2O_8 \text{ or } (H_3PO_4)_2$$

If this acid be heated for a considerable time to 215° C. (419° F.), the two molecules lose one mol. of water and yield *pyrophosphoric acid,* a tetrabasic variety, according to the reaction:

$$H_6P_2O_8 - H_2O = H_4P_2O_7$$

Lastly, at a red heat the ordinary phosphoric acid is converted into *metaphosphoric acid,* a monobasic variety, according to the reaction:

$$H_3PO_4 - H_2O = HPO_3$$

This last variety may also be obtained direct from the oxide by dissolving it in cold water, when it takes up one molecule of water:

$$P_2O_5 + H_2O = H_2P_2O_6 \text{ or } (HPO_3)_2$$

An aqueous solution of either of the three acids, heated so long as water escapes, yields the monobasic or metaphosphoric acid; and as, upon cooling, it becomes a transparent ice-like solid, it has received in this state the name of glacial phosphoric acid. Conversely, this monobasic acid is slowly transformed, in aqueous solution, and more rapidly if the solution is heated, into the tribasic form. John M. Maisch ascertained that nitric acid, added to the solution of the monobasic acid, with the aid of heat, caused the change from the monobasic to the tribasic form, *i.e.,* to the common phosphoric acid, without the intermediate production of the tetrabasic variety. *Pyrophosphorous Acid,* $H_4P_2O_5$, has been obtained by V. Auger in the form of colorless needles, melting at 38° C. (100.4° F.). (*C. R. A. S.,* 136, 814.)

The three forms of phosphoric acid are distinguishable by peculiar reactions. Thus, the *monobasic* is characterized by coagulating albumin, and giving white, gelatinous, uncrystallizable precipitates with the soluble salts of barium, lime, and silver; the *tetrabasic* does not coagulate albumin, and, though it causes a *white* precipitate with silver nitrate, must first be neutralized; the *tribasic* does not coagulate albumin, and, until neutralized, does not precipitate silver nitrate, but after neutralization throws down a *yellow* precipitate of silver phosphate.

Glacial phosphoric acid is most advantageously obtained from calcined bones, by first treating them with sulphuric acid, which produces an insoluble calcium sulphate and soluble acid phosphate; then dissolving out the latter salt, and saturating it with ammonium carbonate, which generates ammonium phosphate in solution; and, finally, obtaining the ammonium phosphate by evaporation to dryness, and then igniting it in a platinum crucible. The ammonia and all the water except the one molecule needed for the formation of metaphosphoric acid are driven off, and the glacial acid remains.

Properties.—Glacial phosphoric acid is in the form of a white, uncrystallizable, fusible solid; inodorous, very sour to the taste, slowly deliquescent, slowly soluble in water, and soluble also in alcohol. Its formula is HPO_3, and it is made up of 11.2 per cent. of water in combination with 88.8 per cent. of phosphoric oxide.

Impurities.—Glacial phosphoric acid is seldom prepared in this country. That found in commerce is almost all imported, and chiefly from Germany. It is often more or less impure, containing (as shown by the experiments of Maisch) silica and calcium and magnesium phosphates, which are precipitated from a neutralized solution of the acid by ammonia. In one instance 8 per cent. of these impurities was found, but in some others little or none. Maisch never found nitric or hydrochloric acid, and sulphuric acid rarely; and, though the presence of ammonia might be suspected from the source whence the acid is obtained, he did not detect it. (*A. J. P.,* 1860, p. 194.) The chief impurity, however, is soda, as has been pointed out by Brescius, Remington, Dohme, Prescott, and others (see *Proc. A. Ph. A.,* 1875, 666, 672); the acid has been found to contain occasionally as much as 60 per cent. of sodium metaphosphate, and rarely less than 55 per cent. (*N. R.,* Feb., 1879.) Hodgkin (*P. J.,* 1891, p. 217) examined eight samples of German and English glacial phosphoric acid, and found in them, respectively, the following proportions of absolute orthophosphoric acid: 92.8, 91.5, 90.8, 85.4, 84.4, 83.8, 80.1, and 78.1 per cent. In consequence of its deliquescence upon exposure to the air, a portion of the monobasic acid passes into the tribasic state. This may be detected, if in considerable quantity, by its giving a yellowish colored precipitate with silver nitrate. The U. S. P. 1870 directed that the acid, in aqueous solution, should yield no precipitate with hydrogen sulphide, showing the absence of metals; should cause a white pre-

cipitate with barium chloride soluble in an excess of acid; with an excess of ammonia should cause only a slight turbidity, proving the almost total absence of earthy salts; and should yield no ammonia when treated with potassium hydroxide in excess. Should the presence of arsenic be ascertained by the tests for that metal, it may be separated by boiling with hydrochloric acid, so as to convert the arsenic into its very volatile chloride, which would escape with vapors of hydrochloric acid.

Glacial phosphoric acid was introduced into the U. S. P. 1860 as affording a convenient method of preparing the medicinal acid, but, owing to its unreliability, was very properly dismissed; 38½ grains, dissolved in a fluidounce of water, form a solution about equal in strength to the diluted acid of U. S. P. 1860.

ACIDUM PHOSPHORICUM DILUTUM.
U. S., Br.

DILUTED PHOSPHORIC ACID **Acid. Phos. Dil.**

(ăç'ĭ-dŭm phŏs-phŏr'ĭ-cŭm dī-lū'tŭm)

"An aqueous solution containing not less than 9.5 per cent. nor more than 10.5 per cent. of H_3PO_4 (98.06). Preserve it in well-stoppered bottles." *U. S.* "Diluted Phosphoric Acid contains 10 per cent. by weight of hydrogen orthophosphate, H_3PO_4." *Br.*

Acide phosphorique médicinale, *Fr.*; Verdünnte Phosphorsäure, *G.*

* "Phosphoric Acid, *one hundred grammes* [or 3 ounces av., 231 grains]; Distilled Water, *seven hundred and sixty-five grammes* [or 26 ounces av., 431 grains], to make *eight hundred and sixty-five grammes* [or 30 ounces av., 224 grains]. Mix them." *U. S.* "Concentrated Phosphoric Acid, 159.5 grammes; Distilled Water sufficient to produce 1000.0 millilitres. Mix." *Br.*

It will be observed that in both Pharmacopœias diluted phosphoric acid is made by simple dilution of the stronger acid, and that the older method of dissolving the glacial acid has been very properly abandoned. (See *Acidum Phosphoricum Glaciale*, p. 58.)

Properties.—Diluted phosphoric acid is a colorless, inodorous, sour liquid, acting strongly on litmus, and possessing powerful acid properties, although when evaporated so as to become dense, it is not corrosive like the other mineral acids. Neubauer found that the strong acid, when pure and warm, was capable of dissolving calcium oxalate. Diluted Phosphoric Acid is officially described as follows: "A clear, odorless liquid; it has a strongly acid taste and is strongly acid to litmus. Specific gravity: about 1.057 at 25° C. (77° F.). Supersaturate 3 mils of Diluted Phosphoric Acid with ammonia water; the addition of magnesium sulphate T.S. (or of magnesia mixture T.S.) produces a white, crystalline precipitate. Collect this precipitate, wash it, and then dissolve it in diluted acetic acid; the solution yields a yellow precipitate with silver nitrate T.S. (distinction from *metaphosphoric or pyrophosphoric acid*). Warm 5 mils of Diluted Phosphoric Acid gently and add a few drops of silver nitrate T.S.; it does not become turbid or brown (*phosphorous or hypophosphorous acid*). Ten mils of Diluted Phosphoric Acid does not respond to the Test for heavy metals (see Part III, Test No. 3). Two mils of Diluted Phosphoric Acid meets the requirements of the Test for arsenic (see Part III, Test No. 1). Diluted Phosphoric Acid is not immediately affected by silver nitrate T.S. (*hydrochloric acid*); nor is it affected, even after one hour, by the addition of an equal volume of tincture of ferric chloride (*pyrophosphoric or metaphosphoric acid*). Evaporate 20 mils of Diluted Phosphoric Acid to a volume of about 4 mils on a water bath. Cool, transfer 2 mils to a graduated cylinder and add 6 mils of ether and 2 mils of alcohol; no turbidity appears (*phosphates*). Mix 1 mil of Diluted Phosphoric Acid with 6 mils of distilled water and add 1 mil of barium chloride T.S.; no immediate precipitate is produced (*sulphuric acid*). Mix equal parts of Diluted Phosphoric Acid and sulphuric acid and, after cooling, add a clear crystal of ferrous sulphate; no brownish color appears around the crystal (*nitric acid*).

"**Assay.**—Pour about 1 mil of Diluted Phosphoric Acid into a tared flask, weigh accurately, transfer it to a 100 mil graduated flask, add a drop of phenolphthalein T.S., neutralize it with sodium hydroxide T.S. (free from chloride), then introduce 50 mils of tenth-normal silver nitrate V.S., agitate the liquid, and gradually add zinc oxide (free from chloride) in small portions until the mixture is neutral to litmus. Now add distilled water to make the product measure 100 mils, agitate it thoroughly, filter through a dry filter, collect 50 mils of the filtrate, add 2 mils of nitric acid and 2 mils of ferric ammonium sulphate T.S. and determine the excess of silver nitrate by titration with tenth-normal potassium sulphocyanate V.S. to the production of a permanent red color. When calculated to the amount of Diluted Phosphoric Acid originally taken, it shows not less than 9.5 per cent. nor more than 10.5 per cent. of H_3PO_4.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.0032687 Gm. of H_3PO_4. Each gramme of Diluted Phosphoric Acid corresponds to not less than 29.0 mils nor more than 32.1 mils of tenth-normal silver nitrate V.S." *U. S.*

"Specific gravity 1.057. 10 millilitres mixed with a solution of 5 grammes of *sodium chloride* in 20 millilitres of *water* require for neutralisation 21.6 millilitres of *N/1 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator." *Br.*

It has been supposed that one-tenth of phosphorous acid would render the diluted acid dangerous to life; but experiments go far to show that this was an erroneous opinion, as half a drachm of that acid given to a dog produced no obvious poisonous effect. (See *A. J. P.*, 1858,

p. 359.) Phosphorous acid may be detected by testing the medicinal acid with a solution of corrosive sublimate, which will be converted into calomel if this impurity be present.

Old diluted phosphoric acid is very apt to contain microscopic plants. The presence of traces of hydrochloric acid is said to prevent their formation. (Rother, *D. C.*, 1886, p. 99; L. E. Sayre, *Proc. A. Ph. A.*, 1885; Samuel G. Ade, *Proc. A. Ph. A.*, 1884.)

Uses.—Diluted phosphoric acid, like other mineral acids, is capable of replacing the hydrochloric acid in peptic digestion and is a useful drug, therefore, in certain types of *dyspepsia*. It is doubtful, however, whether it possesses any advantage over diluted hydrochloric acid. Because of the fact that the nervous system contains a considerable proportion of phosphoric acid in combination with glycerin it has been supposed that this acid might exercise some tonic action in nervous diseases. Accordingly it has been employed to a considerable extent in *neurasthenia* and similar conditions of nerve weakness, but neither scientific evidence nor clinical experience lends any support to this use, such value as it may possess in these conditions being due simply to the improvement of digestion. It is also of service to prevent *phosphatic deposits* in the urine. This it does by increasing the acidity of this secretion through its uniting with the natural sodium and calcium phosphates to form acid salts. For the purpose of increasing acidity of the urine, however, the acid phosphate of sodium is generally preferred to phosphoric acid itself (see page 1037). Diluted phosphoric acid is incompatible with salts of silver, lead, and mercury, and also with many compounds of iron, aluminum and calcium, insoluble precipitates being formed unless the acid be much in excess in which case the precipitate may redissolve.

Dose, from fifteen to sixty minims (0.9–3.75 mils) well diluted.

ACIDUM SALICYLICUM. U. S., Br.

SALICYLIC ACID Acid. Salicyl.

(ăç'ĭ-dŭm săl-ĭ-cŷl'ĭ-cŭm)

"Orthohydroxybenzoic acid, existing naturally in combination in various plants, but generally prepared synthetically. It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99.3 per cent. of $C_7H_6O_3$ or $C_6H_4(OH)COOH$ (138.05). Preserve it in well-closed containers." *U. S.* "Salicylic Acid, $HC_7H_5O_3$, may be obtained from natural salicylates such as the oils of wintergreen (Gaultheria procumbens, *Linn.*) and sweet-birch (Betula lenta, *Linn.*), or by the interaction of sodium phenate and carbon dioxide." *Br.*

Ortho-oxybenzoic Acid; Acidum Spiricum; Acide salicylique, *Fr. Cod.*; Acidum salicylicum, *P. G.*; Salicylsäure, Spirsäure, Salicoylsäure, Spiroylsäure, *G.*; Acido salicilico, *It., Sp.*

In 1834 *salicyl aldehyde* (*salicylous acid*) was discovered by Pagenstecker in the flowers of *Spiræa Ulmaria*, L. In 1837, Piria and Ettling found that by oxidizing agents salicyl aldehyde was converted into a new body, salicylic acid, and in 1839, Löwig and Weidmann derived the latter principle directly from the flowers of the *Spiræa Ulmaria* L. Shortly afterwards Procter (*A. J. P.*, 1843; Aug., 1875) discovered that the acid could be procured from the oil of wintergreen (*Gaultheria procumbens*), which is now known to contain over 98 per cent. of methyl salicylate. Methyl salicylate is indeed obtainable by distillation from very many plants, but the probabilities are that it never exists already formed in the plant, but is produced during the process of distillation. (See *Betula lenta*, Part II.) When potassium hydroxide is added to methyl salicylate, potassium salicylate is formed, and methyl alcohol is also produced. If this latter be volatilized by heating, the acid is readily obtained by means of hydrochloric acid. Notwithstanding the discovery of this fact, and also the invention of still another process of manufacture by Ettling in 1845, salicylic acid remained so expensive as to be of no value in the arts until Kolbe and Lautemann discovered that it could be prepared by uniting phenol with carbon dioxide through the instrumentality of sodium. The article now began to attract some attention, but remained beyond the reach of general use until Kolbe, by continuing his researches, succeeded, in 1874, in producing it at a moderate cost. Traphagen and Burke found salicylic acid to be a natural constituent of many fruits, as follows: strawberries, raspberries, blackberries, currants, plums, black cherries, apricots, peaches, grapes, crab apples, apples, and oranges. (*J. Am. C. S.*, 1903, 242.)

Preparation.—While salicylic acid may be prepared from salicin by fusion with potassium hydroxide, or from oil of wintergreen by saponification with potassium hydroxide solution, practically it is usually obtained, according to Kolbe's patent, by treating sodium phenol (or carbolate) with carbon dioxide gas. For this purpose, the most concentrated caustic soda solution is evaporated with the corresponding amount of phenol to a dry powder, which is then heated to 100° C. (212° F.), while a stream of dry carbon dioxide gas is passed over it. The temperature is gradually raised to 180° C. (356° F.), increased to 220° C. (428° F.) as soon as phenol distils over, and finally raised to 250° C. (482° F.), until no more phenol distils. In the retort, the half of the phenol used remains as basic sodium salicylate, while the other half has distilled over unchanged. The reaction is as follows:

$$2C_6H_5ONa + CO_2 = C_6H_5OH + C_6H_4(ONa)COONa$$

The sodium salt thus obtained is dissolved in water, decomposed by hydrochloric acid, the salicylic acid filtered off, washed, and crystallized out of hot water, or purified by sublimation in a current of superheated steam. P. W. Hofmann subsequently patented a process

whereby distillation with superheated steam, with its attendant loss, is obviated; to the crude solution is added stannous chloride, which precipitates a dark mass containing the impurities, the clear supernatant liquid is then decomposed with hydrochloric acid and the crystals of salicylic acid purified by washing and the use of centrifugals. (*Ph. Centralh.*, 1892, 412.) An important improvement was subsequently made in Kolbe's process whereby all, instead of only half, of the phenol-sodium is converted into salicylate. R. Schmitt has found (Wagner's *Jahresbericht für Chem. Tech.*, 1885, p. 490) that if dry sodium phenolate and dry carbon dioxide are allowed to act on each other at ordinary temperatures, as long as absorption takes place a phenyl-sodium carbonate, $CO\begin{cases}OC_6H_5\\ONa\end{cases}$, is formed. If this is now heated for several hours in a closed vessel to 140° C. (284° F.), a molecular rearrangement takes place, and simple sodium salicylate, $C_6H_4(OH)COONa$, is formed without any separation whatever of phenol. Schmitt's process was purchased by the owners of Kolbe's patent. Lloyd's process for preparing salicylic acid from oil of wintergreen is as follows: Pure wintergreen oil, 3 parts; white potassium hydroxide, 3 parts; hydrochloric acid, 8 parts; water, q. s. Dissolve the potassium hydroxide in two parts of water in a glass or porcelain vessel, and heat to the temperature of 82.2° C. (180° F.). Stir into this gradually the oil, using a glass or porcelain spatula. Into another vessel place 64 parts of cold distilled water, and add the hydrochloric acid. Then with constant stirring add the solution of the potassium salicylate. The magma of minute crystals of salicylic acid must be separated with a thin muslin strainer (previously moistened) and pressed, then dried by exposure to a temperature of 65.5° C. (150° F.). Dissolve this crude acid in six parts of cold alcohol, filter through a funnel stopped with cotton and, with constant stirring, pour the filtrate into 32 parts of cold water. The purified crystals may be separated by straining through muslin, and dried by exposure to a heat of 65.5° C. (150° F.). The yield is a trifle less than 2 parts. For Walter's process, see *Bull. Pharm.*, 1899, 54. Salicylic acid has also been obtained synthetically from copper benzoate and water, which, when heated together in sealed tubes, yield cuprous oxide, free benzoic acid, and salicylic acid. (E. F. Smith, *Am. Chem. J.*, 2, p. 338). A. Rautert has found that the acid volatilizes with steam of 170° C. (338° F.), and has devised a process of purification based upon this, which yields at very little cost a beautiful product. Biel (*Ph. Z. R.*, 1876) reports that the sublimed acid is liable to decompose spontaneously. Dialyzed salicylic acid of beautiful appearance has been in the market since 1876. All traces of tarry matter can be removed by dialysis, and this acid is unexceptionable. Kolbe also obtained salicylic acid from barium and calcium carbolates, but the yield was less than when sodium salt was employed. Potassium phenol yielded only a trace of salicylic acid, but an abundance of *paraoxybenzoic* acid.

Properties.—" Fine prismatic needles, or as a bulky, crystalline powder, having a sweetish, afterwards acrid taste, permanent in the air. Synthetic Salicylic Acid is white and odorless; when prepared from methyl salicylate the Acid may have a slightly yellow or pink tint and a slight, gaultheria-like odor. One Gm. of Salicylic Acid dissolves in 460 mils of water, 2.7 mils of alcohol, 42 mils of chloroform, 3 mils of ether, 135 mils of benzene, or in 52 mils of oil of turpentine at 25° C. (77° F.), also in about 15 mils of boiling water. A saturated aqueous solution of Salicylic Acid is acid to litmus. It melts between 156° and 159° C. (312.8° and 318.2° F.). A saturated, aqueous solution of Salicylic Acid is colored intensely bluish-violet (in high dilution violet-red) by ferric chloride T.S. Incinerate about 1 Gm. of Salicylic Acid; not more than 0.1 per cent. of ash remains. Allow a saturated alcoholic solution of about 1 Gm. of Salicylic Acid to evaporate spontaneously, in a glass or porcelain dish in a place protected from dust; the synthetic Acid yields a perfectly white, crystalline residue; the Acid, prepared from methyl salicylate, yields a white, or not more than a slightly yellow, or slightly pink residue (*iron, phenol, or coloring matter*). Dissolve about 1 Gm. of Salicylic Acid in an excess of cold sodium carbonate T.S., agitate the liquid with an equal volume of ether, and allow the ethereal solution to evaporate spontaneously; the residue, if any, is free from the odor of phenol. A solution of about 0.5 Gm. of the synthetic Salicylic Acid in 10 mils of sulphuric acid at room temperature acquires not more than a light yellow color. The Acid, prepared from methyl salicylate, under similar conditions, may produce a slightly brown color (*organic impurities*). A solution of about 0.5 Gm. of Salicylic Acid in 10 mils of alcohol mixed with a few drops of nitric acid remains unaffected upon the addition of a few drops of silver nitrate T.S. (*hydrochloric acid*).

Assay.—Dissolve about 0.5 Gm. of Salicylic Acid, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed, in 25 mils of diluted alcohol which has previously been neutralized with tenth-normal potassium hydroxide V.S., phenolphthalein T.S. being used as indicator. Titrate this solution with tenth-normal barium hydroxide V.S., using phenolphthalein T.S. as indicator. It shows, in the dried acid, not less than 99.3 per cent. of $C_7H_6O_3$.

" Each mil of tenth-normal barium hydroxide V.S. corresponds to 0.013805 Gm. of $C_7H_6O_3$. Each gramme of Salicylic Acid, previously dried, corresponds to not less than 71.9 mils of tenth-normal barium hydroxide V.S." *U. S.*

" Distinct, prismatic, colorless crystals. Taste at first sweetish, then acid, leaving a burning sensation in the throat. Soluble in about 500 parts of *water*, in 3.5 of *alcohol* (90

per cent.), or in 2 of *ether*. Melting point 156° to 157° C. (312.8°–314.6° F.). Carefully heated it volatilises without decomposition. Dissolves in *solution of ammonium acetate*, and in *solution of sodium phosphate*. *T. Sol. of ferric chloride* gives with the aqueous solution a violet color, or, if the solution be largely diluted, a reddish-violet color. Shaken with a small proportion of *water*, the mixture filtered, and the solution evaporated, there remains a white residue, having no buff-tinted fringe (absence of iron, organic impurities, and coloring matter). Salicylic Acid dissolves in cold *sulphuric acid*, imparting to the liquid not more than a faint brownish tint in fifteen minutes (absence of certain organic impurities). When 1 gramme of the Acid is dissolved in an excess of cold *solution of sodium carbonate*, the liquid shaken with an equal volume of *ether*, and the ethereal solution allowed to evaporate spontaneously, the residue, if any, is free from the odor of phenol (absence of phenol). *Arsenic limit* 2 parts per million. No appreciable ash." *Br.*

When heated rapidly it is converted into phenol and carbon dioxide. It is stated that, by careful heating, glycerin can be made to dissolve 1 part in 50, and that the solution not only remains clear on cooling, but also may be diluted with water without separating. (*A. J. P.*, 1875, p. 212.) Goldsborough affirms that a mixture of the acid with alcohol, 1 to 10, may be diluted with 150 parts of water without crystallizing. By the presence of various neutral salts its solubility is increased without its antiseptic value being interfered with. It dissolves when mixed with 1 part of potassium nitrate, in 50 parts water; 1½ parts of ammonium citrate, in 60 parts water; 2 parts sodium sulphite, in 50 parts water; 2 parts sodium phosphate, in 50 parts water; 2½ parts sodium phosphate, in 12½ parts water. (Allen, *Com. Org. Anal.*, 1879, p. 344; also see Rother, *A. J. P.*, 1886, p. 420.)

On distilling salicylic acid or one of its salts with methyl alcohol and sulphuric acid, acid methyl salicylate is formed, having an agreeable aromatic odor. The reaction with ferric salts is much more delicate (1 in 100,000) than that of phenol with the same reagent (1 in 3000). Commercial salicylic acid was formerly very impure. Sodium chloride, phenol, cresotic acid, and oxybenzoic and paraoxybenzoic acids were the usual impurities. These may be detected by the official tests.

The most sensitive test for it is a ferric salt, with which it develops a beautiful violet color. Goldsborough states that to insure the delicacy of this reaction it is necessary that the iron salt be perfectly neutral; also that with this precaution he has clearly detected 1 part of the acid in 400,000 parts of water. On the addition of ammonia the violet color is changed to a reddish-brown, then to an orange, then to a permanent greenish-yellow. Sulphuric and nitric acids change the violet to a light brown (Goldsborough). It must be remembered that salicylous acid (salicylic aldehyde, C_6H_4OHCHO) reacts similarly with ferric salts. Salicylous acid, however, precipitates the silver potassio- or ammonio-nitrate white, the salicylic acid yellow. A. Fagans (*A. J. P.*, 1893, p. 133) points out that salicylic acid cannot be colorimetrically estimated in aqueous solutions in presence of phenols, but that in alcoholic solution only the former reacts with ferric chloride.

By distilling with alcohol and strong sulphuric acid, salicylic acid forms methyl- and ethyl-salicylic acids.

Uses.—Salicylic acid is an active disinfectant distinctly superior to phenol in its antiseptic properties and probably also in its germicidal effects. De LaCroix (*A. E. P. P.*, 1881, xiii) found that in the proportion of one part in a thousand it was sufficient to prevent the growth of various bacteria, and Kolbe has shown that as little as 0.04 per cent. is sufficient to retard souring of milk. In the experiments of H. C. Wood, Jr. (*U. P. M. B.*, February, 1907), 0.5 per cent. killed the colon bacillus in five minutes' exposure, and De LaCroix found that one in four hundred was germicidal after one and one-half days' exposure. Like many other disinfectants, it retards, and if in sufficient concentration arrests, enzymic fermentation. Locally salicylic acid is strongly irritant to mucous membranes and its irritant action can be demonstrated upon the skin. It has the peculiar property of softening and finally causing the separation of the horny matter of the epiderm.

In ordinary quantities when taken internally the salicylates exercise practically no effect upon the circulation nor respiration. It appears to act upon the central nervous system somewhat like the anilin derivatives, lessening painful sensation and also causing reduction in febrile temperature; in both of these actions, however, it is inferior in power to the coal-tar antipyretics. It appears also to have a distinct action upon the nutritive processes causing a marked increase in the nitrogenous elimination, but especially in the quantity of uric acid. Fine and Chase (*J. Bi. Chem.*, 1915, xxi, 371) have found that the uric acid of the blood is diminished, indicating that the increase in the urine is due to better elimination rather than augmented formation. It has a stimulant action upon the liver, increasing especially the liquid portion of the bile and thereby the total quantity; the solid matters, however, appear to be also slightly augmented.

Whether administered in the form of the acid itself or as one of its salts, salicylic acid circulates in the blood almost entirely in the form of sodium salicylate. Most of it unites with glycocoll in the body and appears in the urine in the form of a new compound known as salicyluric acid; a small amount, however, is probably eliminated unchanged, and some as pyrocatechin which imparts a greenish color to the urine.

After large doses salicylic acid causes symptoms resembling those seen after quinine; there is fulness of the head, roaring in the ears often with headache and sometimes disturbances of hearing and vision. Nausea and vomiting—due to an action upon the emetic center—are also frequent symptoms of large doses. With toxic quantities these symptoms are intensified and there is usually a fall in the bodily temperature with profuse sweating, excessive restlessness passing into delirium, a slow pulse, with at first hurried and later depressed respiration.

Salicylic acid is used both for its local effect and its systemic action. Because of its relative insolubility in water it is rarely of service as a direct surgical germicide but salicylated cotton and gauze are widely used. This may be prepared by dissolving two ounces (62 Gm.) of salicylic acid in two pints (1 liter) of alcohol, diluting with twenty pints (9.5 liters) of water and saturating with this six and one-half pounds (2–4 kilogm.) of absorbent cotton, and drying. Wadding so prepared contains about 2.53 per cent. of salicylic acid. It is also widely used in the form of lotions and ointments in the treatment of various *skin diseases,* especially chronic *eczemas.* Its beneficial action in these conditions is due in part to its antiseptic effect and in part to its softening action upon the corneous layer of the skin. Because of this latter property it is also widely employed for the purpose of removing *corns.* Weinbrenner (*M. M. W.,* lxi) has obtained good results from the local application of crystalline salicylic acid to superficial *cancers* of the skin.

Internally salicylic acid and its salts are used as urinary antiseptics, analgesics, antipyretics, and in the treatment of various forms of rheumatism. As the neutral salicylates are almost without antiseptic influence and as salicylic acid in whatever form exhibited circulates in the blood only in combination with a base, it is evident that any antiseptic action in the urine must depend upon the decomposition of its salt by urinary acids with the liberation of free salicylic acid; therefore it is of service as a urinary antiseptic only when the urine is acid in reaction. As an analgesic or antipyretic it has the same range of usefulness as the aniline derivatives, but except in rheumatic conditions is distinctly inferior to them.

The most important use of the salicylates is in the treatment of various rheumatic conditions. There are two distinct groups of conditions to which the term *rheumatism* is applied. One of these groups, which includes *acute articular rheumatism* and *tonsillitis,* is of infectious origin; in the other group, are included various painful conditions of the muscles, nerves, or joints, occurring in persons of a *lithemic diathesis.* The cause of this latter group of disturbances is unknown. Our theories of the mode of action of the salicylates in rheumatism has varied with our ideas of the pathogenesis of this disease. In former times when an excess of uric acid in the blood was believed to cause the various symptoms, the beneficial effects of the salicylates were attributed to their influence in increasing the elimination of this substance in the urine, but as we now know that uric acid is a result rather than a cause of many of the conditions called rheumatic, this explanation is not at present widely accepted. Some consider that the action of salicylic acid is merely that of an analgesic and antipyretic, but while this may be true of its effects in the *myalgias* and *neuralgias,* the evidence is strong that it exercises a specific curative effect in the infectious type of rheumatism. This is most rationally explained on the ground of its antiseptic action. While the salicylic acid must circulate in the blood as a neutral salt which is very inferior in antiseptic power, it has been shown that an excess of carbon dioxide in the blood may lead to the liberation of the free acid and it is probable that in the congested joints of rheumatic fever there is a sufficient accumulation of carbon dioxide to cause a liberation of salicylic acid. Closely allied to rheumatic fever, and probably due to the same micro-organism, are certain types of *acute tonsillitis* and some cases of *chorea;* in these conditions the salicylates are often of great service, although their action is neither so certain nor so prompt as in the case of joint involvement. It is probable also that there is a type of *chronic arthritis* which is caused by the germ of rheumatic fever. Perhaps also certain inflammations of serous membranes, as *iritis,* may be due to the same cause. In this latter group of diseases the salicylates are often of service.

In *lumbago, pleurodynia* and other myalgias, in certain inflammations of nerves as *sciatica,* in some cases of *chronic arthritis,* and the host of similar conditions which for lack of better diagnostic acumen we are wont to call *rheumatism,* salicylic acid is a valuable palliative and often appears to exercise even a curative effect.

There has been a great deal of discussion concerning the relative value and toxicity of salicylic acid obtained from plants and that manufactured from phenol. There is a widespread belief among clinicians that the so-called "natural salicylates" are superior in power and less prone to cause unpleasant symptoms than those manufactured synthetically. The toxic properties of the synthetic salicylates have been attributed to various phenol bodies, especially *cresotinic acid,* which are present as impurities, but Stockmann (*J. P. Ex. T.,* 1912, iv) has shown that these substances are scarcely more actively poisonous than salicylic acid and are possessed of similar curative properties in rheumatism. In an elaborate investigation undertaken under the auspices of the Council of Pharmacy and Chemistry of the American Medical Association, which included an historical, chemical, pharmacological, and clinical inves-

tigation of this subject, the conclusion was reached that there was no trustworthy evidence of any kind that the natural salicylates were superior to those prepared from phenol. (See *J. A. M. A.*, 1913, lx and lxi.)

Salicylic acid itself is so irritant to the stomach that it is rarely used internally. Because the neutral salicylates are so much less powerfully antiseptic some have believed that the salicylic acid is theoretically preferable in those cases where an antiseptic influence is desired as in *cystitis* and *rheumatic fever*, but as the acid must immediately combine with the excess of alkali in the blood, this theory is erroneous. There is no justification for the internal use of the free acid.

The use of salicylic acid or its salts as preservatives of beer, of milk, or other articles of food, is to be strongly condemned and its use is prohibited under the Federal and most state food and drugs acts.

Salicylic acid is incompatible with compounds of lead, silver, mercury, bismuth, and some other metals with which it produces insoluble precipitates. With ferric salts it produces the well-known violet color which is used as a test for its identity. Oxidizing agents destroy its identity and produce various derivatives.

Dose, five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Unguentum Acidi Salicylici, *Br.;* Collodium Salicylici Compositum, *N. F.;* Glycerogelatinum Acidi Salicylici, *N. F.;* Mulla Creosoti Salicylata, *N. F.;* Mulla Acidi Salicylici, *N. F.;* Pasta Zinci, *N. F.;* Pulvis Antisepticus, *N. F.;* Pulvis Talci Compositus, *N. F.;* Stili Acidi Salicylici Dilubilis, *N. F.*

ACIDUM STEARICUM. U. S.

STEARIC ACID Acid. Stear.

(ăç′ĭ-dŭm stē-ăr′ĭ-cŭm)

"An acid obtained from tallow and other solid fats, consisting chiefly of $C_{18}H_{36}O_2$ or $C_{17}H_{35}$. COOH (284.29)." *U. S.*

Acidum Stearinicum; Acide Stéarique, *Fr.;* Talgsäure, Stearinsäure, *G.*

Preparation.—Stearic acid is obtained from tallow soap by treating it with sulphuric or hydrochloric acid, whereby sodium sulphate or chloride is produced and stearic acid liberated; it is also made on a large scale by purifying the residue left after making glycerin by acting on stearin with superheated steam. (See *Glycerinum.*)

Properties.—It is officially described as "a hard, white, or yellowish-white, somewhat glossy solid, odorless, or having a slight, tallow-like odor, tasteless, and permanent in the air. One Gm. of Stearic Acid dissolves in 21 mils of alcohol, 2 mils of chloroform, or in 3 mils of ether at 25° C. (77° F.); almost insoluble in water; freely soluble in carbon disulphide or carbon tetrachloride. Melting point: not below 56° C. (132.8° F.). Congealing point: not below 54° C. (129.2° F.). Incinerate about 1 Gm. of Stearic Acid; not more than 0.1 per cent. of ash remains. Boil about 1 Gm. of Stearic Acid and about 0.5 Gm. of monohydrated sodium carbonate with 30 mils of distilled water in a capacious flask; the resulting solution while hot is not more than opalescent (*undecomposed fat or paraffin*). Shake melted Stearic Acid with an equal volume of hot distilled water; the separated water, after filtration, is not reddened by the addition of a drop of methyl orange T.S. (*mineral acids*)." *U. S.*

The melting point, 56° C. (132.8° F.), is an important factor in testing stearic acid, as a lower melting point would unfit it for use in making glycerin suppositories.

Uses.—This acid was introduced into the U. S. P. of 1890 and 8th and 9th Rev. solely because of its use in making glycerin suppositories. Stearic acid combines with alkalies to form the corresponding salts and is decomposed by oxidizing agents.

ACIDUM SULPHURICUM. U. S., Br.

SULPHURIC ACID Acid. Sulphuric.

(ăç′ĭ-dŭm sŭl-phū′rĭ-cŭm)

"A liquid containing not less than 93 per cent. nor more than 95 per cent. of H_2SO_4 (98.09). Preserve it in glass-stoppered bottles." *U. S.* "Sulphuric Acid may be obtained by the combustion of sulphur or pyrites and the oxidation and hydration of the resulting sulphur dioxide by means of nitrous and aqueous vapours, and contains not less than 95 per cent. by weight of hydrogen sulphate, H_2SO_4." *Br.*

Oil of Vitriol, Vitriolic Acid; Hydrogen Sulphate; Acide sulfurique; Huile de Vitriol, *Fr.;* Acidum Sulfuricum, *P. G.;* Vitriolöl, Schwefelsäure, *G.;* Acido solforico, *It.;* Acido sulfurico, *Sp.*

Preparation.—Sulphuric acid is obtained by burning sulphur or iron pyrites, FeS_2, and allowing the product of combustion, SO_2, to mix with nitrous fumes obtained from the decomposition of sodium nitrate, which change SO_2 into SO_3, and this uniting with steam yields H_2SO_4. If the sulphur were burned by itself, the product would be sulphurous oxide, which contains only two-thirds as much oxygen as sulphuric oxide. The object of the sodium nitrate is to furnish, by its decomposition, the requisite additional quantity of oxygen. To understand the process, it is necessary to remember that several oxides of nitrogen have oxidizing power. Thus, the main reactions of the sulphuric acid process are

$$2SO_2 + N_2O_4 = 2SO_3 + N_2O_2$$
$$SO_3 + H_2O = H_2SO_4$$
$$N_2O_2 + O_2 = N_2O_4$$

in which the sulphurous oxide from the burning pyrites or sulphur is oxidized to sulphuric oxide by the nitrogen tetroxide, which readily parts with two atoms of oxygen to such bodies as sulphurous oxide, and then takes two

atoms of oxygen again from the atmosphere, regenerating the original tetroxide. The nitrogen tetroxide thus acts simply as a carrier of atmospheric oxygen, whereby the SO_2 is changed into SO_3. This latter compound then unites with steam to form H_2SO_4, the final product. If the supply of steam be insufficient, white crystals (*lead chamber crystals*) will also form, which have the composition $HSO_3(NO_2)$, according to the following reactions:

$$2SO_2 + H_2O + N_2O_3 + O_2 = 2HSO_3(NO_2)$$

when steam enters in larger amount they disappear, with formation of sulphuric acid, while red fumes are given off, thus:

$$2HSO_3(NO_2) + H_2O = 2H_2SO_4 + N_2O_3$$

Thus, here, nitrous oxide, N_2O_3, aids oxidation.

Preparation on the Large Scale.—The manufacture of this most important chemical has grown to enormous proportions. The production of sulphuric acid in the United States in 1916 is given as 4,475,000 tons, reckoned as 50 degree acid, which is a large increase over any previous year. This includes not only acid produced from sulphur and pyrites, but the by-product from copper and zinc smelters, from the latter of which sources nearly 950,000 tons were obtained. Large quantities are manufactured in England, France, and Germany. Smaller amounts are prepared in Austria, Italy, Belgium, Russia and Japan, and additional amounts not definitely ascertained in Spain and in Scandinavian countries.

As made from pyrites, the process is as follows: Beginning with the pyrites-kilns, or burners, the broken mineral is placed in moderate-sized lumps on the bars of the burners, which have previously been heated to redness, and when the burning is once started, the fire is kept up by placing a new charge on the top of that nearly burned out. The ordinary charge for each burner of pyrites, containing about 48 per cent. of sulphur, is from 5 to 6 cwt., which is burnt out in twenty-four hours. The hot sulphur dioxide and air are drawn from the pyrites-burners through the whole system of tubes, towers, and chambers by help of the powerful draught from a large chimney which is placed in connection with the apparatus. These gases then pass either into a tall tower (called the Glover or denitrating tower), where they meet a descending stream of strong sulphuric acid charged with nitrous fumes, which at this moment of descent is mixed with a weaker sulphuric acid, thereby liberating the nitrous fumes which then mix with the sulphur dioxide and air, or they are charged with nitrous fumes direct from the nitre-pots, where a mixture of Chili saltpetre and sulphuric acid liberates them. The mixed gases are then delivered at a temperature of about 75° C. (167° F.) into the first of the leaden chambers. These chambers, of which there are three, are now made of much larger size than was formerly the case, having often a capacity of 38,000 cubic feet. Here the gases meet jets of steam and deposit liquid sulphuric acid, as also in the second chamber. In the third or exhaust chamber all the sulphur dioxide should have been converted into sulphuric acid, and red nitrous fumes must always be visible. These must not be lost, but are drawn into a so-called Gay-Lussac tower filled with coke, over which a finely divided shower of strong acid is allowed to fall. The nitrous fumes are absorbed by this, and give the so-called nitrated acid used as before mentioned in the Glover tower. The acid obtained in the leaden chambers has a sp. gr. of 1.55, or contains 64 per cent. of H_2SO_4. The acid which comes from the Glover tower (or, in case this is not used, is obtained by further concentration of chamber acid in leaden pans) has a sp. gr. of 1.71, and contains 78 per cent. H_2SO_4. The strongest acid must be procured by still further concentration in glass or platinum vessels, and will contain 98 per cent. H_2SO_4. (Roscoe and Schorlemmer, *Chem.*, vol. i, pp. 321–338.) Within recent years it has been found that to continue the concentration to the limit of 98 per cent. acid in platinum vessels is very destructive to these. Therefore it has been proposed, after a strength of 65° B. or about 90 per cent. acid has been reached, to finish in vessels of cast iron. It is found that the concentrated acid does not attack this, and therefore it can be substituted for platinum to advantage.

According to theory, 100 parts of sulphur burnt should yield 305.9 parts of pure sulphuric acid. In practice the yield is 290 to 294. The amount of sodium nitrate used varies very much. Manufacturers who employ Glover and Gay-Lussac towers require from 3.5 to 6.5 parts of nitrate for every 100 of sulphur burnt, while works unprovided with these appliances may take from 12 to 13 parts. (Roscoe and Schorlemmer, *Chem.*, vol. i, p. 337.)

In 1901, the "Badische Anilin and Sodafabrik" began on a large scale the manufacture of sulphuric acid by what is known as the "contact process," and since then this process has developed very successfully, and is now in use in this country in a number of the newer chemical works. It is rather a process for the manufacture, on a commercial scale, of sulphur trioxide, which then can be allowed to take up the necessary amount of water to form acid of any strength. A mixture of sulphur dioxide and purified air is passed over heated platinized asbestos, which is the so-called "contact material." To make the process successful, the sulphur dioxide gas must be washed to free it from dust, and all traces of volatile arsenic compounds (arising from arsenical pyrites) must be absent; in addition, the temperature must be regulated with great care to avoid the dissociation of the sulphur trioxide formed. The sulphur trioxide can be marketed as anhydride or as concentrated sulphuric acid of any desired strength.

One of the methods of obtaining pure sulphuric acid from chamber acid is by distillation.

Owing to the high boiling point of this acid, the operation is rather precarious, in consequence of the danger of the fracture of the retort from the sudden concussions to which the boiling acid gives rise. Ure recommended that a retort of the capacity of from two to four quarts be used in distilling a pint of acid. This is connected, by means of a wide glass tube three or four feet long, with a receiver surrounded with cold water. All the vessels must be perfectly clean, and no luting employed. The retort is then gradually heated by a small furnace of charcoal, or, what is better, by means of a sand bath, the retort being buried in the sand up to the neck. It is useful to put into the retort a few sharp-pointed pieces of glass, slips of platinum foil, or clay tobacco pipe tubes, with the view of diminishing the shocks produced by the acid vapor. The distilled product ought not to be collected until a dense grayish-white vapor is generated, the appearance of which is a sign that the pure concentrated acid is coming over. If this vapor should not immediately appear, it shows that the acid subjected to distillation is not of full strength; and the distilled product, until this point is attained, will be an acid water. In the distillation of sulphuric acid, Lembert uses, instead of pieces of glass or platinum foil, fragments of the mineral called quartzite; these after a time get worn and must be changed. Another method of concentrating is that of Gaillard in which the weak acid is made to fall in the form of a fine spray from the top of a tall tower, being met by a current of hot gases from a coke generator which cause the vaporization of the water, and the acid is thus concentrated to a strength ranging from 92 to 97 per cent. Hundreds of plants are now using this method of concentration.

What is said above relates to the mode of preparing common sulphuric acid; but there is another kind, know on the continent of Europe by the name of the *fuming sulphuric acid of Nordhausen*, so called from its properties, and a place in Saxony where it was first manufactured. This product is known in commerce, in the industries where it is used, simply as *oleum*. This acid is obtained by distilling dried ferrous sulphate in large stoneware retorts, heated to redness, and connected with receivers of glass or stoneware. The fuming acid distils over, and ferric oxide is left in the form of *colcothar* or *polishing rouge*, a material used for polishing metals, particularly gold and silver. The formula usually given for fuming sulphuric acid is $H_2S_2O_7$ or $H_2SO_4 + SO_3$. This would demand about 45 per cent. of sulphuric oxide or SO_3. In fact, the so-called Nordhausen acid seldom contains more than 10 per cent. of SO_3, and to obtain that demanded by the formula a re-distillation is necessary. This product is semi-solid, and is now obtainable in commerce put up in sealed glass flasks. Its sale has been largely curtailed lately, owing to the introduction into commerce of the *anhydride* under the name of *Solid Sulphuric Acid*. When moisture is rigidly excluded, the acid has little action on metals, and it is put up in soldered boxes of tinned sheet-iron; it is used largely in the arts in the manufacture of artificial alizarin and indigo. *Persulphuric acid* and the *persulphates* are among recent products of electrolysis. The ammonium persulphate, $(NH_4)_2S_2O_8$, and potassium persulphate, $K_2S_2O_8$, both form white crystalline salts. The former has already found a considerable technical application as an energetic oxidizing agent in the manufacture of organic dyestuffs and the cyanide extraction of gold.

Properties.—Sulphuric acid (*hydrogen sulphate*), commonly called *oil of vitriol*, is a dense, colorless, inodorous liquid, of an oily appearance, and strongly corrosive. On living tissues it acts as a powerful caustic. It unites with water in all proportions, and much heat is evolved on the mixture of the two fluids. When pure and as highly concentrated as possible, as manufactured in leaden chambers, its sp. gr. is 1.840 (1.8485, Ure), a fluidounce weighing a small fraction over 14 drachms. If its density exceed this, the presence of lead sulphate or other impurity may be inferred. Kohlrausch (*Pogg. Ann. Erganzungs*, Bd. viii, p. 675, Lunge) found the sp. gr. of *pure sulphuric acid, real hydrate*, to be 1.8342, and believes that a higher sp. gr. than this is due to impurities (probably lead sulphate). The commercial acid is seldom of this strength. According to Phillips, it has generally the sp. gr. 1.8433, and this is about the strength of the Br. acid, of which the sp. gr. is stated to be 1.841 at 15.6° C. (60° F.). The specific gravity of the U. S. P. IX acid is about 1.83 at 25° C. (77° F.); the British acid contains about 95 per cent. of absolute sulphuric acid and the U. S. P. IX acid not less than 93 per cent. nor more than 95 per cent. of H_2SO_4. Mendelejeff, after a careful determination, found that pure monohydrated sulphuric acid had the specific gravity 1.8371 at 15° C. (59° F.) compared with water at its maximum density, 4° C. (39.2° F.). (*Am. Drug.*, 1885, p. 16.) The strong acid boils at 338° C. (640.4° F.), and freezes at −26° C. (−14.8° F.). When diluted, its boiling point is lowered. When of the sp. gr. 1.78, it deposits crystals of the formula $H_2SO_4 + H_2O$ at about 0° C. (32° F.), and hence it is hazardous for manufacturers to keep an acid of that strength in glass vessels in cold weather, as they are liable to burst. With salifiable bases it forms a numerous class of salts, called sulphates. It acts powerfully on organic bodies, whether vegetable or animal, depriving them of the elements of water, liberating carbon, and turning them black. A small piece of cork or wood dropped into the acid will for this reason render it of a dark color. It absorbs water with avidity, and is used as a desiccating agent. It has been ascertained by W. B. and R. E. Rogers to be capable of absorbing 94 per cent. of carbon dioxide, a fact having an important bearing

on analytical operations. It is officially described as follows: "Sulphuric Acid is a colorless, odorless liquid, of oily consistence, very caustic and corrosive; it is strongly acid to litmus, even when highly diluted. Specific gravity: about 1.83 at 25° C. (77° F.). Sulphuric Acid is miscible with water or alcohol, with the evolution of much heat; the Acid must be added with great caution to the diluent. When heated on platinum foil, it is vaporized with the evolution of dense fumes. Sulphuric Acid chars cane sugar, wood, and many other organic substances. Pour a layer of ferrous sulphate T.S. carefully upon 3 mils of Sulphuric Acid, contained in a test-tube, and cool the liquid; the zone of contact does not assume a brown or reddish-brown color (*nitric or nitrous acid*). No precipitate is formed within an hour on mixing Sulphuric Acid with 4 or 5 volumes of alcohol (*lead*). Sulphuric Acid conforms to the tests for identity and purity given under *Acidum Sulphuricum Dilutum* when diluted to that strength.

"**Assay.**—Pour about 1 mil of Sulphuric Acid into a tared flask, stopper, weigh accurately, dilute with 50 mils of distilled water, cool the solution and titrate with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 93 per cent. nor more than 95 per cent. of H_2SO_4.

"Each mil of normal potassium hydroxide V.S. used corresponds to 0.049045 Gm. of H_2SO_4. Each gramme of Sulphuric Acid corresponds to not less than 18.96 mils nor more than 19.37 mils of normal potassium hydroxide V.S." *U. S.*

"A colorless, corrosive, intensely acid liquid of oily consistence, evolving much heat on the addition of *water*. Yields, when neutralised, the *reactions* characteristic of sulphates. Specific gravity about 1.841. 1 gramme diluted with 20 or 30 millilitres of *water* requires for neutralisation not less than 19.3 millilitres of *N/1 solution of sodium hydroxide*. Yields no characteristic *reactions* for copper, iron, ammonium, chlorides, nitrates, nitrites, or sulphites. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million. *Hydrochloric acid* to which *sodium sulphite* has been added, when poured carefully upon an equal volume of Sulphuric Acid contained in a test-tube, does not cause a red coloration at the junction of the two liquids, and no red precipitate forms on warming the tube (absence of selenium). Leaves not more than 0.05 per cent. by weight of solid residue on evaporation." *Br.*

Occasionally potassium nitrate is added to render dark samples of acid colorless. This addition gives rise to the impurity of potassium sulphate. These impurities often amount to 3 or 4 per cent. The commercial acid cannot be expected to be absolutely pure; but when properly manufactured it should not contain more than one-fourth of 1 per cent. of impurity. The fixed impurities are discoverable by evaporating a portion of the acid, when they will remain. If lead sulphate be present, the acid will become turbid on dilution with an equal bulk of water. This impurity is not detected by hydrogen sulphide unless the sulphuric acid be saturated with an alkali. If only a scanty white turbidity arise, the acid is of good commercial quality.

Other impurities occur in the commercial sulphuric acid. The several oxides of nitrogen are always present in greater or less amount in lead chamber acid. They may be detected by gently pouring a solution of ferrous sulphate over the commercial acid in a tube, when the solution, at the line of contact, will acquire a deep red color, due to the liberation of nitrogen tetroxide. Another method is to pass into tincture of guaiac the gases proceeding from the suspected acid heated with iron filings. If nitrogen tetroxide be present, the tincture becomes blue. The commercial acid, however, is not to be rejected unless the test shows the presence of nitrogen tetroxide in unusual quantity. Nitrogen tetroxide is an injurious impurity when the sulphuric acid is employed in the manufacture of hydrochloric acid, which is decomposed by the nitrogen tetroxide with evolution of chlorine. To remove this impurity it was recommended by Wackenroder, before distilling it, to heat the acid with a little sugar. This and the N_2O_4 mutually decompose each other, and the products are dissipated by heat. For the removal of the nitrogen acids generally, J. Löwe recommends the addition to the heated sulphuric acid of small portions of dry oxalic acid, so long as it exhibits a yellow tinge. The oxalic acid is decomposed into carbon dioxide and oxide, the latter of which, in becoming carbon dioxide, deoxidizes and destroys the nitrogen acids. A slight excess of oxalic acid produces no harm, as it is immediately decomposed. Perhaps a better method of getting rid of these acids is to distil with a little ammonium sulphate. Potassium sulphate, fraudulently introduced into the acid to increase its density, may be detected by saturating the acid with ammonia and heating to redness in a crucible, when ammonium sulphate will be expelled, and the potassium sulphate left.

Arsenic is sometimes present in sulphuric acid. In consequence of the high price of Sicilian sulphur, most English manufacturers have employed iron pyrites for the purpose of furnishing the necessary sulphurous acid in the manufacture of oil of vitriol. As the pyrites usually contains arsenic, it happens that the sulphurous acid fumes are accompanied by arsenous oxide, and thus the sulphuric acid becomes contaminated. From 22 to 35 grains of arsenic trioxide have been found in 20 fluid-ounces of oil of vitriol, of English manufacture, by G. O. Rees and Watson, and a still larger proportion by J. Cameron of South Wales. It may readily be discovered by the official tests for arsenic (see p. 72).

Until within recent years all the sulphuric acid produced in the United States was made from sulphur. At the present time many

Table of Percentage and Specific Gravity of Sulphuric Acid. U. S. IX

Per cent. H_2SO_4	Sp. gr. app. 25° C. / 25° C.	Sp. gr. app. 15° C. / 15° C.	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal KOH mils.	Per cent. = 0.01 mil normal KOH.
‡0	1.0000	1.0000	0.000180	0.0147	0.000	0.0488
1	1.0068	1.0070	0.000200	0.0152	0.205	0.0483
2	1.0134	1.0139	0.000221	0.0154	0.412	0.0476
3	1.0199	1.0206	0.000241	0.0152	0.622	0.0469
4	1.0265	1.0274	0.000262	0.0152	0.835	0.0465
5	1.0331	1.0342	0.000282	0.0149	1.050	0.0459
6	1.0398	1.0411	0.000302	0.0147	1.268	0.0452
7	1.0466	1.0480	0.000323	0.0147	1.489	0.0446
8	1.0534	1.0550	0.000343	0.0145	1.713	0.0441
9	1.0603	1.0621	0.000363	0.0145	1.940	0.0437
10	1.0672	1.0692	0.000384	0.0143	2.169	0.0429
11	1.0742	1.0764	0.000404	0.0143	2.402	0.0424
12	1.0812	1.0836	0.000424	0.0139	2.638	0.0420
13	1.0884	1.0909	0.000444	0.0141	2.876	0.0413
14	1.0955	1.0983	0.000464	0.0139	3.118	0.0410
15	1.1027	1.1057	0.000484	0.0135	3.362	0.0403
16	1.1101	1.1132	0.000500	0.0135	3.610	0.0398
17	1.1175	1.1207	0.000516	0.0135	3.861	0.0392
18	1.1249	1.1283	0.000531	0.0133	4.116	0.0388
19	1.1324	1.1360	0.000546	0.0132	4.374	0.0385
20	1.1400	1.1437	0.000561	0.0132	4.634	0.0377
21	1.1476	1.1515	0.000574	0.0130	4.898	0.0375
22	1.1553	1.1593	0.000586	0.0128	5.166	0.0368
23	1.1631	1.1671	0.000599	0.0128	5.438	0.0365
24	1.1709	1.1750	0.000611	0.0128	5.712	0.0360
25	1.1787	1.1830	0.000623	0.0127	5.990	0.0356
26	1.1866	1.1910	0.000633	0.0127	6.271	0.0351
27	1.1946	1.1991	0.000642	0.0125	6.556	0.0347
28	1.2026	1.2072	0.000651	0.0123	6.844	0.0342
29	1.2107	1.2153	0.000661	0.0123	7.136	0.0338
30	1.2188	1.2235	0.000670	0.0122	7.432	0.0334
31	1.2270	1.2318	0.000676	0.0122	7.731	0.0330
32	1.2352	1.2401	0.000682	0.0120	8.034	0.0327
33	1.2435	1.2484	0.000688	0.0119	8.340	0.0322
34	1.2519	1.2568	0.000694	0.0119	8.651	0.0318
35	1.2603	1.2653	0.000699	0.0118	8.965	0.0314
36	1.2688	1.2738	0.000702	0.0118	9.283	0.0311
37	1.2773	1.2823	0.000704	0.0116	9.605	0.0307
38	1.2859	1.2909	0.000707	0.0116	9.931	0.0303
39	1.2945	1.2996	0.000709	0.0115	10.261	0.0299
40	1.3032	1.3083	0.000712	0.0114	10.595	0.0296
41	1.3120	1.3171	0.000715	0.0112	10.933	0.0292
42	1.3209	1.3260	0.000717	0.0111	11.276	0.0288
43	1.3299	1.3350	0.000720	0.0110	11.623	0.0285
44	1.3390	1.3441	0.000723	0.0110	11.974	0.0281
45	1.3481	1.3533	0.000726	0.0108	12.330	0.0278
46	1.3574	1.3626	0.000731	0.0108	12.690	0.0273
47	1.3667	1.3721	0.000736	0.0105	13.056	0.0270
48	1.3762	1.3816	0.000741	0.0103	13.426	0.0266
49	1.3859	1.3913	0.000747	0.0103	13.802	0.0263
50	1.3956	1.4011	0.000753	0.0102	14.182	0.0260
51	1.4054	1.4110	0.000759	0.0100	14.567	0.0256
52	1.4154	1.4210	0.000765	0.0100	14.958	0.0253
53	1.4254	1.4311	0.000771	0.0098	15.354	0.0249
54	1.4356	1.4413	0.000777	0.0097	15.755	0.0246
55	1.4459	1.4516	0.000784	0.0096	16.162	0.0243

* Add if the temperature is above, subtract if it is below, the standard.
† Corresponding with a difference in specific gravity of 0.0001.
‡ The figures in this line across the page are for fractional percentages below 1.

Table of Percentage and Specific Gravity of Sulphuric Acid. U. S. IX.—Continued.

Per cent. H_2SO_4	Sp. gr. app. 25° C. / 25° C.	Sp. gr. app. 15° C. / 15° C.	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal KOH mils.	Per cent. = 0.01 mil normal KOH.
56	1.4563	1.4621	0.000790	0.0095	16.574	0.0239
57	1.4668	1.4726	0.000795	0.0094	16.992	0.0236
58	1.4774	1.4832	0.000800	0.0093	17.415	0.0234
59	1.4881	1.4939	0.000805	0.0093	17.843	0.0230
60	1.4989	1.5048	0.000810	0.0092	18.277	0.0228
61	1.5098	1.5157	0.000816	0.0091	18.716	0.0225
62	1.5208	1.5267	0.000822	0.0091	19.161	0.0222
63	1.5318	1.5379	0.000828	0.0090	19.612	0.0219
64	1.5429	1.5491	0.000834	0.0089	20.068	0.0217
65	1.5541	1.5603	0.000841	0.0088	20.529	0.0214
66	1.5654	1.5717	0.000848	0.0088	20.996	0.0211
67	1.5768	1.5831	0.000856	0.0088	21.469	0.0209
68	1.5882	1.5946	0.000864	0.0087	21.947	0.0207
69	1.5997	1.6062	0.000872	0.0087	22.431	0.0204
70	1.6112	1.6178	0.000880	0.0085	22.920	0.0202
71	1.6229	1.6295	0.000888	0.0085	23.416	0.0200
72	1.6346	1.6413	0.000897	0.0085	23.917	0.0197
73	1.6464	1.6531	0.000906	0.0085	24.424	0.0196
74	1.6582	1.6650	0.000915	0.0085	24.935	0.0193
75	1.6700	1.6769	0.000924	0.0085	25.452	0.0192
76	1.6817	1.6888	0.000934	0.0085	25.972	0.0190
77	1.6935	1.7006	0.000947	0.0086	26.498	0.0189
78	1.7051	1.7124	0.000963	0.0087	27.027	0.0188
79	1.7166	1.7240	0.000976	0.0088	27.558	0.0188
80	1.7279	1.7355	0.000987	0.0090	28.090	0.0187
81	1.7390	1.7467	0.000999	0.0093	28.624	0.0188
82	1.7497	1.7575	0.001011	0.0096	29.156	0.0188
83	1.7601	1.7680	0.001022	0.0101	29.687	0.0190
84	1.7700	1.7780	0.001034	0.0109	30.213	0.0193
85	1.7792	1.7873	0.001046	0.0115	30.732	0.0195
86	1.7879	1.7959	0.001043	0.0127	31.244	0.0199
87	1.7958	1.8038	0.001040	0.0139	31.747	0.0203
88	1.8030	1.8110	0.001035	0.0154	32.240	0.0207
89	1.8095	1.8174	0.001030	0.0172	32.724	0.0211
90	1.8153	1.8231	0.001022	0.0196	33.198	0.0216
91	1.8204	1.8282	0.001032	0.0217	33.662	0.0220
92	1.8250	1.8327	0.001043	0.0256	34.116	0.0225
93	1.8289	1.8365	0.001053	0.0303	34.561	0.0230
94	1.8322	1.8397	0.001064	0.0385	34.995	0.0235
95	1.8348	1.8422	0.001074	0.0526	35.420	0.0244
96	1.8367	1.8440	0.001064	0.1111	35.830	0.0256
97	1.8376	1.8448	0.001054	.....	36.221	0.0274
98	1.8372	1.8445	0.001064	0.0555	36.586	0.0297
99	1.8354	1.8427	0.001070	0.0270	36.923	0.0336
100	1.8317	1.8391	0.001074	.....	37.221	.....

Note that the specific gravity diminishes in acids of more than 97.5 per cent. strength as the percentage increases.

NOTE: To find the per cent. of SO_3, multiply the per cent. of H_2SO_4 by 0.81629. To find the per cent. of SO_4 multiply the per cent. of H_2SO_4 by 0.97941. To find the volume per cent. of official Sulphuric Acid (94 per cent.), multiply the "normality" by 2.857. For the volume per cent. of official Diluted Sulphuric Acid (10 per cent.), multiply the "normality" by 46.10.

To find the weight in grammes of H_2SO in 100 mils, multiply the specific gravity by the per cent. of H_2SO_4.

of the sulphuric acid works are using pyrites. Most of the American pyrites ore is entirely free from arsenic. Dupasquier states that tin is sometimes present in commercial sulphuric acid, derived from the solderings of the leaden chambers; but this could scarcely happen now, as care is taken to avoid soldering, and to effect the union of the metal by fusion by means of the blow-pipe. It may be discovered by hydrogen sulphide, which precipitates sulphide of tin, convertible by nitric acid into the white insoluble stannic oxide.

Should the precipitate be the mixed sulphides of arsenic and tin, the former would be converted by nitric acid into arsenic acid and dissolved, and the latter into insoluble stanic oxide and left. Another impurity occasionally existing in French sulphuric acid is selenium, supposed to be derived from copper pyrites sometimes substituted for sulphur in the manufacture of the acid.

Composition.—The normal acid of the sp. gr. 1.842 consists of one molecule of sulphuric oxide and one molecule of water. As the hydrogen acts the part of a metal in the compound, the systematic name would be hydrogen sulphate. The oxide consists of one atom of sulphur and three atoms of oxygen. The ordinary commercial acid consists, according to Phillips, of one molecule of oxide and one and a quarter molecules of water. The hydrated acid of Nordhausen has a density as high as 1.89 or 1.9, and consists of two molecules of oxide and one molecule of water ($2SO_3 + H_2O$). This acid is particularly adapted to the purpose of dissolving indigo for dyeing the Saxon blue. When heated gently in a retort, connected with a dry and refrigerated receiver, sulphuric oxide or anhydride distils over, and the common monohydrated acid remains behind. In performing this operation, much difficulty from concussion is avoided, and the production of oxide increased, by introducing a coil of platinum wire into the retort. The oxide may also be obtained by the action of phosphoric oxide on concentrated sulphuric acid, according to the method of Barreswil. The mixture must be made in a refrigerated retort, and afterwards distilled by a gentle heat into a refrigerated receiver. *Sulphuric oxide* (*solid sulphuric acid*) under 18° C. (64.4° F.) is in small, colorless crystals, resembling asbestos. It is tenacious, difficult to cut, and may be moulded in the fingers like wax, without acting on them. Exposed to the air, it emits a thick opaque vapor of an acid odor. Above 18° C. (64.4° F.) it is a liquid, very nearly of the density 2.

Uses.—For the therapeutic powers and uses of sulphuric acid when administered internally, see *Acidum Sulphuricum Dilutum*. Externally it is sometimes employed as a caustic; but, from its liquid form, it is very inconvenient for that purpose, and should be applied with caution. A plan, however, has been proposed by Simpson by which it becomes very manageable. This consists in mixing it with dried and powdered zinc sulphate sufficient to give it a pasty consistence. *Michel's Paste* consists of strong sulphuric acid three parts, and finely powdered asbestos one part, thoroughly rubbed together. Mixed with saffron to the consistence of a ductile paste, Velpeau found it a convenient caustic not liable to spread or be absorbed, and producing an eschar which is promptly detached.

Toxicological Properties.—The symptoms of poisoning by this acid are the following: Burning heat in the throat and stomach, extreme fetidness of the breath, nausea and excessive vomitings of black or reddish matter, excruciating pains in the bowels, difficulty of breathing, extreme anguish, a feeling of cold on the skin, great prostration, constant tossing, convulsions, and death. Sometimes there is no pain whatever in the stomach, sensibility being apparently destroyed by the violence of the caustic action. The intellectual faculties remain unimpaired. Frequently the uvula, palate, tonsils, and other parts of the fauces are covered with black or white sloughs. The treatment consists in the administration of large quantities of magnesia, or, if this be not at hand, of solution of soap or other alkali. The safety of the patient depends upon the greatest promptitude in the application of the antidotes. After the poison has been neutralized, mucilaginous and other bland drinks must be taken freely.

Upon the skin sulphuric acid acts as a very rapid and powerful corrosive. When it has been spilled or thrown upon the person the part should be immediately washed with a weak solution of sodium carbonate or bicarbonate, or soap may be well rubbed into the surface. After the removal and neutralization of the acid, Carron oil or similar protective may be applied. Further treatment is that of a burn.

The holes burnt in linen by sulphuric acid, so long as the texture is undisturbed, are distinguished from those produced by red-hot coals, by the paste-like characters of their edges.

Uses in the Arts.—Sulphuric acid is more used in the arts than any other acid. It is employed to obtain many of the other acids; to extract soda from common salt; to make alum and ferric sulphate; to refine petroleum and paraffin; to decompose the neutral fats; to dissolve indigo; to prepare phosphorus, chlorinated lime, magnesium sulphate, etc. Petroleum refining, manufacture of smokeless powder and other nitrated explosives, and manufacture of fertilizers from phosphatic materials consume the largest amounts of sulphuric acid in the United States.

Apart from the destructive effect which strong sulphuric acid has upon almost all forms of organic matter, its incompatibilities in general are those of the diluted acids, which see.

Off. Prep.—Acidum Sulphuricum Aromaticum, *U. S., Br.;* Acidum Sulphuricum Dilutum, *U. S., Br.;* Acidum Sulphurosum, *Br.*

ACIDUM SULPHURICUM AROMATICUM.
U. S., Br.

AROMATIC SULPHURIC ACID **Acid. Sulph. Arom.**

(ăç′ĭ-dŭm sŭl-phū′rĭ-cŭm ăr-ǫ-măt′ĭ-cŭm)

"Aromatic Sulphuric Acid contains free sulphuric acid and ethyl-sulphuric acid together equivalent to not less than 19 per cent. nor more than 21 per cent. of H_2SO_4 (98.09). Preserve it in glass-stoppered bottles." *U. S.*

Tinctura Aromatica Acida; Elixir of Vitriol; Elixir vitriolique, Teinture (alcoolé) aromatique sulphurique, *Fr*; Saure Aromatische Tinktur, Elixir Vitrioli Mynsichti, Mynsicht's Elixir, *G.*

* " Sulphuric Acid, *one hundred and nine* mils [or 3 fluidounces, 5 fluidrachms, 29 minims]; Tincture of Ginger, *fifty mils* [or 1 fluidounce, 5 fluidrachms, 31 minims]; Oil of Cinnamon, *one mil* [or 16 minims]; Alcohol, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Add the Sulphuric Acid gradually, and with great caution, to *seven hundred mils* [or 23 fluidounces, 321 minims] of Alcohol, and allow the mixture to cool. Then add to it the Tincture of Ginger and the Oil of Cinnamon, and afterwards enough Alcohol to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Keep the product in glass-stoppered bottles." *U. S.*

" Tincture of Ginger, 250 millilitres; Spirit of Cinnamon, 15 millilitres; Sulphuric Acid. 70 millilitres; Alcohol (90 per cent.), sufficient to produce 1000 millilitres. Mix the Sulphuric Acid gradually with six hundred millilitres of the Alcohol; cool to 15.5° C. (59.9° F.); add the Spirit of Cinnamon and Tincture of Ginger and sufficient of the Alcohol to produce the required volume." *Br.*

The formula adopted at the 1880 revision of the U. S. Pharmacopœia and continued in the 1890 and 8th and 9th Revisions is that recommended by Thomas N. Jamieson, *A. J. P.,* 1867, p. 201. The change in the appearance and properties from the preparation of the U. S. P., 1870, was so marked that the wisdom of making so radical a change was doubted. Experience has proved, however, that the new preparation has not the same tendency to precipitate, and the lightness in color has been offset by more substantial advantages. The British formula has been remodelled to accord with the U. S. P. Spirit of cinnamon is used, however, instead of oil of cinnamon in corresponding amount. The proportion of sulphuric acid was increased in the U. S. P. (8th Rev.) about 10 per cent. over that of the previous Pharmacopœia.

Properties.—It is officially described as follows: " Aromatic Sulphuric Acid is a clear, reddish-brown liquid; it has a pleasant, aromatic odor and is strongly acid to litmus. When added to barium chloride T.S. it produces a white precipitate, insoluble in hydrochloric acid. Specific gravity: about 0.933 at 25° C. (77° F.)." *U. S.*

Aromatic sulphuric acid of the older Pharmacopœias was of a deep reddish-brown, but it is a straw-colored liquid when freshly prepared according to the directions of the U. S. Pharmacopœia IX, of a peculiar aromatic odor, and, when sufficiently diluted, of a grateful acid taste. It cannot, however, be viewed merely as a sulphuric acid diluted with alcohol and containing essential oils, for the difference between fresh and old preparations is quite marked, and a peculiar and agreeable ethereal odor is developed by age. The U. S. official definition recognizes the presence of ethyl sulphuric acid.

" **Assay.**—Pour about 10 mils of Aromatic Sulphuric Acid into a tared flask, stopper, weigh accurately, transfer to a small flask, using 60 mils of distilled water to rinse the weighing-flask, and, having connected the flask with a reflux condenser, boil the liquid for six hours. When cold, dilute it with distilled water to about 100 mils and titrate with normal potassium hydroxide V.S., methyl orange T.S. being used as indicator. It shows not less than 19 per cent. nor more than 21 per cent. of H_2SO_4.

" Each mil of normal potassium hydroxide V.S. used corresponds to 0.049045 Gm. of H_2SO_4. Each gramme of Aromatic Sulphuric Acid corresponds to not less than 3.87 mils nor more than 4.28 mils of normal potassium hydroxide V.S." *U. S.*

" Specific gravity 0.917 to 0.923. 10 millilitres require for neutralisation not less than 24.9 millilitres of *N/1 solution of sodium hydroxide.*" *Br.*

Samples of fresh aromatic sulphuric acid as well as older specimens have been assayed by E. W. Clark, and all were found to be more or less deficient in sulphuric acid; the inference is quite clear that there is some decomposition or combination of sulphuric acid in the preparation upon keeping.

Uses.—This valuable preparation is tonic and astringent. It acts precisely as does the *Acidum Sulphuricum Dilutum.* Water produces a turbidity in this preparation owing to the precipitation of the oil and resin of the aromatics, otherwise the incompatibilities are the same as those of *diluted sulphuric acid,* which see.

Dose, from five to fifteen minims (0.32–1.0 mil), in a wineglassful of water, repeated two or three times a day. Care must be taken that the teeth are not injured.

ACIDUM SULPHURICUM DILUTUM. U. S., Br.

DILUTED SULPHURIC ACID Acid. Sulph. Dil.

(ăç'ĭ-dŭm sŭl-phū'rĭ-cŭm dī-lū'tŭm)

" An aqueous solution containing not less than 9.5 per cent. nor more than 10.5 per cent. of H_2SO_4 (98.09). Preserve it in glass-stoppered bottles." *U. S.* " Diluted Sulphuric Acid contains 10 per cent. by weight of hydrogen sulphate, H_2SO_4." *Br.*

Acide sulphurique dilué, *Fr.;* Acidum sulphuricum dilutum, *P. G.;* Verdünnte Schwefelsäure, *G.*

* " Sulphuric Acid, *fifty grammes* [or 1 ounce av., 334 grains]; Distilled Water, *four hundred and twenty grammes* [or 14 ounces av., 357 grains], to make *four hundred and seventy grammes* [or 16 ounces av., 253 grains]. Pour the Acid gradually, with constant stirring, into the Distilled Water. Keep the product in glass-stoppered bottles.

" Diluted Sulphuric Acid is a colorless, odorless liquid; it has a strongly acid taste and is strongly acid to litmus. Specific gravity: about 1.067 at 25° C. (77° F.). With barium chloride T.S. it yields a white precipitate insoluble in hydrochloric acid. Evaporate 25 mils of Diluted Sulphuric Acid from a platinum or porcelain dish, and ignite the residue; not

more than 0.0015 Gm. of residue remains after ignition (*non-volatile impurities*). Ten mils of Diluted Sulphuric Acid does not at once discharge the color of 0.1 mil of tenth-normal potassium permanganate V.S. (*sulphurous or nitrous acid*). Diluted Sulphuric Acid is not immediately affected by silver nitrate T.S. (*hydrochloric acid*). Ten mils of Diluted Sulphuric Acid does not respond to the Test for heavy metals (see Part III, Test No. 3). Two mils of Diluted Sulphuric Acid meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"**Assay.**—Pour about 20 mils of Diluted Sulphuric Acid into a tared flask, weigh accurately, dilute with 10 mils of distilled water and titrate with normal potassium hydroxide V.S., using methyl orange T. S. as indicator. It shows not less than 9.5 per cent. nor more than 10.5 per cent. of H_2SO_4.

"Each mil of normal potassium hydroxide V.S. used corresponds to 0.049045 Gm. of H_2SO_4. Each gramme of Diluted Sulphuric Acid corresponds to not less than 1.94 mils nor more than 2.14 mils of normal potassium hydroxide V.S." *U. S.*

"Sulphuric Acid, 112.5 grammes; Distilled Water, 940.0 millilitres, or a sufficient quantity. Add the Sulphuric Acid very gradually to one-half of the Distilled Water contained in a glass flask; cool to 15.5° C. (59.9° F.) and add sufficient Distilled Water to make the resulting liquid respond to the following tests.

"Specific gravity 1.069. 10 millilitres require for neutralisation 21.7 millilitres of *N/1 solution of sodium hydroxide.*" *Br.*

This preparation is sulphuric acid diluted to such an extent as to make it convenient for prescription. The British Pharmacopœia, 1914, lowered slightly the specific gravity of this acid to correspond with that of the U. S. IX. The difference is not so great as to be of practical importance. The strong acid is added gradually to the water, to guard against the too sudden production of heat, which might cause the fracture of the vessel. During the dilution, when commercial sulphuric acid is used, the liquid becomes slightly turbid, and in the course of a few days deposits a grayish-white powder, which is lead sulphate, and from which the diluted acid should be poured off. This noxious salt is thus disposed of; but potassium sulphate, another impurity in the strong acid, still remains. The presence of a little potassium sulphate will do no harm; but, if it should be fraudulently introduced into the strong acid to increase its specific gravity, its amount may be ascertained by saturating the acid, after dilution, with ammonia, and expelling by a red heat the ammonium sulphate formed. Whatever potassium sulphate is present will remain behind. If the directions of the Pharmacopœias are strictly carried out, and the kind of sulphuric acid is used which is known in commerce as chemically pure, responding to the tests given under the head of *Acidum Sulphuricum*, the official manipulations will be all-sufficient.

Uses.—Diluted sulphuric acid is tonic, refrigerant, and astringent. It is given in *typhoid fever*, and often with advantage. In the convalescence from protracted fevers it acts beneficially as a tonic, exciting the appetite and promoting digestion. As an astringent, it is employed in *colliquative sweats, passive hemmorrhages,* and *diarrheas* dependent on a relaxed state of the mucous membrane of the intestines, *i.e.*, in *serous diarrheas.* Buxton, of London, called attention to its great value in *choleraic diarrheas;* his assertions have received abundant confirmation both in this country and in England. In incipient *cholera* it is an efficient remedy; diluted with water, it may be given every twenty minutes in ordinary cases, every quarter of an hour in severe cases. For *bilious diarrhea* the acid is not a suitable remedy. It is added with advantage to infusions of cinchona, the alkaloids of which it tends to hold in solution. As it is injurious to the teeth, it is best taken by sucking it through a glass tube or quill. It is much less used in the United States than is the aromatic sulphuric acid. An elegant form for its administration was the Compound Infusion of Rose, U. S., 1870.

All forms of sulphuric acid show incompatibility with salts of lead, barium, strontium, and calcium, forming insoluble precipitates of the corresponding sulphates. With hypophosphorous acid or hypophosphites, it is reduced to sulphurous acid and finally to sulphur.

Dose, ten to thirty minims (0.6–1.8 mils).

ACIDUM SULPHUROSUM. Br.

SULPHUROUS ACID

(ăç'ĭ-dŭm sŭl-phū-rō'sŭm)

"Sulphurous Acid is an aqueous solution containing 6.4 per cent. by weight of hydrogen sulphite, H_2SO_3, corresponding to 5 per cent. by weight of sulphur dioxide, SO_2. The sulphur dioxide may be obtained by heating sulphuric acid with charcoal or sulphur." *Br.*

Acide sulfureux, *Fr.;* Schwefligsäure, Schwefligsäurewasser, *G.*

Sulphurous acid was not admitted to Part I of the U. S. IX, but was placed among the reagents (see Part III) and also in the British Pharm., 1914, although without a process for making it. The U. S. VIII method of preparation is appended:

"Sulphuric Acid, *sixty mils* [or 2 fluidounces, 14 minims]; Charcoal, in coarse powder, *twenty grammes* [or 309 grains]; Distilled Water, *five hundred mils* [or 16½ fluidounces]. Introduce the Charcoal into a glass flask having a capacity of about *five hundred mils* [or 16½ fluidounces], add the Acid, and mix them well. Connect the flask by means of bent glass tubing, about fifty centimeters in length, with a wash bottle having a capacity of about two hundred mils containing about *fifty mils* [or 1 fluidounce, 5 flui-

drachms] of water, so that the end of the inlet tube shall be below the surface of the water. Through the triply perforated rubber stopper of the wash-bottle pass a safety tube, which should reach nearly to the bottom of the bottle, and connect the latter, by means of glass tubing, with a bottle provided with a doubly perforated rubber stopper, having a capacity of about one thousand mils, and containing *five hundred mils* [or 16½ fluidounces] of well-cooled Distilled Water. The inlet tube should dip about twenty-five millimeters below the surface of the Distilled Water. By means of a second tube connect this bottle with another containing water, the end of the tube extending five centimeters below the surface. Having ascertained that all the connections are air-tight, apply a moderate heat to the flask containing the Sulphuric Acid and Charcoal, until the evolution of gas has nearly ceased, and, during the passage of the gas, keep the bottle containing the Distilled Water at or below 10° C. (50° F.), by surrounding it with cold water or ice. Assay a small portion of the Sulphurous Acid by the method given below. Then add to the remainder sufficient Distilled Water to bring the product to the strength of 6.4 per cent., by weight, of sulphur dioxide. Finally pour the Sulphurous Acid into dark, amber-colored, glass-stoppered bottles, which should be completely filled, and kept in a cool place, protected from light. Owing to its rapid deterioration, Sulphurous Acid should be frequently assayed, and none should be dispensed, if it fails to conform to the assay given below." *U. S. VIII.*

The British Pharmacopœia no longer gives a detailed process. The process of the former U. S. Pharmacopœia was essentially that of Wittstein. The sp. gr. of the U. S. preparation was about 1.028, of the British, 1.025, the former being slightly stronger.

The rationale of the process is simple. When the sulphuric acid (H_2SO_4) and charcoal are heated together, two molecules of the former give up each an atom of oxygen to the latter, and there are thus produced sulphur dioxide and carbon dioxide, which, having been first passed through a wash bottle containing a little water to absorb impurities, are received into the distilled water, where the sulphur dioxide is absorbed, while the greater part of the carbon dioxide escapes:

$$4H_2SO_4 + C_2 = 2CO_2 + 4H_2O + 4SO_2$$

The excess of sulphur dioxide or sulphurous acid gas which escapes absorption may be received into a solution of sodium carbonate, to prevent the escape of gas into the room. The point of saturation may be roughly indicated by the bubbles formed by the escape of the gas from the distilled water being equal in size to those formed in the wash bottle. If there is any difficulty in getting the solution up to the official strength, the proportionate amount of sulphuric acid and of charcoal should be increased, and care exercised that the gas pass through the water in an abundant stream. The direction to keep the acid in well-stoppered bottles, in a cool place, is necessary in consequence of the strong tendency of the gas to escape and to undergo oxidation. Old sulphurous acid often contains sulphuric acid, which may be nearly all removed by the cautious addition of barium sulphite and the removal by filtration of the precipitated sulphate.

According to W. L. Scott (*P. J.*, Oct., 1869, p. 217), the best results are obtained when sulphuric acid containing 75 per cent. of anhydrous acid is employed; when a too concentrated acid is used, a part of it is entirely reduced and sulphur deposited, while a too diluted acid causes the evolution of hydrogen sulphide. He also affirms that a purer gas is obtained by placing a little lead sulphite and a few pieces of charcoal in the wash bottles.

F. C. Calvert gives a process for preparing this acid on a large scale by which he avoids all the inconveniences usually attendant on its manufacture, and has prepared thousands of gallons daily of a saturated solution. It consists in burning sulphur in a small furnace, and conducting the acid gas through earthenware tubes surrounded with water so as to cool them. The gas is then made to ascend through a wooden tube 40 feet high and about 4 feet wide, sometimes called a coke scrubber, filled with pumice stone previously washed first with hydrochloric acid and then with water. A certain amount of water is introduced into the tube from above, which, in its descent, meets and dissolves the gas, and runs out saturated from the bottom of the tube into an air-tight reservoir. (*P. J.*, xvii, 512.) Where sulphurous acid is to be used as a disinfectant, carbon disulphide, either pure or mixed with petroleum, or sulphur moistened with wood alcohol, may be burned in the room to be disinfected. Keates (*Chem. News*, Dec. 8, 1876) suggests the use of a suitable lamp. Stevenson uses an open copper dish or porcelain capsule, and simply ignites the liquid; care should be used, however, as the disulphide is very inflammable and volatile. A purer sulphurous acid than the official may be made by John Kennedy's process, that of reducing sulphuric acid with metallic copper and passing the gas through a cylinder containing lumps of moist charcoal and then through a wash bottle. The by-product is available as a copper sulphate. (*A. J. P.*, 1886, p. 226.)

F. L. Cheney devised a method of making sulphurous acid extemporaneously as follows: Dry acid sodium sulphite, 5.7 Gm.; dilute hydrochloric acid, 18.5 mils; water, 25 mils. Add the acid to the salt, placed in a half pint glass-stoppered bottle, stopper immediately and set aside in a cool place. Agitate slowly to aid in the solution of the salt, and when bubbles cease to arise, add the water and shake the bottle for a few minutes. The product should measure 40 mils and assay from 6 per cent. to 6.5 per cent. SO_2. When it is necessary to have a fresh solution of sulphurous acid and the presence of a small amount of sodium chloride is admissible,

this process will be found convenient. (*A. J. P.*, 1906, 333.)

Properties.—Sulphurous acid is a strong solution of sulphurous oxide gas. The oxide is an irrespirable gas, of a suffocating odor familiar to every one as that of burning sulphur, which is converted into it by combustion. If inhaled in the concentrated state, it proves fatal. Cold reduces it to a colorless liquid, which boils at –10.5° C. (13.1° F.). It has the sp. gr. 2.21, liquefies at –10° C. (14° F.), has a strong acid reaction, extinguishes burning bodies, has the power of bleaching many colored substances, and has a strong affinity for oxygen, with which it gradually combines in the presence of water, forming sulphuric acid. Water at 18° C. (64.4° F.) takes up about 50 volumes of gas, and the solution has the sp. gr. 1.04. (Brande and Taylor.) Liquefied sulphurous acid gas (sulphurous oxide) is manufactured by Pictet in Geneva, and others, and is sent into commerce in copper cylinders. It also forms the basis of the Pictet ice making process. The Pictet machines are constructed to use either the pure SO_2 or the "Pictet fluid," a mixture of compressed carbon dioxide and sulphur dioxide.

Sulphurous acid sometimes exists as an impurity in hydrochloric, acetic, and other acids; according to P. Schweitzer, the minutest quantity may be detected by dissolving zinc in the suspected acid, when, if sulphurous acid be present, hydrogen sulphide will be evolved, recognizable by its odor. (*Chem. News*, xxviii, 293.)

When sulphurous acid is exposed to the air it slowly absorbs oxygen, with the formation of sulphuric acid, and acquires a sour taste, and the property of changing vegetable blues to red. When kept in closed vessels exposed to the sunlight, a portion of it is decomposed, sulphur being deposited and sulphuric acid formed by the union of the liberated oxygen with other portions of the acid. (*A. J. P.*, xlii, 352.) It should be entirely volatilized by heat. It decolorizes iodine by producing hydriodic acid, and on this fact is based the Br. test given below. It decomposes bone calcium phosphate.

"A colorless liquid with a pungent, sulphurous odor. Yields, when neutralised, the *reactions* characteristic of sulphites. Yields not more than a slight precipitate with *solution of barium chloride* (limit of sulphates), but a copious precipitate if *solution of chlorine* is also added. Leaves no appreciable residue on evaporation. Specific gravity 1.025. 1 gramme, diluted with 100 millilitres of recently boiled and cooled *water*, requires 15.5 millilitres of *N/10 solution of iodine* for complete oxidation, *mucilage of starch* being used as indicator. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Assay.—The details for its assay will be found in Part III, where this acid appears as a reagent.

Uses.—Sulphurous acid in concentrated solutions is a powerful germicide, but probably no more so than are the other mineral acids. The disinfectant value of burning sulphur is due to the formation of this acid; during the process of combustion sulphur dioxide is formed and if there be present in the air an abundance of aqueous vapors this will unite with the water to form sulphurous acid which has a destructive action on many forms of life including the less resistant bacteria. It is, however, difficult to generate sufficient sulphurous acid by this method to have any real bactericidal effect, and the method of disinfecting sick rooms has been almost completely abandoned in favor of the more efficient and less destructive formaldehyde. It is, however, often useful for the destruction of vermin. It is quite impossible to hope for any true disinfectant action by burning sulphur candles in the manner which is so popularly resorted to; the most that can be hoped for is a deodorizing effect. By virtue of its reducing properties sulphurous acid decomposes hydrogen sulphide, and like other acids will unite with ammonia to form relatively inodorous compounds. It must also be remembered that sulphurous acid has a bleaching effect due to its reducing power and is therefore likely to be injurious to various kinds of clothing and furniture which are exposed to its fumes. Sulphurous acid and sulphites have been widely used for preserving food, but are now prohibited by the laws of many states. They are still permitted for the preservation of dried fruits where the function is to prevent darkening during drying and from which they are largely removed by the preliminary washing and subsequent cooking to which these foods are subjected before being eaten. So-called "sulphite powders" containing either sodium sulphite or calcium or magnesium bisulphites have figured largely as food preservatives. Sulphurous acid is also used for its bleaching properties to decolorize various products and make them look pure and colorless, and as a preliminary step to their subsequent dyeing, as in the so-called "maraschino" or cocktail cherries. For a method of determining sulphurous acid in foodstuffs and allied products, see *Circular of the U. S. Dept. of Agriculture*, 1906, No. 28, pp. 11–12.

Its use in food products, however, should not be encouraged as it is well demonstrated that the continued ingestion of sulphites is injurious to the kidneys.

Externally sulphurous acid is used in various *skin diseases*, such as *scabies*, *ringworm* and *impetigo contagiosa* for its parasiticide effect. For local application it should be diluted with two or three parts of water or glycerin and applied as a lotion or by cloths wet with this solution. Internally it has been used as a gastric antiseptic in *pyrosis* and in cases of *sarcinæ ventriculi*, but has been almost entirely replaced by the acid sulphite of sodium.

The incompatibilities of sulphurous acid are those of any powerful reducing agent. It will decompose many metallic salts, as of mercury, with the liberation of metallic mercury. Oxidiz-

ing compounds readily change it to sulphuric acid.

Dose, one-half to one fluidrachm (1.8–3.75 mils).

ACIDUM TANNICUM. U. S., Br.

TANNIC ACID Acid. Tann. [Gallotannic Acid, Tannin]

(ăç'ĭ-dŭm tăn'nĭ-cŭm)

"A tannin usually obtained from nutgalls. Preserve it in well-closed containers, in a cool place, protected from light." *U. S.* "Tannic Acid, $C_{14}H_{10}O_9$, may be extracted by water-saturated ether from galls which have been subjected to a special fermentation." *Br.*

Digallic Acid, Acidum Gallo-tannicum, Tanninum; Acide tannique, Tannin officinal, *Fr. Cod.;* Acidum tannicum, *P. G.;* Gerbsäure, Gallusgerbsäure, Tannin, *G.;* Acido tannico, *It.;* Acido tanico, *Sp.*

The U. S. IX and the British Pharmacopœia do not give a detailed process for preparing tannic acid; the former British Pharmacopœia adopted a process which was almost identical with that of the U. S. P., 1870, both being essentially the process of Leconnet, modified by Dominé, which had been substituted for that of Pelouze previously employed in both Pharmacopœias. The process of the British Pharmacopœia (1885) was as follows: "Galls in powder, Ether, of each a sufficient quantity. Expose the powdered galls to a damp atmosphere for two or three days, and afterwards add sufficient ether to form a soft paste. Let this stand in a well-closed vessel for twenty-four hours, then, having quickly enveloped it in a linen cloth, submit it to strong pressure in a suitable press, so as to separate the liquid portion. Reduce the pressed cake to powder, mix it with sufficient ether, to which one-sixteenth of its bulk of water has been added, to form again a soft paste, and press this as before. Mix the expressed liquids, and expose the mixture to spontaneous evaporation until, by the aid subsequently of a little heat, it has acquired the consistence of a soft extract; then place it on earthen plates or dishes, and dry it in a hot-air chamber at a temperature not exceeding 212° F. (100° C.)." *Br.* (1885).

While the Pelouze process yields the tannic acid probably in a somewhat purer state than Leconnet's, it is less easy of performance, and much less productive, and the product of the above formula is sufficiently pure for all practical purposes. The addition of a little alcohol —8 per cent., for example—to the ethereal menstruum still further increases the product. The exposure of the powdered galls to a damp atmosphere for two or three days is for the purpose of inducing a special fermentation, whereby the yield of tannin is materially increased. There appear to be two coloring principles in galls, one soluble in ether and not in alcohol, the other in alcohol and not in ether. Hence, while the tannic acid, in whichever way procured, is yellowish, that obtained by ether has a greenish tint, while that obtained by the addition of alcohol is slightly brownish. In consequence of the mode in which the acid is dried, in thin layers, on tinned or glass plates, and equally exposed to the heat above and below, it froths up on the escape of the ether, and concretes in a soft, cellular, friable form, which is strikingly characteristic of the preparation made in strict accordance with the formula.

From a superficial examination of this process, it might appear that the result can be nothing more than an ethereal extract; but it is necessary that the ether employed should contain water, as it is directed to be washed; and yet the quantity of water is so small that it can hardly operate by its mere solvent power. The circumstances attendant upon the process of Pelouze afford the means of a satisfactory explanation, which was first suggested by Beral. In this, the powdered galls are submitted to percolation by watered ether, and the liquid which passes separates into two layers, a heavier which sinks to the bottom and a lighter which floats upon the surface. It is the heavier which contains the tannic acid, and from which the acid is obtained by evaporation. The most probable explanation is that ether, water, and tannic acid unite to form a definite compound, in which the affinities are too feeble to resist the tendency of the ether to rise in vapor, and which is, therefore, decomposed by its evaporation. The proportion of the menstruum to the galls is very small, much smaller than would be employed to obtain an extract; and the whole or nearly the whole of both liquids is probably occupied in the formation of the definite compound referred to, thus leaving little or none to act merely as solvents. Hence the exclusion from the resulting acid, in great measure, of the other soluble constituents of the galls; and the slight amount of impurity really present in the acid is probably owing to the action of that small quantity of the menstruum not occupied in forming the liquid compound. Opinion is not altogether united in this explanation, but it is that which appears to us the best to account for the phenomena of the case. It has been stated that the tannic acid obtained by either process has a more or less yellowish tint. From this, according to F. Kummel, it may be freed by the percolation, through recently ignited animal charcoal, of its solution in a mixture of ether and alcohol. It has, too, a slight odor, which, according to Procter, is derived from a volatile odorous principle existing in galls, which he succeeded in separating from the acid by the action of benzene. From 30 to 35 per cent. of tannic acid is obtained from galls by Pelouze's method; 60 per cent. by that of Leconnet. Alcohol tannin and water tannin are terms used to indicate the method of extraction; in the former the powdered nutgall is percolated with alcohol (50 per cent.) and the solution of tannin evaporated in a vacuum apparatus; in the water tannin, water is used as in the ether process as above described and

the aqueous solution evaporated *in vacuo*. Gartenmeister used acetic ether for a solvent and a patent was secured for this process in Germany.

Crystallized tannic acid is said to be made by forcing a thick syrupy tannin solution through finely perforated sieves and dropping the threads from a height upon rapidly revolving wooden cylinders and scraping off the product. The term crystallized is, of course, a misnomer, as tannin is amorphous. For the preparation of tannin from Chinese galls, Oscar Rothe proposes the following as a superior process. Macerate eight parts of the powdered galls with twelve of ether and three of strong alcohol for two days, decant, renew the menstruum, and finally express. Mix the liquids, and after standing, decant from the sediment, add twelve parts of water, recover the alcohol and ether by distillation, rapidly filter the aqueous solution, and quickly evaporate by means of a steam bath; dry, and pulverize the residue. (*A. J. P.*, xlii, 403.)

Henry Trimble and J. C. Peacock recommend acetone as a valuable solvent for extracting tannin from oak bark (*Proc. A. Ph. A.*, 1893, p. 110), and acetone is now largely used by manufacturers as a solvent in extracting tannin from galls. B. L. DeGraffe (*A. J. P.*, 1896, 313) recorded investigations upon the plants of the Ericaceæ to determine the character of their tannins; acetone and acetic ether were used as solvents. For Sisley's method of preparing *pure* tannin, see *Proc. A. Ph. A.*, 1894, 1087.

The term *tannin* is applied to a class of vegetable principles the aqueous solutions of which give blue or green colors or precipitates with ferric salts, and precipitate solutions of gelatin and albumin. They are mainly glucosides. Chemists have recognized two kinds, one distinguished by producing a bluish-black precipitate with ferric salts, and the other characterized by producing a greenish-black or dark olive precipitate with the same salts. The former is the one which has received most attention, and from an examination of which the characters of tannin have generally been given. It is the substance described in this article. It is called, for the sake of distinction, *gallotannic acid*. According to Pettenkofer, it is found only in perennial plants, indicating some relation to the production of woody fiber. (*Buchner's Neues Repert.*, iii, 74–76.) Henry Trimble (*The Tannins*, vol. ii, p. 132, Phila., 1894) classifies the tannins into two main groups: Group *a*. Gallotannic acid, chestnut wood tannin, chestnut bark tannin, pomegranate bark tannin, and sumac tannin. Group *b*. Oak bark tannin, mangrove tannin, canaigre tannin, rhatany tannin, kino tannin, catechu tannin, and tormentil tannin. R. Wagner (*Bull. Soc. Chem.*, 1866, ii, 461) divides tannin into two great classes: pathological, found only in diseased vegetable tissue, as gallotannic acid, etc.; and physiological, occurring in leaves, bark, wood, etc., in a natural state, as quercitannic acid, etc.

For another scheme of classification of the tannins, based on the products they yield when heated alone, when heated with diluted acid, and when fused with caustic alkali, see Allen, *Com. Org. Anal.*, 2d ed., vol. iii, part i, p. 77.

Properties.—Pure tannic acid is solid, uncrystallizable, white, or slightly yellowish, inodorous; taste strongly astringent without bitterness, very soluble in water, much less soluble in alcohol and ether, especially when anhydrous, insoluble in the fixed and volatile oils.

The United States Pharmacopœia IX describes this acid as follows: "Tannic Acid occurs as a yellowish-white to light brown, amorphous powder, gradually turning darker when exposed to air and light, usually cohering in the form of glistening scales or spongy masses; odorless, or having a faint, characteristic odor, and a strongly astringent taste. One Gm. of Tannic Acid dissolves in 1 mil of glycerin with the application of a moderate heat; very soluble in water and alcohol at 25° C. (77° F.), and in boiling water and boiling alcohol; freely soluble in diluted alcohol, slightly soluble in dehydrated alcohol and almost insoluble in ether, chloroform, benzene, or petroleum benzin. An aqueous solution of Tannic Acid (1 in 20) is acid to litmus. The addition of a small quantity of ferric chloride T.S. to an aqueous solution of the Acid produces a bluish-black color or precipitate. An aqueous solution of Tannic Acid produces precipitates with nearly all alkaloids and glucosides, and with solutions of gelatin, albumin, and starch. Tannic Acid does not lose more than 12 per cent. of its weight when dried to constant weight at 100° C. (212° F.). Incinerate about 1 Gm. of Tannic Acid in a platinum dish; not more than 0.6 per cent. of ash remains. Dissolve about 2 Gm. of Tannic Acid in 10 mils of hot distilled water; the solution is not more than slightly turbid, and no turbidity is produced on diluting 5 mils of the cooled and filtered solution with twice its volume of alcohol (*gum or dextrin*) or with twice its volume of distilled water (*resinous substances*)." *U. S.*

"A light brownish powder consisting of thin glistening scales. Characteristic odor; taste strongly astringent. Reaction acid. Soluble in 1 part of *water* or of *alcohol* (90 per cent.), and, slowly, in 1 part of *glycerin*. It is precipitated from an aqueous solution by many mineral salts and acids. The aqueous solution precipitates *solutions of isinglass, albumen*, alkaloids, and *tartarated antimony*, and gives with *T. Sol. of ferric chloride* a bluish-black color. Ash not more than 0.2 per cent." *Br.*

Commercial tannic acid often has a decided odor, which Procter, after a practical investigation, believed to be owing chiefly to the presence of the odorous principle of the galls, though sometimes to matter derived from the ether with which it is prepared. (*A. J. P.*, 1865, p. 53.) According to Heinz, the odor is due to a greenish resinous principle, which may be

separated by dissolving the acid in twice its weight of hot water, adding one-fourth part of ether, agitating slowly, allowing the coagulated coloring matter to precipitate, filtering, and evaporating. (*J. P. C.*, xv, 308.)

Exposed to heat, tannic acid partly melts, swells, blackens, takes fire, and burns with a brilliant flame. Its solution reddens litmus, and it combines with most of the salifiable bases. It forms with potassium hydroxide a compound but slightly soluble, and is, therefore, precipitated by this alkali or its carbonates from a solution which is not too dilute, though a certain excess of alkali will cause the precipitate to be redissolved. Its combination with soda is much more soluble, and this alkali affords no precipitate, unless with a very concentrated solution of tannic acid. With ammonia its relations are similar to those with potassium hydroxide. Lime and magnesia added in the state of hydroxides, form with it compounds of little solubility. The same is the case with most of the metallic oxides, when presented in the state of salts to a solution of potassium tannate. Tannic acid even when in the uncombined state precipitates many of the metallic salts, especially those of lead, copper, silver, uranium, chromium, mercury, antimony trioxide, and stannous oxide. With ferric salts it forms a black precipitate, which is a compound of tannic acid and the iron, and is the basis of ink. It does not disturb the solutions of the pure ferrous salts. Several of the alkaline salts precipitate it from its aqueous solution, either by the formation of insoluble compounds or by simply abstracting the solvent. Potassium chlorate when rubbed up with it explodes with great violence, and several serious accidents are recorded as having occurred during the attempt to dispense such a mixture.

Tannic acid unites with some of the vegetable alkaloids, forming compounds which are for the most part of a whitish color, and but very slightly soluble in water, though they are soluble in the vegetable acids, especially acetic, and in alcohol. In this latter respect they differ from most of the compounds which tannic acid forms with other vegetable principles. On account of this property of tannic acid, it has been employed as a test for some of these alkaloids.

Tannic acid when in solution affords precipitates with sulphuric, nitric, hydrochloric, phosphoric, and arsenic acids, but not with oxalic, tartaric, lactic, acetic, or citric. The precipitates are considered as compounds of tannic acid with the respective acids, and are soluble in pure water, but insoluble in water with an excess of acid. Hence, in order to insure precipitation, it is necessary to add the acid in excess to the solution of tannic acid. Strecker, however, denies that the precipitates are compounds of the tannin with the acid, and maintains that they are tannin imbued with free acid.

When tannic acid, iodine, and water are mixed, a reaction takes place, by which the water is decomposed, its hydrogen forming with the iodine hydriodic acid, which combines with a portion of the tannic acid and remains in solution, while the oxygen of the water combines with another portion of the tannic acid to form a compound, which, being insoluble, is precipitated. The iodized solution thus obtained is capable of dissolving more iodine, and holding it in permanent solution, however much diluted. (Socquet and Guilliermond, *J. P. C.*, xxvi, 280.) Iodine in a liquid containing tannic acid cannot be detected by starch, but if the liquid is placed in a watch-glass, ferrous sulphate added, and the glass covered with starch paper, ferric tannate being precipitated, the blue color soon appears. (*A. J. P.*, xlvii, 398.)

Griessmayer (*Zeit. An. Chem.*, 1873) proposes a test for tannin and free alkalies. On mixing a drop of a solution of tannin with 1 mil of $\frac{1}{10}$ normal solution of iodine, the reddish color of the iodine solution instantly disappears; if one drop of solution of ammonia be now added (previously diluted with ten times its bulk of water), a brilliant red color is produced which is quite permanent. Tannic acid precipitates solutions of starch, albumin, and gluten, and forms with gelatin an insoluble compound, which is the basis of leather. J. Napier Spence (*J. Soc. Chem. Ind.*, 1891, p. 1114) has reviewed all the current tests for distinguishing between tannic acid and gallic acid. (See *Proc. A. Ph. A.*, 1892, p. 1032.)

Mulder gave for tannic acid the formula $C_{14}H_{10}O_9$; and both Julius Löwe and Hugo Schiff confirmed these figures. (*A. J. P.*, xxv, 223; xlvii, 208.) Schiff asserted that it was not a glucoside; that glucose exists in commercial tannic acid as an impurity, and is not a necessary part of it, and that it is a "first anhydride," formed from two molecules of gallic acid by the abstraction of water, thus:

$$2C_7H_6O_5 - H_2O = C_{14}H_{10}O_9.$$

According to Schiff it is digallic acid; this is not the present view. (See *Acidum Gallicum.*)

Various plans have been proposed for estimating the quantity of tannic acid, which is an object of importance to tanners, as enabling them to judge of their tanning materials. John H. Yocum, after reviewing various methods of estimating tannin, believes the "hide-powder" method most practical and useful. (*Am. Chem. Soc.*, Jan. 9, 1897.) This was the one adopted by the International Congress of Leather Trades Chemists at Turin, Italy, in 1904, and is still used. For other methods, see *A. J. P.*, 1859, p. 427; 1864, p. 314; and Aug., 1877; *P. J.*, 1867, p. 515; and 1885, pp. 121, 850; *J. P. C.*, 1874, p. 445; *N. R.*, 1882, p. 150; *West. Drug.*, 1891, p. 445; and a monograph on the "*The Tannins*," by Henry Trimble. (J. B. Lippincott Company, 1894.)

Uses.—Tannic acid is a powerful astringent and but slightly irritant. It is not capable of being absorbed nor, indeed, of circulating in the blood, because of its property of precipitating

all albumin. When taken by the mouth, however, a portion of it combines with the alkalies of the intestinal tract and is probably absorbed as sodium tannate—which is not astringent—and a portion of it is hydrolized to gallic acid which may also be absorbed. As an astringent it is employed locally in chronic *congestions of the throat,* in local *relaxations, as of the uvula* or in *hemorrhoids,* to check excessive secretion, as in mercurial *salivation* or weeping *ulcers,* and as a styptic in various local *hemorrhages.* In *diarrheas* it is often of much service but is not so generally employed in the pure form as in one of the galenicals of crude vegetables containing it, or as some synthetic derivative. The preference for these various drugs which contain tannic acid over the pure substance is owing to their being less readily precipitated by the albumins of the prima viae before they reach the diseased point. Tannic acid is also widely recommended as a chemical antidote to various poisons, especially to the alkaloids and heavy metals. The tannates of the alkaloids are, however, soluble in dilute acids and the use of tannic acid in alkaloidal poisoning can at best be only partially antidotal.

The principal incompatibilities of tannic acid are salts of the metals, particularly of iron, albumen, gelatin, and iodine, all of which are covered in the foregoing text.

Dose, from three to twenty grains (0.20–1.3 Gm.).

Off. Prep.—Glyceritum Acidi Tannici, *U. S.* (*Br.*); Suppositoria Acidi Tannici, *Br.;* Trochisci Acidi Tannici, *U. S.* (*Br.*); Unguentum Acidi Tannici, *U. S.;* Collodium Stypticum, *N. F.*

ACIDUM TARTARICUM. U. S., Br.

TARTARIC ACID Acid. Tart.

(ăç'ĭ-dŭm tär-tăr'ĭ-cŭm)

"A dibasic organic acid usually obtained from wine lees or argol. It contains not less than 99.5 per cent. of $C_4H_6O_6$ or $C_2H_2(OH)_2(COOH)_2$ (150.05)." *U. S.* "Tartaric Acid may be obtained from acid potassium tartrate, and contains not less than 99 per cent. of hydrogen tartrate, $HC_4H_4O_6$." *Br.*

Dextrotartaric Acid; Sal Essentiale Tartari; Acide Tartrique, *Fr. Cod.;* Acide du Tartre, Acide dextroracémique, *Fr.;* Acidum tartaricum, *P. G.;* Weinsteinsäure, Weinsäure, *G.;* Acido tartarico, *It.;* Acido tartrico, *Sp.*

No formula for the preparation of tartaric acid is given in either Pharmacopœia. It is extracted from *tartar,* or *argol,* a peculiar substance which is deposited on the inside of wine casks during the fermentation. Tartar, when purified and reduced to powder, is the cream of tartar of commerce, and consists of acid potassium tartrate. (See *Potassii Bitartras.*) The following is the former British process:

"Take of Acid Tartrate of Potassium *forty-five ounces* [av.]; Distilled Water *a sufficiency;* Prepared Chalk *twelve ounces and a half* [av.]; Chloride of Calcium *thirteen ounces and a half* [av.]; Sulphuric Acid *thirteen fluidounces.* Boil the Acid Tartrate of Potassium with two gallons [Imp. measure] of the Water, and add gradually the Chalk, constantly stirring. When the effervescence has ceased, add the Chloride of Calcium dissolved in two pints [Imp. meas.] of the Water. When the tartrate of calcium has subsided, pour off the liquid, and wash the tartrate with Distilled Water until it is rendered tasteless. Pour the Sulphuric Acid, first diluted with three pints [Imp. meas.] of the Water, on the tartrate of calcium, mix thoroughly, boil for half an hour with repeated stirring, and filter through calico. Evaporate the filtrate at a low temperature until it acquires the sp. gr. of 1.21, allow it to cool, and then separate and reject the crystals of sulphate of calcium which have formed. Again evaporate the clear liquor till a film forms on its surface, and allow it to cool and crystallize. Lastly, purify the crystals by solution, filtration (if necessary), and recrystallization." *Br.* (1885).

Tartaric acid was first obtained in a separate state by Scheele in 1770. The process consists in saturating the excess of acid in potassium bitartrate or cream of tartar with calcium carbonate, and decomposing the resulting insoluble calcium tartrate by sulphuric acid, which causes the precipitation of calcium sulphate, and liberates the tartaric acid. The equivalent quantities are two molecules of the acid tartrate and one molecule of calcium carbonate. The process, when thus conducted, furnishes one-half of the tartaric acid. The other half may be procured, as in the British process, by decomposing the neutral potassium tartrate remaining in the solution after the precipitation of the calcium tartrate, by calcium chloride in excess. By double decomposition, potassium chloride will be formed in solution, and a second portion of calcium tartrate will precipitate, which may be decomposed by sulphuric acid together with the first portion. The process, when thus conducted, will furnish twice as much tartaric acid as when the acid salt only is decomposed. The reactions are:

$$2KHC_4H_4O_6 + CaCO_3 = K_2C_4H_4O_6 + CaC_4H_4O_6 + H_2O + CO_2$$

$$CaC_4H_4O_6 + H_2SO_4 = CaSO_4 + H_2C_4H_4O_6$$

$$K_2C_4H_4O_6 + CaCl_2 = 2KCl + CaC_4H_4O_6$$

$$CaC_4H_4O_6 + H_2SO_4 = CaSO_4 + H_2C_4H_4O_6$$

Scarlata (*Chem. News,* 1899, 296) has devised a method of making tartaric acid based on the decomposition of potassium and calcium tartrates by *fluosilicic acid;* tartaric acid is liberated and corresponding fluosilicates are formed; the latter may then be decomposed by sulphuric acid and fluosilicic acid reproduced for use in a subsequent operation. By this method tartaric acid of 99 per cent. purity may be obtained. Zinno has prepared tartaric acid synthetically by passing carbon dioxide under pressure over potassium glycerate. (*Proc. A. Ph. A.,* 1902, 263.)

Preparation on the Large Scale.—To obtain tartaric acid from the crude materials (argol and wine lees), the method still largely used is the precipitation of the acid potassium tartrate as calcium tartrate and subsequent preparation of the tartaric acid from the latter. The methods of obtaining the calcium tartrate vary according to the nature of the crude material. A suitable method of producing it from argol is to mix the argol, preferably in the form of a powder, with water, and boil, after the addition of some hydrochloric acid. Milk of lime is then added to the boiling mass until this is nearly neutral, when calcium tartrate is precipitated and neutral potassium tartrate and calcium chloride left in solution. The neutral potassium tartrate is decomposed either by boiling with a sufficient amount of calcium sulphate or by adding calcium chloride solution, an excess of the precipitant being avoided in either case. The small amount of acid potassium tartrate purposely left in the liquid, when treating the latter with milk of lime, is decomposed with pure precipitated calcium carbonate. The object of not adding the milk of lime to the neutral point or in excess is to avoid the precipitation of iron or aluminum oxides. The solution must still remain perceptibly acid after the addition of the calcium carbonate. When cooled to about 40° C. (104° F.), the liquid is filtered with the aid of a suction pump, and the residue washed with water.

In the oldest methods of obtaining calcium tartrate from wine lees the latter were boiled with water and hydrochloric acid, the clear solution removed, and the residue treated with more water. As the extraction was very incomplete, these methods have not been employed of late years. When filtration of the lees was first attempted it was found that the pores of the filter became clogged, and that even under a pressure of four or five atmospheres no liquid would pass through. This difficulty was overcome by the process of Dietrich and Schnitzer, in which the albuminoid substances are coagulated by heating for about six hours under a pressure of four or five atmospheres. Wet lees, when thus treated, can be readily filtered. Dried lees are crushed, stirred in a tank with water, and heated by steam for some time, until air is completely expelled, before being heated in the pressure boiler.

During the process of heating the lees, the steam passing from the apparatus carries with it volatile empyreumatic products derived from the decomposed albuminoids. These have a very offensive odor, and should be conveyed into a factory chimney of sufficient height, so that the evil-smelling vapors are drawn up and decomposed by the furnace gases.

When the heating is finished, the steam outlet pipe is opened and the pressure allowed to fall to from one to one-half atmosphere, this pressure being required to force the lees from the boiler into a tank, which may be suitably constructed of wood. Here they are mixed with water, which has previously been put into the tank, and the requisite quantity of crude hydrochloric acid (21° to 22° B.). Experience has shown that for every 100 parts by weight of argol in the lees 100 parts of acid are required. Too little acid causes deposition of argol in the cloths of the filter-press, while too much destroys the cloths, and more lime is needed to neutralize the filtrate. If the conditions are right, the filtered liquid should have a specific gravity of about 6° B.

The acidified lees are pressed and washed, the washings being used instead of clear water for mixing with the next charge of lees from the pressure boiler. The tartaric acid in the filtrate is precipitated with lime and calcium carbonate, and the remainder of the process is the same as in the case of the argol, with the exception that there is no necessity to add calcium chloride or calcium sulphate.

Calcium tartrate obtained from wine lees is of a clear gray color, which is considerably purer than the dark gray or dark brown product from argol.

L. H. Baekeland patented, in 1916, a synthetic method for the production of tartaric acid: From carbon monoxide and an alkali is obtained an alkaline formate; this is changed into an oxalate by heating under pressure; the latter to glyoxalate by potassium amalgam in the presence of an acid. The glyoxalate is reduced electrolytically to tartaric (racemic) acid.

Oscar Ficinus, of Bensheim, proposes the following process to procure a pure tartaric acid. Saturate the crude tartar with calcium carbonate, and decompose the resulting calcium tartrate with solution of zinc chloride, whereby calcium chloride and zinc tartrate are produced. The latter is almost insoluble, and is completely decomposed by hydrogen sulphide. The liquid filtered from the precipitated zinc sulphide, containing tartaric and sulphydric acids in solution, is heated for some time to 60° to 80° C. (140°–176° F.), in order to dissipate the latter acid, filtered from the precipitated sulphur, and concentrated to the point of crystallization. (*A. Pharm.*, April, 1879, p. 310.)

Properties.—"Tartaric Acid occurs in colorless, translucent, monoclinic prisms, or as a white, granular or fine powder; odorless, having an acid taste; permanent in the air. One Gm. of Tartaric Acid dissolves in 0.75 mil of water and in 3.3 mils of alcohol at 25° C. (77° F.); also in 0.5 mil of boiling water; almost insoluble in chloroform, slightly soluble in ether. An aqueous solution of Tartaric Acid (1 in 20) is acid to litmus. An aqueous solution of the Acid (1 in 2) mixed with an equal volume of an aqueous solution of potassium acetate (1 in 3) yields a white, crystalline precipitate, which is dissolved by solutions of alkalies and by mineral acids, but is insoluble in acetic acid. When slowly ignited it is gradually decomposed, evolving an odor resembling burning sugar. Incinerate about 2 Gm. of Tartaric Acid; not more than 0.05 per cent. of ash remains. The addi-

tion of 1 mil of barium chloride T.S. to 10 mils of an aqueous solution of the Acid (1 in 100), to which has previously been added a few drops of hydrochloric acid, produces no turbidity (*sulphuric acid*). An aqueous solution of the Acid (1 in 10), in which the free acid has been nearly neutralized with ammonia water, is not affected by calcium sulphate T.S. (*oxalic acid*). Ten mils of an aqueous solution of the Acid (1 in 50), mixed with 0.5 mil of hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3). Dissolve 10 Gm. of Tartaric Acid in 20 mils of distilled water, add 2 mils of sulphurous acid and boil the mixture until the odor of sulphur dioxide is barely perceptible. Cool the solution, mix it with 1 mil of sodium cyanide T.S. and follow this immediately with stronger ammonia water until the precipitate formed is redissolved and the solution has a slight odor of ammonia. When cold, transfer the solution to a glass-stoppered cylinder, graduated to 50 mils. Dilute it with sufficient distilled water to measure 50 mils and add 3 drops of sodium sulphide T.S. After mixing well, the color produced in the solution, if any, when viewed downward against a white surface, is not greater than the color of a control solution prepared as follows: Dissolve 2 Gm. of ammonium chloride (see Reagents, Part III) in 20 mils of distilled water, add 4 mils of a solution containing 0.08 Gm. of lead nitrate in 1000 mils of distilled water, and then 1 mil of diluted hydrochloric acid. Treat this solution with the same quantity of sulphurous acid, sodium cyanide T.S. and stronger ammonia water, as directed above, transfer to another 50 mil glass-stoppered cylinder, then dilute it with sufficient distilled water to make 50 mils, and add 3 drops of sodium sulphide T.S. (before adding the sodium sulphide T.S., the liquid must possess a distinct odor of ammonia and the two cylinders used must be matched, be of practically colorless glass, and have the same internal diameter) (*lead*).

"**Assay.**—Dissolve about 3 Gm. of Tartaric Acid, accurately weighed, in 50 mils of distilled water and titrate this solution with normal potassium hydroxide V.S., using phenolphthalein T.S. as indicator. It shows not less than 99.5 per cent. of $C_4H_6O_6$.

"Each mil of normal potassium hydroxide V.S. consumed corresponds to 0.07503 Gm. of $C_4H_6O_6$. Each gramme of Tartaric Acid corresponds to not less than 13.26 mils of normal potassium hydroxide V.S." *U. S.*

"Soluble in less than 1 part of *water*, and in 3 parts of *alcohol* (90 per cent.). Yields, when neutralised, the *reactions* characteristic of tartrates. An aqueous solution is dextrorotatory. 1 gramme dissolved in *water* requires for neutralisation not less than 13.2 millilitres of *N/1 solution of sodium hydroxide*. Yields no characteristic *reactions* for copper, iron, or oxalates, and not more than the slightest *reactions* for calcium. *Lead limit* 20 parts per million. *Arsenic limit* 1.4 parts per million. 1 gramme dissolved in 50 millilitres of *water*, on addition of 0.5 millilitre of *solution of barium chloride*, does not yield a greater opalescence than 1 millilitre of *N/100 solution of sulphuric acid* when precipitated under the same conditions (limit of sulphates). Ash not more than 0.1 per cent." *Br.*

The powder is sometimes directed to be kept in well-stoppered vials; but Otto has shown that this method tends to spoil it. A better plan is to keep the powder in ordinary boxes. The tendency of the powder to form hard masses on keeping has been largely obviated of late years. This was formerly due to the presence of traces of sulphuric acid which caused the absorption from the air of water, but with the greater purity of the commercial product and absence of sulphuric acid the powder retains it pulverulent form much better than formerly.

As found in commerce, it is in the form of a fine white powder, prepared by pulverizing the crystals. A weak solution undergoes spontaneous decomposition when kept, becoming covered with a mouldy pellicle; but, if boiled and filtered, it is said to lose this tendency. It is asserted that the addition of 1-1000th of salicylic acid will effectually preserve solutions of tartaric acid. In uniting with bases it has a remarkable tendency to form double salts, several of which constitute important medicines. It combines with several of the vegetable alkaloids, so as to form salts. It is distinguished from all other acids by forming a crystalline precipitate, consisting of potassium bitartrate, when added to a neutral salt of that alkali. When associated with an excess of boric acid, it is detected with difficulty, potassium hydroxide not precipitating it, even with the addition of acetic or hydrochloric acid. Its separation, however, may be effected, according to Barfoed, by means of potassium fluoride, which detaches the boric acid, to form potassium fluoborate, and renders free the tartaric acid, which then responds to the ordinary test. (*J. P. C.*, 4e sér., ii, 70.) Its most usual impurity is sulphuric acid, which may be detected by the solution affording with lead acetate a precipitate only partially soluble in nitric acid. When incinerated with mercuric oxide, it leaves no residue, or a mere trace.

Denigés gives the following modification of Mohler's test for tartaric acid. A solution of 2 Gm. of resorcinol in sufficient diluted sulphuric acid (1 per cent.) is added to 20 times its volume of strong sulphuric acid. In the presence of tartaric acid this liquid gives with a few drops of the fluid to be tested (which must be free from carbohydrates) a characteristic violet-red color when the mixture is heated to 115° to 140° C. (239°–284° F.). (*Am. Drug.*, 1896, 182.)

Modifications of Tartaric Acid.—Five distinct modifications of tartaric acid exist. Their chief physical and chemical differences are:

a. Dextro-tartaric acid, or ordinary tartaric acid, forms anhydrous, hemihedral, rhombic

crystals, the aqueous solution of which turns the plane of polarization of a luminous ray to the *right*. The crystals fuse at 135° C. (275° F.), have a sp. gr. of 1.74 to 1.75, and are readily soluble in absolute and aqueous alcohol.

b. Lævo-tartaric acid forms anhydrous, hemihedral, rhombic crystals, the aqueous solution of which turns the plane of polarization of a luminous ray to the *left*.

c. Racemic or *para-tartaric* acid forms hydrated, holohedral, triclinic crystals of $H_2C_4H_4O_6 + H_2O$, which are optically *inactive*. The crystals have a sp. gr. of 1.69, and are soluble in five parts of cold water and with difficulty in cold alcohol. The calcium racemate is less soluble in water than calcium dextro-tartrate, and is also distinguished by its insolubility in acetic acid and in ammonium chloride solution. Racemic acid can be prepared by mixing *a*- and *b*-tartaric acids, and can be resolved into them by appropriate methods. Racemic acid exists naturally in small proportion in the juice of grapes growing in particular localities, and was first obtained artificially in 1853 by Pasteur.

d. Inactive or *meso-tartaric* acid, optically inactive, but not resolvable into *a* and *b* acids.

e. Meta-tartaric acid, produced by fusing the ordinary variety. It is deliquescent and uncrystallizable. Its solution and the solutions of its salts are converted by boiling into those of the ordinary modification.

Léger prepares *metatartaric acid* in the following manner. Into a porcelain dish put a small amount of tartaric acid, and heat it, with occasional agitation, on a slow fire until it fuses; then add successively small portions of the acid, so as not to cool the mass, lest it solidify and burn. When the dish is two-thirds full, cease adding the acid, but continue the heat until the mass, at first puffed up and doughy, is completely melted into an amber-colored liquid. Withdraw it from the fire, and when sufficiently cooled form it into pebbles, which must be kept in closely-stoppered bottles on account of their being hygroscopic. This acid is very soluble in water, and in this state greedily attacks the magnesium carbonate, forming with it a salt which is permanent even when in solution. (*J. P. C.*, xix, 226.)

Uses.—Tartaric acid is sometimes used for citric acid in the preparation of refrigerant drinks, especially for decomposing sodium bicarbonate in the preparation of effervescent salts. It differs sharply from citric, acetic, and many other vegetable acids in that it is not oxidized in the system, appearing in the urine unchanged. Acid tartrates, therefore, tend to increase the acidity of the system. Tartaric acid is also more irritant than citric acid and decidedly more laxative in its effects.

Tartaric acid is incompatible with salifiable bases and their carbonates; with salts of potassium, with which it produces a crystalline precipitate of bitartrate, and with the salts of calcium and lead, with which it also forms precipitates. It consists of four atoms of carbon, six of hydrogen, and six of oxygen. Of the six hydrogen atoms, however, only two are replaceable by metal, so that it is dibasic, and can form both acid and neutral salts with monad elements like potassium and sodium. Thus, cream of tartar is the acid potassium tartrate (potassium bitartrate), and the so-called "soluble tartar" is the neutral potassium tartrate.

Dose, five to thirty grains (0.32–2.0 Gm.).

ACIDUM TRICHLORACETICUM. U. S.

TRICHLORACETIC ACID Acid. Trichloracet.

(ăç'ĭ-dŭm trī-ċhlōr-ą-cĕt'ĭ-cŭm)

"A monobasic organic acid. It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99 per cent. of $C_2HO_2Cl_3$ or $CCl_3.COOH$ (163.39). Preserve it in well-stoppered bottles, in a cool place, protected from light." *U. S.*

Acide trichloracétique, *Fr.*; Acidum trichloraceticum, *P. G.*; Trichloressigsäure, *G.*

Three forms of chloracetic acid are known, mono-, di-, and tri-chloracetic acids, having the following formulas, respectively, $C_2H_3ClO_2$, $C_2H_2Cl_2O_2$, and $C_2HCl_3O_2$. *Monochloracetic acid* may be prepared by acting upon glacial acetic acid containing 10 per cent. of iodine with dry chlorine, reserving the portion distilling over between 180° C. and 188° C. (356°–370.4° F.). *Dichloracetic acid* distils over between 189° and 191° C. (372.2°–375.8° F.). *Trichloracetic acid*, discovered by Dumas in 1838, may be most conveniently prepared by treating hydrated chloral with three times its volume of fuming nitric acid, and placing the whole mixture in the sunlight until the red fumes have disappeared; the liquid is then distilled, and the portion coming over at 195° C. (383° F.) is pure trichloracetic acid. All the chloracetic acids are powerful caustics, destroying the epidermis. They form various salts, most of which are easily soluble in water. The mono- and tri- acids are solid, crystalline, deliquescent bodies; dichloracetic acid is a colorless liquid having a suffocating odor, and crystallizing at 0° C. (32°F.).

While trichloracetic acid is usually formed by the oxidation of hydrated chloral with nitric acid, it may also be obtained by the action of potassium permanganate in concentrated solution upon hydrated chloral, the potassium trichloracetate crystallizing out in white silky crystals. The reduction of trichloracetic acid to acetic acid can be accomplished by the use of nascent hydrogen.

It is officially described as in "colorless, deliquescent, rhombohedral crystals, having a slight, characteristic odor. One Gm. of Trichloracetic Acid dissolves in about 0.1 mil of water at 25° C. (77° F.); it is very soluble in alcohol and ether at 25° C. (77° F.). An aqueous solution of Trichloracetic Acid (1 in 20) is acid to litmus. When the Acid is heated with potassium hydroxide T.S., it is decomposed with

the formation of chloroform and potassium carbonate. Incinerate about 2 Gm. of Trichloracetic Acid; not more than 0.05 per cent. of ash remains. Ten mils of a freshly made, aqueous solution of the Acid (1 in 20) does not immediately become more than slightly opalescent upon the addition of a few drops of silver nitrate T. S. (*chlorides*). Dissolve a small crystal of ferrous sulphate in 5 mils of an aqueous solution of Trichloracetic Acid (1 in 20), and pour this solution upon 5 mils of sulphuric acid (free from nitrogen compounds) so as to form a layer above; no brownish-red color is produced at the zone of contact of the two liquids (*nitric acid*).

"**Assay.**—Dissolve about 4 Gm. of Trichloracetic Acid, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed in a tared and stoppered flask, in 50 mils of distilled water, add a few drops of phenolphthalein T.S. and titrate this solution with normal potassium hydroxide V.S. It shows, in the dried acid, not less than 99 per cent. of $C_2HO_2Cl_3$.

"Each mil of normal potassium hydroxide V.S. corresponds to 0.16339 Gm. of $C_2HO_2Cl_3$. Each gramme of Trichloracetic Acid, previously dried, corresponds to not less than 6.06 mils nor more than 6.12 mils of normal potassium hydroxide V.S." *U. S.*

Uses.—Trichloracetic acid is an active caustic which has been largely employed for the destruction of *papillomata, vascular nævi, chancroids,* various small growths in the mouth, and similar minor structures. It is also actively antiseptic and is used in diluted solution, 1 in 1000 to 1 in 2000, in *ozena* and other forms of chronic *inflammation of the nose, pharynx* and *tonsils.* It has also been used for *gleet* in solutions of from 1 to 5 per cent. As its action is purely local it is not employed in internal medicine. When used as a caustic enough water may be added to the crystals to cause liquefaction, and this solution applied by means of a glass rod, the surrounding parts being protected by painting with collodion.

ACONITINA. U. S., Br.

ACONITINE Aconitin.

(ă-cŏn-ĭ-tĭ'na)

"An alkaloid [$C_{34}H_{47}O_{11}N = 645.39$] obtained from aconite. Preserve it in well-closed containers protected from light." *U. S.*

"Aconitine, $C_{34}H_{45}NO_{11}$, is an alkaloid obtained from Aconite Root." *Br.*

Aconitia, Aconitinum, Aconitin; Aconitine, *Fr. Cod.;* Aconitin, *G.;* Aconitina, *It., Sp.*

Formerly a process for the manufacture of aconitine was given in the U. S. and Br. Pharmacopœias, but in the 1880 revision the alkaloid was dropped from the U. S. P., while in the revision of the Br. Ph. (1898) the process of manufacture was omitted. Aconitine was again made official in the U. S. Pharmacopœia, VIII and IX Revisions.

Crystallized aconitine was first made known by the researches of Groves (*P. J.,* 2d ser., viii, 121), but it was elaborately studied by Duquesnel. The methods of obtaining it differ, but, according to Patrouillard (*J. P. C.,* 4e sér., xix, 151), that of Duquesnel gives much the larger yield. It is as follows: 100 parts of the powdered roots having been mixed with one part of tartaric acid, and the whole exhausted by repeated percolation with cold alcohol, the liquid is evaporated at a low temperature on a water bath to the consistence of a fluidextract. To this, distilled water is added, and the precipitated resinous and oily matters removed by filtration. The solution of aconitine tartrate is then precipitated with a slight excess of potassium bicarbonate, agitated with washed ether, and the two fluids separated with a siphon. The ethereal solution is shaken four or five times with a 10 per cent. solution of hydrochloric acid, which takes up the alkaloids from the ethereal solution. The acid liquids are treated with calcium carbonate to saturation in order to prevent the prolonged and injurious action of the acid upon the crystallizable aconitine, the mixture is evaporated at a very gentle heat, filtered, and while still warm mixed with a solution of sodium nitrate (2 of salt to 3 of water) having the same temperature. The whole is allowed to cool slowly during several hours, and set away for several days' rest, when the crystals separate out as a crust on the bottom.

Pure aconitine may exist in an amorphous or in a crystalline form. The official product is always crystalline, but of amorphous aconitine there are two varieties, the hydrated and the anhydrous. When the alkaloid is dried at ordinary temperature, it retains 20 (Hager) or 25 (Hottot) per cent. of water; but when dried at the temperature of the water bath, it is anhydrous, and is then *not* soluble in 50 parts of boiling water. (Hager, *A. J. P.,* xlvii, 210.) For Hottot's process of preparing aconitine, see 15th ed., U. S. D.

The amorphous aconitine of commerce is of very uncertain composition and value, and should never be substituted for official aconitine.

Properties.—The U. S. P. IX describes aconitine as occurring in "colorless or white rhombic tables or prisms, possessing no odor and permanent in the air. *The alkaloid itself must never be tasted, and its solutions only when largely diluted, and then with the utmost caution.* A drop of an aqueous solution of the alkaloid or its salts (1 in 100,000), placed upon the tongue, produces a tingling and numbing sensation. One Gm. of Aconitine dissolves in 28 mils of alcohol, about 65 mils of ether, and in 7 mils of benzene, at 25° C. (77° F.); very slightly soluble in water and almost insoluble in petroleum benzin at 25° C. (77° F.). Aconitine solutions are alkaline to litmus. When heated rapidly, Aconitine melts at about 195° C. (383° F.). Stir about 0.001 Gm. of Aconitine with 2 or 3 drops of nitric or sulphuric acid on a white porcelain surface; it dissolves without colora-

tion. With 2 drops of sulphuric acid containing 0.005 Gm. of ammonium vanadate in each mil an orange color is produced under the same conditions. Dilute solutions of Aconitine salts yield precipitates with mercuric potassium iodide T.S., tannic acid T.S., or gold chloride T.S., but only concentrated solutions yield precipitates with platinic chloride T.S., mercuric chloride T.S., or picric acid T.S. No weighable ash remains on incinerating 0.05 Gm. of Aconitine. Evaporate a solution of 0.01 Gm. of Aconitine to dryness, add 5 drops of fuming nitric acid; evaporate again to dryness; the resulting yellow residue, when cooled, yields no violet color when treated with alcoholic potassium hydroxide T. S. (*pseudaconitine or atropine*)." *U. S.*

Aconitine as defined by the Br. Pharmacopœia is in "colorless, transparent, hexagonal crystals belonging to the rhombic system, prismatic and tabular. Melting point 198° C. (388.4° F.), at which temperature evolution of acetic acid occurs. Almost insoluble in *water, petroleum spirit,* and *carbon disulphide;* readily soluble in *benzene* and in *chloroform,* less readily in *ether* and in *absolute alcohol.* Forms a crystalline hydrochloride which melts at 149° C. (300.2° F.). A drop of an aqueous solution (1 in 10,000) placed upon the tongue produces a characteristic tingling and numbing sensation. An aqueous solution, not more dilute than 1 in 4000, faintly acidified with *acetic acid,* yields a reddish precipitate on the addition of a few drops of *N/10 solution of potassium permanganate.* The ethereal solution obtained by boiling Aconitine with *N/2 alcoholic solution of potassium hydroxide,* removing most of the alcohol by evaporation, diluting with *water,* acidifying, and extracting with *ether,* leaves on evaporation a crystalline residue of benzoic acid. When 0.0002 gramme of Aconitine is gently warmed with 4 drops of *sulphuric acid* an odor of benzoic acid is evolved, and if after five minutes a few crystals of *resorcin* are added and the heat continued, a reddish-yellow color, changing to intense red, is produced. No appreciable ash." *Br.*

Aconitine is precipitated from its solution by caustic alkalies, but not by ammonium carbonate or potassium and sodium bicarbonates. A spurious substance has sometimes been sold under the same name, which is nearly or quite inert; and at best the alkaloid is apt to be of uncertain strength as found in commerce.

Monti proposes a color test for aconitine with resorcinol which is now official in the Br. Pharm., 1914, after some modifications. (See *P. J.,* 1908, 596.)

For E. R. Squibb's physiological tests for aconitine and aconite preparations, see page 87. Its only peculiar color reaction is obtained with difficulty by dissolving in diluted phosphoric acid and evaporating, when at a certain degree of concentration a violet coloration appears.

The investigations of C. R. A. Wright upon *Aconitum Napellus,* which were fully stated in a previous edition (16th ed., p. 125), were corrected in part by later studies by Wyndham Dunstan. (*J. Chem. S.,* May, 1891, April and May, 1892.) He stated that the roots of true *Aconitum Napellus* contain four alkaloids, of which one is crystallized and three are amorphous: *aconitine,* to which he gives the formula $C_{33}H_{45}NO_{12}$ instead of the formula $C_{33}H_{43}NO_{12}$ proposed by Wright; *aconine,* $C_{26}H_{41}NO_{11}$ instead of the formula $C_{26}H_{39}NO_{11}$ proposed by Wright; *napelline,* or *isoaconitine,* was stated by Dunstan (*P. J.,* 1893, 625) to have the composition $C_{33}H_{45}NO_{12}$, and said to be isomeric with aconitine. Schulze reopened the controversy about the molecular composition of aconitine and operating with pure aconitine having a melting point of 197° to 198° C. (386.6°–388.4° F.) stated the composition to be $C_{34}H_{45}O_{11}N$, which was adopted by the British Pharmacopœia (1904). (*Ap. Ztg.,* 1904, 782.) Aconine, when purified, melts at 132° C. (269.6° F.). Dunstan was able, by heating aconine together with ethyl benzoate in a sealed tube to effect the synthesis of the anhydride of aconitine. The *picraconitine* of Wright is considered by Dunstan to have been a mixture. In a later communication (*P. J.,* 1893, p. 1045) Dunstan shows that the roots of *Aconitum Napellus* contain, besides the highly poisonous aconitine, an almost non-poisonous isomeride, *isoaconitine.* Both furnish the same hydrolytic products,—viz., aconine and benzoic acid. Aconitine hydrobromide (melting point 163° C.) (325.4° F.), when heated in aqueous solution, is very gradually changed into isomeric isoaconitine hydrobromide (melting point 282° C.) (539.6° F.). The change is facilitated by the presence of a small quantity (1 to 2 per cent.) of free hydrobromic acid, but is not assisted if sufficient is present to induce hydrolysis of a large proportion of the aconitine. The hydrolysis of napelline, or aconitine, into aconine and benzoic acid is represented by the following equation:

$$C_{33}H_{45}NO_{12} + H_2O = C_{26}H_{41}NO_{11} + C_7H_6O_2$$

Aconitum ferox was examined by Wright. In it he found chiefly the alkaloid *pseudaconitine,* $C_{36}H_{49}NO_{12}$. It crystallizes in transparent needles and sandy crystals, but is apt to separate as a varnish if not evaporated extremely slowly. It forms crystallized salts with difficulty. It can be dehydrated, forming *apo-pseudaconitine,* $C_{36}H_{47}NO_{11}$, and when saponified yields dimethyl-protocatechuic acid instead of benzoic, and a new base, *pseudaconine,*

$$C_{36}H_{49}NO_{12} + H_2O = C_9H_{10}O_4 + C_{27}H_{41}NO_9$$

Pseudaconitine crystallizes with H_2O and melts at 104° to 105° C. (219.2°–221° F.). Dunstan and Carr (*J. Chem. S.,* 1897, 350) give a process for making the very poisonous alkaloid pseudaconitine, which they obtained in crystals; it dissolves in hot water, very slightly in cold water, readily in alcohol, chloroform, and acetone, less readily in ether. The products of

hydrolysis, which occurs in two stages, result in the separation of *veratryl pseudaconine,* $C_{34}H_{47}NO_{11}$, and *pseudaconine,* $C_{25}H_{39}O_8$; *veratric acid* is eliminated. *Pyropseudaconitine,* $C_{34}H_{45}NO_{10}$, an anhydride of veratryl pseudaconine, did not appear to be poisonous. In Japanese aconite roots (species not certainly known) Wright found a larger percentage of active alkaloids than in either of the other varieties. He also considers that he has obtained here a new base, *japaconitine,* $C_{66}H_{88}N_2O_{21}$. This base on saponification splits up into benzoic acid and a base, *japaconine,* $C_{28}H_{41}NO_{10}$.

Pseudaconitine has been physiologically studied by Boehm and Ewens (*A. E. P. P.,* 1873, i) and by Cash and Dunstan (*P. Tr. R. S. L.,* Series B., 1902), who are in accord in finding that its physiological action is that of aconitine save only in regard to strength. 0.4 gr. of it is said to be equivalent in toxic power to 0.45 of true aconitine. *Japaconitine,* the alkaloid of Japanese aconite, *Kuza-ùza, A. japonicum* or *A. Fischeri,* according to Cash and Dunstan, acts physiologically as true aconitine, except that 0.85 gr. is equivalent to 0.9 in toxicity. For local application these three alkaloids may be substituted for aconitine.

Aconitine Derivatives.—Certain alkaloids have been prepared by Cash and Dunstan by the withdrawal of the acetyl group from aconitine (*Philosophical Trans.,* 1898, vol. 190; and 1902, vol. 195); of these *benzaconine,* in which an acetyl group of aconitine is replaced by an atom of hydrogen, has been found to differ physiologically entirely from aconitine: being, in fact, so far as its action on the heart is concerned, antagonistic to the parent alkaloid. *Pyraconitine* differs from aconitine by the loss of one molecule of acetic acid. It differs physiologically from aconitine chiefly in being devoid of local action; it slows the heart by stimulating the vagus, at the same time depressing the heart muscles or its ganglia, and is a powerful respiratory and centric motor depressant. *Methylbenzaconine* differs from aconitine in that an acetyl group has been replaced by a methyl group. It is much less active locally and less poisonous than aconitine; it is a somewhat feeble cardiac depressant, but is especially characterized physiologically by a curare-like action upon the motor nerves. It seems, also, to have influence upon the muscles, producing in the frog marked persistent fibrillary contractions even at a time when the reflexes are abolished.

Aconitine exists in the root in combination with *aconitic acid,* $C_6H_6O_6$. Dragendorff and Spohn (*J. P. C.* (5), 10, 361–368) find in *Aconitum Lycoctonum* two alkaloids; *lycaconitine,* $C_{27}H_{34}N_2O_6 + 2H_2O$, which is not crystalline, nor does it yield a crystalline aurochloride or platinochloride, and *myoctonine,* $C_{27}H_{30}N_2O_6 + 5H_2O$, which is amorphous. The former alkaloid, heated with water under pressure, gives rise to two acids, a volatile one and a crystalline one, *lycoctonic acid,* $C_{17}H_{18}N_2O_7$, while two alkaloids remain dissolved, one, *lycaconine,* soluble in ether, the other soluble in chloroform, and apparently Hübschmann's *acolytine.*

Hübschmann is said to have extracted two alkaloids from *A. Lycoctonum;* one in the form of a white powder, insoluble in ether, but soluble in water and alcohol, which he names *acolytine;* the other crystallizable, very soluble in alcohol, and but slightly so in ether or water, and named by him *lycoctonine.* (*A. J. P.,* 1866, p. 376.) According to Flückiger, *lycoctonine* is in white acicular crystals, melting like aconitine in boiling water, though at a somewhat higher heat. On cooling it crystallizes only when moistened with water, when the amorphous mass is converted into tufted crystals. It loses no water upon melting, and combines with none on crystallizing. It readily dissolves in chloroform, and upon evaporation is left as an amorphous varnish, which on the addition of a little water becomes strikingly crystalline. It is largely dissolved by carbon disulphide, ether, alcohol, the fixed and volatile oils, amyl alcohol, and petroleum benzin; but requires 600 parts of boiling water for solution. The solution is bitter and has an alkaline reaction, and with bromine water produces fine yellow crystals; and this effect results though the solution contain only one part of the alkaloid in 30,000. Lycoctonine is an alkaloid quite distinct from aconitine and pseudaconitine, and is much less poisonous than either. (Flückiger, *P. J.,* 1870, p. 122.) Wright and Luff concluded that lycoctonine and acolytine are identical with *aconine* and *pseudaconine,* decomposition products respectively of aconitine and pseudaconitine, but according to Dragendorff and Spohn they are really decomposition products of two previously unnoticed alkaloids of *A. Lycoctonum,* namely, *lycaconitine* and *myoctonine.* (See *P. J.,* viii, 169, and xv, 104.) Jacobowsky found lycaconitine to resemble curare in its physiological action, but to be of no value in practical medicine.

Even different specimens of apparently pure crystallized aconitine made by the same chemist in the same manner vary greatly in toxic property. (See K. F. Mandelin, *A. Pharm.,* 1885, xxiii; abstracted, *P. J.,* xvi; Bunzen and Madsen, *Trans. Internat. Congress,* Copenhagen, 1884.) Lepine states that the crystallized alkaloid made from plants gathered in Switzerland is much more active than that from plants of the Vosges or of the Pyrenees. (*S. M.,* March 30, 1892.)

Uses.—Aconitine produces effects on the system similar to aconite. Because of its extreme toxicity, as well as its variability, its use is not to be encouraged.

Dose, one eight-hundredth to one four-hundredth of a grain (0.000075–0.00015 Gm.).

Off. Prep.—Unguentum Aconitinæ, *Br.;* Oleatum Aconitinæ, *N. F.*

ACONITUM. U. S. (Br.)

ACONITE Aconit. [Monkshood Aconite Root Aconiti tuber P. I.]

(ăc-o-nī'tŭm)

"The dried tuberous roots of *Aconitum Napellus* Linné (Fam. *Ranunculaceæ*), without the presence or admixture of more than 5 per cent. of stems or other foreign matter, and yielding not less than 0.5 per cent. of the ether-soluble alkaloids of Aconite. If made into a fluidextract and assayed biologically the minimum lethal dose should not be greater than 0.00004 mil for each gramme of body weight of guinea-pig." *U. S.* "Aconite Root is the dried root of Aconitum Napellus, *Linn.*" *Br.*

Aconiti Radix, *Br.;* Aconite Root, Monkshood, Wolfsbane, Wolfroot, Friar's cap, Cuckoo's cap, Blue rocket; Racine d'Aconite, Aconit, Coqueluchon, Aconit Napel, *Fr.;* Tubera Aconiti, *P. G.;* Eisenhut, Eisenhutknollen, Sturmhut, Mönchskappe, Akonitknollen, *G.;* Aconito, *It., Sp.*

The name Aconite is derived, according to Pliny, from the Black Sea port, Acone. While the drug was used by the ancient Chinese as well as by the hill tribes of India, it was introduced into modern medicine by Störck, of Vienna, in 1763. The genus *Aconitum* is a relatively large one, there being some sixty well-defined species, nearly half of which have been used in medicine. The species which is official and recognized by nearly all the Pharmacopœias is *Aconitum Napellus.* It is indigenous to the mountainous regions of Middle Europe and is found growing in Northern Europe, Siberia and Central Asia. It is extensively cultivated in temperate climates for its foliage and flowers and has been successfully grown in the testing garden of the U. S. Department of Agriculture. Schneider reports that it has become naturalized to some extent in California. There are five species of Aconitum which are indigenous to the mountainous regions of the Northern United States, two of these being found in the Rocky Mountains and on the Pacific Coast. Holm describes the morphology and structural characteristics of the wild Monkshood of the United States, *A. uncinatum* L., in *Merck's Rep.,* 1907, p. 65.

The roots or rhizomes of several other species of Aconitum are found in commerce, these being chiefly used in the manufacture of the alkaloids. (1) The tuberous roots of *A. variegatum* L. and of *A. Stoerkianum* Reich, are sometimes found in the commercial drug. These are smaller, not so pungent, although quite active. (2) Japanese Aconite is derived from *A. Fischeri* Reich and *A. japonicum* Thumberg. The roots are light gray in color, fleshy, being smaller than the official tubers. They have a circular cambium and the starch grains are more than 0.015 mm. in diameter. They are largely imported into Europe and to some extent to this country. (3) Indian Aconite is derived from *A. ferox* Wall., a plant growing in the Himalayas and in Nepal. The roots are from 5 to 10 cm. long and from 2 to 4 cm. in diameter, being externally grayish-brown and deeply furrowed. They are hard, the fracture being either horny or mealy and the inner surface is either yellowish-brown or whitish. The cambium is 7- to 9-rayed and the taste resembles that of the official Aconite. (4) Another species of Aconitum that is very poisonous is *A. Lycoctonum* L., of Europe and Northern Asia. This, however, does not produce a tuberous root, but develops an oblique rhizome surrounded with numerous roots. (5) The fleshy roots of *A. heterophyllum* Wallich., a plant growing in the West Himalayas, are somewhat ovoid and flattened at the summit and base. Externally they are grayish-brown. The odor resembles that of black pepper and the taste is bitter and acrid. The rhizome contains an amorphous bitter alkaloid, *atisine,* which is not toxic. Under the name of *Utees, Atees,* or *Atis,* the rhizome and roots of *A. heterophyllum* are said to be largely employed in doses of 20 grains as an antiperiodic. *Wakhma* is the root of *A. palmatum* Don, in which Jowett found *aconitic acid* and the alkaloid *atisine,* $C_{22}H_{33}NO_3$, which, according to Cash, is physiologically very feeble. (*J. Chem. S.,* 1896.)

Aconitum Napellus is a perennial herbaceous plant, with a conical-shaped, tapering root, seldom exceeding 10 cm. in length and 2 cm. in thickness near the summit, brownish externally, whitish and fleshy within, and sending forth numerous long, thick, fleshy rootlets. When the plant is in full growth, there are usually two roots joined together, of which the older is dark brown and supports the stem, while the younger is of a light yellowish-brown, and is destined to furnish the stem of the following year, the old root decaying. The stem is erect, round, smooth, leafy, usually simple, and from two to six or even eight feet high. The leaves are alternate, petiolate, divided almost to the base, from two to four inches in diameter, deep green upon their upper surface, light green beneath, somewhat rigid, and more or less smooth and shining on both sides. Those on the lower part of the stem have long footstalks and five or seven divisions; the upper, short footstalks and three or five divisions. The divisions are wedge-form, with two or three lobes, which extend nearly or quite to the middle. The lobes are cleft or toothed, and the laciniæ or teeth are linear or linear-lanceolate and pointed. The flowers are of a dark violet-blue color, large and beautiful, and are borne at the summit of the stem upon a thick, simple, straight, erect, spike-like raceme, beneath which, in the cultivated plant, several smaller racemes arise from the axils of the upper leaves. Though without calyx, they have two small calycinal stipules, situated on the peduncle within a few millimeters of the flower. The petals are five, the upper helmet-shaped and beaked, nearly hemispherical, open or closed, the two lateral roundish and internally hairy, the two lower oblong-oval. They enclose two

pediceled nectaries, of which the spur is capitate, and the lip bifid and revolute. The fruit consists of three, four, or five follicles. The seeds are wrinkled or scaly and very acrid.

The plant is abundant in the mountain forests of France, Switzerland, and Germany. It is also cultivated in the gardens of Europe, and has been introduced into this country as an ornamental flower. All parts of the plant are acrid and poisonous. The leaves and root are used. The leaves should be collected when the flowers begin to appear, or shortly before. After the fruit has formed, they are less efficacious. The *fresh leaves* have a faint narcotic odor, most sensible when they are rubbed. Their taste is at first bitterish and herbaceous, afterwards burning and acrid, with a feeling of numbness and tingling on the inside of the lips, tongue, and fauces, which is very durable, lasting sometimes many hours. When long chewed, they inflame the tongue. The *dried leaves* have a similar taste, but the acrid impression commences later. Their sensible properties and medicinal activity are impaired by long keeping. They should be of a green color, and free from mustiness. The root is much more active than the leaves, and an extract from the latter is said to have only one-twentieth of the strength of one made from the former. It should be gathered in autumn or winter after the leaves have fallen, and is not perfect until the second year. It has been mistakenly substituted for horseradish root, as a condiment, with fatal effect. The wild plant is said to be more active than the cultivated. (Schroff.) Procter found the roots of the plant cultivated in this country richer in active alkaloidal principles than the imported roots, having obtained as much as 0.85 per cent. from the former. (*Proc. A. Ph. A.*, 1860.) The studies of P. W. Squire seem to show that in the autumn the root is the most active. So far, however, as concerns the whole plant, the practical difficulty is that the root of *A. paniculatum* Lam. cannot be distinguished from that of *A. Napellus*, except by taste; so that the custom which seems to prevail of gathering the root about the flowering period is probably well founded. The plant is being cultivated to some extent for medicinal purposes in England, but much of the stock is of doubtful nature, owing to the extraordinary tendency of *A. Napellus* to hybridize with other species and to alter under cultivation. (See *P. J.*, 1889, 645.) For Keller's test for aconite root and leaves, see *Proc. A. Ph. A.*, 1895, 539.

Aconite root is generally brought into market in packages or bales, either from the continent of Europe or from India. It is of variable quality, some parcels being unobjectionable, while others contain a considerable proportion of inert or defective roots. Among these roots that of *Imperatoria Peucedanum Ostruthium* has been especially observed. (*P. J.*, vii, 749.) The best test is the taste; roots should be rejected which have not in a fair degree the characteristic properties in this respect described below, especially the production of the sensation of numbness and tingling on the tongue, lips, and fauces. One shipment of aconite consisted entirely of Japanese aconite. The powdered drug is sometimes adulterated with the endocarp of the olive or so-called "olive pits." The latter is not easily detected, as aconite contains a large number of stone cells. The latter, however, have relatively thin walls and the various forms have been described by Stingel in *A. J. P.*, 1913, p. 391.

Nepaul aconite, known in India as "*Bikh*" or "*Bish*" aconite, is supposed to be derived from *A. spicatum* or *A. laciniatum*. There is a question about this as the Nepaul aconite of European commerce yields the alkaloid pseudaconitine and this principle is only present in the roots of *A. deinorrhizum* and *A. Balfourii*. (*Bulletin of the Imperial Institute*, 1906, p. 32.) Nepaul aconite is composed of elongated fusiform or nearly cylindrical roots which are more or less flattened, longitudinally furrowed and from 7.5 to 10 cm. in length.

Properties.—The German Pharmacopœia restricts aconite to the bud-crowned tubers of wild growing plants. Most of the other Pharmacopœias permit the use of stem-crowned roots. In the former case the daughter tubers terminated by their buds are employed, whereas in the latter the older tubers which have developed foliage and flower stems are used. The commercial drug shows considerable variation and is usually a mixture of six or seven different kinds of tubers, as follows: 1. Single fleshy tubers which are smooth, light brown and full of starch. 2. Single tubers which are single, somewhat elongated fusiform, crowned with short stems, dark brown and longitudinally furrowed. 3. Twin tubers, one of which is bud-crowned and the other having a short stem at the summit. 4. Very small single tubers usually crowned with stems, the lower portion being acute or pointed. 5. Single tubers which are almost cylindrical, crowned with stems and either fleshy and nearly smooth or more or less shrunken and furrowed. 6. Dark brown resinous tubers. 7. And finally fragments of small and nearly filiform roots.

The *root* has a feeble earthy odor. Though sweetish at first, it has afterwards the same effect as the leaves upon the mouth and fauces. It shrinks much in drying, and becomes darker, but does not lose its acridity. Aconite root is officially described as being "more or less conical or fusiform, from 4 to 10 cm. in length and from 1 to 2 cm. in diameter at the crown; externally dark brown or grayish-brown, smooth or longitudinally wrinkled, the upper end with a bud, remains of bud-scales or stem-scars, the other portions with numerous root-scars or short rootlets; fracture short, horny or somewhat mealy; internally, bark light or dark brown, 1 to 2 mm. in thickness, cambium zone usually 5- to 8-angled, with a small fibrovascular bundle in each angle, pith whitish or light brown,

from 2 to 7 mm. in diameter; odor very slight; taste sweetish, soon becoming acrid and developing a tingling sensation, followed by numbness. Under the microscope transverse sections, made near the middle of the tuberous root of Aconite, show an outer layer consisting of one or more rows of cells with blackish-brown walls; a primary cortex of 8 to 15 rows of parenchymatous cells and interspersed with characteristic stone cells, which occur either singly or in small groups; a more or less modified endodermis; a secondary cortex, consisting chiefly of starch-bearing parenchyma and interspersed with a few small fibrovascular bundles; a more or less star-shaped and characteristic cambium with from 5 to 12 collateral fibro-vascular bundles; and a pith composed of large, starch-bearing parenchyma cells. The powder is grayish-brown; starch grains numerous, spherical, somewhat plano-convex, single or 2- to 5-compound, the individual grains from 0.003 to 0.015 mm. in diameter and frequently with a central cleft; tracheæ mostly with slit-like, simple pores, sometimes with spiral or reticulate thickenings or with bordered pores; stone cells single, tabular, irregular in shape or elongated to fibers, from 0.1 to 0.4 mm. in length, walls from 0.008 to 0.025 mm. in thickness, strongly lignified and having large, simple pores; fragments of cork few, yellowish-brown; fragments of parenchyma numerous, the cells being filled with starch grains; bast-fibers from stems few, very long, with lignified walls about 0.005 mm. in thickness, and marked by transverse or oblique, slit-like pores. Aconite yields not more than 6 per cent. of ash." *U. S.*

The following standards for aconite root are given in the British Pharmacopœia: "From four to ten centimetres long, and from one to two centimetres wide at the upper extremity. Conical, dark brown, with numerous root scars, and crowned with base of the stem or the remains of a bud. Internally solid and starchy. In transverse section a stellate cambium with small vascular bundles at the projecting angles; primary cortex narrow, with isolated thick-walled sclerenchymatous cells; cells of parenchymatous tissue contain numerous small simple or compound starch grains. No marked odor; taste at first slight, followed by persistent sensation of tingling and numbness." *Br.*

The British Pharmacopœia formerly recognized the flowering tops of the Aconite (*Aconiti Folia*). To be effective they should be collected just as the flowers are beginning to expand, at which time they are richest in alkaloid. The dried leaves are stated to contain about 0.3 per cent. and the flower-buds about 0.4 per cent. of aconitine. For an account of the chemistry of aconite, see *Aconitina*, page 83. In the absence of any reliable chemical tests for aconitine E. R. Squibb suggested that a fluidrachm of a highly diluted solution of the various preparations be taken into the anterior part of the mouth (after the latter has been thoroughly rinsed) and held there for one minute exactly, and then discharged. The peculiar numbing sensation should be experienced within fifteen minutes, and it should continue for fifteen or thirty minutes. Tested in this way, he found the commercial aconitines, in solution of the strength of $\frac{1}{500}$ grain in 1 fluidrachm of water, to have the following relative strengths: 1 grain of good powdered aconite root is equal to 1 grain of ordinary commercial aconitine, $\frac{1}{8}$ grain of Merck's ordinary aconitine, $\frac{1}{20}$ grain of Merck's pseudaconitine, $\frac{1}{111}$ grain of Duquesnel's crystallized aconitine (really aconitine nitrate). He also found by this approximate method that 1 grain of powdered aconite root was equivalent to 1.5 minims of Fleming's tincture, 9 grains of powdered aconite leaf, 1.5 grains of alcoholic extract of dried aconite leaf, 1 grain of Allen's English extract of fresh plant, and 72 minims of tincture of aconite leaf. For methods of assaying aconite, reader is referred to A. R. L. Dohme's paper (*Proc. A. Ph. A.*, 1895, 206); also *P. J.*, 1895, 860; *D. C.*, 1900, 69, 132.

Assay.—The quality of aconite root is officially determined by an assay as follows: "Proceed as directed under *Belladonnæ Radix*, using 15 Gm. of Aconite in No. 40 powder and ether only as the immiscible solvent throughout the assay. Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 64.539 milligrammes of ether-soluble alkaloids of Aconite." *U. S.*

"Yields not less than 0.40 per cent. of ether-soluble alkaloids when assayed by the following process: Into a small stoppered glass percolator, provided with a glass tap and suitably plugged with cotton wool, introduce 10 grammes of Aconite Root in No. 40 powder and 75 millilitres of *alcohol* (70 per cent.). Macerate for four hours, shaking occasionally. Then allow percolation to proceed slowly until the liquid ceases to drop. Continue the percolation by the addition of more of the same menstruum until 150 millilitres have been collected or the Root is exhausted. Evaporate the percolate to dryness in a shallow porcelain evaporating basin, at a temperature not exceeding 60° C. (140° F.). Dissolve the residue in 5 millilitres of *N/10 solution of sulphuric acid* diluted with 20 millilitres of *water*. Filter into a separating funnel, washing the dish and filter with about 30 millilitres of *water*. Add to the mixed filtrate and washings 25 millilitres of *ether* and 2 millilitres of *solution of ammonia*, and shake for one minute. After separation draw off the lower layer into a flask, and filter the ethereal solution into a beaker. Return the contents of the flask to the separator, add 20 millilitres of *ether* and again shake for one minute, separating the aqueous liquid and filtering the ethereal solution into the beaker. Repeat the operation with two other portions, each of 20 millilitres, of *ether*. Evaporate the mixed ethereal solutions to dryness, dry the residue at 60° C. (140° F.), dissolve it in 5 millilitres

of *N/20 solution of sulphuric acid* diluted with 20 millilitres of *water,* and titrate back with *N/20 solution of sodium hydroxide, tincture of cochineal* being used as indicator. Deduct the number of millilitres of the alkaline solution required from 5, multiply the difference by 0.3217; the result will be the percentage of ether-soluble alkaloids in the powdered Root." *Br.*

Biologic Assay.—Because of the great variation in the activity of the various alkaloids of aconite a chemical assay does not offer an accurate criterion of the activity of a sample of this drug, and the Pharmacopœia has very properly, therefore, permitted a standard of toxicity. As the different alkaloids resemble each other very closely in the type of their effect varying only in degree, it is not necessary to standardize the drug for any one physiological effect, and, as the sharpest physiological end reaction is death, the best test for the activity of a specimen of aconite is determination of its lethal dose. The test recommended by the Revision Committee for aconite is based upon the determination of the minimum lethal dose for guinea-pigs.

"The guinea-pigs to be utilized should be of average size and not too large; preferably from 250 to 350 Gm. in weight and in healthy condition. The drug may be administered in the form of fluidextract, extract, or tincture, which in the preliminary trial may be injected subcutaneously into a series of guinea-pigs in doses having sufficiently wide limits. If the extract is to be standardized, it must be dissolved in sufficient solvent to produce a liquid preparation before injection. The animals after injection are placed in cages and at the end of the observation (twelve hours), note is taken of those living and dead. After this preliminary test, the limits of the doses for a second series of animals are further narrowed and, if necessary to still further confirm the earlier results, additional series may be injected until the minimum lethal dose for the guinea-pig is found.

"*Standard.*—A satisfactory preparation of the Fluidextract of Aconite should kill guinea-pigs when administered in doses of 0.00004 mil for each gramme of body weight of guinea-pig; a satisfactory Tincture of Aconite should prove fatal to guinea-pigs when given in doses of 0.0004 mil for each gramme of body weight of guinea-pig and a satisfactory Extract of Aconite should have a minimum lethal dose not greater than 0.00001 Gm. for each gramme of body weight of guinea-pig." *U. S.*

It is well to take a series of four guinea-pigs, each of which will be injected respectively with 0.03, 0.04, 0.045, and 0.05 milligramme for each gramme of body weight. If none of the animals survive the drug is too strong, if none of them die it is too weak. If some survive and some die it is necessary to test the drug on a second series in which case the test should be 0.038, 0.04, 0.042 milligramme; it is well to have at least two animals who receive the middle dose of these three. If the drug be of official quality those who receive 0.038 should survive, those which receive 0.042 should die, and of those which receive 0.04 some should die and some survive. In testing the crude drug it may be made up conveniently in the form of a fluidextract and diluted with nine volumes of water. The syringe used must be standardized and graduated in tenths of a mil. The injection should be made subcutaneously, preferably beneath the skin of the abdomen. After the injection the animals are marked or placed in separate cages and at the end of 12 hours notice taken of those living or dead.

Uses.—Aconite was well known to the ancients as a powerful poison, but was first employed as a medicine by Baron Störck, of Vienna, whose experiments were published in the year 1762.

Locally aconite is actively irritant and also a paralyzant to the peripheral sensory nerves. When applied to a mucous surface it produces at first a burning tingling sensation followed in a few minutes by a numbness. This sensation may even be perceptible after the systemic ingestion of very large doses. When administered internally the most marked changes are seen in the circulation. The first effect is generally a slowing of the pulse, due to stimulation of the cardio-inhibitory centers, with consequent fall in the blood pressure. After somewhat larger doses, however, there is a weakening of the force as well as reduction of the rate of the pulse brought about by a direct action on the heart muscle. After poisonous doses various irregularities of heart action are produced and often there will be complete lack of harmony between the contraction of the auricle and ventricle. After fatal doses the heart is arrested in complete diastole and will respond to neither electrical nor mechanical irritation. In the frog, large quantities of aconite produce a loss of reflex activity, which is apparently due to a paralysis of sensation as voluntary motion is preserved for some time later, although it too may eventually be abolished. The drug appears to affect both the sensory nerves and the receptive side of the spinal cord, although the latter is involved comparatively late in the poisoning. In mammals this depressant action upon the nervous system can scarcely be demonstrated because of the powerful depressant effect upon the circulation.

Aconite is used chiefly as a circulatory sedative in conditions attended with excessive action of the heart or high arterial tension. Thus in *valvular lesions of the heart* in which the muscle tone is good, but the heart is over acting, in the so-called *irritable heart* seen in improperly trained athletes and similar conditions, it is often a remedy of great service. The choice between aconite and digitalis in such cases will depend largely upon the condition of the heart muscle; when the latter is strong and of good tone aconite may be used, but if there be a tendency towards dilatation, digitalis is generally preferred. In chronic *high blood pressure,* by retarding the pulse rate it will often produce a

sensible reduction in the tension but in acute hypertension or threatened *apoplexy* it is less certain in its effects than the nitrites, but may at times be advantageously combined with them, By virtue of the lowering of the blood pressure aconite tends to increase the sweat and is frequently used as a sudorific, especially in febrile conditions. In sthenic *fevers* its effect in restraining the heart as well as its diaphoretic tendency often renders it a drug of much use.

Aconite is also frequently employed for its local effects. The combination of local irritant effects with anesthetic action suggests strongly its use in peripheral *neuralgias*. It must not be forgotten, however, that if used too freely for this purpose it may be absorbed through the skin in sufficient quantities to cause serious poisoning. It is also occasionally employed as a local anesthetic to the stomach in various types of *vomiting* or *gastralgia*, but on account of its systemic effect is practically of secondary value.

For internal use the best preparation is the tincture which may be given in doses of from five to fifteen minims (0.3–0.9 mil). For external application the fluidextract may be employed, but generally an ointment is preferred. This may be made by rubbing up the extract with two or three parts of lard, or the *ointment of aconitine* of the British Pharmacopœia may be used. The U. S., 1870, recognized a *plaster of aconite*.

Toxicology.—Aconite is a rapidly acting and powerful poison. The symptoms produced by overdose of it are sensations of warmth in the stomach sometimes with nausea but usually without vomiting, with slowing of the pulse and of the respiration, the skin is cool and moist and there is profound prostration. As the poisoning progresses the respirations become more slow and shallow, the pulse more and more feeble and towards the end may become rapid or very irregular. A characteristic symptom, in fact the only symptom of diagnostic importance, is the peculiar numbness and tingling first felt in the lips and mouth, but later also often in the fingers. At times there is dimness of vision, the pupils may be either contracted or dilated and occasionally delirium and stupor or convulsions may precede the fatal termination.

In the treatment of aconite poisoning the patient should be kept absolutely in a horizontal position or with the feet higher than the head. For the purpose of emptying the stomach the stomach pump is preferable to emetics as the latter involve a more or less serious strain upon circulation. Circulatory stimulants, such as strychnine, ammonia, and atropine, may be given hypodermically. Body temperature should be maintained by external application of heat.

Dose, of aconite root, one-half to one grain (0.032–0.065 Gm.).

Off. Prep.—Extractum Aconiti, *U. S.;* Fluidextractum Aconiti, *U. S.;* Linimentum Aconiti, *Br.;* Tinctura Aconiti, *U. S., Br.;* Linimentum Aconiti et Chloroformi (from Fluidextract), *N. F.*

ADEPS. U. S. (Br.)

LARD

(ăd'ĕps)

"The purified internal fat of the abdomen of the hog (*Sus scrofa*, var. *domesticus* Gray, Fam. *Suidæ*). Preserve it in a cool place in well-closed containers which are impervious to fat." *U. S.* "Prepared Lard is the purified internal fat of the hog, Sus scrofa, *Linn.*" *Br.*

Adeps Præparatus, *Br.;* Axungia Porci, s. Porcina, Axungia; Prepared Lard, Hog's Lard; Axonge, *Fr. Cod.;* Graisse, Graisse de Porc, Saindoux, *Fr.;* Adeps Suillus, *P. G.;* Schweineschmalz, *G.;* Grasso suino, Sugna, Grasso di Porco, Lardo, *It.;* Grasa de cerdo, Manteca de puerco, Lardo, *Sp.*

Preparation.—Lard is the prepared fat of the hog. The Br. Pharmacopœia (1898) gave a process for its preparation; but in this country it is generally purchased already prepared by the druggists. The adipose matter of the omentum and mesentery and that around the kidneys, are usually employed, though the subcutaneous fat is said to afford lard of a firmer consistence. In the crude state it contains membranes and vessels, and is more or less contaminated with blood, from all of which it must be freed before it is fit for use. For purification, the fat, having been deprived of membranous matter as far as possible by the hand, is cut into pieces, washed with water till the liquor ceases to be colored, and then, after carefully separating the water, it is melted in a copper or iron vessel, over a slow fire, or, on the large scale, by steam heat. The heat is continued until all the moisture is evaporated, which may be known by the transparency of the melted fat, and the absence of crepitation when a small portion of it is thrown into the fire. This operation is technically known as "*rendering*." Care should be taken that the heat be not too great, as otherwise the lard might be partially decomposed, acquire a yellow color, and become acrid. This may be guarded against by using a water bath in melting the lard. The process is completed by straining the liquid through linen, and pouring it into suitable vessels, in which it hardens upon cooling. To render it, however, perfectly free from particles of membrane and tissue, which are often the cause of rancidity and unfit lard for its finer and more permanent uses, Ed. Smith of Torquay, insists on the necessity of filtering the lard through paper, after freeing it from its coarser impurities by straining through linen. By this author it is recommended that the process of purification should be completed by remelting the lard, by means of a water bath, and then carefully filtering it through paper in a warm closet. Lard may be rendered quite inodorous by melting it, when fresh, by means of a salt water bath, adding a little alum or common salt, continuing the heat till a scum rises, which is to be skimmed off, and, after the lard has hardened, separating the saline matter by washing it thoroughly with water. For a particular account of the process, see *A. J. P.*, xxviii, 176.

Lard, as offered for sale, often contains common salt, which renders it unfit for pharmaceutical purposes. This may be detected, when the quantity is insufficient to be sensible to the taste, by means of silver nitrate, which will produce a precipitate of silver chloride with water in which the salted lard has been boiled, after cooling and filtration. To free it from this impurity, it may be melted with twice its weight of boiling water, the mixture well agitated and set aside to cool, and the fat then separated. Lard is sometimes adulterated with water, starch, and a small portion of alum and quicklime, which render it whiter, but unfit for medicinal use. But by far the most common adulteration of lard in recent years is through the use of cotton seed oil. Indeed, some specimens of lard consist almost wholly of mixtures of beef stearin and cotton seed oil. Lard of this kind can easily be detected by the disagreeable and characteristic odor of cotton seed oil which is evolved when it is heated. For Taylor's method of differentiation, see *Nat. Drug.*, 1892, p. 103. Crookes (*Analyst*, 1893, p. 221) gives the following very delicate modification of Milliau's test. Pure white filtering paper is first moistened with 12 per cent. solution of silver nitrate and held over a small sample of the lard, which is gradually heated in an oil bath to 115.5° C. (239.9° F.), when, if even less than 1 per cent. of cottonseed oil is present, the paper will turn light brown to nearly black. Pure fresh lard does not affect the paper. The best test for detecting imitation lard is the Halphen test for cottonseed fat, see under *Oleum Olivæ*. Although it is possible at this time to obtain lard of excellent quality in the American market, if due care is observed (Gordon, *Proc. Pa. Pharm. Assoc.*, 1901, 126), there are many grades of lard to be found in commerce, designated by the dealers as follows: 1. Neutral (or Kettle) lard. 2. Leaf lard; made by melting the whole flare with steam, followed by pressure. 3. Choice kettle-rendered lard, chiefly from fat from the back of the hog. 4. Prime steam lard, from all the fatty parts of the hog. 5. Butcher's lard, melted on an open fire. 6. Off grade lard, from salt fat. 7. Dead hog grease, from diseased hogs. 8. Brown grease, from the intestines. 9. White grease, from the other parts. 10. Yellow grease, from the waste of packing warehouses. 11. Pig's foot grease, from glue factories. (*Ph. Ztg.*, 96, 402.)

Lard from hogs which have been fed with cottonseed meal will not only show the tests for cottonseed oil (Becchi and Halphen tests), but even the presence of physosterin or vegetable cholesterin can be shown. (Emmett & Grindley, *J. Am. C. S.*, 1905, 270.)

The slight reaction shown under these conditions is not likely to be confused, however, with the marked reaction which occurs in a sample of lard which is actually adulterated, as has been shown in the examination of hundreds of samples in the enforcement of the food laws.

Properties.—Lard is "a soft, white, unctuous solid, having a faint odor and a bland taste; it is free from rancidity. It is insoluble in water; very slightly soluble in alcohol; readily soluble in ether, chloroform, carbon disulphide, or petroleum benzin. Lard melts between 36° and 42° C. (96.8°–107.6° F.), to a clear liquid, from which no aqueous layer separates. Distilled water boiled with Lard does not acquire an alkaline reaction (*alkalies*). Boil about 1 Gm. of Lard with 20 mils of alcohol and filter the solution after cooling; the filtrate is not rendered more than slightly turbid by the addition of a few drops of a saturated alcoholic solution of silver nitrate (*chlorides*). Dissolve 10 Gm. of Lard in 30 mils of chloroform, mix the solution with 10 mils of neutral alcohol and add 1 drop of phenolphthalein T.S.; not more than 2 mils of tenth-normal potassium hydroxide V.S. is required to produce a pink tint after shaking it vigorously (*free fatty acids*). Intimately mix 5 mils of melted and filtered Lard, while warm, by agitating it in a test tube with 5 mils of an alcoholic solution of silver nitrate (made by dissolving 0.1 Gm. of silver nitrate in 10 mils of alcohol, and adding 2 drops of nitric acid); heat this mixture for five minutes on a water bath. The liquid fat acquires no reddish or brown color, nor is any dark color produced at the line of contact of the hot liquids (*cottonseed fats*). Dissolve 5 Gm. of Lard in 20 mils of ether in a test tube, stopper the tube loosely with purified cotton and allow it to stand for about twelve hours or over night at a temperature of about 20° C. (68° F.). Collect some of the crystals which have separated at the bottom of the test tube, mount them in either alcohol or a fixed oil and examine them under a microscope having a magnifying power of about two hundred diameters. Lard stearin crystallizes in the form of flat and rhomboidal plates, cut off obliquely at one end and grouped irregularly. Beef stearin crystallizes in the form of cylindrical rods or needles with sharp ends, grouped in fan-shaped clusters. Saponification value: not less than 195 nor more than 203 (see Part III, Test No. 9). Iodine value: not less than 46 nor more than 70 (see Part III, Test No. 8)." *U. S.*

"A soft, white, homogeneous, unctuous substance. Odor faint but not rancid. Entirely soluble in *ether*. *Acid value* not more than 1.2; *saponification value* 192 to 198; *iodine value* 52 to 63; *unsaponifiable matter* not more than 0.5 per cent.; *refractive index* at 60° C. (140° F.) 1.4530 to 1.4550. Forms on melting a clear liquid which does not deposit water on standing. *Water* boiled with it does not acquire an alkaline reaction (absence of alkalies), and, after filtering and acidifying with *nitric acid*, does not yield any reaction with *solution of silver nitrate* (absence of chlorides). When a mixture of 20 millilitres of the melted and filtered Lard with 10 millilitres of *hydrochloric acid* containing 1 per cent. of *refined sugar* is shaken for half a minute and allowed to stand,

the acid layer does not become pink (absence of sesame oil). In India, Prepared Suet (Sevum Præparatum) should be employed in making the official preparations for which Prepared Lard is directed to be used." *Br.*

When melted, it readily unites with wax and resins. Like most animal fats and oils, it consists of stearin, palmitin, and olein, its consistence, when pure, depending largely upon the relative proportions of these principles; olein, being the liquid principle, can readily be separated from the other two by subjecting lard in cold weather to strong pressure, when the *olein* (*lard oil*) is pressed out, the solid residue (*stearin*) being used for various purposes, more particularly the manufacture of candles. Olein may also be separated by means of boiling alcohol, which, on cooling, deposits the concrete principles of the lard. Lard oil (see *Oleum Adipis*) was formerly extensively employed for burning in lamps, and is often used as a lubricant, and for greasing wool. Vast quantities of it are prepared in Cincinnati, Chicago, and other centers of the pork slaughtering industry. The exports of lard for 1903 amounted to 535,375,757 lbs., and for 1904 to 563,520,159 lbs.

Exposed to the air, lard absorbs oxygen and becomes rancid. It should, therefore, be kept in well-closed vessels, or procured fresh when wanted for use. In the rancid state, it irritates the skin, and sometimes exercises an injurious reaction on substances mixed with it. Rancidity in lard and other fats is prevented by digesting them with benzoin or poplar buds (see *Adeps Benzoinatus*), and rancid lard may often be greatly improved by washing it with lime water. (See *Unguenta.*) Lard even when fresh is slightly acid, as was proved by Dieterich. (*A. Pharm.*, 1887.)

Uses.—Lard is emollient, and is occasionally employed by itself in frictions, or in connection with poultices to preserve their soft consistence; but its chief use in pharmacy is as an ingredient in the preparation of ointments and cerates.

Off. Prep.—Adeps Benzoinatus, *U. S.* (*Br.*).

ADEPS BENZOINATUS. U. S. (Br.)

BENZOINATED LARD Adeps Benz.

(ăd'ĕps bĕn-zō-i-nā'tŭs)

Adeps Benzoatus, *Br., P. G.;* Benzoated Lard; Ointment of Benzoin; Unguentum Benzoini, *U. S.* 1870; Axungia Balsamica, s. Benzoinata, s. Benzoata; Axonge (Graisse) benzoinée (balsamique), *Fr.;* Benzoinirtes Schmalz, Benzoeschmalz, *G.;* Grasso con benzoino, *It.;* Manteca benzoada, Manteca con benjui, *Sp.*

* "Lard, *one thousand grammes* [or 35 ounces av., 120 grains]; Siam Benzoin, in coarse powder, *ten grammes* [or 154 grains]. To make about *one thousand grammes* [or 35 ounces, 120 grains]. Add the benzoin to the lard and mix thoroughly; then melt the mixture by means of a water bath, and, stirring frequently, continue the heat for two hours, covering the vessel and not allowing the temperature to rise above 60° C. (140° F.). Lastly, strain the liquid through muslin, and stir it occasionally, while it cools. Preserve it in a cool place in well-closed containers which are impervious to fat. For use in southern latitudes and during the heated season in other localities, 50 Gm. of the lard (or more, if necessary) may be replaced by an equal weight of white wax." *U. S.*

"Prepared Lard, 1000 grammes; Benzoin, in coarse powder, 30 grammes. Melt the Lard, add the Benzoin, and maintain at a temperature of 60° C. (140° F.) for one hour, stirring frequently; strain, and stir until nearly cold. In India, Benzoated Suet (*Sevum Benzoatum*) should be employed in making the official preparations for which Benzoated Lard is directed to be used." *Br.*

That the balsamic or resinous principles, in certain substances like benzoin, exercise a valuable function in preserving fats has been proved by abundant experience. It has been shown that when made, as originally suggested by Doliber and directed in the U. S. Pharmacopœia of 1870, by incorporating the tincture with lard, ointment of benzoin was irritating to the skin in certain diseases; hence the return to the old process of digesting the benzoin in lard, kept at a temperature of 60° C. (140° F.). The present U. S. formula does not differ materially from the British. The name "benzoinated lard" is preferred by the U. S. Pharmacopœia to that used by the British Pharmacopœia "benzoated lard" because benzoin is used as a preservative; the word benzoated might imply that a benzoate or benzoic acid is employed. A much pleasanter and more agreeable product is insured by heeding the U. S. directions as to limiting the temperature, a high heat volatilizing the odorous principles and communicating an empyreumatic odor. Benzoinated lard is largely manufactured by several firms in the United States and is usually of excellent quality.

ADEPS LANÆ. U. S., Br.

WOOL FAT Adeps Lan. [Anhydrous Lanolin]

(ăd'ĕps lā'næ)

"The purified fat of the wool of the sheep (*Ovis aries* Linné Fam. *Bovidæ*), freed from water. Preserve it in a cool place in well-closed containers which are impervious to fat." *U. S.* "Wool Fat is the purified fat of sheep's wool, freed from water." *Br.*

Anhydrous wool-fat, *E.;* Suint de laine, *Fr.;* Adeps Lanæ, anhydricus, *P. G.;* Wollfett, *G.;* Lanolinum Anhydricum, *Ph. Aust. VIII;* Lanolinum, *Ph. Belg. III.*

Both the United States and the British Pharmacopœias now recognize wool fat (anhydrous) and hydrous wool fat.

Preparation.—The wool of sheep contains on the average about 45 per cent. of its weight of fat, which must be removed before the wool can be used in the manufacture of woolen fabrics. The crude fat has been termed *œsypus* and *œsypum*. This fat is a mixture of esters

of *cholesterin*, $C_{26}H_{43}(OH)$, with the several fatty acids contained in ordinary fats. Darmstaedter and Lifscheitz obtained from the alkaline washings of partially saponified wool fat two unsaturated alcohols, $C_{10}H_{20}O$ and $C_{11}H_{22}O$, both being colorless, odorless, and tasteless powders; *lanolin alcohol*, $C_{12}H_{24}O$, also a colorless, odorless powder, was isolated by G. Marchetti (*Ber. d. Chem. Ges.*, 1895, No. 19); by the action of chromium trioxide the latter is converted into lanolinic acid, $C_{12}H_{22}O_3$, a white crystalline powder. (*P. J.*, 1895, p. 75.) Wool fat under the name of lanolin was originally recommended by Oscar Liebreich, and may be readily procured from the washings of the wool by a process which was patented by him, or it may be obtained by treating the wool with petroleum benzin and distilling off the benzin. The objection to the latter process is the difficulty of getting rid of the benzin odor. Liebreich's patented process is as follows. The fresh undecomposed waste liquor or lye is passed through a centrifugal machine, in which the dirt and fat are separated from each other, while the cleansed soap liquor is continually drawn off by means of a pipe and led directly into the vat which serves for the acidulation. The raw lanolin thus obtained is thoroughly kneaded by suitable machinery in cold flowing water until the water which flows off is as clear as the water which flows in. The raw lanolin is then heated with water, whereby it is split up into water and fat. The latter is skimmed off from the surface and cooled, and for further purification it can be treated in the centrifugal machine in a melted condition, or it can be dissolved in ether, ethylated or methylated spirits, or other solvents, and the solution can be separated from the residue by filtration or other means. The solvents can be recovered by treatment in suitable stills. After the fat has been cleaned as above stated, it is thoroughly kneaded with water for a long time, and a perfectly white neutral ointment is obtained. From the deposit in the lowest part of the centrifugal machine a further portion of lanolin can be obtained by stirring the same up with clean or salt water and again treating it in the centrifugal machine, or extracting it, either in a wet or a dry condition, by means of a solvent, after which it is treated as above.

Instead of producing lanolin from wool-washing water it may be obtained from commercial wool fat by stirring this wool fat together with water containing sodium carbonate, caustic soda, or a mixture of these to form a thin milky solution, which is treated in the manner above described.

Properties.—Wool fat is "a light-yellow, tenacious, unctuous mass, having not more than a slight odor. It is insoluble in, but miscible with, about twice its weight of water, sparingly soluble in cold alcohol, more soluble in hot alcohol, freely soluble in ether and in chloroform. Wool Fat melts between 38° and 42° C. (100.4°–107.6° F.). At higher temperatures it vaporizes, the vapor igniting and burning with a luminous, sooty flame. A solution of Wool Fat in chloroform (1 in 50), when poured upon the surface of concentrated sulphuric acid, gradually develops a deep brownish-red color at the line of contact of the layers. Dried to a constant weight on a water bath, with frequent stirring, Wool Fat loses not more than 0.5 per cent. of its weight (*water*). Incinerate about 1 Gm. of Wool Fat; not more than 0.1 per cent. of ash remains. The ash, if any, is not alkaline to moistened litmus paper (*alkalies and soaps*). Dissolve about 2 Gm. of Wool Fat in 10 mils of ether and add 2 drops of phenolphthalein T.S.; a colorless liquid is obtained (*free alkalies*) which, on the addition of 0.2 mil of tenth-normal potassium hydroxide V.S., develops a deep red color (*free fatty acids*). Boil about 1 Gm. of Wool Fat with 20 mils of alcohol, and filter the solution after cooling; the filtrate is not rendered more than slightly turbid by the addition of a few drops of saturated alcoholic solution of silver nitrate (*chlorides*). Melt about 10 Gm. of Wool Fat with 50 mils of distilled water on a water bath, with constant stirring; the fat separates completely on cooling, leaving the aqueous layer nearly clear and neutral to litmus. Separate portions of 10 mils each of the filtered aqueous layer leave no sweet residue on evaporation (*glycerin*), emit no ammonia vapors when boiled with 1 mil of potassium hydroxide T.S., and do not completely decolorize 0.05 mil of tenth-normal potassium permanganate V.S. within ten minutes (*soluble oxidizable impurities*). About 0.5 Gm. of Wool Fat dissolves completely in 40 mils of boiling dehydrated alcohol (*petrolatum*). Iodine value not less than 18 nor more than 28 (see Part III, Test No. 8)." *U. S.*

"A yellowish, tenacious, unctuous substance. Almost inodorous. Melting point about 40° C. (104° F.). When a solution of 0.1 gramme in a mixture of 5 millilitres of *chloroform* and 0.5 millilitre of *acetic anhydride* is gently poured upon the surface of 5 millilitres of *sulphuric acid* in a test-tube, a purplish-brown ring, the upper layer of which gradually becomes green, is developed at the surface of contact (presence of cholesterol). A solution of 0.2 gramme in 10 millilitres of *ether* remains colorless on the addition of 2 drops of *solution of phenolphthalein* (absence of free alkali), but becomes deep red on the addition of 1 drop of *N/1 solution of sodium hydroxide* (limit of free acid). Heated with *solution of sodium hydroxide* no ammoniacal odor is evolved (absence of organic nitrogenous matter). Ash not more than 0.3 per cent." *Br.*

Off. Prep.—Adeps Lanæ Hydrosus, *U. S., Br.*

ADEPS LANÆ HYDROSUS. U. S., Br.

HYDROUS WOOL FAT Adeps Lan. Hyd. [Lanolin]

(ăd'ĕps lā'næ hȳ-drō'sŭs)

"The purified fat of the wool of the sheep (*Ovis aries* Linné Fam. *Bovidæ*), combined with

not less than 25 nor more than 30 per cent. of water. Preserve it in a cool place in well-closed containers which are impervious to fat." *U. S.*

Lanoline; Lanolin, Adeps lanæ cum aqua, *P. G.*; Wasserhaltiges Wollfett, *G.*; Lanolina, *It., Sp.*

"Wool Fat, 70 grammes; Distilled Water, 30 millilitres. Mix." *Br.*

Properties.—Hydrous wool fat is officially described as "a yellowish-white, or nearly white, ointment-like mass, having not more than a slight odor. It is insoluble in water; with ether or chloroform it yields turbid solutions which are neutral to moistened litmus paper. Hydrous Wool Fat on heating separates into an upper oily and a lower aqueous layer. When heated on a water bath with stirring until it ceases to lose weight, there remains not less than 70 per cent. and not more than 75 per cent. of residue, which is transparent when melted, and when cold remains as a yellowish, tenacious, unctuous mass, completely soluble in ether or chloroform, and only sparingly soluble in alcohol. Hydrous Wool Fat thus deprived of water responds to the tests under *Adeps Lanæ*." *U. S.*

"10 grammes heated on a water-bath, with stirring, until the weight is constant, yield not less than 7 grammes of a residue which responds to the tests described under 'Adeps Lanæ.'" *Br.*

Uses.—As an ointment base wool fat has the following advantages over lard: it will absorb a larger quantity of water, it is less likely to become rancid, because of its stickiness it adheres more pertinaciously to the skin, and because of the difficulty in saponifying it it is less liable to be washed off. Because of its consistence it usually requires some thinning with cottonseed or other oil. It has been claimed for wool fat that it passes through the skin more readily than other ointment bases and is therefore especially suitable when it is desired to have medicaments absorbed. The fact, however, that this is a sebaceous secretion intended by nature to soften fibers of the wool and not for absorption, a priori would seem to render such a view improbable, and in the experiments of Sutton (*B. M. J.*, May 23, 1908) it was found that wool-fat penetrated the skin much less readily than did lard.

ADRENALINUM. Br.

ADRENALIN

(ăd-rĕn-ą-lĭn'ŭm)

"Adrenalin, or lævo-methylamino-ethanol-catechol, $C_9H_{13}NO_3$, may be obtained from the suprarenal glands of animals." *Br.*

Epinephrine, Suprarenalin, Suprarenin.

In 1897 Dr. John Abel (*J. H. H. B.*, July, 1897) separated from the suprarenal capsule the benzoyl-chloride of a base to which he gave the name epinephrine. The pure base was isolated in 1901 almost simultaneously by von Furth, who named it suprarenin, and Takamine, who named it *adrenalin*, the latter of whom patented the name and product. This substance was not admitted to the U. S. P. IX because of a direction by the U. S. P. Convention not to introduce into the text of the Pharmacopœia patented or proprietary products, but has been recognized by the British Pharmacopœia and by the U. S. P. IX Reagents (see Part III).

Properties.—It is described by the Pharmacopœia as "a light-brown, or nearly white, microcrystalline powder. Very slightly soluble in *water;* almost insoluble in *alcohol* (90 per cent.), in *ether*, and in *chloroform*. Combines with acids to form salts which are readily soluble in *water* and in *alcohol* (90 per cent.). Melts, with partial decomposition, between 205° and 212° C. (401° and 413.6° F.). Alkaline to moistened *litmus paper*. A diluted, slightly acid solution gives with a trace of *ferric chloride* an emerald-green color which is changed to purple or carmine by the cautious addition of a dilute solution of *sodium hydroxide;* readily reduces *solution of auric chloride;* gradually develops a characteristic unpleasant odor when a small quantity is mixed with five times its volume of *solution of sodium hydroxide;* yields no precipitate with *solution of potassio-mercuric iodide* (absence of most alkaloids). No appreciable ash." *Br.*

It has a slightly bitter taste and leaves a numb feeling on the tongue where it has been applied. Although its solutions readily undergo oxidation, in the dry form it is stable. It is easily soluble by dilute acids and by alkali hydroxides, forming salts, although not dissolved by ammonia or the carbonates. The alkaline solution absorbs oxygen very readily, in proportion to its alkalinity.

The following are some of the characteristic reactions: Ferric chloride colors adrenalin solution emerald green. A careful addition of caustic alkali to the green solution produced by ferric chloride, gives rise to the various shades of hue ranging from purple to carmine red, which are destroyed by careful neutralization with acids, restoring its original green color. Iodine as well as oxidizing agents, such as nitric acid, potassium bichromate and ferricyanide, etc., give a vivid pink.

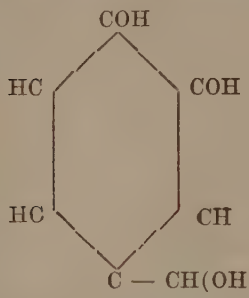
A sensitive color test for *adrenalin* has been proposed by Moreschi (*Gaz. Med. Ital.*, 1913, 41), as follows: A small amount of tincture of iodine is cautiously floated upon the suspected liquid. In the presence of adrenalin a pink ring will be formed at the zone of contact, which gradually spreads into the lower liquid and then rapidly disappears. On then adding a few mils of 1/1000 aqueous solution of sodium persulphate, a reddish or violet color will appear. This test will detect 1 part of adrenalin in two million of solution.

Gold chloride is very energetically reduced by adrenalin and a complete separation of the metal follows, from acid solution, by application of gentle heat; resultant liquid is colored pink or carmine red according to the strength of the solution used, as is the case with different oxidizing agents.

None of the following alkaloidal reagents pro-

duce precipitation: Mercuro-potassium iodide, picric acid, tannic acid, phosphomolybdic acid, phospho-tungstic acid, mercuric chloride, lead acetate, potassium bichromate, and platinum chloride.

As the result of much investigation into the nature of this substance it has been determined to be ortho-dioxyphenyl-ethanol-methyl-amine with the following structural formula:



In 1904 Stolz (*Ber. d. Chem. Ges.*, 1904, xxxvii, p. 4149) succeeded in preparing a compound synthetically which differed from the natural alkaloid only in being optically inert and much weaker physiologically. Flacher (*Z. P. C.*, 1908, lviii, p. 189) showed that the synthetic alkaloid consisted of two principles, one dextro- and the other lævo-rotatory, and Abderhalden and Mueller (*Z. P. C.*, lviii, p. 185, and lxii, p. 484) and Cushny (*J. P.*, 1908, xxxvii and xxxviii) have shown that the lævo-rotatory form was nearly fifteen times as active as the dextro-rotatory.

Epinephrin is a substance of extreme chemical sensitiveness especially easily affected by oxidizing agents, but also being destroyed by alkalies, free halogens, and the salts of easily reducible metals such as iron. Beckwith (*J. A. Ph. A.*, 1914, iii, p. 1547) has shown that if protected from light, heat, and air, solutions of epinephrin will retain their activity for long periods of time. He found that the presence of slight excesses of non-oxidizing acids had a preservative effect. Formaldehyde, he states, if present in as small amounts as one-tenth of 1 per cent. will destroy the activity of epinephrin in a few hours. According to Rowe (*A. J. Pharm.*, 1914, p. 145) boiling for a period of five minutes produces only an imperceptible amount of change in epinephrin solutions. After three boilings of five minutes each, however, there was a distinct loss of physiological activity.

The following method for separating this principle is given by Takamine (*A. J. P.*, 1901, p. 523): The comminuted suprarenal capsules are steeped in acidulated water for five hours at a temperature of from 50° to 80° C. (122°–176° F.) with frequent agitation. At the end of this time the temperature is raised to 95° C. (203° F.) for a period of an hour to coagulate albuminous matters. As the adrenalin is prone to absorb oxygen from the air it is necessary to avoid exposure of the liquid as much as possible; a layer of fat floating on the surface acts well for this purpose and at the same time has the effect of retarding evaporation of the water. The liquid portion is separated by straining and the precipitate expressed and afterwards steeped for several hours in a fresh quantity of acidulated water in order to extract any residual alkaloid. The two liquid portions are united and allowed to separate from the oil and then partially evaporated in a vacuum pan. To this concentrated solution about two or three times its own volume of strong ethyl or methyl alcohol is added which precipitates various inert substances which may be removed by filtration. The alcoholic solution is then partially evaporated and ammonia added until distinct alkalinity. After standing several hours a yellow brownish precipitate is formed which is an impure basic form of adrenalin. This precipitate is washed with water and dried and further purified by dissolving in dilute acid and adding alcohol and ether which precipitate the coloring matter and inorganic impurities. To the filtrate from this precipitation ammonia is added which precipitates the adrenalin as almost colorless crystals. They may be further purified by repetition of the same process.

Uses.—In 1895 Oliver and Schafer (*J. P.*, 1895, xviii) showed that the intravenous injection of the extract of the suprarenal capsules produced an enormous rise in the blood pressure. The rise of blood pressure, after sufficient doses, reaches an extraordinary height and is accompanied with a marked slowing of the pulse. It is due chiefly to a violent contraction of the arterioles which is brought about by the action of the drug upon the nerve endings in the walls of the blood vessels. Although the vascular contraction is the main factor, epinephrine also exercises a marked stimulant action upon the cardiac muscle. The slowing of the pulse which is produced by the drug is not seen if the pneumogastric nerves have been divided previous to the injection, and is probably a reflex inhibition from the excessive rise of pressure. Despite the great degree of the increase of arterial tension the duration is short, after moderate-sized doses not lasting more than five minutes. The injection of a second dose causes circulatory changes of precisely similar kind and extent as the first dose. The cause of this brevity of action is not definitely known, but is probably due to destruction of the drug, perhaps by the walls of the blood vessels themselves. So rapid is the disappearance of the drug from the circulation that its effects are entirely absent after administration by the mouth, and almost imperceptible after hypodermic administration; according to Meltzer and Auer, however, if it be thrown deeply into muscle tissue the effects are but slightly less marked than those following intravenous injection.

The action of epinephrine upon the vasomotor nerves seems to be part of a widespread action upon the nerves of organic life. As a result

of this action upon the sympathetic nerves, there is produced dilatation of the pupil, inhibition of intestinal peristalsis, more or less marked increase in the saliva, and powerful contraction of the pregnant uterus. It is probably also that its power to relax bronchial spasm is through an effect on the sympathetic nerves. Epinephrine in large quantities may give rise to a glycosuria apparently through an action upon the pancreas. (See Frugoni, *B. K. W.*, 1908, p. 1606.)

In 1903, Josué (*C. R. S. B.*, 1903, lv, p. 30), announced that the repeated injection of adrenaline into the rabbit produced a degeneration of the walls of the aorta more or less similar to that seen clinically in atheroma. This effect appears to be due largely to a direct irritant action on the internal coat of the artery, although it is possible that the extremely high blood pressure may be an adjuvant factor. The practical importance of this observation is made questionable by the fact that the arterial changes do not seem to occur in either the dog or cat.

Epinephrine is used in medicine for five distinct purposes: (1) For overcoming local congestions; (2) to check local hemorrhages; (3) as a general circulatory stimulant; (4) for the relief of asthmatic paroxysms, and (5) to cause contraction of the uterus. Each of these requires separate consideration.

While the local application of moderately concentrated solutions of epinephrine in acute inflammatory conditions, such as *conjunctivitis, rhinitis* and the like, will cause an immediate blanching of the part, and often a temporary cessation of the symptoms, it is very questionable if the method of treatment in any way shortens the duration or lessens the real severity of the disease. On the other hand in passive congestions—the so-called *chronic inflammations*—it is often a remedy of much service. Thus, in *hay fever,* it produces temporary relief, at least in a very large proportion of cases. In this connection also might be mentioned the use of epinephrine in prolonging and enhancing the action of the local anesthetics. This effect is probably the result of the stoppage in the local circulation.

For *hemorrhages* from regions to which it can be directly applied to the bleeding point, epinephrine is one of the most valuable remedies that we possess. Its action differs essentially from that of the true styptics, in that the latter act chiefly by coagulating the albumen of the blood, and thus leave behind a hard clot, which is often an objectionable feature, while the hemostasis after epinephrine is due solely to its contraction of the blood vessels. When the torn vessel is of large caliber, epinephrine is a less certain remedy than the older styptics. Although it has been largely used internally in the treatment of non-accessible hemorrhages, it is not demonstrated that its influence in these conditions is beneficial. Some ground is afforded for its use in internal hemorrhages by the findings of Cannon and Grey (*A. J. Phys.*, 1914, xxxiv) that small doses accelerate the coagulation of blood.

As a general circulatory stimulant the fugaciousness of the action of epinephrine limits its usefulness to the very acute forms of *circulatory failure,* such as *surgical shock, collapse* during anesthesia, and similar conditions. Although when injected hypodermically its effects are very slight, if thrown into the substance of a muscle (intramuscular injection) a very considerable degree of activity is obtained. Donaldson (*B. M. J.*, 1914, i, p. 476) has shown that five minims of a one to one-thousand solution so injected will produce in normal men a rise in the blood pressure of from 15 to 45 millimeters, and according to Miller (*J. A. M. A.*, 1908) the rise lasts from one-half to three-quarters of an hour. In cases of degeneration of the heart muscle the drug must be used with great caution as the strong vascular constriction throws an intense strain upon the heart.

In bronchial *asthma* the intramuscular injection of epinephrine will nearly always cause an immediate arrest of the paroxysm. Unfortunately in many instances the relief is only temporary, lasting perhaps an hour or two. According to Ephrain (*D. M. W.*, 1912), however, if the solution is applied directly to the bronchial mucous membrane the effects are much more lasting. When, however, the asthma is dependent upon heart disease it should never be used because the sudden increase in arterial resistance may be sufficient to overcome the resistance of the enfeebled heart. Fredericia (*J. A. M. A.*, Feb. 5, 1916) has reported two deaths following the use of epinephrin for the relief of asthma which had been mistakenly diagnosed as bronchial when it was really of cardiac origin. In cases where evil effects are greatly to be feared from the arterial spasm, it is well to guard the drug with nitroglycerin.

When applied either locally or injected internally, epinephrine causes a violent spasm of the uterus. Although, according to Neu (*Archiv. f. Gynekol.*, 1909, lxxv, p. 618), this occurs in the human being either in the pregnant or non-pregnant condition, the drug is not to be recommended for general uterine hemorrhages, but is of great value in the treatment of *post-partum hemorrhages.*

Various preparations containing epinephrine, as well as the alkaloid itself, have been used, with apparent benefit, in the treatment of *osteomalacia* and also *rickets.*

To obtain its systemic effects epinephrine must be given either intravenously or intramuscularly; ordinary hypodermic injections will not serve the purpose.

The *dose* of epinephrine is from one-two hundredth to three two-hundredths of a grain (0.0003–0.0009 Gm.) or as commonly expressed from 5 to 15 minims (0.3–1 mil) of the one to one thousand solution.

As a local application, epinephrine may be used in strengths of from 1 in 10,000 up to 1 in 1000.

The number of proprietary brands of epinephrine on the market is very large. The more important of these include: *Adnephrin, adrenaline, adrenamine, epirenan, hemisine, hemostatin, paranephrin, renalina, supracapsulin, suprarenalin, supranephrane,* and *suprarenin.*

ÆTHER. U. S. (Br.)

ETHER

(æ'thẹr)

"A liquid containing not less than 95.5 per cent. nor more than 97.5 per cent. of ethyl oxide [$(C_2H_5)_2O = 74.08$], the remainder consisting of alcohol containing a little water. Preserve it in partially filled, well-closed containers, in a cool place, remote from fire, and protected from daylight. When Ether is to be used for anesthesia it is to be dispensed only in small, well-closed containers and is not to be used for this purpose if the container has been opened longer than twenty-four hours." *U. S.* "Ether, also known as ethylic ether, $C_4H_{10}O$, may be obtained by distilling a mixture of ethylic alcohol or industrial methylated spirit and sulphuric acid, and rectifying the distillate. It should be preserved in a cool dark place." *Br.*

Æther Purificatus, *Br.,* Purified Ether; Stronger Ether; Æther sulphuricus, *Ed., Dub.;* Ether, Hydric Ether, Sulphuric Ether, Naphtha Vitrioli, Hydrate of Ethylen, Oxide of Ethyl; Ethoxyethane; Ether officinal, Ether pur, *Fr. Cod.;* Ether, Ether hydrique, ou vinique, ou sulphurique, *Fr.;* Aether, *P. G.;* Reiner Aether, Schwefeläther, *G.;* Etere, *It.;* Eter, Eter sulfurico, *Sp.*

The U. S. Pharmacopœia of 1880 recognized Æther containing about 74 per cent. of ethyl oxide and Æther Fortior containing about 94 per cent. of ethyl oxide. The present Æther of the U. S. Pharmacopœia replaces the Æther Fortior of the U. S. P., 1880, the Æther of the U. S. P., 1880, being dropped, as its deficient strength rendered it of little use. The Æther Purificatus of the British Pharmacopœia and the Æther of the U. S. Pharmacopœia IX are practically identical in strength. The British purified ether on account of its having the alcohol removed by washing with water, is sometimes termed *Æther Lotum,* or washed ether. It still contains a trace of water.

Preparation.—A process for preparing ether upon the small scale was given in the U. S. P., 1870, and a former British Pharmacopœia, (see *U. S. D.,* 18th ed., p. 118), but it was properly abandoned by both Pharmacopœias, as the production of this inflammable and very volatile liquid should be undertaken only in buildings properly safeguarded, and it is now made of excellent quality on a large scale with special apparatus. Ether was made officially by the action of sulphuric acid upon alcohol, in a glass flask, at a temperature ranging between 130° C. (266° F.) and 137.7° C. (279.8° F.), the distillate being afterwards rectified to remove impurities.

In the apparatus employed by E. R. Squibb the ether is made in one operation; the vapors of ether and unchanged alcohol are first washed by a solution of caustic potash maintained at a temperature above the boiling point of alcohol, the alcoholic vapor is then condensed in a worm condenser kept at a suitable temperature and runs back into the still, while the ether vapor, retaining about 4 per cent. of alcohol, is condensed in a well-cooled apparatus. Three hundred and sixty pounds of concentrated sulphuric acid are sufficient to etherify 120 barrels of clean spirit; the acid has then to be changed, chiefly because the impurities of the spirit render the mixture dark and tarry and liable to froth in the still. (*Ephem.,* ii, p. 590.) Kraft proposes to manufacture ether by heating alcohol in contact with the alkyl esters of sulphonic acid. He states that benzene-sulphonic acid under favorable conditions is capable of converting several thousand times its weight of alcohol into ether. The advantage claimed for this method is greater purity of the resulting ether. (*Chem. Ztg.,* 1893, 1876.) Methionic acid, $CH_2(HSO_3)_2$, is used in manufacturing ether under the patents of Schroeter and Sondag. In Senderens' process the alcohol vapor is transformed into ether by passing it over alumina (Al_2O_3) heated to exactly 260° C. (500° F.). Ekenberg purifies ether by mixing it with 5 or 10 per cent. of liquid paraffin, which has a boiling point of about 300° C. (572° F.), and distilling at a temperature of from 40° to 50° C. (104°–122° F.). The liquid paraffin holds the impurities and permits the pure ether to distil over. (*Chem. Ztg.,* 1894, 1240.)

Properties of Ether.—In considering the properties of ether it is necessary to draw a sharp distinction between the official ethers of the two Pharmacopœias. The term Ether (Æther) is used now (1917) for the second grade ether (sp. gr. 0.735) of the British Pharmacopœia as well as for the only ether now recognized by the U. S. Pharmacopœia [sp. gr. 0.713–0.717 at 25° C. (77° F.)]; this latter corresponds with the Purified Ether (Æther Purificatus) of the British Pharmacopœia, which has the sp. gr. 0.720 at 15.6° C. (60° F.). Ether of the U. S. Pharmacopœia IX is described as follows: "A transparent, colorless, mobile liquid, having a characteristic odor, and a burning and sweetish taste. It is soluble in about 12 times its volume of water at 25° C. (77° F.) with slight contraction of volume. Miscible with alcohol, chloroform, petroleum benzin, benzene, or fixed or volatile oils. The color of light blue litmus paper, moistened with water, is not changed to red when the paper is immersed in Ether for ten minutes. Specific gravity: 0.713 to 0.716 at 25° C. (77° F.). Boiling point: about 35° C. (95° F.). Ether is highly volatile and inflammable. Its vapor when mixed with air and ignited may explode violently. It is slowly oxidized by the action of air, moisture, and sun-light with the formation of peroxides. The moist residue left on the spontaneous evaporation of 30 mils of Ether from a shallow dish is odorless and neither reddens nor bleaches blue litmus paper. Dried at 100° C. (212° F.) this residue does not exceed 0.001 Gm. Pour 10 mils of Ether in portions upon clean, odorless blotting paper and allow

it to evaporate spontaneously. No foreign odor is perceptible when the last traces of Ether leave the paper. Shake 10 mils of Ether occasionally during one hour with 1 mil of potassium hydroxide T.S. in a glass-stoppered container, protected from light; no color is developed in either liquid (*aldehyde*). Shake 10 mils of Ether occasionally during one hour with 1 mil of a freshly made solution of cadmium and potassium iodide (1 in 10), in a glass-stoppered cylinder previously rinsed with the Ether under examination and protected from light; no color develops in either liquid (*peroxides*)." *U. S.*

Under the title "Ether" the British Pharmacopœia gives the following description:

"A colorless, very volatile and inflammable liquid. Odor and taste strong and characteristic. Slightly soluble in *water;* miscible in all proportions with *alcohol* (90 per cent.), *chloroform,* and fixed and volatile oils. Specific gravity 0.720. Boiling point from 34° to 36° C. (93.2°–96.8° F.). Its vapor mixed with air is explosive in contact with flame. 5 millilitres, on spontaneous evaporation in a glass dish, leave a film of moisture which does not redden or bleach *blue litmus paper* (absence of free acid, sulphurous acid)." *Br.*

The British Pharmacopœia gives the following tests for purified ether: "Purified Ether possesses the characters and responds to the tests described under 'Æther,'" with the following requirements in addition: "Kept in contact with *potassium hydroxide* freshly broken into small fragments, in a well-stoppered white glass bottle in the dark, no yellow coloration is developed within one hour. Mixed with one-tenth of its volume of freshly prepared *solution of potassium iodide,* it does not develop a yellow color within three hours when kept in a completely filled white glass stoppered bottle in the dark and frequently shaken. Yields no reaction with the following test for methyl compounds: Well shake 2 volumes of the Purified Ether in a separating funnel with 1 volume of *alcohol* (20 per cent.) and 1 volume of *water,* allow the mixture to separate, and draw off the lower layer. Mix 5 millilitres of this lower layer in a wide test-tube with 2.5 millilitres of an aqueous solution (1 in 50) of *potassium permanganate* and 0.2 millilitre of *sulphuric acid.* At the end of three minutes add to the contents of the tube 0.5 millilitre of an aqueous solution (9.6 in 100) of *oxalic acid,* followed by 1 millilitre of *sulphuric acid,* and then by 5 millilitres of *decolorised solution of fuchsin;* mix thoroughly and set aside for twenty minutes. No violet color is produced (absence of methyl compounds)." *Br.*

Commercial ether, which is sometimes used as a solvent, varies in sp. gr. from 0.733 to 0.765. The impurities found in it are excess of alcohol, water, sulphurous and other acids, heavy oil of wine, and various fixed substances.

The ether of U. S. P., 1880, had the sp. gr. 0.750; if heavier than this, it must contain too much alcohol or water. The statement that water takes up only one-tenth of ether, when equal volumes of ether (sp. gr. 0.750) and water are shaken together in a graduated tube, has been shown by Squibb to be erroneous. If it take up more than one-fourth, the ether must contain an excess of alcohol or water, or of both. If the alcohol be in excess, it may be removed by agitating the liquid with twice its bulk of water, which unites with the alcohol, forming a heavier stratum, from which the ether may be poured off. The ether, however, takes up about one-tenth of water, which may be removed by agitation with freshly burned lime, and subsequent distillation. An easy method for detecting and measuring any alcohol present in ether was given by the Edinburgh College; namely, to agitate it, in a graduated cylinder, with half its volume of a concentrated solution of calcium chloride. This will remove the alcohol and the reduction of the volume of the ether, when it rises to the surface, will indicate the amount.

The extreme volatility of ether causes it to evaporate speedily in the open air, with the production of considerable cold. Its inflammability is very great, and the products of its combustion are water and carbon dioxide. In consequence of this property the greatest care should be used not to bring it in the vicinity of a naked flame. One of the great advantages of using steam as the source of heat is that it obviates, in a great measure, the danger of its accidental inflammation. When too long kept it undergoes decomposition, and is converted in part into acetic acid and organic peroxides. It dissolves iodine and bromine freely, and sulphur and phosphorus sparingly. Its power to dissolve corrosive sublimate makes it a useful agent in the manipulations for detecting that poison. It is also a solvent of volatile and fixed oils, many resins and balsams, tannic acid, caoutchouc, and most of the vegetable alkaloids. It does not dissolve potassium or sodium hydroxide, in which respect it differs from alcohol. Ether unites in all proportions with alcohol. According to R. Boettger, water may be detected in ether by agitating the suspected liquid with carbon disulphide; if water be present the mixture becomes milky and turbid, otherwise it remains clear. Stefanelli (*Ber. d. Chem. Ges.,* 8, 439) proposed to shake ether with a small fragment of aniline-violet, which does not impart color to ether free from alcohol. One per cent. of alcohol may be thus detected. A delicate test for the presence of alcohol in ether is that of Lieben, founded on the formation of iodoform by alcohol but not by ether. (See p. 106.) The mere keeping of ether in the presence of moisture is said to generate sufficient alcohol to produce the reaction. (Allen, *Com. Org. Anal.,* 2d ed., i, p. 125.) Ether is usually made anhydrous by allowing it to remain in contact with dry calcium chloride or by distilling it with a small quantity of metallic sodium in a flask or retort.

On filtering an ethereal liquid with free access of air, a frost-like congelation is observed on the upper part of the filter, its appearance and

quantity depending upon the temperature and the hygrometric state of the atmosphere. Tanret has collected some of this *ether hydroxide,* and found that after it had been completely freed from ether by strongly blowing upon it, it had the temperature −3.5° C. (25.7° F.), and on fusion yielded 17 to 18 parts of water for 37 of ether; the formula $(C_2H_5)_2O,2H_2O$ requires 18 parts.

Composition and Theory of Its Production.—The empirical formula of ether is $C_4H_{10}O$, and this is the result both of analysis and of a determination of its vapor density, whereby the molecular weight is established. This formula, however, is better understood when we examine the conditions of its formation. Ether is then found to be the oxide of ethyl (C_2H_5). This is the group which gives character to common alcohol and all its salts, whether with organic or inorganic acids. The group C_2H_5 acts as a monad radical, and common alcohol is its hydroxide, C_2H_5,OH. Its oxide then should be $(C_2H_5)_2O$, and all the reactions by which ether is produced show it to be this oxide. It is commonly formed from common alcohol (ethyl hydroxide) by the action of sulphuric acid, according to the following reactions:

$$C_2H_5OH + SO_2OH.OH = SO_2OH.OC_2H_5 + HOH$$

that is, alcohol reacting with sulphuric acid yields ethyl-sulphuric acid (sulphovinic acid) and water. In the presence of an excess of alcohol and at the proper temperature the ethyl-sulphuric acid then reacts with another molecule of alcohol, as follows:

$$C_2H_5OH + SO_2OH.C_2OH_5 = C_2H_5OC_2H_5 + SO_2OH.OH$$

whereby ethyl oxide (ether) is formed, and sulphuric acid is regenerated. These reactions take place best at a temperature of about 140° C. (284° F.), and if the mixture in the still is kept at this temperature a steady stream of alcohol can be converted into ether, whence the process has been called "the continuous etherification process."

Uses.—As early as 1805, inhalations of ether were recommended by Warren, of Boston, to relieve pulmonary distress in advanced *phthisis,* and in 1812 ether intoxication by inhalation is said to have been frequently practiced. It seems to have been first used as anesthetic by Dr. C. W. Long, of Georgia, but it was not until October, 1846, that Warren, at the instance of W. T. G. Morton, of Boston, used ether as a surgical anesthetic at the Massachusetts General Hospital and made its value public knowledge. A few days subsequently, C. T. Jackson, of Boston, claimed to have first made known to Morton the use of ether for the prevention of pain in dental operations.

Locally, ether is a violent irritant. It is absorbed through the lungs with very great rapidity, and less quickly, but with equal certainty, through the mucous membrane of the gastro-intestinal tract, and is eliminated through the lungs.

Ether is predominantly a paralyzant to the central nervous system affecting first the cerebral centers, then the spinal cord, and at last the vital centers in the medulla. The condition of surgical anesthesia is really one of advanced poisoning which is made reasonably safe only by the fact that the vital centers are involved so late and that the volatility of the ether allows it to be rapidly eliminated through the lungs. Although eventually both sensory and motor apparatus are paralyzed, the effect occurs much earlier in the sensory side of the organism than in the motor. The action upon the circulation is of relatively minor importance, although it is probable that this drug affects the circulatory apparatus much as does alcohol; that is, after small doses there is a slight stimulation of the heart with dilatation of the peripheral blood vessels and generally a slight increase in the blood pressure. After large doses both the heart and vascular system are depressed and the arterial tension greatly reduced. When pushed to a fatal termination ether poisoning nearly always causes death from respiratory failure.

As a practical anesthetic, ether is inferior to chloroform in being distinctly slower in action, more disagreeable to the patient by producing greater excitement and in being more apt to cause prolonged nausea and vomiting after its use. Statistics show, however, that the proportion of deaths due to chloroformization is four to five times greater than after etherization; and only in rare circumstances is the surgeon justified for the sake of convenience in selecting the more dangerous anesthetic.

It being impossible in the space which can be allotted to the subject in the present work to discuss to any advantage the subject of etherization, either in its general, theoretical, or practical aspects, the reader is referred to H. C. Wood, Jr.'s *Textbook of Pharmacology.*

Given by the mouth, ether may be used in *nausea* dependent upon gastric depression, in excessive *flatulence,* especially when attended by colic, and in *gastrodynia.* It has also been administered in the treatment for *gall stones* with the belief, probably not well founded, that it would aid in the solution of the stones. As a constituent of Hoffmann's anodyne it is much used as a stimulant antispasmodic. For administration by the mouth it is best given floating on ice-cold water, though it is sometimes administered in capsules under the name of *pearls,* and a syrup of ether is recognized by the French Codex. According to Regnault and Adrian, the best syrup of ether is to be made by shaking together in a bottle 440 parts of sugar, 490 parts of distilled water, 50 parts of alcohol (sp. gr. 0.833), 20 parts of ether. If the parts taken are represented by grains the formula would give one full dose of the narcotic.

Dose, half to one fluidrachm (1.8–3.75 mils).

ÆTHER ACETICUS. Br.

ACETIC ETHER Æth. Acet. [Ethyl Acetate]

(æ'ther ą-cĕt'ĭ-cŭs)

"Acetic Ether is a liquid obtained by distilling a mixture of ethylic alcohol, acetic acid, and sulphuric acid, and purifying the product. It contains not less than 90 per cent. of ethyl acetate, $C_2H_5C_2H_3O_2$." *Br.* "A liquid containing not less than 96 per cent., by volume, of $C_4H_8O_2$ or $CH_3CO.OC_2H_5$ (88.06), the remainder consisting of alcohol and a little water. Preserve it in well-stoppered bottles, in a cool place, remote from fire and protected from light." *N. F.*

Naphtha Aceti; Ethyl Acetate; Ether acétique, Acétate d'éthyl, *Fr. Cod.*; Naphte acétique, *Fr.* Aether aceticus, *P. G.*; Essigäther, Essignaphtha, *G.*; Etere acetico, *It.*; Eter acetico, *Sp.*

Acetic ether is not official in the U. S. IX. The Br. Pharm., 1914, and N. F. IV retain it.

Preparation.—A process for preparing this ether will be found in a former British Pharmacopœia (1885). It is a modification of the process recommended by W. I. Clark (*P. J.*, 1883, p. 777), and is as follows: "Take of Rectified Spirit, 32¼ fluidounces [Imp. meas.]; Sulphuric Acid, 32½ fluidounces [Imp. meas.]; Acetate of Sodium, 40 ounces [av.]; Carbonate of Potassium, freshly dried, 6 ounces [av.]. To the spirit slowly add the acid, keeping the fluid cool, and, the product being cold, add the acetate, mixing thoroughly. Distil forty-five fluidounces [Imp. meas.]. Digest the distillate with the carbonate of potassium for three days in a stoppered bottle. Separate the ethereal fluid, and again distil until all but about four fluidounces have passed over. Preserve the resulting acetic ether in a well-closed bottle and in a cool place." *Br.*, 1885. In addition to this method, acetic ether may be made by several processes, the chief of which are the following: 1. Mix 100 parts of alcohol (sp. gr. 0.83) with 63 parts of concentrated acetic acid, and 17 parts of strong sulphuric acid, and distil 125 parts into a well cooled receiver. 2. Distil to dryness a mixture of three parts of sodium acetate, three of alcohol, and two of sulphuric acid, mix the distilled product with one-fifth of sulphuric acid, and distil a second time an amount of ether equal to the alcohol employed. 3. Distil two parts of efflorescent lead acetate with one part of alcohol and a little more than one part of sulphuric acid. In the last two processes, the acetic acid is set free by the action of the sulphuric acid on the acetate employed. J. A. Pabst has devised a process for acetic ether in imitation of that for the preparation of common ether. Fifty mils of sulphuric acid and the same quantity of alcohol are heated together in a retort to 140° C. (284° F.), and then a mixture of one liter of 96 per cent. alcohol and one liter of acetic acid (93 per cent.) is allowed to flow in slowly. At first some ethyl ether goes over, and then a liquid which contains, with considerable uniformity, 85 per cent. ethyl acetate. The reaction takes place between 130° C. (266° F.) and 135° C. (275° F.); at 145° C. (293° F.) some sulphurous acid is produced. The yield is about 1350 grammes, or 78 per cent., which is 90 per cent. of the theoretical amount. The methyl acetate can be prepared exactly as the ethyl compound, but in the attempt to prepare the amyl acetate in an analogous manner, side reactions were found to interfere. In order to study the proportional power of combination possessed by the two alcohols, Pabst allowed a mixture of 100 mils methyl alcohol and 100 mils acetic acid to flow into a mixture of 50 mils sulphuric acid and 50 mils ethyl alcohol. The first distillates contained essentially methyl acetate and the latter pure ethyl acetate. In the flask were found remaining nearly equal amounts of sulphuric and ethyl-sulphuric acids, and in addition alcohol, acetic acid, and some residual ethyl acetate. (*Bull. Soc. Chim.*, vol. xxxiii, pp. 350, 351; *A. J. P.*, 1880.)

Ethyl acetate often forms in galenical preparations which contain both acetic acid and alcohol in the menstruum and which have been allowed to stand for some time. This sometimes is a disadvantage, for it causes differences between a freshly made and an old preparation which require an explanation when a change is made from one to the other, as in refilling a prescription.

Properties.—The British Pharmacopœia (1914) describes it as "a colorless liquid with a fragrant odor. Soluble in all proportions in *alcohol* (90 per cent.), in *ether* and in *chloroform*, and in not less than 11 parts of *water*. Specific gravity 0.900 to 0.907 at 15.5° C. (59.9° F.). Moistened *blue litmus paper* introduced into it is not immediately reddened. A little allowed to evaporate from filter paper leaves no extraneous odor. When carefully poured over *sulphuric acid* no dark ring is formed within fifteen minutes at the surface of contact. Contains not less than 90 per cent. of ethyl acetate as determined by the following process: Introduce about 5 grammes into a tared stoppered flask, weigh, and make up to 100 millilitres with *water*. Transfer 10 millilitres of this solution to a titration flask and neutralise with *N/1 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator. Then add 20 millilitres of the alkaline solution, set aside for five minutes, rotating occasionally, dilute with *water* and titrate back with *N/1 solution of sulphuric acid*. Deduct from 20 the number of millilitres of the acid solution required. Each millilitre of the difference corresponds to 0.088 gramme of ethyl acetate." *Br.*

The National Formulary IV describes it as "a transparent, colorless liquid, of a fragrant and refreshing, slightly acetous odor, and a peculiar acetous and burning taste. Specific gravity: 0.887 to 0.895 at 25° C. (77° F.). One mil of Acetic Ether is soluble in about 10 mils of water at 25° C. (77° F.); miscible with alcohol, ether, or fixed or volatile oils. It does not immediately redden blue litmus paper. Boiling point: from 72° to 77° C. (161.6°–170.6° F.).

Acetic Ether is readily volatilized, even at a low temperature. It is inflammable, burning with a yellowish flame and an acetous odor. No weighable residue remains on evaporating 10 mils of Acetic Ether. Allow 10 mils of Acetic Ether to evaporate spontaneously from clean, odorless blotting paper; the final odor does not resemble that of pineapple (*butylic or amylic derivatives*). Pour carefully 2 mils of Acetic Ether on 10 mils of sulphuric acid; no dark ring is developed at the point of contact of the two layers within fifteen minutes (*readily carbonizable organic impurities*). Mix 20 mils of Acetic Ether with a solution of 20 Gm. of sodium hydroxide in 50 mils of distilled water, allow the mixture to stand, agitating occasionally, or heat it gently under a reflux condenser, until a homogeneous liquid results, and then distil about 25 mils. This distillate complies with the Test for absence of methyl alcohol under *Alcohol* in the U. S. Pharmacopœia IX. Shake 25 mils of Acetic Ether in a graduated tube, with 25 mils of distilled water just previously saturated with Acetic Ether; the ethereal layer when separated measures not less than 24 mils (*undue proportion of alcohol or water*)." *N. F. IV.*

With reference to the solubility of acetic ether in saturated calcium chloride solution, it is to be remarked that pure acetic ether is not dissolved, except when it is mixed with 90 per cent. alcohol. One volume acetic ether, one volume alcohol, and two volumes calcium chloride solution give a homogeneous liquid.

Uses.—Acetic ether is occasionally used in medicine as a stimulant and antispasmodic. Its action upon the system is probably very similar to that of ether; but as it is less volatile it is less rapidly absorbed and eliminated, and consequently is much less prompt and fugacious in its influence than is ether. It is locally irritating. H. C. Wood found it to be capable of being used as an anesthetic, but to be too slow in its action for practical purposes. It is sometimes employed externally, by friction, as a resolvent, and for *rheumatic pains*.

Dose, fifteen to fifty minims (0.9–3.1 mils).

ÆTHYLIS CARBAMAS. U. S.

ETHYL CARBAMATE Æthyl. Carbam.

(æ'thyl-is cär'ba-mas)

"The ethyl ester [$C_3H_7O_2N$ or $CO(OC_2H_5)NH_2 = 89.07$] of carbamic acid. Preserve it in well-closed containers." *U. S.*

Ethyl urethane, Urethane; Uréthane, *Fr.*; Carbaminsäureaethylester, Aethyl-urethan, Urethan, *G.*; Uretano, Eter Carbamico, *Sp.*

Ethyl carbamate was introduced into the U. S. Pharmacopœia VIII and retained in the U. S. P. IX. It is made by allowing ammonia to act upon ethyl carbonate, when urethane and ethyl alcohol are produced, or by heating urea nitrate with alcohol to from 120° to 130° C. (248°–266° F.), resulting in the formation of ethyl carbamate and ammonium nitrate.

Properties.—It is officially described as in "colorless, columnar crystals or scales, odorless, and having a cooling, saline taste. One Gm. of Ethyl Carbamate dissolves in 0.45 mil of water, 0.8 mil of alcohol, 2.5 mils of glycerin, 0.9 mil of chloroform, 1.5 mils of ether, and in 32 mils of olive oil, at 25° C. (77° F.). Its aqueous solution (1 in 20) is neutral to litmus. Ethyl Carbamate melts between 48° and 50° C. (118.4° and 122° F.). Add 1 Gm. of Ethyl Carbamate to 5 mils of sulphuric acid and heat it gently; decomposition follows with the evolution of carbon dioxide (alcohol and acid ammonium sulphate remain in solution). Heat 1 Gm. of Ethyl Carbamate with 5 mils of concentrated potassium hydroxide solution; ammonia gas is given off, recognizable by its odor. Dissolve about 0.5 Gm. of Ethyl Carbamate in 5 mils of distilled water with about 1 Gm. of dry sodium carbonate and about 0.01 Gm. of iodine, and warm the solution; yellow crystals of iodoform separate on cooling. Incinerate about 2 Gm. of Ethyl Carbamate; not more than 0.05 per cent. of ash remains. Dissolve about 2 Gm. of Ethyl Carbamate in 2 mils of distilled water and add 5 mils of nitric acid to the solution; no white precipitate is produced (*urea*). Not more than slight opalescence results from the addition of a few drops of silver nitrate T.S. to 10 mils of an aqueous solution of Ethyl Carbamate (1 in 20) (*chloride*). Mix 2 mils of the aqueous solution (1 in 20) with 1 mil of ferrous sulphate T.S. and pour the mixture upon 2 mils of sulphuric acid, so as to form a separate layer; no red or brown zone appears (*nitrate*)." *U. S.* When it is heated with ammonia to 180° C. (356° F.), urea is formed.

Uses.—Ethyl carbamate is one of the safest of the somnifacient drugs. In therapeutic doses it has no perceptible effect upon the respiration or circulation, its physiological action being limited almost solely to a depressant influence upon the cerebrum, although large doses also have a depressant influence upon the motor areas in the spinal cord. In ordinary quantities it does not lessen the susceptibility to pain, but toxic doses will produce a condition of anesthesia. In the lower animals, after fatal doses, the respiration becomes slower, there is complete unconsciousness, loss of reflexes, fall of body temperature, and some depression of the circulation, death being due to asphyxia. Although in the milder forms of *insomnia* its freedom from toxicity makes it a very useful remedy, in severe cases its action is uncertain. According to Rappoport (*Z. E. P. T.*, 1911, ix, p. 39) it greatly enhances the narcotic effects of opiates and bromides. It has also been used by Jackman and others (*L. L.*, June, 1886) in various forms of *convulsions*.

Dose, fifteen to forty-five grains (1–3 Gm.).

ÆTHYLIS CHLORIDUM. U. S. (Br.)

ETHYL CHLORIDE *Æthyl. Chlor.*

(æ'thyl-ĭs ȼhlō'rĭ-dŭm)

"Monochlorethane [C_2H_5Cl or CH_3CH_2Cl = 64.50]. Preserve it in hermetically sealed containers, in a cool place, remote from fire, and protected from light." *U. S.* "Ethyl Chloride, C_2H_5Cl, may be obtained by the action of hydrochloric acid on ethylic alcohol or on industrial methylated spirit; in the latter case it will contain a small but variable proportion of methyl chloride, CH_3Cl." *Br.*

Ethyl Chloridum, *Br.;* Hydrochloric ether; Chlorethyl, Monochlorethane; **Ethylum** chloratum, Æther chloratus; Chlorure d'éthyle, Ether hydrochlorique, *Fr.;* Aethylchlorid, Chlorwasserstoffäther, Chloräthyl, *G.*

Preparation.—Ethyl chloride was discovered by Rouelle, but first obtained in sufficient quantities to permit the examination of its properties by Basse. It may be procured by several processes, but the following is recommended. Distil a mixture of equal measures of concentrated hydrochloric acid and alcohol, and receive the product, by means of a curved glass tube, in a tubulated bottle, half filled with water at a temperature between 21.1 °C. (70° F.) and 26.6° C. (80° F.), and connected by means of a second tube with another bottle, loosely corked, and surrounded by a mixture of common salt with snow or pounded ice. The ethyl chloride, as it enters the first bottle, is mixed with alcohol and acid, which are retained by the water; while the pure ether passes forward, and is condensed in the refrigerated bottle. It must be kept in strong bottles, well secured with ground stoppers covered with leather or in sealed containers. Before being opened, the bottle should be cooled to the freezing point.

Properties.—Like common ether and ethyl nitrite, it dissolves sulphur, phosphorus, the fixed and volatile oils, and many other substances. It consists of one atom of chlorine combined with the monatomic radical or group C_2H_5, *ethyl,* and its composition is sufficiently shown by the reaction for its production:

$$C_2H_5OH + HCl = C_2H_5Cl + H_2O$$

It is officially described as follows: "When liberated at ordinary room temperature from its sealed container Ethyl Chloride vaporizes at once; *the gas is very inflammable, and must not be used in proximity to fire.* At low temperatures or under pressure Ethyl Chloride is a colorless, mobile, very volatile liquid, having a characteristic, ethereal odor, and a burning taste. It is slightly soluble in water, freely soluble in alcohol and in ether. Specific gravity: about 0.921 at 0° C. (32° F.). Ethyl Chloride boils between 12° and 13° C. (53.6°–55.4° F.). It burns with a smoky, greenish flame, with the production of hydrogen chloride. Dissolve about 1 mil of Ethyl Chloride in 20 mils of alcohol, both previously cooled to the temperature of melting ice, and add a few drops of silver nitrate T.S.; no turbidity is produced at once (*hydrochloric acid*). Shake 10 mils of Ethyl Chloride with 10 mils of distilled water, both previously cooled to the temperature of melting ice, and allow the supernatant stratum of Ethyl Chloride to evaporate spontaneously. The residual liquid is neutral to litmus, and on adding to it a few drops of potassium dichromate T.S., followed by some diluted sulphuric acid, and boiling the mixture, no odor of aldehyde is developed, and no greenish or purplish color is produced in the liquid (*alcohol*). On the spontaneous evaporation of 5 mils of Ethyl Chloride, no foreign odor is noticeable while the last portions evaporate and no weighable residue remains." *U. S.*

"Gaseous at normal temperature and pressure, but as usually supplied it is condensed into a colorless, mobile, inflammable, and very volatile liquid. Odor pleasant and ethereal, not alliaceous; if kept in vessels provided with rubber fittings, it may acquire a slight odor of rubber. Specific gravity at 0° C. (32° F.), 0.920 to 0.960. *Water* which has been shaken with twice its volume of liquid Ethyl Chloride is neutral to *litmus,* and gives no opalescence or precipitate with *solution of silver nitrate* (absence of sulphur dioxide and of hydrochloric acid). *Sulphuric acid* does not become colored when shaken with ten times its volume of liquid Ethyl Chloride and, after separation and dilution with an equal volume of *water,* has no unpleasant odor, or odor of ether, and does not become turbid on the addition of *solution of silver nitrate* (absence of ether, empyreumatic matter, and certain other substances). When 0.4 gramme is saponified by heating in a stoppered bottle in a water-bath with 10 millilitres of *N/1 alcoholic solution of potassium hydroxide,* the liquid requires for neutralisation not more than 38.2 millilitres of *N/10 solution of sulphuric acid,* corresponding to a proportion of not less than 99.5 per cent. by weight of esters calculated as ethyl chloride, C_2H_5Cl." *Br.*

Uses.—Ethyl chloride is so extremely volatile that when sprayed upon the skin it absorbs sufficient heat in its vaporization to cause superficial freezing in the area to which it is applied. This freezing destroys functional activity of the peripheral nerve endings and therefore the application of ethyl chloride produces local anesthesia. It is used for this purpose for a large variety of conditions where a short and superficial anesthesia is desired as, for instance, in inserting trocar, for the removal of fluid, and for the application of cautery. This method of anesthesia has also been applied for opening boils and abscesses, but is not to be recommended as it more or less interferes with the nutrition of the part. Seidelin (*L. L.,* 1913, i, 1663) destroys superficial epithelioma by freezing them with ethyl chloride. Ethyl chloride has also been used by inhalation as a general anesthetic. Its action in this regard is extremely rapid and fugacious, comparable to that of nitrous oxide, but it is a much more dangerous anesthetic. The statements concerning the mortality after ethyl chloride anesthesia have been extremely varied. In

a critical study of the statistics of fifty thousand cases H. C. Wood, Jr. (*J. A. M. A.*, 1910, lv) reaches the conclusion that the death rate is in the neighborhood of one in six thousand anesthesias. It is perhaps less dangerous than chloroform but is certainly less safe than ether. In its physiological action it closely resembles chloroform, although it is less powerfully depressant to the heart. On account of its great inflammability it should not be used near a light or flame.

Dose, five to ten minims (0.3–0.6 mil) in alcoholic solution.

ÆTHYLMORPHINÆ HYDROCHLORIDUM U. S.

ETHYLMORPHINE HYDROCHLORIDE

Æthylmorph. Hydrochl. [Ethylmorphine Chloride]

"The hydrochloride [$C_{19}H_{23}O_3NHCl + 2H_2O$ or $C_{17}H_{17}ON(OH)(OC_2H_5).HCl + 2H_2O$ = 385.69] of an alkaloid prepared from morphine by ethylation. Preserve it in well-closed containers, protected from light." *U. S.*

It is the hydrochloride of the ethyl ester of morphine, and is made by acting on morphine in the presence of an alkali with ethyl iodide. The product is purified by treatment with hot alcohol and crystallization from its solution in hydrochloric acid. It was introduced as a proprietary preparation by Merck & Co., under the name of *dionin.* It is officially described as follows: "Ethylmorphine Hydrochloride is a white or yellowish, odorless, microcrystalline powder. One Gm. of Ethylmorphine Hydrochloride dissolves in 8 mils of water and in 22 mils of alcohol at 25° C. (77° F.); slightly soluble in ether or chloroform. An aqueous solution of the salt (1 in 20) is neutral to litmus. It melts at about 123° C. (253.4° F.) with decomposition. Add a drop of ferric chloride T.S. to a solution of about 0.01 Gm. of the salt in 10 mils of sulphuric acid and warm it on a water bath; the color of the mixture will become at first green, then deep violet-blue, and, after the addition of a drop of nitric acid, deep red. Add silver nitrate T.S. to an aqueous solution of the salt (1 in 20); a white precipitate insoluble in nitric acid is produced. No weighable ash remains on incinerating 0.2 Gm. of Ethylmorphine Hydrochloride. Heat 5 mils of an aqueous solution of the salt (1 in 20) with 5 mils of potassium hydroxide T.S. on a water bath; no vapors showing an alkaline reaction with litmus paper are evolved at once (*ammonium compounds*). Dissolve about 0.05 Gm. of potassium ferricyanide in 10 mils of distilled water, add a drop of ferric chloride T.S., then 1 mil of an aqueous solution of the salt (1 in 100); no green or blue color is produced at once (*morphine*)." *U. S.*

Uses.—Ethyl morphine hydrochloride, in its general effect, stands between morphine and codeine, but is somewhat closer to the latter. Although it is more powerful as an analgesic and hypnotic than codeine it is greatly inferior to morphine. Internally ethyl morphine is a useful drug to allay *cough* and to relieve *pain.* As a cough sedative it is inferior in power to either morphine or diacetylmorphine, but has the advantages of being less constipating and less liable to habit formation. As an analgesic, although greatly inferior to morphine, it is useful in the same class of cases. It has also been highly recommended for the quieting of nervousness following the withdrawal of opiates in those who have been accustomed to the habitual use of this drug. Lindenmayr (*B. K. W.*, 1912) reports goods results from the use of ethylmorphine in acute *coryza,* stating that it not only relieves the symptoms, but has a true curative action.

Locally ethylmorphine is decidedly irritant to the more delicate mucous membranes, as conjunctiva or nose, but seems to increase the lymph flow to an extent not explicable purely on its local irritant action. It is widely employed as a local lymphagogue in various inflammations of the eye, such as *iritis, glaucoma, corneal ulcers,* and the like. It has also been employed to a lesser extent for a similar effect upon the mucous membrane of the nose, especially in *ozena.*

Dose, one-quarter to one grain (0.016–0.065 Gm.).

AGAR. U. S.

AGAR [Agar-agar]

(ā'gär)

"The dried mucilaginous substance extracted from *Gracilaria* (*Sphærococcus*) *lichenoides* Greville and other marine algæ growing along the eastern coast of Asia, particularly several species of *Gelidium,* or *Gloiopeltis* (Class *Rhodophyceæ*)." *U. S.*

Quite a number of the algæ belonging to the *Rhodophyceæ,* growing on the coast of Southern and Eastern Asia, contain large quantities of mucilage which is extracted and sold under the name of agar-agar. The most important species are those recognized by the U. S. Pharmacopœia. The algæ are collected, spread out upon the beach until they are bleached and then dried. They are then boiled with water and the mucilaginous solution strained through a cloth. The filtrate is allowed to harden and thoroughly dry in the sun. The algæ are usually collected during the summer and fall, bleached and dried, but the process of the manufacture of agar-agar does not take place until cold weather and usually extends from November to February.

The following varieties of agar are known:

1.—*Ceylon Agar-agar,* consisting chiefly of *Gracilaria lichenoides,* Ag., the alga used by the *Hirundo esculenta* in the formation of its edible nest.

2.—*Macassar Agar-agar,* coming from the straits between Borneo and Celebes, consisting of impure *Eucheuma spinosum,* Ag., incrusted with salt.

3.—*Japanese Agar-agar,* known as *Japanese isinglass,* derived from several algæ, especially

Sphærococcus compressus, Ag., *Gloiopeltis tenax*, J. Ag., *Gelidium corneum* Lam. and *G. cartilagineum* Gaill. It occurs in European commerce either in transparent pieces, two feet long and as thick as a straw, prepared in Singapore by putting the algæ named in hot water, or, more frequently, in yellowish-white masses, a foot long and upward of an inch in width. It is the latter kind of agar-agar that is suitable for the culture of bacteria, and is employed in medicine. (*P. J.*, 1885, 188.)

Morin has investigated the *gelose* of Payen, contained in the agar-agar. When a solution of gelose is cooled, even that of 1 in 500 parts of water, a colorless, transparent, and stiff jelly is obtained, which, when heated with moderately strong nitric acid, yields *mucic* and oxalic acids. It dissolves on heating with acidulated water without yielding a jelly on cooling.

Gelose leaves 3.88 per cent. of ash, and when air-dried contains 22.85 per cent. of moisture. When dissolved there also separates out a flocculent mass amounting to 1.9 per cent. Alcohol precipitates gelose, but it cannot be obtained pure in this manner, as the precipitate contains some ash. (*C. R. A. S.*, No. 90, 924–926.)

Under the name of *gelosine* a mucilaginous substance, extracted from a Japanese alga, has entered commerce in the form of dry, whitish leaves. Gelosine is soluble in alcohol and water, and is said when wet to gradually contract and expel water and the medicinal substances which it may contain. It has been proposed as a pharmaceutical basis for various preparations for local use. (See *B. M. J.*, vol. ii, 1886.) Glycerin suppositories have been made with agar-agar as a vehicle, but they contain only 70 per cent. of glycerin as compared to 90 per cent. in the official suppositories made with sodium oleate.

Properties.—Agar-agar occurs "mostly in bundles from 4 to 6 dm. in length, consisting of thin, translucent, membranous, agglutinated pieces from 4 to 8 mm. in width; externally yellowish-white or brownish-white; tough when damp, brittle when dry; odor slight; taste mucilaginous. A fragment mounted in water and examined under the microscope gradually becomes more transparent, showing a granular structure and a few diatoms, notably the frustules of *Arachnoidiscus Ehrenbergii* Baillon, which are disk-shaped and from 0.1 to 0.2 mm. in diameter, and also fragments of the spiculæ of sponges; upon the addition of iodine some of the granules or hyphal portions are colored bluish-black. Insoluble in cold water, but slowly soluble in hot water. A solution made by boiling 0.1 Gm. of Agar in 100 mils of water, upon cooling yields no precipitate upon the addition of tannic acid T.S. (*gelatin*), and does not produce a blue color upon the addition of iodine T.S. (*starch*). Boil 1 part of Agar for about ten minutes with 100 parts of water, and replace the water lost by evaporation; it yields a stiff jelly upon cooling. The powder is pale buff; when mounted in water and examined under the microscope it shows transparent, more or less granular, striated angular fragments, occasionally containing frustules of diatoms; with iodine T.S., fragments for the most part are colored bright red, certain more less definite areas being stained bluish-black. Agar yields not more than 5 per cent. of ash." *U. S.*

To detect agar in jams, jellies, etc., in which it is often used as an adulterant, it is usually considered necessary to ash the sample and examine the acid insoluble ash for presence of the characteristic diatoms. Albert Schneider (*Pac. Pharm.*, 1912, p. 35) states that the ashing is unnecessary and often destructive of the diatoms and that they may be collected by dissolving 10 Gm. of the sample in 200 mils of distilled water and centrifuging for thirty minutes, after which the sediment may be placed on a microscopic slide and examined.

Uses.—Under the name of agar-agar a jelly-like substance has been used as a culture medium by bacteriologists for many years. (See *Diagnostical Reagents*, Part III.) Although agar contains sixty per cent. of carbohydrates, according to Saiki (*J. B. C.*, 1906), the human digestive tract is able to utilize but a very small percentage of the food value. Its therapeutic importance depends upon the ability of the dry agar to absorb and retain moisture. Being indigestible, it passes through the intestinal tract, swelling up somewhat, owing to the absorption of water from the stomach, and gives bulk to the intestinal contents. In other words, it acts mechanically in an analogous manner to the cellulose of vegetable foods, and aids in maintaining the regularity of the bowel movements. It has been widely used in the treatment of *chronic constipation*. Of itself, when there is more or less atony of the intestinal muscles, it does not originate peristaltic movements, and therefore is frequently combined with small doses of cascara, or one of the other vegetable cathartics. It is best administered cut up in small pieces, and eaten like a cereal with the addition, if desirable, of cream and sugar. Ordinarily, from two to four drachms (7.7–15.5 Gm.) of the dry agar may be administered once a day.

ALCOHOL. U. S. (Br.)

ALCOHOL

(ăl'cọ-hŏl)

"A liquid containing not less than 92.3 per cent. by weight or 94.9 per cent. by volume, at 15.56° C. (60° F.), of $C_2H_5.OH$ (46.05). Preserve it in well-closed containers, in a cool place, remote from fire." *U. S.* "Alcohol (90 per cent.) is a mixture of ethyl hydroxide and water containing in 100 parts by volume 90 parts by volume of ethyl hydroxide, C_2H_5OH, and is obtained by the distillation of fermented saccharine liquids." *Br.*

Spiritus Rectificatus, *Br.*; Ethyl alcohol, Ethyl hydroxide, Rectified Spirit; Spiritus Vini Rectificatissimus, Alcohol ethylicum, Alcohol Vini; Spirit of Wine; Alcool, *Fr. Cod.*; Esprit de Vin, *Fr.*; Spiritus, *P. G.*; Rectificirter Weingeist, Aethyl alkohol, Alkohol, *G.*; Alcool, Acquavite rectificata, *It.*; Alcohol, Espiritu rectificado de vino, *Sp.*

ALCOHOL DEHYDRATUM. U. S. (Br.)

DEHYDRATED ALCOHOL Alcohol Dehyd. [Alcohol Absolutum, U. S. P. VIII]

(ăl'cọ-hŏl dē-hȳ-drā'tŭm)

"A liquid containing not less than 99 per cent. by weight of $C_2H_5.OH$ (46.05). Preserve it in well-closed containers, in a cool place, remote from fire." *U. S.* "Absolute Alcohol is ethyl hydroxide, C_2H_5OH, with not more than 1 per cent. by weight of water; obtained by the dehydration of less strong ethylic alcohol, and subsequent distillation." *Br.*

Alcohol Absolutum, *Br.;* Alcohol absolutus, *P. G.;* Absoluter Alkohol, *G.;* Alcool absolu, *Fr.;* Alcool assoluto, *It.;* Alcohol anhidro, *Sp.*

ALCOHOL DILUTUM. U. S. (Br.)

DILUTED ALCOHOL Alcohol Dil.

(ăl'cọ-hŏl dī-lū'tŭm)

"A liquid containing from 41 to 42 per cent. by weight or from 48.4 to 49.5 per cent. by volume, at 15.56° C. (60° F.), of $C_2H_5.OH$ (46.05). Preserve it in well-closed containers, in a cool place, remote from fire." *U. S.*

"The four official liquids obtained by diluting Alcohol (90 per cent.) with Distilled Water, contain, respectively, 70, 60, 45, and 20 per cent. of ethyl hydroxide by volume." *Br.*

Spiritus Tenuior, *Br.* 1885, Proof Spirit; Alcool dilué, *Fr.;* Spiritus Dilutus *P. G.;* Verdünnter Spiritus, Verdünnter Weingeist, *G.*

From the titles and definitions above given, which include all the forms of alcohol recognized by the U. S. and Br. Pharmacopœias, it will be perceived that there are three U. S. official alcohols, and two alcohols as well as four strengths of diluted alcohol recognized by the British Pharmacopœia, those being considered the same which have nearly the same specific gravities and are employed for similar purposes.

The extensive use of alcohol in pharmacy renders it desirable not only to group the official kinds together here, but to consider each in detail in the subsequent pages. In the U. S. P. (1890) two new kinds of alcohol were made official, "Alcohol Absolutum" and "Alcohol Deodoratum." The former, which had been made official in the Br. Pharm. (1885) under the title "Alcohol Ethylicum," is in the Br. Pharm. (1898) termed "Alcohol Absolutum," so that the two Pharmacopœias were in accord in this. The U. S. Pharmacopœia VIII dismissed Alcohol Deodoratum (U. S. P. 1890), but raised the standards for Alcohol to correspond with those formerly required for the dismissed deodorized alcohol. The U. S. P. IX made no change in the strength of the alcohols, but the title of absolute alcohol was changed to "Alcohol Dehydratum (dehydrated alcohol)," because, strictly speaking, there is no such liquid as absolute alcohol found in commerce. Both pharmacopœias permitted the presence of 1 per cent. of water, and hence the word "absolute" is a misnomer.

Alcohol, in the chemical sense, is a peculiar liquid generated for the most part in vegetable juices and infusions by a *fermentation,* called the *vinous* or *alcoholic.* The liquids which have undergone it are called vinous liquors, and are of various kinds. Thus, the fermented juice of the grape is called *wine;* of the apple, *cider;* and the fermented infusion of malt and hops, *beer.*

With regard to the nature of the liquids susceptible of the vinous fermentation, however various they may be in other respects, one general character prevails; that, namely, of containing sugar in some form or other. It is found, further, that after they have undergone the vinous fermentation the sugar they contain has either wholly or in part disappeared; and it was long believed that the only new products are alcohol which remains in the liquid, and carbonic acid which escapes during the process, and that these, when taken together, are equal in weight to the sugar lost. It was hence inferred that sugar is the subject matter of the changes occurring during the vinous fermentation, and that it is resolved into alcohol and carbon dioxide. It has, however, been shown by Pasteur that, along with alcohol and carbon dioxide, glycerin and succinic acid are generated in small amount, and that the process is not so simple as at first supposed. One of the theories earlier held was that some definite intermediate product was always formed between the sugar and the alcohol. Some authorities, including Baeyer and Buchner, believed this product to be lactic acid. One of the most recent views is that of Fernbach, who holds that the intermediate product is pyruric acid, $CH_3COCOOH$, which is capable of being converted into alcohol by yeast, which lactic acid is not.

Sugar will not undergo the vinous fermentation by itself, but requires to be dissolved in water, subjected to the influence of a ferment, and kept at a certain temperature. Accordingly, sugar, water, the presence of a ferment, and the maintenance of an adequate temperature may be deemed the prerequisites of the vinous fermentation. The water acts by giving fluidity, and the ferment and temperature by commencing and maintaining the chemical changes. The precise manner in which the ferment operates has not been positively determined; but the fermentative change seems to be intimately connected with the multiplication of a microscopic plant, *Torula cerevisiæ.* Pasteur has shown that the yeast plant lives and grows at the expense of the sugar, which is converted partly into the plant's tissue, partly into alcohol and other products. The proper temperature for conducting vinous fermentation ranges from 15.5° C. to 32.2° C. (60°–90° F.).

Certain vegetable infusions, as those of potatoes and rice, readily undergo vinous fermentation, on account of the ease with which their starch is changed into sugar under the influence of certain ferments. Taking the formula of starch as $(C_6H_{10}O_5)_3$ for illustra-

tion, it is first changed under the influence of dilute acids or ferments according to the two reactions:

$$(C_6H_{10}O_5)_3 + H_2O = \underset{\text{Dextrin.}}{(C_6H_{10}O_5)_2} + \underset{\text{Dextrose.}}{C_6H_{12}O_6}$$

$$(C_6H_{10}O_5)_3 + 2H_2O = \underset{\text{Maltose.}}{C_{12}H_{22}O_{11}} + \underset{\text{Dextrose.}}{C_6H_{12}O_6}$$

The two compounds, *dextrin* and *maltose,* then pass gradually into dextrose, according to the reactions:

$$(C_6H_{10}O_5)_2 + 2H_2O = 2C_6H_{12}O_6$$

$$C_{12}H_{22}O_{11} + H_2O = 2C_6H_{12}O_6$$

Neither dextrin nor maltose is directly fermentable. Arnoult has succeeded in obtaining alcohol by fermenting sugar (glucose), formed by the action of sulphuric acid on poplar wood sawdust, which yielded from 70 to 80 per cent. of this kind of sugar. Simmson (*Ap. Ztg.,* 1898, 776) obtained 6.5 liters of absolute alcohol from 100 kilogrammes of air dried sawdust. The action of sulphurous acid upon wood fibre has been found by Clássen to be even more satisfactory as a saccharifying agent, and the process has been successfully used in practice.

Alcohol, being the product of the vinous fermentation, necessarily exists in all vinous liquors, and may be obtained from them by distillation.

A valuable table of the sources whence alcohol may be obtained commercially, together with the estimated yield, was published in the *Kew Bulletin* for 1912, No. 3, and will be found reprinted in the *A. Ph. A. Yearbook of Pharmacy* for 1912, p. 354.

In vinous liquors, the alcohol is largely diluted with water, and associated with coloring matter, volatile oil, extractive, ethereal substances, and various acids and salts. In purifying it, advantage is taken of its volatility, which enables it to be separated by distillation, combined with some of the principles of the vinous liquor employed, and more or less water. The distilled product of vinous liquors forms the different *ardent spirits of commerce.* When obtained from wine, it is called *brandy;* from fermented molasses, *rum;* from grain, such as corn, malted barley, or rye, *whisky;* from malted barley and rye meal with hops, and rectified from juniper berries, *Holland gin;* from malted barley, rye, or potatoes, and rectified from turpentine, common *gin;* and from fermented rice, *arrack.* These spirits are of different strengths, that is, contain different proportions of alcohol, and have various peculiarities by which they are distinguished by the taste. Their strength is accurately judged by the specific gravity, which is always less in proportion as their concentration is greater. When they have the sp. gr. 0.920 (0.91984, Drinkwater), they are designated in commerce by the term *proof spirit.* The United States Custom House and Internal Revenue Service defines the term proof spirit to be alcohol containing 50 per cent. by volume of absolute alcohol at 15.6° C. (60° F.).

Commercial proof spirit is still very far from being pure, being a diluted alcohol, containing about half its weight of water, together with amylic alcohol and other foreign matters. It may be further purified and strengthened by redistillation, or *rectification* as it is called. The average strength of rectified spirit (sp. gr. 0.835), corresponds very nearly with the *Spiritus Rectificatus* of the Br. Pharm. When this is once more cautiously distilled, it may be further purified from water, and the specific gravity attained will be about 0.820, which is the lightest spirit that can be obtained by ordinary distillation, and is practically the pure spirit of the British system of excise. It still, however, contains 11 per cent. of water. In the meanwhile, the spirit, by these repeated distillations, becomes more and more freed from the contaminating oil, called *grain oil* or *fusel oil.* (See *Alcohol Amylicum.*) The synthesis of alcohol from ethylene through the intervention of ethyl-sulphuric acid has long been known to be a scientific possibility; with the production of acetylene industrially from calcium carbide, this synthesis has been asserted to be a commercial possibility. Acetylene, made as stated from calcium carbide and water, is generated in the same flask in which nascent hydrogen is being formed, the result being the production of ethylene gas. This is brought in contact with concentrated sulphuric acid at 80° C. (176° F.), when the two unite to form ethyl-sulphuric acid, which is then condensed and redistilled, when it breaks up into alcohol and sulphuric acid, which later can be used over again. The reactions for this synthesis are:

$$C_2H_2 \text{ (acetylene)} + H_2 \text{ (hydrogen)} = C_2H_4 \text{ (ethylene)}$$

$$C_2H_4 \text{ (ethylene)} + H_2SO_4 = (C_2H_5)HSO_4 \text{ (ethyl-sulphuric acid)}$$

$$C_2H_5HSO_4 + HOH = C_2H_5.OH \text{ (alcohol)} + H_2SO_4$$

Wood (*Chem. News,* 1898, 308), after repeated experiments, doubts the probability of making alcohol synthetically by this process. Berthelot announced the formation of alcohol synthetically, by the union of olefiant gas with water, but in this discovery he was anticipated by Hennel, who published it in 1828.

We shall first consider the general properties of alcohol, and afterwards the different official forms.

Properties.—Alcohol, using this term in a generic sense, is a colorless, transparent, volatile liquid, of a penetrating, agreeable odor, and burning taste. It should be free from foreign odor, which, when present, is usually due to fusel oil. When free from water, it is called *anhydrous* or *absolute alcohol.* It is inflammable, and burns without smoke or residue, forming water and carbon dioxide. Its flame is bluish when strong, but yellowish when weak. It combines in all proportions with water and ether, and, when diluted with distilled water, preserves its transparency. Its density varies with the pro-

portion of water it contains. (See alcohol tables, Part III.) Its value depends upon the quantity of absolute alcohol contained in it; and, as this is greater in proportion as the specific gravity is less, it is convenient to take the density of a sample as a means of estimating its strength.

This is done by instruments called hydrometers or alcoholometers, which, when allowed to float in the spirit, sink deeper into it in proportion as it is lighter. Each hydrometer degree has a corresponding specific gravity, and, by referring to tables constructed for the purpose, the percentage of absolute alcohol is at once shown. Hydrometer manufacturers graduate instruments showing specific gravity and Baumé's degrees upon the same scale in parallel columns, with a thermometer taking the place of the bulb; these are exceedingly convenient. Alcoholometers are also constructed to show the alcohol percentage by weight directly, as well as percentage of proof spirit.

Alcohol is used enormously in the arts as a solvent and for other purposes, and the U. S. government has established suitable regulations permitting the proper use of alcohol in manufacturing and controlling its use as a beverage. The liquid treated so that it is rendered unfit for use in beverages is termed *denatured* or *denaturized alcohol*. The introduction of *methylated spirit* (alcohol with 10 per cent. of methyl alcohol) has not proved effective. The French excise directs that alcohol should be denatured or deprived of its natural properties by the addition of 500 mils of petroleum benzin and 1 Gm. of malachite green to each hectoliter; it has been found, however, that the color can be destroyed by calcium hypochlorite.

The U. S. Internal Revenue Department has authorized the use of a number of formulas for denaturing alcohol, but it must be prepared under the supervision of an official of the Department at special plants. Some of these formulas provide an alcohol for burning purposes or for use as special solvents, others are the preliminary steps to manufacturing processes, such as a mixture of sulphuric acid and alcohol for the subsequent production of ether, while other formulas have now been authorized which are identical with official formulas, such as tincture of iodine, soap liniment, etc., thus making it possible to have these products manufactured from duty-free alcohol at greatly reduced cost. These preparations may therefore be purchased from large dealers at prices which are less than the cost of the raw material if bought through the usual channels of trade.

The dangerous properties of methyl alcohol when taken internally caused the Committee of Revision of the U. S. P. to introduce a test for determining the presence or absence of methyl alcohol, which is sometimes used as an adulterant for alcohol. See p. 108, also *U. S. D.*, 19th ed., p. 105.

Alcohol is capable of dissolving a great number of substances as, for example, sulphur and phosphorus in small quantity, iodine and ammonia freely, and the hydroxides of potassium, sodium, and lithium, but not the carbonates of these metals. Among organic substances, it is a solvent of most of the vegetable alkaloids, urea, tannic, citric, and tartaric acids, sugar, mannite, camphor, resins, balsams, volatile oils, and soap. It dissolves the fixed oils sparingly, except castor oil, which is abundantly soluble in it. It reacts chemically with some acids, forming the ethyl esters, but with others acts only as a solvent. All deliquescent salts are soluble in alcohol, except potassium carbonate; while the efflorescent salts, and those either insoluble or sparingly soluble in water, are mostly insoluble in it. It dissolves ammonium chloride, and most of the chlorides readily soluble in water; also some nitrates, but none of the metallic sulphates.

A method of detecting alcohol in small proportions has been proposed by Carstanjin. The liquid supposed to contain it, having been mixed with platinum black in a small flask, is heated to 51.1° C. (124° F.), well shaken, and filtered. To the filtrate a few drops of solution of potassium hydroxide are added, and the liquor evaporated to dryness on a water bath. The residue is then heated with a little arsenic trioxide, when, if alcohol be present, a garlicky odor will be perceived, owing to the production of cacodyl. According to Nickles, however, propylic alcohol will produce the same result. (*A. J. P.*, 1865, p. 334.) A very delicate test for small quantities of alcohol is that of Lieben as modified by Hager. (*Zeit. An. Chem.*, ix, 492.) It depends on the fact that alcohol under the influence of iodine and an alkali yields iodoform, CHI_3, the properties of which are very characteristic. To 10 mils of the clear suspected liquid five or six drops of a 10 per cent. solution of potassium or sodium hydroxide are added, and the liquid is warmed to about 50° C. (122° F.). A solution of potassium iodide fully saturated with free iodine is next added drop by drop, with agitation, until the liquid becomes permanently yellowish-brown, when it is carefully decolorized by a further cautious addition of the caustic alkali solution. If alcohol be present, iodoform is gradually deposited at the bottom of the tube in yellow crystals of the flat hexagonal type seen in snowflake crystals, which, after standing, may be examined with a lens. Spirit diluted with 2000 parts of water, when treated as above and allowed to stand twelve hours, gives a distinct dust-like deposit of iodoform. Unfortunately, the above delicate reaction is not peculiar to alcohol, being produced by acetone, aldehyde, propylic and butylic alcohols, various ethers, etc. On the other hand, it is not given by pure methyl or amyl alcohol, chloroform, chloral, glycerin, or ether, nor by acetic, formic, or oxalic acids. (Allen, *Com. Org. Anal.*, 2d ed., i, p. 59; see also *A. J. P.*, Feb., 1877, Feb., 1879, Nov., 1879; *N. R.*, Aug., 1876.) Barfoed, of Copenhagen, recommends for an approximate simple test of the strength of an alcoholic fluid, to moisten small slips

of filtering paper thoroughly with the alcohol, and set fire to them. If, when the alcohol has burned out, the paper slip catches fire readily, the alcohol must be stronger than 80 per cent.; if the paper barely catches fire, the strength may be presumed to be between 75 and 80 per cent.; if it does not catch fire at all, the alcohol cannot be stronger than 73 or 75 per cent. (*A. J. P.*, Jan., 1875.)

A new specific reaction for alcohol, which is not interfered with by impurities nor by methyl alcohol or acetone, has been proposed by A. Toninelli (*P. J.*, 93, 47), as follows: The reagents required are (1) 1.5 Gm. of pure crystal dinitritoluol is dissolved in 200 mils of a mixture of 1 part of carbon disulphide and 2 parts of ether; (2) 12 Gm. of iodine is dissolved in 100 mils of ether; (3) 40 Gm. of potassium hydroxide is dissolved in 100 mils of distilled water.

Into a 10 mil graduated glass-stoppered tube are introduced 2 mils of the liquid to be tested, 2 mils of the iodine solution, and after shaking and allowing to stand for two minutes, 4 mils of potassium hydroxide solution is added and the mixture shaken until decolorized. Finally, 2 mils of the dinitritoluol reagent is added with vigorous shaking, the graduated tube is placed upon a white surface and the upper layer closely observed. If ethyl alcohol is present in quantity sufficient to react, an orange-yellow color is developed which passes through various shades, terminating in intense garnet red. With as little as 3 per cent. alcohol the color is a light rose. Some of the higher alcohols give somewhat similar effects, but are readily removed by salting out and shaking with petroleum benzin.

Alcohol tables will be found in Part III, which will give the specific gravities of the various strengths of alcoholic liquids. The temperature at which the specific gravities of these liquids is taken was not changed to 25° C. (77° F.) in the U. S. P. IX, as it was for most liquids, because the temperature 15.6° C. (60° F.) was the one adopted by the U. S. government and still retained by it, for all of the national legal requirements.

ALCOHOL DEHYDRATUM. *Absolute Alcohol, Anhydrous Alcohol, Ethylic Alcohol.*—No process is given in the U. S. Pharmacopœia for the preparation of absolute alcohol; the definition given, however, is "A liquid containing not less than 99 per cent. by weight of $C_2H_5.OH$." *U. S.* The following is the process of the Br. Pharmacopœia (1885): "Rectified Spirit, 1 pint [Imp. meas.]; Carbonate of Potassium, anhydrous, 2 ounces [av.]; Chloride of Calcium, fused, a sufficiency. Add the carbonate of potassium to the spirit in a stoppered bottle, and macerate for twenty-four hours with frequent agitation. Put the chloride of calcium into a covered crucible, and subject it to a red heat for half an hour; then pour the fused salt on to a clean stone slab, cover it quickly with an inverted porcelain dish, and when it has congealed, break it up into small fragments and enclose in a dry stoppered bottle. Put one pound [av.] of this fused chloride of calcium into a flask, pour over it the spirit decanted from the carbonate of potassium, and, closing the mouth of the flask with a cork, shake them together and allow them to stand for twenty-four hours with repeated agitation. Then attaching a dry condenser closely connected with a receiver from which free access of air is excluded, and applying the flame of a lamp to the flask, distil about two fluidounces [Imp. meas.], which should be returned to the flask, after which the distillation is to be continued until fifteen fluidounces [Imp. meas.] have been recovered." *Br.*, 1885. By the term absolute alcohol is meant pure alcohol, entirely free from water. In this state it cannot be obtained by ordinary distillation alone, the purest alcohol thus procured still containing 5 per cent. of water. To separate this it is customary to have recourse to substances having a very strong affinity for water, sufficient not only to abstract it from the alcohol, but to retain it at a temperature at which alcohol will distil over.

In all cases, before decanting or distilling, the alcohol must be digested for two or three days with lime, at a temperature between 35° and 37.7° C. (95°–100° F.). Lime will not answer as a substance to be distilled from, unless it be in sufficient excess; for otherwise, towards the end of the distillation, the calcium hydroxide formed will yield up its water to the alcohol, and weaken the distilled product. J. Lawrence Smith procures an alcohol of 98 to 100 per cent. by macerating 3 pints of alcohol, 94 per cent., in a four-pint bottle with about six troy ounces of well burned lime; well corked and agitated at intervals for ten days, the strengthened alcohol, at the end of this time, is drawn off by a siphon, and may be freed, if desired, of the small trace of lime by redistillation. Yvon prepares absolute alcohol by treating strong alcohol with powdered calcium carbide.

Properties.—Dehydrated alcohol is a colorless, volatile liquid, of an agreeable odor and burning taste. It boils at 78.4° C. (173.1° F.), and is congealed at –130.5° C. (–202.9° F.). Its sp. gr. is 0.7978 at 68° C. (154.4° F.), according to Regnault; 0.79381 at 60° C. (140° F.), according to Drinkwater; 0.794 (equivalent to 99.95 per cent. of ethyl hydroxide by volume and by weight) to 0.7969 (equivalent to 99.4 per cent. of ethyl hydroxide by volume or 99 per cent. by weight), by the British Pharmacopœia; while E. R. Squibb has shown that pure alcohol is obtainable of as low a density as 0.7935, and possibly lower. (*Ephem.*, ii, p. 522.) The sp. gr. of its vapor is 1.59.

"Dehydrated Alcohol is a transparent, colorless, mobile, and volatile liquid having a characteristic odor, and a burning taste. It is very hygroscopic. Specific gravity: not above 0.798 at 15.56° C. (60° F.), the U. S. Government standard temperature for alcohol, nor above 0.790 at 25° C. (77° F.). Shake 10 mils of Dehydrated Alcohol in a stoppered tube with

about 0.5 Gm. of powdered anhydrous copper sulphate; the latter does not become blue (*water*). In other respects Dehydrated Alcohol has the properties and responds to the tests and reactions under *Alcohol.*" *U. S.*

"Specific gravity from 0.794 (equivalent to 99.95 per cent. of ethyl hydroxide by volume and by weight) to 0.7969 (equivalent to 99.4 per cent. of ethyl hydroxide by volume or 99 per cent. by weight). Very volatile and hygroscopic at ordinary temperatures. Anhydrous *copper sulphate* shaken occasionally during two or three hours in a well-closed vessel with about fifty times its weight of Absolute Alcohol does not assume a decidedly blue color (absence of excess of water). Free from the impurities indicated under 'Spiritus Rectificatus,' and resembling it in other general characters." *Br.*

The tests usually given to prove the absence of water by dropping into the absolute alcohol anhydrous barium oxide or anhydrous copper sulphate are not reliable, as Squibb has demonstrated that when half of one per cent. of water was added to absolute alcohol no change in either the barium oxide or the anhydrous copper sulphate took place. Görgeu's test of forming a clear solution when mixed with an equal bulk of pure benzene is more delicate, but a test for determining the presence of as little as one per cent. of water is needed. Dehydrated alcohol should be free from fusel oil. Dehydrated alcohol burns with a pale flame without residue, the products being carbon dioxide and water. Its vapor, passed through a porcelain tube filled with pumice stone and heated to redness, yields carbon, gaseous hydrocarbons, aldehyde, naphthalene, benzene, phenol, and various other substances. (Berthelot.) It unites in all proportions with ether and water. Its union with water is attended by condensation and a rise of temperature. When 52.6 volumes of alcohol are mixed with 47.4 of water, corresponding with one molecule of the former to three of the latter, the decrease of volume is at the maximum, amounting to 3.4 per cent.

Composition.—Absolute alcohol consists of two atoms of carbon, six of hydrogen, and one of oxygen. Its empirical formula is, therefore, C_2H_6O. It is, however, recognized as the hydroxide of the radical ethyl (C_2H_5), so that its rational formula would be $C_2H_5.OH$.

Alcohol. *U. S. Alcohol,* sp. gr. 0.816 at 15.6° C. (60° F.).—This is the so-called "95 per cent. alcohol" of commerce (or 94.9 per cent. by volume); it was an official preparation of the Dublin College, which gave a formula for its preparation, and stated its sp. gr. at 0.818. The Stronger Alcohol introduced into the U. S. P. (1860), though of the sp. gr. 0.817, and therefore a little stronger than the old Dublin preparation, was for all practical purposes identical with it. The British Pharmacopœia (1914), under the title "Spiritus Rectificatus," recognizes alcohol of 90 per cent. by volume or 85.68 by weight, slightly weaker than U. S. P. alcohol. To prepare it on a small scale, potassium carbonate, previously ignited in a heated mortar, may be mixed with ordinary alcohol in a bottle, and shaken occasionally for about four hours, the mixture being, in the meantime, maintained at the temperature of about 37.78° C. (100° F.). Upon standing, the liquid divides into two layers, the lower consisting of an aqueous solution of potassium carbonate, the upper of the stronger alcohol, which is to be separated, and distilled so as to obtain the measure of about nine-tenths of the original alcohol employed.

It is described as follows: "Alcohol is a transparent, colorless, mobile and volatile liquid, having a slight, characteristic odor, and a burning taste. It is miscible with water in all proportions, and without any trace of cloudiness; also miscible with ether or chloroform. It does not affect the color of blue or red litmus paper previously moistened with water. Specific gravity: not above 0.816 at 15.56° C. (60° F.), the U. S. Government standard temperature for Alcohol, nor above 0.810 at 25° C. (77° F.). Alcohol is readily volatilized, even at low temperatures, and boils at about 78° C. (172.4° F.). It is inflammable, and burns with a pale blue, smokeless flame. Evaporate 50 mils of Alcohol in a platinum or porcelain dish on a water bath; the residue does not exceed 0.002 Gm. Mix 10 mils of Alcohol with 5 mils of distilled water and 1 mil of glycerin and allow the mixture to evaporate spontaneously from a piece of clean, odorless blotting paper; no foreign odor is perceptible when the last traces of the Alcohol leave the paper (*fusel oil constituents*). Allow 25 mils of alcohol to evaporate spontaneously in a porcelain evaporating dish, carefully protected from dust, until the surface of the dish is barely moist. No red or brown color is produced upon the addition of a few drops of colorless sulphuric acid (*amyl alcohol or non-volatile, carbonizable organic impurities,* etc.). Mix 10 mils of Alcohol in a test tube with 5 mils of potassium hydroxide T.S.; the liquid does not at once assume a yellow color (*aldehyde or oak tannin*). Shake 20 mils of Alcohol in a clean, glass-stoppered bottle with 1 mil of silver nitrate T.S.; the mixture does not become more than faintly opalescent, or acquire more than a faint brownish tint when exposed for six hours to diffused daylight (*organic impurities, amyl alcohol, aldehyde,* etc.). Dilute the alcohol with distilled water until it contains about 10 per cent., by volume, of ethyl alcohol. Transfer 5 mils of the dilute alcohol to a test tube, add to it 2 mils of a potassium permanganate solution (made by dissolving 3 Gm. of potassium permanganate in 100 mils of distilled water) and 0.3 mil of sulphuric acid, and allow the mixture to stand for five minutes. Now dissolve the precipitate of manganese dioxide by the addition of sulphurous acid, drop by drop with agitation, then add 1 mil of sulphuric acid and 5 mils of fuchsin-sulphurous acid T.S. and mix them. After standing for ten minutes, a colorless liquid results (*methyl alcohol*). A mixture of 5 mils of Alcohol, 2 mils of sodium hydroxide

T.S., and 5 drops of a freshly made aqueous solution of sodium nitro-prusside (1 in 50), rendered slightly acid with acetic acid, shows no violet tint within one minute (*acetone*)." U. S.

"Specific gravity 0.8337. It contains 85.68 per cent. by weight of ethyl hydroxide, C_2H_5OH, and 14.32 per cent. by weight of water. Burns with a blue smokeless flame. Leaves no residue on evaporation (absence of non-volatile matter). Remains clear when mixed with *water* (absence of oily or resinous substances). A little exposed on clean white filter paper leaves no unpleasant smell after the alcohol has evaporated (absence of fusel oil and allied impurities). 100 mils, with 2 mils of *N/10 solution of silver nitrate*, exposed for twenty-four hours to bright light and then decanted from the black powder which has formed, undergo no further change when again exposed to light with more *N/10 solution of silver nitrate* (absence of more than traces of amylic alcohol and of other organic impurities). When mixed with half its volume of an aqueous solution (1 in 5) of *sodium hydroxide*, the mixture does not immediately darken in color (absence of more than traces of aldehyde). No immediate darkening in color is caused by the addition of *solution of ammonia* (absence of tannic acid, excess of aldehyde, and other organic impurities)." *Br.*

On a large scale, alcohol of this strength is now prepared in the United States, very abundantly, by simple distillation by means of a modified distillatory apparatus known as a "still and column." The modification consists in substituting for a single refrigerated receiver a series of receivers, kept at such temperatures that, in the first of them, the aqueous vapor shall condense with comparatively little of the alcoholic, which, as it passes through the successive recipients, is more and more deprived of water, until, when condensed in the last, it yields a spirit at least as strong as the official Alcohol of the sp. gr. 0.816. At the same time that the spirit is thus strengthened, it becomes, through the principle of fractionation which the process introduces, more and more freed from fusel oil, until almost wholly deprived of it.

The British preparation contains 14.32, the U. S. only 7.7 per cent. by weight of water. Official alcohol, though of standard strength, may still be impregnated with a volatile liquid, called *fusel oil*. This is usually separated by digesting the alcohol with charcoal. It, as well as other impurities, may also be removed by passing the impure spirit through a filtering bed, composed of sand, wood charcoal, boiled wheat, and broken oyster shells, arranged in layers. If 5 mils of alcohol be mixed with 6 times its volume of water and then agitated with about 20 drops of chloroform, the latter will, if separated and allowed to evaporate spontaneously, leave the fusel oil, which will be perceptible by its odor; and by treating with a little sulphuric acid and potassium acetate, its peculiar ether may be recognized by its odor. (*Ber. d. Chem. Ges.*, viii; *A. J. P.*, 1875, p. 304.) If a little of the solution of silver nitrate be added to alcohol and the mixture exposed to a bright light, a black powder will be precipitated, if fusel oil be present. Official alcohol will not withstand this test, as the best contains a little of the foreign oil. According to E. N. Kent, of New York, silver nitrate will not detect fusel oil, but affords its indications by reacting with other organic substances. For detecting fusel oil, Kent finds pure sulphuric acid the best test. To apply it he half fills a test tube with the spirit to be tested, and then fills it up very slowly with pure concentrated sulphuric acid. If the spirit be pure, it will remain colorless, otherwise it will become colored, the tint being deeper in proportion to the amount of the impurity. The presence of a small proportion of fusel oil is readily detected by the use of this test.

Deodorized alcohol is, as its name implies, alcohol deprived of foreign odor; there are certain uses in pharmacy for which any other alcohol would be unsuited, such as the solution of volatile oils and essences having delicate odors, the manufacture of compound spirits, etc. This was official in the U. S. P., 1890, under the title *Alcohol Deodoratum*, but, inasmuch as it is easily obtained in the United States, at a slight advance in price over commercial alcohol, its standards of purity, odor and strength were retained for the *Alcohol* of the U. S. P. VIII and IX, see page 108, hence the alcohol used in pharmacopœial preparations should be deodorized alcohol.

Deodorized alcohol is manufactured under Atwood's process, in which manganic acid or potassium or sodium permanganate is used to destroy fusel oil and other foreign substances. This alcohol withstands the tests of silver nitrate and sulphuric acid remarkably well. Pure fused sodium acetate has been proposed as a substance particularly adapted to retain fusel oil, and has been used by adding it to the alcohol to be rectified in the proportion of about 10 pounds to the barrel of forty-five gallons, and redistilling. The purification of alcohol is accomplished, according to Schmitt, by taking crude alcohol containing 30 per cent. by volume, adding potassium carbonate (not enough to cause two layers to form), and agitating with pure petroleum benzin; this solvent removes completely the fusel oil from the alcohol. After separating the light layer, potassium carbonate is added to the alcohol in sufficient quantity to form two layers, the lower one consisting of a saturated solution of potassium carbonate, the upper one of 94 per cent. alcohol containing a small quantity of potassium carbonate. The alcohol layer is siphoned off and mixed with just sufficient strong sulphuric acid to precipitate the potassium salt as sulphate, which is insoluble in alcohol of 94 per cent., and which can then be removed. Alcohol purified in this manner, without distillation, it is stated, cannot be distinguished from that purified by the usual method. F. G. Earl recommends the following method, which has the ad-

vantage of requiring no special apparatus. "Rub four drachms of powdered unslaked lime with two drachms of powdered alum intimately; add one gallon (95 per cent.) alcohol, and shake well, then add one fluidrachm of spirit of nitrous ether, set aside for seven days, and filter through animal charcoal." (*C. D.*, 1895, 35.) *Perfumer's alcohol* can now be had, which is very much cleaner than *cologne spirit*, as the purest alcohol attainable was formerly called. It is termed perfumer's alcohol because it was found necessary to prepare a very high grade of alcohol for those who need a solvent for fine odors, on the score of economy and to insure greater excellence of product.

Alcohol Dilutum. *U. S.*—"A liquid containing from 41 to 42 per cent., by weight, or from 48.4 to 49.5 per cent., by volume, at 15.6° C. (60° F.) [$C_2H_5.OH = 46.05$]." *U. S.* Specific gravity from 0.935 to 0.937 at 15.6° C. (60° F.) and from 0.930 to 0.932 at 25° C. (77° F.).

Diluted alcohol is officially made by mixing equal measures of alcohol and water together. * "Alcohol, *five hundred mils* [or 16 fluidounces, 7 fluidrachms, 15 minims]; Distilled Water, *five hundred mils* [or 16 fluidounces, 7 fluidrachms, 15 minims]. Mix them. Measure the alcohol and water at the same temperature and mix them. If the two liquids are measured at the temperature of 25° C. (77° F.), the mixture, when cooled to the same temperature, will measure about 970 mils. *Diluted Alcohol* may also be prepared as follows: Alcohol, *four hundred and eight grammes* [or 14 ounces av., 171 grains]; Distilled Water, *five hundred grammes* [or 17 ounces av., 279 grains]. Mix them." *U. S.*

The British Pharmacopœia (1914) no longer uses the titles "Spiritus Tenuior" or "Proof Spirit" for diluted alcohol, but admits four official liquids under the name of diluted alcohol, as follows:

"1. **Alcohol (70 per cent.).**—With *one thousand millilitres* of Alcohol (90 per cent.) mix *three hundred and ten and a half* (310.5) *millilitres* of Distilled Water. Specific gravity 0.8899.

"2. **Alcohol (60 per cent.).**—With *one thousand millilitres* of Alcohol (90 per cent.) mix *five hundred and thirty-six and a half* (536.5) *millilitres* of Distilled Water. Specific gravity 0.9134.

"3. **Alcohol (45 per cent.).**—With *one thousand millilitres* of Alcohol (90 per cent.) mix *one thousand and fifty-three and a half* (more accurately 1053.4) *millilitres* of Distilled Water. Specific gravity 0.9435.

"4. **Alcohol (20 per cent.).**—With *one thousand millilitres* of Alcohol (90 per cent.) mix *three thousand five hundred and fifty-eight* (3558.0) *millilitres* of Distilled Water. Specific gravity 0.9760." *Br.*

This is a convenient pharmaceutical method of providing suitable menstrua for making tinctures, fluidextracts, and other galenical preparations, which have been adopted by the British Pharmacopœia.

"Rules for making an alcohol of any required lower percentage from an alcohol of any given higher percentage:

"I. *By Volume.*—Designate the volume-percentage of the stronger alcohol by *V*, and that of the weaker alcohol by *v*.

"*Rule.*—Mix *v* volumes of the stronger alcohol with distilled water to make *V* volumes of product. Allow the mixture to stand until full contraction has taken place, and until it has cooled, then make up the deficiency in the *V* volumes by adding more distilled water.

"*Example.*—An alcohol of 30 per cent. by volume is to be made from an alcohol of 94.9 per cent. by volume.—Take 30 volumes of the 94.9 per cent. alcohol, and add enough distilled water to produce 94.9 volumes.

"II. *By Weight.*—Designate the weight-percentage of the stronger alcohol by *W*, and that of the weaker alcohol by *w*.

"*Rule.*—Mix *w* parts by weight of the stronger alcohol with distilled water to make *W* parts by weight of product.

"*Example.*—An alcohol of 50 per cent. by weight is to be made from an alcohol of 92.3 per cent. by weight.—Take 50 parts by weight of the 92.3 per cent. alcohol, and add enough distilled water to produce 92.3 parts by weight." *U. S.*

"Diluted Alcohol has a specific gravity of from 0.935 to 0.937 at 15.56° C. (60° F.), the U. S. Government standard temperature for alcohol, and from 0.930 to 0.932 at 25° C. (77° F.). It responds to the reactions and tests under *Alcohol*, allowance being made for the difference in strength and the presence of water and the boiling point being omitted." *U. S.*

Uses.—The local action of alcohol is mildly irritant, feebly anesthetic and distinctly germicidal. The most favorable concentration for the destructive action on bacteria is from 60 to 70 per cent.; either higher or lower concentrations are less efficient. This amount of alcohol is capable of destroying most of the pathogenic micro-organisms within a relatively short time, but some of the more resistant spore-bearing germs are not killed even by prolonged exposure. Largely by virtue of its local irritant action upon the mucous membrane of the stomach, but probably also in part through some specific action, small quantities of alcohol excite secretion in the alimentary tract, and thereby improve digestion. If large amounts are taken, however, the direct action of alcohol upon the peptic ferments becomes manifest and digestion is retarded.

Alcohol belongs, physiologically as well as chemically, to the group of aliphatic narcotics. In large doses it will produce a condition of coma which is precisely analogous to the anesthesia produced by ether. A number of authors, however, have maintained that in small quantity it acts as a cerebral excitant. There are arguments in favor of this view, and one may not speak too dogmatically on the subject, but the weight of evidence to-day indicates that any dose

of alcohol sufficient to affect the system at all, lessens, rather than increases, intellectual activity.

The question of its effect on the circulation has been the subject of much study and dispute. When administered in moderate quantity, it usually does not produce any marked change in the blood pressure, although occasionally there may be some elevation. On the other hand, the rapidity of the flow of blood through the vessels is distinctly accelerated. This concordination of effects can be explained only by simultaneous increase in the cardiac action and dilatation of the blood vessels. While there has been in the past a considerable contradiction, the most recent and most trustworthy experimentation has shown clearly that quantities of alcohol equivalent to not over one-half an ounce for the ordinary man, increase the amplitude of the cardiac contractions. The experiments of Dixon (*J. P.*, 1907, xxxv) indicate that this effect is most marked when the heart is partially exhausted. The widening of the blood vessels is most noticeable in the vessels of the skin. Large quantities of alcohol produce a marked fall in the blood pressure which is due not only to paralysis of the vasomotor mechanism, but also to a depressant action upon the heart.

When a moderate quantity of alcohol is ingested, from 90 to 95 per cent. is completely oxidized in the system, only traces of the drug being recoverable from either the urine or breath. The oxidization of this amount of hydrocarbon material must of necessity yield energy. Some have, however, attempted to maintain that this energy was not utilizable by the animal economy. The experiments of Atwater and Benedict (*Memoirs of the National Academy of Science*, 1902, vii) and others, seem to demonstrate beyond cavil that small amounts of alcohol are entirely capable of replacing an equivalent portion of the hydrocarbon foodstuffs. But the amount of alcohol which the system is capable of oxidizing is rather limited, and if the administered dose be increased the drug begins to appear unchanged, or only partially oxidized, in the urine and in the exhalations. Whether the presence of unaltered alcohol in the bodily fluids hastens or retards metabolism is still an unsettled question. It seems, however, to be fairly well established that in some way it distorts metabolism, and that the oxidization, especially or purin-containing bodies, is not so complete as in the normal animal.

Alcohol has a marked influence upon gastric and probably also intestinal digestion. In small amounts it does not influence the activity of the peptic ferments, although concentrations of 10 per cent. or over greatly reduce or completely destroy the enzymic activity of pepsin. It has long been recognized that the swallowing of small quantities of alcoholic liquors increases the flow of gastric juice. While this is in part probably due to the local irritation of the mucous membrane of the stomach there is also some central mechanism involved, as an increase in the gastric secretions and of the pancreas has been shown after the intravenous or rectal administration of alcohol. After section of the vagi or their paralysis by atropine this increase in the digestive secretions does not occur. (For review of literature on the effects of alcohol on digestion, see Salant, *A. J. Phys.*, 1907, xvii, p. 409.)

As a circulatory stimulant there is no doubt that in the past too much confidence has been placed in alcohol. Nevertheless if used circumspectly it is often of great value. It is used especially when it is desired to tide the patient over for a limited period of time, as in cases of depressant *poisonings*. It must never be forgotten in this connection that large doses are depressant to the heart; while a small amount of alcohol may prove useful in cases of *snake bite*, it is no exaggeration to say that the injudicious exhibition of this drug has been responsible for as many deaths in rattlesnake bites as the venom itself. In the circulatory failure due to anesthetics it should be sedulously avoided; on account of its close chemical relation to both ether and chloroform it acts as a synergist rather than an antagonist to these poisons. The use of alcohol in *infectious fevers*, especially *typhoid fever*, involves a large number of factors concerning some of which we have at present no definite knowledge. While it seems to be well established that in large doses alcohol diminishes the resistance of the body to bacterial invasion the influence of small quantities upon the vital resistance is as yet a matter of dispute. The impairment of digestion, which is so universal an accompaniment of these diseases, suggests the use of alcohol both as a stimulant to gastric secretion and as an accessory food. While febrile patients are capable of burning up larger quantities of alcohol than normal individuals, if given too freely the unoxidized alcohol circulating in the blood may prove injurious. An alcoholic odor to the breath is generally a sign that the patient is receiving more than he can oxidize. Many believe that the mild narcotic action of alcohol is also of service in preserving the vitality in these adynamic states.

By dilating the vessels of the skin alcohol tends to increase the sweat and is frequently used as an aid to more powerful diaphoretic measures in the abortion of mild infections, such as *acute coryza*.

Locally it is of service for its disinfectant action not only in cleansing the hands of the surgeon but also as a dressing for local inflammations and *wounds*. Although not infrequently employed for the sterilization of surgical instruments the uncertainty of its effects against spore forming organisms makes it very unreliable for this purpose. Recently it has been widely employed for its local paralytic influence when injected into nerve tissue, as in *sciatica*, but especially in that most intractable disorder *tic douloureux*.

Raw alcohol is rarely used internally, preferance being always shown for one of the alco-

holic beverages, such as whiskey, brandy, or wine.

The purer forms of alcohol, whether strong or diluted, are employed almost exclusively in pharmacy; as in the preparation of medicines, such as ether, into the composition of which they enter; for the preservation of organic substances; in the extraction of the active principles of drugs, as in the tinctures; for dissolving bodies soluble in alcohol much more readily than in water, or insoluble in the latter fluid; and for other pharmaceutical purposes. Diluted alcohol is employed as an addition to some infusions and decoctions, and to some of the distilled waters, in order to preserve them from decomposition; as a menstruum for extracting the virtues of plants, preparatory to the formation of extracts and syrups; and in preparing many of the spirits, and a few of the medicated wines. But it is in forming the tinctures that diluted alcohol is chiefly used. Some of these are made with official alcohol (rectified spirit), but the majority with mixtures of alcohol and water of different percentages. As diluted alcohol contains more than half its weight of water, it is well fitted for acting on organic substances the virtues of which are partly soluble in water and partly in alcohol.

Toxicology.—The symptoms of acute alcohol poisoning are unfortunately so widely known that detailed description is unnecessary, but the striking similarity between the symptoms of alcoholic intoxication and ether anesthesia is worthy of note; in the more profound stages of alcoholism there is the complete loss of consciousness and of sensation, the muscular relaxation, and the slow respiration, which are characteristic of the ether narcosis. It should not be forgotten that acute alcohol poison may, and frequently does, end fatally. The treatment consists in the immediate evacuation of the stomach, the maintenance of the bodily temperature by the use of external heat, the use of respiratory stimulants, such as strychnine, cocaine and atropine, and of cardiac stimulants, as ammonia and digitalis.

The habitual use of alcoholic beverages may lead to profound degenerations of the various internal organs, especially the stomach, liver, and kidney. The changes may be either sclerotic or fatty. Besides these there are often marked symptoms of serious nervous diseases, but whether the latter are organic or toxic is as yet unsettled.

ALOE. U. S., Br.

ALOES

(ăl'o-ē)

"The inspissated juice of the leaves of *Aloe Perryi* Baker, yielding Socotrine Aloes; or *Aloe vera* Linné yielding Curaçao Aloes; or of *Aloe ferox* Miller, yielding Cape Aloes (Fam. *Liliaceæ*)." *U. S.* "Aloes is the juice that flows from the transversely cut leaves of Aloe chinensis, *Baker*, Aloe Perryi, *Baker*, and probably other species of Aloe, evaporated to dryness. Known in commerce as Curaçao aloes, Socotrine aloes, or Zanzibar aloes." *Br.*

Aloe Barbadensis; Aloe Socotrina; Aloes socotrin, ou succotrin, *Fr.*; Aloès hépatique des Barbades, *Fr.*; Socotora oder Socotrinische Aloe, *G.*; Barbados Aloe, *G.*; Musebber, *Ar.*; Acibar Sucotrino, *Sp.*

The 1890 edition of the U. S. Pharmacopœia agreed with the British in recognizing as distinct varieties Barbados and Socotrine aloes; but both standards now recognize only the general title of Aloe.

Most plants belonging to the genus Aloe are capable of yielding a bitter juice from which may be prepared an aloes, and there is little doubt that in many cases a commercial aloes exported from one country is the product of several species.

1. *A. Perryi*, J. G. Baker, *Tr. Linn. Soc.*, xxviii. The true Socotrine aloe plant was first described from specimens sent to Kew Gardens by Wykeham Perry, and was subsequently found by Balfour, of Edinburgh, growing abundantly upon the island of Socotra, especially in the limestone tracts, from the sea level to an altitude of 3000 feet; along with it, but much less abundant, was a dwarf species with spotted leaves. It resembles in its general habit the Barbados aloe, but differs in its shorter leaves, and especially in its flowers, which are arranged in looser racemes on longer pedicels and have the tube much longer than the segments.

The proper aloetic juice was formerly thought to exist in longitudinal vessels beneath the epidermis of the leaves, and readily flows out when these are cut transversely; but, according to E. Robiquet, who made elaborate researches in relation to this drug, these vessels are air ducts, and the juice flows in the intercellular passages between them. The liquid obtained by expression from the parenchyma is mucilaginous, and possessed of little medicinal virtue. After condensation by artificial or natural heat the aloe juice is poured into gourds, more commonly boxes, or into monkey skins, allowed to harden and sent into commerce.

2. *A. vera* L.—This species, which is the source of Curaçao Aloes, has a very short, woody stem, and lanceolate embracing leaves, which are first spreading, then ascending, of a glaucous green color, somewhat mottled with darker spots, flat on the upper surface, convex beneath, and armed with hard reddish spines, distant from each other, and perpendicular to the margin. *A. vera* is a native of Southeastern Europe, Northern Africa, and Madagascar. It is cultivated in Italy, Sicily, Malta, and especially in the West Indies, where it contributes largely to furnish the Barbados aloes.

3. *Aloe chinensis* Baker.—This species was introduced from China into the Dutch Colonies of Curaçao by W. Anderson, in 1817. It was described by Haworth from flowerless specimens as a probable variety of *A. barbadensis*. It is apparently, however, a distinct species and is so recognized in the British Pharmacopœia. The leaves of *A. chinensis* are not more than half the

length of those in *A. barbadensis,* and are more or less copiously spotted on the dorsal surface as in *A. abyssinica.* The flowers have a strong and decidedly unpleasant odor; and occur in loose racemes, the stamens being much shorter than in *A. barbadensis.* Holmes suggests that *A. chinensis* may be a native of Africa, Arabia or India. Engler considers that *A. chinensis* is merely a form related to *A. vera.* (Baker, in *J. L. S.,* xviii, p. 161; Holmes, *P. J.,* xxi, p. 205.)

4. *A. ferox* Miller yields Cape Aloes. It has a simple stem ten to fifteen feet long, four to six inches in diameter; furnished at the top with a dense rosette containing thirty to fifty leaves, which are lanceolate, one and one-half to two feet long, very rigid, with copious prickles on back and face, the margin armed with brown-tipped deltoid or cuspidate prickles one-eighth to one-sixth of an inch long.

According to L. Pappe, Cape aloes of poor quality is obtained from *A. africana* and *A. plicatilis,* of Miller; while in Lindley's *Flora Medica, A. purpurascens* Haworth, *A. arborescens* Mill., *A. Commelyni* Willd., and *A. multiformis* are all said to contribute to commercial Cape aloes. *Curaçao Aloes* is apparently produced by the following species: *A. vera* (L.) Webb, *A. vulgaris* Lam., *A. spicata* L., and *A. socotrina* Lam., all of which have been introduced into the island (see *P. J.,* Jan., Sept., 1890), although E. M. Holmes believes it to be at least in part the product of *A. chinensis* Baker.

Commercial History and Varieties.—Three chief varieties of aloes have been known in comparatively recent commerce: Socotrine, Barbados or Curaçao, and Cape.

Socotrine Aloes.—This variety appears to have been the original aloes, having been produced in the island of Socotra at least as early as the time of Alexander the Great, 333 B.C., who is said to have sent a commission to investigate its manufacture. Very little, however, of the true Socotrine aloes at the present time comes into the Western markets, the aloes which reaches European commerce from Bombay, Muscat, Aden, and Zanzibar having various botanical and geographical origins. This form of aloes under the title of "Aloes Socotrina" alone is official in the Spanish Pharmacopœia. It is said to be derived from *Aloe vera* Mill., *A. spicata* Thumb., *A. ferox* L., *A. arborescens* Mill., and *A. linguæformis* L., and other species of aloes.

It is stated that the production of aloes in Arabia was formerly a government monopoly, but that at present it is entirely free to the inhabitants. The leaves, which are cut at any time of year, are allowed to drain into a goat's or sheep's skin, and the gathered juice permitted to evaporate spontaneously. In the course of about one month, when it has become thick and viscid, it is known by the Arabic name of *Jâyef Gesheeshah;* several weeks subsequently, when it has become hard, it is called *Jâyef Kasahul.* Due to its exposure throughout the long process of desiccation, all the varieties of Socotrine aloes contain much foreign matter, which, according to E. R. Squibb, amounts to from 7 to 22 per cent. of the bulk.

The best Socotrine aloes occurs in pieces varying from a dark ruby-red to a yellowish or reddish-brown, more or less semi-transparent, with a glossy surface and a smooth or ragged but not conchoidal fracture, and yielding a bright golden-yellow powder. Its odor is peculiar, almost fragrant, especially developed by breathing upon the aloes, and its bitter, disagreeable taste has a somewhat aromatic tang. The poorest variety of Socotrine aloes, *Mocha aloes* of the East, is soft, dark, and malodorous. Much of the drug supplied American dealers in recent years has consisted of this variety. Even the finest Socotrine aloes may consist of an orange or yellow colored distinctly fragrant, semi-liquid mass, while the variety known as *Zanzibar aloes* usually occurs in liver-brown masses, with a dull, waxy fracture, a characteristic odor and a nauseous, bitter taste. The variability of Socotrine aloes probably depends upon not only different methods of preparation but a different origin. Both Zanzibar and true Socotrine Aloes "are opaque even in small splinters, exhibit when examined under the microscope numerous minute crystals embedded in a transparent mass, and impart to *nitric acid* a reddish or yellowish-brown color." *Br.,* 1900.

Curaçao or Bonaire Aloes.—This aloes, which is produced in the Dutch West Indian Islands, chiefly in the island of Aruba, appears not to have entered commerce extensively before the early part of the 19th century, but at present constitutes a very large proportion of commercial aloes. It occurs chiefly in three forms; first, an opaque, brittle aloes, showing abundant crystals under the microscope, and sold in gourds usually as Barbados aloes; second, aloes having an appearance like the first variety but sold in cases; third, glossy Curaçao or Capey Curaçao aloes, which occurs in cases and is glossy and transparent.

It is affirmed that the difference in these varieties of Curaçao aloes depends upon the extent of the evaporation by artificial heat, the aloes being dark colored and opaque when poured into the gourds while still soft; glossy and transparent when allowed to evaporate to dryness over the fire. It is said that the juice is obtained by allowing the leaves to drain into V-shaped troughs, and that it is never evaporated spontaneously.

According to P. van der Wielden, shining Curaçao aloes dissolves completely in nitric acid with the production of a red color, while the dull Curaçao aloes, giving the same color reaction, fails to entirely dissolve. Kremel gives a method to distinguish Curaçao aloes from other kinds by adding to it a little cupric sulphate solution, then some saturated solution of common salt, which makes the color an intense carmine. The reaction is due to *cuproaloin.* (*C. D.,* 1895, 759.) Curaçao aloes is sometimes found in the markets which has been deprived of its aloin;

this fraudulent product is then sold as Cape aloes; the odor of the Curaçao variety still remains.

Barbados Aloes.—This aloes appears to have been brought to London as early as 1693, and to have reached its greatest commercial abundance in the year 1843, when 4227 gourds of it are said to have been exported from Barbados, a gourd containing from twenty to sixty pounds. Occasionally small quantities of Barbados aloes are on the American markets. Most of the Barbados aloes was produced from *A. vera*, although *A. socotrina*, *A. purpurascens*, and *A. arborescens* are said to have been cultivated.

The method of obtaining Barbados aloes seems to have varied at different periods of time, and possibly in different portions of the island. According to various authors the lower ends of the freshly cut leaves were put into wooden V-shaped troughs, and the exuding juice collected and dried in the sun or boiled in copper pans; again, a decoction of the chopped-up leaves was boiled to the proper consistency; in either case, when the liquor had become so thick that it hardened on cooling, it was poured into calabashes or gourds.

Barbados aloes, as formerly supplied, varied in color from very dark blackish-brown through reddish-brown and liver-colored to orange-brown. It yielded a dull olive-yellow powder, of a disagreeable, even nauseous odor, and it was described in the British Pharmacopœia as follows: "Fracture either dull and waxy, in which case small splinters are opaque; or smooth and glassy, in which case the splinters are transparent; the opaque variety examined under the microscope exhibits numerous minute crystals embedded in a transparent mass." *Br.*, 1898.

"Mixed with nitric acid, it acquires a red color. Barbados Aloes is not colored, or acquires only a light bluish-green tint, on being mixed with sulphuric acid and blowing the vapor of nitric acid over the mixture (difference from *Natal aloes*)." *U. S.*, 1890.

According to Marais, Barbados aloes could be distinguished by the fact that its solution in distilled water, 1 to 100,000 parts, yielded on the addition of gold chloride or of tincture of iodine a fine rose color, all other varieties of aloes producing with the reagents named either a feeble color of slow development, or no change of color whatever.

Cape Aloes.—The general method of collecting Cape aloes is to allow the excised leaves to drain into a sheep's skin, which has been so placed in a hole in the ground as to force the juice to collect in the center. Later this juice is evaporated by artificial heat, and when sufficiently concentrated, poured into boxes or skins. Cape aloes differs from Socotrine aloes, especially in its brilliant conchoidal fracture and peculiar odor, which is strong, but neither nauseous nor aromatic. When freshly broken it has a very dark olive or greenish color approaching to black, presents a smooth, bright, almost glassy surface, and if held up to the light appears translucent at its edges. The small fragments also are semi-transparent, and have a tinge of yellow or red mixed with the deep olive of the opaque mass. The same tinge is sometimes observable in the larger pieces. The powder is of a fine greenish-yellow color, and, being generally more or less sprinkled over the surface of the pieces as they are kept in the shops, gives them a somewhat yellowish appearance. Cape aloes, when quite hard, is very brittle and readily powdered; but in very hot weather it is apt to become somewhat soft and tenacious, and the interior of the pieces is occasionally more or less so even in winter. This variety alone is official in the Swiss, German, and Austrian Pharmacopœias.

Uganda or *crown aloes* is a brand of Cape aloes produced by manufacturers who buy the aloe juice from the collectors, allow it to undergo a slight fermentation, and dry it in the sun in wooden troughs. It is sent into commerce in bags containing coarse or fine powder, or chips, and in bricks wrapped in red paper; it has a very bitter, aromatic taste and a strongly aromatic odor. The bricks are of a hepatic brown color, with a resinous fracture, which has a bronzy-gold luster by reflected light. Splinters are translucent, but not garnet-red. With nitric acid it forms a brown solution, gradually changing through dull brownish-yellow to a deep green color.

Natal aloes is a variety coming from Natal, on the southeast coast of Africa, which occurs in irregular pieces, with a fracture much less shining than that of Cape aloes and a totally different color, having a greenish slate hue. It yields a greenish-brown powder, which has the odor of Cape aloes. It is less soluble than Cape aloes, and has a peculiar composition, which will be adverted to under the chemistry of the drug.

Besides the chief varieties of aloes, others are, or have been, known in the market. *Hepatic aloes*, as well as *fetid*, *caballine* or *horse aloes*, have no proper claim to be considered distinct varieties, being simply inferior aloes of various origins, the first liver-colored, the second blackish and fetid and full of impurities. *Jafferabad aloes*, supposed to be the same as *Mocha aloes* (*A. J. P.*, 1881, 175), has been shown to be the product of *A. abyssinica* Lam., and is said by Shenstone to contain *b*-barbaloin. (*A. J. P.*, 1883, 92.) Aloes made in India from the *A. vera* is known as *Musambra aloes*. It appears to be a very inferior variety, and rarely, if ever, reaches Europe. (*P. J.*, Aug., 1889.) Occasionally aloes is found on the market in which the aloin has been removed. Noyes has reported the presence of pea flour in the powdered drug.

It is evident that the labels under which aloes are largely sold often have little or no connection with the place of production, or with the variety of aloes in the package. This fact has probably come about through the indifference of retail druggists to the variety of the aloes which they are using, an indifference largely due to their common habit of buying aloes in

powder. Wilbert (*A. J. P.*, 1903) proposed that aloes should be classified as follows:

Aloes A.—Containing barbaloin; responds to Bornträger's test for emodin, but does not give a distinct red color with nitric acid, or with Klunge's test.

Aloes B.—Containing isobarbaloin with barbaloin; responds to Bornträger's test for emodin, and also has a deep red color with strong nitric acid, or with Klunge's test.

Properties.—The commercial aloes are sometimes divided into two groups: 1. Those which are shiny and amorphous, as Cape aloes, and 2. Those which are of a dull color and crystalline. To this latter group most of the other aloes belong. They are also grouped geographically as follows. 1. South African aloes, including Cape and Natal. 2. East African aloes, including Socotrine, the brown and black Zanzibar aloes and Madagascar aloes. 3. The West Indian aloes which includes the Curaçao, Barbados and Jamaica varieties. 4. The East Indian aloes which includes Jafferabad and Musumbra aloes. The official description is limited to the three principal varieties, viz., Socotrine, Curaçao and Cape aloes and is as follows:

"**Socotrine Aloes.**—In yellowish-brown to blackish-brown, opaque or smooth and glistening masses; fractured surface somewhat conchoidal; sometimes soft or semi-liquid; odor aromatic or saffron-like, never fetid or putrid; taste nauseous, bitter. Not less than 50 per cent. of Socotrine Aloes is soluble in cold water, the solution being of a yellowish color. The powder is dark brown; when mounted in expressed oil of almond and examined under the microscope, it shows yellowish- to reddish-brown, irregular or angular fragments. On adding nitric acid, it yields a yellowish- to reddish-brown solution.

"**Curaçao Aloes.**—In orange to blackish-brown, opaque masses; fractured surface uneven, waxy, somewhat resinous; odor characteristic but not aromatic as in Socotrine Aloes. Not less than 60 per cent. of Curaçao Aloes is soluble in cold water, the solution being of a purplish-red color. The powder is deep reddish-brown; when mounted in expressed oil of almond and examined under the microscope, it shows numerous blackish-brown, irregular, more or less opaque and angular fragments. Upon the addition of nitric acid, it yields immediately a deep red liquid.

"**Cape Aloes.**—In reddish-brown or olive-black masses, usually covered with a yellowish powder, or in thin, transparent fragments of a reddish-brown color; fracture smooth and glassy; odor characteristic. Not less than 60 per cent. of Cape Aloes is soluble in cold water, the solution being of a pale yellow color. The powder is greenish-yellow, changing to light brown on aging; when mounted in expressed oil of almond and examined under the microscope, it shows numerous, distinctly angular, bright yellow fragments. Upon the addition of nitric acid, it yields a liquid that is colored reddish-brown, changing to purplish-brown and finally greenish.

The tests which follow apply to Socotrine, Curaçao, and Cape Aloes. Aloes contains not more than 10 per cent. of moisture. Add 50 mils of alcohol to 1 Gm. of Aloes, gently heat the mixture and then cool it; a nearly clear solution is obtained (*gum and inorganic impurities*). Intimately mix 1 Gm. of Aloes with 10 mils of hot water and dilute 1 mil of this mixture with 100 mils of water; a green fluorescence is produced upon the addition of an aqueous solution of sodium borate (1 in 20). Dilute 1 mil of the original aqueous mixture of Aloes with 100 mils of water, and shake it with 10 mils of benzene; upon separating the benzene solution and adding to it 5 mils of ammonia water, a permanent deep rose color is produced in the lower layer. Aloes yields not more than 4 per cent. of ash." *U. S.*

The 1914 British Pharmacopœia gives the following description: "In hard masses, varying in color from yellowish-brown to dark or chocolate-brown. Fractured surface dull, waxy and uniform (Curaçao and Zanzibar aloes), or uneven and somewhat porous (Socotrine aloes). Small splinters examined under the microscope exhibit minute crystals embedded in a transparent mass. Characteristic odor; taste nauseous and bitter. The solution obtained by dissolving 0.1 gramme of Aloes in 10 millilitres of boiling *water* and adding 0.5 gramme of *purified borax* acquires a green fluorescence. *Nitric acid* dropped on a little crushed Aloes acquires a reddish-brown color (Socotrine and Zanzibar aloes), or a crimson color (Curaçao aloes). Almost entirely soluble in *alcohol* (60 per cent.). Loss on drying at 100° C. (212° F.) not more than 10 per cent. Ash not more than 5 per cent." *Br.*

Chemical Properties.—Several distinguished chemists have investigated the nature and composition of aloes. Braconnot found a bitter principle, which he named *resino-amer* (*resinous bitter*), and another substance in smaller proportion, which he designated by the name of *flea-colored principle.* These results were essentially confirmed by Trommsdorff, Bouillon-Lagrange, and Vogel. Robiquet obtained a product from aloes which he called *aloëtin.* (For details, reader is referred to 14th ed., U. S. Dispensatory.)

ALOINS.—The bitter substances noticed above, viz., the resino-amer of Braconnot, and the *aloëtin* of Robiquet, probably contain the active principle of aloes, but combined with impurities which render it insusceptible of crystallization. It has been assumed that there exists not one compound, but a set of three closely related compounds, to which the general name of *aloins* is now given. The first of these, found exclusively in Barbados aloes, and discovered by T. and H. Smith, is called *barbaloin;* the second, discovered by Flückiger in Natal aloes, is called *nataloin;* the third, found by Histed and Flückiger in Socotrine aloes, is called *socaloin.*

The three aloins, *barbaloin, nataloin,* and *socaloin,* are easily distinguished by the following reaction, first noticed by Histed. A drop

of nitric acid on a porcelain slab gives, with a few particles of barbaloin or nataloin, a vivid crimson (rapidly fading in the case of barbaloin, but permanent with nataloin unless heat be applied), but produces little effect with socaloin. To distinguish barbaloin from nataloin, test each by adding a minute quantity to a drop or two of sulphuric acid, then allowing the *vapor* from a rod touched with nitric acid to pass over the surface. Barbaloin (and socaloin) will undergo no change, but nataloin will assume a fine blue. (*Pharmacographia,* 2d ed., p. 688.) E. von Sommaruga and Egger consider that the three aloins form a homologous series possessing the formulas: barbaloin, $C_{17}H_{20}O_7$; nataloin, $C_{16}H_{18}O_7$; socaloin, $C_{15}H_{16}O_7$, and that they are all derived from *anthracene,* $C_{14}H_{10}$. Tilden subsequently assigned a different composition to the aloins: barbaloin and socaloin, each $C_{16}H_{18}O_7$; for nataloin, the formula $C_{25}H_{28}O_{11}$. He further states that barbaloin and socaloin differ in physical and chemical properties on account of the variation in the molecules of water which are associated with them. Léger assigns to nataloin the formula $C_{23}H_{26}O_{10}$. The British Pharmacopœia (1898) assigns to barbaloin the formula $C_{16}H_{16}O_7,3H_2O$. Two bases only are recognized now, *barbaloin* (or simply aloin) and *isobarbaloin.* According to Léger (*P. J.,* 1902, 21) *Cape aloes* contains from 5 to 6 per cent. of aloin (barbaloin) without any admixture of the isomeric isobarbaloin. The Barbadoes aloes of English commerce never gave more than 5 per cent. of barbaloin with but minute traces of isobarbaloin, which, however, is always met with in the so-called Barbados aloes of French commerce. *Curaçao aloes* is rich in aloin, containing 10 per cent., of which half is barbaloin and the other half isobarbaloin. *Jafferabad aloes* is very rich in aloin, yielding 20 per cent., chiefly in the form of isobarbaloin. *Socotrine aloes* does not contain more than 4 per cent. of aloin, almost wholly barbaloin with a very little isobarbaloin. Since barbaloin is found in almost all varieties, the significance of the prefix "barb" is misleading. The only aloes in which it does not occur is that of Natal.

Hugo Borntträger asserted that one part of aloes in 5000 can be detected in the following manner. A little of the suspected liquid is shaken with about twice its bulk of benzin, which is allowed to separate, decanted, and shaken with a few drops of stronger water of ammonia. On separation the ammonia will be of a clear red color. With solids a tincture should first be made. According to R. H. Groves (*P. J.,* 3d ser., xi, 1045), this test will never succeed with a less concentration than 1 part in 250, and with some aloes 1 in 100, and is due to the tannin-like substance of aloes; he also states that extreme care is necessary to have the benzin solution perfectly clear. (*P. J.,* 1885, p. 633. For Hager's quantitative method for determining the percentage of aloin in aloes, see *A. J. P.,* 1885, p. 237.

R. A. Cripps and T. S. Dymond have given the testing of aloes a lengthy investigation, and they recommend the following method. Place 1 grain of the substance in a glass mortar standing on white paper, now add 16 drops of strong sulphuric acid and triturate until dissolved, then add 4 drops of nitric acid, sp. gr. 1.42, and then 1 ounce of distilled water. If aloes be present, a color varying from deep orange to crimson will be produced, according to the kind of aloes that has been used; the color is deepened by the addition of ammonia. The table below is taken from the paper of Bainbridge and Morrow. (*P. J.,* Jan., 1890.) Under the heading of Kew Specimens are given the results obtained with juice of aloes plants grown in Kew Gardens.

Commercial Specimens.	HNO_3.	H_2SO_4 and vapor of HNO_3.	Cripps and Dymond test.	C. and D. test with NH_4HO.	Bromine Test.	$FeCl_3$.
Hepatic aloes . .	Reddish-grown.	Nil.	Orange-red.	Intense brownish-red.	Nil.	All varieties of aloes give an olive-green coloration with the above reagent.
True Socotrine .	Reddish-brown.	Nil.	Orange-red.	Intense brownish-red.	Nil.	
Commercial Socotrine . . .	Faint crimson.	Nil.	Crimson.	Deep claret.	Nil.	
Cape	Permanent green after standing a few minutes.	Nil.	Orange-red.	Pale claret.	Nil.	
Curaçao	Evanescent crimson.	Nil.	Crimson.	Intense claret.	Nil.	
Natal	Permanent crimson.	Deep blue.	Deep crimson.	Intense brownish-red.	Nil.	
Barbadoes . . .	Crimson soon fading.	Slight bluish-green occasionally.	Crimson.	Deep claret.	Nil.	
KEW SPECIMENS.						
Aloe feroz. . . .	Evanescent crimson.	Green.	Pale yellow.	Red.	Violet.	
—*socotrina* . . .	Permanent crimson.	Deep blue.	Crimson.	Intense brownish red.	Deep purplish-red.	
—*vera*	Nil.	Slight green.			Nil.	
—*Perryi*	Nil.	Nil.			Nil.	
—*purpurascens* .	Crimson fading to light red.	Nil.			Violet.	
—*platylepis* . . .	Nil.	Nil.			Nil.	
—*arborescens,* var. *frutescens* .	Nil.	Nil.			Nil.	
—*africana* . . .	Evanescent red, changing after a few minutes to green.	Nil.	Orange-red.	Pale claret.	Nil.	
—*chinensis* . . .	Nil.	Nil.			Nil.	

Tschirch, of Berne, has published (*B. P. G.*, 1898, viii, Heft 6) an important communication, in which he showed that *emodin*, $C_{15}H_{10}O_5$, or *trioxymethylanthraquinone*, is the purgative principle of the aloins. He succeeded in obtaining emodin in orange-red crystals which melt at 216° C. (420.8° F.). Emodin was found in the aloins obtained from Cape, Barbadoes, and Socotrine Aloes; it is extracted by treating barbaloin with ether, which dissolves out the emodin. Tschirch found that if a liquid extract of aloes be deprived of its resin and aloin, an additional quantity of emodin could be obtained by boiling the liquid extract with diluted sulphuric acid, thus pointing to the fact that emodin may be produced through hydrolysis. He also showed that emodin could be obtained from purgative drugs of the same class as aloes: rhubarb, rumex, frangula, cascara, senna, rhamnus catharticus, morinda bark, and parmelia.

Aloes yields its active matter to cold water, and when good is almost wholly dissolved by boiling water; but the inert portion, or apotheme of Berzelius, is deposited as the solution cools. It is also soluble in alcohol, rectified or diluted. Long boiling impairs its purgative properties by oxidizing the aloin and rendering it insoluble. The alkalies, their carbonates, and soap alter in some measure its chemical nature, and render it of easier solution. It is inflammable, swelling up and decrepitating when it burns, and giving out a thick smoke which has the odor of the drug.

Those substances only are incompatible with aloes which alter or precipitate the soluble matter, as the insoluble portion is without action upon the system. Among these is the infusion of galls, which we have found, probably through its tannic acid, to afford a copious precipitate with an aqueous solution of aloes. It is said that such a mixture will keep a long time, even for a period of several months, without mouldiness or putrescence, though it becomes ropy.

A method for the detection of aloes in mixtures containing other cathartic drugs, such as rhubarb, cascara, etc., has been described by Mossley (*Chem. and Drug.*, 1913, 915). The method depends upon the precipitation of the oxymethyl anthraquinones, which usually interfere in such identification tests, and the subsequent detection of aloes by the addition of bromine T.S., which precipitates aloin, and the green fluorescence produced with aloes by borax.

Uses.—Aloes was known to the ancients, being cultivated in the island of Socotra as far back as the time of Alexander the Great, and is mentioned in the works of Dioscorides and of Celsus. Its cathartic action is due to a stimulation of peristalsis, especially in the larger bowel, probably the result of a local irritant effect upon the mucous membrane, although there is some evidence that it exercises a specific stimulant effect upon unstriped muscles. As its action is largely limited to the colon it is not to be recommended in those conditions in which it is desirable to clean out the whole alimentary canal, and as its effect is largely the result of local irritation it should be avoided in inflammatory conditions of the intestines. In *chronic constipation*, however, especially when dependent upon an atonic condition of the lower bowel, it is one of the most useful laxatives that we possess. Many believe that it possesses a direct tonic action, not only evacuating the bowel of its contents but encouraging a restoration toward normal conditions. The presence of bile in the bowel seems in some way to be essential for the best effects of this drug, and in those cases in which this secretion is lacking it is well to exhibit some preparation of bile in conjunction with the aloes. Soap also appears to enhance the cathartic action of this drug. It was formerly almost universally believed that aloes possessed emmenagogue properties and it was accordingly largely used in the treatment of various forms of *amenorrhea*. It is, however, extremely doubtful whether it exercises any action upon the pelvic organs which is not attributable to its cathartic effects.

Crude aloes is rarely used in human medicine, but may be given in *doses* of from two to ten grains (0.13–0.65 Gm.).

Off. Prep.—Extractum Colocynthidis Compositum, *U. S.* (*Br.*); Pilulæ Aloes, *U. S.* (*Br.*); Pilulæ Rhei Compositæ, *U. S.* (*Br.*); Tinctura Aloes, *U. S.*; Tinctura Benzoini Composita, *U. S.* (*Br.*); Decoctum Aloes Compositum, *Br.*; Extractum Aloes, *Br.*; Pilula Aloes et Asafetidæ, *Br.*; Pilula Aloes et Ferri, *Br.*; Pilula Aloes et Myrrhæ, *Br.*; Pilula Colocynthidis Composita, *Br.* (*N. F.*); Extractum Aloes, *N. F.*; Pilulæ ad Prandium, *N. F.*; Pilulæ Aloes et Asafœtidæ, *N. F.*; Pilulæ Aloes et Ferri, *N. F.*; Pilulæ Aloes et Mastiches, *N. F.*; Pilulæ Aloes et Myrrhæ, *N. F.*; Pilulæ Aloes et Podophylli Compositæ, *N. F.*; Pilulæ Aloes, Hydrargyri et Scammonii Compositæ, *N. F.*; Pilulæ Antiperiodicæ (from Extract), *N. F.*; Pilulæ Colocynthidis et Hyoscyami, *N. F.*; Pilulæ Ferri, Quininæ, Aloes et Nucis Vomicæ, *N. F.*; Pilulæ Laxativæ Post Partum, *N. F.*; Pulvis Aloes et Canellæ, *N. F.*; Tinctura Aloes et Myrrhæ, *N. F.*; Tinctura Antiperiodica (from Extract), *N. F.*; Tinctura Zedoariæ Amara, *N. F.*

ALOINUM. U. S., Br.

ALOIN Aloin.

(ăl-ō-ĭ′nŭm)

"A pentoside or mixture of pentosides obtained from aloes, varying in chemical composition, physical and chemical properties according to the source. Preserve it in well-closed containers, protected from light." *U. S.* "Aloin is a crystalline principle obtained from aloes." *Br.*

Although aloin has been used for many years, it was not recognized by the U. S. Pharmacopœia until the revision of 1890.

Preparation.—Aloin may be prepared by W. A. Tilden's process as follows: 1 part of aloes

is dissolved in 10 parts of boiling water acidulated with hydrochloric acid, and allowed to cool. The liquid is then decanted from resinous matter, evaporated to about 2 parts, and set aside two weeks for crystals to form; the liquid portion is poured off, the crystals pressed, and the adherent resinous matter separated by shaking with acetic ether, which dissolves the resin. This process answers fairly well for obtaining aloin from Barbados or Curaçao aloes. Aloin from Socotrine aloes is best obtained by digesting the aloes in 3 parts of alcohol for 24 hours, then transferring to a water bath, and boiling for 2 hours. After cooling, the liquid is filtered and set aside to crystallize. The crystals are washed with a little alcohol and dried. The yield is about 10 per cent. (H. C. Plenge, *A. J. P.*, 1884, p. 507.) According to Lewis Ough (*C. D.*, 1892, 837) Tilden's process, modified, affords the best results; Barbados aloes yielded 12 per cent. of aloin. Schäfer obtains from 15 to 30 per cent. of crystallized aloin from commercial aloes by the following process: 50 Gm. of aloes dissolved in 300 mils of hot water are slightly acidulated with hydrochloric acid. The solution, after standing (for the resins to separate), is decanted, mixed with 50 mils of 20 per cent. ammonia water, followed by a solution of 15 Gm. of calcium chloride in 30 mils of water. The liquid is agitated and the aloin-calcium compound which separates is collected, drained, and mixed in a mortar with a slight excess of hydrochloric acid; the mixture of aloin and calcium chloride is dissolved in the smallest possible quantity of boiling water, filtered, and the filtrate cooled by means of ice; the aloin crystallizes. (*P. J.*, 1897, p. 287.) The yield of aloin from Curaçao aloes varies from 5 to 30 per cent.

Aloin is officially described as in "a microcrystalline powder or minute acicular crystals from lemon-yellow to dark-yellow in color, odorless, or possessing a slight odor of aloes and an intensely bitter taste. It becomes darker on exposure to light and air. Aloin varies in solubility with its composition. It is soluble in water, alcohol or acetone; slightly soluble in ether. A saturated aqueous solution of Aloin is neutral or not more than faintly acid to litmus. Aloin is soluble in ammonia water and alkali hydroxide solutions, forming red solutions (or yellow solutions that soon become red) which exhibit a green fluorescence. When added to alkaline solutions, Aloin is rapidly decomposed; when mixed with acid solutions decomposition is slower. A drop of ferric chloride T.S. added to an alcoholic solution of Aloin produces a brownish-green color. The color of a saturated aqueous solution of Aloin is yellow, but changes to brown on standing. Incinerate about 0.5 Gm. of Aloin; not more than 0.5 per cent. of ash remains. Shake about 1 Gm. of Aloin with 10 mils of benzene for one minute and filter; the filtrate imparts not more than a faint, pink color to an equal volume of dilute ammonia water (5 per cent.), when shaken with it (*emodin*). Dissolve about 1 Gm. of Aloin in 120 mils of distilled water, collect the insoluble residue, if any, on a filter tared after it has been dried at 100° C. (212° F.) and wash the residue with 25 mils of distilled water. This residue, when dried at 100° C. (212° F.), does not exceed 1.5 per cent." *U. S.*

"A pale yellow, microcrystalline powder. Almost inodorous; taste intensely bitter. Almost entirely soluble in 130 parts of *water,* in 18 parts of *alcohol* (90 per cent.), and in 50 parts of *acetone;* very sparingly soluble in *ether, chloroform,* and *benzene;* readily soluble in dilute *solution of ammonia,* the liquid becoming red and acquiring a greenish-red fluorescence. 0.5 gramme of Aloin gently warmed with 25 millilitres of *water* forms an almost clear solution; the filtered liquid remains clear on cooling, but on long standing slowly deposits pale yellow crystals of Aloin. One drop of *solution of copper sulphate* added to 20 millilitres of an aqueous solution (1 in 1000) of Aloin produces a bright yellow coloration, which is changed to red by the addition of 0.5 millilitre of a saturated aqueous solution of *sodium chloride,* and to violet on the further addition of 1 millilitre of *alcohol* (90 per cent.). No appreciable ash." *Br.*

Aloin of commerce is frequently contaminated with resin from aloes, indicating want of care in manufacturing. According to Serre (*D. C.*, 1895, 8), this may be detected by finely powdering 1 grain of the sample, shaking it in a test tube with 20 mils of water, and allowing it to stand one minute. The solution should be perfectly clear. See also paper by C. H. LaWall. (*Proc. Penn. Pharm. Assoc.*, 1895, 92.)

Uses.—The actions of the aloins upon the system are precisely the same as that of aloes (see page 117). Moyer (*A. E. P. P.*, xxviii) has shown that when given hypodermically it is capable of producing purgative effects but it is never employed practically in this manner. There is a marked difference in the cathartic activity of the various kinds of aloin. Barbaloin is more powerful than socaloin and, according to Moyer, nataloin generally fails to purge in man, although acting energetically upon dogs. Aloin is one of the most frequently employed of laxatives in *chronic constipation,* especially in combination with belladonna and strychnine, as in the formerly official Compound Laxative Pill.

Dose, one-sixth to one grain (0.01–0.065 Gm.).

Off. Prep.—Pilulæ Aloini Compositæ, *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ, *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ Compositæ, *N. F.;* Pilulæ Laxativæ Compositæ, *N. F.*

ALSTONIA. Br.

ALSTONIA

"Alstonia is the dried bark of Alstonia scholaris, *R. Br.,* and also of Alstonia constricta, *F. Muell.*" *Br.*

Dita Bark; Australian Fever Bark; Bitter Bark.

Under Alstonia the British Pharmacopœia recognizes the dried barks of *Alstonia scholaris* (L.) R. Br. (*Echites scholaris* L.), of India and the Philippine Islands, and *Alstonia constricta* F. Muell., of Australia, two apocynaceous trees whose barks are quite dissimilar in appearance, and, as far as our present knowledge goes, contain different alkaloids. These barks are respectively described as follows:

"Bark of Alstonia scholaris usually in irregular fragments, three to twelve millimetres thick; texture somewhat spongy, fracture short and coarse; external layer unevenly rough and fissured, brownish-grey with occasional blackish spots; internal layer bright buff. Transverse section shows numerous small medullary rays in inner layer. Almost odorless; taste bitter. Bark of Alstonia constricta usually in curved pieces or quills about sixty millimetres wide, and twelve millimetres thick. Periderm from two and a half to six millimetres thick, rusty brown, strongly rugose, with large deeply fissured reticulations. Bark internally cinnamon-brown, with strong, coarse longitudinal striæ. Transverse section shows dark-brown periderm covering the inner orange-brown tissues, in which numerous small shining particles can be seen with a lens. Fracture short and granular in outer layers, fibrous in inner. Slight aromatic odor; taste very bitter." *Br.*

From the bark of *Alstonia scholaris* M. Gruppe extracted an uncrystallizable, hygroscopic, bitter principle, *ditaine.* (*J. P. C.*, 4e sér., xviii, 225; xix, 84; *P. J.*, Aug., 1875.) Harnack (*Ber. d. Chem. Ges.*, 1878) first obtained ditaine in pure crystallized form, and gave it the formula $C_{20}H_{30}N_2O_4$. O. Hesse (*P. J.*, Oct. 23, 1880) finds in dita the following principles: three alkaloids: *ditamine*, $C_{16}H_{32}O_2N$, the relative amount of which he estimates at 0.04 per cent.; *echitamine*, $C_{32}H_{28}O_4N_2 + H_2O$ (identical, according to Hesse, with Harnack's ditaine); and *echitenine*, $C_{20}H_{27}O_4N$. Of these, the second is the strongest base, and resembles ammonia in its chemical characters; Hesse considers it with one molecule of water to form the hydroxide of a strong basic radical, *echitammonium*, $C_{32}H_{29}O_4N_2$. The solutions of *echitammonium hydroxide* are so strongly basic that they precipitate the hydroxides of copper, iron, aluminum, and lead, and decompose sodium and potassium chlorides, liberating the corresponding hydroxides. Hesse considers echitammonium the most strongly basic of all the alkaloids. Hesse also obtained by extraction with petroleum benzin *echicaoutchin*, *echiretin*, *echicerin*, *echitin*, and *echitein*, of which the three last mentioned are crystalline.

From *Alstonia constricta*, F. V. Müller and A. Rummel obtained *alstonine.* Oberlin and Schlagdenhauffen found in 1879 another alkaloid, *alstonicine.* Hesse subsequently analyzed the bark and found alstonine, the *chlorogenine* of a former investigation, which has the composition $C_{21}H_{20}O_4N_2$, *prophyrine*, $C_{21}H_{25}O_2N_3$, and *alstonidine.* The alkaloids and their salts in acidulated solutions show decided blue fluorescence.

Uses.—This drug has been used for many years in Australia and the Philippine Islands in the treatment of *malarial* and other *fevers*, as well as a simple bitter. The alkaloid ditaine has been scientifically studied by Harnach (*A. E. P. P.*, 1877, xvii, p. 126), who finds that it has a paralyzing effect upon the endings of the motor nerve similar to that produced by curara. In large dose it also paralyzes the cardio-inhibitory nerves and lowers blood pressure. There is nothing in this study, which is, as far as we know, the only scientific investigation of the drug which has been made, to explain any action in malaria. Nevertheless some of the clinical reports, especially from the eclectic physicians, have been extremely laudatory, vaunting it even as a substitute for quinine.

Dose, two to four grains (0.13–0.25 Gm.).

Off. Prep.—Infusum Alstoniæ, *Br.*; Tinctura Alstoniæ, *Br.*

ALTHÆA. U. S.

ALTHÆA [Marshmallow root]

(äl-thæ'a)

"The root of *Althæa officinalis* Linné (Fam. *Malvaceæ*) deprived of the brown, corky layer and small roots, and carefully dried. Preserve Althæa in tightly-closed containers, adding a few drops of chloroform or carbon tetrachloride from time to time, to prevent attack by insects." *U. S.*

Radix Hibisci, Radix Bismalvæ; Wymote, White Mallow, Mortification root; Racine de Guimauve, Guimauve, *Fr.*; Radix Althææ, *P. G.*; Altheewurzel, Althee, Eibischwurzel; Eibisch, *G.*; Altea, Malvavischio, *It.*; Altea, Raiz de Malvavisco, *Sp.*

Althæa officinalis is an herbaceous perennial, with a perpendicular branching root and erect woolly stems, from two to four feet or more in height, branched and leafy towards the summit. The leaves are described under *Folia Althæa*, p. 120. The flowers are terminal and axillary, with short peduncles, each bearing one, two, or three flowers. The corolla has five spreading, obcordate petals, of a pale rose color. The fruit consists of numerous capsules united in a compact circular form, each containing a single seed. The plant grows throughout Europe, inhabiting salt marshes, the banks of rivers, and other moist places. It is found also in this country, from New England to New York and westward to Michigan and Arkansas. It is largely cultivated in Europe for medicinal use, particularly in Germany, Belgium and France.

The roots should be collected in autumn from plants at least two years old. They are usually prepared for the market by removing the outer layers. The commercial drug sometimes consists of the unpeeled root, which is sliced transversely and diagonally.

Properties.—Althæa is "usually cut into

small pieces about 5 mm. in diameter, of a uniform grayish-white color and otherwise having the characters of entire roots; occasionally entire, slenderly tapering, attaining a length of 30 cm. and a thickness of 2 cm.; externally whitish, longitudinally furrowed, frequently spirally twisted and covered with the somewhat loosened bast-fibers; fracture of bark fibrous, of wood short and granular; internally yellowish-white; bark 1 to 2 mm. thick, porous, due to mucilage cells, and separated from the slightly radiating wood by a distinct, grayish cambium zone; odor slight; taste sweetish, mucilaginous. The powder is whitish; starch grains numerous, from 0.003 to 0.02 mm. in diameter, usually with a long cleft at the point of origin of growth; sclerenchymatous fibers in groups, the walls being quite thick and more or less lignified; tracheæ with scalariform thickenings or with bordered pores; calcium oxalate crystals few, in rosette aggregates from 0.02 mm. to 0.03 mm. in diameter. Add 1 Gm. of Althæa to 10 mils of cold water, allow it to stand with occasional stirring during thirty minutes, and filter through cotton; a pale yellow-colored mucilage is obtained, which is neutral to litmus and is colored a deep yellow on the addition of a few drops of potassium hydroxide T.S. The mucilage does not have a sour or ammoniacal odor. Althæa yields not more than 8 per cent. of ash." *U. S.*

The abundant mucilage is situated chiefly in special cells, and can be seen to be in layers when alcohol is added. Kraemer (*A. J. P.*, 1898, p. 285) proposed the use of an alcoholic solution of methylene blue for the differentiation of the mucilage. It, with starch and saccharine matter, is taken out by boiling water. The mucilage, without the starch, is extracted by cold water, which thus becomes ropy. A principle was discovered in the root by Bacon, which has been ascertained to be identical with *asparagin*, $C_4H_8N_2O_3 + H_2O$. Boutron-Charland and Pelouze found it to belong to that class of organic principles which are convertible by strong acids, and other agencies, into ammonia and organic acids, and which are designated by the termination *amide*, being compounds of acid radicals with the group NH_2. When such an amide is acted upon by acids, it is decomposed, the acid radical taking OH to form the free acid and the amide group taking H to form ammonia. Thus asparagin, which in this view should be called *asparamide*, is converted into ammonia and *aspartic acid*, $C_4H_7NO_4$, and one molecule of the resulting ammonium aspartate corresponds with one molecule of asparamide and one of water. (*J. P. C.*, xix, 208.) Asparagin, being now recognized as a derivative of succinic acid, is called *amido-succinamide*, and the aspartic acid is called *amido-succinic* acid. It is found in various other plants besides the marshmallow, as in the shoots of asparagus, in vetches grown in the dark, in all the varieties of the potato, and in the roots of the comfrey and licorice plant. According to Pira, asparagin has acid properties. It has no therapeutic value. *Betaine* (trimethyl-glycocoll) has been obtained from althæa by Orlow. (*Ph. Z. R.*, 1898.)

The roots of other Malvaceæ are sometimes substituted for that of marshmallow, without disadvantage, as they possess similar properties. Among these are *Althæa rosea* Cav., or *hollyhock*, and *Malva Alcea* L. The dark purple flowers of a variety of *A. rosea* have been proposed as a test for acids and alkalies. A strong infusion of these flowers imparts to slips of white filtering paper a permanent purplish-blue color, which is reddened by acids, and rendered bluish-green by alkalies.

Althæa or Marshmallow Leaves, under the title of *Folia Althææ*, are official in the Swiss, German and Austrian Pharmacopœias and as *Althæa Folia* in the National Formulary. The leaves are collected in June or July, while the plant is in flower, and dried. They are described in the N. F. as "the dried leaves of *Althæa officinalis* Linné (Fam. *Malvaceæ*), without the presence of more than 5 per cent. of stems or other foreign matter." *N. F.* As seen in commerce they are "gray-green or yellowish gray-green and densely and finely tomentose throughout; petioles one-sixth to one-fifth as long as the blades; blades varying from 5 to 15 cm. in length and from 3 to 10 cm. in breadth, cordate or rhomboidal-ovate in outline, rounded or occasionally nearly truncate at the base, acute at the summit; margin doubly serrate-dentate, the principal teeth from one to three pairs, the lowest almost large enough to be regarded as lobes, the secondary very irregular, triangulate, acute, broader than long, the sinuses acute; two to four occasionally six principal veins originating with the midrib in the petiole, prominent underneath, terete; branches of the midrib arising at a wide angle, nearly straight, each terminating in a marginal tooth. Leaf thin, but appearing thick because of its hairy covering. Odor slight, scarcely characteristic; taste mucilaginous. The powdered drug is grayish to grayish-green and, when examined under the microscope, exhibits numerous unicellular, non-lignified stellate branching hairs, up to 0.6 mm. in length, usually occurring in clusters of two to six; few, short stalked, multicellular glandular hairs; calcium oxalate in rosette aggregates up to 0.025 mm. in diameter; fragments of the epidermal tissue with stomata, the latter about 0.025 mm. in length; few lamellated mucilage cells; usually a few pollen grains, spherical, spiny, up to 0.1 mm. in diameter. Althæa Leaves yield not more than 16 per cent. of ash." *N. F.*

Uses.—The virtues of marshmallow are exclusively those of a demulcent. The decoction of the root is much used in Europe in irritation and inflammation of the mucous membranes. A syrup of althæa is official in the German Pharmacopœia, and was introduced into the U. S. Pharmacopœias of 1880 and 1890 (see *U. S. D.*, 18th edition, p. 1327). Owing to its tendency to ferment rapidly it was not

retained in the U. S. P. VIII or IX, but is found in the N. F. IV. (See *Syrupus Althææ.*) The roots themselves, as well as the leaves and flowers, boiled and bruised, are sometimes employed as a poultice. In France the powdered root is much used in the preparation of pills and electuaries. It enters, as an ingredient, into one mass and two pills of the U. S. P.

Off. Prep.—Massa Hydrargyri, *U. S.;* Pilulæ Ferri Carbonatis, *U. S.;* Pilulæ Phosphori, *U. S.;* Species Pectorales, *N. F.;* Syrupus Althææ, *N. F.*

ALUMEN. U. S. (Br.)

ALUM

(ą-lū′mĕn)

"It contains not less than 99.5 per cent. of $AlNH_4(SO_4)_2 + 12H_2O$ (453.47), or of $AlK(SO_4)_2 + 12H_2O$ (474.53), the label of the container must indicate whether the salt is Ammonium Alum or Potassium Alum." *U. S.*

"Purified Alum is aluminum and potassium sulphate (Potassium Alum), $Al_2(SO_4)_3,K_2SO_4, 24H_2O$, or aluminium and ammonium sulphate (Ammonium Alum), $Al_2(SO_4)_3$, $(NH_4)_2SO_4, 24H_2O$, and is obtained by the combination of aluminium sulphate with potassium sulphate or with ammonium sulphate." *Br.*

Alumen Purificatum, *Br.;* Potassium Alum, Aluminum and Potassium Sulphate, *U. S. P. VIII.;* Aluminii et Potassii Sulphas, *U. S.* 1870, Potassa Alum; Sulphas Aluminico-potassicus; Alun de potasse, *Fr. Cod.;* Alun, Sulfate d'Alumine et de Potasse, *Fr.;* Alumen, *P. G.;* Alaun, Kalialaun, *G.;* Solfato di allumino e di potassio, Allume, *It.;* Sulfato aluminico-copotasico, Alumbre, *Sp.*

Aluminii et Ammonii Sulphas, Sulphas Aluminico-Ammonicus; Alun ammoniacal, *Fr.;* Ammoniak-Alaun, *G.*

The name alum has been applied indifferently to two salts, one consisting of aluminum trisulphate combined with ammonium sulphate, the other of the same salt of aluminum combined with potassium sulphate, and distinguished as *ammonium alum* and *potassium alum.* The former was official in the U. S. P. 1870, but was replaced by *potassium alum. Ammonium alum* is still retained with potassium alum under the title *Alumen* in the United States and British Pharmacopœias.

The British authority (1914) added the word "Purificatum" to the title.

Ammonium Alum. *Aluminum and Ammonium Sulphate.*—Besides the potassium alum, there are several others, in which the potassium is replaced by some other base, as, for example, ammonium or sodium. Of these, *ammonium alum,* or aluminum and ammonium sulphate, is recognized by both the U. S. and Br. Pharmacopœias. It is made by adding ammonium sulphate to the solution of aluminum sulphate. This kind of alum formerly came into very general use, owing to the comparative cheapness of ammonia, and now (1916), owing to the great advance in the cost of potassium salt, is almost exclusively used. *Scotch alum,* made near Paisley, generally contains both potassium and ammonium. Ammonium alum resembles potassium alum so exactly that it cannot be distinguished by simple inspection; and in composition it is perfectly analogous to the potassium salt. It may be distinguished by subjecting it to a strong calcining heat, after which alumina will be the sole residue; or by rubbing it with potassium hydroxide or lime and a little water, when the odor of ammonia will be perceived.

Potassium Alum. *Aluminum and Potassium Sulphate.*—Potassium alum is manufactured occasionally from earths which contain it ready formed, but most generally from minerals which, from the fact of their containing most or all of its constituents, are called *alum ores.* The principal alum ores are the *alum stone,* which is a native mixture of aluminum sulphate and potassium sulphate, found in large quantities at Tolfa and Piombino in Italy; certain natural mixtures of iron disulphide with alumina, silica, and bituminous matter, called *aluminous schist* or *alum slate; bauxite,* a native aluminum hydroxide, and *cryolite.* (See *Sodii Carbonas.*)

At the Solfatara, and other places in Southern Italy, alum was formerly extracted from earths containing it ready formed. The ground being of volcanic origin, and having a temperature of about 40° C. (104° F.), an efflorescence of pure alum formed upon its surface. This was collected and lixiviated, and the solution crystallized by slow evaporation in leaden vessels sunk in the ground. The alum stone is manufactured into alum by calcination, and subsequent exposure to the air for three months, the mineral being frequently sprinkled with water, in order that it may be brought to a soft mass. This is lixiviated, and the solution obtained crystallized by evaporation. The alum stone may be considered as consisting of alum united with a certain quantity of aluminum hydroxide. The latter, by the calcination, loses its water, and becomes incapable of remaining united with the alum of the mineral, which is consequently set free. Alum of the greatest purity is obtained from this kind of ore.

Alum slate, when compact, is first exposed to the air for a month. It is then stratified with wood, which is set on fire. The combustion which ensues is slow and protracted. The sulphur is in part converted into sulphuric acid, which unites with the alumina; and the aluminum sulphate thus formed generates a portion of alum with the potassium hydroxide derived from the ashes of the wood. The iron, in the mean time, is almost wholly converted into sesquioxide, and thus becomes insoluble. The matter is lixiviated, and the solution crystallized into alum by evaporation. The mother waters, containing aluminum sulphate, are then drawn off, and made to yield a further portion of alum by the addition of potassium sulphate or potassium chloride, the latter being obtained from the soap boilers, or from native potassium chloride of the Stassfurt deposits. When alum slate is easily disintegrated, it is not calcined,

but merely placed in heaps and occasionally sprinkled with water. The iron disulphide gradually absorbs oxygen, and passes into ferrous sulphate, which effloresces on the surface of the heap. Part of the sulphuric acid formed unites with the alumina, so that, after the chemical changes are completed, the heap contains both ferrous sulphate and aluminum sulphate. At the end of about a year, the matter is lixiviated, and the solution of the two sulphates produced is concentrated to the proper degree in leaden boilers. The ferrous sulphate crystallizes, while the aluminum sulphate, being of a more soluble nature, remains in the mother waters.

These are drawn off, and treated with potassium sulphate in powder, heat being at the same time applied. The whole is then allowed to cool, that the alum may crystallize. The crystals are then separated from the solution, and purified by a second solution and crystallization. They are next treated with water just sufficient to dissolve them at the boiling temperature, and the saturated solution is run into casks or tubs so constructed as to be easily taken to pieces and set up again. In the course of ten or fifteen days the alum concretes into a crystalline mass, from which the mother liquor is let off.. The vessel is then taken to pieces, and the salt, having been broken up, is packed in barrels for sale. This process for forming the alum in large masses is called *rocking*.

Alum is largely manufactured by the direct combination of its constituents. With this view, clays are selected as free from iron and calcium carbonate as possible, and calcined to sesquioxidize the iron and render them more easily pulverized; after which they are dissolved, by the assistance of heat, in weak sulphuric acid. Advantage has been found in mixing the clay, previous to calcination, with powdered charcoal, coke, or other carbonaceous matter, in the proportion of about one to six of the clay, and then applying heat by a reverberatory furnace until all the carbon is consumed. It is asserted that the alumina is thus rendered more soluble in the acid. (*P. J.*, Dec., 1857, p. 328.) The aluminum sulphate, thus generated, is next crystallized into alum by the addition of potassium sulphate in the usual manner. Alum is made in this way from the ashes of the Boghead cannel coal, which occurs near Edinburgh. These ashes, which form the residue of the combustion of the coke derived from the coal used for making gas, contain a considerable quantity of alumina in a state readily soluble in acids. For an account of the manufacture of alum in India, see *C. D.*, 1892, 636. *Bauxite*, a hydrated oxide of aluminum, containing from 56 to 60 per cent. of aluminum oxide, has within recent years become one of the most important raw materials for the alum manufacture. It is found in very rich deposits in Georgia and Alabama. *Cryolite*, a double fluoride of sodium and aluminum, also serves as a source of supply, the aluminum hydroxide being produced as an intermediate product.

The elements *rubidium* and *cæsium* are found in *lepidolite*, and, as much of the alum in continental Europe is made from this mineral, Salzer found samples of commercial potassium alum which contained a considerable quantity of rubidium alum; this contaminated potassium alum is less soluble in water than ordinary alum. (*A. Pharm.*, 1887, p. 217.)

The production of crystallized alum in the United States has decreased in recent years, while that of aluminum sulphate (so-called concentrated alum), containing half the usual quantity of water of crystallization, has steadily increased. In 1914, the production of alum in the United States amounted to 18,238 tons, valued at $565,989, while that of aluminum sulphate amounted to 164,954 tons, valued at $2,942,572.

Properties.—Alum, as usually seen, is officially described as follows: "Ammonium Alum and Potassium Alum both occur in large, colorless crystals, crystalline fragments, or as white powders; Alum is odorless and has a sweetish and strongly astringent taste.

"**Ammonium Alum.**—It is somewhat less soluble in water than is Potassium Alum. Potassium hydroxide T.S. added to an aqueous solution of Ammonium Alum (1 in 20) at first causes a precipitate, which completely dissolves in an excess of the reagent, ammonia being evolved. Completely precipitate the aluminum from a boiling solution of 1 Gm. of Ammonium Alum in 100 mils of distilled water by the addition of a slight excess of ammonia water and filter; not more than 0.5 per cent. of residue remains on evaporating the filtrate to dryness and igniting it.

"**Potassium Alum.**—One Gm. of Potassium Alum dissolves in 7.2 mils of water at 25° C. (77° F.), and in 0.3 mil of boiling water; insoluble in alcohol, freely soluble in glycerin. Potassium Alum imparts a violet color to a nonluminous flame. The addition of sodium bitartrate T.S. to a saturated solution of Potassium Alum produces, sometimes slowly, a white crystalline precipitate. Potassium hydroxide T.S. added to an aqueous solution of Potassium Alum (1 in 20) at first causes a precipitate, which completely dissolves in an excess of the reagent, but no ammonia is evolved.

Both Ammonium Alum and Potassium Alum conform to the following tests: An aqueous solution of Alum (1 in 20) is acid to litmus. When heated it fuses, and at about 200° C. (392° F.) it loses all of its water of crystallization. When strongly heated it loses sulphuric anhydride, becoming incompletely soluble in water. An aqueous solution of Alum (1 in 20) yields with ammonia water a white gelatinous precipitate almost insoluble in an excess of ammonia water. With barium chloride T.S., an aqueous solution of Alum (1 in 20) yields a white precipitate insoluble in hydrochloric acid. An aqueous solution of Alum does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of Alum meets the require-

ments of the Test for arsenic (see Part III, Test No. 1). Add 5 drops of potassium ferrocyanide T.S. to 20 mils of an aqueous solution of Alum (1 in 150); no blue color is produced at once (*iron*).

"**Assay.**—Dissolve about 1 Gm. of the Alum, accurately weighed, and about 1 Gm. of ammonium chloride in 250 mils of distilled water and precipitate the aluminum hydroxide by the addition of a slight excess of ammonia water to the boiling solution. Collect the precipitate on a filter, wash it thoroughly with hot distilled water, dry, ignite strongly and weigh it. The aluminum oxide so obtained corresponds to not less than 99.5 per cent. of the Alum assayed. Each Gm. of aluminum oxide corresponds to 8.874 Gm. of $AlNH_4(SO_4)_2 + 12H_2O$, and to 9.286 Gm. of $AlK(SO_4)_2 + 12H_2O$." *U. S.*

"In colorless transparent crystalline masses; taste sweetish, astringent. Soluble in 10 parts of *water*, the solution being clear and having an acid reaction; freely soluble in *glycerin*, insoluble in *alcohol* (90 per cent.). Yields the *reactions* characteristic of aluminium, of potassium or ammonium, and of sulphates. Yields no characteristic *reactions* for copper, lead, zinc, calcium, or sodium, and not more than very slight *reactions* for iron. *Arsenic limit* 5 parts per million." *Br.*

Its sp. gr. is 1.71. It reddens litmus, but changes the blue tinctures of the petals of plants to green. When heated a little above 100° C. (212° F.), it undergoes the aqueous fusion; and, if the heat be continued, it loses its water, swells up, becomes a white, opaque, porous mass, and is converted into the official *exsiccated alum*. (See *Alumen Exsiccatum*.) Exposed to a red heat, it gives off oxygen, together with sulphurous and sulphuric oxides, and the residue consists of aluminum oxide and potassium sulphate. When calcined with finely divided charcoal, it forms a spontaneously inflammable substance, called *Homberg's pyrophorus*, which consists of a mixture of potassium sulphide, alumina, and charcoal.

Several varieties of alum are known in commerce. *Roche alum*, so called from its having come originally from Rocca, in Syria, is a sort which occurs in fragments about the size of an almond, and of a pale rose color, which is given to it, according to Pereira, by bole or rose-pink. *Roman alum*, which is another variety found in commerce, also occurs in small fragments, covered with a reddish-brown powder, resembling ochre, which is put on by the manufacturers. It has been supposed that the powder contains iron, but this is probably a mistake. Roman alum crystallizes in cubes, from the fact that the crystals are deposited from a solution always containing an excess of alumina, which decomposes any iron salt that may be present. This crystalline form of alum is, therefore, an index of its freedom from much contamination with iron.

All the alums of commerce contain more or less ferrous sulphate, varying from five to seven parts in the thousand. The iron is readily detected by adding to a solution of the suspected alum a few drops of potassium ferrocyanide, which will cause a greenish-blue tint, if iron be present. It may be detected also by precipitating the alumina as a subsulphate with a solution of potassium hydroxide, and afterwards adding the alkali in excess. This will redissolve the precipitate, with the exception of any iron, which will be left in the state of sesquioxide. The proportion of iron usually present, though small, is injurious when the salt is used in dyeing. Alum may, however, be purified, either by dissolving it in the smallest quantity of boiling water, and stirring the solution as it cools, or by repeated solution and crystallization.

Incompatibles.—Alum is incompatible with the alkalies and their carbonates, lime and lime water, magnesium oxide and carbonate, potassium tartrate, and lead acetate.

Composition.—Alum was regarded as an aluminum sulphate, until it was proved by Descroizilles, Vauquelin, and Chaptal to contain also potassium sulphate, ammonium sulphate, or both these salts. When its second base is potassium, it consists of one molecule of aluminum sulphate 342.41, one of potassium sulphate 174.27, and twelve of water $429.12 = 942.04$, but one-half of this molecule of alum is now more often written, making its molecular weight 474.53 for the formula $AlK(SO_4)_2 + 12H_2O$. In the ammonium alum, the molecule of potassium sulphate is replaced by one of ammonium sulphate. *Alumina* is classed as an earth, and may be obtained by subjecting ammonium alum to a strong calcining heat. It consists of two atoms of the metal *aluminum* 54.2, and three of oxygen $48 = 102.20$. It is, therefore, a sesquioxide. The existence of this metal was rendered probable by Sir H. Davy in 1808; but it was not fairly obtained until 1828, when Wöhler procured it in an impure state, in globules of the size of a pin's head, by the action of potassium on aluminum chloride. In 1854, Deville succeeded in obtaining the pure metal in ingots by decomposing the same chloride with sodium. The process of Deville remained the only practical process for its manufacture until 1886, when the Messrs. Cowles of Cleveland, Ohio, succeeded in effecting the reduction of corundum, the native oxide, by charcoal with the aid of a powerful electric current from a Brush dynamo-electric machine, using large carbon electrodes. They manufactured the pure aluminum and the alloys of copper known as aluminum bronzes. This process in turn has been practically displaced by the Hall process, as operated by the Pittsburg Reduction Company at Niagara Falls and elsewhere. This is to electrolyze pure alumina dissolved in a bath of melted cryolite. The cryolite (a double fluoride of sodium and aluminum) is continuously regenerated, so that by feeding in the pure alumina the process can be made continuous. A German process, that of Graetzel,

for electrolyzing the fused chloride, is also in successful use.

Aluminum is silver-white, sonorous, unalterable in the air, and lighter than glass, having only the sp. gr. 2.56. Its fusing point is somewhat lower than that of silver. It is not attacked by sulphuric or nitric acid, nor tarnished by hydrogen sulphide. Its best solvent is hydrochloric acid. After silver, gold, and platinum, it is the least alterable of the metals.

The world's production of aluminum for 1915 was 86,240 metric tons, of which the United States produced 45,000 tons, valued at $31,-581,000.

Uses.—Alum is absorbed from the intestinal tract only in relatively small quantities, although Gies (*J. A. M. A.*, 1911, lvii, p. 57) has shown that the former view that it was completely excreted, unabsorbed, with the feces is incorrect. The germicidal power of alum is lower than many of the other salts of aluminum. According to Miquel it will inhibit the multiplication of bacteria when present, in the proportion of about one part to two hundred.

Alum is a powerful astringent with very decided irritant qualities, and when taken internally in sufficient quantities is emetic and purgative, and may even cause gastro-intestinal inflammation. It is widely employed in various conditions in which an astringent or styptic is desired, as for instance, *serous diarrheas, pharyngitis,* local *hemorrhages,* and the like. It has also been used internally in the treatment of *colica pictonum* in which disease it seems to do more than act as a chemical precipitant of any lead in the intestinal tract and to exercise some beneficial action upon the intestines directly. As an emetic it was formerly used to a considerable extent in the treatment of *laryngeal diphtheria,* but has in modern times been largely replaced by various operative procedures. It is occasionally employed to empty the stomach in cases of poisoning, but is inferior for this purpose to zinc sulphate. As a gargle in various *anginas* it has been a favorite remedy, but because of its acidity exercises a destructive influence upon the teeth and is inferior to aluminum acetate.

The most important use of alum to-day is as a local styptic in external *hemorrhages,* in *epistaxis,* and other bleeding from mucous membranes to which it can be directly applied. It is also employed as an astringent in *leukorrhea,* unhealthy *ulcers,* and similar conditions. As an astringent it is usually employed in strengths ranging from 1 to 5 per cent., according to the location to which it is applied. Occasionally powdered alum may be thinly dusted over the area. As a styptic if the bleeding point is easily accessible it may be touched with the alum stick or the powdered alum directly applied. In *epistaxis* it is usually employed by plugging the nares with pledgets of cotton soaked in a saturated solution. When used as an astringent on the more delicate mucous membranes, as in *conjunctivitis,* it is often desirable to modify its action by combining it with albuminous matter as in the form of the *alum curd.* This is made by boiling two drachms of alum in a pint of milk and straining off the whey.

When taken in large dose alum acts as an irritant poison causing burning in the mouth and throat followed by vomiting, purging, collapse, and other symptoms of toxic gastro-enteritis. Ricquet records a fatal case from an ounce of alum. (*J. P. C.*, Oct., 1873, p. 333.) When small quantities of the soluble salts of aluminum are introduced into the circulation they produce a slow form of poisoning characterized by motor palsies and areas of local anesthesia with fatty degeneration in the kidney and liver. The nervous symptoms have been shown by Doellken (*A. E. P. P.*, 1897, xl) to be due to anatomical changes in the nerve centers. There are also often symptoms of gastro-intestinal inflammation which is presumably the result of the effort of the glands of the intestinal tract to eliminate the poisoning.

The question of the toxic effects of repeated small doses of alum has become a matter of some importance because of the widespread use of the salt in baking powder. It has been held by some that under these conditions the aluminum is converted into a form which is non-absorbable and therefore harmless. The experiments of Gies appear to demonstrate that bread stuffs made from alum baking powder yield their alum to absorption, at least partially. The wider question of whether the relatively minute doses of aluminum which enter the system under these conditions is deleterious or not, is still a matter of dispute.

Dose, as an astringent, five to twenty grains (0.32–1.3 Gm.); as an emetic one drachm (3.9 Gm.).

Off. Prep.—Alumen Exsiccatum, *U. S.;* Alumini Hydroxidum, *U. S.;* Glycerinum Aluminis, *Br.;* Alumen Exsiccatum, *Br.;* Liquor Alumini Acetico-Tartratis, *N. F.*

ALUMEN EXSICCATUM. U. S., Br.

EXSICCATED ALUM Alum. Exsic. [Alumen Ustum Dried Alum Burnt (Burned) Alum]

(ą-lū'mĕn ĕx-sĭc-cā'tŭm)

"It contains, when recently dried to constant weight at 200° C. (392° F.), not less than 96.5 per cent. of anhydrous $AlNH_4(SO_4)_2$ (237.28) or of anhydrous $AlK(SO_4)_2$ (258.34), the label of the container indicating whether it is made from Ammonium Alum or from Potassium Alum. Preserve it in well-closed containers and do not dispense it if it contains more than 10 per cent. of moisture." *U. S.*

Alun calciné, desséché, brûlé, *Fr.;* Alumen ustum, *P. G.;* Gebrannter Alaun, Gebrannter Kalialaun, *G.;* Solfato di alluminio e di potassio usto, Allume usto, *It.;* Solfato aluminico-potasico anhidro, Alumbre calcinado, *Sp.*

* "Alum, in small pieces, *one hundred grammes* [or 3 ounces av., 231 grains], to make

fifty-five grammes [or 1 ounce av., 411 grains]. Place the Alum in a tared shallow porcelain dish so as to form a thin layer, and heat it cautiously on a sand-bath until it liquefies. Then continue the application of heat at a temperature not exceeding 200° C. (392° F.) with constant stirring, until aqueous vapor ceases to be evolved, and a dry, white, porous mass is obtained. When cold, reduce the product to a fine powder." *U. S.*

"Potassium Alum, 100 grammes. Heat the Potassium Alum in a porcelain dish or other suitable vessel till it liquefies, then increase and continue the application of heat until aqueous vapor ceases to be disengaged, and the salt has lost from 45 to 46 per cent. of its weight." *Br.*

The object of these processes is to obtain the alum free from its water of crystallization, without otherwise in the least decomposing it. For this purpose a certain degree of heat is necessary; and yet if the heat be too great the salt itself is decomposed, and the desired end is not attained. If the alum employed be the potassium alum, the old indefinite directions will generally be sufficient to secure the requisite result, as this salt will resist a heat short of redness; but this is not the case with the ammonium salt. To guard against failure from this cause, the Pharmacopœias formerly directed 205° C. (401° F.) as the highest heat to be used, and the checking of the operation when nearly all the water has been driven off, as indicated by the weight of the residue. John M. Maisch satisfactorily determined by experiment that, whichever alum may be used, this temperature is quite high enough, and the direction of the Pharmacopœias, as to the weight of the residue, insures that a sufficient heat will be employed. By the official process there is left behind about one and one-fourth per cent. of the water of crystallization, when potassium alum is used.

Properties.—Exsiccated alum is officially described as "white, granular powder, without odor, possessing a sweetish, astringent taste, and attracting moisture on exposure to the air. One Gm. of Exsiccated Alum dissolves very slowly and usually incompletely in about 20 mils of water at 25° C. (77° F.); also in 1.5 mils of boiling water; insoluble in alcohol. Add 2 Gm. of Exsiccated Alum to 40 mils of distilled water and allow it to stand with occasional agitation for twenty-four hours. Collect the insoluble residue on previously dried and counterbalanced filters, wash with 50 mils of distilled water and finally dry at 100° C. (212° F.) until of constant weight; the residue weighs not more than 0.05 Gm. Dry about 1 Gm. of Exsiccated Alum in an air bath, to constant weight at 200° C. (392° F.); the loss does not exceed 10 per cent. An aqueous solution of Exsiccated Alum responds to the reactions and tests for Ammonium Alum or for Potassium Alum given under *Alumen*, allowance being made for the difference in strength.

"**Assay.**—Dissolve about 0.5 Gm. of Exsiccated Alum, previously dried to constant weight at 200° C. (392° F.) and accurately weighed, in 100 mils of distilled water, filter if necessary, thoroughly wash the insoluble residue with distilled water, dilute the filtrate and washings to about 250 mils, with distilled water, and add 1 Gm. of ammonium chloride. Proceed with the assay as directed under *Alumen*, beginning with the words 'and precipitate,' second line of the Assay. The aluminum oxide so obtained corresponds to not less than 96.5 per cent. of the previously dried Exsiccated Alum. Each gramme of aluminum oxide corresponds to 4.643 Gm. of $AlNH_4(SO_4)_2$, and to 5.055 Gm. of $AlK(SO_4)_2$." *U. S.*

"A white powder slowly and completely soluble in 20 parts of *water*. Absorbs moisture on exposure to air. Yields the reactions and is free from the impurities indicated under 'Alumen Purificatum.'" *Br.*

Before pulverization, it is a light, white, opaque, porous mass. During the exsiccation, alum loses 45 per cent. of its weight in dissipated water. Exsiccated alum resists the action of cold water for a long time, showing its altered aggregation. In composition it differs from crystallized alum merely in the absence of water.

Uses.—Exsiccated alum has the same medicinal properties as ordinary alum, except that it is much more powerful and irritant. It is used as a mild escharotic to destroy *exuberant granulations*, on which it should be freely dusted.

ALUMINI HYDROXIDUM. U. S.

ALUMINUM HYDROXIDE Alum. Hydrox. [Alumini Hydras, U. S. 1890]

(ą-lū'mį-nī hȳ-drŏx'į-dŭm)

"A compound consisting principally of aluminum hydroxide [$Al(OH)_3 = 78.12$]." *U. S.*

Aluminum Hydrate, Hydrated Alumina; Argilla Pura, s. Hydrata; Hydrate de l'Alumine, *Fr.*; Thonerdehydrat, *G.*

* "Alum, *one hundred grammes* [or 3 ounces av., 231 grains]; Monohydrated Sodium Carbonate, *forty-five grammes* [or 1 ounce av., 257 grains]; Water, *a sufficient quantity*.

"Dissolve each salt separately in *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of Water, filter the solutions and heat them to boiling. Then having poured the hot solution of Monohydrated Sodium Carbonate into a capacious vessel, gradually pour in the hot solution of Alum with constant stirring, and add *two thousand mils* [or 67 fluidounces, 5 fluidrachms] of boiling Water. Allow the precipitate to subside, decant the clear liquid, and pour upon the precipitate *two thousand mils* [or 67 fluidounces, 5 fluidrachms] of hot Water. Again decant, transfer the precipitate to a strainer, and wash it with hot Water, until the washings produce not more than a faint cloudiness with barium chloride T.S. Allow the precipitate to drain, dry it at a temperature not exceeding 40° C. (104° F.), and reduce it to a uniformly fine powder." *U. S.*

The reaction is as follows: $2KAl(SO_4)_2 + 3Na_2CO_3 + H_2O = 2Al(OH)_3 + 3Na_2SO_4 +$

$K_2SO_4 + 3CO_2$. The alum solution is directed to be added to the sodium carbonate solution, because if the latter is not in excess during the whole period of precipitation a basic sulphate will be produced and contaminate the finished solution.

Properties.—It is "a white, bulky, amorphous powder, odorless and tasteless; permanent in dry air. It is insoluble in water and alcohol; it is dissolved by hydrochloric or sulphuric acid and by the fixed alkali hydroxides. Solutions of Aluminum Hydroxide in hydrochloric or sulphuric acid yield with potassium hydroxide T.S. a white gelatinous precipitate, dissolved by an excess of the reagent but again precipitated by the addition of an excess of ammonium chloride. When heated to redness it loses abo t 34 per cent. of its weight. Boil 1 Gm. of Aluminum Hydroxide with 20 mils of distilled water, and filter the liquid; the filtrate does not show an alkaline reaction, and, on evaporation, does not leave a residue weighing more than 0.005 Gm. (*alkali salts*). Heat 1 Gm. of Aluminum Hydroxide with 10 mils of hydrochloric acid, evaporate the solution to dryness, and dissolve the residue in 50 mils of distilled water. Ten mils of this solution does not respond to the Test for heavy metals (see Part III, Test No. 3). Heat 1 Gm. of Aluminum Hydroxide with 5 mils of sulphuric acid and 5 mils of distilled water, on a water bath, for fifteen minutes. Then dilute it to 25 mils with distilled water and filter. Five mils of this filtrate meets the requirements of the Test for arsenic (see Part III, Test No. 1)." *U. S.*

Uses.—Aluminum hydroxide is feebly astringent and probably slightly antiseptic. It is used chiefly as a protective and astringent application either in the form of an ointment or suspension, or as a dusting powder in the treatment of various inflammatory *skin diseases.*

AMMONIA

AMMONIA

(ạm-mō'nĭ-ạ)

All the compounds of ammonia owe their distinctive properties to their combination with a peculiar gaseous substance, composed of nitrogen and hydrogen (NH_3) called *ammonia.* This is most easily obtained by the action of lime on ammonium chloride,—when the lime unites with the hydrochloric acid, so as to form calcium chloride and water, and expels the ammonia. It is transparent and colorless, like common air, but possesses an acrid taste and an exceedingly pungent odor. It has a powerful alkaline reaction, and, from this property and its gaseous nature, was called the *volatile alkali* by the earlier chemists. Its sp. gr. is 0.56 compared with air. It is irrespirable, the glottis closing spasmodically when the attempt is made to breathe it. Each molecule consists of one atom of nitrogen and three of hydrogen, or, in volumes, of one volume of nitrogen and three volumes of hydrogen, condensed into two. Its formula is NH_3. The sources of ammonia will be mentioned elsewhere (see *Ammonii Chloridum,* p. 133), but a synthesis of ammonia from simple elements may be noted here. Hydrogen, nitrogen, and aqueous vapor in the presence of porous contact substances like pumice, charcoal, etc., unite to form ammonia, and this, in the presence of CO and CO_2, gives rise to ammonium formate or carbonate. These elements in the presence of moisture, as in damp atmosphere, under the influence of an electric discharge, produce ammonium nitrate directly as follows: $N_2 + O + 2H_2O = NO_3NH_4$.

As the gas ammonia exists in the free state, the molecule NH_3 is a definite saturated compound under ordinary conditions. When, however, ammonia gas is mixed with hydrochloric acid gas or its aqueous solution with hydrochloric acid in solution, the two unite to form a new compound, NH_4Cl, which proves to be a definite compound, analogous to potassium or sodium chlorides. Berzelius, therefore, proposed to call this ammonium chloride, assuming that the monad group (NH_4) acted like the monad metal K in forming compounds, and in fact it is found that when sulphuric, nitric, carbonic, and other acids are neutralized by *ammonia* gas or solution, crystallizable salts like $(NH_4)_2SO_4$, NH_4NO_3, and $(NH_4)_2CO_3$ are formed, which are termed ammonium sulphate, nitrate, and carbonate respectively. *Ammonium* is believed to exist, although it has not been isolated in a pure state. *Ammonium amalgam* is a compound of ammonium with mercury.

The atmosphere contains a minute proportion of ammonia, probably in the state of carbonate. (A. Vogel, *N. R. Pharm.,* 1872.)

Ozonized oxygen oxidizes the elements of ammonia, producing water and nitric acid; the latter, uniting with undecomposed ammonia, generates ammonium nitrate. Ordinary oxygen, under the influence of platinum-black, or finely-divided copper, likewise oxidizes the elements of ammonia, the nitrogen to the extent only of forming nitrous acid, with the result of producing ammonium nitrite.

AMMONIACUM. Br.

AMMONIACUM

(ăm-mọ-nī'ạ-cŭm)

"Ammoniacum is a gum-resin exuded from the flowering and fruiting stem of Dorema Ammoniacum, *D. Don,* and possibly other species of Dorema." *Br.*

Gum Ammoniac, Gummi-resina Ammoniacum or Doremæ, Ammoniacum; Ammoniaque, Gomme-résine ammoniaque, Gomme ammoniaque, *Fr.;* Ammoniacum, *P. G.;* Ammoniak, Ammoniak-gummi, *G.;* Gomma ammoniaco, *It.;* Gomo-resina amoniaco, Goma amoniaco, *Sp.;* Ushek, *Ar.;* Semugh belsheren, *Pers.*

This gum-resin was dropped in the Eighth Revision of the U. S. Pharmacopœia on account of its having fallen, at least in America, almost into desuetude. It is, however, official in the British as well as the Swiss and German Pharmacopœias.

The ammoniac plant (*Dorema Ammoniacum*)

grows spontaneously in Farsistan, Irak, Khorassan, and other Persian provinces. Grant found it abundantly in Syghan near Bamian, on the northwest slope of the Hindu-Kush Mountains. It attains the height of six or seven feet, and in the spring and early part of summer abounds in a milky juice, which flows out upon the slightest puncture. From the accounts of travellers, it appears that in the month of May the plant is pierced in innumerable places by an insect of the beetle kind. The juice, exuding through the punctures, concretes upon the stem, and when quite dry is collected by the natives. Fontanier states that the juice exudes spontaneously, and that the harvest is about the middle of June. The gum-resin occurs in special reservoirs near the phloem tissues of the stems, roots and petioles of the leaves. According to Grant, the drug is collected in Syghan, like asafetida, from the root of the plant. The gum-resin is sent to Bushire, whence it is transmitted to India, chiefly to Bombay. A small portion is said to be taken to the ports of the Levant, and thence distributed. The name of the drug is thought to have been derived from the temple of Jupiter Ammon in the Libyan desert, where the ammoniac of the ancients is said to have been collected; but Don considers it a corruption of *Armeniacum,* originating in the circumstance that the gum-resin was formerly imported into Europe through Armenia. The *African Ammoniac,* which is said to have appeared in the London market only in the years 1857 and 1871, has been described by Daniel Hanbury as follows. It is "in large, compact, dark, heavy masses, formed of agglutinated tears of a gum-resin of hard, waxy consistence. The tears are opaque, white or of a pale greenish-yellow, mixed with others of a blackish-brown, which, with vegetable and earthy impurities, constitute a large portion of the mass." The odor of the drug is feeble, and quite different from that of the Persian gum-resin which is the variety that is preferred; its taste slightly acrid and very persistent. (Examined by John Moss, it was found to consist of 67.76 per cent. of resin, 9.1 of gum, 4.29 of water and volatile oil, and 18.85 of bassorin and insoluble matters. (*P. J.*, 1873, p. 742.) It is used chiefly for incense in Mohammedan countries, and is sent eastward by the caravans, or in vessels from the ports of Morocco to Alexandria. Holmes (*P. J.*, 1907, lxxix, p. 570) claims that ammoniac is derived from the *Ferula communis* L., var. *brevifolia.*

Properties.—Ammoniac comes either in the state of tears, or in aggregated masses, and in both forms is frequently mixed with impurities. That of the tears, however, is preferable, as the purest may be conveniently picked out and kept for use. These are of an irregular shape, usually more or less globular, from 5 to 25 mm. in diameter, opaque, yellowish on the outside, whitish within, compact, homogeneous, brittle when cold, and breaking with a conchoidal, shining, waxy fracture. The masses are often of a darker color and less uniform structure, appearing, when broken, as if composed of numerous white or whitish tears, embedded in a dirty-gray or brownish substance, and frequently mingled with foreign matters, such as seeds, fragments of vegetables, and sand or earth. According to the 1890 U. S. Pharmacopœia, only such masses should be considered up to the standard as are composed entirely of tears "without any intervening dark-colored substance."

The odor of ammoniac is peculiar, and stronger in the mass than in the tears. The taste is slightly sweetish, bitter, and somewhat acrid. The sp. gr. is 1.207. When heated, the gum-resin softens and becomes adhesive, but does not melt. It burns with a white flame, swelling up, and emitting a smoke of a strong, resinous, slightly alliaceous odor. It is partly soluble in water, alcohol, ether, acetic acid, and alkaline solutions. The alcoholic solution is transparent, but is rendered milky by the addition of water.

"In small dull white, yellowish-white, or brownish-white tears or in nodular masses varying from about five to twenty-five millimetres in diameter. Hard and brittle when cold, the freshly fractured surface having a waxy lustre; softens when warmed. Internally opaque and varying in color from milky-white to pale brownish-yellow. Faint characteristic but not alliaceous odor; taste bitter, acrid. Triturated with *water* forms a white emulsion. Freshly fractured surface colored yellow by *solution of sodium hydroxide* and dark-red or orange by *solution of chlorinated soda.* The solution obtained by boiling 1 gramme of the powdered gum-resin with 10 millilitres of *water,* filtering, and adding *alcohol* (90 per cent.) till clear, assumes a reddish-violet coloration on the addition of one drop of *T. Sol. of ferric chloride.* The solution obtained by boiling 1 gramme of the coarsely powdered gum-resin for a few minutes with 10 millilitres of *hydrochloric acid* diluted with an equal volume of *water* does not exhibit a blue fluorescence when filtered and made alkaline with *solution of ammonia* (absence of asafetida and African ammoniacum). Ash not more than 7 per cent." *Br.*

Martius found 0.4 per cent. of ethereal oil, Flückiger 0.33 per cent. (*Pflanzenstoffe,* 2d ed., p. 962.) Plugge's analysis gives 1.27 per cent. of volatile oil, 5.10 per cent. of water, 2 per cent. of ash, 65.53 per cent. of resin, and 26.10 per cent. of gum. Hager succeeded in procuring the volatile oil in a separate state by repeated distillation with water. It has a penetrating, disagreeable odor, and a taste at first mild, but afterwards bitter and nauseous. Flückiger says that the oil contains no sulphur. The resin in ammoniacum usually amounts to about 70 per cent. Unlike the gum-resin of allied plants ammoniacum yields no umbelliferone. When melted with potassium hydroxide it affords protocatechuic acid and resorcinol. The resin of ammoniac is dissolved by alcohol, and by the fixed and volatile oils; but it is divided by ether into

two resins, of which one is soluble and the other insoluble in ether. Plugge states that sodium hypobromite, made by dissolving 30 grammes of pure sodium hydroxide in water, adding 20 grammes of bromine, cooling the mixture, and adding distilled water until the whole measures 1 liter, is a sensitive reagent for ammoniac resin. (*A. Pharm.*, 1883.)

Tschirch and Luz have made an elaborate research of the chemistry of ammoniac, and state the following conclusions. Ammoniac contains resin, gum, and volatile oil, together with about 3.5 per cent. of a residue insoluble in water and alcohol. The portion soluble in alcohol and ether is a mixture of a so-called acid resin and a neutral resin, and amounts to 69 per cent. Both resins are free from sulphur, despite the statement of Preiszewski, who considered the latter of them to contain sulphur. The saponification of the so-called acid resin yielded salicylic acid of the formulas $C_6H_4OHCOOH$ and $C_6H_4OHCOOH + \frac{1}{2}H_2O$. Along with this were volatile acids, consisting of valeric and butyric acids, and an alcohol which belongs to the class of *resinotannols*, and has the same formula as galbaresinotannol, $C_{18}H_{30}O_3$. The resin is, therefore, a salicylic ester of resinotannol. From this resinotannol both the acetyl and the benzoyl derivatives were made, and the formula $C_{18}H$ Os thus established. On oxidizing the resinotannol with nitric acid, *styphnic acid* was obtained, and on fusing it with potassium hydroxide, resorcinol. Volatile oil was found in small amount only. It contains no umbelliferone, and is free from sulphur. The crude ammoniac showed traces of a free acid which was recognized as salicylic both by its fusing point and the ferric chloride reaction. The gum contained 3.5 per cent. of ash, of which 1.2 per cent. was calcium oxide, so that the gum is probably related to gum arabic, and is an acid calcium arabinate. (*A. Pharm.*, 1895, p. 571.) Dieterich proposes the following tests: 1. Loss at 100° C. (212° F.). 2. Per cent. of ash. 3. Determination and weighing of alcohol-soluble constituents. 4. Determination and weighing of alcohol-insoluble constituents. 5. Saponification number. 6. Acid number. 7. Ester number. (*Ph. Ztg.*, 96, 401, and *P. J.*, 1900, 647.)

Uses.—This gum-resin is stimulant and expectorant, in large doses cathartic, and, like many other stimulants, may be so given as occasionally to prove diaphoretic, diuretic, or emmenagogue. It has been employed in medicine from the highest antiquity, being mentioned in the writings of Hippocrates, but is now seldom administered. The complaints in which it was most frequently used were *chronic catarrh, asthma*, and other *pectoral affections* attended with deficient expectoration without acute inflammation, or with a too copious secretion from the bronchial mucous membrane, dependent upon debility of the vessels. It is usually administered in combination with other expectorants, with tonics, or with emmenagogues. Externally applied, in the shape of a plaster, it is thought to be useful as a discutient or resolvent in white swellings of the joints, and other indolent tumors. (See *Emplastrum Ammoniaci cum Hydrargyri, U. S. Dispensatory*, 19th edition, p. 437.) It is given in substance, in pill or emulsion. The latter form, however, is preferable. (See *Mistura Ammoniaci*, Br., 1914.)

Dose, from ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Mistura Ammoniaci, *Br.;* Pilula Ipecacuanhæ cum Scilla, *Br.;* Pilula Scillæ Composita, *Br.;* Pilula Ipecacuanhæ cum Urginea, *Br.;* Pilula Urgineæ Composita, *Br.*

AMMONII BENZOAS. U. S., Br.

AMMONIUM BENZOATE Ammon. Benz.

(ąm-mō′nĭ-ī bĕn′zo-ăs)

"It contains, when dried for twenty-four hours in a desiccator over sulphuric acid, not less than 98 per cent. of $NH_4C_7H_5O_2$ or $C_6H_5COONH_4$ (139.08). Preserve it in well-closed containers in a cool place." *U. S.* "Ammonium Benzoate, $NH_4C_7H_5O_2$, may be obtained by neutralising benzoic acid with solution of ammonia." *Br.*

Ammoniæ Benzoas, Ammonium Benzoicum, Benzoas Ammonicus; Benzoate of Ammonia; Benzoate d'Ammoniaque, *Fr. Cod.;* Benzoësaures Ammonium, Ammonium benzoat, *G.;* Benzoato amonico, *Sp.*

The process for the preparation of this salt was omitted in the later editions of the U. S. P. The process of U. S., 1870, is appended. "Take of Benzoic Acid *two troyounces;* Water of Ammonia *three fluidounces and a half,* or a *sufficient quantity;* Distilled Water *four fluidounces.* Dissolve the Acid in three fluidounces and a half of the Water of Ammonia, previously mixed with Distilled Water; evaporate with a gentle heat, occasionally adding Water of Ammonia, if necessary, to maintain a slight excess of the alkali; then set aside to crystallize, and dry the crystals without heat." *U. S.*, 1870.

Although the quantity of ammonia ordered in the formula is in excess, yet, from the feeble action between the constituents, and the consequent escape of ammonia during the evaporation, a portion of the acid benzoate would be formed, if it were not that a little solution of ammonia is from time to time added during or near the close of the evaporation, so as to maintain the alkali in slight excess. The crystals, for the same reason, should be dried without heat. If slightly evaporated, and then allowed to cool, the solution becomes a mass of crystals, retaining so much water as to render it necessary to dry them by means of bibulous paper.

Properties.—"Ammonium Benzoate occurs in thin, white, laminar crystals or as a crystalline powder; gradually losing ammonia on exposure to air; odorless, or having a slight odor of benzoic acid, a saline, bitter afterwards slightly acrid taste. One Gm. of Ammonium Benzoate dissolves in about 10 mils of water, 35.5 mils of alcohol, and about 8 mils of glycerin at 25° C.

(77° F.). When strongly heated it evolves ammonia and benzoic acid, and is finally volatilized leaving not more than 0.05 per cent. of ash. An aqueous solution of the salt (1 in 20) is neutral or not more than slightly acid to litmus. An aqueous solution of Ammonium Benzoate (1 in 10) yields with ferric chloride T.S. a pink precipitate, and when such a solution is gently heated with potassium hydroxide T.S., ammonia is evolved. Acidulate 10 mils of an aqueous solution of the salt (1 in 50) with hydrochloric acid and filter it; the filtrate does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Dissolve about 0.5 Gm. of Ammonium Benzoate, previously dried for twenty-four hours in a desiccator over sulphuric acid and accurately weighed, in 10 mils of distilled water in a separator. Add to the solution 5 mils of diluted sulphuric acid, and extract the liberated benzoic acid by shaking out with 3 successive portions of 25, 15 and 10 mils respectively of chloroform, passing the chloroform solution through a filter previously moistened with chloroform and removing any benzoic acid adhering to the stem of the funnel with a few mils of chloroform. Evaporate the chloroform solution at a low temperature, preferably spontaneously, to about 5 mils, add 25 mils of diluted alcohol which has been previously neutralized with tenth-normal potassium hydroxide V.S., phenolphthalein T.S. being used as indicator, and titrate this solution with tenth-normal barium hydroxide V.S., using phenolphthalein T.S. as indicator. It shows, in the dried salt, not less than 98 per cent. of $NH_4C_7H_5O_2$.

"Each mil of tenth-normal barium hydroxide V.S. corresponds to 0.013908 Gm. of $NH_4C_7H_5O_2$. Each gramme of Ammonium Benzoate, previously dried, corresponds to not less than 70.5 mils of tenth-normal barium hydroxide V.S." *U. S.*

"Colorless lamellar crystals. Taste saline, slightly acrid. Soluble in 6 parts of *water*, and in 30 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of ammonium salts. An aqueous solution yields a pale reddish precipitate on the addition of *T. Sol. of ferric chloride.* A strong aqueous solution, to which a little *hydrochloric acid* is added, yields a crystalline precipitate of benzoic acid. Completely volatilised by heat. If 1 gramme is dissolved in 20 millilitres of *water* and excess of *nitric acid* added, a crystalline precipitate of benzoic acid separates, the filtrate from which remains clear on the addition of *solution of barium chloride,* and does not become more than slightly opalescent on the addition of *solution of silver nitrate. Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million." *Br.*

Gmelin states that by boiling its solution the salt is converted into the acid benzoate, which crystallizes in feathery tufts of needles. (*Handbook,* xii, 38.) According to Lichtenstein, it deliquesces in the air. It gives a copious pink precipitate with ferric salts, and is known to contain benzoic acid and ammonia, by depositing the former when the solution is acidulated with hydrochloric acid, and giving off the latter when it is heated with potassium hydroxide. According to Squire, the acid salt, which is that commonly met with in commerce, is less soluble than the official salt, requiring 60 parts of water and 12 of alcohol for solution. This is a decided objection to it.

Uses.—Ammonium benzoate is a slightly stimulant diuretic, which acts chiefly through its benzoic acid, it being decomposed by the gastric acids, which combine with the ammonia, while the benzoic acid is absorbed, and passes out through the kidneys in the form of hippuric acid. (See *Benzoic Acid.*) Like the other benzoates it is of service in the treatment of various forms of *rheumatism,* but is especially prized as an urinary antiseptic in fermentative *cystitis.* It has the great advantage in this condition that not only is the benzoic acid directly antiseptic but, because the ammonium radical is destroyed in the body, it also tends to increase the acidity of the urine, thereby aiding in the antibacterial effects of other agents.

Dose, from ten to thirty grains (0.65–2.0 Gm.), which may be taken dissolved in water.

AMMONII BROMIDUM. U. S., Br.

AMMONIUM BROMIDE Ammon. Brom.

(ạm-mō'nĭ-ĭ brō'mĭ-dŭm)

"It contains, when dried to constant weight at 100° C. (212° F.), not less than 98.5 per cent. of NH_4Br (97.96). Preserve it in well-closed containers." *U. S.* "Ammonium Bromide may be obtained by neutralising hydrobromic acid with solution of ammonia. When dried at 100° C. (212° F.) it contains not less than 98 per cent. of pure ammonium bromide, NH_4Br." *Br.*

Ammonium Bromatum; Bromhydrate d'Ammoniaque, *Fr. Cod.;* Bromure d'Ammonium, *Fr.;* Ammonium bromatum, *P. G.;* Ammonium bromid, Brom-Ammonium, *G.;* Bromuro di ammonio, *It.;* Bromuro amonico, *Sp.*

Ammonium bromide may be made by dissolving bromine in ammonia water; but the U. S. Pharm., 1870, preferred the method of first forming solution of ferrous bromide, precipitating with ammonia water, separating by filtration the ferric oxide, and obtaining by evaporation the ammonium bromide from the solution. This process is similar to that by which potassium bromide is prepared. According to Procter, a still better method consists in adding to bromine and water sufficient solution of ammonium sulphide to discharge the color, filtering to separate the sulphur, and then evaporating to dryness. Charles Rice (*A. J. P.,* 1873, p. 249) recommends making ammonium bromide by double decomposition between hot solutions of potassium bromide and ammonium sulphate, assisting the precipitation of potassium sulphate by alcohol. W. H. Pile (*Proc. A. Ph. A.,* 1874, p. 434) published a simple process for this salt. Pour the bromine (one pound) carefully into

four times its weight of distilled water in a stone jar, add *very gradually* about one quart of solution of ammonia, cover the top of the jar with a glass plate when vapors arise, and when all the ammonia has been added, and the solution is free from the odor of bromine, it is evaporated and the salt granulated; the yield is about twenty ounces.

Properties.—Ammonium bromide may be obtained in colorless crystals, but the official salt is also a white, crystalline powder. Whether in crystals or in powder, on exposure to the air it gradually becomes yellowish, in consequence of a partial decomposition, by which hydrobromic acid appears to be liberated, as it now changes litmus red. The salt has a saline. pungent taste. Exposed to heat, it sublimes unchanged. It is officially described as in "colorless, transparent, prismatic crystals, or as a white, crystalline or granular powder; odorless, of a pungent, saline taste; somewhat hygroscopic. One Gm. of Ammonium Bromide dissolves in 1.3 mils of water and in 12 mils of alcohol at 25° C. (77° F.); also in 0.9 mil of boiling water and 1.2 mils of boiling alcohol. When heated, Ammonium Bromide volatilizes without fusing. An aqueous solution of the salt (1 in 20) is neutral or not more than slightly acid to litmus. An aqueous solution of Ammonium Bromide when gently heated with potassium hydroxide T.S. evolves ammonia. Silver nitrate T.S. added to an aqueous solution of the salt (1 in 10) produces a yellowish-white precipitate, insoluble in nitric acid or in a moderate excess of ammonia water. Add 2 mils of nitric acid to about 2 Gm. of the salt and evaporate the mixture to dryness in a porcelain dish on a water bath and ignite the residue; it yields not more than 0.05 per cent. of non-volatile matter. Add 1 mil of chloroform to 10 mils of an aqueous solution of the salt (1 in 20) and cautiously introduce chlorine water, which has been diluted with an equal volume of distilled water, drop by drop and with constant agitation. The liberated bromine dissolves in the chloroform and imparts to it a yellow or orange color, which is free from any violet tint (*iodide*). Drop 1 mil of diluted sulphuric acid upon about 1 Gm. of the powdered salt; no yellow color appears at once (*bromate*). A blue color is not produced at once on adding potassium ferrocyanide T.S. to 20 mils of an aqueous solution of the salt (1 in 250) (*iron*). Add 1 mil of potassium sulphate T.S. to 10 mils of an aqueous solution of Ammonium Bromide (1 in 20), acidulated with acetic acid; no turbidity is produced immediately (*barium*); under similar conditions the addition of barium chloride T.S. produces no turbidity (*sulphate*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Proceed as directed under the Assay for bromides (see Part III, Test No. 5), using about 0.4 Gm. of Ammonium Bromide, previously dried to constant weight at 100° C. (212° F.), and accurately weighed. It shows, in the dried salt, not less than 98.5 per cent. of NH_4Br.

"Each mil of tenth-normal silver nitrate V.S. corresponds to 0.009796 Gm. of NH_4Br. Each gramme of Ammonium Bromide, previously dried, corresponds to not less than 100.5 mils nor more than 103.4 mils of tenth-normal silver nitrate V.S." *U. S.*

"Small colorless crystals. Taste somewhat pungent, saline. Soluble in 1.5 parts of *water*, and in 13 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of ammonium salts and of bromides. Loses not more than 1 per cent. of its weight when dried at 100° C. (212° F.). 0.5 gramme of this dried salt dissolved in *water* requires for complete precipitation not less than 50.5 and not more than 51.5 millilitres of *N/10 solution of silver nitrate* (limit of impurities). Completely volatilised by heat. Yields no characteristic *reactions* for iron, bromates, iodides, or nitrates, and not more than the slightest *reaction* for sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Uses.—Ammonium bromide is useful chiefly for the action of its bromic ion. (See page 890) By some it is believed to be less prone to cause disturbances of the digestion than is potassium bromide. Theoretically the ammonium ion should impart to this salt a stimulant action upon the circulation and upon the spinal cord, but for reasons pointed out elsewhere (see *Ammonii Carbonas*) it is doubtful whether this is of any practical importance.

Dose, ten to thirty grains (0.6–1.9 Gm.) well diluted.

Off. Prep.—Elixir Ammonii Bromidi, *N. F.;* Elixir Trium Bromidorum, *N. F.;* Syrupus Bromidorum, *N. F.*

AMMONII CARBONAS. U. S., Br.

AMMONIUM CARBONATE Ammon. Carb.

(ąm-mō'nĭ-ĭ cär'bo-nās)

"It consists of varying proportions of a mixture of acid ammonium carbonate [$NH_4HCO_3 = 79.05$] and ammonium carbamate [$NH_4NH_2CO_2 = 78.07$], and yields not less than 30 per cent. nor more than 32 per cent. of NH_3. Preserve it in well-closed containers in a cool place. For medicinal purposes, use only the translucent portions." *U. S.* "Ammonium Carbonate is a variable mixture of ammonium hydrogen carbonate, NH_4HCO_3, with ammonium carbamate $NH_4NH_2CO_2$. It may be obtained by heating ammonium sulphate or chloride with calcium carbonate." *Br.*

Ammoniæ Carbonas, *Br.* 1867; Ammoniæ Sesquicarbonas, *Lond., Dub.;* Carbonas Ammonicus, Sal Volatile Siccum; Volatile Salt, Sal Volatile; Carbonate d'Ammoniaque, *Fr. Cod.;* Alcali volatil concret, Sel volatil d'Angleterre, *Fr.;* Ammonium carbonicum, *P. G.;* Ammonium-carbonat, Kohlensaures Ammonium, Flüchtiges Laugensalz, Reines Hirschhornsalz, *G.;* Carbonato di ammonio, *It.;* Carbonato amonico, *Sp.*

There have been many methods of obtaining ammonium carbonate, in all of which the ammonia originated in organic decomposition. It was probably originally prepared from putrid urine, and it is sometimes made in Scotland now

from this source. A patent was taken out in England for manufacturing it from guano, and another for making it by the direct combination of its constituents, the carbon dioxide and ammoniacal gases being introduced simultaneously into leaden chambers. (*Chem. News*, Dec. 29, 1865.) At present the salt is manufactured by subliming a mixture of either ammonium chloride or sulphate with chalk. Ammonium chloride and chalk (calcium carbonate) are heated together in iron pots or retorts, and sublimed into large earthen or leaden receivers. By the reciprocal action of the salts employed, the carbon dioxide of the chalk unites with the ammonia of the chloride, generating ammonium carbonate, and the hydrochloric acid with the lime, forming water and calcium chloride. The carbonate and water sublime together as hydrated ammonium carbonate, and the residue is calcium chloride,

$$4NH_4Cl + 2CaCO_3 = NH_4HCO_3NH_4NH_2CO_2 + NH_3 + 2CaCl_2 + H_2O.$$

The relative quantities of chalk and ammonium chloride, for mutual decomposition, are 50 of the former and 53.5 of the latter, or one molecule of each. But a great excess of chalk is usually taken, in order to insure the perfect decomposition of the ammonium chloride, any redundancy of which would sublime with the carbonate and render it impure. Barium carbonate is sometimes used in place of calcium carbonate, barium chloride, the by-product, having a greater commercial value than calcium chloride.

Ammonium sulphate may be substituted for the chloride with much economy, as was shown by Payen. This double decomposition between ammonium sulphate and calcium carbonate takes place in the dry way only—that is, by sublimation. In the wet way, the double decomposition is reversed, ammonium carbonate and calcium sulphate reacting so as to form ammonium sulphate and calcium carbonate. Large quantities of this carbonate are manufactured indirectly from *coal gas liquor* and *bone spirit*, the ammoniacal products in these liquors being converted successively into ammonium sulphate, chloride, and carbonate. (See *Ammonii Chloridum.*) The salt as first obtained has a slight odor of tar, and leaves a blackish carbonaceous matter when dissolved in acids. Hence it requires to be purified, which is effected in iron pots surmounted with leaden heads. The American carbonate has almost supplanted the English article, which was formerly used exclusively.

Properties.—The official salt is described as "white, hard, translucent, striated masses, having a strong odor of ammonia, without empyreuma, and a sharp, ammoniacal taste. On exposure to the air, the salt loses both ammonia and carbon dioxide, becoming opaque, and is finally converted into friable, porous lumps, or a white powder. When heated, Ammonium Carbonate is volatilized, without charring, the vapor showing a strongly alkaline reaction with litmus; not more than 0.05 per cent. of residue remains. One Gm. of Ammonium Carbonate dissolves very slowly in 4 mils of water at 25° C. (77° F.); it is decomposed by hot water, with the elimination of carbon dioxide and ammonia. By prolonged boiling with water the salt is completely volatilized. Alcohol dissolves the carbamate leaving the acid carbonate. An aqueous solution of the salt (1 in 20) effervesces with acids, and is alkaline to litmus. An aqueous solution of the salt (1 in 50), when slightly supersaturated with hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3). Five mils of a similar solution is not immediately affected by barium chloride T.S. (*sulphate*). Ten mils of an aqueous solution of the salt (1 in 20), on the addition of a slight excess of silver nitrate T.S., and subsequent supersaturation with nitric acid, neither assumes a brown color (*thiosulphate*), nor becomes more than slightly opalescent within two minutes (*chloride*). On slightly supersaturating an aqueous solution, containing 1 Gm. of the salt, with nitric acid, and then evaporating it to dryness on a water bath, a colorless and odorless residue is obtained (*empyreumatic matter*).

"**Assay.**—Introduce about 2 Gm. of unaltered, translucent Ammonium Carbonate into a tared weighing-bottle containing 10 mils of distilled water, stopper, weigh accurately and add 40 mils of distilled water and 50 mils of normal sulphuric acid V.S. and when solution is effected titrate the excess of acid with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 30 per cent. nor more than 32 per cent. of NH_3.

"Each mil of normal sulphuric acid V.S. used corresponds to 0.01703 Gm. of NH_3. Each gramme of Ammonium Carbonate corresponds to not less than 17.6 mils nor more than 18.8 mils of normal sulphuric acid V.S." *U. S.*

"Translucent, crystalline masses. Ammoniacal odor; taste pungent, ammoniacal. Alkaline to *litmus*. Soluble in 4 parts of *water*. Exposed to the air it becomes covered with a white efflorescence which is only superficial; this efflorescence should be scraped off before the salt is used for dispensing. Yields the *reactions* characteristic of ammonium salts and of carbonates. 1 gramme dissolved in 40 millilitres of *water* requires for neutralisation not less than 18.0 millilitres of *N/1 solution of sulphuric acid*. Completely volatilised by heat. Yields not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 5 parts per million. *Arsenic limit* 2 parts per million. When its aqueous solution is neutralised with a mineral acid and evaporated to dryness, the residue is colorless and odorless (absence of tarry matters)." *Br.*

If commercial ammonium carbonate be treated with 90 or 91 per cent. alcohol, it is decomposed into the two salts of which it is composed, ammonium carbamate going into solution while the acid ammonium carbonate remains undissolved. This latter compound also remains undissolved when the commercial carbonate is treated with an amount of water insufficient for complete solution. The result of the complete

solution of the commercial salt in water is a mixture of acid and neutral carbonates, the carbamate having been decomposed according to the reaction:

$$(NH_4)HCO_3 + CO\begin{Bmatrix} ONH_4 \\ NH_2 \end{Bmatrix} + H_2O = (NH_4)HCO_3 + (NH_4)_2CO_3$$

When long or insecurely kept, it gradually passes into a bicarbonate, becoming opaque and friable, and falling into powder. When heated in a porcelain dish the commercial carbonate should evaporate without residue, and, if turmeric paper held over it undergoes no change, it has passed into bicarbonate. As prepared from coal gas liquor, it sometimes contains traces of tarry matter, which give a dark color to its solution in acids, but a refined carbonate, made by resubliming the commercial article, is now in the market, and this alone should be dispensed in preparations for internal use. When it is saturated with nitric acid, neither barium chloride nor silver nitrate causes a precipitate. The non-action of these tests shows the absence of ammonium sulphate and chloride. The presence of lead in small quantities was detected by Bennett in commercial ammonium carbonate. (*C. D.*, 1904, 203.) It is decomposed by acids, the fixed alkalies and their carbonates, lime water and magnesia, solution of calcium chloride, alum, acid salts, such as potassium bitartrate and bisulphate, solutions of iron (except the iron and potassium tartrate and analogous preparations), corrosive sublimate, lead acetate and subacetate, and ferrous and zinc sulphates. Traces of chlorine have been noticed in some samples of commercial carbonate, and a sublimed salt which had been sold as carbonate, was *devoid of odor*, hard, crystalline, yet having the external appearance of carbonate, and was proved by Bridges to be anhydrous ammonium bicarbonate. (*A. J. P.*, Nov., 1874.) Although much inferior to the official compound, this salt is often found in the market. For papers on testing commercial ammonium carbonate, see *A. J. P.*, 1890, p. 500, by G. M. Beringer; also *Ph. Era*, 1889, p. 417, by Charles C. Abbey.

Uses.—Locally ammonium carbonate is an active irritant and capable in overdose of causing gastritis. Systemically its action is purely that of its ammonium radical. When injected into the circulation in proper dose ammonium acts as a rapid but fugacious stimulant to both the circulation and nervous system. The blood pressure is elevated partly from an effect on the cardiac muscles and probably also in part from a stimulation of the vasomotor center in the medulla. After toxic doses the rise in blood pressure may be followed by a fall to a point below the norm. There is also an increase in the rapidity of breathing due to an action upon the respiratory center. The action upon the spinal cord is shown by increased activity of reflexes and in sufficient doses it is capable of causing in the lower animals tetanic convulsions. These effects are caused only when it is introduced fairly rapidly into the circulation and do not occur, at least to any practical degree, when the drug is exhibited by the mouth, because the ammonium is so rapidly destroyed in the system that it is scarcely possible for a sufficient quantity to be absorbed through the mucous membrane of the alimentary tract to obtain the necessary concentration in the blood for its physiological effect. It is oxidized in the liver appearing in the urine chiefly as urea, although a small amount seems to be excreted as nitric acid. The irritant salts of ammonium, however, by virtue of their local effects on mucous membranes reflexly, may excite the medullary centers. To this action is due the improvement in circulation and respiration seen in cases of syncope as the result of smelling or swallowing such salts as the carbonate or hydroxide.

Ammonium carbonate is used as an antacid in the treatment of various forms of *gastric disturbances*, especially when associated with *headache*. It is also employed for its expectorant effect. It is probably largely converted in the stomach in to the chloride and exercises the same type of action in *bronchitis* as that salt. As a rapid stimulant in cases of *circulatory failure*, as in adynamic *pneumonias, snake-bite*, and other conditions it may prove of great value if administered hypodermically.

Coarsely bruised with the addition of half its bulk of stronger ammonia water, and scented with oil of lavender, it constitutes the common *smelling-salts*, so much used as a nasal stimulant in *syncope* and *hysteria*. It should never be given in powder or in pill, on account of its volatile nature and its irritant action on the mucous membrane.

Ammonium carbonate is sometimes employed in making effervescing draughts, 20 grains of the salt requiring for this purpose 6 fluidrachms of lemon juice, 24 grains of citric acid, or 25½ grains of tartaric acid.

Dose, five to ten grains (0.32–0.65 Gm.) every two hours.

Off. Prep.—Spiritus Ammoniæ Aromaticus, *U. S., Br.;* Mistura Pectoralis, Stokes, *N. F.*

AMMONII CHLORIDUM. U. S., Br.

AMMONIUM CHLORIDE Ammon. Chlor.

[Ammonium Muriate, Muriate of Ammonia]

(ăm-mō′nĭ-ĭ ĕhlō′rĭ-dŭm)

"It contains, when dried to constant weight at 100° C. (212° F.), not less than 99.5 per cent. of NH_4Cl (53.50)." *U. S.* "Ammonium Chloride, NH_4Cl, may be obtained by neutralising crude solution of ammonia or ammonium carbonate with hydrochloric acid, and purifying the product." *Br.*

Ammonium Muriaticum, s. Hydrochloratum, Chloruretum Ammonicum, Sal Ammoniacum, Ammoniæ Hydrochloras, s. Murias; Sal Ammoniac, Hydrochlorate of Ammonia; Chlorhydrate d'Ammoniaque, *Fr. Cod.;* Hydrochlorate d'Ammoniaque, Muriate d'Ammoniaque, Sel Ammoniac, Chlorure d'Ammonium, Chlorure d'Ammonium pur, *Fr.;* Ammonium Chloratum, *P. G.;* Ammoniumchlorid, Salmiak, Chlorammonium, Reiner (gereinigter) Salmiak, *G.;* Clorurio dammonio, Sale ammoniaco, *It.;* Cloruro amonico, Sal amoniaco, *Sp.*

In the U. S. Pharmacopœia of 1870 both the crude and the purified ammonium chloride were official, under the names *Ammonii Chloridum* and *Ammonii Chloridum Purificatum.* The U. S. P. VIII recognized but one, *Ammonii Chloridum,* but it transferred this title, which formerly was given to the crude sal ammoniac, to the purified salt, without giving a process for preparing it. The U. S. P. IX retained this plan. The U. S. P., 1870, process is as follows: "Take of Chloride of Ammonium, in small pieces, *twenty troyounces;* Water of Ammonia five *fluidrachms;* Water *two pints.* Dissolve the Chloride of Ammonium in the water, in a porcelain dish, with the aid of heat; add the Water of Ammonium, and continue the heat for a short time; filter the solution while hot, and evaporate to dryness, with constant stirring at a moderate heat, until it granulates." *U. S.,* 1870.

This process is used to free the salt from ferric chloride, a frequent impurity of the crude product, derived from the subliming vessels.

Ammonium chloride originally came from Egypt, where it was obtained by sublimation from the soot resulting from the burning of camels' dung, which is used in that country for fuel, and it is still to be found in the Indian bazars in an impure state as it has been obtained from the unburnt residue in the interior of brick-kilns in which camels' manure is used for fuel. The name ammonia is derived from the fact that it was largely thus obtained in the Libyan desert near the temple of Jupiter Ammon. It has long been known in China, where it is obtained from the water of certain volcanic springs, and exists in commerce in various states of purity. It is found in the fumeroles of Vesuvius, Etna, Hecla, and other volcanoes, and in the cracks and fissures in recent lava streams.

Preparation.—At present ammonium chloride is derived from two principal sources, the ammonia liquor, called *gas liquor,* found in the condensing vessels of coal gas works, and the brown, fetid ammonia liquor, known under the name of *bone spirit,* which is a secondary product, obtained from the destructive distillation of bones, in the manufacture of bone black. These two liquors are the chief sources of ammonia compounds, for they are both used to procure ammonium sulphate, and this salt is employed directly or indirectly for obtaining all the other salts of ammonium. A third source of increasing importance is its production as a by-product in ovens for coking coal. Other sources are stale urine, coal soot, guano, peat, and bituminous schist. The census report gives the production of ammonium chloride for 1914 as 11,511,934 pounds, valued at $641,043.

Gas liquor contains ammonium carbonate, cyanide, sulphide, and sulphate, but principally the carbonate. It is saturated with sulphuric acid, and the solution obtained, after due evaporation, furnishes brown crystals of ammonium sulphate. These are then sublimed with sodium chloride in iron pots lined with clay and furnished with an iron dome or head. By the mutual action of the sulphate and chloride, there are formed ammonium chloride which sublimes, and sodium sulphate which remains behind. Thus:

$$(NH_4)_2SO_4 + 2NaCl = 2NH_4Cl + Na_2SO_4$$

Gas liquor is usually distilled with lime with the aid of column stills, whereby a relatively pure and strong solution of ammonia is obtained.

This may be further purified, however, from empyreumatic matter by treatment with potassium permanganate and then driven over by heat and absorbed in hydrochloric acid. In this way, as the solution becomes concentrated, the sal ammoniac crystallizes out in the bottom of the leaden tanks in which the absorption takes place. Impure sal ammoniac may be purified either by crystallization or by sublimation. In the latter case the sal ammoniac is placed in an iron subliming pot coated with a composition of clay, sand, and charcoal and covered with a dome of lead, iron, earthenware, or glass. These pots are sometimes sufficiently large to hold 500 pounds. A gentle fire is kept up under the subliming pot for seven or eight days, when, the dome having cooled down, and the sal ammoniac somewhat contracted, so as to loosen from the sides, the dome is thrown off from the iron pot, and about two or three hundred-weight of white, semitransparent sal ammoniac is obtained.

In the destructive distillation of bones for making bone black, the distilled products are the bone spirit already mentioned, being chiefly an aqueous solution of ammonium carbonate, and an empyreumatic oil, called *animal oil.* Ammonium chloride may be obtained from the bone spirit in the manner just described for procuring it from gas liquor. Sometimes, however, the ammonium sulphate is not made by direct combination, but by digesting the bone spirit with ground plaster of Paris. By double decomposition, ammonium sulphate and calcium carbonate are formed. The ammonium sulphate is then converted into the chloride by sublimation with common salt.

Other processes have been proposed or practised for obtaining ammonium chloride. For an account of the manufacture of ammonia salts, and for a list of the patents issued in Great Britain, since 1827, for their preparation, the reader is referred to *P. J.,* xii, 20, 63, 113.

Properties.—Commercial ammonium chloride is a white, transparent, tough, fibrous salt, occurring in large cakes about two inches thick, convex on one side and concave on the other, due to the shape of the dome of the subliming apparatus; the pieces are frequently tinged on the surface with iron stains, from the iron dome which is used for crude sal ammoniac. It has a pungent, saline taste, but no odor. Its sp. gr. is 1.45. This salt is very difficult to powder in the ordinary way. Its pulverization, however, may be readily effected by making a boiling saturated solution of the salt and stirring it as it cools. The salt is thus made to granulate, and in this state, after draining from the remaining solution and drying, may be easily powdered. At a

red heat it sublimes without decomposition or residue. Exposed to a damp atmosphere it becomes slightly moist. It has the property of increasing the solubility of corrosive sublimate in water. It is decomposed by the strong mineral acids, and by the alkalies and alkaline earths—the former disengaging hydrochloric acid, the latter ammonia, both sensible to the smell. Ammonium chloride is usually employed for obtaining gaseous ammonia, which is conveniently disengaged by lime. It is incompatible with lead acetate and silver nitrate, producing precipitates respectively of lead and silver chlorides.

Ammonium chloride is little subject to adulteration. If not entirely volatilized by heat, and if incompletely soluble in water, it contains impurity. As ordinarily prepared, it contains ferrous chloride, and this may be detected by boiling a small portion of a saturated solution of the salt with a drop or two of nitric acid, and then adding potassium ferrocyanide, when the characteristic blue color occasioned by iron will be produced. If the salt is entirely volatilized by heat, and yet produces a precipitate with barium chloride, the presence of ammonium sulphate is indicated. The description and tests of the official salt are as follows:

"Ammonium Chloride is a white, crystalline or granular powder, without odor, having a cooling and saline taste; somewhat hygroscopic. One Gm. of Ammonium Chloride dissolves in 2.6 mils of water, 100 mils of alcohol and in 8 mils of glycerin at 25° C. (77° F.); also in 1.4 mils of boiling water. Ammonium Chloride on ignition, is volatilized without fusing. An aqueous solution of the salt (1 in 20) in ice-cold water does not show an immediate acid reaction with litmus. Silver nitrate T.S. added to an aqueous solution of the salt (1 in 10) produces a white, curdy precipitate, insoluble in nitric acid but readily soluble in ammonia water. An aqueous solution of the salt, when heated with potassium hydroxide T.S., evolves ammonia. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). When acidulated with hydrochloric acid, 10 mils of an aqueous solution of the salt (1 in 10) does not assume a red color on the addition of a few drops of ferric chloride T.S. (*sulphocyanate*). Add 2 mils of nitric acid to 2 Gm. of the salt and evaporate the mixture to dryness in a porcelain dish on a water bath; a white residue is obtained, which, when ignited, yields not more than 0.05 per cent. of non-volatile substances.

"**Assay.**—Proceed as directed under the Assay for chlorides (see Part III, Test No. 5), using about 0.2 Gm. of Ammonium Chloride, previously dried to constant weight at 100° C. (212° F.), and accurately weighed. It shows, in the dried salt, not less than 99.5 per cent. of NH_4Cl.

"Each mil of tenth-normal silver nitrate V.S. corresponds to 0.005350 Gm. of NH_4Cl. Each gramme of Ammonium Chloride, previously dried, corresponds to not less than 186.0 mils of tenth-normal silver nitrate V.S." *U. S.*

"Colorless, inodorous crystals. Taste saline, cooling. Soluble in 3 parts of *water*, and in 60 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of ammonium salts and of chlorides. Completely volatilised by heat. Yields no characteristic *reactions* for copper, carbonates, or nitrates, and not more than the slightest *reactions* for iron, or for sulphates. *Lead limit* 5 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Uses.—Ammonium chloride possesses the stimulant properties of its basic ion and probably differs but little in its physiological action from the carbonate, although it is believed by some to be less powerful and less fugacious. Clinically it is employed chiefly in the treatment of various types of *bronchitis* for the purpose of increasing the secretions. Its effect in these conditions is probably owing chiefly to its "salt action," a property common to most of the non-toxic salts. Some believe, however, that it exercises a specific stimulant effect upon mucous membranes not only of the lungs but also of the digestive organs. It has been used, therefore, in the treatment of *acute hepatitis, catarrhal jaundice,* and *gastric catarrh,* and with asserted good results. For its old use in *sciatica, dysmenorrhea,* and *glandular enlargements* there is little scientific support, and it has been almost entirely abandoned for these purposes.

Hermann Beigel, of London, strongly recommends its inhalation in the nascent state, resulting from a mixture of the two gases composing it. Three bottles are used, one containing ammonia water, the second an equivalent quantity of liquid hydrochloric acid, and the third half filled with water, connected with the first two by tubes, and supplied itself with a tube for inhalation. By inhalation the patient draws the two gases from their respective bottles into the third, where they combine to form ammonium chloride, which is freed from any excess of either gas by the water. Another mode of inhaling ammonium chloride is in *spray,* by means of the atomizer; ten to twenty grains are dissolved for the purpose in a fluidounce of water. Ammonium chloride has been used in some European countries in place of sodium chloride for salting food before eating it.

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Trochisci Ammonii Chloridi, *U. S.;* Mistura Ammonii Chloridi, *N. F.*

AMMONII IODIDUM. U. S.

AMMONIUM IODIDE Ammon. Iod.

(ąm-mō'nĭ-ī ī-ŏd'ĭ-dŭm)

"It contains, when dried to constant weight at 100° C. (212° F.), not less than 99 per cent. of NH_4I (144.96). Preserve it in small, well-closed containers, protected from light." *U. S.*

Iodhydrate d'ammoniaque, *Fr. Cod.;* Iodure d'Ammonium, *Fr.;* Ammonium jodatum, Jodammonium, *G.;* Yoduro amonico, *Sp.*

No process is given in the U. S. P. IX for this salt; it was formerly prepared according to the method of John A. Spencer, of London, the formula for which is as follows: Add to a portion of iodine, placed in a flask with a little water, a solution of ammonium sulphydrate, until the mixture loses its red color, and is turbid from the separation of sulphur only. Shake the flask, which causes the sulphur, for the most part, to agglomerate, and having poured off the liquid, boil it until all odor of hydrogen sulphide and of ammonia is lost. Then filter the liquid, and, constantly stirring, evaporate it, first with a naked flame until it becomes pasty, and then in a water bath until it forms a dry salt. In 1864 (*A. J. P.*, May, 1864), Jacobson proposed a process in which double decomposition between solutions of ammonium sulphate and potassium iodide was employed. James F. Babcock (*Proc. A. Ph. A.*, 1866) stated that on trial of the first of the above processes, and of all others in which hydrogen sulphide or an alkaline sulphide was employed, the resulting ammonium iodide retained a portion of sulphur, which caused its color to change with time to yellow and ultimately to brown, and rendered it unfit for the accurate solutions required in photography. Having tried also other formulas, which he found objectionable, he at length satisfied himself that Jacobson's process, above described, was the best in use, and with slight modifications would yield an absolutely pure product.

Babcock's process is substantially the following, official in the U. S. P., 1870: "Take of Iodide of Potassium, in coarse powder, *four troyounces;* Sulphate of Ammonium, in coarse powder, a *troyounce* [this should be 867 grains]; Boiling Distilled Water, *two fluidounces;* Alcohol, Water, each, *a sufficient quantity.* Mix the salts, add them to the Boiling Water, stir well, and allow the mixture to cool; then add a fluidounce of Alcohol, mix well, and reduce the temperature, by a bath of iced water, to about 4.4° C. (39.9° F.); throw the mixture into a cool glass funnel, stopped with moistened cotton, and, when the clear solution has passed, pour upon the salt a fluidounce of a mixture containing two parts of Water and one part of Alcohol. Lastly, evaporate the solution rapidly to dryness, stirring constantly; and preserve the residue in a well-stoppered bottle." *U. S.*, 1870. The object of the first step of the process is sufficiently evident. After the double decomposition has occurred, the alcohol is added to complete the precipitation of the potassium sulphate; the pouring of alcohol upon the cotton filter is to remove completely from the sulphate all of the iodide. As made by this process, ammonium iodide always contains a minute proportion of potassium sulphate.

Properties.—Ammonium iodide occurs in "minute, colorless, cubical crystals, or as a white, granular powder, odorless and having a sharp, saline taste. The salt is very hygroscopic, and soon becomes yellow or yellowish-brown on exposure to air and light, owing to the loss of ammonia and the liberation of iodine. One Gm. of Ammonium Iodide dissolves in 0.6 mil of water, 3.7 mils of alcohol and in 1.5 mils of glycerin at 25° C. (77° F.); also in 0.5 mil of boiling water. When strongly heated, Ammonium Iodide evolves vapor of iodine, and volatilizes without fusing, leaving not more than 0.1 per cent. of residue. An aqueous solution of the salt (1 in 20) is neutral or not more than slightly acid to litmus. When heated with potassium hydroxide T.S., ammonia is liberated. Add a few drops of ferric chloride T.S. to 5 mils of an aqueous solution of the salt (1 in 20); iodine is liberated which imparts a violet color to chloroform when shaken with the solution. Ten mils of an aqueous solution of Ammonium Iodide (1 in 20), when acidulated with hydrochloric acid, is not rendered turbid by the addition of 1 mil of potassium sulphate T.S. (*barium*). Ten mils of an aqueous solution of the salt (1 in 150) does not at once assume a blue color upon the addition of 3 drops of potassium ferrocyanide T.S. (*iron*). Shake 5 mils of an aqueous solution of the salt (1 in 150) with 1 mil of chloroform; no violet color is imparted to the latter (*free iodine*). An aqueous solution of Ammonium Iodide does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Proceed as directed under the Assay for iodides (see Part III, Test No. 5), using about 0.5 Gm. of Ammonium Iodide, previously dried to constant weight at 100° C. (212° F.) and accurately weighed in a stoppered weighing-bottle. It shows, in the dried salt, not less than 99 per cent. of NH_4I. Each mil of tenth-normal silver nitrate V.S. corresponds to 0.014496 Gm. of NH_4I. Each gramme of Ammonium Iodide, previously dried, corresponds to not less than 68.3 mils nor more than 70.1 mils of tenth-normal silver nitrate V.S." *U. S.*

Uses.—Ammonium iodide is employed, both externally and internally, as a resolvent, and does not differ perceptibly from the other iodides (see *Iodi*). It is used in *secondary syphilis, chronic rheumatism,* and in *scrofulous disorders* attended with glandular enlargements. Richardson found a liniment, made by dissolving half a drachm of the iodide in an ounce of glycerin, very efficacious in *enlarged tonsils,* applied every night with a large camel's-hair brush, and his practice has been followed to some extent by other members of the profession. Pennock recommends it as an external remedy in certain cases of *lepra* and *psoriasis,* in the form of ointment, applied by friction in the quantity of half an ounce, morning and evening. The proportions employed ranged from 4 per cent., in recent cases, to 12 per cent. in the chronic conditions. As the iodide is decomposed by the air, the ointment should be kept in well-stoppered bottles.

Dose, three to ten grains (0.20–0.65 Gm.).

AMMONII SALICYLAS. U. S.

AMMONIUM SALICYLATE Ammon. Salicyl.

(ąm-mō′nĭ-ī săl-ĭ-cȳ′ląs)

"It contains, when dried for twenty-four hours in a desiccator over sulphuric acid, not less than 98 per cent. of $NH_4C_7H_5O_3$ or $C_6H_4(OH)COONH_4$ (155.08). Preserve it in well-closed containers, protected from heat and light." *U. S.*

Ammonium Salicylicum; Salicylate d'Ammoniaque, *Fr.*; Ammoniumsalicylat, Salicylsaures Ammonium, *G.*

This salt may be made by adding salicylic acid to ammonia water until the acid is in slight excess, then evaporating the solution (which should be slightly acid to litmus paper) and crystallizing. Care should be used to prevent contamination with iron, which would give the product a pinkish or reddish tinge, and overheating, which would cause decomposition, evidenced by a phenol-like odor.

Properties.—Ammonium salicylate is officially described as in "colorless, lustrous, monoclinic prisms, or plates, or as a white, crystalline powder; odorless, and having at first a slightly saline, bitter taste, with a sweetish after-taste. Permanent in dry air. One Gm. of Ammonium Salicylate dissolves in 1 mil of water and in 3 mils of alcohol at 25° C. (77° F.). When heated, the salt fuses with decomposition, giving off inflammable vapors and an odor of phenol, and is finally volatilized, leaving not more than 0.1 per cent. of ash. An aqueous solution of the salt (1 in 10) is colorless and neutral or slightly acid to litmus. When heated with potassium hydroxide T.S. ammonia is evolved. Add a few drops of ferric chloride T.S. to an excess of a concentrated aqueous solution of Ammonium Salicylate (1 in 4); a dark red color and a precipitate are produced. In dilute solution (1 in 100) a deep violet-blue color appears. Diluted hydrochloric or sulphuric acid produces, in a concentrated aqueous solution of the salt, a voluminous, white precipitate. Acidulate 10 mils of an aqueous solution of Ammonium Salicylate (1 in 50) with hydrochloric acid and filter; the filtrate does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Dissolve about 0.5 Gm. of Ammonium Salicylate, previously dried for twenty-four hours in a desiccator over sulphuric acid and accurately weighed, in 10 mils of distilled water in a separator. Add to the solution 5 mils of diluted sulphuric acid, and extract the liberated salicylic acid by shaking out with three successive portions of 25, 15 and 10 mils respectively of chloroform, passing the chloroform solution through a filter previously moistened with chloroform and removing any salicylic acid adhering to the stem of the funnel with a few mils of chloroform. Evaporate the chloroform to about 5 mils, add 25 mils of diluted alcohol which has been previously neutralized with tenth-normal potassium hydroxide V.S., phenolphthalein T.S. being used as indicator, and titrate this solution with tenth-normal barium hydroxide V.S., using phenolphthalein T.S. as indicator. It shows, in the dried salt, not less than 98 per cent. of $NH_4C_7H_5O_3$. Each mil of tenth-normal barium hydroxide V.S. corresponds to 0.015508 Gm. of $NH_4C_7H_5O_3$. Each gramme of Ammonium Salicylate, previously dried, corresponds to not less than 63.2 mils of tenth-normal barium hydroxide V.S." *U. S.*

Uses.—Ammonium Salicylate is one of the best forms of administering salicylic acid. For consideration of its uses, see under *Acidum Salicylicum.*

Dose, ten to twenty grains (0.65–1.3 Gm.).

AMMONII VALERAS. U. S.

AMMONIUM VALERATE Ammon. Valer. [Ammonii Valerianas, U. S. 1890; Ammonium Valerianate]

(ąm-mō′nĭ-ī văl′ę-răs)

"A compound of ammonia and valeric acid having a somewhat varying composition. Preserve it in well-closed containers." *U. S.*

Valérianate d'Ammoniaque, *Fr. Cod.*; Baldriansaures (Valeriansaures) Ammonium, Ammoniumvalerianat, *G.*; Valerianato amonico, *Sp.*

A process for preparing this salt is no longer official; that of the United States Pharmacopœia of 1870 will be found in the United States Dispensatory, eighteenth edition, page 163.

Ammonium valerate was introduced into the U. S. Pharmacopœia of 1860; much difficulty was experienced by manufacturing chemists in procuring a crystallized ammonium valerate, until, after a series of experiments, B. J. Crew of Philadelphia, ascertained that it was necessary to employ the *monohydrated* valeric acid, as the ordinary acid with three molecules of water could not be successfully used for the purpose. The official formula of 1870 was based upon that of Crew, published in the *A. J. P.* (1860, p. 109). In this formula the monohydrated valeric acid, procured by a special process (see *Valeric Acid*), is saturated with gaseous ammonia obtained in the usual manner from a mixture of ammonium chloride and lime. The saturation is known to have been effected when litmus paper is no longer acted on. During the operation heat is developed sufficient to prevent premature crystallization, and, when the saturation is completed, nothing more is necessary than to allow the solution to cool. Crystallization soon begins, and in a few hours the contents of the vessel become a nearly solid mass of crystals; these should be thoroughly drained, and, without unnecessary exposure, at once transferred to well-stoppered bottles.

Properties.—Thus prepared, ammonium valerate is in snow white, pearly, four-sided, tabular crystals, perfectly dry, of an offensive odor like that of valeric acid, and a sharp sweetish taste. Instead of liquefying whenever exposed to the air, as happened to the salt formerly

procured, it undergoes this change only in a moist atmosphere, and effloresces when the air is dry. The normal salt would have the formula $NH_4C_5H_9O_2$. It is very soluble in water, ether, and alcohol. Exposed to heat it is in great measure volatilized unchanged; but a small portion, by giving off a part of its ammonia, is converted into the acid valerate. Hager (*Ph. Centralh.*, 1879, p. 465) states that commercial ammonium valerate is always the acid salt, as is proved by the acid reaction and the strong rotation of the crystals when placed upon cold water; the neutral salt is obtained only with difficulty, is in prismatic crystals, and is easily liquefied by moderate temperatures. It is officially described as in "colorless, or white, quadrangular plates, emitting the odor of valeric acid; it is deliquescent in moist air, and has a sharp and sweetish taste. One Gm. of Ammonium Valerate dissolves in 0.3 mil of water and in 0.6 mil of alcohol at 25° C. (77° F.); soluble in ether. When heated, the salt fuses, gives off vapors of ammonia and valeric acid, and is finally volatilized, leaving not more than 0.05 per cent. of residue. An aqueous solution of the salt (1 in 20) is acid to litmus, and when heated with potassium hydroxide T.S. evolves ammonia. Supersaturate slightly a concentrated aqueous solution of Ammonium Valerate with sulphuric acid; an oily layer of valeric acid rises to the surface. Precipitate completely 10 mils of an aqueous solution of the salt (1 in 20) with ferric chloride T.S.; the filtrate does not possess a deep red color (*acetate*). An aqueous solution of the salt (1 in 50), when slightly acidulated with hydrochloric acid and filtered through a small, wetted filter, does not respond to the Test for heavy metals (see Part III, Test No. 3)." *U. S.*

Uses.—On the theory that valerian owed its activity to valeric acid the ammonium valerate was brought forward many years ago as a nerve sedative in *hysteria, epilepsy, neuralgia,* and other nervous infections. Physiologically, however, it is practically inert and any beneficial result which may have followed its administration in these conditions may more reasonably be attributed to the psychic effect than to any direct action upon the nervous system. *Pierlot's solution* should be made by dissolving a drachm of valeric acid in thirty-two drachms of distilled water, saturating the solution with ammonium carbonate, and adding to the salt formed forty grains of the alcoholic extract of valerian. According to Pierlot, the latter addition is necessary to preserve the preparation from change, for a simple solution of the ammonia salt is rapidly decomposed. It will keep still better if the extract, when added to the solution, be mixed with a fluidounce of diluted alcohol, with only 24 drachms of distilled water. The solution of Pierlot is neutral, color brown, odor of valerian strong. It contains one twenty-fifth of its weight of the pure salt. The dose is six to thirty minims (0.4–1.8 mils), given in water or on a lump of sugar.

Dose, of ammonium valerate, two to ten grains (0.13–0.6 Gm.).

Off. Prep.—Elixir Ammonii Valeratis, *N. F.*

AMYGDALA AMARA. Br.

BITTER ALMOND

(ą-mŭg'dą-lą ą-mā'rą)

"Bitter Almond is the ripe seed of Prunus Amygdalus, *Stokes, var.* amara, *Baill.*" *Br.*

Semen Amygdali Amarum; Amandes amères, *Fr. Cod.*; Amygdalæ Amaræ, *P. G.*; Bittere Mandeln, *G.*; Mandorle amare, *It.*; Almendra amarga, *It.*

Bitter almond was not made official in the U. S. P. IX.

The almond tree resembles that of the cherry. The leaves are elliptical, petiolate, minutely serrated, and are of a bright green color. The flowers are large, of a pale red color varying to white, with very short peduncles, and petals longer than the calyx, and usually stand in pairs upon the branches. The fruit is a drupe with the outer covering thin, tough, dry, and marked with a longitudinal furrow, where it opens when fully ripe. Within this covering is a rough shell, containing the kernel or almond.

There are several varieties of this species of Amygdalus, differing chiefly in the size and shape of the fruit, the thickness of the shell, and the taste of the kernel. The two most important are the var. *dulcis* and the var. *amara,* the former bearing sweet, the latter bitter almonds. Both of these varieties have been known since ancient times. The var. *dulcis* yields the hard and paper-shelled variety. The latter, owing to the thin endocarp, is particularly suitable for table use. Another variety grows wild in Turkestan and has a nearly smooth endocarp or "stone." The almond tree is a native of sub-tropical China, Middle Asia and probably also Turkestan. It is now cultivated not only in the Orient, but in the Mediterranean countries of Southern Europe and Northern Africa, and also in Southern England, Scandinavia and California. Bitter almonds are chiefly imported from Morocco and Sicily.

Bitter Almonds.—These are smaller than the sweet almonds, and are "ovate or oblong-lanceolate, 20 to 30 Mm. long; seed-coat thin, brown, finely downy; embryo straight, white, and with two plano-convex cotyledons; taste bitter and oily; when triturated with water Bitter Almond yields a milk-white emulsion which emits an odor of hydrocyanic acid." *U. S. VIII.*

"Resembles the Sweet Almond in general appearance, but is distinguished by being shorter and proportionally broader, by its bitter taste, and by the characteristic odor resembling that of prussic acid given off by its aqueous emulsion." *Br.*

They have the bitter taste of the peach kernel, and, though when dry, inodorous or nearly so, have, when triturated with water, the fragrance of the peach blossom. They contain nearly the same ingredients as sweet almonds, and like them form a milky emulsion with water. It was formerly supposed that they

also contained hydrocyanic acid and volatile oil, to which their peculiar taste and odor and their peculiar operation upon the system were ascribed. It was, however, ascertained by Robiquet and Boutron that these principles do not pre-exist in the almond, but result from the reaction of water; and Wöhler and Liebig proved, what was suspected by Robiquet, that they are formed out of a peculiar substance denominated *amygdalin*, which is the characteristic constituent of bitter almonds. This substance, which was discovered by Robiquet and Boutron in 1830, is white, crystallizable, inodorous, of a sweetish bitter taste, unalterable in the air, freely soluble in water and hot alcohol, very slightly soluble in cold alcohol, and insoluble in ether. It is decomposed by the action of diluted acids or in the presence of water by the nitrogenous ferments, like *emulsin*, which accompany it in the bitter almond. The reaction is as follows:

$$\underset{\substack{\text{Crystallized}\\\text{amygdalin}}}{C_{20}H_{27}NO_{11}} + 3H_2O =$$

$$2(\underset{\text{Dextro-glucose.}}{C_6H_{12}O_6}) + \underset{\text{Hydrocyanic acid.}}{HCN} + \underset{\text{Benzal-dehyde.}}{C_7H_6O} + H_2O$$

It is recognized as belonging to the glucoside class, compounds which, when decomposed by diluted acids, alkalies, or ferments, yield glucose and some other characteristic decomposition product. They may be considered as esters of glucose analogous to the esters of glycerin which exist in the fats under the name of *glycerides*. Liebig and Wöhler give the following process for obtaining amygdalin, in which the object of the fermentation is to destroy the sugar with which it is associated. Bitter almonds, previously deprived of their fixed oil by pressure, are to be boiled in successive portions of alcohol till exhausted. From the liquors thus obtained all the alcohol is to be drawn off by distillation, care being taken, near the end of the process, not to expose the syrupy residue to too great a heat. This residue is then to be diluted with water, mixed with good yeast, and placed in a warm situation. After the fermentation which ensues has ceased, the liquor is to be filtered, evaporated to the consistence of syrup, and mixed with alcohol. The amygdalin is thus precipitated in connection with a portion of gum, from which it may be separated by solution in boiling alcohol, which will deposit it upon cooling. If pure, it will form a perfectly transparent solution with water. Any oil which it may contain may be separated by washing with ether. One pound of almonds yields at least 120 grains of amygdalin. (*Ann. Pharm.*, xxii, 329.) Amygdalin appears to be extensively diffused in plants, having been noticed not only in the different genera of the Rosaceæ, as *Amygdalus, Cerasus*, and *Prunus*, but also by Wicke in various Pomaceæ, as *Pyrus Malus, Sorbus Aucuparia, Sorbus hybrida, Sorbus torminalis, Amelanchier vulgaris, Cotoneaster vulgaris*, and *Cratægus Oxyacantha*. (*Ann. Ch. Ph.*, lxxix, 79.) It may be advantageously procured from peach kernels, which have been found to yield 80 grains for each avoirdupois pound, or more than 1 per cent. (*A. J. P.*, xxvii, 227.) According to the researches of Johannen, the emulsin is contained in the radicle and plumule, and in the vascular bundles of the cotyledons, while the parenchyma of the cotyledons contains the amygdalin. (*P. J.*, March, 1888.)

Amygdalin, mixed with emulsion of sweet almonds, gives rise, among other products, to the volatile oil of bitter almond and hydrocyanic acid,—the emulsin in the sweet almonds acting the part of a ferment, by causing a reaction between the amygdalin and water; and the same result is obtained when pure *emulsin* is added to a solution of amygdalin. It appears, then, that the volatile oil and hydrocyanic acid developed in bitter almonds when moistened result from the mutual reaction of amygdalin, water, and emulsin. Certain substances have the effect of preventing this reaction, as, for example, alcohol and acetic acid. It is asserted that emulsin procured from other seeds, as those of the poppy, hemp, and mustard, is capable of producing the same reaction between water and amygdalin, though in a less degree. (*Ann. Pharm.*, xxviii, 290.) Amygdalin appears not to be poisonous when taken pure in the stomach, unless there be emulsin in the food in the stomach.

Bitter almonds yield their fixed oil by pressure, and at the present time this oil is an article of commerce, and is frequently sold as expressed oil of almond, this being now officially permitted. It is usually produced from North African bitter almonds; the volatile oil, impregnated with hydrocyanic acid, may be obtained from the residue by distillation with water. (See *Oleum Amygdalæ Amaræ.*)

Uses.—Bitter almonds are used solely for their flavoring powers. For medicinal purposes the oil is preferable. (See *Oleum Amygdalæ Amaræ.*) It has been ascertained that bitter almond paste, and other substances which yield the same volatile oil, such as bruised cherry-laurel leaves, peach leaves, etc., have the property of destroying the odor of musk, camphor, most of the volatile oils, creosote, cod liver oil, the balsams, etc.; and Mahier, a French pharmacist, has employed them successfully to free mortars and bottles from the odor of asafetida and other substances of disagreeable odor. All that is necessary is first to remove any oily substance by means of an alkali, and then to apply the paste or bruised leaves.

Bitter almonds, on account of the hydrocyanic acid developed in them, have sometimes proved poisonous.

AMYGDALA DULCIS. U. S., Br.

SWEET ALMOND Amygd. Dulc.

(ă-mŷg'dą-lą dŭl'cĭs)

"The ripe seeds of *Prunus Amygdalus dulcis* De Candolle (Fam. *Rosaceæ*). Preserve Sweet

Almond in tightly-closed containers, adding a few drops of chloroform or carbon tetrachloride from time to time to prevent attack by insects." *U. S.* "Sweet Almond is the ripe seed of Prunus Amygdalus, *Stokes, var.* dulcis, *Baill.* Known in commerce as the Jordan almond." *Br.*

Semen Amygdali Dulce; Amandes douces, *Fr. Cod.;* Amygdalæ Dulces, *P. G.;* Süsse Mandeln, *G.;* Mandorle dolci, *It.;* Almendra dulce, *Sp.*

We are supplied with sweet almonds chiefly from Spain, Italy, France, and Southern California. They are separated into the soft-shelled and hard-shelled, the former of which come from Marseilles and Bordeaux, the latter from Malaga. From the latter port they are sometimes brought to us without the shell. In British commerce, the two chief varieties are the *Jordan* and *Valencia* almonds, the former imported from Malaga, the latter from Valencia. The former are longer, narrower, more pointed, and more highly esteemed than the latter.

Properties.—The shape and appearance of almonds are too well known to require description. Each kernel consists of two white cotyledons, enclosed in a thin, yellowish-brown, bitter skin, which is easily separable after immersion in boiling water. Deprived of this covering, they are called *blanched almonds.* On exposure to the air they are apt to become rancid; but, if thoroughly dried and kept in well-closed glass vessels, they may be preserved unaltered for many years.

Sweet almonds, when blanched, are without odor, and have a sweet, very pleasant taste, which has rendered them a favorite article of diet in all countries where they are readily attainable. They are, however, generally considered difficult of digestion. They are officially described as: "Ovate or oblong lanceolate, 17 to 25 mm. in length, 10 to 13 mm. in breadth and 4 to 7 mm. in thickness; seed-coat light brown with numerous parallel veins, thin and easily removed on soaking the seed in water; embryo straight, white, and with two plano-convex cotyledons; taste bland, sweet. Triturate Sweet Almond with water; a milk-white emulsion is produced which is not acid to litmus, and has no odor of benzaldehyde or hydrocyanic acid (*bitter almond*). The powder is creamy-white, exhibiting numerous very small oil globules, 0.001 mm. or less in diameter, and larger oil globules and crystalloids, the latter sometimes with adhering globoids; fragments of parenchyma of endosperm, containing oil globules and aleurone grains; also occasional fragments of seed-coat with characteristic, more or less scattered, large, elliptical, thin-walled, strongly lignified epidermal cells and narrow, closely spiral tracheæ. Starch grains are absent. Sweet Almond yields not more than 4 per cent. of ash." *U. S.* "About two and a half centimetres or somewhat more in length, nearly oblong in outline, more or less compressed, pointed at one extremity and rounded at the other. Testa cinnamon-brown, thin and scaly. Seed exalbuminous, containing two large planoconvex oily cotyledons. Taste bland; when triturated with *water* forms a white emulsion with no marked odor." *Br.* Shelled almonds are sometimes substituted by the kernels of the peach, plum and apricot. The stone cells in the epidermal layer of the almond are much larger than in the kernels of the substitutes. For microscopic distinctions see Winton and Moeller, "*The Microscopy of Vegetable Foods.*" Almond cake a by-product in the manufacture of almond oil is largely used in the preparation of a class of detergent powders known as "almond meal." It is also used as a diabetic food and sometimes as an adulterant of ground spices and powdered drugs. By the analysis of Boullay, it appears that almonds contain 54 parts of fixed oil, 24 of protein, 6 of uncrystallizable sugar, 3 of gum, 9 of fibrous matter, 3.5 of water, and 0.5 of acetie acid, comprising loss. The protein is somewhat peculiar, consisting of *amandin* and *emulsin,* the latter being an enzyme. It may be obtained separate by treating the emulsion of almonds with ether, allowing the mixture, after frequent agitation, to stand until a clear fluid separates at the bottom of the vessel, drawing this off by a siphon, adding alcohol to it so as to precipitate the emulsin, then washing the precipitate with fresh alcohol, and drying it under the receiver of an air pump. In this state it is a white powder, inodorous and tasteless, soluble in water, and insoluble in ether and alcohol. Its solution has an acid reaction, and, if heated to 100° C. (212° F.), becomes opaque and milky, and gradually deposits a snow-white precipitate, amounting to about 10 per cent. of the protein employed. The distinguishing characteristic of the emulsin is that of producing certain changes noticed previously in amygdalin, which property it loses when its solution is boiled, although not by exposure in the solid state to a heat of 100° C. (212° F.). It consists of nitrogen, carbon, hydrogen, and oxygen, with a minute proportion of sulphur, and is probably identical with the *synaptase* of Robiquet. L. Portes has reported *asparagin* in sweet almonds. (*N. R.,* January, 1877.) The fixed oil is described under the head of *Oleum Amygdalæ Expressum,* to which the reader is referred. Sweet almonds, when rubbed with water, form a milky emulsion, free from the odor of hydrocyanic acid, the insoluble matters being suspended by the agency of the albuminous, mucilaginous, and saccharine principles.

Uses.—Sweet almonds have no other influence on the system than that of a nutrient and demulcent. The emulsion formed by triturating them with water is a pleasant vehicle. From their nutritive properties, and the absence of starch in their composition, they are much used in the diet of *diabetics,* as originally recommended by Pavy. (*Guy's Hosp. Rep.,* 1862, p. 213.) *Almond meal* or almond press cake is used for cosmetic purposes as an addition to

the bath or to the water used in washing the face and hands. Much of the so-called almond meal used for this purpose is factitious or adulterated.

Off. Prep.—Emulsum Amygdalæ, *U. S.;* Mistura Amygdalæ, *Br.;* Pulvis Amygdalæ Compositus, *Br.*

AMYLIS NITRIS. U. S. (Br.)

AMYL NITRITE Amyl. Nitris
[Amyl Nitris, U. S. 1890]

(ăm'y-lis nī'tris)

"A liquid containing not less than 80 per cent. of $C_5H_{11}NO_2$ (117.10) (chiefly iso-amyl nitrite). Preserve it in hermetically sealed glass bulbs, or in glass-stoppered vials, in a cool place, protected from light." *U. S.* "Amyl Nitrite is a liquid obtained by the interaction of amylic alcohol [which has been distilled between 128° and 132° C. (262.4° and 269.6° F.)] and nitrous acid. It consists chiefly of iso-amyl nitrite, $C_5H_{11}NO_2$, but contains also other nitrites of the homologous series. It should be kept in small, stoppered bottles in a cool, dark place." *Br.*

Amyl Nitris, *Br.;* Amylo-nitrous Ether, Amylæther Nitrosus; Ether amylnitreux, *Fr. Cod.;* Ether amylazoteux, Azotite d'Amyl, *Fr.;* Amylium Nitrosum, *P. G.;* Amynitrit, *G.;* Etere isoamilnitroso, *It.;* Nitrito de amilo, *Sp.*

This substance, which was discovered by Balard in 1844, should not be confounded with *amyl nitrate,* $C_5H_{11}NO_3$, which is not used as a medicine.

Preparation.—Amyl nitrite may be prepared by passing a stream of nitrous acid (hyponitric acid) gas through purified amyl alcohol at a temperature of 132° C. (269.6° F.), or by acting upon amyl alcohol with nitric acid, as originally suggested by Balard. The alcohol should always first be purified according to the method of Hirsch (*A. J. P.,* 1862, pp. 139, 328), by agitating with an equal bulk of strong solution of common salt, then distilling in a retort with a thermometer, collecting what comes over between 125° C. (257° F.) and 140° C. (284° F.), and redistilling this until it has a boiling point near 132° C. (269.6° F.). The purified alcohol should be mixed with about an equal bulk of nitric acid in a capacious glass retort, being gradually heated until it approaches boiling, when the fire is to be removed. As soon as a thermometer inserted into the tubulures rises above 100° C. (212° F.) the receiver is changed, because both ethyl-amylic ether and amyl nitrate at such temperatures come over freely and would contaminate the product. The distillate obtained below 100° C. (212° F.) is agitated with a solution of potassium carbonate, and the oily liquid which separates is very slowly heated in a clean retort to 96° C. (204.8° F.), then the receiver is changed and the distillate collected as before, until the thermometer reaches 100° C. (212° F.). That which comes over between the two temperatures is pure amyl nitrite. It is essential to this process that in every case the heating be very gradual. (*A. J. P.,* 1871, p. 148.) Allen states (*Com. Org. Anal.,* 2d ed., i, 159) that the use of nitric acid is certain to result in the formation of much valeric aldehyde and more or less amyl nitrate, and the boiling point of the former of these bodies precludes the possibility of subsequently separating it by fractioning the crude product. He therefore prefers the passing of nitrous acid gas into purified amyl alcohol. John M. Maisch attempted to produce amyl nitrite by Redwood's process (*A. J. P.,* 1867, p. 330) for the production of nitrous ether, substituting amyl for ethyl alcohol. He found that the reactions occurred with such excessive violence as to render the preparation of the nitrite in this way impracticable. Subsequently, however, Alfred Tanner pointed out (*P. J.,* Nov., 1871, also *A. J. P.,* 1872, p. 21) that Maisch used a nearly anhydrous amyl alcohol, and that the reactions are equally violent with ethyl alcohol of similar strength. He finds no difficulty when the fusel oil is diluted with water, and prefers the process, especially for the production of the drug upon a small scale. Having introduced the purified amyl alcohol into a tubulated retort containing copper wire, he adds one-tenth of its bulk of strong sulphuric acid, and then the same quantity of nitric acid, previously diluted with an equal bulk of water, and heats gently to 63° C. (145.4° F.). At this temperature the reaction commences, and goes on very manageably, until a bulk about equal to double the quantity of nitric acid collects in the receiver. The chemical movement now ceases, and the temperature, which has risen to near 100° C. (212° F.), begins to fall. More diluted nitric acid is added, and the process carried out as before. These additions are repeated until the amyl alcohol is exhausted, which is known by the appearance of red fumes in the retort. The whole product is washed with caustic soda, to remove hydrocyanic and other acids, and rectified over potassium carbonate, to get rid of moisture. The portion which distils over between 95° C. (203° F.) and 100° C. (212° F.) is medicinally pure amyl nitrite. Amyl nitrite is also manufactured by distilling a mixture of amylic alcohol, sodium nitrite, and diluted sulphuric acid,

$$2C_5H_{11}OH + 2NaNO_2 + H_2SO_4 = 2C_5H_{11}NO_2 + Na_2SO_4 + 2H_2O.$$

D. B. Dott (*P. J.,* Aug. 31, 1878) called attention to the difficulties in the way of fixing a standard boiling point for amyl nitrite, and W. H. Greene (*A. J. P.,* 1879, p. 65) shows that nitropentane (an isomer of amyl nitrite) is almost invariably a constituent of amyl nitrite, and he believes that commercial amyl nitrite is frequently put upon the market unrectified, specimens examined having boiling points varying from 70° C. (158° F.) to 180° C. (356° F.). J. M. Francis examined amyl nitrite of commerce in 1905 and found many samples of inferior grade. He stated that 80 per cent. of the total volume should distil between 90° C. (194° F.) and 100° C. (212° F.).

Dunstan and W. Lloyd Williams (*P. J.*, 1888, p. 487) have shown that the supposed pure amyl nitrite is a mixture of α-amyl nitrite and β-amyl nitrite, arising from the fact that the amyl alcohol used is always a mixture of α-amyl alcohol and β-amyl alcohol in varying proportions. They find the α-amyl nitrite to be optically inactive and to boil at 97° C. (206.6° F.), while the β-amyl nitrite has dextro-rotatory power and boils at about 94° C. (201.2° F.). Much of the commercial amyl nitrite also contains isobutyl nitrite, boiling at 67° C. (152.6° F.). It is a question whether the physiological action of commercial amyl nitrite is really due to the amyl nitrite or to impurities, especially to the iso-butyl nitrite, but the experiments of Brunton and Bokenham (*P. J.*, xix, 490) indicated that the commercial, impure nitrite is stronger than either pure α- or β-amyl nitrite. According to Bals and Broglio, the *tertiary amyl nitrite* differs from amyl nitrite in not giving rise to toxic symptoms, and in being slightly hypnotic.

Properties.—It is officially described as follows: "A clear, yellowish liquid, of a peculiar, ethereal, fruity odor and a pungent, aromatic taste. It is almost insoluble in water, miscible with alcohol or ether. Specific gravity: 0.865 to 0.875 at 25° C. (77° F.). Amyl Nitrite is very volatile, even at a low temperature, and is inflammable, burning with a yellow, luminous and sooty flame. Add 2 mils of sulphuric acid to a mixture of 2 drops of Amyl Nitrite and 2 drops of water; amyl valerate is produced, recognizable by its odor on dilution with water. Add a few drops of Amyl Nitrite to a mixture of 1 mil of ferrous sulphate T.S. and 5 mils of diluted hydrochloric acid; a greenish-brown color is produced. Mix 1 mil of normal potassium hydroxide V.S. and 10 mils of distilled water in a test tube with a drop of phenolphthalein T.S. and add 5 mils of Amyl Nitrite; after inverting the tube a few times, the red tint of the aqueous layer is still perceptible (*free acid*). A mixture of 1.5 mils of silver nitrate T.S. and 1.5 mils of alcohol with a few drops of ammonia water does not become brown or black on adding 1 mil of Amyl Nitrite and gently heating the mixture (*aldehyde*)." *U. S.*

"A volatile liquid of a yellowish color, fragrant odor, and not more than the faintest acid reaction. Almost insoluble in *water;* soluble in *alcohol* (90 per cent.) in all proportions. Specific gravity 0.870 to 0.880. Not less than 90 per cent. distils below 100° C. (212° F.). A mixture of 5 volumes with sufficient *alcohol* (90 per cent.) to form 100 volumes yields a liquid of which a portion tested in a nitrometer as described under 'Spiritus Ætheris Nitrosi' yields not less than 7.9 times its volume of nitric oxide gas. On shaking with an equal volume of *solution of sodium hydroxide* the aqueous portion acquires not more than a pale yellow color (limit of aldehyde). Remains transparent when cooled to 0° C. (32° F.) (absence of water)." *Br.*

Assay.—"Transfer about 3 mils of Amyl Nitrite, which has been previously shaken with 0.5 Gm. of potassium bicarbonate and carefully decanted, to a tared 100 mil measuring-flask, containing about 20 mils of alcohol, and weigh it accurately. Add sufficient alcohol to bring the volume to exactly 100 mils and mix thoroughly. Introduce into a nitrometer (see Part III, Test No. 19) exactly 10 mils of the alcoholic solution, followed by 10 mils of potassium iodide T.S., and afterwards by 5 mils of diluted sulphuric acid. When the volume of gas has become constant (within thirty to sixty minutes), note the amount collected, multiply this volume in mils by 4.8 and divide the product by the original weight in grammes of the Amyl Nitrite. At standard temperature and pressure, the quotient represents the percentage of Amyl Nitrite in the liquid. The temperature correction is one-third of one per cent. of the total percentage just found for each degree—additive if the temperature is below 25° C. (77° F.), and subtractive if it is above 25° C. (77° F.). The barometric correction is four-thirtieths of one per cent. of the total percentage just found for each millimeter,—additive if it is above 760 mm., and subtractive if it is below 760 mm." *U. S.*

Uses.—Physiologically, amyl nitrite acts precisely like sodium nitrite (see p. 1032), except that it is much quicker and more evanescent. Amyl nitrite is used in medicine for three purposes: to relax spasms in the arteries, to control convulsions, and for the relief of the asthmatic paroxysm. In all its usages it is to be borne in mind that its action while extremely rapid is very fleeting and it is therefore of service only where an immediate effect is desired. In the circulatory conditions in which it is of service the most important is *angina pectoris.* This disease is probably associated with spasms of the coronary arteries, but whatever be its pathology, clinical experience has demonstrated the extreme value of inhalations of amyl nitrite. In convulsive disorders, amyl nitrite is of service only when it is necessary to cause immediate relaxation; thus in *tetanus,* because of the duration of the convulsive tendency, the fugaciousness of its action renders it of relatively small service; on the other hand, in *strychnine poisoning,* by restraining the convulsions long enough for more durable motor depressants to act, it may prove a life-saving remedy. In ordinary *epilepsy* it is of little service, but in that condition known as *status epilepticus* in which the patient passes from one convulsion to another, the drug may be of great benefit. Again, in those occasional cases of epilepsy in which the seizure is preceded by an aura of sufficient length, if the patient carry in the pocket pearls of amyl nitrite and inhale the vapor as soon as the aura commences the paroxysm may usually be aborted. In many cases of *asthma* it will cause an immediate, if only temporary, cessation of the paroxysm. Whether this effect is due to the action of the nitrite radical upon the circulation or whether it is the result of some narcotic effect of the amyl group is at present uncertain.

The claim of Hare that amyl nitrite is of great value for the relief of *hemoptysis* has been confirmed by a number of observers. (See *B. M. J.*, July 15, 1911.) Its action in this condition is probably the result of dilatation of the splanchnic and contraction of the pulmonary blood-vessels.

Amyl nitrite is generally administered by inhalation, usually in doses of from three to five drops, although much larger quantities have been given without bad results. The rule is to commence with three drops on a handkerchief held close to the nose, and then gradually to increase *pro re nata*. The handkerchief should always be withdrawn so soon as the face flushes or the heart begins to become excited, as the effects always increase for some time, even if no more be inhaled. The best method, however, of administering the very volatile liquid is by the use of glass pearls,—small flask-shaped vessels containing two, five, or ten minims of the nitrite; these are crushed in a handkerchief or towel when wanted for inhalation, the thin and fragile glass causing no inconvenience. The drug may also be given by the mouth.

When inhaled in doses of from five to ten drops, amyl nitrite produces in man violent flushing of the face, accompanied with a feeling as though the head would burst, and a very excessive action of the heart. Along with these symptoms, after a larger quantity, there is a sense of suffocation, and more or less marked muscular weakness. No case of serious poisoning from amyl nitrite has occurred in man.

Dose, from three to five minims (0.2–0.3 mil), if given by mouth it may be dissolved in alcohol.

AMYLUM. U. S., Br.

STARCH Amyl. [Corn Starch]

(ăm'y-lŭm)

"The starch separated from the grain of *Zea Mays* Linné (Fam. *Gramineæ*)." *U. S.* "Starch is procured from the grains of (1) common wheat, Triticum sativum, *Lam.;* (2) maize, Zea Mays, *Linn.;* and (3) rice, Oryza sativa, *Linn.*" *Br.*

Amylum Tritici, *P. G.;* Amylum Zeæ, Wheat Starch; Amidon, *Fr. Cod.;* Fécule de Froment, de Blé, de Maïs, *Fr.;* Stärkmehl, Stärkes, Kraftmehl, Maisstärke, Weizenstärke, *G.;* Amido, *It.;* Almidon, *Sp.*

Starch is a proximate vegetable principle contained in most plants, and especially abundant in the various grains, such as corn, wheat, rye, and barley; in seeds, as peas, beans, chestnuts, acorns, etc.; and in numerous rhizomes and tuberous roots, as those of the potato, the sweet potato, the arrow-root, canna, cassava, sago, yam, curcuma and erythronium. The starch is always in the form of grains, which are contained within the parenchymatous cells, and is procured by reducing the substances in which it exists to a state of minute division, agitating or washing them with cold water, straining or pouring off the liquid, and allowing it to stand till the fine grains which are held in suspension have subsided. This, when dried, is starch, more or less pure, according to the care taken in conducting the process. Electricity has been used to bleach starch and thus raise its commercial value. (*D. C.*, 1893, 203.) In the U. S. P. of 1880 the official starch was that derived from wheat, but in the revision of 1890 corn starch was substituted, and this kind of starch was made official in the U. S. P. VIII and IX. In most of the European Pharmacopœias the official starch is derived from wheat. In some of them rice is also recognized. The starch of European commerce is largely obtained from the potato, while in the United States corn starch is almost exclusively in use, wheat and rice starch coming next in importance. For a description of the differences, see page 144.

Properties.—Starch is white, inodorous and tasteless, pulverulent, opaque, and, as found in commerce, is usually in columnar or irregular angular masses (wheat starch), which are easily reduced to powder, which produces a peculiar sound when pressed between the fingers. Its specific gravity is 1.505 at 19.4° C. (66.9° F.) (Payen.) It is composed of minute microscopic granules, in starch from the same plant nearly uniform in size, more or less plainly striate, and having a distinct hilum or point of origin of growth. In the different species of plants the starch granules differ in their characteristic forms. When exposed to a moist air, it absorbs a considerable quantity of water, which may be driven off by a gentle heat. It is insoluble in alcohol, ether, and cold water, but unites with boiling water, which, on cooling, forms with it a soft semi-transparent paste or a gelatinous opaline solution according to the proportion of starch employed. The paste placed on folds of blotting-paper, renewed as they become wet, loses water, contracts, and assumes the appearance of horn. If the proportion of starch be very small, the solution, after slowly depositing a very minute quantity of insoluble matter, continues permanent, and upon being evaporated yields a semi-transparent mass, which is partially soluble in cold water. The starch has, therefore, been modified by the combined agency of water and heat; nor can it be restored to its original condition. Heating with glacial acetic acid to 100° C. (212° F.), or with glycerin to 190° C. (374° F.), will also make starch soluble. Corn starch is officially characterized as "in fine powder, or irregular, angular, white masses; consisting chiefly of polygonal, rounded or spheroidal starch grains from 0.003 to 0.035 mm. in diameter, usually with a lenticular or 3- to 4-rayed central cleft, or in the rounded grains, with a circular marking; inodorous; taste slight, characteristic. The individual starch grains are colored a deep blue by iodine T.S. Corn starch is insoluble in cold water and in alcohol; upon boiling 1 Gm. of Starch with 15 mils of water and cooling, it yields a translucent, whitish jelly. Incinerate

about 0.5 Gm. of Starch; not more than 0.5 per cent. of ash remains. Triturate about 0.5 Gm. of Starch with 5 mils of distilled water; the mixture is neutral to litmus." *U. S.*

"In fine powder or in irregular angular or columnar masses, which are readily reduced to powder; white, inodorous. Cold *water* mixed with an equal weight of Starch does not become more than faintly acid or alkaline to *litmus*. Boiled with *water* and cooled, it gives a deep blue color with *N/10 solution of iodine*. Under the microscope the several varieties of Starch present the following characters:—1. Wheat Starch: A mixture of large and small granules, the former lenticular in shape, and marked with faint concentric striæ surrounding a nearly central hilum. 2. Maize Starch: Granules more uniform in size, frequently polygonal, somewhat smaller than the large granules of wheat starch, and having a very distinct hilum, but without evident concentric striæ. 3. Rice Starch: Granules extremely minute, nearly uniform in size, polygonal, without evident hilum or striæ. Starch is free from granules other than those described." *Br.*

At a temperature of 160° C. (320° F.) for air-dried starch, and 200° C. (392° F.) for starch previously dried at 100° C. (212° F.), it is changed into *dextrin* (*British gum*), and at 200° C. (392° F.) to 215° C. (419° F.) forms a transparent fused mass, which consists exclusively of dextrin (Payen); at 220° C. (428° F.) to 230° C. (446° F.) it undergoes further change and yields chiefly *pyrodextrin*, a brown, tasteless, and odorless compound, readily soluble in water, insoluble in alcohol and ether. (Gelis, *Ann. Ch. Phys.*, (3) lii, 388.)

Composition and Nature.—The formula of starch is generally taken as $C_6H_{10}O_5$, or a multiple of this. This formula does not give us a clear idea of the nature of the starch grain. It consists of at least two or three substances. The wall or membrane is very distinct and clearly differentiated from the rest of the grain. The inner portion consists of two substances which are distributed in alternate layers. The one is colloidal, taking up aniline stains, and the other is made up of soluble starch. (See Kraemer, *A. J. P.*, 1907, pp. 217 and 412; 1914, p. 81.)

Musculus, in 1861, showed that by the action of diluted acids or of *diastase*, starch is resolved into *dextrin*, $C_{12}H_{20}O_{10}$, and *dextrose*, $C_6H_{12}O_6$, so that its formula, in simplest terms, would be $(C_6H_{10}O_5)_3$. Recent determinations of its molecular weight by Brown and Morris make it as high as $5(C_{12}H_{20}O_{10})_{20}$. Iodine forms with starch, whether in its original state or in solution, a blue compound; and the tincture of iodine is the most delicate test for its presence. The color varies somewhat according to the proportions employed. When the two substances are about equal, the compound is of a beautiful indigo blue; if the iodine be in excess, it is blackish-blue; if the starch, violet blue. This reaction is not altogether characteristic of starch; Barger and Starling (*P. J.*, 1912, xcii, 146) have compiled a list of over sixty organic substances which give a blue color with iodine. A singular property of starch iodide is that its solution becomes colorless if heated to about 93.5° C. (200° F.), and afterwards recovers its blue color upon cooling. By boiling, the color is permanently lost, while Puchot states that certain nitrogenized organic bodies, as albumin, prevent the reaction of iodine on starch or destroy it. Alkalies unite with starch, forming soluble compounds, which are decomposed by acids, the starch being precipitated. It is thrown down from its solution by lime water and baryta water, forming insoluble compounds with these earths. The solution of lead subacetate precipitates it in combination with the oxide of the metal. Starch may be made to unite with tannin by boiling their solutions together; and a compound results, which, though retained by the water while hot, is deposited when it cools. By long boiling with diluted sulphuric, hydrochloric, or oxalic acid, it is converted into *dextrin* and glucose or grape sugar. A similar conversion into dextrin and glucose is effected by means of *diastase*, which change can be represented as taking place in several stages:

$$3C_6H_{10}O_5 + H_2O = \underset{\text{Dextrin}}{C_{12}H_{20}O_{10}} + \underset{\text{Dextrose}}{C_6H_{12}O_6}$$

$$C_{12}H_{20}O_{10} + H_2O = \underset{\text{Maltose}}{C_{12}H_{22}O_{11}}$$

$$C_{12}H_{22}O_{11} + H_2O = 2\underset{\text{Dextrose}}{C_6H_{12}O_6}$$

Many observers claim to recognize the production of other intermediate substances, as *amylodextrin* (soluble starch), *erythrodextrin, achroodextrin, maltodextrin,* none of which reduce Fehling's solution, followed by *maltose*, which does reduce Fehling's solution. Strong hydrochloric and nitric acids dissolve starch; and the latter acid, by the aid of heat, converts it into oxalic and malic acids. By the action of strong nitric, sulphuric, or crystallizable acetic acid, used with certain precautions, the starch is rendered soluble, and may be obtained in this state by separating the acid by means of alcohol. By the continued action of concentrated sulphuric acid it is decomposed. When it is dissolved in strong nitric acid, and precipitated by water, a white powder is thrown down, called *xyloidin*, $C_6H_9(NO_2)O_5$ (Braconnot), in which one atom of the hydrogen of the starch is replaced by one group, NO_2, furnished by the nitric acid. Mixed with hot water and exposed to a temperature of 27° C. (80.6° F.), it undergoes chemical changes, which result in the formation of several distinct principles, among which are sugar, a gummy substance (perhaps *dextrin*), and a soluble modification of starch. With yeast, starch undergoes the vinous fermentation, being, however, first converted into sugar. Mixed with cheese and chalk it is said to yield alcohol without the previous saccharin conversion. (Berthelot, *J. P. C.*, 3e sér., xxxii, 260.) All plants which contain chlorophyll have the power of using the chem-

ical rays of sunlight in producing from carbon dioxide and water a substance which is organic. There is first formed in the centre of the chlorophyll granule a minute speck, which is believed to be starch; this new starch granule is incapable of solution, but by conversion into sugar or dextrin is rendered soluble, and in this form is carried in the juices of the plant. One of two destinies there awaits it. It may be converted into the permanent compound cellulose which constitutes the woody tissue, or it may be reconverted to its original form and be deposited in the buds, seeds, barks, roots or rhizomes of the plant. These stores of starch are usually accumulated for future growth, and are especially seen in plants which flower in the spring before the leaves are put forth, or which reproduce the species without seeding.

The structure and nature of the starch granule has been the subject of much investigation and discussion. Its microscopic appearance supports, but of course does not prove, the original theory advanced by Schleiden, that it is composed of concentric layers of similar chemical composition, in which the outer layer has been the first formed while the inner layers have been successively deposited in its interior. The microscopic characters, however, are just as readily explained on the theory that the central layer was the first formed and that the peripheral layers have been deposited around the point of the hilum. This view, originally advanced by Fritsche in 1834, has been widely supported by various observers. Other authorities have come to the conclusion that the starch grains grow as do ordinary vegetable cells, but the theory brought forward in 1880 by Schimper, that all starch grains develop within plastids, *i.e.*, in protoplasmic masses or cells, and that in starch which is stored, the leucoplastids finally disappear, is the theory which has been of recent times most widely believed and is probably correct. In stating his views, Schimper further came to the conclusion that the outer portion of the grain is the part most recently produced. That there is a marked difference in the layers of the starch grains is shown by the varying effects of staining reagents, certain parts of the grains being much more affected by safranin and gentian-violet than others. It would further appear that though the starch layers each contain colloidal substances besides crystalloidal cellulose, the proportion of their constituents varies so much that the alternate layers are different, one set being colloidal and others crystalloidal, in their general nature. For details see Kraemer, *Botan. Gaz.*, vol. 24, Nov., 1902; also *Proc. Am. Philosoph. Soc.*, vol. xli.

Varieties.—Starch, as obtained from different substances, is somewhat different in its characters. *Wheat starch*, when examined with a microscope, is found to consist of more or less rounded or biscuit-shaped grains, from 0.005 to 0.035 mm. in diameter, the smaller being spheroidal, the larger rounded and flattened, and are without distinct markings, except when heated with chemical solutions. The granules are mixed with loose integuments, resulting from the process of grinding. This variety of starch has a certain degree of hardness and adhesiveness, owing, according to Guibourt, to the escape of a portion of the interior substance of the broken granules, which attracts some moisture from the air, and, thus becoming glutinous, acts as a bond between those which remain unbroken. Another opinion attributes this peculiar consistence to the retention of a portion of the gluten of the wheat flour, which causes the granules to cohere. Under the name of *corn starch*, a variety of starch obtained from the meal of maize or Indian corn is much used for nutritive purposes in the United States. It is now the official starch. The granules of maize starch are very small, with a diameter not exceeding, according to Payen, one-sixth of that of the potato, and little more than one-half of that of the wheat granules. They have a very distinct hilum which is either circular or in the form of a 3- to 5-rayed cleft, but no evident concentric striæ. *Rice starch* has extremely minute granules, nearly uniform in size, polygonal, without evident hilum or striæ. *Potato starch* is employed in various forms, being prepared so as to imitate more costly amylaceous substances, such as arrow-root and sago. In its ordinary state it is more pulverulent than is wheat starch, has a somewhat glistening appearance, and may be distinguished, with the aid of the microscope, by the size of its granules, which are larger than those of any other known fecula except canna, or *tous les mois*. They are exceedingly diversified in size and shape, though their regular form is said to be ovate or shell-shaped, the grains varying from 0.005 to 0.125 mm. in long diameter. The characters of other kinds of fecula will be given under the heads of the several official substances of which they constitute the whole or a part. According to Chevallier, starch is sometimes adulterated with calcium carbonate and calcium sulphate; and the fraud is also practised of saturating it with moisture, of which it will absorb 12 per cent. without any obvious change.

Several authors have recently reported upon the value of the micro-polariscope in the examination of commercial starches. (See Ewers, *Zeitschr. f. öffentl. Chem.*, 1908, pp. 8 and 150; Herman, *Bull. Soc. Chim. Belg.*, 1908, p. 340.) For a report on the ultra-microscopic structure of the starches, their constituents and a method of separating the latter, see *Compt. rend.*, 1908, pp. 285, 599 and 978.

Uses.—Starch is demulcent and, when cooked, nutritive; in the raw state it is not affected by human digestive secretions. Powdered and dusted upon the skin, it is sometimes used to absorb irritating secretions and prevent excoriation. Mixed with water it forms the basis of several pastes used in dermatological practice. Dissolved in hot water and allowed to cool, it is often employed in enemata, either as a vehicle,

or as a demulcent application in irritated states of the rectum; this liquid may also be used as an antidote in iodine poisoning, and given freely in other cases where amylaceous or mucilaginous drinks are indicated. It is also used officially as a diluent for powdered extracts.

Dextrin is a substance resembling gum in appearance and properties, but differing from it in not affording mucic acid by the action of nitric acid. Large quantities of dextrin are now made both here and abroad and employed for various purposes in the arts, under the name of *artificial gum* or *British gum.* It is found in the market usually in the form of a yellowish or brilliant white powder, and in small masses or fragments resembling natural gum. It is made by the action either of acids or of diastase on starch, or by heating starch slightly moistened with nitric acid as follows: Dextrin is made according to the Heuse process. One thousand kilos of starch are moistened with 2 kilos of nitric acid diluted with 300 liters of water, the mass is then made into loaves which are dried in the air, ground finely, and heated for about two hours at 100° to 120° C. (212°–248° F.). The powder is then heated in a suitable oven or placed in a circular Uhland apparatus, it is heated with superheated steam, and continually stirred to secure intimate mixture. If the temperature is raised to 130° to 140° C. (266°–284° F.) the duration of heating is shortened, but yellow and not white dextrin is obtained. For further detail, consult *General and Industrial Chemistry,* Molinari.

White Dextrin under the title *Dextrinum Album* is official in the National Formulary IV. It is "a mixture of soluble carbohydrates, amylodextrin, achroodextrin, erythrodextrin and maltodextrin, together with a variable amount of unconverted starch, obtained by the incomplete hydrolysis of starch by the action of an acid." *N. F.*

It occurs as "a white, glistening, non-hygroscopic, amorphous powder producing a peculiar and characteristically harsh sensation when rubbed in the hand; odorless and having a sweetish taste. Only partly soluble in cold water, but completely soluble in three parts of water on boiling. An aqueous solution prepared in the cold and filtered is colored wine-red by iodine T.S.; an aqueous solution prepared with boiling water is colored blue by iodine T.S. Alkaline cupric tartrate V.S. is not changed by a solution of White Dextrin in the cold, but is reduced on boiling. Separate portions of a freshly prepared, filtered solution in cold water do not become turbid on the addition of calcium chloride T.S. or of calcium hydroxide T.S. (*oxalic acid*). Not more than 5 per cent. of White Dextrin is soluble in boiling alcohol (*dextrose*). Dry White Dextrin at 110° C. (230° F.); it loses not more than 10 per cent. in weight (*moisture*). Separate portions of a filtered aqueous solution of White Dextrin (1 in 20) are not immediately precipitated by lead acetate T.S., or by basic lead acetate T.S., but upon the addition of a few drops of ammonia water to the mixtures, precipitation occurs (difference from *natural gums*). A solution of White Dextrin does not darken on the addition of hydrogen sulphide T.S. even when supersaturated with ammonia water (*metals*). White Dextrin yields not more than 0.5 per cent. of ash." *N. F.*

Dextrin, according to Payen, is converted into glucose through the action of diastase; but the glucose impedes the action unless removed; as, however, during alcoholic fermentation the glucose is consumed, the influence of diastase is not retarded. Hence dextrin by conversion into sugar may contribute to the alcoholic product.

Off. Prep.—Glyceritum Amyli, *U. S.* (*Br.*); Pulvis Tragacanthæ Compositus, *Br.*

ANETHI FRUCTUS. Br.

DILL FRUIT

(ą-nē'thī frŭc'tŭs)

"Dill Fruit is the dried ripe fruit of Peucedanum graveolens, *Benth. and Hook. f.*" *Br.*

Garden Dill, Dilly, Anet; Aneth, *Fr. Cod.;* Fenouil puant, *Fr.;* Dill, *G.;* Eneldo, *Sp.*

Peucedanum graveolens (*Anethum graveolens* L.), or garden dill, resembles the fennel plant, but is smaller. It is an annual plant, three or four feet high, with a long spindle-shaped root; an erect, striated, jointed, branching stem; and bipinnate or tripinnate, glaucous leaves, which stand on sheathing footstalks and have linear and pointed leaflets. The flowers are yellow, and in large, flat, terminal umbels, destitute of involucre. The plant is a native of Spain, Portugal, and the south of France, and is found growing wild in various parts of Africa and Asia. It is cultivated in all the countries of Europe, and has been introduced into our gardens. The whole plant is aromatic, the leaves are used as a flavor for soups, sauces and pickles. For a paper by J. C. Umney describing the commercial varieties, see *Year Book of Pharmacy,* 1898, 374. The seeds, as the fruit is commonly called, are the only part used. They are "composed of two mericarps usually separate and freed from the pedicel; each broadly oval, about four millimetres long, and two to three millimetres broad; brown; very strongly compressed dorsally; dorsal ridges inconspicuous, but the lateral ridges prolonged into paler brown wings. In transverse section, six vittæ in each mericarp. Odor and taste agreeably aromatic." *Br.* These properties depend on a volatile oil, which is present in the fruits to the extent of 2.8 to 4 per cent. (See *Oleum Anethi.*) The bruised fruits impart their virtues to alcohol and to boiling water.

Uses.—Dill seeds have the properties common to the aromatics, but are very seldom used in this country. They may be given in powder or infusion.

Dose, of the fruit, from fifteen grains to a

drachm (1–3.9 Gm.); of the oil, two or three minims (0.12–0.2 mil).

Off. Prep.—Aqua Anethi, *Br.*

ANISUM. U. S. (Br.)

ANISE Anis. [Aniseed]

(ą-nī'sŭm)

"The dried ripe fruit of *Pimpinella Anisum* Linné (Fam. *Umbelliferæ*) without the presence or admixture of more than 3 per cent. of foreign seeds or other vegetable matter." *U. S.* "Anise Fruit is the dried ripe fruit of Pimpinella Anisum, *Linn.*" *Br.*

Anisi Fructus, *Br.;* Fructus (Semen) Anisi, s. Anisi vulgaris; Aniseed, Anny, Aneys, Annyle; Anis, Anis vert, Grgaines d'Anis, *Fr.;* Fructus Anisi, *P. G.;* Anissame, Anis, *G.;* Anice, Anace, Semi d'Aniso, *It.;* Anis (Fruto de), Simiente de Anis, *Sp.;* Anison, *Ar.*

Pimpinella Anisum is an annual plant, about a foot in height, with an erect, smooth and branching stem. The leaves are petiolate, the lower roundish-cordate, lobed, incised-serrate, the middle pinnate-lobed with cuneate or lanceolate lobes, the upper trifid, or undivided, linear. The flowers are white, and in terminal compound umbels, destitute of involucres.

The anise plant is a native of Egypt and the Levant, but has been introduced into Southern Europe and is cultivated in all warm climates, especially Germany, Russia, Italy, Spain, France, Turkey, India, Japan and Chili. It is also cultivated occasionally in the gardens of this country. The Spanish is smaller than the German or French, and is usually preferred; the Russian fruit is very short. It is said also to be extensively cultivated in India and South America, although we are not aware that the product ever comes into American commerce. It is estimated that over a million pounds of anise are imported annually.

It is one of the oldest aromatics, having been used by the old Egyptians, and is spoken of by Theophrastus and cultivated in the imperial German farms of Charlemagne. In 1305 Edward I granted a patent giving the right to levy tolls upon it at the Bridge of London for the purpose of repairing the bridge.

Anise seeds (botanically, fruit) are officially described as follows: "Cremocarp broadly ovoid or pyriform, laterally compressed, from 3 to 6 mm. in length and from 2 to 3 mm. in breadth; mericarps usually cohering and attached to a slender pedicel from 2 to 12 mm. in length; summit with a ring-like disk and 2 projecting, diverging styles; externally grayish or greenish-gray, seldom grayish-brown, slightly pubescent; each with five light brown filiform ridges and in cross-section with from 15 to 45 vittæ. Odor and taste agreeable and aromatic. Under the microscope transverse sections of Anise show an epidermal layer with numerous papillæ and short, one-celled, non-glandular hairs having very thick papillose walls; primary ribs each with a small fibro-vascular bundle, surrounded by a few sclerenchymatous fibers; vittæ or oil-tubes from 15 to 45 in number, extending as a more or less interrupted circle in the tissues of the mesocarp on the dorsal side of each mericarp; 2 large vittæ on the commissural surface, each separated from the other tissues of the mericarp by a large cavity due to shrinkage of the seed-coat; inner epidermis of pericarp consisting of a layer of narrow, tangentially elongated cells closely united with the 1-layered seed-coat, the inner walls of which are yellowish-brown and considerably thickened; endosperm of polygonal, thick-walled cells filled with spherical or ellipsoidal aleurone grains, each containing a small rosette aggregate of calcium oxalate; the aleurone grains surrounded with an oily protoplasm, the oil of which is liberated upon mounting sections in hydrated chloral T.S., in the form of small globules; epidermal layer near the middle of the commissural surface composed of 2 or 3 rows of cells with thick porous walls, and beneath which occur small groups of thick-walled cells resembling stone cells. The powder is yellowish-brown; consisting of numerous irregular fragments of pericarp showing portions of the yellowish vittæ, fragments with tracheæ and sclerenchymatous fibers of carpophore; cells of endosperm filled with aleurone grains about 0.006 mm. in diameter, each usually enclosing a rosette aggregate crystal of calcium oxalate about 0.002 mm. in diameter; non-glandular hairs 1-celled, from 0.025 to 0.2 mm. in length, either straight or curved and with numerous, slight, centrifugal projections on the outer surface. Heat 1 Gm. of the whole drug or powdered drug with 10 mils of potassium hydroxide T.S.; no mouse-like odor develops (fruits of *Conium maculatum* Linné). Anise yields not more than 9 per cent. of ash." *U. S.*

"Ovoid, somewhat compressed laterally; about five millimetres long and two millimetres broad. Mericarps usually united and attached to the pedicel. Rough from the presence of short, bristly hairs. Greenish-grey or greyish-brown; primary ridges pale, slender and entire. In transverse section, numerous vittæ in each mericarp; commissural surface of the endosperm not deeply grooved. Agreeably aromatic odor; taste aromatic and sweet. Ash not more than 11 per cent." *Br.*

Their odor and taste, which depend upon a peculiar volatile oil existing to the extent of from 1.5 to 3.5 per cent., are imparted sparingly to boiling water, but freely to alcohol. (See *Oleum Anisi.*) The endosperm of the fruit contains a bland fixed oil. By expression, a greenish oil is obtained, which is a mixture of the two. The fruits are sometimes adulterated with fine gravel and small fragments of an argillaceous earth which resembles them in color. This accounts for the fact that the amount of ash may run as high as 30 per cent., greatly exceeding the official requirements. Their aromatic qualities are occasionally impaired by a slight fermentation, which they are apt to undergo in the mass, when collected before maturity. Russian anise is sometimes admixed with as much as 30 per cent. of

coriander. Anise is also contaminated with weed seeds and stems of the anise plant.

The Italian anise not infrequently is admixed with from 2 to 10 per cent. or even 50 per cent. of the fruits of conium. A case of poisoning is on record from the accidental admixture of the fruits of *Conium maculatum,* which latter may be distinguished by their crenate or notched ridges and the absence of oil tubes; by their mericarps being smooth, grooved upon the face, and having crenate or notched ridges with wrinkles between them. The conium fruits are, moreover, broader in proportion to their length, and are generally separated into half fruits (or single mericarps), while those of anise are whole (double mericarps).

Star aniseed, the *Cardamomum Siberiense* or *Annis de Sibérie* of the seventeenth century and the *badiane* of the French writers, is the product of *Illicium verum* Hook. f., Gaertn., and is fully described under the heading *Illicium,* Part II. They contain about 4 per cent. of a volatile oil very closely resembling that of anise. There are no known chemical differences between these oils, although dealers distinguish them by their odor and taste.

Ruschenberger, U. S. N., has shown that oil of anise has a remarkable power of masking the odor of potassium sulphide; a drop of the oil having entirely deprived of offensive odor a drachm of lard with which five grains of the sulphide had been incorporated. (*Am. J. M. S.,* N. S., xlviii, 419.)

Uses.—Anise, a grateful aromatic carminative, may be used in flatulent *colic,* and as a corrigent of griping or unpleasant medicines.

Dose, eight to fifteen grains (0.5–1.0 Gm.); of the oil, which should always be preferred, three to eight minims (0.2–0.5 mil).

Off. Prep.—Aqua Anisi, *U. S.* (from Oil of Anise), *Br.;* Species Laxativæ, *N. F.;* Species Pectorales, *N. F.;* Tinctura Rhei Dulcis, *N. F.*

ANTHEMIDIS FLORES. Br.

CHAMOMILE FLOWERS [Chamomile, English Chamomile, Roman Chamomile]

(ăn'thẹ-mīs flō'rēs)

"Chamomile Flowers are the expanded flower-heads of Anthemis nobilis, *Linn.,* collected from cultivated plants, and dried." *Br.*

Anthemis, *U. S. VIII;* Flores Chamomillæ Romanæ, *P. G.;* Roman, Low, Garden, White or English Chamomile, Chamomile Flowers, Camil, Camovyne, Whig-plant; Camomille Romaine, *Fr.;* Römische Kamille, *G.;* Camomilla Romana, Camomilla Ingleses, *It.;* Manzanilla (Flor de), Manzanilla Romana, *Sp.*

Chamomile flowers were formerly recognized by the U. S. Pharmacopœia. They still receive official recognition in the British, Austrian and Swiss Pharmacopœias.

Several species of anthemis have been employed in medicine. *A. nobilis,* which is the subject of the present article, is by far the most important. *A. Cotula* L., *Dog Fennel,* or *mayweed,* was formerly recognized by the U. S. Pharmacopœia. *A. arvensis* L. (*corn chamomile*), a native of Europe, naturalized in this country, bears flowers which have an acrid bitter taste and possess medicinal properties analogous though much inferior to those of common chamomile. They may be distinguished by their want of odor. *A. tinctoria* L. is occasionally employed as a tonic and vermifuge in Europe. *Matricaria suaveolens* is said to yield the chamomile of the Indian bazaars.

Anthemis nobilis is an herbaceous plant with a perennial root. The stems are from six inches to a foot long, round, slender, downy, trailing, and divided into branches, which turn upward at their extremities. The leaves are bipinnate, the leaflets small, thread-like, somewhat pubescent, acute, and generally divided into three segments. The flowers are solitary, with a yellow convex disk, and white rays. The involucre is of a hemispherical form, and composed of several small imbricated hairy scales. The receptacle is convex, prominent, and furnished with rigid bristle-like paleæ. The ray florets are numerous, narrow and terminated with three small teeth. The whole herb has a peculiar fragrant odor, and a bitter aromatic taste.

This plant is a native of Europe, and grows wild in all the temperate parts of that continent. It is also largely cultivated for medicinal purposes. In France, Germany, and Italy, it is generally known by the name of *Roman chamomile.* By cultivation the yellow disk florets are often converted into the white ray florets. Thus altered, the flowers are said to be *double,* while those which remain unchanged are called *single;* but, as the conversion may be more or less complete, it generally happens that with each of the varieties there are intermingled some flowers of the other kind, or in different stages of the change. The double flowers are generally preferred; though, as the sensible properties are found in the greatest degree in the disk florets, the single flower heads are the more powerful. It is rather, however, in aromatic flavor than in bitterness that the radial florets are surpassed by those of the disk. If not well and quickly dried, the flowers lose their beautiful white color, and are less efficient. The flowers which are largest, most double, and whitest should be preferred. They are thus described: "Flower-heads hemispherical, from about twelve to twenty millimetres in diameter, white or pale buff in color. Involucre composed of several rows of oblong bracts with membranous margins; receptable solid, conical, and densely covered with concave, blunt, narrow, scaly bracts; florets mostly ligulate and white, the ligula possessing four veins and terminating in three teeth. Strong aromatic odor; taste bitter." *Br.*

The seeds yield by expression a fixed oil, which is said to be applied in Europe to various economical uses.

Though not a native of America, chamomile grows wild in some parts of this country, and is occasionally cultivated in our gardens for family use, the whole herb being employed. The

medicine, as found in commerce, consists chiefly of the double flowers, and is imported from Germany and England. From the former country the flowers of *Matricaria Chamomilla* are also occasionally imported, under the name of chamomile. (See *Matricaria.*) In Europe the flowers of *A. arvensis* L., corn chamomile, are sometimes substituted for the official drug. In France corn chamomile flowers are sold in commerce indiscriminately with those of *Anthemis nobilis,* of *Chrysanthemum Parthenium* Bernh. (*Pyrethrum Parthenium* Smith), or of *Anthemis parthenoides* De Cand. (*Matricaria parthenoides* Desf.). (*J. P. C.,* May, 1859, p. 347.) For the peculiar character by which these two flowers may be distinguished from the chamomile, see *Pyrethrum parthenium* in PART II.

Properties.—Chamomile flowers, as usually found in commerce, are large, almost spherical, of a dull white color, a fragrant odor, and a warmish, bitter, aromatic taste. When fresh, their odor is much stronger, and was fancied by the ancients to resemble that of the apple. Hence the name *chamæmelum* (*χαμαί*, on the ground, and *μῆλον*, an apple); and it is somewhat singular that the Spanish name *manzanilla* (a little apple) has a similar derivation. The flowers impart their odor and taste to water and alcohol, the former of which, at the boiling temperature, extracts only one-fourth of their weight. The investigations of several chemists made in 1878–1879, in Fittig's laboratory at Strassburg, have shown the *oil of chamomile* to contain the following constituents: a fraction distilling at 147° to 148° C. (296.6°–298.4° F.) consisting of *isobutylic esters* and hydrocarbons; *isobutyl angelicate* at 177° C. (350.5° F.); *isoamyl angelicate* at 200° to 201° C. (392°–394° F.); *isoamyl tiglinate* at 204° to 205° C. (399°–401° F.) (both of these esters answering to the formula $C_5H_{11},C_5H_7O_2$). In the residual portion, hexylic alcohol, C_6H_{13},OH, and an alcohol of the formula $C_{10}H_{16}O$ isomeric with camphor, to which the name of *anthemol* has been given (see *Chem. Cb.,* 1903 (1), 1226), are met with, both probably occurring in the form of esters. By decomposing the angelicates and the tiglinate with potassium hydroxide, *angelic acid,* $C_5H_8O_2$, and *tiglinic acid* (or *methyl-crotonic*), isomeric with the former, are obtained to the extent of about 30 or more per cent. of the crude oil. In the oil examined by Fittig, angelic acid prevailed; from another specimen E. Schmitt (1879) obtained but very little of it, tiglinic acid prevailing. Naudin (*Bull. Soc. Chim.,* 1884, 41, 483) extracted also a solid paraffin, $C_{18}H_{38}$, to which the name of *anthemene* was given; Klopp obtained another body, *anthesterin,* from chamomile. (*P. J.,* 1903, 458.) Umney states that pure oil of chamomile has the sp. gr. 0.905 to 0.912 at 15° C. (59° F.) (*P. J.,* 1895, p. 949). The oil from *Anthemis Cotula* closely resembles that from *A. nobilis,* see *A. J. P.,* 1885, pp. 376, 381. E. Amerman (*A. J. P.,* 1889, p. 69) obtained a wax which was nearly white, bitter, and crystalline, melting at about 130° C. (266° F.), and a crystalline substance distinctly acid and of a glucosidal nature. There was no evidence of the presence of an alkaloid. (See *Oleum Anthemidis,* Br., and *Extractum Anthemidis,* Br. Pharm., 1898.)

Uses.—Chamomile is a mild tonic, in small doses acceptable and corroborant to the stomach, in large doses capable of acting as an emetic. In cold infusion it is often advantageously used in cases of *enfeebled digestion* in convalescence, of *general debility,* with languid appetite, which often attends convalescence from infectious fevers. The flowers are sometimes applied externally in the form of fomentation, in cases of irritation or inflammation of the abdominal viscera, and as a gentle incitant in flabby, ill-conditioned *ulcers.* The infusion is usually preferred. The decoction or extract cannot exert the full influence of the medicine, as the volatile oil is driven off.

Dose, of the powder as a tonic, from half a drachm to a drachm (2.0–3.9 Gm.) three or four times a day, or more frequently.

ANTIMONII ET POTASSII TARTRAS.
U. S. (Br.)

ANTIMONY AND POTASSIUM TARTRATE Antim. et Pot. Tart. [Tartar Emetic; Tartarated Antimony; Antimonyl Potassium Tartrate, Tartrated Antimony. Potassio tartrate of Antimony, Emetic Tartar]

(ăn'tĭ-mō'nĭ-ī ĕt pŏ-tăs'sĭ-ī tär'trās)

"It contains not less than 98.5 per cent. of $K(SbO)C_4H_4O_6 + \frac{1}{2}H_2O$ (332.34). Preserve it in well-closed containers." *U. S.* "Tartarated Antimony may be obtained by setting aside a mixture of antimonious oxide and acid potassium tartrate, made into a paste with a little water, until combination has taken place, and then purifying by crystallisation from water. Contains not less than 99 per cent. of antimonium potasso-tartrate, $(KSbOC_4H_4O_6)_2,H_2O$." *Br.*

Antimonium Tartaratum, *Br.;* Potassium antimonyl tartrate, Antimonium Tartarizatum, Tartarized Antimony, Tartrated Antimony; Potassio-Tartrate of Antimony, Antimonii Potassio-Tartras, Tartarus Emeticus, Stibio-Kali Tartaricum; Tartrate d'Antimoine et de Potasse, *Fr. Cod.;* Emétique, Tartre stibié, *Fr.;* Tartarus Stibiatus, *P. G.;* Brechweinstein, *G.;* Tartrato di antimonico e di potassio, *It.;* Tartrato antimonico potasico, *Sp.*

A process for Tartar Emetic not now being given in the U. S. Pharmacopœia, that of 1870 follows: "Take of Oxide of Antimony, in very fine powder, *two troyounces;* Bitartrate of Potassium, in very fine powder, *two troyounces and a half;* Distilled Water, *eighteen fluidounces.* To the Water, heated to the boiling point in a glass vessel, add the powders, previously mixed, and boil for an hour; then filter the liquid while hot, and set it aside that crystals may form. Lastly, dry the crystals, and keep them in a well-stoppered bottle. By further evaporation the mother-water may be made to yield more crystals, which should be purified by a second crystallization." *U. S.,* 1870. This compound is a normal tartrate. Tartaric acid is dibasic. In

acid potassium tartrate (cream of tartar) one of the two hydrogen atoms is replaced by potassium, while the other is unreplaced; in neutral potassium tartrate (soluble tartar) both are replaced by potassium; in tartar emetic one is replaced by potassium, while the other is replaced by the group (SbO) antimonyl, which is an univalent group, exactly replacing one hydrogen atom.

In the preparation of tartar emetic the cream of tartar should not be in excess, as in that case it is apt to crystallize, upon cooling, with the tartar emetic. To avoid such a result it is better to have a slight excess of antimonial oxide. The hot filtration, directed in the U. S. Pharmacopœia of 1870, may be conveniently performed by a jacketed funnel filled with hot water. In all cases the salt should be obtained in well-defined crystals, unmixed with those of cream of tartar, as the best index of its purity. The practice of some manufacturing chemists of boiling the filtered liquor to dryness, whereby an impure mass is obtained, consisting in part only of the antimonial salt, is very reprehensible.

It is not easy to decide as to the relative eligibility of the different forms of antimonial oxide used for preparing tartar emetic. The preference, however, was given to the oxychloride (*powder of Algaroth*) by Berzelius; and M. Henry, an eminent pharmaceutist of Paris, after a careful comparison of the different processes, declared also in its favor; his process will be found in detail in the U. S. D., 17th ed., p. 175.

Tartar emetic is not usually prepared by the apothecary, but made on a large scale by the manufacturing chemist. Different processes are pursued in different manufactories; it is not material what plan is adopted, provided the crystals of the antimonial salt be carefully purified. Mohr prefers the use of a moist oxide, prepared by adding gradually an intimate mixture of one part, each, of antimony trisulphide and potassium nitrate to a boiling mixture of one part of sulphuric acid and two of water. The liquid is boiled down nearly to dryness and allowed to cool. The grayish-white mass thus formed is then washed thoroughly with water. The details of this process are given by Soubeiran, by whom it is praised, in the *J. P. C.*, 3e sér., iii, 327. Yuntz (*A. Pharm.*, 1887, p. 641) communicates the following process for *Antimony Tartrate* ($SbO)O_6,C_4H_5$. An excess of antimony oxide is boiled with solution of tartaric acid, the clear solution evaporated to a syrupy consistence, allowed to cool, and the crystalline precipitate which forms washed with alcohol to free it from any excess of tartaric acid.

Properties.—Antimony and potassium tartrate occurs as "colorless, transparent crystals of the rhombic system, or as a white granular powder; without odor, and having a sweet, afterwards disagreeable, metallic taste. The crystals effloresce upon exposure to the air. One Gm. of Antimony and Potassium Tartrate dissolves in 12 mils of water and in 15 mils of glycerin at 25° C. (77° F.); also in 3 mils of boiling water; insoluble in alcohol. Its aqueous solution (1 in 20) is slightly acid to litmus. When heated to redness it chars, emits an odor resembling that of burning sugar, and leaves a blackened residue having an alkaline reaction and imparting a violet color when a small fragment is held in a non-luminous flame. In an aqueous solution of Antimony and Potassium Tartrate (1 in 20), acidulated with hydrochloric acid, hydrogen sulphide T.S. produces an orange-red precipitate, which is soluble in ammonium sulphide T.S. or potassium hydroxide T.S. Ten mils of an aqueous solution of the salt (1 in 100), acidulated with acetic acid, does not at once assume a blue color on the addition of 5 drops of potassium ferrocyanide T.S. (*iron*). Dissolve 0.2 Gm. of Antimony and Potassium Tartrate in 5 mils of hydrochloric acid; the solution does not respond to Bettendorf's Test for arsenic (see Part III, Test No. 2).

"**Assay.**—Dissolve about 0.5 Gm. of Antimony and Potassium Tartrate, accurately weighed, in 30 mils of distilled water, add 25 mils of a cold, saturated solution of sodium bicarbonate and a few drops of starch T.S. and immediately titrate this solution with tenth-normal iodine V.S., to the production of a permanent blue color. It shows not less than 98.5 per cent. of $K(SbO)C_4H_4O_6 + \frac{1}{2}H_2O$.

"Each mil of tenth-normal iodine V.S. used corresponds to 0.016617 Gm. of $K(SbO)C_4H_4O_6 + \frac{1}{2}H_2O$. Each gramme of Antimony and Potassium Tartrate corresponds to not less than 59.3 mils of tenth-normal iodine V.S." *U. S.*

"Soluble in 17 parts of *water*, forming a slightly acid solution; almost insoluble in *alcohol* (90 per cent.), moderately soluble in weak alcoholic liquids. Taste sweet and metallic. Precipitated from its solutions by *solution of tannic acid*. Yields the *reactions* characteristic of antimony, of potassium, and of tartrates. The solution obtained by dissolving 0.5 gramme in 25 millilitres of *water*, and adding 5 grammes of *sodium potassium tartrate* and 1.5 grammes of *sodium bicarbonate*, discharges the color of not less than 29.8 or more than 30.2 millilitres of *N/10 solution of iodine*. Yields no characteristic *reactions* for lead, copper, iron, sodium, ammonium, chlorides, or sulphates. Does not effervesce with an aqueous solution of *sodium bicarbonate* (absence of acid potassium tartrate)." *Br.*

Antimony and potassium tartrate was discovered in 1631 by Adrian de Mynsicht. When prepared from the oxychloride it crystallizes in tetrahedrons. As it occurs in commerce, it is often in the form of a white powder, resulting from the pulverization of the crystals. It is insoluble in alcohol, but dissolves in proof spirit or wine. (See *Vinum Antimonii.*) Its aqueous solution slightly reddens litmus, and undergoes decomposition by keeping. If one-fifth of its bulk of alcohol be added, to the water, this decomposition is prevented. It is incompatible with acids, alkalies and their carbonates, some of

the earths and metals, calcium chloride, and lead acetate and subacetate. It is incompatible also with astringent infusions and decoctions, as of rhubarb, cinchona, catechu, galls, etc.; but these substances, unless galls be an exception, do not render it inert, though they lessen its activity to a greater or less extent.

Tartar emetic, when pure, exhibits its appropriate crystalline form. A crystal or two, dropped into a solution of hydrogen sulphide, will be covered with an orange-colored deposit of antimony trisulphide. Entire solubility in water is not a character belonging exclusively to the pure salt, for, according to Hennell, tartar emetic may contain 10 per cent. of uncombined cream of tartar and yet be wholly soluble in the proper proportion of water. Hennell's method of detecting uncombined bitartrate is to add a few drops of a solution of sodium carbonate to a boiling solution of the antimonial salt. If the precipitate formed be not redissolved, no bitartrate is present.

The impurities found in tartar emetic are uncombined cream of tartar from faulty preparation or fraudulent admixture, calcium tartrate, iron, sulphates, and chlorides. The mode of detecting cream of tartar has been indicated above. Calcium tartrate is derived from the cream of tartar, which often contains this impurity. It is apt to form on the surface of the crystals of tartar emetic in crystalline tufts, which are easily brushed off. Iron is sometimes present, especially when the antimonial salt has been prepared from glass of antimony. It is detected by a blue color being *immediately* produced by potassium ferrocyanide, added after a little acetic acid. If the blue color be *slowly* produced, it may arise from reactions on the iron of the ferrocyanide itself. If much iron be present the solution of the tartar emetic will be yellow instead of colorless. According to Sérullas, tartar emetic, except when well crystallized, and all the other antimonial preparations usually contain a minute proportion of arsenic, derived from the native antimony trisulphide, which almost always contains this dangerous metal. Subsequently, however, Thos. Williams (*P. J.*, July, 1874, p. 63) examined a number of samples of various antimonial preparations and found them remarkably free from arsenic. The U. S. test rigidly restricts the amount of arsenic which may be present in the official salt. Tartar emetic loses water of crystallization on exposure to dry air and is sometimes two per cent. stronger than the official product on this account.

It has been already stated in general terms that tartar emetic in solution is incompatible with acids and alkalies, and with some of the earths; but this salt is so important that some details in regard to the effects of particular reagents, included under these titles, seem to be necessary. Hydrochloric and sulphuric acids, added to a solution of the antimonial salt, not too dilute, throw down a white precipitate of antimony trichloride or subsulphate, mixed with cream of tartar, which is redissolved by an excess of the precipitant. Nitric acid throws down a subnitrate, which is taken up by an excess of acid. When solution of potassium hydroxide is added to a concentrated solution, it produces at first no effect, and then a precipitate of trioxide, which is redissolved on the continued addition of the alkali. Lime water acts in a weaker solution, and throws down a white precipitate, consisting of the mixed calcium and antimony tartrates. Potassium carbonate affects still weaker solutions, throwing down a white precipitate of trioxide; but this test does not act in solutions containing less than a quarter of a grain to the fluidounce. Ammonia, both pure and carbonated, precipitates a solution of tartar emetic, throwing down the pure trioxide. To these reagents may be added infusion of galls, which, when fresh and strong, causes a dirty-yellowish-white precipitate of antimony tannate.

Uses.—When tartar emetic is given in minute doses (gr. $\frac{1}{12}$, or 0.005 Gm.) to a healthy man it produces only a slight lessening of the force of the pulse and a tendency to increased secretion from the skin. After somewhat larger amounts these symptoms are more pronounced, and have nausea added to them. If a grain be ingested, the nausea and vomiting will be severe and persistent, and accompanied by severe purging and marked prostration, both of the circulation and of the muscular strength. In the lower animals antimony causes symptoms similar to those which it produces in man. It has been experimentally proved that the fall of the arterial pressure is produced, at least in part, by a direct action upon the heart. The loss of muscular power, of reflex activity, and of sensibility is believed to be due to depression of the spinal centers, and the disturbance of respiration to a direct influence upon the nerve-centers which preside over that function. The purging and vomiting are connected with an effort at elimination, the poison escaping through the gastro-intestinal mucous membrane, as well as through the kidneys. After death from antimony, fatty degeneration of the liver, kidneys, and other organs has been found, indicating that the poison has a powerful influence upon nutrition. It is evident that in small doses tartar emetic is powerfully depressant to the circulation and stimulant to the secretion of the skin.

At one time tartar emetic was very largely used in medicine; at present it is employed almost solely as a diaphoretic and expectorant, having been supplanted by other less dangerous remedies as a circulatory depressant. In the first stage of a *bronchitis* in a sthenic subject it is often of great service. Its emetic action is very certain, powerful, prolonged, but accompanied with much depression. It is very badly borne by children. Tartar emetic is occasionally used as a counter-irritant in the form of an ointment or plaster, whose application produces sooner or later a burning sensation accompanied by a very painful pustular eruption with ulcerations.

The salts of antimony are highly poisonous to certain pathogenic parasites, especially the trypanosome of *sleeping sickness,* and apparent cures have been reported not only in the lower animals but also human beings. Various salts of the metal, both organic and inorganic, have been employed in this condition. Which preparation will prove the most useful and what channel of exhibition is the best, remains to be determined by future trials. Castellani (*Pediatria,* 1915, xxiii) says tartar emetic acts as a specific in *kala-azar.* Klemperer (*D. M. W.,* 1911) also reports favorable results from the use of tartar emetic in *pernicious anemia.* He gave hypodermically one sixty-fourth of a grain (1 mgm.) daily. The drug has also been employed in veterinary medicine as a vermifuge.

Poisoning.—Symptoms of acute poisoning by the drug are an austere metallic taste, excessive nausea, copious vomiting, frequent hiccough, burning pain in the stomach, colic, frequent stools and tenesmus, fainting, rapid and feeble pulse, coldness of the skin, and even of the internal organs, difficult and irregular respiration, cutaneous anesthesia, convulsive movements, painful cramps in the legs, prostration, and death. Ten grains (0.65 Gm.) is the smallest dose reported to have proved fatal. In rare cases vomiting and purging do not take place, and when they are absent, the other symptoms are aggravated. Sometimes a pustular eruption is produced, like that caused by the external application of the antimonial.

When given in repeated small doses, tartar emetic produces both in man and in the lower animals a chronic poisoning, in which the chief symptoms are nausea, vomiting, watery purging, often followed by constipation, failing circulation, and a general asthenia, deepening into death from exhaustion. After death from antimonial preparations, decided evidences of gastro-intestinal irritation are apt to be present, but they have been in some cases wanting. The blood is often markedly fluid. Intense venous congestion, especially of the lungs, is usually present, and in some cases pulmonary apoplexy, atelectasis, or other structural lesion of the lungs has been found. A wide-spread fatty dégeneration has been noted as constant in chronic poisoning in animals, and probably occurs also in man.

The treatment of tartar emetic poisoning consists, first, in washing out the stomach with a solution of tannic acid; second, in meeting the symptoms as they arise, especially by the use of opiates, which should be administered hypodermically and by rectal suppositories; external warmth, stimulants, etc., should be used *pro re nata.* Rosenthal and Severn (*A. E. P. P.,* 1912, lxvii, p. 275) assert that potassium hexatantalate is a valuable antidote in poisoning by antimony, being capable of following the drug after its absorption and producing a non-toxic compound in the system. In all cases of suspected poisoning, the vomit, the passages from the bowels, and especially the urine should be saved. The metal has been found in all the tissues of the body, but in the experiments of B. W. Richardson it was most abundant in the liver.

Dose, as a diaphoretic or expectorant, one-twentieth to one-sixth of a grain (0.003–0.01 Gm.); as an emetic, half a grain (0.032 Gm.).

Off. Prep.—Mistura Glycyrrhizæ Composita, *U. S.;* Pilulæ ad Prandium (Cole's), *N. F.;* Syrupus Scillæ Compositus, *U. S.;* Vinum Antimonii, *N. F.* (*Br.*).

ANTIMONII OXIDUM. Br.

ANTIMONIOUS OXIDE [Antimony Trioxide]

(ăn-tĭ-mō′nĭ-ī ŏx′ĭ-dŭm)

"Antimonious Oxide, Sb_2O_3, may be obtained by pouring solution of antimonious chloride into water, and decomposing the precipitated antimony oxychloride with sodium carbonate." *Br.* "It contains not less than 97 per cent. of antimonous oxide [$Sb_2O_3 = 288.4$]." *N. F. IV.*

Antimonious Oxide, Oxide of Antimony; Stibium Oxydatum, Oxydum Antimonicum s. Stibicum; Oxyde d'Antimoine, *Fr.;* Antimonoxyd, *G.;* Oxido de antimonio, *Sp.*

This compound is no longer official in the U. S. Pharmacopœia, but has been introduced into the N. F. IV. The process of the U. S. P., 1870, was as follows: "Take of Sulphuret of Antimony, in very fine powder, *four troyounces;* Muriatic Acid *eighteen troyounces;* Nitric Acid, *a troyounce and one hundred and twenty grains;* Water of Ammonia, *a fluidounce and a half;* Water, Distilled Water, each, *a sufficient quantity.* Introduce the Sulphuret into a flask, of the capacity of two pints, and, having added the Muriatic Acid, digest, by means of a sand-bath, until effervescence ceases. Then, having removed the flask from the sand-bath, add the Nitric Acid gradually; and, when nitrous acid vapors cease to be given off, and the liquid has grown cold, add to it half a pint of Water, and filter. Pour the filtered liquid gradually into twelve pints of Water, constantly stirring, and allow the precipitate to subside. Decant the supernatant liquid, and wash the precipitate twice by decantation, using, each time, eight pints of Water. Then transfer it to a muslin filter to drain, and, after the draining is completed, wash it with Water until the washings cease to have an acid reaction. Next introduce it into a suitable vessel, and subject it to the action of the Water of Ammonia for two hours; at the end of which time transfer it to a moistened muslin filter, and wash it with Distilled Water as long as the washings produce a precipitate with nitrate of silver. Lastly, dry the precipitate upon bibulous paper with the aid of a gentle heat." *U. S.,* 1870.

When antimony trisulphide is digested with hydrochloric acid, a chemical reaction takes place as follows:

$$Sb_2S_3 + 6HCl = 2SbCl_3 + 3H_2S$$

the hydrogen of the acid uniting with the sul-

phur of the antimonia., and escaping as hydrogen sulphide, while the chlorine and antimony combine to form antimony trichloride, which is held in solution. The effect of the nitric acid is supposed to be to render the oxide whiter, by decomposing any remaining hydrogen sulphide, and thus preventing it from contaminating the product. Though the result thus far is an aqueous solution of the trichloride, this cannot be diluted beyond a certain degree without decomposition. Hence, if largely diluted, as when poured into an excess of water, decomposition takes place, and a white powder is precipitated, formerly called *powder of Algaroth,* which is mainly an oxychloride. The decomposition of the powder, however, is not uniform, as it contains more trioxide the greater the proportion of water used in the decomposition. The pure oxychloride, SbOCl, is formed when the proportion of 4 molecules of water to 1 molecule of antimony chloride exists, but with a relatively larger proportion of water the average composition of the powder is $Sb_4O_5Cl_2$, which may be considered as made up of $(SbOCl)_2 + Sb_2O_3$. The oxychloride is first washed with abundance of water to separate adhering hydrochloric acid, and then acted upon by an alkaline solution (ammonia or sodium carbonate) to decompose the oxychloride, with the effect of adding to the amount of teroxide; after which the teroxide requires only to be washed with water in order to render it pure. The last washing separates the ammonium or sodium chloride resulting from the decomposition of the oxychloride; and the water of this washing is tested by silver nitrate, until the presence of chlorine ceases to be indicated.

Properties.—Antimony trioxide is a heavy, grayish-white powder, permanent in the air, almost insoluble in water, insoluble in alcohol and nitric acid, readily soluble in hydrochloric or tartaric acid, or in boiling solution of potassium bitartrate. Heated in close vessels it becomes yellow, fuses at a full red heat, and finally sublimes in crystalline needles. When cooled from a state of fusion, it forms a fibrous crystalline mass, of pearl color. Heated in open vessels it suddenly becomes red hot, and, by the absorption of oxygen, changes into Sb_2O_4 (antimony antimonate), which differs from the trioxide in being insoluble in hydrochloric acid, less fusible, and not volatile.

"A greyish-white powder, fusible at a low red heat. Insoluble in *water.* Readily soluble in *hydrochloric* acid, the solution yielding the *reactions* characteristic of antimony. The solution obtained by dissolving 0.25 gramme in *diluted hydrochloric acid,* adding 5 grammes of *sodium potassium tartrate* and then a slight excess of *sodium bicarbonate,* discharges the color of 34.5 millilitres of *N/10 solution of iodine.* Yields no characteristic *reactions* for lead, copper, arsenium, calcium, sodium, or potassium, not more than slight *reactions* for iron, and not more than the slightest *reactions* for chlorides or sulphates. Dissolves entirely when boiled with an excess of an aqueous solution of *acid potassium tartrate.*" *Br.*

The National Formulary description is as follows: "Antimony Oxide is a white or grayish-white powder, odorless and tasteless. It is insoluble in water, alcohol or nitric acid; readily dissolved by hydrochloric acid without effervescence, and also by a warm aqueous solution of tartaric acid or by a boiling aqueous solution of potassium bitartrate. When heated Antimony Oxide turns yellow, but it again becomes white on cooling. At a dull red heat it fuses to a yellowish liquid and at a higher temperature it volatilizes. Dissolve Antimony Oxide in a slight excess of hydrochloric acid and dilute the solution with a large volume of distilled water; a white precipitate is produced which is changed to orange by hydrogen sulphide. A solution of 0.1 Gm. of the Oxide in 3 mils of hydrochloric acid and 5 mils of distilled water is not rendered turbid at once by a few drops of barium chloride T.S. (*sulphate*). A solution of 0.1 Gm. of the Oxide in 10 mils of distilled water and 1 Gm. of tartaric acid does not become more than slightly opalescent on the addition of 0.2 mil of nitric acid and 0.2 mil of silver nitrate T.S. (*chloride*). Dissolve 0.5 Gm. of the Oxide in 10 mils of hydrochloric acid, dilute the solution with distilled water until it begins to become permanently turbid and then precipitate with hydrogen sulphide. This precipitate when thoroughly washed with distilled water dissolves in ammonium sulphide T.S. or sodium sulphide T.S., without leaving a black insoluble residue (*copper or lead*). A solution of 0.1 Gm. of Antimony Oxide in 5 mils of hydrochloric acid does not respond to Bettendorf's Test for arsenic (see Part III).

"**Assay.**—Dissolve about 0.2 Gm. of Antimony Oxide, accurately weighed, by warming it in a solution of 1 Gm. of tartaric acid in 10 mils of distilled water (adding a few drops of hydrochloric acid to aid the solution). Nearly neutralize the solution with sodium carbonate, then add 40 mils of a cold saturated solution of sodium bicarbonate and titrate at once with tenth-normal iodine V.S., using starch T.S. as indicator. It shows not less than 97 per cent. of Sb_2O_3.

"Each mil of tenth-normal iodine V.S. corresponds to 0.00721 Gm. of Sb_2O_3. One gramme of Antimony Oxide corresponds to not less than 134.5 mils of tenth-normal iodine V.S." *N. F.*

It is frequently impure from the presence of the before-mentioned antimony antimonate, in which case it is not *entirely* soluble in hydrochloric acid. If it contain oxychloride, which it is apt to do from the imperfect action of the alkaline solutions employed in its purification, its solution in tartaric acid will be precipitated by silver nitrate. When antimony antimonate is substituted for it, the fraud may be detected by the spurious preparation being entirely insoluble in hydrochloric acid.

Uses.—This oxide, which must not be confounded with the powder of Algaroth, has the

general therapeutic properties of the antimonials. Like antimonial powder, it is not uniform in its effects, and ought not to be used in practical medicine. The inequality of action is plausibly explained by the state of the stomach as to acidity, the presence of acids giving the medicine activity, and this explanation is confirmed by the experiments of Osburn, of Dublin. As to the French Codex oxide, prepared by boiling the oxychloride with a solution of potassium bicarbonate, the inequality is attributed by Durand, of Caen, to the presence of more or less trichloride, which is separated with difficulty. Objecting to the Codex oxide, Durand proposes to prepare the trioxide by precipitating tartar emetic with ammonia in excess. Thus obtain it contains no trichloride, and does not cause vomiting. (*J. P. C.*, 3e sér., ii, 364.) It was introduced into the British Pharmacopœia as an ingredient in *Pulvis Antimonialis*.

Dose, of antimony trioxide, three grains (0.20 Gm.) every two or three hours, but the drug should not be employed as a medicine.

Off. Prep.—Pulvis Antimonialis, *Br., N. F.*

ANTIMONIUM

ANTIMONY

(ăn'tĭ-mō'nĭ-ŭm)

Stibium, *Lat.*; **Antimoine**, *Fr.*; **Antimon, Spiessglanz Metall**, *G.*; **Antimonia**, *It.*; **Antimonio**, *Sp.*

Metallic antimony, sometimes called *regulus of antimony*, is not official in the British or United States Pharmacopœia, but, as it enters into the composition of a number of important pharmaceutical preparations, we have thought it proper to notice it under a distinct head

Antimony exists in nature: (1) uncombined; (2) as an oxide; (3) as antimonous sulphide (tersulphide), and (4) as an oxysulphide. It is found in France, Japan, and Hungary, but most largely in China which it is stated yields 85 per cent. of the world's production, and has been discovered also in Ontario, Alaska, and in smaller amounts in California and Nevada.

Extraction.—Much of the antimony of commerce is extracted from the native sulphide. The ore is first separated from its gangue by fusion. It is then reduced to powder, and placed on the floor of a reverberatory furnace, where it is subjected to a gentle heat, being constantly stirred with an iron rake. This process of roasting is known to be completed when the matter is brought to the state of a dull, grayish-white powder called *antimony ash*. By this treatment the antimony is partly trioxidized, and partly converted into antimonous acid, while nearly all the sulphur is dissipated in the form of sulphurous acid gas; a portion of trisulphide, however, remains undecomposed. The matter is then mixed with charcoal impregnated with a concentrated solution of sodium carbonate, and the mixture heated in crucibles, in a melting-furnace. The charcoal reduces the antimony trioxide, while the alkali unites with the undecomposed trisulphide, and forms melted scoriæ, which cover the reduced metal and diminish its loss from volatilization. Antimony is also frequently obtained by the reduction by iron of the native sulphide. The reduction of the antimony sulphide by iron takes place at a red heat, but as iron sulphide needs a higher temperature for its fusion, and its specific gravity is not much less than that of the metallic antimony, the mass must be heated to a white heat to effect a perfect separation, and this occasions a loss of antimony. In order to avoid this, sodium sulphide is added in practice, which unites with the iron sulphide to form a more fusible and lighter slag of double sodium and iron sulphide. For 100 parts of antimony sulphide are taken 42 parts of iron, 10 parts of anhydrous sodium sulphate, and 2½ to 3½ parts of carbon.

The purest commercial antimony is not entirely free from foreign metals, chiefly iron, lead, and arsenic. Lefort purifies it for the purposes of pharmacy by gradually adding twenty-five parts of the metal, in fine powder, to fifty parts of nitric acid, by the action of which the antimony is precipitated as antimonous acid, while the foreign metals remain in solution. The precipitate is then thoroughly washed with water containing a hundredth part of nitric acid, drained completely, mixed with three or four parts of powdered sugar, and reduced to the metallic state by being heated to redness in a Hessian crucible. Antimony is imported into the United States in the form of antimony sulphide, as antimony regulus or metal, and most largely as "*hard lead*" or *antimonial lead* obtained as a by-product in smelting lead or silver ores which contain from 3 to 10 per cent. of antimony. The production of metallic antimony in the United States in 1915, was 3,288 tons, while the importations for the same year amounted to 8,742 tons of metallic antimony and 1,682 tons in ore.

Properties.—The time of the discovery of antimony is not known, but Basil Valentine was the first to describe the method of obtaining it, in his work entitled "*Currus Triumphalis Antimonii*," published towards the end of the fifteenth century. It is a brittle, brilliant metal, ordinarily of a lamellated texture, of a silver-white color when pure, but bluish white as it occurs in commerce. Its atomic weight is 120.2, symbol Sb, sp. gr. 6.7, and fusing point 630° C. (1166° F.). On cooling, after fusion, antimony assumes an appearance on the surface bearing some resemblance to a fern leaf. When strongly heated, it burns with the emission of white vapors, consisting of teroxide, formerly called *argentine flowers of antimony*. A small portion being fused and then thrown upon a flat surface divides into numerous globules, which burn rapidly as they move along. It forms three combinations with oxygen, *antimony trioxide* (antimonous oxide), Sb_2O_3, *antimony tetroxide*, Sb_2O_4 (by some considered to be an antimonate of the radical *antimonyl*, SbO.SbO$_3$), and *antimony pentoxide* (antimonic oxide), Sb_2O_5. The

first of these unites with water to form antimonous acid, the salts of which are called *antimonites,* the third unites with water to form antimonic acid, the salts of which are called *antimonates.* The trioxide was noticed under the head of *Antimonii Oxidum.* The tetroxide is a white powder, yellowish when hot, and difficultly soluble in acids. It forms when either of the other two oxides is strongly heated in air. *Antimony ash,* described above, is also an impure tetroxide. *Antimonic acid* is a lemon-colored powder, which may be prepared by oxidizing the metal by digestion in nitric acid, and then driving off the excess of the acid by a heat not exceeding 315.5° C. (600° F.). When exposed to a red heat, it parts with oxygen, and is converted into the *antimony tetroxide* just described. This, though medicinally inert, frequently forms a large proportion of the preparation called antimonial powder. (See *Pulvis Antimonialis.*)

The activity of antimonials is proportional not merely to their solubility in the gastric juices but, according to the researches of Brunner (*A. E. P. P.,* 1912, lxviii, p. 186), especially depends upon whether the metal is in the trivalent or pentavalent condition, the latter being comparatively innocuous.

ANTIMONIUM SULPHURATUM. Br.

SULPHURATED ANTIMONY [Kermes Mineral]

(ăn'tĭ-mō'nĭ-ŭm sŭl-phū-rā'tŭm)

"Sulphurated Antimony is a mixture containing antimony sulphides and oxides, and sulphur." *Br.* "Chiefly antimony trisulphide [$Sb_2S_3 = 336.6$] with small quantities of antimony trioxide, sodium pyroantimonate, and free sulphur. It contains not less than 45 per cent. of antimony (Sb). Preserve it in well-closed containers, protected from light." *N. F. IV.*

Antimonium Oxysulphuratum, Antimonii Oxysulphuretum, *Lond.;* Antimonii Sulphuretum Aureum, *Ed.;* Precipitated Sulphide of Antimony; Sulphur Stibiatum Aurantiacum, Sulphur Auratum Antimonii; Golden Sulphuret of Antimony, Golden Sulphur; Soufre doré d'Antimoine, *Fr. Cod.;* Stibium Sulfuratum Aurantiacum, *P. G.;* Goldschwefel, Gefälltes Schwefelantimon, *G.;* Kermes minerale, *It.;* Quermes mineral, Oxisulfuro de antimonio hidratado, *Sp.*

Sulphurated antimony was not introduced into the U. S. P. VIII or IX, but is official in the N. F. IV; the U. S. Pharmacopœia of 1890 added the synonym "Kermes mineral" to this preparation, intending that it should be used when "Kermes" was ordered in prescriptions.

The process of the British Pharmacopœia (1914) is as follows: "Antimonious sulphide ('black antimony') of commerce, 200 grammes; Sublimed Sulphur, 200 grammes; Caustic soda of commerce, 100 grammes; Diluted Sulphuric Acid, Distilled Water, of each a sufficient quantity. Dissolve the caustic soda in two thousand millilitres of the Distilled Water; with this solution mix the antimonious sulphide and the Sublimed Sulphur; boil for two hours with frequent stirring, adding Distilled Water occasionally to maintain the same volume; then, while the mixture is still hot, add three thousand six hundred millilitres of boiling Distilled Water; strain the product through calico; before the strained liquid cools add to it by degrees Diluted Sulphuric acid till the latter is in slight excess; collect the precipitate on a calico filter; wash with Distilled Water till the washings are free from sulphates; dry at a temperature not exceeding 100° C. (212° F.)." *Br.*

There are three preparations containing antimony and sulphur,—viz., the *amorphous precipitated antimony sulphide,* Sb_2S_3, which while orange-red in color corresponds to the black native sulphide; a reddish-brown mixture known as "*Kermes mineral,*" which contains both antimony sulphide and oxide, and has an average composition $2Sb_2S_3 + Sb_2O_3$; and the *golden sulphide,* which is antimonic sulphide, Sb_2S_5, and is obtained by decomposing sulphantimonates like *Schlippe's salt,* $SbS_4Na_3 + 9H_2O$, by the addition of a strong mineral acid.

The first of these may be obtained by dissolving the powdered native sulphide in potassium hydroxide solution with the aid of heat, and then adding to this solution, which contains the antimony combined as potassium antimonite and sulphantimonite, sulphuric acid, when a reddish precipitate is formed which dries to a reddish-brown powder.

The second may be obtained by boiling the native sulphide or the red amorphous sulphide just described with sodium carbonate, and then allowing the compound to settle out from the hot filtered liquid as it cools.

The third may be obtained by first forming a sulphantimonate by boiling finely-powdered antimony sulphide and sodium hydroxide with sulphur (or sodium carbonate and chalk instead of the sodium hydroxide), and then adding the solution of this to diluted hydrochloric or sulphuric acid, when yellow Sb_2S_5 separates, according to the reaction:

$$2(SbS_4Na_3 + 9H_2O) + 3H_2SO_4 = 3Na_2SO_4 + Sb_2S_5 + 3H_2S + 18H_2O$$

Ten parts of Schlippe's salt yield in theory 4.17 parts of antimony pentalsulphide. The U. S. 1890 sulphurated antimony belonged to the first kind above mentioned, the British (1898) to the third variety. E. G. Eberhardt recommends the more direct preparation of sulphurated antimony by treating the native sulphide with hydrochloric acid and precipitating the solution with hydrogen sulphide. The objection that arsenic might be found in the product was met by an examination which showed that traces of arsenic present were not more than when the then official process had been employed. (*A. J. P.,* 1886, p. 229.) The color of sulphurated antimony or Kermes mineral is influenced by porphyrization, with the admixture of a little sugar or gum; if hastily porphyrized, the mixture has a violet tint; if carefully and slowly, it has a russet color.

Properties.—"An orange-red powder, readily dissolved by hot *hydrochloric acid* with evolution of hydrogen sulphide and separation of sulphur. 1 gramme digested with 20 millilitres of hot *water* yields a filtrate which, after acidification with *diluted nitric acid,* becomes not more than slightly cloudy on the addition of *solution of barium chloride* (limit of sulphates). *Arsenic limit* 1000 parts per million. 3 grammes moistened with *diluted nitric acid,* warmed with successive portions of *fuming nitric acid* until red fumes cease to be evolved, and then dried and carefully heated to redness, leave a whitish residue weighing not less than 1.6 or more than 1.8 grammes." *Br.*

The N. F. description and tests are as follows: "It occurs as a red-brown powder, becoming lighter in color on exposure to light; odorless and tasteless. Insoluble in water and in alcohol. One gramme of Sulphurated Antimony, warmed, with 10 mils of hydrochloric acid dissolves with the evolution of hydrogen sulphide, leaving a small amount of residue composed chiefly of sulphur. Its hydrochloric acid solution, after the removal of the hydrogen sulphide by boiling, yields a white precipitate when greatly diluted with water; the liquid separated from this precipitate yields an orange-red precipitate with hydrogen sulphide. Shake about 1 Gm. of Sulphurated Antimony with 20 mils of distilled water and filter. The filtered liquid is neutral to litmus and a portion of it remains clear upon the addition of ammonium oxalate T.S. (*calcium*); another portion does not become more than slightly turbid upon the addition of barium chloride T.S. (*sulphate*). Boil 1 Gm. of Sulphurated Antimony with 100 mils of distilled water until the volume is reduced to about 10 mils, filter it and thoroughly wash the residue on the filter with distilled water. The combined filtrate and washings, after evaporation to about 1 mil, does not respond to Bettendorf's Test for arsenic (see *U. S. P.*, Test No. 2, Part III). Mix about 1 Gm. of Sulphurated Antimony, accurately weighed, with 20 mils of hydrochloric acid and then add 5 Gm. of tartaric acid dissolved in 20 mils of distilled water. Heat the mixture on a water bath until the vapors evolved no longer blacken lead acetate test paper, then filter, wash the residue on the filter until the washings are neutral to litmus and dry it at 100° C. (212° F.). The weight of this residue does not exceed 4 per cent. of the weight of Sulphurated Antimony taken, and it should burn with the odor of sulphur dioxide, leaving an ash not exceeding 0.2 per cent. of the Sulphurated Antimony taken.

"**Assay.**—Dilute the combined filtrate and washings from the preceding test to 200 mils. Neutralize 50 mils of this solution with sodium carbonate, add 25 mils of a cold saturated aqueous solution of sodium bicarbonate and at once titrate with tenth-normal iodine V.S., using starch T.S. as indicator. It shows not less than 45 per cent. of antimony.

"Each mil of tenth-normal iodine V.S. corresponds to 0.00601 Gm. of antimony (Sb). Each gramme of Sulphurated Antimony requires not less than 74.9 mils of tenth-normal iodine V.S." *N. F.*

Water in which this preparation has been boiled should not yield a white precipitate with ammonium oxalate. The non-action of this test shows the absence of lime. When pure, precipitated antimony sulphide is completely soluble in a hot solution of potassium hydroxide; but, as it is found in commerce, a white substance is usually left undissolved.

John Moss asserted before the London Pharmaceutical Society that the British process always yields a dark reddish or reddish-brown powder, but that the Kermes mineral in English commerce is golden yellow or yellowish-red, and must be prepared by some other method. He was confirmed by Redwood and Attfield, the latter explaining that the official Kermes contains antimony trisulphide, the commercial antimony pentasulphide.

Uses.—Precipitated antimony sulphide (*sulphurated antimony*) is alterative, diaphoretic, and emetic. It is, however, an uncertain medicine, and is very little used. In combination with calomel and guaiac (*Plummer's pill*), it was formerly employed in *secondary syphilis* and *cutaneous eruptions.* (See *Pilulæ Antimonii Compositæ,* U. S. P. 1890.) During its use the patient should abstain from acidulous drinks.

Golden sulphide acts like Kermes mineral, but is much weaker, and must be given in a larger dose.

Dose, as an alterative, from one to two grains (0.065–0.13 Gm.), given twice a day, in the form of a pill; as an emetic, from five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Pilula Hydrargyri Subchloridi Composita, *Br.;* Pilulæ Antimonii Compositæ, *N. F.*

ANTIPYRINA. U. S. (Br.)

ANTIPYRINE Antipyr. [Phenazone]

(ăn-tĭ-pȳ-rī'nȧ)

"Phenyldimethylpyrazolon [$C_{11}H_{12}ON_2$ or $C_3HON_2(CH_3)_2.C_6H_5 = 188.12$]. Preserve it in well-closed containers." *U. S.* "Phenazone, or phenyl - dimethyl - iso - pyrazolone, $C_{11}H_{12}N_2O$, may be obtained from phenyl-hydrazine by interaction with aceto-acetic ether, and the subsequent interaction of the resulting phenyl-methyl-iso-pyrazolone with methyl iodide." *Br.*

Phenazonum, *Br.;* Phenazone; Phenyldimethylisopyrazolone, Methozine, Dehydrodimethylphenylpyrazine; Analgésine, *Fr. Cod.;* Antipyrine, Parodyne, Anodynine, *Fr.;* Pyrazolonum phenyldimethylicum, *P. G.;* Phenyldimethylpyrazolon, Antipyrin, *G.;* Antipirina, *It., Sp.*

Antipyrine was made official for the first time in the U. S. P. VIII, the patent having expired. It was retained in the U. S. P. IX. The British Pharm. (Additions 1885) introduced it under the specially coined word "Phenazone," by which name it was introduced in the Br. Pharm. 1898 and 1914.

Preparation.—This compound is one of the first important synthetical remedies introduced into medicine; it is now generally conceded to be a derivative of pyrrol, C_4H_5N, a base found in coal tar and in bone oil. From this base, $\begin{matrix}HC=CH\\|\\HC=CH\end{matrix}>NH$, pyrazole, $\begin{matrix}HC=N\\|\\HC=CH\end{matrix}>NH$, is derived (see Part II); from this pyrazolon, $\begin{matrix}HC=N\\|\\H_2C-CO\end{matrix}>NH$, which by molecular rearrangement yields isopyrazolon, $\begin{matrix}CH-NH\\||\\CH-CO\end{matrix}>NH$. Phenyldimethylisopyrazolon, $\begin{matrix}(CH_3)C-N(CH_3)\\||\\HC-CO\end{matrix}>N(C_6H_5)$, is a substitution product from this. Practically it is made by Knorr's patented process of acting upon phenylhydrazine, $C_6H_5-HN-NH_2$, with ethyl acetoacetate, $(CH_3.CO)CH_2.CO.C_2H_5$, when phenyl-methyl-pyrazolon, $\begin{matrix}(CH_3)C=N\\|\\H_2C-CO\end{matrix}>N(C_6H_5)$, is formed. This is then methylated by treatment with methyl iodide, when the hydriodide of the finished base results. Another reaction's product—viz., that of halogen butyrate acting upon phenyl-hydrazine with the subsequent oxidation and methylation of the compound so obtained, which is also a phenyldimethylpyrazolon—it is only an isomer of true antipyrine; not identical with it.

Properties.—It is officially described as "a white, almost odorless, crystalline powder or in tabular crystals, with a slightly bitter taste. One Gm. of Antipyrine dissolves in less than 1 mil of water, in 1.3 mils of alcohol, 1 mil of chloroform, and in 43 mils of ether, at 25° C. (77° F.). Its aqueous solution (1 in 20) is neutral to litmus. It melts between 111° and 113° C. (231.8° and 235.4° F.). The addition of tannic acid T.S. to an aqueous solution of Antipyrine produces an abundant white precipitate. Mix 0.1 Gm. of sodium nitrite and 12 mils of an aqueous solution of Antipyrine (1 in 100); a nearly colorless liquid is obtained, which, upon the addition of 1 mil of diluted sulphuric acid, develops a deep green color due to the formation of isonitroso-antipyrine. One drop of ferric chloride T.S. added to 2 mils of a dilute aqueous solution of Antipyrine (1 in 1000) produces a deep red color, which, upon the addition of 10 drops of sulphuric acid, is changed to light yellow. Incinerate about 1 Gm. of Antipyrine; not more than 0.1 per cent. of ash remains. Antipyrine is completely soluble in 1 part of cold distilled water, the solution being colorless or at most slightly yellow when viewed crosswise in a test tube of about 20 mm. in diameter. An aqueous solution of Antipyrine does not respond to the Test for heavy metals (see Part III, Test No. 3)." *U. S.*

It is described in the British Pharmacopœia as "small colorless, scaly crystals. No odor; taste bitter. Soluble in 1.2 parts of *water,* in 1.3 parts of *alcohol* (90 per cent.), and in 1.3 parts of *chloroform.* Melting point from 111° to 113° C. (231.8–235.4° F.). Aqueous solution neutral to *litmus.* An aqueous solution (1 in 100) responds to the following tests:—Mixed with an equal volume of *nitric acid* it assumes a yellow color passing to crimson on warming; 2 millilitres are colored green by 2 drops of *fuming nitric acid,* and the color is changed to red by boiling with an additional 3 or 4 drops of the *fuming nitric acid;* 12 millilitres remain nearly colorless on the addition of 0.1 gramme of *sodium nitrite,* but turn deep green on the further addition of 1 millilitre of *diluted sulphuric acid;* 1 millilitre, diluted with 9 millilitres of *water,* is colored deep red by *T. Sol. of ferric chloride,* the color being nearly discharged by excess of *diluted sulphuric acid.* An aqueous solution (1 in 20) gives with *T. Sol. of mercuric chloride* a white precipitate which disappears on boiling, but reappears on cooling. Aqueous solution not affected by *hydrogen sulphide.* No appreciable ash." *Br.*

Uses.—Locally antipyrine exercises an anesthetic effect upon the nerve endings and causes constriction of the superficial blood vessels. When taken into the stomach it is absorbed rapidly and eliminated unchanged chiefly through the kidneys, although it has been demonstrated in various other secretions. In appropriate dose it causes in the lower animals increased activity of reflexes through an action upon the spinal cord, a rise in the blood pressure through an influence upon the cardiac and vascular muscles, and a slight stimulation of the respiratory center. These actions, however, are of little importance from a standpoint of the clinical use of the drug. The medicinal value of antipyrine, aside from its local uses, is based on effects on the pain-perceiving mechanism and upon the thermoregulator apparatus, similar to that described under acetanilid, see page 8. As far as at present known, the action of antipyrine upon these centers is precisely analogous to that of the anilin derivatives, but it is somewhat more prompt in its action and some believe also more prone to produce collapse than either acetanilid or acetphenetidin.

Antipyrine is useful in medicine most largely for the relief of pain, especially of nervous origin, as *neuralgias, migraine,* crises of *locomotor ataxia,* and similar conditions. In so-called *muscular rheumatism* many believe that it is not merely of value as a symptomatic drug, but that it possesses some curative effect. As an antipyretic it is employed in the same class of cases as the aniline derivatives. It is also used in certain spasmodic disorders, especially *whooping-cough* and *epilepsy.* In the latter disease it usually fails when given alone, but appears to enhance the action of the bromides. It has been recommended for the purpose of checking excessive secretion, especially in the treatment of *diabetes insipidus* and as an anti-

galactogogue. It is valuable as a local remedy in the treatment of various inflammatory conditions of the mucous membranes, especially *rhinitis* and *laryngitis*, both for its local anesthetic and vaso-constricting effects. For this latter purpose it may be employed in strengths of from five to fifteen per cent. It is also occasionally employed as a styptic in *nasal hemorrhage*.

Antipyrine, like the other coal-tar derivatives, is prone to produce unpleasant and sometimes alarming symptoms, even after doses which would scarcely be regarded as excessive. The most common type of antipyrine poisoning is characterized by giddiness, tremor, free sweating with more or less collapse, a peculiar lividity with, in many cases, eruption of the skin most commonly morbilliform, but sometimes erythematous or urticarial. When these skin symptoms are severe, the mucous membranes may share in the irritation, and a general rise of temperature, dyspnea, hysterical unrest, and even more severe constitutional symptoms come on. In some cases of poisoning the chief symptoms have been those of profound progressive collapse with excessive sweating, increased frequency of the pulse, often accompanied by precordial anguish, fall of temperature arrested respiration, exaggeration of the reflexes, followed, if the dose has been large enough, by somnolence deepening into coma, and passing into profound stertorous unconsciousness, with dilatation of the pupil and epileptiform convulsions. Various irregular symptoms have been noted, such as amaurosis, pseudo-membranous stomatitis, swelling of the lips and tongue, laryngeal interference with the respiration. The treatment of antipyrine poisoning is purely symptomatic. Circulatory stimulants, as ammonia, strychnine and atropine, should be given and the bodily temperature maintained by the external application of heat.

Antipyrine is incompatible with nitrites and ferric salts, which produce marked color reactions. It forms eutectic mixtures which liquefy when triturated with many other organic compounds like salol, etc.

Dose, three to fifteen grains (0.2–1.0 Gm.).

APOMORPHINÆ HYDROCHLORIDUM.
U. S., Br.

APOMORPHINE HYDROCHLORIDE, APOMORPHINE CHLORIDE Apomorph. Hydrochl. [Apomorphinæ Hydrochloras, U. S. 1890. Apomorphine Hydrochlorate]

(ăp-o-mŏr-phī'næ hȳ-dro-ȼhlō'rı̣-dŭm)

"The hydrochloride [$C_{17}H_{17}O_2NHCl + \frac{1}{2}H_2O = 312.62$] of an alkaloid prepared from morphine by the abstraction of one molecule of water. Preserve it, protected from light, in small, well-stoppered vials, which have been previously rinsed with diluted hydrochloric acid and dried. Apomorphine Hydrochloride must be rejected if it imparts at once an emerald-green color to 100 parts of distilled water when shaken with it in a test tube." *U. S.* "Apomorphine Hydrochloride, $(C_{17}H_{17}NO_2,HCl)_2$, H_2O, is the hydrochloride of an alkaloid which may be obtained from morphine by the abstraction of the elements of a molecule of water." *Br.*

Hydrochlorate of Apomorphine; Chlorhydrate d'Apomorphine, *Fr. Cod.*; Apomorphinum Hydrochloricum, *P. G.*; Apomorphinhydrochlorid, *G.*; Cloridrato di apomorfina, *It.*; Cloruro de apomorfina, *Sp.*

Apomorphine was discovered by Matthiessen and C. A. Wright. It is prepared by heating morphine in a closed tube with a great excess of hydrochloric acid for two or three hours to the temperature of 140° to 150° C. (284°–302° F.). The contents of the tube are then dissolved in water, an excess of sodium bicarbonate added, and the precipitate exhausted with ether or chloroform. On the addition to the solution of a very small quantity of hydrochloric acid, crystals of apomorphine hydrochloride form. The process is one of dehydration; the morphine parting with one molecule of water, the formula of apomorphine being $C_{17}H_{17}NO_2$. Apomorphine may also be made by the action of hydrochloric acid upon codeine, and it is affirmed that the best method in practice is that of E. Mayer, in which morphine is treated with a solution of zinc chloride, at 120° C. (248° F.) (*Ber. d. Chem. Ges.*, Berlin, 1871, iv, 121.) Codeine, $C_{18}H_{21}NO_3$, when treated with hydrochloric acid, yields first $C_{18}H_{20}ClNO_2$, and then splits off methyl chloride, CH_3Cl, and leaves apomorphine, $C_{17}H_{17}NO_2$. Pschorr (*Ber. d. Chem. Ges.*, 1902, 4377) believes that apomorphine is a derivative of phenanthrenequinoline.

Properties.—Apomorphine Hydrochloride is officially described as in "minute, white or grayish-white, glistening, monoclinic prisms; odorless, and acquiring a greenish tint upon exposure to light and air. One Gm. of Apomorphine Hydrochloride dissolves in 50 mils of water and in 50 mils of alcohol at 25° C. (77° F.); also in 17 mils of water at 80° C. (176° F.); very slightly soluble in chloroform or ether. Its saturated aqueous solution is neutral to litmus. The salt loses its water of crystallization slowly over sulphuric acid and the anhydrous salt regains the water lost when exposed to the air. The addition of a solution of sodium bicarbonate to an aqueous solution of the salt (1 in 100) produces a white or pale greenish-white precipitate, which rapidly becomes green on exposure to air and then dissolves in ether with a violet color and in chloroform with a violet-blue color. The salt dissolves in nitric acid with a dark purple color. Silver nitrate T.S., added to an aqueous solution of the salt, produces a white precipitate, insoluble in nitric acid; the precipitate soon turns black by reduction to metallic silver, and is instantly reduced by the addition of ammonia water. No weighable ash remains on incinerating 0.2 Gm. of Apomorphine Hydrochloride. Shake about 0.1 Gm. of the salt with 10 mils of ether; the

latter acquires not more than a pale reddish color (*decomposition products*)." *U. S.*

"Small, greyish-white, shining, acicular crystals, turning green on exposure to air and light. Soluble in 60 parts of *water* and in 50 parts of *alcohol* (90 per cent.) The solutions decompose on boiling or keeping, with production of a green color; but remain unchanged for a considerable time if acidified with a trace of *hydrochloric acid.* Yields the *reactions* characteristic of chlorides. Gives a deep red color with dilute *T. Sol. of ferric chloride.* The addition of an aqueous solution of *sodium bicarbonate* to an aqueous solution (1 in 100) of Apomorphine Hydrochloride produces a white precipitate rapidly changing to green; this precipitate forms a purple solution with *ether,* a bluish solution with *chloroform,* and a green solution with *alcohol* (90 per cent.)." *Br.*

The alkaloid is colored dark red by nitric acid and rose red by ferric chloride, changing to violet, and finally black, on exposure. The aqueous and alcoholic solutions are at first colorless, if heated becoming pinkish, but change rapidly to greenish, finally becoming deep emerald green in color. This change in color has been attributed to oxidation, and it has been noticed that the solution on standing loses its power; for this reason it is best not to keep the solution, but to make it as wanted. C. Bernbeck affirms that the change in the solution to a green color may be prevented by the addition of a small quantity of hydrochloric acid, the decomposition being due to ammonia. (*Ph. Ztg.,* 1885.)

According to Max Quehl and H. Koehler apomorphine is precipitated from its solutions, greenish by tannic acid, lemon yellow by picric acid, bluish-white, and turning to sap-green by copper sulphate on boiling, purplish by gold chloride, white, turning to blackish-violet by potassium ferricyanide on boiling, blood-red by iodine in solution of potassium iodide, the precipitate disappearing on boiling, white and curdy by potassium sulphocyanate. (*A. J. P.,* 1873, p. 166.) With potassium dichromate and concentrated sulphuric acid it turns a dark red; with the potassium salt alone, a deep yellow-orange; with neutral iron chloride, an amethyst color.

According to Harnack and Hildebrand (*A. E. P. P.,* 1911, lxv, p. 38) apomorphine hydrochloride is sometimes contaminated with *chloromorphine,* whose action is very similar to that of acetyl-morphine. Frerichs (*P. J.,* lxxxiv, p. 293) reports having examined two samples of apomorphine hydrochloride which consisted almost entirely of *trimorphine hydrochloride.*

Uses.—Apomorphine hydrochloride was first brought forward by Gee as a prompt and efficient emetic. According to the researches of Eggleston and Hatcher (*J. P. Ex. T.,* 1912, iii, p. 551) the vomiting is due solely to an action on the vomiting center. Aside from its emetic effects therapeutic doses of apomorphine ordinarily have very little influence upon the system. Rosenwasser (*N. Y. M. R.,* July, 1907), however, and some other writers maintain that it has narcotic properties, but it is not impossible that the effects they have observed have been due to impurities in the drug. It has the great advantages of smallness of dose and freedom from irritating properties, so that it can be used hypodermically. When from one-fifteenth to one-tenth of a grain (0.004–0.006 Gm.) of it is injected under the skin of a man, free emesis usually occurs in from 5 to 20 minutes; the dose may be repeated at intervals if necessary. The effects upon the general system are usually not marked; but in some cases very alarming syncopal symptoms have been produced, and death is said to have resulted from one-sixteenth of a grain (0.004 Gm.) in a feeble adult worn out with chronic bronchitis and emphysema. (*Med. Rec.,* 1877, p. 664.) Apomorphine hydrochloride is a very useful emetic in cases of *poisoning* or *acute gastritis* or any other condition where it is desired to promptly evacuate the stomach. Its advantages are, first, lack of irritation of the gastric mucosa, secondly, the smallness of dose which makes it possible to carry it in the form of a hypodermic tablet, and thirdly, the promptness of its effect. In cases of *narcotic poisoning,* however, it frequently fails to act, because of the depression of the vomiting centers. Given in doses too small to act as an emetic it is a valuable nauseating expectorant in the early stages of *acute bronchitis.* One drawback to its wider use for this purpose is its instability when in solution. The green substance formed does not seem to be toxic, but it does not possess the peculiar therapeutic properties of the drug. Under no circumstances should more than one-fourth of a grain (0.016 Gm.) by mouth, or one-eighth of a grain (0.008 Gm.) hypodermically, be given at a dose.

Dose, as an expectorant, one-twentieth to one-fifteenth of a grain (0.003–0.004 Gm.); as an emetic, one-tenth to one-fourth of a grain (0.006–0.016 Gm.).

Off. Prep.—Injectio Apomorphinæ Hypodermica, *Br.*

AQUA. U. S.

WATER

(ă'quą)

Ὕδωρ, Gr.; Eau, *Fr.;* Wasser, *G.;* Acqua, *It.;* Agua, *Sp.*

Water has always been included in the U. S. Pharmacopœia, on account of its great importance as a medicinal and pharmaceutical agent. In the U. S. P. VIII it was defined as "Potable Water in its purest obtainable state." It was not admitted into the official lists of the British Pharmacopœias until 1839, when it was first recognized by the Edinburgh College, but it was dropped at the last revision of the British Pharmacopœia. It is more or less concerned in almost all the changes which take place in inorganic matter, and is essential to the growth and existence of living beings, whether animal or vegetable. In treating of a

substance of such diversified agency, our limits will allow of a sketch only of its properties and modifications. We shall speak of it under the several heads of *pure water, common water,* and *mineral waters.*

Pure Water.—Water, in a pure state, is a transparent liquid, without color, taste, or odor. Its sp. gr. is assumed to be unity, and forms the term of comparison for that of solids and liquids. A cubic inch of it, at the temperature of 15.5° C. (59.9° F.), weighs very nearly 252.5 grains; when weighed in air with brass weights at 25° C. (77° F.) it weighs 251.91 grains. In the metric system the weight of 1 mil of distilled water taken at 4° C. (39.2° F.) is made equal to 1 gramme, the unit of weight in this system. Water is compressible to a small extent, as was proved first by Canton, and afterwards, in an incontestable manner, by Perkins. Reduced in temperature to 0° C. (32° F.), it becomes a solid or ice, with the sp. gr. 0.9175 (Dufour, *C. R. A. S.*, Juin, 1860); and raised to 100° C. (212° F.), an elastic gas called steam. In the latter state its bulk is increased nearly 1700-fold, and its sp. gr. so far lessened as to be not much more than half that of atmospheric air. At the temperature of 4° C. (39.2° F.), its density is at the maximum; and consequently, setting out from that point, it is increased in bulk by being either heated or cooled. It has the power of dissolving more or less of all gases, including the constituents of common air, which are always present in natural water in variable proportions. It uniformly exists in the atmosphere, in the form of invisible vapor.

Water consists of two atoms of hydrogen and one of oxygen; or, in volumes, of two volumes of hydrogen and one volume of oxygen condensed into two volumes of aqueous vapor or steam. On these data, it is easy to calculate the sp. gr. of steam; which will be 0.0693 (sp. gr. of hydrogen) + 0.5528 (half the sp. gr. of oxygen) = 0.6221.

Common Water.—By reason of its extensive solvent powers, water, in its natural state, must be more or less contaminated with foreign matter. Thus, it becomes variously impregnated, according to the nature of the strata through which it percolates. When the foreign substances present are in so small an amount as not materially to alter its taste and other sensible qualities, it constitutes the different varieties of *common water.*

There are almost innumerable shades of difference in common water, as obtained from different localities and sources; but all its varieties may be conveniently arranged under the two heads of soft and hard. A *soft water* is one which contains but inconsiderable impurities, and which, when used in washing, readily forms a lather with soap. By a *hard water* is understood a variety of water which contains calcium or magnesium salts, through which it curdles soap, and is often unfit for domestic purposes. Solution of soap is a good test liquid for ascertaining the hardness of water. In distilled water it produces no effect; in soft water, only a slight opalescence; but in hard water, a milky appearance or a curdy precipitate which is due to the formation of an insoluble compound between the fatty acids of the soap and the lime or magnesia of the foreign salt. The hardness may be classed as temporary or permanent, as in waters which contain much free carbon dioxide, the hardness is removed or diminished by boiling, which causes a loss of the gas and a deposition of the calcium and magnesium salts which produce the hardness and which have been held in solution as bicarbonates. The hardness may be estimated by means of a volumetric soap solution which is added in small quantities to a measured quantity of the water, shaking after each addition and noting the volume of the soap solution which is required to produce a lather which will remain on the surface for five minutes.

The most usual foreign substances in solution in common water, besides oxygen and nitrogen, and matters held in a state of mechanical suspension, are carbon dioxide, calcium sulphate, magnesium carbonate, and sodium chloride. Carbon dioxide is detected by lime water, which produces a precipitate before the water is boiled, but not afterwards, as ebullition drives off the dioxide. The presence of calcium sulphate is shown by precipitates being produced by barium nitrate, and, after ebullition, by ammonium oxalate. The former test shows the presence of sulphuric acid, and the latter, after boiling the water, indicates lime not held in solution by carbon dioxide. Calcium carbonate, when held in solution by an excess of carbon dioxide, may be detected by boiling the water, which causes it to precipitate; but even after ebullition and filtration the water will retain enough calcium carbonate to give a precipitate with lead acetate, calcium carbonate being itself to a minute extent soluble in water. Silver nitrate will produce a precipitate if any soluble chloride be present; and, ordinarily, the one present may be assumed to be common salt. Arsenic in minute quantity has been found in some waters used as drink. At Whitbeck, in Cumberland, England, the inhabitants employ, both as drink and for culinary purposes, a water holding enough arsenic in solution to be quite sensible to tests, without any known injurious consequences. Small amounts of iron and aluminum salts and silica are almost always found in potable waters.

Clark has proposed to purify hard water, when the hardness arises from calcium bicarbonate, by a process which he calls *liming.* This consists in adding to the water sufficient lime water to convert the bicarbonate into the very sparingly soluble carbonate. This procedure renders the water soft, and gets rid of all the lime, except that in the minute portion of carbonate dissolved. The merit of this process consists chiefly, not in the removal of lime, but in preventing the formation of organic growths, principally confervæ, the decomposi-

tion of which renders the water offensive and unwholesome. River water containing the usual amount of calcareous matter, if allowed to stagnate in open reservoirs, in the summer, will become contaminated with myriads of microscopic plants and animals. This change is prevented, according to Clark, by his peculiar treatment, which deprives the living organisms of the nutriment derived from loosely combined carbon dioxide.

The oxygen and nitrogen present in neutral waters are not usually in the same proportion as in atmospheric air; the oxygen in atmospheric air amounts to about 20 per cent. in volume, while the usual gaseous mixture expelled from fresh water by boiling contains 32 per cent. (See table on page 164.) The important discovery has been made by Moore and Kellerman of the U. S. Department of Agriculture, that copper sulphate, if present in amounts such as 1 in 4,000,000 will be toxic to algæ, destroying them and preventing their reappearance; this statement has been confirmed by Gildersleeve (*Am. J. M. S.*, 1905, 129, p. 757), Stewart (*Am. J. M. S.*, 1905, p. 761), Kraemer (*A. J. P.*, 1906, 140), and others. They state that one part of copper sulphate in 100,000 of water will destroy typhoid and cholera germs in from three to four hours, and it appears to be established that waters not containing too large amounts of organic matter, exposed to the action of copper foil, kept in copper vessels, or treated with small amounts of copper sulphate (1 to 500,000), will destroy all typhoid bacilli and many other organisms in from 3 to 6 hours. On the other hand as shown by Doty (*N. Y. M. R.*, cxvii, p. 90), and Fowler (*Jour. Roy. Army Med. Corps*, 1905, v, 391), in the presence of even moderate quantities of organic matter the bactericidal power of copper is much reduced, while in foul waters it is almost nil. See "The Use of Copper in Destroying Typhoid Organisms and the Effects of Copper on Man," Henry Kraemer. (*A. J. P.*, 1905, p. 265.)

Common water is also divided into varieties according to its source. Thus, we have rain, snow, spring, river, well, lake, and marsh water.

Rain (*aqua pluvialis*) and *snow water* (*aqua nivalis*) are the purest kinds of natural water. Rain water, to be obtained as pure as possible, must be collected in large vessels in the open fields, at a distance from houses, and some time after the rain has commenced falling; otherwise it will be contaminated with the dust which floats in the atmosphere, and with other impurities derived from roofs. The rain water of large cities contains nitrogenized organic matter, as shown by the odor produced by burning the residue left after the water has been evaporated. In districts near the sea coast rain water usually contains appreciable quantities of chlorides.

Rain water ordinarily contains atmospheric air, and, according to Liebig, a little nitric acid, the amount of which is increased when the rain descends during a thunder storm. Chabrier states as the result of his observations that rain water contains either nitrous or nitric acid, the one or the other predominating according to the condition of the weather, the nitrous acid being relatively in excess in mild weather, but the nitric when the rain is attended with tempestuous winds. According to an analysis, made by Martin, of rain water which fell at Marseilles during a violent storm, 1000 parts by weight contained 0.004 of chlorine and 0.003 of ammonia. Not a trace of iodine or of nitric acid was discovered. Boussingault has ascertained that the rain which falls in towns contains considerably more ammonia than that which falls in the country. Thus the rain of Paris was found by him to contain three or four parts of ammonia per million, while that collected in a mountainous region contained about four-fifths of one part only in a million. The average results of J. B. Lawes and J. H. Gilbert give one part of ammonia to the million of rain water. Snow water has a peculiar taste, which was supposed to depend on the presence of air more oxygenated than that of the atmosphere; but in point of fact it contains no air, and this accounts for its vapid taste. Rain and snow water are sufficiently pure for most chemical operations.

Spring water (*aqua fontana*) depends entirely for its quality on the strata through which it flows, being purest when it passes through silicious sand or gravel, or where the prevailing rock formation is granitic. On the contrary, where the formation is limestone, the water will, because of the carbon dioxide dissolved in it, take up calcium carbonate, convert it into a bicarbonate, and become what is called a *hard water*. It almost always contains a trace of common salt, and generally other impurities, which vary according to the locality of the spring.

River water (*aqua fluvialis*) is, generally speaking, less impregnated with saline matter than spring water, because made up in considerable part of rains, while its volume bears a larger proportion to the surface of its bed. It is, however, much more apt to have mechanically suspended in it insoluble matters, of an earthy nature, like clay and silt, which impair its transparency. It is frequently rendered more sightly by being run through porous stone, carbon, or sand filters. The coarse particles are by this filtration removed; but sewage or injurious products resulting from decomposition which are dissolved in the water are not removed, so that such clean filtered water may be a very deadly poison. Water may be purified for manufacturing purposes by what is termed the alum process,—*i.e.*, by adding 2 grains of alum to a gallon of water, and permitting the impurities to subside for 48 hours. (*Chem. News*, July 23, 1886.) River water is purified now at Philadelphia and other cities on the large scale by filtration through sand. (See *U. S. D.*, 19th ed., p. 163.)

Well water, like that from springs, is liable to contain various impurities. As a rule, the purity of the water of a well will be in proportion to its depth and the constancy with which it is used. Well water in large cities always contains a large amount of impurity, both organic and inorganic, the result of sewage contamination. R. D. Thomson found 147.6 gr., per Imperial gallon, of impurity in a well in London. (*P. J.,* 1856, p. 27.) The presence of nitrates in water is destructive to many forms of organic life. *Artesian Wells,* from their great depth, generally afford a pure water, although on analysis they frequently show a larger proportion of solid constituents on evaporation than do waters from rivers.

Lake water cannot be characterized as having any invariable qualities. The water of most of the lakes in the United States is pure and wholesome except where it is near large centers of population, when it is usually contaminated by sewage.

Marsh water is generally stagnant, and contains vegetable matter undergoing decomposition. It is unwholesome, and ought never to be used internally.

All water which is exposed to the air dissolves a quantity of oxygen, nitrogen, and carbon dioxide, in obedience to the laws of gaseous absorption. It is indeed upon this dissolved oxygen that the life of water-breathing animals depends. In every pure water the proportion between the dissolved nitrogen and oxygen is found to be constant, and it is represented by the following numbers:—oxygen 34.91, and nitrogen 65.09 per cent.; 1000 parts of pure water, such as rain water, when saturated dissolves 17.95 parts of air. If the water be rendered impure by the introduction of organic matter undergoing oxidation, the proportion between the dissolved oxygen and nitrogen becomes different, owing to the oxygen having been partly or wholly used for the oxidation of this material.

Analysis of the gases dissolved in water may prove of much help in ascertaining whether the water is pure or whether it has been contaminated with putrescent organic matter. Miller concludes that whenever the proportion between dissolved oxygen and nitrogen falls to less than 1 to 2 the water is unfit for drinking purposes. (Roscoe and Schorlemmer, *Treatise on Chem.,* i, 245.)

The second class of dissolved impurities consists of inorganic salts, even rain water washing some of these out of the atmosphere. It invariably contains ammonia salts, sodium chloride, and particles of organic matter, living and dead. In towns the rain water also contains a larger proportion of nitrates than that falling in the country. It is, however, the spring waters especially which contain the largest amount of mineral matter in solution. The salts which most commonly occur in solution in spring water are: (1) Calcium, magnesium, iron, and manganese carbonates, dissolved in an excess of carbon dioxide. (2) Calcium and magnesium sulphates. (3) Alkaline carbonates, chlorides, sulphates, nitrates, or silicates.

Spring waters which issue from considerable depths, or which originate in volcanic districts, are always hotter than the mean annual temperature of the locality where they come to the surface.

The term *Aqua,* in the United States Pharmacopœia, may be considered as designating any natural water of good quality which answers well for cooking and does not curdle soap. "Water is a colorless, limpid liquid, practically tasteless and odorless. When heated nearly to the boiling point and agitated, no disagreeable odor is evolved. Water is neutral to litmus. Evaporate 100 mils of Water in a platinum dish; it leaves a residue weighing not more than 0.03 Gm. (*solids*), and this residue, when carefully heated to redness, evolves no visible fumes and shows no appreciable charring (*organic impurities*). Add 1 mil of hydrochloric acid to 100 mils of Water and then add 50 mils of hydrogen sulphide T.S.; it shows no darkening after standing fifteen minutes (*lead or copper*). Add 1 mil of hydrochloric acid to 100 mils of Water and then add 1 mil of potassium ferrocyanide T.S.; no blue coloration is produced immediately (*iron*). Add 0.5 mil of tenth-normal silver nitrate V.S. to 200 mils of Water, heat to boiling, filter and add to the filtrate 3 drops of potassium chromate T.S.; a red precipitate is produced (*chloride*). Add 1 drop of hydrochloric acid, 1 mil of sulphanilic acid T.S. and 1 mil of naphthylamine hydrochloride T.S. to 100 mils of Water in a Nessler jar, stirring with a glass rod after each addition. Closely cover the jar with a glass plate, place it upon a white surface and view it from above; no pink coloration appears within five minutes (*nitrite*). Add 1 mil of sodium carbonate T.S. to 100 mils of Water and evaporate the liquid in a small porcelain dish just to dryness. Moisten the residue thoroughly with 2 mils of phenolsulphonic acid T.S., gently warm the dish, add 20 mils of ammonia water and sufficient distilled water to measure 100 mils. Any yellow color produced is not greater than that obtained by evaporating 0.0021 Gm. of potassium nitrate, dissolved in 3 mils of distilled water and 1 mil of sodium carbonate T.S., to dryness and treating the residue in the same manner as the residue from the Water. The comparison of colors must be made in Nessler jars of the same diameter and size (*nitrate*). Add 2 mils of alkaline mercuric potassium iodide T.S. to 100 mils of Water in a Nessler jar and mix thoroughly. Place the jar on a white surface and view the contents from above; the water does not at once assume a deep yellow or orange color (*ammonium compounds*). Mix 100 mils of Water with 10 mils of diluted sulphuric acid in a clean porcelain dish and heat it rapidly to boiling, then add 0.4

mil of tenth-normal potassium permanganate V.S. and boil the liquid for ten minutes; the color of the liquid is not completely destroyed (oxygen consuming capacity as a measure of *organic impurities*)." *U. S.*

The British Pharmacopœia no longer includes *"Aqua"*; it recognizes *"Aqua Destillata,"* and gives appropriate tests. (See page 175.)

Water should never be kept in leaden cisterns, on account of the risk of its dissolving a small portion of lead. This risk is greater in proportion to the softness and purity of the water; for it is found that the presence of a minute proportion of saline matter, as for example of calcium sulphate, protects the water from the slightest metallic impregnation. The chlorides are not protective, as they give rise to lead chloride, which is slightly soluble. The protection has been ascribed to an insoluble film on the surface of the lead, formed by the decomposition of the saline matter. Upon this principle is based a plan of protection by Schwartz of Breslau, who proposes to fill leaden pipes through which water is conducted, with a strong solution of an alkaline sulphide, which forms a perfectly insoluble coating of lead sulphide (*sulphuret*), said to be quite impermeable by the water afterwards introduced. Galvanized iron (zinc coated) does not rust as readily as iron which is unprotected, because as the zinc has the greater solution tension it protects the iron, which remains unacted upon. On the other hand, tinned iron (tin plate) rusts more readily than iron alone if the iron is exposed at any point; the iron being the anode end is at once attacked. The action of water upon various metals has been exhaustively studied by Jorissen (*Compt. Rend.*, xi; *Internat. Pharm. Cong.*, 1914, 696) who found that aluminum was but slightly affected by distilled water; ordinary water acted upon it decidedly, producing crater-shaped corrosions. Magnalium (an alloy of magnesium and aluminum) is less liable to corrosion. Copper is only slightly affected by distilled water; sea water, free from air, does not act upon copper, but in the presence of air, corrosion readily occurs with formation of carbonates and chlorides. Lead is affected by water which is free from CO_2, especially when dissolved oxygen is present. The presence of CO_2 considerably lowers the percentage of dissolved lead. Nickel is not corroded even by sea water; over 35 per cent. of nickel will prevent iron from rusting. Tin is proof against the action of pure water. Ordinary water acts upon it slightly. Sea water containing air acts upon it at first, but it is soon protected by a layer of basic salts. Zinc in distilled water free from CO_2 and oxygen preserves its shining surface for years. When oxygen is present zinc hydroxide is produced, which is slightly soluble, and when CO_2 is present, a slightly soluble carbonate is also formed.

A very important class of dissolved impurities is made up of organic compounds. This organic matter may be derived from a vegetable source, such as leaf-mould and the decomposition products of wood, in which case it is practically harmless, or it may be derived from animal sources, in which case it almost always proves a serious impurity.

The careful observations of students of public health leave no doubt that a number of epidemic diseases, especially cholera and typhoid fever, are often contracted and spread by means of drinking water contaminated with germs of disease from excreta and general sewage. This impure water may be clear and may have filtered through considerable distances of soil, and yet may contain these poisonous germs. Now, nitrogen is one of the characteristic constituents of animal matter as contrasted with vegetable matter, relatively few forms of which contain it, and those are of a character not likely to be found in natural waters. Hence, if water should be impregnated with animal matter, this would be indicated by the presence of nitrogen in solution, either in the form of albumin or albuminous matter, if the animal matter in the water is still unchanged, or, if the animal matter has undergone oxidation, in the form of ammonia or nitrous or nitric acid.

There are, therefore, to be determined in the examination of a water with reference to this presence of organic nitrogenous matter, (1) the ammonia, (2) the unchanged albuminous matter, which, as it is changed into and determined as ammonia, is called "albuminoid ammonia," and (3) the nitrates and nitrites present.

The ammonia is first determined by distilling the water made alkaline with sodium carbonate as long as the distillate carries enough ammonia to be recognized by *Nessler's solution.* (See Part III.) For this purpose the distillate is collected successively in volumes of 50 mils and the amount of ammonia in each of these separate distillates determined. The smallest quantity of ammonia will produce a yellow color, the tint of which is to be compared with that obtained from the Nessler solution treated with a standard ammonium chloride solution.

After the free ammonia has been distilled off, a solution of sodium hydroxide and potassium permanganate is added and the distillation is continued. Another portion of ammonia now comes off, owing to the action of the permanganate on the nitrogenous organic matter. The amount of ammonia thus obtained is determined, and is tabulated as "albuminoid ammonia," because albumin is one of the bodies which is decomposed in this way. L. de Konnick found that the Nessler test in ammonia liquids does not produce the usual yellowish-brown precipitate, nor even a coloration, in the presence of alcohol. (*Am. Drug.*, 1893, p. 386.)

Instead of this method proposed by Wanklyn and Chapman, another process, described by Frankland and Armstrong, is often used. In this case, the water having been evaporated, the dry residue is submitted to an organic

combustion analysis, which gives the "organic nitrogen" and the "organic carbon," and the ratio of these gives an indication as to the presence of albuminous matter rich in nitrogen. If the amount of albuminoid nitrogen indicated by either of these processes exceeds 0.15 part for one million of water, the latter should be rejected as a drinking water. In some large towns, however, the surface well waters have shown albuminoid nitrogen to the amount of 0.3 to 0.8 part per million. Such waters are little better than sewage. The free ammonia, moreover, should not exceed 0.08 part per million, or the water must be considered as containing sewage contamination.

Nitrates may be estimated by the following process: A measured volume (15–25 mils) of the water is evaporated just to dryness in a flat-bottomed porcelain dish, 1 mil of phenoldisulphonic acid (made by heating 37 grammes of strong sulphuric acid with 3 grammes of pure phenol for 6 hours in a water bath) is added and thoroughly mixed with the residue by means of a glass rod. It is then diluted with about 25 mils of water, solution of ammonium hydroxide added in excess and the volume of the solution made up to 50 mils. The nitrates present in the residue convert the phenoldisulphonic acid into picric acid, which, by the action of ammonium hydroxide forms ammonium picrate; this imparts to the solution a yellow color which is proportional in its intensity to the amount of nitrates present in the water, and by carrying out a similar test with a standard solution of potassium nitrate similarly evaporated, the amount may be accurately estimated. Nitrites may be estimated by the sulphanilic acid and naphthylamine hydrochloride test given for the qualitative detection of nitrites by the U. S. Pharmacopœia (see page 161), by carrying out a similar test with a standard solution of sodium nitrite and making a comparison of the relative intensity of the color which is produced in each.

The determination of chlorides is also frequently of great importance, for although mineral waters may be rich in chlorides, ordinary well waters or river waters, which are the chief sources of supply, will not contain much chlorine unless they have been contaminated. Both urine and sewage may contribute this chlorine, as they are highly charged with sodium chloride. As a rule, it may be said that water containing more than two grains of chlorine per gallon must be looked upon with suspicion, unless some good reason for the presence of sodium chloride can be assigned.

MINERAL WATERS.—When natural spring waters are so far impregnated with foreign substances as to have a decided taste, and to operate in a peculiar manner upon the human economy, they are called *mineral waters.* There has been an enormous amount of fraud perpetuated in connection with the mineral waters. The so-called natural "lithium waters" contain only traces of that element and a number of them have been proven misbranded within the meaning of the Food and Drugs Act. Mineral waters are conveniently arranged under the heads of *carbonated, alkaline, sulphuretted, saline* (including *magnesian, chalybeate,* and *chlorinated*), and *siliceous.* For a more comprehensive and detailed classification of this class of waters see *Mineral Waters of the United States,* U. S. Department of Agriculture, Bulletin No. 91.

1.—*Carbonated waters* are cold, and are characterized by containing an excess of carbon dioxide, which gives them a sparkling appearance, and the power of reddening litmus paper. These waters frequently contain calcium, magnesium, and iron, which are held in solution by the excess of carbon dioxide as bicarbonates. The waters of Seltzer, Spa, Apollinaris, and Pyrmont in Europe, and of the sweet springs in Virginia, belong to this class. For Artificial Carbonic Acid Water, the reader is referred to page 165.

2.—*Alkaline waters* contain a large quantity of sodium bicarbonate, as well as common salt and Glauber's salt. These are sometimes warm, such as the springs at Ems and Vichy, but generally cold. Gettysburg spring water is of this class.

3.—*Sulphuretted waters* are such as contain hydrogen sulphide, and are distinguished by the peculiar fetid odor of that gas, and by yielding a brown precipitate with the salts of lead or silver. Examples of this kind are the waters of Aix-la-Chapelle and Harrogate in Europe, and those of the White, Red, and Salt sulphur springs in Virginia.

4.—*Saline waters* are those the predominant properties of which depend upon saline impregnation. The salts most usually present are sodium, calcium, and magnesium sulphates and carbonates, in which latter case the name *magnesian* is given to them, the presence of the chlorides of these alkalies making the class *chlorinated* waters, which reach their maximum concentration in sea waters; while the presence of ferrous salts makes another class, the *chalybeate.* Among magnesium waters may be mentioned those of Friedrichshall, Hunyádi Janos, and Epsom; among chalybeate waters, those of Tunbridge and Brighton in England, of Pyrmont, Wiesbaden, and Spa on the Continent, and of Bedford, Pittsburg, and Brandywine in the United States. Potassium sulphate is occasionally present, and lithium has been detected by Berzelius in Carlsbad and other salt springs of Germany, and is also found in some American spring waters. Boric acid, usually in the form of an alkaline borate, is of frequent occurrence in mineral waters of certain portions of the United States. Cæsium and rubidium have also been detected in certain mineral waters, such as the Dürkheim and Baden-Baden waters, in the former of which

these elements were first discovered by Bunsen. Bromine is found in the saline at Theodorshalle, in Germany, as also in the salt wells of Western Pennsylvania, Ohio, Michigan, and West Virginia. The mineral springs at Saratoga contain a small proportion of iodine and bromine. The principle saline waters are those of Seidlitz in Bohemia, Cheltenham and Bath in England, and Harrodsburg and Saratoga in the United States.

5.—*Siliceous waters* are those in which the contents consist chiefly of alkaline silicates, such as the hot spring waters of Iceland and the geysers of Fire-hole Basin and Gardiner's River, Yellowstone National Park, U. S.

6.—*Sea water* (*English Channel*).—In a thousand grains: water 964.744 gr.; sodium chloride 27.059; potassium chloride 0.765; magnesium chloride 3.667; magnesium bromide 0.029; magnesium sulphate 2.296; calcium sulphate 1.407; calcium carbonate 0.033. Total 1000 gr. (Schweitzer.) The proportion of sodium chloride is from 36 to 37 parts in 1000 in the ocean, at a distance from land. Its amount is small in the interior of the Baltic. It is perceived that bromine is present in very minute amount, 100 pounds of sea water yielding only 3⅓ gr. of this element. Iodine exists in the water of the Mediterranean, and it has been found in ocean water. Besides these ingredients, others are alleged to exist in minute proportion in sea water, as fluorine by G. Wilson; lead, copper, and silver by Malaguti, Durocher, and Sarzeau; and iron and manganese by Uziglio. Gold in very minute quantity has been found in sea water. Prior to Wilson's researches, Middleton and Silliman, Jr., had inferred the existence of fluorine in sea water, from its presence in marine animals. The lead and copper above mentioned were found in certain fuci only, the silver in the sea water itself. The presence of silver in sea water has been demonstrated by F. Field, by a comparative analysis of the same copper sheathing, when new, and after having been on a vessel for many years. The old sheathing was always found to contain more silver than the new; and the observations of Field have been subsequently confirmed by others. Schweitzer's analysis gives a small proportion of calcium carbonate, but Bibra could not detect any. John Davy's examinations of sea water show that calcium carbonate does not exist at a great distance from land, except in very minute proportion, but becomes quite evident at a distance of from fifty to a hundred miles from coasts. Boric acid has been found by Veatch in the sea water on the coast of California. (See *A. J. P.*, 1860, p. 330.)

The following analysis of sea water, taken at two leagues from Fécamp, on the coast of France, merits special notice from the care with which it was made, and the large quantity operated on. The sp. gr. was 1.026, at 13.9° C. (59° F.).

Gaseous Contents.	*In one kilo. Liters.*	*In one liter. Liters.*
Atmospheric air	0.0120	0.0123
Free carbonic acid	traces	traces
" hydrogen sulphide	traces	traces
Solid Contents.	*Gm.*	*Gm.*
Potassium chloride	0.09763	0.10019
Sodium "	26.09300	26.78913
Lithium "	0.00042	0.00043
Ammonium "	0.00178	0.00183
Magnesium "	3.19300	3.27700
Sodium iodide	0.00920	0.00944
" bromide	0.10605	0.10882
Magnesium bromide	0.03084	0.03163
Calcium sulphate	0.09017	0.92540
Potassium "	0.00919	0.00943
Sodium "	2.57250	2.64012
Magnesium sulphate	0.32736	0.33597
" phosphate	0.00046	0.00047
(Ammonio-magnesian) phosphate	signs	signs
Calcium carbonate	0.13600	0.13959
Magnesium "	traces	traces
Iron "	0.00021	0.00021
Manganese "	signs	signs
Silicic acid	0.01420	0.01457
Organic matter	signs	signs
Pure water	966.50646	991.91577
Total	1000.00000	1026.30000

(*J. P. C.*, 4e sér., i, 381, 1865.)

Sea water, filtered, and charged with five times it volume of carbon dioxide, forms, according to Pasquier, a gentle purgative, which keeps very well, and is not disagreeable to take. The dose is from half a pint to a pint.

By freezing, sea water is almost entirely freed from saline matter, the ice being nearly pure water. It is obvious that the unfrozen water contains much more than its ordinary proportion of salts; and this is one of the methods of concentrating this and other saline solutions.

Medicinal Properties of Water.—Water is a remedy of great value in a large number of complaints either internally or externally. When taken internally the important effects depend upon the temperature. At low temperatures, below 10° C. (50° F.) it inhibits the secretion of the digestive juices and therefore delays digestion. If at a temperature of from 15° to 21° C. (60°–70° F.) it is almost without effect; the elaborate studies of Hawk (*J. Am. C. S.*, 1911, xxiii, and 1912, xxxiv) have completely dissipated the old superstition that water lowered digestive activity by diluting the ferment in the stomach. At tepid temperatures, 26° to 32° C. (80°–90° F.), it is likely to nauseate, and if taken in large quantities may even produce emesis. After its absorption water has a profound influence in increasing all the bodily secretions, notably those of the kidney and sweat glands. It is therefore frequently used as diuretic when it is desired either to wash out toxic substances from the system or, by dilution, to make an irritating urine more bland. In conjunction with external heat, or diaphoretic drugs, it is also of much service to increase the perspiration in various morbid conditions. When the systemic effects of water are desired quickly it may frequently be given advantageously in the form of salt solution, either hypodermically or intramuscularly. (See *Liquor Sodii Chloridi Physiologicus.*) Although a very potent agent for good in proper cases it should not be forgotten that the too free drinking of water may

prove harmful, especially in patients with feeble heart muscle.

Externally, although occasionally useful for the purpose of softening the skin, water is mostly applied as a means of conveying other medicinal forces either chemical, thermal or mechanical. Over small areas it may be applied either very hot, 49° to 60° C. (120.2°–140° F.), or ice cold, for its counter-irritant effect in various internal inflammations. The use of hot and cold baths has become one of the most important methods of treatment, and for consideration of the subject the reader is referred to text-books on hydrotherapy.

Frequently various chemicals are added to increase the effects of the bath. Of these forms of saline baths the most important is the so-called *Nauheim* or *carbonated baths.* For this purpose a naturally effervescent springs, Bad Nauheim in the Grand Duchy of Hesse, was originally used. *Artificial Nauheim baths,* however, have been widely employed. For this purpose the following formula may be used: In one package a mixture of sodium carbonate 1½ pounds, sodium bicarbonate ½ pound, calcium chloride 3 pounds, sodium chloride 2 pounds. This is dissolved in the bath of about 50 gallons, and then afterward 1 pound of sodium bisulphate is added slowly. This bath is used chiefly in the treatment of certain forms of *heart disease.* Another and very old bath which is used both as a diaphoretic and as a stimulant in various forms of *shock,* especially in young children, is the *mustard bath,* which is made by adding ground mustard in the proportions of 1 or 2 ounces for each gallon of water.

Aqua Acidi Carbonici, *Carbonic Acid Water,* or *Soda Water* (so called), (*Aqua acidula simplicior,* F. P.; *Eau gazeuse simple,* Fr.; *Kohlensaurewasser,* G.), which was formerly official in the U. S. Pharmacopœia, consists of water highly charged with carbonic acid.

Preparation.—Water is found to take up its volume of this gas under the pressure of the atmosphere; and Henry ascertained that precisely the same *volume* of the compressed gas is absorbed under a higher pressure. From this law, the bulk taken up is constant, the quantity being different in proportion as there is more or less driven into a given space. As the space occupied by a gas is inversely as the compressing force, it follows that the quantity of the acid forced into the water will be directly as the pressure. From the principles above laid down it follows that, to saturate water with five times its volume of carbon dioxide, it must be subjected to a pressure of five atmospheres. Carbonic acid gas compressed into the liquid state is now manufactured on an immense scale and supplied in 20-pound and 50-pound steel cylinders. This allows of convenient transportation, and the purity of the gas is usually excellent.

Carbonic acid water is familiarly called in this country "*mineral water,*" "*plain soda,*" and "*soda water*"; the latter names originally applied to the preparation when it contained sodium carbonate, being from habit continued since the alkali has been omitted.

Carbonic acid water is dispensed in most of the pharmacies in this country. The fountain is usually placed in the cellar, and the tube proceeding from the fountain is made to pass through the floor and counter of the store, and to terminate in a draught tube, by means of which the carbonic acid water may be drawn off at pleasure. In order to have the liquid cool, the tube from the cellar generally terminates in a strong metallic vessel of convenient shape, or a series of block tin pipes called coolers, placed inside the counter apparatus, and surrounded with ice.

Properties.—Carbonic acid water is a sparkling liquid, possessing an agreeable, pungent, acidulous taste. It reddens litmus deeply from its state of concentration, and is precipitated by lime water in excess. Being impregnated with a large quantity of the acid gas under the influence of pressure, it effervesces strongly when freed from restraint. Hence, to preserve its sparkling qualities, it should be kept in strong vessels or in strong, well-corked bottles placed inverted in a cool place. Several natural waters contain an excess of carbonic acid, such as those of Seltzer, Spa, Pyrmont, Apollinaris, etc., but the artificial water has the advantage of a stronger impregnation with the acid gas. Carbonic acid water should be made with every precaution to avoid metallic impurity. Hence the necessity of having the fountain well protected on the inner surface. Even with this precaution, a slight metallic impregnation is not always avoided, especially in the winter season, when the water is less consumed as a drink, and, therefore, allowed to remain longer in the tubes and stop-cocks. Iron fountains lined with a hard enamel are preferred to those of copper, but the best fountains are made of cast steel, lined with block tin. When leaden tubes are employed to convey the water, it is liable to be contaminated with this metal, which renders it deleterious. Tubes of pure tin are free from objection, and should be exclusively used.

Copper fountains, well tinned, are liable to the objections that the tin lining wears away by use, and that there is no convenient means of inspecting the interior, owing to the solder joint which permanently unites the two sections of the fountain. Sometimes drops of solder and chips of copper are carelessly left in the fountain, and form an additional source of danger. There can be no doubt that carbonic acid water is not unfrequently rendered poisonous by metallic impregnation. R. O. Doremus has proved by a chemical examination that lead and copper are sometimes present. Lead is detected by hydrogen sulphide, which gives with it a black precipitate, and copper by potassium ferrocyanide, which causes a brown precipitate. In testing for copper, a few drops of the reagent should be added to a glass of the suspected water, placed on a sheet of white paper,

when, if even a minute proportion of copper be present, a brownish discoloration will be seen, upon looking down through the liquid. Fortunately copper fountains have largely gone out of use, having been supplanted by those made of steel.

Uses.—Carbonic acid water is a grateful drink to *febrile patients*, allaying thirst, lessening *nausea* and *gastric distress*, and promoting the secretion of urine. The quantity taken need only be regulated by the reasonable wishes of the patient. It also forms a very convenient vehicle for the administration of magnesia, the carbonated alkalies, magnesium sulphate, and the saline cathartics generally, rendering these medicines less unpleasant to the palate, and, in irritable states of the stomach, increasing the chances of their being retained. When used for this purpose, six or eight fluidounces (180–240 mils) will be sufficient.

AQUA AMMONIÆ. U. S. (Br.)

AMMONIA WATER Aq. Ammon.

(ā'quą ąm-mō'nĭ-æ)

"An aqueous solution of ammonia [$NH_3 = 17.03$] containing not less than 9.5 per cent. nor more than 10.5 per cent. by weight of NH_3. This solution deteriorates on keeping, and must be tested frequently. Preserve it in a cool place in glass-stoppered bottles made of hard glass free from lead." *U. S.* "Solution of Ammonia is an aqueous solution containing 10 per cent. by weight of ammonia, NH_3." *Br.*

Liquor Ammoniæ, *Br.*; Solution of Ammonia; Water of Ammonia; Spiritus Salis Ammoniaci Causticus, Ammoniaque liquide officinale, *Fr. Cod.*; Eau (Solution, Liqueur) d'Ammoniaque, *Fr.*; Liquor Ammonii Caustici, *P. G.*; Salmiakgeist, Aetzammoniak, Ammoniak-Flüssigkeit, *G.*; Ammoniaca, *It.*; Amoniaco, Amoniaco liquido, *Sp.*

The U. S. Pharmacopœia IX omits a process for preparing Ammonia Water. The U. S. P., 1870, contains an excellent process, which is as follows: "Take of Chloride of Ammonium, in small pieces, Lime, each, *twelve troyounces;* Water, *six pints;* Distilled Water, *a sufficient quantity*. Pour a pint of the Water upon the Lime, in a convenient vessel; and, after it has slaked, stir the mixture so as to bring it to the consistence of a smooth paste. Then add the remainder of the Water, and mix the whole thoroughly together. Decant the milky liquid from the gritty sediment into a glass retort, of the capacity of sixteen pints, and add the Chloride of Ammonium. Place the retort on a sand-bath, and adapt to it a receiver purposely connected with a two-pint bottle, by means of a glass tube, reaching nearly to the bottom of the bottle, and containing a pint of Distilled Water. Surround the bottle with ice-cold water; and apply heat, gradually increased, until ammonia ceases to come over. Remove the liquid from the bottle, and add to it sufficient Distilled Water to raise its specific gravity to 0.960. Lastly, keep the liquid in small bottles, well stopped."

"Strong Solution of Ammonia, 500 millilitres; Distilled Water, 1000 millilitres. Mix." *Br.*

The title of this preparation was changed, at the revision of the U. S. Pharmacopœia in 1860, from Liquor Ammoniæ to Aqua Ammoniæ, that it might conform in name as well as character with the Waters, among which the official preparations consisting of aqueous solutions of gaseous bodies are included. In the revision of 1890 the English name was changed from Water of Ammonia to Ammonia Water.

In the U. S. P., 1870, process the ammonium chloride is decomposed by the superior affinity of the lime for its acid, ammonia is disengaged, and the lime, combining with the acid, forms calcium chloride and water,

$$2NH_4Cl + Ca(OH)_2 = CaCl_2 + 2H_2O + 2NH_3$$

This differs from the former process in introducing the materials into the retort with a large quantity of water, instead of in the dry state. In both cases the gas is driven over by heat, but in the moist plan it is accompanied with more aqueous vapor than in the dry. If the object were to obtain ammonia water in the highest concentrated state, there might be some advantage in the dry method; but, as a weak solution is contemplated, the wet method is equally efficient, while in all respects it is more convenient, and productive of better results, for, according to E. R. Squibb, the ammonia water made by the older official process has invariably an empyreumatic odor, from which that made by the present process is free. The receiver is intended to retain any water holding in solution undecomposed chloride, or the oily matter sometimes contained in the salt, as well as other impurities, which may be driven over by the heat while the pure gas passes forward into the bottle containing the distilled water, which should not fill it, on account of the increase in the bulk of the water during the absorption of the gas. The tube should extend to near the bottom of the bottle, and pass through a cork loosely fitting its mouth. To prevent the regurgitation of the water from the bottle into the intermediate vessel, the latter should be furnished with a Welter's safety tube.

In preparing solution of ammonia, equal weights of ammonia chloride and lime are used for generating the gaseous ammonia. This proportion gives a great excess of lime, compared with the quantity required if determined by the molecular weights; but in practice it is found advantageous to have an excess, in order to insure the full decomposition of the ammonium chloride, as well as to make up for accidental impurities in the lime.

The British Pharmacopœia gives directions for diluting *Liquor Ammoniæ Fortis* so as to reduce it to the strength of *Liquor Ammoniæ*. This is effected by mixing one measure of their stronger preparation with two measures of distilled water. The ammonia water of commerce is sometimes known as "Aqua Ammoniæ F. F. F.," or "20° ammonia"; it may be diluted by adding 2 volumes of water to 4 volumes of 20° ammonia water to make official ammonia water. Ammonia water of other strengths may be diluted

by consulting the table given on page 168, and applying the rules given in Remington's *Practice of Pharmacy*, 5th ed., p. 98.

Ammonia water of the various commercial strengths is one of the few substances which continue to be designated by strength in terms of the specific gravity expressed in degrees Baumé. Thus "*16° ammonia*" is equivalent to 10 per cent., and "*26° ammonia*" is equivalent to 28 per cent.

Properties.—Ammonia water is "a colorless, transparent liquid, having a very pungent characteristic odor and a caustic, alkaline taste. Dense white fumes are produced on bringing a glass rod, dipped into hydrochloric acid, near the surface of Ammonia Water. Ammonia Water is strongly alkaline to litmus. Specific gravity: about 0.958 at 25° C. (77° F.). Add 0.1 mil of tenth-normal potassium permanganate V.S. to 10 mils of Ammonia Water, which has been slightly supersaturated with diluted sulphuric acid; the pink color is not completely destroyed within ten minutes (*oxidizable and empyreumatic substances*). When neutralized and made slightly acid with hydrochloric acid, 10 mils of Ammonia Water does not respond to the Test for heavy metals (see Part III, Test No. 3). Twenty-five mils of Ammonia Water, when evaporated to dryness in a platinum or porcelain dish and heated to constant weight at 120° C. (248° F.), leaves not more than 0.005 Gm. of residue.

"**Assay.**—Pour about 5 mils of Ammonia Water into a tared, stoppered weighing-bottle containing about 10 mils of distilled water and weigh accurately. Dilute the liquid with 50 mils of distilled water and titrate with normal sulphuric acid V.S., using litmus or methyl orange T.S., as indicator. It shows not less than 9.5 per cent. nor more than 10.5 per cent., by weight, of NH_3.

"Each mil of normal sulphuric acid V.S. used corresponds to 0.01703 Gm. of NH_3. Each gramme of Ammonia Water corresponds to not less than 5.57 mils nor more than 6.16 mils of normal sulphuric acid V.S." *U. S.*

"Specific gravity 0.959. 3 grammes require for neutralisation 17.6 millilitres of *N/1 solution of sulphuric acid.* Responds in other respects to the tests and possesses the general characters described under 'Liquor Ammoniæ Fortis.'" *Br.*

Ammonia Water is incompatible with acids, and with acidulous and many earthy and metallic salts; but it does not decompose the salts of lime, barium, or strontium, and only partially decomposes those of magnesium. Commercial solution of ammonia sometimes contains *pyrrol, naphthalene, aniline,* and *pyridine.* These may be detected by the solution being reddened by nitric acid, and, after having been supersaturated with hydrochloric acid, by its tingeing a slip of fir wood a rich purple color, characteristic of pyrrol. (Maclagan.) The source of these impurities is coal gas liquor, from which the ammonia compounds are largely obtained. Donath (*Dingler's Polytechnisches Journal,* vol. iv, p. 229) tested some ammonia prepared from gas liquor, by neutralizing with diluted sulphuric acid, when the liquid assumed a rose color, and a solution of the sulphate emitted the characteristic odor of naphthalene.

According to Eber (*Ph. Centralb.,* 1892, 238) the well-known test for ammonia of exposing a glass rod dipped into hydrochloric acid to the fumes, is rendered more sensitive by using a mixture of hydrochloric acid 1 part, alcohol 3 parts, and ether 1 part, shaken together.

Composition.—Water is capable of absorbing 670 times its volume of ammonia gas at 10° C. (50° F.), and increases in bulk about two-thirds. But the official solution of ammonia is by no means a saturated one. Thus, the ammonia contained in the strongest U. S. preparation is about 28 per cent. The official table on page 168 gives the percentage of ammonia gas in aqueous solutions of different densities at the temperatures of 25° C. (77° F.) and 15° C. (59° F.).

Uses.—When brought into contact with living tissue ammonium hydroxide acts as a stimulant, irritant, or caustic according to the strength of its solution. The official water of ammonia if applied for a short time to the skin produces burning pain and redness, but if contact be maintained is capable of destroying the whole dermal tissue. The irritant effects of ammonia water are due to the hydroxyl ion, not to the ammonium. When injected into the circulation the water of ammonia produces the characteristic effects of the ammonium salts but for the reasons pointed out on page 132 it cannot be absorbed from the stomach in sufficient quantity to exercise any direct influence upon the general system. It is, however, often of service in sudden *syncope,* especially of nervous origin, even when given by the mouth. Its effects under these circumstances are due to the reflex stimulation of the vasomotor center from the irritation of the gastric mucous membrane. Still more marked action of the same nature may be elicited by smelling the fumes which arise from the ammonia water. When injected hypodermically, however, it is a powerful direct stimulant to the heart and vasomotor system, although somewhat fleeting in its effects. It was at one time brought forward as an antidote for *snake-venom,* but the only value it has in this condition is due to its stimulant effect upon the circulation. It is widely employed to correct *hyperacidity of the stomach,* especially where a local stimulant as well as an antacid effect is required.

In serious *collapse,* as pointed out above, it is necessary to inject the ammonia hypodermically, or better, intravenously. Half a drachm to a drachm diluted with half an ounce to an ounce of water may be slowly thrown directly into a vein. In some cases the drug has been simply used hypodermically, but is almost certain to cause severe local symptoms. On account of its cheapness, ammonia water is much used as an ingredient in stimulating liniments, especially combined with olive or other oil.

Table of Percentage and Specific Gravity of Ammonia. U. S. P. IX.

Per Cent NH_3	Sp. gr. app. 25° C. / 25° C.	Sp. gr. app. 15° C. / 15° C.	Correction of specific gravity for 1° C.*	Fractional per cent.†	Normality. 1 mil requires normal HCl mils.	Per cent. = 0.01 mil normal HCl.
‡0	1.00000	1.00000	0.00017	0.0227	0.000	0.0172
1	0.99560	0.99573	0.00018	0.0230	0.583	0.0173
2	0.99126	0.99151	0.00020	0.0233	1.160	0.0175
3	0.98696	0.98735	0.00021	0.0236	1.733	0.0176
4	0.98272	0.98324	0.00023	0.0239	2.301	0.0178
5	0.97854	0.97918	0.00024	0.0240	2.864	0.0179
6	0.97437	0.97517	0.00026	0.0243	3.422	0.0181
7	0.97025	0.97121	0.00028	0.0246	3.976	0.0182
8	0.96618	0.96730	0.00029	0.0249	4.525	0.0184
9	0.96216	0.96344	0.00030	0.0252	5.069	0.0185
10	0.95819	0.95964	0.00032	0.0267	5.609	0.0186
11	0.95445	0.95604	0.00033	0.0270	6.146	0.0188
12	0.95074	0.95249	0.00035	0.0273	6.679	0.0189
13	0.94708	0.94898	0.00036	0.0276	7.207	0.0190
14	0.94346	0.94551	0.00037	0.0279	7.732	0.0192
15	0.93987	0.94208	0.00039	0.0282	8.253	0.0193
16	0.93633	0.93869	0.00040	0.0286	8.770	0.0195
17	0.93283	0.93533	0.00042	0.0289	9.283	0.0196
18	0.92937	0.93202	0.00043	0.0292	9.793	0.0198
19	0.92594	0.92874	0.00045	0.0295	10.299	0.0199
20	0.92255	0.92550	0.00046	0.0295	10.801	0.0200
21	0.91916	0.92230	0.00047	0.0299	11.300	0.0202
22	0.91581	0.91914	0.00049	0.0301	11.796	0.0204
23	0.91249	0.91601	0.00050	0.0307	12.287	0.0205
24	0.90923	0.91292	0.00052	0.0309	12.776	0.0206
25	0.90599	0.90987	0.00053	0.0317	13.262	0.0207
26	0.90286	0.90685	0.00055	0.0321	13.744	0.0209
27	0.89974	0.90385	0.00057	0.0324	14.223	0.0210
28	0.89665	0.90087	0.00058	0.0326	14.699	0.0212
29	0.89358	0.89791	0.00059	0.0329	15.171	0.0213
30	0.89054	0.89498	0.00060	0.0339	15.640	0.0214
31	0.88759	0.89212	0.00061	0.0353	16.108	0.0214
32	0.88476	0.88938	0.00062	0.0368	16.575	0.0215
33	0.88204	0.88674	0.00063	0.0382	17.040	0.0215
34	0.87942	0.88421	0.00064	0.0394	17.505	0.0216
35	0.87688	0.88176	0.00064	.....	17.968	.....

* Add if the temperature is above, subtract if it is below, the standard.

† Corresponding with a difference in specific gravity of 0.0001.

‡ The figures in this line across the page are for fractional percentages below 1.

NOTE: To find the per cent. of NH_4 multiply the per cent. of NH_3 by 1.0592. To find the volume per cent. of official Ammonia Water (10 per cent.) multiply the "normality" by 17.83. For the volume per cent. of official Stronger Ammonia Water (28 per cent.), multiply the "normality" by 6.803.

Toxicology.—The symptoms of poisoning by ammonia are solely those of local irritation: pain in the mouth, throat, and epigastrium; vomiting and collapse from the severity of the gastritis. In some cases the irritation of the throat is so severe as to produce an acute edema of the glottis which may mechanically obstruct respiration, and rapid death from asphyxia has occurred. In the treatment of the condition, diluted acetic acid in the form of vinegar may be used as an antidote; olive oil or other fatty substance is useful not only because it combines with the caustic alkali to form a comparatively non-irritant soap, but also by virtue of its local soothing action upon the inflamed mucosa. In case of edema of the larynx tracheotomy is indicated; it should not be forgotten that this accident may be postponed for an hour or two after the ingestion of the poison and the physician should remain ready for immediate operation if necessary. The subsequent treatment is purely symptomatic.

Dose, ten to thirty minims (0.6–1.8 mils), largely diluted.

Off. Prep.—Linimentum Ammoniæ, *U. S., Br.;* Linimentum Hydrargyri, *Br.;* Lotio Ammoniacalis Camphorata, *N. F.;* Spiritus Ammonii Aromaticus, *U. S.;* Linimentum Opii Compositum, *N. F.;* Linimentum Saponato-Camphoratum, *N. F.;* Spiritus Ammonii Anisatus, *N. F.*

AQUA AMMONIÆ FORTIOR. U. S. (Br.)

STRONGER AMMONIA WATER Aq. Ammon. Fort.

(ă'quą ąm-mō'nĭ-æ för'tĭ-ǫr)

"An aqueous solution of ammonia [NH_3 = 17.03] containing not less than 27 per cent. nor more than 29 per cent., by weight, of NH_3. This solution deteriorates on keeping, and must be tested frequently. Preserve it in a cool place in partially filled, strong, glass-stoppered bottles made of hard glass free from lead. *Great caution should be used in handling this liquid.*" *U. S.* "Strong Solution of Ammonia is an aqueous solution containing 32.5 per cent. by weight of ammonia, NH_3. It may be obtained by heating a mixture of ammonium chloride and slaked lime, and passing the resulting ammonia into distilled water." *Br.*

Liquor Ammoniæ Fortis, *Br.*; Strong Solution of Ammonia; Eau d'Ammoniaque forte, *Fr.*; Stärker Salmiakgeist, *G.*

This preparation is too strong for internal exhibition, but forms a convenient ammonia solution for reduction, by dilution with two measures of distilled water, to the strength of ordinary Ammonia Water, or for preparing strong rubefacient liniments.

The U. S. Pharmacopœia does not give a process. The process of the British Pharmacopœia (1885) will be found in detail in the U. S. D., 17th ed., p. 202.

Stronger Ammonia Water is seldom made by this process, but is prepared on a large scale, from one of the products of the coal gas manufacture, by the more economical process of distilling *gas liquor;* the distillate, which is principally ammonium sulphide, is then converted into ammonium sulphate by sulphuric acid. The sulphate is gently distilled with milk of lime, the still being connected with a series of glass carboys, arranged like Woulf's bottles, and three-fourths filled with distilled water. In this way solution of ammonia may be obtained of maximum strength. It is also made by diluting the concentrated liquid ammonia.

Anhydrous liquefied ammonia is now an article of commerce, being used on a large scale in the manufacture of artificial ice and in refrigerating plants, where the cold produced by its rapid evaporation under a partial vacuum is utilized to furnish the necessary lowering of temperature. The apparatus used for its production is almost identical with that employed in the manufacture of liquid carbon dioxide, and consists of a combination of vacuum and condensing pumps. The gas is obtained from the strongest ammonia water by heating, with application of a partial vacuum, and must be well dried before the compression. To obtain a pure product, it has been found best to allow the liquefied ammonia to expand several times in a gasometer, in which case, the larger part of the impurities are left behind in liquid form. These consist of water, alcohol, acetone, traces of the lubricating oil from the compressing pumps, and a little ammonium carbonate. In ammonias made from the distillation of bones, pyridine is also found to occur as an impurity. Liquefied ammonia comes into commerce in steel cylinders which have been tested to stand 100 atmospheres internal pressure, and are provided with well fitting screw valves. Anhydrous ammonia is said to dissolve metallic sodium, and the solution is intensely blue. (*Chem. News,* Nov. 4, 1870, p. 217.)

Properties of Stronger Ammonia Water.—This has similar properties to those above mentioned. Its sp. gr. is 0.897 at 25° C. (77° F.), *U. S.,* 0.888 at 15.5° C. (59.9° F.), *Br.* When of the former density, it contains 28 per cent. of the gas; when of the latter, 32.5 per cent. It is "a colorless, transparent liquid, having an excessively pungent, characteristic odor and a very caustic and alkaline taste. *Stronger Ammonia Water must never be tasted unless greatly diluted.* Stronger Ammonia Water is strongly alkaline to litmus. Specific gravity: about 0.897 at 25° C. (77° F.). Stronger Ammonia Water, when diluted with twice its volume of distilled water, responds to the tests for identity and purity under *Aqua Ammoniæ.*

"**Assay.**—Pour about 2 mils of Stronger Ammonia Water into a tared flask containing about 50 mils of distilled water, weigh accurately, and titrate with normal sulphuric acid V.S., using litmus or methyl orange T.S. as indicator. It shows not less than 27 per cent. nor more than 29 per cent., by weight, of NH_3.

"Each mil of normal sulphuric acid V. S. used corresponds to 0.01703 Gm. of NH_3. Each gramme of Stronger Ammonia Water corresponds to not less than 15.8 mils nor more than 17 mils of normal sulphuric acid V.S." *U. S.*

"A colorless liquid, with a characteristic, very pungent odor. Strongly alkaline. Specific gravity 0.888. 1 gramme requires for neutralisation 19.1 millilitres of *N/1 solution of sulphuric acid.* When mixed with an equal volume of *water* and a slight excess of *sulphuric acid* no color or odor is developed (absence of tarry matters). Yields no characteristic *reactions* for aluminium, zinc, calcium, magnesium, potassium, sodium, carbonates, sulphates, or sulphides, and only the slightest *reactions* for chlorides. 0.5 millilitre of *solution of sodium sulphide* added to 50 millilitres of Strong Solution of Ammonia contained in a Nessler glass produces no change of color (absence of copper, iron, and lead). *Arsenic limit* 0.5 part per million. Leaves no appreciable residue on evaporation." *Br.*

The stronger ammonia water of commerce usually ranges in density from 0.900 to 0.920. Even when of proper official strength at first, it gradually becomes weaker by the escape of ammonia. To prevent its deterioration, it should be kept in closely-stoppered bottles in a cool place.

When purchasing Stronger Ammonia Water the pharmacist should not trust to its being of the official strength, but should ascertain the point by taking its density, either by the specific gravity bottle or the hydrometer. Another

method of ascertaining its density is by the *ammonia-meter* of J. J. Griffin, of London, described and figured in *P. J.* (x, 413). Although the U. S. Pharmacopœia states that "if stronger ammonia water be diluted with twice its volume of distilled water it should respond to the reactions and tests described under *Aqua Ammoniæ*," it will be usually found in practice that two volumes of water will be too much; in any event it is safer to use a smaller quantity of water (one and a half volumes), and, if the mixture should not have the sp. gr. 0.958, it should be brought to that density by the addition either of the stronger solution or of distilled water, as the case may require. *Great care should be exercised in opening bottles containing stronger ammonia water.* It is safer, if the ammonia water has been kept in a warm room, to cool it with ice before attempting to withdraw the stopper, as the liberated gas, when warm, frequently is forced out with extreme violence, and accidents which have resulted in injury to the sight of the operator are recorded.

Uses.—This solution is too strong for medicinal use in its unmixed state. Sufficiently diluted with spirit of camphor and rosemary, it was formerly much employed as a prompt and powerful rubefacient, vesicatory, or escharotic, in various *neuralgic, gouty, rheumatic, spasmodic,* and *inflammatory affections* in which strong and speedy counter-irritation is indicated. When mere rubefaction is desired five parts of the stronger ammonia water may be mixed with eight parts of the diluent. This will answer even for blistering or cauterizing, unless a very prompt effect be necessary. In the latter case a lotion may be resorted to consisting of five measures of the ammonia to three of the diluent liquid. These mixtures are applied by means of linen folded several times, or a thick piece of flannel saturated with the liniment. A convenient mode of applying is to fill the wooden cover of a pill or ointment box, an inch or two in diameter, with purified cotton, saturate this with the liquid, and press it upon the part. The ammonia is thus prevented from escaping, and a definite boundary given to the inflammation. The application will generally produce rubefaction in from one to eight minutes, vesication in from three to ten minutes, and a caustic effect in a somewhat longer time.

When a solution of ammonia of 25° C. (77° F.) (sp. gr. 0.905) is mixed with fatty matter, the mixture forms the *vesicating ammoniacal ointment* of Gondret. The revised formula of this ointment is as follows: Take of lard 32 parts, oil of sweet almond 2 parts. Melt them together by a *gentle* heat, and pour the melted mixture into a bottle with a wide mouth. Then add 17 parts of solution of ammonia of 25° C. (77° F.), and mix with continued agitation until the whole is cold. The ointment must be preserved in a bottle with a ground stopper, and kept in a cool place. When well prepared, it vesicates in ten minutes. There may be danger of excessive irritation and inflammation of the nostrils, mouth, and air passages, from the inadvertent inhalation of the gas escaping from a bottle of the stronger ammonia water, when freshly opened; and serious consequences have occurred from this cause, or from the accidental breaking of the bottle. The best antidote, under these circumstances, is the inhalation of the vapors of vinegar or acetic acid.

Dose, three to six minims (0.2–0.4 mil), largely diluted.

Off. Prep.—Linimentum Camphoræ Ammoniatum, *Br.;* Liquor Ammoniæ, *Br.;* Spiritus Ammoniæ Aromaticus, *Br.;* Spiritus Ammoniæ Fetidus, *Br.*

AQUA AMYGDALÆ AMARÆ. U. S.

BITTER ALMOND WATER Aq. Amygd. Amar.

(ă'quą ą-mŷg'dą-læ ą-mā'ræ)

Eau d'Amandes ameres, *Fr.;* Aqua Amygdalarum Amararum, *P. G.;* Bittermandelwasser, *G.;* Acqua distillata di mandorle amare, *It.;* Agua de almendras amargas, *Sp.*

* "Oil of Bitter Almond, *one mil* [or 16 minims]; Distilled Water, recently boiled, *nine hundred and ninety-nine mils* [or 33 fluidounces, 6 fluidrachms, 14 minims], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the oil of bitter almond in the recently boiled distilled water by agitation, and filter. Note: Bitter Almond Water contains a mere trace of hydrocyanic acid and differs from the preparation of the same name, recommended by the International Protocol, 1906, which contains 0.1 per cent. of hydrocyanic acid." *U. S.*

Owing to the almost universal employment at this time of artificial oil of bitter almond (or benzaldehyde), which is free from hydrocyanic acid (such oil being much cheaper than that made from bitter almond), the bitter almond water of pharmacy cannot be relied upon as a medicinal agent, but is used mainly as a pleasant vehicle, but the requirements of the U. S. P. IX are that the oil of bitter almond shall contain not less than 85 per cent. of benzaldehyde, and not less than 2 per cent. nor more than 4 per cent. of hydrocyanic acid, hence the use of benzaldehyde (see *Benzaldehydum*) is no longer permissible and care must be exercised not to prescribe a larger dose of the water to begin with than two teaspoonfuls (7.5 mils). Its principal use in this country is as a vehicle, many physicians prescribing it not for its medicinal virtues, but on account of its agreeable taste and powers of masking the taste of saline substances. The process for *Aqua amygdalarum amararum* of the German Pharmacopœia directs that 12 parts of bruised bitter almonds shall be expressed without heat, so as to remove as much fixed oil as possible; the press-cake is powdered, mixed thoroughly with 20 parts of water, and 9 parts distilled off into a receiver containing 3 parts of alcohol; the distillate is assayed to determine the percentage of hydrocyanic acid, and then diluted with a mixture of 1 part of alcohol and 3 parts of water, so that 1000 parts of the final product shall contain 1 part of hydrocyanic acid.

Under the name of *chloral hydrocyanate* a substance has been introduced for making cherry-laurel or bitter almond water extemporaneously. It occurs in white, translucent, rhombic prisms, soluble in water, alcohol, and ether. It has the odor of hydrocyanic acid and chloral, and is said to be a very stable compound. A solution of 6.5 grains of the salt in 1000 grains of distilled water corresponds with the official bitter almond water of the German Pharmacopœia, which is 1 to 1000. (*Merck's Bulletin.*)

For a method of determining the amount of hydrocyanic acid in bitter almond water, see *A. Pharm.*, Nov., 1878, 408; *A. J. P.*, Feb., 1879; *Zeit. Oest. Apoth. Ver.*, 1893, 45, 344, 387, 391.

Dose, one fluidrachm (3.75 mils).

AQUA ANETHI. Br.

DILL WATER

(ă'quạ ạ-nē'thī)

Eau d'Aneth, *Fr.;* Dillwasser, *G.*

"Dill Fruit, 100 *grammes;* Water, 2000 *millilitres.* Distil one thousand millilitres. In preparing this and other similar aqueous liquids by distillation, only good natural potable water must be employed, as directed for 'Distilled Water.'" *Br.*

"This Water may be prepared by triturating the oil of dill with twice its weight of calcium phosphate and five hundred times its volume of distilled water and filtering the mixture. In tropical and subtropical parts of the Empire this Water way be used in placed of the corresponding Water of the text of the British Pharmacopœia." *Br.*

This water, which is frequently prescribed in Great Britain, is occasionally used here; it closely resembles caraway water, over which it has no advantages. It is used only as a vehicle.

AQUA ANISI. U. S., Br.

ANISE WATER Aq. Anisi

(ă'quạ ạ-nī'sī)

Eau d'Anis, *Fr.;* Aniswasser, *G.;* Acqua distillata di anice, *It.;* Agua de anis, *Sp.*

* "Oil of Anise, *two mils* [or 32 minims]; Purified Talc, *fifteen grammes* [or 231 grains]; Distilled Water, recently boiled, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Triturate the Oil of Anise with the Purified Talc, add the recently boiled Distilled Water gradually with continued trituration, filter, and pass the filtrate through the filter repeatedly until the Anise Water is perfectly clear." *U. S.* See also *Aquæ Aromaticæ,* page 179.

"Anise Fruit, 100 *grammes;* Water, 2000 *millilitres.* Distil one thousand millilitres." *Br.*

"This water may be prepared by triturating the oil of anise with twice its weight of calcium phosphate and five hundred times its volume of distilled water and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

Anise water is rarely made by distillation, although the product thus secured has a more delicate flavor than the U. S. preparation. It is used solely as a vehicle.

AQUA AURANTII FLORUM. U. S. (Br.)

ORANGE FLOWER WATER Aq. Aurant. Flor.

(ă'quạ âu-răn'tĭ-ī flō'rŭm)

Aqua Aurantii Floris, *Br.,* Aqua Florum Naphæ; Eau distillée (Hydrolat) de Fleurs d'Oranger, *Fr. Cod.;* Eau de Naphe, *Fr.;* Orangenblüthenwasser, *G.;* Acqua distillata di arancio, *It.;* Agua destilada de azahar, *Sp.*

* "Stronger Orange Flower Water, Distilled Water, recently boiled, each, *one volume.* Mix them immediately before use. Orange Flower Water complies with the tests for identity and purity given under *Aqua Aurantii Florum Fortior." U. S.* "Orange-flower Water is the orange-flower water of commerce, prepared by distillation from the flowers of the Bitter Orange tree, Citrus Aurantium, var. Bigaradia, *Hook., f.,* diluted, immediately before use, with twice its volume of Distilled Water." *Br.*

The U. S. Pharmacopœia, 1890, and the U. S. P. VIII and IX introduced "Stronger Orange Flower Water," providing for its dilution with an equal volume of distilled water to make "orange flower water." This plan enables American pharmacists to employ the imported "triple" water, as it is known in commerce. This retains its fragrance longer than a weaker water; moreover, economy is effected through saving customs duty and freight, and a fresh, delicate water can be dispensed.

"Colorless or with a slight yellowish tint; odor very fragrant. Yields no *reactions* for lead or copper. The orange-flower water of commerce is a saturated solution of the volatile oil of the fresh flowers." *Br.*

This preparation is also considered by the British Pharmacopœia as an object of importation. According to this authority, it is obtained from the flowers of the bitter orange tree; this is concurred in by our own official standard. In Italy and France, where it is largely made, the flowers of the bitter orange have long been preferred, as yielding the most fragrant product. It may be prepared in the most southern districts of our country from the fresh flowers; and these may be brought to the North for the same purpose, if previously incorporated with one-third or one-fourth of their weight of common salt. The proper method is to arrange the flowers and salt in successive layers in jars of stoneware or glass. They may also be preserved by means of glycerin. Notwithstanding, however, the facility of preparing this water here, it is generally imported from the south of France, whence it usually comes in cans of tinned copper.

L. Malenfant observed that fresh orange flowers, mixed with cold water, yield, on distillation over the naked fire, a milky water,

possessing a somewhat empyreumatic odor and a strong, somewhat acrid taste. Kept for twelve or eighteen months in glass vessels covered with parchment, it loses its empyreuma, and after filtering has an agreeable odor and taste. If the flowers be mixed with boiling water and immediately distilled, the water is limpid, and gradually separates some thick oil of a brownish color; the water has the odor and taste of the flowers, but complicated with an odor of the still, which it loses after long keeping; it seems to alter less rapidly than that obtained by the former process. Distilled by steam, limpid water of a pure odor and taste it at once obtained, free from empyreuma; it may be at once used, and keeps better in the light than when obtained by the two former processes. (*A. J. P.*, June, 1874.) Hesse and Zeitschel (*J. Pr. Chem.*, 1901, 525) found by exhausting with ether the orange flower water obtained in the distillation of the orange blossoms that the quantity of oil dissolved in the water represented about one-third of the total amount of oil from the blossoms. A distilled water of the leaves is also prepared, and sometimes a mixture of the leaves and flowers is employed. But this is a fraud, as the distilled water of the leaves never has the sweet perfume of that of the flowers. (*J. P. C.*, 4e sér., iii. 249.) Orange flower water is used exclusively on account of its agreeable odor as a flavoring agent.

Orange flower water is stored in large glass vessels or carboys in cool cellars by the manufacturers in Grasse, France, care being taken not to stopper them tightly, but simply cover the orifice with a piece of paper or coarse cloth.

Nitric, sulphuric, or hydrochloric acid produces a red coloration with orange flower water, particularly if the water be shaken with ether to take up the oil, and the acid added to the ethereal solution. (*P. J.*, 1878, 248.) It is used as a vehicle, and to flavor syrups and elixirs.

Off. Prep.—Syrupus Aurantii Florum, *U. S.*

AQUA AURANTII FLORUM FORTIOR. U. S. (Br.)

STRONGER ORANGE FLOWER WATER

Aq. Aurant. Flor. Fort. [Triple Orange Flower Water]

(ā'quạ âu-răn'tī-ī flō'rŭm fōr'tī-ọr)

"The saturated aqueous distillate prepared by distilling the fresh flowers of *Citrus Aurantium amara* Linné (Fam. *Rutaceæ*) with water. Preserve it in bottles stoppered with a pledget of purified cotton and in a dark, cool place." *U. S.* The orange flower water of commerce is a saturated solution of the essential oil of the fresh flowers, and the British Pharmacopœia uses this in several preparations, terming it "Orange-flower water of commerce, undiluted." (See *Aqua Aurantii Florum*, p. 171.)

Orange flower water is nearly colorless, though often of a pale yellowish tint. "Stronger Orange Flower Water is colorless and clear or only faintly opalescent, and possesses a strong and pleasant odor and taste of orange blossoms, and must be free from empyreuma, mustiness, or mucoid growths. It is neutral or only slightly acid to litmus, and 100 mils, when evaporated to dryness on a water bath and the residue subsequently dried in an oven to constant weight at 100° C. (212° F.), yields not more than 0.001 Gm. of residue. It gives no reaction with hydrogen sulphide T.S. or with sodium sulphide T.S. (*metallic impurities*)." *U. S.* From being kept in tinned copper cans, it sometimes contains metallic impurity, which is said to be chiefly lead carbonate, derived from the lead used as a solder in making the cans. The means of detecting metallic impurity is also mentioned under the general observations on distilled water. Much color, offensive odor, or mouldiness indicates impurity derived from the flowers in distillation.

Off. Prep.—Aqua Aurantii Florum, *U. S.;* Syrupus Aurantii Floris, *Br.;* Elixir Amygdalæ Compositum, *N. F.;* Elixir Aurantii Amari, *N. F.;* Elixir Glycyrrhizæ Aquosum, *N. F.*

AQUA CAMPHORÆ. U. S., Br.

CAMPHOR WATER Aq. Camph.

(ā'quạ căm'phọ-ræ)

Aqua Camphorata; Eau camphrée, *Fr. Cod.;* Kampherwasser, *G.;* Agua alcanforada, *Sp.*

* "Camphor, *eight grammes* [or 123½ grains]; Alcohol, *eight mils* [or 130 minims]; Purified Talc, *fifteen grammes* [or 231 grains]; Distilled Water, recently boiled, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Triturate the camphor with the alcohol in a mortar, add the purified talc; continue the trituration until the alcohol has evaporated and add the recently boiled distilled water. Filter the mixture, and pass the filtrate repeatedly through the filter until the Camphor Water is perfectly clear." *U. S.*

"Camphor, 1 *gramme;* Alcohol (90 per cent.), 2 *millilitres;* Distilled Water, 1000 *millilitres.* Dissolve the Camphor in the Alcohol; add the solution in successive portions to the Distilled Water, shaking after each addition; finally shake occasionally until all the Camphor is dissolved." *Br.*

In both of these processes the sole object is to effect a solution; water is capable of dissolving but a very small proportion of camphor, but the quantity varies with the method employed. The present official process is an improvement on former methods. Magnesium carbonate is to be preferred to purified talc as a distributing agent were it not for the fact that it is slightly soluble in water. The present British process is more efficient than the old formula, a definite quantity of camphor being dissolved in a small quantity of alcohol and this solution gradually added to the proper quantity of water; it is questionable, however, whether it would not be advantageous to use an insoluble powder to aid in the solution and

thus obtain quickly a clear liquid, as the water made by the British process is sometimes cloudy. In the former British process no trouble was taken even to comminute the camphor, or to shake it with the water, which was thus allowed to take up what it might be disposed to do by contact with the camphor contained in a bag. The solution thus effected was extremely feeble, containing probably less than one part in a thousand; this proportion, according to Berzelius, is taken up by water when triturated with camphor. It was, besides, of uncertain strength, varying with the size of the fragments of camphor. Wm. B. Addington proposed to add to the camphor just enough alcohol to dissolve it, and triturate the liquor with magnesia, during which process he affirmed that the alcohol evaporated (*A. J. P.*, xlv, 209); and F. T. Hartzell substituted ether for alcohol, a few drops of which enabled him to bring the camphor to an impalpable powder. John K. Thum states that in the U. S. process part of the camphor remains with the talc on the filter and proposes to make camphor water by using eight grammes of camphor in small pieces and adding it to 1000 mils of distilled water, shaking the bottle until the solution is saturated and filtering through sterilized gauze. (*Proc. Pennsylvania P. A.*, 1913, 364.) Camphor is separated from its aqueous solution by a solution of pure potassium hydroxide, and, according to Paris, by magnesium sulphate and several other salts. J. Murray proposes a solution of camphor and magnesium bicarbonate, which contains three grains of the former and six grains of the latter in each fluidounce.

Camphor water has this advantage over camphor in substance, that the latter is with difficulty dissolved by the liquors of the stomach; but it is too feeble a preparation for use when a decided effect is desired; it is, however, an excellent vehicle for the administration of more active substances.

Dose, half to one fluidounce (15–30 mils), repeated every one or two hours.

Off. Prep.—Mistura Camphoræ Acida, *N. F.*; Mistura Camphoræ Aromatica, *N. F.*

AQUA CARUI. Br.

CARAWAY WATER

(ă'quạ căr'ù-ī)

Aqua Carvi; Eau Distillée de Carvi, *Fr.*; Kümmelwasser, *G.*

"This Water may be prepared by triturating the oil of caraway with twice its weight of calcium phosphate and five hundred times its volume of distilled water and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

"Caraway Fruit, 100 *grammes;* Water, 2000 *millilitres.* Distil one thousand *millilitres.*" *Br.*

Distilled Caraway Water has the flavor of the fruit or seeds, but is seldom used in the United States. The water made from the volatile oil (16 minims in a pint), in the same manner as is cinnamon water, is largely employed. It is used only as a vehicle.

AQUA CHLOROFORMI. U. S., Br.

CHLOROFORM WATER Aq. Chlorof.

(ă'quạ ȼhlō-rọ-fôr'mī)

Eau de Chloroforme, *Fr.*; Chloroformwasser, *G.*; Agua chloroformada, *Sp.*

* "Chloroform, Distilled Water, recently boiled, each, *a sufficient quantity.* To a convenient quantity of recently boiled distilled water, contained in a dark amber-colored bottle, add enough chloroform to maintain a slight excess of the chloroform after the contents have been repeatedly and thoroughly shaken. Preserve it in a cool, dark place. When Chloroform Water is required for use, pour off the needed quantity, refill the bottle with recently boiled distilled water and saturate it by thorough agitation, taking care that there be always an excess of chloroform present." *U. S.*

"Chloroform, 2.5 *millilitres;* Distilled Water sufficient to produce 1000.0 *millilitres.* Dissolve." *Br.*

The water should be fully saturated, in which case it should contain one-half per cent. of chloroform. Chloroform water has been proved to be an excellent vehicle for administering active remedies, and, owing to its antiseptic properties, mixtures having it for a basis resist decomposition longer than those made with ordinary water.

Dose, one-half to two fluidounces (15–60 mils).

AQUA CINNAMOMI. U. S., Br.

CINNAMON WATER Aq. Cinnam.

(ă'quạ cĭn-nạ-mō'mī)

Eau distillée de Cannelle, *Fr. Cod.*; Aqua Cinnamomi, *P. G.*; Zimmtwasser, *G.*; Acqua distillata di canella, *It.*; Agua destilada de canela, *Sp.*

* "Oil of Cinnamon, *two mils* [or 32 minims]; Purified Talc, *fifteen grammes* [or 231 grains]; Distilled Water, recently boiled, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Triturate the Oil of Cinnamon with the Purified Talc, add the recently boiled Distilled Water gradually with continued trituration, filter, and pass the filtrate through the filter repeatedly until the Cinnamon Water is perfectly clear." *U. S.* See also *Aquæ Aromaticæ,* page 179.

"Cinnamon Bark, bruised, 100 *grammes;* Water, 2000 *millilitres.* Distil *one thousand millilitres.*" *Br.* "This Water may be prepared by triturating the oil of cinnamon with twice its weight of calcium phosphate and five hundred times its volume of distilled water and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

Of these processes, that of the U. S. Pharmacopœia is the easier, though the second, the British, may yield a sweeter product. On standing, cinnamon water, made from oil of Ceylon cinnamon, is apt to precipitate, owing to the gradual oxidation and formation of cinnamic acid, which is comparatively insoluble in water: this can be prevented, according to E. Backhaus, by passing a stream of carbon dioxide through the fresh water for a few minutes. We have never seen the precipitation successfully prevented, notwithstanding the application of numerous so-called preventives; these usually delay the precipitation, but in a few weeks' time the cloudiness due to the formation of minute crystals of cinnamic acid invariably appears. When oil of cinnamon (*Oleum Cassiæ*) is used as directed in the U. S. P. IX process precipitation rarely occurs. E. Holmes recommends glycerin as an excellent intermedium between the oil of cinnamon and water. Ten drops of glycerin will effect the solution of a drop of the oil in a fluidounce of water.

Cinnamon water is much used as a vehicle for other less agreeable medicines, but should be given cautiously in inflammatory affections. For ordinary purposes the U. S. preparation is sufficiently strong when diluted with an equal measure of water.

Off. Prep.—Infusum Digitalis, *U. S.;* Mistura Cretæ, *U. S., Br.;* Mistura Guaiaci, *Br.* (*N. F.*)*;* Mistura Olei Ricini, *Br.;* Mistura Spiritus Vini Gallici, *Br.;* Syrupus Aromaticus, *Br.;* Syrupus Cascaræ Aromaticus, *Br.;* Syrupus Cinnamomi, *N. F.;* Syrupus Ipecacuanhæ et Opii, *N. F.;* Tinctura Ferri Pomata, *N. F.;* Tinctura Rhei Aquosa, *N. F.*

AQUA CREOSOTI. U. S.

CREOSOTE WATER Aq. Creosot.

(ā'quą crē-ǫ-sō'tī)

Creasote Water; Eau créosotée, *Fr.;* Kreosotwasser, *G.*

℞ "Creosote, *ten mils* [or 162 minims]; Distilled Water, recently boiled, *nine hundred and ninety mils* [or 33 fluidounces, 228 minims], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Agitate the creosote vigorously with the recently boiled distilled water and filter, returning the filtrate to the filter until it is perfectly clear. This preparation must not be dispensed unless it has been recently prepared." *U. S.*

Creosote Water contains 1 per cent., or about 4.8 minims, of creosote in each fluidounce, and is too feeble where a full systemic action of creosote is desired. It is, however, actively germicidal and may be used for its local effects in various infections of the mouth or throat or to gently stimulate *indolent surfaces.*

Dose, from one to four fluidrachms (3.75–15 mils).

AQUA DESTILLATA. U. S., Br.

DISTILLED WATER Aq. Dest.

(ā'quą dēs-tĭl-lā'tą)

"Water [$H_2O = 18.016$] purified by distillation." *U. S.* "Distilled Water is prepared by distillation from good natural potable water." *Br.*

Eau distillée, *Fr. Cod.;* Aqua distillata, *P. G.;* Destillirtes Wasser, *G.;* Acqua distillata, *It.;* Agua destilada, *Sp.*

℞ "Water, *one thousand volumes,* to make *seven hundred and fifty volumes.* Distil the water from a suitable apparatus provided with a block-tin or glass condenser. Collect the first *one hundred volumes* and reject this portion. Then collect *seven hundred and fifty volumes* and keep the Distilled Water in glass-stoppered bottles, which have been rinsed with hot distilled water immediately before being filled." *U. S.*

No natural water is sufficiently pure for certain pharmaceutical purposes; and hence the necessity of the above process for its distillation. It is best to reject the first portion which comes over, as this may contain carbon dioxide and other volatile impurities; and the last portion of the water ought not to be distilled, lest it should pass over with an empyreumatic taste. The distillation is usually performed with the ordinary still and worm; but, to avoid any impurity from the worm or the receiver, the condenser is directed in the U. S. Pharmacopœia to be of block tin or glass. The large stills for making distilled water commercially are not run upon the principle of the rejection of the first and the last portions, as they are continuous in their operation. They are all provided with a vent at the highest portion of the condensing system where a small amount of steam escapes, carrying with it the gases which ordinarily would contaminate the condensed distillate. Commercial distilled waters are frequently passed through charcoal filters to aerate the water and remove the flat insipidity of taste. Brande states that distilled water often derives from the still a foreign flavor, which it is difficult to avoid. He therefore recommends that a still and condenser be kept exclusively for distilling water; or, where this cannot be done, that steam be driven through the worm for half an hour, for the purpose of steaming it out, before it is used, the worm-tub having been previously emptied. J. N. Hurty prefers well water as the source of distilled water, and that it be boiled before collecting the distillate, to get rid of ammonia, and, to prevent access and growth of spores, that the water be heated to boiling before introducing it into the container, and that it be drawn off by a siphon tube reaching to the bottom of the vessel, the mouth of which is loosely stoppered with cotton. (*West. Drug.,* 1887, p. 4.) Even the use of pure tin, which is generally considered unexceptionable, does not give perfect security against impurity, as water distilled from metallic alembics with the head and worm of this metal has a peculiar odor which it retains for some time. Ordinary distilled water invariably contains ammonia, as

may be proved by adding a few drops of Nessler's reagent. (See Part III.) In order to free distilled water from volatile nitrogenous bodies, it is necessary to redistil it after it has been placed in contact with potassium permanganate and potassium hydroxide. After about one-twentieth of the water has come over, the distillate is usually free from ammonia, and leaves no residue on evaporation. If traces of ammonia remain, acid potassium sulphate is added, and it is redistilled. (Stas.) Distilled water when kept long in glass vessels dissolves a minute quantity of the glass and the official test permitting 0.075 Gm. of residue in 1000 mils after evaporation to dryness, was inserted to avoid unnecessary severity in the test for a solvent used for pharmaceutical purposes.

Properties.—Distilled water, as usually obtained, has a vapid and disagreeable taste, and is not perfectly pure; water, to be rendered so, requiring to be distilled in silver vessels. The properties of pure water have already been given under the head of *Aqua*. "Distilled Water is a colorless, limpid liquid, without odor or taste, and neutral to the official indicators (see Part III). Separate portions of 100 mils each of Distilled Water are not affected by the addition of barium chloride T.S. (*sulphate*); silver nitrate T.S. (*chloride*); ammonium oxalate T.S. (*calcium*); hydrogen sulphide T.S., or sodium sulphide T.S. (*metals*). Distilled Water shows no deep yellow, orange or brown coloration when 1 mil of Nessler's reagent is added to 100 mils of the Water (*ammonia*). Add 50 mils of calcium hydroxide T.S. to 25 mils of Distilled Water; the mixture remains clear and transparent (*carbon dioxide*). Evaporate 100 mils of Distilled Water to dryness on a water bath and subsequently dry the residue in an oven to constant weight at 100° C. (212° F.); not more than 0.001 Gm. of residue remains. Heat 100 mils of Distilled Water to boiling, acidulate it with 10 mils of diluted sulphuric acid, and subsequently add 0.1 mil of tenth-normal potassium permanganate V.S. The color of the liquid is not completely destroyed by boiling it for ten minutes (*organic or other oxidizable substances*)." *U. S.*

The British Pharmacopœia requires distilled water to be "colorless, odorless, and tasteless. Yields no *reactions* for sulphates, chlorides, or nitrates. 100 millilitres evaporated to dryness on a water-bath leave not more than 0.005 gramme of solid residue. 50 millilitres with one drop of *solution of sodium sulphide* remain colorless when viewed in a Nessler glass standing on a white tile (absence of lead, copper, and iron). 250 millilitres with a mixture of 3 millilitres of *sulphuric acid* and 0.1 millilitre of *N/10 solution of potassium permanganate*, after standing for three hours at about 15.5° C. (59.9° F.), are colored blue on the addition of a crystal of *potassium iodide* and 1 millilitre of *mucilage of starch* (absence of more than traces of organic matter). 50 millilitres mixed with 2 millilitres of *alkaline solution of potassio-mercuric iodide* when viewed in a Nessler glass standing on a white tile do not, after five minutes, yield a more intense color than that yielded by 50 millilitres of ammonia-free water with 0.5 millilitre of *dilute solution of ammonium chloride* (*Nessler's*) when tested under similar conditions (limit of ammonia)." *Br.*

It is needlessly employed in some formulas, but is essential in others. As a rule, when small quantities of active medicines are to be given in solution, and in the preparation of collyria, distilled water should be directed. The following list contains the chief substances which require distilled water as a solvent: tartar emetic, corrosive sublimate, silver nitrate, barium and calcium chlorides, lead acetate and subacetate, potassium permanganate, iron and zinc sulphates, quinine sulphate, morphine sulphate, hydrochloride, and acetate, and, in general terms, all the alkaloids and their salts. Distilled water is used in preparing the official diluted acids, for absorbing gaseous ammonia, and for forming nearly all the official aqueous solutions.

AQUA DESTILLATA STERILISATA. U. S.

STERILIZED DISTILLED WATER **Aq. Dest. Steril.**

(ă'quạ dĕs-tĭl-lā'tạ stĕr-ĭl-ī-sā'tạ)

* "Water, freshly distilled, *a sufficient quantity*. Transfer the necessary quantity of freshly distilled water to a flask of hard glass of sufficient size which has previously been cleansed and sterilized as described under *Sterilization* (see Part III). Close the mouth of the flask with a pledget of sterilized purified cotton, boil the contents for thirty minutes and allow the water to cool without removing the cotton plug. Finally protect the mouth of the flask and the cotton pledget from infection through dust by wrapping the top of the flask tightly with paper. Sterilized Distilled Water should be used within forty-eight hours after its preparation." *U. S.*

Distilled water is ordinarily not sterile, due to the contamination of the vessels in which it is collected or by air-borne organisms. For the preparation of hypodermic injections, therefore, and for some other purposes it is necessary to re-sterilize the distilled water, hence the admission of this sterilized water into the Pharmacopœia.

It is of the utmost importance that the water to be sterilized shall be freshly distilled, since distilled water which has stood even for a short time will contain many bacteria which, if present, would be killed by the sterilization process, but subsequently form a bacterin (a suspension of dead bacteria), and this if used for dissolving salts for hypodermic injection is apt to cause febrile and other systemic disturbances. If the U. S. method is followed the flask must be of so-called insoluble glass, such as Jena glass, or the solution will contain silicates which are likely to separate as needle-like spicula. Sterilized distilled water may to advantage be prepared in an autoclave.

AQUA FŒNICULI. U. S., Br.

FENNEL WATER Aq. Fœnic.

(ăʹquạ fœ-nĭcʹû-lī)

Eau de Fenouil, *Fr.;* Aqua Fœniculi, *P. G.;* Fenchelwasser, *G.;* Acqua distillata di finocchio, *It.;* Agua de hinojo, *Sp.*

* "Oil of Fennel, *two mils* [or 32 minims]; Purified Talc, *fifteen grammes* [or 231 grains]; Distilled Water, recently boiled, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Triturate the Oil of Fennel with the Purified Talc, add the recently boiled Distilled Water gradually with continued trituration, filter, and pass the filtrate through the filter repeatedly until the Fennel Water is perfectly clear." *U. S.*

"Fennel Fruit, 100 *grammes;* Water, 2000 *millilitres.* Distil one thousand *millilitres.*" *Br.*

"This Water may be prepared by triturating the oil of fennel fruit with twice its weight of calcium phosphate and five hundred times its volume of distilled water and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

Uses.—Fennel water is a pleasant vehicle for other medicines, and useful when a mild aromatic is indicated. The distillation process of the British Pharmacopœia, although more troublesome, furnishes a more delicate and agreeable water than does that of the U. S. Pharmacopœia.

AQUA HAMAMELIDIS. U. S. (Br.)

HAMAMELIS WATER Aq. Hamam. [Witch Hazel Water Distilled Extract of Witch Hazel]

(ăʹquạ hăm-ạ-mĕlʹĭ-dĭs)

Liquor Hamamelidis, *Br.;* Solution of Hamamelis, Witch-hazel extract; Eau distillée de hamamelis, *Fr.;* Hamameliswasser, *G.*

* "A saturated aqueous liquid obtained by distilling with steam or water the bark, twigs, smaller stems or the entire shrub of *Hamamelis virginiana* Linné (Fam. *Hamamelidaceæ*) collected in the autumn, and adding *one hundred and fifty mils* [or 5 fluidounces, 35 minims] of alcohol to each *eight hundred and fifty mils* [or 28 fluidounces, 356 minims] of distillate. Preserve it in tightly-closed containers in a cool place." *U. S.* "Fresh Hamamelis Leaves, 1000 *grammes;* Distilled Water, 2000 *millilitres;* Alcohol (90 per cent.), 160 *millilitres.* Macerate for twenty-four hours; then distil one thousand *millilitres.*" *Br.*

The U. S. P. VIII directed that this water be made from Hamamelis Bark, the Br. Pharm. (1914) directs fresh Hamamelis leaves; the U. S. P. IX uses the bark, twigs, smaller stems, or the entire shrub of Hamamelis.

Hamamelis Water or, as it is popularly called, "Distilled Extract of Witch Hazel," has been found on the market containing very little alcohol, formaldehyde being used as a preservative. Methyl alcohol has also been found in place of ethyl alcohol in many samples. The U. S. Pharmacopœia IX describes Hamamelis Water as "a clear and colorless, or not more than faintly opalescent or slightly yellowish liquid having a characteristic odor and taste. It is neutral or only faintly acid to litmus. Specific gravity: 0.979 to 0.982 at 25° C. (77° F.). It must be free from mucoid or fungous growths and must not have an acetous odor. It gives no reaction with hydrogen sulphide T.S. or with sodium sulphide T.S. (*metallic impurities*). Evaporate 100 mils of Hamamelis Water to dryness on a water bath; not more than 0.025 Gm. of residue remains (*dissolved impurities*). It contains not less than 14 per cent. of absolute alcohol, by volume, when estimated as directed under Determination of alcohol in official preparations (see Part III, Test No. 14). Add 8 drops of an aqueous solution of resorcinol (1 in 200) to 5 mils of Hamamelis Water and then carefully pour this upon 5 mils of sulphuric acid, contained in a test tube, in such a manner that the two liquids do not mix. After standing for three minutes a rose-red ring does not appear at the line of contact of the liquids nor does a distinct, white layer appear above this zone (*formaldehyde*). Ten mils of Hamamelis Water gives no reaction for methyl alcohol when tested as directed under *Alcohol* for the detection of methyl alcohol." *U. S.*

Uses.—This water was probably introduced into the British Pharmacopœia and U. S. Pharmacopœia IX on account of the large demand for it which has grown out of the wide advertisements of a certain proprietary medicine, and the universally recognized need in American families for an embrocation which appeals to the psychic influence of faith. As the tannic acid of hamamelis bark does not come over into the distillate the water is therapeutically a mixture of water and alcohol, the volatile oil being found in too minute a proportion to possess any therapeutic value.

AQUA LAUROCERASI. Br.

CHERRY-LAUREL WATER

(ăʹquạ lâuʹrō-çĕrʹạ-sī)

Eau distillée de Laurier-cerise, *Fr. Cod.;* Kirschlorbeerwasser, *G.;* Agua destilada de laurel-cerezo, *Sp.*

"Cherry-Laurel Leaves, crushed, 800 *grammes;* Water, 2500 *millilitres.* Distil one thousand *millilitres;* shake the product; filter, if necessary; adjust the strength of the finished product either by adding hydrocyanic acid or Distilled Water, so that, when tested as described under 'Acidum Hydrocyanicum Dilutum,' it contains 0.1 per cent. by weight of hydrocyanic acid, HCN." *Br.*

The International Protocol (1906) fixed the strength of Cherry-Laurel Water at 0.1 per cent. of hydrocyanic acid which corresponds with the strength of the Br. Pharm, 1898 and 1914.

It is greatly to be regretted that this uncertain, dangerous, and troublesome preparation should retain a place in European pharmacopœias, inasmuch as it could easily be replaced

by a flavored water containing a definite amount of a soluble cyanide. See *S. W. P.*, 1909, No. 10, 147, and 1909, No. 36, 542.

As the cherry-laurel is little cultivated in the United States, the water is not official; but from several experiments by William Procter there is little or no room to doubt that a preparation identical in its effects might be made from the leaves of our common wild cherry, *Prunus serotina*. The imported cherry-laurel water, as found in commerce, is generally impaired by age, and not to be relied on.

Cherry-laurel leaves contain 65 per cent. of water, sufficient to provoke the reaction which results in the formation of a volatile oil and hydrocyanic acid. Water is very prone to hasten the conversion of the benzaldehyde, contained in the volatile oil, into benzoic acid by oxidation, and it has been found by C. Umney (*P. J.*, x, 467) and by Moore (*Ibid.*, 604) that the water distilled without previous maceration is somewhat stronger in hydrocyanic acid and decidedly stronger in oil (Umney) than the official product. The strength of cherry-laurel water was formerly very variable, but the present Pharmacopœias require 0.1 per cent. of hydrocyanic acid. The proportion of hydrocyanic acid in the water diminishes with time. It has been ascertained by Deschamps that if a drop of sulphuric acid be added to a pint of the preparation it will keep unchanged for at least a year. It is best preserved by the entire exclusion of air and light. Lepage found that, preserved in full and perfectly air-tight bottles, both this and bitter almond water remained unchanged at the end of a year; while if freely exposed to the air, they lost all their hydrocyanic acid and essential oil in two or three months. (*J. P. C.*, xvi, 346.) For Denigés's method of assaying the water, see *Proc. A. Ph. A.*, 1894, 556.

Uses.—Cherry-laurel water is employed in Europe as a sedative narcotic, identical in its properties with a diluted solution of hydrocyanic acid; but it is of uncertain strength, and should not be allowed to supersede the preparation of the acid now in use.

Dose, twenty minims to a fluidrachm (1.3–3.75 mils).

AQUA MENTHÆ PIPERITÆ. U. S., Br.

PEPPERMINT WATER Aq. Menth. Pip.

(ă'quą měn'thæ pĭp-ę-rĭ'tæ)

Eau distillée de Menthe poivrée, *Fr. Cod.*; Aqua Menthæ Piperitæ, *P. G.*; Pfefferminzwasser, *G.*; Acqua distillata di menta piperita, *It.*; Agua destilada de menta piperita, *Sp.*

• "Oil of Peppermint, *two mils* [or 32 minims]; Purified Talc, *fifteen grammes* [or 231 grains]; Distilled Water, recently boiled, a *sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Triturate the Oil of Peppermint with the Purified Talc, add the recently boiled Distilled Water gradually with continued trituration, filter, and pass the filtrate through the filter repeatedly until the Peppermint Water is perfectly clear." *U. S.* See *Aqua Aromaticæ*, page 179. "Oil of Peppermint, 1 *millilitre;* Water, 1500 *millilitres*. Distil one thousand *millilitres*." *Br.*

"This Water may be prepared by triturating the oil of peppermint with twice its weight of calcium phosphate and five hundred times its volume of distilled water, and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

Uses.—Peppermint water is one of the most popular of the aqueous vehicles. It is especially useful as an ingredient in mouth washes because the menthol content produces a pleasant and cool sensation on mucous membranes.

Off. Prep.—Liquor Sodæ et Menthæ (Alternative with Spearmint), *N. F.*

AQUA MENTHÆ VIRIDIS. U. S., Br.

SPEARMINT WATER Aq. Menth. Vir.

(ă'quą měn'thæ vĭr'ĭ-dĭs)

Eau de Menthe verte, *Fr.*; Römisch-Minzwasser, *G.*; Agua de yerba buena, *Sp.*

• "Oil of Spearmint, *two mils* [or 32 minims]; Purified Talc, *fifteen grammes* [or 231 grains]; Distilled Water, recently boiled, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Triturate the Oil of Spearmint with the Purified Talc, add the recently boiled Distilled Water gradually with continued trituration, filter, and pass the filtrate through the filter repeatedly until the Spearmint Water is perfectly clear." *U. S.*

"Oil of Spearmint, 1 *millilitre;* Water, 1500 *millilitres*. Distil one thousand *millilitres*." *Br.*

"This Water may be prepared by triturating oil of spearmint with twice its weight of calcium phosphate and five hundred times its volume of distilled water and filtering the mixture. In tropical and subtropical parts of the Empire this Water may be used in place of the corresponding Water of the text of the British Pharmacopœia." *Br.*

There would seem to be no good reason for distilling the mint waters from their respective volatile oils, as directed in the British processes. If the fresh plants were available, a good source for a distilled water could be provided; but if a volatile oil must be used with its uncertainty of freshness always present, the quicker process of the U. S. P. is greatly preferable.

Uses.—Spearmint water is used solely as a vehicle. Its flavor to most persons is inferior to that of peppermint, and it lacks the characteristic cooling effect of the menthol which is found in peppermint.

Off. Prep.—Liquor Sodæ et Menthæ, *N. F.*

AQUA ROSÆ. U. S., Br.

ROSE WATER Aq. Ros.

(ă'quạ rō'ṣæ)

Eau distillée de Rose, *Fr. Cod.;* Aqua Rosæ, *P. G.;* Rosenwasser, *G.;* Acqua distillata di Rose, *It.;* Agua destilada de rosas, *Sp.*

* "Stronger Rose Water, Distilled Water, recently boiled, *one volume* [or 1 pint]. Mix them immediately before use." *U. S.* "Rose Water is the rose water of commerce, prepared by distillation from the flowers of Rosa damascena, *Linn.*, diluted, immediately before use, with twice its volume of Distilled Water. The rose water of commerce is a saturated solution of the volatile oil of the fresh rose flowers." *Br.*

"Rose Water complies with the tests for identity and purity described under *Aqua Rosæ Fortior.*" *U. S.*

The British Pharmacopœia of 1898 abandoned the former process of distilling the petals and followed the method adopted by the U. S. Pharmacopœia of diluting the so-called triple rose water of commerce with distilled water. This, however, does not make rose water identical in strength in these authorities, the U. S. preparation being the stronger.

Although domestic rose water of fair quality may be made by distilling fresh rose petals, it does not possess the strength or delicacy of the by-product obtained from abroad, as officially described under *Aqua Rosæ Fortior;* hence the above process of diluting this stronger rose water. The process of distilling the fresh petals of the hundred-leaved rose is sometimes practised. These are usually preferred in the recent state; but it is said that, when preserved by being incorporated with one-third of their weight of common salt, they retain their odor, and afford a water equally fragrant with that prepared from the fresh flowers. Indeed, Haselden prefers the salted roses, believing that the water prepared from them is less mucilaginous, less apt to become sour, and keeps its odor better than that prepared from the fresh flowers. (*P. J.*, xvi, 15.) It is not uncommon to employ the whole flower, including the calyx; but the product is less fragrant than when the petals only are used, as officially directed. A. Monthus states that the petals of the hundred-leaved rose are more odorous the nearer they are to the center of the flower, and, contrary to what is said in the text, thinks that the calyx should not be rejected in preparing the distilled water. He maintains that so far from injuring the product it in fact contributes to its preservation, and that the water obtained from the whole flower is less liable to that mucosity which is the commencement of decomposition. This effect he ascribes to the astringent matter of the calyx, coagulating the mucilaginous matter of the petals, and preventing it from passing over in the distillation. (*J. P. C.*, 1863, p. 497.) Rose water is sometimes made by distilling together water and the oil of rose. This is best performed by dropping 10 drops of oil of rose on a sponge and adjusting it in the upper part of a still in the body of which a gallon of water is placed; the steam from the boiling water will carry over portions of the oil, and the distillate will thus be impregnated. Alpers (*Am. Drug.*, 1896, 384) prepares rose water by dropping 10 drops of oil of rose into a liter of hot distilled water, agitating and filtering. Rauschenberger improves the flavor by adding a trace of oil of cloves; 2.5 Gm. of oil of rose, 0.25 Gm. of oil of cloves are added to sufficient alcohol to make 100 mils; then 10 mils of this solution is added to 1000 mils of boiling water and the liquid cooled and filtered.

Rose water when properly prepared, has the perfume of the rose in great perfection. It is most successfully made on a large scale. Like the other distilled waters, it is liable to spoil when kept; and the alcohol which is sometimes added to preserve it is incompatible with some of the purposes to which the water is applied, and is even said to render it sour through acetous fermentation. It is best, therefore, to avoid this addition, and to substitute a second distillation. It may be kept in a bottle stoppered with a plug of absorbent cotton. This distilled water is chiefly employed, on account of its agreeable odor, in collyria and other lotions. It is wholly destitute of irritating properties, unless it contain alcohol.

Off. Prep.—Mistura Ferri Composita, *Br.;* Linimentum Terebinthinæ Aceticum, *N. F.;* Mistura Ferri Composita, *N. F.;* Unguentum Aqua Rosæ, *Br.*

AQUA ROSÆ FORTIOR. U. S. (Br.)

STRONGER ROSE WATER Aq. Ros. Fort.

(ă'quạ rō'ṣæ fōr'tī-ọr)

Rose Water of Commerce, *Br.*, [Triple Rose Water] Aqua Rosæ, *U. S.* 1880; Stärkeres Rosenwasser, *G.*

"The saturated aqueous distillate prepared by distilling the fresh flowers of *Rosa centifolia* Linné (Fam. *Rosaceæ*) with water. Preserve it in bottles stoppered with a pledget of purified cotton, in a cool, dark place." *U. S.*

This has been introduced for the purpose of making rose water. (See the preceding article.)

"Stronger Rose Water is colorless and clear, and possesses a strong and pleasant odor, and a taste of fresh rose blossoms, and must be free from empyreuma, mustiness, or mucoid growths. It is neutral or only slightly acid to litmus, and 100 mils, when evaporated to dryness on a water bath and the residue subsequently dried in an oven to constant weight at 100° C. (212° F.), yields not more than 0.001 Gm. of residue. It gives no reaction with hydrogen sulphide T.S. or with sodium sulphide T.S. (*metallic impurities*)." *U. S.*

Off. Prep.—Aqua Rosæ, *U. S., Br.;* Unguentum Aquæ Rosæ, *U. S., Br.;* Confectio Rosæ, *N. F.*

AQUÆ AROMATICÆ

AROMATIC WATERS

(ă'quæ ăr-ǫ-măt'ĭ-cæ)

[Medicated Waters] Aquæ stillatitiæ; Distilled Waters; Eaux Medicinales, *Fr. Cod.*; Eaux distillées, Hydrolats, *Fr.*; Aquæ Destillatæ, *P. G.*; Destillirte Wässer, *G.*; Acque distillate, *It.*

"Aromatic Waters, when prepared from volatile oils, are intended to be, as nearly as practicable, saturated solutions, which must be clear and free from solid impurities, and, unless otherwise directed, should be made by the following general process: * Volatile Oil, *two mils* [or 32 minims]; Purified Talc, *fifteen grammes* [or 231 grains]; Distilled Water, recently boiled, *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Triturate the volatile oil with the purified talc, add the recently boiled distilled water gradually with continued trituration, filter, and pass the filtrate through the filter repeatedly until the Aromatic Water is perfectly clear. If preferred, the solution of the volatile oil may be made by replacing the purified talc by purified siliceous earth, or by pulped filter paper; or a solution of the volatile oil may be prepared with recently boiled distilled water, by direct addition and filtration, after shaking. Aromatic Waters may also be made by the distillation of a mixture of the drug or volatile oil with water. In each case the method used must yield a finished product which meets the official requirements and corresponds with that obtained by the general process. Aromatic Waters should not be permitted to freeze." *U. S.*

Under this head are included, in the U. S. Pharmacopœia, preparations consisting of water holding volatile substances in solution, many of which were formerly obtained by distillation, and some of which still continue to be so. They include the preparations formerly specially designated as "Distilled Waters," having been made by distilling water from plants or parts of plants containing volatile oil.

The Distilled Waters, as thus defined, hold a much more prominent position in the pharmacy of Europe, particularly of continental Europe, than in that of the United States; and a great deal of thought and elaborate investigation has been bestowed there upon the various conditions calculated to furnish the best products by the most convenient method. The British Pharmacopœia (1914) directs the distillation process for the waters, but provides for certain medicated waters the alternative process as follows:

"**Aquæ Olei Anethi, Anisi, Carui, Cinnamomi, Fœniculi, Menthæ Piperitæ, Menthæ Viridis.**—Each of these Waters may be prepared by triturating the corresponding Oil with twice its weight of Calcium Phosphate and five hundred times its volume of Distilled Water and filtering the mixture. In tropical and subtropical parts of the Empire these Aquæ Olei may be used in place of the corresponding Aquæ of the Text of the Pharmacopœia." *Br.*

Many vegetable substances impart their peculiar flavor to water distilled from them, and more or less of their medicinal properties. The Distilled Waters chiefly used are those prepared from aromatic plants, the volatile oils of which rise with the aqueous vapor and are condensed with it in the receiver. But as water is capable of holding but a small proportion of the oil in solution, these preparations are generally feeble, and are employed chiefly as pleasant vehicles or corrigents of other medicines.

In the preparation of the Distilled Waters, dried plants are sometimes used, because fresh plants are not to be had at all seasons; but the latter, at least in the instance of herbs and flowers, should be preferred if attainable. Flowers which lose their odor by desiccation may be preserved by incorporating them intimately with one-third of their weight of common salt, and in this state afford Distilled Waters of delicate flavor. Some pharmacists prefer to employ the salted flowers in certain instances, believing that the waters distilled from them keep better than when prepared from the fresh flowers. C. R. Tichborne proposed a method of preserving flowers which is said to answer even better than the use of salt. It consists simply in immersing the fresh flowers in glycerin, which preserves them with all their aromatic properties wholly unimpaired. The flowers, as of the elder, rose, or orange, should be gathered after full expansion, and packed firmly in wide-mouthed bottles or jars, but without crushing them. The glycerin is then to be poured on until it covers them, and the vessel closed. Tichborne has kept flowers in this way for two years, and at the end of that time procured from them Distilled Waters, of which the perfume has equalled that of the waters prepared from recent flowers. It is not necessary that the glycerin should be perfectly pure, but it should be without odor. (*P. J.*, 2d ser., vii, 135.)

The idea at one time prevailed, to a considerable extent, that Waters kept better if distilled from dried herbs than from fresh, and the opinion was true in regard to those prepared with the defective alembics of former times and by a naked fire; but experiment has sufficiently established the fact that, with a suitable apparatus, and a regular heat, the fresh herbs yield products which not only have a more agreeable odor of the plant, but keep quite as well as those from dried herbs.

It is necessary to observe certain practical rules in conducting the process of distillation. When the substance employed is dry, hard, and fibrous, it should be mechanically divided, and macerated in water for a short time previous to the operation. The quantity of materials should not bear too large a proportion to the capacity of the still, as the water might otherwise boil over into the receiver. The water should be brought quickly to the state of ebullition, and continued in that state until the end of the process. Care should be taken to leave

sufficient water undistilled to cover the whole of the solid matter, lest a portion of the latter, coming in contact with the sides of the vessel, be decomposed by the heat, and yield empyreumatic products. Besides, when the operation is urged too vigorously, or carried too far, a slimy matter is apt to form, which adheres to the sides of the still above the water, and is thus exposed to igneous decomposition. To obviate these disadvantages, the heat may be applied by means of an oil bath, regulated by a thermometer, or of a bath of solution of calcium chloride, by which any temperature may be obtained between 100° C. (212° F.) and 132.2° C. (270° F.), according to the strength of the solution; or, when the process is conducted upon a large scale, by means of steam introduced under pressure into a space around the still termed a "jacketed body." To prevent the disagreeable effects of charring and the excessive empyreumatic odor frequently noticed in Distilled Waters, caused by the solid contents of the still coming into direct contact with the heated bottom, Remington devised an expedient which prevents the herb from touching the bottom and yet permits the water and steam to have free access to all parts of it. (See Pharmaceutical Still, under *Extracta.*) A hemispherical No. 12 copper sieve with a handle and loosely fitting lid is filled with the herb and placed in the water in the still. If the bottom of the still be flat or nearly so, the rounded bottom of the cage must have a very slight point of contact, and thus charring will be prevented. A convenient mode of applying heat by steam is by means of a coil of metal tubing placed in the bottom of the still, having one end connected with a boiler, and the other passing out beneath or at the side, and furnished with a steam-cock, by which the pressure may be increased or the condensed water drawn off at will. If any volatile oil floats upon the surface of the Distilled Water, it may be separated.

This direction is generally given; but, in a communication to the Pharmaceutical Society of Great Britain, Haselden recommends the excess of oil to be well shaken with the water, and the whole to be transferred to the stock vessel, where it may be allowed to rest, and the oil to separate. He thinks the water keeps better when thus treated, and the full strength is always insured. The stock vessel he prefers made of stoneware, and furnished with a tap placed two inches from the bottom, whereby the water may be drawn off clear when wanted for the ordinary shop bottles, the oil rising to the top, or sinking to the bottom, according to its sp. gr. (*P. J.*, xvi, 14, 15.)

From a series of experiments made in Paris in reference to the best mode of applying heat, it was concluded that as regards the great majority of aromatics the direct application of steam was preferable, because the Distilled Waters prepared by means of it have a freshness of aroma that is wanting in the others, are always free from the odor of the still, are much more limpid, are less apt to deposit mucilaginous matter, and keep better; but that exceptions to the general rule are afforded by bitter almonds, cherry-laurel leaves, mustard, and horse-radish, in all of which the oil does not pre-exist in the plant, but is formed upon contact with water; by woods, barks, and roots, the tissue of which cannot be sufficiently penetrated by steam; and by roses. (*J. P. C.*, Mai, 1861, p. 364.) Later experiments have led to the conclusion that even these substances are most advantageously treated by distillation with steam, and that, in fact, there is no exception to the rule.

But, however carefully the process may be conducted, the Distilled Waters prepared from plants always have at first an unpleasant smoky odor. They may be freed from this by exposure for a short time to the air before being enclosed in well-stoppered bottles, in which they should be preserved. When long kept, a viscid ropy matter is apt to form in them, and they become sour. To prevent this decomposition, a little alcohol is sometimes added to the water employed in its distillation. But this addition is inadequate, and is in fact injurious, as the alcohol by long exposure to the air undergoes the acetous fermentation. A better plan is to redistil the Waters. When thus purified, it is said that they may be kept for several years unchanged.

Robiquet considered the mucosity which forms in Distilled Waters to be the result of a vegetable process, for which the presence of air is essential. He stated that so long as the water is covered with a layer of essential oil it undergoes no change, but that the oil is gradually altered by exposure to the air, and, as soon as it disappears, the water begins to be decomposed. He stated that camphor exercises the same preservative influence over the Distilled Waters by resisting the vegetation, and that those in which the odor of camphor is developed keep better on that account. Finally, he observed that the more Distilled Water is charged with volatile oil, the more abundant is the mucosity when it has begun to form. Robiquet united with Henry and Guibourt, and with Virey, in recommending that all these waters, when intended to be kept for a considerable time, should be introduced, immediately after distillation, into bottles of a size proportionate to the probable consumption of the water when brought into use, and that the bottles should be quite filled, and then sealed or otherwise well stoppered, so as entirely to exclude the air. It is best that they should be small, and be closed with well-fitting glass stoppers. Thus treated, the Waters may be preserved without change for many years. This view is opposed to the experience of large producers of Distilled Waters; we have seen at Grasse hundreds of carboys stored away, containing distilled rose and orange flower waters, not only uncorked, but having only a thin piece of muslin laid over the lips to exclude dust. We were informed by the distillers that the waters retained their qualities for years far better when treated in this way than if stoppered tightly. We have frequently noticed microscopic

plants belonging to the *Confervoideæ* in the Distilled Waters contained in shop bottles standing on the shelves in the dispensing room, and if it be desired to keep Distilled Waters, the only sure way is to destroy the spores and prevent the admission of fresh ones by placing the bottles, filled to the lip with the Distilled Water, into a bath of boiling water, and, when thoroughly sterilized by the heat, inserting a plug of purified cotton if for immediate use; or if the waters are to be kept for a longer period, the well soaked corks should be driven into the mouths of the bottles, and immediately tied down, the top of the bottle dipped into melted sealing wax, and the bottle stored in a cool place.

Another mode of preparing the Distilled Waters is to substitute the volatile oil, previously separated from the plant, for the plant itself in the process. This mode is directed in the British Pharmacopœia in several instances. It is said to afford a more permanent product than the preceding, but does not always preserve the flavor of the plant.

In relation to most of the aromatic waters, the U. S. Pharmacopœia formerly directed that water should be impregnated with the volatile oil by trituration with magnesium carbonate, and subsequently filtered. This was by far the most simple and easy process. The resulting solution is nearly pure and permanent, and is perfectly transparent, the magnesium carbonate being separated by the filtration. Magnesium carbonate is preferable to magnesium oxide, as the latter sometimes gives a brownish color to the liquid, and requires to be used in larger proportion. But both these substances are dissolved in minute quantities, and are apt to occasion a slight flocculent precipitate. They may also possibly prove injurious by decomposing certain substances given in very small doses, as salts of the alkaloids, mercuric chloride, and silver nitrate. The object of the magnesium carbonate is simply to enable the oil to be brought to a state of minute division, and thus presented with a larger surface to the action of the solvent. Precipitated calcium phosphate was used in the U. S. P., 1890, and used in the Br. Pharm. (1914) as a substitute for magnesium carbonate, but this has been shown to be slightly soluble in water; notwithstanding this objection, its use was sanctioned by the U. S. Pharmacopœia of 1890. W. S. Thompson, of Washington, D. C., suggested the use of absorbent cotton as being free from all of these objections, and his views were substantially adopted by the Committee of Revision of the Pharmacopœia of 1880. E. V. Zoeller proposes to use a hand cotton-card to aid in pulling the filaments of cotton apart when a large quantity of medicated water is needed. (*N. R.*, 1883, p. 56.) Experience has shown, however, that the use of an insoluble powder to effect the minute division of the particles of oil, so as to present a large surface to the solvent, is a more practical and convenient method of making medicated waters. According to Robert Warington, this object may be better accomplished by porcelain clay, finely powdered glass or pumice-stone, which are wholly insoluble; and the London College employed finely powdered silica for the purpose. Talc or soapstone in powder, purified by washing with diluted hydrochloric acid, was adopted by the Committee on National Formulary (1888). (See *Talcum Purificatum;* also paper recommending it by Curtman, *Proc. A. Ph. A.*, 1887.) Purified Siliceous earth or Kieselguhr (see *Terra Silicea Purificata*) was added to the list of powders to facilitate solution in the U. S. P. IX; this was recommended by C. H. LaWall. (*Proc. New Jersey Pharm. Assoc.*, 1908, p. 47.) The U. S. P. IX recommends the use of purified talc, although several alternative processes are allowed; *i.e.*, the shaking of the oil with hot water until saturated and afterwards filtering; the use of paper pulp; or the distillation from the volatile oil or drug macerated in water, but the finished water must in all cases correspond to the product resulting from the use of talc. (See page 179.) A very good way to make medicated waters when a volatile oil is directed, is that proposed by Percival, which is to heat the water required, pour it into a bottle and add the oil, cork tightly, shake occasionally until cool, then pour off and filter; this secures a medicated water free from foreign substances, and a saturated solution, most oils being more soluble in hot than in cold water. Thum (*Proc. P. P. A.*, 1916, p. 225) suggests that the use of talc or any other intervening filtering agent is unnecessary if a large stock bottle is used in which distilled water and an excess of the oil are kept, occasionally agitating to insure saturation. When the dispensing container is to be filled, all that is necessary is to filter some of the water through a well wetted filter paper. Waters made in this manner compare favorably with those made by the more tedious processes, both in aroma and degree of saturation and are less likely to develop microscopic organisms. The Dublin College prepared its Waters by agitating an alcoholic solution of the oil with distilled water, and filtering. They consequently contained alcohol, and were liable to the objection, already mentioned, against the medicated waters thus impregnated. They were, besides, feeble in the properties of their respective oils. In the preparation of the aromatic waters by these processes, it is very important that the water should be pure. The presence of a sulphate causes a decomposition of the oil, resulting in the production of hydrogen sulphide and a carbonate, and the aromatic properties are quite lost. (See *A. J. P.*, xix, 303.) Hence the propriety of the official direction to employ distilled water.

The Distilled Waters are liable to contain various metallic impurities, derived from the vessels in which they are prepared or preserved. The metallic salts which have been found in them are those of iron, zinc, copper, and lead. With potassium ferrocyanide, iron will give a blue color, zinc and lead white precipitates, and

copper a rose color followed by a chestnut brown precipitate. Sodium sulphide causes with salts of iron, copper, or lead, a brown discoloration more or less deep, followed by precipitates varying from brown to black; with those of zinc a white precipitate. The volatile oils may be recovered from the Waters containing them, or at least may be transferred to a spirituous menstruum, by mixing olive oil with the water, adding a little solution of potassium hydroxide so as to form a soap, and a consequent emulsion with the liquid, and then neutralizing by an acid. The fixed oil will rise to the surface, bringing the volatile oil along with it. The latter may then be separated from the former by agitation with alcohol. (T. P. Groves, *P. J.*, Feb., 1864.)

ARAROBA. Br.

ARAROBA [Goa Powder; Crude Chrysarobin]

(ăr-ą-rō'bą)

Crude Chrysarobin, Goa Powder, Poh di Bahia; Poudre de Goa, *Fr.*; Goa-Pulver, *G.*

"Araroba is a substance found in cavities in the trunk of Andira Araroba, *Aguiar*, freed as much as possible from fragments of wood, dried and powdered." *Br.*

Under the name of Chrysarobin, or Araroba, a medicine has long been used in Brazil; it is exported in considerable quantities to Portugal, whence it found its way through the Portuguese colonies into Eastern commerce. It is officially recognized, after being purified, in the British, Swiss and German Pharmacopœias In the East Indies it is usually known as Goa Powder. Indeed, the identity of the two powders was first proved in 1875 by J. F. Dasilva Lima. (*P. J.*, v.) It has been supposed to be yielded by certain lichens, but was shown by R. A. Monteiro to be obtained from a leguminous tree abundant in the forests of the Brazilian province of Bahia, which was referred by E. M. Holmes to the genus Cæsalpinia, but which was determined by studies made in its native forests by J. M. de Aguiar to be an undescribed Andira.

Andira Araroba is a large tree, attaining a height of 100 feet, with a smooth trunk, common in the province of Bahia, Brazil. The wood is yellowish, with numerous longitudinal canals, besides abundant irregular interspaces or lacunæ, in which the chrysarobin is deposited. (See *P. J.*, ix, 755; x, 42, 814.) The oldest trees yield the largest amount of the powder; the parts containing it are finely chipped or scraped off. The workmen who procure it often suffer severely from irritation of the eyes and face. As first obtained, chrysarobin is stated to be of a pale primrose yellow, but it rapidly darkens with age, so that in commerce it varies from a dull ochre to a dark chocolate or maroon-brown. It is sometimes a rather fine powder, but is usually more or less agglomerated, and not rarely contains fragments of woody tissue.

"The powder varies in color from brownish-yellow to umber-brown. Yields to hot *benzene* not less than 50 per cent. of a substance which, on evaporating the filtrate, drying and powdering the residue, has the characters described under 'Chrysarobinum.'" *Br.*

It has been stated that Goa powder of late years is much weaker in its properties than that formerly obtained; this has been attributed to the scraping of the product from immature or young trees. This statement was not confirmed by the analysis of ten samples from the London market by Duncan and Tweedie. (*P. J.*, 1892, 543.) Its taste is bitter. It is insoluble in water and most menstrua, but yields as much as 80 per cent. of its weight to solutions of caustic alkalies and to benzene. Attfield analyzed Goa powder, and found, along with 2 per cent. of resin, 5.5 per cent. of woody fiber, 7 per cent. of bitter extractive, and from 80 to 84 per cent. of what he considered to be chrysophanic acid; but Liebermann and Siedler showed that this was not chrysophanic acid, but a substance easily convertible into the acid, which substance they called *chrysarobin*, and gave to it the formula $C_{30}H_{28}O_7$. (See *Chrysarobinum.*)

For consideration of the therapeutic uses of Araroba, see *Chrysarobin.*

ARGENTI NITRAS. U. S., Br.

SILVER NITRATE Arg. Nit.

(ăr-ģĕn'tī nī'trās)

"It contains, when finely powdered and dried to constant weight in a desiccator over sulphuric acid, in the dark, not less than 99.8 per cent. of $AgNO_3$ (169.89). Preserve it in dark amber-colored vials, protected from light." *U. S.*

"Silver Nitrate, $AgNO_3$, may be obtained by the interaction of nitric acid and silver." *Br.*

Nitrate of Silver, Lunar Caustic; Azotas (Nitras) Argenticus; Azotate d'Argent cristallisé, *Fr. Cod.*; Nitre lunaire, *Fr.*; Argentum Nitricum Crystallisatum, *P. G.*; Salpetersäures Silberoxyd, Silbersalpeter, Silbernitrat, *G.*; Nitrato di argento cristallizzato, *It.*; Nitrato argentico cristalizado, Nitrato de plata, *Sp.*

The U. S. and Br. Pharmacopœias do not give processes for making this salt. The U. S. Pharmacopœia, 1870, gave the following: "Take of Silver, in small pieces, *two troyounces;* Nitric Acid, *two troyounces and a half;* Distilled Water, *a sufficient quantity.* Mix the Acid with a fluidounce of Distilled Water in a porcelain capsule, add the Silver to the mixture, cover it with an inverted glass funnel, resting within the edge of the capsule, and apply a gentle heat until the metal is dissolved, and red vapors cease to be produced; then remove the funnel, and, increasing the heat, evaporate the solution to dryness. Melt the dry mass, and continue the heat, stirring constantly with a glass rod, until free nitric acid is entirely dissipated. Dissolve the melted salt, when cold, in six fluidounces of Distilled Water, allow the insoluble matter to subside, and decant the clear solution. Mix the residue with a fluidounce of Distilled Water, filter through paper, and, having added the filtrate to the decanted solution, evaporate the liquid until a pellicle begins to form, and set it aside in a warm place

to crystallize. Lastly, drain the crystals in a glass funnel until dry, and preserve them in a well-stoppered bottle. By evaporating the mother-water, more crystals may be obtained." *U. S.*, 1870.

In the above process two details deserve notice. One of these is the direction to cover the materials in the evaporating dish, during the continuance of the reaction, with a glass funnel. This is in order to prevent the escape of fumes and to economize the nitric acid, a portion of which rises in vapor, and, being condensed on the inner surface of the funnel, falls again into the dish. The second detail is the fusion of the salt before being dissolved; the effect is to decompose any copper nitrate that might have been derived from the silver, which, if coin be employed, always contains copper. The heat decomposes the copper nitrate, and the comparatively insoluble oxide is formed, which remains on the filter when the mass is subsequently dissolved in water and filtered, the silver nitrate not being decomposed by the heat used.

A practical method used in Calcutta for separating the copper nitrate depends upon the fact that strong nitric acid only slightly dissolves silver nitrate in the presence of copper nitrate. The silver nitrate is crystallized out from the first solution as long as it can be obtained pure, and the bluish-green mother liquor is evaporated to dryness; the powdered salt, placed in a funnel stopped with asbestos, is percolated with nitric acid (sp. gr. 1.42). This washes out all of the copper nitrate, and the silver nitrate can be freed from the adhering nitric acid by heat. (*P. J.*, 1897, 61.)

During the solution of silver in nitric acid, part of the acid is decomposed and nitric oxide is given off, which becomes red by contact with the atmosphere, and the oxygen oxidizes the silver. This is taken up by the remainder of the acid, and produces silver nitrate in solution, which, by due evaporation, furnishes crystals of the salt. The silver should be pure, and the acid diluted for the purpose of promoting its action. If the silver contain copper, the solution will have a greenish tint, not disappearing on the application of heat; and if a minute portion of gold be present, it will be left undissolved as a black powder. The acid also should be pure. The commercial nitric acid, as it frequently contains both hydrochloric and sulphuric acids, should never be used. The hydrochloric acid gives rise to an insoluble chloride, and the sulphuric, to the sparingly soluble silver sulphate. It is desirable that pure silver, free from copper, should be used in this process. As silver coin always contains copper, it should be purified before being employed. For this purpose, according to the method of Lienau, it should be dissolved in nitric acid, and the solution precipitated by chlorine water, which throws down the silver only in the form of chloride. The precipitate is to be well washed with chlorine water, then dissolved in solution of ammonia, and precipitated by clean copper wire. The silver is deposited as a black powder, which, when washed with solution of ammonia, is perfectly pure. (*A. J. P.*, 1862, p. 368.) For an account of the manufacture of silver nitrate, see *D. C.*, 1887, p. 3.

Properties.—Silver nitrate is in "colorless, transparent, tabular, rhombic crystals, becoming gray or grayish-black on exposure to light in the presence of organic matter; without odor, but having a bitter, caustic and strongly metallic taste. One Gm. of Silver Nitrate dissolves in 0.4 mil of water and in 30 mils of alcohol at 25° C. (77° F.); also in slightly more than 0.1 mil of boiling water and in 6.5 mils of boiling alcohol; slightly soluble in ether. When heated in a porcelain crucible to about 200° C. (392° F.), the salt melts, forming a faintly yellow liquid, which, on cooling, congeals to a pure white, crystalline mass. At a higher temperature it is gradually decomposed with the evolution of nitrogen oxides. An aqueous solution of the salt (1 in 10) is clear and colorless and is neutral to litmus. Hydrochloric acid added to an aqueous solution of the salt (1 in 50) produces a white, curdy precipitate, insoluble in nitric acid, but readily soluble in ammonia water. Mix an aqueous solution of the salt (1 in 10) in a test tube with a drop of diphenylamine T.S. and then carefully pour on sulphuric acid so as to form a separate layer; a deep blue color appears at the line of contact. An aqueous solution of the salt (1 in 10) is not colored even faintly blue by the addition of an excess of ammonia water (*copper*).

"**Assay.**—Dissolve about 0.8 Gm. of finely powdered Silver Nitrate, previously dried in a desiccator over sulphuric acid, in the dark, and accurately weighed, in 50 mils of distilled water, add 2 mils of nitric acid and 2 mils of ferric ammonium sulphate T.S. and titrate the mixture with tenth-normal potassium sulphocyanate V.S. It shows, in the dried salt, not less than 99.8 per cent. of $AgNO_3$.

"Each mil of tenth-normal potassium sulphocyanate V.S. used corresponds to 0.016989 Gm. of $AgNO_3$. Each gramme of Silver Nitrate, dried to constant weight, corresponds to not less than 58.7 mils of tenth-normal potassium sulphocyanate V.S." *U. S.*

"In colorless tabular crystals. Taste bitter, metallic. Soluble in less than its own weight of *water*, slightly soluble in *alcohol* (90 per cent.); soluble in *ether*, and in *glycerin*. Yields the *reactions* characteristic of silver and of nitrates. 1 gramme dissolved in 15 millilitres of *water* yields with *hydrochloric acid* a precipitate, which, when washed and dried, weighs 0.845 gramme. The filtrate, when evaporated to dryness on a water bath, leaves no appreciable residue. Yields no characteristic *reactions* for lead, copper, iron, or sulphates." *Br.*

The solution stains the skin an indelible black color, and is itself discolored by the most minute portion of organic matter, for which it forms a delicate test. The affinity of this salt for animal matter is evinced by its forming definite com-

pounds with albumin and fibrin. The solution also stains linen and muslin in a similar manner, and hence its use in making the so-called indelible ink. To remove these stains, W. B. Herapath advises to let fall on the moistened spots a few drops of tincture of iodine, which converts the silver into silver iodide. The iodide is then dissolved by a solution of sodium thiosulphate, made with from half a drachm to a fluidounce of water, or by a moderately diluted solution of potassium hydroxide, and the spots are washed out with warm water. Silver stains may also be taken out by a solution of two and a half drachms of potassium cyanide, and fifteen grains of iodine, in three fluidounces of water. H. Kraetzer recommends, instead of potassium cyanide, a solution of 10 parts ammonium chloride and 10 parts corrosive sublimate in 100 parts of water, with which the stains are said to be removed readily from the hands, and from linen, wool, and cotton without injuring the fabric. (*A. Pharm.*, 1880, 52.) Silver nitrate is incompatible with most spring and river waters, on account of the chlorides usually contained in them; with soluble chlorides; with hydrogen sulphide, sulphuric, hydrochloric, and tartaric acids, and their salts; with the alkalies and their carbonates; with lime water, and with astringent infusions. It is sometimes improperly prescribed in pills with tannic acid, by which it is decomposed. Silver nitrate is an anhydrous salt, consisting of one atom of silver, combined with the monivalent group characteristic of nitric acid.

Impurities and Tests.—Hydrochloric acid or a solution of sodium chloride, added in excess to one of silver nitrate, should throw down the whole of the silver as a white curdy precipitate (darkening on exposure to light), and nothing besides. This precipitate should be entirely soluble in ammonia. If not so, the insoluble part is probably lead chloride. If the supernatant liquid, after the removal of the precipitate, be discolored or precipitated by hydrogen sulphide, the fact shows the presence of metallic matter, which is probably copper or some remains of lead, or both. The solution, after precipitation by hydrochloric acid and filtration, should leave no residue when evaporated. A piece of the salt, heated on charcoal by the blowpipe, melts, deflagrates, and leaves behind a whitish metallic coating.

Uses.—When silver nitrate in a pure state is brought in contact with a living tissue, it acts as an escharotic. Owing to the formation of a dense film of coagulated albumin, the depth of its action is very limited; the albuminous coating is at first white, but soon becomes black, owing to the reduction of the silver. Silver nitrate is among the most powerful of the chemical germicides. According to Boer, one part in four thousand is sufficient to destroy the viability of the typhoid bacillus in two hours, and Behring (*D. M. W.*, 1887) found that as dilute as 1 part in 10,000 it was capable of destroying the highly resistant anthrax spores if the exposure was sufficiently long (48 hours). It is antiseptic in proportions of 1 part in 30,000. Despite the fact that it is so easily precipitated it retains a considerable degree of germicidal power even in the presence of large quantities of albuminous material. When applied to the human tissues in dilute solution it is an active astringent; in concentrated form it is mildly caustic, but the depth of its action is very limited because the dense film of silver albuminate which is rapidly formed prevents further penetration.

Although silver nitrate, because of its affinity for proteins, cannot exist unchanged in the blood, but when taken into the stomach the silver is absorbed in some form, perhaps as a peptonate. When a non-precipitable salt of silver is introduced into the blood in sufficient quantities it causes convulsions followed by paralysis through its effect upon the spinal cord, weakening of the circulation with pulmonary edema, and respiratory embarrassment. There is, however, no known physiological action which lends any support to its use as a systemic drug.

The most important use of silver is locally as an astringent and germicide, especially in infections of the mucous membranes. The strength employed varies greatly according to the location and nature of the infection, thus in *diphtheria* or *tonsillitis* it may be used as concentrated as 4 or 5 per cent., while in *urethritis* at times it cannot be borne in higher concentrations than one part in ten thousand. In *ophthalmia neonatorum* it is useful either as a prophylactic or a curative. As a preventive the instillation of one or two drops of a 2 per cent. solution is advised in all cases of suspicious birth. In sluggish *ulcers* its astringent and stimulating effect is often of great value. It has been widely employed as an astringent in treatment of various types of *gastritis*, especially in *ulcer of the stomach*. Colonic injections of silver nitrate in strengths of ten to twenty grains to the quart have been highly lauded not only in *chronic colitis* but also in *dysentery*.

Internally silver nitrate was formerly used to some extent in the treatment of various chronic diseases of the nervous system, as *epilepsy*, *locomotor ataxia*, etc., but has largely passed out of vogue. The prolonged use internally of silver leads to a peculiar slate blue discoloration of the skin known as *argyria*. This discoloration may also appear on the mucous membrane and is probably due to a deposit of metallic silver. When once produced it is usually permanent, although Yandel has reported its disappearance under a course of potassium iodide. (*N. R.*, July, 1873.)

For internal exhibition, the physician should always prescribe the crystals, and never direct the fused nitrate, which may not be pure. Silver nitrate should always be given in pill, as the solution is decomposed by the liquids of the mouth. It should not be made up into pill with crumb of bread, as this contains common salt, but with kaolin and petrolatum, cacao butter, or other media not readily oxidizable. But, as all

organic substances decompose it more or less, Vée proposes the use of inorganic matter, such as potassium nitrate, or preferably pure silica obtained by precipitating one of the silicates by an acid, and washing it. The least possible proportion of tragacanth may be used to give adhesiveness to the mass. (*J. P. C.*, May, 1864, p. 408.)

When ingested in sufficient dose, silver nitrate is a violent poison, and upon several occasions caused death. The symptoms are those of toxic gastro-enteritis, with marked constitutional disturbance, especially coma, convulsions, paralysis, and profound alteration of the respiration. The treatment of the poisoning resolves itself into the use of the ordinary antidotes (common salt, soap, alkalies, etc.), and the use of stimulants to maintain the circulation if needed.

Dose, one-fourth to one-half grain (0.016–0.032 Gm.).

Off. Prep.—Argenti Nitras Fusus, *U. S.* (*Br.*); Argenti Nitras Induratus, *Br.*; Argenti Nitras Mitigatus, *Br.*

ARGENTI NITRAS FUSUS. U. S. (Br.)

MOULDED SILVER NITRATE Arg. Nit. Fus. [Fused Silver Nitrate, Lunar Caustic, Toughened Caustic]

(ăr-gĕn'tī nī'trăs fū'sŭs)

"It contains not less than 94.5 per cent. of $AgNO_3$ (169.89)." *U. S.*

Argenti Nitras Induratus, *Br.*; Fused Nitrate of Silver; Lapis Infernalis, Argentum Nitricum Fusum; Crayons d' Azotate d'Argent, *Fr. Cod.*; Azotas (Nitras) Argenticus Fusus, Azotate d'Argent 'fondu, Pierre Infernale, *Fr.*; Gehärteter Höllenstein, Geschmolzenes Salpetersaures Silberoxyd, Silbernitrat, *G.*; Nitrato di argento fuso, *It.*; Nitrato argentico fundido, Piedra infernal, *Sp.*

• "Silver Nitrate, *one hundred grammes* [or 3 ounces av., 231 grains]; Hydrochloric Acid, *four grammes* [or 62 grains]." *U. S.*

"Add the hydrochloric acid to the silver nitrate, contained in a porcelain dish, and melt the mixture at as low a temperature as possible. Stir it well, and pour the melted mass into suitable moulds. Preserve it in dark amber-colored vials, protected from light." *U. S.*

"Silver Nitrate, 95 grammes; Potassium Nitrate, 5 grammes. Fuse together, mix and pour into suitable moulds." *Br.*

For most purposes it is desirable to have the silver nitrate less brittle than in its pure state. J. L. Smith, of Louisville, Ky., found that this could be effected by adding a little silver chloride, which rendered the stick tough, without materially impairing its efficiency. E. R. Squibb proposed to accomplish the object by adding 40 grains of hydrochloric acid, with half a fluidounce of distilled water, to two ounces of silver nitrate, heating the mixture by means of a sand bath to dryness, and then melting and casting into moulds. (*Proc. A. Ph. A.*, 1858.) This process has been practically adopted in the U. S. Pharmacopœia. In order to keep the stick from becoming discolored during the casting process, it is advisable to add a diluted nitric acid (1 in 5) occasionally to the melted nitrate, and carefully prevent the mass from becoming overheated. In the British process the "toughening" is effected by the addition of 5 per cent. of potassium nitrate. In our opinion, this is not as efficient as is the use of hydrochloric acid. As the salt while melting penetrates a common crucible, the fusion is performed in a porcelain dish or preferably a casserole, the size of which should be sufficient to hold five or six times the quantity of the salt operated on, in order to prevent its boiling over. Sometimes small portions of the liquid are spurted out, and the operator should be on his guard against this occurrence. When the mass flows like oil, it is completely fused, and ready to be poured into the moulds. These should not be greased, as the organic matter would partially decompose the fused salt.

Properties.—Moulded silver nitrate, as prepared by the above process, is in the form of hard brittle sticks of the size of a goose quill, at first translucent, but quickly becoming gray or more or less dark under the influence of light, owing to the reduction of the silver, through organic matter or conversion through hydrogen sulphide contained in the atmosphere. That the change does not depend on the sole action of light has been proved by Scanlon, who finds that silver nitrate in a clean glass tube hermetically sealed undergoes no change by exposure to light. The sticks often become dark colored and nearly black on the surface, and when broken across, exhibit a crystalline fracture with a radiated surface. Fused silver nitrate, when pure, is wholly soluble in distilled water; but even fair samples of the moulded salt will not totally dissolve, a very scanty black powder being left of reduced silver, arising probably from the salt having been exposed to too strong a heat in fusion. Stein (*S. W. P.*, 6, 10, 1877) recommends a plan for obtaining sticks of lunar caustic of special diameter or length by taking a glass tube or rod of the required outside diameter and wrapping around it moistened parchment paper, pasting the edges, tying the lower end, and drying. The melted lunar caustic is poured into the paper mould, held upright in a test tube, and allowed to cool by standing. *Elastic crayons* of silver nitrate may be made by taking a laminaria tent one-tenth of an inch (0.002 mm.) in diameter, dipping it into thick mucilage, rolling it in finely powdered lunar caustic, and drying it. (Pajot.) Entirely black lunar caustic is sometimes seen in France, which contains about 2 per cent. of potassium nitrate and the same quantity of black manganese oxide. *Heller's caustic pencils* look like ordinary lead pencils, and consist of long, thin sticks of lunar caustic, encased in wood; they may be sharpened like lead pencils, and the point protected by a cap to prevent injury when not in use. "Moulded Silver Nitrate is a white, hard solid, generally in the form of pencils or cones, showing a fibrous fracture, becoming gray or grayish-black on exposure to light; odorless, and having a bitter, caustic, and strong metallic taste. One

Gm. of Moulded Silver Nitrate, with the exception of about 5 per cent. which is silver chloride, dissolves in 0.4 mil of water and in 30 mils of alcohol at 25° C. (77° F.); also in slightly more than 0.1 mil of boiling water and in 6.5 mils of boiling alcohol; slightly soluble in ether. A filtered, aqueous solution of Moulded Silver Nitrate (1 in 10) is neutral to litmus, and responds to the tests for identity and purity under *Argenti Nitras.*

"**Assay.**—Add about 0.8 Gm. of Moulded Silver Nitrate, accurately weighed, to 50 mils of distilled water and, when the silver nitrate has dissolved, filter the solution. Thoroughly wash the filter and sediment with distilled water, add 2 mils of nitric acid and 2 mils of ferric ammonium sulphate T.S. to the mixed filtrate and washings and titrate this liquid with tenth-normal potassium sulphocyanate V.S. It shows not less than 94.5 per cent. of $AgNO_3$. Each mil of tenth-normal potassium sulphocyanate V.S. used corresponds to 0.016989 Gm. of $AgNO_3$. Each gramme of Moulded Silver Nitrate corresponds to not less than 55.6 mils of tenth-normal potassium sulphocyanate V.S. It shows

"White or greyish-white cylindrical rods or cones. Freely soluble in *water*, but only sparingly in *alcohol* (90 per cent.). Yields the *reactions* characteristic of silver, of potassium, and of nitrates. 1 gramme, dissolved in 15 millilitres of *water*, yields with *hydrochloric acid* a precipitate which, when washed and dried, weighs 0.8 gramme, and the filtrate when evaporated leaves a white residue." *Br.*

Impurities and Tests.—Moulded silver nitrate is liable to contain free silver from having been exposed to too high a heat, lead and copper nitrates from the impurity of the silver dissolved in the acid, and potassium nitrate from fraudulent admixture or otherwise. Free silver will be left undissolved as a black powder, after the action of distilled water. A very slight residue of this kind is hardly avoidable; but if there be much free silver it will be shown by the surface of a fresh fracture of one of the sticks presenting an unusually dark gray color. The mode of detecting lead and copper is explained under silver nitrate. (See *Argenti Nitras.*) In order to detect potassium nitrate, a solution of the suspected salt should be treated with hydrochloric acid in excess, to remove silver, and with hydrogen sulphide, to throw down other metals if they happen to be present. The filtered liquid, if the salt be pure, will entirely evaporate by heat; if it contains potassium nitrate, this will be left, easily known by its properties as a nitrate. This impurity sometimes exists in moulded silver nitrate in large amount, varying, according to different statements, from 10 to 75 per cent. (See *Argenti Nitras Mitigatus.*) According to Christison, it may be suspected if the sticks present a colorless fracture. Pollacci (*J. P. C.*, 4e sér., xvii, 160) states that if silver nitrate, after having been heated in a porcelain capsule to redness and cooled, imparts an alkaline reaction to water, it contains nitre.

Uses.—Lunar caustic affords a convenient method for applying silver nitrate locally in the concentrated form, especially where combined escharotic and germicidal action is desired. It is of special service in *aphthous stomatitis, exuberant granulations, chancroids,* and various other *ulcers.* The mode of application consists in dipping the stick into distilled water and applying to the part for a greater or less period of time according to the degree of action which is desired.

The moulded silver nitrate has also been used as a counter-irritant. If it be rubbed gently back and forth over the moistened skin until the latter assumes a grayish color, it generally vesicates, usually with less pain than is produced by cantharides. As a counter-irritant it has been employed in the treatment of violent inflammations of the subcellular tissue and it is asserted that it will sometimes avert a felon or an *epididymitis.*

Lunar caustic is also frequently used as a topical remedy in various superficial inflammations. The method, originated in 1820 by John Higginbottom, of treating *erysipelas* by silver nitrate still finds favor with some of the profession. After thorough washing of the skin with soap and water, and afterwards with pure water, and subsequent drying, a concentrated solution of twenty grains of silver nitrate to a drachm of distilled water is applied freely on the inflamed surface and beyond it on the healthy skin by means of a linen mop. It has been employed by injection for the radical cure of *hydrocele,* and in solid stick applied as a fine point to each *pustule of small-pox* upon the face for the prevention of pitting.

ARGENTI NITRAS MITIGATUS. Br.

MITIGATED CAUSTIC

(ăr-gĕn'tī nī'trās mĭt-ĭ-gā'tŭs)

Mitigated Silver Nitrate [Argenti Nitras Dilutus, U. S. 1890, Diluted Silver Nitrate, Mitigated Caustic] Silver and Potassium Nitrate; Lapis infernalis nitratus; Crayons d'Azotate d'Argent mitigé, Pierre infernale diluée, *Fr.;* Argentum Nitricum cum Kalio nitrico, *P. G.;* Salpeterhaltiges Silbernitrat, Salpeterhaltiger Höllenstein, *G.;* Nitrato di argento fuso con nitrato di potassio, *It.;* Nitrato argentico mitigado, Piedra infernal mitigada, *Sp.*

"Silver Nitrate, 20 *grammes;* Potassium Nitrate, 40 *grammes.* Fuse together, mix and pour into suitable moulds." *Br.*

Mitigated silver nitrate was dismissed from the U. S. Pharmacopœia IX, but was retained in the Br. Pharm., 1914. The process was practically the same in both pharmacopœias, the strength is 33.3 per cent. of pure silver nitrate.

The introduction of these preparations grew out of the frequent demand for a fused silver nitrate which would not be so severe in its action as the pure article. The manufacturers have been furnishing for many years a "*No. 2 Lunar Caustic,*" which contains 67 per cent. of pure silver nitrate; the diluted nitrate of the

U. S. P. 1880 contained 50 per cent. of lunar caustic.

Properties.—"White or greyish-white cylindrical rods or cones. Freely soluble in *water*, but only sparingly in *alcohol* (90 per cent.). Yields the *reactions* characteristic of silver, of potassium, and of nitrates. 3 grammes, dissolved in 15 millilitres of *water*, yield with *hydrochloric acid* a precipitate which, after washing with hot *water* and drying, weighs 0.843 gramme." *Br.*

Uses.—This preparation is used only externally. It is similar in its action to the fused nitrate, but less energetic.

ARGENTI OXIDUM. U. S.

SILVER OXIDE Arg. Oxid.

(ăr-gĕn'tī ŏx'ĭ-dŭm)

"It contains, when dried to constant weight at 120° C. (248° F.), not less than 99.6 per cent. of Ag_2O (231.76). Preserve it in well-stoppered, dark amber-colored vials. It must not be triturated with readily oxidizable or combustible substances, and must not be brought in contact with ammonia." *U. S.*

Argentum Oxydatum, Argentic Oxide; Oxyde d'Argent, *Fr.*; Silberoxyd, *G.*

Silver Oxide was dismissed from the British Pharmacopœia (1914), but retained in the U. S. P. IX. The U. S. P. 1870 process for preparing it, follows: "Take of Nitrate of Silver *four troyounces;* Distilled Water *half a pint;* Solution of Potassa *a pint and a half,* or *a sufficient quantity.* Dissolve the Nitrate of Silver in the Water, and to the solution add Solution of Potassa so long as it produces a precipitate. Wash this repeatedly with water until the washings are nearly tasteless. Lastly, dry the precipitate and keep it in a well-stopped bottle, protected from the light."

Silver oxide was introduced into the U. S. P. of 1850, and was adopted in the Br. Ph. from the Dublin. In the processes for making it, silver nitrate is decomposed by potassium hydroxide or lime, the oxide being precipitated, and potassium nitrate or calcium nitrate, as the case may be, remaining in solution. When thus obtained, the oxide is an olive-brown powder. If the potassium hydroxide used be not wholly free from carbon dioxide the precipitated oxide will be contaminated with some silver carbonate. According to Borland of London, the carbonate is sometimes sold for the oxide. A third process for obtaining this oxide, by Gregory, consists in boiling the moist, recently prepared silver chloride with a strong solution of potassium hydroxide (sp. gr. 1.25 to 1.30), when by double decomposition, silver oxide and potassium chloride are formed.

Properties.—"Silver Oxide is a heavy, dark brownish-black powder, easily reduced by exposure to light; odorless, and having a metallic taste. Silver Oxide is very slightly soluble in water, to which, however, it imparts an alkaline reaction; insoluble in alcohol; it is dissolved by nitric acid. When heated in a porcelain crucible to about 250° to 300° C. (482°–572° F.), Silver Oxide is rapidly decomposed, with the evolution of oxygen, leaving a residue of metallic silver. Dissolve about 0.2 Gm. of the Oxide in a mixture of 1 mil of nitric acid and 2 mils of distilled water, add 10 mils of ammonia water and dilute the liquid to 60 mils; 10 mils of this solution does not immediately become cloudy upon the addition of 1 mil of nitric acid (*chloride*). A solution of the Oxide in nitric acid is colorless, and responds to the tests for identity and purity under *Argenti Nitras* when the tests are applied to a solution of proportionate strength.

"**Assay.**—Dissolve about 0.5 Gm. of Silver Oxide, previously dried to constant weight at 120° C. (248° F.) and accurately weighed, in 3 mils of nitric acid and 50 mils of distilled water in a flask, add 2 mils of ferric ammonium sulphate T.S. and titrate the mixture with tenth-normal potassium sulphocyanate V.S. It shows, in the dried Silver Oxide, not less than 99.6 per cent. of Ag_2O. Each mil of tenth-normal potassium sulphocyanate V.S. used corresponds to 0.011588 Gm. of Ag_2O. Each gramme of Silver Oxide, dried to constant weight, corresponds to not less than 86.0 mils of tenth-normal potassium sulphocyanate V.S." *U. S.*

When its solution in nitric acid is precipitated by sodium chloride in excess, the supernatant liquid is not discolored by ammonium sulphide. It parts with its oxygen with great facility, being decomposed by many organic substances; in this way it causes sulphur, amorphous phosphorus, or tannin to take fire when rubbed with it, in a mortar.

Uses.—This oxide has been proposed as a substitute for silver nitrate, as having the general therapeutic virtues of the latter, without its escharotic effect and its objectionable property of discoloring the skin. Experience, however, has shown that it will tint the skin. (*N. Y. M. J.*, June, 1869; *P. M. T.*, vi.) It may be used in *gastric* and other *catarrhs,* but is inferior to the nitrate. If pills are ordered, they should not be made with honey, confection of rose, or other excipient containing glucose; and, indeed, most organic substances, especially in a moist state, deoxidize the oxide, reviving the silver. A case is recorded in which pills containing it exploded violently in the pocket of the patient. (See Jackson, *P. J.*, xi, 552.) An ointment from five to ten grains to the drachm, has been used as an application to *venereal sores,* and to the urethral membrane in *gonorrhea;* it should be smeared on a bougie.

Dose, one grain (0.065 Gm.).

ARGENTUM

SILVER

(ăr-gĕn'tŭm)

Argentum purificatum; Argent raffiné, Argent, *Fr.*; Silber, Raffinirtes Silber, *G.*; Argento, *It.*; Plata, *Sp.*

Silver is found at times in the metallic state, usually crystallized, also associated with gold,

antimony, arsenic, or mercury; but usually it occurs as a sulphide, pure or mixed with other sulphides, as those of copper, lead, and antimony. It is sometimes found as a chloride.

The most productive mines of silver are found on this continent, being those of Mexico and Peru and our own Rocky Mountain States and Territories; the richest in Europe are those of Norway, Hungary, and Transylvania. Mines have been opened and profitably worked in California and Nevada, but at present it is chiefly Colorado and Montana which furnish the great bulk of the American silver production. Idaho, Utah, and Arizona also contain very rich silver deposits. The principal ore is the sulphide. The mineral containing silver which is most disseminated is argentiferous galena, which is lead sulphide containing a little silver sulphide. Argentiferous galena exists in several localities in the United States. Native silver is associated, in small quantities, with the native copper of the Lake Superior region, and a little of it has come into the market. The two metals, though more or less mixed, are yet quite distinct, never being alloyed to any considerable extent, showing conclusively that the deposits have not undergone igneous fusion at any time, but that the metals have deposited from solution. The production of silver in the United States in 1915 amounted to 74,961,075 ounces, valued at $37,397,300.

Extraction.—Silver is extracted from its ores by two principal processes, *amalgamation* and *cupellation*. When the ore is principally the sulphide, it is mixed with a tenth of sodium chloride and roasted in reverberatory furnaces. As fast as the sulphide is oxidized to sulphate, this reacts with the sodium chloride, forming silver chloride and sodium sulphate. The roasted mass is then reduced to very fine powder, mixed with half its weight of mercury, one-third of its weight of water, and about one-seventeenth of iron in flat pieces, and subjected for sixteen or eighteen hours to constant agitation in barrels turned by machinery. The chlorine combines with the iron, and remains in solution as iron chloride, while the reduced silver forms an amalgam with the mercury. The amalgam is then subjected to pressure in leather bags, through the pores of which the excess of mercury passes, a solid amalgam being left behind. This is then subjected to heat in a distillatory apparatus, by means of which the mercury is separated from the silver, which is left in a porous mass. In Peru and Mexico the process is similar to that above given, common salt and mercury being used; but slaked lime and iron sulphide are also employed, with little effect.

When argentiferous galenas are worked for the silver they contain, they are at first reduced, and the argentiferous lead obtained is fused on a large, oval, shallow vessel called a test, and exposed to the blast of a bellows, whereby the lead is oxidized, half vitrified, and driven off the test in scales, in the form of litharge. The operation being continued on successive portions of argentiferous lead, the whole of the lead is separated, and the silver, not being oxidizable, accumulates on the test as a brilliant fused mass, until its amount is sufficient to be removed. The time required for the separation is much abridged by the process of Pattinson. This consists in allowing the melted alloy to cool slowly, and separating the crystals which first form, consisting mainly of lead, by means of a perforated ladle. The residue is a very fusible alloy of lead and silver, in which the latter metal is in large proportion, and from which it can be easily separated by cupellation or other means. In recent years much gold and silver have been extracted from tailings and so-called "slimes" by the *cyanide* process and most recently by the *oil flotation* process.

Properties.—Silver is a white metal, very brilliant, tenacious, malleable, and ductile. In malleability and ductility it is inferior only to gold. It is harder than gold, but softer than copper. Its atomic weight is 107.88, symbol Ag, and sp. gr. from 10.4 to 10.5. What is termed "molecular silver" is obtained as a very fine powder, by reducing freshly precipitated silver chloride with formaldehyde in the presence of potassium carbonate. "*Colloidal silver*" is obtained by heating to 100° C. (212° F.) silver citrate in a stream of hydrogen or by passing an electric current between silver electrodes in water. It dissolves in water to a red solution which does not dialyze. Both these allotropic forms are converted into ordinary silver by fusion. (For further description, see Part II.) Silver forms but one well-characterized oxide. Exposed to a full red heat, it enters into fusion, melting at 954° C. (1749.2° F.), and exhibits a brilliant appearance. It is not oxidized in the air, but contracts a superficial tarnish of silver sulphide by the action of hydrogen sulphide in the atmosphere, from which it may be freed by washing it with a strong solution of potassium cyanide, and, as soon as it becomes bright, washing it with water and drying it. It is entirely soluble in diluted nitric acid. If any gold be present, it will remain undissolved as a dark-colored powder. From the nitric solution the whole of the silver may be thrown down by sodium chloride, as a white precipitate of silver chloride, characterized by being completely soluble in ammonia. If the remaining solution contain copper or lead, it will be affected by hydrogen sulphide. "The solution, deprived of silver by means of sodium chloride, and filtered, is not colored, *or but slightly so*, and is not precipitated by hydrosulphuric acid." *U. S.* 1870. "If ammonia be added in excess to a solution of the metal in nitric acid, the resulting fluid exhibits neither color nor turbidity" (*Br.* 1885); proving the absence of copper, lead, and other metals. "10 grains dissolved in a little nitric acid, the solution diluted with water, and diluted hydrochloric acid added in slight excess, yields a white precipitate which, when thoroughly washed, dried, and heated, weighs 13.25 grains." *Br.* 1885.

ARMORACIÆ RADIX. Br.

HORSERADISH ROOT

(ăr-mo-rā'cī-æ rā'dix)

"Horseradish Root is the fresh root of Cochlearia Armoracia, *Linn.*, collected from cultivated plants." *Br.*

Armoracia, Br. 1864; Raifort sauvage, Moutarde des Moines, Radis de Cheval, Cran de Bretagne, *Fr.*; Meerrettig, *G.*; Rabano rusticano (Raiz de), *Sp.*

Cochlearia Armoracia L. (also known as *Roripa Armoracia* (L.) Hitch. and *Radicula Armoracia* (L.) Robinson) is a native of the marshy districts of Great Britain. It is cultivated very largely for its roots which are used as a condiment, being considered stimulating to the digestive organs. It has escaped from our gardens, growing in moist grounds, especially along streams. The root of this plant is perennial, sending up numerous very large radical leaves from the midst of which a round, smooth, erect, branching stem rises two or three feet in height. The radical leaves are lance-shaped, waved, scolloped on the edges, sometimes pinnatifid, and stand upon strong footstalks. Those of the stem are much smaller, without footstalks, sometimes divided at the edges, sometimes almost entire. The flowers are numerous, white, peduncled, and form thick terminal clusters.

The root, which is official in its fresh state, is long, conical at top, then nearly cylindrical for some inches, at last tapering, whitish externally, very white internally, fleshy, of a strong pungent odor when scraped or bruised, and of a hot, biting, somewhat sweetish, and sometimes bitterish taste. "Nearly cylindrical, except at the crown, where it is somewhat enlarged, and marked with closely approximated semi-amplexicaul leaf-scars. Diameter from twelve to twenty-five millimetres, length commonly thirty centimetres or more; pale yellowish-white or brownish-white externally, whitish within. Inodorous when unbroken, but yielding a characteristic pungent odor when scraped or bruised; taste very pungent." *Br.* Its virtues are imparted to water and alcohol. They depend upon a *volatile oil*, which is dissipated by drying, the root becoming at first sweetish, and ultimately insipid and quite inert. Its acrimony is also destroyed by boiling. The oil may be obtained by distillation with water. It is colorless or pale yellow, heavier than water, very volatile, excessively pungent, acrid, and corrosive, exciting inflammation and even vesication when applied to the skin. Hubatka considers it as identical with the volatile oil of mustard. He combined it with ammonia and obtained crystals of *thiosinamin*, $NH_2.CS.N(C_3H_5)H$, which agreed with that produced from mustard oil. (*J. P. C.*, 3e sér., v, 42.) According to Gutret, only six parts of it are obtained from 10,000 of the root. Besides this principle, the fresh root contains, according to the same chemist, a bitter resin in minute quantity, sugar, extractive, gum, starch, albumen, acetic acid, calcium sulphate and acetate, water, and lignin. A. Hilger found in the ashes of the root of horseradish the following: calcium, magnesium, potassium, a trace of sodium and iron in combination with sulphuric, hydrochloric, carbonic, phosphoric, and silicic acids. (*Chem. Cb.*, p. 597, 1878; *A. J. P.*, 1879, p. 21.) From observations made by F. L. Winckler, it may be inferred that *myronic acid* exists in the root combined with potassium, and that it is from the reaction between this potassium myronate, *myrosine*, an enzyme, also existing in the root, and water, that the volatile oil is produced, in the same manner as oil of mustard from mustard seed. (See *Sinapis.*) Horseradish when distilled with alcohol yields none of the oil. Buried in cool sand the root may be kept for some time without material injury.

It is said that if to the powder of the dried root which has become apparently inert, the emulsion of white mustard seed containing myrosin be added, it reacquires its original irritant properties; so that it is the myrosin and not the potassium myronate which is injured by drying. Hence the powdered root may be added with advantage to mustard in preparing cataplasms, pediluvia, etc. (*J. P. C.*, xxvii, 268.)

The French Codex contains a formula for *compound syrup of horseradish* under the name of *Sirop de Raifort Composé.* It was formerly called *Sirop Antiscorbutique.*

Uses.—Horseradish is highly stimulant, exciting the stomach when swallowed, and promoting the secretions, especially that of urine. Externally it is rubefacient. Its chief use is as a condiment to promote appetite and invigorate digestion.

Dose, fifteen to thirty grains (1–2 Gm.) or more, grated or cut into small pieces.

Off. Prep.—Spiritus Armoraciæ Compositus, *Br.*

ARNICA. U. S. (Br.)

ARNICA Arnic. [Arnicæ Flores, U. S. 1890 Arnica Flowers]

(ăr'nĭ-cą)

"The dried flower-heads of *Arnica montana* Linné (Fam. *Compositæ*)." *U. S.* "Arnica Flowers are the dried flower-heads of Arnica montana, *Linn.*" *Br.*

Arnicæ Flores, *Br.*; Leopard's Bane, Wolf's Bane, Mountain Tobacco; Fleurs d'Arnique, *Fr.*; Flores Arnicæ *P. G.*; Wohlverleihblüthen, Arnicablüthen, Arnika, Blutblume, Gemsblume, Fallkraut, *G.*; Fiori di arnica, *It.*; Flor de arnica, *Sp.*

Arnica montana is a perennial herbaceous plant, having a woody, brownish, horizontal rhizome, from 2 to 10 cm. long, and 0.5 to 5 mm. thick, ending abruptly, and sending forth numerous slender fibers of the same color. The stem is about 3 dm. high, cylindrical, striated, hairy, and terminating in one, two, or three peduncles, each bearing a flower. The radical leaves are ovate, entire, ciliated, and obtuse; those of the stem, which usually consist of two opposite pairs, are lance-shaped. Both are

bright green, and somewhat pubescent on their upper surface. The flowers are yellow.

This plant is a native of the mountainous districts of western and central Europe, and is found, according to Nuttall, in the northern regions of this country, west of the Mississippi. It has been introduced into England, and might no doubt be cultivated in the United States. The flowers, leaves, and root are employed; but the flowers only are official in the U. S. P. (9th Rev.). In the Swiss and German Pharmacopœias the definition of arnica flowers is restricted to the flowers separated from the receptacles, this being done as the latter contain the larvæ of *Trypeta arnicivora*. On the other hand the Austrian Pharmacopœia permits the use of the entire flower heads, but the receptacles containing larvæ must be removed.

Properties.—The whole plant, when fresh, has a strong, disagreeable odor, which is apt to excite sneezing, and is diminished by drying. The taste is acrid, bitterish, and durable. Water extracts its virtues. The U. S. Pharmacopœia thus describes the flowers: "Consisting chiefly of the tubular and ligulate flowers, occasionally with the involucre and receptacle present; involucral bracts narrowly lanceolate, about 1 cm. in length, dark green and pubescent; receptacle slightly convex, deeply pitted and densely short-hairy; ray flowers bright yellow, the ligulate portion 2 cm. in length, more or less folded lengthwise, 3-toothed, 7- to 12-veined, pistillate; tubular flowers perfect, reddish-yellow, stamens without a tail-like appendage (distinguished from anthers in flowers of *Inula Helenium* Linné, which have two bristles or long tails at the base); the achenes spindle-shaped, from 5 to 7 mm. in length, dark brown, finely striate, glandular-pubescent and surmounted by a pappus a little longer than the achene and composed of a single circle of nearly white barbellate bristles; odor characteristic and agreeable; taste bitter and acrid. The powder is yellowish-brown; pollen grains numerous, from 0.025 to 0.035 mm. in diameter, spherical, triangular in section and spinose; non-glandular hairs of three kinds, either unicellular, 4- to 6-celled, or consisting of a pair of unicellular hairs with numerous pores on the dividing wall; glandular hairs of three kinds, either with a large unicellular stalk and a unicellular, glandular head, or with a 4-celled stalk and a unicellular, glandular head, or a stalk of a double row of 5 cells and a 2-celled, glandular head; pappus consisting of a multicellular axis with unicellular branches. Arnica yields not more than 9 per cent. of ash." *U. S.*

"Receptacle nearly flat, bristly, with two rows of dark-green, linear-lanceolate, acute, hairy bracts. Each ray-floret possesses a much shrivelled dark yellow ligulate corolla which, after expansion in water, exhibits from eight to twelve veins and three terminal teeth. Disc-florets numerous, yellow. Fruits slender, shrivelled, with numerous appressed hairs, and crowned with a single row of stiff, whitish, barbed bristles. Slight aromatic odor; taste bitter and acrid." *Br.*

Arnica flowers of commerce are not infrequently admixed with and substituted by other composite flowers. Farwell states that the heads of *Lapachis columnaris* T. et G., a western composite, have been offered in large quantities for arnica. Hartwich has recently found a sample of arnica adulterated with the flowers of the common dandelion. Beilstein reported having found in one lot approximately 90 per cent. of the flowers of *Inula*. The following flowers also have been used: *Anthemis tinctoria* L., *Calendula officinalis* L., *Doronicum Pardalianches* L., *Inula britannica* L., and *Scorzonera humilis* L. The first three of these are distinguished by the fact that the achenes do not have any pappus. In *Inula* the receptacle is naked and the lingulate flowers are four-nerved. In *Scorzonera* the flowers are all ligulate and the pappus is feather-shaped.

The rhizome which was formerly official in both the British and U. S. Pharmacopœias was described by the latter as follows:

"Rhizome about 5 Cm. long, and 3 or 4 Mm. thick; externally brown, rough from leaf-scars; internally whitish, with a rather thick bark, containing a circle of resin-cells, surrounding the short, yellowish wood-wedges, and large, spongy pith. The roots numerous, thin, fragile, grayish-brown, with a thick bark containing a circle of resin-cells. Odor somewhat aromatic; taste pungently aromatic and bitter." *U. S.*, 1890.

Arnica rhizome is at the present time officially recognized only by the Austrian Pharmacopœia. It is frequently substituted by or admixed with the rhizomes of other plants. Of these the following are easily recognized because of their absence of balsam canals: *Achyrophorus maculatus* Scop., *Hieracium murorum* L., *Fragaria vesca* L., and *Betonica officinalis* L. The rhizomes of *Eupatoria cannabinum* L. are completely surrounded with small roots. The rhizome of *Solidago Virgaurea* L. has a thicker and yellowish rhizome, the taste being very faintly aromatic. The rhizome of *Geum urbanum* L. has an odor resembling cloves.

Bastick (*P. J.*, x, 389) separated what he believed to be an alkaloid from the flowers, to which he gave the name of *arnicine*. The *arnicin* of Walz (*N. Jahrb. Pharm.*, xiii), extracted from both the root and the flowers, is a different substance; it is an amorphous yellow mass of acrid taste, slightly soluble in water, freely in alcohol or ether, and dissolving also in alkaline solutions. It is precipitable from its alcoholic solution by tannic acid or by water. Walz assigns to arnicin the formula $C_{20}H_{30}O_4$; other chemists that of $C_{35}H_{54}O_7$. Arnicin has not been proved to be a glucoside, although it is decomposed by diluted acids. Sigel (1873) obtained from dried arnica root about ½ per cent. of essential oil, and 1 per cent. from the fresh; the oil of the latter had a sp. gr. of 0.999 at 18° C. (64.4° F.). The oil was found to be a mixture of various bodies, the principal

being the *dimethyl ether of thymohydroquinone*, $C_{10}H_{12}\begin{cases}OCH_3\\OCH_3\end{cases}$, boiling at about 235° C. (455° F.), and with this, *phloryl isobutyrate* to the extent of one-fifth of the oil, and the *methyl ether of a phlorol.* (*Pflanzenstoffe*, 2d ed., p. 1530.) Kondakow (1910) confirmed the results of Sigel's investigations. (*J. P. Chem.*, ii, 79.) (See also Gildemeister and Hoffmann, *Die Aetherische Oele*, p. 900.) The water from which the oil separates contains *isobutyric acid*, probably also a little *angelic* and *formic acids*, but neither capronic nor caprylic acid, which had been pointed out by Walz. Arnica root contains *inulin*, which Dragendorff extracted from it to the extent of about 10 per cent. (*Pharmacographia*, 2d edition, p. 391.) Klobb reported the presence in arnica flowers of a colorless, crystalline body which he at first named *arnisterin*, but in 1905 he changed its name to *arnidiol.* (*Ph. Ztg.*, 1905, xl, p. 846.)

Uses.—Arnica is an active irritant, which is capable when taken in overdose of producing symptoms of violent toxic gastro-enteritis, with great nervous disturbance, reduction or increase of the pulse rate, and collapse. In a number of cases of severe or even fatal poisoning by it, the symptoms have been burning pains in the stomach, vomiting, choleraic diarrhea, giddiness, intense muscular weakness, dilated pupils, finally complete insensibility and collapse. In some cases the disturbances of the gastro-intestinal canal have been absent, and the symptoms have chiefly been of cerebral origin. An ounce of the tincture (*L. L.*, Nov., 1864) has produced serious but finally not fatal symptoms.

Arnica has been used in Germany in the treatment of *palsies* and various other diseases, but we have very little positive knowledge concerning its action upon the system, and there is no sufficient reason for believing that it is valuable in the treatment of internal diseases. It is largely employed externally in the treatment of *bruises* and *sprains*, generally in the form of the tincture.

The powdered flowers and leaves are employed as a sternutatory; and the inhabitants of Savoy and the Vosges are said to substitute them for tobacco. They may be given in substance or infusion. The dose of the powder is from five to twenty grains (0.32–1.3 Gm.), frequently repeated. The infusion may be prepared by digesting an ounce of the flowers in a pint of water, of which from half a fluidounce to a fluidounce (15–30 mils) may be given every three hours. It should always be strained through linen, in order to separate the fine fibers, which might irritate the throat. A tincture of the root was official in the British Pharmacopœia, 1898, this would be preferable for internal use. (See *Tinctura Arnicæ.*)

Dose, of the flowers, fifteen grains (1 Gm.).

Off. Prep.—Tinctura Arnicæ, *U. S.* (*Br.*) (from flowers); Fluidextractum Arnicæ, *N. F.*

ARSENI IODIDUM.—U. S. (Br.)

ARSENOUS IODIDE Arsen. Iod. [Arsenic Iodide]

(ăr'sẹ-nī ī-ōd'ī-dŭm)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99 per cent. of AsI_3 (455.72). Preserve it in amber-colored, glass-stoppered vials, in a cool place, protected from light." *U. S.* "Arsenious Iodide, AsI_3, may be obtained by the direct combination of iodine and arsenium, and purification of the product by crystallisation." *Br.*

Arsenii Iodidum, *Br.*; Arsenici Iodidum, *U. S.* 1870; Iodide of Arsenic, Arsenious Iodide; Iodure d'Arsenic, *Fr.*; Arsenicum jodatum, Arsenik Jodür, Arsentrijodid, *G.*

This iodide was introduced into the U. S. Pharmacopœia for the purpose of being used in preparing the solution of arsenous and mercuric iodides. It may be made by the direct combination of its constituents, with the aid of a gentle heat, but this form readily decomposes, the iodine subliming and condensing in crystals upon the upper portion of the bottle containing it. The orange red crystalline powder now official is much more permanent.

Nickle's process enables the operator to obtain the salt in a crystalline condition. Arsenic and iodine in equivalent proportions are heated together with carbon disulphide in a flask, to which an upright condenser is attached, until the iodine color disappears. The solution is then evaporated to the crystallizing point.

In the *Ber. d. Chem. Ges.*, 1881, 2643, may be found a process for obtaining this salt chemically pure, by making a hot solution of arsenic trioxide in hydrochloric acid, and mixing it with a concentrated solution of potassium iodide, whereupon the triiodide separates as a crystalline powder; this may be washed with hydrochloric acid, sp. gr. 1.120, until a portion of the washings on evaporation ceases to leave a residue of potassium chloride.

Properties.—Arsenous iodide is described as "an orange-red, inodorous, crystalline powder, stable when protected from direct sunlight and kept in a cool place. One Gm. of Arsenous Iodide dissolves in about 12 mils of water at 25° C. (77° F.), with partial decomposition; soluble in alcohol, chloroform, ether, or carbon disulphide. No loss of iodine occurs when dry Arsenous Iodide is heated on a water bath, but at higher temperatures it volatilizes, leaving not more than 0.5 per cent. of residue. When warmed with a few drops of nitric acid, brown vapors of nitrogen oxides are evolved, followed by violet vapors of iodine. A freshly prepared aqueous solution of the salt is colorless, but upon standing it gradually decomposes with the formation of arsenous and hydriodic acids and becomes yellow. Add hydrogen sulphide T.S. to an aqueous solution of Arsenous Iodide, acidulated with hydrochloric acid; a lemon-yellow precipitate of arsenous sulphide is produced. Add 1 mil of chlorine water to 5 mils of an aqueous solution of the salt (1 in 20); iodine is liberated and imparts to the solution a light red-

dish-brown color. Agitate this mixture with 1 mil of chloroform; the latter acquires a violet color.

"**Assay.**—Proceed as directed under the Assay for iodides (see Part III, Test No. 5), using about 0.5 Gm. of Arsenous Iodide, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed. It shows, in the dried salt, not less than 99 per cent. of AsIs.

"Each mil of tenth-normal silver nitrate V.S. corresponds to 0.015191 Gm. of AsIs. Each gramme of Arsenous Iodide, dried to constant weight, corresponds to not less than 65.2 mils of tenth-normal silver nitrate V.S." *U. S.*

"Small orange-colored crystals. Soluble in *water*, and in *alcohol* (90 per cent.). The aqueous solution is acid to *litmus*, and yields the *reactions* characteristic of arsenic and of iodides. Heated in a test-tube it entirely volatilises, violet vapors of iodine being set free." *Br.*

It has a tendency to decompose even at ordinary temperatures, iodine separating and volatilizing, oxygen being absorbed and arsenic trioxide formed.

Uses.—Following the suggestion of Biett arsenous iodide has been somewhat extensively used in the treatment of *lupus* and other skin conditions in which a powerful stimulant is desired; Biett employed the oirtment of the strength of three grains to the ounce. The iodide has also been given internally as an alterative, in *cancer*, in *scrofula*, *lepra*, etc., and probably does not differ in its action from other preparations of arsenic. In large doses it acts as a violent gastro-intestinal irritant and poison.

Dose, one-tenth of a grain (0.006 Gm.).

Off. Prep.—Liquor Arseni et Hydrargyri Iodidi, *U. S.* (*Br.*).

ARSENI TRIOXIDUM. U. S. (Br.)

ARSENIC TRIOXIDE Arsen. Triox. [Acidum Arsenosum, U. S. 1890, Arsenous Acid, Arsenous Anhydride, Arsenous Oxide, White Arsenic]

(ăr'sẹ-nī trī-ŏx'ĭ-dūm)

"It contains, when dried to constant weight at 100° C. (212° F.), not less than 99.8 per cent. of As_2O_3 (197.92)." *U. S.* "Arsenious Anhydride may be obtained by roasting certain arsenical ores, and contains not less than 99.8 per cent. of arsenious oxide, As_4O_6." *Br.*

Acidum Arseniosum, *Br.*; Arsenicum Album, *Ed.*; Arsenic, Acide arsénieux, *Fr. Cod.*; Arsenic blanc, Fleurs d'Arsenic, *Fr.*; Acidum Arsenicosum, *P. G.*; Arsenigesäure, Arsenichte Säure, Weisser Arsenik, *G.*; Anidride arseniosa, Acido arsenioso, Arsenico bianco, *It.*; Anhidrido arsenioso, Arsenico blanco, *Sp.*; Arsenik, *Dan., Swed., Pol.*

Arsenic trioxide is prepared in Bohemia and Saxony, where it is procured on a large scale as a collateral product during the smelting of cobalt ores, which are almost invariably accompanied by arsenic, and in England from the mineral *arsenopyrite*, also called *mispickel* or *arsenical iron*, which is associated with the ores of tin and copper. Most of the arsenous oxide produced in the United States is from this latter mineral. The German process is that usually quoted as the older and better known. According to this, the ores are roasted in reverberatory furnaces with long horizontal flues. The arsenic is converted by combustion into arsenic trioxide, which rises in vapor and condenses on the sides of the flues. In this state it is impure, and requires a second sublimation, which is performed in cast iron vessels, fitted with conical heads of the same material, having an opening at the summit. The vessels are placed over a furnace, and brought to a red heat, when a portion of the impure arsenic trioxide is thrown in through the opening, which is immediately stopped. This portion being sublimed, a second portion is introduced in a similar manner. Finally, the vessels are allowed to cool; and upon removing the heads the purified oxide is found attached to them, in vitreous layers, at first as transparent as glass, but gradually becoming, by contact with the air, opaque at their surface. These are broken into fragments of a convenient size, and thus enter commerce. The arsenic trioxide so obtained is generally packed in casks, containing from two to five hundred pounds, and is shipped principally from the ports of Hamburg and Bremen. The English process differs somewhat in its details, and essentially in its final product, which is fine and crystalline rather than amorphous. In this process the crude arsenic of the first sublimation is refined by introducing it into another furnace or series of furnaces, where it is again volatilized by the heat. When it condenses in the long series of chambers through which the vapors are carried, it is, if the process be fully successful, in the form of a perfectly white crystalline solid, which needs only to be ground and packed into kegs to be made ready for the market. The unground arsenic is, as stated, all in the *crystalline* condition, the temperature of the chambers being too low to permit the formation of the glassy variety. The production of arsenous oxide in the United States in 1915 was 5195 tons, largely from the flue dust of arsenical copper and lead ores.

Properties.—Arsenic trioxide is entirely volatilized by heat. As the German make of arsenic occurs in commerce, it is in masses, with a vitreous fracture, and of a milk-white color externally, but, internally, often perfectly transparent. As first sublimed, the whole mass is transparent; but it gradually becomes white and opaque, the change proceeding progressively from the surface inwards. This change has not been well explained, but probably depends upon the absorption of moisture, causing a gradual passage of the acid from the amorphous to the crystalline state. The U. S. Pharmacopœia IX describes arsenic trioxide as follows: "An opaque, white powder, or in irregular masses of two varieties: one, amorphous, transparent, and colorless, like glass; the other, crystalline, opaque, and white, resembling porcelain. Frequently the same piece has an opaque, white outer crust enclosing the glassy variety. Contact with moist air gradually changes the glassy into the white, opaque variety. Both are odorless. Arsenic Trioxide is soluble in water, the amorphous or glassy variety being somewhat more soluble than the crystalline variety; it is

slightly soluble in alcohol and in ether and freely soluble in glycerin and is dissolved by hydrochloric acid and alkaline solutions. An aqueous solution of Arsenic Trioxide is faintly acid to litmus. When slowly heated in a dry test tube of hard glass, Arsenic Trioxide yields a sublimate of minute, brilliant, transparent, octahedral crystals and does not show a yellow color (*arsenous sulphide*). When heated rapidly to about 200° C. (392° F.), the amorphous variety fuses, then sublimes, while the crystalline variety sublimes without fusing. Not more than 0.1 per cent. of residue remains after sublimation. When covered with charcoal in an ignition tube, and strongly heated, Arsenic Trioxide is reduced, and metallic arsenic is deposited on the cooler portion of the tube as a mirror, having a metallic luster, and this mirror is readily dissolved by solutions of sodium or calcium hypochlorite. Hydrogen sulphide T.S. colors an aqueous solution of Arsenic Trioxide (1 in 100) yellow; on adding a few drops of hydrochloric acid to the colored solution, a lemon-yellow precipitate of arsenic trisulphide is produced, which is completely soluble in ammonium carbonate T.S. (*antimony, tin, and cadmium*). Dissolve 1 Gm. of Arsenic Trioxide in 10 mils of ammonia water with the aid of a gentle heat; a colorless solution is produced.

"**Assay.**—Dissolve about 0.2 Gm. of Arsenic Trioxide, previously dried to constant weight at 100° C. (212° F.) and accurately weighed, in 20 mils of boiling distilled water by the gradual addition of sodium hydroxide T.S. until complete solution results. Neutralize this solution with diluted sulphuric acid V.S., using phenolphthalein T.S. as indicator, cool, dissolve in it 2 Gm. of sodium bicarbonate and titrate the mixture with tenth-normal iodine V.S., using starch T.S. as indicator. It shows, in the dried Arsenic Trioxide, not less than 99.8 per cent. of As_2O_3.

"Each mil of tenth-normal iodine V.S. used corresponds to 0.004948 Gm. of As_2O_3. Each gramme of Arsenic Trioxide, dried to constant weight, corresponds to not less than 201.7 mils of tenth-normal iodine V.S." *U. S.*

"A heavy white powder, or broken white lumps which have a vitreous fracture and usually appear stratified. Very slowly soluble in 65 parts of *water*. Slowly heated in a test-tube it yields a sublimate of minute, brilliant, transparent, octahedral crystals. Its aqueous solution, which is odorless, tasteless, and faintly acid to *litmus*, gives with *solution of silver ammonionitrate* a canary-yellow precipitate readily dissolved by *solution of ammonia* and by *nitric acid*. Sprinkled on ignited charcoal, it emits an alliaceous odor. Entirely volatilised by heat. 0.1 gramme, dissolved in boiling *water* with the aid of a little *solution of sodium hydroxide*, the cooled solution being slightly acidified with *hydrochloric acid* and then made alkaline with excess of *sodium bicarbonate*, decolorises not less than 20.1 millilitres of *N/10 solution of iodine*. Dissolves completely in *solution of ammonia*, and the resulting liquid, when diluted with an equal volume of *water* and acidified with *hydrochloric acid*, is not yellow (absence of arsenious sulphide)." *Br.*

According to Guibourt, the sp. gr. of the transparent variety is 3.73, of the opaque 3.69. The experiments, however, of J. K. Mitchell and Durand make the density of the former variety from 3.208 to 3.333. The English make of arsenic is always powdered, and, under a lens, is seen to consist of small crystals perfect in form, or of small fragments of larger crystals. In a poisoning case in 1880 (State of Conn. *vs.* Hayden) much was made to hinge upon the differences observed between this crystalline English arsenic and the commoner amorphous or German arsenic. (*Microscop. Exam. of Samples of Commercial Arsenic,* E. S. Dana. F. D. Linn & Co., Publishers, Jersey City, 1880.) As it occurs in commerce for medicinal use, it is often in the form of a white powder, almost as fine as flour. In this state it is sometimes adulterated with powdered lime or chalk, or calcium sulphate or arsenite, a fraud which is very easily detected by exposing the powder to a heat sufficient to evaporate the arsenic trioxide, when these impurities will be left behind. In consequence of the liability of the oxide to contain impurities when in powder, it was directed in the U. S. Pharmacopœia of 1870 to be kept in masses, so that the apothecary may powder it for himself as it is wanted. It has been erroneously stated to have an acrid taste. Christison asserts that it possesses hardly any taste, inasmuch as it produces merely a faint sweetish impression on the palate. In strong hot solution, it has an austere taste, most nearly resembling that of zinc sulphate. (Mitchell and Durand.) It has no odor, even in vapor; but when thrown on ignited charcoal it emits a garlicky odor, in consequence of its deoxidation, and the volatilization of the reduced metal. Its point of sublimation, according to Berzelius, is at an incipient red heat; but, according to Mitchell and Durand, it is lower than that of metallic arsenic, being only 218° C. (424.4° F.). In the British Pharmacopœia, 1898, it is said to be volatilized at a temperature not exceeding 204.4° C. (400° F.). When slowly sublimed it condenses in regular octahedral crystals of a sparkling luster. It may also be obtained crystallized in fine octahedral by the slow-cooling of a solution of the oxide in boiling diluted hydrochloric acid.

The following is given on the authority of Bussy. The transparent variety dissolves much more rapidly than the opaque. By prolonged ebullition with water, the opaque variety attains the same solubility as the transparent, and may be supposed to be converted into the latter. Thus, at the boiling temperature, a pint of water dissolves 807 grains of either variety. The transparent variety, in cold saturated solution, gradually lessens in solubility, until it reaches the solubility of the opaque, no doubt in consequence of being changed into the latter. Pulverization lessens the solubility of the transparent variety, without affecting that of the opaque. The mixture of the two varieties of the oxide

in the same solution serves to explain the anomalies heretofore observed in its solubility. Experiments of M. L. A. Buchner on the solubility of arsenic trioxide in its various forms gave the following results. A liter of water saturated at 15° C. (59°F.) with crystallized arsenic trioxide contains gr. 2.821; with the amorphous and vitreous variety, gr. 9.306; while the same solutions, made by boiling and then allowed to cool for twenty-four hours, down to 15° C. (59° F.), contain of the crystallized oxide gr. 27.839 per liter, and of the amorphous and vitreous, gr. 34.056 per liter.

Uses.—The official preparations of arsenic are all of them, when in sufficient concentration, violent irritants or escharotics. Taken internally in sufficient dose they are exceedingly poisonous to both man and the lower animals. When preparations of arsenic are given for their tonic effect only, they should be used in doses so small as not to cause any general symptoms; but when a specific action, as in *chorea,* is desired, it is proper to begin with small doses and rapidly increase them until the limit of tolerance is reached. Not rarely, such doses produce gastro-intestinal irritation, especially pain and diarrhea. To avoid this as much as possible, the remedy should be given after meals. When either gastro-intestinal irritation, puffiness under the eyes, or other of the peculiar effects of arsenic are caused, the drug should be, at least temporarily, withdrawn. The specific symptoms of *arsenicalism* are a general disposition to edema, especially of the face and eyelids, a feeling of stiffness in these parts, itching of the skin, tenderness of the mouth, loss of appetite, and uneasiness and sickness of the stomach, usually with diarrhea. The peculiar swelling produced is called *œdema arsenicalis.* In some instances the internal use of arsenic causes a rash not unlike that of measles, and, as in that affection, attended with catarrhal symptoms. (Tilbury Fox, *M. T. G.,* March, 1868.) Sometimes salivation is produced, and occasionally the hair and nails fall off. It is stated by Charcot that he has seen, in two cases, decided anaphrodisiac effects from the prolonged use of arsenic, which disappeared several months after its discontinuance, and in one instance returned upon its resumption. (*Ann. Thér.,* 1865, p. 267.)

Although in large doses arsenous oxide depresses the central nervous system and also the vasomotor center, these effects have no connection with its therapeutic uses. The properties for which it is employed in practical medicine, so far as they are at all explicable, may be ascribed to its influence on the nutritive processes and the blood making organs, or to its toxic action on certain lower forms of life. Arsenic in sufficient strength is capable of destroying the vitality of all forms of living matter but appears to be especially poisonous to certain pathogenic microorganisms. While because of its general protoplasmic toxicity it has a certain degree of power as an antibacterial, it is too poisonous to man for use as a medical germicide.

The most important physiological action of arsenic is its power of inhibiting chemical activity of the bodily cells; in other words, it lessens destructive metabolism. Because of the diminished katabolism there is a tendency for the body to take on weight. This effect is especially marked in growing animals. Gies found that newly born rabbits after four weeks of arsenical treatment averaged 30 per cent. heavier than normal. The gain in weight was not due merely to the deposition of fat, for the bones were longer and thicker, and there was a proportional increase in the muscular tissue. Especially marked in the human being have been the nutritive changes in the skin. The mode of action of arsenic in dermatological conditions is not well understood, but in cases of chronic arsenic poisoning one of the most remarkable symptoms has been the overgrowth of the horny layer and appendages, such as the nails. After small doses of arsenic there has been demonstrated, in the lower animals, hyperemia of the bone marrow and an increase in the number of white blood corpuscles. We have, however, no knowledge of any physiological action which would explain its beneficial influence in anemia; the proof of its value in this condition rests entirely on clinical evidence.

The therapeutic uses of arsenic may be divided into six categories: (1) to stimulate nutrition, (2) for its effect on the blood, (3) in the treatment of certain skin diseases, (4) for its effect upon the bronchial mucous membrane, (5) for the destruction of certain pathogenic microörganisms, and (6) as a local remedy.

In chronic wasting diseases, as in *tuberculosis* or in certain types of *neurasthenia* with malnutrition, arsenic is one of the most powerful drugs that we possess. It is one of the very few substances which really deserves the name of a general tonic since it increases both the weight and strength of the patient. It is perhaps due to its effect on nutrition that it owes its value in certain obscure nervous diseases, especially *chorea* and *migraine.* It is also sometimes a powerful remedy in various chronic types of *arthritis.*

In *chlorosis,* as shown by Seiler (*D. M. W.,* 1911, xxxvii, 1340), arsenic by itself has little if any beneficial power, but in some way greatly enhances the action of iron. In other types of *anemia,* in which iron is of little value, especially the so-called *pernicious anemia,* arsenic often produces marked amelioration. In the various types of *leukemia* it frequently produces marked temporary improvement but rarely permanent cures. It is possible that its value in these latter dyscrasias of the blood as well as in *malarial anemia,* is due to an action upon some causative parasite. In skin diseases its use should be avoided in the acute inflammatory forms, reserving it for the more sluggish lesions, such as certain types of chronic *eczema* or *psoriasis.*

While the inorganic forms of arsenic are highly toxic to many of the hematozoa they are usually less successful in the treatment of para-

sitic infections of the blood than the organic forms, because the latter can be given in so much larger doses without danger to the human host. (See *Atoxyl* and *Salvarsan.*) To what action arsenic owes its value in pulmonary diseases is entirely unknown, but there is strong clinical evidence that in chronic *bronchitis,* especially of the aged, and in *asthma* it is often of much service.

In most of the conditions in which it is useful arsenic must be given in large doses before any pronounced benefit is obtained. This is possible only because of the extraordinary tolerance which is acquired under the continual use of it. One of the most interesting examples of this fact is found in certain portions of the Archduchy of Styria where the peasants are in the habit of taking routinely considerable quantities of a native arsenical earth. The quantities employed by these so-called *arsenic eaters* have been greatly exaggerated, but there is no doubt that they can take more than half a grain of arsenic daily over long periods of time. Locally arsenic is a valuable caustic for the destruction of *malignant growths.* While a universal poison, the cells of unhealthy tissue are more readily affected by it than normal structure and it is therefore used widely for the destruction of *cancers,* especially of the skin. It is an ingredient of nearly all the proprietary and semi-proprietary cancer pastes. *Plunket's caustic* consists of *Ranunculus acris* and *Ranunculus flammula,* each one ounce, bruised and mixed with sixty grains of arsenic trioxide and one hundred grains of sulphur; beaten into a paste and dried in the sun. *Arsenical paste of Frére Côme* was made by mixing water with a powder consisting of ten grains of arsenic trioxide, forty grains of red mercuric sulphide, and ten grains of powdered animal charcoal.

Febure's remedy for cancer consisted of ten grains of arsenic trioxide, dissolved in a pint of distilled water, to which were added an ounce of extract of conium, three fluidounces of solution of lead subacetate, and a fluidrachm of tincture of opium. With this the cancer was washed every morning. Febure's formula for internal exhibition was, arsenic trioxide two grains, rhubarb half an ounce, syrup of chicory q. s., distilled water sufficient to make a pint. Of this mixture, a tablespoonful, containing about the sixteenth of a grain of the oxide, was given every night and morning. The dose was gradually increased to six tablespoonfuls a day.

Arsenic trioxide may be given in doses of from one-fiftieth to one-twentieth of a grain (0.0013–0.003 Gm.), three times a day, in the form of pill. It is often combined with opium, which enables the stomach to bear the medicine better. The *Asiatic pills,* so called, consist of arsenic trioxide and black pepper, in the proportion of 1 part of the former to 80 parts of the latter. A preparation much used on the continent of Europe is *Boudin's solution,* which is simply an aqueous solution of arsenic trioxide with the addition of wine, and is made by boiling one gramme (15.4 grains) of the oxide with one liter (2.1 pints) of distilled water till entirely dissolved, then cooling, filtering, adding enough distilled water to supply the loss, and finally mixing with one liter of white wine. Of this solution a fluidounce contains about one-quarter of a grain of arsenic trioxide.

Toxicology.—Arsenic is one of the most commonly used poisons for criminal purposes. The symptoms, which generally do not appear for a period of from one-half to one hour after the ingestion of the poison, are somewhat varied in different cases. The most frequent symptoms are pain in the epigastrium, vomiting, the vomitus being occasionally bloody, more commonly not, profuse serous purging, great thirst, rapid, weak pulse, prostration and weakness, and restlessness, sometimes with delirium and convulsions. Any or all of these symptoms, however, may be lacking, death occasionally taking place with no prodromal symptoms except heart failure or stupor. Death usually occurs in the fatal cases after about twenty-four hours but may occur within an hour, or may be delayed for more than a week. At post-mortem examination there will be found evidence of inflammation of the alimentary canal and of the kidney and frequently fatty degeneration in various of the internal organs.

There can be no doubt that, when applied to any ulcerated surface, arsenic may be absorbed with fatal result; death has indeed occurred in a number of cases from the use of arsenic as an escharotic to tumors, cancerous ulcers, etc. As indicated by Blackader, absorption is less likely to follow the use of large than of small quantities, the larger amount probably killing the part to which it is applied, and thereby preventing absorption. If this dangerous caustic be used at all, it should be in accordance with these facts. Harles's observations also seem to show that when the surface is that of a chronic ulcer, either simple or malignant, absorption is less prone to occur than from a fresh wound.

The diagnosis of acute arsenical poisoning is sometimes impossible without chemical examination. For the methods of detecting arsenic in the human body, see *U. S. D.,* 19th edition, p. 202. It should be remembered that even after the post-mortem injection of arsenic, as in the use of embalming fluids, the poison may be diffused throughout the entire body.

In the treatment of poisoning by arsenic it is necessary to prevent the absorption of the drug by early emesis and the use of a chemical antidote. Probably the most useful antidote is ferric hydroxide or preferably ferric hydroxide with magnesium oxide, in the moist or pulpy state. (*Ferri Oxidum Hydratum cum Magnesii Oxido.*) As soon as it is ready, it must be given in doses of a tablespoonful to an adult, of a dessertspoonful to a child, every five or ten minutes, until the urgent symptoms are relieved. It is calculated that the quantity taken should be at least twelve times the supposed amount of the poison swallowed; but, as the antidote is per-

fectly innocent, it is prudent to give it in larger quantities. According to the experiments of E. Riegel, one part of arsenic trioxide in solution is so fully precipitated by ten parts of the ferric hydroxide, that, after its action, not a trace of the poison can be detected, even by Marsh's test. Its efficacy is, of course, greater the sooner it is administered after the ingestion of the poison; but even after delay its use will prove advantageous, so long as any portion of the poison still remains in the stomach. Ferric hydroxide acts by producing with the poison, by a transfer of oxygen from the oxide to the acid, an insoluble, and therefore inert, ferrous arsenate: $4Fe(OH)_3 + As_2O_3 = Fe_3(AsO_4)_2 + 5H_2O + Fe(OH)_2$.

It should always be freshly prepared immediately before use. (See *Ferri Hydroxidum cum Magnesii Oxido.*) Dialyzed iron has been suggested as an antidote but is condemned by Hirschsohn. Köhler (*B. F. M. R.*, 1870) reports successful use of the saccharated oxide of iron. The light magnesium oxide has also shown itself possessed of antidotal properties, and the U. S. has authorized the alternative use of magnesia magma. For the full precipitation of arsenic trioxide eighteen parts by weight of the anhydrous magnesia are required.

If the antidote (see *Ferri Hydroxidum cum Magnesii Oxido*) be not directly at hand, or a soluble ferric salt and some form of alkaline hydroxide from which ferric hydroxide may be prepared, free vomiting should be induced by the finger, the feather part of a quill, or the administration of an emetic; or the poison may be removed by the use of the stomach tube. Demulcent drinks should be freely given, such as milk, white of eggs and water, or flour and water, which serve to encourage the vomiting and to envelop the poison.

The antidote having been faithfully applied, the subsequent treatment consists in the administration of mucilaginous drinks, and the treatment of symptoms as they arise. Convalescence is generally long and distressing; usually dyspeptic symptoms mark the presence of gastro-intestinal inflammation or even ulceration, while not rarely violent neuralgic pains, with loss of power, wasting of the muscle, and other trophic changes, show that a peripheral neuritis has been produced.

Chronic arsenical poisoning has occurred either as a result of the inhalation or the swallowing of the poison. Wall paper which is colored with arsenical dyes has been shown to be capable of giving off a fine poisonous dust. (See *Chem. News*, March, 24, 1860.) Chronic arsenic poisoning has also occurred from various foodstuffs colored with arsenic containing dyes, and a large epidemic which occurred in Manchester in the year 1900 was traced to glucose used in the manufacture of beer, originating in this case in the arsenic containing sulphuric acid used in making the glucose. The symptoms are so protean as to defy detailed description. The most important are *peripheral neuritis*, inflammation or overgrowth of the skin and dermal appendages, and irritation of the alimentary canal; when the poison has been inhaled to these are often added the signs of laryngitis and bronchitis.

Dose, of arsenic trioxide, one-fortieth to one-twentieth of a grain (0.0016–0.003 Gm.).

Off. Prep.—Liquor Acidi Arsenosi, *U. S.* (*Br.*); Liquor Potassii Arsenitis, *U. S.* (*Br.*); Liquor Arsenicalis, Clemens', *N. F.*; Liquor Auri et Arseni Bromidi, *N. F.*; Pilulæ Ferri, Quininæ, Strychninæ et Arseni Fortiores, *N. F.*; Pilulæ Ferri, Quininæ, Strychninæ et Arseni Mites, *N. F.*

ARSENUM.

ARSENIC

(ăr'sę-nŭm)

As = 74.96

Arsenicum, *U. S.* 1870; Arsenium; Arsenic, *Fr.*; Arsen, Arsenik, *G.*; Arsenico, *It.*; *Sp.*

This metal was introduced into the U. S. and Dublin Pharmacopœias in 1850, for the purpose of making arsenous iodide, and the solution of arsenous and mercuric iodide. It has been rejected by the compilers of the U. S. and the British Pharmacopœias. The Dublin College gave the following formula:

"Take the White Oxide of Arsenic of Commerce two drachms [*Dub. weight*]. Place the Oxide at the sealed end of a hard German glass tube, of about half an inch in diameter and eighteen inches long, and, having covered it with about eight inches of dry and coarsely pulverized charcoal, and raised the portion of the tube containing the charcoal to a red heat, let a few ignited coals be placed beneath the Oxide, so as to effect its slow sublimation. When this has been accomplished, the metallic arsenic will be found attached to the interior of the tube at its distant or cool extremity.

"In conducting this process, the furnace used in the performance of an organic analysis should be employed, and the fuel should be ignited charcoal. It will be proper also to connect the open extremity of the tube with a flue, for the purpose of preventing the possible escape into the apartment of arsenical vapors; and, with the view of keeping it from being plugged by the metal, to introduce occasionally into it, as the sublimation proceeds, an iron wire through a cork, fixed (but not air-tight) in its open extremity."

In the above process, the white oxide (arsenic trioxide) is reduced by the agency of ignited charcoal, and acts as a reducing agent, liberating the metal by combining with the oxygen. On the large scale, metallic arsenic is generally obtained by heating arsenical pyrites (FeAs, FeS_2) in earthen tubes, when the metal sublimes, and two molecules of ferrous sulphide, FeS, are left.

Properties.—Arsenium is a brittle, crystalline metal, of a steel-gray color, and possessing much brilliancy when recently broken or sublimed. Exposed to the air, its surface becomes dull and

blackish. Its texture is granular, and sometimes a little scaly. Rubbed on the hands, it communicates a peculiar odor, but it is devoid of taste. Its sp. gr. is about 5.73 (5.88). When heated to about 180° C. (356° F.) it sublimes, giving rise to white vapors having a garlicky odor. The statement that arsenic on being heated sufficiently, passes at once into the state of vapor without fusing was disproved by experiments of Dunnington and Odger, made under direction of Mallet. They succeeded in fusing arsenic without great difficulty. An amorphous modification results from the decomposition of hydrogen arsenide by heat, the arsenic appearing as a dark brown deposit. There is also a yellow modification which is formed when arsenic vapor is strongly cooled. It resembles yellow phosphorus, as it is soluble in carbon disulphide and oxidizes in the air with luminosity. Its atomic weight is 74.96. It forms two combinations with oxygen, arsenous and arsenic oxides, As_2O_3 and As_2O_5 respectively, to each of which the corresponding acid is known, and three with sulphur, namely, the disulphide, or realgar, As_2S_2; the trisulphide, or orpiment, As_2S_3, corresponding in composition to arsenous oxide; and the pentasulphide, As_2S_5, corresponding to arsenic oxide. (See *Arseni Trioxidum;* also *Realgar* and *Orpiment* in Part II of this work.) *Arsenic oxide* is obtained by distilling off a mixture of twelve parts of nitric and one of hydrochloric acid from four parts of arsenic trioxide, until the whole acquires the consistence of a thin syrup. The liquid is then poured into a porcelain dish, and evaporated at a moderate heat. Suddenly the arsenic oxide concretes into an opaque white mass, which should be transferred, while warm, to a well-stoppered bottle. Arsenic oxide is white, solid, deliquescent, and soluble in six parts of cold and two of boiling water. It forms several acids, corresponding to the several varieties of phosphoric acid, to which it bears a close analogy. With silver nitrate it gives a brick-red precipitate of silver arsenate. As a poison it is even more virulent than arsenous oxide. It consists of two atoms of arsenic and five of oxygen (As_2O_5).

The world's supply of arsenic and arsenic compounds at the present time is obtained from Germany, Spain, England and Canada, although in Montana and Washington considerable quantities of arsenic are being produced as a by-product in the smelting of copper ores. In 1903 the German production of arsenic was 2768 metric tons; that of Spain, 1088 tons; of England, 917 tons, and of Canada, 233 tons, while the United States produced 554 tons. The importations of arsenic, arsenous oxide, and arsenic sulphides into the United States for 1903 amounted to 8,357,661 lbs., valued at $294,602.

Arsenic is much diffused. Besides being present in a great many minerals, it has been detected, in minute proportion, in the earth of cemeteries by Orfila; in certain soils and mineral waters by Walchner; in the ashes of various plants by Stein; in various mineral coals; also in the incrustation formed in the boiler of a sea-going steamer, by Daubrée. Recently it has been found in minute quantities in many plants and even in the tissues of the human body.

ASAFŒTIDA. U. S. (Br.)

ASAFŒTIDA Asafœt. [Gum Asafetida]

(ăs-ą-fœt'ĭ-dą)

"The gum-resin obtained by incising the rhizomes and roots of *Ferula Asafœtida* Linné and *Ferula fœtida* Regel and of some other species of *Ferula* (Fam. *Umbelliferæ*), indigenous to Persia and adjacent countries, and yielding not less than 60 per cent. (or if powdered 50 per cent.) of alcohol-soluble constituents." *U. S.* "Asafetida is an oleo-gum-resin obtained by incision from the root of Ferula fœtida, *Regel*, and probably other species of Ferula." *Br.*

Asafetida, *Br.;* Stercus Diaboli, Cibus Deorum; Gummiresina Asafœtida; Asa fœtida, Asse-fétide, Assafœtida, *Fr.;* Asa fœtida, *P. G.;* Asant, Stinkasant, Teufelsdreck, *G.;* Assa fetida, *It.;* Asafetida, *Sp.;* Ungoozeh, *Pers.;* Hilteet, *Arab.;* Hing, *India;* Angusa-kema, *Afgh.*

Ferula Asafœtida was first described from actual observation by H. Falconer, who found it near Kashmir, and has long been successfully cultivated in the Edinburgh Botanical Gardens. It is distinguished by the greater height of the stem (6 to 10 feet), and by the numerous stem leaves furnished with wide sheathing petioles. The flowers are pale yellow, and the oval fruit thin, flat, foliaceous, and reddish brown, with pronounced vittæ. It yields a milky juice having a powerful odor of asafetida.

Ferula fœtida is a coarse umbelliferous plant, growing from five to seven feet high, with a large fleshy root, the crown of which is covered with coarse bristly fibers, and gives origin to large bipinnate radical leaves and a nearly naked stem which has only a few bipinnate leaves without wide sheathing petioles, and ends at the top in very numerous umbels. The flat-winged fruit have the vittæ almost obsolete. This plant was first discovered in the sandy desert near the sea of Aral, by Lehmann, in 1844. Bunge found it in Persia about twenty years later. It would seem to be native all through Afghanistan.

It is possible that asafetida is obtained from various species of *Ferula,* yet the bulk of the drug probably comes from the official plants. Among the other plants yielding asafetida is *Ferula Narthex* Boiss. While this is disputed by Aitchison yet it appears that it is the source of the gum-resin obtained from certain portions of Afghanistan. Tschirch describes this plant with illustrations in *S. W. P.,* 1910, p. 289. E. M. Holmes's discussion of the asafetida plants (*P. J.,* ser. iii, xix, 1888–1889) still remains one of our chief sources of information on the subject. (See also article on the sources of the fetid gum-resins by James Small, *P. J.,* 1913, vol. xc, p. 287.) *Ferula Jæschkeana* Vatke, which has been believed to be the source of asafetida, ac-

cording to E. M. Holmes, has, at least in its dried state, not the slightest odor of asafetida, and yields a strongly celery-scented juice. (*P. J.*, 1894, xxv.)

The asafetida plants are indigenous to Western Afghanistan and Eastern Persia. In 1687 the collection of asafetida was witnessed by Kaempfer, whose description of the method is very similar to that given by H. W. Bellew in 1872, and by J. E. T. Aitchison in 1884. According to Aitchison, the high plains of Afghanistan, two to four thousand feet above the sea, are arid and bare in winter, but in the early summer are covered with a thick growth of *Ferula fœtida, Dorema ammoniacum,* and *Ferula glabaniflua.* The great cabbage-like heads of the asafetida plant, representing the primary stage of the flower heads covered over by the stipules of its leaves, are eaten raw by the natives as a sort of green. In June the asafetida is obtained. The root stock is first laid bare to the depth of a couple of inches, those plants only which have not reached their flower-bearing stage being selected. A slice is then taken from the top of the root stock, which is immediately covered with twigs and clay, forming a sort of dome, with an opening towards the north, so that the sun cannot get at the exposed root. About five or six weeks later, a thick, gummy, not milky, reddish substance found upon the exposed surface of the root in more or less irregular lumps is scraped off with a piece of iron hoop or removed with a slice of the root and at once placed in a leather bag. The asafetida is conveyed to Herat, where it is adulterated with red clay before being sent into commerce. It is brought to this country directly from India, whither it is conveyed from Bushire and down the Indus, or it is shipped first to London and then to America. It sometimes comes in mats, but more frequently in cases, the former containing eighty or ninety pounds, the latter from two hundred to four hundred pounds. Asafetida is sometimes also imported in casks.

The fruit of the asafetida is said to be sent to India, where it is highly esteemed as a medicine.

Properties.—As usually found in commerce, asafetida is in irregular masses, soft when not long exposed, of a yellowish or reddish-brown color externally, exhibiting when broken an irregular, whitish, somewhat shining surface, which soon becomes red on exposure, and ultimately passes into a dull yellowish-brown. This change of color is characteristic of asafetida, and is ascribed to the influence of air and light upon its resinous ingredient. The masses appear as if composed of distinct portions agglutinated together, sometimes of white, almost pearly tears, embedded in a darker, softer, and more fetid paste. Occasionally the tears are separate, though rarely in the commerce of this country. They are roundish, oval, or irregular, and generally flattened, from the size of a pea to that of a large almond, sometimes larger, yellowish or brownish externally and white within, and not unlike ammoniac tears, for which they might be mistaken except for their odor, which, however, is weaker than that of the masses. A very fine variety of asafetida is spoken of by Bellew as being procured from the leaf bud in the center of the root. It does not come into European commerce, but is the *Kandaharee Hing* of the Indian bazaars. (*P. J.*, viii, 103.) It occurs in moist flaky pieces and tears, yielding a reddish-yellow oil on pressure, and mostly mixed with the remains of leaf buds. The ordinary asafetida of the Indian bazaars is known in the superior grade as *Hing,* in the inferior grade as *Hingra.* The odor of asafetida is alliaceous, fetid, and tenacious; the taste, bitter, acrid, and persistent. The effect of time and exposure is to render it more hard and brittle, and to diminish the intensity of its odor and taste, particularly the former. Kaempfer assures us that one drachm of the fresh juice diffuses a more powerful odor through a close room than one hundred pounds of the drug as usually kept in the stores. The color, which is at first white, becomes pink, and finally the well known brown, on exposure. Asafetida softens by heat without melting, and is difficult of pulverization. Its sp. gr. is 1.327. (Berzelius.) It is inflammable, burning with a clear, lively flame. It yields all its virtues to alcohol, and forms a clear tincture, which becomes milky on the addition of water.

The description in the U. S. P. IX has been considerably enlarged and is as follows: "In a soft mass, sometimes almost semi-liquid, or in irregular, more or less pliable masses composed of agglutinated tears of variable size imbedded in a yellowish-brown or dark brown matrix, or in loose ovoid tears, from 1 to 5 cm. in diameter, the surface sometimes containing streaks of violet, yellowish-red or brownish-red and with a few vegetable fragments; when fresh the mass is either soft or tough, becoming hard and occasionally even brittle on drying; the surface of the freshly fractured tears is milky-white and opaque, changing gradually on exposure to a pinkish or reddish-purple or even reddish-brown; on moistening with water, the tears become milky-white; odor persistent, alliaceous; taste bitter, alliaceous and acrid. Triturate one part of Asafetida with three parts of water; it forms a milk-white emulsion which becomes yellowish on the addition of alkalies. Heat a fragment of one of the tears of Asafetida with sulphuric acid; a reddish-brown solution is formed; greatly dilute the latter with water, filter, and add an excess of any of the alkalies; the solution acquires a blue fluorescence, which becomes more pronounced upon the addition of a slight excess of ammonia water. An alcoholic solution of Asafetida, on the addition of a few drops of phloroglucinol T.S. and a fews drops of hydrochloric acid, acquires a cherry-red color. Add a few drops of ferric chloride T.S. to a portion of the alcoholic solution of Asafetida, obtained in the assay process given below; an olive-green color is produced (*most foreign resins*). Add hydrochloric acid to another portion of the same

alcoholic solution of Asafetida until a faint turbidity results; a bluish-green color is developed, which fades on standing (*galbanum*). Evaporate a quantity of the same alcoholic solution, representing 5 Gm. of Asafetida, to 25 mils, mix it with 25 mils of petroleum benzin, in a separatory funnel, and afterwards add to it twice its volume of water and agitate. The petroleum benzin layer, after washing with water and subsequent separation, exhibits no green color when shaken with 30 mils of a freshly made aqueous solution of copper acetate (1 in 20) (*rosin*). Mix 2 mils of emulsion, prepared as directed under *Emulsum Asafœtida,* with 5 mils of water and add 5 mils of sodium hypobromite T.S., so as to form a separate layer; a red color is not produced (*ammoniac*). The yield of ash of the gum-resin does not exceed 15 per cent. The powder is prepared by drying the gum-resin over freshly-burnt lime or by exposure to currents of warm air until it ceases to lose weight and then reducing it to a powder at a low temperature. Diluents of starch or magnesium carbonate may be added in order to maintain the powdered form. The color of powdered Asafetida is light brown. The yield of ash of powdered Asafetida does not exceed 30 per cent.

"**Assay.**—Introduce about 10 Gm. of Asafetida into a tared, 250 mil Erlenmeyer flask, determine the exact weight of the drug, add 100 mils of alcohol, and having connected the flask with an upright condenser, boil the mixture in the flask during one hour or until the drug is completely disintegrated. Then transfer the contents of the flask to two counterpoised, plainly folded filters one within the other, so that the triple fold of the inner filter is laid against the single side of the outer, and wash the flask and filter with consecutive, small portions of boiling alcohol until the washings no longer produce a cloudiness when dropped into water. Collect and reserve the mixed alcoholic solutions, for the qualitative tests given above. Dry the filters and flask to a constant weight at a temperature of about 115° C. (239° F.). Now determine the weight of the residue on the filter and in the flask and calculate its percentage from the amount of Asafetida originally taken. This percentage of alcohol-insoluble material, when subtracted from 100, gives the percentage of alcohol-soluble constituents contained in the Asafetida." *U. S.*

"Rounded or flattened tears from twelve to twenty-five millimetres in diameter, or masses containing tears, greyish-white to dull yellow, darkening on keeping. Fresh tears usually tough at ordinary temperatures, hard when cold. Internally yellowish and translucent, or milk-white and opaque; freshly exposed surfaces often slowly become pink, then red, and finally reddish-brown. Odor strong, alliaceous and persistent; taste bitter, acrid and alliaceous. When triturated with *water* Asafetida forms a white emulsion. When the freshly fractured surface of a tear is touched with *sulphuric acid,* a bright red or brownish-red color is produced. The tincture obtained by macerating 0.5 gramme of Asafetida with 10 millilitres of *alcohol* (90 per cent.), filtered, made alkaline with *strong solution of ammonia,* and then largely diluted with *alcohol* (90 per cent.), does not exhibit a blue fluorescence (distinction from and absence of galbanum). Contains not more than 50 per cent. of matter insoluble in *alcohol* (90 per cent.). Ash not more than 15 per cent." *Br.*

Much commercial asafetida of prime appearance fails to come up to the requirements of the U. S. Pharmacopœia. Large quantities are said to be returned from the United States ports to Europe on account of their failure to contain the proper percentage of material soluble in alcohol, and in reducing the requirements from 60 to 50 per cent. the revisers of the U. S. P. VIII yielded to a slight extent to the necessities of the situation, but the U. S. P. IX raised the percentage of alcohol-soluble constituents to 60 per cent. for asafetida and to 50 per cent. of powdered asafetida. Macerated in water it produces a turbid red solution, and triturated with that fluid it gives a white or pinkish milky emulsion of considerable permanence. Touched with nitric acid (sp. gr. 1.2) the tear becomes of an evanescent green color. In 100 parts, Pelletier found 65 parts of resin, 19.44 of gum, 11.66 of bassorin, 3.60 of volatile oil, with traces of acid calcium malate. J. Polásek examined the pure tears of *Asafœtida amygdaloides,* finding the following constituents: 61.40 per cent. of resin soluble in ether, which is regarded by him to be the ferulaic acid ester of *asaresino-tannol;* 0.60 per cent. of resin insoluble in ether, regarded to be free asaresino-tannol; 25.10 per cent. of gum; 6.70 per cent. of volatile oil; 0.06 per cent. of vanillin; 1.28 per cent. of free *ferulaic acid;* 2.36 per cent. moisture; 2.50 per cent. impurities. *Asaresino-tannol* has the composition corresponding to the formula $C_{24}H_{35}O_5$. The author has prepared a benzoyl derivative, $C_{24}H_{33}O_5.C_6H_5CO$, and an acetyl derivative, $C_{24}H_{33}O_5.CH_3CO$, which prove it to contain a hydroxyl group—viz., $C_{24}H_{33}O_4.OH$. Umbelliferone was obtained as a secondary product of hydrolysis with sulphuric acid from asaresino-tannol, and was also obtained from ferulaic acid synthetically, guaiacol being produced at the same time. By nitrification of asaresino-tannol, picric acid is produced. (*A. Pharm.,* 1897, ccxxxv, 125, 132.) The odor of the gum-resin depends on the *volatile oil,* which may be procured by distillation with water or alcohol, and amounts to from 6 to 9 per cent., according to Flückiger. It is lighter than water, colorless when first distilled, but becomes yellow with age, of an exceedingly offensive odor, and of a taste at first flat, but afterwards bitter and acrid. Hlasiwetz (*Ann. Ch. Ph.,* lxxi, 23) considers it a mixture, in variable proportions, of the sulphide and disulphide of a compound radical consisting of carbon and hydrogen (C_6H_{11}). Allyl persulphide, which is sublimed when oil of mustard is heated with potassium persulphide, is said by Wertheim to have an extremely

intense odor of asafetida, a fact which justifies the supposition that it may be identical with the oil of that gum-resin. (Gmelin, ix, 377.) Semmler, in a later study (*Ber. d. Chem. Ges.*, 23, p. 3530, and 24, p. 78), states that it contains *pinene* and a second terpene in smaller amount, and in the higher boiling fractions, a disulphide, $C_7H_{14}S_2$; a disulphide, $C_{11}H_{20}S_2$; a body $(C_{10}H_{16}O)n$; a disulphide, $C_8H_{18}S_2$; and $C_{10}H_{18}S_2$.

The resin is, according to Hlasiwetz and Barth (*Ann. Ch. Ph.*, cxxviii, 61), a mixture containing *ferulaic acid,* $C_{10}H_{10}O_4$, crystallizing in iridescent needles, and obtained by precipitating the alcoholic solution with lead acetate, washing the precipitate, and decomposing it with diluted sulphuric acid. Submitted to dry distillation, the resin yields *umbelliferone,* $C_9H_6O_3$, and blue-colored oils. Fused with potassium hydroxide, ferulaic acid yields oxalic acid and carbon dioxide, several acids of the fatty series, and protocatechuic acid. The resin itself treated in like manner, after it has been freed from gum, yields resorcinol. Tschirch (*Harze und Harzebehälter,* 1900, p. 234) states that the resin is the *ferulaic ester of asaresino-tannol* containing some free *ferulaic acid,* and some *vanillin,* which latter is a product of the oxidation of the ferulaic acid.

Impurities and Adulterations.—Asafetida is often purposely adulterated; it frequently comes of inferior quality, and mixed with various impurities, such as sand and stones. It is generally conceded to be the worst adulterated drug upon the market, the chief adulterant being gypsum. Portions which are very soft, dark brown, or blackish, with few or no tears, and indisposed to assume a red color when freshly broken, should be rejected. We have been informed that a case seldom comes without more or less of this inferior asafetida, and of many it forms the larger portion. It is sold chiefly for horses. A factitious substance, made of garlic juice and white pitch with a little asafetida, has occurred in commerce. Asafetida is said to be sometimes mixed with wheat or barley flour or with earthy matters at the place of its production, the impurities sometimes exceeding 30 per cent. The gum-resin imported from the Persian Gulf and Bombay is largely adulterated with sand and other gum-resins. *Hingra* of the Bombay bazaars is a very stony variety, composed largely of earthy matter. Gaul has recently reported having met with an asafetida containing 45 per cent. of sand. Patch (*Proc. A. Ph. A.*, 1905, p. 183) has found asafetida on the market which yielded 62, 62.5 and 73.3, respectively, of material insoluble in alcohol. The Belgian inspectors reported in 1905 finding as high as 75 per cent. of ash in some commercial samples. In spite of these figures Gehe & Co. report that the quality of the available asafetida has materially improved.

J. U. Lloyd, after examining a large number of samples of commercial asafetida, was convinced that it is impracticable to obtain the crude drug of the official standard, gypsum, carbonates, and other insoluble matters being present in large amounts. He did not find white turpentine or rosin in any of the samples; exhausting asafetida with alcohol and evaporating the alcohol carefully, he obtained an extract for which he proposed the name of *Purified Asafetida.* (*Ph. Rev.*, 1896.) H. William Jones (*Y. B. P.*, 1900, 503) purifies asafetida by pouring a concentrated alcoholic solution into water slightly acidulated with hydrochloric acid, collecting the precipitate, washing and drying it.

A few years ago a new method was proposed for the detection of adulteration in asafetida which depended upon the combining power of the purified resins with the lead in a standard solution of lead acetate. This method, the details of which will be found in *J. A. C.*, vol. ii, p. 86, is called the lead number and has hardly been in use long enough to warrant its adoption as an official method. Some observers, including Rippetoe (*A. J. P.*, 1913, p. 199) find it to be subject to fluctuations as yet unexplained. Harrison and Self (*Ph. J.*, 1912, 205) present what they term a preliminary report on the investigation of this drug for the purpose of suggesting an improved method of standardization. They claim that there is good reason to believe that the virtues of asafetida are due not only to the volatile oil, but to the sulphur containing constituents of the volatile oil. They give abundant analytical data in support of their views and as showing how adulterations with other gum-resins may be readily detected. They state that if a gum-resin contains not less than 1.5 per cent. of sulphur it may unhesitatingly be pronounced as genuine asafetida. Bernegau and E'we propose a method for estimating asafetida in commercial tablets, pills, etc., depending upon extractions with hot chloroform under specified conditions. (*Proc. P. P. A.*, 1912, p. 305.)

Asafetida is sometimes kept in a powdered state, but this is objectionable, as the drug is thus necessarily weakened by the loss of volatile oil, and is more liable to adulteration. Powdered asafetida is best prepared by exposing the gum-resin to a low temperature for several hours or several days.

Uses.—Asafetida appears to have been used in the East from the earliest times of which we have any record and notwithstanding its repulsive odor is at present much used in India and Persia as a condiment. It is by some believed to have been imported into Europe as far back as the second century, but the earliest undoubted reference to it in European medical literature is in the twelfth century. Although it is without doubt capable of being absorbed from the intestinal tract in greater or lesser quantities there is no convincing evidence that after its absorption it exercises any distinct effect upon the system. Pidoux took a half an ounce at one dose without perceptible effects not ascribable to its local action. It has in the past been supposed

to exercise a stimulant action upon the cerebral centers. The evidence in favor of this view is based upon the beneficial effects which have followed its administration in *hysteria* and conditions of *nervous exhaustion.* Its effects in these conditions, however, is entirely explicable on the grounds of the psychical impression made by taking a drug of so powerful odor and taste. On the other hand as a local stimulant to the mucous membranes, especially of the alimentary tract, it is a remedy of much value, thus it is a favorite carminative in the treatment of *flatulent colic;* it is often useful as an addition to laxative drugs in various types of *constipation.* There is evidence that after its absorption the volatile oil of asafetida is eliminated through the lungs and consequently it has been used as a stimulating expectorant in various forms of *bronchitis,* in *whooping cough,* and in *asthma.*

When used internally in adults it is generally preferable to administer it in the form of a pill on account of its disagreeable taste. In *colic,* especially in infants, it is often administered per rectum. For this purpose the emulsion of asafetida in the proportion of from one-half to one fluidounce to a pint of water may be employed.

Asafetida may be given in pill or emulsion. The tincture is official, and is much used. It may also sometimes be conveniently used in the form of a suppository, or plaster. (See *Emplastrum Asafœtidæ,* 18th ed. U. S. D., p. 238.) A syrup has been recommended in which the fetid odor of the drug is disguised by the use of the infusion of wild cherry bark. (See *A. J. P.,* 1871, p. 397.)

J. W. Wood prepared *syrup of asafetida* by dissolving 256 grains of asafetida in two fluidounces of glycerin by the aid of a gentle heat and straining. He then dissolved 15 drops of oil of wintergreen, 5 drops of oil of cinnamon and 1 drop of oil of bitter almond in 3 fluidrachms of 95 per cent. alcohol, and added to it the above, together with enough syrup to make one pint. Each teaspoonful represents two grains of asafetida. (*A. J. P.,* 1874.)

Dose, of asafetida, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Emulsum Asafœtidæ, *U. S.;* Pilula Aloes et Asafœtidæ, *Br., N. F.;* Pilulæ Asafœtidæ, *U. S.;* Spiritus Ammoniæ Fetidus, *Br.;* Tinctura Asafœtidæ, *U. S., Br.;* Mistura Magnesiæ, Asafœtidæ et Opii (from Tincture), *N. F.*

ASPIDIUM. U. S. (Br.)

ASPIDIUM [Male Fern]

(ąs-pĭd'ĭ-ŭm)

"The rhizome and stipes of *Dryopteris Filix-mas* (Linné) Schott, or of *Dryopteris marginalis* (Linné) Asa Gray (Fam. *Polypodiaceæ*), collected in the autumn, freed from the roots and dead portions of rhizome and stipes and dried at a temperature not exceeding 70° C. (158° F.). Preserve Aspidium in tightly-closed containers and protect from light." *U. S.* "Male Fern is the rhizome of Dryopteris Filix-mas, *Schott.* Collected late in the autumn, divested of its roots, leaves, and dead portions, and carefully dried. Should not be kept more than a year." *Br.*

Filix Mas, *Br.,* and *U. S.* 1870; Stipites aspidii, Radix Filicis maris, Male Shield Fern, Knotty or Sweet Brake, Basket Fern, Bear's-paw Root; Fougère Mâle, *Fr.;* Rhizoma Filicis, *P. G.;* Wurmfarnwurzel, Waldfarnwurzel, Johanniswurzel, Farnwurzel, *G.;* Felce maschio, *It.;* Helecho macho (Rhizoma de), *Sp.*

As the term Dryopteris was first used by Amman in 1739, and applied in 1763 by Adamson, as the name of the genus to which the Aspidium was applied in 1800 by Swartz the use of the generic term Dryopteris would seem to be necessitated by the ordinary laws of botanic nomenclature. The synonyms of the male fern are extraordinarily numerous. We append some of them: *Aspidium Filix-mas,* of many authors; *Polypodium Filix-mas* Linn.; *Polystichum Filix-mas* Roth.; *Nephrodium Filix-mas* Rich.; *Lastrea Filix-mas* Presl.; *Tectarea Filix-mas* Cavan.; *Dryopteris Filix-mas* (L.) Schott; *Lophodium Filix-mas* Newm.; *Polypodium memorale* Salisb.; *Polystichum durum et induratum* Schur.; *Polystichum abbreviatum* De Candolle; *Aspidium mildeanum* Göppert; *Dryopteris affinis; Polypodium heleopteris.* Under the name of *inkomankomo* or *uncomocomo,* the rhizome of *Aspidium athamanticum* (Hook.) Kuntze, has long been used by the South African Kaffirs, and has entered European commerce as *pannum.*

The male fern has a perennial, horizontal rhizome, from which numerous annual fronds or leaves arise, forming tufts from a foot to four feet in height. The stipe, or footstalk, and midrib are thickly beset with brown, tough, transparent scales; the frond itself is ovate-oblong in outline, the pinnæ being lanceolate, acuminate, slightly broadest above the base (*D. marginalis*), or lanceolate, the pinnæ being linear-lanceolate, tapering from base to apex (*D. Filix-mas*). The fructification is in small dots on the back of each lobe, occurring close to the margin in *D. marginalis* and nearer the midvein than the margin in *D. Filix-mas.* The latter is a native of Europe, Asia, and the north of Africa. It is also found in some of the Polynesian islands, and grows in British America, following the Rocky Mountain chain through Mexico, Venezuela, etc., as far south as Peru.

D. marginalis is common in the Eastern United States, especially northward, on rocky hillsides and in the woods.

It is probable that most species of the genus, if not of the family, are medicinally active. J. L. Patterson (*A. J. P.,* 1875) found that the *D. marginalis* contained all of the active principles of *D. Filix-mas,* and Chas. H. Cressler has demonstrated the activity of its oleoresin. (*Ibid.,* 1878.) According to Rosendahl (*P. J.,* 1911, lxxxvii, p. 35) the *Dryopteris dilatata* is indeed four times as active a poison to the tapeworm as the true aspidium. According to V. Penndorf (*Ap. Ztg.,* 1903), in Germany the rhizomes of *D. spinulosum* and *Athyrium Filix-fœmina* are frequently found mixed with those

of the true male fern, in quantities varying from five to ninety per cent. The rhizomes of *D. Filix-fœmina* are readily recognized by having only two large dumb-bell-shaped steles. The rhizomes of *D. spinulosum* closely resemble those of the genuine drug, but it is stated that they can be distinguished by the numerous small glands found on the margin of their scales, the scales of *D. Filix-mas* having only two upon each. On account of this substitution, many of the German extracts of the male fern are said to contain *aspidin*, a yellow crystalline substance having a melting point of 124° to 125° C. (255.2°–257° F.), which is found only in *D. spinulosum*. (*Ap. Ztg.*, 1903.) Lauren of Helsingsfors states that the extract of *A. spinulosum* is a very active tenicide, and is less apt to produce disagreeable sensations in the patient than is the official drug. He gives the dose as sixty grains (3.9 Gm.), followed by a laxative, and states that some Finnish apothecaries are especially noted for their fern extracts, because they use only the rhizome of *A. spinulosum*. (*Ap. Ztg.*, 1903.) Under the name of *filicone* there is used what is asserted to be the active principle of *Aspidium spinulosum*. The dose is thirty grains. On the Pacific slope the indigenous *A. rigida* Underw. is locally used against the tapeworm, and W. J. Bowman has found in it filicic acid and resin. Popular belief has long ascribed tenicidal virtues to our native *Asplenium Filix-femina*, commonly known as *Lady Fern*. It occurs in conical pieces from 8 to 13 cm. long, 2 to 5 cm. in diameter, of a reddish-brown color, covered with root fibers and leaf scars. According to R. Kürsten (*P. J.*, xxii, 1891), its active principle is closely allied to filicic acid, differing in being especially soluble in strong alcohol, in subliming at 80° C. (176° F.), and is not yielding isobutyric acid when heated in a sealed tube with water. *Pannic acid* crystallizes in thin, shining, light yellow, rectangular prisms, melting at 187° C. (368.6° F.).

Heffter (*A. E. P. P.*, 1897, 458) finds three well characterized and crystallized principles in pannum: *flavopannin*, $C_{21}H_{36}O_7$, crystallizing in citron-yellow prisms, melting at 151° C. (303.8° F.), and soluble in ether, benzene, acetic ether, acetone, and boiling methyl and ethyl alcohols, insoluble in petroleum, ether and water; *albopannin*, $C_{21}H_{34}O_7$, crystallizing in silky-white needles, which melt at 147° C. (296.6° F.); and *pannol* (pannic acid of Kürsten), $C_{11}H_{14}O_4$, fusing at 192° C. (377.6°F.), which is easily soluble in hot glacial acetic acid and acetone, more difficultly soluble in alcohol and ether, and very slightly soluble in petroleum benzin, benzene, and water. The alcoholic solution is colored intensely dark green with ferric chloride. Heffter compares these three compounds with the three obtained from *D. Filix-mas*, and finds a close chemical and therapeutic correspondence between *aspidin* and *flavopannin*, between *albaspidin* and *albopannin*, and between *aspidinol* and *pannol*. According to the experiments of A. Heffter, both *flavopannin* and *albopannin* are powerful muscle poisons, directly affecting the heart. (*A. E. P. P.*, Bd. xxxviii.)

Aspidium deteriorates rapidly when kept, and in about two years becomes entirely inert. The rhizomes of other species of fern are frequently substituted for the official, and in the dried state it is difficult to distinguish them. The varying results reported by physicians when using this drug, can undoubtedly be ascribed to the employment of spurious male fern, or old brownish rhizomes which should have been thrown away.

Properties.—As taken from the ground, the rhizome consists of a long cylindrical caudex, around which are closely arranged, overlapping each other like the shingles of a roof, the remains of the leafstalks or stipes, which are 2 to 5 cm. in length, from 3 to 8 mm. thick, somewhat curved and directed upwards, angular, brown, shining, and surrounded near their origin from the rhizome with thin silky scales of a light brown color. From between these remains of the footstalks emerge numerous small radical fibers. The whole rhizome, thus constituted, presents a somewhat flexible, cylindrical mass, 2.5 to 5 cm. thick, and from 7 cm. to 4 dm. in length. In this form, however, it is not usually found in commerce. The whole is ordinarily broken up into fragments, consisting of the separated remains of the leafstalks before described, with a small portion of the substance of the rhizome attached to their base, where they are surrounded by the silky scales. These fragments, as seen in commerce, often appear as if long kept, and are probably, in general, much deteriorated by time. The official description is as follows:

"Usually with the blackish-brown outer layers removed; rhizome 1 to 3 cm. in thickness, cylindraceous and nearly straight, or curved and tapering toward one end, usually split longitudinally, roughly scarred with remains of the stipe-bases, or bearing several coarse longitudinal ridges and grooves; stipes cylindrical, 3 to 5 cm. in length, about 6 mm. in thickness, nearly straight or somewhat curved, tapering toward one end, and with occasional elongated patches of the still-adhering, blackish-brown outer layers; fracture short, pale green in the inner half, the texture rather spongy, and exhibiting, in an interrupted circle, from 6 to 12 vascular bundles, each surrounded with an endodermis; odor slight; taste sweetish, astringent, bitter, acrid. Use only such portions as have retained their green color. Aspidium yields not more than 3 per cent. of ash." *U. S.*

"From seven to fifteen centimetres or more in length; the rhizome itself about two centimetres in diameter. Entirely covered with the hard, persistent, curved, angular, dark brown bases of the petioles, which bear numerous brown membranous scales. Petioles green internally and exhibiting in transverse section about eight pale yellow fibrovascular bundles arranged in a diffuse circle (distinction from the petioles of Athyrium Filix fœmina, *Roth.*). Rhizomes brown externally, green internally. In transverse section, stalked secreting glands in intercellular spaces. Margins of the membranous scales with two-

celled projections but no glands; at the base two minute glands (distinction from the rhizomes of certain other ferns). Feeble but disagreeable odor; taste sweetish and astringent at first, but subsequently bitter and nauseous." *Br.*

In collecting male fern, all the black discolored portions should be cut away, the fibers and scales separated, and only the sound green parts preserved. These should be immediately but carefully dried, and then pulverized; and the powder should be kept in small well-stoppered glass bottles. Powdered althæa leaves are sometimes used as an adulterant of powdered aspidium, giving the desirable light-green tint indicative of a good quality of drug. At other times the powder is said to consist entirely of the chaff and other inert material which the Pharmacopœia directs should be rejected.

Kraemer has reported that much of the aspidium in the American market consists of the large rhizomes of *Osmunda Claytonia.* For distinction see *Proc. A. Ph. A.*, 1906, p. 345. Capelle discusses the characteristics of genuine aspidium and the differentiation of related species. (*Ap. Ztg.*, 1907, p. 433.)

Microscopic examination shows that aspidium is composed of polyhedral parenchyma and vascular bundles containing scalariform ducts; in *D. Filix-mas* ten of these bundles are arranged in an interrupted circle near to the surface; while in *D. marginalis* there are only six bundles in the circle. It has been analyzed by H. Bock, who gives as its constituents volatile oil, fixed oil, resin, starch, vegetable jelly, albumen, gum, sugar, tannic and gallic acids, pectin, lignin, and various salts. (See *A. J. P.*, xxiv, 64.) Peschier ascertained that its active properties reside in the ethereal extract, which is the fixed oil in an impure state, containing volatile oil, resin, coloring matter, etc. It is a thick dark liquid, with the odor of the fern, and a nauseous, bitterish, somewhat acrid taste. E. Luck found in it a peculiar acid, which he denominated *filicic acid.* Daccomo gives to filicic acid the formula $C_{14}H_{16}O_5$, and finds in addition a white waxy substance, melting at 80° C. (176° F.), with the formula $(C_{13}H_{26}O)n$, glucose, tannin, a red coloring matter (*filix red*), a green oil which he separated into several fractions, and two resins, one brick-red, melting at 85° to 93° C. (185°–199.4° F.), the other black and plastic. He considers that filicic acid is probably an isobutyric acid derivative of hydroxynaphthaquinone. Poulson (*A. E. P. P.*, 1891) states that, when pure, crystalline, inactive filicic acid is dissolved in alkalies and reprecipitated by an acid, the amorphous precipitate possesses the active properties of the extract. He thinks that the inactive crystalline body is an anhydride or lactone of the amorphous filicic acid, and should be called *filicin.* Böhm announced three additional substances which he named *flavaspidic acid, albaspidin* and *aspidinol.* Kraft (*Ph. Ztg.*, 1903, p. 275) confirms this and finds in addition, *flavaspidin,* and an amorphous acid which he names *filmaron,* which pharmacological examination has proven conclusively to be the true anthelmintic constituent of male fern. *Filmaron* is a bright yellowish-brown powder, insoluble in water, difficultly soluble in cold alcohol, but very soluble in other general solvents. The rhizome contains about 5 per cent. of *filmaron.* Its formula is $C_{47}H_{54}O_{16}$. The other different constituents seem to be largely decomposition products of filmaron. For an assay method for male fern extract, see *Am. Drug.*, 1897, 73.

Uses.—Male fern was used by the ancients, and is mentioned as a vermifuge in the works of Dioscorides, Theophrastus, Galen and Pliny, and by some of the earlier modern writers. But it does not appear to have been generally known till about the year 1775, when the King of France purchased from Madame Nouffer, the widow of a Swiss surgeon, a secret remedy for tapeworm, which proved to be the powdered root of the male fern. As was first demonstrated by Straub (*A. E. P. P.*, 1902, xlviii, p. 1) the principles of aspidium paralyze the voluntary muscles of the higher animals as well as the analogous contractile tissue of the invertebrates. In smaller quantities these principles are stimulant to the central nervous system and may cause even tetanic convulsions.

Aspidium is used in medicine almost solely for the purpose of getting rid of various intestinal parasites, especially the *tapeworm.* As to its value in other forms of *helminthiasis* there is difference of opinion. Schultz (*J. A. M. A.*, 1911, lvii) reports 75 per cent. of cures in cases of *hookworm* infection, but Patterson (*T. G.*, 1908, xxxii), on the other hand, states that it has been found absolutely without value in this infection. Its action appears not to be so much to kill the parasite as to paralyze it so that it can be washed out of the alimentary canal with an active purge. For the latter purpose castor oil is often employed, but there is little doubt that its use increases the absorbability of the drug and hence adds to the danger of poisoning. For this reason calomel is generally to be preferred.

Besides as a vermifuge aspidium has been recommended by La Nara (*J. des Pract.*, 1910) as a local application in *eczema* and *acne.*

Aspidium is a violent poison, the relative rarity of serious symptoms from its use being due to its non-absorbability. Under certain conditions, probably when there is a large amount of fatty matter in the bowel, it may be absorbed with unexpected readiness and give rise to serious and even fatal poisoning. Six drachms of it have caused death. (*L. L.*, 1882.) The common symptoms have been vomiting, diarrhea, vertigo, headache, tremors, cold sweats, dyspnea, cyanosis, convulsions and mental disturbances. In nearly half of the cases there was disturbance of vision and even blindness, which in a few instances remained permanently. According to Harnack (*M. M. W.*, 1912, lix, 1941) the blindness is due to spasm of the retinal vessels and subsequent optic atrophy. Prevost and Binet have found that in the lower animals, given hypodermically, the oleoresin produces

violent dyspnea and death from arrest of the heart in systole, and Fröhner has found parenchymatous nephritis in animals fatally poisoned by it.

Dose, sixty to one hundred and twenty grains (3.–7.7 Gm.). Filmaron has been used clinically in doses of fifteen to twenty grains (1.0–1.3 Gm.).

Off. Prep.—Oleoresina Aspidii, *U. S.* (*Br.*).

ASPIDOSPERMA. U. S.

ASPIDOSPERMA Aspidosp. [Quebracho]

(ăs-pĭ-dō-spĕr'mą)

"The dried bark of *Aspidosperma Quebracho blanco* Schlechtendal (Fam. *Apocynaceæ*), without the presence or admixture of more than 2 per cent. of wood or other foreign matter." *U. S.*

Aspidosperma Quebracho. Quebracho Bark. Quebracho Blanco.

Quebracho is an evergreen tree which sometimes reaches the height of one hundred feet, and is remarkable for its erect stem and its wide-spreading crown reaching out over the cacti and lower bushes among which it grows. The tree is indigenous to the western provinces of Argentine and is also found growing in Chili, Bolivia and Southern Brazil. The bark has been used for a long time in South America as a febrifuge and was not introduced into Europe until about 1878. The name quebracho is derived from the two Spanish words, *quebrar* and *hacha*, signifying "The axe breaks." The wood of the quebracho tree is not met with in commerce, but is said to be very hard, distinctly marked with rings of growth, and of a bright chocolate-brown color, except the very young wood, which is yellowish or reddish. According to Hesse and Penzoldt, the wood contains no alkaloids; it is used for tanning. In addition to *Aspidosperma quebracho blanco* there are two other plants which are known as quebracho. (1) The wood and bark of *Schinopsis Lorentzii* (Grisebach) Engl. (Fam. *Anacardiaceæ*) are extensively used in tanning. The plant was formerly known as *Aspidosperma quebracho colorado* and the wood is sold in commerce as "quebracho wood." Under the name of "quebracho flojo," the wood and bark of *Iodina rhombifolia* Hook. et Arn. (Fam. *Santalaceæ*) are substituted and sold for quebracho colorado in Southern Brazil to Argentina and Uruguay.

Properties.—Quebracho bark is remarkable for the extreme thickness of the corky layer which often constitutes more than half of its entire substance, and is separated from the lower layer by a more or less sharply defined outline. The corky layer is usually externally dirty gray, or where it has been rubbed appears yellowish-red. "In irregular chips or in longitudinal pieces attaining a length of 14 cm. and a thickness of 35 mm.; outer corky layer from 3 to 25 mm. in thickness, brownish-gray or reddish-brown and deeply furrowed, frequently somewhat reticulate with longitudinal and shallow transverse fissures, the crevices being occasionally lined with the mycelia of a grayish mould; outer surface of bark, from which the cork has been separated, light brown or reddish-brown and usually more or less roughened; inner surface occasionally with adhering wood, otherwise light yellowish-brown to light reddish-brown, longitudinally finely striate and finely porous; fracture short-fibrous with projecting bast-fibers; nearly inodorous, taste bitter and slightly aromatic. Under the microscope, transverse sections of Aspidosperma show a number of successive layers of cork separated by large groups of stone cells, isolated bast-fibers and parenchyma; inner bark with starch-bearing medullary rays 1 to 5 cells in width, separating narrow wedges composed of large prominent groups of stone cells in which are occasionally included one or more thick-walled bast-fibers; bast-fibers usually single, very thick-walled, strongly lignified and surrounded with crystal fibers and starch-bearing parenchyma. The powder is reddish-brown; bast-fibers single, very long and surrounded by crystal fibers, the crystals being in prisms frequently terminated by pyramids and from 0.008 to 0.03 mm. in length; stone cells in large thick groups composed of numerous more or less tabular cells; cork cells more or less polygonal in outline with thick, slightly lignified walls; starch grains single or 2- to 4-compound, the individual grains spherical, ovoid or more or less plano-convex, from 0.003 to 0.025 mm. in diameter." *U. S.*

In 1878, Fraude (*Ber. d. Chem. Ges.*, 1878, p. 2189; 1879, p. 1560) discovered in the quebracho blanco an alkaloid, *aspidospermine*, $C_{22}H_{30}N_2O$, but Hesse has found five other alkaloids, *aspidospermatine*, $C_{22}H_{28}N_2O_2$, and isomeric with it *aspidosamine*, $C_{22}H_{28}N_2O_2$, *quebachine*, $C_{21}H_{26}N_2O_3$, and isomeric with this *hypoquebrachine*, $C_{21}H_{26}N_2O_2$, and *quebrachamine*, *quebrachol*, $C_{20}H_{24}O + H_2O$, *quebrachit*, $C_6H_{11}(OCH_3)O_5$. (*Ber. d. Chem. Ges.*, xiii, 2308.) *Aspidospermine* is a brownish-yellow amorphous powder or needle-shaped crystals, fusing at 205° to 206° C. (401°–403° F.), is soluble in about 6000 parts of water at 15° C. (59° F.), the solution having a decidedly bitter taste, soluble in about 48 parts of absolute alcohol, in 106 parts of ether, insoluble in glycerin; it dissolves readily in fats and fixed oils, cod liver oil dissolving a larger proportion than it does of quinine. Its *sulphate* and *hydrochloride* are very soluble in water. The *citrate* is crystallizable, and very soluble. The yield of aspidospermine is small, 0.33 per cent. of the bark. *Aspidospermatine* is crystalline, and fuses at 162° C. (323.6° F.); *aspidosamine* is amorphous, and fuses at 100° C. (212° F.); *quebrachine* in colorless crystals fuses at 214° to 216° C. (417.2°–420.8° F.); *hypoquebrachine* is a yellowish mass resembling albumin, and fuses at 80° C. (176° F.); *quebrachamine* forms colorless silky needles, only slightly soluble in alcohol, ether, chloroform, and benzin, and fuses at 142° C. (287.6° F.). Two new sugars have also been extracted by Tanret, *quebrachite* and *lævogyrate inosite*. Tannin and starch have also been found in the bark. Accord-

ing to H. C. Wood, Jr., the most important principle is *quebrachine.* (*U. P. M. B.*, 1910, xxiii.)

Uses.—When a preparation of aspidosperma is injected into the circulation it causes an enormous increase in the rate and depth of the respiration with some fall in the blood pressure. Pentzold, who first described the effects of this drug on the respiration, believed that the breathing was dyspneic in type and that the drug acted by preventing the red corpuscles from giving up their oxygen. He based his belief on the fact that after death from the poison the blood had the same color in both arteries and veins, but Wood and Hoyt (*U. P. M. B.*, Sept., 1903) showed that the blood retained its normal oxidizing powers after aspidospermin and believed that the arterial hue in the veins was due to the violence of the respiration. The fall of blood pressure is due primarily to weakness of the heart, although larger doses also cause dilatation of the blood vessels—according to Cow (*J. P. Ex. T.*, 1914, v, p. 341), by a depressant action on the medullary centers. The increase in the respiration which is the most marked effect of aspidosperma appears to be due to a direct action upon the respiratory center as H. C. Wood, Jr. (*U. P. M. B.*, 1910, xxiii), has shown that it does not affect the circulation in the lungs, and Cow that it does not affect the bronchioles.

All of the alkaloids of aspidosperma as far as they have been studied are possessed of similar physiological properties, although to different degree. Both Wood and Cow agree that quebrachine is the most active alkaloid in the drug.

Aspidosperma is used in medicine for the relief of various types of dyspnea, especially in *emphysema* and *asthma.* In the latter condition it is not generally useful to interrupt the paroxysm, but in many cases if used continuously will greatly reduce the frequency and severity of attacks.

Under the name of *amorphous aspidospermine* there has entered in commerce a mixture of the various alkaloids of this drug. *Dose* of this preparation is from a quarter to one grain (0.016–0.065 Gm.); that of the crystalline aspidospermine is from one-fortieth to one-twentieth of a grain (0.0016–0.003 Gm.).

Dose, of aspidosperma, fifteen grains (1 Gm.); it is not, however, used in the crude state.

Off. Prep.—Fluidextractum Aspidospermatis, *U. S.*

ATROPINA. U. S., Br.

ATROPINE Atrop.

(ăt-rō-pī′nạ)

"An alkaloid [$C_{17}H_{23}O_3N = 289.19$] obtained from belladonna and from some other plants of the *Solanaceæ.* Preserve it in well-closed containers, protected from light." *U. S.* "Atropine, $C_{17}H_{23}NO_3$, is an alkaloid obtained from Atropa Belladonna, *Linn.*, and other plants of the natural order Solanaceæ." *Br.*

Atropia; Atropine, *Fr. Cod.*; Atropinum, *P. G.*; Atropin, *G.*; Atropina, *It., Sp.*

Because atropine cannot profitably be manufactured on a small scale, both Pharmacopœias have omitted the processes of preparation and furnish only qualitative tests. For the U. S. process of 1870, see U. S. D., 14th edition.

Properties and Tests.—"Atropine occurs in white rhombic prisms; odorless. *Great caution must be used in tasting it and then only in very dilute solution.* One Gm. of Atropine dissolves in 455 mils of water, 2 mils of alcohol, about 27 mils of glycerin, 1 mil of chloroform, and in 25 mils of ether at 25° C. (77° F.); also in 90 mils of water at 80° (176° F.) and in 1.2 mils of alcohol at 60° C. (140° F.). Its saturated aqueous solutions are alkaline to litmus, and to phenolphthalein T.S. It melts between 114° and 116° C. (237.2° and 240.8° F.). Gold chloride T.S. yields in a solution of Atropine in dilute hydrochloric acid (1 in 50) a lusterless precipitate (distinction from *hyoscyamine,* which yields a lustrous precipitate). Evaporate about 0.01 Gm. of Atropine to dryness in a porcelain dish on a water bath with a few drops of nitric acid; a yellow colored residue is produced. Cool this residue and add a few drops of alcoholic potassium hydroxide T.S. and a fragment of potassium hydroxide; an intensely violet color is produced. Hyoscyamine and hyoscine produce the same color, but the presence of strychnine or other alkaloids masks the reaction. No weighable ash remains on incinerating 0.1 Gm. of Atropine. About 0.1 Gm. of Atropine, dissolved in 2 mils of sulphuric acid, does not produce more than a slightly yellow solution (*readily carbonizable impurities*) and only a light yellow color is produced upon the further addition of 0.1 mil of nitric acid (*foreign alkaloids*). In a solution of Atropine in dilute hydrochloric acid (1 in 50) platinic chloride T.S. produces no precipitate (*foreign alkaloids*). An aqueous solution of Atropine (1 in 60), made with the aid of a slight excess of diluted sulphuric acid, is rendered turbid by the addition of a slight excess of sodium hydroxide T.S., but no turbidity is produced immediately upon the addition of 2 mils of ammonia water to 5 mils of the solution (*apoatropine, belladonnine*)." *U. S.*

"Colorless acicular crystals. Soluble in about 500 parts of *water,* readily soluble in *alcohol* (90 per cent.), in *chloroform,* and in *ether.* Melting point 114.5° to 115.5° C. (238°–240° F.). Its aqueous solution has an alkaline reaction and powerfully dilates the pupil of the eye. 0.05 gramme dissolved in 5 millilitres of *water* acidified with *hydrochloric acid* yields with *solution of auric chloride* a lemon-yellow precipitate which, after recrystallisation from boiling *water* acidified with *hydrochloric acid,* has a minutely crystalline character, is dull and pulverulent when dry, and melts at 137° to 139° C. (278.6°–282.2° F.) (distinction from hyoscyamine). 0.01 gramme with 5 drops of *nitric acid* yields, when evaporated to dryness on a water bath, a residue scarcely yellow in color which, after cooling, assumes a violet color on moistening with freshly prepared *alcoholic solution of potassium hydroxide.* 0.05 gramme dissolves in 1 millilitre

of *sulphuric acid* without coloration, and the solution remains colorless on the addition of 1 drop of *nitric acid*. 10 millilitres of a solution containing 1 part of Atropine in 80 parts of *water* slightly acidified with *hydrochloric acid* does not at once become cloudy on the addition of 4 millilitres of *solution of ammonia* (absence of apoatropine)." *Br.*

For further information, see *Belladonna;* also *A. J. P.*, 1884, 206.

It is inflammable, giving off an odor like that of benzoic acid, and, when burned in the open air, leaves no residue. By distilling it with potassium dichromate and sulphuric acid, E. Pfeiffer succeeded in obtaining crystals of benzoic acid and propylamine. (*A. J. P.*, 1864, 226.) Kraut, by heating it with baryta water, succeeded in obtaining a peculiar acid and peculiar base, the former of which he calls *tropic acid*, $C_9H_{10}O_3$, melting at 117° C. (242.6° F.), and oxidizable by diluted potassium permanganate to bitter almond oil and benzoic acid, and the latter *tropine*, $C_8H_{15}NO$, melting at 62° C. (143.6° F.). Ladenburg (*Ber. d. Chem. Ges.*, 12, 942, and 13, 104) has succeeded in effecting the synthesis of atropine from these two constituents, which, when heated over a water bath in the presence of diluted hydrochloric acid, unite to form the alkaloid; later (*Ph. Ztg.*, 1902, 355), he produced tropine by the direct action of hydrobromic acid on tropidine. Willstätter produced tropidine synthetically and the following synthetic chain was completed: Glycerin, glutaric acid, suberone, tropidine, tropine, tropic acid, and atropine. Ladenburg also succeeded in forming a series of compound esters of tropine with other organic acids to which the general name of *tropeines* has been given. Some of these have pronounced toxic effects, and one (homatropine) has found use as a valuable substitute for atropine. The list of artificial tropeines thus prepared includes:

Benzoyl-tropeine, $C_{15}H_{19}NO_2 + 2H_2O$, not mydriatic; *salicyl-tropeine*, $C_{15}H_{19}NO_3$, strong base, weak poisonous action; *m-oxybenzoyl-tropeine*, $C_{15}H_{19}NO_3$; *p-oxybenzoyl-tropeine*, $C_{15}H_{19}NO_3 + 2H_2O$; *phenylacet-tropeine*, $C_{16}H_{21}NO_2 + H_2O$; *oxytoluyl-tropeine* (homatropine), $C_{16}H_{21}NO_3$, has mydriatic action, and is less poisonous than atropine; *cinnamyl-tropeine*, $C_{17}H_{21}NO_2$, strong base, but without mydriatic action; *atropyl-tropeine*, $C_{17}H_{21}NO_2$; *atrolactyl-tropeine*, $C_{17}H_{23}NO_3$, has similar action to atropine; *phthalyl-tropeine*, $C_{24}H_{32}N_2O_4$; *lactyl-tropeine*, $C_{11}H_{19}NO_3$.

Hinterberger states that an alcoholic solution of atropine, when cyanogen is passed through it, assumes a blood-red color, and, on spontaneous evaporation, deposits a red, syrupy liquid insoluble in water. (Gmelin.) The detection of atropine in small quantity is a matter of great difficulty; the best test is the physiological, which consists in placing the suspected liquid in the eye of a cat, or other animal, when, if the alkaloid be present, dilatation of the pupil will occur. According to Brunner, the best chemical test is the aromatic odor which is produced by adding the alkaloid and a little water to a hot mixture of sulphuric acid and potassium dichromate or ammonium molybdate. (*P. J.*, iv, 385.) Fabris believes that strychnine in the presence of atropine interferes with the toxicological identification of the latter by chemical tests, but a physiological test reveals the presence of both alkaloids. (*B. S. Ph. Br.*, 1894.) Wormley made comparative examinations of various tests for atropine, hyoscyamine, and hyoscine. (*A. J. P.*, 1894, 513.)

Uses.—The effects of atropine upon the system are due chiefly to two actions, namely, a stimulation of certain higher nerve centers and a paralysis of the peripheral endings of the nerves known as the autonomic (or parasympathetic) system. The autonomic nerves carry impulses to certain organs of unconscious life; among them the secretory nerves for salivary, sweat, gastric, and probably all other glands except the kidney and mammæ; the vagus which carries inhibitory impulses to the heart, motor fibers to the bronchi and to a part of the intestines; the oculo-motor nerve which supplies the sphincter pupillæ and ciliary muscle. As atropine affects all of these nerves it is evident that it will produce a large number of changes in the bodily functions.

The earliest symptom of atropine poisoning is usually dryness of the throat. This is due to a paralytic action of the drug not only upon the chorda tympani nerve which supplies the salivary gland, but also probably to an action upon the mucus glands throughout the oral cavity. There is a corresponding decrease—although ordinarily only after somewhat larger dose—in the secretion of the sweat glands, of the digestive glands, and of the lachrymals; neither the kidney nor liver are affected. Concerning the mammary glands there is still some difference of opinion; pharmacologists have failed to demonstrate any effect upon these organs but clinicians continue to believe that the drug will cause a diminution in the secretion of milk. A little later in the action of atropine the pulse rate is increased through a paralysis of the cardio-inhibitory mechanism. As a result of the more rapid heart action, but also largely from the effect upon the vasomotor center in the medulla, there is an increase in the blood pressure. The question of whether atropine has a direct stimulant influence upon the heart muscle is as yet undecided, but if it possesses any such action it is a feeble one. Its stimulant action upon the medullary center is also shown in the increased rapidity of breathing, while that it possesses an action upon the cerebral centers is manifest by the delirium which follows toxic doses. The action upon intestinal peristalsis is probably a combination of various factors; through its paralytic action upon the branch of the pneumogastric nerve supplying the intestinal muscles it tends to counteract various spasmodic influences. At the same time, as has been shown by Magnus (*A. G. P.*, 1905, cviii, p. 1),

it possesses an action upon the so-called Auerbach plexus by virtue of which it increases the size of the peristaltic wave and also tends to restore their rhythmicity. When directly applied in sufficient concentration it is capable of paralyzing the unstriped muscle. The dilatation of the pupil which may be caused by the systemic action of toxic doses of atropine, but is more commonly the result of its local application, is due to an action upon the peripheral endings of the oculo-motor nerve. At the same time there is paralysis of accommodation through an effect upon the branches of this nerve which run to the ciliary muscle.

In the lower animals very large doses of atropine may cause increased reflexes, and even convulsions, through its effect upon the motor centers of the spinal cord, but this action is rarely seen in human poisoning. When brought in direct contact with either motor or sensory nerve endings it produces more or less complete abolition of their function.

Atropine is used in medicine for five purposes, namely, to check secretion, stimulate circulation, stimulate respiration, to overcome spasm of the involuntary muscles, locally for its effect upon the eye and externally as a local anodyne.

In the various forms of *colliquative sweating*, such as seen, for example, in *phthisis*, in *salivation*, as for instance, in mercurial poisoning, in *hyperchlorhydria*, atropine ranks as one of our most useful remedies. It is also of service to check the nasal secretions, as for instance in *acute coryza* or *hay fever*. In *galactorrhea* and threatened *mammary abscesses* belladonna plasters are routinely applied with the idea that the atropine in them may diminish the lacteal secretions, but as pointed out above, it is doubtful whether the drug possesses any such power.

As a circulatory stimulant atropine is of great value in severe emergencies, such as *surgical shock* or *collapse*. Its value in these conditions is due in part to the stimulating action on the vasomotor center and also in part to the effect upon the nerves of the skin which tend to check the excessive sweating which is characteristic of these states and thereby prevent the loss of animal heat. In the milder forms of circulatory failure it is ordinarily not to be recommended because the drying up of the secretion is often a source of great discomfort to the patient. As a respiratory stimulant it is of service, especially in the treatment of *poisoning* by various depressants, such as opium, chloral, and the like. It should be borne in mind that large doses of atropine are depressant and the physician should never give more than one-fiftieth of a grain when used either as a circulatory or respiratory stimulant.

In spasmodic affections involving the unstriped muscles, such as the *colica pictonum* and the *asthmatic paroxysm*, atropine is perhaps the most certain symptom remedy which we possess. In the latter affection it is usually best administered by inhalation; for this purpose it may be volatilized by burning one of the plants containing it. (See *Stramonium.*) In *whooping cough* and *dysmenorrhea* it is sometimes of value, but its action is much less certain. Certain cases of nocturnal *enuresis* appear to be due to a hyper-irritability of the muscle in the walls of the bladder and in these patients full doses of atropine are of the greatest service. The injection of atropine into the substance of the torticollis muscle in cases of *wry-neck*, for the purpose of paralyzing the motor nerve supplying it, while commonly recommended in textbooks, generally does not prove of avail. Allied to its antispasmodic action is the power of atropine to regulate as well as increase the movements of the bowel. For this purpose it is habitually added to laxative mixtures for the purpose of preventing griping as well as to enhance the aperient effect. Massive doses (as high as one-twentieth grain) have also been used with apparent favorable results in the treatment of *ileus*.

In ophthalmology atropine is a remedy of extreme service. It is used both for the purpose of dilating the pupil and paralyzing the muscles of accommodation. Its action is so slow and persistent that in cases where only temporary effects are desired, as, for example, the fitting of glasses, it has been largely abandoned for more rapidly acting drugs, but in inflammatory conditions of the eye, as in *iritis*, *keratitis*, etc., the very persistency of its effect makes it of extreme usefulness. For this purpose one or two drops of a 1 per cent. solution may be instilled into the eye at such intervals as may be deemed necessary. The same purpose may be accomplished by inserting beneath the eyelid small gelatin disks containing atropine. (See *Lamellæ Atropinæ.*)

Locally atropine in the form of an ointment and the plaster of belladonna is largely used in various painful conditions, but its use does not seem highly rational for this purpose.

Toxicology.—Atropine poisoning may occur from the ingestion of any of the numerous plants of which it is the active principle, most frequently, however, from either belladonna or the widespread stramonium. It should be remembered that severe poisoning may follow the external application either of the ointment or plaster of belladonna. The symptoms are dryness of the throat, dilatation of the pupil, rapid hard pulse, hurried respirations, the skin warm and dry, the face flushed and frequently there is an erythematous rash somewhat resembling that of scarlet fever. The most striking of the symptoms, however, is the peculiar delirium. In the earlier stages this manifests itself simply by profuse and somewhat incoherent talkativeness, but later there is complete obfuscation often with hallucinations, sometimes more or less maniacal in character. After large doses a stage of depression may develop with stupor, weakening of the pulse, and respiratory failure. The condition, though alarming, usually ends in recovery. In case of doubt as to the cause of the condition a presumptive diagnosis can be made by in-

stilling a drop or two of the urine from the patient into the eye of a cat. In most cases of atropine poisoning sufficient of the drug is eliminated through the kidneys to cause dilatation of the pupil. In the treatment of atropine poisoning after emptying the stomach with the stomach tube or suitable emetics, twenty minims of the compound solution of iodine should be given as the best chemical antidote. Morphine may be used cautiously for the purpose of quieting the delirium, but as the real danger in the case is from respiratory failure it should not be given in large dose. Physostigmine is almost a complete physiological antagonist of atropine and would probably prove useful in cases of poisoning. Symptoms of respiratory and circulatory failure may best be met by the use of strychnine and caffeine.

The hypodermic dose of atropine may be set down as the one-hundredth of a grain (0.0006 Gm.), the dose by the mouth as the one-seventy-fifth of a grain (0.0008 Gm.), although in serious cases these amounts may be much exceeded. Thus in *ileus* German clinicians have given as high as the one-twentieth of a grain (0.003 Gm.) as a dose. On the other hand in susceptible persons, one-hundredth of a grain (0.0006 Gm.) will produce decided dryness of the throat, and one-fiftieth of a grain (0.0013 Gm.) is alleged to have caused toxic symptoms. As atropine itself is nearly insoluble, the sulphate should always be preferred. For application to the sound skin, the form of ointment or oleate is most convenient. The ointment may be made by rubbing a grain of the alkaloid first with four minims of alcohol, and then with a drachm of lard. The ointment of belladonna is, however, usually preferred.

When solution of atropine sulphate is used for *dilating the pupil*, it may be either dropped into the eye within the lower lid, or introduced on small slips of paper previously saturated with the solution and dried, or, what is still more convenient, by means of minute circular disks of gelatin, made by mixing the solution with gelatin and evaporating so as to produce a thin film, which is to be cut into circular pieces. (See *Lamellæ Atropinæ.*) These have the advantage over paper that they do not require to be subsequently removed from the eye.

The solution of atropine or its salts is very prone to have developed in it a fungous growth with consequent decomposition of the alkaloid.

Dose, of atropine, one two-hundredth to one-fiftieth of a grain (0.0003–0.0013 Gm.).

Off. Prep.—Oleatum Atropinæ, *N. F.*; Unguentum Atropinæ, *Br.*

ATROPINÆ SULPHAS. U. S., Br.

ATROPINE SULPHATE Atrop. Sulph.

(ăt-rŏ-pī'næ sŭl'phās)

"The sulphate $[(C_{17}H_{23}O_3N)_2H_2SO_4 + H_2O = 694.49]$ of the alkaloid atropine." *U. S.*

"Atropine Sulphate, $(C_{17}H_{23}NO_3)_2,H_2SO_4$, is the sulphate of the alkaloid Atropine." *Br.*

Sulphate of Atropia; Sulfate d'Atropine, *Fr. Cod.*; Atropinum Sulfuricum, *P. G.*; Schwefelsaures Atropin, Atropinsulfat, *G.*; Solfato di atropina, *It.*; Sulfato de atropina, *Sp.*

Neither the U. S. nor the Br. Pharmacopœia gives a process for preparing this salt. The official formula of 1870 is essentially the process of Ch. Maitre, which is as follows: "Take of Atropia, *sixty grains;* Stronger Ether, *four fluidounces and a half;* Sulphuric Acid, *six grains;* Stronger Alcohol, *a fluidrachm.* Dissolve the Atropia in the Ether; then mix the Acid and Alcohol, and add the mixture, drop by drop, to the ethereal solution until the Atropia is saturated. Allow the liquid to stand until the precipitate formed is deposited. Then decant the ether, and expose the residue to spontaneous evaporation until the salt is dry." *U. S.*, 1870. Atropine being soluble in ether, while its sulphate is insoluble in that fluid, a convenient method is afforded for preparing the sulphate with little evaporation. By adding the mixed acid and alcohol to the ethereal solution, the sulphate is formed, and, being insoluble in the ether, is deposited, while the little left dissolved in the alcohol is obtained by spontaneous evaporation. The quantity of acid added is intended to be just sufficient to saturate the alkaloid; but if the saturation should not be exact, it would be easy to render it so by the addition of a little more alkaloid or a little more acid, as required.

From the great facility with which atropine undergoes change, much caution is necessary in preparing its salts, and the process was arranged in reference to this caution. Upon the addition of the mixed acid and alcohol to the ethereal solution, the liquid becomes milky, and deposits on the sides of the vessel a copious precipitate of a viscid appearance, which soon dries upon the decantation of the ether and the placing of the vessel in a drying-room. To succeed with this process it is necessary that the liquids employed should be carefully freed from water, the sulphuric acid being monohydrated, and that the temperature should be kept as low as possible. There should be no excess of acid; and, if such an excess should be found upon applying the test of litmus paper, the solution should be neutralized by a portion of reserved solution of atropine. (*A. J. P.*, xxviii, 361; from *Répert. de Pharm.*)

Properties.—"Atropine Sulphate occurs as a white, crystalline powder or in microscopical needles and prisms; efflorescent in dry air; odorless. *Great caution must be used in tasting it and then only in very dilute solution.* One Gm. of Atropine Sulphate dissolves in 0.4 mil of water, 5 mils of alcohol, 2.5 mils of glycerin, 420 mils of chloroform and in 3000 mils of ether at 25° C. (77° F.); also in 2.5 mils of boiling alcohol. An aqueous solution of the salt (1 in 20) is neutral to litmus. It usually melts between 188° and 191° C. (370.4°–375.8° F.); but when anhydrous and free from hyoscyamine, it melts between 181° and 183° C. (357.8°–361.4° F.). It responds to the other tests of identity and purity under *Atropina.*" *U. S.*

"Nearly colorless, crystalline, somewhat hygroscopic. Soluble in less than 1 part of *water*, and in 4 parts of *alcohol* (90 per cent.), the solutions being neutral to *litmus* and, even when largely diluted, dilating the pupil of the eye. Melting point from 189° to 190° C. (372.2°–374° F.). 0.05 gramme dissolves in 1 millilitre of *sulphuric acid* without coloration, and the solution remains colorless on the addition of 1 drop of *nitric acid*. 10 millilitres of an aqueous solution (1 in 60) do not at once become cloudy on the addition of 4 millilitres of *solution of ammonia* (absence of apoatropine). An aqueous solution, not too dilute, yields with *solution of sodium hydroxide* a white precipitate which, when washed and dried, responds to the tests described under 'Atropina.' Yields the *reaction* characteristic of sulphates. Loses not more than 2 per cent. of moisture when dried at 105° C. (221° F.)." *Br.*

If it be required to procure the sulphate in the form of crystals, which may sometimes be desirable to avoid adulteration, the process of Laneau may be employed. A solution of crystallized atropine in absolute alcohol, in the proportion of 2.89 parts of the former to 4 parts of the latter by weight, having been made with the assistance of a gentle heat, 0.4 part of sulphuric acid of the sp. gr. 1.85, diluted with 3 parts of absolute alcohol, is to be gradually added, and stirred with a glass rod, until saturation, as shown by test paper, is effected. The solution is then allowed to evaporate spontaneously, and the thinner the stratum the sooner will the process be completed. The crystals are in colorless needles more or less interlaced. (See *A. J. P.*, 1863, p. 315.)

Uses.—The effects of the salt on the system are precisely the same as those of atropine, and it may be used in the same dose. Its great advantage over the alkaloid is its solubility in water.

Dose, one two-hundredth to one one-hundredth of a grain (0.0003–0.0006 Gm.).

Off. Prep.—Lamellæ Atropinæ, *Br.;* Liquor Atropinæ Sulphatis, *Br.*

AURANTII AMARI CORTEX. U. S. (Br.)

BITTER ORANGE PEEL Aur. Amar. Cort.

(âu-răn'tĭ-ī ą-mā'rī cör'tĕx)

"The dried rind of the fruit of *Citrus Aurantium amara* Linné (Fam. *Rutaceæ*)." *U. S.* "Dried Bitter-Orange Peel is the dried outer part of the pericarp of Citrus Aurantium, var. Bigaradia, *Hook. f.*" *Br.*

Aurantii Cortex Siccatus, *Br.*; Aurantii Pericarpium; Cortex Aurantiorum, Cortex Pomorum Aurantii; Seville Orange Peel, Wild Orange Peel; Ecorce (Zestes) d'Oranges amères, Ecorce de Bigarade, *Fr.;* Cortex Aurantii Fructus, *P. G.;* Pomeranzenschale, *G.;* Corteccia di arancio amaro, *It.;* Corteza de naranja amarga, *Sp.*

Bitter Orange Peel of the U. S. P. IX is the dried rind. In the Br. Pharm., 1914, both the dried and the fresh rind are official, while under the name of *Aurantii Cortex Indicus*, Indian Orange Peel, the British Pharmacopœia, 1914, recognizes the bitter orange peel obtained from varieties of the *Citrus Aurantium*, grown in India and Ceylon. For description and properties, see under *Aurantii Dulcis Cortex.*

Off. Prep.—Fluidextractum Aurantii Amari, *U. S.;* Infusum Aurantii, *Br.;* Infusum Aurantii Compositum, *Br.;* Tinctura Aurantii Amari, *U. S.* (*Br.*); Syrupus Aurantii (from Tincture), *Br.;* Vinum Aurantii Compositum, *N. F.*

AURANTII CORTEX INDICUS. Br.

INDIAN ORANGE PEEL

(âu-răn'tĭ-ī cör'tĕx ĭn'dĭ-cŭs)

"Indian Orange Peel is the fresh and the dried outer part of the pericarp of varieties of Citrus Aurantium, *Linn.*, grown in India and Ceylon." *Br.*

It is thus described: "Possesses the pleasant aromatic odor and bitter taste characteristic of Bitter-Orange Peel derived from Citrus Aurantium, var. Bigaradia, *Hook, f.* Inner surface retains not more than a very small amount of the white spongy part of the pericarp." *Br.*

In India and the Eastern divisions of the Empire, Indian Orange Peel, fresh or dried, may be employed in making the official preparations for which Fresh or Dried Bitter-Orange Peel is directed to be used.

AURANTII CORTEX RECENS. Br.

FRESH BITTER-ORANGE PEEL

(âu-răn'tĭ-ī cör'tĕx rē-cĕns)

"Fresh Bitter-Orange Peel is the fresh outer part of the pericarp of Citrus Aurantium, var. Bigaradia, *Hook. f.*" *Br.*

It is thus described: "Outer surface red or deep orange-red in color, and generally rough. Inner surface retains not more than a very small amount of the white spongy part of the pericarp; in transverse section numerous large oil-glands below the epidermis. Pleasant aromatic odor; taste aromatic, bitter." *Br.*

AURANTII DULCIS CORTEX. U. S.

SWEET ORANGE PEEL Aurant. Dulc. Cort.

(âu-răn'tĭ-ī dŭl'cĭs cör'tĕx)

"The outer rind of the fresh, ripe fruit of *Citrus Aurantium sinensis* Gallesi (Fam. *Rutaceæ*)." *U. S.*

Cortex Aurantiorum Dulcium; Ecorce (Zestes) d'Oranges douces, *Fr.;* Apfelsinenschalen, *G.;* Scorze del frutto dell' arancio, *It.;* Corteza de naraja dulce, *Sp.*

The U. S. Pharmacopœia includes two kinds of orange peel, bitter and sweet, the former dried and the latter fresh. On the other hand, the British Pharmacopœia recognizes bitter orange peel in three forms, the fresh and the dried, under the respective names of Aurantii Cortex Recens, fresh bitter orange peel, Aurantii Cortex Siccatus, dried bitter orange peel, and Indian Orange Peel; but the orange peel which is called sweet by the U. S. Pharmacopœia—*i.e.*,

Citrus Aurantium—is termed *C. Aurantium* var. *Bigaradia*, bitter orange peel, by the British authority.

The orange tree grows to the height of about thirty feet. Its stem is rounded, much branched, and covered with a smooth, shining, greenish-brown bark. In the wild state, and before inoculation, it is often furnished with axillary spines. The leaves are ovate, pointed, entire, smooth, and of a shining pale green color. When held between the eye and the light, they exhibit numerous small transparent vesicles, filled with volatile oil, and when rubbed between the fingers, are highly fragrant. Their footstalks are about an inch long, and have wings or lateral appendages. The flowers, which have a delightful odor, are large, white, and attached by short peduncles, singly or in clusters, to the smallest branches. The calyx is saucer-shaped, with pointed teeth. The petals are oblong, concave, white, and beset with numerous small glands. The filaments are united at their base in three or more distinct groups, and support yellow anthers. The ovary is roundish, and bears a cylindrical style, terminated by a globular stigma. The fruit is a spherical berry, often somewhat flattened at its base and apex, rough, of a yellow or orange color, and divided internally into a number of vertical loculi, each containing from two to four seeds, surrounded by a pulp. The rind of the fruit consists of a thin exterior layer, abounding in schizo-lysigenous cavities filled with a fragrant volatile oil, and of an interior one, which is thick, white, spongy, insipid, and inodorous.

According to Lloyd, the orange was unknown to the ancient Greeks and Romans and was probably introduced into Europe by the Arabians. (*Bull. Lloyd Libr.*, 1911, p. 7.) According to Tschirch, the word orange is derived from the Sanscrit, Nagaranga or Naranga. (*J. P. C.*, 1910, p. 2.)

There are two varieties of *C. Aurantium*, considered by some as distinct species. They differ chiefly in the fruit, which in one is sweet, in the other is sour and bitterish and often has a darker and rougher rind. The sweet is officially recognized as *Citrus Aurantium sinensis* L., and the bitter or Seville variety as *Citrus Aurantium amara* L. The latter is ascribed by the British authority to *Citrus Aurantium* var. *Bigaradia* Hook, f., which is the Mandarin Orange. This is probably a native of China, but cultivated in Sicily, the south of Italy, and Florida, bears a fruit much smaller than the common orange, round, but flattened above and below, with a smooth, thin, delicate rind, and a very sweet delicious pulp. A volatile oil is obtained from the rind by expression, of a yellow color, a very bland agreeable odor, different from that of the orange or lemon, and a not unpleasant taste, like that of the rind. When freed from coloring matter by distillation, it was found by M. S. de Luca to be a pure hydrocarbon, with the formula $C_{10}H_{16}$. (*J. P. C.*, 3e sér. xxxiii, 52.) This constituent is now recognized as *d-limonene*.

The orange tree is a beautiful evergreen, in which the fruit is mingled, in every stage of its growth, with the blossoms and foliage and has been applied to numerous purposes of utility and ornament. A native of China and India, it was introduced into Europe at a very early period, was transplanted to America soon after its first settlement, and is now found in every civilized country where the climate is favorable. The fruit is brought to us chiefly from California, Florida, Southern Europe, and the West Indies. The Florida and Havana oranges are the sweetest. A seedless variety termed the *navel orange* is rapidly replacing all others in cultivation.

Various parts of the plant are used medicinally. The leaves, which are bitter and aromatic, are employed in some places in the form of infusion as a gently stimulant diaphoretic. They yield by distillation with water a volatile oil, which is said to be often mixed by the distillers with the oils obtained from the flowers and unripe fruit. In regard to polarized light it has a rotary power to the left, which is considerably weakened by the prolonged action of heat. (Chautard, *J. P. C.*, 3e sér. xliv, 28.) The fresh flowers may be kept for some time by mixing them well with half their weight of sodium chloride, pressing the mixture in a suitable jar, and keeping it well closed in a cool place. They were formerly recognized by the U. S. P. under the name of *Aurantii Flores*, and were officially described as "about half an inch (12 mm.) long; calyx small, cup-shaped, five-toothed; petals five, oblong, obtuse, rather fleshy, white and glandular-punctate; stamens numerous, in three or more sets; ovary globular, upon a small disk, with a cylindrical style, and a globular stigma; odor very fragrant; taste aromatic and somewhat bitter." *U. S.*, 1880. The dried flowers are used on the continent of Europe as a gentle nervous stimulant, in the form of infusion, two drachms to the pint of boiling water, taken in the dose of a teacupful. The flowers should be dried in the shade, at a temperature between 24° C. (75° F.) and 35° C. (95° F.).

An oil is obtained also from the flowers by distillation, which is called *oil of neroli*, and is much used in perfumery, and in the composition of *liqueurs*. It is an ingredient of the famous Cologne water. That obtained from the flowers of the Seville or bitter orange is deemed the sweetest. It was introduced into the Edinburgh Pharmacopœia, with the title of *Aurantii Oleum*, to serve for the preparation of orange flower water. Soubeiran considers this oil rather as a product of the distillation than as pre-existing in the flowers. The fact may thus be explained that orange flower water made by dissolving even the finest neroli oil in water has not the precise odor of that procured by distillation from the flowers.

The fruit is applied to several purposes. Small unripe oranges, about the size of a cherry or less, previously dried, and rendered smooth by a turning-lathe, were sometimes employed to

maintain the discharge from issues. They were preferred to peas on account of their agreeable odor, and by some were thought to swell less with the moisture; but this was denied by others, and it was asserted that they required to be renewed at the end of twenty-four hours. These fruits are sometimes found in commerce under the name of *orange berries.* They are sub-globular, 5 to 20 mm. in diameter, of a grayish or greenish-brown color, fragrant odor, and bitter taste, and are said to be used for flavoring cordials. A volatile oil is obtained from them by distillation, known to the French by the name of *essence de petit grain,* and employed for similar purposes with that of the flowers. The oil, however, which now goes by this name is said to be distilled from the leaves, and those of the bitter orange yield the best. The oils from the unripe and the ripe fruit have a rotating power to the right, the latter much greater than the former; and this property might serve to distinguish them from the oil of the leaves. Several of the oils from the *Rutaceæ* deposit a crystalline substance, differing from camphor. (Chautard.) The juice of the Seville orange is sour and bitterish, and forms with water a refreshing and grateful drink in febrile diseases. It is employed in the same manner as lemon juice, which it resembles in containing citric acid, though in much smaller proportion. The sweet orange is more pleasant to the taste, and is extensively used as a light refrigerant article of diet in inflammatory diseases, care being taken to reject the membranous portion. The best mode of separating the outer rind, when its desiccation and preservation are desired, is to pare it from the orange in narrow strips with a sharp knife, as we pare an apple. When the object is to use the fresh rind for certain pharmaceutical purposes, as for the preparation of the *confection of orange peel,* it is best separated by a grater, carefully avoiding the grating of the white portion which contains the bitter principle. The dried peel sold in the shops is usually that of the Seville orange, and is brought chiefly from countries adjacent to the Mediterranean.

Properties.—*Bitter orange peel* has a grateful aromatic odor, which depends upon the volatile oil contained in its schizo-lysigenous cavities, and a warm, bitter taste. Bitter orange peel occurs "in narrow, thin bands (ribbons), or more often elliptical, flattened, more or less curved, pieces (quarters), varying from 3 to 6 cm. in length; outer surface convex, varying from reddish- or yellowish-brown (ribbons) to greenish-brown (quarters), coarsely reticulate and with the edges recurved; inner surface concave, whitish, with numerous conical projections and yellowish-white, linear, more or less anastomosing fibro-vascular bundles; fracture hard; transverse section light brown, somewhat spongy, outer layer with 1 or 2 rows of oil reservoirs; odor fragrant; taste aromatic and bitter. The powder is yellowish-white or light brown; fragments of parenchyma cells numerous, the walls from 0.004 to 0.012 mm. in thickness; few fragments of tracheæ with close spiral markings or simple pores; occasional membrane crystals of calcium oxalate in monoclinic prisms, from 0.02 to 0.035 mm. in diameter. Powdered Bitter Orange Peel is colored yellowish upon the addition of potassium hydroxide T.S. Bitter Orange Peel yields not more than 7 per cent. of ash." *U. S.*

"In thin strips. Outer surface deep orange-red and rough. Inner surface retains not more than a very small amount of the white spongy part of the pericarp; in transverse section numerous large oil-glands below the epidermis. Pleasant aromatic odor; taste aromatic, bitter." *Br.*

The Br. Pharmacopœia requires that the outer surface both of the fresh and of the dried bitter orange peel shall be of a deep orange-red color, and rough and glandular.

The sweet peel is described officially as having "the outer, orange-yellow layer recently separated by grating or paring and consisting of epidermal cells, parenchyma cells of the sarcocarp with chromoplastids, oil reservoirs and globules of volatile oil; odor highly fragrant; taste pungently aromatic." *U. S.*

For the preparation of powdered bitter orange peel the German Pharmacopœia directs that the drug should be previously dried over freshly burnt lime. For histological study of orange fruit, see Winton and Moeller, "The Microscopy of Vegetable Foods." Bitter orange peel is sometimes adulterated with sweet orange peel. The latter is distinguished by the pieces being thinner and of a more orange-red color. They are less aromatic and bitter. The following test which is distinctive for bitter orange peel is recognized by the Netherland Pharmacopœia: the section of the fruit is mounted in a solution of potassium bichromate slightly heated when the tissues become colored brown. This reaction does not take place with sweet orange peel. A distinctive test for the latter is the use of fuming nitric acid (containing 55 per cent. N_2O_5) which gives a dark green color distinguishing it from bitter orange peel which is colored brown.

Both orange peels yield their sensible properties to water and alcohol. The bitter principle, *hesperidin,* $C_{22}H_{26}O_{12}$, was discovered by Lebreton in 1828, but its character as a glucoside was first established by Hilger and Hoffmann. (*Ber. d. Chem. Ges.,* 9, 26, 685.) Treated with diluted acids it yields *hesperetin,* $C_{16}H_{14}O_6$, and glucose. It is crystalline (fusing point 250° to 251° C. (482°–483.8° F.), and may be prepared by Paterno and Briosi's process, as follows: The cut and bruised oranges are covered with diluted alcohol, solution of potassium hydroxide added in excess, the liquor filtered after two days, and impure hesperidin precipitated by hydrochloric acid; the precipitate is boiled with acetic acid for ten minutes, and, after cooling, filtered from the resinous mass left. The hesperidin gradually separates from the filtrate upon standing, in white fine needles. From 4000 oranges about 6 ounces av. of the principle were

obtained. (*Ber. d. Chem. Ges.*, 1876, 250–252.) Tanret found in the rind of the bitter orange, (1) a crystalline acid, $C_{44}H_{28}O_{14}$; (2) a non-crystalline resinous body; (3) *hesperidin;* (4) *isohesperidin,* a crystalline glucoside isomeric with hesperidin; (5) *aurantiamarin,* another glucoside to which, in part, the bitterness of the peel is due. (*P. J.*, 1886, 839.) Orange peel contains also albumen, gum, resin, a trace of fixed oil, volatile oil, and a principle resembling tannin in its action on salts of iron. The bitter principles are much more abundant in the white spongy inner portion of the peel than in the outer yellowish layer. The volatile oil, *Oleum Aurantii,* U. S., may be obtained by expression from the fresh grated rind, or by distillation with water. It is imported into the United States in tinned copper cans. It has properties resembling those of the oil of lemons, but spoils more rapidly on exposure to the air, acquiring a terebinthinate odor. The perfumers use it in the preparation of Cologne water, and for other purposes; and it is also employed by the confectioners. According to Imbert-Gourbeyre, persons who are much exposed to the inhalation of the oil of bitter oranges are apt to be affected with cutaneous eruptions, and various nervous disorders, as headache, tinnitus aurium, oppression of the chest, gastralgia, want of sleep, and even muscular spasm. (*Ph. Cb.*, Feb., 1854, 128.)

Uses.—Bitter orange peel is a mild tonic, carminative, and stomachic; the sweet is simply aromatic; but neither is much used alone. They are chiefly employed to communicate a pleasant flavor to other medicines, to correct their nauseating properties, and to assist their stimulant impression upon the stomach. They are a frequent and useful addition to bitter infusions and decoctions, such as those of gentian, quassia, calumba, and Peruvian bark. It is obviously improper to subject orange peel to the action of heat, as the volatile oil is thus driven off. Violent colics, convulsions, and even death have been caused in children by eating large quantities of the rind. When orange peel is used simply for its agreeable flavor, the rind of the sweet orange is preferable; as a tonic, that of the Seville orange.

Dose, from half a drachm to a drachm (2.0–3.9 Gm.).

Off. Prep.—Syrupus Aurantii, *U. S.*, *Br.* (from Tincture); Tinctura Aurantii Dulcis, *U. S.;* Vinum Aurantii (from Fresh Peel), *Br.*

AURI ET SODII CHLORIDUM. U. S.

GOLD AND SODIUM CHLORIDE Aur. et Sod. Chlor.

(âu'rĭ ĕt sō'dĭ-ĭ ȼhlō'rĭ-dŭm)

"A mixture of equal parts of anhydrous gold chloride [$AuCl_3$ = 303.58] and anhydrous sodium chloride [NaCl = 58.46], representing, when dried to constant weight in a desiccator over sulphuric acid, not less than 30 per cent. of metallic gold [Au]. Preserve it in well-stoppered, amber-colored vials." *U. S.*

Chlorure d'Or et de Sodium, *Fr. Cod.;* **Chlorosaurate de Soude,** *Fr.;* **Natriumgoldchlorid,** *G.;* **Cloruro di oro e sodio,** *It.*

Gold and sodium chloride may be prepared by dissolving gold in nitrohydrochloric acid, evaporating the solution to dryness, weighing, and dissolving the dry mass in eight times its weight of distilled water. To this solution a weight of pure decrepitated common salt equalling that of the dry gold chloride is added, previously dissolved in four parts of water. The mixed solutions are then evaporated to dryness, being in the meantime constantly stirred with a glass rod. A process for making this salt from gold coin without requiring the preliminary purification necessary in the above process may be found in *Proc. A. Ph. A.*, 1882, p. 311. (See Kebler's paper, *A. J. P.*, 1900, 325; and one by Averkief, *Chem. News,* 1903, 84.)

Properties.—The pure crystallized salt, $AuCl_3$, $NaCl.2H_2O$, is of a golden-yellow color, and is in the form of prismatic crystals. The mixture of the U. S. P. is described as "an orange-yellow powder, odorless, having a saline and metallic taste, and deliquescent when exposed to damp air. Gold and Sodium Chloride is very soluble in water; alcohol or ether dissolves the gold chloride leaving the sodium chloride. A fragment imparts a persistent, intensely yellow color to a non-luminous flame. An aqueous solution (1 in 100) shows a slightly acid reaction, and yields with silver nitrate T.S. a white precipitate insoluble in nitric acid but readily soluble in ammonia water. Hold a glass rod, moistened with ammonia water, close to a portion of Gold and Sodium Chloride; no white fumes appear (*free hydrochloric acid*). The filtrate from the precipitated gold in the following assay process, after acidulation with hydrochloric acid, is not affected by hydrogen sulphide T.S. (*metallic impurities*).

"**Assay.**—Dissolve about 0.5 Gm. of Gold and Sodium Chloride, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed in a stoppered flask, in 10 mils of distilled water in a porcelain dish. Render the solution alkaline by the addition of 10 mils of potassium hydroxide T.S., heat it for five minutes on a water bath, add 25 mils or an excess of solution of hydrogen dioxide and continue the heating for an hour on a water bath, or until the addition of a few drops of solution of hydrogen dioxide produces no further precipitation in the clear liquid. (During the heating on the water bath occasionally replace the liquid lost by evaporation by the addition of hot distilled water.) Wash the precipitate of metallic gold with distilled water slightly acidulated with hydrochloric acid, dry and ignite it. Its weight corresponds to not less than 30 per cent. of the weight of the dried Gold and Sodium Chloride taken." *U. S.*

Uses.—The precise action of this salt upon the system is not known, but it is thought to affect the general nutrition, and is by some believed to affect the central nervous system. It has been used in various chronic nervous dis-

eases as *locomotor ataxia, neurasthenia,* etc. By many gynæcologists it is believed to have a specific direction to the genital organs, and it is used in *hysteria, ovarian irritation,* and even *chronic uterine inflammation.* It has also been commended in *syphilis, chronic rheumatism, diabetes mellitus,* and other chronic disorders affecting nutrition. The double salt of gold and sodium chloride has been very largely used in the treatment of the *alcoholic habit.* It would seem certain that no medication can suffice for moral reformation and any benefit from the drug must be by toning up the nervous system and bringing about a general increase of nutritive tone.

Dose, one-twelfth to one-quarter of a grain (0.005–0.016 Gm.).

AURUM
GOLD
(âu'rŭm)

Or, *Fr.*; Gold, *G.*; Oro, *It., Sp.*

The preparations of gold were introduced into medical practice in 1810 by Chrestein, of Montpellier. They have been especially recommended in various chronic diseases of the nervous system and skin, also in inveterate constitutional *syphilis* and allied disorders. The U. S. Pharmacopœia recognizes one preparation. (See p. 212.) For a discussion of various non-official preparations which have been used in medicine, see *Gold,* Part II.

BALSAMUM PERUVIANUM. U. S., Br.
BALSAM OF PERU Bals. Peruv. [Peru Balsam]
(bâl'sạ-mŭm pẹ-rû-vĭ-ā'nŭm)

"A balsam obtained from *Toluifera Pereiræ* (Royle) Baillon (Fam. *Leguminosæ*)." *U. S.* "Balsam of Peru is a viscid balsam exuded from the trunk of Myroxylon Pereiræ, *Klotzsch,* after the bark has been beaten and scorched." *Br.*

Balsamum Peruvianum Nigrum, Balsamum Indicum; Baume des Indes, Baume de Pérou noir, Baume de Sonsonate, *Fr.*; Balsamum peruvianium, *P. G.*; Peruvianischer Balsam, Indischer Balsam, Perubalsam, *G.*; Balsamo peruviano, Balsamo del Peru, *It.*; Balsamo del Peru liquido, Bálsamo de San Salvador, Balsamo negro, *Sp.*

The origin of Peru balsam has been the subject of considerable investigation (see *U. S. D.,* 19th ed.), and while the U. S. Pharmacopœia in conjunction with the Swiss Pharmacopœia ascribes it to *Toluifera Pereiræ,* the British authority ascribes it to *Myroxylon Pereiræ.* Tschirch, who has given a great deal of attention to the origin of Peru balsam, has come to the conclusion that it is merely a physiological variety of the same tree that yields Balsam of Tolu, and has designated it as *Toluifera Balsamum* L., var. phys. *Pereiræ.*

Toluifera Pereiræ is a handsome tree, with a straight, round, lofty stem, a smooth ash-colored bark, and spreading branches at the top. The leaves are alternate, petiolate, and unequally pinnate. The leaflets are from five to eleven, shortly petiolate, oblong, oval-oblong, or ovate, about three inches long by somewhat less than an inch and a half in breadth, rounded at the base, and contracting abruptly at top into an emarginate point. When held up to the light they exhibit, in lines parallel with the primary veins, beautiful rounded and linear pellucid spots. The common and partial petioles and midribs are smooth to the naked eye, but when examined with a microscope are found to be furnished with short hairs. The fruit, including the winged footstalks, varies from two to four inches in length. At its peduncular extremity it is rounded or slightly tapering; at the top enlarged, rounded, and swollen, with a small point at the side. The mesocarp, or main investment of the fruit, is fibrous, and contains in distinct receptacles a balsamic juice, which is most abundant in two long receptacles or vittæ, one upon each side. The yellowish-white beans yielded to Rother (*P. J.,* xv, 244) two per cent. of coumarin; the husks, a brown, extremely bitter, somewhat acrid resin. A gum-resin exudes in small quantities from the trunk of the tree, which, though containing, besides gum and resin, a small proportion of volatile oil, is distinct from the proper balsam, and yields no cinnamic acid. (Attfield, *P. J.,* Dec., 1863.) The valuable wood of the tree resembles mahogany.

This tree grows in Central America, in the State of San Salvador, upon the Pacific coast. It is found in the wild forests, singly or in groups, but the trees are owned by individuals. Charles Dorat states that it is never found at a greater height on the mountains than one thousand feet, that it begins to be productive after five years, and continues to yield for thirty years or more, and that the aroma of its flower is perceived at the distance of one hundred yards. (*A. J. P.,* xxxii.) The balsam is collected by the aborigines, on lands reserved to them, within a small district denominated the Balsam Coast, extending from Acajutla to La Libertad. Early in November or December the bark is beaten on four sides of the trunk, so as to separate it from the wood without breaking it, intermediate strips being left sound, in order not to destroy the life of the tree. The bruised bark soon splits, or cuts are made in it. Five or six days after the beating the injured surface is set on fire, and about a week later the bark, if it has not fallen off spontaneously, is removed. The juice now begins to exude freely from the exposed wood, which the natives cover with rags. The latter, when saturated, are boiled in water in large jars, and the liquid allowed to stand, whereupon the water rises to the top, and is poured off, leaving the balsam, which is put into calabashes or bladders. Seven to ten days later a second flow of balsam occurs, and is secured as before. Subsequently the exposed parts are scraped or otherwise wounded, and a third balsam is obtained. These three grades of balsam are said to be known respectively as *Tagauzonte, balsam de trapo, balsamo de contrapique.* The balsam is then taken for sale to the neighboring towns,

where it is purified by subsidence and straining and put into jars or metallic drums for exportation. The destroyed bark is said to renew itself in two years, so that by care a tree can be worked for a long time; two pounds is stated to be the average yearly yield. In 1861 the tree was introduced in Ceylon with complete success.

The term Balsam of Peru is a survival of the times when the products of the Spanish colonial coast were assembled at Callao, Peru, for shipment to Europe. This fact has caused Gane and Webster to assert that Balsam of Peru is misbranded under the Foods and Drugs Act in that it does not come from Peru. (*Drug Topics,* 1910, p. 4.) It is estimated that the Republic of Salvador exports annually about 130,000 pounds of Balsam of Peru. In spite of this there is a good deal of factitious balsam on the market which consists chiefly of synthetic cinnamein which is often added to exhausted tolu. Riedel reports having found a sample of balsam on the market, which was apparently derived from *Myroxylon punctatum* Klotzsch, and which contained none of the active principles of Balsam of Peru.

A substance called *white balsam* (*Balsamo blanco*) is procured from the fruit. This has been confounded with the balsam of Tolu, but is wholly distinct. It is of a semi-fluid or soft-fluid consistence, somewhat granular, and, on standing, separates into white, resinous crystalline deposit, and a superior, translucent more fluid portion. The odor, though quite distinct from that of the balsams of Tolu and Peru, is not disagreeable. Stenhouse has obtained from it a peculiar resinous body, readily crystallizable, and remarkably indifferent in its chemical affinities, which he denominated *myroxocarpin.* (*P. J.,* x, 290.) Tschirch (*Harze und Harzbehälter,* 1900, p. 166) gives the compound the name *myroxoresene,* and the formula, $C_7H_{10}O$. Dorat, however, denies that the white balsam is produced by the same tree, or in the same vicinity.

Another substance obtained from the same tree, and much used in Central America, is a tincture of the fruit made by digesting it in rum. It is called *balsamito* by the inhabitants, and is said to be stimulant, anthelmintic, and diuretic. It is also used as an external application to gangrenous or indolent ulcers, and as a wash to the face to remove freckles. According to Dorat, the balsamito is not the tincture, but an alcoholic extract of the young fruit. Neither this nor the white balsam reaches the markets of this country.

Balsam of Peru was named from its place of exportation, and it was long thought to be a product of Peru. It is now shipped partly from the Pacific coast, and partly from the Balize or other Atlantic ports, whither it is brought across the country. It was Guibourt who first made known the fact of its exclusive production in Central America. As imported, it is usually in tin canisters, with a whitish scum on its surface, and more or less deposit, which is dissolved with the aid of heat.

Besides the official species, there are others of the genus which possess medicinal virtues, and have been more or less employed. (See 14th ed., *U. S. D.*) The pod of *M. frutescens* Jacq., growing in Trinidad, is popularly used in that island as a carminative, and externally, in the form of a tincture, as a lotion in rheumatic pains, and by incisions in the stem a small quantity of balsamic juice is obtained not distinguishable from balsam of Tolu. (*P. J.,* Sept., 1862, p. 108.) Another species is known in Paraguay under the name of *quino-quino,* the bark of which is used, in powder and decoction, as a remedy in wounds and ulcers, and from the trunk of which a juice is obtained which in its concrete state closely resembles dried balsam of Peru. (*P. J.,* Oct., 1862, p. 183.) A product of *T. peruiferum,* sometimes known as *Brazilian balsam* or as *Oleo-balsam* has been offered for sale as genuine Peru balsam. In bulk it is of a dark brown color, but in thin layers it is dark red. Its odor is smoky, feebly fragrant; its taste slightly pungent, leaving a choking, disagreeable, persistent feeling. It is entirely soluble in ether and in rectified spirits. It also mixes with castor oil in all proportions, and forms with carbon disulphide a clear light brown solution with residue, also a deposit, in its chloroform solution, which becomes a powdery precipitate upon standing. At 17° C. (62.6°F.) its specific gravity is 1.031. Its general constitution is very similar to that of balsam of Peru, containing volatile oil, myroxylin, cinnamic and tannic acids, and resin. (*P. J.,* 3d sér. xi, 818.) It is especially to be distinguished from Peru balsam by its behavior with sulphuric acid. When Peru balsam is treated with sulphuric acid, and cold water poured upon it, a beautiful violet color is imparted to the surface, and the whole mass has a bright shade. The same procedure yields with the oleo-balsam a gray mass. For further information, see *P. J.,* xv, 771.

Properties.—"Balsam of Peru is a viscid liquid of a dark brown color; free from stringiness or stickiness; transparent and reddish-brown in thin layers; of an agreeable, vanilla-like odor and a bitter, acrid taste, with a persistent after-taste. When swallowed it leaves a burning sensation in the throat. It does not harden on exposure to the air. It is soluble in alcohol, chloroform, and glacial acetic acid with not more than a slight opalescence; only partly soluble in ether or petroleum benzin. Water, when agitated with the Balsam, is acid to litmus. Specific gravity: 1.130 to 1.160 at 25° C. (77° F.). One Gm. of the Balsam forms a clear solution when shaken with a solution of 3 Gm. of hydrated chloral in 2 mils of distilled water (*fixed oils*). Shake about 1 Gm. of the Balsam with 5 mils of purified petroleum benzin, and warm the mixture on a water bath for 10 minutes, adding a sufficient quantity of the solvent to replace the loss by evaporation. On evaporating 2 mils of the benzin solution, no odor of turpentine is noticeable, and when the residue is treated with a few drops of nitric acid, no green or bluish

color is produced (*turpentine or rosin*). Weigh accurately about 1 Gm. of the Balsam and dissolve it in 100 mils of alcohol, add 1 mil of phenolphthalein T.S. and titrate the solution with half-normal potassium hydroxide V.S. The acid number thus obtained is not less than 56 nor more than 84. Mix about 3 Gm. of the Balsam, accurately weighed, with 30 mils of sodium hydroxide T.S. and shake the mixture for a few minutes with 60 mils of ether. Then add about 3 Gm. of powdered tragacanth, filter and transfer 50 mils of the ethereal filtrate (representing five-sixths of the weight of the Balsam taken) into a tared, conical flask. Evaporate the ether and dry the residue to constant weight at 100° C. (212° F.). The weight of the residue of cinnamein so obtained is not less than 50 per cent. nor more than 56 per cent. of the weight of the Balsam represented by the 50 mils of ethereal solution taken. Dissolve this residue in 25 mils of alcohol, add 25 mils of half-normal alcoholic potassium hydroxide V.S. and heat the mixture carefully in a flask provided with a reflux condenser, during half an hour on a water bath. Then add 1 mil of phenolphthalein T.S. and titrate the excess of alkali with half-normal hydrochloric acid V.S. The amount of half-normal alcoholic potassium hydroxide V.S. consumed corresponds to a saponification value for the cinnamein of from 235 to 238 (see Part III, Test No. 10)." *U. S.*

"A viscid liquid, in bulk nearly black but in thin layers deep orange-brown or reddish-brown and transparent. Agreeable balsamic odor; taste acrid, leaving when swallowed a burning sensation in the throat. Insoluble in *water;* soluble in *chloroform.* 1 volume is soluble in 1 volume of *alcohol* (90 per cent.), but on the further addition of 2 or more volumes of the *alcohol* the mixture becomes turbid. Specific gravity between 1.140 and 1.158. Does not diminish in volume when shaken with an equal bulk of *water* (absence of ethylic alcohol). When tested by the following method it yields not less than 57 per cent. of cinnamein, the saponification value of which is not less than 235:—Dissolve 1 gramme of the Balsam in 30 millilitres of *ether* and shake in a separating funnel with two successive quantities of 20 and 10 millilitres of *N/2 solution of sodium hydroxide.* Separate the alkaline solutions, mix and shake with 10 millilitres of *ether.* Draw off and reject the alkaline solution. Add the second ethereal solution to that previously obtained. Wash the mixed ethereal solutions with two successive quantities of 5 millilitres of *water.* Transfer the ethereal solution thus washed to a tared wide-mouthed flask, evaporate at a gentle heat until the odor of ether has disappeared, add 1 millilitre of *absolute alcohol,* dry at 100° C. (212° F.) for half an hour, and weigh. The weight of the cinnamein thus obtained is not less than 0.57 gramme. To this residue add 20 millilitres of *N/2 alcoholic solution of potassium hydroxide* and 20 millilitres of *alcohol* (90 per cent.). Attach a reflux condenser, boil for half an hour, and titrate back with *N/2 solution of sulphuric acid, solution of phenolphthalein* being used as indicator. Each gramme of the residue thus treated requires not less than 8.4 millilitres of the alkaline solution for complete saponification (corresponding to a saponification value of not less than 235)." *Br.*

Boiling water extracts the acid. The oily liquid which separates on agitating Peru balsam with potassium or sodium hydroxide, called *Peru balsam oil* by Stolze, and *cinnamein* by Frémy, may be separated by fractional distillation into three portions, viz., *benzyl alcohol,* C_7H_8O, passing over at about 200° C. (392° F.); *benzyl benzoate,* $C_7H_5O_2.C_7H_7$, the principal portion boiling at 303° to 304° C. (577.5°–579° F.); and *benzyl cinnamate,* $C_9H_7O_2.C_7H_7$, passing over at about the boiling point of mercury. The crude oil likewise contains small quantities of free cinnamic and benzoic acids, resulting from the decomposition of the benzylic ether by the alkali used in separating it. According to Kraut (*Ann. Ch. Ph.,* cliii, p. 129), the benzyl cinnamate constitutes nearly 60 per cent. of the balsam; but Trog (*A. Pharm.,* 1894, 70–98) states that it is the benzyl benzoate which makes up the bulk of the oily portion and amounts to from 63 to 64 per cent. Tschirch (*loc. cit.*) states that in the sample of Peru balsam investigated by him benzyl benzoate was the main constituent, but small amounts of benzyl cinnamate were also present, and he considers that the relative proportions of the two esters may vary greatly in different samples of the balsam. The odor of the balsam Tschirch considers to be due to the *peruviol,* $C_{13}H_{22}O$, discovered by Thoms.

Peru balsam appears to contain only a single resin, yielding, by analysis, 66.3 to 67.25 per cent. of carbon, and 6.22 to 6.32 per cent. of hydrogen. (Kraut, *loc. cit.*) This resin separated from the alkaline solution of the balsam by hydrochloric acid is brown, has a faint odor of vanilla, and when fused with potash yields protocatechuic acid, together with a little benzoic acid. Tschirch has studied this resin and finds it to be the *cinnamic ester* of an alcoholic body called *peru-resino-tannol,* with the formula $C_6H_5.CH.COOC_{18}H_{19}O_4$. The tree also exudes a gum-resin, which, according to Attfield (*P. J.,* 1864, p. 248), contains 77.4 per cent. of a resin, and is non-aromatic, devoid of cinnamic acid, and entirely distinct from balsam of Peru. The leaves of the tree contain a fragrant oil. Like benzoin, balsam of Peru appears to be a pathological product.

The balsam is said to be adulterated in Europe (especially at Bremen) with castor oil, copaiba, Canada turpentine, etc. (*P. J.,* xii, 549), and a factitious substance has been sold in this country for the genuine balsam, prepared by dissolving balsam of Tolu in alcohol. This may be distinguished by its taking fire readily and burning with a blue flame, but a skillfully prepared product known commercially as *Perugen* is furnished, of which K. Enz (1913) states that the only constants of the German Pharmacopœia

available for detection are the acid number, iodine number, isolated cinnamein nitric acid reaction, and behavior in contact with benzin; the other pharmacopœial constants are of no value. "*Synthetic Balsam of Peru*" (*Ph. Ztg.*, No. 79, 828), is defended by Dr. F. Evers on the ground that it is equivalent to the natural balsam therapeutically and in some respects superior. Caesar and Soretz state that the characteristic odor and taste of the natural balsam are absent in the substitute.

For additional tests, see *Proc. A. Ph. A.*, 1894, 903; also 1895, 866, and *D. C.*, 1898, 60. A method of detecting castor oil, proposed by Wagner, is to expose a small portion of the suspected balsam to distillation until somewhat more than one-half has passed, shake the distillate with baryta water, remove by means of a pipette the layer of oil floating on the surface, and shake this with a concentrated solution of sodium bisulphite. If castor oil be present, the liquid will immediately become a crystalline mass. (*A. J. P.*, xxx, 570.)

A color test to distinguish true Peru Balsam from the factitious variety is as follows: One drop of Peru Balsam is shaken with 5 mils of petroleum benzin, and to 2.5 mils of this liquid 5 mils of ether is added. Sulphuric acid is then added, drop by drop, until from 10 to 15 drops have been added. Genuine Peru Balsam gives a beautiful violet to cornflower blue color in the lower layer, while the artificial products give either no color or very different shades.

Flückiger relied upon the specific gravity, which should be between 1.140 and 1.145, and the *lime test*, in which 10 drops of the balsam are shaken with 6 grains (0.4 Gm.) of slaked lime, forming, if there be no adulteration, a soft mixture, which does not harden. *Grote's test* consists in shaking 3 drops of balsam with 2 mils of official ammonia water; if, after standing, the mixture solidifies, rosin or other adulterant is present; benzoin, storax, and certain other substances cannot be detected by this test. (*A. J. P.*, 1881, 302, 361.)

As stated by Trog and others, the percentage of cinnamein should approximate 60. The saponification number should be between 235 and 238.

Uses.—Balsam of Peru is useful internally as a stimulating expectorant in *asthma* and *chronic bronchitis*, especially when of tuberculous origin. Although not so agreeable as balsam of Tolu it is much more active. Externally it affords a valuable stimulating dressing in indolent *ulcers* and local *tuberculosis* of the skin, bone, larynx, etc. It has also been highly lauded by Malannik (*M. M. W.*, 1912) as a first dressing for military *wounds*. He asserts that it is not only bactericidal of itself but that it stimulates the local resistance of the tissues and that it exercises a valuable protective action. Extensive erythema has followed its local application. (Hazen, *J. A. M. A.*, 1910, liv.) Internally it is best administered suspended in water by the yolk of egg or acacia.

Dose, from five to fifteen minims (0.3–0.9 mil).

Off. Prep.—Mistura Oleo-Balsamica, *N. F.*

BALSAMUM TOLUTANUM. U. S., Br.

BALSAM OF TOLU Bals. Tolu. [Tolu Balsam]

(bâl'sa-mŭm tō-lū-tā'nŭm)

"A balsam obtained from *Toluifera Balsamum* Linné (Fam. *Leguminosæ*)." *U. S.* "Balsam of Tolu is a solid balsam obtained from incisions made in the trunk of Myroxylon toluiferum, *H. B. and K.*" *Br.*

Balsamum Americanum; Baume de Tolu, Baume de Carthagène, *Fr.*; Balsamum Tolutanum, *P. G.*; Tolubalsam, *G.*; Balsamo Tolutano, Balsamo del Tolu, *It.*; Bálsamo de Tolu, *Sp.*

This balsam like balsam of Peru, has been the subject of much controversy. This is not only seen in the distinct sources above given by the U. S. and British Pharmacopœias, but is rendered more confusing by the fact that the German Pharmacopœia prescribes "the air hardened balsam of *Myroxylon balsamum* (L.) Harms var. *genuinum* Baillon." In addition to this Tschirch regards the tree yielding balsam of Tolu like that of the tree yielding balsam of Peru, merely physiological varieties of *Toluifera Balsamum* L. Schaer has recently reported on *Myrocarpus Balsam* (*Cabureiba Balsam*, of Piso; *Baume du Perou en coques*, of Guibourt), and concludes that it has intermediate properties between balsam of Tolu and balsam of Peru. It did not contain cinnamic acid an the benzoic acid which he obtained had a melting point from 3° to 4° higher than normal benzoic acid. (*Arch. d. Pharm.*, 1909, p. 176.)

The balsam is said to be produced normally in the tree only in young growing tissues such as the young twigs and leaves, and to be formed in the older tissues only as the result of injuries received. It is procured by making V-shaped incisions in the trunk quite through the bark. The juice is received in small calabash cups, which are inserted in slight excavations beneath the point of the two vertical incisions meeting at the lower end; and Weir has seen as many as twenty cups at a time on one tree. The collectors go from tree to tree, emptying the cups into flasks of raw-hide. In these skin vessels the juice is taken to the different ports on the river, where it is transferred to tin cans. It is brought from Carthagena in calabashes or baked earthen jars, or in tin or glass vessels.

Properties.—As first imported, balsam of Tolu has a soft tenacious consistence, which varies considerably with the temperature. By age it becomes hard and brittle like rosin. It is shining, translucent, of a reddish or yellowish-brown color, a highly fragrant odor, and a warm, somewhat sweetish and pungent, but not disagreeable taste. Exposed to heat, it melts, inflames, and diffuses an agreeable odor while burning. It is entirely soluble in volatile oils. The official description is as follows: "Balsam of Tolu is a yellowish-brown, or brown, plastic solid, becom-

ing brittle when old, dried, or exposed to cold. It is transparent in thin layers, has a pleasant, aromatic odor, resembling that of vanilla, and a mild aromatic taste. Balsam of Tolu is nearly insoluble in water and in petroleum benzin. It is soluble in alcohol, chloroform, and ether. It is dissolved by solutions of the fixed alkalies, usually leaving an insoluble residue. An alcoholic solution of the Balsam (1 in 20) is acid to litmus. Shake about 1 Gm. of the Balsam with 25 mils of carbon disulphide, allow it to stand for thirty minutes, filter the liquid and evaporate 15 mils of the filtrate to dryness. The residue thus obtained, when dissolved in glacial acetic acid, does not show a green color on the addition of a few drops of sulphuric acid (*rosin*). The remaining portion of the filtrate, when shaken with an equal volume of an aqueous solution of copper acetate (1 in 1000), does not acquire a green color (*rosin or copaiba*). Dissolve about 1 Gm. of the Balsam, accurately weighed, in 50 mils of alcohol, add 1 mil of phenolphthalein T.S. and titrate the solution with half-normal alcoholic potassium hydroxide V.S. The acid number thus obtained is not less than 112 nor more than 168. Now add sufficient half-normal alcoholic potassium hydroxide V.S. to the neutralized liquid to make the total amount of the volumetric alkali solution exactly 20 mils; heat the liquid on a water bath for half an hour, under a reflux condenser, and allow it to cool. Mix this liquid with 200 mils of distilled water, or more if necessary, and titrate the excess of potassium hydroxide with half-normal sulphuric acid V.S.; the total amount of half-normal potassium hydroxide V.S. consumed corresponds to a saponification value of not less than 154 nor more than 220 (see Part III, Test No. 10)." *U. S.*

"A soft, tenacious solid when first imported, becoming harder and finally brittle. Transparent and yellowish-brown in thin films. Pressed between pieces of glass with the aid of heat, and examined with a lens, it exhibits crystals of cinnamic acid. Odor fragrant, especially when warmed; taste aromatic and slightly acid. Soluble in *alcohol* (90 per cent.), the solution being acid to *litmus*. *Acid value* 107.4 to 147.2; *saponification value* 170 to 202. If 5 grammes are gently warmed with three successive portions of 25, 15, and 10 millilitres of *carbon disulphide*, the solution yields, when evaporated to dryness, a distinctly crystalline residue, which, when tested as described under 'Styrax Præparatus' yields not less than 1.25 grammes of benzoic acids." *Br.*

The carbon disulphide test is based upon Braithwaite's researches upon spurious balsams of Tolu. (See *P. J.*, 1895, 145; also 1897, 307.)

Boiling water extracts its acid. Distilled with water it affords a small proportion of volatile oil, and, if the heat be continued, an acid matter sublimes. Hatchett states that when dissolved in the smallest quantity of solution of potassium hydroxide it loses its own characteristic odor and acquires that of the clove pink. G. L. Ulex gives as a test of the purity of the balsam, that if heated in sulphuric acid it dissolves without disengagement of sulphurous acid, and yields a cherry-red liquid. (*A. Pharm.*, Jan., 1853.) A modification of this test is that of R. A. Cripps (*P. J.*, xix, 1888), who states that by a comparative test of the suspected balsam with a pure specimen 1 per cent. of storax or other resinous adulterant can be detected. Thirty grammes of the sample are digested in carbon disulphide for fifteen minutes with gentle warmth, the clear liquid decanted, evaporated to dryness, and dissolved in sulphuric acid. A bright red rose color is produced, remaining rose for a length of time if the balsam be pure, rapidly becoming brown if the balsam has been adulterated. The balsam is a mixture of volatile oil, free acid, and resin. The volatile oil is obtained by distilling the balsam with water, and may amount to a little over 1 per cent. This oil is chiefly *tolene*, $C_{10}H_{16}$, boiling at 170° C. (338° F.), and rapidly hardening by absorption of oxygen from the air. The free acid, according to Deville and Scharling, consists of benzoic and cinnamic acids, which statement has been confirmed by Flückiger. (*Pharmacographia*, 2d ed., 204.) Buse (*Ber. d. Chem. Ges.*, 1876, 833) has shown that the benzylic esters of these two acids are present in the balsam, the benzyl cinnamate in larger amount.

Tschirch (*Harze und Harzbehälter*, 1900, p. 173) found that the ester mixture in Tolu balsam amounted to 7.5 per cent. against 62 to 64 per cent. in Peru balsam. Trommsdorff obtained 88 per cent. of resin, 12 of acid, and only 0.2 of volatile oil. According to Heaver, the balsam yields by distillation about one-eighth of its weight of pure cinnamic acid. The acid distils over in the form of a heavy oil, which condenses into a white crystalline mass. It may be freed from empyreumatic oil by pressure in bibulous paper, and subsequent solution in boiling water, which deposits it in minute colorless crystals upon cooling. (*A. J. P.*, xv, 77.) A later investigation by Tschirch and Oberländer shows that the resinous portion of the balsam consists of *tolu-resino-tannol* in combination with cinnamic and benzoic acids, the latter in small proportions only. It contains, in addition, 7.5 per cent. of an aromatic, acid, oily liquid, composed mainly of benzyl benzoate, with a little benzyl cinnamate and a trace of vanillin. (*A. Pharm.*, 1894, 599.) A factitious balsam described by R. V. Mattison (*A. J. P.*, 1876, 51) contained 63 per cent. of storax.

Tolu balsam is sometimes adulterated with rosin and pine resins, both of which are readily detected, as they are soluble in carbon disulphide and benzol. The Balsam of Tolu of commerce is sometimes deficient in alcohol-soluble contents. Occasionally, the cans of shipment of tolu contain large pieces of red brick with enough melted balsam poured in to completely cover the bricks and fill the cans.

Uses.—Balsam of Tolu is a feeble stimulant expectorant; the syrup of Tolu is much used, on account of its agreeable flavor, as the basis of cough mixtures. Old and obstinate *catarrhs*

are said to be sometimes greatly relieved by the inhalation of the vapor proceeding from an ethereal solution of this balsam. The best form of administration is that of emulsion, made by triturating the balsam with mucilage and loaf sugar, and afterwards with water.

Dose, ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Syrupus Tolutanus, *U. S.* (from the tincture), *Br.;* Tinctura Benzoini Composita, *U. S., Br.;* Tinctura Tolutana, *U. S., Br.*

BARBITONUM. Br.

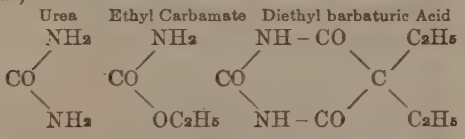
BARBITONE [Diethyl-barbituric Acid, Malonurea, Diethyl-malonyl-urea]

(bär-bĭ-tō'nŭm)

"Barbitone, $C_8H_{12}N_2O_3$, may be obtained by the interaction of the diethyl ester of malonic acid, and carbamide." *Br.*

Veronalum, Veronal, Acidum Diæthyl-barbituricum; Malourea.

The coined word barbitone is used in the British Pharmacopœia 1914 to designate the patented product, U. S. 782,739, termed "Veronal" by the Farbenfabriken (Friedr. Bayer & Co.), of Germany. It is related chemically to urea and ethyl carbamate or urethane, thus,



It is described by the British Pharmacopœia as "A white crystalline powder. Inodorous; taste faintly bitter. Slightly soluble in cold *water*, the solution being neutral to *litmus;* more soluble in hot *water*, and in *alcohol* (90 per cent.); freely soluble in aqueous solutions of the alkalies. Melting point 191° C. (375.8° F.). When fused with a caustic alkali, ammonia is evolved; and, when the cooled residue is dissolved in *water* and the solution acidified with *diluted sulphuric acid*, carbon dioxide is liberated, and a characteristic odor resembling that of fatty acids is developed. A few drops of *solution of mercury nitrate* added to 25 millilitres of a saturated aqueous solution acidified with *nitric acid* produces a gelatinous precipitate. No appreciable ash." *Br.*

Barbitone unites with various bases to form salts, many of which are soluble. One of these, the sodium salt, is used in medicine.

Uses.—Diethyl-barbituric acid is absorbed with moderate rapidity through the intestinal mucous membrane, its effects generally being manifest in about thirty minutes after its ingestion. It is eliminated solely through the kidneys, although Bachem (*A. E. P. P.*, 1910, lxiii, p. 228) believes that a considerable proportion is destroyed in the system. After small doses it is practically all eliminated within twelve hours, but when large quantities have been taken it may be retained in the system for long periods of time and when used repeatedly tends to accumulate in the body. In small doses it produces in the lower animals usually no symptoms but sleep, although after even moderate quantities the blood pressure may be reduced. In large doses it causes decided fall in the blood pressure through dilatation of the abdominal blood vessels, muscular weakness in the posterior extremities without loss of reflex, muscular fibrillation which may be sufficiently violent to simulate convulsions, diminution of respiration, and fall of bodily temperature. After very large poisonous doses there is loss of pain perception and diminution of reflex. (Roemer, *J. P. Ex. T.*, 1911, vi, p. 241.)

Veronal is a powerful somnifacient useful in many forms of *agrypnia* when not due to pain. Its effects are generally manifest in from a half to one hour and last over the greater portion of the night. Generally the patients awake without showing any symptoms of veronal action, but House (*T. G.*, May, 1913) reports that occasionally patients complain of slight vertigo in the morning, which he attributes to the reduction in blood pressure. The drug is far from being the harmless remedy that it has been deemed in some quarters. In the first place, because of its tendency to accumulate in the body, it is not fitted for continual uninterrupted use. There have been reported a number of cases of fatal poisoning from large doses and Wilcox (*B. M. J.*, 1913, ii, p. 663) states that as small a quantity as fifteen grains has proven fatal. In 1909 there were reported in England and Wales thirteen deaths from this agent. (*P. J.*, 1911, lxxxvi, p. 235.) In many persons who possess an idiosyncrasy against the drug, it produces violent eruptions, usually of a scarlatinoform character and often accompanied with considerable fever.

Diethylbarbituric acid has also been used as a general sedative in *hysteria, chorea,* and especially in *sea-sickness.* Hildebrandt (*Zeitschrift für ärztliche Fortbildung,* 1913, No. 12, p. 366) recommends it for the relief of *night sweats* in pulmonary tuberculosis.

The *dose* is from five to ten grains (0.32–0.65 Gm.), stirred up in water or enclosed in a gelatin capsule. It should not be given in pill form.

BELÆ FRUCTUS. Br.

BAEL FRUIT

(bēl'æ frūc'tŭs)

"Bael Fruit is the fresh half-ripe fruit of Ægle Marmelos, *Correa.*" *Br.*

Fructus Baël, Béla; Bael fruit, Indian Bael, Befigal Quince; Marmelos de Benguala, Cirifole, Beli; Indische Quitten, Marmelosbeeren, Marmelosfrüchte, *G.*

The so-called *Bengal quince* is a rather large tree (fam. *Rutaceæ*), extensively cultivated in India, with an erect stem, few and irregular branches, an ash-colored bark, strong, very sharp, axillary thorns, single or in pairs, leaves and large white flowers, ternate. The fruit is a berry of delicious flavor, of about the size of

a large orange, with a hard smooth shell, and from ten to fifteen loculi containing besides the compressed, woolly seeds a large quantity of exceedingly tenacious mucilage, which when dried is hard and transparent. "Fruit about 7 or 8 cm. in diameter, globular, ovoid or pyriform, greyish or yellowish-brown. Outer surface hard, nearly smooth. Rind about three millimetres in diameter, and adherent to a pale-reddish juicy pulp in which are ten to fifteen cells, each containing several woolly seeds. Faint aromatic odor; taste mucilaginous, acidulous, and slightly astringent." *Br.* The mucilage about the seeds is applied to various purposes in the arts, on account of its viscid properties. The rind is used in dyeing. The flowers are deemed refrigerant by the native physicians. The fresh leaves yield by expression a bitterish and somewhat pungent juice, which, diluted with water, is occasionally used in the early stage of catarrhal and other *fevers*. The bark of the stem and root is thought to possess febrifuge properties.

The fruit yields its virtues to water by maceration or decoction. Pollock found in it traces of tannic acid, an essential oil, and a vegetable acid. (*M. T. G.*, Feb., 1864.) It also contains mucilage, pectin, sugar and a bitter principle. (Badakow, *Apoth. Zeit.*, 1894, p. 773.)

The difficulty of obtaining bael in England is said to have led to the substitution for it of *mangosteen*, the fruit of *Garcinia Mangostana* L. This is in irregular fragments of the rind, without adhering pulp. The pieces are convex, three or four lines or more in thickness, externally covered with a smooth, deep reddish-brown, easily separable coating, and internally pale reddish-brown or reddish-yellow, smooth, with projecting vertical lines. (*P. J.*, May, 1867.)

Uses.—Bael fruit has been used in India in the treatment of *diarrhea* and *dysentery* for many years. It is also asserted to have laxative properties. Whether it has any real therapeutic activity is, at present, very doubtful. The *decoction*, two ounces of dried fruit in a pint of water boiled down to four fluidounces, is used in *doses* of one to two fluidounces (30–60 mils) every two to six hours; or the *Liquid Extract of Bael, Br.*, may be given in *doses* of 1 to 2 fluidrachms (3.75–7.5 mils).

Off. Prep.—Extractum Belæ Liquidum, *Br.*

BELLADONNÆ FOLIA. U. S., Br.

BELLADONNA LEAVES Bellad. Fol. [Deadly Nightshade Leaves Belladonnæ folium P. [.]

(bĕl-la-dŏn'næ fō'lĭ-a)

"The dried leaves and tops of *Atropa Belladonna* Linné (Fam. *Solanaceæ*), without the presence or admixture of more than 10 per cent. of its stems or other foreign matter, and yielding not less than 0.3 per cent. of the total alkaloids of Belladonna Leaves." *U. S.* "Belladonna Leaves are the leaves of Atropa Belladonna, *Linn.*, collected when the plant is in flower, and dried." *Br.*

Folia (s. Herba) Belladonnæ, Black Cherry, Poison black cherry, Deadly Nightshade, Doft-berry, Dwayberry, Devale (Dwale), Mad, Great Morel, Mekilwort; Feuilles de Belladone, *Fr.*; Folia Belladonnæ, *P. G.*; Belladonnablätter, Tollkirschen-Blätter. Solfskirschen-Blätter, Tollkraut, *G.*; Foglie di belladonna, *It.*; Hoja de belladona, *Sp.*

Off. Prep.—Emplastrum Belladonnæ, *U. S.* (from extract); Extractum Belladonnæ Foliorum, *U. S.*; Extractum Belladonnæ Siccum, *Br.*; Tinctura Belladonnæ Foliorum, *U. S.* (*Br.*); Unguentum Belladonnæ, *U. S.* (from extract); Pilulæ Aloes et Podophylli Compositæ (from Pilular Extract), *N. F.*; Pilulæ Aloini Compositæ (from Pilular Extract), *N. F.*; Pilulæ Aloini, Strychninæ et Belladonnæ (from Pilular Extract), *N. F.*; Pilulæ Aloini, Strychninæ et Belladonnæ Compositæ (from Pilular Extract), *N. F.*; Pilulæ Antidyspepticæ (from Pilular Extract), *N. F.*; Pilulæ Laxativæ Compositæ (from Pilular Extract), *N. F.*

BELLADONNÆ RADIX. U. S., Br.

BELLADONNA ROOT Bellad. Rad. [Deadly Nightshade Root]

(bĕl-la-dŏn'næ rā'dĭx)

"The dried root of *Atropa Belladonna* Linné (Fam. *Solanaceæ*), without the presence or admixture of more than 10 per cent. of its stem-bases or other foreign matter, and yielding not less than 0.45 per cent. of the total alkaloids of Belladonna Root. Preserve Belladonna Root in tightly-closed containers, adding a few drops of chloroform or carbon tetrachloride from time to time to prevent attack by insects." *U. S.* "Belladonna Root is the root of Atropa Belladonna, *Linn.*, collected in the autumn and dried." *Br.*

Racine de Belladone, Belladone, *Fr.*; Gemeine Tollkirsche, Wolfskirsche, Tollkirschen-wurzel, Wolfskirschen-Wurzel, *G.*; Radice di Belladonna, Belladonna, *It.*; Raiz de Belladona, Belladona, Belladama, *Sp.*

The belladonna, or *deadly night-shade* (*Atropa Belladonna*) is an herbaceous perennial, with a fleshy, creeping root, from which rise several erect, round, purplish, branching stems, to the height of about three feet. The leaves, which are attached by short footstalks to the stem, are in pairs of unequal size, oval, pointed, entire, of a dusky green on their upper surface, and paler beneath. The flowers are large, bell-shaped, pendant, of a brownish-purple color, with solitary peduncles, rising from the axils of the leaves. The fruit is a roundish berry with a longitudinal furrow on each side, at first green, afterwards red, ultimately deep purple and containing, in two loculi, numerous seeds and a sweetish violet-colored juice. The calyx adheres to the base of the fruit.

The plant is a native of Central and Southern Europe, where it grows in shady places, along walls, and amidst rubbish, flowering in June and July, and ripening its fruit in September. It grows vigorously under cultivation in England, France and the United States. During the past few years there has been very great interest in the cultivation of belladonna in the United States. The results of all experiments show

that a high grade of belladonna can be grown in this country. (Consult Borneman, *A. J. P.*, 1909, p. 1; Miller, *A. J. P.*, 1913, p. 291; Carr, *Ibid.*, 1913, p. 487; Severs, *Ibid.*, 1914, pp. 47 and 483, also 1916, p. 193; Newcomb, *Ibid.*, 1914, p. 531, and 1915, p. 1.) Plants cultivated in California are very rich in active constituents. (*Pacific Pharmacist*, 1907–1908, pp. 97 and 172.) The yield, per acre, of stems and leaves is somewhat less than one ton. The experiments in California seemed to show that the alkaloidal contents of belladonna stems is equal to that of the leaves, ranging from 0.51 to 0.82 per cent. of total alkaloids. (*Pacific Pharmacist*, 1909–1910, p. 295.) Belladonna leaves grown in the shade are uniformly larger, though somewhat thinner. It is quite likely that the percentage of alkaloids can be increased through selection. (*A. J. P.*, 1914, pp. 97 and 483.) All parts of it are active. Hirtz, of Strassburg, inferred from his experiments that the root yields an extract five times stronger than that obtained from the leaves, but did not determine the relative yield of extract, while Lefort obtained from young roots 0.6, from old roots 0.25, and from dried leaves 0.44 per cent. of atropine; Dragendorff obtained 0.66 from dried leaves, and 0.4 per cent. from the roots. (*Jahresb.*, 1874, p. 96.) The leaves and roots are directed by the United States and British Pharmacopœias, the latter including the branches, which, if young, are probably not less efficient. The leaves should be collected in June or July, when the plant is in flower, the roots in the autumn or early in the spring, and from plants three to four years old. Leaves which have been kept long should not be used, as they undergo change through absorption of atmospheric moisture, emitting ammonia, and probably losing a portion of their active nitrogenous matter. It has been affirmed that the finest looking leaves are to be rejected, as probably being those of cultivated plants, and inferior in strength to the smaller and less sightly leaves of the wild plant. (*A. J. P.*, xxvii, 455.) This is, however, probably an error, as the analyses made by A. W. Gerrard (*P. J.*, xv, 153) show that while the wild belladonna plant contains a little more alkaloid than the cultivated, the difference is not sufficient to be of material consequence. The same investigator found that the leaf yields the alkaloid most abundantly, the root, fruit, and stem being the next in order, and that the period of flowering (between two and four years of age), is the best time for collecting the plant. The dried leaves as they occur in the American market vary remarkably in the percentage of alkaloid; the best are fully equal to the finest English leaves. Specimens which contain much stem or are musty should always be rejected, as weak in active principle. Holmes has found in the English market the root of *Medicago sativa* used as an adulterant. (*P. J.*, 1882.)

Properties.—Officially the leaves are described as "usually much twisted and matted together; leaves much crumpled; when soaked in water and spread out, the entire leaves from 6 to 20 cm. in length, 4 to 12 cm. in breadth, broadly ovate, summits acute, margins entire, narrowed into the long petioles; upper surfaces brownish-green, lower surfaces grayish-green, epidermis more or less papillose and slightly hairy; flowers with yellowish-purple, campanulate corollas; fruits globular, subtended by the calyx, dark green or greenish-brown, and with numerous small seeds; odor distinct, especially on moistening; taste somewhat bitter and acrid. Stems of variable length not exceeding 7 mm. in diameter, longitudinally wrinkled, older parts smooth and usually hollow, younger parts flattened and finely hairy. The powder is dark green, consisting of irregular fragments of leaf tissues and woody elements; calcium oxalate in sphenoidal micro-crystals; hairs few, the non-glandular being simple, 2- to 5-celled, the glandular with stalks of 1 to 3 cells; tracheæ with annular, spiral, scalariform or reticulate thickenings and with bordered pores; starch grains and pollen grains few; occasional fragments of the stems of Belladonna with long, thin-walled and slightly lignified bast-fibers. Raphides must not be present (leaves and stems of *Phytolacca decandra* Linné). Belladonna Leaves yield not more than 20 per cent. of ash." *U. S.*

"Eight to twenty centimetres long, broadly ovate, acute, entire, glabrous or nearly so. Transverse section exhibits bi-collateral vascular bundles; mesophyll contains numerous cells filled with very minute crystals of calcium oxalate; epidermal cells of both surfaces possess a delicately striated cuticle. Yields not less than 0.30 per cent. of alkaloids when assayed as directed on page 222." *Br.*

The roots occur in "cylindrical or somewhat tapering, usually split into longitudinal pieces, from 0.5 to 2.5 cm. in thickness; externally pale brownish-gray, longitudinally wrinkled, outer layers of the periderm rather soft, frequently abraded, and thus showing lighter patches; fracture nearly smooth, mealy, on breaking, emitting a puff of dust consisting chiefly of starch grains; internally whitish, with a distinct cambium zone and yellowish wood wedges; nearly inodorous; taste sweetish, afterwards bitterish and strongly acrid. Transverse sections of Belladonna Root when moistened with iodine T.S. are colored bluish-black and by transmitted light show an imperfectly radiate structure within and near a conspicuous cambium line. Under the microscope, sections exhibit a bark and wood composed mainly of parenchyma, the cells being filled with starch grains, single and 2- to 6- or more compound, the individual grains being somewhat spherical and from 0.003 to 0.03 mm. in diameter. A section cleared with hydrated chloral T.S. shows in both bark and wood occasional cells of parenchyma filled with sphenoidal micro-crystals of calcium oxalate; bark free from bast-fibers; wood containing scattered groups of large tracheæ with simple and bordered pores or reticulated thickenings,

and associated in older roots with wood-fibers. Stem fragments of Atropa Belladonna occur either separate or attached to the roots; light brown or greenish-brown; finely, longitudinally wrinkled, with transverse leaf-scars; pith frequently hollow. Under the microscope, sections of Belladonna stem show beneath the endodermis an interrupted circle of bast-fibers either singly or in small groups, the walls of which are relatively thin and slightly lignified. In the internal phloem also occur isolated small groups of bast-fibers similar to those found in the inner bark. The powder is light brown; starch grains numerous, from 0.003 to 0.030 mm. in diameter, spherical, plano-convex, polygonal, and 2- to 6- or more compound; sphenoidal micro-crystals numerous, from 0.003 to 0.010 mm. in length; fragments of cork cells and tracheæ with wood-fibers few; occasional fragments of stems of Belladonna showing long, thin-walled and slightly lignified bast-fibers. Belladonna Root yields not more than 7 per cent. of ash." *U. S.*

"Nearly cylindrical pieces, entire or longitudinally split, usually ten to twenty millimetres in diameter, and fifteen to thirty centimetres or more in length. Externally pale greyish-brown, and finely wrinkled longitudinally. Transverse fracture short. Internally whitish and starchy. Within and mostly near to the cambium ring are numerous scattered groups of vessels and fibers which do not exhibit a prominently radiate arrangement. Most of the parenchymatous cells contain small compound starch grains; some are filled with numerous very minute crystals of calcium oxalate. Taste slightly bitter." *Br.*

The usual adulterants of belladonna leaves are the leaves of *Phytolacca* and *Ailanthus*. The commercial article may consist as high as 75 per cent. of foreign material. (See Allen and Deane, *P. J.*, 1914, p. 121.) For distinction between belladonna and scopola leaves see article by Kraemer. (*Proc. A. Ph. A.*, 1908, p. 819.) Guérin and Giullaume describe the anatomical differences in the leaves of belladonna, phytolacca and ailanthus. (*Bull. Soc. Pharmacol.*, 1908, p. 213.)

Belladonna root is not infrequently of inferior quality because of the presence of large quantities of the stem-bases of the plant. Reports still come in that the root is adulterated with phytolacca and replaced by 15 to 20 per cent. of scopola. Rusby has reported the presence of 25 per cent. of some inert root, apparently wild althæa, or a relative of that plant. For article on the distinction between belladonna root and scopola rhizome, consult Kraemer. (*Proc. A. Ph. A.*, 1908, p. 819.)

Scopola root has been largely used by manufacturers of belladonna plasters in the place of belladonna root.

Both the leaves and root, as well as all other parts of the plant, impart their active properties to water and alcohol. Its activity is attributable to the alkaloid atropine discovered by Brandes, but first procured in a state of purity by Mein, a German apothecary, who extracted it from the root. It is generally recognized that the following mydriatic alkaloids are found in the solanaceous plants; *atropine, hyoscyamine, scopolamine, atroscine,* and *belladonine.* The first two of these, atropine and hyoscyamine, are isomeric, having the formula $C_{17}H_{23}NO_3$, and yield the same decomposition products. They differ, however, in their physical constants, especially in their relation to polarized light. Whereas hyoscyamine is strongly lævo-rotatory, atropine is optically inert. Will (*Ber. d. Chem. Ges.*, 1888, p. 1717) has shown that hyoscyamine is readily changed into atropine and that varying proportions of the two alkaloids may be obtained from the same specimen of belladonna, according to the method of extracting from the crude drug. Atropine appears to be a mixture of lævo-rotatory and dextro-rotatory hyoscyamines. The dextro-hyoscyamine does not appear to occur in nature, but has been prepared artificially. Of these, atropine occurs in the *Atropa Belladonna* and in *Datura Stramonium*, hyoscyamine in these plants and also in *Hyoscyamus niger* and *Duboisia myoporoides;* hyoscine is found in *Hyoscyamus niger* (and under the name of scopolamine in *Scopola carniolica*), and belladonine in belladonna root alone. Atropine fuses when pure at 115.8° C. (240.4° F.), and forms a double gold chloride, fusing at 135° to 137° C. (275°–278.6° F.); *hyoscyamine* fuses at 108.5° C. (227.5° F.), and yields a gold salt fusing at 160° C. to 162° C. (320°–323.6° F.). In *Duboisia myoporoides* (see Part II) the chief alkaloid present seems to be hyoscyamine, and the complete identity of it with the purified alkaloid of hyoscyamus has been established byLadenburg, both by analysis of the free alkaloid and its salts, and by study of the action of different reagents upon it. Hyoscyamine is more soluble in water and diluted alcohol than is atropine, and, as already stated, forms a gold salt of different fusing point. Its decomposition products under the influence of caustic baryta or hydrochloric acid are the same as those of atropine,—viz., *tropine* and *tropic acid.* Hübschmann (*Schweiz. Zeits. Pharm.*, 1858, 123) and Kraut (*Ann. Ch. Ph.*, 148, 236) both described, under the name of *belladonine,* a second alkaloid extracted from belladonna root. This *belladonine* and another alkaloid, *atropamine,* found at times in belladonna root, and obtained from the by-products of the manufacture of atropine, possess the formula $C_{17}H_{21}NO_2$, and are considered as anhydro-atropines. Both bases form varnish-like masses. Merck has isolated a base isomeric with Hesse's atropamine, which has been termed *apoatropine,* the salts of which are easily crystallizable. He asserts that atropamine and apoatropine are identical. Hesse, on the other hand, denies this assertion. (*Ann. Ch. Ph.*, cclxxi, 10.) W. Will in 1888 as the result of an investigation undertaken at the request of the Schering Company to determine why the proportion of hyoscyamine and atropine in a root seems to vary

with the method of working, found that hyoscyamine can be changed into atropine under a variety of circumstances, such as fusion, action of weak soda solution (even at ordinary temperature), and of ammonia. The conversion of the optically active hyoscyamine into the optically inactive atropine was proved by the alteration of fusing point in the two alkaloids, and of their double gold chloride salts. (*Ber. d. Chem. Ges.*, 1888, p. 1717.) The results were also confirmed by Schmidt, and it is now generally admitted that the two alkaloids are stereoisomeric, and capable of such change. For the mode of preparing atropine, and its properties, see *Atropina*, page 206. Dunstan and Ransom have devised processes for isolating the alkaloids from the root and leaves which they assert are simple and accurate. (See *A. J. P.*, 1884, 277; *Proc. A. Ph. A.*, 1886, 392.) A. W. Adams states that only 53 per cent. of the atropine in belladonna leaves can be separated by these processes. (*Am. Drug.*, 1891, 328.) For other assays of belladonna leaves and root, and comments, see Schwickerath (*Ph. Rund.*, 1893, 282); Keller (*Ph. Ztg.*, 1894, 345); Moerk (*A. J. P.*, 1899, 105); LaWall and Pursell (*A. J. P.*, 1899, 394); Puckner (*Ph. Rev.*, 1898, 180, 324; 1902, 457); Bird (*P. J.*, 1900, 195); Kebler (*Am. Drug.*, 1902, 215); Schmidt (*Ap. Ztg.*, 1900, 13).

Assay of Belladonna Root.—"Introduce 15 Gm. of Belladonna Root, in No. 60 powder, into a 250 mil flask and add 150 mils of a mixture of chloroform, 1 volume, and ether, 2 volumes. Stopper the flask, shake it well and allow it to stand ten minutes, then add 5 mils of ammonia water and shake the flask vigorously every ten minutes during two hours. Now add 15 mils of distilled water, again shake the flask well, and, when the drug has settled, decant 100 mils of the solution, representing 10 Gm. of Belladonna Root. Filter the solution through a pledget of purified cotton into a separator, and rinse the graduate and cotton with a little ether. Completely extract the alkaloids from the solution by shaking out repeatedly with weak sulphuric acid. Collect the acid washings in a separator, add ammonia water until the solution is decidedly alkaline to litmus, and completely extract the alkaloids by shaking out repeatedly with chloroform. Evaporate the combined chloroform washings to dryness, dissolve the alkaloids from the residue in exactly 5 mils of tenth-normal sulphuric acid V.S., and titrate the excess of acid with fiftieth-normal potassium hydroxide V.S., using cochineal T.S. as indicator. Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 28.92 milligrammes of the total alkaloids of Belladonna Root (see *Proximate Assays*, Part III)." *U. S.*

Assay of Belladonna Leaves.—"Proceed as directed under *Belladonnæ Radix*, using 15 Gm. of Belladonna Leaves, in No. 60 powder, increasing the amount of water added after maceration to 25 mils and, before titration, treating the final residue twice with 5 mils of ether, evaporating to dryness each time. Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 28.92 milligrammes of the total alkaloids of Belladonna leaves." *U. S.*

"Into a small stoppered glass percolator provided with a glass tap and suitably plugged with cotton wool introduce 10 grammes of Belladonna Leaves in No. 60 powder and 50 millilitres of a mixture of *chloroform* 1 volume and *ether* 4 volumes. Shake; set aside for ten minutes; then add 2 millilitres of *solution of ammonia* diluted with 3 millilitres of *water*, and set aside for one hour, shaking frequently. Then allow percolation to proceed slowly, receiving the percolate in a separator containing 6 millilitres of *N/1 solution of sulphuric acid* diluted with 20 millilitres of *water*. When the liquid ceases to pass continue the percolation with a further 50 millilitres or more of the ether-chloroform mixture, added in small quantities, until the Leaves are exhausted. Shake the separator well and, after separation, draw off the acid liquid into a second separator. Repeat the extraction of the ether-chloroform solution with two successive portions, each of 10 millilitres, of the diluted acid. Make the mixed acid solutions alkaline with *solution of ammonia*, and shake out with three successive portions of 15, 15, and 5 millilitres of *chloroform*. Evaporate the mixed chloroformic solutions to dryness, dissolve the residue in 3 millilitres of *ether*, and again evaporate to dryness. Dissolve the residue in 10 millilitres of *N/20 solution of sulphuric acid*, and titrate with *N/20 solution of sodium hydroxide, tincture of cochineal* being used as indicator. Deduct the number of millilitres of the alkaline solution required fro 10, multiply the difference by 0.1446; the product will be the percentage of alkaloids in the Leaves." *Br.*

Uses.—All parts of the belladonna plant are poisonous. It is not uncommon in countries where it grows wild, for children to pick and eat the berries, allured by their fine color and sweet taste. The symptoms of belladonna poisoning are precisely the same as those of atropine poisoning, see page 207.

It is believed by some that the active principle of belladonna is hyoscyamine rather than atropine. This idea receives certain clinical support because practical experience has shown that, although qualitatively indistinguishable in its action from atropine, belladonna is efficacious in doses considerably smaller than might be expected from its content of alkaloid if the latter were atropine. For description of the physiological and therapeutic properties of belladonna, see under *Atropine*, page 206.

The various preparations are much used locally. Rubbed upon the areola of the breast, it has been believed to arrest the *secretion of milk* and is frequently employed in *mastitis*. The decoction or extract, applied to the neck of the uterus, is asserted to have hastened *tedious labor* dependent on rigidity of the os cervicis; and spasmodic *stricture of the urethra, neck of the bladder*, and *anal fissures* and *painful uterine*

affections have been relieved by the local use of the extract, either smeared upon bougies or administered by injection. In the latter mode it has relieved *strangulated hernia.* It is asserted also to be useful in *paraphimosis.* The inhalation of the vapor from a decoction of the leaves or extract has been recommended in *spasmodic asthma.* For this purpose, two drachms of the leaves, or fifteen grains of the aqueous extract, are employed to the pint of water. A much better plan is to smoke the dried leaves in the form of a cigarette or in a pipe.

Belladonna should never be given in substance, but in the form of extract or tincture, or, when accuracy or quickness of action is desired, of atropine. (See *Atropina.*)

Dose, one grain (0.065 Gm.)

Off. Prep.—Emplastrum Belladonnæ *Br.* (from liquid extract); Fluidextractum Belladonnæ Radicis, *U. S.* (*Br.*); Linimentum Belladonnæ, *U. S.*, *Br.* (from liquid extract); Suppositoria Belladonnæ, *Br.* (from alcoholic extract); Unguentum Belladonnæ, *Br.* (from liquid extract).

BENZALDEHYDUM. U. S.

BENZALDEHYDE Benzaldehyd.

(bĕn-zăl-dē-hī′dŭm)

"An aldehyde produced synthetically or obtained from oil of bitter almond and containing not less than 85 per cent. of C_7H_6O or $C_6H_5.CHO$ (106.05). Preserve it in small, well-stoppered bottles, protected from light." *U. S.*

Benzoic aldehyde; Oleum Amygdalarum Æthereum Sine Acido Prussico; Oleum Amygdalarum Æthereum Artificiale; Aldéhyde Benzoique, *Fr.*; Benzaldehyd, Künstliches Bittermandelöl, *G.*

Preparation.—Benzaldehyde is the first in the series of aromatic aldehydes, being the first oxidation product of benzyl alcohol, $C_6H_5.CH_2OH$, and going in turn into the fuller oxidation product, benzoic acid, $C_6H_5.COOH$. It is mainly produced artificially from toluene by the following reactions:

$$C_6H_5.CH_3 + 2Cl_2 = C_6H_5.CHCl_2 + 2HCl$$
$$C_6H_5.CHCl_2 + HOH = C_6H_5.COH + 2HCl$$

Exposed to the air, benzaldehyde tends to pass by oxidation into benzoic acid, which latter is therefore liable to be found as a contamination of the sample of benzaldehyde if not freshly rectified. Benzaldehyde is officially described as "a colorless, or yellowish, strongly refractive liquid, having a bitter-almond-like odor, and a burning, aromatic taste. It is slightly soluble in water, miscible with alcohol, ether, or fixed or volatile oils. Specific gravity: about 1.045 at 25° C. (77° F.). Shake 10 drops of Benzaldehyde with 5 mils of distilled water, add 0.5 mil of potassium hydroxide T.S. and 0.1 mil of ferrous sulphate T.S., and warm the mixture gently. Now add a slight excess of hydrochloric acid to the mixture; no greenish-blue color nor blue precipitate is produced within fifteen minutes (*hydrocyanic acid*). Hold the looped end of a piece of clean copper wire in a non-luminous flame until it glows, without coloring the flame green, cool the wire, dip the loop into Benzaldehyde, ignite the latter and hold it so that the liquid burns outside of the non-luminous flame. On slowly bringing the flame from the burning Benzaldehyde on the loop in contact with the lower outer edge of the non-luminous flame, no green tinge is discernible (*chlorinated products*). Dissolve 1 mil of Benzaldehyde in 20 mils of alcohol, add distilled water until a slight turbidity is produced, and maintain a brisk evolution of hydrogen for one hour by the addition of zinc and diluted sulphuric acid. Filter and evaporate the liquid to about 20 mils and boil 10 mils of the evaporated liquid with 1 drop of potassium dichromate T.S.; no violet color is produced (*nitrobenzene*).

"**Assay.**—Dissolve about 3 mils of freshly redistilled phenylhydrazine in 60 mils of alcohol and titrate 25 mils of the solution, which must always be freshly prepared, with half-normal hydrochloric acid V.S., using methyl orange T.S. as indicator. To about 1 Gm. of the Benzaldehyde, accurately weighed, add 25 mils of the phenylhydrazine solution just prepared and allow it to stand for thirty minutes Add a drop of methyl orange T.S., and acidify the mixture by adding a measured excess of half-normal hydrochloric acid V.S. Filter the mixture and wash the precipitate with small portions of distilled water until the washings cease to redden blue litmus paper. Then titrate the excess of hydrochloric acid in the filtrate with half-normal potassium hydroxide V.S. Subtract the number of mils of half-normal hydrochloric acid V.S. consumed from the number of mils of half-normal hydrochloric acid V.S. used in titrating the 25 mils of phenylhydrazine solution; the difference multiplied by 0.053, gives the weight of the Benzaldehyde present." *U. S.*

Uses.—Benzaldehyde is used as a flavoring agent, in place of the oil of bitter almond, from which it differs in containing no hydrocyanic acid; it is often called *artificial* or *synthetic oil of bitter almond.* (See *Oleum Amygdalæ Amaræ.*) It is not poisonous if pure.

Dose, half to one minim (0.03–0.06 mil).

BENZAMINÆ LACTAS. Br.

BENZAMINE LACTATE

(bĕn-zą-mī′næ lăc′tăs)

"Benzamine Lactate, $C_{15}H_{21}NO_2,C_3H_6O_3$, is the lactate of benzoyl-vinyl-diaceton-alkamine, from which it may be obtained by neutralising with lactic acid." *Br.*

Betaeucaine Lactate; Eucaine Lactate.

"A white crystalline powder. Taste slightly bitter followed by a sensation of numbness. Soluble in 5 parts of *water,* and in 8 parts of *alcohol* (90 per cent.). Its aqueous solution yields with an aqueous solution of *salicylic acid*

a white precipitate, and with *solution of ammonia* a white precipitate readily soluble in excess of the reagent. Treated with *nitric acid* and *alcoholic solution of potassium hydroxide* as described under 'Cocainæ Hydrochloridum' a characteristic odor is evolved, recalling peppermint. Does not darken in color when moistened with *alcohol* (90 per cent.) and triturated with *mercurous chloride* (distinction from cocaine and *a*-eucaine). An aqueous solution (1 in 100) gives no precipitate with *solution of potassium iodide* (distinction from *a*-eucaine). Dissolves in *sulphuric acid* and in *nitric acid* without coloration. No appreciable ash." *Br.*

Benzamine lactate was made official in the Br. Pharm. 1914; it is the same as *Beta-eucaine lactate,* a proprietary preparation made by E. Schering, of Berlin. (U. S. Patent No. 657,880, which expired in 1917.) It is used solely as a local anesthetic. It has the advantages over cocaine in being much less poisonous and of possessing no action on either the pupils or blood pressure when applied locally. (See *Betaeucainæ Hydrochloridum.*)

BENZENUM. Br.

BENZENE

(bĕn-zē'nŭm)

"Benzene, C_6H_6, is a liquid hydrocarbon obtained from light coal-tar oil." *Br.*

Benzene, Benzole, Phenyl Hydride, Benzen; Benzenum Medicinale, *N.N.R.* Benzine, *Fr.*; Phenylwasserstoff, Steinkohlenbenzin, *G.*; Benzolo, *It.*

It is to be regretted that the British Pharmacopœia 1914 has abandoned the name "Benzol" and adopted the name "Benzene" for this product, and that the French Codex uses the word "Benzine" for crystallizable benzene. Benzol (Benzene, Br. Pharm. and U. S. P. reagent) must not be confounded with the commercial article *benzin,* which is a mixture of various hydrocarbons of light specific gravity, obtained in the distillation of petroleum. (See *Benzinum Purificatum.*) Originally the two names benzol and benzin were applied to the same substance, but after the discovery of petroleum it was found that the liquid obtained by distillation from coal tar was quite different from that obtained from petroleum. In the United States it has become the custom to call the liquid obtained by the fractional distillation of petroleum, having the specific gravity 0.638 to 0.660 at 25° C. (77° F.), *benzin.* It is unfortunate that in Europe, and on the Continent especially, the term benzin was used for both liquids. The two substances are essentially different, although resembling each other somewhat in their solvent powers. Benzol is a definite hydrocarbon of fixed constitution, petroleum benzin a complex body of varying constitution. Benzol can be frozen; petroleum benzin has never yet been congealed. Petroleum benzin boils at from 45° to 60° C. (113°–140° F.), while benzol boils at 79° to 80° C. (174.2°–176° F.). Benzol can be converted into nitrobenzol, and by further treatment into aniline colors; petroleum benzin cannot. When petroleum benzin is shaken in the cold with one-third of its volume of fused crystals of absolute phenol, the latter remains undissolved, while benzol is miscible with absolute phenol in all proportions. (Allen.) According to Pusch, benzol can be distinguished from petroleum benzin by the fact that benzol forms a violet-red and petroleum benzin a raspberry-colored solution with iodine. The term *benzene* is gradually becoming limited to the pure hydrocarbon, C_6H_6, while *benzol* is applied to the mixture of benzene with its homologues *toluene, paraxylene, metaxylene, mesitylene, pseudocumene,* etc. This view was probably in the minds of the revisers of the British Pharmacopœia (1914) and caused them to abandon the name "Benzol" and adopt "Benzene," thus signifying the purified product.

Benzol was discovered by Faraday in the condensed liquid from oil gas, and was next obtained by Mitscherlich by distilling benzoic acid with lime. It was afterwards discovered by Hofmann as a constituent of coal gas tar. This tar, when distilled, furnishes *coal naphtha* or light oil of tar, a complex substance, containing a number of hydrocarbons, among which is benzol. Upon distilling this naphtha from a metallic still, surmounted by an open vessel filled with water, and containing a worm terminating in a refrigerated receiver, the benzol will pass over and condense in the receiver; while the other substances associated with it, having higher boiling points, will condense in the worm and fall back into the still. The benzol is then purified by distillation at a heat between 80° C. and 90° C. (176°–194° F.), and by subjecting the product to a new distillation from one-fourth of its volume of sulphuric acid. E. Kopp purifies benzol by taking advantage of its high congealing point. He exposes the impure mixture containing it to a degree of cold sufficient to solidify it (–15° C. or 5° F.), presses the congealed mass to separate the liquid hydrocarbons, allows it to become fluid, then again freezes and presses it, and thus obtains it almost entirely pure, when it is known as "crystallizable benzene." He obtains the impure mixture containing the benzol by decomposing the heavier tar oils by a high degree of heat.

Calvert, of Manchester, purifies coal naphtha, so as to render it a sufficiently pure benzol to be usefully applied to the purpose of removing fatty and oil matters from animal and vegetable substances, by subjecting it to the action of sulphuric acid, added in small quantities, so long as coloration is produced, then washing it with pure water, and afterwards subjecting it to distillation in an ordinary still. The sulphuric acid combines with the less volatile hydrocarbons present, which interfere with the solvent power of the benzol.

Prolonged treatment with sulphuric acid is also necessary to free the benzol from *thiophene,*

C_4H_4S, an impurity which to the extent of about 0.6 per cent. is always present in commercial benzol. Its complete removal from the benzol is to be tested for by the *indophenin reaction* (blue coloration in presence of concentrated sulphuric acid and a small quantity of isatine).

In consequence of the great volatility and extreme inflammability of benzol and its attendant hydrocarbons, much care is necessary both in their preparation and in their subsequent use in order to avoid any possible exposure to flame. Very serious accidents have taken place from want of the proper caution in this respect.

Properties.—The British Pharmacopœia describes benzene as "a colorless, mobile, inflammable liquid. Insoluble in *water,* but miscible with *absolute alcohol* or *ether.* Specific gravity 0.880 to 0.887. 95 per cent. distils between 79° and 82° C. (174.2° and 179.6° F.). It solidifies when cooled to 0° C. (32° F.), and if the temperature be allowed to rise, does not entirely re-melt below 4° C. (39.2° F.)." *Br.*

"Benzene, C_6H_6, is a colorless, transparent, inflammable liquid of a peculiar, aromatic odor; specific gravity about 0.876 at 25° C. (77° F.); congealing at about 5.2° C. (41.36° F.); boiling between 79° and 80.4° C. It is insoluble in water, but soluble in 4 parts of alcohol and also in ether. When equal volumes of benzene and concentrated sulphuric acid are shaken together, the latter is not colored. Shake 2 mils of benzene with 0.5 mil of sulphuric acid and 1 drop of fuming nitric acid; no green or blue tint is produced (*thiophene*)." *U. S.* (*Reagents.*)

Its powers as a solvent are very extensive. Among the substances soluble in it are sulphur, phosphorus, and iodine, and most resins and fats. It dissolves quinine, but not cinchonine, with which it forms a bulky gelatinous mass. Morphine and strychnine are sparingly soluble. Its solvent power over some of the organic alkaloids led John Williams, of London, to employ it in extracting them. Dragendorff has corroborated and extended this use of benzol for obtaining the alkaloids, whose salts are, however, not usually soluble in the menstruum. Benzol is also a solvent of many of the resins, of mastic, camphor, wax, fatty and oily substances, essential oils, caoutchouc, and gutta-percha. It often becomes a matter of great importance commercially to test the purity of commercial benzol, and a very thorough method of assay based on fractional distillation is proposed by A. H. Allen, in his *Commercial Organic Analysis,* 1882. The following method, originating with Schorlemmer, is based on the conversion of this hydrocarbon into aniline, and of that into one of the characteristic colors derived from it. That part of the mixture which volatilizes at 150° C. (302° F.) is operated on. This is treated with fuming nitric acid, which, if benzol be present, gives rise to a nitrobenzol with its bitter-almond odor. The nitrobenzol is then converted by the action of granulated tin and hydrochloric acid into aniline, which is isolated by distilling the product with potassium hydroxide. The aniline floats on the top of the liquid that passes. A little of this gives with sodium hypochlorite a fine purple color; and a drop of it, if heated with a little corrosive sublimate, will yield the beautiful color of rosaniline. (*J. P. C.,* 4e sér., ii, 177.) According to Balls, magnesium ribbon, with the addition of a few drops of solution of platinic chloride, rapidly and completely reduces nitrobenzene in alcoholic solution to aniline, giving a solution which can be at once decanted and tested with bleaching powder. (Allen.)

Uses.—Benzol has been shown by Chassevant (*Archiv. de Pharmacodyn,* 1896, ii) to be depressant to the central nervous system and to the vasomotor system. It was experimented with as an anesthetic by Simpson, but was found scarcely capable of producing unconsciousness. In 1897 Guyot reported that habitual exposure to the fumes of benzol during its manufacture produced a chronic poisoning characterized by uncertainty of gait, mental disturbance, loss of sexual power, and epileptiform convulsions. Sanlessen found that, in lower animals, after death from benzol poison, there were hemorrhages into the lungs and the stomach, with various fatty degeneration, and a plastic bone-marrow. Selling (*J. H. H. B.,* 1910, xxi) reported fatal cases of human poison, showing the same lesions. His studies of these cases led Von Koranyi (*B. K. W.,* 1912, xlix) to the use of benzol in the treatment of *leukemia.* Since this a large number of authors has reported favorable results in this intractable disease. Barker has also reported favorable effects (*J. H. H. B.,* 1913) in *Hodgkin's disease* and McLester (*J. A. M. A.,* 1914, lxii) in *polycythemia.* It is best administered by mixing with equal parts of olive oil and emulsifying with mucilage of acacia.

The remedy is evidently not harmless. Neumann (*Ther. Geg.,* 1913, p. 56) reports a case of leukemia in which benzol was given for thirty-six days with great reduction in the number of leukocytes, but after the drug was stopped the action continued, the leukocytes fell to 200, the patient developed fever, weakness, diarrhea and epistaxis, and died thirty-nine days after the last dose. Pappenheim (*W. K. W.,* 1913, p. 48) from experiments upon the lower animals finds that benzol is injurious to both the liver and kidney. Koranyi, however (*W. K. W.,* 1913), insists that in quantities of not over 3 Gm. per day benzol is perfectly safe, but generally smaller quantities are sufficient for therapeutic purposes. It should be noted that commercial benzol often contains toxic impurities, especially nitrobenzol and aniline. A crystallizable benzol is described in the *N. N. R.,* under the name of *Benzenum medicinale;* it is liquid at ordinary temperatures.

The beginning *dose* is generally fifteen minims (0.9 mil) cautiously increased to forty-five minims (2.8 mils).

BENZINUM PURIFICATUM. U. S

PURIFIED PETROLEUM BENZIN Benzin. Purif. [Petroleum Ether]

(bĕn-zī'nŭm pū-rĭ-fĭ-cā'tŭm)

"A purified distillate from American petroleum consisting of hydrocarbons, chiefly of the marsh-gas series. Preserve it carefully in well-closed containers, in a cool place, remote from fire." *U. S.*

Benzin, Petroleum Ether; Æther Petrolei; Esprit (naphte, Ether) de Pétrole, *Fr.*; Benzinum Petrolei, *P. G.*; Petroleumbenzin, Petroläther, *G.*; Benzina del petrolio, *It.*

Purified petroleum benzin was introduced into the U. S. Pharmacopœia VIII and IX, and is used mainly as a solvent. The process of purification was not introduced into the U. S. IX, as the liquid is very inflammable and not suited for purification on the small scale by the pharmacist. The U. S. VIII process was as follows:

* "Potassium Permanganate, *ten grammes* [or 154 grains]; Sodium Hydroxide, *two grammes* [or 31 grains]; Sulphuric Acid, *sixty mils* [or 2 fluidounces, 14 minims]; Petroleum Benzin, *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]; Water, *a sufficient quantity.*

"Add the Acid to *five hundred and fifty mils* [or 18 fluidounces, 287 minims] of Water, and when the mixture has become cold, pour it into a bottle having the capacity of about two liters. Add *eight grammes* [or 123½ grains] of Potassium Permanganate and agitate until it is dissolved, then add the Petroleum Benzin, in four portions, shaking the liquid after each addition. Allow the liquids to remain in contact for twenty-four hours, shaking the bottle at frequent intervals; then decant the Petroleum Benzin into another bottle of the same capacity, and having dissolved *two grammes* [or 31 grains] of Potassium Permanganate in *two hundred and forty mils* [or 8 fluidounces, 55 minims] of Water, in which the Sodium Hydroxide has previously been dissolved, mix the liquids and agitate the mixture frequently during several hours, then decant, repeat the washing with Water, and again decant the Purified Petroleum Benzin." *U. S. VIII.*

"Purified Petroleum Benzin is a clear, colorless, non-fluorescent, volatile liquid, of an ethereal or faint, petroleum-like odor, and having a neutral reaction. It is highly inflammable and its vapor, when mixed with air and ignited, explodes violently. It is practically insoluble in water; freely soluble in alcohol, and miscible with ether, chloroform, benzene, volatile oils, and fixed oils, with the exception of castor oil. Specific gravity: 0.638 to 0.660 at 25° C. (77° F.). It distils completely between 40° and 80° C. (104° and 176° F.). Evaporate 10 mils of Purified Petroleum Benzin from a piece of clean filter paper; no greasy stain remains, and the odor is not disagreeable nor notably sulphuretted. Not more than 0.0015 Gm. of residue remains on evaporating 50 mils of Purified Petroleum Benzin at a temperature not exceeding 40° C. (104° F.). Boil 10 mils of Purified Petroleum Benzin for a few minutes with one-fourth its volume of an alcoholic solution of ammonia (1 in 10) and a few drops of silver nitrate T.S.; the liquid does not turn brown (*pyrogenous products and sulphur compounds*). Add 5 drops of Purified Petroleum Benzin to a mixture of 40 drops of sulphuric acid and 10 drops of nitric acid in a test tube, warm the liquid for about ten minutes, set it aside for half an hour, and dilute it in a shallow dish with water; no odor of nitrobenzene is evolved (*benzene*)." *U. S.*

This useful product of petroleum was first introduced into the U. S. Pharmacopœia 1880; it is obtained in the process of purifying petroleum by fractional distillation. (See *Petroleum*, Part II.) Petroleum benzin must be carefully distinguished from benzene (official in the British Pharmacopœia under the name of *Benzenum* and a reagent in the U. S. P.), a product derived from coal tar. Although the U. S. Pharm. gives a test to distinguish an admixture with benzene, this adulteration of petroleum benzin is hardly likely to take place here in the near future, because of the great difference in price. The principal consumption of petroleum benzin at present is in the arts as a solvent, especially as a substitute for oil of turpentine, which it resembles very much in its solvent properties. In pharmacy it has been used to deprive powdered drugs of their fixed oil by percolation; to obtain volatile oils by percolating the oily drug with the benzin and subsequently evaporating the mixture spontaneously; as a substitute for ether in making oleoresins; and for many other purposes to which it is adapted on account of its powers as a solvent. Petroleum benzin is a good solvent for fats, resins, rubber, and some of the alkaloids.

Dragendorf recommends the rectification of benzin by fractional distillation from lard, collecting the portion which distils below 45° C. (113° F.). We have found petrolatum to be efficient in retaining the impurities in the still.

Uses.—Not only benzin, but various other commercial mixtures derived from petroleum, such as gasoline and naphtha, have been used by depraved humanity for the purpose of producing intoxication. (See *Petroleum*, Part II.)

Jaffé (*M. M. W.*, 1914, lxi) concludes from an experimental investigation, as well as from the study of cases of human poisoning, that the most marked effect of benzin is extensive hemorrhage in the lungs, which he believes is due to an effort at elimination. It has been largely used as a solvent for iodine in the disinfection of the skin, but if evaporation is prevented it has a marked irritant effect and even a caustic action, indeed Senrwald (*D. M. W.*, 1913, p. 318) has recommended it clinically as a counter-irritant.

Purified benzin is official in the Pharmacopœia purely for pharmaceutical properties. It is not used in medicine. It was at one time suggested

by Schleich as a diluent for chloroform in producing surgical anesthesia, but H. C. Wood, Jr. (*P. M. J.*, April 15, 1899) showed that it was a direct depressant to both the heart and vasomotor system far beyond its power as a narcotic, and the method practically yielded such unfavorable results that it was soon abandoned.

A number of cases of benzin poisoning, both acute and chronic, have been reported. In the acute cases the most constant symptom has been disturbance of intellection or unconsciousness, with slowing of the respirations. The pulse is generally somewhat slower than normal, pupils dilated, the surface cold, and frequently there has been cyanosis and occasionally convulsions. In most of the cases whether the poison has been swallowed or inhaled, the benzin odor can be perceived upon the breath. (For report of cases see Wichern, *M. M. W.*, lvi, p. 11.) In the chronic cases the symptoms have been headache, giddiness, numbness and paresthesia of the extremities, vomiting, loss of memory, general weakness, especially in the legs, tenderness and pain along the nerve trunks, and progressive anemia. In acute cases it causes a peculiar intoxication, having the appearance, at the onset, of an attack of hysteria, with laughing, tremors, mydriasis, nystagmus, loss of power in the legs and bladder, failing heart action, delirium, coma and death. In nine fatal cases of chronic poisoning by petroleum benzin, Santesson found a widespread fatty degeneration affecting especially the liver, kidneys and cardiac muscles.

Off. Prep.—Used as a solvent for the fatty substances in various drugs.

BENZOINUM. U. S., Br.

BENZOIN Benzoin. [Gum Benjamin]

(bĕn-zo-ĭ'nŭm)

"A balsamic resin obtained from *Styrax Benzoin* Dryander and some other species of *Styrax* (Fam. *Styracaceæ*) growing in the East Indies and known in commerce as Sumatra Benzoin and Siam Benzoin." *U. S.* "Benzoin is a resinous solidified balsam obtained from the incised stem of Styrax Benzoin, *Dryand.* Known in commerce as Sumatra benzoin." *Br.*

Resina Benzoe, Asa Dulcis; Gum Benjamin; Benjoin, *Fr.*; Benzoë, *P. G.*; Benzoëharz, *G.*; Benzoino, *It.*; Benjui, *Sp.*

It is generally believed that Siam Benzoin is obtained from *Styrax Benzoin* Dryander. It appears to closely resemble the tree growing in Sumatra, which yields a balsamic resin bearing this name. Tschirch considers that the trees yielding Siam and Sumatra Benzoin are physiological varieties of the same species. (Tschirch, "*Harze*," II. Aufl., p. 195.) Strueff presents a careful morphological paper on the trees of *Styrax Benzoin*, growing in Siam, Sumatra and Java, in *Arch. d. Pharm.*, 1911, p. 10.

Styrax Benzoin, or *Benjamin Tree*, is a tall tree of quick growth, sending off many strong round branches, covered with a whitish downy bark. Its leaves are alternate, entire, oblong, pointed, smooth above and downy beneath. The flowers are in compound, axillary clusters, nearly as long as the leaves, and usually hang, all on the same side, upon short slender pedicels. The tree is a native of Sumatra, Java, Borneo, and other islands in the vicinity. By wounding the bark near the origin of the lower branches, a juice exudes, which hardens upon exposure and forms the *Sumatra benzoin* of commerce. According to the researches of A. Tschirch (*Journ. Roy. Microscop. Soc.*, 1890), the exudation is purely the result of pathological processes, the plant containing no resin receptacles. The trees, which are either wild or cultivated, are deemed of a proper age to be wounded at six years, when the trunks are usually about seven or eight inches in diameter. The operation is performed annually, and the product on each occasion from one tree never exceeds three pounds. The juice which first flows is the purest, and affords the whitest and most fragrant benzoin.

The tree which yields the Siam benzoin is stated to grow in an extremely circumscribed locality, on the bank of the river Mekong, occurring on high ground in clusters of from fifty to sixty trees. According to E. M. Holmes, its leaves are thinner and less distinctly venated than are those of the true *Styrax Benzoin*. In July and August the Siam trees are notched, and from these notches three months later the hardened benzoin is picked out. According to later studies (*Kew Bulletin*, 1912, p. 391) the Siam benzoin is derived from a new species, *Styrax benzoides* Craib. This view is also held by Hartwich. The benzoin of farther India is probably derived from *Styrax tonkimensis*.

Siam benzoin is usually imported in cubical blocks, which take their form from the wooden boxes in which the soft resin has been packed. It is brittle, with a peculiar, vanilla-like fragrance, but bitter taste. It may be a compact mass, containing more or less numerous opaque white tears embedded in a rich amber-colored translucent resin, mixed to a greater or less extent with bits of bark, wood, etc. In some specimens these tears are exceedingly small, in others almost wanting. The finest variety is composed almost entirely of these tears, loosely agglutinated together. *Sumatra benzoin* is sent into commerce chiefly from Acheen in Sumatra. It differs from the Siam varieties in having a much grayer color; the resin is grayish-brown, the tears are usually fewer than in the finer variety, and the bits of wood, etc., more abundant. The odor differs from, and is less agreeable than, that of Siam benzoin. *Palembang benzoin* resembles Sumatra benzoin, but is somewhat more transparent, and is stated to yield a larger percentage of benzoic acid. It is also asserted that it can be distinguished by its tincture, when dropped into water, not producing milkiness, but a flocculent deposit. *Penang benzoin* also resembles Sumatra benzoin, but has an odor which is more like that of storax, and it is probably yielded by the *Styrax Benzoin;* possibly it is the product of one of the Sumatran

species, *S. subdenticulata* Mig. For an account of the cultivation and collection of benzoin in Sumatra, by L. M. Vonck, see *C. D.*, 1891, 486–488; also *D. C.*, 1891, 258. Lüdy made an investigation of the bark and wood of a benzoin tree which was brought from Java by Tschirch. He reached the conclusion that benzoin balsam was produced from the tannin of the bark. (*A. Pharm.*, 1893, 43, 95.) A variety of benzoin known as *Estoraque* or *Benjui*, is produced in Bolivia from the *Styrax Pearcei* Perk. var. *bolivianus*. This has been shown by Wichmann (*S. W. P.*, 1912, p. 237) to be of similar composition to the Asiatic resin. According to this author resins are also collected from a number of other species of styrax in South America.

Properties.—Benzoin has a fragrant odor, with very little taste, but when chewed for some time leaves a sense of irritation in the mouth and fauces. It breaks with a resinous fracture, and presents a mottled surface of white and brown or reddish-brown; the white spots being smooth and shining, while the remainder, though sometimes shining and even translucent, is usually more or less rough and porous, and often exhibits impurities. In the inferior kinds the white spots are very few, or entirely wanting. Benzoin is easily pulverized, and, in the process of being powdered, is apt to excite sneezing. Its sp. gr. is from 1.063 to 1.092. The U. S. Pharmacopœia recognizes both Sumatra and Siam benzoins. The official descriptions of these follow:

"**Sumatra Benzoin.**—In blocks or lumps of varying size, made up of tears, compacted together with a reddish-brown, reddish-gray, or grayish-brown resinous mass; tears externally yellowish or rusty-brown, milky-white on fresh fracture; hard and brittle at ordinary temperatures, but softened by heat and becoming gritty on chewing; odor aromatic and upon digesting with boiling water suggesting the odor of cinnamic acid or storax; taste aromatic and slightly acrid. Heat a few fragments of Sumatra Benzoin in a test tube; a sublimate is formed consisting of plates and small, rod-like crystals that strongly polarize light. Add carefully an ethereal solution of Sumatra Benzoin to a small quantity of sulphuric acid contained in a porcelain dish; the solution is colored a brownish-red. Not less than 75 per cent. of Sumatra Benzoin dissolves in alcohol; the alcoholic solution, upon the addition of water, becomes milky and is acid to litmus. Sumatra Benzoin does not yield more than 2.5 per cent. of ash.

"**Siam Benzoin.**—In pebble-like tears of variable size, compressed, yellowish-brown to rusty-brown externally, milky-white on fracture, separate or very slightly agglutinated; hard and brittle at ordinary temperatures, but softened by heat and becoming plastic on chewing; odor agreeable, balsamic, vanilla-like; taste slightly acrid. Heat a few fragments of Siam Benzoin in a test tube; a sublimate is formed directly above the melted mass consisting of numerous long, rod-shaped crystals, which do not strongly polarize light. Add carefully an ethereal solution of Siam Benzoin to a small quantity of sulphuric acid contained in a porcelain dish; the solution is colored purplish-red. Not less than 90 per cent. of Siam Benzoin dissolves in alcohol; the alcoholic solution upon the addition of water becomes milky and is acid to litmus. Siam Benzoin does not yield more than 2 per cent. of ash. *The tests which follow apply to Sumatra and Siam Benzoin:* Heat gently 1 to 2 Gm. of Benzoin with 15 mils of purified petroleum benzin, and, after cooling, transfer the supernatant liquid to a separatory funnel, wash once with 10 mils of saturated sodium bicarbonate solution and then with water until free from bicarbonate; on the addition of 20 mils of a copper acetate solution (1 in 200) and vigorously shaking the mixture, no green color is noticeable in the petroleum benzin layer (*rosin and foreign resins*). Treat about 1 Gm. of powdered Benzoin with 15 mils of warm carbon disulphide, filter the solution, wash the filter with an additional 5 mils of carbon disulphide and allow the mixed liquids to evaporate spontaneously; not less than 12.5 per cent. of residue remains, which corresponds to the tests for identity under *Acidum Benzoicum.*" *U. S.*

"Hard brittle masses consisting of numerous whitish tears embedded in a greyish-brown translucent matrix. Odor agreeable, similar to that of storax; taste slightly acrid. When cautiously heated in a dry test-tube it melts and evolves whitish fumes with an irritating odor. When 0.5 gramme is slowly heated to about 40° C. (104° F.) with 10 millilitres of *solution of potassium permanganate* an odor of benzaldehyde is evolved (distinction from Siam benzoin). Not more than 15 per cent. insoluble in *alcohol* (90 per cent.). Ash not more than 5 per cent.

When heated it melts, and emits thick, white, pungent fumes, which excite coughing when inhaled, and consist chiefly of benzoic acid. It is wholly soluble, with the exception of impurities, in alcohol, and is precipitated by water from the solution, rendering the liquid milky. It yields to boiling water a notable proportion of benzoic acid. Lime water and the alkaline solutions partially dissolve it, forming benzoates, from which the acid may be precipitated by the addition of other acids. Its chief constituents are resin and benzoic acid, and it therefore belongs to the balsams. The white tears and the brownish connecting medium are said by Stolze to contain nearly the same proportion of acid, which, according to Bucholz, is 12.5 per cent., to Stolze, 19.8 per cent. In a more recent examination by Kopp, the white tears were found to contain from 8 to 10 per cent. of acid, and the brown 15 per cent. (*J. P. C.*, 3e sér., iv, 46.) The resin is of three kinds, one extracted with the benzoic acid by a boiling solution of potassium carbonate in excess, another dissolved by ether from the residue, and the third affected by neither of these solvents. Besides benzoic acid and resin, the balsam contains a little extractive

and traces of volatile oil. Benzoin retards the oxidation of fatty matters, and thus tends to prevent rancidity.

The percentage of soluble matter required to be present by the U. S. Pharm. in benzoin is very high, and if rigidly enforced by the customs would exclude Sumatra benzoin in all but its very finest varieties. Robt. C. Pursel and Willard Graham obtained from five commercial varieties of Sumatra benzoin, in the American market, an average of 86 per cent. of soluble matter. (*Proc. Pennsylvania Pharm. Assoc.*, 1902.) John Barclay, in England, found the average of ten samples to be 69.9 per cent. (*P. J.*, Jan., 1903.)

It appears from various researches that benzoin, besides its own characteristic acid, often contains also cinnamic acid, which is found more especially in the white tears. Indeed, Hermann Aschoff obtained from some benzoin of Sumatra a pure cinnamic acid, without any benzoic; and Kolbe and Lautermann, upon examining a specimen of the tears, discovered what they at first supposed to be a peculiar acid, but which on further investigation proved to be a mixture of cinnamic and benzoic acids. H. Beckurts and W. Brueche confirm the statement that Siam benzoin contains no cinnamic acid, which is usually present in Sumatra benzoin. They found the specific gravity from 1.120 to 1.171; ash from 0.05 to 2.38 per cent.; portion insoluble in alcohol from 2.1 to 9 per cent. On the other hand, Tschirch and Lüdy (*A. Pharm.*, 1893, 500) extracted benzoic acid from Siam benzoin by the wet process. They found Sumatra benzoin to contain esters which yielded by saponification 32.9 per cent. of cinnamic acid, the proportion of esters being *benzoresinol cinnamate*, 7.4 per cent., and *resinotannol cinnamate*, 92.6 per cent., at least 75 per cent. of Sumatra benzoin consisting of cinnamates yielding from 20 to 24 per cent. of cinnamic acid. (See also *A. Pharm.*, 1893, 461; *A. J. P.*, 1893, 223; and *J. P. C.*, 1894, 172.) In a later research they found that Siam benzoin did not contain cinnamic acid, either free or in combination as ester. Besides some free benzoic acid and vanillin it contains only esters of benzoic acid. These, on saponification, yielded 38.2 per cent. of *benzoic acid*, 56.7 per cent. of *isoresinotannol*, and 5.1 per cent. of *benzoresinol*. (Tschirch, *Harze und Harzbehälter*, 1900, p. 155.) Benzoin may be rapidly tested for cinnamic acid by heating a small quantity with a little soda and water and warming the filtrate with potassium permanganate, when the odor of bitter almond will be developed. (*A. Pharm.*, 1892, ccxxx.)

Aschoff recommends the following method of detecting cinnamic acid. Boil the benzoin with milk of lime, filter, decompose with hydrochloric acid, and add either potassium dichromate with sulphuric acid, or potassium permanganate, when, if cinnamic acid be present, the odor of oil of bitter almond will be perceived.

According to T. T. Cocking and J. D. Kettle (*Tr. Br. Ph. Conf.*, 1914, 357), the important analytical data to be considered in valuing benzoin are (1) the percentage soluble in 90 per cent. alcohol, and (2) the quantity of aromatic acids present, both free and combined. Methods of obtaining these factors are given in detail and also tables giving the results of such examinations of a number of commercial samples. Reinitzer (*A. Pharm.*, cclii) has made an exhaustive study of *Siam benzoin*, in which he contradicts some of the previously published statements of Tschirch and Ludy. He claims that the resinotannol of these authors does not exist in the drug, but is an oxidation product created during the analysis.

Rump (1878) treated Siam benzoin with caustic lime, precipitated the benzoic acid with hydrochloric acid, and agitated the liquid with ether. The latter on evaporating afforded a mixture of benzoic acid and *vanillin*, $C_8H_8O_3$. Subjected to dry distillation, benzoin affords as the chief product benzoic acid, together with empyreumatic products, among which Berthelot has proved the presence (in Siam benzoin) of *styrol*, C_8H_8. The latter was also obtained in 1874 by Theegarten from Sumatra benzoin by distilling it with water. (*Ber. d. Chem. Ges.*, 1874, p. 727.)

Sumatra benzoin is sometimes heavily adulterated with stony debris, sand and bark. Schneider reports finding as much as 75 per cent. of bark in a commercial article.

Uses.—Benzoin is stimulant and expectorant, and was formerly employed in pectoral affections, but, except as an ingredient of the compound tincture of benzoin, it has fallen into disuse. Trousseau and Pidoux recommend strongly its inhalation in *chronic laryngitis*. Either the air of the chamber may be impregnated with its vapor by placing a small portion upon some live coals, or the patient may inhale the vapor of boiling water to which the balsam has been added. It is occasionally employed in pharmacy for the preparation of benzoic acid (see *Acidum Benzoicum*); the milky liquor resulting from the addition of water to its alcoholic solution is sometimes used as a cosmetic, under the impression that it renders the skin soft. A tincture has been strongly recommended in *anal fissure*. In the East Indies, the balsam is burnt by the Hindus as a perfume in their temples of worship.

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Adeps Benzoinatus, *U. S.* (*Br.*); Tinctura Benzoini, *U. S.*; Tinctura Benzoini Composita, *U. S., Br.*; Sevum Benzoatum, *Br.* (*N. F.*); Unguentum Picis Compositum (from Tincture), *N. F.*

BENZOSULPHINIDUM. U. S. (Br.)

BENZOSULPHINIDE SACCHARIN
Benzosulphinid. [Saccharin Glusidum]

(bĕn-zō-sŭl-phĭ-nĭ'dŭm)

"The anhydride [$C_7H_5O_3NS$ or $C_6H_4SO_2.CONH$ = 183.12] of orthosulphamide-benzoic acid." *U. S.* "Gluside, or benzoic sulphinide,

$C_7H_5NSO_3$, the anhydride of orthosulphamidobenzoic acid, may be prepared from toluene." *Br.*

Glusidum, *Br.;* Gluside, Saccharin, Neo-Saccharin; Glucusimide; Benzoyl-Sulphonicimide; Anhydro-orthosulphamidebenzoic Acid; Glukusin; Acide Anhydroorthosulfamidebenzoique, *Fr. Cod.;* Sulfinide-benzoique, Sucre de Houille, *Fr.;* Benzoësauresulfimid, Sycose, Saccharol, Toluolsüss, Zuckerin, *G.;* Sacarina, *Sp.*

Preparation.—This artificial sweetening substance, which is known commonly as "saccharin," is made from toluene by first forming the ortho-sulphonic acid $C_6H_4\begin{cases}SO_3H\\CH_3\end{cases}$; from this the sulphamide $C_6H_4\begin{cases}SO_2NH_2\\CH_3\end{cases}$; from this, by oxidation, the sulphamide-benzoic acid $C_6H_4\begin{cases}SO_2NH_2\\COOH\end{cases}$, of which the anhydride is the official compound. When dissolved in alkaline hydroxide solutions the salt of the sulphamide-benzoic acid is formed as $C_6H_4\begin{cases}SO_2NH_2\\COONa\end{cases}$. (See *Sodii Benzosulphinidum.*)

Properties.—A white powder, melting at 200° C. (392° F.) with partial decomposition, evolving the odor of bitter almonds. It is soluble in water, from which it can be crystallized; also in alcohol, ether, glycerin, and glucose. Its taste in diluted solutions is intensely sweet, so that 1 part of saccharin will sweeten quite strongly 10,000 parts of water. Saccharin may be detected in sugar solutions by extracting with ether, evaporating and fusing the residue, which, if saccharin, will melt at about 220° C. (428° F.), and fused with potassium nitrate and sodium carbonate will show sulphuric acid. The weight of $BaSO_4$ obtained in this way from 100 Gm. of sugar multiplied by 0.785 will give the weight of saccharin extracted.

The aqueous solution of saccharin has a distinctly acid reaction and forms salts. Its most remarkable property is its sweet taste, which is said to be three hundred times more intense than that of sugar. The commercial product, according to Pope, frequently contains para-sulphamide-benzoic acid, from which impurity it can be freed by recrystallization, acetone being used as the solvent. Hefelman has furnished a process for assaying saccharin. (See *Proc. A. Ph. A.*, 1895, 701.) The difference in melting points of pure saccharin and para-sulphamide-benzoic acid is also used for distinguishing them; the former melts at 220° C. (428° F.) and the latter at 286.5° C. (547.7° F.). (*Ph. Cb.*, 1896, 279.)

Saccharin is officially described "as white crystals or as a white, crystalline powder; odorless, or having a faint, aromatic odor; its solutions have an intensely sweet taste. One Gm. of Benzosulphinide dissolves in 290 mils of water and in 31 mils of alcohol at 25° C. (77° F.); also in about 25 mils of boiling water; slightly soluble in chloroform or ether. It is easily dissolved by ammonia water, by alkali hydroxide solutions, also by a solution of sodium bicarbonate, with the evolution of carbon dioxide. A saturated aqueous solution of Benzosulphinide is acid to litmus. It melts between 219° and 222° C. (426.2° and 431.6° F.). When Benzosulphinide is fused at a low temperature with about 5 times its weight of sodium hydroxide, ammonia vapors are evolved; continue the heating until the evolution of ammonia has ceased, treat the residue with 10 mils of distilled water, neutralize the solution with diluted hydrochloric acid, and filter; the filtrate becomes violet on the addition of a drop of ferric chloride T.S. Incinerate about 1 Gm. of Benzosulphinide; not more than 0.5 per cent. of ash remains. A solution of 0.2 Gm. of Benzosulphinide in 10 mils of sulphuric acid kept at a temperature of from 48° to 50° C. (118.4°–122° F.), on a water bath, develops not more than a brown color within ten minutes (*carbonizable impurities*). A solution of about 0.2 Gm. of Benzosulphinide in 5 mils of potassium hydroxide T.S. remains clear, and, when mixed with 5 mils of alkaline cupric tartrate V.S., does not deposit cuprous oxide on heating (*glucose, milk-sugar*). Add ferric chloride T.S., drop by drop, to 10 mils of a hot, saturated aqueous solution of Benzosulphinide; no precipitate nor violet color appears (*benzoic or salicylic acid*). An aqueous solution of Benzosulphinide (1 in 10,000) has a distinctly sweet taste, comparable with that of an aqueous solution of sugar (1 in 20). No odor of ammonia is noticeable on warming about 0.5 Gm. of Benzosulphinide with about 1 Gm. of magnesia and 10 mils of distilled water (*ammonium compounds*)." *U. S.*

"A white crystalline powder. Taste in dilute solution, intensely sweet. Soluble in 400 parts of *water,* and in 38 parts of *alcohol* (90 per cent.); soluble also in solutions of alkalies and of alkaline carbonates, the neutral sodium salt being known as 'soluble gluside.' Completely soluble in 12 parts of *acetone.* 1 gramme heated for four hours on a water-bath with 10 millilitres of a mixture of 4 volumes of *sulphuric acid* and 3 volumes of *water* completely dissolves, and when the solution is diluted with an equal volume of *water* and allowed to stand for twenty-four hours no crystals separate. Gently warmed for a short time with *sulphuric acid* no blackening occurs. Ash not more than 0.5 per cent." *Br.*

Saccharin may be readily estimated in food products, etc., with no danger of emulsification, by the following method: 100 mils of the liquid under examination are added to 10 to 15 mils of a 10 per cent. solution of tannic acid, and then lead subacetate solution is added. Filter and acidify an aliquot portion of the filtrate with phosphoric acid and extract by shaking out with a mixture of ether and petroleum ether. Upon evaporating the ethereal mixture the saccharin is left in a pure state.

Uses.—Taken internally saccharin is rapidly absorbed and eliminated unchanged through the kidneys. It is almost free from general physiological activities. Mosso and Aducco have given

seventy-five grains to a man without sensible effect, and 600 grains to a dog within ten days without any change in the weight, general health or metabolism as indicated by urinalysis. On the other hand it has a slight local irritant action and according to the referee board of the U. S. Bureau of Chemistry, doses of more than 0.3 Gm. per day are liable, if used over periods of time, to impair digestion. The statement sometimes made that it is irritant to the kidneys seems to lack positive confirmation. Its use in medicine is purely as a sweetening agent in those diseases such as *diabetes* and *obesity* where sugar is contraindicated. It has also been widely employed in preserves, canned foods, and beverages for the same purpose, but this latter act, according to the decision of the U. S. Department of Agriculture, constitutes adulteration of the food, as it allows the omission of cane sugar.

Dose, three to five grains (0.2–0.32 Gm.).

BERBERIS. Br.

BERBERIS

(bĕr'bę-rĭs)

"Berberis is the dried stem of Berberis aristata, *DC.*" *Br.* "The rhizome and roots of species of the section *Odostemon* Rafinesque of the genus *Berberis* Linné (Fam. *Berberidaceæ*), without the presence of more than 5 per cent. of the overground parts of the plant or other foreign matter. Berberis without the bark should be rejected." *N. F.*

Oregon grape root; Nepaul Barberry; Barberry; Epine-vinette, Vinettier, Ecorce de Racine de Berbérides, *Fr.;* Fauerach, Gemeiner Sauerdorn, Berberitze, Berberitzen-(Saurach-) Wurzelrinde, *G.;* Berbero, *It., Sp.*

The genus *Berberis* (Fam. *Berberidaceæ*) is a large one, comprising shrubs or trees which are widely distributed throughout temperate regions and in the mountains of the tropics. There are three well-defined medicinal groups: (1) The Rocky Mountain group, including *Berberis Aquifolium,* which yields the Oregon Grape Root. (2) The Asiatic group, which includes *B. aristata* DC., a shrub indigenous to India and Ceylon, and is recognized by the British Pharmacopœia. (3) The European group, which includes the common Barberry (*B. vulgaris* L.), which is naturalized in New England. According to Dragendorff (*Die Heilpflanzen*), about forty different species of berberis have been used in medicine.

Berberis aristata, which furnishes the Berberis of the British Pharmacopœia, is a shrub indigenous to the temperate Himalayas, extending from Bhután to Kanawar, the Nilgiri Hills, Ceylon. It is erect and branching, the leaves being evergreen, obovate or oblong entire, sometimes possessing spinose teeth. The flowers are yellow and occur in compound, often corymbose racemes. The stigmas are distinguished by being small and subglobose. The berries are few-seeded and taper into a short style. Several varieties of this species are recognized, viz., *floribunda* and *micrantha.* The type *B. aristata* closely resembles *B. asiatica* Roxb., *B. Lycium* Royle and *B. vulgaris* L., and consequently are mistaken throughout India. The same vernacular names are frequently applied to each of these plants and the same medicinal properties attributed to all.

The berberis of the British Pharmacopœia occurs "in undulating pieces from two and a half to five centimetres in diameter. Cork orange-brown, removed in places showing the subjacent darker brown cortex; marked with slightly wavy longitudinal striæ and occasional shallow transverse depressions. Transverse section shows a narrow brown cork; a broad, dark brown bast traversed by conspicuous yellow medullary rays; a bright yellow wood composed of numerous narrow vascular rays, containing many vessels, separated by narrow paler medullary rays. Slight odor; taste bitter." *Br.*

For a description of the bark of *B. aristata* DC., by Hartwick, see *Ph. Rev.,* 1896, 232.

"Cylindrical, more or less knotty, strongly branched, usually cut into pieces of varying length and up to 45 mm. in diameter; externally light yellowish-brown, longitudinally wrinkled and short scaly; fracture hard and tough; bark 1 mm. in thickness, easily separable into layers; wood yellow, the color more pronounced upon wetting, distinctly radiate, and showing rings of growth; pith of rhizome small, sometimes excentral. Slightly odorous; taste distinctive, very bitter; on chewing it tinges the saliva yellow. The powder is yellowish-brown; composed chiefly of fragments of wood fibers associated with a few tracheæ and medullary rays; wood fibers yellowish, scarcely giving any reaction with phloroglucinol T.S. and hydrochloric acid, and with large, simple, transverse pores; tracheæ chiefly with bordered pores, occasionally reticulate; medullary rays one to twelve cells wide, and in very long rows; starch grains simple or two- to three-compound, the individual grains being irregularly spherical, from 0.003 to 0.01 mm. in diameter, and occasionally larger. Berberis yields not more than 5 per cent. of ash." *N. F.*

The N. F. IV recognizes, under the title Berberis, "the rhizome and roots of species of the section *Odostemon* Rafinesque, of the genus Berberis." This section corresponds to the genus *Mahonia* of Nuttall, and includes *B. Aquifolium* and *B. Nervosa.*

Berberis Aquifolium Pursh., *Berberis,* U. S. VIII, *Oregon Grape Root, Rocky Mountain Grape, California Barberry, Holly-leaf Barberry, Trailing Mahonia.*

The *Oregon grape* is a tall shrub, about six to seven feet high, with evergreen, coriaceous, bright and shining leaves, and having numerous small, yellowish-green flowers in the early Spring, and later clusters of purple berries containing an acid pulp. It is a native in woods from Colorado to the Pacific Ocean, especially abundant in Oregon and Northern California. The root, which was formerly official, occurs in pieces about a foot long, one-fourth of an inch thick, of a brownish exterior, but yellowish

within, yielding a bright lemon-colored bitter powder. The rhizome was officially described as "in more or less knotty irregular pieces of varying length and from 3 to 20 Mm. in diameter; bark from ½ to 2 Mm. thick; wood yellowish, distinctly radiate with narrow medullary rays, hard and tough; rhizome with a small pith; odor distinct; taste strongly bitter. Pieces without the bark should be rejected." *U. S. VIII.*

Rusby believes that a large part of the berberis collected in Oregon is obtained from *B. Nervosa.* (*Ph. Era,* 1909, p. 633.)

Nepaul Barberry—*Berberis vulgaris* L. (*Barberry*). *B. vulgaris* is a native of Europe, but grows wild in waste ground in the eastern parts of New England, and is sometimes cultivated in gardens on account of its berries. It is a spreading shrub, from four to six feet or more in height, with thorny branches, a light gray bark and a fine yellow wood.

The *berries* of *B. vulgaris,* which grow in loose bunches, are oblong and of a red color, have a grateful, sour, astringent taste, and contain malic and citric acids. They are refrigerant, astringent, and antiscorbutic, and are used in Europe, in the form of drink, in *febrile diseases* and *diarrheas.* An agreeable syrup is prepared from the juice, and the berries are sometimes preserved for the table. The bark of the root of *B. vulgaris* L. was formerly included in the secondary list of the U. S. Pharmacopœia, under the name of *Berberis.* The *root* and *inner bark* have been used for dyeing yellow. The bark of the root is grayish on the outside, yellow within, very bitter, and stains the saliva when chewed. Brandes found in 100 parts of the root 6.63 of bitter, yellow extractive (impure berberine), 1.55 of brown coloring matter, 0.35 of gum, 0.20 of starch, 0.10 of cerin, 0.07 of stearin, 0.03 of chlorophyll, 0.55 of a subresin, 55.40 of lignin, and 35.00 of water.

Lycium, or λύκιον of the ancients, highly valued as a local application in affections of the eye and eyelids, and used for various other purposes, is supposed to be the medicine still used in India for the same affections, under the name of *rusot* or *ruswut.* According to Royle, extracts from various species of berberis enter into this substance, which, combined with opium and alum, was much used in *ophthalmia.* (*P. J.,* Dec., 1865.)

Algerita Root, which has been used by Mexicans and old settlers in Western Texas, is derived from *Berberis trifoliatus* Moricand [*Odostemon trifoliatus* (Moric.) Heller]. The shrub grows in Western Texas and New Mexico and extends into Mexico. The root contains, according to Hart (*A. J. P.,* 1916, p. 301) 1.3 per cent. of berberine and 0.1 per cent. of associated alkaloids. Hydrastine is absent. Infusions of algerita root are used for *eye sores,* while chewing the roots is considered reliable as a corrective for *sore mouths.* Injections of an infusion have been used for *gonorrhea.*

Hesse found in berberis root four alkaloids besides *berberine* (see *Hydrastis*), the mother liquor from berberine hydrochloride when precipitated with sodium hydroxide yielded to ether three alkaloids, a fourth, which is amorphous, remaining undissolved. One of the alkaloids in the ethereal solution crystallized from alcohol in small tabular crystals, and is named by the author *berbamine.* It has the composition $C_{18}H_{19}NO_3 + 2H_2O$. (*Ber. d. Chem. Ges.,* 19, 3190.) To a second alkaloid the name of *oxyacanthine* has been applied.

For additional information concerning the constituents of berberis berries and root, see *U. S. D.,* 19th ed., p. 1412.

B. aquifolium contains the alkaloids *berberine,* $C_{20}H_{17}NO_4$; *oxyacanthine,* $C_{18}H_{19}NO_3$; and *berbamine,* $C_{18}H_{19}NO_3$, together with phytosterin, gum, fat, resin and wax. Berberine and oxyacanthine were isolated by H. B. Parsons (*N. R.,* 1882, 83), the percentage of the former is said to be 2.35 and of the latter 2.82. Jungk and Stubbe investigated the alkaloids from berberis, and found that the three alkaloids in *B. aquifolium* are identical with those found in *B. vulgaris.* Rüdel examined and described these alkaloids. (*J. C. S.,* 1892, 641.) Gordin and Merrell (*Proc. A. Ph. A.,* 1901, 228) objected to the method of Gaze (*Chem. Ch.,* 1890, 590) for making berberine from acetone-berberine.

Uses.—The various species of *Berberis* appear to have similar medical properties. The alkaloid berberine is physiologically very feeble. (See *Hydrastis.*) Antiperiodic properties have been attributed to it, and T. Lascarato (*La Grèce médicale,* 1899, No. 2) affirms that it has a specific action upon the spleen which renders it very valuable in the treatment of malarial *splenic enlargement,* and that it is so powerful in producing contraction that when the spleen is softened large doses may produce splenic rupture, with *fatal hemorrhage.* The crude drug probably has no real medicinal effect, except that of a bitter tonic and mild laxative. It is by some believed to have an especial tendency towards the liver and hence is used in *jaundice* and *chronic hepatitis.* It is also stated to have alterative powers and has been employed in *syphilis* and *scrofula.*

Off. Prep.—Tinctura Berberidis, *Br.;* Fluidextractum Berberidis, *N. F.*

BETAEUCAINÆ HYDROCHLORIDUM

BETAEUCAINE HYDROCHLORIDE Betaeucain. Hydrochl. [Eucaine Chloride, Eucaine]

(bē-tạ-eū-cạ-I'næ hȳ-drọ-ȼhlō'rị-dŭm)

"A synthetic derivative of piperidine, containing, when dried to constant weight at 100° C. (212° F.), not less than 99 per cent. of the hydrochloride of 2, 6, 6-trimethyl-4 benzoyl-oxypiperidine [$C_{15}H_{21}O_2NHCl$ or $C_5H_7N(CH_3)_2O(C_6H_5CO)\,HCl = 283.65$]." *U. S.*

This derivative of piperidine was introduced by E. Schering under the name of Eucaine, German patent No. 97,672, U. S. patent No. 657,880 (the latter expired Sept. 11, 1900). It is made

by acting on diacetonamine with paraldehyde and metallic sodium. The product is treated with benzoyl chloride and the trimethyl-benzoxy-piperidine which is formed is neutralized with hydrochloric acid and the resulting crystals are purified. It is officially described as "a white, crystalline powder; odorless. It is permanent in the air. One Gm. of Betaeucaine Hydrochloride is soluble in 30 mils of water, 35 mils of alcohol and 6 mils of chloroform at 25° C. (77° F.); it is more soluble in boiling water and boiling alcohol. Its saturated aqueous solution is neutral to litmus. Silver nitrate T.S. produces in an aqueous solution of the salt (1 in 100) a white precipitate insoluble in nitric acid. About 0.1 Gm. of Betaeucaine Hydrochloride dissolved in 20 mils of distilled water yields with one drop of ammonia water a white precipitate, which dissolves on agitation. On now adding three more drops of ammonia water to this solution, a white precipitate is again produced, which is dissolved on the addition of an equal volume of distilled water. The further addition of ammonia water again produces a precipitate, which dissolves on adding 10 mils of distilled water, but this solution is not affected by the further addition of ammonia water. Separate portions of 10 mils each of a saturated aqueous solution of the salt yield a white, curdy precipitate on the addition of a few drops of mercuric chloride T.S., and a yellow, curdy precipitate on the addition of a few drops of a mixture of equal volumes of potassium chromate T.S. and diluted sulphuric acid. No color is produced when 0.1 Gm. of Betaeucaine Hydrochloride is dissolved in 1 mil of sulphuric acid (*readily carbonizable impurities*). Five mils of an aqueous solution of the salt (1 in 100) gives no permanent precipitate on the addition of 5 mils of mercuric chloride T.S. (*cocaine and alpha-eucaine*). No weighable ash remains on incinerating 0.5 Gm. of Betaeucaine Hydrochloride.

"**Assay.**—Dissolve about 0.5 Gm. of Betaeucaine Hydrochloride, previously dried to constant weight at 100° C. (212° F.) and accurately weighed, in 100 mils of alcohol, which must be previously neutralized with tenth-normal potassium hydroxide V.S., using phenolphthalein T.S. as indicator, and titrate this alcoholic solution with tenth-normal potassium hydroxide V.S. until the pink color is restored. It shows, in the dried salt, not less than 99 per cent. of $C_{15}H_{21}O_2NHCl$.

"Each mil of tenth-normal potassium hydroxide V.S. used corresponds to 0.028365 Gm. of $C_{15}H_{21}O_2NHCl$. Each gramme of Betaeucaine Hydrochloride, previously dried, corresponds to not less than 34.9 mils of tenth-normal potassium hydroxide V.S." *U. S.*

Uses.—Betaeucaine is used solely as a local anesthetic. It differs from cocaine in that it is not stimulant to the central nervous system, that it does not dilate the pupil nor contract the blood vessels. It is one of the least poisonous of all the cocaine substitutes, its toxicity being estimated at from one-fourth to one-sixth that of cocaine. While it is apparently slightly less powerful as a local anesthetic than cocaine, because of its greatly reduced poisonous action it is a far safer drug to use. Moreover, it is free from the danger of habit formation which is always such an imminent evil with cocaine; and, although at first included in the Harrison Anti-narcotic Law as a restricted drug, the Department has ruled that it is no longer subject to the provisions of the Act. As a local anesthetic it may be used in strengths of from 1 to 5 per cent. It is not used internally except for its anesthetic action upon the stomach in cases of *gastric ulcer*, or other painful conditions of the stomach. For this purpose from one-half to two grains (0.032–0.13 Gm.) may be given at a *dose*.

BETANAPHTHOL. U. S. (Br.)

BETANAPHTHOL Betanaph. [Naphtol, U. S. 1890, Naphthol]

(bē-ta-năph'thŏl)

"A monohydroxyphenol [$C_{10}H_7OH = 144.06$] of the naphthalene series. Preserve it in well-closed containers protected from light." *U. S.*

"Beta-naphthol, or beta-mono-hydroxy-naphthalene, $C_{10}H_7OH$, may be obtained from naphthalene-sulphonic acid." *Br.*

Naphthol, *Br.*; β-Naphthol, Beta-mono-hydroxy-naphthalene, Iso-naphthol; Naphtol β, *Fr. Cod.*; Naphtholum, *P. G.*; Beta-Naphtholum, *G.*; Naftol β, *It.*

Preparation.—On digesting four parts of naphthalene with three parts of sulphuric acid at 80° C. (176° F.) there is formed α- and *β-naphthalene sulphonic acids*, $C_{10}H_7SO_3H$, which may be separated by means of the barium or lead salts. When heated with sulphuric acid, the α acid passes into the β variety; therefore the latter acid is exclusively produced at higher temperatures, 160° C. (320° F.). Both of the naphthalene sulphonic acids, when fused with alkaline hydroxides, yield the corresponding naphthols, which are designated as α- and *β-naphthol*, respectively. The second of these, betanaphthol, is the official naphthol, $C_{10}H_7OH$. It bears to naphthalene the same relation that phenol does to benzene. It is officially described as in "colorless or pale buff-colored, shining crystalline laminæ, or as a white or yellowish-white, crystalline powder, having a faint, phenol-like odor and a pungent taste. Permanent in the air. One Gm. of Betanaphthol dissolves in about 1000 mils of water, 0.8 mil of alcohol, 17 mils of chloroform and in 1.3 mils of ether at 25° C. (77° F.); also in 80 mils of boiling water; soluble in glycerin and olive oil and easily dissolved by alkali hydroxide solutions. A hot, saturated aqueous solution of Betanaphthol is neutral to litmus. Betanaphthol melts between 120° and 122° C. (248°–251.6° F.). Betanaphthol sublimes readily when heated and volatilizes with the vapors of alcohol or water. A cold, saturated aqueous solution of Betanaphthol, when mixed with ammonia water, exhibits a faint, bluish fluorescence. Add about 0.1 Gm. of Betanaphthol to 5 mils of an aqueous solution

of potassium hydroxide (1 in 4), then add 1 mil of chloroform, and gently warm the mixture; the aqueous layer acquires a blue color, changing afterwards to green and brown. Ferric chloride T.S. colors a cold, saturated aqueous solution of Betanaphthol greenish, and after some time causes the separation of whitish flakes, which turn brown upon the application of heat. Incinerate about 2 Gm. of Betanaphthol; not more than 0.05 per cent. of ash remains. Dissolve 0.5 Gm. of Betanaphthol in 25 mils of ammonia water; no residue remains (*naphthalene*), and the solution does not have a deeper color than pale yellow (*other organic impurities*). A cold, saturated aqueous solution of Betanaphthol, on the addition of a few drops of iodine T.S., followed by sodium hydroxide T.S. in excess, shows no violet color (*alphanaphthol*)." *U. S.*

The British Pharmacopœia describes it as "white, or nearly white, crystalline lamellæ, or in powder. Odor resembling that of phenol; taste sharp, pungent. Soluble in about 1000 parts of *water*, and in 75 parts of boiling *water*, the solutions being neutral to *litmus;* soluble in less than 2 parts of *alcohol* (90 per cent.); very soluble in *ether*, in *chloroform*, and in *solution of sodium hydroxide*. Melting point 122° C. (251.6° F.). A hot saturated aqueous solution develops a blue fluorescence on the addition of 1 drop of *solution of ammonia*. A cold saturated aqueous solution yields a white turbidity with *solution of chlorine*, which, on the addition of excess of *solution of ammonia*, gives place to a green or brown coloration. 0.1 gramme dissolved in 10 millilitres of boiling *water* yields with 10 drops of an aqueous solution (1 in 30) of *ferric chloride* a white precipitate becoming brown, but not violet (absence of alpha-naphthol). No appreciable ash." *Br.*

For Yvon's tests to distinguish between alpha- and betanaphthol, see *Proc. A. Ph. A.*, 1892, 955; see also *Chem. News*, 1892, 18. For Liebman's test for the presence of alphanaphthol, see *M. R.*, 1897, 281. See *Alphanaphthol* (Part II).

Uses.—Betanaphthol is locally irritant to mucous membranes, but on account of its insolubility cannot exercise a caustic effect in aqueous solutions. It is powerfully germicidal. Sternberg found that a solution of 1 part in 2000 would destroy the cholera spirillum after 15 minutes' exposure, and Schneider (*Z. Hyg.*, 1906, lii) finds that it is four times as active as lysol. As an antiseptic it is still more efficient, 1 part in 10,000, according to Maximovitch, being sufficient to prevent the development of all bacteria tested. Probably because of its slight solubility it appears to be very sparingly absorbed from the alimentary canal, but even after its direct introduction into the system is much less toxic than phenol or cresol. Freeman (*M. A.*, 1908, x, p. 11) has frequently given it in sixty-grain doses without any toxic manifestations. According to Vander Hoeve (*Arch. f. Ophthalm.*, 1913, lxxxv), however, when used in large quantities it may cause hyperemia and even degenerative changes in the retina.

Naphthol was originally introduced by Kaposi as a local remedy in skin diseases, and more recent studies have confirmed his conclusions as to its value in *favus, chronic eczema, scabies,* and other parasitic diseases of the skin. For this purpose it may be applied in the form of an ointment in strengths of from ½ to 5 per cent. Internally it is one of the most valuable intestinal antiseptics that we possess in the treatment of *enteritis, intestinal fermentation,* and similar conditions. It is also a useful vermifuge, especially in *uncinariasis*. According to Schultz (*J. A. M. A.*, 1911, lvii, p. 1103), when used as anthelmintic fifteen to thirty grains mixed with one-third its weight of milk sugar and enclosed in a capsule should be given at a dose and followed by an active cathartic. It has been used to some extent as a food preservative, but is prohibited specifically by many state food laws and it is rarely used at present.

Dose, as an intestinal antiseptic, two to five grains (0.13–0.32 Gm.).

Off. Prep.—Liquor Zinci et Alumini Compositus, *N. F.;* Liquor Zinci et Ferri Compositus, *N. F.;* Pasta Betanaphtholis, *N. F.;* Petroxolinum Betanaphtholis, *N. F.*

BETEL. Br.

BETEL

(bē'tĕl)

"Betel consists of the dried leaves of Piper Betle, *Linn.*" *Br.*

Betel, Betle, Pawn, or *Pinang* are popular Oriental names for *Piper Betle* L. and *P. Siriboa* L., the leaves of which are used by the Malays as a masticatory. The leaves are usually admixed with scrapings of the Areca nut and shell lime. The Betel plants are indigenous throughout the entire Indian-Malay region and cultivated in Madagascar, Bourbon and West Indies. The plants are climbing shrubs and trained upon trellises and poles in shady but hot places. The leaves are picked while green, pressed together by means of stones and dried. The Betel leaves of the British Pharmacopœia are described as follows: "About fifteen centimetres long, broadly ovate, acuminate, obliquely cordate at base; thin and brittle, upper surface glossy, five or seven conspicuous lateral veins. Mesophyll contains abundant oil-cells filled with brown oleo-resin. Taste warm, aromatic, bitter. As found in commerce the leaves are frequently tied up or stitched together into packets." *Br.*

The warm aromatic taste of the betel leaves is due to an essential oil known as *betel oil.* This is of a color varying from clear yellow to dark brown and of aromatic, somewhat creosote-like, odor and burning sharp taste. The specific gravity ranges from 0.958 to 1.044, the lighter oil being that obtained from the fresh leaves. The alcoholic solution of the oil gives a greenish to bluish-green color with ferric chloride.

The betel oil from Siam contains *cadinene* and

a characteristic phenol named *betelphenol,* isomeric with eugenol; the oil from Java contains in addition to the betelphenol, *chavicol* and a *sesquiterpene;* while the Manila oil contains betelphenol as the sole phenolic constituent. (Gildemeister and Hoffmann, *Die Ætherische Oele, Berlin,* 1899.)

Uses.—The essential oil of betel is an active local stimulant and has been used in *doses* of one to two minims (0.06–0.12 mil) in the treatment of various respiratory *catarrhs,* and as a local application, either by gargle or inhalation, in *diphtheria.* It is said that the juice of four leaves is equivalent in power to one drop of the oil. In India betel leaves are used locally to a considerable extent for the purpose of counter-irritation and applied to the mammary glands for the purpose of suppressing the secretion of milk in *mammary abscesses.* The essential oil has been given internally in doses of from one to two minims (0.06–0.12 mil).

BISMUTHI BETANAPHTHOLAS.

BISMUTH BETANAPHTHOL Bism. Betanaph.

(bĭs-mū'thī bē-ta-năph'thŏ-lăs)

"A compound of bismuth and betanaphthol of somewhat varying composition, yielding not less than 15 per cent. of betanaphthol [$C_{10}H_7OH$] and, upon ignition, not less than 73 per cent. nor more than 78 per cent. of bismuth oxide [Bi_2O_3]." *U. S.*

This compound has been introduced into the U. S. P. IX. It is sometimes known as *Orpholvon Heyden.* The United States patent has expired and it is now made in this country by several manufacturers. It is obtained by precipitating solution of sodium betanaphtholate with an acetic acid solution of bismuth nitrate with the addition of solution of sodium hydroxide. It is officially described as "a buff-colored to grayish-brown, amorphous powder; odorless or having a faint odor of betanaphthol; tasteless; permanent in the air. Bismuth Betanaphthol is nearly insoluble in water, alcohol, chloroform or ether; partially dissolved by mineral acids with the formation of the corresponding bismuth salts and the liberation of betanaphthol. When strongly heated Bismuth Betanaphthol chars and finally leaves a grayish-yellow residue, which is blackened by hydrogen sulphide T.S. Shake about 1 Gm. of Bismuth Betanaphthol, accurately weighed, with 20 mils of chloroform, filter the mixture, allow the filtrate to evaporate spontaneously and dry the residue in a desiccator over sulphuric acid; the weight of this residue does not exceed 1 per cent. (*free betanaphthol*). Shake about 0.5 Gm. of Bismuth Betanaphthol with 10 mils of distilled water and filter; the filtrate is colorless and neutral to litmus. Heat gently a mixture of about 0.2 Gm. of Bismuth Betanaphthol with 5 mils of potassium hydroxide T.S. and about 0.2 Gm. of aluminum wire; the vapors evolved do not turn red litmus blue (*nitrates*). Incinerate about 2 Gm. of Bismuth Betanaphthol in a porcelain crucible, cool the residue and add just sufficient nitric acid to form a solution with the aid of heat. This solution, when poured into 100 mils of distilled water, produces a white, crystalline precipitate. Now filter the mixture, evaporate the filtrate to 30 mils and again filter if not clear; the clear filtrate does not respond to the tests for *lead, copper, sulphate, or silver* given under *Bismuthi Subcarbonas.* The bismuth oxide obtained in the following assay does not respond to Bettendorf's Test for arsenic (see Part III, Test No. 2).

"**Assay for Betanaphthol.**—Dissolve about 2 Gm. of Bismuth Betanaphthol, accurately weighed, in 20 mils of hydrochloric acid with the aid of heat, cool the liquid and then shake it in a separator with successive portions of chloroform until the extraction of the betanaphthol is complete. Combine the chloroform solutions, allow the liquid to evaporate spontaneously and dry the residue in a desiccator; the weight of the residue corresponds to not less than 15 per cent. of the weight of Bismuth Betanaphthol taken. This residue, crystallized from a solution in boiling distilled water, responds to the tests for identity under *Betanaphthol.*

"**Assay for Bismuth Oxide.**—Incinerate about 2 Gm. of Bismuth Betanaphthol, accurately weighed, in a porcelain crucible, cool the residue and dissolve it in nitric acid. Evaporate the solution to dryness and carefully ignite the residue until of constant weight; the bismuth oxide (Bi_2O_3) so obtained corresponds to not less than 73 per cent. nor more than 78 per cent. of the original weight of the Bismuth Betanaphthol taken." *U. S.*

Uses.—This salt of bismuth is employed especially in the treatment of *enteritis* on the supposition that when the salt is broken up in the intestinal tract it will liberate betanaphthol, and therefore exercise a more powerful antiseptic action than the other salts of bismuth.

Dose, from five to twenty grains (0.32–1.3 Gm.).

BISMUTHI ET AMMONII CITRAS. U. S.

BISMUTH AND AMMONIUM CITRATE Bism. et Ammon. Cit. [Bismuth Ammonio-Citrate]

(bĭs-mū'thī ĕt ăm-mō'nĭ-ī cī'trās)

"Bismuth citrate rendered soluble by the presence of ammonium citrate; when dried to constant weight in a desiccator over sulphuric acid, it yields, upon ignition, not less than 46 per cent. nor more than 52 per cent. of bismuth oxide [Bi_2O_3]. Preserve it in well-closed containers protected from light." *U. S.*

Bismuthi Ammonio-citras; Bismuthum Citricum Ammoniatum; Citrate of Bismuth and Ammonium; Citrate de Bismuth et d'Ammoniaque, *Fr.;* Citronensaures Wismutoxyd-Ammonium; Wismutammoncitrat, Citronensaures Wismutammonium, *G.*

No process is given in the U. S. IX for this compound. The process of the U. S. VIII is appended.

* "Bismuth Citrate, *one hundred grammes,* [or 3 ounces av., 231 grains]; Ammonia Water, Distilled Water, each, *a sufficient quantity.* Mix the Bismuth Citrate with *two hundred mils* [or

6 fluidounces, 366 minims] of Distilled Water and rub it to a smooth paste, heat the mixture on a water-bath, and gradually add Ammonia Water until the salt is dissolved and the liquid is neutral or has only a faintly alkaline reaction. Then filter the solution, evaporate it on a water-bath to a syrupy consistence, and spread it upon plates of glass, so that, when dry, the salt may be obtained in scales. Keep the product in amber-colored, well-stoppered bottles, protected from light." *U. S. VIII.*

The British Pharmacopœia does not recognize this salt, which has been used quite extensively during the last twenty years, principally for preparing extemporaneously the London Liquor Bismuthi originally suggested by Schacht. The Br. Pharm., 1914, gives a process for a solution in which bismuth citrate is produced. (See *Liquor Bismuthi et Ammoniæ Citratis*, Br.) The N. F. IV solution of bismuth contains bismuth and sodium tartrate. (See Part III.)

Properties.—The U. S. Pharmacopœia describes it as in "shining, pearly or translucent scales, or white powder, becoming opaque with loss of ammonia on exposure to the air; it is odorless and has a metallic taste. Bismuth and Ammonium Citrate is very soluble in water and sparingly soluble in alcohol. When strongly heated, the Bismuth and Ammonium Citrate fuses and finally leaves a blackened residue, having a yellow surface. A solution of this residue in a slight excess of nitric or hydrochloric acid produces a white turbidity when added to 25 volumes of distilled water. An aqueous solution of Bismuth and Ammonium Citrate (1 in 20) is neutral or faintly acid to litmus. Ammonia is evolved when Bismuth and Ammonium Citrate is boiled with a slight excess of sodium hydroxide T.S. An aqueous solution of the Bismuth and Ammonium Citrate, when treated with an excess of hydrogen sulphide, yields a black precipitate. The filtrate from the latter, when deprived by heat of the excess of hydrogen sulphide and boiled with an excess of lime water, yields a white precipitate. Dissolve about 0.05 Gm. of Bismuth and Ammonium Citrate in 1 mil of distilled water, in a test tube, add 5 mils of sulphuric acid (free from nitrous compounds), cool the mixture and carefully pour over it 5 mils of ferrous sulphate T.S. without mixing; no red or brown zone appears immediately (*nitrate*). Dissolve 1 Gm. of Bismuth and Ammonium Citrate in 50 mils of distilled water, precipitate the bismuth completely with hydrogen sulphide, filter, evaporate the filtrate to dryness and ignite. The weight of the residue does not exceed 0.005 Gm. (*alkalies or alkali earths*). Ignite 3 Gm. of the Bismuth and Ammonium Citrate, dissolve the residue in just a sufficient quantity of warm nitric acid, and pour the solution into 100 mils of distilled water; a white precipitate is produced. Filter this mixture, evaporate the filtrate on a water bath to 30 mils, again filter the liquid and divide the new filtrate into portions of 5 mils each. These portions do not respond to the tests for *lead, copper, sulphate, or silver* given under *Bismuthi Subcarbonas.* The residue resulting from the ignition and subsequent treatment of 2 Gm. of Bismuth and Ammonium Citrate, as described in the following test, does not respond to Bettendorf's Test for arsenic (see Part III, Test No. 2).

"**Assay.**—Take about 1 Gm. of Bismuth and Ammonium Citrate, previously dried to constant weight in a desiccator over sulphuric acid, and weigh accurately. Ignite it in a porcelain crucible and, after cooling, add 5 mils of nitric acid to the residue, drop by drop, warming until solution is effected. Evaporate this solution to dryness, and carefully ignite it at red heat. It leaves a residue of bismuth oxide (Bi_2O_3) corresponding to not less than 46 per cent. nor more than 52 per cent. of the original weight of Bismuth and Ammonium Citrate taken." *U. S.*

As frequently seen in commerce it is not entirely soluble in water; this is due to the loss of ammonia through exposure, and a few drops of ammonia water added to the turbid solution are generally sufficient to restore its transparency. The Committee of Revision very properly omitted to give its chemical formula, as it is by no means proved that it has a definite composition. Some believe it to be a true double citrate. $BiC_6H_5O_7(NH_4)_3C_6H_5O_7$. On the other hand, Bartlett (*Zeit. An. Chem.*, 1865, p. 305) obtained on evaporation of the ammoniacal solution $BiC_6H_5O_7.NH_3 + 3H_2O$, and Rother (*Jahresb.*, 1876, p. 564) obtained on crystallizing from warm ammonia $BiC_6H_5O_7.3NH_3 + 3H_2O$.

Uses.—This salt, because of its solubility, lacks the therapeutic virtues of the other official preparations of bismuth. It is actively astringent, and more irritant in its action. It is occasionally of service in *serous diarrheas*, but should not be used when there is much inflammation.

Dose, one to three grains (0.065–0.20 Gm.).

BISMUTHI SUBCARBONAS. U. S. (Br.)

BISMUTH SUBCARBONATE Bism. Subcarb.

(bĭz-mū'thī sŭb-cär'bo-năs)

"A basic bismuth carbonate of varying chemical composition, which, when dried to constant weight at 100° C. (212° F.), yields, upon ignition, not less than 90 per cent. of bismuth oxide [Bi_2O_3]." *U. S.* "Bismuth Oxycarbonate, $(Bi_2O_2CO_3)_2,H_2O$, may be obtained by the interaction of bismuth nitrate and ammonium carbonate." *Br.*

Bismuthi Carbonas, *Br.*; Carbonate of Bismuth, Oxycarbonate of Bismuth, Bismuthyl carbonate; Bismuthum Subcarbonicum, Subcarbonas Bismuthicus; Sousearbonate de Bismuth, *Fr.*; Basisches Kohlensaures Wismutoxyd, Wismutsubcarbonat, *G.*

A process for this salt is no longer official; that of the U. S. P., 1870, will be found in U. S. D., 19th edition, p. 239.

Properties.—Bismuth subcarbonate is "a white or pale yellowish-white powder; odorless and tasteless, and permanent in the air. Bismuth Subcarbonate is insoluble in water or alcohol;

completely dissolved by nitric or hydrochloric acid with copious effervescence. Its solution in a slight excess of nitric acid, when added to 25 volumes of distilled water, produces a white turbidity. When heated to redness, the salt loses water and carbon dioxide, and leaves a yellowish residue, which is soluble in nitric or hydrochloric acid and blackened by hydrogen sulphide T.S. Dissolve 1 Gm. of the salt in 2 mils of nitric acid, add distilled water to make the solution measure 25 mils, then add 0.35 mil of tenth-normal silver nitrate V.S. and remove the precipitate, if any, by filtration; the clear filtrate remains unaffected by the further addition of a few drops of silver nitrate T.S. (*chloride*). Dissolve 3 Gm. of the salt in just a sufficient quantity (about 4 mils) of warm nitric acid, and pour the solution into 100 mils of distilled water; a white precipitate is produced. Filter, and evaporate the filtrate on a water bath to 30 mils, again filter the liquid, divide the latter filtrate into portions of 5 mils each and subject these several portions to the following tests: Mix one portion with an equal volume of diluted sulphuric acid; it does not become cloudy (*lead*). Precipitate another portion with a slight excess of ammonia water; the supernatant liquid does not exhibit a bluish tint (*copper*). Another portion is not immediately affected by barium nitrate T.S. (*sulphate*). In another portion hydrochloric acid does not produce a precipitate which is insoluble in a slight excess of hydrochloric acid, but soluble in ammonia water (*silver*). Boil 1 Gm. of the salt with 20 mils of a mixture of equal parts of acetic acid and distilled water, cool the solution and filter. Free the filtrate from bismuth by the addition of hydrogen sulphide, boil the mixture and again filter. The latter filtrate leaves not more than 0.003 Gm. of residue on evaporation and gentle ignition (*alkalies or alkali earths*). Agitate about 0.05 Gm. of Bismuth Subcarbonate with 5 mils of a solution of equal parts of distilled water and ferrous sulphate T.S. and cautiously pour the mixture over 5 mils of sulphuric acid (free from nitrous compounds), so as to form a layer above; no brownish-red zone forms at the line of contact of the two liquids (*nitrate*). The residue resulting from the ignition of 2 Gm. of Bismuth Subcarbonate does not respond to Bettendorf's Test for arsenic (see Part III, Test No. 2)." *U. S.*

"A whitish, inodorous powder. Insoluble in *water;* soluble in *nitric acid* diluted with half its volume of *water*. Yields the *reactions* characteristic of bismuth and of carbonates. Yields when strongly heated from 89 to 91 per cent. of bismuth oxide. Yields no characteristic *reactions* for silver, lead, copper, calcium, selenium, tellurium, or chlorides, and not more than the slightest *reaction* for sulphates. *Arsenic limit* 2 parts per million. On mixing 0.02 gramme with 5 drops of *phenoldisulphonic acid,* adding after five minutes, 10 millilitres of *solution of ammonia,* filtering, washing the precipitate with *water* and adding *water* to the filtrate until it measures 100 millilitres, the color of the filtrate is not deeper than that obtained by similarly treating 0.00013 gramme of *potassium nitrate* (limit of nitrate). The solution obtained by exhausting 5 grammes with boiling *water* requires for neutralisation not more than 1 millilitre of *N/10 solution of sulphuric acid* (limit of alkaline carbonates)." *Br.*

Its sp. gr. is about 4. It effervesces with acids, and, when exposed to heat, loses 9.5 per cent. of its weight (*U. S.,* 1870) in consequence of the escape of carbon dioxide, and is converted into the anhydrous trioxide, of a slight yellow color.

Assay.—"Ignite thoroughly at red heat in a porcelain crucible about 1 Gm. of Bismuth Subcarbonate, previously dried to constant weight at 100° C. (212° F.), and accurately weighed. The residue of bismuth oxide (Bi_2O_3) corresponds to not less than 90 per cent. of the original weight of Bismuth Subcarbonate taken." *U. S.*

Uses.—Bismuth subcarbonate has the general properties of the insoluble salts of bismuth. (See page 240.) In cases of *gastritis* and especially in *gastric ulcer* the fact that it acts as an alkali gives it preference over the subnitrate which is usually acid in reaction. It is especially preferred over the subnitrate when large quantities are to be taken, as in röntgenography, because of its lower toxicity. For the purpose of rendering opaque to the X-ray the walls of the intestines it is the habit to give one to two ounces of an insoluble salt of bismuth. This quantity of the subcarbonate produces absolutely no disturbances of either the general system or the alimentary canal.

Dose, ten to thirty grains (0.65–2.0 Gm.).

BISMUTHI SUBGALLAS. U. S.

BISMUTH SUBGALLATE Bism. Subgal. [Dermatol]

(bĭs-mū'thĭ sŭb-găl'lās)

"A basic bismuth gallate of varying chemical composition which, when dried to constant weight at 100° C. (212° F.), yields, upon ignition, not less than 52 per cent. nor more than 57 per cent. of bismuth oxide [Bi_2O_3]." *U. S.*

Bismuthyl Gallate; Gallate Basique de Bismuth, *Fr. Cod.;* Sousgallate de Bismuth, *Fr.;* Bismutum subgallicum, *P. G.;* Basisches Wismutgallat, *G.;* Gallato basico de bismuto, *Sp.*

Preparation.—Bismuth Subgallate was originally prepared by Bley in 1841; Fischer again prepared and described it in 1891. It was introduced to the medical profession under the proprietary name of "Dermatol," but as it was found to be bismuth monogallate, it is now known under its chemical name. Its composition has been stated to be $C_6H_2(OH)_3.COOBi(OH)_2$. F. T. Greene proposes the following process: Normal bismuth nitrate, 1 oz. av.; glacial acetic acid, 2 fl. oz. or q. s.; gallic acid, 250 grains. Dissolve the normal bismuth nitrate in the glacial acetic acid; add a pint of water. If bismuth salts should precipitate, add more glacial acetic acid until clear. Filter off impuri-

ties. Dissolve the gallic acid in a pint of warm water; mix the solutions; allow the precipitate to subside; decant; wash by decantation with warm water until washings no longer show acid reaction. Dry at 100° C. (212° F.); rub to powder. See *Ph. Rund.*, 1896, 85; *Ph. Ztg.*, 1901, 1033.

Properties.—It is officially described as "an amorphous, bright yellow powder, odorless; tasteless, and permanent in the air. Bismuth Subgallate is insoluble in water, alcohol, or ether; readily soluble, with decomposition, in warm hydrochloric, nitric or sulphuric acid; insoluble in very dilute mineral acids; readily soluble in alkali hydroxide solutions, forming a clear, yellow solution which rapidly changes to a deep red. When heated to redness it at first chars, leaving finally a yellow residue, which is blackened by hydrogen sulphide T.S. A solution of this residue in a slight excess of warm nitric or hydrochloric acid produces a white turbidity when added to 25 volumes of distilled water. Agitate thoroughly about 0.1 Gm. of Bismuth Subgallate with an excess of hydrogen sulphide T.C.; a brownish-black precipitate results. Filter this mixture, boil the filtrate to remove the dissolved gas, and then cool; the addition of 1 drop of ferric chloride T.S. produces a blue-black coloration in the liquid. Shake 1 Gm. of the salt with 20 mils of alcohol for one minute, filter and evaporate the filtrate to dryness on a water bath; not more than 0.005 Gm. of residue remains (*free gallic acid*). Boil 1 Gm. of Bismuth Subgallate with 20 mils of a mixture of equal parts of acetic acid and distilled water, cool the solution and filter. Free the filtrate from bismuth by the addition of hydrogen sulphide, boil the mixture and again filter. The latter filtrate leaves not more than 0.005 Gm. of residue on evaporation and gentle ignition (*alkalies or alkali earths*). Mix thoroughly about 0.05 Gm. of Bismuth Subgallate with 5 mils of diluted sulphuric acid and 5 mils of ferrous sulphate T.S., filter the mixture and then cautiously pour the filtrate, without mixing, over 5 mils of sulphuric acid (free from nitrous compounds), contained in a test tube; no brownish-red zone forms immediately (*nitrate*). Ignite 3 Gm. of Bismuth Subgallate in a porcelain crucible, cool and cautiously add just sufficient nitric acid, drop by drop, warming until the residue is dissolved. Evaporate the solution to dryness, again ignite and cool. Cautiously dissolve this residue in just sufficient nitric acid by the aid of gentle heat, concentrate the solution to about 4 mils, pour it into 100 mils of distilled water, filter, evaporate the filtrate on a water bath to 30 mils, again filter and divide this filtrate into portions of 5 mils each. These portions do not respond to the tests for *lead, copper, sulphate, or silver* given under *Bismuthi Subcarbonas*. The residue resulting from the ignition and subsequent treatment of 2 Gm. of Bismuth Subgallate as described in the following test does not respond to Bettendorf's Test for arsenic (see Part III, Test No. 2).

"Assay.—Take about 1 Gm. of Bismuth Subgallate, previously dried to constant weight at 100° C. (212° F.), and weigh accurately. Ignite in a porcelain crucible and, after cooling, add 5 mils of nitric acid to the residue, drop by drop, warming until complete solution has been effected. Evaporate this solution to dryness and carefully ignite at red heat; it leaves a residue of bismuth oxide (Bi_2O_3) corresponding to not less than 52 per cent. nor more than 57 per cent. of the original weight of Bismuth Subgallate taken." *U. S.*

Uses.—Bismuth subgallate was originally introduced into medicine as a substitute for iodoform in the treatment of *eczema* and other skin diseases and in surgical dressings. It does not, however, act like iodoform, and is only a feeble germicide which resembles closely in all its medicinal activities the older insoluble preparations of bismuth, than which it is, however, thought by some practitioners to be more astringent, and therefore preferable in *diarrhea;* otherwise its rank in internal medicine is precisely that of the subnitrate.

Dose, seven to thirty grains (0.45–2.0 Gm.).

BISMUTHI SUBNITRAS. U. S., Br.

BISMUTH SUBNITRATE Bism. Subnit.

[Bismuth Oxynitrate]

(bĭz-mū'thī sŭb-nī'trās)

"A basic bismuth nitrate of varying chemical composition, which, when dried for twenty-four hours in a desiccator over sulphuric acid, yields, upon ignition, not less than 79 per cent. of bismuth oxide [Bi_2O_3]." *U. S.* "Bismuth Oxynitrate, $BiONO_3,H_2O$, may be obtained by the interaction of bismuth nitrate and water." *Br.*

Subnitrate of Bismuth; Bismuthum Album, *Br.* 1864; Bismuthyl Nitrate; Magistery of Bismuth; White Bismuth; Bismuthum Hydrico-nitricum, Magisterium Bismuthi, Subazotas (s. Subnitras) Bismuthicus; Azotate (sous) de Bismuth, *Fr. Cod.;* Sous-nitrate de Bismuth, *Fr.;* Bismutum subnitricum, *P. G.;* Basisches Salpetersaures Wismutoxyd, Basisches Wismutnitrat, Wismutsubnitrat, *G.;* Nitrato basico di bismuto, *It.;* Nitrato (sub) bismutico, Magisterio de bismuto, *Sp.*

A process for bismuth subnitrate is no longer official in the U. S. or Br. Pharmacopœias. The process of the U. S. P. (1870) will be found in the U. S. D., 19th edition, p. 242.

The process frees the subnitrate from any arsenic that might be present in the bismuth used. This is accomplished by first preparing the carbonate, by adding the nitric acid solution of bismuth to a solution of sodium carbonate in excess, whereby most of the arsenic is retained in the solution, probably as sodium arsenate, while the insoluble carbonate is precipitated. The latter is dissolved, with the aid of heat, in nitric acid, so as to make a very concentrated solution of the nitrate, to which, when cold, just enough water is added to begin to produce a permanent turbidity. The object of this is to allow any arsenic that may be still present to be deposited. The deposited matter having been precipitated, only the pure nitrate remains in solution, which is made to yield the subnitrate

by large dilution with water, and still more completely by the addition of ammonia. In the former British formula, the method pursued was that of dissolving the bismuth, which has been previously purified, in nitric acid somewhat diluted, concentrating the solution, and precipitating by adding it to a large quantity of water.

When bismuth is added to diluted nitric acid, red fumes are copiously given off, and the metal, oxidized by the decomposition of part of the nitric acid, is dissolved by the remainder so as to form a solution of bismuth trinitrate. It is unnecessary to have the metal in powder, as it dissolves with great facility when added to the acid in fragments. When the solution is completed, the liquor should be added to the water, and not the water to the solution. In order to have a smooth light powder, which is most esteemed, the precipitate should be well washed to remove every trace of free nitric acid, and dried as speedily as possible. In the use of this formula it is taken for granted that the bismuth has been ascertained to be free from arsenic; and if it prove upon the application of Marsh's test to be otherwise, means should certainly be employed to purify it before using it. Methods for this purpose are mentioned under *Bismuthum*. Should the subnitrate or subcarbonate be ascertained to contain arsenic, it may, as suggested by Herapath, be purified by boiling it with solution of sodium hydroxide twice successively, then thoroughly washing the residue, which will be yellow oxide of bismuth, dissolving it again in nitric acid, and precipitating by water as before. (*Chem. News*, 1863, p. 77.) In the washing of bismuth subnitrate, the salt is asserted to lose a portion of its nitric acid; and the change may be considerable, if the washing be continued so long as the liquid comes away in any degree acidulous. It has been ascertained by Julius Löwe that this effect may be avoided by washing with a very diluted solution of ammonium nitrate, containing one part in 500 parts of water. (*Chem. Gaz.*, March 15, 1859, 119.) A. de Schulten obtained *crystallized bismuth subnitrate*, $5Bi_2O_3.5N_2O_5.9H_2O$, by dissolving 50 Gm. of bismuth subnitrate in 50 mils of nitric acid (sp. gr. 1.2) and adding 300 mils of water while stirring; the crystals which are produced are pressed between folds of filter paper and dried. (*Chem. News*, 1904, 87.) *Bismuth nitrate*, a crystalline salt ($Bi3NO_3.5H_2O$), is deposited from a solution of bismuth in nitric acid. Bismuth nitrate has been used by Balmanno Squire dissolved in glycerin, under the name of *Glycerole of Nitrate of Bismuth*. (*P. J.*, Nov. 11, 1876.) W. W. Moorhead prepares it by taking two troyounces of crystalline bismuth nitrate and dissolving in sufficient glycerin to make eight fluidounces. No heat should be used. This preparation can be diluted with an equal bulk or less of water, or one part can be added to forty-eight of water without precipitation, but one part to twelve, eight, or six of water soon precipitates. (*A. J. P.*, 1877, p. 98; also pp. 23 and 89.)

Properties.—"White powder; odorless, almost tasteless, and slightly hygroscopic. Bismuth Subnitrate is almost insoluble in water, insoluble in alcohol, and readily dissolved by hydrochloric or nitric acid. Its solution in a slight excess of warm nitric or hydrochloric acid produces a white turbidity when added to 25 volumes of distilled water. When heated to redness it evolves nitrous vapors, leaving a yellow residue, which is blackened by hydrogen sulphide T.S. When brought in contact with moistened blue litmus paper, the salt shows a slightly acid reaction. Boil 1 Gm. of Bismuth Subnitrate with 20 mils of a mixture of equal parts of acetic acid and distilled water, cool the solution and filter. Free the filtrate from bismuth by the addition of hydrogen sulphide, boil the mixture and again filter. The latter filtrate leaves not more than 0.003 Gm. of residue on evaporation and gentle ignition (*alkalies or alkali earths*). Boil about 0.1 Gm. of the salt with 5 mils of potassium hydroxide T.S.; no odor of ammonia is perceptible nor does the vapor turn moistened red litmus paper blue. The residue resulting from the ignition of 2 Gm. of the salt does not respond to Bettendorf's Test for arsenic (see Part III, Test No. 2). Add 3 Gm. of the salt to 3 mils of warm nitric acid; no effervescence occurs (*carbonate*), and no residue remains (*insoluble foreign salts*). Pour this solution into 100 mils of distilled water, a white precipitate is produced. Filter, evaporate the filtrate on a water bath to 30 mils, again filter the liquid and divide the new filtrate into portions of 5 mils each. These portions do not respond to the tests for *lead, copper, sulphate, or silver* given under *Bismuthi Subcarbonas*." *U. S.*

"A white, inodorous, microcrystalline powder, with not more than a slight action on *litmus*. Yields the *reactions* characteristic of bismuth and of nitrates. Yields, when strongly heated, from 79 to 82 per cent. of bismuth oxide. Yields no characteristic *reactions* for silver, lead, copper, calcium, selenium, or tellurium, and not more than the slightest *reactions* for chlorides or sulphates. *Arsenic limit* 2 parts per million." *Br.*

Lassaigne has found as much as 27 per cent. of bismuth chloride in this preparation, when obtained by precipitating with water, a solution of bismuth in a mixture of nitric and hydrochloric acids. The same impurity is introduced, to a small extent, by using common water containing chlorides; and bismuth sulphate renders the preparation impure, when the water used contains calcium sulphate. These facts show the necessity of using distilled water. As regards the origin of the chlorine sometimes existing in commercial bismuth subnitrate, it was asserted by R. C. Tichborne to be a common practice with the manufacturer, in order to save the bismuth existing in the mother liquor after the decomposition of the subnitrate, to precipitate it with sodium chloride, thus obtaining an insoluble bis-

muth oxychloride, which is then added to the previous product. The metal thallium is said to be present in some specimens of the pharmaceutical preparations of bismuth, while the fetid odor of the breath so often produced when the subnitrate is administered is believed to be due to traces of tellurium. It has also been said that the arsenic usually present in minute quantities is the cause of the garlicky odor of the breath. E. R. Squibb (*Ephem.*, Sept., 1882) states, however, that the "bismuth breath" has been noticed in patients who were taking a preparation of bismuth in which the absence of both tellurium and arsenic was conclusively shown. The cause of the peculiar odor is, therefore, at present doubtful. Calcium phosphate has been ascertained to be an occasional adulteration of the subnitrate. A ready method of detecting it suggested by Roussin, has proved to be fallacious, and may lead to false decisions as to the presence of the phosphate. There can be no difficulty in detecting the adulteration by the U. S. P. tests. Bismuth subnitrate is incompatible with potassium iodide (slowly forming a brick-red bismuth iodide) and with alkaline bicarbonates. For examination of commercial bismuth subnitrate by Curtman, see *A. J. P.*, 1896, 422; *Ph. Era*, 1896, 43; also a paper by F. A. Upsher Smith (*P. J.*, 1900, 15).

Assay.—"Ignite thoroughly at red heat in a porcelain crucible about 1 Gm. of Bismuth Subnitrate, previously dried for twenty-four hours in a desiccator over sulphuric acid and accurately weighed. The residue of bismuth oxide (Bi_2O_3) corresponds to not less than 79 per cent. of the original weight of Bismuth Subnitrate taken." *U. S.*

Uses.—The almost complete insolubility of the bismuth subnitrate has led to the belief that it is incapable of being absorbed from the gastro-intestinal tract, but a number of chemists have found traces of bismuth in the urine and in various internal organs after its oral exhibition. It is evident, therefore, that it may be slowly absorbed from the bowels, but apparently unlimited quantities can be given by the mouth without enough of the metal being absorbed to produce any sign of bismuth intoxication. Although serious symptoms have been reported from the ingestion of doses of two ounces of bismuth subnitrate administered for röntgenographic purposes, it has been shown that the condition was due to the formation of nitrous acid in the intestinal tract and not to the bismuth. When applied to raw surfaces, however, the subnitrate of bismuth undergoes some chemical change and sufficient of the metal may be absorbed to cause fatal poisoning. The symptoms of bismuth poisoning which have followed the surgical use of bismuth subnitrate are as follows: There appears first a bluish line on the edges of the gum which spreads and becomes darker in color until the whole tongue and pharynx are almost black. There also develops ulcerative stomatitis with salivation, nephritis, vomiting, and in some cases mental disturbances and methemoglobinemia. The mortality in this poisoning is high. (See David and Kauffmann, *J. A. M. A.*, 1909, lii.)

The insoluble salts of bismuth because of their heaviness, as well as their insolubility, tend to cling to any surface to which they are applied; therefore when they are brought in contact with the mucous membrane they form over it a coating which protects the membrane against the action of a local irritant. Chiefly because of this protective action, but probably also in part because of a feeble antiseptic influence, the insoluble salts of bismuth are of great value in the treatment of all forms of *catarrh*, especially of the acuter types, such as *rhinitis*, *gastritis*, or *enteritis*. Although in no proper sense an antemetic, in cases of *vomiting* dependent upon irritation of the stomach, bismuth by its sedative influence upon the mucous membrane may relieve the emesis. In the same way in cases of *gastric ulcer* it assuages the pain by protecting the ulcerated surface from the irritant secretion of the stomach. When used in cases of gastric disease it should be given when the stomach is empty, preferably in the form of a suspension or as a dry powder, so that it will spread of itself out over the mucous membrane of this organ before it is carried out into the duodenum by peristaltic movements. On the other hand, in *enteritis* it should be given after meals. The bismuth salts are also useful as topical applications in the treatment of *coryza*, *gonorrhea*, *dysentery*, and similar conditions. For this purpose from 1 to 4 per cent. should be suspended by means of mucilage of acacia. When administered by mouth in fairly large quantities bismuth often causes blackish discoloration of the stools. As a form of suspension of bismuth subnitrate less liable to produce bismuth poisoning, it has been suggested to use 20 Gm. of bismuth subnitrate, 70 Gm. of liquid petrolatum, and 10 Gm. of petrolatum. This preparation is not readily absorbed and may be sweetened and flavored and used for a bismuth meal for radioscopy.

As was first shown by Kocher the insoluble salts of bismuth possess considerable antiseptic virtues when applied to raw surfaces. The subnitrate of bismuth was at one time largely, and it still is to a less extent, used as a dusting powder in various *wounds* and *ulcers*. In 1908 Beck (*J. A. M. A.*, March 14, 1908) described the favorable results following the injection of a mixture containing one part of bismuth subnitrate and two parts of petrolatum into the chronic *fistulas* of *bone tuberculosis*. His method has been followed by a large number of surgeons with mostly favorable results, although in a number of cases the injection of the bismuth paste into abscess cavities has led to bismuth poisoning. This mixture is known as *Beck's bismuth paste*, and it is important that it shall be sterile.

Dose, five to thirty grains (0.32–2.0 Gm.).

Off. Prep.—Unguentum Resorcinolis Compositum, *N. F.*

BISMUTHI SUBSALICYLAS. U. S. (Br.)

BISMUTH SUBSALICYLATE Bism. Subsalicyl.

(bĭs-mū'thī sŭb-săl-ĭ-cȳ'lăs)

"A basic bismuth salicylate of varying chemical composition, which, when dried to constant weight at 100° C. (212° F.), yields, upon ignition, not less than 62 per cent. nor more than 66 per cent. of bismuth oxide [Bi_2O_3]. Protect it from light." *U. S.* "Bismuth Salicylate, or oxysalicylate, $BiOC_7H_5O_3$, may be obtained by the interaction of bismuth hydroxide and salicylic acid." *Br.*

Bismuthi Salicylas, *Br.;* Bismuth Salicylate; Bismuthyl Salicylate, Bismuth Oxysalicylate; Salicylate Basique de Bismuth, *Fr. Cod.;* Sous-salicylate de Bismuth, *Fr.;* Bismutum subsalicylicum, *P. G.;* Basisches Wismutsalicylat (salicylsaures Wismutoxyd), Wismutsubsalicylat, *G.;* Salicilato de bismuto, *Sp.*

Preparation.—This salt is a bismuthyl salicylate of indefinite composition, the bismuth oxide resulting from its ignition being about 64 per cent. Samples which show a higher percentage than this either contain bismuth subnitrate or hydroxide. It may be made by Wolff's process, by diluting a glycerin solution of crystallized bismuthous nitrate with one or two parts of water, and decomposing this with a concentrated aqueous solution of sodium salicylate, then washing the precipitate well with hot water and carefully drying. Another method for its preparation will be found in *A. J. P.,* 1891, 401. Fischer and Grützner (*A. Pharm.,* 1894, 680) object to the variable composition of commercial bismuth salicylate, and recommend the following process for making a basic salt of constant composition. Crystallized bismuth nitrate is dissolved in four times its weight of diluted acetic acid, the solution diluted with about forty times its weight of water, and the bismuth precipitated as hydroxide by ammonia water. The precipitate is washed and mixed with the molecular proportion of salicylic acid. After heating on a water bath, a magma of crystals of basic bismuth salicylate is formed; these are drained and dried. B. Fischer recommended the following process: one molecule each of salicylic acid and freshly precipitated bismuth hydroxide are heated together with the necessary amount of water on the water bath; filter, collect and dry the residue at 80° to 100° C. (176°–212° F.) on porous tiling. (*Ph. Centralh.,* 1895, 92, 169.) Duyk prepares bismuth salicylate as follows: 100 Gm. of pure bismuth subnitrate are treated for one or two days with one liter of water, to which 50 Gm. of ammonia water have been added. After shaking sufficiently the subnitrate is completely changed into an oxide, which is collected and carefully washed with water. This oxide, after expression, is heated, under constant stirring, with 25 Gm. powdered salicylic acid on a water bath. After the union has been effected, the salicylate is washed and dried at a gentle heat. (*B. S. Ph. Br.,* 1891.) Thibault prefers the use of crystallized bismuth nitrate and solution of sodium hydroxide to precipitate the bismuth hydroxide. (*Bull. Soc. Chem.,* xxv, No. 16.)

Properties.—Bismuth subsalicylate is officially described as "a white, or nearly white, amorphous or crystalline powder; odorless, tasteless, and permanent in the air. Bismuth Subsalicylate is almost insoluble in cold water; upon prolonged boiling with water a portion of the salicylic acid passes into solution with the formation of a more basic bismuth subsalicylate. It is partly soluble, with decomposition, in hydrochloric or nitric acid, a white, flocculent precipitate of salicylic acid separating. When heated to redness it at first chars, finally leaving a yellow residue, which is blackened by hydrogen sulphide. A solution of this residue in a slight excess of warm nitric or hydrochloric acid produces a white turbidity when added to 25 volumes of distilled water. Agitate about 0.1 Gm. of Bismuth Subsalicylate with a solution of 5 drops of ferric chloride T.S. in 10 mils of distilled water; a deep violet-blue coloration is produced. Agitate 1 Gm. of the salt with 20 mils of chloroform, filter the liquid and evaporate the filtrate to dryness; not more than 0.005 Gm. of residue remains (*free salicylic acid*). Ignite 3 Gm. of Bismuth Subsalicylate in a porcelain crucible, cool and cautiously add just sufficient nitric acid to the residue, drop by drop, warming until it is dissolved. Pour this solution into 100 mils of distilled water, filter, evaporate the filtrate on a water bath to 30 mils, again filter and divide the filtrate into portions of 5 mils each. These portions do not respond to the tests for *lead, copper, sulphate, or silver* given under *Bismuthi Subcarbonas.* Boil 1 Gm. of Bismuth Subsalicylate with 20 mils of a mixture of equal parts of acetic acid and distilled water, cool the solution and filter. Free the filtrate from bismuth by the addition of hydrogen sulphide, boil the mixture and again filter. The latter filtrate, on evaporation and ignition, leaves not more than 0.005 Gm. of residue (*alkalies or alkali earths*). Triturate about 0.05 Gm. of Bismuth Subsalicylate with 0.1 Gm. of sodium salicylate and 5 mils of distilled water, and carefully pour it without mixing over 5 mils of sulphuric acid (free from nitrous compounds) contained in a test tube; no pink to brownish-red zone forms immediately (*nitrate*). The residue resulting from the ignition and subsequent treatment of 2 Gm. of Bismuth Subsalicylate, as described in the test below, does not respond to Bettendorf's Test for arsenic (see Part III, Test No. 2)." *U. S.*

"A white or nearly white amorphous powder, insoluble in *water.* Yields the *reactions* characteristic of bismuth. When shaken with diluted *T. Sol. of ferric chloride* a violet color is produced. Yields not more than the slightest characteristic *reaction* with the copper test for nitrates. *Arsenic limit* 2 parts per million. When 5 grammes are shaken with 50 millilitres of *ether,* the ethereal solution filtered off and evaporated to dryness leaves not more than 0.005 gramme of residue (limit of free salicylic acid).

Yields when strongly heated from 62 to 65 per cent. of bismuth oxide. Free from the impurities indicated under 'Bismuthi Carbonas.'" *Br.*

Assay.—"Take about 1 Gm. of Bismuth Subsalicylate, previously dried to constant weight at 100° C. (212° F.), and weigh accurately. Ignite in a porcelain crucible, and, after cooling, add 5 mils of nitric acid to the residue, drop by drop, warming until solution has been effected. Evaporate this solution to dryness and carefully ignite it at red heat. It leaves a residue of bismuth oxide (Bi_2O_3) corresponding to not less than 62 per cent. nor more than 66 per cent. of the original weight of Bismuth Subsalicylate taken." *U. S.*

Uses.—Bismuth subsalicylate differs from the subnitrate in that it exercises a distinctly antiseptic as well as protective effect in the bowels. It is used to a considerable extent in the treatment of chronic *intestinal catarrhs* and subacute *diarrheas* with marked tendency to intestinal fermentation; also as a local antiseptic remedy for *wounds* and various inflammations of the mucous membrane.

Dose, from ten to twenty grains (0.65–1.3 Gm.), every four to eight hours.

BISMUTHUM.

BISMUTH

(bĭz-mū'thŭm)

Bi = 208.0

Etain de Glace, Bismuth, *Fr.*; Wismuth, Wismut, *G.*; Bismuto, *It.*, *Sp.*

Bismuth occurs usually in the metallic state, occasionally as a sulphide or a telluride, and rarely as an oxide. It is found largely in Saxony, Schneeberg being the chief point of production. It has been found, mainly as telluride of bismuth, in Colorado with gold and silver ores. Small quantities have been found in Utah and Wyoming. It has also been discovered in Southern Australia, from whence a quantity of it has been sent into commerce. It is obtained almost entirely from native bismuth ore, which is heated by means of wood or charcoal, whereby the metal is fused, and separated from its gangue. Most of the bismuth of commerce formerly came from Germany and Austria, but it is now largely mined in Bolivia and Australia. The bismuth ore from South America is said to be naturally free from arsenic, and to be therefore preferable for pharmaceutical purposes.

As the production of bismuth in the world far exceeds the demand, there is no regular American production, much of that which accompanies the gold and silver in the ore being allowed to go to waste in the slag.

Bismuth was first recognized as a metal by Agricola in 1520. Before that period it was confounded with lead. It is a brittle, pulverizable, brilliant metal, of a crystalline texture, and of a white color with a slight reddish tint. Its crystals are rhombohedral, but with an angle of 87° 40′, which makes it difficult to distinguish them from cubes, in which the angle would be 90°. Indeed, many books still refer to it as cubical in form. It undergoes but a slight tarnish in the air. Its sp. gr. is 9.8 (B. P., 1885, purified 9.83), melting point 264° C. (507° F.). When impure bismuth solidifies after fusion, globules of the metal, nearly pure, are thrown up from the mass. This takes place when the metal contains as much as 50 per cent. of impurity. The same phenomenon does not occur when pure bismuth is melted. (R. Schneider.) At a high temperature, in close vessels, bismuth volatilizes, and may be distilled over. When heated in the open air to a full red heat, it takes fire, and burns with a faint blue flame, forming an oxide of a yellow color. This is the *trioxide,* or *bismuthous oxide,* and consists of two atoms of bismuth and three of oxygen. There is another compound of bismuth and oxygen consisting of two atoms of the former and five atoms of the latter, which is called *bismuthic oxide,* Bi_2O_5. It is obtained in the form of a hydroxide by boiling bismuth nitrate in solution of potassium hydroxide, washing the precipitate, and mixing it while moist with solution of potassium hydroxide into which chlorine is passed. A mixture of bismuthous and bismuthic oxides is precipitated, from which the former is separated by digestion with nitric acid. The hydroxide remaining, when washed and dried, is in the form of a red powder, which gives up its water at 130° C. (266° F.), and at a higher heat loses oxygen. Bismuth is acted on feebly by hydrochloric acid, but violently by nitric acid, which dissolves it with a copious liberation of red fumes. Sulphuric acid, when cold, has no action on it, but at a boiling heat effects its solution with the liberation of sulphurous acid. As it occurs in commerce, it is generally contaminated with other metals, among which are arsenic in minute quantity, traces of silver, cadmium, nickel, lead and iron, and sometimes a very small proportion of thallium. Claassen has found in so-called "purissimus" bismuth, lead, copper, and iron, and in one sample of bismuth, sold as suitable for scientific purposes, he obtained from 500 grammes 10 grammes of lead chloride. (*Ap. Ztg.*, 1891, p. 121; see also *Chem. News,* 1892, lxv, 28.) It may be purified from all contaminating metals by dissolving the bismuth of commerce in diluted nitric acid, precipitating the clear solution by adding it to water, and reducing the white powder thus obtained with black flux. The same precipitate is obtained by adding ammonia to the nitric solution; if the supernatant liquid is blue, the presence of copper is indicated; if the precipitate is yellowish, iron is present.

Uses.—Bismuth is not used in medicine in an uncombined state, but is employed pharmaceutically to obtain bismuth subcarbonate, subnitrate, subgallate, subsalicylate and other medicinal preparations formed from this metal. In the arts its oxychloride is used to form a cosmetic for the complexion, called *pearl white,* and the metal as an ingredient of the best pewter.

BROMOFORMUM. U. S.

BROMOFORM Bromof.

(brō-mo-fôr'mŭm)

"A liquid consisting of about 96 per cent., by weight, of $CHBr_3$ (252.77) and about 4 per cent. of dehydrated alcohol. Preserve it in glass-stoppered bottles, in cool place, protected from light." *U. S.*

Tribrommethane, Formyl Tribromide; Bromo-formium, *P. G.;* Bromoform, Tribrommethan, *G.;* Bromoformo, *Sp.*

This compound, the analogue of chloroform, is prepared by methods similar to those used for the manufacture of chloroform. It is made, for instance, by the action of bromine in the presence of calcium hydroxide upon alcohol or acetone, or by the decomposition of bromal (the analogue of chloral) by alkalies. It is found as an impurity, at times, in commercial bromine.

Bromoform is officially described as "a heavy, transparent, colorless, mobile liquid, with an ethereal odor, and a penetrating, sweet taste, resembling that of chloroform. Bromoform is slightly soluble in water; miscible with alcohol, chloroform, ether, benzene, petroleum benzin or fixed or volatile oils. Specific gravity: 2.595 to 2.620 at 25° C. (77° F.). Bromoform is slightly volatile at ordinary temperatures. Bromoform is not inflammable, but when vaporized by the application of heat, its vapors may be ignited. Evaporate 10 mils of Bromoform from a porcelain dish on a water bath; not more than 0.006 Gm. of residue remains after drying at 100° C. (212° F.). Shake 10 mils of Bromoform with 10 mils of distilled water, and allow the liquids to separate completely. The water removed from the layer of Bromoform is neutral to litmus (*free acid*); 5 mil portions, tested separately, show not more than a slight opalescence on the addition of a few drops of silver nitrate T.S. (*bromides or brominated compounds*), and no blue color on the addition of a few drops each of potassium iodide T.S. and of starch T.S. (*free bromine*). Agitate 10 mils of Bromoform with 10 mils of distilled water, and allow the liquids to separate completely. Remove the aqueous layer from the Bromoform, treat it with an excess of ammonia water, and then with a solution of iodine and ammonium iodide, until the black precipitate of nitrogen iodide, which sometimes forms, slowly disappears; it does not become milky in appearance, due to the separation of iodoform, recognizable by its odor (*acetone*)." *U. S.*

Uses.—As long ago as 1849, Nunneley and Schuchard suggested the use of bromoform as a general anesthetic. The later experience of practical surgeons has shown, however, that although bromoform produces a rapid narcosis when inhaled, its employment is attended with excessive danger. When taken internally by the mouth it is capable of acting like the older bromides, over which, however, it has no advantages and than which it is probably more dangerous. In the recorded cases of poisoning by it the symptoms have been pallor, titubation, dilatation of the pupils, coma, heart failure and collapse.

The original statement by Stepp, that bromoform is especially efficient in *whooping cough*, has been confirmed by various clinicians. Stepp administered in a teaspoonful of water to children three or four weeks old, one drop three or four times daily; in older, nursing children, three drops; in children from two to four years of age, four to five drops three or four times daily; up to seven years of age six to seven drops three or four times daily. These doses are, however, probably dangerous. Three drops are said to have produced very serious symptoms in a child of four years, and two drops in one of fifteen months. For cases of poisoning, see *Cb. I. M.*, No. 50, 1902; *B. M. J.*, vol. i, 1900; *T. G.;* 1903; *Ap. Ztg.*, July, 1898, March 24, 1900. A saturated aqueous solution of bromoform (containing about 0.3 per cent.) has been recommended by Desesquell (*B. M.*, 1907) for the relief of *sea-sickness*, in tablespoonful doses.

Dose, one to five minims (0.06 to 0.3 mil), best administered in capsules, dropped on sugar, or mixed with an equal quantity of olive oil and emulsified.

BUCHU. U. S. (Br.)

BUCHU

(bū'ȼhū)

"The dried leaves of *Barosma betulina* (Thunberg) Bartling and Wendland, known in commerce as Short Buchu; or of *Barosma serratifolia* (Curtis) Willdenow, known in commerce as Long Buchu (Fam. *Rutaceæ*), without the presence or admixture of more than 10 per cent. of stems or other foreign matter." *U. S.* "Buchu Leaves are the dried leaves of Barosma betulina, *Bart. and Wendl.*" *Br.*

Buchu Folia, *Br.;* Folia Bucco, Folia Diosmæ, s. Barosmæ; Feuilles de Bucco (Booko, Buchu), *Fr.;* Buckublätter, Buccoblätter, *G.*

The leaves of the official and other *Barosmas* (so named from βαρύς, heavy, and ὀσμή, odor), and of some *Agathosmas*, are collected by the Hottentots, who value them on account of their odor, and under the name of *bookoo* or *buchu*, rub them, in the state of powder, upon their greased bodies.

Buchu leaves are not recognized except in the U. S. and British Pharmacopœias. The definitions for this drug do not show any great stability, at one time the "short" buchu being official and then again both the "short" and the "long" buchus are included in one definition. This latter is a mistake as the oils in the several buchus are quite distinct. The drug was exploited in the 70's in the United States by Helmbold who was one of the most eccentric and fantastic exploiters of proprietary medicines. (See *A. J. P.*, 1916, p. 23.) The medicinal species of Barosma are all erect, slender shrubs with opposite leaves, dotted with con-

spicuous pellucid oil glands, smooth, angular, purplish branches, often of a purplish color, white flowers, and a fruit of five erect carpels. They are chiefly distinguished by their leaves.

Barosma betulina is a small shrubby plant indigenous to Cape Colony. The leaves are collected while the plant is in flower and fruit, then dried and shipped to London. *B. serratifolia* is a well developed shrub growing in the mountains of the southwest of Cape Colony. The leaves usually command a higher price and are only employed when the supplies of short buchu are reduced. The exports of buchu from South America in 1908 were 243,742 pounds, in 1912, 223,000 pounds, in 1913, 163,000 pounds, and in 1914 about 75,000 pounds. According to Schimmel and Co., the buchu plant thrives best in a very sandy soil, but it is rather difficult to cultivate as the cuttings do not root readily. The buchu of commerce always contains more or less foreign material, such as stems, twigs and old worthless leaves, and the U. S. Pharmacopœia has wisely limited the amount of such admixture to 10 per cent.

The non-official species, which have been seen in European markets occasionally, are said to be used in South Africa as substitutes for the official buchu; they are:

Barosma crenulata (L.) Hook.—The leaves are opposite, ovate or obovate, acute, serrated and glandular at the edge, coriaceous, and full of small pellucid dots on the under surface. The flowers are white or of a reddish tint, and stand solitarily at the end of short, lateral leafy shoots. C. J. S. Thompson has found that the leaves of *B. serratifolia* yield only 3.45 per cent. of resin and 1 per cent. of volatile oil, while those of *B. crenulata* yield 3.75 per cent. of resin and 1.6 per cent. of volatile oil, and those of *B. betulina* give 4.25 per cent. of resin and 1.45 per cent. of volatile oil; so that *B. serratifolia* would seem to be the least active of the species. (*P. J.*, xxi, 1890.)

Barosma Ecklóniana Barth., a plant which has been considered to be only a variety of *B. crenulata*, has leaves which are rounded at the base, shorter and proportionately wider than those of *B. crenulata*, and also grow upon pubescent shoots.

The leaves of *Barosma venusta* which are said to have appeared in the London markets, are readily distinguished by their being very much smaller than those of *B. betulina*, which they otherwise resemble.

Barosma pulchellum (L.) Bartl. and Wendl.—The leaves closely resemble those of the *B. betulina*, being ovate instead of obovate, that is, they are wider at the base. Their odor is quite different, strongly recalling that of citronella, and Schimmel and Company have demonstrated the presence in them of citronellal.

Under the name of *Karoo buchu*, in 1904 the leaves of the *Diosma succulenta* L., var. *Bergiana* H. and S., appeared in London; they are small and heath-like, thick, obtuse, and slightly recurved, and yielded to C. E. Sage (*C. D.*, lxv, 506, 787) a small semi-solid volatile oil having the odor of peppermint. Recently a new buchu has appeared on the market, the leaves resembling very closely those of *Barosma scoparia* E. and Z. (*Perf. & Ess. Oil Rec.*, 1914, p. 375.)

Buchu is subject to many adulterations both by the leaves of other species of the genus as well as more distantly related leaves. The most important of these adulterations are as follows: *Psoralea obliqua* E. Mey, or *P. bracteata* (*P. J.*, 1910, pp. 69 and 464), and *Empleurum serrulatum* Ait. The leaves of the latter are lanceolate or narrowly linear, about 4 cm. in length, yellowish-green and very acute at the summit. They furthermore do not contain any oil canals at the base of the teeth. (For description of many other adulterants, see Holmes, *P. J.*, 1910, lxxxv, p. 464.)

Properties.—Buchu leaves are officially described as follows:

"**Short Buchu.**—Rhomboidally oval or obovate; from 9 to 25 mm. in length and from 4 to 13 mm. in breadth; summit obtuse, and recurved; margin somewhat serrate or finely dentate with an oil gland at the base of each tooth; the base more or less wedge-shaped; color varying from vivid green to yellowish-green, occasionally a few olive-gray leaves; glandular-punctate; both surfaces papillose; under surface longitudinally striate; texture coriaceous; petiole 1 mm. in length; odor and taste characteristic, aromatic and mint-like.

"**Long Buchu.**—Linear-lanceolate, from 2.5 to 4 cm. in length and from 4 to 6 mm. in breadth; summit somewhat rounded or truncate with an oil gland at the apex; margin sharply serrate and glandular; otherwise resembling Short Buchu.

"Stems in both Short and Long Buchu about 1 mm. in diameter, yellowish-green or brownish-red, cylindrical, longitudinally furrowed, with prominent leaf-scars nearly opposite to each other giving the stems a jointed character. The yield of ash does not exceed 4 per cent." *U. S.*

"From twelve to twenty millimetres long, rhomboid-obovate, dull yellowish-green, rigid, cartilaginous when slightly moist. Surface glabrous, bearing small scattered prominences; margin usually sharply denticulate, apex blunt and recurved. Oil glands visible in the leaf, especially near the margin. Transverse section exhibits in epidermis cells containing yellow sphero-crystals; inner walls of these cells thick and rich in mucilage. Odor and taste strong and characteristic." *Br.*

The leaves of *B. crenulata* constitute the *short buchu* or *round buchu*, while those of *B. serratifolia* are the *long buchu* of commerce. The leaves of *B. crenulata* are at present comparatively infrequent in commerce, the parcels usually consisting of those of one of the other species almost unmixed. The species can be recognized by the characters already given. The leaves of the *Empleurum serrulatum* sometimes occur mixed with buchu leaves occasionally constituting the bulk of the parcel. They are to

be distinguished by their acrid taste and peculiar odor and by being longer and narrower than any buchu leaf, with a sharp-pointed apex, parallel sides, and coarse denticulation. Further, according to Holmes, when the leaf of a Barosma is held up to the light the lateral veins appear straighter, longer, and more strongly developed than in the leaves of the Empleurum. John C. Umney (*P. J.*, March, 1895) finds that the leaves of the latter contain 0.64 per cent. of a peculiar volatile oil. There is no reason to believe that they possess the therapeutical properties of buchu. Holmes enumerated a number of plants used in South Africa as substitutes. (See *P. J.*, 1900, 70.)

Flückiger obtained from *B. betulina* 1.56 per cent. of volatile oil, which had the odor of peppermint rather than of buchu, and deviated the plane of polarization considerably to the left. On exposure to cold it furnished a camphor, which, after re-solution in alcohol, crystallized in needle-shaped forms. After repeated purification in this manner, the crystals of *Barosma camphor,* or *diosphenol,* $C_{10}H_{16}O_2$, have a peppermint odor; they fuse at 85° C. (185° F.) and begin to sublime at 110° C. (230° F.). After fusion they again solidify only at 50° C. (122° F.). Barosma camphor is abundantly soluble in carbon disulphide. The crude oil from which the camphor had been separated had a boiling point of about 200° C. (392° F.), quickly rising to 210° C. (410° F.), or even higher. The oil which distilled between these temperatures, rectified over sodium, gave approximately the formula $C_{10}H_{18}O$. (*Pharmacographia,* 2d ed., p. 109.) Spica examined *B. crenulata* and found the volatile oil to differ from that obtained by Flückiger from *B. betulina;* the solid body was similar to diosphenol, but upon analysis gave the figures $C_{10}H_{16}O_2$, and hence is regarded by Spica as an oxycamphor. The liquid portion was a greenish-yellow oil, having a pleasant odor and a pungent, peppermint-like taste; by fractioning, it was separated into a portion isomeric with borneol, resembling thymol in odor and taste, to which the name of *dioscamphor* was given. A substance extracted by alcohol from the residue after the removal of the oil Spica named *diosmin.* (*P. J.*, 1885, p. 106.) The results of Spica were confirmed by Shimoyama (*A. J. P.*, 1888, p. 624), who made several simple derivatives of diosphenol and then prepared from it, by prolonged digestion with alcoholic potash, *diolic acid,* $C_{10}H_{18}O_3 + H_2O$, forming white crystalline needles, melting at 96° to 97° C. (204.8°-206.6° F.), and a compound to which he gave the name *diolalcohol.* Wayne's experiments (*A. J. P.*, 1876, p. 19) appear to indicate that the oil also contains a substance capable of being converted into salicylic acid. J. M. Maisch believed that buchu leaves do not contain salicylic acid, although the stearopten of the oil gives a blackish color with ferric chloride. (*A. J. P.*, July, 1881.) The yield of ash varies, according to the researches of H. W. Jones (*P. J.*, ix, 673), from 4.69 to 4.40 in *B. betulina,* 4.32 to 5.39 in *B. crenulata,* 5.03 to 5.22 in *B. serratifolia;* the ash itself was remarkable as containing a great deal of manganese. The short leaved buchu was found by P. W. Bedford to yield an average of 1.21 per cent. of volatile oil; while the long leaved, though more highly valued in the market, gave only 0.66 per cent., showing its great inferiority in strength. (*Proc. A. Ph. A.*, 1863, p. 211.)

Uses.—Buchu, originally employed by the Hottentots, has long since come into general use. Its activity depends upon the volatile oil, which is eliminated by the kidneys. Under its action there is no marked increase in the amount of the urine, hence the remedy is of no value in *dropsies,* but the oil affects very decidedly the mucous membrane of the genito-urinary tract. The remedy is useful in diseases of the urinary organs, such as *gravel, chronic catarrh of the bladder, morbid irritation of the bladder and urethra, diseases of the prostate,* and *retention or incontinence of urine* from a loss of tone in the parts concerned in its evacuation. It should be given when the inflammation is not severe, but when it is in that condition of chronicity requiring oil of turpentine, tincture of cantharides, or other stimulant diuretics. An infusion (one ounce in a pint of boiling water) may be given in the dose of one to two fluidounces (30–60 mils), but the best preparation is the fluidextract.

Dose, one-half to one drachm (2.0–3.9 Gm.).

Off. Prep.—Fluidextractum Buchu, *U. S.;* Infusum Buchu, *Br.;* Tinctura Buchu, *Br.;* Elixir Buchu (from Fluidextract), *N. F.;* Elixir Buchu Compositum (from Compound Fluidextract), *N. F.;* Elixir Buchu et Potassii Acetatis (from Elixir of Buchu), *N. F.;* Fluidextractum Buchu Compositum, *N. F.*

BUTEÆ GUMMI. Br.

BUTEA GUM [Bengal Kino]

(bū-tē'æ gŭm'mĭ)

"Butea Gum is the inspissated juice obtained from incisions in the stem of Butea frondosa, *Roxb.*" *Br.*

For description and uses, see under butea seeds.

BUTEÆ SEMINA. Br.

BUTEA SEEDS

(bū-tē'æ sē'mĭ-nă)

"Butea Seeds are the seeds of Butea frondosa, *Roxb.*" *Br.*

The *Sacred Tree, Butea frondosa* (Fam. *Leguminosæ*), enters largely into the religious rites of the Hindoos. Its red flowers are offered at the bloody sacrifice of the goddess Kali. Its leaf with three spreading leaflets is supposed to represent the Hindoo deity, and furnishes platters used when the Hindoo boy becomes of age.

Butea gum, which has sometimes been mistaken for African kino, is the concrete juice of

the *Butea frondosa* Roxb., or *Dhak-tree* of Hindostan, and also to some extent of *B. superba.* The juice flows from natural fissures, and from wounds made in the bark of the tree, and quickly hardens. It is in small elongated tears, or irregular angular masses, less in size than a grain of barley, apparently black and opaque, but translucent and of a ruby-red color when examined in small fragments by transmitted light; in some specimens the tears are much paler than described, and of a very beautiful ruby tint. Many of the tears have small portions of bark adhering to them. They are very brittle, and readily pulverizable, yielding a reddish powder. They are very astringent to the taste, do not adhere to the teeth when chewed, and tinge the saliva red. The solubilities and reactions of this product to water, alcohol, and other chemical reagents are nearly the same as those of ordinary kino. When freed from impurities, consisting of from 15 to 25 per cent. of wood, bark, and sand, etc., it contains, according to E. Solly, 73.26 per cent. of tannin, 5.05 of soluble extractive, and 21.67 of gum and other soluble substances. It is used in the arts in India, and might undoubtedly be employed as kino in medicine. It is, however, very seldom imported into England, and never, at present, into this country. Pereira found a quantity in an old drug store in London, and sent a portion to Guibourt, from which that writer drew up his description of African kino. It is possible that the kino which formerly reached us, full of small pieces of wood, bark, etc., may have been the *Butea gum.*

Butea gum occurs in "small irregular shining fragments, very dark ruby color, thinnest flakes transparent when examined by transmitted light. Partially soluble in *water;* about 40 per cent. soluble in hot *alcohol* (90 per cent.), the solution being scarcely colored. No odor; taste astringent. Free from corky or woody particles. On keeping, the fragments may become dull and blackish." *Br.*

It is said (Hanbury) to yield 1.8 per cent. of ash and 13.5 per cent. of water, and to be composed of about equal parts of kino-tannic acid and a soluble mucilaginous substance. On dry distillation it yields pyrocatechin, which, according to Eissfel, does not preëxist in it. "In India and the Eastern Divisions of the Empire, Butea Gum may be employed in making the official preparations for which kino (distinguished in commerce as East Indian, Malabar, Madras, or Cochin kino) is directed to be used." *Br.*

The British Pharmacopœia describes the seeds as "flat, reniform, from twenty-five to thirty-eight millimetres long, sixteen to twenty-five millimetres wide, and one and a half to two millimetres thick. Testa thin, glossy, veined, wrinkled, dark reddish-brown. Cotyledons large, leafy, yellow. Faint odor; taste slightly acrid." *Br.*

For a description of the seeds of *B. frondosa,* see *Ph. Rev.,* 1896, 232.

Uses.—Butea Gum is used for the same purposes and in the same doses as kino. The seeds have been used by the native practitioners in India as vermifuges against both the *tape worm* and the *round worm.* According to the *Pharmacographica Indica,* the infusion of three seeds exercises a laxative effect. Before being used, the seeds should be soaked in water and the integument carefully removed. The powdered dried kernels may be given in doses of ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Pulvis Buteæ Seminum, *Br.*

BUTYL-CHLORAL HYDRAS. Br.

BUTYL-CHLORAL HYDRATE

(bū'tĭl-klō'răl hī'drăs)

"Butyl-Chloral Hydrate, or trichlorbutylidene glycol, $C_4H_7Cl_3O_2$, is a crystalline hydrate obtained by adding water to the liquid butyl-chloral produced by the action of chlorine gas on aldehyde." *Br.*

Butylchloralum Hydratum, Chloralhydratum Butyli; Trichlorbutylidene Glycol; Hydrous Butyl Chloral; Croton Chloral Hydrate (wrongly so called); Chloralum Butyli Hydratum; Butyl Chloralhydrate; Hydrate de Chloral Butylique, *Fr.*; Butylchloralhydrat, Trichlorbutylaldehydhydrat, *G.*

This substance was discovered by Krämer and Pinner, of Berlin, during an examination of the accumulated by-products of the chloral factory of Schering. It was named croton-chloral hydrate because it was believed to bear a relationship to crotonic acid, the peculiar acid of croton oil; this was subsequently disproved by Pinner, who showed that it belonged to the butyl series. (*Ber. d. Chem. Ges.,* vii, 1321, 1561.) It is made by passing dry chlorine through aldehyde cooled to –10° C. (14° F.), in an apparatus similar to that used in making chloral. Fractional distillation is resorted to, and the product boiling between 163° C. (325.4° F.) and 165° C. (329° F.) is reserved; this is butyl-chloral, a colorless oily fluid. The necessary amount of water is added, and butyl-chloral hydrate is obtained.

Properties.—Butyl-chloral hydrate occurs in the form of crystalline, micaceous scales of a pungent odor, sparingly soluble in water, freely soluble in alcohol, hot water, and glycerin, but insoluble, or nearly so, in chloroform, a property which may be employed to separate it from ordinary hydrated chloral. When treated with caustic alkalies it is converted into formic acid, potassium chloride, and allylene dichloride, $C_3H_4Cl_2$. The British Pharmacopœia describes it as "pearly-white, trimetric laminæ. Odor pungent but not acrid; taste acrid and nauseous. Melts at about 78° C. (172.4° F.) to a transparent liquid, which, on cooling, begins to solidify at about 71° C. (159.8° F.). Soluble in about 40 parts of *water,* and in less than 1 part of *glycerin* or of *alcohol* (90 per cent.). The aqueous solution is neutral or but slightly acid to *litmus.* When 0.5 gramme is gently warmed for a short time with 10 millilitres of *solution of sodium hydroxide,* 3 drops of *aniline* added and the mixture well shaken and heated to boiling, no odor of phenyl iso-cyanide is perceptible (absence of chloral hydrate)." *Br.*

Uses.—Butyl-chloral hydrate was proposed by Liebreich, in 1870, as a remedy in the treatment of *trigeminal neuralgia.* He states that a drachm (3.9 Gm.) of it causes deep sleep, accompanied by anesthesia of the head, with complete loss of irritability of the eyeball and of the trigeminal nerve. The circulation is kept up with great tenacity, and, if the dose has been large enough, death results from the arrest of respiration. These statements of Liebreich were contradicted by the research of J. von Mering and of H. W. Schmidt, who found that no anesthesia was produced unless sufficient doses were given to cause complete narcosis, and that the general course of the symptoms caused by the butyl-chloral hydrate was exactly parallel to that of those produced by hydrated chloral. But a number of observers have used butyl-chloral hydrate with asserted good results in *tic douloureux.* The relief obtained is, unfortunately, only temporary and palliative. The drug has been commonly administered in doses of from 5 to 20 grains (0.32–1.3 Gm.) in syrup. The safer plan is to give 5 grains (0.32 Gm.) every half hour until 30 grains (2.0 Gm.) have been taken or relief afforded. The original formula of Liebreich was: butyl-chloral hydrate 5 to 10 parts, glycerin 20 parts, distilled water 130 parts. Dose, half a fluidounce (15 mils), followed in five minutes by a second dose, ten minutes later by a third dose, unless relief is afforded. That such medication is safe is not certain. For experiments in making and dispensing solutions of butyl-chloral hydrate, see *Proc. A. Ph. A.,* 1894, 578.

Dose, of British Pharmacopœia, from five to twenty grains (0.32–1.3 Gm.).

CAFFEINA. U. S., Br.

CAFFEINE Caffein. [Theine]

(căf-fe-ĭ'nă)

"A feebly basic substance [$C_8H_{10}O_2N_4 + H_2O$ or $C_5H(CH_3)_3O_2N_4 + H_2O = 212.14$] obtained from the leaves of *Thea sinensis* Linné (Fam. *Ternstræmiaceæ*), or from the seeds of *Coffea arabica* Linné (Fam. *Rubiaceæ*); also occurring in some other plants; or prepared synthetically." *U. S.* "Caffeine, $C_8H_{10}N_4O_2,H_2O$, is an alkaloid obtained from the dried leaves of Camellia Thea, *Link,* or from certain other plants." *Br.*

Trimethyl-xanthine, Methyl-theobromine; Caffeia, Theina, Guaranina, Caféine, *Fr. Cod.;* Coffeïnum, *P. G.;* Koffein, Kaffein, Thein, *G.;* Caffeina, *It.;* Cafeina, *Sp.*

Caffeine (*Caffeia*) was first discovered by Runge, and afterwards by Pelletier, Caventou and Robiquet. Strecker first proved it to be methyl-theobromine by making it from theobromine synthetically. (*Ann. Ch. Ph.,* 118, 170.) It is now recognized as an immediate derivative of xanthine, $C_5H_4N_4O_2$, being the trimethyl-derivative of the same, and it belongs to the purine group, of which xanthine is the dioxy-derivative. Emil Fischer has accomplished the conversion of uric acid, $C_5H_4N_4O_3$, into xanthine, and this into caffeine. The United States Pharmacopœia allows caffeine to be prepared from either one of the ordinary commercial sources, but because tea leaves contain a much larger percentage of the alkaloid than does the coffee berry, and are frequently thrown into commerce in a damaged condition, unfit for use as a beverage, commercial caffeine is almost always prepared from them. Mays (*M. News,* xlviii) asserted that theine differed from caffeine in being a local anesthetic, but his views have not received general acceptance. Dunstan and Shepheard (*J. Chem. S.,* 1893, 195) reviewed the question of the identity of caffeine and theine with great care, and established the complete chemical identity of the two by a study of a number of derivatives.

Caffeine may be made as follows: Exhaust bruised coffee by two successive portions of boiling water, unite the infusions, add lead acetate in order to precipitate various principles accompanying the caffeine, filter, decompose the excess of lead acetate in the filtered liquor by hydrogen sulphide, concentrate by evaporation, and neutralize with ammonia. The caffeine is deposited in crystals upon cooling, and may be purified by redissolving in water, treating with animal charcoal, and evaporating. H. Leuchsenring obtains caffeine by availing himself of its property of subliming unchanged by heat. He precipitates a concentrated decoction of coffee by a weak solution of lead acetate, filters, evaporates to dryness, mixes the residue with sand, and sublimes as in Mohr's process for procuring benzoic acid. (*A. J. P.,* xxxii, 25.) Still another method, proposed by Vogel, is to treat coffee, ground to powder, with petroleum benzin, which dissolves the caffeine and an oily substance, separate the petroleum benzin by distillation and treat the residue with boiling water, which dissolves the caffeine, and deposits it in a crystalline form, after filtration and concentration. (*J. P. C.,* 3e sér., xxxv, 436.) Paul and Cownley's process for estimating the caffeine in coffee is to mix finely powdered coffee with moist lime, and exhaust with alcohol by hot repercolation. The alcohol is evaporated off, and the residue mixed with water and a few drops of diluted sulphuric acid; the mixture is filtered, and the filtrate and washings, when cool, treated with chloroform to wash out the alkaloid; the chloroformic solution is evaporated in a tared dish, and the residue weighed as caffeine. (*P. J.,* 1887, p. 565.) Petit and Terrat subsequently found that the presence of lime or magnesia retards the extraction of the caffeine; they recommend direct extraction by chloroform containing a trace of water. (*J. P. C.,* 1896, 529.) For another method, by E. D. Smith, see *Ph. Era,* 1887, 17; see also *A. J. P.,* 1892, 468, and 1893, 338; *J. P. C.,* 1893, 545; *Ap. Ztg.,* 1893, 132; *C. D.,* 1893, 210; *Ph. Era,* 1897, 391.

Caffeine is prepared on a considerable scale from damaged tea. The tea is exhausted with boiling water, the decoction boiled with litharge

or lead acetate, and the filtered solution evaporated till the alkaloid crystallizes out on cooling. The product can be purified by resublimation or by crystallization from hot water. (Allen, *Com. Org. Anal.*, 2d ed., vol. iii, part ii, 474.)

Properties.—Caffeine is a feeble base, capable of forming definite compounds with mineral acids but not with organic acids; the latter, however, increase its solubility in water and other liquids. (See *Caffeina Citrata.*) Caffeine is "in white, flexible, silky, glistening needles, usually matted together in fleecy masses; odorless, and having a bitter taste; efflorescent in dry air. One Gm. of Caffeine dissolves in 46 mils of water, 66 mils of alcohol, 5.5 mils of chloroform and in 530 mils of ether at 25° C. (77° F.); also in 5.5 mils of water at 80° C. (176° F.), and in 22 mils of alcohol at 60° C. (140° F.). A saturated aqueous solution of Caffeine is neutral to litmus. Caffeine, rendered anhydrous, melts between 235° and 237° C. (455°–458.6° F.). Dissolve about 0.01 Gm. of Caffeine in 1 mil of hydrochloric acid in a porcelain dish, add 0.1 Gm. of potassium chlorate and evaporate the solution to dryness on a water bath. Invert the dish over a vessel containing a few drops of ammonia water; the residue acquires a purple color, which is destroyed by fixed alkalies. An aqueous solution of Caffeine yields a precipitate with tannic acid T.S., soluble in an excess of the reagent. Caffeine loses not more than 9 per cent. of its weight when dried to constant weight at 80° C. (176° F.). Incinerate about 2 Gm. of Caffeine; not more than 0.05 per cent. of ash remains. About 0.5 Gm. of Caffeine dissolves in 5 mils of sulphuric or nitric acid without producing more than a faint, yellowish color (*organic impurities*). Its aqueous solution is not precipitated by mercuric potassium iodide T.S. (*alkaloids*)." *U. S.*

The Br. Ph. describes it as "colorless, silky, acicular, inodorous crystals. Soluble in 80 parts of *water*, somewhat more soluble in *alcohol* (90 per cent.), readily soluble in *chloroform*, sparingly in *ether*. Melting point 235° C. (455° F.). Aqueous solution neutral to *litmus* and faintly bitter. Loses part of its water of crystallization on exposure to the air. Loss when dried at 100° C. (212° F.) not more than 8.5 per cent.; the dry alkaloid begins to volatilise at a slightly higher temperature and sublimes readily at about 180° C. (356° F.).) A cold saturated aqueous solution is not precipitated by *N/10 solution of iodine*, or by *solution of potassio-mercuric iodide*, but gives a white precipitate with *solution of tannic acid*, soluble in excess of the reagent. 0.1 gramme dissolves without color in 1 millilitre of *sulphuric acid*, and also in 1 millilitre of *nitric acid*. When treated with a crystal of *potassium chlorate* and a few drops of *hydrochloric acid*, the mixture being evaporated to dryness in a porcelain dish, a reddish residue remains which becomes purple when exposed to the vapor of *solution of ammonia*." *Br.*

The apparent difference in solubilities of caffeine between the U. S. and British Pharmacopœias is due to the fact that the standard temperature of the U. S. is 25° C. (77° F.), and of the British 15.5° C. (60° F.). The U. S. solubilities are based upon the studies of Seidell (*J. Am. C. S.*, 1907, xxix, p. 1091).

Tanret proposes to increase the solubility of caffeine by adding definite proportions of sodium benzoate, cinnamate or salicylate, which form with it compounds rich in alkaloid (45.8, 58.9, and 61 per cent., respectively). These are well adapted for hypodermic administration as they are all freely soluble in water. The proportions recommended are as follows: *caffeine-sodium benzoate* (caffeine, 244, sodium benzoate, 288); *caffeine-sodium cinnamate* (caffeine, 244, sodium cinnamate, 170); *caffeine-sodium salicylate* (caffeine, 244, sodium salicylate, 160). (*L'Union Pharm.*, xxxvii, 394.) Caffeine is remarkable for containing a larger proportion of nitrogen than does almost any other proximate vegetable principle, in this respect equalling some of the highly animalized products. A new method of determining caffeine in either raw or roasted coffee, suggested by Fendler and Stüber (*Z. Nahr. Genuss.*, 1914, H. 1), gives a very white and pure alkaloid. The method is as follows: The coffee is first extracted with chloroform and ammonia. The residue from the chloroformic filtrate is taken up in hot water and treated with a solution of potassium permanganate in excess and the excess of manganese removed by adding a little solution of hydrogen dioxide, acidulated with acetic acid. After filtration the aqueous liquid is rendered alkaline and extracted with chloroform and the residue dried at 100° C. (212° F.) to constant weight.

Uses.—There have been a few cases of poisoning by caffeine; a drachm of citrated caffeine swallowed by an adult was followed by burning in the throat, giddiness, faintness, nausea, tremor of the extremities, abdominal pain, mental distress, great cardiac oppression and finally collapse. Consciousness was not impaired and there was no headache until the patient began to recover. A decoction of 8 ounces of freshly roasted coffee, taken for the purpose of producing abortion, caused pronounced choreic tremors, great restlessness, quickened respiration, and rapid pulse, with very strong, even violent, heart beats. In doses of 3 to 5 grains caffeine produces in the healthy individual a peculiar wakefulness, with stimulation of the cerebrum, and some increase of the urinary secretion and force of the pulse. There is usually marked increase of the mental activity and of the capability for sustaining mental work. About two hours after the ingestion of 12 grains by Pratt, there were intense physical restlessness and mental anxiety, with obstinate sleeplessness, active and persistent thinking, general muscular tremulousness, and frequent urination.

Given in large dose to the lower animals, caffeine produces hurried respiration, restlessness,

slightly lowered, followed by markedly elevated, temperature, tetanic and clonic convulsions, progressive paralysis, and finally death from paralytic arrest of respiration. The cause of the convulsions in mammals is not determined, but in the frog they are of spinal origin, for both Pratt and Le Blond have found that cutting of the cord does not arrest them below the point of section, while destruction of the cord (Pratt and Leven) prevents their development. It would appear, therefore, that caffeine acts upon the frog as a stimulant to the motor side of the spinal cord and a similar effect has been demonstrated in the human being by H. C. Wood, Jr. (*T. G.*, Jan., 1912.) In moderate doses, caffeine exercises a marked stimulating influence upon the muscle, increasing not only the irritability and contractile power of the muscle, but also the resistance to fatigue. When the drug is applied locally, in concentrated solution, it produces death of the muscle, with a condition simulating that of rigor mortis. In certain species of frogs a generalized rigidity of the muscles can be caused by the hypodermic administration of the drug, but it is improbable that sufficiently large quantities could be introduced into the system of any warm blooded animal to exercise this effect.

The effect of caffeine upon the circulation is less powerful than has been believed in the past. After moderate doses, there is generally, although not always, a slight rise in the blood pressure, with usually some slowing of the pulse. The rise in the blood pressure, as has been demonstrated by Sollmann and Pilcher (*J. P. Ex. T.*, 1911, iii, p. 19), is due solely to an increase in the vigor of the contraction of the heart, the blood vessels being usually somewhat dilated. After large doses the pulse becomes extremely rapid, apparently through a direct action upon the muscle of the heart, and the blood pressure shows a tendency to fall. The drop in the blood pressure after these large quantities appears to be due both to a widening of the vessels, and a diminution of the amplitude of the cardiac contractions.

In sufficient quantities, caffeine produces a very marked increase in the quantity of urine. Although the increase is more marked in the watery constituents, and the percentage of solid matter falls, the total quantity of solids eliminated in a given time is somewhat increased. The diuresis is accompanied with a marked widening of the renal vessels. This increase in the flow of urine appears to be due to a direct action on the renal epithelium, for Richards and Plant have shown (*J. P. Ex. T.*, 1915, vii, 485) that diuresis can be caused in the artificially perfused kidney without any acceleration of the blood flow.

The early belief that caffeine exercised some influence upon metabolism and the output of nitrogen has been entirely disproven. The only change in the amount or character of nitrogenous material in the urine is that which is due to the presence of caffeine itself, or its various decomposition products. Caffeine undergoes demethylization in the body, appearing in the urine as a dimethyl- or monomethyl-xanthine. If the dose is small this reduction is complete, but after large quantities some of the drug may escape unaltered.

The dominant action of caffeine in the human being is upon the cerebrum. The experiments of Hollingworth (*T. G.*, Jan., 1912) have demonstrated that in those forms of psychological tests which involve purely intellectual processes there is a distinct increase in the rapidity and accuracy, an observation which is in entire harmony with the daily experience of millions of men. Not only is the mental activity temporarily stimulated, but the capability for prolonged work is also increased. After large quantities, this cerebral excitation shows itself in nervous restlessness, and a tendency to insomnia.

Although widely employed as a mental stimulant in daily life, caffeine is rarely used medically for this purpose, unless it be that its value in certain types of *headache* is associated with its action upon the cerebrum. Its most important medical uses are as a diuretic, and as a cardiac and respiratory stimulant.

As a diuretic, caffeine is of service, especially in the treatment of *dropsies*. When the dropsy is due to *nephritis* it must be used with some caution because of the possibility of an irritating action upon the diseased kidneys. Its value as a diuretic is lessened by its tendency to produce wakefulness, and because of this objection it has largely been displaced by the closely allied drugs, theobromine and theophylline. It is generally advisable, if using caffeine freely, not to administer the remedy in the latter part of the day.

As a circulatory stimulant, caffeine is of little value as a cardiac tonic in cases of chronic *heart disease*, but finds its chief application in more or less acute *heart failure*, whether occurring during the course of a chronic cardiac condition, or as the result of the ingestion of the depressant *poisons*. In *surgical shock* the fact that it does not stimulate the vasomotor mechanism—which is generally believed to be the essential factor in these cases—makes it a remedy of only secondary value.

As a stimulant of the respiration it is a remedy of much usefulness, especially when used in connection with other agents of this class. It is more especially employed in cases of *narcotic poisoning*, such as morphine or chloral, in which it is useful, not only because of its direct action upon the respiratory center, but also because it counteracts, to some degree, the tendency to sleep.

Dose, one to five grains (0.065–0.32 Gm.).

Off. Prep.—Caffeina Citrata, *U. S.* (*Br.*); Caffeinæ Citras Effervescens (from Citrated Caffeine), *U. S.*; Pulvis Acetanilidi Compositus, *N. F.*; Caffeinæ Sodio-Benzoas, *U. S.*; Caffeinæ Sodio-Salicylas, *N. F.*; Sal Potassii Bromidi Effervescens Compositus, *N. F.*

CAFFEINA CITRATA. U. S. (Br.)

CITRATED CAFFEINE Caffein. Cit.

[Caffeine Citrate]

(căf-fe-ĭ'nă cĭ-trā'tă)

"Citrated Caffeine contains, when dried to constant weight at 80° C. (176° F.), not less than 48 per cent. of anhydrous caffeine [$C_8H_{10}O_2N_4 = 194.12$]." *U. S.* "Caffeine Citrate, $C_8H_{10}N_4O_2,C_6H_8O_7$, is an unstable compound of Caffeine and Citric Acid." *Br.*

Caffeinæ Citras, *Br.*; Citrate de Caféine, *Fr.*; Koffeïncitrat, Citronensaures Koffeïn, *G.*; Citrato cafeico, *Sp.*

* "Caffeine, *fifty grammes* [or 1 ounce av., 334 grains]; Citric Acid, *fifty grammes* [or 1 ounce av., 334 grains]; Distilled Water, hot, *one hundred mils* [or 3 fluidounces, 183 minims]. Dissolve the Citric Acid in the hot Distilled Water, add the Caffeine, and evaporate the resulting solution to dryness on a water-bath, constantly stirring toward the end of the operation. Reduce the product to a fine powder and transfer it to well-closed containers." *U. S.*

"Caffeine, 100 grammes; Citric Acid, in powder, 100 grammes; Distilled Water, 16 millilitres. Mix the Caffeine with the Citric Acid, moisten the mixture with the Distilled Water, and dry on a water-bath with constant stirring." *Br.*

In this preparation Merson (*P. J.*, 1904, 8) prefers to mix the caffeine with the citric acid without the aid of a liquid; he uses a sieve, water bath, and granulating tray, and asserts that the process yields a superior product. It is not regarded by chemists as a chemical salt, but as a mechanical mixture of the two substances composing it. The British Pharmacopœia gives the following as its chemical formula: $C_8H_{10}N_4O_2,C_6H_8O_7$.

It is described by the U. S. Pharm. as "a white powder, odorless and having a slightly bitter, acid taste. Citrated Caffeine gives a clear, syrupy solution with a small quantity of water, but caffeine precipitates on dilution. This precipitate redissolves on the further addition of water. Its aqueous solution (1 in 30) is acid to litmus. Dissolve about 0.02 Gm. of Citrated Caffeine in 1 mil of hydrochloric acid in a porcelain dish, add 0.1 Gm. of potassium chlorate, evaporate the mixture on a water bath and invert the dish over a vessel containing a few drops of ammonia water; the residue acquires a purple color, which is destroyed by alkalies. About 2 mils of a filtered aqueous solution of Citrated Caffeine (1 in 10) mixed with 50 mils of lime water remains clear in the cold, but becomes turbid when heated to boiling. When dried to constant weight at 80° C. (176° F.) it loses not more than 5 per cent. of its weight. Incinerate about 1 Gm. of Citrated Caffeine; not more than 0.1 per cent. of ash remains. Heat a mixture of 0.25 Gm. of Citrated Caffeine and 5 mils of sulphuric acid in a porcelain dish on a water bath for fifteen minutes, protecting it from dust; it may become yellow in color but not brown or black (*tartaric acid*). An aqueous solution of Citrated Caffeine does not respond to the Test for heavy metals (see Part III, Test No. 3). The addition of a few drops of barium chloride T.S. to 10 mils of an aqueous solution of Citrated Caffeine (1 in 100), previously treated with a few drops of hydrochloric acid, produces no turbidity (*sulphuric acid*).

"**Assay.**—Dissolve about 0.5 Gm. of Citrated Caffeine, previously dried to constant weight at 80° C. (176° F.) and accurately weighed, in 10 mils of hot distilled water, add an excess of sodium hydroxide T.S., cool the solution, and shake it in a separator with three successive portions of 20 mils, 10 mils, and 5 mils, respectively, of chloroform, or more if necessary to complete the extraction. Evaporate the combined chloroform solutions on a water bath and dry the residue to constant weight at 80° C. (176° F.). The weight of anhydrous caffeine ($C_8H_{10}O_2N_4$) so obtained corresponds to not less than 48 per cent. of the weight of Citrated Caffeine taken. This residue, when recrystallized from hot water, and dried to constant weight at 80° C. (176° F.), has the melting point given under *Caffeina.*" *U. S.*

The British Pharm. describes it as "a white powder with an acid reaction. Inodorous; taste acid and faintly bitter. Soluble in 4 parts of hot *water,* but dissociating on the further addition of *water* with separation of caffeine, which completely redissolves in 32 parts of *water.* Loses not more than 1 per cent. of its weight when dried at 100° C. (212° F.). When 1 gramme is dissolved in hot *water,* the solution made alkaline with *solution of sodium hydroxide* and shaken with three successive portions, each of 10 millilitres, of *chloroform,* the mixed chloroformic solutions, washed with a little *water,* leave on evaporation a residue weighing not less than 0.45 gramme, and responding to the test with *potassium chlorate* and *hydrochloric acid* described under 'Caffeina.' Caffeine Citrate yields the *reactions* characteristic of citrates." *Br.*

Uses.—Citrated caffeine is possessed of the physiological and therapeutic properties of caffeine, but is more liable to disagree with the digestive functions.

Dose, from three to eight grains (0.2–0.5 Gm.).

Off. Prep.—Caffeina Citrata Effervescens, *U. S.* (*Br.*).

CAFFEINA CITRATA EFFERVESCENS. U. S. (Br.)

EFFERVESCENT CITRATED CAFFEINE Caff. Cit. Eff.

(căf-fe-ĭ'nă cĭ-trā'tă ĕf-fẽr-vĕs'cens)

"It contains not less than 1.9 per cent. of anhydrous caffeine [$C_8H_{10}O_2N_4 = 194.12$]." *U. S.*

Caffeinæ Citras Effervescens, *Br.*; Effervescent Caffeine Citrate; Coffeïnum Citricum Effervescens; Brausendes Koffeïncitrat, *G.*

* "Citrated Caffeine, *forty grammes* [or 1 ounce av., 180 grains]; Sodium Bicarbonate,

dried and powdered, *five hundred and seventy grammes* [or 20 ounces av., 46 grains]; Tartaric Acid, dried and powdered, *three hundred grammes* [or 10 ounces av., 255 grains]; Citric Acid, unefflouresced crystals, *one hundred and ninety-five grammes* [or 6 ounces av., 384 grains], to make about *one thousand grammes* [or 35 ounces av., 120 grains]. Powder the citric acid and mix it intimately with the citrated caffeine and tartaric acid, then thoroughly incorporate the sodium bicarbonate. Place the mixed powders on a plate of glass or in a suitable dish in an oven heated to between 93° and 104° C. (199.4°–219.2° F.). Manipulate the mixture carefully with a wooden spatula, and, when it has become moist, rub it through a No. 6 tinned-iron sieve, and dry the granules at a temperature not exceeding 54° C. (129.2° F.). Immediately transfer the product to suitable containers, and seal them tightly. Care must be used to prevent the preparation from coming in contact with air containing moisture." *U. S.*

"Assay.—Dissolve about 5 Gm. of Effervescent Citrated Caffeine, accurately weighed, in 10 mils of hot distilled water. When effervescence has ceased, add an excess of sodium hydroxide T.S., cool the mixture and shake it in a separator with three successive portions of 20 mils, 10 mils, and 5 mils, respectively, of chloroform, or more if necessary to complete the extraction. Evaporate the combined chloroform solutions on a water bath and dry the residue to constant weight at 80° C. (176° F.). The weight of anhydrous caffeine ($C_8H_{10}O_2N_4$) so obtained corresponds to not less than 1.9 per cent. of the weight of Effervescent Citrated Caffeine taken. This residue, when recrystallized from hot water, responds to the tests for identity and, when dried to constant weight at 80° C. (176° F.), has the melting point given under *Caffeina*." *U. S.*

"Sodium Bicarbonate, in powder, 510 grammes; Tartaric Acid, in powder, 270 grammes; Citric Acid, in powder, 180 grammes; Refined Sugar, in powder, 140 grammes; Caffeine Citrate, 40 grammes. Mix the Caffeine Citrate, Tartaric Acid, and Citric Acid; with this mixture thoroughly incorporate the mixed Sodium Bicarbonate and Refined Sugar; place in a dish or pan of suitable form heated to between 90° and 105° C. (194–221° F.). When the mixture, by aid of careful manipulation, has assumed a granular character, separate it into granules of uniform and convenient size by means of suitable sieves. Dry the granules at a temperature not exceeding 55° C. (131° F.). The product weighs about one thousand grammes." *Br.*

This compound contains about two per cent. of caffeine; the proportion was about one per cent. in the U. S. P., 1890. The old expensive process in which alcohol was used to make the mass, was abandoned, the amount of water of crystallization liberated from the citric acid on decomposition proving sufficient to moisten the mass; this effects a saving in the expense of manufacturing, while the use of heat with skilful manipulation has been found to produce equally good results. The U. S. product differs from that of the British Pharmacopœia in containing no sugar. Samples of effervescent citrated caffeine have been found in the market very deficient in caffeine; the sweetening is sometimes effected by the use of saccharin instead of sugar. The powder affords an agreeable method of administering citrated caffeine.

Dose, one to two drachms (3.9–7.5 Gm.) in water, to be taken during effervescence.

CAFFEINÆ SODIO-BENZOAS. U. S.

CAFFEINE SODIO-BENZOATE Caff. Sod. Benz.

(kăf-fe-ĭ'næ sō'dĭ-ō bĕn'zo-ăs)

"A mixture of caffeine and sodium benzoate. It contains, when dried to constant weight at 80° C. (176° F.), not less than 46 per cent. nor more than 50 per cent. of anhydrous caffeine [$C_8H_{10}O_2N_4 = 194.12$], the remainder being sodium benzoate [$NaC_7H_5O_2 = 144.04$]. Preserve it in well-closed containers." *U. S.*

This caffeine compound was introduced for the first time into the U. S. P. IX. It is a mixture and not a definite chemical salt. It is made by dissolving 50 Gm. each of caffeine and sodium benzoate in 100 mils of water and evaporating the solution on a water bath to dryness.

It is official in the Austrian and Hungarian Pharmacopœias, and also in the Danish, Japanese, Swiss, Dutch, and Italian Pharmacopœias. It is officially described as "a white powder; it is odorless and has a slightly bitter taste. One Gm. of Caffeine Sodio-Benzoate dissolves in 1.1 mils of water, some caffeine separating on standing, and in 30 mils of alcohol, at 25° C. (77° F.); partly soluble in chloroform. An aqueous solution (1 in 20) may be neutral, slightly acid, or slightly alkaline to litmus, but is not reddened by phenolphthalein T.S. On heating the compound, it is decomposed with the evolution of white vapors, leaving a carbonaceous residue which effervesces with acids and colors a non-luminous flame intensely yellow. Ferric chloride T.S produces a salmon-colored precipitate in an aqueous solution of the compound. The addition of diluted hydrochloric acid produces a white precipitate of benzoic acid. About 0.1 Gm. of Caffeine Sodio-Benzoate dissolves in 2 mils of sulphuric acid without producing more than a slight, yellow color (*readily carbonizable organic matter*). An aqueous solution (1 in 50), acidulated with hydrochloric acid and filtered, does not respond to the Test for heavy metals (see Part III, Test No. 3). When dried to constant weight at 80° C. (176° F.), it loses not more than 5 per cent. of its weight.

"**Assay for Caffeine.**—Dissolve about 1 Gm. of Caffeine Sodio-Benzoate, previously dried to constant weight at 80° C. (176° F.), and accurately weighed, in 5 mils of distilled water in a separator, add 5 mils of sodium hydroxide T.S.

and shake the mixture with four successive portions of 20 mils, 10 mils, 10 mils, and 5 mils, respectively, of chloroform. Evaporate the combined chloroform solutions on a water bath and dry the residue to constant weight at 80° C. (176° F.). The weight of anhydrous caffeine ($C_8H_{10}O_2N_4$) so obtained corresponds to not less than 46 per cent. nor more than 50 per cent. of the weight of dried Caffeine Sodio-Benzoate taken. This residue, when recrystallized from hot water, responds to the tests of identity and, when dried to constant weight at 80° C. (176° F.) has the melting point given under *Caffeina*.

" Assay for Sodium Benzoate.—When dried to constant weight at 80° C. (176° F.) and estimated as directed under the Assay for alkali salts of organic acids (see Part III, Test No. 6) it shows, in the dried mixture, not less than 50 per cent. nor more than 54 per cent. of sodium benzoate ($NaC_7H_5O_2$)." *U. S.*

Uses.—This compound has the physiological effects and therapeutic uses of caffeine. It has the advantage over the alkaloid of being freely soluble in water, and over the citrated caffeine of being less irritant to the stomach; whenever it is desired to exhibit caffeine in solution the preference should be given to caffeine and sodium benzoate. It is especially suitable for hypodermic administration for which purpose it may be dissolved in three parts of water and from ten to twenty minims (0.6–1.3 mils) of this solution injected at a dose.

Dose, three to ten grains (0.2–0.6 Gm.).

CALCII BROMIDUM. U. S.

CALCIUM BROMIDE Calc. Brom.

(kăl'cĭ-ī brō'mĭ-dŭm)

"A hydrated form of Calcium Bromide containing not less than 84 per cent. of $CaBr_2$ (199.91). Preserve it in well-closed containers." *U. S.*

Calcium Bromatum, Bromure de Calcium, Bromure de Chaux, *Fr.*; Brom Kalk, Calciumbromid, *G.*

In the U. S. P. IX the hydrated form, 84 per cent. of $CaBr_2$, replaced the anhydrous form, 97 per cent. of the U. S. P. VIII. The former is believed to be more stable.

The process of Boedecker for its preparation consists in first forming a sulphur bromide, by the addition of 20 parts of the flowers of sulphur to 240 parts of bromine; this is added to a milk of lime containing 140 parts of fresh lime. Calcium bromide and sulphate are formed and are readily separated. (*J. P. C.*, 4e sér., viii, 463.) By the process of Jas. R. Mercein, five ounces of bromine and two and a half pints of water are put in a half-gallon specie jar, a stream of hydrogen sulphide passed through the bromine until it is all taken up, the liquid filtered, excess of hydrogen sulphide driven off by heat, and the solution of hydrobromic acid thus obtained distilled until four-fifths have passed over; the distillate is saturated with excess of precipitated calcium carbonate, filtered, and evaporated. (*A. J. P.*, xliv, 100.) Macdonald's method (*A. J. P.*, 1873) is as follows: Dissolve 4 ounces of ammonium bromide in a pint of water. Put into a flask and bring to the boiling point. Keep boiling, and add milk of lime (made from *pure* calcined lime) in small quantities, until ammoniacal vapors cease to be evolved. The operator can easily tell when this point has been reached, by the sense of smell. Filter the solution, evaporate to a syrupy consistency, remove from the fire, and stir until cold. Tasilly prepares *calcium oxybromide* by adding three parts of calcium oxide in small portions to a solution of one hundred parts of calcium bromide in seventy-five parts of hot water; acicular crystals of calcium oxybromide $CaBr_23CaO, 16H_2O$, are deposited on cooling the filtered solution.

Properties.—It is officially described in the United States Pharmacopœia IX as "white, granular salt; odorless, of a sharp, saline taste, and very deliquescent. One Gm. of Calcium Bromide dissolves in 0.7 mil of water and in 1.3 mils of alcohol at 25° C. (77° F.); also in 0.4 mil of boiling water; insoluble in chloroform or ether. An aqueous solution of the salt (1 in 20) is neutral or slightly alkaline to litmus. An aqueous solution of the salt (1 in 20) yields with ammonium oxalate T.S. a white precipitate, insoluble in acetic acid but soluble in hydrochloric acid. Silver nitrate T.S. added to an aqueous solution of the salt (1 in 20) produces a yellowish-white precipitate, insoluble in nitric acid or in a moderate excess of ammonia water. Add 1 mil of chloroform to 10 mils of an aqueous solution of the salt (1 in 20) and cautiously introduce chlorine water, which has been diluted with an equal volume of distilled water, drop by drop, with constant agitation. The liberated bromine dissolves in the chloroform and imparts to it a yellow to orange color, which is free from any violet tint (*iodide*). Drop 1 mil of diluted sulphuric acid upon about 1 Gm. of the powdered salt; no yellow color appears at once (*bromate*). Dissolve about 0.1 Gm. of the salt in 5 mils of distilled water, add an excess of silver nitrate T.S. and a few drops of nitric acid, filter, wash the precipitate with distilled water, digest it for ten minutes with 5 mils of ammonia carbonate T.S. and filter. On supersaturating the filtrate with nitric acid not more than a slight turbidity is produced at once (*chlorides*). Twenty mils of an aqueous solution (1 in 250) does not at once assume a blue color with potassium ferrocyanide T.S. (*iron*). Five mils of an aqueous solution (1 in 20), when acidulated with 1 drop of hydrochloric acid, shows no immediate turbidity with 1 mil of barium chloride T.S. (*sulphate*). Dissolve 1 Gm. of Calcium Bromide and 1 Gm. of sodium acetate in 5 mils of distilled water and render the solution slightly acid by the addition of a sufficient quantity (from 3 to 5 drops) of diluted acetic acid. After boiling and thoroughly cooling the solution, it does not become cloudy within five minutes after the addition, with agitation,

of 5 drops of potassium dichromate T.S. (*barium*). Precipitate the calcium completely from 10 mils of an aqueous solution of the salt (1 in 20) by adding ammonium oxalate T.S. and filtering. The filtrate on evaporation and ignition leaves not more than 0.004 Gm. of fixed residue (*magnesium and alkalies*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Proceed as directed under the Assay for bromides (see Part III, Test No. 5), using about 0.4 Gm. of Calcium Bromide, accurately weighed in a stoppered weighing-bottle. It shows not less than 84 per cent. of $CaBr_2$.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.0099955 Gm. of $CaBr_2$. Each gramme of Calcium Bromide corresponds to not less than 84.0 mils of tenth-normal silver nitrate." *U. S.*

Uses.—If the calcium salts have, as there is reason to believe, anticonvulsant properties (see under *Calcium Chloride*) then the combination in calcium bromide is a rational one. Its action upon the lower animals has been partially investigated by Guttmann (*P. M. T.*, iv, p. 361) who finds that it is a sedative to the nerve centers and does not depress the heart. It may be used in the place of the other bromides in the treatment of *epilepsy, tetany,* or *hysteria,* but is not largely employed. It is sometimes of service in *asthma.*

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Elixir Calcii Bromidi, *N. F.;* Syrupus Bromidorum, *N. F.*

CALCII CARBONAS PRÆCIPITATUS.
U. S., Br.

PRECIPITATED CALCIUM CARBONATE Calc. Carb. Præc. [Precipitated Chalk]

(kăl'cĭ-ī kär'bo-năs præ-cĭp-ĭ-tā'tŭs)

"It contains, when dried to constant weight at 200° C. (392° F.). not less than 98 per cent. of $CaCO_3$ (100.07)." *U. S.* "Precipitated Calcium Carbonate, $CaCO_3$, is obtained by the interaction of calcium chloride and sodium carbonate." *Br.*

Carbonas Calcicus Præcipitatus, Creta Præcipitata, Calcaria Carbonica Præcipitata; Precipitated Carbonate of Lime; Carbonate de Chaux Precipité, *Fr. Cod.;* Craie Precipitée, *Fr.;* Calcium carbonicum præcipitatum, *P. G.;* Calciumcarbonat; Präcipitirter kohlensaure Kalkerde, *G.;* Carbonato di calcio precipitato, *It.;* Carbonato de cal, *Sp.*

This salt may be made by the process of the U. S. P., 1870. It is as follows: "Take of Solution of Chloride of Calcium *five pints and a half;* Carbonate of Sodium *seventy-two troy-ounces;* Distilled Water *a sufficient quantity.* Dissolve the Carbonate of Sodium in six pints of Distilled Water. Heat this solution and the Solution of Chloride of Calcium, separately, to the boiling point, and mix them. After the precipitate has subsided, separate it from the supernatant liquid by decantation, and wash it with boiling Distilled Water until the washings cease to be affected by a solution of nitrate of silver. Lastly, dry the precipitate on bibulous paper."

A mutual interchange of elements takes place, resulting in the production of sodium chloride which remains in solution, and calcium carbonate which is deposited,

$$CaCl_2 + Na_2CO_3 = CaCO_3 + 2NaCl$$

Any peculiar advantage of the preparation must depend on the minute division of its particles. According to Bridges, this effect is best obtained by employing the solutions at the boiling temperature, a precaution which is observed in most processes. "Precipitated Calcium Carbonate is a fine, white, micro-crystalline powder, without odor or taste, and permanent in the air. Precipitated Calcium Carbonate is nearly insoluble in water; the solubility is increased by the presence of ammonium salts and especially by carbon dioxide; alkali hydroxides diminish its solubility; insoluble in alcohol; dissolved with effervescence by diluted acetic, hydrochloric, or nitric acid. When heated to full redness, the salt gradually loses carbon dioxide, and a residue of calcium oxide remains. For applying tests of identity and purity, mix 1 Gm. of Calcium Carbonate with 50 mils of distilled water, and add hydrochloric acid, drop by drop, with agitation, until solution takes place. The resulting solution, after boiling and cooling, should be acid, and should not impart a green or crimson color to a non-luminous flame, nor leave more than 0.002 Gm. of insoluble matter. Neutralize a portion of this acid solution with ammonia water, and add ammonium oxalate T.S.; a white precipitate is produced which is insoluble in acetic acid, but soluble in hydrochloric acid. Another portion of the solution, as prepared above does not respond to the Test for heavy metals (see Part III, Test No. 3). Agitate 1 Gm. of the salt with 50 mils of distilled water, which has previously been boiled and cooled, and then filter; the filtrate is not alkaline to litmus, and, on evaporation, leaves not more than 0.005 Gm. of residue (*soluble impurities*)." *U. S.*

"A white microcrystalline powder insoluble in *water.* Yields the *reactions* characteristic of calcium and of carbonates. Yields no characteristic *reactions* for iron, aluminium, phosphates, or sulphates, and not more than the slightest *reactions* for magnesium or chlorides. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Assay.—"Dissolve about 0.3 to 0.4 Gm. of Calcium Carbonate, previously dried to constant weight at 200° C. (392° F.), and accurately weighed, in 10 mils of distilled water and 10 mils of diluted hydrochloric acid and boil the solution to expel all carbon dioxide. Transfer this solution to a 200 mil graduated flask, add 100 mils of tenth-normal oxalic acid V.S., render it alkaline with ammonia water, shake the mixture well and allow to stand for three hours at from 60° to 70° C. (140°–158° F.) or over night at room temperature. Cool the liquid if necessary, fill the flask with distilled water to the

mark, mix it well, filter through a dry filter into a dry flask, reject the first 20 mils of the filtrate, and proceed as follows: Add diluted sulphuric acid to 100 mils of the filtrate (representing one-half of the Calcium Carbonate taken) until of acid reaction, then add 25 mils more of the diluted sulphuric acid, warm the solution to from 60° to 70° C. (140°–158° F.), and titrate with tenth-normal potassium permanganate V.S. It shows, in the dried salt, not less than 98 per cent. of $CaCO_3$.

"Each mil of tenth-normal oxalic acid V.S. used corresponds to 0.0050035 Gm. of $CaCO_3$. Each gramme of dried Calcium Carbonate corresponds to not less than 195.9 mils of tenth-normal oxalic acid V.S." *U. S.*

Uses.—For ordinary purposes, it probably has no such superiority over prepared chalk as to counterbalance its greater expensiveness, but it is preferred by some in the preparation of tooth powders.

Dose, from ten to forty grains (0.65–2.6 Gm.).

Off. Prep.—Trochiscus Bismuthi Compositus, *Br.*

CALCII CHLORIDUM. U. S., Br.

CALCIUM CHLORIDE Calc. Chlor.

(kăl'cĭ-ĭ ghlō'rĭ-dŭm)

"A hydrated form of Calcium Chloride containing not less than 75 per cent. of $CaCl_2$ (110.99). Preserve it in well-stoppered bottles." *U. S.* "Calcium Chloride, $CaCl_2$, may be obtained by neutralising hydrochloric acid with calcium carbonate, and carefully desiccating at a temperature not exceeding 200° C. (392° F.)." *Br.*

Calcium Chloratum; Calcaria Muriatica, Chloridum Calcium; Muriate of Lime, Hydrochlorate of Lime; Chlorure de Calcium Fondu, Hydrochlorate de Chaux, *Fr.*; Chlorcalcium, Calciumchlorid, Salzsaures Kalk, *G.*; Cloruro di calcio, *It.*; Cloruro calcico, *Sp.*

The hydrated form of this salt has replaced the fused calcium chloride which was formerly official. Anhydrous calcium chloride may be readily formed by saturating hydrochloric acid with chalk or marble, evaporating to dryness, and heating to redness. The hydrochloric acid, by reacting with the calcium carbonate, forms calcium chloride, carbon dioxide, and water, the latter of which is dissipated at a red heat, $CaCO_3 + 2HCl = CaCl_2 + CO_2 + H_2O$. The crystallized or partly hydrated salt is prepared by allowing a concentrated solution to crystallize in a cool temperature. The Br. Ph. (1885), after neutralizing the acid with calcium carbonate, adds a little solution of chlorinated lime and slaked lime, filters, evaporates until the chloride becomes solid, and, instead of igniting the residue, dries it at about 204.4° C. (400° F.).

Properties.—Calcium chloride is in "white, slightly translucent, hard fragments, granules, or sticks; odorless, having a sharp, saline taste. It is very deliquescent. One Gm. of Calcium Chloride dissolves in 1.2 mils of water and in about 10 mils of alcohol at 25° C. (77° F.); also in 0.7 mil of boiling water and about 2 mils of boiling alcohol. Its aqueous solution (1 in 20) is neutral or slightly alkaline to litmus. An aqueous solution of the salt (1 in 20) yields, with ammonium oxalate T.S., a white precipitate insoluble in acetic acid, but soluble in hydrochloric acid. Silver nitrate T.S. added to an aqueous solution of the salt (1 in 10) produces a white precipitate insoluble in nitric acid but readily soluble in ammonia water. Add ammonia water to an aqueous solution of the salt (1 in 20) until of alkaline reaction; no turbidity or precipitation occurs either before or after boiling (*iron, aluminum, phosphates, etc.*). Precipitate the calcium completely from 10 mils of an aqueous solution of the salt (1 in 20) by adding ammonium oxalate T.S. and filtering. The filtrate on evaporation and ignition leaves not more than 0.004 Gm. of fixed residue (*magnesium and alkalies*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3)." *U. S.*

"Dry, white, very deliquescent masses. Taste warm, slightly bitter. Soluble in 1.5 parts of *water*, and in 3 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of calcium and of chlorides. Yields no characteristic *reactions* for iron, aluminium, or carbonates, and not more than the slightest *reaction* for magnesium. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million. Evolves no chlorine or hypochlorous acid on the addition of *hydrochloric acid* (absence of hypochlorite). Loses not more than 5 per cent. of its weight when dried at 200° C. (392° F.)." *Br.*

On account of its avidity for water, the fused salt is used for drying gases. The crystallized salt is also very deliquescent, and has the form of colorless, transparent, striated, six-sided prisms. The crystals, on exposure to heat, first dissolve in their water of crystallization, and, after this has evaporated, undergo igneous fusion. With ice or snow they form a powerful frigorific mixture. Calcium chloride exists in the water of the ocean and of many springs. It is usually associated with common salt and magnesium chloride, from which it is separated with difficulty. When crystallized it normally contains six molecules of water, but other crystalline hydrates have also been obtained.

Assay.—"Proceed as directed under the Assay for chlorides (see Part III, Test No. 5), using about 0.3 Gm. of Calcium Chloride, accurately weighed in a stoppered weighing-bottle. It shows not less than 75 per cent. of $CaCl_2$.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.00555 Gm. of $CaCl_2$. Each gramme of Calcium Chloride corresponds to not less than 135.1 mils of tenth-normal silver nitrate V.S." *U. S.*

Liquor Calcii Chloridi was official in the U. S. P., 1870. A convenient method of making this preparation is to dissolve 228 grains of fused calcium chloride in 1 fluidounce of distilled water, and filter if necessary.

Uses.—Because of its easy solubility calcium chloride offers one of the best means of intro-

ducing lime into the system. The healthy functioning of the body organs is contingent upon the proper balance between the sodium, potassium and calcium in the blood and other fluids of the body. A relative excess of calcium, as of other salts, will be rapidly removed from the system, and will, therefore, do little harm, but there are morbid states which are apparently dependent upon the reduction in the amount of bodily lime. It has been shown by MacCallum and Voegtlin (*J. Ex. M.*, 1909, xi, p. 118) and others, that an insufficiency of calcium in the blood increases the irritability of the motor cortex of the brain and of muscle substance, and that conversely an excess of lime diminishes motor irritability. Stone (*J. A. M. A.*, 1909, lii, 1102) has employed calcium salts successfully in *tetany;* Ohlmacher (*J. A. M. A.*, 1910, liii, 527) recommends it in *epilepsy,* and Emmerich (*M. M. W.*, 1915, lxi) in various *tics.* It has long been known that the removal of calcium from the blood prevents the formation of clots, and the suggestion of Wright, many years ago, for the use of calcium chloride in hemorrhagic conditions, is theoretically, at least, well founded. The clinical reports on this subject are very numerous, and although somewhat contradictory, on the whole the evidence is favorable to the use of the salts of lime in conditions of internal *hemorrhages,* as *hemoptysis, menorrhagia* and in *hemophilia.*

While in the ordinary cases of *rickets,* calcium salts are of no value, it is probable that there are occasional cases of softening of the bones which are dependent upon an insufficient amount of lime in the food. These cases, of course, will be much benefited by the administration of lime salts.

In some way not at present evident the lime salts diminish the susceptibility of guinea-pigs to the condition known as *anaphylaxis* which follows the injection of foreign proteins. It has, therefore, been used clinically and with apparent good results not only to prevent the *serum disease* after the injection of antitoxins, but in the treatment of *hay fever, asthma, urticaria, laryngismus stridulus, hemoglobinuria,* etc.

The *dose* ordinarily recommended is five to fifteen grains (0.32–1.0 Gm.), but it is very doubtful whether such a quantity can exercise any distinct effect on the system, and as the salt is relatively innocuous larger doses would seem more rational; H. C. Wood, Jr., recommends twenty to thirty grains (1.3–2.0 Gm.) every two or three hours.

Off. Prep.—Liquor Hydrastinæ Compositus, *N. F.*

CALCII GLYCEROPHOSPHAS. U. S.

CALCIUM GLYCEROPHOSPHATE Calc. Glycerophos. [Calcium Glycerinophosphate]

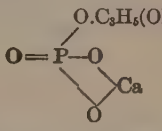
(kăl'cĭ-ī glĭc'ĕr-ō-phŏs'phăs)

"The normal calcium salt of glycerophosphoric acid [$C_3H_5(OH)_2PO_4H_2 = 172.11$], containing, when dried to constant weight at 130° C. (266° F.), not less than 98 per cent. of $CaC_3H_7PO_6$ or $C_3H_5(OH)_2PO_4Ca$ (210.17). Preserve it in well-closed containers." *U. S.*

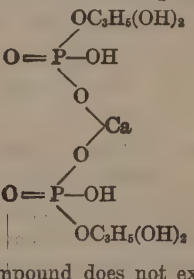
Glycerophosphate of Lime, Calcium Phosphoglycerate; Glycerophosphate de chaux, *Fr.*

There are several theoretically possible *glycerides of phosphoric acid,* but the only one of any practical significance is the *monoglyceride of ortho-phosphoric acid,* of the composition $CH_2OH.CHOH.CH_2O.PO(OH)_2$. This compound, called for brevity's sake *glycerophosphoric acid,* was discovered by Pelouze in 1846, while studying glycerol-sulphuric acid, an analogous compound. Other authors soon discovered the presence of salts of this new acid in yolk of egg, brain tissue and other organic sources. Being called to the attention of the medical profession, a demand soon arose for the glycerophosphates of the various elements, which in some cases, as that of sodium, was supplied by the furnishing of spurious articles, mixtures of inorganic salts and glycerin being substituted for them, as well as hypophosphites.

Glycerophosphoric acid is a dibasic acid and therefore is capable of combining with bases to form normal or acid salts, which occur in varying conditions of hydration. The official calcium glycerophosphate is the normal salt and has the following structural formula:



The acid salt has the following formula:



This latter compound does not exist as a solid salt, but is usually found in the form of a 50 per cent. solution, higher concentrations being unstable. The advantage of the acid salts is their more ready solubility, which, however, is counter-balanced by the acidity, which prevents their use subcutaneously. The solubility of the normal salts can be greatly increased by the addition of a small proportion of lactic acid.

The normal salt was introduced into the U. S. P. IX. It is made by treating glycerophosphoric acid with calcium hydroxide and purifying the product by treatment with alcohol. It is officially described as follows: "Calcium Glycerophosphate occurs as a fine white powder; odorless and almost tasteless, somewhat hygroscopic. One Gm. of Calcium Gly-

cerophosphate dissolves in about 50 mils of water at 25° C. (77° F.); soluble in less water at a lower temperature; citric acid increases its solubility; insoluble in alcohol. A saturated aqueous solution of the salt is alkaline to litmus and to phenolphthalein. A cold, saturated aqueous solution of the salt yields white, iridescent scales of anhydrous calcium glycerophosphate when heated to boiling. When heated above 170° C. (338° F.) the salt is decomposed, evolving inflammable vapors, and at a red heat it is converted into calcium pyrophosphate. A saturated aqueous solution of the salt yields with ammonium oxalate T.S. a white precipitate, insoluble in acetic acid but soluble in hydrochloric acid. With lead acetate T.S. the saturated solution yields a white curdy precipitate which is soluble in nitric acid. Dissolve 1 Gm. of Calcium Glycerophosphate in 10 mils of diluted nitric acid and add an equal volume of cold ammonium molybdate T.S.; no precipitate is formed within one hour (*phosphates*) but on heating the mixture a yellow precipitate is is formed. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). Dissolve 0.1 Gm. of the salt in 10 mils of diluted nitric acid and add 1 mil of silver nitrate T.S.; an opalescence but no precipitate may appear within one minute (*chloride*). Dissolve 0.1 Gm. of the salt in 10 mils of diluted hydrochloric acid and add 1 mil of barium chloride T.S.; no distinct turbidity appears within one minute (*sulphate*). Shake 1 Gm. of finely powdered Calcium Glycerophosphate with 25 mils of dehydrated alcohol, filter the mixture, evaporate the filtrate on a water bath and dry the residue for an hour at a temperature not exceeding 70° C. (158° F.). The resulting residue weighs not more than 0.01 Gm. (*alcohol-soluble impurities, etc.*). Dry a portion of the finely powdered salt to constant weight at 130° C. (266° F.); the loss does not exceed 10 per cent. (*water*).

" **Assay.**—Dissolve about 0.4 Gm. of the salt, previously dried to constant weight at 130° C. (266° F.) and accurately weighed, in 20 mils of a 5 per cent. solution of acetic acid and add 30 mils of distilled water. Heat the mixture to boiling and add an excess of ammonium oxalate T.S. Collect the resulting precipitate, wash, dry, and then ignite it until of constant weight. This residue of calcium oxide corresponds to not less than 26.1 per cent. of the weight of Calcium Glycerophosphate taken. Dry a portion of Calcium Glycerophosphate to constant weight at 130° C. (266° F.), and ignite it to constant weight; the weight of calcium pyrophosphate corresponds to not less than 59.2 per cent. of the weight of Calcium Glycerophosphate taken." *U. S.*

Uses.—The phosphorus of the central nervous system exists in the form of an organic combination of glycerophosphoric acid. On the theory that glycerophosphoric acid could be directly absorbed and utilized as a nutriment for the central nervous system, various salts of the glycerophosphates have been introduced into medicine. There is, however, no convincing evidence that the central nervous system can metabolize the glycerophosphates any better than ordinary phosphates; moreover in conditions of nerve weakness in which this group of remedies is supposed to be indicated, the fault is due not to the absence of phosphorus in the food but to errors in the metabolic processes of the nervous system. Theory does not support the use of glycerophosphates as nerve tonics. On the other hand there is considerable clinical evidence as to their value in conditions of *debility*, as *neurasthenia*. The calcium glycerophosphate represents any virtue that may pertain to the glycerophosphoric acid and adds to it the value of the calcium. It has been used also in various *bone diseases*, such as *rickets* and also in *tubercular* complaints. Blackader (*J. A. M. A.*, 1912, lix) believes that any therapeutic value that calcium glycerophosphate may possess is due to its content of lime.

Dose, three to eight grains (0.2–0.5 Gm.).

Off. Prep.—Elixir Calcii et Sodii Glycerophosphatum, *N. F.*; Elixir Glycerophosphatum Compositum, *N. F.*

CALCII HYDRAS. Br.

CALCIUM HYDROXIDE

(căl'cĭ-ī hȳ'drăs)

" Calcium Hydroxide, $Ca(OH)_2$, is the product, recently prepared, of the interaction of water and Lime." *Br.*

Calcis Hydras; Slaked Lime; Hydrate of Lime; Chaux Eteinte, *Fr. Cod.*; Idrato di calcio, *It.*

The British Pharmacopœia no longer gives a detailed process for slaked lime. The process of the Br. Pharm. (1885) is as follows: " Take of Lime *two pounds* [avoirdupois]; Distilled Water *one pint* [Imperial measure]. Place the lime in a metal pot, pour the water upon it, and when vapor ceases to be disengaged cover the pot with its lid and set it aside to cool. When the temperature has fallen to that of the atmosphere, put the slaked lime on an iron-wire sieve, and by gentle agitation cause the fine powder to pass through the sieve, rejecting what is left. Put the powder into a well-stoppered bottle, and keep it excluded as much as possible from the air. Slaked lime should be recently prepared." *Br.*, 1885. Calcium hydroxide " is a soft, white powder. Yields the *reactions* characteristic of calcium. Strongly heated it loses nearly one-fourth of its weight of water. Yields not more than the slightest characteristic *reactions* for iron, carbonates, chlorides, sulphates, or silica. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million." *Br.*

For an account of the physical and medicinal properties of slaked lime, see *Calx.*

Off. Prep.—Liquor Calcis, *Br.*; Liquor Calcii Saccharatus, *Br.*

CALCII HYPOPHOSPHIS. U. S., Br.

CALCIUM HYPOPHOSPHITE Calc. Hypophos.

(kăl'cĭ-ī hȳ-pŏ-phŏs'phĭs)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 98 per cent. of $Ca(PH_2O_2)_2$. (170.18). Preserve it in well-closed containers. Caution should be observed in dispensing Calcium Hypophosphite as an explosion is liable to occur when it is triturated or heated with nitrates, chlorates, or other oxidizing agents." *U. S.*

"Calcium Hypophosphite may be obtained by the interaction of phosphorus, calcium hydroxide, and water. It contains not less than 98 per cent. of pure calcium hypophosphite, $Ca(PH_2O_2)_2$." *Br.*

Calcis Hypophosphis; Calcium Hypophosphorosum, Hypophosphite of Lime; Calcaria Hypophosphorosa, Hypophosphis Calcicus; Hypophosphite de Chaux, *Fr. Cod.*; Unterphosphorigsaure Kalkerde, Calcium hypophosphit, *G.*; Hipofosfito calcico, *Sp.*

Attention has been called to the hypophosphites as a class of salts, in consequence of their recommendation by Churchill, of Paris, in the treatment of *phthisis,* in which they were thought to be useful by furnishing phosphorus to the tissues. One of the first papers on their mode of preparation and qualities was communicated by Wm. Procter. (See *A. J. P.,* xxx, 118.) Hypophosphorous acid consists of one atom of phosphorus, two of oxygen, and three of hydrogen, of which latter, however, only one atom is replaceable by metal. It has a strong affinity for oxygen, and acts as a powerful deoxidizing or reducing agent, which property is attributed to the presence of the unreplaceable hydrogen atoms, sometimes termed "aldehydic" hydrogen. When heated, it is resolved into hydrogen phosphide and phosphoric acid. Its salts are generally soluble in water and deliquescent, and many are soluble in alcohol. They are converted into phosphates by heat, with the escape of hydrogen phosphide; some are explosive. *Calcium hypophosphite* has been most largely employed.

To prepare it Procter gave the following formula. Slake four pounds (avoirdupois) of lime with a gallon of water, add it, in a deep boiler, to four gallons of boiling water, and mix thoroughly. To the mixture add a pound (av.) of phosphorus, and continue the boiling, adding hot water from time to time to keep up the measure, until the combination is complete, and hydrogen phosphide is no longer evolved. It is necessary to provide for the escape of the gas, which takes fire spontaneously in contact with air. There are formed in the liquid calcium phosphate and hypophosphite, the phosphorus oxidizing at the expense of the water, the hydrogen of which has escaped in combination with another portion of phosphorus, which is therefore lost. The liquid is filtered to separate the insoluble phosphate and residuary lime, then concentrated, and refiltered to separate the calcium carbonate formed by the action of the air on a little lime held in solution, and lastly evaporated until a pellicle appears; after which the salt may be allowed to crystallize by setting the liquid aside, or may be obtained in the granular form by continuing the heat and stirring. The salt should be introduced into bottles. The former Br. Pharm. practically adopted this process, but any uncombined lime remaining in the solution was separated by passing carbonic acid gas through it.

Properties.—"Calcium Hypophosphite occurs as colorless, transparent, monoclinic prisms, as small lustrous scales, or as a white, crystalline powder; odorless, having a nauseous and bitter taste, permanent in the air. One Gm. of Calcium Hypophosphite is slowly soluble in 6.5 mils of water at 25° C. (77° F.); insoluble in alcohol. When heated the salt decrepitates and begins to decompose, giving off water and evolving spontaneously inflammable hydrogen phosphide, and on complete ignition leaving a residue of calcium pyrophosphate. When an aqueous solution of the salt (1 in 20), acidulated with hydrochloric acid, is added, drop by drop with agitation, to an excess of mercuric chloride T.S., a white precipitate of mercurous chloride is formed. Upon the further addition of the solution of Calcium Hypophosphite the precipitate becomes gray from reduction to metallic mercury. An aqueous solution of Calcium Hypophosphite (1 in 20) yields with ammonium oxalate T.S. a white precipitate, insoluble in acetic acid, but soluble in hydrochloric acid. Dissolve 1 Gm. of the salt in 20 mils of distilled water; it requires not more than 1 mil of tenth-normal potassium hydroxide V.S. to produce a pink color, phenolphthalein T.S. being used as indicator. When 1 Gm. of the salt is dissolved in 20 mils of distilled water, not more than 0.005 Gm. of residue remains (*phosphate*). Mix 5 mils of an aqueous solution of the salt (1 in 10) in a test tube with 0.5 mil of diluted hydrochloric acid and heat on a water bath; no offensive odor develops within thirty minutes. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). Pour 5 mils of an aqueous solution of the salt (1 in 25) into a beaker containing 3 mils of nitric acid, diluted with about 10 mils of distilled water, and evaporate it to dryness on a water bath. The residue meets the requirements of the Test for arsenic (see Part III, Test No. 1)." *U. S.*

"A white crystalline salt, with a pearly lustre; taste bitter, nauseous. Soluble in 8 parts of *water;* insoluble in *alcohol* (90 per cent.). When strongly heated evolves spontaneously-inflammable hydrogen phosphide and hydrogen, and leaves a reddish residue. Yields the *reactions* characteristic of calcium. Its aqueous solution yields with *T. Sol. of mercuric chloride* a white precipitate turning grey. Yields no characteristic *reactions* for copper or iron, and not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million. Contains not less than 98 per cent. of pure calcium hypophosphite, $Ca(PH_2O_2)_2$, as determined by the

following process: Dissolve 2.5 grammes in 40 millilitres of *water;* add 5 millilitres of *solution of lead acetate* and sufficient *water* to produce 50 millilitres; shake the mixture well and allow it to stand for one hour for the precipitate to subside. To 10 millilitres of the clear liquid add 50 millilitres of *N/1 solution of potassium bichromate* and 10 millilitres of *sulphuric acid;* heat on a water-bath for one hour, cool, and add sufficient *water* to produce 250 millilitres. To 25 millilitres of this solution add 2 grammes of *potassium iodide* and titrate the liberated iodine with *N/10 solution of sodium thiosulphate, mucilage of starch* being used as indicator; not more than 27 millilitres are required." *Br.*

The solubility of calcium hypophosphite is increased by the addition of hypophosphorous acid. For a method of purifying alkaline hypophosphites, see *J. P. A.*, 1879, 57; *N. R.*, 1879, 142.

Assay.—" Dissolve about 0.75 Gm. of Calcium Hypophosphite, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed, in 10 mils of distilled water, add 10 mils of nitric acid and evaporate to dryness on a water bath. Add 5 mils of nitric acid to the residue, again evaporate to dryness on a water bath and dissolve the residue in sufficient distilled water to measure 100 mils. Transfer 10 mils of this solution to a 100 mil graduated flask, add sodium hydroxide T.S. (free from chloride) until a slight permanent precipitate is produced; then add 50 mils of tenth-normal silver nitrate V.S. and proceed as directed in the assay under *Sodii Phosphas.* When calculated to the amount originally taken it shows not less than 98 per cent. of $Ca(PH_2O_2)_2$. Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.002836 Gm. of $Ca(PH_2O_2)_2$. Each gramme of Calcium Hypophosphite, dried to constant weight, corresponds to not less than 345.5 mils of tenth-normal silver nitrate V.S." *U. S.*

As the soluble salts of mercury, copper, and silver are reduced by the hypophosphites, they are of course incompatible with it in prescriptions. With calcium hypophosphite all the soluble sulphates and carbonates produce precipitates. As the hypophosphites are insoluble in cod liver oil, they should be dissolved in syrup or water before being added to the oil. (See *Syrupus Hypophosphitum* and *Emulsum Olei Morrhuæ cum Hypophosphitibus.*) W. A. H. Naylor considers the presence of sulphites in commercial hypophosphites to be the source of the disagreeable odor of hydrogen sulphide sometimes found in the compound syrup of hypophosphites. (*P. J.*, 1895, 144.)

Uses.—Calcium hypophosphite was at one time largely used in *chronic phthisis,* in various *scrofulous affections,* in *neurasthenia,* and other conditions of impaired nutrition of the nerve centres. It seems in none of these cases to be really efficient, but is harmless.

Dose, ten to thirty grains (0.65–2.0 Gm.), three times a day.

Off. Prep.—Syrupus Hypophosphitum, *U. S.;* Elixir Calcii Hypophosphitis, *N. F.;* Elixir Cinchonæ Alkaloidorum et Hypophosphitum, *N. F.;* Elixir Hypophosphitum, *N. F.;* Elixir Hypophosphitum et Ferri, *N. F.;* Emulsum Olei Morrhuæ cum Hypophosphitibus, *N. F.;* Liquor Hypophosphitum, *N. F.;* Liquor Hypophosphitum Compositus, *N. F.;* Syrupus Calcii et Sodii Hypophosphitum, *N. F.;* Syrupus Calcii Hypophosphitibus, *N. F.;* Syrupus Hypophosphitum Compositus, *N. F.*

CALCII LACTAS. U. S., Br.

CALCIUM LACTATE Calc. Lact.

(căl'cĭ-ī lăc'tăs)

" The hydrated form of Calcium Lactate [$Ca(C_3H_5O_3)_2 + 5H_2O = 308.23$]. It contains, when dried to constant weight at 120° C. (248° F.), not less than 98 per cent. of $Ca(C_3H_5O_3)_2$ (218.15). Preserve it in well-closed containers." *U. S.* " Calcium Lactate may be obtained by neutralising dilute lactic acid with calcium carbonate and evaporating the resulting solution. It contains not less than 93 per cent. of pure calcium lactate, $Ca(C_3H_5O_3)_2,5H_2O$." *Br.*

This salt was introduced into the U. S. P. IX and the Br. Pharm., 1914. The experiments of C. A. Hill and T. T. Cocking demonstrate that calcium lactate is liable to vary in composition according to the method of preparation, varying particularly in the amount of water of crystallization. It may be neutral or contain either lactic acid, calcium hydroxide, or calcium carbonate. *Pure* calcium lactate is readily prepared by precipitation of its cold saturated solution with acetone, washing the precipitate with acetone and then with ether. (*Y. B. P.*, 1912, 481.)

It is officially described as follows: " Calcium Lactate occurs in white, granular masses or powder; odorless and nearly tasteless. It is somewhat efflorescent; at 120° C. (248° F.) it becomes anhydrous. When dried to a constant weight at that temperature the loss is not more than 29.2 per cent. (corresponding to 5 molecules of water of crystallization) nor less than 25 per cent. One Gm. of Calcium Lactate dissolves in 20 mils of water at 25° C. (77° F.); almost insoluble in alcohol. An aqueous solution of Calcium Lactate (1 in 20) is neutral, slightly acid, or slightly alkaline to litmus, but is not reddened by phenolphthalein T.S. Acidulate an aqueous solution of the salt (1 in 20) with sulphuric acid, add potassium permanganate and heat the mixture; the odor of acetaldehyde is developed. With ammonium oxalate T.S. an aqueous solution (1 in 20) yields a white precipitate, insoluble in acetic acid but soluble in hydrochloric acid. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). Add ammonium oxalate T.S. to 20 mils of a hot aqueous solution of the salt (1 in 20) until no further precipitate is produced, filter the mixture after three hours, and wash the precipitate with 50 mils of distilled water. The combined filtrate and washings leave not

more than 0.01 Gm. of residue on evaporation and subsequent ignition (*magnesium and alkalies*). Stir about 0.5 Gm. of the salt with 1 mil of sulphuric acid; the mixture does not emit an odor of volatile fat-acids, even on warming.

"**Assay.**—Incinerate in a crucible about 2 Gm. of the salt, previously dried to constant weight at 120° C. (248° F.) and accurately weighed, dissolve the residue in 50 mils of half-normal hydrochloric acid V.S. and titrate the excess of acid with half-normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows, in the dried salt, not less than 98 per cent. of $Ca(C_3H_5O_3)_2$. Each mil of half-normal hydrochloric acid V.S. used corresponds to 0.05454 Gm. of $Ca(C_3H_5O_3)_2$. Each gramme of dried Calcium Lactate corresponds to not less than 17.97 mils of half-normal hydrochloric acid V.S." *U. S.*

"A white powder; almost tasteless. Slowly soluble in 18.5 parts of *water*, forming a clear, colorless solution. Yields the *reactions* characteristic of calcium. The aqueous solution, acidified with *sulphuric acid* and warmed with *potassium permanganate*, develops the odor of aldehyde. A solution of 5 grammes in hot *water* does not become pink on the addition of a few drops of *solution of phenolphthalein*, and requires not more than 0.5 millilitre of *N/1 solution of sodium hydroxide* to produce a pink coloration (limit of acidity). One gramme, treated with *sulphuric acid* and incinerated in a crucible, cooled, again treated with *sulphuric acid* and incinerated, leaves a white residue weighing not less than 0.410 and not more than 0.450 gramme. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Uses.—Calcium lactate affords an excellent means of obtaining the therapeutic effects of lime. It is asserted that it not only is less likely to disturb the stomach than the chloride, but is more readily absorbed. It is used in the treatment of *hemorrhage, rickets, scrofula,* and other diseases in which the lime salts are indicated.

The *dose* is fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Syrupus Calcii Lactophosphatis, *Br.*

CALCII PHOSPHAS. Br.

CALCIUM PHOSPHATE

(kăl'cĭ-ī phŏs'phăs)

"Calcium Phosphate may be obtained by the interaction of calcium chloride with sodium phosphate and excess of ammonia at a boiling temperature." *Br.* "Calcium Phosphate [$Ca_3(PO_4)_2 = 310.29$] losing, when dried at 200° C. (392° F.), not more than 4 per cent. of moisture." *N. F.*

Calcii Phosphas Præcipitatus, *N.F.IV*, Precipitated Calcium Phosphate; Tricalcium Phosphate, Calcaria Phosphorica; Phosphas Calcicus Præcipitatus; Precipitated Phosphate of Lime; Phosphate of Calcium; Phosphate Tricalcique, *Fr. Cod.*; Phosphate de Chaux hydraté, *Fr.*; Phosphorsaure Kalkerde, Calciumphosphat, *G.*; Fosfato calcico, *Sp.*

A formula for this precipitate was given in the U. S. Pharmacopœia of 1870. For description of an apparatus for preparing calcium phosphate on a large scale, see *J. P. C.*, Sept. 1, 1875, 193. The salt has been very properly retained in the Br. Pharmacopœia, but was deleted from the U. S. P. IX. There was no necessity for retaining the word "præcipitatus" in the N. F. title, as it is never seen in commerce except as a precipitate. One of its uses has been to replace magnesium carbonate and absorbent cotton in the process for medicated waters; but it has now been superseded by purified talc.

In the process of the Br. Pharm., 1885, the hydrochloric acid dissolves the calcium phosphate of the bones, from which it is precipitated, on the addition of ammonia, in a state of minute division. It is then washed to free it from adhering ammonium chloride. The salt thus obtained is, for the sake of distinction, called *bone calcium phosphate.*

In the Br. Pharm., 1914, solutions of calcium chloride and sodium phosphate are mixed with an excess of ammonia at a boiling temperature.

Properties.—The N. F. IV describes precipitated calcium phosphate as follows: "Precipitated Calcium Phosphate occurs as a white, amorphous or micro-crystalline, bulky powder, odorless and tasteless; permanent in the air. At an intense white heat the salt fuses without decomposition. Almost insoluble in cold water; partly decomposed by boiling water; almost insoluble in acetic acid, except when freshly precipitated; easily dissolved by hydrochloric or nitric acid; insoluble in alcohol. When moistened with silver nitrate T.S., either before or after ignition, the salt acquires a yellow color (distinction from *acid calcium phosphate*, which, after ignition, when moistened with silver nitrate T.S., remains white). For applying tests of identity and of purity, prepare a solution by shaking 2 Gm. of Precipitated Calcium Phosphate with 20 mils of distilled water, adding nitric acid, drop by drop, until solution is effected, and then sufficient distilled water to make the liquid measure 40 mils. While making this solution, no effervescence occurs on adding the acid (*carbonate*). To a portion of this solution add a slight excess of ammonia water, then an excess of silver nitrate T.S. and afterwards acetic acid, drop by drop, until the excess of ammonia is neutralized; the color of the precipitate changes from white to yellow. Ammonium molybdate T.S. precipitates from the solution yellow ammonium phosphomolybdate; the reaction is accelerated by a gentle heat, not exceeding 65° C. (149° F.). Add to five mils of the solution, acidulated with nitric acid, 0.5 mil of silver nitrate T.S.; not more than a slight turbidity is produced (*chloride*). Add to five mils of the solution, strongly acidulated with nitric acid, 1 mil of potassium sulphate T.S.; no turbidity appears within fifteen minutes (*barium*). An aqueous solution of Precipitated Calcium Phosphate (1 in 50), obtained by shaking the salt with distilled water, adding hydrochloric acid, drop by drop, and heating until solution is effected, does not respond to the Test

for heavy metals (see page 357). Five mils of a solution of Precipitated Calcium Phosphate in diluted nitric acid (1 in 25), heated with 1 mil of sulphuric acid until fumes of sulphur trioxide appear, does no respond to the Test for arsenic (see Part III)." *N. F.*

"A light, white, amorphous powder, permanent in the air. No odor or taste. Almost insoluble in *water.* Yields the *reactions* characteristic of calcium and of phosphates. Dissolves without residue and without effervescence (absence of carbonate) in *diluted hydrochloric acid* or *diluted nitric acid.* Yields no characteristic *reactions* for barium, ammonium, or silica, and no more than the slightest *reactions* for aluminium or magnesium. *Arsenic limit* 5 parts per million. Its solution in slight excess of *diluted nitric acid* is not rendered more than slightly opalescent by *solution of silver nitrate* (limit of chlorides), or by *solution of barium chloride* (limit of sulphates). Its solution in slight excess of *diluted hydrochloric acid* is not affected by *hydrogen sulphide* (absence of copper and lead), and, on the subsequent addition of excess of *solution of ammonia,* the precipitate produced is quite white (limit of iron)." *Br.*

Joly and Sorel record (*C. R. A. S.,* 1894, 738) the precipitation of tricalcium phosphate by adding crystals of hydrated bicalcium phosphate to boiling water; the acid liquid remaining contains monocalcium phosphate.

Uses.—The question of whether it is possible to influence phosphorus metabolism by the administration of inorganic phosphates cannot at present be answered positively, although the bulk of the scientific evidence indicates that the body is unable to synthesize organic phosphates from inorganic. (For review of the literature on this subject see Forbes and Keith, *Ohio Technical Bulletin* No. 5, 1914.) There is therefore no rational basis for the use of calcium phosphate or other inorganic phosphates in the treatment of nervous diseases and any value which it may possess in diseases of the bones must be ascribed to the calcium rather than to the phosphoric acid. The same thing is true of its use in *scrofula, rickets,* and *tuberculosis.* Its relative insolubility would seem to give an inferior position to either the chloride or lactate as a mode of exhibiting lime. It is best administered in acid solution, and is at present used dissolved in lactic acid and administered with emulsion of cod-liver oil.

Dose, ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Emulsum Olei Morrhuæ cum Calcii Phosphate, *N. F.*

CALCII SULPHIDUM CRUDUM. U. S. (Br.)

CRUDE CALCIUM SULPHIDE Calc. Sulphid. Crud.
[Calx Sulphurata, U. S. VIII Sulphurated Lime]

(căl'cĭ-ī sŭl-phīd'ŭm crûd'ŭm)

"It contains not less than 55 per cent. of CaS (72.14). Preserve it in well-closed containers." *U. S.* "Sulphurated Lime is a mixture consisting chiefly of calcium sulphide and calcium sulphate. It may be obtained by heating calcium sulphate with carbon. Contains not less than 50 per cent. of calcium sulphide, CaS." *Br.*

Calx Sulphurata, *Br.;* Calcium Sulphuratum, Calcii Sulphidum; Calcaria Sulfurata, Hepar Sulphuris Calcareum, Hepar Calcis; Sulphide of Calcium; Sulfure de Chaux, *Fr.;* Kalkschwefelleber, *G.*

The name of this preparation was changed in the U. S. P. IX to "Crude Calcium Sulphide," but the British Pharm. retained the name "sulphurated lime." No process is at present official. The process of the U. S. P. VIII is as follows:

"Exsiccated Calcium Sulphate, in fine powder, *seventy grammes* [or 2 oz. av., 205 grains]; Charcoal, in fine powder, *ten grammes* [or 154 grains]; Starch, *two grammes* [or 31 grains]. Mix the powder thoroughly, pack the mixture lightly into a crucible, cover this loosely, and heat it to bright redness, until the contents have lost their black color. Allow the crucible to cool, reduce the product to powder, and at once transfer it to small, glass-stoppered vials." *U. S. VIII.*

By subjecting a mixture of seven parts of calcium sulphate and one part of charcoal to a red heat, in a covered crucible, carbonic oxide is formed, and calcium sulphide is produced,

$$CaSO_4 + 2C = CaS + 2CO_2$$

A less convenient method is to pass hydrogen sulphide over red-hot lime, but if the lime be pure a better product is insured.

Properties.—Crude calcium sulphide is officially described as "a pale gray or yellowish powder, having a faint odor of hydrogen sulphide and a nauseous and alkaline taste. It gradually decomposes on exposure to moist air. Crude Calcium Sulphide is very slightly soluble in cold water; more readily soluble in boiling water with partial decomposition; readily dissolved by solutions of ammonium salts; insoluble in alcohol. When Crude Calcium Sulphide is decomposed by diluted acetic acid, hydrogen sulphide is evolved and a residue of calcium sulphate and carbon frequently remains. The filtered solution yields with ammonium oxalate T.S. a white precipitate insoluble in acetic acid, but soluble in hydrochloric acid." *U. S.*

"A greyish-white powder with an odor of hydrogen sulphide; taste nauseous. Yields the *reactions* characteristic of calcium. When 0.8 gramme is mixed in a stoppered flask with a cold solution of 1.4 grammes of *copper sulphate* in 50 millilitres of *water,* and, after the addition of a little *hydrochloric acid,* the mixture is heated to a temperature approaching that of ebullition, well shaken for ten minutes, and then filtered, the filtrate gives no red color with *solution of potassium ferrocyanide* (presence of a due proportion of sulphide)." *Br.*

Calcium sulphydrate, or *calcium hydrosulphide,* $Ca(SH)_2$, is formed when hydrogen sulphide is passed into milk of lime as long as it is absorbed. It is in the form of a paste of a greenish-gray color, and exhales a strong odor of hydrogen sulphide.

Assay.—"Introduce about 0.2 Gm. of Crude Calcium Sulphide, accurately weighed, into a glass-stoppered bottle or flask; add 50 mils of distilled water, mix, and quickly introduce 30 mils of a 10 per cent. ammonium chloride solution and immediately stopper the flask. Agitate the contents for a few minutes, add quickly 20 mils of a 10 per cent. cadmium chloride solution, immediately insert the stopper and again agitate well for a few minutes. Then add 5 mils of acetic acid, heat the mixture on a water bath for fifteen minutes, decant the supernatant liquid through a filter, agitate the remaining precipitate with 10 mils of diluted acetic acid, transfer the precipitate to the filter and wash with 10 mils of diluted acetic acid. Return the filter and precipitate to the original flask, add 50 mils of tenth-normal iodine V.S. and 20 mils of a mixture of equal volumes of hydrochloric acid and water. Stopper the flask and agitate it vigorously for a few minutes, and then titrate the excess of iodine with tenth-normal sodium thiosulphate V.S. It shows not less than 55 per cent. of CaS. Each mil of tenth-normal iodine V.S. used corresponds to 0.003607 Gm. of CaS. Each gramme of Crude Calcium Sulphide corresponds to not less than 152.5 mils of tenth-normal iodine V.S." *U. S.*

Uses.—Sulphide of lime owes its therapeutic virtues chiefly to the hydrogen sulphide which is evolved during its decomposition. This gas is locally irritant and actively poisonous, not only to bacteria, but to more highly organized forms of life. Because of this latter property calcium sulphide is a useful agent in the treatment of various parasitic *skin diseases,* such as *scabies, ring-worm,* etc. Because of its local stimulating action it is also employed in various other skin diseases, such as *acne.* Its use as a depilatory depends upon its solvent powers towards keratin. It should be stirred up with enough water to form a paste and spread in a thin layer over the area from which it is desired to remove the hair. At the end of fifteen minutes it is removed with a wet sponge, the hair generally coming away at the same time. See Brayton. (*J. A. M. A.,* April 16, 1898.) For the treatment of skin diseases it may generally be employed in strengths of from twenty to thirty grains to the ounce. It is very widely used in the form of *Vleminck's solution.* (*Liquor calcis sulphurati,* N. F.) Internally calcium sulphide has been highly recommended by Duhring and other dermatologists in the treatment of *furunculosis* and *acne.*

Dose, one-fourth to one grain (0.015–0.065 Gm.).

CALCIUM

CALCIUM

(kăl'cĭ-ŭm)

This is the metal characteristic of lime, and, consequently, of all calcareous substances. It was obtained by Matthiessen, in 1855, in masses of the size of a pea, by the electrolysis of calcium chloride with a Bunsen battery. It has been recently made on a much larger scale by electrolysis and has become better known. It is, when pure, a yellowish-white crystalline metal, ductile and malleable, with a specific gravity of 1.58 and melting at 760° C. (1400° F.). It oxidizes slowly in dry air, more rapidly in moist air, and it must therefore be kept under petroleum.

Calcium is a very abundant element in nature, existing in the mineral kingdom chiefly as a carbonate, in the form of limestone, marble, chalk, and calcareous spar; and as a phosphate and carbonate in the bones and shells of animals, and as a sulphate in gypsum and selenite.

CALUMBA. U. S. (Br.)

CALUMBA Calumb. [Columbo, Columba, Colombo]

(cą-lŭm'bą)

"The dried root of *Jateorhiza palmata* (*Lamarck*) Miers (Fam. *Menispermaceæ*)." *U. S.* "Calumba Root is the root of Jateorhiza Columba, *Miers,* cut in transverse slices and dried." *Br.*

Calumbæ Radix, *Br.;* Calumba Root; Radix Columbo; Colomba, *U. S.* 1850; Racine de Colombo, *Fr. Cod.;* Colombo, *Fr.;* Radix Colombo, *P. G.;* Kolombowurzel, *G.;* Colombo, *It.;* Colombo, Raiz de colombo, *Sp.;* Kalumbo, *Port.;* Calumb, *Mozambique.*

Calumba is official in nearly all pharmacopœias. The difference in botanical origin as given in the definition in the U. S. and British Pharmacopœias is merely one of synonymy, as *J. palmata* (Lamarck) Miers is merely another name for *J. Columba* Miers. There is considerable confusion in the spelling of both the generic and specific names: *Jateorhiza* is spelled by most of the European Pharmacopœias *Jatrorrhiza.* In the same way the specific name is usually given as *Calumba* and not *Columba.*

Jateorhiza palmata is a dicœcious climbing plant, with a perennial root consisting of several fasciculated, fusiform tuberous portions. The stems are twining, cylindrical, hairy and simple in the staminate plant, being branched in the pistillate plant. The leaves, which stand on rounded, glandular, hairy footstalks, are alternate, distant, cordate, with three, five, or seven entire, acuminate, wavy, somewhat hairy lobes, and as many nerves, each running into one of the lobes. The flowers are small and inconspicuous, and arranged in solitary axillary racemes, which in the staminate plant are compound, in the pistillate simple, and in both plants are shorter than the leaves.

The Calumba plant is indigenous to Mozambique, on the southeastern coast of Africa, where it grows wild in great abundance in the thick forests extending from the sea many miles into the interior. It is more particularly abundant in the region between the Zambezi and Rovuma. (*Ap. Ztg.,* 1912, p. 147.) The root is dug up in March, when dry weather prevails. From the base of the root numerous fusiform offsets proceed, less fibrous and woody than the parent stock. These offsets are separated and cut into

transverse slices, which are dried in the shade. The old root is rejected.

The plant is said to be cultivated both in Africa and the East Indies for the sake of its root, which under the name of *Calumb* is used in dyeing.

Calumba is sent from the Portuguese dominions in Southeastern Africa into India, from whence it goes into general commerce. At one time, when thought to be a product of Ceylon, it was supposed to have derived its name from Columbo, a city of that island, but a much more probable derivation is from the African name of the root above given. (See Lloyd's history of colombo root, *West. Drug.*, 1898, 8.)

Properties.—It is officially described in the U. S. P. as "in circular or oval disks attaining a diameter of 9 cm. and seldom exceeding 2 mm. in thickness, or in longitudinal or in oblique slices attaining a length of 30 cm., a breadth of 35 mm. and a thickness of 16 mm.; externally brown and roughly wrinkled; cut surface varying from yellowish-brown to grayish-yellow, the transverse slices distinctly radiate in the outer portion and with a dark cambium; central portion often depressed; fracture short, mealy; odor slight; taste slightly aromatic, very bitter. The powder is greenish-brown to grayish-yellow; starch grains numerous, mostly single, occasionally 2- to 3-compound, the individual grains from 0.003 to 0.085 mm. in the long diameter, ovoid, ellipsoidal, frequently very irregular, slightly lamellated, with an excentral linear x-shaped or branching cleft; stone cells few with irregularly thickened, strongly lignified, coarsely porous walls and containing one or more prisms of calcium oxalate from 0.01 to 0.03 mm. in length, or numerous sphenoidal micro-crystals; fragments with tracheæ few, the latter with reticulate thickenings or bordered pores, and associated with wood-fibers having long, oblique, slit-like pores. Calumba yields not more than 8 per cent. of ash." *U. S.*

The drug is described in the British Pharmacopœia as follows: "Cork thin, brownish and wrinkled; cortex thick, yellowish and separated by a dark line from the greyish wood, in which the parenchymatous tissue is largely developed and the vessels arranged in narrow elongated groups. In the cortex, in transverse section, numerous isolated sclerenchymatous cells, with yellow, irregularly thickened walls enclosing small prismatic crystals of calcium oxalate; in the wood, vessels with yellow reticulated walls. The parenchymatous cells of both wood and cortex filled with starch grains, which are irregularly ovoid in outline, from 20 to 70 microns in length, and exhibit a conspicuous, excentric, radiate or cleft hilum." *Br.*

Along with the disks are sometimes a few cylindrical pieces an inch or two in length. The cortical portion is thick, of a bright yellow, slightly greenish color internally, but covered with a brownish, wrinkled epidermis. The interior or medullary portion, which is readily distinguishable from the cortical, is light, spongy, yellowish, usually more or less shrunk, so that the pieces are thinnest in the centre; and is often marked with concentric circles and radiating lines. Those pieces are to be preferred which have the brightest color, are most compact and uniform, and least worm eaten.

The odor of calumba is slightly aromatic. The taste is very bitter, that of the cortical much more so than that of the central portion, which is somewhat mucilaginous. The root is easily pulverized. The powder is greenish, becoming browner with age, and deepening when moistened. As it attracts moisture from the air, and is apt to undergo decomposition, it should be prepared in small quantities.

The crude drug, as well as the powder, is liable to be attacked by insects if kept for any length of time. This can be guarded against by thoroughly drying the drug, keeping it in a dry place, and adding either carbon tetrachloride or chloroform. According to the U. S. P. microscopical description, it is inferred that the calcium oxalate crystals occur only in the stone cells. Tunmann (*Ph. Zentralh.*, 1906, p. 1069) asserts that the crystals are distributed throughout the woody portion of the root as well as in the bark, and outlines a method for readily demonstrating their presence.

Adulterations.—Formerly the high price of calumba led to its frequent adulteration, especially, it is said, with the roots of the *white bryony*, and of *Frasera carolinensis* or *American calumba*, and with the stem of *Coscinium fenestratum*, the *columbo wood* or *false columbo* of Ceylon. According to Stolze of Halle, the American calumba can be readily detected by the fact that while the tincture of true calumba is not affected by ferric sulphate or sesquichloride, and yields with tincture of galls a dirty precipitate, the tincture of Frasera becomes dark green with the former and is not affected by the latter reagent. *Coscinium fenestratum*, a bitter tonic used in Ceylon, is at once to be distinguished by its being a stem, not a root, and is said not to have appeared upon the market for many years. At present, owing to its great cheapness, calumba root seems to be very rarely adulterated (see *P. J.*, 1901, 502, and Dec., 1904), although a specimen of calumba yielded, on incineration, 16 per cent. of ash. Holmes believes that the fictitious drug is the overground portion of *Jateorrhiza palmata*, while Wardleworth believed that the drug is a product of *Tinospora Bakis* (A. Rich.) Miers which is used in Senegal as an antiperiodic.

Chemistry.—Planche analyzed calumba in 1811, and found it to contain a nitrogenous substance, probably albumen, in large quantity, a bitter yellow substance not precipitated by metallic salts, and one-third of its weight of starch. He obtained also a small proportion of volatile oil, salts of calcium and potassium, ferric oxide, and silica. Wittstock, of Berlin, afterwards isolated a principle, which he called *columbin*. This crystallizes in beautiful transparent quadrilateral prisms of the

formula $C_{21}H_{22}O_7$, is without odor, and is extremely bitter. It is but very slightly soluble in water, more soluble in alcohol, ether, or chloroform, and imparts to these fluids a strongly bitter taste. It is more soluble in boiling alcohol, which deposits it upon cooling. The best solvent is diluted acetic acid. It is taken up by alkaline solutions, from which it is precipitated by acids. It is obtained by exhausting calumba by means of alcohol of the sp. gr. 0.835, distilling off three-quarters of the alcohol, allowing the residue to stand for some days until crystals are deposited, and lastly treating these crystals with alcohol and animal charcoal. The mother waters still contain a considerable quantity of columbin, which may be separated by evaporating with coarsely powdered glass to dryness, exhausting the residue with ether, distilling off the ether, treating the residue with boiling acetic acid, and evaporating the solution to crystallization.

P. E. Alessandri (*L'Orosi*, v, 1; *P. J.*, 1882, p. 995) isolated *calumbine* (which he considers an alkaloid) by the following process: An infusion of calumba is made with a 3 per cent. solution of oxalic acid; the yellow bitter liquid is neutralized with ammonia and evaporated to one-third its bulk; it is, when cooled, treated with ether, separated, and the ethereal solution on evaporation yields pure white calumbine. Allesandri obtained what he called *berberine* from calumba by neutralizing a cold infusion, made with diluted oxalic acid (3 per cent.), with baryta; the precipitate which is produced is separated. The liquid is heated, allowed to stand for twenty-four hours to allow the barium oxalate to deposit, filtered, and then a current of carbonic acid is passed through to remove barium oxide. It is then treated by shaking the ammoniacal liquid with ether as in Alessandri's process for calumbine (see above), and, after the ethereal layer is separated, the aqueous liquid is evaporated to dryness. *Columbic acid* may be obtained from the precipitate produced by the addition of barium oxide to the oxalic acid infusion. Bocchiola (*Y. B. P.*, 1891, p. 162) states that the older roots contain more of the active principles than the younger ones. He found that the inner and the outer portions of calumba also vary in their constituents; thus in the woody or inner part he found the following percentages: calumbine 1.90, berberine 0.72, ether extract 0.80, alcoholic extract 3.86, diluted alcoholic extract 17.80, ash 6. In the cortical or outer part he found calumbine 1.42, berberine 1.43, ether extract 0.70, alcoholic extract 3.89, diluted alcoholic extract 17.96, ash 5. He assigns to columbin the formula $C_{21}H_{24}O_7$, and to columbic acid $C_{21}H_{22}O_6$. (*Zeit. Oest. Apoth. Ver.*, 1896, No. 1, 8–14.) Gordin questioned the presence of berberine in calumba and Gadamer, Feist and Günzel proved the absence of berberine and stated that calumba contains *calumbamine*, $C_{21}H_{22}O_5N.OH$, *jateorrhizine*, $C_{20}H_{20}O_5N.OH$, and probably *palmatine*, $C_{23}H_{24}O_5N.OH$, the last formula not having been positively proved. (*A. Pharm.*, 1907, No. 8, 586.) Haensel (*P. J.*, 1904, 216) obtained from calumba a volatile oil which exists in very small quantities (0.00568 per cent.). It has a peculiar odor and bitter taste.

There can be little doubt that both columbin and the alkaloids contribute to the remedial effects of calumba. The virtues of the root are extracted by boiling water and by alcohol. Precipitates are produced with the infusion and tincture by infusion of galls, and by solutions of lead acetate and subacetate, but the bitterness is not affected.

Uses.—Biberfeld (*Z. E. P. T.*, 1909, vii) has shown that all the alkaloids of calumba root are depressant to the central nervous system and especially to the respiratory center; palmatine indeed exceeds morphine in its respiratory toxicity; columbamine and jateorrhizine increases intestinal tonus. Despite these findings, however, it is improbable that calumba has any medical virtue aside from that of a mild bitter, free from astringency. It is useful in functional atonic conditions of the digestive organs, especially with other tonics, aromatics, or cathartics. A favorite remedy of the late George B. Wood for the cure of a disposition to the accumulation of *flatus* in the bowel was an infusion made with half an ounce of calumba, half an ounce of ginger, a drachm of senna, and a pint of boiling water, and given in doses of a wineglassful three times a day. By the natives of Mozambique it is used in *dysentery* and various other diseases.

Dose, of the powder, from ten to thirty grains (0.65–2.0 Gm.), which may be repeated three or four times a day.

Off. Prep.—Fluidextractum Calumbæ, *N. F.*; Infusum Calumbæ, *Br.*; Tinctura Calumbæ, *U. S.*, *Br.*

CALX. U. S., Br.

CALCIUM OXIDE [Lime Quicklime]

(călx)

"It contains, when freshly ignited to constant weight with a blast lamp, not less than 95 per cent. of CaO (56.07). It loses not more than 10 per cent. of its weight on ignition. Preserve it in air-tight containers in a dry place." *U. S.* "Lime, CaO, is calcium oxide obtained by calcining marble." *Br.*

Calcii Oxidum, Calcium Oxydatum; Calcaria Usta, Calx Viva, Calx Usta, Oxydum Calcicum; Burned Lime; Chaux Commune, *Fr. Cod.*; Chaux, Chaux vive, *Fr.*; Calcaria Usta, *P. G.*; Aetzkalk, Kalk, Gebrannter kalk, *G.*; Ossido di calcio, Calce, *It.*; Cal viva, *Sp.*

Calcium, which is ranked among the alkaline earths, is a very important pharmaceutical agent, and forms the principal ingredient in several standard preparations. It is a very abundant natural production. It is never found free, but mostly combined with acids, as with carbonic acid in chalk, marble, calcareous spar, limestone, and shells; with sulphuric acid in the different kinds of gypsum; with phosphoric acid in the bones of animals; and with silica in a great variety of minerals.

Preparation.—Lime is prepared by calcining, by a strong heat, some form of the native carbonate. The carbon dioxide is thus expelled, and the lime remains. When the lime is intended for delicate chemical operations, it may be obtained from Iceland spar. For the purpose of the arts it is procured from common limestone, by calcining it in kilns of peculiar construction. When obtained in this way it is generally impure, being of a grayish color, and containing alumina, silica, ferric oxide, and occasionally a little magnesia and manganese oxide.

The official lime of the United States and British Pharmacopœias is the lime of commerce, and not quite pure. It may be obtained purer by exposing pure white marble, broken into small fragments, in a covered crucible, to a full red heat for three hours, or until the residue, when slaked and suspended in water, no longer effervesces on the addition of hydrochloric acid.

Properties.—Lime is in "hard, white or grayish-white masses or granules, or as a white powder; odorless and having a caustic taste. One Gm. of Calcium Oxide dissolves in 840 mils of water at 25° C. (77° F.); also in 1740 mils of boiling water; soluble in glycerin and syrup; insoluble in alcohol. When moistened with water, Calcium Oxide becomes heated, and is gradually converted into a white powder (calcium hydroxide or slaked lime). When this is mixed with about 3 or 4 times its weight of water, it forms a smooth magma (milk of lime). Water, when agitated with Calcium Oxide, becomes alkaline to litmus. Slake 1 Gm. of Calcium Oxide, thoroughly mix it with 50 mils of water, and decant the greater portion of the milky liquid; the addition of an excess of diluted hydrochloric acid to the residue does not cause more than a slight effervescence (*carbonate*). Mix 5 Gm. of Calcium Oxide, after slaking, with 100 mils of distilled water, followed by hydrochloric acid, drop by drop, with agitation until solution takes place. The resulting solution, after boiling and cooling, should be acid and should not deposit more than 0.05 Gm. of insoluble matter. Ammonium oxalate T.S. added to a portion of this solution, after neutralizing it with ammonia water, yields a white precipitate, insoluble in acetic acid, but soluble in hydrochloric acid. Ignite to constant weight with a blast lamp in a tared platinum crucible a portion of Calcium Oxide; it loses not more than 10 per cent. in weight of the Calcium Oxide taken (*volatile substances*).

"**Assay.**—Dissolve about 1 Gm. of Calcium Oxide, previously ignited to constant weight over a blast lamp and accurately weighed, in 20 mils of diluted hydrochloric acid, cool the solution, dilute with distilled water to 100 mils and mix well. Transfer 20 mils of this solution to a 200 mil graduated flask and proceed with the assay as directed under *Calcii Carbonas Præcipitatus*. Each mil of tenth-normal oxalic acid V.S. corresponds to 0.0028035 Gm. of CaO. Each gramme of freshly ignited Calcium Oxide corresponds to not less than 338.9 mils of tenth-normal oxalic acid V.S." *U. S.*

"Compact whitish masses, which readily absorb water. When rather less than their weight of water is added, the masses swell and fall to powder with the development of much heat. The powder obtained by this process of slaking, when shaken with *water*, gives, after filtration, a clear alkaline solution which yields the *reactions* characteristic of calcium. Yields not more than the slightest characteristic *reactions* for iron, silica, carbonates, chlorides, or sulphates. *Arsenic limit* 5 parts per million." *Br.*

Lime is calcium oxide 56.07, and consists of one atom of calcium 40.07, and one of oxygen 16.00. Its sp. gr. is 3.15 to 3.40, while the hydroxide has the sp. gr. 2.078. (Filhol.) Its solubility in water is greatly increased by the addition of sugar or glycerin. (See *Liquor Calcis Saccharatus.*) It is distinguished from the other alkaline earths by forming a very deliquescent salt (*calcium chloride*) by reaction with hydrochloric acid, and a sparingly soluble one with sulphuric acid. All acids, acidulous, ammoniacal, and metallic salts, borates, alkaline carbonates, and astringent vegetable infusions are incompatible with it.

Uses.—Lime acts externally as an escharotic, and was formerly applied to ill-conditioned *ulcers*. The *lime ointment* of Spender is made by incorporating four parts of washed slaked lime with one part of fresh lard and three parts of olive oil, previously warmed together. Mixed with potassium hydroxide, lime forms *Potassa cum Calce*, official in the U. S. P. 1890. As an internal remedy, it is converted into hydroxide and this is administered in solution. (See *Liquor Calcis.*)

Off. Prep.—Liquor Calcis, *U. S.* (*Br.*); Liquor Calcis Saccharatus, *Br.*; Liquor Calcis Sulphuratæ, *N. F.*; Potassa cum Calce, *N. F.*; Soda cum Calce, *N. F.*

CALX CHLORINATA. U. S., Br.

CHLORINATED LIME CHLORINATED CALCIUM OXIDE Calx Chlorin. [Calx Chlorata, Pharm. 1890, Chloride of Lime]

(călx ¢hlo-rī-nā'tą)

"A product resulting from the action of chlorine upon calcium hydroxide, and containing not less than 30 per cent. of available chlorine [Cl = 35.46]. Preserve it in air-tight containers, in a cool and dry place." *U. S.* "Chlorinated Lime is obtained by exposing slaked lime to the action of chlorine gas until absorption ceases." *Br.*

Hypochlorite of Lime or Calcium, Oxymuriate of Lime or Calcium, Chloris Calcicus, Chloruretum Calcis, Calcis Chloridum, Calcii Hypochloris, Calcium hypochlorite, Bleaching Powder; Chlorure de Chaux sec, *Fr. Cod.*; Poudre de Tennant ou de Knox, *Fr.*; Calcaria Chlorata, *P. G.*; Chlorkalk, Bleichkalk, *G.*; Cloruro di calcio, *It.*; Hipoclorito calcico clorurado, *Sp.*

This compound, originally prepared as a bleaching agent in 1798 by Tennant, of Glasgow, is now enormously used both in the arts

and in medicine. (For a process of manufacture, see *U. S. D.*, 19th ed., p. 267.)

A more expeditious method of manufacture is now used, both in Germany (where it originated) and in this country, where bleaching powder is made from electrolytic chlorine. A series of horizontally placed drums or cylinders provided with revolving endless screws receive the dry calcium hydroxide, which, from its entering the top cylinder until discharged from the bottom one, meets a continuous stream of chlorine gas going in the opposite direction.

Several electrolytic processes for the decomposition of sodium and potassium chlorides have been introduced in recent years, whereby caustic alkali on the one hand and chlorine on the other hand are produced. The chlorine liberated is almost entirely utilized in the manufacture of bleaching powder. Large quantities are thus produced at present at Niagara Falls.

The production of bleaching powder in the United States in 1914 amounted to 111,076 tons, valued at $2,578,269, of which approximately two-thirds was produced electrolytically.

Properties.—Chlorinated lime is "a white, or grayish-white, granular powder, having the odor of chlorine. It becomes moist and gradually decomposes on exposure to the air and when in such condition must not be used or dispensed. It is partially soluble in water or alcohol. The insoluble portion settles readily when it is mixed with water. If lumps are present they readily break down and leave no core. Shake 1 Gm. of Chlorinated Lime with 50 mils of distilled water and filter; the filtrate at first colors red litmus blue, and then bleaches it. Dissolve Chlorinated Lime in diluted acetic acid; an abundance of chlorine gas is evolved, and only a trifling residue remains undissolved. Ammonium oxalate T.S. added to this solution yields a white precipitate, insoluble in acetic acid, but soluble in hydrochloric acid.

"**Assay.**—Introduce into a tared, stoppered weighing-bottle, containing 10 mils of distilled water, between 3 and 4 Gm. of Chlorinated Lime and weigh accurately. Triturate this thoroughly with 50 mils of distilled water, transfer the mixture to a graduated liter flask, rinse the mortar with distilled water, add the rinsings to the mixture and then sufficient distilled water to make 1000 mils, stopper the flask and allow it to stand for ten minutes. Shake it thoroughly, add to 100 mils of the mixture 1 Gm. of potassium iodide and 5 mils of acetic acid, and titrate with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. When calculated to the weight of Chlorinated Lime taken, it shows not less than 30 per cent. of available chlorine. Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.003546 Gm. of available chlorine (Cl). Each gramme of Chlorinated Lime corresponds to not less than 84.6 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

"A dull white powder with a characteristic chlorinous odor, becoming moist and gradually decomposing on exposure to air. Partially soluble in *water*. The solution yields the *reactions* characteristic of calcium and of chlorides, and evolves chlorine copiously upon the addition of an acid. 0.5 gramme of Chlorinated Lime, mixed with 1.5 grammes of *potassium iodide* dissolved in 200 millilitres of *water*, gives, when acidified with 6 millilitres of *hydrochloric acid*, a reddish solution, which requires for decolorisation not less than 42.3 millilitres of *N/10 solution of sodium thiosulphate*, corresponding to not less than 30 per cent. of available chlorine." *Br.*

When perfectly saturated with chlorine it dissolves almost entirely in water. When exposed to heat, it gives off oxygen and some chlorine, and is converted into calcium chloride. It is incompatible with the mineral acids, carbon dioxide, and the alkaline carbonates. The acids evolve chlorine copiously, and the alkaline carbonates cause a precipitate of calcium carbonate. (See *Liquor Sodæ Chlorinatæ*).

Chlorinated lime is an oxidizing agent, the oxygen being derived from water, the hydrogen of which unites with the chlorine to form hydrochloric acid. It has a powerful action on organic matter, converting sugar, starch, cotton, linen, and similar substances into formic acid, which unites with the lime. (W. Bastick.) It also acts energetically on the volatile oils, including oil of turpentine, producing chloroform. (*J. P. C.*, March, 1855.)

Chlorinated lime constantly becomes weaker on exposure to air, giving off chlorine or hypochlorous acid, probably through the influence of the atmospheric carbon dioxide, which sets them free by combining with the lime. But it would seem that, even when closely confined, it sometimes at least gives off gaseous matter, as we have an account of a well-stoppered bottle containing it having been broken by a violent explosion, without any peculiar exposure to heat. (See *A. J. P.*, 1861, p. 72.) Barreswil has found that the subjection of chlorinated lime to strong pressure greatly diminishes the tendency to decomposition. It is rendered in this way as hard as a stone, and may be kept long without undergoing change. (*Chem. News*, No. 58, p. 33.)

According to Lunge's investigations, the best temperature for the absorption of chlorine by calcium hydroxide is 40° to 45° C. (104°–113° F.); from pure calcium hydroxide a bleaching powder of 43 per cent. active chlorine can be produced, in which case allowance for 4 per cent. of moisture in the hydroxide is made; strong mineral acids, when not used in excess, liberate only hypochlorous acid; dry carbon dioxide at normal temperature does not set free any chlorine, but at moderately elevated temperature drives off almost all the chlorine.

Composition.—The composition of chlorinated lime is represented by the formula $CaOCl_2$, and it was formerly supposed to be a direct compound of lime with chlorine. This view, however, is not consistent with its reactions, for when distilled with diluted nitric

acid it readily yields a distillate of aqueous hypochlorous acid, and when treated with water it is resolved into calcium chloride and hypochlorite, the latter of which may be separated in crystals by exposing the filtered solution to a freezing mixture, or by evaporating it in a vacuum over oil of vitriol and leaving the dense frozen mass to thaw upon a filter. A solution of calcium chloride mixed with hypochlorite then passes through, and feathery crystals remain on the filter, very unstable, but consisting, when recently prepared, of hydrated calcium hypochlorite, $Ca(OCl)_2.4H_2O$. This seems, at first sight, to show that the bleaching powder is a mixture of calcium chloride and hypochlorite, formed according to the equation

$$2CaO + Cl_4 = CaCl_2 + Ca(ClO)_2$$

but if this were its true constitution, the powder when digested with alcohol ought to yield a solution of calcium chloride containing half the chlorine of the original compound, which is not the case. Its constitution is, therefore, better represented by the formula $Ca\begin{cases} Cl \\ OCl \end{cases}$ suggested by Odling, this molecule being decomposed by water into chloride and hypochlorite in the manner just explained, and yielding with diluted nitric acid or sulphuric acid a distillate containing hydrochloric and hypochlorous acids,

$$CaCl(OCl) + 2HNO_3 = Ca(NO_3)_2 + HCl + HClO$$

(Lunge and Schaeppi, *A. J. P.*, 1881; Lunge and Naef, *Ber. d. Chem. Ges.*, 1883.) Lunge and Bachofen (*Zeit. angew. Chem.*, 1893, 326) have determined the specific gravities of chlorinated lime solutions at 15° C. (59° F.). (See *Proc. A. Ph. A.*, 1894, 579.)

Impurities and Tests.—Chlorinated lime may contain a great excess of lime, from imperfect impregnation with the gas. This defect will be shown by the large proportion insoluble in water. If it contain much calcium chloride, it will be quite moist, which is always a sign of inferior quality. When long and insecurely kept, it deteriorates from the gradual formation of calcium chloride and calcium carbonate. Several methods have been proposed for determining its bleaching power, which depends solely on the proportion of loosely combined chlorine. Walter proposed to add a solution of the bleaching powder to a standard solution of indigo sulphate, in order to ascertain its decolorizing power; but the objection to this test is that the indigo of commerce is very variable in its amount of coloring matter. The oxidation of an arsenous acid solution is largely used in practice. Lunge (*Ber. d. Chem. Ges.*, 1886, p. 869) has also proposed to use hydrogen dioxide (H_2O_2) solution for the valuation of bleaching powder. The two solutions liberate oxygen in exactly equal amount. This is measured in a nitrometer.

The following is the test given in the British Pharmacopœia: "0.5 gramme of Chlorinated Lime, mixed with 1.5 grammes of *potassium iodide* dissolved in 200 millilitres of *water*, gives, when acidified with 6 millilitres of *hydrochloric acid*, a reddish solution, which requires for decolorization not less than 42.3 millilitres of *N/10 solution of sodium thiosulphate*, corresponding to not less than 30 per cent. of available chlorine." *Br.*

This is similar in principle to the U. S. P. assay method previously described. In this process iodine is separated by the chlorine in equivalent quantity, and imparts color to the liquid, which is removed by the sodium thiosulphate, by forming colorless compounds with the iodine, and the quantity required for this purpose measures the quantity of iodine, and consequently that of the chlorine, present in the chlorinated solution. (See *Sodii Thiosulphas.*)

Uses.—As the therapeutic virtues of chlorinated lime depend largely upon the chlorine gas which is liberated from it, it may be well to discuss in this place the effects of chlorine. This gas is an extraordinarily powerful germicide, according to Geppert (*B. K. W.*, 1890) 0.03 per cent. being sufficient to kill the highly resistant anthrax spores in two minutes. It should be noted, however, that in the absence of moisture its germicidal power is comparatively slight. Gaseous chlorine has been used for the purpose of disinfecting inclosed spaces, such as ships' holds, but although highly efficient, if properly used, has largely passed out of vogue. Not only is chlorine actively germicidal, but because of its oxidizing effect decomposes hydrogen sulphide and other malodorous substances, thereby acting as a deodorant. For the same reason it is a powerful bleaching agent and destructive to many kinds of organic matters.

Chlorinated lime possesses desiccant, disinfectant, deodorizant, and bleaching powers. As a bleaching agent it is widely used in the arts. As regards its antibacterial properties it probably ranks, except the salts of mercury and silver, as the most active germicide official. Bolton has shown that one part in two thousand of chlorinated lime is sufficient to destroy the viability of the typhoid bacillus within two hours, and that a one per cent. solution would kill the anthrax spores in the same time. Niessen (*Z. Hyg.*, vii, p. 62) finds that a one per cent. solution can be relied on to destroy either typhoid or cholera germs in the feces within ten minutes, while Stokes and Hatchel (*J. A. M. A.*, li, p. 1505) report that chlorinated lime equivalent to from 0.4 to 1.5 parts per million of chlorine killed ninety per cent. of the bacteria in drinking water.

The most important use of chlorinated lime is as a disinfectant. For the purpose of destroying disease germs in urine, feces, sputa, or similar matters it is, taking all things into consideration, the best of all chemical agents. Its advantages are its relative cheapness, the promptness and certainty of its action, and its oxidizing power whereby it tends to destroy the breeding places of the germs. For this purpose sufficient chlorinated lime to equal about two parts for each hundred of excre-

ment should be intimately mixed and the mixture allowed to stand for one or two hours in an agate-ware, china, or glass receptacle. A solution of one pound of chlorinated lime to a bucketful of water makes an excellent disinfectant for washing the walls and floors of dissecting rooms, privies, docks, and other places with offensive effluvia, not only for its germicidal, but especially for its deodorizing effect. The same solution is also serviceable for sterilizing dishes and other utensils which have been used by patients with infectious diseases. Because of its decolorizing effect it is not a suitable agent for the sterilization of colored goods or clothing.

For more directly medicinal purposes chlorinated lime has been used in solution externally as an application to ill-conditioned *ulcers, burns, chilblains,* and the *itch,* also as a gargle in *angina* and as a disinfectant and deodorizant mouth wash in *ulcerated gums* and similar conditions. Binz (*B. K. W.,* 1909) recommends an ointment containing from 10 to 20 per cent. of chlorinated lime for the treatment of *chilblains* and of *erysipelas.* This ointment must be made with petrolatum as the true fats rapidly render the salts inert. For external application the solution may be made of the strength of from one to four drachms (3.9–15.5 Gm.) to a pint (500 mils) of water. Vincent (*Press. Mèd.,* 1914, Oct. 8) has had success in the treatment of *hospital gangrene* by powdering the wound with a mixture of 1 part of chlorinated lime to 10 parts of boric acid. Internally it has been used as an intestinal disinfectant in *typhoid fever* and other conditions, but the compound solution of chlorine is usually preferred. Riehl (*W. M. W.,* 1907) has confirmed the findings of Calmette regarding the value of calcium hypochlorite as an antidote for *snake bite.* For this purpose ten mils (2½ fluidrachms) of a 1 per cent. solution should be immediately injected in the neighborhood of the wound. Under the name of *Dakin's solution* a preparation which combines the advantages of nascent chlorine without the irritating effect of the alkalies which are usually present, has been largely used in some of the European hospitals during the present war. (See *Liquor Sodæ Chlorinatæ.*)

Chlorinated lime acts exclusively by its chlorine which being loosely combined is disengaged by the slightest affinities. It should, therefore, be carefully kept from contact with the air and organic substances, which cause rapid loss of chlorine, and the modern method of putting it up for ordinary use in hermetically sealed zinc boxes is a great convenience. R. C. Bicknell examined commercial chlorinated lime put up in boxes for available chlorine. He found the top layers usually deficient in strength, but in the interior from 30 to 35 per cent. of chlorine. Some of the packages assaying 30 per cent. of chlorine were more than a year old. (*A. J. P.,* 1886, p. 593.) Investigations made more recently show that variations in the percentage of chlorine are found in the chlorinated lime put up in packages. See Puckner, Stephens, Harding. (*Proc. A. Ph. A.,* 1898, 905.) All acids, even carbonic, disengage it, and, as this acid is a product of animal and vegetable decomposition, noxious effluvia furnish the means, to a certain extent, of their own disinfection; but the stronger acids disengage the chlorine far more readily, and among these sulphuric acid is the most convenient. Accordingly, the powder may be dissolved in a very dilute solution of this acid, or a small quantity of the acid may be added to an aqueous solution ready formed, if a more copious evolution of chlorine be desired than that which takes place from the mere action of the carbon dioxide of the atmosphere.

From one to four drachms of the powder added to a pint of water, and the solution filtered, will form a liquid within the limits of strength ordinarily required. For the cure of *itch,* Derheims has recommended a much stronger solution—three ounces of the chloride to a pint of water, the solution being filtered, and applied several times a day as a lotion, or constantly by wet cloths. When applied to *ulcers,* their surface may be covered with lint dipped in the solution. When used as an ointment to be rubbed upon *scrofulous enlargements* of the lymphatic glands, this may be made of a drachm of the chloride to an ounce of lard.

It has been used occasionally internally, in *adynamic dysentery, typhus fever,* and various other *low diseases;* it may be considered as therapeutically equivalent to chlorine. The dose internally is from three to six grains (0.2–0.4 Gm.), dissolved in one or two fluidounces (30–60 mils) of water, filtered and sweetened with syrup. It should never be given in pills.

Chlorinated lime may be advantageously applied to the purpose of purifying offensive water, a property which makes it invaluable on long voyages. When used for this purpose, from one to two ounces of the chloride may be mixed with about sixty-five gallons of the water. The water must afterwards be exposed for some time to the air, and allowed to settle, before it is fit to drink. As a general water purifying agent, however, the amount to be used is sufficient to represent about one part of available chlorine per million parts of water. This destroys all pathogenic bacteria and communicates scarcely any taste or odor to the water. A new and valuable reagent for the qualitative detection of free or available chlorine, capable of showing a positive reaction in water containing as small a proportion as 0.01 part of chlorine to the million, has been described in the *Amer. Journ. of Pub. Health* for 1916, p. 160, by the Committee on Standard Methods of Water Analysis. It consists of a solution of 1 Gm. of orthotolidin in 1000 mils of 10 per cent. hydrochloric acid. In the presence of chlorine this reagent gives a yellow or greenish-yellow color. It may also be used for quantitative determinations of free or available chlorine by using colorimetric methods of comparison, and permanent comparison standards may be made from

copper sulphate solutions according to the directions given in the article.

Chlorinated lime is less eligible for some purposes than the solution of chlorinated soda. (See *Liquor Sodæ Chlorinatæ.*)

Dose, four grains (0.26 Gm.).

Off. Prep.—Liquor Calcis Chlorinatæ, *Br.;* Liquor Sodæ Chlorinatæ, *U. S., Br.;* Liquor Potassæ Chlorinatæ, *N. F.*

CAMBOGIA. U. S.

GAMBOGE Cambog. [Pipe Gamboge]

(kăm-bō'jĭą)

"A gum-resin obtained from *Garcinia Hanburii* Hooker filius (Fam. *Guttiferæ*)." *U. S.*

Cambogia, *Br.* 1898; Gambogia, *U. S. Pharm.* 1870; Gummi-resina guttæ (s. gutti), Gutta Gamba, Cambodia; Gommegutte, *Fr. Cod.;* Gutte, *Fr.;* Gutti, *P. G.;* Gummigutt, *G.;* Gumma gotta, *It.;* Gutagamba, Goma gutta, *Sp.*

Under the name of *Cambogia Indica, Indian Gamboge,* the British Addendum formerly recognized a gum-resin obtained from the *Garcinia Morella* Desrouss. Several plants belonging to the family of *Guttiferæ,* growing in the equatorial regions, yield on incision a yellow opaque juice, which hardens on exposure and bears a close resemblance to gamboge; but it is only from a particular tree, growing in Siam, that the official gum-resin is procured. According to observations of Baildon and Jamie, gamboge is obtained exclusively from the province of Cambodia, the plant not being found in any other part of Siam nor in Cochin China. (*J. P. C.,* Juillet, 1874.) Several years since, Christison received from Singapore specimens of the gamboge plant cultivated in that island, and derived from Siam, which proved to be a Garcinia, differing from the *G. elliptica* of Wallich chiefly in having its male flowers upon pedicels. Subsequently Hanbury obtained from the same source numerous specimens of the same plant, and was enabled to confirm the statement of Christison; but he also found that the plant approached very near to the *Garcinia Morella* of Desrousseaux, from which it could be distinguished only by its pedicellate flowers. These specimens were afterwards submitted to the inspection of Thwaites in Ceylon, who is perfectly familiar with the Garcinias of that island, and were pronounced by him to belong to a variety of *G. Morella,* scarcely differing from the Ceylon plant, except in having pedicelled instead of sessile flowers; for these two varieties the names of *G. Morella,* var. *sessile,* and *G. Morella,* var. *pedicellata,* were proposed. Sir Joseph Hooker, however, determined (*Journ. Linn. Soc.,* xiv, 485) that the var. *pedicellata* is a distinct species, differing from *G. Morella* in having not only its flowers pedicellate, but also its leaves more ovate and much larger, and its fruit larger; he very properly gave it the specific name of *Hanburii* to commemorate the contributions of the late Mr. Hanbury to pharmaceutical science, and his connection with the history of the present plant. According to the researches of Beckett, *G. Hanburii* is confined to the islands and sea coast of the Gulf of Siam, where it is known as "*Ton Rong,*" and where it grows to the height of fifty feet, with a diameter of twelve inches.

It is doubtful if all of the Gamboge of commerce is obtained from *Garcinia Hanburii.* Some of it is probably obtained from *G. Morella* Desr. and *G. Roxburghii* Engler, plants growing in Canara; *G. Wightii* T. Anders, a plant of Southern Farther India; *G. tetranda* Wall., *G. Gaudichaudii* Planch. et Triana growing in Cochin China and *G. pictoria* (Roxb.) Engl., a plant found in Ceylon and Farther India.

Ceylon gamboge, derived from *G. pictoria,* Roxb., is procured by incisions, or by cutting away a portion of the bark, and scraping off the juice which exudes. The specimens sent to Christison were in flattish or round masses, eight or nine inches in diameter, apparently composed of aggregated irregular tears, with cavities which are lined with a grayish and brownish powdery incrustation. It resembled coarse gamboge, and was identical in composition. In Ceylon it is used as a pigment and purgative. (Christison.) *New Caledonian Gamboge,* derived from *Garcinia collina* Vieil, is described by Heckel and Schlagdenhauffen as very similar in its appearance and reactions to ordinary gamboge; its color is, however, deep orange. A white crystalline compound, which when heated beyond 235° C. (455° F.) produced pyrocatechin, was found in it, and marked the point of difference between it and other varieties of gamboge. (*Rép. de Pharm.,* 1893, 193.)

Gamboge is said to be procured in Siam by breaking off the leaves and shoots of the tree; the juice, which is contained in ducts or latex vessels in the bark, issues in drops, and, being received in suitable vessels, gradually thickens, and at length becomes solid. Jamie, of Singapore, states that incising the trunk and larger branches is often practised. The juice is frequently received into the hollow joints of the bamboo, and the water expelled by mild continuous heat. In this way the so-called pipe gamboge is formed, the contraction during drying causing the cylinders to be hollow. According to Beckett, Siam gamboge is obtained only from trees of not less than ten years of age and during the rainy months, from June to October, by cutting long, spiral grooves into the bark and collecting in hollow bamboos the sap which trickles down in a viscous stream. (*Kew Bulletin,* 1895.)

The name *gummi gutta,* by which gamboge is generally known on the continent of Europe, probably originated from the circumstance that the juice escapes from the plant by drops. The official title was undoubtedly derived from the province of Cambodia, in which the gum-resin is collected. Gamboge was first brought to Europe by the Dutch, about the middle of the seventeenth century. We import it from

Canton and Calcutta, whither it is carried by the native or resident merchants. There is no difference in the appearance or character of the drug as brought from these two ports—an evidence that it is originally derived from the same place.

Varieties.—The best gamboge is in cylindrical rolls, from two to five centimeters in diameter, sometimes hollow in the centre, sometimes flattened, often folded double, or agglutinated in masses so that the original form is not always easily distinguishable. The pieces sometimes appear as if rolled, but are in general striated longitudinally from the impression made by the inner surface of the bamboo. They are externally of a dull orange color, which is occasionally displaced by greenish stains, or concealed by the bright yellow powder of the drug, slightly adhering to the surface. In this form the drug is sometimes called *pipe gamboge.* Another variety is imported under the name of *cake* or *lump gamboge.* It is in irregular masses weighing a kilo or more, often mixed with sticks and other impurities, containing many air-cells, less dense, less uniform in texture, and less brittle than the former variety, and breaking with a dull and splintery instead of a shining and conchoidal fracture. The worst specimens of this variety, as well as of the cylindrical, are sometimes called by the druggists *coarse gamboge.* They differ, however, from the preceding only in containing a greater amount of impurities. Indeed, it would appear from the experiments of Christison that all the commercial varieties of this drug have a common origin, and that cake or lump gamboge differs from the cylindrical only in the circumstance that the latter is the pure concrete juice, while to the former, farinaceous matter and other impurities have been added for the purpose of adulteration. The inferior kinds of gamboge may be known by their greater hardness and coarser fracture; by the brownish or grayish color of their broken surface, which is often marked with black spots; by their obvious impurities, and by the green color which their decoction, after cooling, gives with tincture of iodine (starch). When pure, the gum-resin is completely dissolved by the successive action of ether and water, so that the amount of residue left by any specimen treated in the manner just spoken of indicates approximately the measure of the adulteration.

Properties.—The official description is as follows: "In hard, brittle, cylindrical pieces, usually hollow in the center, from 2 to 5 cm. in diameter, from 10 to 20 cm in length, externally grayish-orange-brown, longitudinally striate; fracture conchoidal, smooth, orange-red: odorless; taste very acrid. When rubbed with water it yields a yellow emulsion which becomes darker and almost transparent upon the addition of ammonia water. The emulsion turns green upon the addition of iodine T.S. (*starch*). The powder is bright yellow, containing few or no starch grains. When mounted in hydrated chloral T.S. and examined under the microscope the particles, for the most part, slowly dissolve, leaving scattered fragments of vegetable tissues. Not less than 65 per cent. of Gamboge is soluble in alcohol. Gamboge yields not more than 2 per cent. of ash." *U. S.*

From the brilliancy of its color, gamboge is highly esteemed as a pigment. It has no odor, and little taste, but, after remaining a short time in the mouth, produces an acrid sensation in the fauces. Its sp. gr. is 1.221. "When *solution of iodine* is added to a cooled aqueous decoction, the color should not become distinctly green (absence of more than a trace of starch). When incinerated it should not yield more than 3 per cent. of ash." *Br.* 1898. It is a gum-resin, without volatile oil. Christison has shown that the proportion of gum and resin varies in different specimens even of the purest drug. In one experiment, out of 100.8 parts he obtained 74.2 of resin, 21.8 of gum, and 4.8 of water. The gum is quite soluble in water, and of the variety denominated arabin. Flückiger, however, says that the gum is not identical with gum arabic, as its solution does not redden litmus, and is not precipitated by neutral lead acetate, nor by ferric chloride, nor by sodium silicate or biborate. By fusing purified gamboge resin with potassium hydroxide, Hlasiwetz and Barth (*Ann. Ch. Ph.*, 138, 61) obtained acetic and other acids of the same series, together with *phloroglucin*, $C_6H_3(OH)_3$, *pyrotartaric acid*, $C_5H_8O_4$, and *isouvitinic acid*, $COOH.C_6H_4.CH_2COOH$. Sassarini found gamboge to contain the following constituents: 1. Gum analogous to arabin. 2. Volatile oil, consisting of terpene and a camphor. 3. Isouvitinic and acetic acids. 4. A phenol ester. 5. Resin. 6. Methyl alcohol and some higher homologues. 7. A liquid having a fruity odor resembling aldehyde or acetone. He believes phloroglucin found by others to be a decomposition product. (*Ann. di Chim. Farm.*, 1897.) Gamboge is readily and entirely diffusible in water, forming a yellow opaque emulsion, from which the resin is very slowly deposited. It yields its resinous ingredient to alcohol, forming a golden-yellow tincture, which is rendered opaque and bright yellow by the addition of water. Its solution in ammoniated alcohol is not disturbed by water. Ether dissolves about four-fifths of it, taking up only the resin. It is wholly taken up by alkaline solutions, from which it is partially precipitated by the acids. The strong acids dissolve it; the solution when diluted deposits a yellow sediment. The color, acrimony, and medicinal power of gamboge are thought to reside in the resin. Hirschsohn gives a method for detecting gamboge in mixtures in *Ph. Z. R.*, xxiv. (*A. J. P.*, 1885.)

Uses.—Gamboge is a powerful, drastic, hydragogue cathartic, so very apt to produce nausea and vomiting and much griping when given in the full dose that it is almost never employed except in combination with other cathartics. In large quantities it is capable of

causing fatal effects, and death has resulted from a drachm. The full dose is from two to six grains (0.13–0.4 Gm.), which in cases of *tenia* has been raised to ten or fifteen grains (0.65–1.0 Gm.). It may be given in pill or emulsion, or dissolved in an alkaline solution. In the dose of five grains (0.32 Gm.) the resin is said to produce copious watery stools, with little or no uneasiness. If this be the case, it is probable that, as it exists in the gum-resin, its purgative property is somewhat modified by the other ingredients.

Dose, two grains (0.13 Gm.).

Off. Prep.—Pilulæ Catharticæ Compositæ, *U. S.*

CAMPHORA. U. S., Br.

CAMPHOR Camph.

(căm'phọ-rạ)

"A ketone [$C_{10}H_{16}O$ or $C_9H_{16}CO = 152.13$] obtained from *Cinnamomum Camphora* (Linné) Nees et Ebermaier (Fam. *Lauraceæ*); it is dextrorotatory. Preserve it in well-closed containers, in a cool place." *U. S.* "Camphor, $C_{10}H_{16}O$, is a white crystalline substance obtained from Cinnamomum Camphora, *T. Nees and Eberm.*, purified by sublimation." *Br.*

Camphre du Japon, *Fr. Cod.;* Camphre, *Fr.;* Camphora *P. G.;* Kampher, Kampfer, Campher, *G.;* Canfora, *It.;* Alcanfor, *Sp.*

The name of camphor has been applied to various concrete, white, odorous, volatile products, found in different aromatic plants, and resulting probably from chemical change in their volatile oil. But commercial camphor is derived exclusively from two plants, the *Cinnamomum Camphora* (L.) of Nees or *Laurus Camphora* of Linnæus (Fam. *Lauraceæ*) and the *Dryobalanops Camphora* Colebrooke (Fam. *Dipterocarpaceæ*); the former of which yields our official camphor, the latter, the Borneo or Baras camphor, a product much valued in the East, but unknown in the commerce of this country and of Europe. Borneo camphor resembles true camphor, but is distinguished by being heavier than water and not being volatile at ordinary temperatures. On treatment with nitric acid it is converted into true camphor.

The camphor tree (*Cinnamomum Camphora*) is an evergreen which sometimes attains great size, having the aspect of the linden, with a trunk straight below, but divided above into many branches, which are covered with a smooth, greenish bark. Its leaves, which stand alternately upon long foot-stalks, are ovate-lanceolate, entire smooth and shining, ribbed, of a bright yellowish-green color on their upper surface, paler on the under, and two or three inches in length. The flowers are small, white, pedicelled, and collected in clusters, which are supported by long axillary peduncles. The fruit is a red berry, resembling that of the cinnamon. The camphor tree is a native of China, Japan, and adjacent portions of Eastern Asia, but is capable of cultivation in most sub-tropical countries, where the minimum winter temperature is not below −6.6° C. (20° F.), and the summers are warm. It thrives in Formosa, Madagascar, Argentina, Egypt, Canary Islands, Southern Europe, Southern Florida, Southern California, and is being cultivated in India and Ceylon. The chief obstacle to its cultivation seems to be the extreme slowness of growth of the tree, and the corresponding slowness of returns from the investment. For an account of cultivation in Florida see *D. C.*, Sept., 1902; also True and Hood, *Proc. A. Ph. A.*, 1909, p. 719.

In Japan and Formosa the drug is obtained chiefly from the root, trunk, and branches by the process of sublimation, but in the American plantations the leaves and small twigs are utilized, thus avoiding injury to the trees. Only the older trees are employed; indeed, it is said that a tree must be fifty years old before it should be considered available. The trees are marked in the forest after investigation by an expert, the lower part of the trunk, with roots, chopped up in small fragments, and some form of heat applied. In Japan the chips are said to be placed with a little water in iron vessels, surmounted by earthenware capitals furnished with a lining of rice straw. A moderate heat is then applied, and the camphor, volatilized by the steam, rises into the capital, where it is condensed upon the straw. In China the comminuted plant is said to be first boiled with water until the camphor adheres to the stick used in stirring, when the strained liquor is allowed to cool, and the camphor which concretes, being alternated with layers of earth, is submitted to sublimation. In the island of Formosa, where the camphor tree abounds, the chips are heated in a rough still. This is usually composed of a furnace surmounted with a trough or similar rude vessel, which is protected by clay. In this reservoir the chips are placed, with water upon them, and a perforated board luted upon the top; on this are set earthenware pots. A fire having been lighted, steam rises through the chips and carries the camphor with it to deposit it in the pots. The crude camphor is taken to the towns in baskets and then put into large vats, with holes in the bottom, through which an oil escapes called *camphor oil,* much used by the Chinese for medicinal purposes. It is said that of recent years hydraulic pressure is largely substituted for drainage.

Oil of Camphor.—Two substances occur in commerce under the name of oil of camphor: the one derived from the *Cinnamomum Camphora,* known as the *Formosa* or *Japanese Oil of Camphor,* and formerly official under the name of *Oleum Camphoræ* in the U. S. P.; the other the product of *Dryobalanops aromatica,* the *East India oil of camphor,* not occurring in American and European commerce. The commercial oil of camphor, as found in our markets, is a colorless fluid or of a light yellowish-brown color, having a strong odor precisely like that of camphor, a bitterish camphorous taste, and a specific gravity, according to Wm. Procter, of

0.940. It acts strongly on polarized light, and is dextrogyrate. It has been considered to be simply a mixture of camphor, $C_{10}H_{16}O$, and a hydrocarbon, $C_{10}H_{16}$, but is in reality much more complex. Yoshida (*A. J. P.*, 1886, p. 99) found in it *terebinthene,* $C_{10}H_{16}$, which differs in physical respects, however, from the terebinthene of oil of turpentine; a hydrocarbon boiling at 172° to 173° C.(341.6°–343.4° F.) and having a pleasant lemon odor, and, he thinks, is identical with the *citrene* of lemon oil; and an oxygenated oil, which constituted half of the crude oil, to which he gave the formula $C_{10}H_{16}O,H_2O$, and calls it *camphorogenol.* Schimmel & Co. of Leipsic, have since extracted *safrol* commercially from the Japanese oil of camphor, and give a different account of its composition. They state (*Schim. Rep.,* 1888) that it contains *camphor, safrol, eugenol,* a *sesquiterpene,* $C_{15}H_{24}$, and possibly *terpinol.* They do not consider Yoshida's camphorogenol to be a distinct substance.

Within the last few years there has appeared in the American and English markets in considerable quantity an oil of camphor produced in Japan. It is imported in tin cans, and varies in tint from the colorless transparency of water, through pale straw and yellow, to deep black. The specific gravity varies from 0.898 in the colorless oil to 0.990 in the very dark. The oil seems to vary greatly in the amount of camphor it contains, much of it having nearly all the solid principle removed before exportation. The odor is distinctly camphoraceous, with a peculiarity that suggests the odor of sassafras. It is said by Peter MacEwan to differ from the Formosa oil in its behavior towards nitric acid. If half a drachm of the acid be allowed to act upon half a drachm of Japanese oil, and then diluted with half a drachm of water, a crimson color will be produced. The Formosa oil so treated yields a milky color with a scarcely perceptible green shade; hydrochloric acid gives with each oil a salmon color, more marked, however, with the Japanese oil. For further details, see *P. J.,* vols. xv, xvi, and *J. C. S.,* Oct., 1885. The oil is said to be used in Japan for the preparation of Chinese ink and varnishes, and for burning. As a diluent for artists' colors it is useful because its capacity for dissolving resins is greater than that of oil of turpentine and similar liquids.

The oil of camphor has properties similar to those of camphor, but more stimulant, and is especially applicable to affections of the stomach and bowels in which an anodyne and stimulant impression is indicated, as *flatulent colic* and *spasmodic cholera.* It may also be used externally, as a rubefacient and anodyne liniment, diluted with soap, liniment, or olive oil, in *local rheumatism* and *neuralgic pains, bruises, sprains,* etc. The dose is two or three minims (0.12–0.2 mil).

The *Dryobalanops oil of camphor* is said to be found in trees too young to produce camphor, and is supposed to constitute the first stage in the development of this substance, as it occupies the cavities in the trunk which are afterwards filled with the camphor. The chief constituent of it is a peculiar volatile oil, which is termed *borneene;* it is isomeric with oil of turpentine, $C_{10}H_{16}$, and holds in solution borneol and resin. By fractional distillation this oil may be separated into two portions, the one more volatile than the other, but not differing in composition.

Commercial History.—The commerce of the world is supplied with camphor from China, Japan, and Formosa, the great bulk of the product coming from the latter island. After the annexation of Formosa by the Japanese, that Government, led by the unnecessary destruction of the camphor trees of the island, the inferiority of the camphor obtained, and the waste of the processes employed, and especially by the desire for revenue, made a governmental monopoly of the camphor trade which went into operation in 1900. From the first it was found necessary to afford military protection to the gatherers, from the abounding savage tribes, and during the Russo-Japanese war irregularities in this regard are said to have greatly diminished the product and to have caused a marked rise in the price of camphor. The camphor is sold by the Japanese government through a single London firm or company, Samuel Samuels, with sub-agencies at Hamburg, New York, and perhaps other cities. From these agencies refiners in different parts of the world buy it by contract for a year at a time. The statement freely made that camphor is sold at a fixed price by the Japanese government is incorrect, and the extraordinary rise of camphor in price is shown by the fact that in Nov., 1895, the average wholesale price of refined camphor was 58 cents per pound; in Nov., 1900, 62.5 cents per pound; in Nov., 1905, 83 cents per pound, and in the importations of crude camphor from Japan and Formosa are about 4,000,000 kilos annually. (See *Schim. Rep.,* April, 1914, 36.) Camphor is now cultivated on a commercial scale in Florida. According to an article in the *Oil, Paint, and Drug. Rep.,* Feb. 26, 1917, p. 18, one grove in Florida produces 40 tons of crude camphor annually.

The importations of crude camphor into the United States for 1916 were 4,574,430 pounds, and of refined and synthetic camphor 1,806,184 pounds.

There are two very distinct varieties of the crude camphor—namely, the Chinese and the Japanese, the Japanese camphor being divided into the Japanese camphor proper and the Formosa camphor. Of the two commercial varieties the Chinese comes in chests lined with lead, each containing about 130 pounds. It occurs in small grains or granular masses, of a dirty white color, frequently mixed with impurities. Japanese camphor (formerly known as *Dutch camphor* or *"tub camphor"* because it was exported through Batavia) is sent into market in tubs, covered with a peculiar matting, and in its general aspect resembles Chinese camphor. The value and purity of both

Chinese and Japanese camphor vary greatly in different specimens, but recently much of the Chinese crude camphor has been whiter and cleaner than the Japanese. It is always small grained and yields on sublimation crystals much smaller than are obtained from Japanese camphor, and is therefore less esteemed. A dark inferior grade of camphor is also obtained in the United States from commercial oil of camphor.

Sumatra Camphor. Borneo Camphor. Dryobalanops Camphor. Bhimsaim Camphor. Baros Camphor. Borneol.—This camphor is produced in the islands of Sumatra and Borneo, by *Dryobalanops Camphora* Coleb. This tree is very large, often exceeding one hundred feet in height, with a trunk six or seven feet in diameter, and ranks among the tallest and largest trees in India. (*A. J. P.,* xxiv, 329.) It is found in Sumatra and Borneo, and is abundant on the northwest coast of the former island. The camphor exists in concrete masses, which occupy longitudinal cavities or fissures in the heart of the tree, from a foot to a foot and a half long, at certain distances apart. The younger trees are generally less productive than the old. The only method of ascertaining whether a tree contains camphor is by incision. A party proceed through the forest, wounding the trees until they find one which will answer their purpose; and hundreds may be examined before this object is attained. When discovered, the tree is felled and cut into logs, which are then split, and the camphor removed by means of sharp-pointed instruments. It is stated that the masses are sometimes as thick as a man's arm, and that the product of a medium-sized tree is nearly eleven pounds; of a large one, double that quantity. The trees which have been wounded and left standing often produce camphor seven or eight years afterward. Ida Pfeiffer states, in her *Second Journey Round the World* (Am. ed., p. 183), that the camphor is also found in a concrete state under the bark and is swept down with long brooms. The whole tree is pervaded more or less by the camphor or the oil. The wood retains a fragrant odor, and, being on this account less liable to the attacks of insects, is highly esteemed for carpenter work.

Borneo camphor resembles in appearance ordinary camphor, but has, according to Christison, a specific gravity of 1.009, and sinks in water. Its odor is also distinctly different from that of camphor. It usually pulverizes without the addition of alcohol, is less volatile than ordinary camphor and does not crystallize in the interior of the bottles in which it is kept. It fuses at 206° C. (402.8° F.) and boils at 212° C. (413.6° F.); is dextrogyrate; has a formula of $C_{10}H_{17}(OH)$; and by the action of boiling nitric acid is converted into common camphor. It does not reach European commerce, being largely consumed in the Batta provinces, especially in funeral rites; and any that is exported is bought up at enormous prices for China, where it is preferred for embalming purposes on account of its being less volatile than the ordinary drug.

Borneo camphor is also produced in Johore, a province of the Malay peninsula, where it is sold in four qualities. The first is composed of transparent crystals, generally a quarter of an inch and upwards in length; the second of brown crystals, inferior in size; the third of powdery coherent and slightly colored grayish crystals, which resemble Japanese camphor; the fourth quality is brownish, pulverulent, and looks like seashore sand. (See *P. J.,* xvii.)

Ngai camphor is yielded by the *Blumea balsamifera* DC. (Fam. *Compositæ*) which occurs in India, China, Formosa, etc. The crude drug is known to the Chinese as *ngai-fêu,* and when refined in Canton as *ngai-p'ien.* About ten thousand pounds annually are exported from Canton. The refined camphor in appearance, odor, hardness, specific gravity, and volatility agrees almost precisely with Borneo camphor. According to Plowman, it has the chemical composition of Borneo camphor, but differs from it in its alcoholic solution, being lævogyrate, and in being converted by boiling nitric acid into a substance thought to be identical with the stearoptene of *Chrysanthemum Parthenium* Pers.

The physiological action of *Borneo* and *Ngai camphor* and of artificial *borneol* has been studied by R. Stockman (*J. P.,* 1888, ix) who finds that the action of the three substances is practically identical and closely resembles that of true camphor. The results obtained by A. Lapin (*Med. Age,* 1894, xii) confirm those of Stockman, and show that in its proper dose the drug increases the energy of the heart, and that in frogs it is an especial motor nerve paralyzant.

Artificial Camphor.—Camphor can be made artificially by the oxidation of *camphene,* $C_{10}H_{16}$, with chromium trioxide mixture. Camphene is obtained from either *pinenehydrochloride* (so-called artificial camphor) or from bornyl chloride by treatment with alcoholic potash, and is a solid crystalline mass, fusing at 49° C. (120.2° F.). In the patented process of Nathan Thurlow, camphor is made by submitting oil of turpentine to the action of anhydrous oxalic acid in steam-jacketed reaction tanks. The liquid mass, containing *pinyl oxalate* and *pinyl formate,* is then distilled in the presence of an alkali with live steam, the resultant products being camphor, Borneol camphor, and certain oily products, which are separated from one another and purified by a somewhat complicated process. It is stated that turpentine yields in this process from 25 to 35 per cent. of its weight, and that oil of lemon and other essential oils, and terpenes are obtained as secondary products. This artificial camphor is either optically inactive or has a very slight dextrorotation, but in general physical properties exactly resembles natural camphor. So far, however, it seems to be difficult to work the process upon a large scale and the artificial product has had no effect upon the general camphor market. Camphor can also be produced from isoborneol, by the action of oxidizing mixtures. The method patented in France, which

is said to yield from 95 to 100 per cent. of camphor, consists in suspending ten kilogrammes of isoborneol in ten kilogrammes of benzol, and adding ten kilogrammes of potassium permanganate dissolved in one thousand liters of water, until the color of the permanganate is discharged. The camphor produced is separated by distillation and crystallized from petroleum benzin. (*Chem. Ztg.*, 28.)

Refined Camphor.—The process for refining camphor was first practised in Europe by the Venetians, who probably derived it from the Chinese. It was afterwards transferred to the Dutch, who long enjoyed a monopoly of this business; and it is only within recent years that the process has been generally known. It is now practised largely in this country, and the camphor refined in our domestic establishments is equal to any formerly imported. Crude camphor is mixed with about one-fiftieth of quick-lime, and exposed, in an iron vessel placed in a sandbath, to a gradually increasing heat, by which it is melted and ultimately converted into vapor, which condenses in a suitable receiver. Refined in this manner, it is usually in the form of large circular cakes, one or two inches thick, slightly convex on one side and concave on the other, and perforated in the centre. Much refined camphor comes into the market in the form of compressed blocks, this being especially true of camphor refined in Philadelphia and Japan. It is stated that in Japan the refining of camphor is done by the Government and also by individuals, the process being probably that employed in the Philadelphia laboratories, as the first refining of camphor was done in Japan by a man who had been thoroughly educated in these laboratories. Japanese refined camphor occurs in rather thin, oblong cakes, enclosed in small tin boxes which have been hermetically sealed by a paper pasted over their edges. Camphor is refined in Philadelphia as follows: The vessels in which the camphor is put are of cast iron, circular, from 12 to 15 inches or more in diameter, and 4 inches deep, with perpendicular sides, and a ledge at top, on which the cover rests. This consists of sheet iron, with a hole through the center about an inch in diameter, over which a small hollow cone of sheet iron is placed loosely. The crude camphor mixed with the lime, the object of which is said to be to combine with the moisture present, which interferes with the due solidification of the camphor vapor, is placed in the iron vessels described, of which from 20 to 50 are arranged in a long sand bath. Heat is then applied until the camphor melts, after which the temperature is kept as nearly uniform as possible, so that the vaporization may take place regularly, without violent ebullition. The vapor condenses on the lower surface of the lid, and care is taken, by the occasional removal of the iron cone, and clearing of the opening by means of a knife, to allow the escape of any accidental excess of the vapor. A study of natural and synthetic camphor, by P. A. Houseman, giving a complete review of all processes for producing the synthetic article and illustrated with structural formulas, is found in *A. J. P.*, 1915, p. 49.

Properties.—"Camphor occurs in white, translucent masses or granules of a tough consistence and having a penetrating, characteristic odor, and a pungent, aromatic taste. It is readily pulverizable in the presence of a little alcohol, ether or chloroform. Camphor is slightly soluble in water and freely soluble in alcohol, chloroform, ether, carbon disulphide, petroleum benzin, or in fixed or volatile oils. Specific gravity: about 0.990 at 25° C. (77° F.). Camphor melts between 174° and 177° C. (345.2° and 350.6° F.). The specific rotation $[a]_D$ of Camphor in a solution in alcohol at 25° C. (77° F.) is between $+41°$ and $+42°$ in a 200 mm. tube, containing 10 Gm. of Camphor in each 100 mils of solution. The alcohol must be of the strength of about 95 per cent. by volume. It volatilizes at ordinary temperatures. On gradually heating about 2 Gm. of Camphor, it sublimes without carbonization and without leaving more than 0.05 per cent. of ash. A solution of Camphor in petroleum benzin (1 in 10) is clear (*moisture*). Hold the looped end of a piece of clean copper wire in a non-luminous flame until it glows, without coloring the flame green, then dip the loop into Camphor, ignite the adhering Camphor, and hold it so that the liquid burns outside of a non-luminous flame. On slowly bringing the flame from the burning Camphor on the loop in contact with the lower outer edge of the non-luminous flame, no green tinge is discernible (*chlorinated products*)." *U. S.*

"Colorless, transparent crystals or crystalline masses of tough consistence; also in rectangular tablets or in pulverulent masses known as 'flowers of camphor.' Penetrating and characteristic odor; taste pungent and somewhat bitter, followed by a sensation of cold. Specific gravity about 0.995. Melting point about 175° C. (347° F.). Soluble in about 700 parts of *water*, in 1 part of *alcohol* (90 per cent.), in 0.25 part of *chloroform*, and in 4 parts of *olive oil*; very soluble in *ether*. Burns readily with a bright smoky flame, volatilises even at ordinary temperatures, and sublimes without residue when heated. Forms a liquid when triturated with chloral hydrate, menthol, phenol, thymol, and certain other substances. A solution of 5 grammes in sufficient *alcohol* (90 per cent.) to produce 20 millilitres exhibits at 15.5° C. (60° F.) an *optical rotation* of about $+10°$ (distinction from synthetic camphor)." *Br.*

Camphor has a peculiar, strong, penetrating, fragrant odor, and a bitter, pungent taste, with a slight sense of coolness. It is beautifully white and pellucid, somewhat unctuous to the touch, brittle, and yet possessed of a tenacity which renders its reduction to a fine powder very difficult, unless its cohesion be overcome by the addition of a minute proportion of alcohol, ether, chloroform, glycerin, essential or fatty oils, or other volatile liquid for which it has an affinity. It may be obtained in powder by pulverizing with an equal weight of sugar,

by precipitating the tincture with water, or by grating and afterwards sifting it, or by sublimation. A still better plan is to dissolve camphor in one and a half parts of alcohol, and pour this solution with stirring into four parts of water. Collect the precipitate, wash with water, and dry. By noting the quantity of camphor used, the amount left dissolved in the diluted alcohol can be calculated, and this solution used in making tincture. The fracture of camphor is shining, and its texture crystalline. Its sp. gr. varies from 0.9857 to 0.996. When thrown in small fragments upon water, it assumes singular circulatory movements, which cease upon the addition of a drop of oil; and this property has been applied to the detection of grease in liquids, a very small proportion of which is sufficient to prevent the movements. Its volatility is so great that, even at ordinary temperatures, it is wholly dissipated if left exposed to the air. When it is confined in bottles, the vapor condenses on the inner surface, and, in large bottles partially filled, sometimes forms, after long standing, large and beautiful crystals. It melts at 175° C. (347° F.), boils at 204° C. (399.2° F.), and, in closed vessels, sublimes unchanged.

When allowed to concrete slowly from the state of vapor, it assumes the form of hexagonal plates. It is not altered by air and light. It readily takes fire, burning with a brilliant flame, with much smoke, and without residue. Water triturated with camphor dissolves, according to Berzelius, not more than a thousandth part; which, however, is sufficient to impart a decided odor and taste to the solvent. By the intervention of sugar or magnesia a much larger proportion is dissolved. (See *Aqua Camphoræ.*) Carbon dioxide increases the solvent power of water, as also does the spirit of nitrous ether. Ordinary alcohol will take up 75 per cent. of its weight of camphor, which is precipitated upon the addition of water. Berzelius states that 100 parts of alcohol, of the sp. gr. 0.806, dissolve 120 parts at 10° C. (50° F.). It is soluble without change in ether, the volatile and fixed oils, strong acetic acid, and diluted mineral acids, and is extremely soluble in chloroform. Nitric acid on prolonged boiling with camphor oxidizes it into *camphoric acid,* $C_{10}H_{16}O_4$ (see page 1301), and *camphoronic acid,* $C_9H_{14}O_6$. Schwanert's *camphresinic acid,* $C_{10}H_{14}O_{12}$, is, according to Kachler, a mixture of these two. Sulphuric acid in the proportion of ten parts to one gives, when heated with camphor, an oil isomeric with camphor, boiling at 200° C. (392° F.), and yielding a solid camphor when distilled repeatedly over potassium hydroxide. Sulphuric acid, in the proportion of four to one with camphor, gives, according to Chautard, a volatile product which he calls *camphrene,* and to which Schwanert gives the formula $C_9H_{14}O$. Kachler (*Ann. Ch. Ph.,* 164, p. 90) considers, however, that camphrene is only *phorone* (a condensation product of acetone) with slight impurities. Alcoholic potassium hydroxide solution heated with camphor gives a derivative called *campholic acid,* $C_{10}H_{18}O_2$, a white solid, fusing at 95° C. (203° F.), and boiling at 250° C. (482° F.). Resins unite with camphor, forming a soft tenacious mass, in which the odor of the camphor is sometimes almost extinguished, and frequently diminished; and a similar softening effect results when it is triturated with the concrete oils. Exposed to a strong heat, in closed vessels, camphor is resolved into carbonic acid gas and hydrocarbons, among which cymol is especially to be recognized.

Camphor, $C_{10}H_{16}O$, and borneol, $C_{10}H_{18}O$, are classified together as belonging to the group called in general *camphors,* which occur with the *terpenes* or essential oils, $C_{10}H_{16}$, and are to be considered as oxidation products of these latter.

Borneol is an alcohol, yielding esters when heated to about 200° C. (392° F.) with organic acids. It is a secondary alcohol, and therefore contains the group CH.OH linked to a more complex group. Secondary alcohols by oxidation yield *ketones,* by the change of the CH.OH group to CO. Common camphor bears this relation to borneol, and is therefore considered as a ketone, and can be formed from borneol by the action of mild oxidizing agents. The action of metallic sodium, on the other hand, upon common camphor, $C_{10}H_{16}O$, yields borneol, $C_{10}H_{18}O$.

Genuine camphor is said to be sometimes adulterated with the artificial, which may be detected by the action of ammonia upon its alcoholic solution, causing a flocculent precipitate, which does not redissolve, and the quantity of which is proportionate to that of the artificial product in any mixture of the two. (*A. J. P.,* xxxiv, 189.) As a means of distinguishing camphor from the artificial camphor resulting from the reaction between the oil of turpentine and hydrochloric acid, J. W. Bailey recommends that a drop of alcohol, holding in solution a little of the camphor to be tested, be allowed to evaporate on the slide of a microscope. The crystals then formed produce with polarized light, beautiful colors, if of natural camphor, but not, if of the artificial. (*Neues Repertorium,* xvi, 763, 1867.)

Uses.—Locally camphor is irritant, with probably a benumbing influence upon the peripheral sensory nerves, and somewhat antiseptic. It is absorbed through mucous membranes not very readily, but easily from subcutaneous tissue. It combines in the body with glycuronic acid and is eliminated in this combination by the kidneys. The systemic action of camphor is not well understood. In frogs it is depressant to the spinal cord and produces no motor disturbance except gradually increasing paralysis. In the mammalia, including man, it causes convulsions which are apparently due to an affect upon the motor tract of the brain. It appears also to have some stimulant action upon the intellectual centers and antagonizes the somnifacient drugs. On the other hand in conditions of nervous excitement it will frequently produce a sensation of quietude. The effects of

camphor upon the circulation have been the subject of an immense amount of scientific investigation but with very contradictory results. The majority of authorities have found that the drug increases the force of the cardiac contractions in cold-blooded animals, but in the studies upon warm-blooded animals the results have been so contradictory that it seems impossible to harmonize them. Most investigators have found that camphor does not produce any consistent change in the blood pressure until large doses are given, when it is likely to cause a fall, but on the other hand, Pilcher and Sollman (*J. P. Ex. T.*, 1915, vi, p. 349) have found that in the great majority of cases it causes a definite rise in the blood pressure. While Gottlieb (*Z. E. P. T.*, 1905, ii) and others have obtained evidence of a stimulant action upon the heart muscle of warm-blooded animals, the majority of experimenters have been unable to determine such an effect. (For review of the literature on this subject, see *J. P. Ex. T.*, 1914, v, p. 571.) On the other hand, the clinical evidence of the stimulating effect of camphor upon the circulation seems incontestable. In cases of heart failure whether due to diseases of the heart itself or secondary to infectious fevers, such as *typhoid* or in *pneumonia*, it is one of the most valued excitants that we possess. In the latter infection its value is not merely that of a circulatory stimulant, but it seems to have some direct restraining influence upon the growth of pneumococci. Several investigators have found that it will save a large proportion of the lower animals experimentally affected with pneumococcus.

Camphor is used in medicine internally for its calmative influence in *hysteria, general nervousness* and *neuralgia;* as a cardiac stimulant in all forms of heart failure, especially those occurring during low fevers and in pneumonia; and in the treatment of *serous diarrheas.* Externally it is widely employed as a counter-irritant in *sprains, rheumatic affections, bronchitis,* and other inflammatory conditions. It is also employed as a local application, especially in conjunction with menthol or phenol, in inflammations of the upper respiratory tract.

When a profound influence is desired, as in heart failure, it is necessary to give the drug hypodermically. For this purpose from three to five grains may be dissolved in twenty to thirty minims of sterile olive oil. The effect of a single injection lasts usually about two hours. In nervous diseases it may be given in substance, in capsule, or as the spirit; the water contains so little camphor that it is scarcely more than a vehicle.

Dose, two to five grains (0.13–0.32 Gm.).

Off. Prep.—Aqua Camphoræ, *U. S., Br.;* Ceratum Camphoræ (from camphor liniment), *N. F.;* Ceratum Plumbi Subacetatis, *N. F.;* Linimentum Aconiti, *Br.;* Linimentum Belladonnæ, *U. S., Br.;* Linimentum Camphoræ, *U. S., Br.;* Linimentum Camphoræ Ammoniatum, *Br.;* Linimentum Chloroformi (from Soap Liniment), *U. S.* (*Br.*); Linimentum Hydrargyri (from camphor liniment), *Br.;* Linimentum Opii, *Br.;* Linimentum Saponis, *U. S., Br.;* Linimentum Sinapis, *Br.;* Linimentum Terebinthinæ, *Br.;* Linimentum Terebinthinæ Aceticum (from camphor liniment), *Br.;* Spiritus Camphoræ, *U. S., Br.;* Tinctura Camphoræ Composita, *Br.;* Tinctura Opii Camphorata, *U. S.* (*Br.*); Unguentum Hydrargyri Compositum, *Br.;* Chloral Camphoratum, *N. F.;* Emplastrum Fuscum Camphoratum, *N. F.;* Linimentum Ammonii Iodidi, *N. F.;* Linimentum Opii Compositum, *N. F.;* Linimentum Saponato-Camphoratum, *N. F.;* Linimentum Sinapis Compositum, *N. F.;* Lotio Ammoniacalis Camphorata (from Spirit of Camphor), *N. F.;* Menthol Camphoratum, *N. F.;* Mistura Camphoræ Acida (from Water), *N. F.;* Mistura Camphoræ Aromatica (from Water), *N. F.;* Mistura Opii et Chloroformi Composita (from Spirit), *N. F.;* Mistura Opii et Rhei Composita (from Spirit), *N. F.;* Nebula Aromaticum, *N. F.;* Nebula Mentholis Composita, *N. F.;* Petroxolinum Chloroformi Camphoratum, *N. F.;* Petroxolinum Phenolis Camphoratum, *N. F.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodicæ sine Aloes, *N. F.;* Pilulæ Opii et Camphoræ, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodicæ sine Aloes, *N. F.;* Tinctura Kino et Opii Composita (from Spirit), *N. F.;* Tinctura Pectoralis (from Spirit), *N. F.;* Unguentum Camphoræ, *N. F.*

CAMPHORA MONOBROMATA. U. S.

MONOBROMATED CAMPHOR Camph. Monobrom.

(kăm′phọ-rą mŏn-ọ-brō-mā′tą)

"Ortho-monobromcamphor [$C_{10}H_{15}OBr$ or $C_8H_{15}Br.CO = 231.04$]. Preserve it in well-closed containers, protected from light." *U. S.*

Bromated Camphor, Brominated Camphor, Bromcamphor, Bromo-camphor; Camphre Monobromé, *Fr. Cod.;* Monobrom Camphor, Bromkampher, Kampher-monobromid, *G.;* Canfora monobromata, *It.;* Alcanfor monobromado, Bromuro de alcanfor, *Sp.*

This substance was discovered in 1861 by Th. Swarts, who prepared it by heating dibromide of camphor in a sealed tube to 100° C. (212° F.). It may also be made by heating bromine and camphor in the proper chemical proportions for three hours in a sealed tube, on a water bath. The crystalline mass is washed with water, recrystallized from alcohol after treatment with animal charcoal, washed with an alcoholic solution of potassium hydroxide, then with much water, and finally recrystallized from a mixture of alcohol and ether. It is very easy to prepare the monobromide on a small scale in this way. There is, however, at all times a very great pressure upon the inside of the tube, and the attempt to practise the method upon a large scale is very likely to result in shattering the tubes. This has led to numerous experiments as to the best method of preparing it. (See *Chem. News,* 1896, 208.) Maisch's method is as follows: Introduce 4 ounces of bromine gradually into a retort in which 13 ounces of camphor have been previously placed. In 15

or 20 minutes a brisk reaction will commence. When this subsides, 8 or 9 ounces more of bromine are to be poured in, in four portions, waiting after each addition until the reaction ceases. The liquid in the retort is now to be heated to about 132° C. (270° F.), then cooled, and sufficient petroleum benzin added to dissolve the crystalline mass. The crystals which are formed on cooling may be purified by recrystallization from benzin or hot alcohol. (*A. J. P.*, 1872, 339.) Various modifications of this process have been proposed. J. U. Lloyd (*A. J. P.*, April, 1875) directs the addition of water to the camphor and bromine in the retort, and boils the mixture for two hours, or until all the water is evaporated. Then the contents are poured into a dish and treated with warm alcohol, and allowed to crystallize, the mother liquor being drained off and the product recrystallized from hot alcohol. C. C. Keller (*S. W. P.*, 1880, p. 50) uses chloroform (instead of water, as proposed by Lloyd) with the camphor and bromine, and washes the crystals with absolute alcohol, crystallizing them finally from an ethereal solution. 300 parts of camphor yield 340 parts of monobromated camphor, the theoretical yield being about 456 parts.

Properties.—"Monobromated Camphor occurs in colorless, prismatic needles or scales, or as a powder having a mild but characteristic, camphoraceous odor and taste; permanent in the air. It is decomposed by prolonged exposure to sun-light. One Gm. of Monobromated Camphor dissolves in 6.5 mils of alcohol, 0.5 mil of chloroform, and in 1.6 mils of ether at 25° C. (77° F.); almost insoluble in water. It melts between 74° and 76° C. (165.2° and 168.8° F.). Heat a mixture of about 0.1 Gm. each of Monobromated Camphor and silver nitrate and 2 mils each of nitric acid and sulphuric acid until nitrous vapors are no longer evolved; a yellowish precipitate of silver bromide is obtained. Incinerate about 2 Gm. of Monobromated Camphor; not more than 0.05 per cent. of ash remains. Shake about 0.5 Gm. of powdered Monobromated Camphor with 10 mils of distilled water and filter. The filtrate is neutral to litmus and is not rendered more than slightly opalescent by the addition of a few drops of silver nitrate T.S. (*soluble bromide*)." *U. S.*

Uses.—Monobromated camphor was first proposed as a medicine by Deneffe, and has been used as a nerve sedative in *delirium tremens, hysteria, convulsive irritation* of teething, *sleeplessness*, etc. According to the experiments of Bourneville (*Prog. Med.*, 1874) and of Lawson, it produces in mammals muscular weakness, passing into paralysis, very decided progressive reduction of temperature, decrease in the respiration rate, sleep passing into stupor, and finally death. Bourneville states that the vessels of the ear and eyelids in the rabbit are contracted. Its therapeutic action resembles, but is not identical with, that of other bromides; in the experience of H. C. Wood, it has seemed to be of value in *spermatorrhea*. It is not safe to give it too freely, as in some cases its ingestion has been followed by epileptiform convulsions. The emulsion may be made by dissolving it in six times its weight of expressed oil of almonds, and then forming an emulsion with gum and water in the usual manner.

Elixir of Monobromated Camphor is proposed by Munday. (*P. J.*, March 3, 1877.) Monobromated camphor 3 parts, alcohol (90 per cent.) 120 parts, orange-flower water 80 parts, glycerin 100 parts. Mix the alcohol and glycerin; dissolve the monobromated camphor by the use of a gentle heat, and add the orange-flower water. It contains 1 per cent. of monobromated camphor.

Dose, two to five grains (0.13–0.32 Gm.), repeated as required.

CANNABIS. U. S. (Br.)

CANNABIS Cannab. [Indian Hemp Cannabis Indica U. S. VIII, Guaza, Ganjah]

(kăn'na-bĭs)

"The dried flowering tops of the pistillate plants of *Cannabis sativa* Linné, or of the variety *indica* Lamarck (Fam. *Moraceæ*), freed from the thicker stems and large foliage leaves and without the presence or admixture of more than 10 per cent. of fruits or other foreign matter. Cannabis, made into a fluidextract in which *one hundred mils* represent *one hundred grammes* of the drug, when assayed biologically, produces incoördination when administered to dogs in a dose of not more than 0.03 mil of fluidextract per kilogramme of body weight." *U. S.* "Indian Hemp consists of the dried flowering or fruiting tops of the pistillate plant of Cannabis sativa, *Linn.*, grown in India; from which the resin has not been removed." *Br.*

Cannabis Indicæ, *Br.*; Hemp, Indian Hemp; **Herba Cannabis Indicæ**; Chanvre, *Fr. Cod.*; Chanvre de l'Inde, *Fr.*; Indischer Hanf, *G.*; Cañamo, *Sp.*

For many years the official *cannabis* was restricted to the drug which was used for centuries in India. The reason for this was that the Indian cannabis was more uniformly active. Recently the Indian Government has placed a high tax on every pound of the drug grown. The result has been that other markets have been sought and the hemp plant has been grown in other parts of Asia, Africa and America. While of course, much of this material is not equal to that grown in India yet the fact that it can be grown, as shown by experiments in the United States (see Hamilton, *J. A. Ph. A.*, 1913, ii; 1915, iv, 389) of a very high quality has caused the framers of the U. S. Pharmacopœia to permit the use of a cannabis, no matter where it may be grown, provided it comes up to the biological standard as given in the definition. Physiologically active cannabis is obtained at the present time not only from India, but Africa, Turkey, Turkestan, Asia Minor, Italy, Spain and the United States.

The *Cannabis sativa*, or hemp plant, is an

annual, from four to eight feet or more in height, with an erect, branching, angular stem. The leaves are alternate or opposite, and digitate, with five to seven linear-lanceolate, coarsely serrated segments. The stipules are subulate. The flowers are axillary; the staminate in long, branched, drooping racemes; the pistillate in erect, simple spikes. The stamens are five, with long pendulous anthers; the pistils two, with long, filiform, glandular stigmas. The fruit is ovate and one-seeded. The whole plant is covered with a fine pubescence, scarcely visible to the naked eye, and somewhat viscid to the touch. The hemp plant of India has been considered by some as a distinct species, and named *Cannabis indica;* but the most observant botanists, upon comparing it without cultivated plant, have been unable to discover any specific difference. It is now, therefore, regarded merely as a variety, and is distinguished by the epithet *indica.* Pereira states that in the female plant the flowers are somewhat more crowded than in the common hemp, but that the male plants in the two varieties are in all respects the same.

C. sativa is a native of the Caucasus, Persia, and the hilly regions in Northern India. It is cultivated in many parts of Europe and Asia, and largely in our Western States. It is from the Indian variety exclusively that the medicine was formerly obtained, the heat of the climate in Hindostan apparently favoring the development of its active principle. H. C. Wood, many years ago, obtained a parcel of the male plant of *C. americana* (*C. sativa*) from Kentucky, made an alcoholic extract of the leaves and tops, and, upon trying it on the system, found it effective in less than a grain, and, having inadvertently taken too large a dose, experienced effects which left no doubt of the powers of the medicine, and of the identity of its influence with that of the Indian plant. (*Proc. Am. Philos. Soc.,* vol. xi, p. 226.) The results obtained by H. C. Wood have been confirmed by a number of observers.

The fruits or "so-called" seeds, though not now official, have been used in medicine. They are from three to five millimeters long and about two millimeters broad, roundish-ovate, somewhat compressed, of a shining ash-gray color, and of a disagreeable, oily, sweetish taste. For a comprehensive monograph on the morphology of cannabis fruits, as well as their history and chemical composition, see Tschirch, "*Handbuch der Pharmakognosie,*" p. 555. They yield by expression about 20 per cent. of a fixed oil, which has the drying property, and is used in the arts. They contain also uncrystallizable sugar and albumen, and when rubbed with water form an emulsion, which may be used advantageously in inflammations of the mucous membrane, though without narcotic properties. The seeds are much used as food for birds, as they are fond of them. They are generally believed to be in no degree poisonous; but Michaud relates the case of a child in whom serious symptoms of narcotic poisoning occurred after taking a certain quantity of them. It is probable that some of the fruit eaten by the child was unripe, as in this state it would be more likely to partake of the peculiar qualities of the plant. (*Ann. Thér.,* 1860.)

In Hindostan, Persia, and other parts of the East, hemp has long been habitually employed as an intoxicating agent. The parts are the tops of the plant, and a resinous product obtained from it. *Bhang* is the selected, dried and powdered leaves. *Ganjah* or *gunjah* is the tops of cultivated female plants, cut directly after flowering, and formed into round or flat bundles from two to four feet long by three inches in diameter. It is stated that in the province of Bengal great care is taken to eradicate the male plants from the fields before fertilization of the female, and that thereby the yield and quality of the resin is greatly increased. In Bombay this matter is commonly neglected, so that Bengal ganjah is much superior to Bombay ganjah. It is recognized in India that ganjah rapidly deteriorates on keeping, that which is one year old being not more than one-quarter as potent as the fresh drug, while two-year-old ganjah is practically inert and is required by the Indian government to be burned in the presence of excise officers. It is probable, however, that much old ganjah finds its way into the markets of the world. All importations of ganjah or hemp from India should be made directly after the harvesting of the new crop in April or May, and the extract should be prepared at once and kept in hermetically sealed jars. There is on the surface of the plant a resinous exudation to which it owes its stickiness. According to Hooper (*P. J.,* 1909, lxxxi, 347) only small amounts of charas are raised in India, that which is being consumed there being mostly imported. The method of collection in Baluchistan is to gently rub the dried plant between carpets. The dust which comes off contains the active principle and is known as "rup." The second shaking produces an inferior variety, known as "tahgalim," and the third shaking is known as "ganja." In Nepal the plant is squeezed between the palms of the hands, and the resin scraped off from the hands. These balls, and also masses formed out of resin mechanically separated from the hemp plant are called *charas* or *churrus.* This is the *hashish* or *hasheesh* of the Arabs.

Hashish is also produced in considerable quantities in Persia by rolling and rubbing the flowers, stalks and leaves of hemp on rough woolen carpets and subsequently scraping off with a knife and making into balls or sticks the adherent resinous substance. The carpets are afterwards washed with water and the extract obtained by evaporation sold at a low price. The dose for smoking of the best hashish is said to be one-fourth to one grain (0.016–0.065 Gm.). The fanatics are affirmed to be generally hashish devotees.

The dealing in hashish in India is said to be a Government monopoly, and a very heavy license is required for the right to even purchase it in quantity. The importation of it into Egypt

is so strongly interdicted that the mere possession of it is a penal offence; H. C. Wood found it, however, readily procurable. It is said to be brought into the country in pigs' bladders, in the Indo-European steamers, and thrown out at night during the passage into the Suez canal, to be picked up by the boats of confederates. Notwithstanding the Governmental interdiction, it is largely used by smoking in Egypt, as an intoxicant. The statement of W. E. Dixon (*B. M. J.*, Nov., 1899) that the inhalations of hemp smoke produces great exhilaration and causes muscular fatigue to disappear for the time being is undoubtedly correct, but his further belief that the habit is not apt to grow upon the hemp votary is more doubtful.

Momea or *mimea* is a hemp preparation said to be made in Thibet with human fat. From gunjah the Messrs. Smith, of Edinburgh, obtained a purer resin by the following process: Bruised ganjah is digested, first in successive portions of warm water, until the expressed liquid comes away colorless; and afterwards for two days, with a moderate heat, in a solution of sodium carbonate, containing one part of the salt for two of the dried herb. It is then expressed, washed, dried, and exhausted by percolation with alcohol. The tincture, after being agitated with milk of lime containing one part of the earth for twelve of the gunjah used, is filtered; the lime is precipitated by sulphuric acid; the filtered liquor is agitated with animal charcoal, and again filtered; most of the alcohol is distilled off, and to the residue twice its weight of water is added; the liquor is then allowed to evaporate gradually; and, finally, the resin is washed with fresh water until it ceases to impart a sour or bitter taste to the liquid, and is then dried in thin layers. Thus obtained, it retains the odor and taste of gunjah, which yields from 6 to 7 per cent. of it.

Properties.—Fresh hemp has a peculiar narcotic odor, which is said to be capable of producing vertigo, headache, and a species of intoxication. It is much less in the dried tops, which have a feeble bitterish taste. According to Royle, *churrus* is, when pure, of a blackish-gray, blackish-green, or dirty olive color, of a fragrant and narcotic odor, and a slightly warm, bitterish, and acrid taste. Cannabis is officially described as "in dark green or greenish-brown and more or less agglutinated fragments, consisting of the short stems with their leaf-like bracts and pistillate flowers, some of the latter being replaced with more or less developed fruits; stems cylindrical, of varying length, not more than 3 mm. in diameter, longitudinally furrowed, light green to light brown, strigose-pubescent; leaves digitately compound; leaflets, when soaked in water and spread out, linear-lanceolate, nearly sessile, margin deeply serrate, bracts ovate, pubescent, each enclosing one or two pistillate flowers, or more or less developed fruits; calyx dark green, pubescent and somewhat folded around the ovary or fruit; styles two, filiform and pubescent; ovary with a single campylotropous ovule; fruit light green to light brown, broadly ellipsoidal, about 3.5 mm. in length, finely wrinkled and slightly reticulated; odor agreeably aromatic; taste characteristic. The powder is dark green, giving a strong effervescence on the addition of dilute hydrochloric acid; numerous sharp pointed fragments of upper portion of non-glandular hairs and fragments of bracts and leaves showing yellowish-brown laticiferous vessels, rosette aggregates of calcium oxalate from 0.005 to 0.025 mm. in diameter; non-glandular hairs unicellular, with a very slender pointed apex and a considerably enlarged base containing, usually in the lumen, some calcium carbonate; glandular hairs of two kinds, one with a short, one-celled stalk and the other with a multicellular, long, tongue-shaped stalk, the glandular portion being globular and consisting of from 8 to 16 cells, fragments of fruits with palisade-like, non-lignified sclerenchymatous cells, walls yellowish-brown, finely porous, the lumina usually containing air; tissues of embryo and endosperm with numerous oil globules and aleurone grains, the latter from 0.005 to 0.01 mm. in diameter and consisting of large crystalloids and globoids. The yield of alcohol extractive is not less than 8 per cent. and the alcoholic solution is of a bright green color. Cannabis yields not more than 15 per cent of ash." *U. S.*

The British Pharmacopœia describes Indian cannabis as follows:

"In compressed, rough, dusky-green masses, consisting of the branched upper part of the stem, bearing leaves and pistillate flowers or fruits, matted together by a resinous secretion. Upper leaves simple, alternate, 1–3 partite; lower leaves opposite and digitate, consisting of five to seven linear-lanceolate leaflets with distantly serrate margins. Fruit one-seeded and supported by an ovate-lanceolate bract. Both leaves and bracts bear external oleo-resin glands and one-celled curved hairs, the bases of which are enlarged and contain cystoliths. Strong, characteristic odor; taste slight. When a mixture of 10 grammes of finely powdered Indian Hemp and 100 millilitres of *alcohol* (90 per cent.) is shaken occasionally during twenty-four hours and then filtered, 20 millilitres of the filtrate, evaporated in a flat-bottomed dish, yield a residue weighing, when dried at 100° C. (212° F.), not less than 0.250 gramme. Ash not more than 15 per cent." *Br.*

For a histological description of the leaf by A. R. L. Dohme, see *Proc. A. Ph. A.*, 1897, 569. The Cannabis of the market may consist of fruiting tops and stems and occasionally the staminate tops are admixed with it.

Hooper (*P. J.*, lxxxi, p. 80) describes a method for the chemical standardization of cannabis indica based upon its iodine value. He finds that the alcoholic extract of old samples has a lower iodine value than that from recent specimens, and there is more or less constancy of relation between the age and the iodine value.

For description of the U. S. method of physiological assay, see page 279.

Indian churrus or hasheesh is a hard resinous

mass of a greenish-gray color, containing much gritty earth, and, as it occurs in Egypt, of a feeble, hemp-like odor and taste. Schlesinger found in the leaves a bitter substance, chlorophyll, green resinous extractive, coloring matter, gummy extract, extractive, albumen, lignin, and salts. The plant also contains volatile oil in very small proportion, which probably has narcotic properties. The resin obtained by T. & H. Smith of Edinburgh, in 1846, has been thought to be the active principle, and received the name of *cannabin*. By repeated distillation of the same portion of water from relatively large quantities of hemp renewed at each distillation, M. J. Personne obtained a volatile oil, of a stupefying odor, and an action on the system such as to dispose him to think that it was the active principle of the plant. As the water distilled was strongly alkaline, he supposed that his volatile principle might be a new alkaloid; but the alkaline reaction was found to depend on ammonia; and the liquid obtained proved to be a volatile oil, lighter than water, of a deep amber color, a strong odor of hemp, and composed of two distinct oils, one colorless, with the formula $C_{15}H_{20}$, the other a hydride of the first, $C_{15}H_{22}$, which was solid, and separates from alcohol in plate-like crystals. For the former Personne proposes the name of *cannabene*. It is affirmed that when this is inhaled, or taken into the stomach, a singular excitement is felt throughout the system, followed by a depression, sometimes amounting to syncope, with hallucinations which are generally disagreeable, but an action on the whole slighter and more fugitive than that of the resin. The various substances of alkaloidal nature that have been described by different investigators as found in Indian hemp are now recognized as due to decomposition products of *choline*, which was identified as present by Jahns. (*P. J.*, 1887, xvii, 1049.) *Cannabindon*, $C_8H_{12}O$, is a dark red syrupy liquid obtained by Kobert (*Chem. Ztg.*, 1894, 741) from Cannabis Indica; it is soluble in alcohol, ether and oils; it is affirmed to be narcotic in doses of from half a grain to two grains (0.032–0.13 Gm.). As a result of a reinvestigation of charras (churrus) from Indian hemp, Wood, Spivey, and Easterfield (*J. Chem. S.*, vol. lxix, 539) have found the following principles: 1, a *terpene*, boiling between 150° and 180° C. (302° and 356° F.); 2, a *sesquiterpene*, boiling at 258° to 259° C. (496.4°–498.2° F.); 3, a *crystalline paraffin* of probable formula $C_{29}H_{60}$, melting at 63.5° C. (146.3° F.); and 4, a *red oil*, boiling at 265° to 270° C. (509°–518° F.) under a pressure of 20 mm., to which they give the name *cannabinol*, and the formula $C_{15}H_{24}O_2$. This latter constituent they consider the only active ingredient. It is probably the same substance as the dark red syrup of Kobert, mentioned above under the name cannabindon. The authors found that cannabinol readily underwent superficial oxidation, at the same time losing its toxic activity. Famulener and Lyons (*A. Pharm.*, 1904) believe that the only reliable preparation of cannabis is a fluidextract made from the *fresh* drug. I. Roux (*A. Pharm.*, 1887) has experimented upon extracts made by treating purified extract of hemp with petroleum benzin and ether. The ether extract produced insignificant results. The petroleum extract was excitant and convulsant. The alcoholic extract was a feeble narcotic. The resin "cannabin" of which *cannabinol* is the chief constituent, appears to be active. Fränkel (*A. E. P. P.*, 1903, p. 266) claims to have isolated the active principle of hashish as a pure and chemically well defined body. It has the formula $C_{21}H_{30}O_2$, and is a phenol-aldehyde. It is of a pale yellow color and of a thick consistency. When heated it becomes quite fluid and distils at 215° C. (419° F.), under a pressure of 0.5 mm. It oxidizes in the air, acquiring a brown tint. It responds to Millon's reaction, and can be acetylized, showing thus its phenol character. Fränkel proposes that the name *cannabinol* be given to it and that the term *pseudo-cannabinol* be given to the inactive substance of Wood, Spivey and Easterfield.

Assay.—"Prepare a fluidextract and proceed as directed below." *U. S.*

Attempts have been made to apply physiological tests to the standardization of cannabis indica. Up to the present no means have been suggested for determining the relative potency of different samples of cannabis indica, the physiological test simply demonstrating that the drug possesses a certain indefinite amount of physiological action. This test is carried out upon dogs in the following manner: It is advisable to use the same animal for repeated tests, because the individual susceptibility of the dog varies so greatly, and the experimenter gradually learns the degree of reaction to be expected from a certain dog. A tincture of the specimen to be tested is either evaporated into a soft extract and given in the form of a pill or mixed with an inert absorbing powder and enclosed in a capsule; it must not be given hypodermically. The symptoms caused by cannabis indica in the dog recall those of alcoholism in the human being. There is at first a slight loss of control in the hind legs so that the animal staggers as he walks, later the ataxia becomes so marked that the dog is unable to stand up without leaning against some object, and about this time begins to show distinct drowsiness, and may eventually pass into a heavy sleep.

The details of assay as directed by the U. S. are as follows: "The assay of Cannabis and its preparations has been made a requirement and is based upon the fact that this drug produces certain symptoms of muscular incoördination. The method consists of ascertaining the dose of the preparation to be tested which will produce these symptoms of incoördination in dogs and then adjusting its strength by comparison with a standard preparation.

"*Dogs.*—The animals differ considerably in susceptibility to the drug and therefore it is best to make preliminary tests upon several

dogs with average-sized doses and select from among them the animals which react easily to the drug. As a rule, fox terriers serve very well for the purpose, but any dog may prove satisfactory. It is best to provide at least two dogs for each assay, but if many samples are to be examined more dogs will be needed. The dogs should be at least one year old and in normal health and must be kept under the best sanitary conditions. They may be used repeatedly for the purpose but not at shorter intervals than three days. Each series of tests should be conducted by the same person, who should be perfectly familiar with the peculiarities of each animal in order that he may recognize more certainly deviations from the normal. While the tests are being made the animals should be kept in a perfectly quiet room, free from disturbance and separated so that they cannot see each other.

"*Preparation of the Drug.*—The drug may be given most conveniently in the form of the fluidextract which is administered in gelatin capsules, or the extract made into soft pills may be used; but whichever form is chosen the same should be used for both the standard and the preparation that is to be tested.

"Before administration the animal should not be fed for twenty-four hours in order to hasten absorption. The head of the animal being held, its mouth is opened and the capsule or pill is placed upon the back of the tongue. Usually the drug is easily swallowed when given in this way, but this may be facilitated by giving the animal a small amount of water to drink.

"*Assay.*—An average dose of the known or standard preparation is given to one of the dogs and a like dose of the preparation to be standardized is given the second dog. After one hour both dogs are observed very carefully for symptoms of muscular incoördination. The incoördination is manifested differently in different animals, but in small doses it shows itself most frequently in slight swaying, when the animal is standing quietly, or in some ataxia when it runs about. The observation should be made frequently during the second hour following the administration of the drug.

"The results obtained from the first test should be confirmed after an interval of not less than three days by repeating the administration, but reversing the order, that is, giving the known strength drug to the dog which received that of unknown strength before and *vice versa*.

"In subsequent tests which are carried out, the dose of the preparation of unknown strength is modified so as to produce similar symptoms to those produced by the standard. If the preparation to be tested is below the standard in strength, its dose must be increased, or if it is above strength its dose is lessened until equivalent doses of the two are found. Dogs may be used over long periods of time, even for some years, but occasionally they have to be discarded, as in some cases they seem to learn the effects of the drug and so refuse to stand up. A certain degree of tolerance is sometimes gained which necessitates larger doses.

"*Standard.*—As there is no chemical substance of definite composition which can be adopted as a standard, a Fluidextract of Cannabis or an extract which has been carefully prepared and suitably preserved may be utilized for this purpose. A standard Fluidextract will produce incoördination when administered to dogs in the dose of 0.03 mil for each kilogramme of body weight of dog. When administered in the form of the Extract a dose of 0.004 Gm. for each kilogramme of body weight of dog should produce similar symptoms, and the requirement for a standard tincture is a dose of 0.3 mil for each kilogramme of body weight of dog." *U. S. IX.*

Uses.—Aside from a slight local irritant effect the action of cannabis seems to be limited almost exclusively to the higher nerve centers. In man this is first manifested by a peculiar delirium which is accompanied with exaltation of the imaginative function and later by a remarkable loss of the sense of time. The delirium is often accompanied with motor weakness and diminished reflexes and generally followed by drowsiness. In the dog the earliest manifestation of the drug's action is a slight degree of restlessness which is soon followed by disturbances of equilibrium and later weakness of the legs and drowsiness.

Cannabis is used in medicine to relieve pain, to encourage sleep, and to soothe restlessness. Its action upon the nerve centers resembles opium, although much less certain, but it does not have the deleterious effect on the secretions. As a somnifacient it is rarely sufficient by itself, but may at times aid the hypnotic effect of other drugs. For its analgesic action it is used especially in pains of neuralgic origin, such as *migraine,* but is occasionally of service in other types. As a general nerve sedative it is used in *hysteria, mental depression, neurasthenia,* and the like. It has also been used in a number of other conditions, such as *tetanus* and *uterine hemorrhage,* but with less evidence of benefit. One of the great hindrances to the wider use of this drug is its extreme variability. Formerly many of the preparations of cannabis were inert before they left the manufacturers' hands, and the present requirements of the U. S. P. that the drug be tested upon dogs to insure its activity is an important step in the right direction. But even granted an active preparation when manufactured, so rapidly does the drug deteriorate that by the time the drug reaches the patient it has lost a large proportion of its activity. The only way of determining the dose of an individual preparation is to give it in ascending quantities until some effect is produced. The fluid extract is perhaps as useful a preparation as any; one may start with two or three minims of this three times a day, increasing one minim every dose until some effect is produced. According to C. R. Marshall (*L. L.,* 1897, i, also *J. A. M. A.,* Oct., 1898) the deterioration of cannabis is due to the oxidation

of cannabinol, which he has found to act upon dogs and cats as the crude drug.

Dose, of cannabis, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Extractum Cannabis, *U. S.* (*Br.*); Fluidextractum Cannabis, *U. S.*; Tinctura Cannabis (from Extract), *U. S.* (*Br.*); Collodium Salicylici Composita (from Fluidextract), *N. F.*; Mistura Chlorali et Potassii Bromidi Composita (from Extract), *N. F.*; Mistura Chloroformi et Morphinæ Composita (from Tincture), *N. F.*

CANTHARIDINUM. Br.

CANTHARIDIN

(kăn-thą-rĭ-dĭ′nŭm)

"Cantharidin, $C_{10}H_{12}O_4$, may be obtained from various species of Cantharis or of Mylabris." *Br.*

Cantharidin is the anhydride (lactone) of cantharidic acid and is officially recognized by the Br. Pharm. (1914) and the Swiss and French Pharmacopœias. Preparations made from cantharidin are believed to be more uniform in quality than those made from cantharides because they are made from a definite crystallizable product and it is not always easy to extract all of the cantharidin from powdered Spanish flies by the usual methods, as in making the vinegar, tincture, collodion, cerate or plaster. (See *Cantharis,* page 282.)

E. Dieterich prepares cantharidin by macerating 1000 parts of coarsely powdered cantharides in 1500 parts of acetic ether mixed with 20 parts of sulphuric acid; after adding 40 parts of barium carbonate to neutralize the excess of sulphuric acid, the mixture is exhausted with acetic ether in an extraction apparatus, the liquid is distilled, and the residue, consisting of cantharidin, resin, fat, etc., is set aside for eight days to allow the cantharidin to crystallize; 200 parts of petroleum benzin (sp. gr. 0.740) are then added, gently heated in order to dissolve the fatty matter, the liquid filtered, and the cantharidin washed with petroleum benzin and recrystallized from its solution in 90 per cent. alcohol. If perfectly pure cantharidin is needed, the cantharidin may be dissolved in acetic ether or chloroform and the solution passed through animal charcoal, filtered, and allowed to crystallize. (*J. P. C.,* 1893, 375.) For assay of cantharides for cantharidin see *P. J.,* 1903, 558 and 783.

Properties.—"Colorless glistening crystals, inodorous. Very slightly soluble in *water, petroleum spirit,* or *alcohol* (90 per cent.); more soluble in *chloroform,* in *acetic ether,* and in *acetone;* soluble also in fixed oils. A 0.1 per cent. solution in a fixed oil raises blisters when kept in contact with the skin. Melting point 210° to 212° C. (410°–413.6° F.). Slowly volatilises at 100° C. (212° F.), more rapidly at higher temperatures. Soluble in *solution of sodium hydroxide,* the solution depositing crystals of Cantharidin when acidified. Gently warmed with *sulphuric acid* it yields a colorless solution, from which it is separated unchanged when freely diluted with *water.*" *Br.*

Cantharidin is in the form of white crystalline scales, of a shining micaceous appearance, inodorous, tasteless, almost insoluble in water and in cold alcohol, but soluble in ether, chloroform, benzene, the oils, and in hot alcohol and acetic acid, which deposit it upon cooling. According to Procter it is insoluble in water. Cold alcohol dissolves it slightly, hot alcohol freely. It is more soluble in ether, which also dissolves it more freely hot than cold. Chloroform, cold or hot, is its best solvent; and acetone ranks next to it in this respect. Olive oil, at 121.1° C. (250° F.), dissolves one-twentieth of its weight, and oil of turpentine, boiling hot, one-seventieth; and both deposit the greater portion on cooling. The olive oil solution after deposition vesicates, the terebinthinate does not. Strong acetic, sulphuric, and nitric acids dissolve it, with the aid of heat, and deposit it unchanged on cooling. It is also dissolved by solutions of potassium or sodium hydroxide, and to a small extent by a strong solution of ammonia. (*A. J. P.,* xxiv, 296.) Formic acid is said to be the best solvent. Somewhat different results in relation to the solubility of cantharidin have been obtained by M. E. Rowan. Careful experimentation with distilled water showed that, when agitated for eight days at ordinary temperatures with pure cantharidin, it was capable of dissolving 0.0266 per cent. of that principle; boiling water dissolves 0.297 per cent.; boiling alcohol (99° Tralles) 2.168 per cent. (*J. P. C.,* May, 1873, 409.) It fuses at 210° C. (410° F.), is volatilizable by heat without decomposition, and its vapor condenses in acicular crystals. As determined by the experiments of Wm. A. Guy, the subliming heat of isolated cantharidin is 100° C. (212° F.), or the temperature of boiling water. (*P. J.,* Feb., 1868, 373.)

According to Masing and Dragendorff, cantharidin, $C_{10}H_{12}O_4$, is capable of combining with water, and thus becomes cantharidic acid, $C_{10}H_{14}O_5$, and in this state forms definite compounds with bases, such as $K_2C_{10}H_{12}O_5$ and $Na_2C_{10}H_{12}O_5$, which are crystallizable. These may be obtained by heating cantharidin with an alkaline hydroxide solution. (*J. P. C.,* January, 1868, 79.) Cantharidin itself has been found to combine like an acid with salifiable and earthy bases, forming soluble compounds with potassium, sodium, and lithium hydroxides, salts of very sparing solubility with baryta, strontia, and lime, and with magnesia a salt which, though feebly soluble in water (100 parts of water dissolving only 0.24 of the salt) (see *P. J.,* March 13, 1880), is much more largely dissolved in cold than hot water, and in cold than in hot alcohol. Cantharidin is therefore recognized as the lactone or inner anhydride of cantharidic acid. The potassium salt crystallizes with 3 molecules of water, and is soluble in 25 parts of water. On the addition of strong acids to this solution, cantharidic acid is not precipitated, as might be expected, but the lactone cantharidin. This potassium

salt has been recommended by Liebreich for use in subcutaneous injections in cases of *phthisis*, but is of very doubtful value. The most satisfactory test of cantharidin is its vesicating property. Notwithstanding the insolubility of this principle in water and cold alcohol, the decoction and tincture of cantharides have the medicinal properties of the insect; and Lewis ascertained that both the aqueous and alcoholic extracts act as effectually in exciting vesication as do the flies themselves, while the residue is in each case inert. Cantharidin consequently exists in the insect so combined with the yellow matter as to be rendered soluble in water and cold alcohol. If, as stated by E. Dieterich (1883), formic acid is present in the Spanish fly, it is probable that the solution of the cantharidin is due to its presence. He also showed that cantharidin was not volatilized with the vapor of benzin, a fact which may prove useful in preparing blistering plasters coated with a benzin solution of cantharidin. (*Ph. Centralh.*, 1901, 464.) H. G. Greenish calls attention to the fact that much loss of cantharidin takes place in making the various pharmaceutical preparations, through insufficient exhaustion by the use of the ordinary solvents. He obtained 0.822 per cent. of cantharidin from exhausted residues. Homolka records (*Ber. d. Chem. Ges.*, xix, 1082) the results of an investigation of the chemical decompositions of cantharidin.

Uses.—Cantharidin is used for the same purposes as *Cantharides* (see page 285). Liebreich strongly recommended hypodermic injections of cantharidin in the treatment of *phthisis*, but general clinical experience has not confirmed the value of the remedy. *Liebreich's cantharidal solution* was made by heating 20 mils of water with 0.2 Gm. of cantharidin and 0.4 Gm. of potassium hydroxide until solution was obtained, then adding enough water to make 1000 mils. Of this solution he injected from 0.5 to 1.0 mil at a dose.

Dose of cantharidin is from one-two-hundred-and-fortieth to one-one-hundred-and-twentieth grain (0.00025–0.0005 Gm.).

Off. Prep.—Acetum Cantharidini, *Br.;* Emplastrum Calefaciens, *Br.;* Emplastrum Cantharidini, *Br.;* Liquor Epispasticus, *Br.;* Tinctura Cantharidini, *Br.;* Unguentum Cantharidini, *Br.;* Collodium Vesicans (from Liquor Epispasticus), *Br.*

CANTHARIS. U. S.

CANTHARIDES Canthar. [Blistering Flies, Spanish Flies, Russian Flies]

(kăn'thą-rĭs)

"The dried beetles, *Cantharis vesicatoria* (Linné) De Geer (Fam. *Meloideæ*, Order *Coleoptera*), yielding not less than 0.6 per cent. of cantharidin. Preserve Cantharides in tightly-closed containers, adding a few drops of chloroform or carbon tetrachloride, from time to time, to prevent attack by insects." *U. S.*

Muscæ Hispanicæ; Cantharide, *Fr. Cod.;* Cantharides, *P. G.;* Spanische Fliegen, Kantharide, Cantharidien, *G.;* Cantaride, Cantarella, Mosca di Spagna, *It.;* Cantaridina, *Sp.*

Cantharis is recognized in all of the European Pharmacopœias, but has been dropped by the British authority, being replaced by Cantharidin which it is stated "may be obtained from various species of Cantharis or Mylabris."

The Br. Add. under the name of *Mylabris* formerly recognized not only the dried beetle, *Mylabris phalerata* Pallas, but also allowed the use in the Colonies of other species of the genus, provided that they yield a similar proportion of cantharidin. Mylabris was characterized in the Br. Add. as "usually an inch (twenty-five millimetres) or rather more long, and three-eighths of an inch (nine millimetres) broad; with two long elytra, each three times as long as broad, black with two broad wavy transverse orange-colored bands and a large orange-colored spot at the base of each; one pair of brown membranous wings."

The term *Cantharis* was employed by the ancient Greek writers to designate many coleopterous insects or beetles. Linnæus gave the title to a genus not including the official blistering insect, and placed this in the genus *Meloë*, which, however, has been since divided into several genera. Geoffrey made the Spanish fly (beetle) the prototype of a new genus, *Cantharis*, substituting *Cincindela* as the title of the Linnæan genus. Fabricius altered the arrangement of Geoffrey, and substituted *Lytta* for *Cantharis* as the generic name. The former was adopted by the London College, and at one time was in extensive use; but, the latter, having been restored by Latreille, is now recognized in the British and U. S. Pharmacopœias, and is universally employed. By this naturalist the vesicating insects were grouped in a small tribe, corresponding very nearly with the Linnæan genus *Meloë*, and distinguished by the title *Cantharidæ*. This tribe he divided into eleven genera, among which is Cantharis. Two others of these genera, *Meloë* properly so called, and *Mylabris*, have been employed as vesicatories. *Mylabris cichorii* is thought to be one of the insects described by Pliny and Dioscorides under the name of cantharides, and is to this day employed in Italy, Greece, the Levant, and Egypt; and another species, *M. pustulata*, is used for the same purpose in China. W. R. Warner has found 500 parts of *M. cichorii* to yield 2.13 parts of cantharidin, which somewhat exceeds the yield of Spanish flies. (*A. J. P.*, xxviii, 195); and R. Wolff has obtained by ethereal extraction more than 4 parts of cantharidin in 500 of the *Lytta aspersa* of Buenos Ayres. The *M. cichorii* has been recently imported to some extent under the name of *Chinese blistering fly* It is black, with the powder blackish gray and free from shining particles; it yielded to Maisch (*Proc. A. Ph. A.*, 1872) 1.016 per cent., and to L. Fahnestock 1.25 per cent. of cantharidin. (*A. J. P.*, 1879.)

Cantharis vesicatoria is one of the *Coleopteræ* or beetles. It is from 15 to 25 mm. long, and of a shining, golden-green color. The head is large and heart-shaped, bearing a pair of stout mandibles and filiform antennæ; the thorax short

and quadrilateral; the wing-sheaths long and flexible, covering brownish membranous wings. (Snyder, *A. J. P.*, 1908, p. 545.) When alive, the Spanish flies have a strong, penetrating, fetid odor, compared to that of mice, by which swarms of them may be detected at a considerable distance. They attach themselves preferably to certain trees and shrubs, such as the white poplar, privet, ash, elder, and lilac, upon the leaves of which they feed. They are most abundant in Spain, Italy, and Southern France, but are found also in all the temperate parts of Europe, and in Western Asia. According to the researches of Lichtenstein, the eggs are laid by the female in the latter part of June in small cylindrical holes made in the ground. A week later the larvæ hatch out. They are a millimeter long, with two long caudal threads, and of a brown color. After many efforts, Lichtenstein succeeded in getting them to feed on the honey contained in the stomach of bees. In a few days they changed into milk-white larvæ, and about a month after this buried themselves in the ground, to assume the chrysalis stage and to hatch out the following spring as perfected beetles. In the wild state the larvæ are said to crawl up flowers and attach themselves to bees or other hymenopterous insects; carried by the bee to the hive, the larvæ feed upon the young bees and the honey and beebread stored up for use. The beetles usually make their appearance in swarms upon the trees in May and June, when they are collected.

The time preferred for this purpose is in the morning, at sunrise, when they are torpid from the cold of the night, and easily let go their hold. Persons with their faces protected by masks, and their hands with gloves, shake the trees, or beat them with poles; and the insects are received as they fall upon linen cloths spread underneath. They are then plunged into vinegar diluted with water, or exposed in sieves to the vapor of boiling vinegar, and, having been thus deprived of life, are dried either in the sun, or in apartments heated by stoves. This mode of killing the flies by the steam of vinegar is as ancient as the times of Dioscorides and Pliny. In some places they are gathered by smoking the trees with burning brimstone. It has been proposed by Lutrand to destroy them by the vapor of chloroform. When perfectly dry, they are introduced into casks or boxes lined with paper and carefully closed, so as to exclude as much as possible the atmospheric moisture. According to Neutwich, the young fly has no vesicating power (*P. J.*, Nov. and Dec., 1870, p. 355); but this is denied by H. Beauregard. (*Ibid.*, xv, 873.)

Cantharides come chiefly from Spain, Southern Russia and Hungary, and other parts of the Mediterranean as Sicily, Poland and Roumania. The Russian flies are most esteemed. They may be distinguished by their greater size, and their color approaching to that of copper.

In the United States are several species of Cantharis, which have been employed as substitutes for *C. vesicatoria* and found equally efficient; but none of them are now recognized by the U. S. Pharmacopœia, even *C. vittata*, which was at one time official, having been discarded. For description of unofficial blistering beetles, see *U. S. D.*, 19th edition, p. 284.

Cantharis vittata. Latreille, *Gen. Crust. et Insect.;* Durand, *A. J. P.*, ii, 274, Fig. 4.—The *"potato fly"* is rather smaller than *C. vesicatoria*, which it resembles in shape. Its length is about six lines. The head is light red, with dark spots upon the top; the feelers are black; the elytra or wing-cases are black, with a yellow longitudinal stripe in the center, and with a yellow margin; the thorax is also black, with three yellow lines; and the abdomen and legs, which have the same color, are covered with a cinerous down. It inhabits chiefly the potato vine, and appears about the end of July or beginning of August, in some seasons very abundantly. It is found on the plant in the morning and evening, but during the heat of the day descends into the soil. The insects are collected by shaking them from the plant into hot water, and are afterwards carefully dried in the sun. They are natives of the Middle and Southern States. This species of Cantharis was first described by Fabricius in the year 1781, and was introduced to the notice of the profession by Isaac Chapman, of Bucks County, Pennsylvania, who found it equal if not superior to the Spanish fly as a vesicatory. The testimony of Chapman has been corroborated by that of many other practitioners. It may be applied to the same purposes, treated in the same manner, and given in the same dose as the foreign insect. W. R. Warner obtained 1.99 parts of cantharidin from 500 parts of this beetle, but by improved methods Fahnestock procured 1⅓ per cent. of the active principle. (*A. J. P.*, xxviii, 195; li, 298.) According to the researches of Jos. Leidy, the vesicating principle resides in the blood, the eggs, and a peculiar fatty matter of certain accessory glands of the generative apparatus (*A. J. M. S.*, Jan., 1869, p. 60); while H. Beauregard (*P. J.*, xv, 873) found that the blood, the seminal vesicles of the male, the eggs, and all parts of the generative organs of the female are active. This insect must not be confounded with the "potato bug" the *Colorado potato beetle* (*Doryphora decemlineata*), which has proved so destructive to potato plants, and which, according to the researches of L. Dembinski (*A. J. P.*, 177, p. 550), contains no cantharidin.

Properties.—"From 15 to 25 mm. in length, 5 to 8 mm. in breadth, oblong, somewhat compressed above; of a brilliant green or bluish-green metallic luster, changing in different parts, especially beneath, to a golden-green; head triangular, separated into two lateral lobes by a faint median line; mandibles stout and partly concealed; antennæ filiform, of 11 conical joints; the upper ones being black; eyes comparatively small; prothorax angulate; legs with five tarsal joints; wings membranous and brownish; elytra or wing sheaths each with two parallel lines and finely wrinkled; odor strong,

disagreeable; taste slight, afterwards acrid. Cantharides with an ammoniacal odor must not be used. The powder is grayish-brown, with shining green particles and a number of long, pointed, 1-celled hairs 0.5 mm. in length and 0.02 mm. in width. Cantharides does not contain more than 10 per cent. of moisture. Cantharides yields not more than 9 per cent. of ash.

"**Assay.**—Introduce 15 Gm. of Cantharides, in No. 40 powder, into a stout bottle of not less than 250 mils capacity, add 150 mils of a mixture of benzene, two volumes, and purified petroleum benzin, one volume, and then add 2 mils of hydrochloric acid. Stopper the bottle tightly, shake it well, and allow it to stand about ten hours. Now gradually warm the bottle and its contents to about 40° C. (104° F.), and maintain it at that temperature with frequent shaking during three hours. Cool the mixture, decant or filter off 100 mils of the clear solution and evaporate this rapidly in a tared beaker or wide-necked flask to a volume of about 5 mils. Now add 5 mils of chloroform to the residue and set it aside in a moderately warm place. When the solvent has all evaporated, add to the crystals 10 mils of a mixture of equal volumes of dehydrated alcohol and purified petroleum benzin, which has previously been saturated with pure cantharidin, allow the mixture to stand during fifteen minutes and then decant the liquid through a pellet of purified cotton. Wash the crystals with successive portions of a saturated solution of cantharidin, similar to that directed above, until it is free from fat and coloring matter, and pass the washings through the same pellet of purified cotton. Then wash the cotton with a very small quantity of warm chloroform to dissolve any adhering crystals, collect the chloroform in the tared flask or beaker containing the washed crystals, evaporate the solvent with the aid of a blast of air, dry the crystals at 60° C. (140° F.) for one-half hour and weigh. The resulting weight will be the amount of cantharidin obtained from ten grammes of Cantharides." *U. S.*

Dried Spanish flies preserve the form and color, and, to a certain extent, the disagreeable odor, of the living insect. They have an acrid, burning, and urinous taste. Their powder is of a grayish-brown color, interspersed with shining green particles, which are the fragments of the feet, head, and wing-cases. If kept perfectly dry, in well-stoppered glass bottles, they retain their activity for a great length of time. A portion which had been preserved by Van Swieten for thirty years, in a glass vessel, was found still to possess vesicating properties. But exposed to a damp air they quickly undergo putrefaction, and this change takes place more speedily in the powder. Hence the insects should either be kept whole, and powdered as they are wanted for use, or, if kept in powder, should be well dried immediately after pulverization, and preserved in air tight vessels. They should never be purchased in powder, as, independently of the consideration just mentioned, they may in this state be more easily adulterated. Davis (*Proc. Mich. Ph. Ass.*, 1910, p. 62) reports that when cantharis is subjected to a microscopical examination the presence of other kinds of beetles and insects may be detected. But, however carefully managed, cantharides are apt to be attacked by mites, which feed on the interior soft parts of the body, reducing them to powder, while the hard exterior parts are not affected. An idea was at one time prevalent that the vesicating property of the insect was not injured by the worm, which was supposed to devour only the inactive portion. But this has been proved to be a mistake. Farines, an apothecary of Perpignan, has satisfactorily shown that, though the hard parts left by these mites possess some vesicating power, and the powder produced by them still more, yet the sound flies are much stronger than either. Camphor, which has been recommended as a preservative, does not prevent the destructive agency of the worm. It appears from the experiments of Nivet that, though camphor does not preserve the entire fly from the attacks of the larvæ of the *Anthrenus*, it actually destroys the mites of the Cantharis so often found in the powder, and may, therefore, be introduced with advantage, in small lumps, into bottles containing powdered cantharides. (*J. P. C.*, xix, 604.) Ammonium carbonate has also been recommended as a preservative. Pereira has found that a few drops of strong acetic acid, added to the flies, are very effectual. Among the best means of preserving them, whether whole or in powder, is the application of the process of Apert, which consists in exposing them for half an hour, confined in glass bottles, to the heat of boiling water, which destroys the eggs of the insect, without impairing the virtues of the flies. (*J. P. C.*, xxii, 246.) Of course, the access of water to the flies should be carefully avoided. Lutrand recommends chloroform as the best preservative that he has tried. (*J. P. C.*, xviii, 214.) The U. S. Pharmacopœia directs the use of chloroform or carbon tetrachloride and either of these are among the simplest, safest and best preservatives to prevent the development of insects in drugs. It is stated by Farines that when the flies are destroyed by the vapor of pyroligneous acid, instead of common vinegar, they acquire an odor which contributes to their preservation. Cantharides will bear a very considerable heat without losing the brilliant color of their elytra; nor is this color extracted by water, alcohol, ether, or the oils, so that the powder might be deprived of all its active principle and yet retain the exterior characters unaltered. The wing-cases resist putrefaction for a long time, and the shining particles have been detected in the human stomach months after interment.

So early as 1778, Thouvenel attempted to analyze cantharides, and the attempt was re-

peated by Beaupoil in 1803; but no very interesting or valuable result was obtained until 1810, when Robiquet discovered in them a crystalline substance, which proved to be the vesicating principle of the insect and received the name of *cantharidin*. The constituents, according to Robiquet, are (1) a green oil, insoluble in water, soluble in alcohol, and inert as a vesicatory; (2) a black matter, soluble in water, insoluble in alcohol, and inert; (3) a yellow viscid matter, soluble in water and alcohol, and without vesicating powers; (4) cantharidin; (5) a fatty matter, insoluble in alcohol; (6) calcium and magnesium phosphates, acetic acid, and, in the fresh insect, a small quantity of uric acid. Orfila afterwards discovered a volatile principle, upon which the fetid odor of the fly depends. It is separable by distillation with water. Dragendorff has found a volatile principle which acts on the system in the same manner as cantharidin. When powdered flies are moistened with water and distilled, the part which passes over, at or below 100° C. (212° F.), contains this principle. (*Chem. News*, May 31, 1867.) That the green coloring matter is chlorophyll seems to be shown by the experiments of Pocklington, who (*P. J.* [3], iii, p. 681) found that when cantharides was treated with alcohol, ether, and carbon disulphide, the solutions yielded absorption spectra agreeing with that of chlorophyll. Cantharidin exists in commercial cantharides to the extent of from 0.6 to 0.9 per cent. (See also *Ph. Centralh.*, 1901, 674.)

Adulterations.—These are not common. Occasionally other insects, or even beads, are added, purposely or through carelessness. These may be readily distinguished by their appearance. Flies exhausted of their cantharidin are sometimes substituted for the genuine drug. They are worthless, and are to be distinguished by their lack of substance and their yielding a nearly colorless ethereal tincture. Pereira states that powdered flies are sometimes adulterated with euphorbium. According to the researches of Fahnestock (*A. J. P.*, 1879, p. 298), age destroys the activity of the drug without of necessity impairing its physical appearance.

The percentage of cantharidin found in cantharides furnishes the best test of their virtues. Wm. Procter succeeded, by means of chloroform, in isolating cantharidin with great facility. He treated the flies with chloroform by percolation, displacing the last portion by means of alcohol, and allowing the resulting solution to evaporate spontaneously. Cantharidin is thus obtained in crystals mixed with the green oil, the greater portion of which may be removed by bibulous paper. The residuary crystals are dissolved in a mixture of ether and alcohol, which, by the spontaneous evaporation of the ether, yields the cantharidin nearly pure. Mortreux, having ascertained that the cantharidin is insoluble in carbon disulphide, proposed to use this fluid for removing the fatty matter associated with the cantharidin crystals obtained by the use of chloroform. He employed the same liquid in estimating the proportion of cantharidin, which he found to be about 20 centigrammes for 40 grammes of the flies, or half of one per cent. (*J. P. C.*, 3e sér., xlvi, 33, 1864.) Wittstein obtains it by digesting coarsely powdered flies repeatedly with water, straining through linen and expressing, allowing the liquid to settle for a day, separating the supernatant oil, adding a little wood charcoal, evaporating to dryness, treating the residue with ether so long as the solution affords a laminated substance on evaporation, evaporating the ethereal solution, treating the residue with cold alcohol of 80 per cent. for one day with frequent shaking, and finally drying the scales. (See *A. J. P.*, xxviii.) Williams has obtained it by means of benzene. (*Ibid.*, xxvi.) For a method of assaying cantharides and its official preparations by H. G. Greenish and Harold Wilson, see *P. J.*, 1898, 255, or *Am. Drug.*, 1898, 224.

Uses.—Internally administered, cantharides are a powerful irritant, with a peculiar direction to the urinary and genital organs. Genito-urinary irritation is ordinarily the first symptom produced by small doses of cantharides, and, if the dose has been large enough, it may amount to violent strangury, attended with excruciating pain, and the discharge of bloody urine. Toxic doses of Spanish fly produce obstinate and painful priapism, vomiting, bloody stools, severe pains in the whole abdominal region, excessive salivation with a fetid breath, hurried respiration, a hard and frequent pulse, burning thirst, exceeding difficulty of deglutition, sometimes a dread of liquids, frightful convulsions, tetanus, delirium, and death. Orfila has known twenty-four grains of the powder to prove fatal. Dissection reveals inflammation and ulceration of the mucous coat of the whole intestinal canal. According to Poumet, if the intestines be inflated, dried, cut into pieces, and examined in the sun between two pieces of glass, they will exhibit small shining yellow or green points, strongly contrasting with the matter around them. (*J. P. C.*, 3e sér., iii, 167.)

The poisonous effects are to be counteracted by the use of emetics, cathartics, and opiates by the stomach and rectum. From the experiments of Schroff it seems that oils somewhat accelerate the poisonous action, probably by dissolving the cantharidin. (See *A. J. P.*, xxviii, 365.) By experiments upon dogs, Thouery, a French apothecary, has satisfied himself that animal charcoal possesses a real antidotal power. (*J. P. C.*, 1858, p. 65.)

Cantharides have been long and beneficially used in medicine. Either these or other vesicating insects appear to have been given by Hippocrates in *dropsy* and *amenorrhea*, in the latter of which complaints, when properly prescribed, they are a highly valuable remedy.

They are also useful in obstinate *gleet, leucorrhea,* and *seminal weakness,* and in *paralytic incontinence of urine.* They are used also in certain cutaneous eruptions, especially those of a scaly character, and in chronic *eczema.* Their unpleasant effects upon the urinary passages are best obviated by the free use of diluent drinks, or when severe, by opiate enemata.

Externally applied, cantharides excite inflammation in the skin, which terminates in a copious secretion of serum under the cuticle. It may be employed either as a rubefacient, or to blister. In the former capacity it is seldom used, but as an epispastic it is preferred to all other substances. When blisters are allowed to stay on only long enough to irritate the skin, but not to blister, they are known as *flying blisters.* Used in this way, they are sometimes of service in *neuralgias,* applied directly over the seat of pain. Their chief value is, however, found in cases of severe internal irritation. It is of great importance that the practitioner should clearly comprehend the distinct uses of the rubefacient and the blister. The rubefacient is to be employed as a revulsive when the internal irritation is severe but is not connected with pronounced organic change. The immediate impression of a rubefacient, acting as it does upon a much larger surface than does the blister, is greater than that of the blister, but the permanent revulsive action is much less. The blister is, therefore, to be used when the internal disease is connected with inflammatory structural change. Thus, in a case of *gastrodynia,* a rubefacient is of much more service than a blister, while the blister is decidedly more effective in *peritonitis.* In a general wide-spread *congestion of the lung* the rubefacient is to be preferred to the blister, but in *pneumonia* the blister to the rubefacient. As, however, congestion of neighboring parts usually accompanies a localized inflammation, a rubefacient is sometimes to be employed as a temporary substitute for or adjuvant to a blister. The amount of serous discharge produced by blisters appears to be sometimes of service in almost directly evacuating local serous exudations. Thus, not rarely, repeated blistering affords the best treatment of a *serous pleurisy.* Possibly, however, even in these cases, the blister acts purely as a counter-irritant, as it certainly does in *chronic rheumatism* and *neuritis.* In all *chronic joint inflammations* the best results may often be obtained by a reblistering, extending, if necessary, over weeks and months. In some cases of *skin disease* blisters are capable of substituting their own action for the original morbid disease, and they are still occasionally used for this purpose in *tinea capitis,* obstinate *herpes,* and other affections. The length of time that a blister should be applied varies with the individual and with the position of the disease. In some constitutions they produce a poisonous impression, attended with frequent pulse, dryness of the mouth, subsultus tendinum, and even convulsion. Such symptoms are probably the results of an intense peripheral nervous irritation acting upon very susceptible centers. Such is not, however, the case with the strangury which may follow absorption of the cantharidin, and which is always the result of the direct action of the cantharidin upon the genito-urinary tract. In order to avoid such genito-urinary irritation, and also as much as possible the pain at the seat of application, the blister should be left on only until it distinctly reddens the skin, when a flaxseed poultice may be applied, and in the course of two or three hours the blister is formed. The time necessary for such reddening of the skin is usually from four to six hours, if the cantharides be active. (See *Ceratum Cantharidis.*)

The dose of cantharides is one-half to one grain (0.032–0.065 Gm.) of the powder, which may be given twice a day, in the form of a pill, but it is rarely used internally. The tincture, however, is more frequently employed.

Off. Prep.—Ceratum Cantharidis, *U. S.;* Collodium Cantharidatum, *U. S.;* Emplastrum Cantharidis (from Cerate), *U. S.;* Tinctura Cantharidis, *U. S.*

CAPSICUM. U. S. (Br.)

CAPSICUM Capsic. [Cayenne Pepper, African Chillies]

(kăp'sĭ-cŭm)

"The dried ripe fruits of *Capsicum frutescens* Linné (Fam. *Solanaceæ*), without the presence or admixture of more than 2 per cent. of stems, calyxes or other foreign matter." *U. S.* "Capsicum is the dried ripe fruit of Capsicum minimum, *Roxb.*" *Br.*

Capsici Fructus, *Br.;* Piper Hispanicum; Capsicum Fruit, African or Pod Pepper, Red Pepper, Chillies, Bird Pepper, Spur Pepper; Fructus Capsici, *P. G.;* Spanischer Pfeffer, Schlotenpfeffer, *G.;* Piment de Cayenne, Piment des Jardins, Poivre d' Espagne, Poivre de Guinée, Poivre d'Inde, Poivre de Cayenne, Piment rouge, Capcique, *Fr.;* Peperone, *It.;* Pimiento, Chile, Aji, *Sp.*

Owing probably to its widespread cultivation, the genus Capsicum contains a large number of plant forms whose specific relations afford a very difficult problem to the systematic botanist. The probability is that the entire genus was originally confined to the American tropics, although it has been cultivated since the time of Columbus in the temperate and tropical zones of almost the whole world. Its first appearance in literature seems to be in an epistle by Peter Martyn, dated September, 1493, speaking of its having been brought by Columbus. Neither in ancient Sanscrit, Chinese, Greek, Latin, or Hebrew is there a name for it. In 1887 Asa Gray expressed his belief that there are only two species in the genus, although in the last previous revision of the genus, in 1852, Dunal had recorded fifty species. After a very thorough and careful study of the subject, including the cultivation of every procurable va-

riety and species for four years in the Missouri Botanical Garden, H. C. Irish has reached the conclusion that the dictum of Gray was correct, and that there are really only two species of the genus, one of which is herbaceous and annual or biennial, the other shrubby and perennial, a conclusion which seems to be accepted.

The first of these species is the one most extensively cultivated in Europe and in this country; it is the *C. annuum* L. The second is in its varieties very largely grown in the tropical and subtropical latitudes, its fruit not ripening at all or only to a slight degree in the temperate zone. It is the species which was described under the name of *C. frutescens*, by Linnæus, in 1737. By Irish it is divided into two varieties—*C. frutescens* proper, which is characterized by its fruit being oblong, acuminate, and usually embraced by the calyx, and *C. frutescens baccatum*, which is characterized by its ovate or subround fruit, usually seated on the calyx. This variety is the *C. baccatum* of Linnæus, 1767. In the first of these varieties are comprised the *C. fastigiatum* of Blume and the *C. minimum* of Miller and of Roxburgh, which yield most of the Cayenne pepper produced in the tropics, although, especially in the West Indies and South America, *C. baccatum* is largely cultivated. It is even doubtful whether *C. annuum* should be considered as a distinct species from *C. frutescens*, as in tropical climates varieties have been produced which are perennial and somewhat woody.

The British Pharmacopœia seems to be in error in ascribing the original description of the *Capsicum minimum* to Roxburgh, since his *Flora Indica* did not appear until 1832, whereas the species was described by Miller, in the *Garden Dictionary*, in 1771.

The following are the characteristics of *C. frutescens*, the shrubby capsicum, as given by Irish: "Plants shrubby, perennial, two and a half to six feet high. Branches angular, often channelled, puberulent or pubescent, especially on the younger portions; usually greatly enlarged and slightly purple at the nodes, green or sometimes purplish striate. Leaves broadly ovate, acuminate, 7.5 to 15 cm. long, usually puffed or wrinkled, more or less pubescent, especially around the veins. Petioles medium, usually subciliate; peduncles slender, 2.5 to 5 cm. long, often in pairs, usually longer than the fruit. Calyx usually cup-shaped, embracing base of the fruit; teeth short, corolla white or greenish white, spreading 10 to 20 mm. long, often with ocherous markings in the throat. Fruit red, ovate, obtuse or oblong acuminate, 20 to 30 mm. long and 6 to 18 mm. in diameter."

Capsicum annuum is largely cultivated both in the United States and in Europe, flowering in the early or middle summer, and ripening its fruit in the early autumn. There are numerous varieties of it differing in the shape of their fruit. That which is chiefly cultivated in the United States for market, to be used in the green state in pickling, or cooked for the table, is a large irregularly ovate or conical berry, depressed or horned at the extremity, and when ripe varying in color from yellowish to scarlet. A variety with a long, conical, pointed and recurved fruit, which is usually not thicker than the finger, is said to be especially used in the making of red pepper. In another variety the berries are not more than an inch in diameter, spherical and slightly compressed.

When ground into powder the fruit of the *Capsicum annuum* constitutes *paprika*, or as it is sometimes called, *sweet pepper;* it is very little used by itself but is largely employed for the mixing with the powder of chillies or true cayenne pepper; it has scarcely more than one-sixth the pungency of real cayenne pepper, so that the addition of it to powdered chillies may almost be considered an adulteration.

Paprika or *Hungarian Pepper* is recognized by the German Pharmacopœia. It is usually imported into the United States in a ground condition, three grades being recognized. 1. *Rosén-paprika* or *Rozsapaprika*, the best grade possesses a beautiful red color and has a savory taste. It is prepared from the selected pericarp and seeds which are carefully washed before being ground, the stems and placentæ being removed. 2. *Königs-paprika* or *Kiralypaprika* is prepared by grinding the entire pods, including not only the seeds but the stems. 3. *Mercantil-paprika* is prepared from the spotted pods, remaining from the selection for the finer grades, and from the pods containing flaws and also contains the stems, seeds and other parts. The last grade has a pale yellow color and is much more pungent. (Tolman and Mitchell, *Bull. No. 163, Bureau of Chemistry, U. S. Dept. of Agriculture.*) The cayenne pepper of the grocery stores is very largely a mixture of paprika and true pepper. The microscopic characteristics in the fruits of the two species are not sufficiently pronounced to be of avail in detecting the presence of the feebler substance in the powdered pepper, although, according to T. Edward Wallis, the outer portions of the pericarp of *Capsicum annuum* are cuticularized or suberized, while in *Capsicum fastigiatum* all the cells are composed purely of cellulose. True cayenne pepper, *chillies* or *bird pepper*, is produced in almost all tropical and subtropical countries, but is said to come in very large proportion from Zanzibar. The pod is at once distinguished by the peculiar thinness and tendency to wrinkle of its outer coating.

The varieties of cayenne pepper are numerous as they occur in the American market—the pods of the *East African pepper* are about 12 mm. in length, flattened, almost cylindrical, although showing distinctly the conical form; the pods of the *Madagascar peppers* reach the length of 6 to 7 cm. and a breadth of about 20 mm.; those of the *Bombay* or *cherry pepper* are very dark in color, 3.5 to 5 cm. in length,

and 12 mm. or more in breadth at the base. They are strictly conical and less likely to be flat than those of the other varieties. *Zanzibar pepper* is smaller than the *East African pepper* but otherwise similar to it. *Japanese capsicum*, whose botanical source is not positively known, occurs in the market in two forms, one in which the pods are large, reaching the length of about 6 cm.; the other in which the small pods are not 2.5 cm. in length. The larger pods are scarcely to be distinguished from *Madras chillies;* the smaller resemble, but are nearly twice the size of, the East African pepper. The color of the pods varies from light yellowish-brown to deep red.

about twelve to twenty millimetres in length and about six millimetres in diameter; sometimes attached to a five-toothed inferior calyx, and long, straight, slender peduncle. Pericarp somewhat shrivelled, glabrous, translucent and leathery, containing from ten to twenty small flat seeds, either loose or attached to a thin reddish dissepiment. The cells of the outer epidermis of the pericarp have moderately thick walls, are often arranged in rows of five to seven, and exhibit a cuticle uniformly striated (distinction from the fruits of other species of Capsicum). Characteristic odor; taste intensely pungent. Ash not more than 7 per cent." *Br.*

T. Edward Wallis believes that the different cayenne peppers can be distinguished from one another when powdered by the character of their epidermis and the tissue immediately below it, and gives the following tabulated summary of the differences. (*P. J.*, July, 1902.)

	C. minimum.	*C. annuum.*	*Japanese Chillies.*
Epidermis.	Thick and straight-walled rectangular cells with few pits; often arranged in groups of five to seven in a row and with a uniformly striated cuticle. Size of cells, 25 mkm. to 60 mkm. in either direction.	Irregular polygonal cells with evenly thickened walls, traversed by numerous well-marked, simple pits. The cuticle shows striated ridges. Size of cells, 60 mkm. to 100 mkm. long, and 25 mkm. to 50 mkm. wide.	Cells with strongly thickened walls and a radiated lumen. The pits only rarely penetrate the whole thickness of the wall. No visible striation. Size of cells, 30 mkm. to 80 mkm. long, and 15 mkm. to 45 mkm. wide.
Hypodermis.	Delicate thin-walled cellulose cells.	Several layers of cuticularized collenchymatous cells, having a rounded outline and very few pits.	A single layer of regular polygonal cells with cuticularized, fairly thick walls, traversed with numerous pits, which give them a beaded appearance.

The U. S. Pharm. describes the fruit of *C. frutescens* as follows: "Oblong-conical, from 8 to 20 mm. in length and from 2 to 15 mm. in diameter; pericarp brownish-red or orange, shining, membranous and translucent; 2- or 3-locular, united below, and containing 6 to 17 flat, reniform, yellowish seeds attached to the placenta or frequently separated from it; odor characteristic, sternutatory; taste intensely pungent. The calyx, when present, light greenish-brown, inferior, inconspicuous, 5-toothed, usually attached to a long straight peduncle. The powder is yellowish-brown; mounts made with hydrated chloral T.S. and examined under the microscope show yellowish-red oil globules; stone cells of two kinds, those of the endocarp being more or less elongated, walls yellowish, uniformly and moderately thickened, wavy in outline, porous and slightly lignified, those of the seed-coat being yellowish, irregular and strongly thickened, wavy in outline and strongly lignified. Capsicum yields not less than 15 per cent. of non-volatile extractive, soluble in ether (see Part III, Test No. 13). Capsicum yields not more than 7 per cent. of ash. The amount of ash, insoluble in hydrochloric acid, does not exceed 1 per cent. of the weight of Capsicum taken." *U. S.*

The Br. Pharm. gives the characteristics of the fruit of *C. minimum* as "Dull orange-red, oblong-conical, obtuse, two-celled fruits, from

The difficulty of distinguishing the source of powdered capsicum is increased by the fact that the red color fades upon exposure to light, and that the powdered African pepper, though very powerful, is a light brownish-yellow. The value of any specimen may be, however, fairly estimated by the intensity of its odor, which is peculiar, somewhat aromatic, and extremely irritant, and by its acrid, burning taste. The pungency appears to depend on a peculiar principle, which was obtained, though not in a perfectly isolated state, by Braconnot, and named *capsicin*. It is obtained as a thick yellowish-red liquid, but slightly soluble in water. When gently heated it becomes very fluid, and at a higher temperature is dissipated in fumes which are extremely irritating if inhaled. Capsicin is a mixed substance, consisting of resinous and fatty matters. In 1876, Thresh isolated a well defined active principle, *capsaicin*, from the extract which he obtained by exhausting Cayenne pepper with petroleum. From the red liquor dilute caustic alkali removes capsaicin, which is to be precipitated in minute crystals by passing carbon dioxide through the alkaline solution. The crystals may be purified by recrystallizing them from either alcohol, ether, petroleum benzin, glacial acetic acid, or hot carbon disulphide; in petroleum, capsaicin is but sparingly soluble, yet it is dissolved abundantly on the addition of fatty oil. The

crystals of capsaicin are colorless, and answer to the formula $C_9H_{14}O_2$; they melt at 59° C. (138.2° F.), and begin to volatilize at 115° C. (239° F.), but decomposition can be avoided only with great care. The vapors of capsaicin are of the most dreadful acridity, and even the ordinary manipulation of that substance requires much precaution. Felletar (*J. P. C.*, April, 1870, p. 347) first obtained from capsicum fruits a volatile alkaloid, which resembles coniine in odor, but is distinguished by the different shape of its hydrochloride crystals. H. Pabst (1892) made a thorough investigation of the fruit of *C. annuum*. He does not think that an alkaloid exists originally in the fruit, but believes that the alkaloidal reactions are due to a decomposition product. He finds, besides capsaicin, a red coloring matter, and oleic, palmitic, and stearic acids. The red coloring matter, by saponification, was shown to be a cholesterin ester of the fatty acids. (*A. J. P.*, 1892, 370.) Moerbitz (1898) isolated a pungent principle having a bitter taste, which he states is neither capsicin nor capsicol, and names *capsicutin*. He gives it the formula $C_{35}H_{54}N_3O_4$, and states that it is neither an alkaloid nor glucoside; it does not have acid properties. Red lead oxide is sometimes added to the powdered capsicum sold in Europe; it may be detected by digestion in diluted nitric acid, and precipitating the lead by sodium sulphate. Capsicum is said to be sometimes adulterated with colored sawdust, which may be recognized by the microscope. It is often adulterated with inert vegetable substances. The British Pharmacopœia requires that capsicum should yield on incineration not more than 6 per cent. of ash; this test would detect the presence of most adulterants. It is occasionally attacked by insects.

Uses.—Capsicum is a very powerful local stimulant, producing, when swallowed, a sense of heat in the stomach, and a general glow over the body without any narcotic effect. It is much employed as a condiment, especially in hot climates, and is useful in cases of *atony of the stomach* or *intestines*. It is strongly contraindicated by the existence of gastric catarrh of the ordinary type, but in the chronically inflamed stomachs of persons of intemperate habits it frequently appears to do good, probably by lessening the size of the dilated blood vessels and thereby relieving chronic congestion. It is often added with advantage to tonic prescriptions in cases of *neurasthenia*.

Applied externally, Cayenne pepper is a powerful rubefacient, which has the advantage of acting speedily without danger of producing vesication. It may be applied in the form of cataplasm, or more conveniently and efficiently as a liniment. It may be used in strengths of from 10 to 20 per cent. mixed either with alcohol or cotton-seed oil. The powder or tincture brought into contact with a *relaxed uvula* often acts very beneficially. The tincture has also been used advantageously in *chilblain*. The fluidextract and the oleoresin (*Oleoresina Capsici, U. S.*) are powerfully rubefacient. A gargle may be prepared by infusing half a drachm of the powder in a pint of boiling water, or by adding half a fluidounce of the tincture to eight fluidounces of rose water.

Dose, of the powder, from one to ten grains (0.065 to 0.65 Gm.), which is most conveniently given in the form of pill. Of an infusion prepared by adding two drachms to half a pint of boiling water, the dose is half a fluidounce (15 mils).

Off. Prep.—Oleoresina Capsici, *U. S.;* Pilulæ Podophylli, Belladonnæ et Capsici, *U. S.;* Tinctura Capsici, *U. S., Br.;* Unguentum Capsici, *Br.;* Mistura Chloroformi et Morphinæ Composita (from Tincture), *N. F.;* Mistura Opii et Chloroformi Composita (from Tincture), *N. F.;* Mistura Opii et Rhei Composita (from Tincture), *N. F.;* Pulvis Aromaticus Rubefaciens, *N. F.;* Pulvis Myricæ Compositus, *N. F.;* Tinctura Capsici et Myrrhæ, *N. F.*

CARBO

CARBON

(cär-bō)

C = 12.

Carbone, *Fr.;* Kohlenstoff, *G.;* Carbone, *It.;* Carbon, *Sp.*

Carbon is an element of great importance, and very extensively diffused in nature. It exists in large quantity in the mineral kingdom, and is the most abundant constituent of animal and vegetable matter. In the crystallized state it constitutes the diamond; and, more or less pure, it forms the substances called *graphite* (or black lead and *plumbago*), anthracite and bituminous coal, coke, animal charcoal, and vegetable charcoal. Combined with oxygen it forms carbon dioxide, or carbonic acid gas, which is a constituent of the atmosphere, and present in many natural waters, especially those which have an effervescing quality. United with oxygen and a base it forms the carbonates, among others calcium carbonate, which is one of the most abundant minerals. There are three allotropic conditions of carbon, represented respectively by the diamond, graphite, and charcoal.

The *diamond* has been found in quantity in India, in Brazil, and in South Africa, but at the present time is obtained almost exclusively from the last named locality. Several diamonds have been found in the gold regions of Georgia and North Carolina. This gem is perfectly transparent, and the hardest and most brilliant substance in nature. Its sp. gr. is about 3.5. It is fixed and unalterable in the fire, provided air be excluded, but is combustible in air or oxygen, the product being the same as when charcoal is burned, namely, carbon dioxide. It has been made artificially at the temperature of the electric arc (2500° to 3000° C.) by Moissan.

Next to diamond, *graphite* or *plumbago* is the purest natural form of carbon. Graphite is the substance of which black-lead crucibles and pencils are made. It is found in greatest purity in the mine of Borrowdale, in England, and in Ceylon, from which latter place most of the graphite of commerce is now obtained, but it also occurs very pure in this country, and in deposits at Ticonderoga, N. Y., at Stourbridge, Mass., and in Canada and Brazil. In physical characters it is utterly different from the diamond; it crystallizes in hexagonal plates, is very soft and unctuous, of 2 to 2.5 sp. gr., and generally contains a little ash. In connection with the production of silicon carbide (carborundum) in the electric furnace, Acheson has produced a very pure artificial graphite by simply increasing the heat until the silicon was volatilized. This artificial graphite has a specific gravity of 2.5, is soft and of high metallic lustre. It is extensively used for electrodes in the electrolysis of brine and similar operations, and for graphite paint.

Anthracite, the purest variety of natural coal, occurs in different parts of the world, but particularly in the State of Pennsylvania. It contains from 90 to 95 per cent. of carbon, and several per cent. of ash. *Bituminous coal* is another variety, containing, besides the fixed or free carbon, some 10 to 15 per cent. of volatile hydrocarbons or gas-making material. When this is driven off by the process of charring, as in the manufacture of coal-gas, a kind of mineral charcoal, called *coke,* is obtained, very useful in the arts as a fuel. When peat is charred, it is converted into *peat charcoal,* which forms a cheap deodorizer, applicable to the purification of hospitals, dissecting-rooms, factories, privies, etc.

Carbon may be obtained in a state approaching to purity by several processes. One method is to expose lamp-black to a full red heat in a close vessel. It may also be obtained, in a very pure state, by passing the vapor of volatile oils through an ignited porcelain tube, whereby the hydrogen and oxygen of the oil will be dissipated, and the charcoal left in the tube. The purest lamp-black is now made from natural gas in Western Pennsylvania and in Ohio. This lamp-black is miscible with water, does not color ether, and is free from oily matter.

Colloidal carbon may be easily prepared by gradually adding 2 Gm. of sugar to 20 Gm. of sulphuric acid with continuous agitation and then pouring the mixture into 80 mils of water and filtering. The sulphuric acid may be removed by dialysis and a clear black solution of colloidal carbon remains.

Properties.—Carbon, in its uncrystallized state, is an insoluble, infusible solid, generally of a black color, and without taste or odor. It burns when sufficiently heated, uniting with the oxygen of the air, and generating carbon dioxide. Its sp. gr. in the solid state, apart from its pores when in mass, is 3.5; but with the air of the pores included, it is only 0.44. It is an almost unalterable and indestructible substance, and has great power in resisting and correcting putrefaction in other bodies. When properly prepared, it possesses the property of absorbing the coloring and odorous principles of most liquids. See (*Carbo Animalis.*) Its other physical properties differ according to its source and peculiar state of aggregation. As a chemical element it enjoys a very extensive range of combination. It forms two compounds with oxygen, *carbon dioxide* (carbonic acid gas) and *carbon monoxide* (carbonous oxide). With hydrogen it forms a number of compounds, called *hydrocarbons,* of which the most interesting are light carburetted hydrogen or marsh-gas, olefiant gas, acetylene, the hydrocarbons constituting petroleum, coal tar hydrocarbons, as benzol, and naphthalene, and some essential oils. With nitrogen, carbon constitutes cyanogen, the compound radical of hydrocyanic or prussic acid, and when united in minute proportion with iron as carbide it is present in cast iron and steel.

CARBO LIGNI. U. S., Br.

WOOD CHARCOAL Carbo. Lig. [Charcoal]

(cär'bō lig'nī)

"Charcoal prepared from soft wood, and very finely powdered. Preserve it in well-closed vessels." *U. S.* "Wood Charcoal is wood charred by exposure to a red heat without access of air." *Br.*

Carbo Præparatus, Carbo e Ligno, Carbo Vegetabilis; Wood Charcoal, Vegetable Charcoal; Charbon Végétal, Charbon de bois, *Fr.;* Carbo Ligni Pulveratus, *P. G.;* Gepulverte Holzkohle, Holzkohle, Präparirte Kohle, *G.;* Carbone Vegetale, Carbone di legno, *It.;* Carbon vegetal medicinal, Carbon de lena, *Sp.*

Preparation on the Large Scale.—Billets of wood are piled in a conical form, and covered with earth and sod to prevent the free access of air, several holes being left at the bottom and one at the top of the pile, in order to produce a draught to commence the combustion. The wood is then kindled from the bottom. In a little while the hole at the top is closed, and, after the ignition is found to have pervaded the whole pile, those at the bottom are stopped also. The combustion taking place with a smothered flame, the volatile portions of the wood, consisting of hydrogen and oxygen, are dissipated, while the carbon is left, a portion of it, however, being lost by combustion. Wood, thus carbonized, yields not more than 17 or 18 per cent. of charcoal. A better method is to char the wood in iron cylinders, when it yields from 22 to 23 parts in 100 of excellent charcoal; and, at the same time, the means are afforded for collecting the volatile products, consisting of pyroligneous acid, empyreumatic oil, and tar. This process for obtaining charcoal has been described under another head. (See *Acidum Aceticum.*) A method of preparing charcoal by subjecting wood to super-

heated steam has been invented by Violette. When the temperature of steam is 300° C. (572° F.), the wood is converted into a peculiar charcoal, called *red charcoal,* which is intermediate in its qualities between wood and ordinary charcoal. When the temperature is lower, the carbonization is incomplete; when higher, the product is black charcoal. The steam process yields a uniform charcoal for a given temperature, which may be easily regulated, and a product about double that obtained in closed cylinders. Charcoal contains *carbon,* approximately in proportion to the temperature at which it is formed; varying from 65 per cent. when made at 250° C. (482° F.) to 80 per cent. when made at 400° C. (752° F.). The gaseous matter present, on the other hand, decreases with the temperature of carbonization. Thus, for charcoal made at 300° C. (572° F.), it is one-third of its weight; at 350° C. (662° F.), one-fourth.

E. C. C. Stanford has called attention to a variety of vegetable charcoal, obtained by charring a species of sea weed, *Laminaria digitata,* gathered on the shores of the Hebrides, which, on account of the large proportion of calcium carbonate contained in it (20 per cent.), is unfit for use in refining sugar; it, however, possesses more of the deodorizing and decolorizing power than animal charcoal itself, which, with the exception referred to, it closely resembles in chemical composition.

Preparation for Medicinal Use.—Belloc recommends charcoal for this purpose to be obtained from poplar shoots, cut at the time the sap rises, and deprived of their bark. The carbonization should be performed in cast iron vessels at a red-white heat. The product is a light and brilliant charcoal, which must be purified by being macerated for three or four days in water, frequently renewed. It is then dried, powdered, and placed in bottles, which should be well-stoppered. The charcoal made from willow is generally preferred, although that obtained from maple is also largely employed. A fine charcoal is also made in Europe from the linden and poplar. The charcoal most esteemed in Philadelphia for medicinal purposes is that prepared by Dupont, near Wilmington, Delaware, for the manufacture of gunpowder; it is made from young willow shoots of two or three years' growth.

Properties.—Charcoal is a black, shining, brittle, porous substance, tasteless and inodorous, and insoluble in water. It is a good conductor of electricity, but a bad one of heat. It possesses the remarkable property of absorbing many times its own bulk of certain gases. "Wood charcoal is a black, odorless, and tasteless powder, free from gritty matter. It burns without a luminous flame. Incinerate about 1 Gm. of Charcoal; not more than 7.5 per cent. of ash remains. Boil about 1 Gm. of Charcoal with a mixture of 3 mils of potassium hydroxide T.S. and 10 mils of distilled water for one-half minute; the filtrate shows only a slight brown color." *U. S.*

The British Pharmacopœia describes it as "A black powder without odor or taste, free from gritty matter. When 1 gramme of the Charcoal is boiled for a few minutes with 5 millilitres of *solution of sodium hydroxide* diluted with 15 millilitres of *water* and the mixture filtered, the color of the filtrate is not deeper than pale yellow (absence of insufficiently carbonised wood). Ash not more than 7.5 per cent." *Br.*

When exposed to the air after ignition, charcoal increases rapidly in weight, absorbing from 12 to 14 per cent. of moisture. As ordinarily prepared, it contains the incombustible part of the wood, amounting to 1 or 2 per cent., which is left as ashes when the charcoal is burned. This inorganic material may be removed by digesting the charcoal in diluted hydrochloric acid, and afterwards washing it thoroughly with boiling water. Havenhill examined the wood charcoal of the western markets and found the ash to vary from 0.62 to 16.80 per cent. (*D. C.* 1914, p. 260.) Gane states that imperfectly carbonized samples are of frequent occurrence (*J. A. Ph. A.* 1912, p. 375). Knecht claims that the more closely the substance approaches in composition to pure carbon the less is its decolorizing power. (*Proc. VIIth Internat. Congress App. Chem.,* Sec. IVb., Coloring, 1909, London, 1910, pp. 17, 18.)

For internal use charcoal is preferred by some in the *granular form.* W. Lascelles Scott employs the following method of preparing it. He prefers the wood of the box, willow, or linden, which, after being charred, should be allowed to cool out of contact with air, then boiled for some time in diluted hydrochloric acid, and afterwards, having been thoroughly washed with pure water, in a little weak ammonia. The fragments are again ignited, and then quickly powdered, and passed through a sieve of 80 or 100 apertures to the inch. Nine pounds of this powder are mixed with one pound of pure sugar passed through a 30 sieve, and 4 ounces of gum arabic in impalpable powder. The whole is then moistened with a few ounces of warm distilled water, to which have been added an ounce and a quarter of tincture of benzoin, and a little mucilage. The mass is now granulated on flat steam pans, in the usual manner, at a temperature of 101.6° to 107.2° C. (215° to 225° F.). When perfectly dry it is sifted, and secured in well-stoppered bottles. (*Chem. News,* 1867, p. 204.)

Stenhouse has devised a process for combining alumina with common vegetable charcoal, forming what he calls *aluminized charcoal,* which is an economical substitute for purified animal charcoal, and equally efficacious as a decolorizer. It is prepared by digesting finely powdered charcoal with sufficient of the solution of aluminum sulphate to give an impregnation of 7.5 per cent. of alumina. The whole is evaporated to dryness, and ignited in a covered

Hessian crucible, until the water and acid have been dissipated. Aluminized charcoal is perfectly black, though thoroughly impregnated with anhydrous alumina, and only requires to be carefully pulverized to be ready for use. On similar principles, Stenhouse prepares his *artificial bone black,* by impregnating powdered wood charcoal with 7.5 per cent. of calcium phosphate, by digesting it in a solution of this salt in hydrochloric acid, evaporating to dryness, and igniting in covered vessels. This charcoal decolorizes well, but can be used only for neutral solutions.

Uses.—Charcoal is used in medicine chiefly for its absorbent properties, thus it is used locally in *gangrene* and *foul ulcers* to absorb the putrid gases. Internally it has been used in *meteorism* and *fermentative dyspepsia* with the idea of absorbing the gas. In many cases of *dyspepsia,* however, it appears to have some further action than that of a mere absorbent. As is well known, charcoal is capable of absorbing not only coloring matter but many other organic substances and it has been lauded by Kraus and Barbara (*D. M. W.,* 1915, xli) as an absorbent for toxins. For this action they recommend it internally in the treatment of *diarrhea* and *dysentery* and locally for various infected *wounds;* see also Eisner. (*Ther. Geg.* lvi.)

At one time it was much used as a dressing for ulcers but is at present rarely employed, though the *Cataplasma Carbonis* or charcoal poultice is still occasionally prescribed in Great Britain. Several of its varieties are used as tooth powder. Those generally preferred are the charcoals of the cocoa-nut shell and of bread. It is said that charcoal proves useful in preserving the teeth by absorbing the acid sometimes morbidly present in the mucus of the mouth. The dose of charcoal varies from one to four teaspoonfuls (3.9 to 15.5 Gm.) or more. Daniel gave it in his case of constipation in doses of a teaspoonful (3.9 Gm.), repeated every half hour. *Charcoal biscuits* have been prepared, containing 15 or 20 per cent. of charcoal in fine powder, while *charcoal lozenges,* either of charcoal alone or associated with bismuth, have been employed with asserted good results in certain forms of gastric disturbances. Scoville states that charcoal is a good antidote for phenol poisoning. It acts by absorbing phenol and eliminating it through the intestines rather than through the kidneys. (*Bull. Pharm.,* 1913, p. 393.)

Dose, five to twenty grains (0.32 to 1.3 Gm.)

Off. Prep.—Trochisci Carbonis Ligni, *N.F.*

CARBON DISULPHIDUM. Br.

CARBON DISULPHIDE [Carbon Bisulphide]

(cär'bŏn dī-sŭl'phī-dŭm)

CS_2=76.14

"Carbon Disulphide, CS_2, may be obtained by combining carbon and sulphur at a high temperature, the product being subsequently condensed and purified." *Br.*

Carbonis Bisulphidum, *Br.,* 1898; Carbonii Bisulphidum; Carbon Bisulphide; Carbon Sulphide; Sulfure de Carbone, *Fr. Cod.;* Carboneum Sulfuratum, Alcohol Sulfuris, Schwefelkohlenstoff, Kohlensulfid, Schwefelalkohol, *G.;* Solfuro di carbonio, *It.;* Sulfuro de carbono, *Sp.*

This compound, corresponding to carbon dioxide (carbonic acid gas), CO_2, is prepared by the direct combination of carbon and sulphur at a moderate red heat. To effect this, charcoal is heated to redness in a vertical cylinder, while sulphur is admitted through a lateral tubulure near the bottom. As the sulphur melts and vaporizes, it combines with the carbon, and the carbon disulphide formed distils over through a series of condensing tubes, which, while they serve to collect the crude carbon disulphide, allow of the escape of the hydrogen sulphide formed at the same time. The crude product is then rectified, first over a solution of chlorinated lime to break up any hydrogen sulphide gas remaining, and then repeatedly either over mercury, mercuric chloride, anhydrous cupric sulphate, or over a pure fatty oil, which withdraws from it all free sulphur and malodorous sulphur compounds. The manufacture of carbon disulphide has assumed large proportions. In the works of Deiss at Pantin, near Marseilles, France, 5000 kilogrammes were turned out daily, and their annual production exceeds 1,200,000 kilogrammes.

The most decided improvement in the manufacture of carbon disulphide was made by E. R. Taylor of Penn Yan, New York, who introduced a patented electrothermal process which can be worked continuously. In large furnaces 41 feet high by 16 feet in diameter an alternating current is applied through carbon electrodes. The metallic sulphur passing over the electrodes is vaporized and rises through the glowing carbon, the carbon disulphide being taken off as vapor through a side connection near the top of the furnace. The impure carbon disulphide is purified by forcing lime water in a fine spray through the disulphide liquor until the water runs out of the tank colorless. The carbon disulphide is finally rectified by steam heat. It is used in the arts for the extraction of oils from different oil seeds, for the extraction of sulphur from some varieties of sulphur ores, for the cleansing of wool and recovering the fat, as a solvent for caoutchouc in the manufacture of india rubber goods, for the extraction of perfumes, and on an enormous scale in France as a remedy against the *phylloxera.* Von Lengyel describes a carbon sulphide having the composition C_3S_2. (*Proc. A. Ph. A.,* 1893, 1021.)

Properties.—Carbon disulphide is official in Part II of the U. S. P. IX and is described as follows: "Preserve in partially filled, well-stoppered bottles, or in tin cans, in a cool place, remote from flame or fire. A clear, colorless, highly refractive liquid, very volatile, having a strong, characteristic but not fetid odor, and a sharp, aromatic taste. Specific gravity between 1.256 and 1.257 at 25° C. (77° F.) Soluble in about 530 parts of water at 25° C.

(77° F.); very soluble in alcohol, ether, chloroform, or fixed or volatile oils. Carbon disulphide vaporizes rapidly at the ordinary temperature, is highly inflammable, boils between 46° and 49° C. (114.8°–120.2° F.), and when ignited, burns with a bluish-white flame, producing carbon dioxide and sulphur dioxide. It does not affect the color of blue litmus paper moistened with water (*sulphur dioxide*). Twenty mils when allowed to evaporate spontaneously in a glass dish and finally on a water bath leaves not more than 0.001 Gm. of residue (*dissolved sulphur*). No discoloration is produced in 10 mils of lead acetate T.S. after agitating with 25 mils of carbon disulphide, when viewed from above in a test tube of about 2 cm. in diameter (*hydrogen sulphide*)." *U. S.*

"A clear, colorless, highly refractive liquid. Odor characteristic but not fetid. Specific gravity 1.268 to 1.269. Highly inflammable, burning with a blue flame and giving off carbon dioxide and sulphur dioxide. Boiling point 46° to 47° C. (114.8°–116.6° F.). Vapor mixed with air is explosive in contact with flame. Evaporated spontaneously in a glass vessel, it leaves no residue (absence of free sulphur)." *Br.*

Uses.—Although carbon disulphide has been recommended by Taar (*B. Thier., W.*, 1907, p. 406) for the destruction of intestinal parasites in the horse, it has not found its way into human medicine as an internal remedy. It is, however, occasionally used externally as a counter-irritant and local anesthetic. Turnbull especially recommended it as an external application in *enlarged lymphatic glands*. He applied it by means of a bottle with a proper sized mouth, containing a fluidrachm of the disulphide, imbibed by a piece of sponge; the skin over the gland is first well moistened with water. He employed the vapor also with benefit in deafness, when dependent on want of nervous energy and a deficiency of wax. For this purpose, the bottle containing the disulphide is made with a neck to fit the meatus, and, being applied to the ear, is held there until considerable warmth is produced. The remedy has been used often with very good results, in a similar manner, in *facial* and other *neuralgias* and various local *pains*. It causes a good deal of smarting, but its disagreeable odor is the chief objection to it. In France the disulphide has been used in *diarrhea* in 3.5 per cent. solution, of which the dose is two tablespoonfuls (30 mils) four or five times a day.

Its most important use is as a solvent, especially for rubber. Carbon disulphide is an active poison and workmen exposed to the fumes of the disulphide are affected with headache, vertigo, and over-excitement of the nervous system, as evinced by voluble talking, incoherent singing, or immoderate laughter, or sometimes by weeping; and a continuance of the exposure is apt to finally cause a state of cachexia, characterized by general weakness, loss of sexual appetite, dullness of sight and hearing, and impairment of memory Later writers assert that these phenomena are hysterical, and that what the carbon disulphide does is to produce an hysterical neurosis. (See *Annales de Hygiène*, 1895, xxxiii.) The swallowing by a man of half an ounce of carbon disulphide was followed in half an hour by absolute unconsciousnes, very rapid, feeble pulse, slow and stertorous respiration, cold and clammy surface of body, and insensitive conjunctiva, with mobile pupils. Two hours later, death occurred. The blood was found fluid, but there were no marked lesions of irritation in the gastro-intestinal mucous membrane. (*L. L.*, July 17, 1886.) India rubber workers, by whom the disulphide is largely used, are said to suffer frequently from paralytic symptoms. (*L. L.*, Jan., 1886.)

CARDAMOMI SEMEN. U. S. (Br.)

CARDAMOM SEED Cardam. Sem. [Cardamomum U.S. VIII Cardamom]

(kär-da-mō'mī sē'mĕn)

"The dried seeds of *Elettaria Cardamomum* White et Maton (Fam. *Zingiberaceæ*), recently removed from the capsules." *U. S.* "Cardamom Seeds are the dried ripe seeds of Elettaria Cardamomum, *Maton*. The seeds should be kept in their pericarps and separated when required for use." *Br.*

Cardamomi Semina, *Br.;* Cardamomum Minus, Cardamomum Malabaricum; Malabar Cardamoms, Cardamoms; Cardamome du Malabar, *Fr. Cod.;* Petit Cardamome, *Fr.;* Fructus Cardamomi, *P. G.;* Malabar Kardamomen, Cardamomen, Kleine Kardamomen, *G.;* Cardamomo minore, *It.;* Cardamomo, Cardamomo menor, *Sp.;* Ebil, *Arab.;* Kakelah seghar, *Pers.;* Capalaga, *Malay;* Gujaratii elachi, *Hindost.*

The fruit of cardamom is official in most of the Pharmacopœias. The U. S. Pharmacopœia in its definition confines cardamom to the seeds. In this it follows the British Pharmacopœia which has always limited the drug to the seeds, but specifically states that the fruit should be kept intact and the seeds separated when required for use. This step was probably a wise one as there has always been some confusion by manufacturers as to whether the article designated as cardamom is a formula was restricted to the seeds or not. On the other hand the pericarp contains some oil and forms an excellent surface for the grinding of the seeds. Furthermore, the decorticated seeds are liable to adulteration with seed of wild cardamom and other foreign seeds which are not detected except upon careful examination.

The subject of cardamom has been involved in some confusion and uncertainty, both in its commercial and botanical relations. The name has been applied to the aromatic capsules of various Indian plants belonging to the family of *Zingiberaceæ*. Three varieties have long been designated by the several titles of the *lesser, middle, and larger—cardamomum minus, me-*

dium, and *majus;* but these terms have been used differently by different writers, so that their precise signification remains doubtful. To Pereira we are mainly indebted for the clearing up of this confusion. It is well known that the *lesser cardamom* of most writers is the variety recognized by the Pharmacopœias and generally kept in the shops. The other varieties, though circulating to some extent in European and Indian commerce, are little known in this country.

Ceylon Cardamom.—This has been denominated variously *cardamomum majus* and *cardamomum longum,* and is sometimes termed in English commerce *wild cardamom.* It is the *large cardamom* of Guibourt. In the East it is sometimes called *grains of Paradise;* but it is not the product known with us by that name. (See below.) It is derived from a plant cultivated in Candy, in the Island of Ceylon, and also growing wild in the forests of the interior, which was designated by Sir James Edward Smith *Elettaria major,* but is now generally acknowledged to be only a variety of the official plant. (*Elettaria Cardamomum* var. *β-Major* Smith.) It is affirmed that the annual product reaches nearly 750,000 pounds. The fruit is a lanceolate-oblong, acutely triangular capsule, somewhat curved, about 3.5 cm. long and 6 to 8 mm. broad, with flat and ribbed sides, tough and coriaceous, brownish or yellow ash-colored, having frequently at one end the long, cylindrical, three-lobed calyx, and at the other the fruit-stalk. It is three-locular, and contains angular, rugged, yellowish-red seeds, of a peculiar fragrant odor and spicy taste. Its effects are analogous to those of the official cardamom.

Round or *Siam Cardamom.*—This is probably the *Αμωμον* of Dioscorides and the *Amomi uva* of Pliny, and is believed to be the fruit of *Amomum cardamomum,* Willd., growing in Sumatra, Java, and other East India islands. The capsules are usually smaller than a cherry, roundish or somewhat ovate, with three convex sides, more or less striated longitudinally, yellowish or brownish-white, and sometimes reddish, with brown, angular, cuneiform, shrivelled seeds, which have a spicy camphorous flavor. They are sometimes, though rarely, met with connected in their native clusters, constituting the *amomum racemosum,* or *amome en grappe,* of the French. They are similar in medicinal properties to the official, but are seldom used except in the southern parts of Europe.

Java Cardamom.—The plant producing this variety is supposed to be the *amomum maximum* of Roxburgh, growing in Java and other Malay islands in the East. The capsules are oval, or oval-oblong, often somewhat ovate, from 1.5 to 3 cm. long, and from 8 to 15 mm. broad, usually flattened on one side and convex on the other, sometimes curved, three-valved, and occasionally imperfectly three-lobed, of a dirty grayish-brown color, and coarse fibrous appearance. When soaked in water, they exhibit as their distinguishing character from nine to thirteen ragged membranous wings along their whole length. The seeds have a feebly aromatic taste and odor. This variety of cardamom affords but a very small proportion of volatile oil, is altogether of inferior quality, and, when imported into London, is usually sent to the continent.

Madagascar Cardamom.—This is the *Cardamomum majus* of Geiger and some others, and is thought to be the fruit of *Amomum angustifolium,* of Sonnerat, growing in marshy grounds in Madagascar. The capsule is ovate, pointed, flattened on one side, striated, with a broad circular scar at the bottom, surrounded by an elevated, notched, corrugated margin. The seeds have an aromatic flavor similar to that of official cardamom.

Bengal or *Nepal Cardamom.*—The fruit of *Amomum subulatum,* Roxb., sometimes known by the name of winged Bengal cardamom. *Morung elachi,* or *Buro elachi,* is about 2.5 cm. in length, obscurely three-sided, ovoid or somewhat obconic, with nine narrow, jagged ridges or wings (best seen after soaking in water) upon its distal end, which terminates in a truncate bristly nipple. The pericarp is coarsely striated, of a deep brown, splitting into three valves, disclosing a three-lobed mass of seeds, 60 to 80 in number.

Nepal Cardamom i. produced by an Amomum of undetermined species, and resembles the Bengal cardamom, except in having a long tubular calyx on its summit, and in being usually attached to a stalk.

Grains of Paradise. Grana Paradisi.—Under this name and that of *Guinea grains,* and *Melegueta* or *Mallaguetta pepper,* are found in commerce small seeds of a round or ovate form, often angular, and somewhat cuneiform, minutely rough, brown externally, white within, of a feebly aromatic odor when rubbed between the fingers, and of a strongly hot and peppery taste. Two kinds of them are known in the English market, one larger, plumper, and more warty, with a short conical projecting tuft of pale fibers on the umbilicus; the other smaller and smoother and without the fibrous tuft. The latter are the more common. It is probable that one of the varieties is produced by *Amomum Grana Paradisi* of Sir J. E. Smith, and the other by Roscoe's *Amomum Melegueta.* (Pereira's *Mat. Med.,* 3d ed., p. 1134.) W. F. Daniell, who has published (*P. J.,* xiv 312 and 356) an elaborate paper on the Amoma of Western Africa, states that the true Mallaguetta pepper is obtained exclusively from varieties of the same species to which belong the *Amomum Granum Paradisi* of Afzelius and the *A. Melegueta* of Roscoe; while the *A. Grana Paradisi* of Sir J. E. Smith is a different plant, and yields a different product. These grains are imported from Guinea, and other parts of the western coast of Africa. Similar grains are taken to England from Demerara, where they are ob-

tained from a plant cultivated by the negroes, supposed to have been brought from Africa, and believed by Pereira to be the *Amomum Melegueto* of Roscoe. (*P. J.*, vi, 412.) Their effects on the system are analogous to those of pepper; but they are seldom used except in veterinary practice, and to give artificial strength to spirits, wine, beer, and vinegar. Pereira points out seven distinct Scitamineous fruits to which the name of grains of Paradise has been applied by different authors. J. C. Thresh made a proximate analysis of the seeds, and found volatile oil, resin, tannin, starch, albuminoids, and an active principle in the form of a straw-colored viscid, odorless fluid, pungent, but not so hot as capsaicin. (*P. J.*, 1884, p. 297.) Fred'k Schwartz found in the seeds a reddish-brown acrid resin, and an oil having a burning aromatic taste, upon which the virtues probably depend. (*A. J. P.*, 1886, 118; consult also Hanausek's researches on grains of Paradise in *Chem. Ztg.*, 1893, 1765.)

Bastard Cardamom, the seeds of *Amomum Xanthioides* Wall., resembles true cardamom in appearance, but is of a dirty green color, and has a very biting camphor-like taste. B. Niederstadt gives the following as the results of analysis of the true (hulled) seed and of the bastard cardamom:

	True.	Bastard.
Water	15.25	15.50
Ether soluble extract	5.10	4.04
Ash	6.55	7.50
Starch and sugar	28.84	24.00
Cellular tissue, nitrogenous matters and extractive	44.26	48.96

A cardamom from East Africa, with a flavor resembling that of official cardamom and of the Korarima cardamom, is said to have been seen in the London market, but apparently has not been identified.

The official cardamoms are produced solely in India, chiefly in Malabar, Mysore, and adjacent regions. Malabar cardamoms are rather smaller than Mysore cardamoms.

The cardamom plant has a tuberous horizontal rhizome, sending up from eight to twenty erect, simple, smooth, green and shining, perennial stems, which rise from six to twelve feet in height, and bear alternate elliptical-lanceolate sheathing leaves. The flower-stalk proceeds from the base of the stem, and lies upon the ground, with the flowers arranged in a panicle. The fruit is a three-celled capsule, containing many seeds; during drying it is said to lose three-fourths of its weight.

This valuable plant is a native of the mountains of Indo-China, where it springs up spontaneously in the forests after the removal of the undergrowth, and is very extensively cultivated by the natives. Recent reports indicate that the cultivation of cardamom is being discontinued in favor of cinchona and rubber plantations on both the Malabar Coast as well as in Ceylon. For a detailed account of culture, see *A. J. P.*, 1877, 605; also *P. J.*, 1888, and *Bull. des Sc. Pharmacol.*, Paris, 1906, pp. 114 and 584. Cardamoms have also been cultivated to some extent in tropical America. The plant begins to yield fruit at the end of the fourth year, and continues to bear for several years afterwards. The capsules when ripe are picked from the fruit-stems, dried over a gentle fire or by sun-heat, and separated, by rubbing with the hands, from the footstalks and adhering calyces. J. W. Mollison describes the method of washing and curing cardamoms employed in the Bombay Presidency, India. The washing and manipulation is performed by women, and water from special wells is employed. The cardamoms are first washed in earthenware vessels containing a mixture of the well water with pounded soap nut and a species of acacia, in the proportion of two pounds of the former to a quarter pound of the latter. About ten pounds of cardamoms are treated at one time. Two women stir them vigorously in the mixture for about one minute and then allow them to rest about an equal length of time, and again stir for another minute. A thick lather results. This completes the first washing, after which the cardamoms are baled out by hand into a basket where they are allowed to drain for a few seconds, and then subjected to a second washing similar to the first except that the mixture contains less of the soap nut preparation and an additional quantity of soap solution. They are then thrown upon a mat and sprinkled with water from the special well at intervals of a half hour, until the next morning, when they are spread upon the roof of a house and allowed to dry for four or five hours. After nipping off the short stalk, an operation performed with a large pair of shears, the cardamoms are sorted, only the most plump fruits being prepared for the foreign market. Besides bleaching by this process, cardamoms are also subjected to starching in India. The starched product has a whiter appearance than the bleached cardamoms. The starch is prepared by pounding together rice, wheat, country soap and buttermilk. The paste is diluted with water and sprinkled over the cardamoms as they are rubbed by hand. (*B. C. D.*, 1904, see also *Ph. Era*, 1904, 137.) Most of the cardamom is sent to Bombay, from whence it is shipped to London, about 250,000 pounds being marketed annually. Thus prepared, they are ovate-oblong, from 10 to 17 mm. long, from 6 to 8 mm. thick, three-sided with rounded angles, obtusely pointed at both ends, longitudinally wrinkled, and of a yellowish-white color. The seeds constitute about 74 parts per cent. by weight. According to Pereira, three varieties are distinguished in commerce: 1, the *shorts*, from 6 to 12 mm. long, from 4 to 6 mm. broad,

browner and more coarsely ribbed and more highly esteemed than the others; 2, the *long-longs,* from 14 to 25 mm. in length by 4 to 6 mm. in breadth, elongated, and somewhat acuminate; and 3, the *short-longs,* which are somewhat shorter and less pointed than the second variety. The odor of cardamom is fragrant, the taste warm, slightly pungent, and highly aromatic.

"Mostly agglutinated in groups of from 2 to 7, the individual seeds, oblong-ovoid in outline, 3- or irregularly 4-sided, convex on the dorsal surface, strongly longitudinally grooved on one side, from 3 to 4 mm. in length; externally reddish-gray-brown, coarsely tuberculated, and with more or less adhering portions of the membranous aril; in section showing a thin reddish-brown seed-coat, a large white perisperm and a central, greenish endosperm enclosing a small straight embryo; odor aromatic; taste aromatic, pungent. The powder is greenish-brown; consisting chiefly of coarse angular fragments of cells of the reserve layers and seed-coat; cells of endosperm and perisperm filled with compound starch grains, the individual grains from 0.001 to 0.004 mm. in diameter; fragments of seed with dark brown stone cells, which are polygonal in surface view and about 0.02 mm. in diameter; in mounts made with hydrated chloral T.S. single prisms or crystals in rosette aggregates may separate in the cells of the endosperm and perisperm; fragments of spiral tracheæ with accompanying slightly lignified bast-fibers relatively few. Cardamom Seed yields not more than 8 per cent. of ash." *U.S.*

"Fruits from one to two centimetres long, ovoid or oblong, bluntly triangular in section, shortly beaked at the apex, pale buff in color, plump and nearly smooth or with slight longitudinal striations. Seeds dark reddish-brown, about three millimetres in length and the same in breadth and thickness, irregularly angular, transversely wrinkled, and enclosed in a thin, colorless, membranous aril. The powdered Seeds exhibit abundant, minute, angular starch grains, often compacted into masses; but no spiral vessels, sclerenchymatous fibres, or strongly elongated sclerenchymatous cells (absence of pericarps). Aromatic odor; taste agreeably warm and aromatic. Ash not more than 6 per cent." *Br.*

Cardamom yields its virtues to water and alcohol, but more readily to the latter. The seeds contain 4.6 per cent. of volatile oil, 10.4 of fixed oil, 2.5 of a salt of potassium mixed with a coloring principle, 3.0 of starch, 1.8 of nitrogenous mucilage, 0.4 of yellow coloring matter, and 77.3 of ligneous fiber. (Trommsdorff.) The volatile oil is colorless, of an agreeable and very penetrating odor, and of a strong aromatic, burning, camphorous, and bitterish taste. It is dextrogyrate, and consists essentially of a terpene, $C_{10}H_{16}$, with small quantities of formic and acetic acids. From old specimens of oil Dumas and Peligot claim to have separated crystals of *terpene hydrate,* $C_{10}H_{20}O_2 + H_2O$, while Flückiger has obtained a crystalline deposit from Ceylon oil which he considers identical with common camphor. Weber (*Ann. Ch. Ph.,* ccxxxviii, 98) found a small amount of a crystalline non-volatile compound which fuses at 60° to 61° C. (140°–141.8° F.). Schimmel & Co. published in their semi-annual reports for April and October, 1897, some results of investigation of several varieties of cardamom oil. The terpenes of Ceylon oil they state to be *terpinene* and *dipentene;* both Ceylon and Bengal cardamom contain *cineol,* $C_{10}H_{18}O$; Malabar cardamom yields *terpineol* as well as cineol, while Siam cardamom yields a crystalline sediment composed of borneol and camphor in approximately equal proportions. The sp. gr. of the oil is between 0.92 and 0.94. It cannot be kept long without undergoing change, and finally, even though excluded from the air, loses its peculiar odor and taste. If ether be made to percolate through the powdered seeds, and the liquor obtained be deprived of the ether, a light greenish-brown fluid remains, consisting almost exclusively of the volatile and fixed oils. It has the odor of cardamom, and keeps better than the oil obtained by distillation. (*A. J. P.,* xxi, 116.) The oil of cardamom of commerce is often factitious, being composed of several cheap volatile oils, oils of cajuput, nutmeg, and others being used. Schimmel & Co. announced in 1901 that they no longer distilled the oil from the fruit of *Elettaria cardamomum,* but from the seeds of another species; this oil makes a clear solution with three parts by volume of 70 per cent. alcohol. (*Schim. Rep.,* 1901, 14.) See *Oil of Cardamom,* N. F. IV., Part II. The seeds should be powdered only when wanted for use, as they retain their aromatic properties best while in the capsule.

Cardamoms are sometimes adulterated; G. W. Kennedy reported nearly 4 per cent. of orange seeds and unroasted grains of coffee admixed with cardamom. Solstein (1892) found that pure powdered cardamom yields 8.36 per cent. of ash; three commercial samples of powdered cardamom that he examined contained sodium carbonate.

Uses.—Cardamom is a grateful aromatic, not strongly heating or stimulating, and useful chiefly as an adjuvant. Throughout the East Indies it is largely consumed as a condiment. It was known to the ancients, and derived its name from the Greek language. In this country it is employed chiefly as an ingredient in compound preparations.

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Fluidextractum Aromaticum (from Aromatic Powder), *U. S.;* Pulvis Aromaticus, *U. S.* (*Br.*); Pulvis Cretæ Aromaticus, *Br., N. F.;* Tinctura Cardamomi, *U. S.;* Tinctura Cardamomi Composita, *U. S., Br.;* Tinctura Aromatica, *N. F.*

CARUM. U. S. (Br.)

CARAWAY [Carawayseed, Caraway Seed]

(cā'rŭm)

"The dried fruit of *Carum Carvi* Linné (Fam. *Umbelliferæ*). Without the presence or admixture of more than 3 per cent. of other fruits, seeds or foreign matter. Preserve Caraway in tightly-closed containers, adding a few drops of chloroform or carbon tetrachloride, from time to time, to prevent attack by insects." *U. S.* "Caraway Fruit is the dried ripe fruit of Carum Carvi, *Linn.*" *Br.*

Carui Fructus, *Br.*; Caraway Fruit; Carvies, Cumin des Prés, Carvi, *Fr. Cod.*; Fructus Carvi, *P. G.*; Gemeiner Kümmel, Kümmel, Garbe, *G.*

The caraway plant is biennial and umbelliferous, with a spindle-shaped, fleshy, whitish root, and an erect stem, about two feet in height, branching above, and furnished with doubly pinnate, deeply incised leaves, the segments of which are linear and pointed. The flowers are small and white, and in erect terminal umbels, with an involucre, consisting sometimes of three or four bracts, sometimes of one only, and are destitute of partial involucre.

It is a native of Europe, growing wild in meadows and pastures, and cultivated in many places. It has been introduced in many places in this country, especially in the North. The flowers appear in May and June, and the seeds, which are not perfected until the second year, ripen in August. The root, when improved by culture, resembles the parsnip, and is used as food in Northern Europe. The fruits are the part used in medicine. They are collected by cutting down the plant, and threshing it on a cloth. Our markets are supplied partly from Europe, partly from our own gardens. The American fruits are usually rather smaller than the German. Under the name of *Ajowan,* the fruits of the *Carum Ajowan,* Bentham & Hooker (*Ammi copticum* L.) are largely used in India. (See *Ajowan,* Part II.) They contain about 4 per cent. of a volatile oil, which has the odor of the oil of thyme, and contains thymol; it may be used as an aromatic carminative. (See *B. M. J.,* June 6, 1885.) For a description of the *oil of ajowan,* see p. 745.

Caraway is officially described as follows: "Mericarps usually separated, crescent-shaped, 3 to 7 mm. in length, 1.5 mm. in diameter; externally dark brown with 5 yellowish filiform ribs; in transverse section nearly equilaterally pentagonal, the commissural surface with two vittæ, the dorsal surface with a vitta between each of the primary ribs; oily endosperm large, enclosing a small embryo; odor and taste agreeably aromatic. Under the microscope, transverse sections of Caraway show an epidermal layer of slightly tangentially elongated cells with thick outer walls; a layer of several rows of tangentially elongated parenchyma cells, frequently more or less collapsed; a single, large, elliptical, brown vitta or oil-tube between each of the ribs and surrounded by small epithelial or secretion cells; in each of the ribs a single fibrovascular bundle surrounded by a layer of thick-walled sclerenchymatous fibers; inner epidermis of broadly elongated cells with very thin side walls, being very frequently broken and closely coherent with the more or less brownish collapsed cells of the seed-coat; commissural surface with 2 large vittæ and at the middle portion 2 large tranverse hollow spaces formed by the separation of the tissues of the seed-coat on one side and the pericarp on the other, otherwise, the cells resemble those on the dorsal surface; endosperm large, cells polygonal with thick walls and containing a fixed oil and aleurone grains, the latter not infrequently containing a small rosette aggregate or prism of calcium oxalate. The powder is yellowish-brown, mostly of irregular, angular fragments; cells of endosperm with aleurone grains each usually containing a rosette aggregate of calcium oxalate about 0.001 mm. in diameter; fragments with light-yellow vittæ, together with nearly isodiametric or polygonal, yellowish-brown, inner epidermal cells of pericarp; fragments with tracheæ and sclerenchymatous fibers, the latter 0.01 mm. in width, slightly lignified and with numerous oblique pores. Caraway yields not more than 8 per cent. of ash." *U. S.*

"Mericarps usually separate; each from about four to six millimetres long and about one millimetre broad; brown with paler primary ridges; slightly curved, tapering towards each end, and glabrous. In transverse section, six vittæ in each mericarp. Odor and taste aromatic. Ash not more than 9 per cent." *Br.*

They have an agreeable aromatic odor, and a sweetish, warm, spicy taste. These properties depend on an essential oil, which they afford largely by distillation. (See *Oleum Cari.*) The residue is insipid. They yield their virtues readily to alcohol and more slowly to water.

"Drawn caraway seeds," a term applied to such as have been recovered from the still residue after obtaining the volatile oil, are used to adulterate caraway; the exhausted "seeds" are much darker in color than are the genuine and are less odorous. (*P. J.,* 1896, 150.) While this is the principal form of adulteration, they may contain large amounts of stems, gravel, sand, dust, weed seeds and other impurities.

Uses.—Caraway is a pleasant stomachic and carminative, occasionally used in *flatulent colic,* and as an adjuvant or corrective of other medicines. The dose in substance is from fifteen to thirty grains (1–2 Gm.). An infusion may be prepared by adding two drachms of the seeds to a pint of boiling water. The volatile oil, however, is most employed. (See *Oleum Cari.*) Three and a half ounces of the oil of caraway caused violent vomiting and abdominal pain, with loss of consciousness, ending, however, in recovery. The urine contained both acetone and albumin. (*Cb. I. M.,* xxii, 1902.) In culinary operations the seeds are added to cakes, to

which they communicate an agreeable flavor, while they stimulate the digestive organs.

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Aqua Carui, *Br.*; Confectio Piperis, *Br.*; Pulvis Opii Compositus, *Br.*; Tinctura Cardamomi Composita, *U. S.*, *Br.*; Tinctura Sennæ Composita, *Br.*

CARYOPHYLLUS. U. S. (Br.)

CLOVE Caryoph. [Cloves]

(căr-ȳ-o-phȳl'lŭs)

"The dried flower-buds of *Eugenia aromatica* (Linné) O. Kuntze, *Jambosa Caryophyllus* (Sprengel) Niedenzu (Fam. *Myrtaceæ*), without the presence or admixture of more than 5 per cent. of the peduncles, stems or other foreign matter." *U. S.* "Cloves are the dried flower-buds of Eugenia caryophyllata, *Thunb.*" *Br.*

Caryophyllum, *Br.*; Caryophylli Aromatici; Girofle, *Fr. Cod.*; Géroflе, Clous Aromatiques, Clous de Girofle, *Fr.*; Caryophylli, *P. G.*; Gewürznelken, Nägelein, *G.*; Garofani, *It.*; Clavo de especia, *Sp.*; Cravo da India, *Portug.*; Kruidnagel, *Dutch*; Kerunfel, *Arab.*

Eugenia aromatica (L.), O. Kuntze, is a small tree inhabiting the Molucca Islands and Southern Philippines. It has a pyramidal form, is always green, and is adorned throughout the year with a succession of beautiful rosy flowers. The stem is of hard wood, and covered with a smooth, grayish bark. The leaves are opposite, petiolate, about four inches in length by two in breadth, obovate-oblong, acuminate at both ends, entire, sinuated, with many parallel veins on each side of the midrib. They have a firm consistence and a shining green color, and when bruised are highly fragrant. The flowers are disposed in terminal corymbose panicles, and exhale a strong, penetrating, and grateful odor.

The natural geographical range of the clove is extremely limited, being confined to the Molucca or, as they were one time called, Clove Islands. According to Flückiger, cloves were known in Western Europe as early as the sixth century, long before the discovery of the Moluccas by the Portuguese. After the conquest of the Molucca Islands by the Dutch, the monopolizing policy of that commercial people led them to extirpate the trees in nearly all the islands except Amboyna and Ternate, which were under their immediate inspection. Notwithstanding their jealous vigilance, a French governor of the Islands of France and Bourbon, named Poivre, succeeded, in the year 1770, in obtaining plants from the Moluccas and introducing them into the colonies under his control. Five years afterwards the clove-tree was introduced into Cayenne and the West Indies, in 1803 into Sumatra, and in 1818 into Zanzibar. At present the spice is cultivated both in the West and East Indies, in tropical Africa, and in Brazil. Approximately seven-eighths of the world's clove supply is grown in Zanzibar, the deliveries in 1911 totaled over 20,000,000 pounds. The amount imported in the United States is approximately 3,500,000 pounds annually.

The unexpanded flower buds are the part of the plant employed under the ordinary name of cloves. They are first gathered when the tree is about six years old. The fruit has similar aromatic properties, but much weaker. The buds are at first white, then become green, and then bright red, when they must be at once collected, which is done by hand picking, or by beating the trees with bamboos and catching the falling buds. In the Moluccas they are said to be sometimes immersed in boiling water and afterwards exposed to smoke and artificial heat before being spread out in the sun. In Zanzibar, Cayenne, and the West Indies they are dried simply by solar heat. The stems of the flowers also enter commerce. They possess the odor and taste of the cloves, but they are worth only about one-fifth the price of the cloves, as they are deficient in volatile oil. They are largely used as an adulterant in ground cloves, and are used in the manufacture of oil of cloves. In France they are generally known by the name of *griffes de girofle*.

Although it is stated that as early as 266 B.C., during the reign of the Han dynasty, the Chinese court officers were accustomed to hold cloves in their mouths before addressing the sovereign, that their breath might have an agreeable odor, the spice seems to have been first introduced into Europe in the fourth century, and became a great source of wealth to the enterprising merchants of mediæval Venice, who obtained it from the Arabians. After the discovery of the southern passage to India, the trade in this spice passed into the hands of the Portuguese, but was subsequently wrested from them by the Dutch, by whom it was long monopolized. The United States derive much of their supply from the West Indies and Guiana; but the great sources of cloves have been recently the islands of Zanzibar and Pemba, on the east coast of Africa. In 1872 the clove orchards in Zanzibar were nearly nestroyed by a hurricane, but they have been replanted. (For detailed information as to method of growth, see *P. J.*, June, 1890.) In commerce the varieties of cloves are known by the names of the localities of their growth, and so closely resemble one another as to be distinguished only by experts. The *Penang cloves* have been especially esteemed. The *Bencoolen cloves* from Sumatra are by many druggists deemed equal to them. The Amboyna and Molucca cloves are stated to be thicker, darker, heavier, more oily, and more highly aromatic than those cultivated elsewhere. Formerly cloves were frequently adulterated, but the comparatively low price of later times has discouraged this fraud. (See Kraemer, *Proc. A. Ph. A.*, 1894, 159.)

Properties.—Cloves resemble in shape a nail with a round head with four spreading points beneath it.

"From 10 to 17.5 mm. in length, of a dark

brown or brownish-black color, consisting of a stem-like, solid, inferior ovary, obscurely four-angled or somewhat compresed, terminated by four calyx teeth, and surmounted by a nearly globular head, consisting of four petals, which enclose numerous curved stamens and one style; odor strongly aromatic; taste pungent and aromatic, followed by slight numbness. When Clove is pressed strongly between the thumbnail and finger the volatile oil becomes visible. Stems either separate or attached to the flower-buds; sub-cylindrical or four-angled, attaining a length of 25 mm. and a diameter of 4 mm., either simple, branching or distinctly jointed, and less aromatic than the flower-buds. The powder varies from dark brown to reddish-brown and consists chiefly of cellular fragments showing the large oil reservoirs, spiral tracheæ and a few somewhat thick-walled, slightly-lignified, spindle-shaped bast-fibers; calcium oxalate in rosette aggregates, from 0.01 to 0.015 mm. in diameter; pollen grains numerous, tetrahedral, somewhat ellipsoidal, from 0.015 to 0.02 mm. in diameter. The presence of stems in the powder is shown by stone cells of irregular, polygonal shape, 0.07 mm. in diameter, with thick porous walls and large lumina, the latter frequently filled with a yellowish-brown amorphous substance. Clove yields not less than 10 per cent. of volatile extractive soluble in ether (see Part III, Test No. 12). Clove yields not more than 8 per cent. of ash. The amount of ash, insoluble in hydrochloric acid, does not exceed 0.5 per cent. of the weight of clove taken." *U. S.*

"About fifteen millimetres long, each consisting of a dark-brown, wrinkled, subcylindrical, somewhat angular calyx tube which tapers below and is surmounted by four thick, rigid, patent teeth, between which are four paler, imbricated petals enclosing numerous stamens and a single style. Odor strong, fragrant and spicy; taste very pungent and aromatic. Cloves emit oil when indented with the finger-nail. Ash not more than 7 per cent." *Br.*

Their color is externally deep brown, internally reddish; their odor strong and fragrant; their taste hot, pungent, aromatic, and very permanent. The best cloves exude a small quantity of oil on being pressed or scraped with the nail. When light, soft, wrinkled, pale, and of feeble taste and odor, they are inferior. Those from which the essential oil has been distilled are sometimes fraudulently mixed with the genuine. For monograph on the microscopical structure of cloves, clove stems and clove fruit see Winton and Moeller, "*The Microscopy of Vegetable Foods.*" Powdered cloves sometime contain an excess of clove stems, and may be adulterated with allspice, wheat middlings and powdered peas or beans. Occasionally clove stems alone are ground and sold as cloves. It is claimed that an enormous quantity of exhausted cloves are dishonestly marketed. The amount of volatile ether extract is the best criterion of the value of cloves.

Trommsdorf obtained from 1000 parts of cloves 180 of volatile oil, 170 of a peculiar tannin, 130 of gum, 60 of resin, 280 of vegetable fiber, and 180 of water. Wm. L. Peabody (1895) found the percentage of tannin in cloves to range from 10 to 13 per cent., and that it has the same chemical composition as gallotannic acid. Lodibert afterwards discovered a fixed oil, aromatic and of a green color, and a white resinous substance which crystallizes in fasciculi composed of very fine diverging silky needles, without taste or odor, soluble in ether and boiling alcohol, and exhibiting neither alkaline nor acid reaction. This substance, called by Bonastre *caryophyllin*, was found in the cloves of the Moluccas, of Bourbon, and of Barbados, but not in those of Cayenne, from which, however, it has since been procured. To obtain it, the ethereal extract of cloves is treated with water, and the white substance thrown down is separated by filtration, and treated repeatedly with ammonia to deprive it of impurities. The most recent determination of its formula by Mylius (*Ber. d Chem. Ges.*, 1873, p. 1053) makes it $C_{20}H_{32}O_2$. Theod. Martius obtains it cheaply by exposing cloves, previously deprived as far as possible of oil by distillation with water, to distillation at a higher temperature, redistilling the brown liquid obtained until the distillate nearly ceases to have the taste or odor of cloves, and then purifying the residue by washing with water, and treating it with boiling alcohol and animal charcoal repeatedly until the caryophyllin, which is deposited by the alcohol on cooling, is perfectly white. (See *A. J. P.*, xxxii, 65.) Dumas has discovered another crystalline principle, which forms in the water distilled from cloves, and is gradually deposited. Like caryophyllin, it is soluble in alcohol and ether, but differs from that substance in becoming red when touched with nitric acid. Bonastre proposed for it the name of *eugenin*. (*J. P. C.*, xx, 565.) It has the formula $C_{10}H_{12}O_2$, and is isomeric with eugenol or eugenic acid, a constituent of oil of cloves. Water extracts the odor of cloves with comparatively little of their taste. All their sensible properties are imparted to alcohol; and the tincture when evaporated leaves an excessively fiery extract, which becomes insipid if deprived of the oil by distillation with water, while the oil which comes over is mild. Hence it has been inferred that the pungency of this aromatic depends on a union of the essential oil with the resin. *Caryophyllic acid*, $C_{20}H_{32}O_3$, is obtained by gradually adding caryophyllin to fuming nitric acid, kept cool by immersing the vessel in water until crystals begin to separate; these are purified by dissolving them in ammonia, precipitating with hydrochloric acid, and redissolving in alcohol and crystallizing. For an account of the oil, see *Oleum Caryophylli*. The infusion and oil of cloves are reddened by nitric acid, and rendered blue by tincture of ferric

chloride, facts of some interest, as morphine gives the same reactions.

Uses.—Cloves are among the most stimulant of the aromatics, but, like others of this class, act less upon the system at large than on the part to which they are immediately applied. They are sometimes administered in substance or infusion to relieve *nausea* and *vomiting*, correct *flatulence*, and excite *languid digestion;* but their chief use is to assist or modify the action of other medicines. They enter into several official preparations.

The French Codex directs a *tincture of cloves* to be prepared by digesting for ten days, and afterwards filtering, a mixture of three ounces of powdered cloves and sixteen of 80 per cent. alcohol.

Dose, in substance, from five to ten grains (0.32 to 0.65 Gm.).

Off. Prep.—Infusum Aurantii Compositum, *Br.;* Infusum Caryophylli, *Br.;* Pulvis Cretæ Aromaticus, *Br., N. F.;* Tinctura Lavandulæ Composita, *U. S.;* Cordiale Rubi Fructus, *N. F.;* Elixir Rubi Compositum, *N. F.;* Pulvis Aromaticus Rubifaciens, *N. F.;* Pulvis Cretæ et Opii Aromaticus (from Aromatic Chalk Powder), *N. F.;* Pulvis Myricæ Compositus, *N. F.;* Tinctura Aromatica, *N. F.*

CASCARA SAGRADA. U. S., Br.

CASCARA SAGRADA. Casc. Sagr. [Rhamnus Purshiana U.S. VIII]

(kăs-kă'ra sa-grä'da)

"The dried bark of the trunk and branches of *Rhamnus Purshiana* De Candolle (Fam. *Rhamnaceæ*)." *U. S.* "Cascara Sagrada is the dried bark of Rhamnus Purshianus, *DC.*, collected at least one year before being used." *Br.*

Rhamni Purshiani Cortex, *Fr. Cod.;* Sacred Bark; Chittem Wood Bark, Dogwood bark, Coffee-berry bark, Pigeonberry bark, Bear-berry bark, Bitter bark and Yellow bark; Cascara Sagrada, *Sp.*

A number of species of Rhamnus have been described as growing in California, but according to the best authority there are only four species,—*R. alnifolia,* L'Her., *R. crocea,* Nutt., *R. Purshiana,* DC., and *R. californica,* Esch. Of these species, *R. alnifolia* is too rare in the Cascara district to be important; while the spinescent twigs, the very thick oval or roundish leaves, and the small roundish red fruit of *R. crocea* make it so distinct that it cannot be confounded with the Cascara, whose bark, moreover, it does not resemble. On the other hand, *R. californica* appears to be very commonly confounded with the official species by collectors, and to have yielded some of the cascara sagrada bark of commerce. *R. californica* is rare in Northern California, but abundant in the countries lying south and southeasterly, while *R. Purshiana* is abundant in Northern California, but scarce in the south, so that any bark collected in Northern California is probably genuine. *R. californica* is chiefly distinguished from the official species by its leaves being thin, and, when not smooth, having a short close pubescence, and the primary veins of the under surface not nearly so numerous, straight, or fine as those of *R. Purshiana.* Rusby thinks that its leaves are especially distinguished by the channel of the midrib of *R. californica* being altogether absent, or shallow, or inconspicuous. Nevertheless the species so run into one another that competent botanists believe them identical.

The *Rhamnus Purshiana* is a small tree, attaining a height of twenty feet. Its leaves are rather thin, elliptic, for the most part briefly acutely pointed, finely serrated, at the base obtuse, somewhat pubescent beneath, from two to seven inches long and from one to three wide. The rather large flowers are in somewhat umbellate cymes; the sepals five; the minute cucullate petals bifid at the apex. The fruit is black, broadly obovoid, four lines long, three-lobed, and three-seeded. The seeds are convex on the back, with a lateral raphe. It is found in California, extending northward to the British territories. For details of manner of collecting the bark see an elaborate and illustrated article by Johnson and Hindman, *A. J. P.*, 1914, p. 387. The amount of Cascara that is collected annually varies between 3,000,000 and 4,000,000 pounds. Because of the rapid destruction of natural sources of the bark in the Western United States, experiments have been conducted by the Bureau of Plant Industry, U. S. Department of Agriculture, Washington, D. C., to cultivate it.

The *Rhamnus californica,* or *Californian buckthorn* or *California coffee-tree,* yields a bark which is of a dark brown color externally and bright yellow internally, having an intensely bitter taste, with a persistent nauseous aftertaste, and very little odor. It is said to be much more distinctly purgative than that of *R. crocea.*

It does not seem possible to distinguish with certainty between the barks of the two species by their macroscopic appearance. The bark of *R. Purshiana* is usually more red than is that of *R. californica,* but it may be of a distinctly gray color. The microscopic structure of the two barks is, however, different. The medullary rays in *R. Purshiana* are numerous, thin, for a long distance nearly parallel and straight (according to L. E. Sayre, they converge at their outer ends), run nearly three-quarters of the distance through the bark, and are commonly composed of two rows of cells. In *R. californica* the medullary rays are much broader, much shorter, and are composed usually of three or more rows of cells; further, they are crooked and not parallel throughout their course. Again, the zone of resin spaces is much broader in *R. californica,* and the spaces themselves much larger and more numerous than in the official species. For further details and elaborations, see papers by H. H. Rusby, *Proc. A. Ph. A.*, 1890, and by Gathercoal, *J. A. Ph. A.*, 1915, p. 15. According to L. E.

Sayre (*A. J. P.*, March, 1897), the powder of the barks can be distinguished by paying attention to the fact that *R. Frangula* contains no stone cells, while in *R. californica* and *R. Purshiana* such cells are abundant, occurring in large, irregular groups below the cork and usually outside the region of the bast: *R. Purshiana* may also be distinguished from *R. californica* by color tests. After several days' maceration in dilute alcohol the powder of *R. Purshiana* appears of an orange-yellow color, *R. californica* of a purplish color; or if 0.2 Gm. of the powdered bark be placed in a small test tube, and there be added 2 mils of potassium hydroxide test solution, *R. californica* will give a blood-red and *R. Purshiana* an orange-red color.

The bark of the *Rhamnus crocea*, the so-called *California mountain holly*, occurs in slightly curved pieces, externally of a dark brown color, internally of a characteristic red delicately streaked with numerous white veins. The odor is somewhat aromatic, the taste warming and not unpleasantly bitter. It is affirmed to be a tonic and mild laxative.

Properties.—Cascara sagrada occurs in commerce in the form of small broken pieces, often more or less flattened out into a somewhat compressed mass, and also as separated quills of varying length and size. The bark is "Usually in flattened or transversely curved pieces, occasionally in quills; bark from 1 to 5 mm. in thickness; outer surface dark brown or brownish-red, longitudinally ridged, often nearly covered with grayish or whitish lichens, bearing small blackish apothecia, sometimes with numerout lenticels, and occasionally with mosses; inner surface light yellow, light brown, or reddish-brown, longitudinally striate, turning red when moistened with solutions of the alkalies; fracture short, with projections of bast-fibers in the inner bark; in cross section inner bark shows diagonal or curved medullary rays, forming converging groups, the outer bark showing yellowish groups of stone cells which are especially apparent on moistening the freshly cut surface with phloroglucinol T.S. and hydrochloric acid; odor distinct; taste disagreeable, bitter, and slightly acrid. Under the microscope, a transverse section of Cascara Sagrada shows an outer yellowish-brown or reddish-brown corky layer consisting of 10 to 15 or more rows of cells; stone cells in outer bark in tangentially elongated groups of 20 to 50 cells, the walls being very thick and finely lamellated; medullary rays 1 to 4 cells wide, 15 to 25 cells deep, the contents being colored red upon the addition of solutions of the alkalies to the sections; bast-fibers in tangentially elongated groups in the inner bark, the walls being thick and strongly lignified; crystal fibers around the bast-fibers with individual crystals from 0.008 to 0.015 mm. in length; parenchyma with spheroidal starch grains about 0.003 to 0.008 mm. in diameter, or with calcium oxalate either in rosette aggregates or prisms from 0.01 to 0.02 mm. in diameter. Add 0.1 Gm. of powdered Cascara Sagrada to 10 mils of hot water, shake the mixture occasionally until cold, filter it and add sufficient water to make 10 mils; on the addition of 10 mils of ammonia water to this liquid, it is colored an orange-yellow. Macerate 0.1 Gm. of powdered Cascara Sagrada with 10 drops of alcohol, boil the mixture with 10 mils of water, when cold filter it and shake the filtrate with 10 mils of ether; a yellow ethereal solution separates. Shake 3 mils of this ethereal solution with 3 mils of ammonia water; the separated ammoniacal solution still possesses, on diluting with 20 mils of water, a distinct, yellowish-red color. The powder is light brown to olive brown, showing characteristic elongated groups of bast-fibers associated with crystal fibers, the crystals in the latter being in the form of monoclinic prisms from 0.008 to 0.015 mm. in length; stone cells in large groups, the cells having thick and finely porous walls; fragments of parenchyma and medullary ray cells colored red upon the addition of solutions of the alkalies; starch grains either free or in parenchyma cells, the individual grains being somewhat spheroidal, from 0.003 to 0.008 mm. in diameter; calcium oxalate in monoclinic prisms or rosette aggregates from 0.01 to 0.02 mm. in diameter; occasional fragments of reddish-brown cork." *U. S.*

"In quilled, channelled, or nearly flat pieces from one to two millimetres thick, but varying in length and width. Cork nearly smooth, dark purplish-brown, marked with transversely elongated lenticels, but usually more or less covered with patches of silvery-grey lichen. Inner surface reddish-brown, with faint transverse corrugations and longitudinal striations. Fracture short, but near the inner surface somewhat fibrous. In transverse section, scattered groups of sclerenchymatous cells in both cortex and bast; the parenchymatous cells contain a yellow substance which is colored violet by *solution of sodium hydroxide*. Odor characteristic but not powerful; taste nauseous, bitter and persistent." *Br.*

For articles illustrating the pharmacognosy of Cascara bark see Kraemer, *A. J. P.*, 1912, p. 385; Miller, *J. A. Ph. A.*, 1912, p. 1207; and Farwell, *J. A. Ph. A.*, 1914, p. 649. According to the analysis of A. B. Prescott (*N. P.*, Feb., 1879), it contains a very bitter brown resin (which is colored a vivid purple-red by potassium hydroxide); a red resin; a light yellow resin; tannic, malic, and oxalic acids; a neutral crystallizable substance; and a volatile oil. H. F. Meier and J. Le Roy Webber have pointed out in addition the presence of a ferment, glucose, and ammonia. According to these investigators, to the action of the ferment are attributed the unpleasant results attending the administration of "fresh bark"; "seasoned bark" —*i.e.*, such as has been kept a year or two— owes its valuable properties as a laxative, *free from griping*, to the fact that the ferment has

exhausted itself; the laxative properties, they state, reside in the resins, and the tonic effects are due to the crystalline principle. (*A. J. P.*, 1888, 91). Schwabe (*A. Pharm.*, ccxxvi, 569) found *emodin*, or trioxymethylanthraquinone, which he believes is the active principle. Dohme and Engelhardt (*Proc. A. Ph. A.*, 1897, 193) have shown the analogy of cascara sagrada with *Rhamnus Frangula* by obtaining a glucoside to which they give the name of *purshianin*. This decomposes, yielding emodin and a dextro-rotatory non-fermentable sugar, while the frangulin of buckthorn yields emodin and rhamnose as the sugar. Purshianin forms brown-red needles, melting at 237° C. (458.6° F.). Dohme and Engelhardt failed to obtain in a pure form (*Proc. A. Ph. A.*, 1898, 340) the bitter principle of cascara sagrada. Le Prince (*C. R. A. S.*, 1892, 286) claimed to have obtained the active principle of cascara bark in a crystalline form, which he named *cascarine;* his results are doubted by Jowett who believes that cascarine and purshianin are impure forms of emodin. Jowett (*Proc. A. Ph. A.*, 1904, 288) in an exhaustive paper concludes that the active principle of cascara is contained in that portion of an alcoholic extract which is soluble in water and precipitable by lead subacetate and in that portion of the regenerated lead subacetate precipitate which is soluble in ethyl acetate. Pietsch states that a glucoside from the bark of cascara sagrada which has been named *peristaltin* has the composition $C_{14}H_{18}O_8$. (*Th. M.*, 1910, No. 1, p. 35.)

Uses.—Cascara sagrada belongs to the group of vegetable cathartics whose activity depends upon the presence of one or more oxides of methylanthraquinone. This group includes aloes, cascara, rhubarb, and senna. In cascara the active principle appears to be emodin, which is trioxymethylanthraquinone, and which appears also to be the purgative principle of aloes. The action of this principle is chiefly to excite peristalsis in the colon, although after large doses there is probably also some effect upon the upper bowel. As the action is chiefly upon the lower intestine it is not to be recommended as a laxative where it is desired to clean out the bowel, but in the treatment of *chronic constipation* it acts very favorably. It often appears to restore tone to the relaxed bowel and in this way produce a permanent beneficial effect. The bark itself is rarely used, either the extract or fluidextract being eligible preparations.

The addition of belladonna to overcome any tendency to gripe is an advantage. Ordinarily a single dose is given at bedtime but in some cases better results are obtained by exhibiting smaller doses after meals.

Dose, ten to thirty grains (0.6–2.0 Gm.).

Off. Prep.—Extractum Cascaræ Sagradæ, *U. S.* (*Br.*); Fluidextractum Cascaræ Sagradæ, *U. S.* (*Br.*); Fluidextractum Cascaræ Sagradæ Aromaticum, *U. S.;* Syrupus Cascaræ Aromaticus, *Br.;* Elixir Cascaræ Sagradæ (from Aromatic Fluidextract), *N. F.;* Elixir Cascaræ Sagradæ Compositum (from Aromatic Fluidextract), *N. F.;* Fluidglyceratum Cascaræ Sagradæ, *N. F.;* Fluidglyceratum Cascaræ Sagradæ Aromaticum, *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ Compositæ (from Extract), *N. F.;* Syrupus Ficorum Compositus (from Aromatic Fluidglycerate), *N. F.*

CASCARILLA. Br.

CASCARILLA

(căs-cą-rĭl'lą)

"Cascarilla is the dried bark of Croton Eluteria, *J. J. Benn.*" *Br.* "The dried bark of *Croton Eluteria* (Linné) Bennett (Fam. *Euphorbiaceæ*), without the presence of more than 5 per cent. of adhering wood." *N. F.*

Cascarillæ Cortex, *Br.* (1885), Cascarilla Bark, Sweet Bark, Sweetwood Bark; Cascarille officinale, *Fr. Cod.;* Cortex Eluteriæ, Cortex Thuris; Chacrille, Ecorce éleuthérienne Cascarille, *Fr.;* Cortex Cascarillæ, *P. G.;* Cascarillrinde; Cascarilla, Kaskarillrinde, *G.;* Cascarilla, Cascariglia, *It.*, Chacarilla, Quina aromatica, *Sp.*

Croton Eluteria is a shrub or a small tree with a stem from four to eight inches in diameter. The stem is straight, and marked at intervals with white or grayish stains. The leaves are petiolate, often somewhat cordate at the base, obtusely acuminate, pale or grayish-green above, and densely covered beneath with shining silvery scales, appearing white at a distance. They are smaller and narrower in the plants of arborescent growth. The flowers, which have a delicious odor, are monœcious, small, white, petiolate, and closely set in simple terminal or axillary spikes. The shrub is a native of the Bahamas, scarce at present in the island of New Providence, but still abundant in Andros, Long, and Eleutheria islands, from the latter of which is derived its botanical title. Daniell calls the plant *sweetwood*. The name of *sea-side balsam* belongs to another species, *C. balsamiferum* of Linnæus, which grows in the Bahamas and other West India islands, and owes its name to the exudation of a balsamic juice from its young branches when wounded.

Under the name of "cascarilla," also "*Quina morada*," the bark of the *Pogonopus febrifugus* is said to be used in the Argentine Republic as a substitute for cinchona bark. There has been separated from it a blue fluorescent substance, *moradin*, and an alkaloid, *moradeine*. (*P. J.*, xx, 854.)

Copalchi bark has been mistaken not only for cascarilla, but also for a variety of cinchona. Portions of it, having been taken to Europe, attracted the attention both of pharmacologists and physicians. Two kinds were noticed: one, in small slender quills, of an ash color, bearing some resemblance to a variety of pale cinchona, but having the flavor of cascarilla, and burning with a similar odor; the other in larger quills, with a thick cork-like epidermis, very bitter, and yielding an aromatic odor when burnt. The former is the product of *Croton Pseudochina*,

Schlechtendal (*C. niveus* Jacquin); the latter is of unknown origin, but conjecturally referred to *C. suberosus*. J. E. Howard states that the quilled copalchi bark contains a bitter alkaloid, soluble in ether, and precipitable as a white hydroxide from its acid solution. (*P. J.*, xiv, 319.) Copalchi bark is an aromatic tonic, employed in Mexico in intermittents, and capable of useful application in all cases requiring a mild aromatic bitter. Stark has employed it advantageously in feeble states of digestion with irritable bowels, and found it in one or two cases, to exhibit antiperiodic properties. It may be given in infusion, made with half an ounce of the bark to a pint of water, in the dose of one or two fluidounces three times a day. (*Ed. Med. and Surg. Journ.*, April, 1849, p. 410; see also *P. J.*, 1886, p. 917.)

Croton Cascarilla Bennett, known in the West Indies as *wild rosemary*, was at one time said to furnish the cascarilla of commerce. The bark is also substituted by the barks of *Croton glabellus* L. and *C. lucidus* L. of the Bahamas and which were formerly designated as the "mother plants" of Cascarilla. They are not aromatic but astringent and slightly bitter. They are also distinguished by the presence of stone cells which are wanting in true Cascarilla. (See *U. S. D.*, 19th ed.)

Cascarilla is brought to this market from the West Indies, and chiefly, we have been informed, from the Bahamas. It comes in bags or casks. We have observed it in commerce in two forms, so distinct as to merit the titles of varieties. In one, the bark is in rolled pieces of every size, from three or four inches in length and half an inch in diameter to the smallest fragments, covered externally with a dull whitish or grayish-white epidermis, which in many portions is partially, sometimes wholly removed, leaving a dark brown surface, while the inner surface has a chocolate color, and the fracture is a reddish-brown. The small pieces are sometimes curled, but have a distinct abrupt edge as if broken from the branches. The second variety consists entirely of very small pieces, not more than an inch or two in length, very thin, without the white cork, not regularly quilled, but curved more or less in the direction of their length, often having a small portion of woody fiber attached to their inner surface, and appearing precisely as if shaved by a knife from the stem or branches. Whether these two varieties are derived from distinct species, or differ only because of the mode of collection, it is difficult to determine. A. W. Southall describes a bark (believed to belong to the genus *Croton*, and obtained from Colombia) in *P. J.*, 1894, 574.

"In quills usually from three to ten centimetres in length and from four to twelve millimetres in diameter, or in small curved pieces. Cork greyish-white, easily detached, and often more or less completely removed disclosing a dull brown cortex. Both cork and cortex frequently marked with numerous longitudinal and transverse cracks. Fracture short, the fractured surface exhibiting under a lens a dark reddish-brown bast traversed by numerous, thin, whitish medullary rays. In transverse section cork cells with strongly thickened outer walls, but thin inner walls, in which minute crystals of calcium oxalate are embedded; both cortex and bast free from sclerenchymatous cells. Aromatic odor, especially when burned; taste aromatic and bitter. Ash not more than 11 per cent." *Br.*

The National Formulary describes it as "in quills or curved pieces from 0.5 to 2.5 mm. in thickness, externally gray, somewhat fissured; the corky layer easily detached, more or less coated with a white lichen; the uncoated surface dull-brown, inner surface smooth; fracture short, the fractured surface having a resinous and radially striate appearance. Odor characteristic, strong and musk-like when the bark is burned; taste warm, aromatic and very bitter. The powdered drug is pale-brown and has an odor resembling that of clove. When examined under the microscope, it exhibits simple starch grains up to 0.013 mm. in diameter and occasionally two- to three-compound; calcium oxalate in monoclinic crystals or rosette aggregates up to 0.025 mm. in diameter; fragments of parenchyma tissue, some of the cells containing starch, calcium oxalate or tannin; cells filled with reddish-brown resin or yellow oil; somewhat lignified cork cells, polygonal in outline with evenly thickened, lamellated walls and irregular lumina; non-porous bast fibers, some with lignified walls, up to 0.016 mm. in diameter; tracheæ with bordered pores very few or absent. Cascarilla yields not more than 10 per cent of ash." *N. F.*

Cascarilla should yield not more than 10 per cent. of ash.

Properties.—Cascarilla has an aromatic odor, rendered much more distinct by friction, and a warm, spicy, bitter taste. It is brittle, breaking with a short fracture. When burned it emits a pleasant odor, closely resembling that of musk, but weaker and more agreeable. This property serves to distinguish it from other barks. It was analyzed by Trommsdorff, and more recently by Duval of Lisieux, in France. The constituents found by the latter were albumen, a peculiar kind of tannin, a bitter crystallizable principle called *cascarillin*, a red coloring matter, fatty matter of a nauseous odor, wax, gum, volatile oil, resin, starch, pectic acid, potassium chloride, a salt of calcium, and lignin. The oil, according to Trommsdorff, constitutes 1.6 per cent., is of a greenish-yellow color, has a penetrating odor analogous to that of the bark, and is of the sp. gr. 0.938. G. Feudler (*A. Pharm.*, 1900, p. 671) finds the oil to contain about 2 per cent. of free acid, which consists of a liquid acid, $C_{11}H_{20}O_2$, to which the name of *cascarillic acid* was given, and a solid portion made up of a mixture of palmitic and stearic acids. The oil contains 0.3 per cent. of eugenol, a terpene differing from pinene, cymene, possibly some l-limonene, two sesqui-

terpenes and an alcohol, $C_{15}H_{23}OH$. To obtain cascarillin, Duval treated the powdered bark with water, added lead acetate to the solution, separated the lead by hydrogen sulphide, filtered, evaporated with the addition of animal charcoal, filtered again, evaporated at a low temperature to a syrupy consistence, and having allowed the semi-liquid substance thus obtained to harden by cooling, purified it by twice successively treating it, first with a little cool alcohol, to separate the coloring and fatty matters, and afterwards with boiling alcohol and animal charcoal. The last alcoholic solution was allowed to evaporate spontaneously. Thus obtained, cascarillin is white, crystalline, inodorous, bitter, very slightly soluble in water, soluble in alcohol and ether. (*J. P. C.*, 3e sér., vii, 96.) It melts at 205° C. (401° F.), is not volatile nor a glucoside. Its composition answers to the formula $C_{12}H_{18}O_4$. P. E. Alessandri regards *cascarilline* as an alkaloid, and obtains it economically by mixing powdered cascarilla with sufficient 3 per cent. aqueous solution of oxalic acid to cover it, shaking the mixture, and heating it to 60° C. (140° F.), then allowing it to cool, expressing the mixture and saturating the filtered liquor with ammonia, then evaporating at a low temperature to two-thirds of its bulk, allowing it to cool, and separating any deposit. The clear liquid is then shaken with ether; this takes up the cascarilline, which may be obtained through evaporation of the ethereal liquid. (*L'Orosi*, v, 1; *P. J.*, 1882, 993.) R. A. Cripps was unable to obtain the alkaloid by Alessandri's method, and suggests that the bitterness of the so-called cascarilline might be due to adherent resin. (*P. J.*, 1886, 1103.) Either alcohol or water will partially extract the active matters of cascarilla; but diluted alcohol is the proper menstruum. Naylor and Littlefield have reviewed the processes of Duval and Alessandri for preparing cascarilline, and find that Duval's method gives the purer product. They find its melting point to be 203.5° C. (398.3° F.), and give it the formula $C_{16}H_{24}O_5$. (*Y. B. P.*, 1896, 301.) W. A. H. Naylor subsequently found betaine in cascarilla. (*P. J.*, 1898, 279.)

Uses.—This bark is aromatic and tonic. It was known in Germany as early as the year 1690, and was much used as a substitute for Peruvian bark by those who were prejudiced against that febrifuge in the treatment of *remittent* and *intermittent fevers*. It has, however, lost its reputation, and is now employed only where a pleasant and gently stimulant tonic is desirable, as in *atonic dyspepsia*, and other cases of debility of the stomach or bowels, especially in combination with the more powerful bitters. It may be given in powder or in infusion. In consequence of its pleasant odor when burned, some smokers mix it in a small quantity with their tobacco; but it is said to occasion vertigo and intoxication.

Dose, twenty to thirty grains (1.3–2.0 Gm.).

Off. Prep.—Infusum Cascarillæ, *Br.*; Tinctura Cascarillæ, *Br.*

CASSIÆ FRUCTUS. Br.

CASSIA PODS [Purging Cassia]

(kăs'sĭ-æ frŭc'tŭs)

"Cassia Pods are the ripe fruits of Cassia Fistula, *Linn.*" *Br.* "The dried fruit of *Cathartocarpus Fistula* (Linné) Persoon (Fam. *Leguminosæ*)." *N. F.*

Cassia Fistula. *N. F. IV*, Purging Cassia, Pudding-stick (or pipe); Fructus Cassiæ Fistulæ; Casse Officinale, *Fr. Cod.*; Casse en bâtons, Pulpe de Casse, Casse Mondée, Casse, *Fr.*; Röhrenkassie, Purgircassie, Fistelkassie, *G.*; Cassia, *It.*; Cana fistula, *Sp.*

Cassia Fistula L. (*Cathartocarpus Fistula* Persoon). This is a large tree, with a trunk of hard, heavy wood, dividing towards the top into numerous spreading branches, and covered with a smooth ash-colored bark. The leaves are commonly composed of five or six pairs of opposite leaflets, which are petiolate ovate, pointed, undulated, smooth and of a pale green color. The flowers are large, of a golden yellow color, and arranged in long, pendent, axillary racemes. The fruit consists of long, cylindrical, woody, dark-brown, pendulous pods, which when agitated by the wind strike against each other and produce a sound that may be heard at a distance. This species of Cassia is a native of Upper Egypt and India, whence it is generally supposed to have been transplanted to other parts of the world. It is at present very extensively diffused through the tropical regions of the old and new continents, being found in Insular and Continental India, Cochin China, Egypt, Nubia, the West Indies, and the warmer parts of the continent of America. Under the name of *Golden Shower* it is known as an ornamental shade tree in all tropical countries. The fruit is the official part of the plant. It is imported from the East and West Indies, chiefly the latter, and from South America. Under the name of Cassia Fistula they were for a long time official.

Properties.—Cassia pods are a foot or more in length, straight, or but slightly curved, cylindrical, less than an inch in diameter, with a woody shell, externally of a dark-brown color, and marked with three longitudinal shining bands, extending from one end to the other, two of which are in close proximity, appearing to constitute a single band, and the third is on the opposite side of the pod. These bands mark the place of junction of the valves of the legume, and are represented as sometimes excavated in the form of furrows. There are also circular depressions at unequal distances. It is described as follows: "Long, narrow, cylindrical, shortly stalked fruits about thirty-five to fifty centimetres in length, and fifteen to twenty-five millimetres in diameter. Pericarp nearly smooth, dark chocolate-brown or nearly black, thin and hard. Internally divided by thin transverse dissepiments into numerous

compartments, each of which contains a smooth, oval, reddish-brown seed surrounded by a nearly black, sweet pulp." *Br.*

The N. F. describes it as in "cylindrical, from 25 to 50 cm. in length, about 20 mm. in diameter, chestnut-brown in color, on one side a longitudinal groove and on the other a smooth line or slight ridge, indicating the sutures; indehiscent, the cavity divided transversely into numerous compartments, each containing a reddish-brown, glossy, flattish-ovoid seed embedded in a blackish-brown sweet pulp. Odor resembling that of prunes." *N. F.*

The pods brought from the East Indies are smaller, smoother, have a blacker pulp, and are more esteemed than those from the West Indies. We have seen pods in the American market sold as cassia pods, which were an inch and a half in diameter, flattened on the sides, exceedingly rough on the outer surface, and marked by three longitudinal very elevated ridges, corresponding to the bands or furrows of the common cassia. The pulp was rather nauseous, but in other respects seemed to have the properties of the official purging cassia. They corresponded exactly with a specimen of the fruit of *Cassia brasiliana*, Lam., brought from the West Indies, and were probably derived from that plant.

The heaviest pods, and those which do not make a rattling noise when shaken, are to be preferred, as they contain a larger portion of the pulp, which is the part employed. This should be black and shining and have a sweet taste. It is apt to become sour if long exposed to the air, or mouldy if kept in a damp place. The pulp is extracted from the pods by first bruising them, then boiling them in water, and afterwards evaporating the decoction; or, when the pods are fresh, by opening them at the sutures and removing the pulp with a spatula.

CASSIÆ PULPA. Br.

CASSIA PULP

(kăs'sĭ-æ pŭl'pą)

"Exhaust crushed Cassia Pods by percolation with Distilled Water; strain; evaporate on a water bath to the consistence of a soft extract." *Br.*

Cassia pulp has a slight odor, and a sweet mucilaginous taste. According to Henry it contains sugar, gum, coloring matter, and a tannin-like substance; while Haensel obtained from it by steam distillation a dark yellow volatile oil, also butyric acid. (*Ph. Cb.*, 41.)

Uses.—Cassia pulp is laxative, and may be advantageously given in small doses in cases of *habitual costiveness*. In quantities sufficient to purge, it occasions nausea, flatulence, and griping. In this country it is rarely prescribed, except as an ingredient in the confection of senna, which is a pleasant and useful laxative preparation.

Dose, of the pulp as a laxative, one or two drachms (3.9 or 7.7 Gm.), as a purge one or two ounces (31–62 Gm.).

Off. Prep.—Confectio Sennæ, *Br.*

CATECHU. Br.

CATECHU [Catechu Pallidum]

(kăt'ē-ȼhū)

"Catechu is an extract of the leaves and young shoots of Uncaria Gambier, *Roxb.*" *Br.*

Catechu is described in the Br. Pharm., 1914, as follows: "In cubes, sometimes more or less agglutinated, each side measuring about twenty-five millimetres. Dark reddish-brown externally, pale cinnamon-brown internally, porous and friable. When examined under the microscope they are found to consist chiefly of minute acicular crystals. No odor; taste at first bitter and very astringent, but subsequently sweetish. Almost entirely soluble in boiling *water*. Not less than 80 per cent. is soluble in *alcohol* (90 per cent.); the alcoholic solution made strongly alkaline with *solution of sodium hydroxide* and shaken with *petroleum spirit* imparts to the latter a brilliant green fluorescence (distinction from Black Catechu); the residue insoluble in *alcohol* (90 per cent.) exhibits no starch grains when examined under the microscope. Ash not more than 5 per cent.; ash of the powder not more than 8 per cent." *Br.*

(See *Gambir.*)

CATECHU NIGRUM. Br.

BLACK CATECHU

(kă'tē-ȼhū nī'grŭm)

"Black Catechu is an extract prepared from the wood of Acacia Catechu, *Willd.*" *Br.*

Cutch, Cachou, *Fr.*; Phgu, Katechu, *G.*; Caticu, Catto, *It.*; Catecu, *Sp.*; Cutt, *Hindostanee.*

The U. S. P. (8th Rev.) dismissed catechu and introduced gambir because of the greater uniformity in quality of the latter. See *Gambir*, p. 507.

The U. S. P. 1890 defined catechu as "an extract prepared from the wood of *Acacia Catechu* (Linné fil.) Willdenow (Fam. *Leguminosæ*)."

Acacia Catechu is a small tree, seldom more than twelve feet in height, with a trunk one foot in diameter, dividing towards the top into many close branches, and covered with a thick, rough, brown bark. This species of Acacia is a native of the East Indies, growing abundantly in various provinces of Hindostan, and in the Burmese Empire. It is also common in eastern Africa where it is valued for its wood; but no extract appears to be made from it. Pereira says that its is common in Jamaica.

This drug had been long known before its source was discovered. It was at first called *Terra japonica*, under the erroneous impression

that it was an earthy substance derived from Japan. When ascertained by analysis to be of vegetable origin, it was generally considered by writers on the Materia Medica to be an extract of the *betel nut.* Its true origin was made known by Kerr, assistant surgeon of the civil hospital in Bengal. According to Kerr, the manufacturer, having cut off the exterior white part of the wood, reduces the interior brown or reddish-colored portion into chips, which he then boils in water in unglazed earthen vessels until all the soluble matter is dissolved. The decoction thus obtained is evaporated first by artificial heat, and afterward in the sun, until it has assumed a thick consistence, when it is spread out to dry upon a mat or cloth, being, while yet soft, divided by means of a string into square or quadrangular pieces. The account subsequently given by Royle, of the preparation of the extract in Northern India, is essentially the same. The process, as he observed it, was completed by the pouring of the extract into quadrangular earthen moulds. It is said that the unripe fruit and leaves are also sometimes submitted to decoction. Three colors of catechu are prepared; the light red or red, which is considered best and is especially employed in Burmah and India to chew with the betel nut; the dark red and black, which are made especially for European and American markets, and which are apt to suffer adulteration *en route* in China.

The name *catechu* in the native language signifies the *juice of a tree,* and appears to have been applied to astringent extracts obtained from various plants. Commerce is chiefly supplied with catechu from Bahar, Northern India, and Nepaul through Calcutta, from Canara through Bombay, and from the Burmese dominions. It is frequently called *cutch* by the English traders, a name derived from the Hindostanee word *cutt.*

It enters commerce in large masses, sometimes of one cwt., consisting of layers of flat cakes, frequently wrapped in the leaves of the *Dipterocarpus tuberculatus* Roxb. In this form, however, we do not see it in drug stores, but almost always in angular, irregular fragments, in which portions of two layers sometimes cohere with leaves between them, indicating their origin. It is characterized by its compactness, shining fracture, and blackish-brown or dark port-wine color, so that when finally broken it bears considerable resemblance to kino. This is an excellent variety of catechu.

Catechu is inodorous, with an astringent and bitter taste, followed by a sense of sweetness. It is brittle, and breaks with a fracture which is rough in some specimens, in others uniform, resinous, and shining. That which is preferred in our market is of a dark color, easily broken into small angular fragments, with a smooth glossy surface, bearing some resemblance to kino. Catechu is often mixed with sand, sticks, and other impurities.

Black catechu is described in the Br. Pharm., 1914, as follows: "In irregular masses of a dark brown color, brittle, having a porous, glossy, somewhat conchoidal fracture. Partially soluble in cold *water,* almost entirely soluble in boiling *water.* Not less than 60 per cent. is soluble in *alcohol* (90 per cent.). No odor; taste sweetish, astringent. Its dilute aqueous solution gives a dark green color with *T. Sol. of ferric chloride,* changing to purple when made slightly alkaline with *solution of sodium hydroxide.* Ash not more than 5 per cent.; ash of the powder not more than 8 per cent. In India, in the Eastern, and in the North American Divisions of the Empire, Black Catechu may be employed in making the official preparations for which Catechu is directed to be used." *Br.*

The proportion of tannic acid, which may be considered the efficient principle, varies from about 45 to 55 per cent. in catechu or cutch, and from 36 to 40 per cent. in gambir. The portion designated by Davy as extractive is said to contain, if it does not chiefly consist, of a principle discovered by Buchner, and now called *catechin, catechuin,* or *catechuic acid,* to which Etti gives the formula $C_{15}H_{18}O_8$, and *catechu red,* $C_{36}H_{34}O_{15}$, which is evidently the first anhydride of catechin. The *catechu tannic acid* is of the variety which precipitates iron of a greenish-black color, and differs from most of the other varieties in not yielding grape sugar when digested with diluted sulphuric acid. It is not, therefore, a glucoside. It precipitates gelatin, but not tartar emetic (Kane), and is not, like the tannic acid exposure of galls, converted into gallic acid by the access of the air. Catechu is almost wholly soluble in a large quantity of water, to which it imparts a brown color. The extractive or catechuic acid is much less soluble than the astringent principle, which may be almost entirely separated from it by the frequent application of small quantities of cold water. Boiling water dissolves it much more readily than cold, and deposits it of a reddish-brown color upon cooling. Both principles are readily dissolved by alcohol or proof spirit, and also by ether.

De Meyer affirms that the best method of detecting adulteration of catechu is to treat the suspected drug with ether. Catechu of good quality, after repeated treatment with ether, loses 53 per cent. of its weight, and the dried residue weighs only 47 per cent. of the catechu employed. If this be exceeded, the drug must be proportionately impure. (*J. P. C.,* June, 1870, 479.) A. Jossart (*J. P. A.,* 1881, 41) examined a catechu which was adulterated with from 60 to 65 per cent. of ferrous carbonate. For methods of assaying catechu and gambir, see Trimble's *The Tannins,* 43; also *Ph. Rev.,* 1897, 27. (See also *Gambir,* p. 507, and *U. S. D.,* 19th ed., p. 1436.)

Catechu is used for the same purposes and in the same proportions as *Gambir,* see page 507.

Dose, five to fifteen grains (0.3–1.0 Gm.).

Off. Prep.—Pulvis Catechu Compositus, *Br.;* Tinctura Catechu, *Br.;* Trochiscus Catechu, *Br.*

CERA ALBA. U. S., Br.

WHITE WAX Cer. Alb.

(cē'rą ăl'bą)

"Yellow Wax, bleached." *U. S.* "White Beeswax is Yellow Beeswax, bleached." *Br.*

White Beeswax; Cire Blanche, *Fr. Cod.;* Cera alba, *P. G.;* Weisses Wachs, *G.;* Cera bianca, *It.;* Cera blanca, *Sp.*

CERA FLAVA. U.S., Br.

YELLOW WAX Cer. Flav. [Beeswax]

(cē'rą flā'vą)

"A product obtained by melting and purifying the honey-comb of the bee, *Apis mellifera,* Linné (Fam. *Apidæ*)." *U. S.* "Yellow Beeswax is obtained from the honeycomb of the Hive Bee, Apis mellifica, *Linn.,* and possibly other species of Apis." *Br.*

Yellow Beeswax; Cera Citrina; Beeswax; Cire Jaune, Cire d'Abeilles, *Fr.;* Cera Flava, *P. G.;* Gelbes Wachs, *G.;* Cera gialla, Cera vergine, *It.;* Cera amarilla, *Sp.*

The name *Apis mellifera* was given to the honey-bee of Linnæus in 1758, *Systema Naturæ,* 10th edition; subsequently (*Ibid.,* 12th edition, 1767), Linnæus changed the name to *mellifica,* but according to the established rules of scientific nomenclature the first name must hold, and the revisers of the United States Pharmacopœia were therefore correct in adopting it. It was at one time doubtful whether the wax which constitutes the walls of the honey-comb is elaborated or merely gathered by the insect. Huber, however, by feeding bees exclusively on honey and water, determined that under these circumstances wax is produced in the form of scales under the rings of the abdomen. But wax also exists in plants, bearing in this, as in other respects, a close analogy to the fixed oils. Besides the official species other bees are used as honey makers. The extremely vicious, blackish-brown *Apis fasciata* was kept by the ancient Egyptians on floating apiaries, which as the season progressed slowly drifted down the Nile, following the successive opening of the flowers. In Senegal, *Apis adansonii,* and in Southern Africa *Apis caffra* and *Apis scutellata* produce honey; while the *Apis unicolor* of Madagascar has been domesticated in that island and introduced into other parts of the world. In India honey is made in large quantities by *Apis dorsata* (the largest of known bees) (*Apis indica, Apis florea*). *India Wax* differs from official wax chiefly in its lower acid value. A wax is also produced in India by the so-called *Kota bees,* belonging to the genus *Melipona;* they are minute stingless insects, which furnish a sticky, dark-colored wax, resembling in physical and chemical characteristics the propolis of the honey bee rather than the true wax.

1. Cera Flava, or *Yellow Wax.*—This is obtained by slicing the comb taken from the hive, draining and afterwards expressing the honey, and melting the residue in boiling water, which is kept hot for some time in order to allow the impurities to separate and either subside or be dissolved by the water. When the liquid cools the wax concretes, and, having been removed and again melted in boiling water, is strained and poured into pans or other suitable vessels. The labor saving device is sometimes adopted of stretching a strainer of cheese cloth upon a hoop and wedging the latter down into the hot mixture below the level of the water; as this cools, the melted wax slowly rises through the cloth, and thus a perfectly clean cake of wax is formed on top on cooling. It is usually brought to market in round flat cakes of considerable thickness.

Properties.—Yellow wax is "a yellow to gray-brown solid, having an agreeable, honey-like odor, and a faint characteristic taste. It is somewhat brittle when cold, and when broken presents a dull, granular, not crystalline fracture. By the heat of the hand, it becomes plastic. Yellow wax is insoluble in water, sparingly soluble in cold alcohol; boiling alcohol dissolves the cerotic acid and a portion of the myricin. It is completely soluble in chloroform, ether, or in fixed or volatile oils; partly soluble in cold benzene or carbon disulphide, and completely soluble in these liquids at a temperature of from 25° to 30° C. (77° to 86° F.) Specific gravity: 0.950 to 0.960 at 25° C. (77° F.) determined as follows: Melt the wax at a low temperature and allow it to fall in separated drops from just above the surface into alcohol that has been warmed to from 45° to 50° C. (113°–122° F.). Allow the globules to remain in the alcohol until it has cooled spontaneously to room temperature (20° to 25° C.) (68° to 77° F.), then remove the wax and keep it at room temperature for 24 hours. Prepare a mixture of 4 volumes of alcohol and enough distilled water to make 10 volumes and allow it to stand until free from air bubbles. Moisten the globules of wax with distilled water, by means of a brush, and place them by means of forceps in the alcohol solution just prepared contained in a beaker. Then add alcohol or air-free distilled water as required to the mixture, kept at 25°C. (77° F.) until the globules of wax float or rest indifferently in the liquid, and finally determine the specific gravity of the alcoholic liquid. The figure thus obtained is the specific gravity of the wax examined. It melts between 62° and 65° C. (143.6° and 149° F.). Boil 1 Gm. of yellow wax for half an hour with 35 mils of an aqueous solution of sodium hydroxide (1 in 7), the volume being preserved by the occasional addition of distilled water; the wax separates on cooling without rendering the liquid opaque, and no precipitate is produced in the liquid after filtration through glass wool or asbestos, on the addition of hydrochloric acid in excess (*fats or fatty acids, Japan wax, or rosin*). Hydrochloric acid produces no precipitate in water which has been boiled with a portion of the wax (soap). Warm about 3 Gm. of yellow wax, accurately weighed, in a 200 mil flask with 25 mils of neutral dehydrated alcohol

until melted, then add 1 mil of phenolphthalein T.S. and titrate the mixture while warm with half-normal alcoholic potassium hydroxide V.S. to a faint pink color. The acid value so obtained is not less than 18 nor more than 24. Now add 25 mils of half-normal alcoholic potassium hydroxide V.S. and 50 mils of alcohol, boil the mixture for two hours under a reflux condenser and titrate the excess of the alkali with half-normal hydrochloric acid V.S. The ester value so obtained is not less than 72 nor more than 77." *U. S.*

"A yellowish-brown solid; somewhat brittle when cold, but becoming plastic by the heat of the hand. Agreeable, honey-like odor. Fracture granular, not crystalline. Soluble in *chloroform*, and in fixed and volatile oils. Specific gravity 0.958 to 0.970. Melting point 61° to 64° C. (141.8°–147.2° F.). *Refractive index* at 80° C. (176° F.) 1.4380 to 1.4420. When 5 grammes are boiled for ten minutes with 80 millilitres of an aqueous solution (1 in 10) of *sodium hydroxide*, the water lost by evaporation being made up, the resulting solution, cooled, and filtered through asbestos, does not become turbid when acidified with *hydrochloric acid* (absence of fats, fatty acids, Japan wax, resin). 5 grammes heated with 20 millilitres of *absolute alcohol*, and shaken until uniformly distributed, require for neutralisation at boiling temperature not less than 1.5 and not more than 2.0 millilitres of *N/1 alcoholic solution of potassium hydroxide, solution of phenolphthalein* being used as indicator (limits of free acid). Upon the further addition of 20 millilitres of *N/1 alcoholic solution of potassium hydroxide*, and on well boiling for one and a quarter hours in a flask to which a reflux condenser is attached, not less than 13.2 and not more than 13.8 millilitres of *N/1 solution of sulphuric acid* are required for neutralisation. When 5 grammes are boiled with a mixture of 15 millilitres of *N/1 alcoholic solution of potassium hydroxide* and 15 millilitres of *absolute alcohol* until completely saponified, the alcohol evaporated, the residue dissolved in 20 millilitres of *glycerin* on a water-bath and 80 millilitres of boiling *water* added, a clear or translucent solution is obtained (absence of ceresin, paraffin and other waxes). Not more than 1 per cent. is soluble in boiling *water* (limit of honey)." *Br.*

Dieterich examined hundreds of specimens annually, and found the wax to vary in sp. gr. from 0.963 to 0.966. He also determined the specific gravities of the following substances some of which are used to adulterate wax: white wax, 0.973; cera japonica, Japan wax, 0.975; ceresin, half white, 0.920; ozokerite, crude, 0.952; rosin, common, 1.108; cacao butter, 0.980 to 0.981; pure rosin, 1.045; beef suet, 0.952 to 0.953; yellow wax, 0.963 to 0.964; ceresin, white, 0.918; ceresin, yellow, 0.922; spermaceti, 0.960; French rosin, 1.104 to 1.105; paraffin, med. hard, 0.913 to 0.914; stearin, A No. 1, 0.971 to 0.972; mutton suet, 0.961.

Various adulterations have been practised, most of which may be readily detected. Meal, earth, and other insoluble substances are at the same time discovered and separated by melting and straining the wax. When the fracture is smooth and shining instead of being granular, the presence of rosin may be suspected. This is dissolved by cold alcohol, while the wax is left untouched. Yellow wax is frequently adulterated with a mixture of paraffin and rosin; such wax is usually translucent on the edges. For other adulterating substances used, and the modes of detecting them, see the remarks which follow on white wax.

Yellow wax is used chiefly as an ingredient of plasters and cerates.

2. Cera Alba, *Bleached Yellow Wax*, or *White Wax.*—The color of yellow wax is discharged by exposing it, with an extended surface, to the combined influence of air, light and moisture. The process of bleaching is carried on to a considerable extent in this country. The wax, previously melted, is made to fall in streams upon a revolving cylinder, kept constantly wet, upon which it concretes, forming thin ribbon-like layers. These, having been removed, are spread upon linen cloths stretched on frames and exposed to the air and light, care being taken to water and occasionally turn them. In a few days they are partially bleached; but, to deprive the wax completely of color, it is necessary to repeat the whole process once, if not oftener. When sufficiently white, it is melted and cast into small circular cakes. Yellow wax may also be decolorized by treatment with animal charcoal or with potassium permanganate, potassium dichromate and sulphuric acid, and hydrogen peroxide. White wax sometimes contains one or more free fatty acids, consequent probably upon the employment of alkalies in bleaching it, which render it an unfit ingredient in the unctuous preparations of certain salts. It may be deprived of these acids by means of alcohol.

Perfectly pure wax is white, shining, diaphanous in thin layers, inodorous, insipid, harder and less unctuous to the touch than the yellow, soft and ductile at 35° C. (95° F.) and fusible at 65° C. (149° F.), retaining its fluidity at a lower temperature. The U. S. Pharmacopœia describes it as "a yellowish-white solid somewhat translucent in thin layers, having a faint, characteristic odor; it is free from rancidity, and nearly tasteless. Specific gravity: 0.950 to 0.960 at 25° C. (77° F.), as determined by the method given under *Cera Flava.* It melts between 62° and 65° C. (143.6°–149° F.). The acid value is not less than 17 nor more than 23, and the ester value not less than 72 nor more than 79, as determined by the methods given under *Cera Flava.* In other respects White Wax has the characteristics of Yellow Wax and responds to the tests for identity and purity under *Cera Flava.*" *U. S.*

"Hard, nearly white, translucent cakes or

masses. 5 grammes heated with a mixture of 10 millilitres of *alcohol* (90 per cent.) and 10 millilitres of *absolute alcohol,* and shaken until evenly distributed, require for neutralisation at boiling temperature not less than 1.5 and not more than 2.2 millilitres of *N/1 alcoholic solution of potassium hydroxide, solution of phenolphthalein* being used as indicator (limits of free acid). In other respects White Beeswax responds to the tests described under '*Cera Flava.*'" *Br.*

By a great heat it is partly volatilized, partly decomposed; and, when flame is applied to its vapor, it takes fire and burns with a clear bright light. It is insoluble in water, and in cold alcohol or ether, but is slightly soluble in boiling alcohol and ether, which deposit it in a great measure upon cooling. The volatile and fixed oils dissolve it with facility, rosin readily unites with it by fusion, and soaps are formed by the action of sodium and potassium hydroxides. It is not affected by the acids at ordinary temperatures, but is converted into a black mass when boiled with concentrated sulphuric acid. Bleached wax contains, according to Lewy's analysis, 80.2 per cent. of carbon, 13.4 of hydrogen, and 6.4 of oxygen. It is a mixture of three different substances, which may be separated from one another by alcohol. —viz.: 1, *myricin,* insoluble in boiling alcohol, and consisting chiefly of myricyl palmitate ($C_{16}H_{31}O.OC_{30}H_{61}$),—that is, a compound of *palmitic acid,* $C_{16}H_{31}O.OH$, and *myricyl alcohol,* $C_{30}H_{61}OH$; 2, *cerotic acid,* $C_{27}H_{54}O_2$ (formerly called *cerin* when obtained only in an impure state), which is dissolved by boiling alcohol, but crystallizes out on cooling; 3, *cerolein,* which remains dissolved in the cold alcoholic liquid. This latter is probably a mixture of fatty acids, as indicated by its acid reaction. Schwalb (*Ann. Chem.,* ccxxiv, 225) found melissic acid and some unsaturated acids of the oleic series; also higher solid hydrocarbons of the saturated series, such as $C_{27}H_{56}$ and $C_{31}H_{64}$. Kebler states that the hydrocarbons in beeswax amount to from 12.72 to 13.78 per cent. (*A. J. P.,* 1893, 587.) T. Marie believes that cerotic acid, as ordinarily obtained, is a mixture of two distinct acids. He gives $C_{30}H_{60}O_2$ as the formula for melissic acid and $C_{25}H_{50}O_2$ for pure cerotic acid.

Wax has been variously adulterated. Heavy substances sink to the bottom of the vessel when the wax is melted. Starch, meal, and other insoluble substances remain behind when the wax is dissolved in oil of turpentine or petroleum benzin. Water, which is said to be sometimes fraudulently incorporated with it, by agitation when partially melted, is driven off by heat. Fatty substances render lime water turbid when agitated with it and allowed to stand. For the detection of stearin and stearic acid, Lebel dissolves the suspected wax in two parts of oil, beats the cerate thus formed with its weight of pure water, and then adds a few drops of solution of lead subacetate. If stearin be present, there will be an immediate decomposition, and the mixture will acquire an extraordinary solidity from the formation of lead stearate. (*J. P. C.,* 3e sér., xv.) Vogel proposes chloroform as a means of detecting the adulteration with fatty matters. That liquid dissolves only 25 per cent. of wax, but stearin and stearic acid completely. If, therefore, wax treated with 6 to 8 parts of chloroform loses more than one-quarter of its weight, it may be considered as impure. (*J. P. C.,* 3e sér., xvii.) Overbeck detects stearic acid by the abundant effervescence produced from the escape of carbon dioxide when a small portion of the suspected wax is boiled in a solution composed of one part of sodium carbonate and fifty of distilled water. (*P. J.,* xi, 128.) The best test for fats, fatty acids, or rosin is the pharmacopœial test of boiling with sodium hydroxide solution and testing the filtrate obtained after cooling. For the detection of rosin, cold alcohol is sufficient. It dissolves the rosin, and yields it on evaporation, attended with a very small portion of pure wax, which yields 2.4 per cent. to cold alcohol. (Ed. Davies, *A. J. P.,* 1870, p. 537.) F. Jean states that a few drops of sulphuric acid added to the melted wax adulterated with rosin, cause a red color, or, if only 1 per cent. be present, a green tint. (*A. J. P.,* 1881, p. 307.) *Japan wax* is said also to be largely employed for adulterating beeswax; so that sometimes but little of the product of the bee is to be found in the mixture. To detect Japan wax, Dullo boils together for a minute 10 Gm. of wax, 120 Gm. of water, and 1 Gm. of sodium hydroxide; if Japan wax be present, a soap will immediately form, which will slowly solidify on cooling. Beeswax does not saponify under these circumstances. (*J. P. C.,* 4e sér., i, 448.) Ceresin, a principle obtained from ozokerite (see Part II), is also employed as an adulterant, and is manufactured largely for that purpose in Vienna. It is only native paraffin, and of course answers to the tests for that substance. There are other less precise methods of detecting adulterations. Thus, spermaceti and lard render wax softer and less cohesive, of a smoother and less granular fracture, and of a different odor when heated. The melting point and specific gravity are lowered by tallow, suet, lard, and especially by paraffin. *Legrip's cereometer* is based upon the altered specific gravity of wax when adulterated. Anyone may apply this principle by making such a mixture of alcohol and water that pure wax will neither sink nor rise in it, but remain wherever placed. Adulterated wax would either float or sink in this liquid. The most valuable information, however, is obtained by the determination, according to Hübl's process, of the chemical constants—viz., acid value, ester value; and saponification value. In yellow wax the iodine value is also of use; in white wax the bleaching process has altered the bodies which absorb the iodine. See also *Chem. Ztg.,* 1893, 918; *Proc. A. Ph. A.,* 1894, 957; *D. C.,*

1898, 33; *Am. Drug.*, 1898, 97, and 1904, 103, 105.) According to G. Brehner (*Ztsch. Off. Ch.*, 1912, No. 5), who has investigated many samples of beeswax of normal and abnormal character, beeswax may be divided into three groups, according to source, as follows: (1) Ordinary normal beeswax in which the ratio of acid number to ester number is 1 : 3.6 to 1 : 4. (2) Beeswax of African origin in which the ratio is 1 : 3. (3) Beeswax of Indian origin in which the ratio is 1 : 12. A. Leijs (*J. P. C.*, 1912, No. 12) has made an extensive investigation of beeswax and *carnauba wax* by new methods, which he describes and which enable him with certainty to separate *paraffin, ceresin,* and *carnauba wax* readily from beeswax. The method depends upon the relative solubility of the substance in fuming hydrochloric acid.

Under the name of White Wax No. 2 or White Wax for technical use, there has been found in commerce a product put up in exact imitation of white beeswax, and consisting of over 90 per cent. of paraffin.

Vegetable Wax.—Many vegetable products contain wax. It exists in the pollen of numerous plants, and forms the bloom or glaucous powder which covers certain fruits, and the coating of varnish with which leaves are sometimes supplied. In some plants it is so abundant as to be profitably extracted for use. Such is the *Ceroxylon andicolum* Humb., a lofty palm growing in the South American Andes. Upon the trunk of this tree, in the rings left by the fall of the leaves, is a coating of wax-like matter, about one-sixth of an inch thick, which is removed by the natives and employed in the manufacture of tapers. It contains, according to Vauquelin, two-thirds of a resinous substance and one-third of pure wax. Two kinds of wax are collected in Brazil, one called *carnauba,* from the leaves of the *Copernicia cerifera,* a palm, which forms large forests in the provinces of Ceara, the other *ocuba,* from the fruit of a shrub of the province of Para. (*J. P. C.*, 3e sér., v, 154.)

Carnauba Wax is collected by cutting out the leaf buds of *Copernicia cerifera* (Arruda) Mart. (fam. *Palmaceæ*), commonly called the *Brazilian Wax Palm,* drying and beating them, and melting the powder thus detached, in water. H. Stürke has stated as the result of an investigation that carnauba wax contains: a hydrocarbon, melting at 59° C. (138.2° F.); an alcohol, $C_{27}H_{55}OH$, melting at 76° C. (168.8° F.); myricyl alcohol, $C_{30}H_{61}.OH$, melting at 85.5° C. (185.9° F.); a diatomic alcohol, $C_{25}H_{50}.(OH)_2$, melting at 103.5° to 103.8° C. (218.3°–218.8° F.); an acid, $C_{24}H_{48}O_2$, isomeric with lignocerotic acid, melting at 72.5° C. (162.5° F.); an acid, $C_{27}H_{54}O_2$, isomeric with cerotic acid, melting at 79° C. (174.2° F.) and an acid, or rather the lactone (anhydride) of an acid, $C_{19}H_{38}\begin{cases} CH_2OH \\ COOH \end{cases}$, melting at 103.5° C. (218.3° F.), from which an acid, $C_{19}H_{38}(COOH)_2$, melting at 90° C. (194° F.) has been prepared. (Schaedler, *Technol. der Fette und Oele,* 2te Auf., p. 884.) It is hard, brittle, and buff-colored, yellow, or greenish, resembling the resins more than wax, and melts at 84° C. (183.2° F.) which is much higher than the fusing point of other kinds of vegetable wax. It takes a fine polish when rubbed with any soft material, does not receive impressions from the finger at the natural temperature of the hand, and is adapted for polishing furniture, either alone or mixed with wax. 2,000,000 pounds of it are said to be annually produced in Brazil, where it is largely used, mixed with tallow, in making candles, etc. (See also *P. J.*, 1904, 246.) (See also *Carnauba Root,* Part II.)

A form of vegetable wax sometimes seen in this country is that derived from *Myrica cerifera* L., and commonly called *myrtle wax.* The *wax myrtle* is an aromatic shrub, from one to twelve feet high, growing in the United States, from New England to Louisiana, and flourishing especially on the sea coast. The fruit, which grows in clusters closely attached to the stems and branches, is small, globular, and covered with a whitish coat of wax, which may be separated for use. Other parts of the plant are said to possess medicinal virtues. The bark of the root is acrid and astringent, and in large doses emetic, and has been popularly employed in jaundice. The process for collecting the wax is simple. The berries are boiled in water, and the wax, melting and floating on the surface, is either skimmed off and strained, or allowed to concrete as the liquor cools, and then removed. To render it pure, it is again melted and strained, and cast into large cakes. It is collected in New Jersey, North Carolina, and New England, and particularly in Rhode Island.

China wax, called *pe-la* by the Chinese, resembles spermaceti in whiteness and crystalline appearance, but is distinguished by greater hardness and friability and a somewhat fibrous fracture. It melts at about 83° C. (181.4° F.), is very slightly soluble in alcohol or ether, is insoluble in cold oil of turpentine and rectified petroleum, but is dissolved with the aid of heat, and is very soluble in benzene. These solubilities distinguish it from spermaceti. (*P. J.*, xiv, 9.) It was formerly supposed to be of vegetable origin, but has been ascertained to be the product of an insect, *Coccus ceriferus,* deposited on the twigs of the Chinese Ash, *Fraxinus Chinensis* (Roxburgh), and investing them closely; the insect becomes embedded in a waxy material, which is scraped off with the insects, and constitutes the crude wax. It is purified by melting and straining. It is one of the chief industries in the province of S'zchuan, second only in importance to the silk culture. It is used over the entire Empire for candles and as medicine. (For details of its collection see *U. S. D.*, 19th ed., p. 307; also *P. J.*, 1885, xv.)

Under the name of *Ocotilla wax,* Helen Abbott Michael described (*A. J. P.*, Feb., 1885) a vegetable wax which she obtained from the bark

of *Fouquiera splendens,* and believed to be a new variety. A wax which is said to be used, under the name of *Arbol de la Cera,* in Mexico not only for domestic purposes, but also as a remedy in diarrhea and jaundice, is that obtained by boiling the fruit of the *Myrica jalapensis* in water. It is greenish or yellow, more brittle and unctuous than beeswax, has a feeble odor, a slightly bitter taste, and a density nearly equal to that of water, and melts at 43° C. (109.4° F.); but on exposure the fusing point rises to 47.5° C. (117.5° F.). It is wholly soluble in boiling ether, insoluble in water, sparingly soluble in cold alcohol, and dissolves in twenty parts of boiling alcohol, depositing the greater part on cooling; alkalies saponify it readily. (*A. J. P.,* xv, 339, 1885.)

Pisang Wax from *Ficus cerifera,* according to Greshoff and Sack, occurs in white crystalline cakes, having the sp. gr. 0.963 to 0.970 at 15° C. (59° F.), and melting at 79° to 81° C. (174.2°–177.8° F.). It is very sparingly soluble in ethyl alcohol, even when boiling, but readily soluble in boiling oil of turpentine, amyl alcohol, and carbon disulphide. Its acid number is 2 to 3, its saponification number 109. *Pisang-cerylic acid,* obtained by saponification, melts at 71° C. (159.8° F.), and has the composition $C_{24}H_{48}O_2$; while *pisang-cerylic alcohol,* which was also isolated, melts at 78° C. (172.3° F.), and has the formula $C_{13}H_{18}O$.

Gondang Wax occurs in brown pieces which are yellowish internally and have a sp. gr. of 1.015. In distinction from pisang wax, gondang wax is soluble in all the usual solvents at a boiling temperature, and it may be almost completely dissolved by prolonged boiling with ethyl alcohol, being however again deposited on cooling. Gondang wax purified in this way melted at 61° C. (141.8° F.), and yielded *fico-cerylic acid* on saponification, which has the formula $C_{13}H_{26}O_2$, and melts at 57° C. (134.6° F.), while *fico-cerylic alcohol* has the formula $C_{17}H_{28}O$, and melts at about 198° C. (388.3° F.). In its general character gondang wax is intermediate between wax and caoutchouc. (*Ph. Ztg.,* 1901, 563.)

Japanese Wax has been imported into Europe in considerable quantities, either directly from Japan, or through the Chinese ports. It is obtained from the berries of the *Rhus succedaneum* of Linnæus, and in small amount from the *R. sylvestris* and *R. vernicifera,* or lacquer plant. The partially dried berries are crushed, winnowed, steamed, placed in hemp cloth bags, steamed again, and pressed in a wooden wedge press. They yield about 15 per cent. of a coarse greenish tallowy mass. It has come in two forms, the one, as originally distinguished by Hanbury, of circular cakes, about four inches in diameter, and an inch thick, flat on one side and somewhat convex on the other; the second, as brought directly from Japan, of large rectangular blocks weighing, it may be, as much as 1 picul (133⅓ lbs.) which are packed in chests. It bears a considerable resemblance to purified beeswax, but is not quite so white, having a slightly yellowish tint, is softer, more friable, and has a somewhat rancid odor and taste. Its melting point is below that of wax, varying from 42° C. (107.6° F.) to 55° C. (131° F.). It is much more soluble in alcohol than is beeswax, is saponifiable with the alkalies, and is in the main a glyceride of palmitic acid with smaller amounts of the glycerides of stearic and arachidic acids. It has been employed in the preparation of candles, which yield as brilliant light as those made of common wax. It has been found useful in the preparation of cerates, etc. From Roucher's experiments it appears that there are two melting points of this wax, one corresponding closely with Procter's results, while the same wax rapidly heated to a point above that of fusion and then allowed to cool, if plunged into water at 42° C. (107.6° F.), melts into a transparent liquid; consequently melting at a point 12° C. below its freezing point in the ordinary state, which was 54° C.; the two temperatures being about equivalent in Fahrenheit's scale to 107° and 129°. (*P. J.,* Aug., 1872.)

Myrtle wax is of a pale grayish-green color, somewhat diaphanous, more brittle and unctuous to the touch than beeswax, of a feeble odor, and a slightly bitterish taste. It is about as heavy as water, and melts, according to G. E. Moore, at from 46.6° to 48.8° C. (116°–120° F.). It is insoluble in water, scarcely soluble in cold alcohol, soluble, excepting about 13 per cent., in twenty parts of boiling alcohol, which deposits the greater portion on cooling, soluble also in boiling ether, and slightly so in oil of turpentine. It is readily saponifiable with the alkalies. Myrtle wax is a mixture of glycerides and not a true wax. This variety of wax has been popularly employed in the United States as a remedy for *dysentery;* in which disease Fahnestock gave the powdered wax in doses of a teaspoonful frequently repeated, with alleged advantage. (*Am. J. M. S.,* ii, 313.) It is occasionally substituted by apothecaries for beeswax in the formation of plasters, and is used in the preparation of tapers and candles. It is somewhat fragrant when burning, but emits a less brilliant light than common lamp oil.

Uses.—Wax has little effect upon the system. Under the impression that it sheathed the inflamed mucous membrane of the bowels, it was formerly prescribed in *diarrhea* and *dysentery;* and it is mentioned by Dioscorides as a remedy in the latter complaint; but at the present time, we suppose, no one would think of employing wax for such purposes. Its sole use in modern medicine is in the formation of ointments, cerates, plasters, suppositories, and surgical dressings, etc.; in which it acts mechanically, either giving stiffness or serving to protect from water. It is an ingredient in almost all the official cerates, which owe to it their general title.

Off. Prep.—*White wax.*—Ceratum, *U. S.;* Ceratum Camphoræ, *N. F.;* Unguentum, *U. S.,*

Unguentum Aquæ Rosæ, *U. S., Br.;* Unguentum Cetacei, *Br.;* Unguentum Paraffini, *Br.;* Petroxolinum Spissum, *N. F.*

Yellow wax.—Ceratum Cantharidis, *U. S. (Br.);* Ceratum Resinæ, *U. S. (Br.);* Ceratum Resinæ Compositum, *N. F.;* Linimentum Terebinthinæ (from Rosin Cerate), *Br.*

CERATA.

CERATES

(cę-rā'tą)

Cérats, Céréolés, Elæocéréolés, *Fr.;* **Cerate, Wachssalben,** *G.*

These are unctuous substances consisting of oil or lard, mixed with wax, spermaceti, or rosin, to which various medicaments are frequently added. Their consistence, which is intermediate between that of ointments and that of plasters, is such that they may be spread at ordinary temperatures upon linen or leather, by means of a spatula, and do not melt or run when applied to the skin. In preparing them, care should always be taken to select the oil or lard perfectly free from rancidity. In reference to the wax, too, there would seem to be a choice, as experience has shown that cerates mades with yellow wax keep longer unchanged than those made with white or bleached wax, probably because there is in yellow wax some principle which corrects the tendency of fatty matters to become rancid. The liquefaction should be effected by a very gentle heat, which may be applied by means of a water bath, and during the refrigeration the mixture should be well stirred, and the portions which solidify on the sides of the vessel should be made to mix again with the liquid portion, until the whole assumes the proper consistence, or, as some prefer, the melted cerate is allowed to cool quickly without stirring. When a large quantity is prepared, the mortar or other vessel into which the mixture may be poured for cooling should be previously heated by means of boiling water. It has been proposed to substitute paraffin for wax in the preparation of the cerates, but the great tendency to produce granulation in the finished cerate has largely prevented its use.

It is, we think, unfortunate that this class of preparations has been abandoned in the British Pharmacopœia, the several cerates having been rejected, or transferred to the class of ointments. Independently of the connection between the name and one of the characteristic constituents of the cerates, there is ground for difference between them and the ointments in their consistence, that of the cerates being such as to render them especially suitable for spreading on linen, while that of ointments is peculiarly adapted to inunction. W. H. Mielcke (*Ph. Cb.*, 1881, Nos. 20, 21) proposes a class of preparations, to which he has given the name "*Steatins*," "*Steatinum*." These are of about the consistence of cerates, of varied composition, and contain usually a considerable portion of tallow. The *Steatinum Iodoformi* offers a fair specimen of the class. "Take of mutton tallow 18 parts, expressed oil of nutmeg 2 parts, iodoform, in fine powder, 1 part. Melt the tallow and add the other ingredients." For other formulas, see the N. F. IV (Part III), and *A. J. P.*, 1881, p. 404.

CERATUM. U. S.

CERATE Cerat. [Simple Cerate]

(cę-rā'tŭm)

Ceratum Adipis, *U. S.* 1860; **Ceratum Simplex,** *U. S.* 1850; **Cérat Simple,** *Fr. Cod.;* **Unguentum cereum,** *P. G.;* **Einfaches Cerat, Wachssalbe,** *G.;* **Cerato simple,** *Sp.*

"White Wax, *three hundred grammes* [or 10 ounces av., 255 grains]; Benzoinated Lard, *seven hundred grammes* [or 24 ounces av., 303 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Melt the white wax, by the heat of a water bath, add the benzoinated lard, continue the heat until the mixture is liquefied, strain if necessary, and stir constantly until it congeals. For use in southern latitudes, and during the heated season in other localities, *fifty grammes* [or 1 ounce av., 334 grains] of the benzoinated lard (or more, if necessary) may be replaced by an equal quantity of white wax." *U. S.*

In the U. S. Pharmacopœia (VIII) 20 per cent. of white petrolatum, and 50 per cent. of benzoinated lard were directed in place of the 70 per cent. of lard used in the U. S. P. 1890 process. In the present official cerate the white petrolatum was omitted. In the preparation of cerate, peculiar care should be taken that the oleaginous ingredient be entirely free from rancidity, and that the heat employed be not sufficient to produce the slightest decomposition, for the value of the preparation depends on its perfect blandness. To avoid change, it should be put up in small jars, and covered closely with tin foil so as to exclude the air. It is used for dressing *blisters, wounds,* etc., in all cases in which the object is to prevent the contact of air and preserve the moisture of the part and at the same time to avoid all irritation. It is sometimes improperly employed as the vehicle of substances to be applied by inunction. For this purpose benzoinated lard should be used in winter, and simple ointment in summer, the cerate having too firm a consistence. George W. Sloan recommended the use of simple cerate as a pill excipient for certain oxidizable substances and special uses. (*Proc. A. Ph. A.*, 1884.)

CERATUM CANTHARIDIS. U. S.

CANTHARIDES CERATE Cerat. Canthar. [Blistering Cerate]

(cę-rā'tŭm cąn-thăr'į-dīs)

Emplastrum Cantharidini, *Br.;* **Cantharides Plaster; Emplastrum Epispasticum, s. Vesicatorium, s. Vesicans, Emplastrum Lyttæ; Blistering Cerate or Plaster; Emplâtre Vesicatoire,** *Fr. Cod.;* **Pommade Epispastique, Emplâtre de Cantharides,** *Fr.;* **Emplastrum Cantharidum Ordinarium,** *P. G.;* **Spanischfliegen Pflaster, Blasenpflaster,** *G.;* **Pomata di cantaridi,** *It.;* **Unguento de cantharidas,** *Sp.*

* "Cantharides, in No. 60 powder, *three hundred and fifty grammes* [or 12 ounces av., 151

grains; Glacial Acetic Acid, *twenty-five mils* [or 406 minims]; Oil of Turpentine, *one hundred and fifty mils* [or 5 fluidounces, 35 minims]; Yellow Wax, *one hundred and seventy-five grammes* [or 5 ounces av., 513 grains]; Rosin, *one hundred and seventy-five grammes* [or 5 ounces av., 513 grains]; Benzoinated Lard, *two hundred grammes* [or 7 ounces av., 24 grains], to make *one thousand grammes.* Moisten the cantharides with the oil of turpentine and the glacial acetic acid, previously mixed, and set the mixture aside in a well-covered container, in a warm place, for forty-eight hours. Melt together the rosin, yellow wax, and benzoinated lard; strain the mixture through muslin, add the macerated cantharides and keep the mixture in a liquid condition by heating it on a water bath with occasional stirring, until it is reduced in weight to *one thousand grammes.* Then withdraw the heat and stir the Cerate until it becomes firm." *U. S.*

This is the commonly called *blistering plaster.* As it can be readily spread without the aid of heat, it is properly a cerate, and is, therefore, correctly named in the U. S. Pharmacopœia. The U. S. P. IX has recognized a plaster in which this cerate is spread upon fabric, while the British Pharmacopœia contains a preparation similar to the U. S. cerate, under the title *Emplastrum Cantharidini.* In the Br., however, cantharidin is used instead of cantharides. (See also *Emplastrum Cantharidis.*)

"Cantharidin, 2 *grammes;* Chloroform, 100 *millilitres;* Yellow Beeswax, 450 *grammes;* Wool Fat sufficient to produce 1000 *grammes.* Dissolve the Cantharidin in the Chloroform by the aid of heat, add to the other ingredients previously melted on a water-bath, and stir until cold. This Plaster contains 0.2 per cent. of Cantharidin, which is approximately the proportion contained in the Emplastrum Cantharidis of the British Pharmacopœia, 1898." *Br.*

The process for the cerate, now official, differs from that of previous Pharmacopœias in the use of glacial acetic acid, and oil of turpentine; the previous digestion of the cantharides with this mixed solvent has for its object the softening of the drug and extraction of the cantharidin; the present cerate is somewhat firmer in consistence than that made by the U. S. P., 1890.

There can be no question of the advantage of retaining the cantharides in contact with hot of the cantharidin.

From the experiments of Donovan, and those of Procter (*A. J. P.*, xiii, 302 and xxiv, 296), it may be inferred that the vesicating principle of Spanish flies is not injured or dissipated by a heat under 148.8° C. (300° F.), and that a limited elevated temperature, instead of being hurtful, is positively advantageous in the preparation of the cerate. The cantharidin is thus more thoroughly dissolved by the oleaginous matter, and consequently brought more efficiently into contact with the skin, than when retained in the interior of the tissue of the fly. Another advantage, stated by Donovan, is that the moisture usually existing to a certain extent in all the ingredients of the cerate is thus dissipated, and the preparation is less apt to become mouldy, or otherwise to undergo decomposition. Donovan recommends that, as soon as the other ingredients are melted, the powdered flies should be added, and the mixture stirred until the heat is shown by a thermometer to have risen to 121.1° C. (250° F.), when the vessel is to be removed from the fire, and the mixture stirred constantly until cool. At the heat mentioned, ebullition takes place in consequence of the escape of the moisture contained in the materials. In the cerate thus prepared, the active matter has been dissolved by the lard, and the powder may be separated, if deemed advisable, by straining the mixture before it solidifies. Care should be taken that the temperature be not so high as to decompose the ingredients; and it would be better to keep it within 100° C. (212° F.), by means of a water bath, as in the U. S. process, than to incur any risk from its excess. Violent irritation and even vesication of the face of the operator are stated to have resulted from exposure to the vapors of the liquid, at a temperature of 121.1° C. (250° F.). (*P. J.*, ii, 391.) From an experiment, however, of Procter, it appears that, though cantharidin begins to volatilize slightly at 121.1° C. (250° F.), and rapidly rises in vapor and sublimes at from 205.5° C. to 211.1° C. (402° F.–412° F.), yet it is not decomposed unless by increasing the heat considerably above the last-mentioned point. (*A. J. P.*, xxiv, 296 and 298.) Dieterich states that the activity is greatly increased by the use of acid in the manufacture. Thus, for every 250 Gm. of powdered flies used he adds to the melted mass 1 Gm. sulphuric acid and 10 Gm. alcohol (90 per cent.), keeps the mass for two hours at 70° C. (158° F.), and finally adds 2 Gm. barium carbonate rubbed up with 6 Gm. alcohol. (*Ph. Centralh.*, 1892, 425.) It is desirable that the flies should be very finely pulverized. Coarsely powdered cantharides should not be used, because of the imperfect and unequal distribution of the vesicating agent. Powdered euphorbium is said to be sometimes fraudulently added.

Uses.—The cerate will raise a blister in ordinary conditions of the system, if the flies are good, and not injured in the preparation. It should be spread preferably on soft leather, though linen or even paper will answer the purpose when leather is not to be had. The official directions for this plaster mention the use of the commercial rosin plaster, but further state that it may be spread upon any other suitable material. Heat is not a requisite, and should not be employed in spreading the cerate. Some operators sprinkle powdered flies upon the surface of the plaster, press them lightly with a roller, and then shake off the portion which has not adhered; but, if the flies

originally employed were good, this addition is superfluous. The practice of applying over the surface with a brush an ethereal tincture of cantharides, which leaves a thin coating of extract, renders the preparation more certain.

Previous to the application of the plaster, the skin should be moistened with warm vinegar or other liquid. In adults, when the full action of the flies is desired, and the object is to produce a permanent effect, the application should be continued for eight hours, and on the scalp for twelve hours. In very delicate persons, however, or those subject to strangury, or upon parts of a loose texture, or when the object is merely to produce a blister to be healed as quickly as possible, the plaster should remain no longer than is necessary for the production of full redness of the skin, which generally occurs in five or six hours, or even in a shorter time. It should then be removed, and followed by a flaxseed poultice, or some other emollient dressing, under which the cuticle rises, and a full blister is usually produced. By this management the patient will generally escape strangury, and the blister will very quickly heal after the discharge of the serum. In young children, cantharides sometimes produce alarming and even fatal ulceration, if too long applied, and from two to four hours are usually sufficient for any desirable purpose. When the head, or other hairy part, is to be blistered, an interval of ten or twelve hours should, if possible, be allowed between the shaving of the part and the application of the plaster, so that the abrasions may heal, and some impediment be offered to the absorption of the cantharidin. After the blister has been formed, it should be opened at the most depending parts, and, the cuticle being allowed to remain, should be dressed with simple cerate; but, if it be desirable to maintain the discharge for a short time, rosin cerate should be used, and the cuticle removed if it can be done without inconvenience. When it is wished that the blistered surface should heal as soon as possible, the application of an antiseptic desiccant powder, as iodoform or thymol iodide, is advantageous.

Various preparations of cantharides have been proposed and employed as substitutes for the cerate. They consist for the most part of cantharidin, more or less pure, either dissolved in olive oil, and applied to the skin by means of a piece of paper saturated with it, or incorporated with wax and spread in a very thin layer upon fine waxed cloth, silk, or paper, constituting *blistering cloth, blistering paper, vesicating taffeta,* etc. (See *Emplastrum Cantharidis.*) The advantages of these preparations are that they occupy less space, are more portable, and, being very pliable, are more easily adapted to irregularities of the surface. Absolutely pure cantharidin is expensive and not requisite, as extracts of cantharides, made with ether, alcohol, or boiling water, will answer every purpose. Henry and Guibourt give the following formula. Digest powdered cantharides in ether, distil off the ether, evaporate the residue by means of a salt water bath, until ebullition ceases, melt the mass which remains, with twice its weight of wax, and spread the mixture upon waxed cloth. The *waxed cloth* may be prepared by spreading upon linen or muslin a mixture composed of 8 parts of white wax, 4 of olive oil, and 1 of turpentine, melted together. An extract of cantharides of a buttery consistence, said to act very efficiently when applied by means of paper greased with it, is prepared by digesting 4 parts of flies with one part of strong acetic acid and 16 of alcohol, straining, filtering, and evaporating at a moderate heat. *A cerate of the extract of cantharides* was formerly official (see *U. S. D.,* 18th ed., p. 358.)

A preparation which received the favorable report of a committee of the Society of Pharmacy, at Paris, is the following, proposed by Dubuisson. Four parts of a hydro-alcoholic extract of the flies, made by maceration, are mixed with an aqueous solution of one part of pure gelatin, so as to obtain a solution of suitable consistence, which is then applied upon a piece of stretched waxed cloth, care being taken that the strokes of the brush should always have the same direction. When the first layer has dried, a second and a third are to be applied in the same manner. The gelatin renders the plaster more adhesive and gives consistence. The hydro-alcoholic extract is preferred to the alcoholic, because it contains less of the green oil, which does not readily mix with the other ingredients. The committee, however, preferred the aqueous extract, as cheaper and more active. This taffeta has been tried, and found to raise blisters in four hours. (*J. P. C.,* 3e sér., viii, 67.) For very speedy vesication, an infusion of the flies in strong acetic acid is sometimes employed. None of these preparations are likely to supersede the cerate, but the demand for them was met by introducing into the Pharmacopœia *Collodium Cantharidatum.*

Off. Prep.—Emplastrum Cantharidis, *U. S.*

CERATUM RESINÆ. U. S. (Br.)

ROSIN CERATE Cerat. Res. [Basilicon Ointment]

(cę-rā'tŭm rę-sī'næ)

Unguentum Resinæ, *Br.;* Resin Ointment, Ointment of Resin, Unguentum Basilicum; Unguentum Tetrapharmacum; Resin Ointment, Resin Cerate; Onguent Basilicum, *Fr. Cod.;* Cérat de Résine Anglais, *Fr.;* Harzcerat, Harzsalbe, Königsalbe, Zugsalbe, *G.*

℞ "Rosin, *three hundred and fifty grammes* [or 12 ounces av., 151 grains]; Yellow Wax, *one hundred and fifty grammes* [or 5 ounces av., 127 grains]; Lard, *five hundred grammes* [or 17 ounces av., 279 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Melt the rosin, add the yellow wax and the lard, and continue the heat until liquefied, then strain the liquid through muslin, and allow it to congeal with occasional stirring. In cold weather *five hundred and thirty*

grammes [or 18 ounces av., 304 grains] of lard, and *one hundred and twenty grammes* [or 4 ounces av., 102 grains] of yellow wax may be used." *U. S.*

"Resin, 26 *grammes;* Yellow Beeswax, 26 *grammes;* Olive Oil, 26 *grammes;* Prepared Lard, 22 *grammes.* Melt together; strain; stir until cold. In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

The U. S. preparation does not differ greatly from that formerly official except that occasional stirring while congealing is directed; the U. S. P. 1890 process forbade stirring. The British process (1898) discards the simple ointment and almond oil previously used (1885), and substitutes lard and olive oil. *Ceratum Resinæ Composition*—Compound rosin cerate. *Deshler's Salve* was dropped from the U. S. P. IX. It is retained in the N. F. IV (see Part III). It is made from rosin, yellow wax, prepared suet, turpentine (white) and linseed oil, and is used for the same purposes as Ceratum Resinæ. Rosin cerate, commonly called *basilicon ointment,* is much used as a gently stimulating application to *blistered surfaces, indolent ulcers, burns, scalds,* and *chilblains.* We have found no application more effectual in disposing the *ulcers* which follow *burns* to heal.

Off. Prep.—Linimentum Terebinthinæ, *U. S.*

CERII OXALAS. U. S.

CERIUM OXALATE Cerii Oxal. [Cerous Oxalate]

(cē'rĭ-ī ŏx'ą-lās)

"A mixture of the oxalates of cerium, didymium, lanthanum, and other associated elements." *U. S.*

Oxalate of Cerium; Cerium Oxalicum, Oxalas Cericus; Oxalate de Cérium, *Fr.;* Oxalsaures Ceroxydul, Cerium Oxalat, Ceroxalat, *G.*

Cerium = 140.25, is a metal which was discovered in 1803 by Berzelius and Hisinger, and about the same time by Klaproth, who, however, described it as an earth. By the two former chemists it was recognized as a metal, and named cerium in honor of the goddess Ceres. It was obtained from a Swedish mineral, formerly from its great weight called *heavy stone of Bastnas* (*Bastnas Schwerstein*), but now named *cerite,* after the metal extracted from it. Besides cerite, it has been found in several other minerals, as *gadolinite, orthite,* and *monazite,* etc. It is not easy to obtain it pure in the metallic state, as its oxides and salts are difficult of reduction. Berzelius describes cerium as in the form of pulverulent masses, of a deep chocolate-brown color which exhibit, however, under the burnisher a metallic appearance and a dark gray color. Hildebrand and Norton have since prepared it in large quantity by the electrolysis of its chloride. It is a poor conductor of electricity. Sp. gr. 6.92 at 25° C. (77° F.), melting point 645° C. (1193° F.). Heated in the air it takes fire before the point of ignition, and burns vividly, passing to the state of peroxide. At ordinary temperatures it is oxidized in a moist atmosphere, giving out a strong and disagreeable odor. In water, especially when moderately heated, it rapidly oxidizes, with the evolution of hydrogen and the water does not become alkaline. There are two cerium oxides, Ce_2O_3 and CeO_2. Sulphur and phosphorus combine with it. Of its compounds two only have been introduced into medicine, the nitrate and the oxalate.

Cerium oxalate may be obtained from cerite, and F. F. Mayer gave a process for the purpose, of which the following is an outline. The mineral consists of cerium, lanthanum, and didymium silicates, with numerous other substances in smaller proportion, the cerium oxide constituting about 39 per cent. of the whole. The powdered mineral is made into a paste with sulphuric acid, and then heated over a lamp until the mass ceases to swell and no longer absorbs sulphuric acid very cautiously added. Upon the cooling of the mass, it is powdered, and exposed in a crucible to the heat of an anthracite fire until it assumes a pale brownish-red color. It is now lixiviated first with hot water and then with nitric acid, and the solution treated with hydrogen sulphide in order to get rid of various metals by precipitation. To the clear liquid some hydrochloric acid is first added, and then a solution of oxalic acid, the former of which holds in solution the calcium oxalate produced, the latter throws down cerium oxalates and oxalates of other metals. The precipitate, having been washed with warm water, is formed into a paste with a quantity of magnesium carbonate equal to half that of the mineral employed; and the paste is dried on porous fire brick, finely powdered, and calcined until it becomes of a cinnamon color. It now contains all of the cerium in the form of ceroso-ceric oxide. To separate this the mass is treated with an excess of nitric acid, the solution evaporated to get rid of the excess of acid, then diluted with warm water, and lastly poured into a vessel containing boiling water acidulated with a little more than half of one per cent. of sulphuric acid. A yellow precipitate of basic cerium sulphate is formed, while a little of the neutral sulphate, and all the lanthanum and didymium, remain dissolved. The precipitate is now dissolved in stronger sulphuric acid, the solution digested with a few crystals of sodium thiosulphate, in order to reduce the ceroso-ceric oxide to cerous oxide, and the liquid, having been filtered, is treated with solution of oxalic acid, which causes a precipitate of cerium oxalate. This is washed with warm water, and dried.

The cerium compounds were formerly obtained chiefly from cerite, which occurs in considerable amounts in Sweden, and affords at least 50 per cent. of *cerium oxide.* The thorium salts were obtained from the mineral *thorite,* which is found in Norway, and contains about 60 to 70 per cent. of its peculiar earth. According to O. N. Witt, it was soon found that the supplies of thorite were not sufficient to even approximately meet the de-

mand for thorium salts required for the incandescent gas mantle industry. A new source of supply was therefore sought for, and this has been found in the mineral monazite, which occurs in considerable quantities in North Carolina and in the Province of Bahia, in Brazil. It is from the latter source that the German industries now chiefly draw their supplies. Monazite is a cerous phosphate, in which a portion of the cerium is replaced by the other cerite earths. The thorium earth is not an integral constituent of the mineral, and, although quite regularly admixed with it, its amount varies within very broad limits. It is further stated by Witt that the monazite from Bahia contains at the most from 5 to 6 per cent. of thorium earth, while the earths of the cerite group amount to from 50 to 60 per cent. or more, of which about one-half is cerium itself. The occurrence of these two earths in nature is therefore in inverse proportion to the requirements for industrial purposes. As enormous quantities of monazite have to be worked up in order to obtain the necessary supplies of thorium salts, and as only a very small proportion of the cerite earths which are obtained at the same time can be utilized in the form of cerium nitrate, it is evident that these must accumulate in considerable amounts. It has thus become an important problem, upon which technical chemists have been engaged for some time, to devise a practical method for the separation of the cerite earths, with the hope that they might then find some industrial applications for which the complex mixtures now available are not adapted. From the existing conditions of this industry, as briefly outlined, it may be inferred that the cerium oxalate of commerce, which, although used medicinally, likewise consists of such a complex mixture of the oxalates of cerium, lanthanum, and didymium, is at present more or less a by-product in the manufacture of thorium salts. See Power and Shedden, on the Composition and Determination of Cerium Oxalate. (*J. Soc. Chem. Ind.*, xix, No. 7; also *Ph. Ztg.*, 1902, 297.)

Metallic cerium has come into prominence recently as an essential constituent of a class of alloys known as *pyrophoric alloys*, of which ferro-cerium is the commonest and cheapest. These are used to set fire to inflammable gases, in what are called mechanical or automatic gas lighters, by means of a shower of bright sparks which is emitted when one of these alloys is filed. This property of certain alloys of cerium and other metals was discovered in 1903 by Welsbach, who found the best results to follow the use of a combination carrying about 65 per cent. of cerium earth metals and 35 per cent. of iron. Other alloys have also been experimented with, the one with zinc being used in practice in connection with automatic lighting mine lamps. The greatest pyrophoric power of any alloy yet experimented with was found to be developed in a platinum cerium alloy, but, of course, this is too expensive for practical use. Various theories have been advanced to explain the reason for the spark producing power of these alloys, it being claimed that the property is due to the presence of nitrides, hydrides, etc. None of these theories have been substantiated and the cause remains a mystery.

Properties.—It is officially described as "a fine white or slightly pink powder, without odor or taste; permanent in the air. It is insoluble in water, alcohol, ether, and in solutions of potassium or sodium hydroxide; insoluble in cold, diluted sulphuric or hydrochloric acid, but dissolved by these acids when heated. When heated to redness it is decomposed, leaving not less than 47 per cent. of a reddish-brown residue. Boil Cerium Oxalate with potassium hydroxide T.S.; an insoluble precipitate of white hydroxides is produced. Filter and supersaturate the filtrate with acetic acid; the addition of calcium chloride T.S. produces a white precipitate, insoluble in acetic acid but soluble in hydrochloric acid. From a solution of Cerium Oxalate in diluted hydrochloric or sulphuric acid, potassium hydroxide T.S., added in slight excess, precipitates white hydroxides, which do not redissolve in a larger excess of the reagent, but gradually turn yellow in contact with air. Ammonium carbonate T.S. added in slight excess to a similar acid solution produces a white precipitate of the mixed carbonates of cerium and associated elements, which is somewhat soluble in a larger excess of the reagent. Dissolve 0.1 Gm. of Cerium Oxalate in 1 mil of sulphuric acid and add 2 mils of potassium sulphate T.S.; small, colorless crystals of double sulphates of potassium and the rare-earth elements in the mixture are deposited after some time. No effervescence occurs when Cerium Oxalate is dissolved in diluted hydrochloric acid (*carbonates*). A solution of Cerium Oxalate (1 in 50) in diluted hydrochloric acid does not respond to the Test for heavy metals (see Part III, Test No. 3). A solution of Cerium Oxalate (1 in 25) in hot dilute sulphuric acid (1 in 3) meets the requirements of the Test for arsenic (see Part III, Test No. 1). Boil 0.3 Gm. of Cerium Oxalate with 15 mils of potassium hydroxide T.S. and filter. No precipitate is produced in 5 mils of the filtrate by boiling with an excess of ammonium chloride T.S. (*aluminum*) or in another 5 mil portion of the filtrate by the addition of sodium sulphide T.S. (*zinc*)." *U. S.*

As usually seen in commerce it has a pinkish tinge, due to the presence of a trace of a compound of didymium. The British Pharmacopœia, 1898, state that it was "an almost white granular powder, insoluble in *water*, decomposed at a dull red heat, yielding a reddish-brown powder which dissolves completely and without effervescence in boiling *hydrochloric acid;* the resulting solution gives with a saturated solution of *potassium sulphate* a white crystalline precipitate. When incinerated it loses 53 per cent. in weight. It should yield no characteristic reaction with the tests for arsenium, iron, aluminium, zinc, calcium, carbonates, or phosphates."

Uses.—Bachem (*A. I. P. T.*, xvii, p. 363)

has shown that cerium, didymium and lanthanum are all practically non-toxic although some of their salts possess antiseptic virtues. The commercial cerium oxalate being almost insoluble is not absorbed when given by the mouth and escapes wholly through the feces. It was originally brought forward by Sir James Y. Simpson as a remedy for the *vomiting of pregnancy* and has been used extensively in this affection and also in various other gastric disturbances attended with vomiting. Baehr and Wessler (*A. in M.*, 1909) have shown, however, that it has no effect in vomiting which is of central origin. Its value as an antemetic is probably precisely parallel to that of the insoluble salts of bismuth; when used in large quantities it forms a protective coating over the mucous membrane of the stomach.

The soluble cerium nitrate was believed by Simpson to be a nerve tonic and useful in irritable *dyspepsia* and chronic *vomiting* in doses of from one-half to one grain (0.032–0.065 Gm.).

Dose of cerium oxalate, one to ten grains (0.065–0.65 Gm.) three or more times a day.

CETACEUM. U. S., Br.

SPERMACETI Cetac.

(cē-tā′cē-ŭm)

"A concrete, fatty substance, obtained from the head of the sperm whale, *Physeter macrocephalus* Linné (Fam. *Physeteridæ*)." *U. S.* "Spermaceti is a solid wax obtained from the Sperm Whale, Physeter macrocephalus, *Linn.*, and possibly other species." *Br.*

Blanc de Baleine ou Cétine, *Fr. Cod.*; Spermacéti, Cétine, Ambre Blanc, *Fr.*; Cetaceum, *P. G.*; Walrat, Wallrath, Spermaceti, *G.*; Cetina, Spermaceti, *It.*; Esperma de ballena, Sperma ceti, *Sp.*

The spermaceti whale is from sixty to eighty feet long, with an enormous head, not less in its largest part than thirty feet in circumference, and constituting one-third of the whole length of the body. The upper part of the head is occupied by large cavities, separated by cartilaginous partitions, and containing an oily liquid, which, after the death of the animal, concretes into a white spongy mass consisting of spermaceti mixed with oil. This mass is removed, and the oil allowed to separate by draining. The crude spermaceti obtained from a whale of the ordinary size is more than sufficient to fill twelve large barrels. It still contains much oil and other impurities, from which it is freed by expression, washing with hot water, melting, straining, and repeated washing with a weak boiling potash lye. Common whale oil and the oil of other cetaceous animals contain small quantities of spermaceti, which they slowly deposit on standing. According to W. Gilmour, *sperm oil* should contain not less than 4 per cent. of cetin, and if much less be obtained by the following process, adulteration has been practised. Shake one part by weight of sulphuric acid (sp. gr. 1.84) with four parts of the oil; allow to stand 20 minutes, shaking twice; add three parts of distilled water; shake this thoroughly, and allow to stand from 16 to 20 hours; dilute with 3 or 4 times its volume of distilled water; agitate thoroughly. On standing, the cetin floats upon the top, and can readily be skimmed off, washed, dried, and weighed. (*P. J.*, vii, 328. See also *Chem. Ztg.*, 1893, 1453, and *Am. Drug.*, 1895, 105.)

Properties.—Spermaceti is officially described as in "white, somewhat translucent, slightly unctuous masses, with a scaly, crystalline fracture, a pearly luster, a very faint odor and a bland, mild taste. It becomes yellowish in color and rancid on prolonged exposure to air. It is insoluble in water and nearly so in cold alcohol; soluble in boiling alcohol, in ether, chloroform, carbon disulphide, or fixed or volatile oils; only slightly soluble in cold petroleum benzin. Specific gravity: 0.938 to 0.944 at 25° C. (77° F.) as determined by the method given under *Cera Flava*. It melts between 42° and 50° C. (107.6° and 122° F.). It dissolves completely in 50 parts of boiling alcohol (*paraffin*), and the solution is neutral or not more than slightly acid to moistened litmus paper. Warm a mixture of about 1 Gm. of Spermaceti and 10 mils of ammonia water until the Spermaceti is melted, then shake it thoroughly in a stoppered vessel for a few minutes, cool and filter. The filtrate, upon supersaturation with hydrochloric acid, may become turbid, but yields no precipitate (*stearic acid*)." *U. S.*

"Translucent, pearly-white, glistening masses, with a leafy, crystalline structure; slightly unctuous to the touch. Almost inodorous. Specific gravity 0.950 to 0.960; *acid value* not more than 1.0; *saponification value* 125 to 136; *iodine value* 3 to 4.4; *refractive index* at 80° C. (176° F.) about 1.4330. Soluble in 50 parts of hot *alcohol* (90 per cent.), the greater proportion separating again in thin laminæ on cooling. Reducible to powder with the aid of a little *alcohol* (90 per cent.). When 1 gramme is boiled with 10 millilitres of *alcohol* (90 per cent.) for one minute, and the mixture cooled to, and filtered at 0° C. (32° F.) the filtrate when poured into *water* may become opalescent, but does not afford a precipitate (absence of stearic acid)." *Br.*

As found in commerce it is not chemically pure, containing a fixed oil, and often a peculiar coloring principle. From these it is separated by boiling in alcohol, which on cooling deposits it in crystalline scales. Thus purified, it does not melt under 49° C. (120° F.), is soluble in 40 parts of boiling alcohol of the sp. gr. 0.821 (Thénard), and is harder, more shining, and less unctuous than ordinary spermaceti. Spermaceti is a mixture of various fats. When recrystallized from alcohol as just described, the purified *cetin* is obtained, while the alcohol on evaporation deposits an oil (mechanically admixed sperm oil). The cetin which crystallizes out of the alcohol is essentially *cetyl palmitate*, $C_{16}H_{33}(C_{16}H_{31}O_2)$—that is, a compound of *cetyl alcohol* (*ethal* of Chevreul), $C_{16}H_{33}.OH$, and *palmitic acid*, $C_{16}H_{32}O_2$. According to Heintz, however, there

are small amounts of other fats with the cetin; fats containing the acids *stearic*, $C_{18}H_{36}O_2$, *myristic*, $C_{14}H_{28}O_2$, and *lauro-stearic*, $C_{12}H_{24}O_2$, and the alcohol radicals corresponding to these acids.

L. F. Kebler, after examining about twenty samples of spermaceti, found that commercial specimens have a melting point of from 42° to 47° C. (107.6°–116.6° F.), a specific gravity ranging from 0.905 to 0.945 at 15° C. (59° F.) and saponification numbers from 125.8 to 134.6. (*A. J. P.*, 1896, 7, and 1897, 104.)

Uses.—Spermaceti exercises emollient effects like other fatty substances, but it has no other remedial properties. It is used chiefly to add firmness to ointment bases. It may be reduced to powder by the addition of a little alcohol or almond oil, or by melting it at a very low heat, pouring into a warm mortar, and agitating it until perfectly cold; an emulsion may be made by mixing spermaceti first with half its weight of olive oil, then with powdered gum arabic, and lastly with water. Spermaceti Cerate (*Ceratum Cetacei*, U. S. 1890) was made by melting together 10 parts of spermaceti and 35 parts of white wax and then adding 55 parts of warmed olive oil.

Off. Prep.—Unguentum Aquæ Rosæ, *U. S., Br.;* Unguentum Capsici, *Br.;* Unguentum Cetacei, *Br.*

CHIRATA. Br.

CHIRETTA

(chĭ-rā'tą)

"Chiretta is the plant, Swertia Chirata, *Buch.-Ham.*, collected when in flower, and dried." *Br.* "The dried plant of *Swertia Chirayita* (Roxburgh) Hamilton (Fam. *Gentianaceæ*)." *N. F.*

East Indian Balmony; Chiretta; Chirette, *Fr.;* Chiretta Ostindischer Enzian, *G.*

Chirata was for many years official in the U. S. Pharmacopœia and is still retained by the British authority and in the N. F. According to Lloyd, this drug has long been held in esteem by the Hindoos. It first attracted attention in England in 1829 and was introduced into the Edinburgh Pharmacopœia in 1839.

Swertia Chirayita (Roxb.), Hamilton (*Ophelia Chirata*, Griesbach).—The *chirayta*, or *chirata*, is an annual plant, about three feet high, with a branching oblique root, and an erect, smooth, slightly winged branching stem, and furnished with opposite, lanceolate, very acute, entire, smooth, three or five-nerved leaves. The flowers are numerous, peduncled, yellow, with a four-cleft calyx having linear acute divisions, the limb of the corolla spreading and four-parted, four stamens, a single style, and a two-lobed stigma. The capsules are unilocular. The plant is a native of Nepaul and other parts of Northern India. The whole of it is gathered when the flowers are well advanced. In the Indian bazaars the name chirata is applied to various dried gentianaceous plants; the most important of these is the *Ophelia angustifolia* (Buch.-Ham.). It yields the *Paharee* or *Hill chirata*, which is distinguished by its inferior bitterness, and its rectangular, winged stems, whose section presents a thick woody ring and a centre nearly or entirely hollow, with only traces of pith. A false chirata, which also found its way into the London markets, and resembles the official variety in having a well developed pith, but which is completely lacking in bitterness, is affirmed to be the product of *Ophelia alata*. (*P. J.*, xvii, 903.) Under the name of *Indian chirata*, the dried plant of the *Andrographis paniculata* Nees has appeared in the London market. It resembles much more closely recently dried broom tops than the true chirata. It is a little more than two feet long. The branching stems are from ⅛ to ¼ inch in thickness near the base, woody, quadrangular, furrowed, smooth, slightly knotted at the point from which the branches spring, the longitudinal furrows are continued through the roots, which have numerous fine radicles, the leaves are opposite decussate, branches erect or forming an acute angle with the stem, terminal shoots extremely slender.

The dried plant is imported into Europe in bundles, consisting mainly of the stems, with portions of the root attached. The stems contain a yellowish pith. The drug is officially described as "Stem about one metre long, smooth, brown, or purplish-brown, slightly winged and much branched above, rounded below and containing a large, continuous, easily separable pith. Root oblique. Branches slender, elongated, decussate. Leaves opposite, ovate, glabrous, entire, usually with three to seven lateral veins. Flowers small, numerous, panicled. Fruits superior, bicarpellary, unilocular. No odor; taste extremely bitter." *Br.*

It is described in the N. F. as "smooth, root simple, about 7 mm. in thickness near the crown, stem about 1 M. in length, externally yellowish- or purplish-brown; cylindrical near the base, quadrangular and slightly winged above, with numerous opposite, ascending branches; wood yellowish, thin, enclosing usually a large yellowish easily separable pith; leaves opposite, sessile, ovate-lanceolate, entire, five nerved, about 6 cm. in length; flowers numerous, panicled, small, with a four-lobed calyx and corolla, capsule ovoid, acute, one-celled, many-seeded. Odor slight; taste intensely bitter. Chirata yields not more than 6 per cent. of ash." *N. F.*

The virtues of chirata are imparted to water and alcohol, and are retained in the extract. According to Lassaigne and Boissel, the stems contain resin, a yellow bitter substance, brown coloring matter, gum, and various salts. Flückiger and Höhn, who subsequently examined the stems and roots of chirata, extracted from them sugar, wax, chlorophyll, soft resin, tannin, an acid which they name *ophelic*, possessing the formula $C_{13}H_{20}O_{10}$, and a peculiar bitter substance, denominated *chiratin*, $C_{26}H_{48}O_{15}$. The acid is syrupy, deliquescent, yellowish-brown, at first slightly sour, afterwards intensely bitter. It is soluble in water, with some turbidness, probably owing to resin mixed with it, and com-

pletely soluble in alcohol, or a mixture of this with ether. It decomposes certain salts, and forms amorphous compounds with acids. Chiratin is a yellow, hygroscopic powder, but feebly crystallizable, very bitter, sparingly soluble in cold water, more so in hot water, and readily dissolved by alcohol and ether. It is neutral to test paper, and yields a copious precipitate with tannic acid. By the action of acids, chiratin is separated into ophelic acid, and a yellowish-brown, amorphous substance, bitter, scarcely soluble in water, readily soluble in alcohol, and not reducing copper solutions, as the ophelic acid does. Höhn gives it the formula $C_{13}H_{24}O_3$, and names it *chiratogenin*.

Uses.—Chirata has long been used in India. It has been introduced into Europe, and appears to be highly esteemed, but has not been employed to any considerable extent in this country. Its properties are those of the pure bitters, and probably do not differ from those of the other members of the family of *Gentianaceæ*. (See *Gentiana*.) Like these, in overdoses it nauseates and oppresses the stomach. Some have supposed that, in addition to its tonic properties, it exerts a peculiar influence over the liver, promoting the secretion of bile and correcting it when deranged, and restoring healthy evacuations in cases of habitual costiveness. It has been used in *dyspepsia*, and in the *debility* of convalescence, and generally in cases in which corroborant measures are indicated. In India it has been employed in *intermittents* and *remittents*, combined with the seeds of *Guilandina Bonducella* L. It may be given in powder, infusion, tincture, or fluidextract.

Dose, ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Infusum Chiratæ, *Br.*; Tinctura Chiratæ, *Br.*; Fluidextractum Chiratæ, *N. F.*

CHLORAL FORMAMIDUM. Br.

CHLORAL FORMAMIDE [Chloralamide]

(ȼhlō'rạl för-mạ-mī'dŭm)

"Chloral Formamide, $C_3H_4Cl_3NO_2$, may be obtained by the direct combination of formamide with anhydrous chloral. Should be preserved in amber-colored bottles." *Br.* "A crystalline solid [$CCl_3.CH(OH)NH.COH$], made by the direct union of formamide with anhydrous chloral. It should be kept in amber-colored, well-stoppered vials. "*U. S.* VIII.

Chloralamide; Chloralum formamidatum, *P. G.*; Chloralformamid, *G.*

Chloralformamide was dropped from the U. S. P. IX. It is made by mixing 45 Gm. of formamide with 147 Gm. of anhydrous chloral, when combination ensues; the crystalline mass is purified by recrystallization.

Properties.—Chloralformamide is officially described in the Br. Pharm. as in "colorless lustrous crystals. No odor; taste slightly bitter. Soluble in 21 parts of *water;* very soluble in *alcohol* (90 per cent.), the solution being neutral to *litmus;* very soluble in *ether;* slowly soluble in 12 parts of *glycerin.* Melting point 114° to 115° C. (237.2°–239° F.); decomposes at a higher temperature. Hydrolyses in aqueous solution at 60° C. (140° F.), yielding chloral hydrate and formamide. Unaffected by dilute acids, but decomposed when warmed with *solution of sodium hydroxide,* chloroform separating and ammonia and sodium formate being produced. Heated with free access of air it volatilises completely without the evolution of inflammable vapors (absence of certain organic impurities). Its solution in *alcohol* (90 per cent.) is not immediately altered in appearance by *solution of silver nitrate* (absence of certain decomposition products)." *Br.*

Chloralimide, $CCl_3.CH{=}NH$, should not be confounded with chloralamide. Chloralimide is in colorless, inodorous, and insipid, long crystalline needles; melting at about 166° C. (330.8° F.); insoluble in water; readily soluble in alcohol, in ether, in chloroform, and in oils. Concerning its physiological action we have no certain knowledge; it is asserted to be hypnotic in doses of from fifteen to sixty grains (1 to 3.9 Gm.).

Uses.—Locally, chloralformamide is scarcely at all irritant, and when taken internally is quickly absorbed and is eliminated chiefly as urochloralic acid. When given to the lower animals, it produces lethargy, sleep, muscular relaxation, arrested respiration, followed by coma, failing respiration, and, if the dose has been sufficient, death by centric respiratory paralysis. As shown by the experiments of H. C. Wood and Cerna, subsequently confirmed by various observers, its influence upon the circulation and the spinal cord is extremely feeble, and it has no perceptible effect upon the nerve trunks and the muscles. As an hypnotic it resembles hydrated chloral, but its action is more slowly developed and is less positive. Confusion, giddiness and headache are the only unpleasant effects following its use, and they rarely occur.

Dose, fifteen to forty-five grains (0.9–3.0 Gm.), half an hour before the desired time of sleep.

CHLORALUM HYDRATUM. U. S. (Br.)

HYDRATED CHLORAL Chloral. Hydrat. [Chloral, U. S. 1890, Chloral Hydrate]

(ȼhlō'rạl-ŭm hȳ-drā'tŭm)

"A compound of trichloraldehyde or chloral, with the elements of one molecule of water. It contains not less than 99.5 per cent. of $C_2HCl_3O + H_2O$ or $CCl_3.COH + H_2O$ (165.4). Preserve it in tightly-stoppered bottles, in a cool place, protected from light." *U. S.* "Chloral Hydrate, $C_2Cl_3H_3O_2$, may be obtained by the addition of water to the liquid chloral, C_2Cl_3HO, produced by the action of dry chlorine gas on ethylic alcohol." *Br.*

Chloral Hydras, *Br.*; Trichloraldehyd Hydrate, Trichlorethylidene Glycol; Hydrous Chloral; Chloral Hydraté *Fr. Cod.*; Hydrate de Chloral, *Fr.*; Chloralum Hydratum, *P. G.*; Chloral hydrat, *G.*; Cloralio idrato, *It.*; Hidrato de cloral, *Sp.*

Perhaps no medicine ever came so rapidly into extensive use as that now under consideration. Though discovered by Liebig in 1832, it was not until 1869 that its remedial properties were first made known by their discoverer, Otto Liebreich of Berlin; in 1878 the consumption of chloral was estimated at one ton daily in England and America alone; and, although not used now to this extent, it is still largely employed.

Anhydrous Chloral.—In preparing anhydrous chloral, the simple method originally employed by Liebig, of acting directly on alcohol by chlorine, is generally preferred, even, we believe, by the larger manufacturers. The following details of the manufacture of hydrated chloral as carried out on a commercial scale have been supplied by E. Schering of Berlin, who has been for years the largest manufacturer of it.

Absolute alcohol, in lots of 50 pounds each, is placed in large glass flasks and saturated with chlorine, which is passed in a continuous stream for 6 to 8 weeks. The chlorine is led into cold alcohol at first, and when no more is is absorbed, the alcohol is heated at first gently and then to 60° C. (140° F.). When saturated, the mixture formed, in which the chloral now exists as chloral alcoholate, is agitated with sulphuric acid at a temperature of 60° C. (140° F.) for several hours, during which time most of the hydrochloric acid escapes. The separated chloral is then rectified over calcium carbonate. The pure chloral so obtained is then mixed in glass flasks with the necessary amount of water, and the resulting hydrated chloral either cast into cakes or purified by crystallization. As solvents for this purpose certain of the side products of the chloral manufacture, after being purified and rectified, are used, for instance, ethylene and ethylidene chlorides; or in their absence chloroform is used; petroleum benzin and carbon disulphide have also been recommended. The action of chlorine upon alcohol is said to be aided by the presence of "chlorine carriers," such as iodine, ferric chloride, thallium chloride, etc. The formula of anhydrous chloral is C_2Cl_3HO; in other words, aldehyde, C_2H_4O, in which 3 atoms of hydrogen have been replaced by 3 atoms of chlorine. The name of chloral was derived from the *chlor*ine and *al*cohol from which it is formed. The anhydrous chloral thus formed is a colorless liquid, of penetrating disagreeable odor, of little taste, of the sp. gr. 1.502, and boiling at 94° C. (201.2° F.). It is soluble in ether or chloroform without change. According to A. Trillat, in the formation of chloral from alcohol, the latter is first changed by the action of the chlorine into aldehyde; this unites with alcohol to form acetal, which is changed successively into mono-, di-, and trichloracetal; the action of hydrochloric acid decomposes this latter with the formation of chloral alcoholate and ethyl chloride; sulphuric acid decomposes the alcoholate, liberating chloral, which then is made to combine with water to form the crystalline hydrated chloral. (*Bulletin*, 1897, 17, 230.) As the union of hydrated chloral with water develops heat, it is supposed to be more than the formation of a hydrate, and the formula $CCl_3.CH{-}OH$ is assigned to the

$$\diagdown OH$$

resulting compound. It does not show all the reactions of an aldehyde, as, for example, the red color of a magenta solution that has been decolorized with sulphurous acid, is not restored by it.

Meta-chloral.—By continued contact of anhydrous chloral and concentrated sulphuric acid, a change is effected in the chloral, by which it becomes a solid insoluble in water, which is designated as *insoluble chloral*, or *meta-chloral*. It is tasteless, of a white color resembling porcelain, and insoluble in alcohol and ether. Its formula is $C_6H_3Cl_9O_3$, being formed by the union of three molecules of chloral. It is stated that when perfectly pure, chloral does not become polymerized; the change is also said to be prevented by the addition of a little chloroform. When heated to 180° C. (356° F.), metal-chloral distils with reversion to liquid chloral. (Allen, *Com. Org. Anal.*, 2d ed., i, p. 171.)

Chloral Alcoholate.—A compound obtained by Roussin, which he announced as pure hydrated chloral, was found by Personne to contain no water, but to be in fact a compound of alcohol and chloral, and is now known by the name of *chloral alcoholate*, C_2HCl_3O,C_2H_6O. It results directly from the action of absolute alcohol on anhydrous chloral, and is now known to be formed as a stage in the manufacture of chloral from alcohol. As it is very likely to be confounded with hydrated chloral, the following points of difference should be noted. It forms white crystals melting at 46° C. (114.8° F.), and boils at 113.5° C. (236.3° F.), while hydrated chloral crystals melt at 58° C. (136.4° F.), and boiling at 97.5° C. (207.5° F.); chloral alcoholate melts without complete solution when warmed with two volumes of water, and, on cooling, congeals below the surface of the water, while hydrated chloral is soluble in one and one-half times its weight of water; chloral alcoholate, gently heated with nitric acid of 1.2 sp. gr., is violently attacked, while hydrated chloral is scarcely acted on; chloral alcoholate, when heated on platinum foil, inflames readily, while hydrated chloral scarcely burns. (Allen, *Com. Org. Anal.*, 2d ed., i, p. 172.)

The three related products, *anhydrous chloral*, polymeric *meta-chloral*, and *alcoholate*, described above, have been more or less introduced into the European markets, and have required some notice to prevent them from being confounded with hydrated chloral, which is alone official. The following observations will be confined to this last compound, and the reader will note that whether the simple term chloral, or the exact designation, hydrated chloral, is used, the same substance is intended.

Properties of Hydrated Chloral.—This is made by simply mixing anhydrous chloral

with water. Acicular crystals soon form, which result from the union of a molecule each of the chloral and water, constituting hydrated chloral. As employed in the United States, this comes from Europe. It was at one time made in this country by E. R. Squibb of Brooklyn. It occurs in commerce mainly in two forms; in distinct crystals, which is the official form, or in crystalline plates, about three lines in thickness, broken into small, irregular pieces, so as to be readily introduced into broad-mouthed bottles. These pieces, while retaining their tabular form, are somewhat translucent, but usually covered with a white powder, which somewhat conceals that property. This is the more common form and the cheaper; but the crystals are to be preferred, as their purity may be relied on. Guerin adds his testimony to the necessity for dispensing only hydrated chloral which has been recrystallized and which is in the form of distinct crystals. He examined many samples, and found acidity in the cake variety, due, as he believes, to the formation of hydrochloric and formic acids, produced by the action of water retained in the cake during the manufacture, and this remaining in contact with the crystals excites decomposition.

Hydrated chloral is white, possessing a peculiar pungent odor, and an acrid pungent taste, especially affecting the velum pendulum. The odor has been compared to that of an overripe melon. Exposed to the air it very slowly volatilizes, and, like camphor, when enclosed in a bottle, covers the interior surface with numerous minute crystals. The boiling point of the pure crystals is 97.5° C. (207.5° F.). If the boiling point be under 95° C. (203° F.), it indicates an under-hydrated preparation; if above 98° C. (208.4° F.), an over-hydrated one. (E. R. Squibb.) The pure hydrated chloral does not take fire when heated in a spoon, but evaporates without residue. With the aid of heat, its solution may be effected readily in chloroform; and the solution, on cooling, deposits it in beautiful crystals, which are generally needle-shaped, while those deposited from a solution in carbon disulphide are prisms. The aqueous solution is prone to decomposition, which is ultimately attended with the development of low organisms. Hydrated chloral should not, therefore, be kept long in this state. (E. Labbée, *A. G. M.*, Sept. 1, 1870.)

In its relation to acids and alkalies it is neutral or, according to E. Schering, slightly acid when perfectly pure. When equal parts of hydrated chloral in crystals and of camphor in small fragments are shaken together in a bottle, and allowed to stand, they liquefy, forming a clear solution. When hydrated chloral and sulphuric acid are mixed, the temperature is greatly reduced. A solution of hydrated chloral dissolves morphine, quinine, and most of the vegetable alkaloids. (R. F. Fairthorne, *A. J. P.*, Oct., 1871, p. 447.) When ammonium sulphide is added to an aqueous solution of hydrated chloral, the mixture rapidly turns yellow, and, after passing through several shades of color, finally becomes dark brown. From this liquid diluted sulphuric acid throws down a bulky brown precipitate. This, purified from precipitated sulphur and dried, is a light-brown powder of the composition $C_{18}H_{24}S_{13}N_4O_6$. Hydrogen sulphide gas forms a sulphydrate by its action on hydrated chloral. These reactions are important, as the detection of metallic poisons in toxicological cases by hydrogen sulphide has been complicated by the presence of hydrated chloral. A still more important chemical reaction of hydrated chloral is that which takes place when the hydrated, or either of its other forms, is placed under the influence of an alkali. Chloroform is developed, and along with it a formate of the alkali employed. Thus, in a strong solution of potassium hydroxide, put a pinch of powdered hydrated chloral, and almost instantly the odor of chloroform becomes sensible, and some oil-like globules of chloroform may be seen at the bottom of the vessel. The reaction is as follows:

$C_2HCl_3O.H_2O$	+	KOH	=
Hydrated chloral		potassium hydroxide	
$CHCl_3$	+ $CHO.OK$	+	H_2O
chloroform	potassium formate		water

This relation of hydrated chloral to chloroform would serve as a ready test of the former, and may be used also to determine its quality, for pure hydrated chloral ought by calculation to yield 76.35 per cent. of chloroform, and the best known yields, according to the table of Mason, 71.5 (72.20 Selden) per cent. If, therefore, the product of chloroform should fall much below the latter percentage, the parcel acted on is probably impure. For other methods of assaying hydrated chloral see Allen, *Com. Org. Anal.*, i, pp. 174 and 175. The following description and tests are given in the U. S. Pharmacopœia: "Hydrated Chloral occurs in rhomboidal, colorless, transparent crystals which do not readily attract moisture. It has an aromatic, penetrating, and slightly acrid odor, and a bitterish, caustic taste. It is slowly volatilized when exposed to the air. One Gm. of Hydrated Chloral dissolves in 0.25 mil of water, 1.3 mils of alcohol, 2 mils of chloroform, and 1.5 mils of ether at 25° C. (77° F.); very soluble in olive oil, freely soluble in oil of turpentine. Hydrated Chloral is decomposed by caustic alkalies, alkaline earths, and ammonia, chloroform and a formate of the base being produced. When warmed with a few drops of aniline and sodium hydroxide T.S., the intensely disagreeable odor of phenylisocyanide is produced. Gently ignite 2 Gm. of Hydrated Chloral; no inflammable vapors are evolved (distinction from *chloral alcoholate and ethyl carbamate*). On complete incineration not more than 0.05 per cent. of ash remains. Ten mils of an alcoholic solution of Hydrated Chloral (1 in 20) does not at once redden moistened blue litmus paper, nor at once become opalescent on the addition of a few drops of silver nitrate

T.S. (*hydrochloric acid and chlorides*). Shake about 0.5 Gm. of Hydrated Chloral, at intervals of five minutes during one hour, with 5 mils of sulphuric acid in a glass-stoppered tube, which has previously been rinsed with sulphuric acid. The acid remains colorless, or very nearly so when viewed transversely in a tube of about 20 mm. diameter (*organic impurities*)." *U. S.*

"In colorless, non-deliquescent, nonoclinic plates. Pungent, but not acrid odor; taste pungent and rather bitter. Soluble in less than 1 part of *water, alcohol* (90 per cent.), or *ether,* and in 3 parts of *chloroform.* Aqueous solution neutral or only slightly acid to *litmus.* Melting point 49° to 53° C. (120.2°–127.4° F.); at a slightly higher temperature it volatilises without residue. Decomposed by alkalies with liberation of chloroform. A solution in *chloroform,* shaken with *sulphuric acid,* imparts no color to the acid (absence of certain organic impurities). When 1 gramme of Chloral Hydrate is warmed with 6 millilitres of *water* and 0.5 millilitre of *solution of sodium hydroxide,* the mixture filtered, sufficient *N/10 solution of iodine* added to impart a deep brown color, and the whole set aside for an hour, no yellow crystalline precipitate is produced (absence of chloral alcoholate). Its aqueous solution yields no precipitate with *solution of silver nitrate* (absence of free chlorides.)" *Br.*

The most delicate test for the presence of chloral alcoholate in hydrated chloral is said to be that with nitric acid. When 1 mil of nitric acid (1.38 sp. gr.) is poured over 1 Gm. of hydrated chloral a yellow color should not appear within 10 minutes, even if the mixture be warmed. (*A. J. P.,* 1894, 191.) For other tests for hydrated chloral by Jaworowski, the reader is referred to *Ph. Z. R.,* 1894, 373.

"**Assay.**—Dissolve about 4 Gm. of Hydrated Chloral, accurately weighed, in 10 mils of distilled water, add 30 mils of normal potassium hydroxide V.S., and allow the mixture to stand two minutes; then add phenolphthalein T.S., and determine the residual alkali at once by titration with normal sulphuric acid V.S. It shows not less than 99.5 per cent. of $C_2HCl_3O+H_2O$. Each mil of normal potassium hydroxide V.S. consumed corresponds to 0.1654 Gm. of $C_2HCl_3O+H_2O$. Each gramme of Hydrated Chloral corresponds to not less than 6.02 mils of normal potassium hydroxide V.S." *U. S.*

Uses.—The physiological action of hydrated chloral may be summed up as follows:—its dominant effect is to depress the centers of consciousness, the soundness of the sleep produced being proportional to the quantity ingested. In somewhat larger doses it is depressant to the motor side of the spinal cord and respiratory center but the sensory apparatus is unaffected except after poisonous doses. In full dose it tends to lower blood pressure probably chiefly through an action upon the vasomotor center, although after large quantities there is a direct depressant influence upon the heart muscle. In poisonous doses it produces profound coma with anesthesia. After fatal quantities death is generally due to stoppage of the respiration through paralysis of the nerve centers, although sometimes due to sudden heart failure. Chloral has little effect on the secretions, although it is stated to somewhat increase the flow of urine. It escapes from the body through the kidneys, probably in part unchanged, although partially in the form of urochloralic acid. This latter body has the property of reducing Fehling's solution. The theory of Liebreich which led to the introduction of this drug into medicine, that it was decomposed by the alkalies of the body with the gradual liberation of chloroform, has been abundantly disproven.

Hydrated chloral is used internally in medicine as a somnifacient, as an antispasmodic, and externally as a local anesthetic, disinfectant and deodorizer. For the relief of *insomnia* not caused by pain it is one of the most certain hypnotics which we possess and is therefore especially employed in the more obstinate forms of sleeplessness such as in *delirium tremens* and certain types of *insanity.* Its action is very prompt, sleep generally beginning within fifteen minutes or half an hour after its oral administration. The effects, however, do not usually last over three or four hours. When the wakefulness is caused by pain it is greatly inferior to the opiates but even here is often of service as an adjuvant. In cases of circulatory weakness it should be used always with great caution if at all, on account of its liability to depress the heart. As a somnifacient it is rarely necessary to give more than 15 grains at a dose.

It is also a remedy of great value in the treatment of various *convulsive disorders.* The determination whether or not to administer chloral in an individual case should be based upon the severity, rather than the type, of the convulsions, thus in *tetanus* and *strychnine poisoning* in which death may be the direct result of the spasm, it is one of the most frequently employed of remedies and justly so. On the other hand, in *epilepsy* ordinarily the convulsions are of no importance and, as the chloral does not lessen the convulsive tendency, it is not often of service; but in the condition known as *status epilepticus* it may prove of great value. It is also occasionally demanded in severe cases of *hysteria* and *chorea.* Certain local spasms, such as *laryngismus stridulus, asthma,* and *hiccough,* are at times greatly benefited by its employment.

Locally it is used to a larger extent in combination with camphor or methyl salicylate as an anodyne and counter-irritant. Occasionally it is employed as a stimulating antiseptic to *wounds,* although its antibacterial powers are comparatively feeble. It has, however, been highly recommended by Siegmund (*Th. M.,* 1909) as a deodorizant in *gangrene of the lung* and various other malodorous conditions. It is said also that it is valuable for washing the hands after post-mortem examinations, acting both as a disinfectant and deodorizer. A two per cent. solution has been recommended by Quincke as a spray in *tonsilitis* and other in-

flamed conditions of the oral or nasal cavities.

Occasionally hydrated chloral in even not excessively large doses may produce very unpleasant symptoms, such as various skin lesions or circulatory failure. The latter may be very alarming and at least one case is recorded in which a single dose of thirty grains caused death. The common symptoms of chloral poisoning are: Deep sleep, passing into coma, the pupil at first contracted, later dilates; the respirations fall in number; the pulse is weakened and rendered slower, but later may become rapid and irregular; the temperature is reduced; the muscular system is relaxed, and both sensibility and reflex action are diminished or completely abolished. The immediate cause of death is generally a paralytic arrest of respiration but in many cases there appears to have been a simultaneous arrest of the cardiac action, and it is very possible that fatal syncope may at times occur. At post-mortem examination, congestion of the meninges and substance of the brain and cord, and of the lungs, is commonly found. The blood is thought by Richardson (*M. T. G.*, Sept. 4, 1870) to coagulate less firmly than normal.

In the treatment, if the case be seen early, the stomach should be thoroughly evacuated by a rapidly acting emetic, as zinc sulphate, or the stomach tube, and atropine, strychnine, cocaine, and caffeine, employed as respiratory and circulatory stimulants; at the same time external heat should be applied to maintain the bodily temperature and efforts made to keep the patient awake. For the latter purposes, however, those measures which throw an added strain upon the heart, such as walking, must be sedulously avoided; the electric brush affords the most efficient and least injurious method of preventing sleep.

Hydrated chloral is best administered in solution with syrup of orange flowers, or some simple aromatic. The French sometimes employ *chloral cream,* made of hydrated chloral 5 parts, water 15 parts, white sugar finely powdered 100 parts, flavored with mint, orange, or vanilla. One grain of hydrated chloral is contained in 24 grains of the cream, and a teaspoonful is equivalent to about 3 grains of hydrated chloral. This preparation keeps well, and the dose may be dissolved in a little water. *Chloral liniment* may be made by dissolving 6 parts of hydrated chloral in 30 parts of oil of sweet almonds. *Chloral ointment,* 6 parts hydrated chloral, 3 parts white wax, 27 parts lard; the lard and wax are melted at a gentle heat, the hydrated chloral added in powder and dissolved. *Chloral plaster,* to produce counter-irritant effects, is prepared by spreading powdered hydrated chloral on Burgundy pitch plaster; care should be taken to distribute it uniformly.

Dose, ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Syrupus Chloral, *Br.* Chloral Camphoratum, *N. F.;* Mistura Chloralis et Potassii Bromidi Composita, *N. F.*

CHLOROFORMUM. U.S., Br.

CHLOROFORM Chlorof.

(ĕhlō-rō-fôr′mŭm)

"A liquid consisting of not less than 99 per cent. nor more than 99.4 per cent., by weight, of $CHCl_3$ (119.39), and not less than 0.6 per cent. nor more than 1 per cent. of alcohol. Preserve it in well-stoppered bottles, in a cool place, protected from light. Caution: Care should be used in vaporizing Chloroform in the presence of a naked flame, as noxious gases are produced." *U. S.* "Chloroform is trichlormethane, $CHCl_3$, to which 2 per cent. of Absolute Alcohol has been added. It may be obtained from ethylic alcohol, industrial methylated spirit, or acetone, by heating with chlorinated lime, slaked lime, and distilled water, and subsequent purification. Should be kept cool and in a dark place." *Br.*

Trichlormethane, Methenyl Trichloride; Chloroformum Purificatum, *U. S.* 1880; Formylum Trichloratum; Chloroforme Officinal, *Fr. Cod.;* Chloroformium, *P. G.;* Reines Chloroform, Chloroform, *G.;* Cloroformio, *It.;* Chlorido ormico, Cloroformo, *Sp.*

Neither the U. S. nor British Pharmacopœias give detailed processes for chloroform or for its purification. (See U. S .D., 17th ed., 370, and 19th ed., p. 327.)

It sometimes happens that the chloroform purified with sulphuric acid, though apparently pure at first, will not keep, but after some time becomes so loaded with chlorine and hydrochloric acid as to be altogether unfit for respiration. Squibb attributed the fact that chloroform purified by concentrated sulphuric acid does not keep well, to the very purity attained. He believed that perfectly pure chloroform is prone to decomposition, and is rendered more stable by the addition of a small proportion of alcohol, so as to reduce its density to the official standard. This he effected by adding alcohol in the proportion of ten drops to each fluidounce of good chloroform of maximum density (see *Amer. Med. Monthly,* July, 1857). This recommendation was carried into effect in the U. S. 1880 process, and explains the addition of alcohol before distillation. Gregory also attributes the tendency to decomposition to its purity, and to the action of sunlight; having found that those portions which he had purified with the greatest care were soonest decomposed under the influence of light. For methods of preserving chloroform by the use of sulphur, hypophosphorous acid, etc., see *P. J.,* 1895, 261; also 1896, 249.

The intermediate formation of hydrated chloral as a result of the reaction between alcohol and chlorinated lime suggested the preparation of chloroform from hydrated chloral. The advantages which were anticipated from decomposing pure hydrated chloral with alkalies have not altogether been realized, for the product is much more expensive, and the claim of greater stability has not been sustained, as it requires just as much alcohol to preserve it as that made in the usual way.

Chloroform is now made on a large scale by the distillation of acetone with chlorinated lime; indeed, this process has entirely replaced the manufacture from alcohol. Liebig, as long ago as 1832, described the reaction, but it was thought to be not adapted for commercial use. In 1882 the manufacture was begun on a commercial scale at Mannheim, Germany, and since June, 1885, in this country. To get a satisfactory yield a very pure acetone is necessary. When such acetone is taken, a yield of nearly or quite 200 per cent. of chloroform can be obtained. (For an account of the methods of purifying the acetone and distilling with chlorinated lime, see *A. J. P.*, 1889, p. 321.) In July, 1885, a patent was taken out by G. Michaelis of Albany, for the manufacture of chloroform from the liquid products resulting from the decomposition of crude acetates at high temperatures. These liquid products are acetone and other higher ketones. The purified chloroform from acetone has a small quantity of alcohol added to prevent decomposition and bring it to pharmacopœial requirements. Pure methyl alcohol, on the other hand, does not yield chloroform. The erroneous statements on this point generally current are probably due to the fact that commercial wood spirit contains a large percentage of acetone.

E. R. Squibb preferred acetic acid to the acetates in the intermediate step of making acetone, thus avoiding impurities likely to be present in acetates; he believed that the grant of a patent for "acetone chloroform" was deficient in equity. (*Ephem.*, 1896, 1743 to 1757.)

Still another method for the manufacture of chloroform from acetone is described in the French technical journals,—viz., to electrolyze a solution of common salt mixed with acetone. A retort of enamel-lined iron, jacketed at the bottom so as to be heated by steam, and provided with a delivery and condensing tube, is used. A 20 per cent. solution of common salt is introduced into the retort and heated to boiling, when the current is made to pass and a continuous stream of acetone is run in. The nascent chlorine liberated rapidly converts the acetone into chloroform, and it distils over. It is claimed that 190 per cent. of the weight of the acetone taken is obtained as chloroform. Lead electrodes were used at first, but these have been replaced by carbon rods which can be attached to a vertical shaft and made to serve as stirrers. The negative electrode consists of a copper cylinder. (*Revue Scientifique*, Feb., 1893.)

Carbon tetrachloride (CCl_4) has also been proposed (1896) as a source of chloroform, and as it is now made cheaply on a large scale, it may come into use. By the action of hydrochloric acid and zinc, hydrogen is liberated and attacks the carbon tetrachloride, forming chloroform and hydrochloric acid,

$$CCl_4 + H_2 = CHCl_3 + HCl$$

As hydrochloric acid is a product of the reaction, fresh quantities of zinc are attacked, and a new liberation of chloroform follows.

Discovery and History.—Chloroform was discovered by Samuel Guthrie of Sackett's Harbor, N. Y., in 1831, and about the same time by Soubeiran in France, and Liebig in Germany. Guthrie obtained it by distilling a gallon from a mixture of three pounds of chlorinated lime and two gallons of alcohol of the sp. gr. 0.844, and rectifying the product by redistillation, first from a great excess of chlorinated lime, and afterwards from potassium carbonate. (*Silliman's Journal*, vol. xxi, Jan., 1832, p. 64.) In a subsequent letter to Silliman, dated Feb. 15, 1832, Guthrie states that the substance which he had obtained, "distilled of sulphuric acid, has the specific gravity of 1.486, or a little greater, and may then be regarded as free from alcohol; and if a little sulphuric acid which sometimes contaminates it be removed by washing it with a strong solution of potassium carbonate, it may then be regarded as *absolutely pure.*" (*Ibid.*, vol. xxii, July, 1832, p. 105.) It is thus evident that Guthrie obtained, in a pure state, the substance now called chloroform; but he erroneously supposed his product to be the well known oily liquid of the Dutch chemists, which it greatly resembles, and for the preparation of which he believed he had fallen on a cheap and easy process. Under this impression he called the substance, in his communications, *chloric ether*, one of the names by which *Dutch Liquid*, or *ethene dichloride*, is designated. He was induced to make the preparation from noticing in Silliman's *Elements of Chemistry* a reference to the Dutch liquid as a grateful diffusible stimulant when properly diluted with alcohol and water. (See also *West. Drug.*, 1894, 51.)

Properties.—Chloroform is "a clear, colorless, mobile liquid, of a characteristic, ethereal odor, and a burning, sweet taste. Chloroform dissolves in 210 times its volume of water; miscible with alcohol, ether, benzene, petroleum benzin, or with fixed or volatile oils. Specific gravity: 1.474 to 1.478 at 25° C. (77° F.). Chloroform is volatile at a low temperature and boils at about 61° C. (141.8° F.). It is not inflammable, but its heated vapor burns with a green flame. Pour 20 mils of Chloroform upon a piece of clean, odorless filter paper laid flat upon a warmed glass plate, and rock the plate from side to side until the liquid is all evaporated. No foreign odor becomes perceptible as the last portions disappear from the paper, and the paper remains odorless. Agitate 10 mils of Chloroform with 25 mils of distilled water, and allow the liquids to separate completely; the aqueous layer is neutral to litmus and separate portions of 10 mils each are not affected by a few drops of silver nitrate T.S. (*chlorides*) nor colored blue by the addition of a few drops each of potassium iodide T.S. and starch T.S. (*free chlorine*). Transfer 40 mils of Chloroform from the container, by means of a clean pipette, to a 50 mil glass-stoppered cylinder of colorless glass having an internal diameter of about 20 mm. and previously rinsed with sulphuric acid, add 4 mils of colorless sulphuric acid and shake the mixture vigorously during five minutes.

Then allow the liquids to separate completely, so that both are transparent. The Chloroform remains colorless, and the acid is colorless or very nearly so when viewed horizontally in the cylinder held in a vertical position (*impurities decomposable by sulphuric acid*). Dilute 2 mils of the sulphuric acid, separated from the Chloroform in the preceding test, with 5 mils of distilled water; the liquid is colorless and clear, and, while hot from the mixing, emits but a faint, vinous or ethereal odor (*odorous decomposition products*). When further diluted with 10 mils of distilled water, it remains clear and is not affected within one minute by the addition of 3 drops of silver nitrate T.S. (*chlorinated decomposition compounds*)." *U. S.*

"A colorless, volatile liquid. Characteristic odor; taste pungent, sweet. Specific gravity 1.483 to 1.487. Does not begin to boil below 60° C. (140° F.). On allowing 10 millilitres to evaporate from a large piece of filter paper placed on a warm plate, no extraneous odor is perceptible at any stage of the evaporation. *Water* which has been shaken for five minutes with half its volume of Chloroform, and separated from the undissolved Chloroform, is neutral to *litmus* (absence of acid), does not give any color with 1 millilitre of *solution of cadmium iodide* and 2 drops of *mucilage of starch* (absence of free chlorine), and yields not more than a very slight opalescence with 4 drops of *solution of silver nitrate* (absence of chlorides). After shaking *sulphuric acid* with twice its volume of Chloroform for five minutes, and setting aside for fifteen minutes, both the acid and the Chloroform are nearly colorless. 2 millilitres taken from the layer of *sulphuric acid*, and diluted with 5 millilitres of *water*, remain very nearly colorless, and have a pleasant odor. When this acid liquid is further diluted with 10 millilitres of *water*, and stirred with a glass rod, it is transparent and colorless, and the addition of 4 drops of *solution of silver nitrate* causes not more than a slightly diminished transparency. *Water* which has been shaken with half its volume of Chloroform, previously treated with *sulphuric acid* as described above, yields not more than a slightly diminished transparency with *solution of silver nitrate*. Evaporates without residue." *Br.*

Besnou gives the densities of various mixtures of alcohol and the purest commercial chloroform at 4.5° C. (40° F.) as follows:

Specific Gravity.	Chloroform, per cent.	Alcohol, per cent.	Specific Gravity.	Chloroform, per cent.	Alcohol, per cent.
1.4945	100.0	0.0	1.4772	97.5	2.5
1.4908	99.5	0.5	1.4602	95.0	5.0
1.4874	99.0	1.0	1.4262	90.0	10.0
1.4840	98.5	1.5	1.4090	87.5	12.5

When pure, it has no action on potassium, except to cover the surface of the metal with small bubbles of gas. Chloroform is a powerful antiseptic. Like creosote, it does not coagulate albumin. It is scarcely acted on by sulphuric acid in the cold, but dissolves readily in alcohol and ether.

The alcoholic solution, when moderately diluted with water, forms a sweetish, aromatic liquid of a very grateful taste. A strong alcoholic solution is decomposed by an abundance of water, the chloroform separating and subsiding, and the alcohol uniting with the water.

It is liable to decomposition by sunlight, or even diffused daylight; and hence the propriety of keeping it in bottles covered with dark paper, in a rather dark place. Chloroform has extensive solvent powers, being capable of dissolving caoutchouc, gutta-percha, mastic, elemi, tolu, benzoin, and copal. Amber, sandarac, lac, and wax are only partially soluble. It also dissolves iodine, bromine, many alkaloids, the fixed and volatile oils, most resins, and fats. It dissolves sulphur and phosphorus sparingly.

It possesses the power of dissolving a large quantity of camphor. As a general solvent, it has the advantage over ether of not being inflammable, the inflammability of the latter being the cause of frequent accidents. For an extensive list of substances soluble, insoluble, and partly soluble in chloroform, see a paper by Lepage of Gisors, France, copied into *A. J. P.*, 1852, p. 147. It has been found by J. B. Barnes that chloroform has the power of preventing the alcoholic, lactic, and other fermentations, probably by killing the organisms that provoke these processes. Twenty minims preserved sixteen ounces of malt, to which two drachms of yeast had been added, as long as the experiment lasted. The same quantity kept fresh eight fluidounces of milk in a warm place for five days. Mucilage and infusions were preserved for weeks with one minim or even less to the ounce. Similar results were reached by F. J. Barrett and others. (*P. J.*, 1874, pp. 441, 442, 455.) The active properties of chloroform forbid its use as a preservative of medicinal infusions, but from milk it could always be removed by boiling. A. Munz (*P. J.*, 1875, p. 967) proposes the employment of chloroform as a test between chemical and living ferments, since he has found it to have no effect upon the former, though absolutely destructive to the latter.

Composition.—Chloroform is composed of one atom of carbon, one of hydrogen, and three of chlorine. Its simplest derivation in theory is from marsh-gas (*methane*), CH_4, whence it is often called *trichloro-methane*. While it can be thus produced, by the action of chlorine upon marsh-gas, in practice, it is formed either from alcohol by the action of bleaching powder, from

chloral by an alkaline hydroxide, or latterly from acetone and bleaching powder.

Tests.—Chloroform is liable to contain alcohol and ether, both of which lower its specific gravity. If it have a less density than 1.38, it will float instead of sinking in a mixture of equal weights of concentrated sulphuric acid and water after it has cooled. M. Mialhe has proposed the following tests for the presence of alcohol. Drop into distilled water a small quantity of the chloroform. If pure, it will remain transparent at the bottom of the glass; but if it contain even a small proportion of alcohol, the globules will acquire a milky appearance. Soubeiran's method was to agitate almond oil and chloroform together in a tube. If the chloroform is pure, it remains clear; if it contains as much as 5 or 6 per cent. of alcohol, it becomes milky. (*J. P. C.*, Août, 1860, p. 95.) Procter detected alcohol by adding the suspected chloroform to an oxidizing mixture of potassium dichromate and sulphuric acid. If alcohol be present, the deep orange color of the chromic mixture will gradually become green; if absent, no change of color will take place. (*A. J. P.*, 1856, p. 213.) Hoffmann's violet has been suggested as a test. If a small portion is added to chloroform containing alcohol, the solution is colored a deep purple. Boettger recommends adding to the chloroform a solution of molybdic acid in pure, strong sulphuric acid, when even a trace of alcohol will cause an intense blue color. (1879.) Chloroform, when pure, upon being mixed with an equal volume of sulphuric acid, does not color it; but when contaminated with pyrogenous oils it gives the acid a color varying from yellow to reddish-brown, according to the amount of impurity. Alcohol also is detected and removed by sulphuric acid. In applying this test, several fluidounces of chloroform should be used, as a slight change of color cannot be easily seen in a test tube, and care must be taken to see that mechanical impurities, like cork dust, dirt, etc., have been filtered out of the specimen, or the acid will be discolored from this cause. A still more delicate test of the oily impurities, according to Gregory, is the odor which they leave. If chloroform thus contaminated be poured upon the hand, it quickly evaporates, leaving the oily impurities, recognizable by their offensive odor, now no longer covered by that of the chloroform. The pure substance, rubbed on the skin, quickly evaporates, and leaves scarcely any odor. Chloroform sometimes contains Dutch liquid, which may be discovered by adding an alcoholic solution of potassium hydroxide, when the mixture, if this impurity be present, will heat and give off a permanent gas, which is *acetyl chloride*, C_2H_3OCl. (Geuther.) Fuming nitric acid, heated with chloroform to 100° C. (212° F.) in a closed tube for 120 hours, forms a new substance, *chloropicrine*.

These tests imply the presence of but a minute proportion of alcohol, and the total absence of chlorine and those volatile and empyreumatic substances which constitute the most injurious impurities of chloroform. A heat that would be felt through the bottle, on the admixture of sulphuric acid with chloroform would evince the presence of too much alcohol or water. The want of discoloration from the contact of the two liquids shows the absence of empyreumatic oily matter. A color bordering on that of sherry wine would imply an objectionable amount of impurities. The volatile impurities are less volatile than chloroform, and would consequently be the last to escape on the evaporation of the liquid. Impure chloroform, therefore, leaves a foreign odor behind it when allowed to evaporate from a clean porcelain plate, in the amount and manner indicated.

Two methods for purifying chloroform, one physical and the other chemical, have attracted much attention. The first of these is the Pictet method of purifying the chloroform by submitting it to very low temperatures, whereby the impurities are first frozen out and filtered off from the chloroform at −70° C. (−94° F.) and then the chloroform itself is solidified at from −80° to −100° C. (−112° to −148° F.) and separated from any liquid impurities. It was at first claimed for this "Chloroform Pictet" that it would not be decomposed by sunlight and did not require the addition of alcohol to preserve it. These claims do not seem to be substantiated by later tests. The other method is based on the discovery of R. Anschütz, that chloroform crystallizes out with salicylid, $C_6H_4\left\{\begin{matrix}CO\\O\end{matrix}\right>$, and *o*-homosalicylid, $C_6H_3(CH_3)\left\{\begin{matrix}CO\\O\end{matrix}\right>$, while the impurities of chloroform remain. These crystalline compounds contain respectively 33.24 and 30.80 per cent. of chloroform, and this can be liberated from its combination by very moderate heating. The compounds can be kept for a long time in closed vessels in a slight atmosphere of chloroform, and the salicylid and *o*-homosalicylid can be used over and over again. After becoming acid, through exposure to light, chloroform may be readily regenerated, by agitating it with solution of sodium carbonate, and distilling from a little unslaked lime. From what has been said above, chloroform to be kept for use should have the sp. gr. 1.476, and if denser than this, should be brought to it by the addition of alcohol. It is best kept in cork stoppered bottles. As the cork is not acted on by chloroform, if it become yellow and softened it will indicate the presence of an acid, and thus act as a test. (*A. J. P.*, 1868, p. 289.)

Uses.—Locally chloroform is actively irritant and somewhat anesthetic. When applied to the skin in ordinary manner it produces pain and redness but if evaporation be prevented will frequently blister. The pain is followed by a sensation of numbness. According to Fornié

the vapor from a mixture of equal parts of glacial acetic acid and chloroform is more effectual as a local anesthetic and will produce complete insensibility of the skin in five minutes. (*P. J.*, 1862, p. 385.) Chloroform is also distinctly antiseptic.

Taken into the stomach in doses of about five minims (0.3 mil), it induces only gastric symptoms, chiefly due to its irritant properties; but when there is excessive flatulence, colic, or gastralgia, it not only causes an increased peristalsis and expulsion of any flatus present, but evinces a distinct local narcotic influence by quieting pain and spasm. Taken in doses of 1 to 2 fluidrachms (3.75–7.5 mils), it produces a narcotism similar to that seen when it is administered by inhalation, the narcotism, however, developing and passing off much more slowly than in the latter case. Chloroform was used internally in *asthma* and other conditions as early as 1832 by Ives of New Haven (*Silliman's Journ.*, xxi, 406, 407), and subsequently in various conditions by several European physicians, but it was not until November, 1847, that Simpson of Edinburg brought it forward as more agreeable, efficacious, and convenient in general anesthesia than ether.

The action of chloroform upon the system like that of ether, is predominantly upon the central nervous system. The first portion to feel the effect of the drug is the higher cerebral centers. After larger quantities there is depression of the spinal cord, first of the sensory side and later of the motor tract, and finally paralysis of the medullary centers, especially the respiratory and vasomotor. It differs from ether not only in the power of its action but especially in the fact that it is directly depressant to the heart. A discussion of the relative advantages and disadvantages of these two great anesthetics would occupy too much space to be permissible here and the reader is referred for details to H. C. Wood, Jr.'s *Text-book of Pharmacology*. It may, however, be remarked that under ordinary circumstances chloroform, although more pleasant to take than ether, is much more dangerous. It should also be remembered that it can be absorbed readily through the mucous membrane of the alimentary canal, and in doses of one or two fluidrachms it will produce a narcosis very similar to that which is caused by its inhalation.

Aside from its use in surgery chloroform is sometimes used to relieve severe *pain*, as in *neuralgia, gallstone colic*, and the like. It is also capable of relieving the asthmatic paroxysm. For these properties it is generally administered by inhalation but should only be employed with the greatest caution. Internally it is used as a carminative in *flatulent colic* and as a stimulant in combination with other drugs in the treatment of *serous diarrheas*. It has also been recommended as an anthelmintic, especially in the treatment of *hookworm*, but appears to be more dangerous than other equally efficient drugs. Externally it is very widely employed as a counter-irritant, especially in the form of the liniment. Langenbeck, of Berlin, prefers chloroform to tincture of iodine as an injection for the radical cure of *hydrocele*.

Chloroform ointment is made by adding twenty parts of chloroform to a mixture of ten parts of white wax and ninety parts of lard, previously melted together, and allowing the whole to cool. Chloroform may be gelatinized by agitating it with an equal weight of white of egg in the cold. In three hours it takes the gelatinous form. A stronger preparation may be made by shaking together, in a bottle, four parts of chloroform and one of white of egg, and placing the mixture in water at 60° C. (140° F.). In four minutes the gelatinization is completed. *Gelatinized chloroform* may be applied to the skin, spread on linen, or by friction. *Syrup of chloroform* may be made by adding one fluidounce of spirit of chloroform to fifteen fluidounces of syrup.

When an overdose of chloroform is taken by the mouth, it is essential to empty the stomach by the pump or siphon tube, and then treat the case much as in serious narcosis from inhalation. In a case of suicide by swallowing chloroform in which death took place in about thirty-four hours, the lining membrane of the larynx and trachea was found inflamed, the bronchi were loaded with a dirty-gray purulent fluid, the lungs were inflamed as in the first stage of pneumonia, and the brain and its membranes congested; but these morbid appearances are not constant.

In relation to the preparations, consisting of chloroform and alcohol, which have been used under the name of "chloric ether," the reader is referred to *Spiritus Chloroformi*.

Dose, of chloroform, five to fifteen minims (0.3–0.9 mil).

Off. Prep.—Aqua Chloroformi, *U. S., Br.;* Linimentum Chloroformi, *U. S., Br.;* Spiritus Chloroformi, *U. S., Br.;* Tinctura Chloroformi et Morphinæ Composita, *Br.;* Linimentum Aconiti et Chloroformi, *N. F.;* Mistura Chloroformi et Morphinæ Composita, *N. F.;* Mistura Olei Picis, *N. F.;* Mistura Opii et Chloroformi Composita, *N. F.;* Petroxylinum Chloroformi Camphoratum, *N. F.;* Syrupus Pini Strobi Compositus, *N. F.;* Syrupus Pini Strobi Compositus cum Morphina, *N. F.*

CHONDRUS. U. S.

CHONDRUS [Irish Moss]

(ĉhŏn'drus)

"The dried plant of *Chondrus crispus* (Linné) Stackhouse or of *Gigartina mamillosa* (Goodenough et Woodward) J. Agardh (Fam. *Gigartinaceæ*)." *U. S.*

Carrageen, Caragahen, Fucus Crispus, Pigwrack, Killeen, Pearl Moss; Carragheen; Carragaheen; Carrageen ou Mousse perlée, *Fr. Cod.;* Mousse Marine perlée, *Fr.;* Carrageen, *P. G.;* Irländisches Moos, Perlmoos, Knorpeltang, *G.;* Fuco carageo, Musco d'Irlanda, Fuco crispo, *It.;* Caragaen, Musgo marino perlado, *Sp.*

Chondrus crispus grows upon rocks and stones on the coast of Europe, and is especially abun-

dant on the southern and western coasts of Ireland, where it is collected. It is also a native of the United States, and is gathered largely on the coast of Massachusetts, below Boston, where it is partly torn from the rocks and partly collected upon the beach, on which it is thrown up during storms. It is prepared for market by spreading it out high on the beach, to dry and bleach in the sun. (Aug. P. Melzar, *Proc. A. Ph. A.*, 1860.) For elaborate accounts of the plant, of its distribution on the sea coast of Massachusetts, and of the mode of gathering and curing, see *U. S. Agricultural Report*, 1866; also *A. J. P.*, 1868, 417; 1895, 596; 1899, 483. Henry Kraemer witnessed the methods pursued on the Massachusetts coast in the collection of Irish moss at Scituate, which appears to be a particularly favorable situation. The season for collection begins late in May and continues to September, June and July being the best months. The moss at present is only found on rocks that are from 15 to 20 feet below the tide, hence women no longer engage in its collection. The men go out in their sail boats or dories at half tide, and come in at half flood. With their long rakes they scrape the moss off the rocks, collecting thus about 50 pounds to the boat, the total for the season at Scituate being about 10,000 pounds. The moss is spread out on the high beach for a week or so, the action of the sun and dew bleaching it. It is then enclosed in hogsheads, in which it is again saturated with sea water by rolling them in the marshes; after which it is again spread out and subjected to the bleaching process, this alternate treatment being repeated four or five times, until the product is of a yellowish or white color. The final drying is done in barns, where the moss is stored until it is packed in 100 lb. barrels at the end of the season. In the course of his journey he had opportunity to observe the *Chondrus* growing and gathered in different localities along the coast, and found it to consist chiefly, if not entirely, of *Chondrus crispus*. While it is stated in Dr. Farlow's "The Marine Algæ of New England" that the closely resembling *Gigartina mamillosa* is common from Boston northward, Kraemer is inclined to believe that *Chondrus crispus* (L.), Lyngbye, is practically the only source of the American drug. (See *Proc. Penn. Pharm. Assoc.*, 1899, 113–116.) Tunmann (*Apoth. Zeit.*, 1909, pp. 91 and 151) has given an elaborate account of the morphology and composition of *Chondrus*.

Gigartina mamillosa Ag. resembles the true Irish moss, and, growing with it upon the rocks, is often gathered with it. It can, however, be at once distinguished by the numerous papillæ which cover the surface and margins of the fronds and bear the fruit (cystocarps). In chemical and medicinal properties it is probably identical with *C. crispus*.

Irish moss when collected is washed and dried. It is probably sometimes bleached by the use of potassium permanganate and sodium thiosulphate by the same process as that used for bleaching sponge. Herr Schack was led to suspect this through discovering the presence of sulphurous acid in a German specimen. (*Ph. Ztg.*, 1886, p. 87.) The presence of arsenic has been determined in some commercial lots, being caused, no doubt, by the impurities in the sulphur used for bleaching Chondrus. Some "faked" samples have yielded as much as 35 per cent. of ash which contained a large quantity of calcium sulphate. The gelatinizing value of specimens of this kind is about 60 per cent. below normal. In the fresh state it is of a purplish color, but, as found in the shops, is yellowish or yellowish-white, with occasionally purplish portions. It is officially described as: "Entire plants more or less matted together, consisting of a slender stalk from which arises a series of dichotomously branching, more or less flattened segments, emarginate or deeply cleft at the tips; from 5 to 15 cm. in length, and 1 to 10 mm. in width; yellowish-white, translucent, frequently coated with a calcareous deposit which effervesces with hydrochloric acid; sometimes with fruit bodies or sporangia embedded near the apex of the segments (in *C. crispus*) or with sporangia borne on short tuberculated projections or stalks, more or less scattered over the upper portion of the segments (in *G. mamillosa*); somewhat cartilaginous; odor slight, seaweed like; taste mucilaginous, saline. Boil one part of Chondrus for about ten minutes with 30 parts of water, replacing the water lost by evaporation; the strained liquid forms a thick jelly upon cooling. When softened in cold water Chondrus becomes gelatinous and transparent, the thallus remaining nearly smooth and uniform and not swollen except slightly at the tips; a solution made by boiling 0.3 Gm. of the drug in 100 mils of water and filtering gives no precipitate on the addition of tannic acid T.S. (*gelatin*), and when cold does not give a blue color on the addition of iodine T.S. (*starch*)." *U. S.*

It swells in cold water, but does not dissolve. Boiling water dissolves a large proportion of it, and the solution, if sufficiently concentrated, gelatinizes on cooling. Herberger found 79.1 per cent. of a so-called pectin (mucilage), and 9.5 of mucus, with fatty matter, free acids, chlorides, etc., but neither iodine nor bromine. Dupasquier discovered in it both of these elements, which had generally escaped attention in consequence of their reaction, as soon as liberated, upon the sodium sulphide resulting from the decomposition of the sodium sulphate of the moss when charred. (*J. P. C.*, 3e sér., iii, 113.) The analysis made by Church in 1877 gave: mucilage, 55.4; water, 18.8; mineral matter, 14.2; albuminoids, 9.4; and cellulose, 2.2 per cent. The pectin Pereira thought peculiar, and proposed to call it *carrageenin*.

It is distinguished from gum by affording, when dissolved in water, no precipitate with alcohol; from starch, by not becoming blue with tincture of iodine; from pectin, by yielding

no precipitate with lead acetate and from mucic acid by the action of nitric acid. Ch. Blondeau gives the name of *goëmine* to a substance obtained by boiling carrageen (*goëmon*, Fr.) for several hours in distilled water, and precipitating the mucilaginous liquid by alcohol. Flückiger, who analyzed this mucilage with care, found in it *no* sulphur, and only 0.88 per cent. of nitrogen. The drug itself yielded not more than 1.012 per cent. of nitrogen. (*Pharmacographia*, 2d ed., 748.) Haedicke, Bauer, and Tollens obtained, on extraction with water containing 0.6 per cent. of sulphuric acid, and further purification by alcohol, a small quantity of a crystalline compound which resembles galactose in its composition, in its action on polarized light, and in its behavior with nitric acid. On oxidation with nitric acid, the dry moss yields from 21.6 to 22.2 per cent. of mucic acid. Carrageenin is said to have been used as a substitute for acacia, under the name of *imitation gum arabic;* the latter occurs in three forms, white, light yellow, and yellow. They all have similar properties, swelling up like tragacanth when mixed with cold water, but not forming a clear solution unless the mixture be boiled, in this latter respect differing from tragacanth or albumen; iodine does not give a blue color, and alcohol does not precipitate the solution, even when 50 per cent. of it is added. It has mild adhesive properties. (E. C. Federer, *Ph. Era*, 1887, 146.) The mucilage of Irish moss has come into considerable use as an emulsifying agent. (*Proc. A. Ph. A.*, 1887; *A. J. P.*, 1888, 170.)

Uses.—Chondrus is nutritive and demulcent, and, being easy of digestion and not unpleasant to the taste, forms a useful article of diet in cases in which the farinaceous preparations, such as tapioca, sago, barley, etc., are usually employed. It has been particularly recommended in *chronic pectoral affections, scrofulous complaints, dysentery, diarrhea,* and *disorders of the kidneys and bladder.* It may be used in the form of decoction, made by boiling a pint and a half of water with half an ounce of the moss down to a pint. Sugar and lemon juice may usually be added to improve the flavor. Milk may be substituted for water when a more nutritious preparation is required. It is recommended to macerate the moss for about ten minutes in cold water before submitting it to decoction. Any unpleasant flavor that it may have acquired from the contact with foreign substances is thus removed.

Dose, four drachms (15.5 Gm.).

Off. Prep.—Gelatinum Chondri, *N. F.;* Mucilago Chondri, *N. F.*

CHROMII TRIOXIDUM. U. S. (Br.)

CHROMIUM TRIOXIDE Chrom. Triox. [Acidum Chromicum, Pharm. 1890, Chromic Acid, Chromic Anhydride]

(ȼhrō'mĭ-ī trī-ŏx'ĭ-dŭm)

"It contains not less than 95 per cent. of CrO_3 (100.00). Preserve it in glass-stoppered bottles. Caution: Chromium Trioxide should not be brought into contact with organic substances, as serious accidents are liable to result." *U. S.* "Chromic Anhydride, CrO_3, may be obtained by the interaction of sulphuric acid and potassium bichromate. It should be preserved in well-stoppered bottles." *Br.*

Acidum Chromicum, *Br.*, Anhydrous Chromic Acid, Acide Chromique Cristallisé, *Fr. Cod.;* Acidum Chromicum; *P. G.;* Chromsäure, *G.;* Anidride cromica, Acido cromico, *It.;* Acido cromico, *Sp.*

This is not a true acid, but an acid anhydride. It may be obtained by the process official in the former British Pharmacopœia: "Bichromate of Potassium, 30 ounces (av.); Sulphuric Acid, 57 fluidounces (Imp. meas.); Distilled Water, a sufficiency. Dissolve the bichromate of potassium in a mixture of 50 fluidounces (Imp. meas.) of the water and 42 fluidounces (Imp. meas.) of the acid. Set aside for twelve hours, and decant the liquor from the crystals of acid sulphate of potassium that have separated. Heat the liquor to about 85° C. (185° F.), and add the remainder of the acid, and water sufficient to just redissolve any crystals of chromic acid that may have been formed. Allow to cool, collect and drain the crystals, and dry them on porous tiles at a temperature not exceeding 37.8° C. (100° F.) in an air-bath. From the mother liquor more crystals may be obtained on evaporation." *Br.* 1885.

This process yields crystals which are more or less contaminated with sulphuric acid. Vulpius (*A. Pharm.*, 1886, p. 964) shows that commercial chromium trioxide sometimes contains as much as 7 per cent. of sulphuric acid, and that pure chromium trioxide is not scarlet in color, but dark brown-red and steel-glistening, and not deliquescent in ordinary air.

The best yield of pure crystals is said to be according to the method of Zettnow (*Pogg. Ann.*, cxliii, 471), in which 300 Gm. of potassium dichromate are mixed with 500 mils of water, and 420 mils of concentrated sulphuric acid added, and the mixture allowed to stand for twelve hours in order that the acid potassium sulphate may crystallize out. The mother liquor is then heated to from 80° to 90° C. (176°–194° F.), and 150 mils of sulphuric acid added, together with enough water to dissolve the crystals of trioxide which at first separate out. After standing for twelve hours the liquid is poured off from the crystals which have separated, and a second and a third crop may be obtained by concentration. The crystals, having been drained upon a porous plate and washed with pure nitric acid, sp. gr. 1.46, are dried in a current of warm air. For a method by Duviller, in which barium chromate is treated by nitric acid, and chromium trioxide crystallized out of the mother liquor, see *A. J. P.*, 1873, p. 23.

Properties.—Chromium trioxide, as ordinarily seen in commerce, is in the form of anhydrous, acicular crystals, of a brilliant crimson red color and an acid metallic taste, deliquescent, and very soluble in water, forming an

orange-red solution; but according to Kebler there may also be found in commerce an impure "chromic acid" made by mixing a solution of sodium dichromate with sulphuric acid and drying the product; it sometimes contains 60 per cent. of acid sodium sulphate (*Am. Drug.*, 1901, 344). The requirements of the U. S. Pharmacopœia IX are that even traces of sulphuric acid shall be absent, and that the color of the crystals be not scarlet. "Chromium Trioxide occurs as small, needle-shaped crystals or rhombic prisms, of a dark purplish-red color and metallic luster; odorless; destructive to animal and vegetable tissues; deliquescent in moist air. One Gm. of Chromium Trioxide dissolves in 0.6 mil of water at 25° C. (77° F.); also in 0.5 mil of boiling water; when brought into contact with organic solvents (*e.g.*, alcohol), decomposition takes place, sometimes with dangerous violence. When Chromium Trioxide is heated, it darkens, and finally becomes black, but the color is restored on cooling. At about 193° C. (379.4° F.) it fuses to a reddish-brown liquid, which, on cooling, forms a dark red, brittle mass (often enclosing cavities filled with crystals), furnishing a scarlet powder. Above 250° C. (482° F.) it begins to decompose into green chromic oxide and free oxygen, and, after protracted heating, leaves a residue of chromic oxide. When warmed with hydrochloric acid, chlorine is evolved. A solution of 1 Gm. of Chromium Trioxide in 100 mils of distilled water, previously acidulated with 3 mils of hydrochloric acid, is not rendered turbid within one minute on the addition of 1 mil of barium chloride T.S. (*sulphuric acid*)." *U. S.*

"Crimson acicular crystals, very deliquescent, inodorous, acting corrosively on the skin. Very soluble in *water* and in *ether*. Strongly heated it first melts and then evolves oxygen, leaving, after heating to redness, a green residue, which yields little or nothing to *water*. Warmed with *hydrochloric acid*, chlorine is evolved. In contact with relatively small proportions of *alcohol* (90 per cent.), *ether, glycerin*, or certain other organic substances, sudden combustion or explosion may ensue. When 4 grammes are dissolved in a mixture of 20 millilitres of *water* with 10 millilitres of *hydrochloric acid*, 5 millilitres of *solution of barium chloride* added and the mixture filtered, the filtrate yields no further precipitate on the addition of more of the reagent (limit of sulphates)." *Br.*

Chromium trioxide at a heat above the melting point, gives off half its oxygen, and is converted into the green sesquioxide, Cr_2O_3. It is a powerful oxidizing and bleaching agent, and gives up its oxygen with great facility to organic matter. The oxidation of weaker alcohol is attended with the production of aldehyde, recognized by the odor; that of stronger alcohol, by inflaming.

"**Assay.**—Dissolve about 1 Gm. of Chromium Trioxide, accurately weighed in a stoppered weighing-bottle, in sufficient distilled water to make a volume of 100 mils. Mix 15 mils of this solution with 3 mils of hydrochloric acid and 2 Gm. of potassium iodide in a glass-stoppered container, agitate the mixture, allow it to stand for five minutes, then dilute it with 100 mils of distilled water and titrate with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 95 per cent. of CrO_3. Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.003333 Gm. of CrO_3. Each gramme of Chromium Trioxide corresponds to not less than 285.0 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

Uses.—In dilute solution chromium trioxide is a powerful coagulant of albumen and is therefore astringent. In more concentrated solution because of its oxidizing power it destroys all forms of tissue and is a rapid and powerful caustic. It is also an active germicide, Dougall (*L. L.*, Dec. 16, 1871) having found it to surpass phenol; according to Koch a 1 per cent. solution is sufficient to destroy anthrax spores after two days' exposure. By virtue of its oxidizing effect it destroys decaying organic matter, combining with and neutralizing the ammonia and decomposing hydrogen sulphide, thereby acting as a deodorizant.

As a caustic the liquid formed by the spontaneous deliquescence of the crystals may be used; it is most frequently applied by means of a glass rod.

Much care should be exercised in the use of this agent as it is a powerful poison both because of its local irritant effect and its systemic action. A single drop of the saturated solution taken internally has caused violent symptoms and fatal results have followed the too free external use of the drug. (See Shaw, *Virginia Med. Semi-monthly*, 1901, v.)

In dilute solution (5 per cent.) it is used as an antiseptic and astringent wash in *leucorrhea, ozena*, and *hyperidrosis*. In the Prussian army it has been found useful as a foot wash for preventing *sweating of the feet* and to harden the skin. In more concentrated solution it is used as a caustic for the removal of *warts, syphilitic condylomata, nasal, polypi*, and other foreign growths.

Although chromium oxide has not been used internally in medicine Kolipinski (*Monthly Cyclopedia of Pract. Med.*, Sept., 1908) asserts that *chromium sulphate* is a valuable remedy in the treatment of various chronic nervous diseases as *alcoholism, neurasthenia, locomotor ataxia, exophthalmic goiter*, etc. He administers it in doses of from one to eight grains (0.065–0.5 Gm.).

Those whose work brings them in contact with chromic acid or its salts, according to Hermann (*M. M. W.*, April 2, 1901) often suffer with lesions, the result of the local irritant action of these compounds either upon the mucous membrane of the respiratory tract or upon the skin. In a large number of cases there was ulceration of the nasal mucosa eventually with perforation of the septum while other patients developed

bronchitis, eczema, gastritis, or other inflammatory disorders.

Dose, of chromium trioxide, should not exceed one-fourth of a grain (0.016 Gm.). It is very rarely, if ever, used internally.

Off. Prep.—Liquor Acidi Chromici, *Br.*

CHRYSAROBINUM. U. S., Br.

CHRYSAROBIN Chrysarob.

(ĕhrĭs-ą-rō-bĭ'nŭm)

"A mixture of neutral principles extracted from Goa powder, a substance found deposited in the wood of *Vouacapoua Araroba* (Aguiar) Druce (Fam. *Leguminosæ*). Preserve it in well-closed containers, protected from light." *U. S.* "Chrysarobin is a mixture of substances extracted from Araroba by hot benzene. It consists of a definite chemical compound, $C_{15}H_{12}O_3$, also known as pure chrysarobin, or chrysophanolanthranol, associated with certain other substances of similar composition." *Br.*

Chrysarobine, *Fr.*; Chrysarobinum, *P. G.*; Chrysarobin, *G.* Crisarobina, *It.*

The British Pharmacopœia recognizes under distinct headings Crude Chrysarobin (Goa Powder or Araroba) and the Purified Chrysarobin. (See *Araroba,* p. 182.)

Properties.—"Chrysarobin is a brownish to orange-yellow, micro-crystalline powder, tasteless, odorless, and irritating to the mucous membrane. One Gm. of Chrysarobin dissolves in 385 mils of alcohol, 12.5 mils of chloroform; 16 mils of ether, 30 mils of benzene and in 180 mils of carbon disulphide at 25° C. (77° F.); very slightly soluble in water, and in boiling water; it dissolves in solutions of the fixed alkali hydroxides, producing a red liquid. It dissolves in sulphuric acid, producing a deep red solution. On pouring this liquid into water, Chrysarobin is deposited unchanged. Incinerate about 0.5 Gm. of Chrysarobin; not more than 0.25 per cent. of ash remains. Mix about 0.001 Gm. of Chrysarobin with 2 drops of fuming nitric acid; a red mixture is produced, which turns violet-red on the addition of a few drops of ammonia water (distinction from *chrysophanic acid,* which produces a yellow liquid). Boil about 0.1 Gm. of Chrysarobin with 20 mils of distilled water and filter; the filtrate is neutral to litmus and is not changed in color by a few drops of ferric chloride T.S. (*chrysophanic acid*)." *U. S.*

"A light, microcrystalline, yellowish powder; inodorous; tasteless. Entirely soluble in hot *chloroform* and in hot *benzene,* almost entirely soluble in hot *alcohol* (90 per cent.), partially and sparingly soluble in *petroleum spirit,* almost insoluble in *water.* Almost entirely soluble in hot *solution of sodium hydroxide,* with production of a deep brownish-red color. Shaken with *solution of ammonia* the liquid slowly becomes violet. About 1 milligram mixed on a white tile with a drop of *fuming nitric acid* produces a brownish-red liquid, becoming violet on the addition of excess of *solution of ammonia.* Melts when heated, giving off yellow fumes. Ash not more than 1 per cent." *Br.*

Chrysarobin in alkaline solution takes up oxygen readily, even from the air, and changes into chrysophanic acid according to the reaction:

$$C_{30}H_{26}O_7 + 4O = 3H_2O + 2C_{15}H_{10}O_4$$

The difference in physical properties between chrysarobin and chrysophanic acid is well described by Andouard. (See *Proc. A. Ph. A.,* 1895, 864.) When chrysarobin is distilled with zinc dust it yields *methyl-anthracene,* $C_{15}H_{12}$. Liebermann has since established clearly the relationship of chrysarobin to chrysophanic acid, as the latter is a dioxymethyl-anthraquinone, the former is a reduced quinone. Hence its affinity for oxygen, as the reduction products of the quinone class almost always tend to absorb oxygen and again go back to their original condition. Liebermann, in observing the chemical relationship of chrysophanic acid to commercial alizarine and purpurine, was led to study their reduction products (or leuco-compounds), and so discovered a class known as *anthrarobins,* having medicinal properties similar to chrysarobin. (See *Anthrarobin,* Part II.)

Hesse (*Ann. Ch. Ph.,* 1912, p. 388) found that chrysarobin is a complex body containing at least five different substances, namely chrysophanol-anthranol, its methyl ether emodinol and its methyl ether, and chrysarobol. Of these chrysophanol-anthranol is the one to which the drug owes its characteristic properties. This work has been confirmed by Tutin and Clewer (*Tr. Chem. Soc.,* 1912), but the latter find other constituents in addition.

Lenirobin, made by the action of acetic acid on chrysarobin, and described as a tetracetate, and *Eurobin,* the triacetate, are recommended as substitutes for chrysarobin, having the advantage of not staining linen indelibly. (*M. R.,* 1898, 466.)

Uses.—When taken internally in sufficient amount, chrysarobin acts as a decided gastro-intestinal irritant, producing large, very watery, brownish stools, and repeated vomiting without much nausea; it has, however, failed to secure a place as an internal remedy. Chrysarobin has long been used in South America and India as a remedy in skin diseases, but the attention of the general profession was first called to it in 1874 by Sir Joseph Fayrer. It is a remedy of the greatest value in the treatment of *psoriasis* and is also of service in chronic *eczema.* Schamberg, Kolmer and Raiziss (*Jour. of Cutaneous Dis.,* 1915, xxxiii) in an elaborate research on its mode of action reach the conclusions that chrysarobin is without germicidal properties and that its beneficent effects are probably due to its chemical affinity for the keratin elements of the skin, the drug abstracting the oxygen for its oxidation, which takes place simultaneously with this union, from the epithelium.

It may be applied in the form of an oint-

ment with good success, although this method of application has the objection of staining the clothing. For this reason a number of dermatologists prefer the solution in collodium, which may be prepared by dissolving a drachm of chrysarobin in a fluidounce of the official flexible collodion. This is painted over the lesions with a camel's hair brush and after it is thoroughly dried the film may be coated with plain collodium as a further protection against staining the clothing. Another method of applying the drug is to dissolve it in chloroform in the proportion of one to two drachms to the ounce. This solution is painted on the skin, the chloroform evaporating and leaving a thin film of chrysarobin behind. Kossobudskji highly recommends in the treatment of *hemorrhoids* an ointment containing twenty-five grains of chrysarobin, nine grains of iodoform, and eighteen grains of extract of belladonna to the ounce of petrolatum. Benzin is said to be useful for removing the stains caused by chrysarobin.

Dose, official, one-half grain (0.032 Gm.).

Off. Prep.—Unguentum Chrysarobini, *U. S., Br.*

CIMICIFUGA. U. S.

CIMICIFUGA Cimicif. [Black Cohosh, Black Snakeroot, Macrotys]

(cim-ĭ-cif'ū-gą)

"The dried rhizome and roots of *Cimicifuga racemosa* (Linné) Nuttall (Fam. *Ranunculaceæ*), without the presence or admixture of more than 2 per cent. of stems or foreign matter." *U. S.*

Cimicifugæ Rhizoma, *Br.*, 1898, Acteæ Racemosæ Radix; Cohosh; Macrotys; Rattleroot; Squaw Root; Rattle Snake Root; Bugbane; Rattle Weed; Richweed; Bugwort, Rattletop; Racine d'Actée à Grappes, *Fr.*; Schwarze Schlangenwurzel, *G.*

Cimicifuga was dismissed from the Br. Pharm., 1914.

Cimicifuga racemosa is a tall stately plant, having a perennial root, and a simple herbaceous stem, which rises from four to eight feet in height. The leaves are large, and ternately decompound, having oblong-ovate leaflets, incised and toothed at their edges. The flowers are small, white, and disposed in a long, terminal, wand-like raceme, with occasionally one or two shorter racemes near its base. The calyx is white, four-leaved, and deciduous; the petals are minute, and shorter than the stamens; the pistil consists of an oval ovary and sessile stigma. The fruit is an ovoid capsule containing numerous flat seeds. The plant grows in shady or rocky woods from Southern New England to Wisconsin and southward, flowering in June and July. The name Cimicifuga is derived from the Latin *Cimex,* bug; and *fugare,* to drive away.

Properties.—It is officially described as follows: "Rhizome horizontal, more or less branching, from 2 to 12 cm. in length, and from 1 to 2.5 cm. in thickness; externally dark brown, slightly annulate from circular scars of bud scale-leaves, the upper surface with numerous stout, erect or somewhat curved branches terminated by deep, cup-shaped scars, each of which usually shows a distinct radiate structure; inferior and lateral portions with numerous root-scars and a few short roots; fracture horny; internally whitish and mealy or dark brown and waxy, bark thin, wood distinctly radiate and of about the same thickness as the pith; odor slight; taste bitter and acrid. Roots somewhat cylindrical or obtusely quadrangular, from 1 to 3 mm. in thickness, externally dark brown, longitudinally wrinkled; fracture short; internally bark dark brown, wood yellowish, 4 to 6-rayed. Under the microscope, sections of the rhizome of Cimicifuga show a yellowish-brown suberized epidermis, a cortex made up of about 30 layers of starch-bearing parenchyma cells; the fibro-vascular bundles collateral, the xylem consisting of tracheæ with bordered pores, and resembling tracheids in that the ends are rather acute; wood-fibers numerous, thin-walled, strongly lignified and with simple, oblique pores, the bundles separated by starch-bearing parenchyma strands from 5 to 30 cells wide; pith cells numerous, resembling those of the cortex. Under the microscope, sections of the root of Cimicifuga show a hairy epidermis, which becomes suberized in older roots; the cortex shows about 12 rows of starch-bearing parenchyma cells; endodermis distinct; fibro-vascular bundles 4 to 6, showing in older roots as separate collateral bundles. The powder is light to dark brown; starch grains numerous, single or compound, the individual grains spherical or more or less polygonal, each with a somewhat central cleft, from 0.003 to 0.015 mm. in diameter; fragments showing tracheæ with bordered pores and lignified wood-fibers; irregular, yellowish-brown fragments of suberized epidermis made up of more or less tabular cells, sometimes elongated and considerably thickened. Cimicifuga yields not more than 10 per cent. of ash." *U. S.*

For a detailed description of the microscopic character of the root, see *A. J. P.*, 1884, 460; also 1895, 121; Holm., *M. R.*, 1911, p. 6.

The roots "exhibit in transverse section from three to five wedge-shaped wood-bundles, separated by as many broad medullary rays. Both rhizome and roots are blackened by *test-solution of ferric chloride* (presence of tannic acid)." *Br.*, 1898.

The odor, though not strong, is peculiar and rather disagreeable, and is gradually lost with age. The drug of commerce is likely to be unintentionally admixed with other species of *Cimicifuga* and *Actæa.* Cimicifuga yields its virtues to boiling water.

Tilghman found gum, starch, sugar, resin, wax, fatty matter, tannic and gallic acids, a black coloring matter, a green coloring matter, lignin, and salts of potassium, calcium, magnesium, and iron. (*A. J. P.*, vi.) It no doubt also contains, when fresh, a volatile principle,

with which its virtues may be in some degree associated. Davis separated by distillation a small proportion of volatile oil having decidedly the peculiar odor of the root. He also found albumen, extractive, and silica. The sugar noticed by him was of the uncrystallizable variety, and the resin of two kinds, one soluble in alcohol but not in ether, the other soluble in both these menstrua. (*A. J. P.*, xxxiii.) A crystallizable principle has been obtained by T. Elwood Conard from a strong tincture of the root by treating with solution of lead subacetate to precipitate resin, tannin, and coloring matters, then filtering, and precipitating the lead by hydrogen sulphide in excess, and allowing the tincture to evaporate spontaneously; and, finally, having treated the residuary powder with petroleum benzin, afterwards washing it with water, dissolving it to saturation in strong alcohol, and treating the solution with alumina. The mixture was allowed to evaporate to a dry mass, which was nearly exhausted with alcohol. The solution, being allowed to evaporate, left behind a crystalline mass, somewhat resembling alum. This substance has little taste, on account of its extreme insolubility in the saliva, but in alcoholic solutions has very strongly the acrid taste characteristic of the fresh root. The crystals are very soluble in cold, and more so in hot alcohol, soluble also in chloroform, and slightly so in ether. They are fusible and inflammable. They are neutral, possessing neither acid nor alkaline properties. Their effects on the system were not determined. (*A. J. P.*, 1871.) L. F. Beach (*A. J. P.*, 1876) obtained from commercial resin of cimicifuga (the so-called cimicifugin or macrotin) a crystalline principle by Conard's process. M. S. Falck (*A. J. P.*, 1884) found in the juice of the fresh plant a crystalline principle resembling the principle announced by Conard. On the other hand, neither F. H. Trimble (*A. J. P.*, 1878) nor Warder and Coblentz were able to obtain a crystalline principle, while C. S. Gallagher obtained crystals of cane sugar from the fluidextract. (*A. J. P.*, 1887.) In view of these facts, it would appear that the active principle is a resinous amorphous body. (See *Drugs and Medicines of North America*, vol. i.) Finnemore reports on the chemical examination of the rhizome of cimicifuga. A systematic examination has resulted in the isolation and identification of *isoferulic acid*, also a minute quantity of an acid whose melting point was unaffected by admixture with salicylic acid. Palmitic, oleic, and other unsaturated acids, and phytosterol, are also present, and distinct reactions for alkaloids have been found, but the amount present is very small. (*P. J.*, 1910, 31 (85), pp. 142–144, 178.)

Uses.—In 1831 cimicifuga was introduced to the notice of the profession by Young. In overdoses it is said to cause general relaxation, vertigo, tremors, decided reduction of the pulse; occasionally it causes vomiting, but its emetic action is never violent, and is probably simply the result of a mild gastric irritation. It certainly, in large doses, produces giddiness, with intense headache and prostration. It has been found by R. Hutchinson to cause in frogs complete anesthesia by a direct action upon the sensory side of the spinal cord. The same observer noted that toxic doses produce in mammals slowing of the pulse and fall of the arterial pressure, results which appear to be due in part to a direct depressant action upon the heart muscle or its ganglia, in part to a paralysis of the vasomotor center. Clinical experience has shown this drug to be a useful remedy in the treatment of *chorea*. It has also been employed, though with less certainty of benefit, in *chronic rheumatism, urticaria, neuralgia,* and *dysmenorrhea*. It is also asserted to act as a specific in *tinnitus aurium*.

In *chorea* it is necessary to give large doses. The proper method of administration is to start with about fifteen minims of the fluidextract three times a day, increasing one minim daily until the occurrence of frontal headache or improvement in the condition. The practitioners calling themselves eclectics use, under the name of *cimicifugin*, or *macrotin*, an impure resin obtained by precipitating a saturated tincture of the root with water; dose, a grain or two (0.065–0.13 Gm.). (See *N. J. Med. Rep.*, viii, 247.)

Dose, of powdered cimicifuga, five to thirty grains (0.3–2.0 Gm.).

Off. Prep.—Extractum Cimicifugæ, *U. S.*; Fluidextractum Cimicifugæ, *U. S.*; Elixir Sodii Salicylatis Compositum (from Fluidextract), *N. F.*; Syrupus Cimicifugæ Compositus (from Fluidextract), *N. F.*; Tinctura Cimicifugæ, *N. F.*

CINCHONA. U. S.

CINCHONA Cinch. [Peruvian Bark, Yellow Peruvian Bark]

(cĭn-ko̍'nă)

"The dried bark of *Cinchona Ledgeriana* Moens, *Cinchona Calisaya* Weddell, and of hybrids of these with other species of *Cinchona* (Fam. *Rubiaceæ*), yielding not less than 5 per cent. of the alkaloids of Cinchona." *U. S.* (See page 350.)

Cinchonæ Flavæ Cortex; Yellow Cinchona Bark, Cinchona Flava, *U. S.* 1880, Yellow Cinchona, Calisaya Bark; Cortex Chinæ Calisayæ, Cortex Chinæ Regiæ; China Regia; Königschina, Calisayarinde, *G.*; Quinquina jaune royal, Quinquina Calisaya, *Fr. Cod.*; China gialla, *It.*; Quina calisaya, Quina amarilla, *Sp.*

CINCHONA RUBRA. U. S. (Br.)

RED CINCHONA Cinch. Rub.

(cĭn-ko̍'nă rū'bră)

"The dried bark of *Cinchona succirubra* Pavon (Fam. *Rubiaceæ*), or of its hybrids, yielding not less than 5 per cent. of the alkaloids of Red Cinchona." *U. S.* "Red Cinchona Bark is the dried bark of the stem and branches of cultivated plants of Cinchona succirubra, *Pav.*" *Br.*

Cinchonæ Rubræ Cortex, *Br.*; Red Cinchona Bark; Cortex Chinæ Ruber, China Rubra; Red Peruvian Bark; Red Bark; Quinquina rouge, *Fr.*; Cortex Chinæ, *P. G.*; Chinarinde, Rothe Chinarinde, *G.*; China rossa, *It.*; Quina roja, *Sp.*

Botanical History.

Though the Peruvian bark was introduced into Europe so early as 1640, it was not until the year 1737 that the plant producing it was known to naturalists. In that year La Condamine, on a journey from Quito to Lima, through the province of Loxa, had an opportunity of examining the tree, of which, upon his return, he published a very complete description, with plate, under the name *Quinquina*, stating that three species were recognized. (*Mém. Ac.*, Paris, 1738, p. 226.) Four years later, Linné proposed a new name, *Cinchona*, in honor of the Countess of Chinchon, who first made the bark known in Europe. Linné recognized but one species, which he called *C. officinalis*, and this continued for a long time to be recognized by the Pharmacopœias as the only source of the Peruvian bark of commerce. But a vast number of plants belonging to the Linnæan genus Cinchona were in the course of time discovered; and the list became at length so unwieldy and heterogeneous that botanists were compelled to distribute the species into several groups, each constituting a distinct genus, and all associated in the natural family of Rubiaceæ.

For our knowledge of these plants as they existed naturally, we are chiefly indebted to the following botanists, besides La Condamine, of whom we have before spoken: Joseph de Jussieu, who, in the year 1739, explored the country about Loxa, and gathered specimens which still exist in the cabinets of Europe; Mutis, who in 1772 discovered Cinchona trees in Colombia, and afterwards, aided by his pupil, Zea, made further investigations and discoveries in the same region; Ruiz and Pavon, who in 1777 began a course of botanical inquiries in the central portions of Lower Peru, and discovered several new species; Humboldt and Bonpland, who visited several of the Peruvian bark districts, and published the results of their observations after 1792; Pöppig, who travelled in Peru so late as 1832, and published an account of his journey about the year 1835; Weddell, whose researches in Bolivia are so well known and have been productive of valuable information in relation to the Calisaya bark and allied species; while Karsten, Caldas, Martius, Ledger, Markham, and other intrepid explorers have in later times largely added to our information. At the present time (1917) thirty or forty more or less clearly defined species of Cinchona are recognized. Of all of these probably but four with their cultivated hybrids yield the Cinchona Bark of commerce. The principal sources of information bearing on this phase of the subject are the several reports of the plantations in Java, India, and Jamaica. Howard's *Quinology of the East Indian Plantations*, Markham's *Peruvian Bark*, Kuntze's *Arten, Hybriden und Cultur der Chininbäume*, Hooper in the *Pharmacographia Indica*, several contributions by Trimen to the *Tropical Agriculturist*, and Rusby in the *Pharmaceutical Record*, October, 1887. The literature of the cinchona hybrids is hopelessly confused by the same name being frequently used by different authorities for the different hybrids and the one hybrid having various names. Thus, *C. robusta* of Trimen is known in Ceylon as *C. lanosa*, and in the Neilgherry Hills as *C. magnifolia*, also as *C. pubescens*.

C. Calisaya Weddell, is tall, usually surpassing those about it, the trunk often more than two feet in diameter. Leaves petiolate, the blade ovate-oblong to slightly obovate, 7 to 17.5 cm. long by 2.5 to 7 cm. broad, obtuse, the base acute or slightly attenuated, very thin, smooth, and, especially below, with a satiny luster, above dark green, below emerald-green or deep purple-green, scrobiculate, the glands scarcely visible above. Stipules oblong, about equalling the petioles, very smooth, very obtuse. Panicles ovate to subcorymbose. Calyx pubescent, with a cup-shaped limb and short triangular teeth. Corolla rose-colored (in cultivation often white or nearly so), the tube cylindrical and about 8 mm. long, the laciniæ more deeply colored, the edges white-hairy. Stamens included. Capsule ovate, scarcely as long as the flowers. Seeds elliptical lanceolate, the margin irregularly fimbriate-toothed. Bolivia and Southern Peru, 4000 to 6000 feet. Source of the Calisaya or Yellow Bark. The species presents many forms, and two varieties are recognized.

C. Ledgeriana Moens., formerly recognized as a variety of *C. Calisaya*, differs from the type chiefly in its thicker, narrower, oblong leaves, with attenuate base, often bluish-green below. It yields a thick and remarkably rich bark, and is probably the most valued of all the cinchonas. This species was named in honor of Ledger, who first brought seed of this species from Bolivia.

C. succirubra Pavon, Mss. (Howard in *P. J.*, Oct., 1856, p. 209, with a figure). Extreme size even greater than that of the last. Branches silvery. Petiole pubescent, leaf ovate to oval, acute with a very short point, the base more or less narrowing, often 6 by 9 inches, dark green and smooth above, below paler and pubescent to a variable degree, especially on the veins, not scrobiculate, the margin slightly revolute. Stipules entire, oblong, obtuse, subamplexicaul. Flowers much as in the last, but rather smaller. Fruit lanceolate. Western slopes of Mt. Chimborazo. The source of the Red Bark.

C. officinalis Hooker fil.—Petioles smooth, cylindrical, and, like the veins, reddish; blade 10 to 12.5 cm. long, varying from broadly oval to lanceolate, acute at both ends, the margins usually recurved, smooth and deep green above, paler, but bright green below, scrobiculate, the principal veins pubescent. Stipules equalling the petioles, ovate, acute, entire, pubescent. Flowers and fruit much as in *C. Calisaya*. Widely distributed in the equatorial Andes, at an elevation of from 5000 to 7500 feet. The source of the barks known as Pale, Crown,

Loxa, Cuenca, and Huanuco. This is the original species, upon which the genus *Quinquina* or *Cinchona* was founded. All things considered, it is, perhaps, to be regarded as the principal species of the genus and its variability is extreme.

The specific variations produced by hybridization in the above characters may not be here considered, though it may be stated that they are entirely characteristic. The parentage of a hybrid is ordinarily fully and strongly indicated in its appearance. As a rule, also, the alkaloidal yield takes a mean between that of the parents, but sometimes this is conspicuously not the case. Goris and Reimers (*Trav. Lab. Nat. méd. Ecol. supe. Pharm.*, in *Bot. Centralbl.*, 1906, p. 462) pointed out the use of *Cinchona robusta* Trimen as a collective name for all hybrids of *C. succirubra* and *C. officinalis*. Rosenthaler gives an account of the structural characteristics and alkaloidal content of *C. robusta* and other cinchona hybrids produced by grafting. (*B. P. G.*, 1908, p. 126.)

Geographical Distribution.

The genuine Cinchona trees are natives exclusively of South America. In that continent, however, they are widely diffused, extending from the 19th degree of south latitude, considerably south of La Paz, in Bolivia, to the mountains of Santa Marta, or, according to Weddell, to the vicinity of Caracas, on the northern coast, in about the 10th degree of north latitude. They follow, in this distance, the circuitous course of the great mountain ranges, and for the most part occupy the eastern slope of the second range of the Cordilleras. Except northward from Guayaquil, both the western slope and the plateau are entirely too dry or too cold for these plants, which require a moderate and equable temperature and an abundant and fairly constant supply of water. Irrigation cannot supply the place of a humid climate, for the atmosphere as well as the soil must be well charged with moisture. A certain amount of dry weather is, however, required for the ripening of the capsules. Free drainage is an important condition. Cross and others, who have personally inspected the region in the Andes where the best barks are obtained, have found the Cinchona trees only on the well drained slopes, and never on wet ground. With regard to temperature, Cross found that in the region of the *C. officinalis* the variation was from 1.1° to 21.1° C. (34°–70° F.), a fall below 40° or a rise above 65° being rare, and the mean range being from 45° to 60°.

The limits of altitude and climatic conditions are closely drawn. In the most southern districts, the trees descend to about 2500 feet, while in the warmest regions they scarcely ascend to the 10,000-foot level. The individual species are for the most part rigidly restricted as to altitude and latitude, and, indeed, it has not always been found easy to detect the climatic conditions which would cause one species or variety to thrive while another very near it would languish. This is especially true of the more valuable forms.

It is to be noted that at present the stocks of wild barks have been enormously reduced, as detailed under Commercial History. Indeed, in certain sections, as the Calisaya district, the tree was practically exterminated in the wild state, so far as relates to a bark supply. From the far interior, however, occasional bales of wild Calisaya have been received. The low price of cultivated bark since 1885 has resulted in checking the destruction of the wild trees, which have begun again to multiply, so that they may possibly become once more common or even abundant. The Crown Bark region of Ecuador is still fairly productive, and in Colombia and Venezuela there are vast supplies of more or less inferior barks which await some favorable change in the market—never very likely to take place—that will render their collection profitable. Even at present a limited and irregular supply of one of these barks is furnished. With the exceptions here noticed, our present supplies of bark are entirely the product of cultivation, to which, therefore, we must give our chief attention.

Cultivation and Production.

The alarming prospect of the failure of the supply of Cinchona bark (see Commercial History) induced Europeans, about the middle of the nineteenth century, to turn their attention to the possibility of introducing the trees to cultivation. So early as 1737, La Condamine had collected a large number of young plants, with a view of conveying them to Europe; but, after having descended the Amazon in safety for more than a thousand leagues, they were washed overboard, near the mouth of that river, from the boat containing them, and were all lost. After this failure, though the idea of transplanting the Cinchonas was occasionally suggested, nothing was done until 1846, when Weddell, now celebrated for his successful exploration of the region of the Calisaya bark, sent some seeds to France, which were planted with success in the Jardin des Plantes, and thus supplied some of the conservatories of Europe with specimens of the plant. But the first successful effort with a view to great practical results was made in 1853 by the Dutch government, by which Hasskarl, formerly superintendent of the Botanical Garden in Java, was sent to South America on this important mission. Five hundred Calisaya seedlings were forwarded by him directly across the Pacific to Batavia, which they reached before the close of 1854. From these, and from seeds obtained from other sources, which were planted in the mountains of Java, in sites selected for their supposed conformity in climate with the native locality of the Cinchona, have sprung the most important plantations now in existence.

Stimulated by the suggestions of Royle, and by the partial success of the Dutch, the English

government engaged, in 1859, the services of Clements R. Markham, who proceeded to Bolivia, in South America, and, after almost incredible hardships, arising partly from the nature of the country and partly from the jealousy of the native authorities, succeeded in collecting and transmitting to England upwards of 400 Calisaya plants. Most of these, however, were so much injured on their way from England to India, by the excessive heat of the Red Sea, that very few, on their arrival in Hindostan, had sufficient life remaining to grow when planted. Happily, the deficiency was supplied by seeds of *C. Calisaya* sent from Java, to Calcutta, at the request of the English Governor-General. While Markham was in Bolivia, other agents were collecting other species in Peru and Ecuador, whence seeds of the pale and red bark Cinchonas reached India, and, being planted in the selected sites, proved to be very productive.

Careful attention to the conditions of growth enumerated under Geographical Distribution was found essential in the selection of sites for the plantations. Those selected were near the Sanitary Station of Ootacamund in the Neilgherry Hills of Southern India, at heights varying from 5000 to 7450 feet. These positions unite the peculiar characters of the native regions of the Cinchonas in the Andes, not only as regards elevation and latitude, but also as to atmospheric moisture. Other sites were selected for experimental plantations, and since the first introduction of the Cinchona trees, their culture has been extended to various points from Hakgalla, in the island of Ceylon, to the Himalaya Mountains,—as in the Wynaad, the Coorg, the hills of Travancore, and especially at Peermede in the Presidency of Madras; in Sikkim and Darjeeling in the Presidency of Bengal; at Lingmulla in the Presidency of Bombay; and in the valley of Kangra in the Punjab,—from the southern to the northern extremity of British India. Outside of India and Ceylon, culture by the British has been undertaken in the West Indies, particularly Jamaica, in Guiana, and in the Fiji Islands. The first plants taken by Weddell from Peru to Paris all perished, but the French afterward established plantations in the Isle of Bourbon, at Guadeloupe, and in Algiers, none of which are known now to exist. The Portuguese have established plantations upon the west coast of Africa, and these now yield considerable quantities of bark. Very extensive plantations have been formed, chiefly by the Germans, in Bolivia. A rather large plantation in Colombia is now old enough to be productive. In Mexico and Central America various attempts to introduce the industry have been made. The question of introducing it into the United States has frequently been raised, but it may be stated that there is no spot in North America where the conditions warrant the slightest hope of success in this direction.

The history of Cinchona cultivation affords a striking illustration of the importance of government aid in the establishment of a new industry of this kind. The early and repeated disappointments and failures, owing to the natural obstacles in the way of securing stocks, and to an almost total ignorance of the conditions determining the successful propagation and growth of the plant, and the composition of its bark, were such as to have discouraged the most hopeful of private enterprises. Repeated and expensive expeditions were necessary before the first transplantings were accomplished, and these stocks were preserved and propagated only through the instrumentality of well appointed public gardens and plantations. In Java, after these early difficulties had been surmounted and success apparently attained, it was found that owing to cross fertilization much of the progeny was entirely worthless, and the work of propagation had to be begun anew. The same difficulty was encountered elsewhere, and the slow and expensive method of propagation by cuttings was largely resorted to. In Ceylon the public were slow to become interested, and the officials were obliged not only to give away the young plants, but to solicit experiments with them as a personal favor. In Jamaica a hurricane visited the young and flourishing plantations and almost completely destroyed them. But at length, in spite of all, not only were thriving and permanent government plantations established, but private capital and enterprise upon a vast scale were enlisted. The question of commercial success is dominated not simply by climatological surroundings, but also by the price of labor. It is stated that both in India and Java the natives who work in the cinchona forests are paid from one dollar to one dollar and seventy cents per month, without food, according to the age and sex. The ability to extract the bark upon the spot is capable of largely counterbalancing a lack of market facilities; but it so happens that this advantage also inures to the benefit of the Eastern countries. Originally undertaken in India for the purpose of affording a cheap antiperiodic (the crude alkaloids known as "*febrifuge*" or "*quinetum*") home extraction has become a most important industry, and has assumed various forms. In Java the powdered bark is thrown into a 5 per cent. solution of caustic soda at 50° C. (122° F.) treating this with Java petroleum, separating, treating the petrolic solution with water acidulated with sulphuric acid and evaporating; the result is said to be a quinine containing less than 1 per cent. of cinchonine. (*J. P. C.*, 1901.) It is imported largely into the United States—50,000 kilogrammes a year—but on account of its yellow color is chiefly employed in the making of proprietary medicines rather than tablets. Through the influence of the above conditions the locations of the important industry of Cinchona cultivation have been gradually wrought out, and at present about four-fifths of the cinchona barks of the world, outside of India, are furnished by Java. The first shipment from

Java was of 900 pounds, in 1869. In 1902 it was 14,700,000 pounds and in 1911 over 20,000,000 pounds. India produces annually over 2,000,000 pounds; Ceylon about 400,000 pounds; Portuguese West Africa about 180,000 pounds, and South America 775,000 pounds. Tunmann estimates that the yearly output of cinchona bark is about 10,000,000 kilogrammes, and the production of quinine as about 500,000 kilogrammes. (*Apoth. Zeit.*, 1910, p. 565.)

It is to be remembered that a great part of the Indian product is not exported.

Methods of Cultivation.

The history of Cinchona cultivation teems with evidence as to the difficulty of obtaining pure seeds, owing to the tendency of the plants towards cross-pollination. In every locality where the industry has been established has the disgust of the gardener been excited by the discovery that the plants which he had reared with great care, and upon which he had based great expectations, were contaminated by the admixture of foreign pollen. This was especially true in case of the earlier attempts, before this tendency had become known. Experience at length established the fact that absolute isolation of the seed-trees was essential. One of the curious developments of these experiments was the fact, already referred to, that the value of the progeny was not always assured by the value of its parentage. Some of the hybrids, even when least expected, would develop a surprisingly rich yield; and this tendency has been utilized to develop the most valuable stocks in existence. So certain is it that some of the plants from the best seed will prove worthless, that the careful selection of the seedlings while young is deemed necessary, and in South America, at least, all planting contracts are based upon this expectation, the contractor not being paid for his work until the plants have become old enough to show with certainty the proportion of good plants contained. Both in the selection of the young seedlings and the acceptance of the plantation, the test of identity is found in the leaf. Propagation by cuttings, extensively practised in some localities, has been found too slow and expensive to become general. A thorough preparation of the soil is as beneficial in the case of Cinchona as in that of other crops. Thorough tillage after transplantation is also essential, a free growth of weeds meaning destruction to a large number of the young trees. The cultivation of a secondary crop between the rows of trees is, however, practicable. A large percentage of profit depends upon the selection of a suitable age for collecting the bark. There comes a time when the use of the ground for starting a new crop is more valuable than the gain by permitting the present crop to remain, and after some years an actual deterioration of the bark sets in. This age is not the same for all the trees in the plantation. Several years' difference may occur in the maturing of trees germinated at the same time. In the case of Calisaya it occurs at from six to nine years from seed, and its indication is the "chicken-leg" scaliness of the bark, as described under Classification. The "officinalis" matures somewhat less early. In the Bolivian plantations the most experienced hand is selected as the marker, and the cutters follow him, peeling the trees which he has indicated. How far these careful methods of selection are followed elsewhere, the writer is not informed.

Collection of Bark.

Four principal methods of collecting the bark are in vogue, these being variously modified in different sections. The first is *uprooting*, the most primitive, by which the trees are simply uprooted at the proper age, and the ground replanted. The barks of root, stem, and branches are preserved and marketed separately. The second method is *coppicing*, by which, after peeling a quill from the lower portion of the trunk, the latter is cut a few inches from the ground and the remainder of the stem bark and the branch bark are removed. The "coppice" is formed by a second growth of two shoots from each of the stumps. A second coppice is commonly grown, and this is harvested by uprooting. By the third method, *scraping*, the outer bark is scraped off, leaving the liber untouched. This has been found especially applicable to young trees, in which the second growth of bark is rapidly formed and contains 20 to 30 per cent. more alkaloid than that which has been taken off. It seems to be a general opinion among the planters that scraping checks the growth of the tree after it is five years old, so that from three to five years is the age at which it is best practised. The fourth method is known as *mossing*. It having been noticed that the Cinchona alkaloids, especially in any other form than that of sulphate, were apt, on exposure to the direct light of the sun, to become reddened by the generation of coloring matter, at the expense of the alkaloid, it was a very natural inference that a similar change might take place in the living plant, as a consequence of which the proportion of alkaloids they were capable of producing might be greatly diminished. It was also observed that the bark upon that side of the tree where the sun struck it was less rich than that upon the shady side. To obviate this presumed effect, MacIvor was induced to make the experiment of covering the stems of the growing trees with a layer of moss, so as to completely protect the bark against the influence of sunlight. The result was favorable beyond all expectation, and the yield of alkaloids in the bark thus protected is said to be doubled, tripled, or increased even in larger proportion. A tree can thus be made continuously productive; for if a slip is removed longitudinally from the trunk, from top to bottom, by covering the decorticated portion with moss, the bark is renewed at least as rich as previously in the

alkaloids, while from time to time other strips may be taken, until the whole of the old bark is removed, and the new ready for removal by a repetition of the same process; and the tree is thus preserved indefinitely, probably for the whole normal length of its life. Hooper says that renewed bark is always of greater value than the mossed, and mossed than the natural, so long as the trees are under twenty years old, for it has been found that after that time the bark ceases to thicken, and the alkaloids remain stationary or even decrease. Perhaps twenty years is even too old. The practical difficulty with the process is that it requires skilled workmen, not always attainable, and hence the "coppicing system" still largely prevails in India.

The methods of packing the bark have also undergone important modifications since the early days of cultivation. The extensive adulteration practised when the wild bark brought very high prices led to a demand for it in large pieces which could be readily and quickly examined; hence the appearance of the large *tabla* and *quill* forms, the latter afterwards becoming the standard for the cultivated bark. The bark of the trunk, and sometimes of the branches when very large, is cut into two-foot lengths, and each length removed in a single piece, which in drying rolls up to form a quill. Such peeling can of course be successfully practised only at the appropriate season of the year. The bark or the roots, branches, and dead or dry trunks must be removed by chipping, scraping, or shaving, commonly the latter. The quills, after thoroughly drying, are carefully packed in bales, or preferably in boxes, to avoid breakage, and are marketed in packages of from 100 to 250 pounds. Large quantities of cultivated bark are still marketed in this way, but, increasing competition having lowered prices so that economy in freight has become a very important item, most of the bark is now broken up, and its bulk even reduced by high pressure, and in fact only a trifling amount of wild South American bark comes into commerce. Cultivation has very greatly increased, not only the quantity, but also the quality of bark. For some years, in India the attempt was made largely to increase the general average in total alkaloids rather than in quinine, so as to increase the production of the impure alkaloids which are so largely used as febrifuges in the British East Indies. Of recent years, however, even in India, efforts have been directed to the obtaining of quinine rather than of inferior alkaloids. The barks of Ceylon have always been of poor quality, while those of Java to-day are probably the best that have ever been put upon the market. The effect of the efforts of arborculturists is well shown by the facts that in 1889 the average percentage of quinine in Java bark was 4; in 1893 it had risen to 4.6; while in the five years, from 1900 to 1904 inclusive, the average quinine percentage of all the Java barks sold in the Amsterdam market was 5.37. The result does great credit to Java, for during the early history of her bark enterprise her plantations were stocked with discouraging quantities of poor or even worthless barks, which have been eliminated by the most steady enterprise and patient industry. David Howard presented a comprehensive survey of cinchona barks and their cultivation. (*J. Soc. Ch. Indus.*, 1906, p. 97.) Winkler describes the methods employed in the cultivation of Cinchona in Java, also the manner of collecting the bark and preparing it for market. (*Der Tropenpflanzer*, 1906, p. 222.) Böhringer gives a review of the progress in the cultivation of Cinchona in Ceylon. (*Tropenpflanzer*, 1909, p. 269.) Schneider discusses the possibility of cultivating Cinchona in California. (*W. D.*, 1906, p. 136.)

Commercial History.

The above general history of Cinchona leaves little necessary to be said of its commercial history, except to deduce from the facts already presented certain practical conclusions showing the present conditions of supply and demand, these bearing especially upon our concluding remarks concerning pharmacognosy and classification.

For more than a century after Peruvian bark came into use, it was procured almost exclusively from the neighborhood of Loxa. In a memoir published in 1738, La Condamine speaks of the bark of Riobamba, Cuenca, Ayavaca, and Jaen de Bracomoros. Of these places, the first two, together with Loxa, lie within the ancient kingdom of Quito, at the southern extremity; the others are in the same vicinity, within the borders of Peru.

Towards the end of the eighteenth century, however, the trees were discovered to exist in Colombia, in central Peru, near Lima (whence the name *Lima bark*, at one time applied to the drug) and in Bolivia.

The consequence of these discoveries was a vast increase in the supply of bark, which was now shipped from the ports of Guayaquil, Payta, Lima, Africa, Buenos Ayres, Cartagena, and Santa Marta. At the same time the average quality was probably deteriorated; for, though many of the new varieties were possessed of excellent properties, yet equal care in superintending the collection and assorting of the bark could scarcely be exercised in a field so much more extended. The varieties poured into the market soon became so numerous as to burden the memory if not to defy the discrimination of the druggist, and the best pharmacologists found themselves at a loss to discover any permanent peculiarities which might serve as the basis of a proper and useful classification. More or less perplexity attending the recognition of the barks continued until after the firm establishment of the bark culture and the cheapening of the price, to the exclusion of the worthless varieties, as already described.

One of the most important developments of the modern bark trade is the fixing of the price in accordance with the quality as determined

by assay. The most accurate method of selecting a characteristic sample for assay is a subject which has received much study, without the discovery of any method which does not depend for its value upon the discrimination and care exercised in its employment. The plan which is regarded as the safest, is to take a given weight, say eight ounces, from the inner portion of each package constituting the lot, mix and powder the whole of it, and furnish to applicants the required amount of the resulting powder. If any portion of any bale or bales is damaged, care is taken to add a proportionately large fragment of such portion. The bark is then recorded as containing so many units, a "unit" being each per cent. of quinine contained in a pound of bark. In rich bark the units are of course worth more than in poor, owing to the increased yield of alkaloid for the same cost of manufacture.

In the United States, at least, some difficulty has been experienced by druggists in securing the better grades of bark at regular rates, owing to the activity of the manufacturers in draining the market of the most desirable stock. The finer appearing packages of unbroken bark, having been marketed at greater cost, are necessarily held at higher prices. Possessing no special value for manufacturing purposes, these fall to the share of the druggist, but at higher prices than broken bark of the same richness. This fact has led to the recognition of two distinct classes, known as *manufacturers' bark* and *druggists' bark*. Druggists' bark, though in quills or unbroken pieces, and of a much finer appearance than manufacturers' bark, is on the average, inferior in quinine percentage. The druggists' bark finds its entrance into commerce through various channels but the bulk of the cinchona trade, including practically all that is known as manufacturers' bark, centres in Amsterdam and London; of these marts that at Amsterdam is much the more important. In 1916 there were imported into the United States 3,947,320 pounds of cinchona barks, and 1,791,738 pounds of quinine sulphate and other salts of the cinchona alkaloids. The bark which is sold in Amsterdam comes almost exclusively from Java; that in London from India, Ceylon, and South America. Manufacturers' bark is sold, without respect to its physical characters or place of origin, entirely by its chemical analysis, the buyer in London being furnished with samples of the different lots of the bark sufficient time before the sale to enable him to make his own analysis, while in Amsterdam the percentage of quinine sulphate in any lot is given in the catalogue and often tagged upon the bale.

Formation of the Alkaloids.—In a very careful series of experiments made at the Java governmental cinchona plantations, Lotsy (*Bull. Inst. Botanique Buitenzorg*, 3, 1900) found that the seeds of *C. succirubra* and *C. Ledgeriana* contain no alkaloids, but that these alkaloids appear in the cotyledons shortly after they become green. They exist chiefly in the bark in combination with a tannic acid. Lotsy found that the percentage of alkaloids is ten times greater in young than in old leaves; also that the petioles are richer in alkaloids than is the blade, and that the branch bark contains more than the trunk bark, and that the root bark is practically free from alkaloids. During the active life of the parenchymatous cells of the leaves, wood, and cortex, the alkaloids can always be found in the active protoplasmic contents, but when these cells pass into the inactive condition, are deposited in the cell-walls. The alkaloids found in the leaves are, however, never crystalline, hence it would appear that these organs produce by direct synthesis, probably as the result of the action of cinchonic acid with ammonia, a fundamental alkaloidal base, which probably in the cambium layer of the tree, and during its deposition in the growing bark, is elaborated into the true cinchona alkaloids.

Classification.

Extreme difficulty attended the earlier attempts to classify the Cinchona barks of commerce,—difficulties not probably encountered elsewhere in the Materia Medica. The varieties have, however, been reduced to a very few, and the whole subject decreased greatly in importance by the chemical method of the sale now in vogue. Most of the discarded barks will be found described in previous editions of this work. We find it necessary to enumerate and describe here only the Pale bark, from *C. officinalis*, the Red bark, from *C. succirubra*, the Yellow bark, from *C. Calisaya* and its var. *Ledgeriana*, and the Hard Yellow or Maracaibo bark, and to refer briefly to the hybrid forms. First, a few words concerning the forms in which Cinchona bark occurs. We have (1) the large flat pieces or chips of irregular shape and size,—this referring at present almost wholly to the Maracaibo variety; (2) the small chips or broken bark, referring in large part to the root bark, and to other bark broken for close packing; (3) the shaved bark, referring to some root bark and to stem bark taken from dry stems, but chiefly to branch bark; (4) the quill bark, referring to natural bark taken from the stem and root in quill form, this including the uncultivated pale bark and all the varieties of cultivated bark; and (5) the renewed and mossed bark, which may be of any cultivated variety. The classification of all varieties and forms into druggists' and manufacturers' barks enables us to dispense in great part with a description of some of these forms. The manufacturer cares nothing for form, appearance, or structure, and but little for the variety of his supplies. He is interested wholly in its composition, and this he determines by assay. For this reason most of the broken bark goes to him. The druggist requires the quill or large chip bark; so that the great bulk of the branch bark is also thrown, at low prices, upon the hands of the manufacturer.

As regards the root barks, no classified description is available. In their structure they correspond very closely to the stem barks of the same variety. They can be readily distinguished from the latter by being thinner, having lighter external and darker inner color, greater softness, and twisted or contorted structure. They occur in short, irregular quills or chips, or sometimes as shavings, and contain very much more dust than any other form. Except partly as regards structure, the description of stem barks will not apply to branch barks of the same variety, for the characteristic markings do not appear in the young condition. The branch bark appears in shavings, to the inner surfaces of many of which more or less wood adheres. If the branches were shaved while yet fresh, these shavings will be more or less rolled up and curled; but if dry before being removed, this rolling and curling will not occur. Shaved bark taken from living trees is thin, soft, and brittle, consisting of the outer bark only. The large quills are of uniform length from the same plantation, but not necessarily so from different plantations or different sections. They are commonly from two to three feet in length, but some have been marketed having a length of five feet. Usually they represent the entire circumference of the stem, but occasionally only half of it. In drying they roll up very tightly from one or both edges, and rarely one will be wholly or partly involved in another. The periderm, with all its markings, remains intact, and no other form so well displays the natural appearance as this. Mossed bark differs from natural stem bark in its great thickness and weight, less breadth of the quills, freedom from lichens, very dark color, and rough, corrugated or warty surface. The outer bark or cellular portion bears a greater ratio to the inner or fibrous portion than in natural bark. Renewed bark is lighter, both in color and weight, thinner, soft and brittle, and marked by a very peculiar external smoothness, sometimes very marked indeed. In its general appearance it is strikingly like a root bark, except for the relative straightness of its fibres. Like the mossed bark, it is in narrow, only partly rolled quills or bands, and is entirely free from lichens.

As they differ so greatly among themselves in coloration, lichen-growth, degree and form of exfoliation, structure and consequent fracture, there are but few characters which can be combined in a general description of the Cinchona barks which we consider. The external color varies from light ashy gray to nearly black, the inner varies less in its shades of yellow-brown and red-brown. All are more or less bitter, and most are astringent, but only Loxa bark has a distinctive odor. The fracture is never very long-splintery and never tough. As to structure, the bast fibers are loosely arranged, the radial rows being neither continuous nor very long. The fibers themselves are always unbranched, which distinguishes the true from the false barks, are rather short and obtuse, brittle, and usually easily detached from the bark. Laticiferous ducts and stone-cells may or may not be present. The former become less conspicuous as the bark grows older, so that their relative absence becomes indicative of a stage in which the due proportion of alkaloid should have been acquired.

It may be noted here that by far the greater portion of the alkaloid, particularly quinine, is stored in the outer bark, though that in the inner bark is in a purer state. The latter is not stored in the fibers, but in the cellular tissue between them.

As regards the former classification of barks by color, it referred only in small part to the external color, chiefly to the powder. These colors were never regarded as absolutely characteristic, as the three barks, yellow, red and pale, exhibited gradations by which they mingled at their extremes. Under present conditions, the lines of demarcation have become even more indistinct, and, as a matter of fact, in the market the terms "yellow" and "red" are used with great looseness. It is true that we receive much pure-blooded Yellow Bark, *Ledgeriana* from the East, and *Calisaya* both from there and from South America; but it is also undeniable that much of the bark sold under the several names is of mixed hybrid, and the typical characters are often greatly obscured. The presence in our market of these mixed forms has made the terms even less valuable than they once were, and dealers cannot be found to agree as to the character of many samples. Nevertheless, the occurrence of the typical forms, and appearance in a hybrid of the blended characters, render it desirable to preserve this classification, and to group the new forms around the types.

Yellow or Calisaya Bark. Cinchona Flava.

The official description is as follows: "In quills or curved pieces of variable length, bark from 3 to 5 mm. in thickness, or in small broken fragments or in transversely curved pieces from 3 to 7 mm. in thickness, externally gray, rarely brownish-gray, with numerous intersecting transverse and longitudinal fissures having nearly vertical sides, and usually with patches of foliaceous lichens with their small, brownish-black apothecia; when the outer bark is absent, the color externally is cinnamon-brown; inner surface light cinnamon-brown, finely striate; fracture of the outer bark short and granular, of the inner bark finely splintery; odor faintly aromatic; taste very bitter and somewhat astringent. The powder is reddish-brown; bast-fibers spindle-shaped, yellowish, from 0.3 to 1.35 mm. in length, with thick, strongly lignified, lamellated walls having slit-like, oblique pores; starch grains single or 2- to 5-compound, the individual grains spherical or plano-convex and from 0.003 to 0.015 mm. in diameter; sphenoidal micro-crystals of calcium oxalate numerous. Heat 1 Gm. of powdered Cinchona in a dry test tube; a tarry distillate forms, having a

purplish color and a somewhat granular appearance." *U. S.*

Its lichens are thin and closely adherent, not rendering it shaggy. External markings very characteristic, consisting of a very light longitudinal ridging or none at all, but of numerous transverse and longitudinal fissures or cracks, the presence and arrangement of which constitute the chief characteristic of Calisaya. Upon the young stems and branches they do not appear. The first to appear are the usually large primary fissures, which encircle the stem at the nodes, or points where pairs of leaves once stood. Subsequently, numerous smaller secondary transverse fissures appear upon the internodes, and these quickly become connected and crossed by longitudinal cracks, thus dividing the periderm up into more or less quadrangular checks, which may remain attached or fall away. This gives to mature Calisaya bark an appearance of scaliness like that upon the tarsus of a fowl, and this is known to the South American collectors by a term which signifies the "chicken-leg appearance." It has also been spoken of as a "carving-like" marking. Like the roughness upon a musk-melon, its great development is regarded as an indication of high quality, and especially is this true of a close proximity of the primary fissures. This roughness is also regarded as a sure indication of maturity. There are excellent distinctions between these and the somewhat similar fissures upon the bark of *C. officinalis*. In the latter they are coarser and more gaping. Even more important is the absence from Pale Bark of most of the longitudinal cracks, so that it does not become "chicken-legged," or at most only very slightly so. The external color of Yellow Bark is lighter than that of the Pale Bark. Longitudinal ridges are few if any, short, irregular, and inconspicuous. In fine South American bark some very small bright-red spots can be detected upon the periderm. East Indian Calisaya can commonly be recognized by its somewhat dingy or brownish shade of gray, the gray of the South American bark being bright and somewhat bluish-steel-colored.

In structure, the zone of large, rather numerous laticiferous ducts just outside the bast is conspicuous in young, and therefore inferior, samples. The rather small bast fibers are loosely scattered, almost uniformly single or a radial arrangement being apparent. The fracture is rough-splintery, though not coarse. Stone cells few or none. Odorless, more bitter, and less astringent than the Pale Bark. Ledger bark is the same as Calisaya in all its essential characters, but does not reach so great a size. In hybrids of Calisaya with succirubra the characters and quality of the latter appear to predominate.

This bark is scarcely collected in a wild state, but cultivated in all plantations. It is the largest quinine yielder, its amount being 70 to 80 per cent. of the total alkaloids contained in the bark. The var. *Ledgeriana* yields a very valuable hybrid bark with *C. succirubra*. *C. Calisaya* also hybridizes with the latter species. Hartwich describes the microscopical characteristics of Cinchona and related barks in *S. W. P.*, 1909, p. 249. Grutterink discusses the microchemistry of Cinchona alkaloids, with illustrations in *Zeit. anal. Chem.*, 1912, p. 215. Rosenthaler reviews the pyro-analytical results that have been obtained with Cinchona bark and describes the crystals found in the tar. (*B. P. G.*, 1911, p. 203.)

Red Bark. Cinchona Rubra.

This bark is recognized by the U. S. and Br. Pharmacopœias (for definition, see page 333). It is described in the U. S. P. IX as "in quills or curved pieces of variable length, bark from 2 to 4 mm. in thickness, or in small broken fragments or in transversely curved pieces from 3 to 7 mm. in thickness; externally gray, grayish-brown, or reddish-brown, more or less rough from corky protuberances, occasionally with transverse fissures which are rarely numerous or much intersected, and having their sides sloping, and with occasional patches of foliaceous lichens; inner surface reddish or orange-brown, distinctly striate; fracture short and granular in the outer bark, shortly and rather coarsely splintery in the inner bark; odor slight; taste very bitter and astringent. The powder is light brown; bast-fibers and sphenoidal micro-crystals of calcium oxalate, resembling those in cinchona; starch grains resembling those of cinchona relatively few, from 0.003 to 0.01 mm. in diameter. Heat 1 Gm. of powdered Red Cinchona in a dry test tube; a tarry distillate forms having a bright red color." *U. S.*

In the British Pharmacopœia it is described as "In quilled or curved pieces, length varying from 5 to 30 cm. or more; usually from about 2.5 to 6 mm. thick; cork brownish or reddish-brown, with longitudinal ridges which are most apparent in the branch bark, and sometimes with reddish warts; inner surface brick-red or deep reddish-brown, irregularly and coarsely striated; fracture shortly fibrous in the smaller, and finely fibrous in the larger, pieces. In transverse section in the cortex, cells filled with minute crystals of calcium oxalate, and also large secretion tubes; in the bast numerous, large, strongly-thickened fibers usually 0.050 to 0.070 mm. wide and about 1 mm. long, isolated or in small groups. The powdered Bark is brownish or reddish-brown, exhibits abundant parenchymatous tissue with brownish cell-walls, and often with brownish contents, small starch grains, and large isolated bast fibers about 0.060 mm. in diameter, with distinctly striated walls. No marked odor; taste bitter and somewhat astringent."

The quills are similar to those of Calisaya, though running somewhat broader and thicker. Externally of a dingy brown gray, less lichen-bearing than either of the others. Inner surface of a more reddish cinnamon-brown than in Calisaya. Powder reddish-brown.

The important characteristic of red bark is the prominent longitudinal ridges, many of them short and confluent, with intervening furrows or elongated meshes. The ridges are suberous, bear numerous small warty protuberances, and may be traversed by faint fissures. Transverse fissures may or may not be present in red bark. If so, they are few, short, and irregularly disposed, and not connected by longitudinal cracks to give the checkered appearance of Calisaya. Hybrids with "officinalis" display numerous transverse fissures, and the external color is lighter and more dingy. Fracture short-splintery, not coarse. Odor none. Taste bitter and astringent.

It is scarcely collected in a wild state, but cultivated in all plantations except those of South America. Demand and production rapidly decreasing. A large alkaloid yielder, but of this only about 20 per cent. is quinine. Largely hybridized with *C. officinalis*. Also hybridized with *C. Calisaya* and its var. *Ledgeriana*.

Pale Bark.

Varieties and Synonyms.—Crown Bark, Loxa or Loja Bark, Cuenca Bark, Huanuco Bark. Derived from *C. officinalis*. Collected in a wild state above Loxa and other parts of Ecuador, and cultivated in all plantations except the South American, especially in India. Demand and production decreasing. Quinine constitutes 60 to 70 per cent. of the total alkaloids. Largely hybridized with *C. succirubra*.

Description.—Quills single or double, irregularly broken or entire, attaining a length of nearly 2 dm., a width of nearly 2.5 cm., and having a very wide range in thickness, the natural mostly 2 to 4 mm. thick. Shaggy, with more abundant lichens than in any other species, the abundance of these having been considered, not entirely without reason, as an indication of the relative quality. Color of periderm darker than in the other species, but varying much from a brown gray to nearly black. Inner surface of a paler brown than in the other species, finely striate. Color of powder pale brown. The external markings consist of transverse fissures and longitudinal ridges, some of them wart-bearing. It is only in the thinner samples, in which the warts and fissures scarcely appear, that the ridges are continuous and conspicuous. In the prominence and breadth of its fissures and the inconspicuousness of its ridges, this bark is most distinct from the Red Bark. These characters are yet sufficiently distinct from the somewhat similar ones of Calisaya, as noted in describing that bark.

Fracture short, the inner fibrous zone sharp and narrow. Taste not so bitter as in the others. Odor of the genuine Loxa variety peculiar and characteristic. Its structure shows the rather short and not numerous bast fibers in short interrupted single or double radial rows, and much disposed to occur in bundles of three to six or more. Stone cells rarely seen, and laticiferous ducts conspicuous only when young.

Hard Yellow, or Maracaibo Bark. Puerto Cabello Bark.

Derivation not at all certain. Collected only in a wild state in the mountains of Southern Colombia, and yielding almost the whole of the inferior wild bark now collected for market. Importation and sale in the United States quite irregular and unimportant. One of the best of the lower-grade barks, but not to be compared with any of those already described. Said to yield about 2 per cent. of crystallizable sulphates, three-fourths of which is quinine sulphate, but a characteristic specimen assayed for this investigation by Virgil Coblentz yielded 2.65 per cent. of total alkaloids, only a trace of which was quinine. Contains a large amount of resin. The common or commercial names by which have been designated the several barks of the northern countries related to this one are of very irregular application. At the time when the trade in them was large and important, the term "Maracaibo Bark" was restricted to the less resinous variety, derived from *C. cordifolia*. It was also formerly sold simply as "Yellow Bark," and it is not impossible that it was sometimes accepted, under this synonym, for Calisaya. The investigations of Morgenthau into the value of certain derivatives of cuprein may give these barks a real value. For a description of *Cuprea Bark*, see 19th ed., *U. S. D.*, p. 349.

Description.—Rusby described it as occurring in irregular broken pieces, mostly from 5 to 15 cm. long, 2.5 to 7 cm. broad, and 3 to 10 mm. thick. Formerly it included many much smaller fragments as well as much dust, but these portions are now mostly sifted and winnowed out before marketing. The pieces are more or less flat, the thinner and narrower ones somewhat incurved, the broader and thicker recurved. The bark is compact, heavy, and fibrous. Most of the pieces display upon the outer surface more or less of the periderm, forming silvery-white or yellowish-white patches, very thin and rather soft. Occasionally the periderm is instead dark, hard, very rough, and much fissured. From many pieces the entire periderm is absent, disclosing the outer face of the bast, very similar to the inner face. This is compactly and rather finely fibrous, of a deep yellow, with a slight rust-brown tinge. Throughout, the bast is of this structure and color. Between it and the periderm there may be seen with varying distinctness, in most pieces, a characteristic resinous band of irregular width, dark reddish-brown and waxy-lustrous on the cut surface. The radial rows of bast fibres are irregular. The fracture is long-fibrous. The odor is distinct, and the taste quite bitter.

Chemical History.

In the analysis of Cinchona bark, the attention of chemists was at first directed exclusively to the action of water and alcohol upon it, and to the determination of the relative proportions of its gummy or extractive and resinous matter.

The presence of tannin and of various alkaline or earthy salts in minute quantities was afterwards demonstrated. Fourcroy made an elaborate analysis, which proved the existence of other principles in the bark besides those previously ascertained. Westring was the first who attempted the discovery of an active principle in the bark, on which its febrifuge virtues might depend; but he was not successful. Seguin afterwards pursued the same track, and endeavored, by observing the effects of various reagents, to discover the relative value of different varieties of the drug; but his conclusions were not supported by subsequent experiment. Deschamps, an apothecary of Lyons, obtained from the bark a crystallizable salt of lime, the acid of which Vauquelin afterwards separated, and called *kinic acid* (*quinic acid*). The latter chemist also pushed to a much greater extent the researches of Seguin as to the influence of reagents, and arrived at the conclusion that those barks were most efficient which gave precipitates with tannin or the infusion of galls. Ruess, of Moscow, succeeded in isolating a peculiar coloring matter from red bark, which he designated by the name of *cinchonic red,* and obtained a bitter substance which probably consisted in part of the peculiar alkaline principles subsequently discovered. The first step, however, towards the discovery of cinchonine and quinine appears to have been taken by Duncan of Edinburgh, so early as 1803. He believed the precipitate afforded by the infusion of cinchona with that of galls to be a peculiar vegetable principle, and accordingly denominated it *cinchonin.* Gomez, a Portuguese physician, convinced that the active principle of bark resided in this cinchonin, but mixed with impurities, instituted experiments upon some pale bark, which resulted in the separation of a white crystalline substance, considered by him to be the pure *cinchonin* of Duncan. It was obtained by the action of potassium hydroxide upon an aqueous infusion of the alcoholic extract of the bark, and was undoubtedly the principle now universally known by the name of *cinchonine* or *cinchonia.* But Gomez was ignorant of its precise nature, considering it to be analogous to resin. Laubert afterwards obtained the same principle by a different process, and described it under the name of *white matter,* or *pure white resin.* To Pelletier and Caventou was reserved the honor of crowning all these experiments, and applying the results which they obtained to important practical purposes. In 1820 they demonstrated the alkaline character of the principle discovered by Gomez and Laubert, and gave it definitively the name of *cinchonine.* They discovered in the yellow or Calisaya bark another alkaline principle, which they denominated *quinine.* Both these bases they proved to exist in the bark, combined with *quinic* or *kinic acid.* It was, moreover, established by their labors that the febrifuge property of bark depends upon the presence of these two principles. In 1833, O. Henry and Delondre discovered a new alkaloid, but afterwards, finding its composition in its anhydrous state the same as that of quinine, concluded that it was a hydrate of that base. About 1844, Winckler announced anew the existence of the same principle, which he considered distinct, and named *chinidine,* and, under the similar title of *quinidine,* it has now taken its place among the cinchona alkaloids. In 1853, Pasteur found that what had been considered as quinidine consisted in fact of two alkaloids, for one of which he retained the name of quinidine, and called the other *cinchonidine,* and, on pushing his investigations further, he ascertained that no less than six alkaloids may be obtained from different varieties of Peruvian bark,—namely, *quinine* and *quinidine* isomeric with each other, *cinchonine* and *cinchonidine* also isomeric, and two others, derivatives from the preceding through the agency of heat, viz., *quinicine* from quinine, and *cinchonicine* from cinchonine, each being isomeric with the alkaloid from which it is derived.

The table (page 344) of the natural Cinchona bases is given by A. H. Allen on the authority of Paul and Cownley. In it the alkaloids are arranged according to formulas.

Besides these natural bases we have a number of alkaloids formed by the alteration or treatment of these natural bases, or in some cases molecular compounds of two of the natural bases. They will be noted later in the description of individual bases.

Chinoidine or *Quinoidine* is a term now applied to the resinous substance consisting not only of the *amorphous* natural alkaloids, but of those which are produced artificially through the action of the heat and acids upon the crystalline alkaloids. It was formerly official, but was dropped at the 1890 revision. The following list of bases from Cinchona or allied sources is arranged alphabetically.

APOQUINAMINE. See *Homocinchonine.*

ARICINE, $C_{23}H_{26}N_2O_4$. *Cinchovatine.*—This alkaloid, found in cusco bark and in Cuprea bark, was formerly believed by Hesse to be identical with cinchonidine. Pelletier and Corriol obtained *aricine* as far back as 1829 (see note, p. 308, 14th ed., *U. S. D.*). Its separate existence is now not doubted. It crystallizes in prisms, and its salts are of sparing solubility.

CHAIRAMIDINE, $C_{22}H_{26}N_2O_4 + H_2O$, is an alkaloid obtained from *Remijia Purdieana.*

CHAIRAMINE, $C_{22}H_{26}O_4N_2$, discovered by Hesse in *Remijia Purdieana,* occurs in white needles which are readily soluble in ether and chloroform. (*Ann. Ch. Ph.*, ccxxv, p. 211.)

CINCHAMIDINE, $C_{19}H_{24}ON_2$, is identical with hydrocinchonidine.

CINCHONAMINE, $C_{19}H_{24}ON_2$.—This alkaloid was discovered in 1881 by Arnaud in *Remijia Purdieana* (false cuprea bark). It exists in the proportion of 0.2 per cent., and is usually associated with cinchonine. His process is to treat the bark with milk of lime, dry the mixture, exhaust with boiling alcohol, distil off the

alcohol, and take up the residue with diluted hydrochloric acid; cinchonamine hydrochloride crystallizes out, cinchonine hydrochloride remaining in solution. Cinchonamine is insoluble in cold water, soluble in thirty parts of alcohol, more soluble in hot alcohol, and in 100 parts of ether. It is dextrogyrate. For formulas for salts of cinchonamine, see *A. J. P.*, 1884, 156. Physiologically, cinchonamine, according to the experiments of Sée and Bochefontaine, has six times the toxic power of quinine, and has decided sialagogue properties. (*P. J.*, 1885, 791.)

CINCHONICINE, $C_{19}H_{22}ONa$, being a derivative of cinchonine, will be treated elsewhere. (See Index.)

CINCHONIDINE, $C_{19}H_{22}ONa$.—This alkaloid is treated under the head of its sulphate, which is official in both the U. S. and Br. Pharmacopœias.

CINCHONINE, $C_{19}H_{22}ONa$, was dismissed from the U. S. (8th Rev.) but its sulphate has been retained and a description of it will be found on page 353.

CINCHOTINE, $C_{19}H_{24}ONa$, is isomeric with cinchonamine and hydrocinchonine; it dissolves very sparingly in ether.

CONCHAIRAMIDINE, $C_{22}H_{26}O_4N_2 + H_2O$, crystallizes in white needles, and is very soluble in ether, chloroform, alcohol, benzene and acetone. (*Ann. Ch. Ph.*, CCXXV, p. 211.)

CONCHAIRAMINE, $C_{22}H_{26}O_4N_2 + H_2O + C_3H_8O$, also discovered by Hesse, crystallizes with both water and alcohol of crystallization. It is soluble in hot alcohol, ether, and chloroform. The alcoholate dissolves in sulphuric acid containing molybdic acid, giving a brown coloration, which soon becomes intensely green. (*Ann. Ch. Ph.*, CCXXV, p. 211.)

CONCUSCONINE, $C_{23}H_{26}O_4N_2$, discovered by Hesse, occurs in the barks of *Remijia*. It is tasteless.

CONQUINAMINE, $C_{19}H_{24}O_2N_2$, occurs with quinamine. According to Allen, it is easily soluble in ether, chloroform and benzene and closely resembles quinamine.

CUPREINE, $C_{19}H_{22}O_2N_2$, was discovered by Paul and Cownley in the bark of *Cinchona cuprea*, or *Remijia pedunculata*, on the upper

Alkaloid.	Formula.	Melting Point, °C.	Optical Rotation, SD.[1]	Chief Source.
I. *Cinchonine Class:*				
Paricine	$C_{16}H_{18}N_2O$	130	0	*C. lutea* and *C. succirubra* from Darjeeling.
Cinchotine	$C_{19}H_{24}N_2O$	277	+	Crude cinchonine sulphate
Cinchonamine		194	+121.1	*Remijia Purdieana.*
Hydrocinchonine		256	. .	*C. cuprea.*
Hydrocinchonidine, (Cinchamidine)		. . . 229	—98.4	Mother liquors of homocinchonidine.
Cinchonine	$C_{19}H_{22}N_2O$	255	+226.5	Various species of *cinchona.* Almost always present.
Cinchonidine		202	—70	Especially *C. rubra.*
Homocinchonidine		207	—107	With cinchonidine.
Cinchonicine		50	+20.1	By heating cinchonine.
Paytine	$C_{21}H_{24}N_2O$	156	—49.5	From white bark of Payta.
Paytamine		. .	. .	
II. *Quinamine Class:*				
Quinamine	$C_{19}H_{24}N_2O_2$	172	+104.5	*C. succirubra* from British India and Java.
Conquinamine		121	+204.6	*C. officinalis, C. Calisaya.*
Javanine		. . .	. .	*C. Calisaya* from Java.
Cupreine	$C_{19}H_{22}N_2O_2$	198	—175.3	*C. cuprea* or *Remijia pedunculata.*
III. *Quinine Class:*				
Hydroquinine	$C_{20}H_{26}N_2O_2$	168	—142.2	In mother liquors from quinine sulphate.
Hydroquinidine		166	+	
Quinine	$C_{20}H_{24}N_2O_2$	172	—145.2	*Calisaya officinalis*, etc.
Quinidine		168	+236.8	
Quinicine		60	+44	By heating quinine sulphate.
IV. *Cusconine Class:*				
Chairamine	$C_{22}H_{26}N_2O_4$	233	+100	*Remijia Purdieana* (Cusco or False Cuprea Bark).
Conchairamine		120	+68.4	
Chairamidine		127	+7.3	
Conchairamidine		114	—60	
Concusconine		144	+40.8	
Aricine	$C_{23}H_{26}N_2O_4$	188	—58.2	
Cusconine		110	—54.3	
Cusconidine	$C_{23}H_{28}N_2O_4$	. .	. .	
Cuscamine	. . . . .	218	. .	*C. Pelletierana.*
Cuscamidine		. .	. .	
V. *Anhydro-bases:*				
Dicinchonicine	$C_{38}H_{44}N_4O_2$	40	+66	*C. rosulenta* and *C. succirubra.*
Diquinicine	$C_{40}H_{46}N_4O_2$	. .	+	*C. rosulenta* and "quinoidine."

[1] The values for the specific rotatory power refer to solutions of the free alkaloids in nearly absolute alcohol.

Orinoco. It crystallizes from alcohol in anhydrous form, but from ether in prisms with $2H_2O$. Cupreine is sparingly soluble in ether or chloroform, but readily soluble in alcohol. This solution is lævogyrate, alkaline, gives a dark reddish-brown color with ferric chloride, and responds to the thalleioquin test. It forms with sodium hydroxide a definite crystallizable compound, $C_{19}H_{21}N_2O.ONa$, from the solution of which the alkaloid cannot be extracted by ether. This cupreine-soda is important as furnishing a synthesis of quinine, according to the reaction:

$$C_{19}H_{21}N_2O.ONa + CH_3I = C_{20}H_{24}N_2O_2 + NaI$$

(See *Optochin*, Part II.)

CUSCAMIDINE, obtained from *C. Pelletierana.*

CUSCAMINE, obtained from *C. Pelletierana.*

CUSCONIDINE is an amorphous alkaloid found in cusco bark, accompanying cusconine.

CUSCONINE, $C_{23}H_{26}O_4N_2.2H_2O$.—This was discovered by Leverköhn. It is a constituent of the *cusco bark* (*C. pubescens* var. *Pelletierana*), and Hesse has found it in Cuprea bark. It is nearly insoluble in water, soluble in thirty-five parts of ether, more easily in alcohol, very soluble in chloroform. It may be distinguished from other cinchona alkaloids by forming with sulphuric acid a neutral sulphate, which is amorphous, gelatinous, and yellow, and insoluble in an excess of the acid.

DICINCHONICINE, $C_{38}H_{44}O_2N_4$, *dichonchinine* or *apodicinchonine*, is prepared from cinchonine and cinchonidine, and found in commercial chinoidine. It probably exists in bark in an amorphous condition.

DICINCHONINE, $C_{38}H_{44}O_2N_4$, exists in the bark of *C. rosulenta* and *C. succirubra*, and may also be obtained by fractional precipitation from the mixed amorphous alkaloids before melting, but not from commercial chinoidine.

DIHOMOCINCHONINE, $C_{38}H_{44}O_2N_4$, is an amorphous alkaloid obtained from *C. rosulenta*. It is dextrogyrate.

DIQUINICINE, $C_{40}H_{46}O_3N_4$, also termed *disconchinine* and *apodiquinidine*, is one of the chief amorphous alkaloids in commercial chinoidine; its formula indicates its relation to quinine or quinidine. By deducting one molecule of water from a double molecule of either there results diquinicine, thus:

$$2C_{20}H_{24}O_2N_2 - H_2O = C_{40}H_{46}N_4O_3$$

DIQUINIDINE, *dichonchinine* of Hesse, $C_{40}H_{46}N_4O_3$, is found principally in chinoidine which has been obtained from barks containing quinine and quinidine. It is dextrogyrate, produces a fluorescent solution with diluted sulphuric acid, and responds to the thalleioquin reaction.

HOMOCINCHONICINE is prepared from homocinchonidine just as cinchonicine and quinicine are prepared from cinchonine and quinine—*i.e.*, by heating their sulphates.

HOMOCINCHONIDINE, $C_{19}H_{22}ON_2$, is also obtained from *C. rosulenta*. It crystallizes in large prisms, and forms a neutral sulphate containing six molecules of water, and may be found in commerce. Its existence is denied by Skraup.

HOMOCINCHONINE, $C_{19}H_{22}ON_2$, *cinchonidine of Koch*, is obtained from the bark of *C. rosulenta;* it is lævogyrate, and crystallizes from its alcoholic solution in large prisms. It has been mistaken for *aricine*. Homocinchonine is isomeric with *apoquinamine*, which is prepared by boiling quinamine or quinamidine with hydrochloric acid for a short time. It is white, amorphous, soluble in ether, alcohol, and diluted hydrochloric acid.

HOMOQUININE, $C_{39}H_{46}O_4N_4 + 4H_2O$, was discovered in 1881 simultaneously by D. Howard and J. Hodgkin, B. H. Paul, A. J. Cownley, and T. G. Whiffen (*P. J.*, 1881, p. 497; 1882, p. 905.) It was first noticed by Paul and Cownley on account of the readiness with which it crystallized from its ethereal solution, and is now recognized as a molecular compound of quinine and cupreine of the formula $C_{20}H_{24}O_2N_2.C_{19}H_{22}O_2N_2 + 4H_2O$, and can be obtained by precipitating a solution of sodium cupreinate with one of quinine hydrochloride. It can be resolved into its constituent parts by precipitating the solution with solution of sodium hydroxide, when the quinine may be shaken out with ether, while the cupreine remains in the alkaline liquid as sodium cupreinate. It is freely soluble in alcohol and chloroform, sparingly in ether, from which it crystallizes in proportion as it can take up water. (Hesse.) It is also soluble in diluted sulphuric acid, producing fluorescence, and gives with chlorine water and ammonia a green coloration (thalleioquin). The sulphate coincides exactly in properties with quinine sulphate, except in its behavior with ether. Its tartrate closely resembles cinchonidine tartrate. Homoquinine and its salts behave towards polarized light like quinine.

HYDROCINCHONIDINE, $C_{19}H_{24}N_2O$, bears the same relation to cinchonidine that hydroquinine does to quinine. It is found associated with homocinchonidine in commercial cinchonidine. (*A. J. P.*, 1883, p. 20.)

HYDROCINCHONINE, $C_{19}H_{24}ON_2$, discovered by Caventou, is obtained by treating cinchonine with potassium permanganate. It is soluble in 1300 parts of water, more soluble in alcohol and in ether. The statement that it may be found in commercial cinchonine has not been confirmed. Hesse states that it may be found in Cuprea bark. It is also called *cinchotine*. Von Arlt has shown that the *pseudocinchonine* of Hesse is identical with hydrocinchonine.

HYDROQUINICINE, $C_{20}H_{26}O_2N_2$, an amorphous alkaloid obtained by fusing dry hydroquinine sulphate.

HYDROQUINIDINE (*hydroconchinine*), $C_{20}H_{26}O_2N_2 + 2\frac{1}{2}H_2O$, is found in commercial quinidine and may be separated by potassium permanganate treatment. It is crystalline, dissolving freely in hot alcohol and in chloroform, but less freely in ether. It gives the thalleioquin reaction like quinine. (*P. J.*, 1882, p. 904.)

HYDROQUININE, $C_{20}H_{26}O_2N_2$, was discovered by Hesse in the mother liquors from which quinine sulphate has been crystallized; he afterwards found it in the commercial quinine salt to the extent of 4 per cent. Quinine cannot be perfectly freed from hydroquinine even by repeated crystallization of the neutral sulphates, but the hydroquinine can be completely separated by converting the alkaloid into the acid sulphate and recrystallizing this from water or alcohol, when the hydroquinine remains in the mother liquor. (Allen.) According to Hesse, it dissolves freely in alcohol and ether, and, ac-

cording to Allen, also in chloroform, benzene and ammonia water, and gives the thalleioquin reaction with chlorine water and ammonia like quinine. (*P. J.*, 1882, p. 904.)

JAVANINE, obtained by Hesse from *C. Calisaya* var. *javanica.*

PARICINE, $C_{18}H_{18}ON_2$, is found with quinamine in the bark of *C. succirubra* of Darjeeling, and, according to Hesse, it may be separated from all the cinchona alkaloids with which it associates in solution by treating with sodium carbonate, which precipitates paricine first.

PAYTAMINE, $C_{20}H_{24}ON_2$, is an amorphous alkaloid accompanying paytine.

PAYTINE, $C_{21}H_{24}O_2N_2,H_2O$, was discovered by Hesse in the white Payta bark.

PROTOQUINAMICINE (see *Quinamicine*).

QUINAMICINE is isomeric with quinamidine; it with protoquinamicine is an artificial base, they are both amorphous, and are produced by heating quinamine in contact with diluted sulphuric acid. If the action of sulphuric acid be continued at 120° C. (248° F.) to 130° C. (266° F.), an amorophous brownish substance is formed which may be precipitated by sodium carbonate, and is insoluble in ether. Hesse has named this protoquinamicine.

QUINAMIDINE, *Quinidamia* (*Conchinamine of Hesse*), $C_{19}H_{24}O_2N_2$, is found in *C. rosulenta* and *C. succirubra,* and probably exists in other species of red bark. It crystallizes in long, brilliant prisms, which melt at 123° C. (253.4° F.). A crystalline hydriodide has been produced. Its gold salt like that of quinamine soon decomposes. It may be formed in acid solutions of quinamine through decomposition.

QUINAMINE, *Quinamia,* $C_{19}H_{24}O_2N_2$.—Hesse discovered this cinchona alkaloid in the bark of *C. succirubra* from Darjeeling in 1872. He has since found it in all the East Indian succirubra barks, as well as in the barks of *C. nitida, C. Calisaya,* var. *Schuhkraffti, C. erythrantha, C. erythroderma, C. rosulenta,* and *C. Calisaya* (Para bark), and particularly in *C. Ledgeriana.* De Vrij (*L'Union Pharm.*, 1877, p. 204; *N. R.*, 1877, p. 300) published a process for its preparation. It crystallizes in very long, asbestos-like, white prisms, without water of crystallization. It is nearly insoluble in cold water and in solution of potassium or ammonium hydroxides, more easily in boiling water; is readily dissolved by hot alcohol, which deposits it in crystals, and less readily by diluted alcohol. Ether, petroleum benzin, and benzene dissolve it rather easily at ordinary temperature, more readily when boiling hot, and give it up crystallized on cooling and evaporation. In alcoholic solution it has an alkaline reaction. It neutralizes sulphuric and hydrochloric acids, forming with the latter an amorphous salt, but with the former one that crystallizes with difficulty in hexagonal scales and short prisms. Its solution is dextrogyrate. Quinamine is almost tasteless, but its solutions in acids are very bitter. Its sulphuric acid solution unlike that of quinine is not fluorescent. Its reaction with gold chloride is very characteristic, the solution of the chloride producing with it a yellowish-white precipitate, which soon becomes purple, and separates gold, the supernatant liquid assuming a purplish-red and afterwards a brown color. (For other characters, see *A. J. P.*, 1872, p. 302.)

QUINIDINE, $C_{20}H_{24}O_2N_2$, is isomeric with quinine. It was discovered in 1833 by O. Henry and Delondre, but they afterwards concluded that it was quinine hydroxide, as it had the same composition as quinine. Winckler, in 1844, announced anew the existence of the same alkaloid, which he considered distinct, and named it "*chinidine*"; this substance was not pure, and Pasteur, in 1853, proved that it really consisted of two alkaloids, one of which he called *cinchonidine,* and the other *quinidine.* This view is now generally accepted, although Hesse insists on calling quinidine "*conchinine*"; but the latter name is used to only a limited extent in Germany, and scarcely at all elsewhere.

Quinidine crystallizes from alcohol with $2\frac{1}{2}H_2O$ in large lustrous monoclinic prisms or needles, efflorescent in the air; from ether, permanent rhombohedra with $2H_2O$ are obtained; from boiling water permanent plates with $1\frac{1}{2}H_2O$. (Hesse.) It effloresces on exposure to the air. It is sublimable by heat without change, and is condensed in a crystalline form. It resembles quinine not only in composition, but also in its chemical relations with chlorine and ammonia, being rendered green by the successive action of those agents. According to Herapath, it resembles it also in causing a fluorescent appearance when dissolved in water, which is not the case with either cinchonine or cinchonidine, or is so, at least, in a much less degree. It differs, however, in its greater facility of crystallization, in its much less solubility in ether, and in its influence on polarized light, quinidine producing deviation to the right, and quinine to the left. De Vrij states, as the result of his observation, that quinidine forms a salt of very difficult solubility with hydriodic acid, and that, consequently, when a solution of potassium iodide is added to a solution of quinidine sulphate a white precipitate is deposited. By this test quinidine may be distinguished from the other cinchona alkaloids, and detected when mixed with them in solution, no other yielding a precipitate with potassium iodide. (See *A. J. P.*, xxix, 233.) Herapath proposes another test to distinguish this alkaloid from quinine. If to a solution of quinine sulphate in acetic acid, tincture of iodine be added, and the mixture heated and then allowed to cool, a beautiful emerald-green compound is formed, while quinidine sulphate treated in the same way yields a brown precipitate. When the mixture of this alkaloid with cinchonidine is exposed to hot air, the crystals of quinidine effloresce, and may be distinguished from the others by their opaque whiteness. Vreven (*C. D.*, March 5, 1898, 400) states that

the crystals yielded by Marmé's reagent (potassio-cadmium iodide) with quinidine are different from those obtained from any of the other cinchona alkaloids. They are seen under the microscope to consist of bundles of fine needle-like crystals quite different from those of quinine, cinchonine, and cinchonidine.

Commercial quinidine, consisting generally of quinidine with a much larger proportion of cinchonidine, and sometimes, there is reason to believe, exclusively, or nearly so, of the latter alkaloid, was carefully examined by H. G. Leers. It readily crystallizes from its alcoholic solution, by spontaneous evaporation, in hard, shining, colorless crystals, which are easily pulverized and yield a snow-white powder. They melt without decomposition or loss of water at 175° C. (347° F.), and on cooling concrete into a grayish-white crystalline mass. At a higher heat they take fire, and burn with an odor resembling that of the volatile oil of bitter almond. Their taste is bitter, but less intensely so than that of quinine. Quinidine is soluble, according to Hesse, in 2000 parts of water at 15° C. (59° F.); in 750 parts of boiling water; in 26 parts of 80 per cent. alcohol at 20° C. (68° F.); in 22 parts of ether of sp. gr. 0.729 at 20° C. (68° F.), or in 35 parts of the same at 10° C. (50° F.) (Hesse, 1868); according to Dragendorff, in 76.4 parts of ether at 10° C. (50° F.); but the solubilities of commercial quinidine vary more or less according to the relative quantities of quinidine proper and cinchonidine contained in it. With the acids it forms salts, most of which are beautifully crystallizable, and much more soluble than those of quinine. There are, as of quinine and cinchonine, two classes of the salts of quinidine, which may be considered either as neutral and acid or as basic and neutral. It differs from quinine by its much slighter solubility in ether. From the aqueous solution of its salts the alkalies and their carbonates and bicarbonates throw down pulverulent precipitates not soluble in an excess of the precipitant. With sodium phosphate, silver nitrate, and mercuric chloride it forms white, with gold trichloride light yellow, and with platinic, orange-yellow precipitates. It may be obtained by first precipitating it from the solution of one of its salts by an alkali, and then repeatedly dissolving in alcohol and crystallizing, until it is entirely freed from a greenish-yellow resinous substance which is apt to attend it. From quinine it may be separated by repeated washing with ether.

The sulphate of this alkaloid was official in the U. S. P. 1890, and described as follows:

QUINIDINÆ SULPHAS. U. S. 1890, *Quinidine Sulphate.* $(C_{20}H_{24}N_2O_2)_2H_2SO_4.2H_2O = 780.42$.

"The neutral sulphate of an alkaloid obtained from the bark of several species of Cinchona (fam. *Rubiaceæ*). Quinidine Sulphate should be kept in well-stoppered bottles, in a dark place." *U. S.* 1890.

Quinidine sulphate is obtained from the quinidine barks by the same process as that by which quinine sulphate is procured from the quinine-yielding barks. When the two alkaloids are contained in the same bark, the quinidine sulphate (commercial) remains in the mother waters in consequence of its greater solubility. By the addition to its solution of a quantity of sulphuric acid equal to that which it already contains, it is converted into fine acicular crystals like asbestos, and possessing the formula $C_{20}H_{24}N_2O_2H_2SO_4 + 4H_2O$. Quinidine sulphate was officially described as in "white, silky needles, odorless, and having a very bitter taste; permanent in the air. Soluble, at 15° C. (59° F.), in 100 parts of water, and in 8 parts of alcohol; in 7 parts of boiling water, and very soluble in boiling alcohol; also in 14 parts of chloroform, and in acidulated water; almost insoluble in ether. When heated to 120° C. (248° F.), the salt loses its water of crystallization (4.6 per cent.). Upon ignition, it is slowly consumed, leaving no residue. The salt is neutral or faintly alkaline to litmus paper. An aqueous solution of the salt, when acidulated with sulphuric acid, has a decided, blue fluorescence. On treating 10 mils of an aqueous solution (about 1 in 1600) of the salt with 2 drops of bromine water, and then with an excess of ammonia water, the liquid will acquire an emerald-green color. With proper adjustment of the reagents, more dilute solutions will give a paler tint, while more concentrated ones will acquire a deeper color, or deposit a green precipitate. A cold, saturated aqueous solution of the salt yields a white precipitate with potassium iodide test-solution (difference from *quinine sulphate*). An aqueous solution of the salt yields, with barium chloride test-solution, a white precipitate insoluble in hydrochloric acid. Quinidine Sulphate should not impart more than a faintly yellowish tint to concentrated sulphuric acid (limit of *readily carbonizable, organic impurities*), nor produce a red color with nitric acid (difference from *morphine*). If a small quantity of ammonia water be added to 3 mils of an aqueous solution of the salt saturated at 15° C. (59° F.), a white precipitate (quinidine) will be produced, which requires more than 30 mils of ammonia or more than 30 times its weight of ether to dissolve it (absence of more than small proportions of *other cinchona alkaloids*)." *U. S.* 1890.

The action of quinidine sulphate upon the system is similar to that of quinine, but is less powerful in the proportion of three to two.

QUINICINE, $C_{20}H_{24}O_2N_2$, being a derivative of quinine, will be treated under that head.

QUININE, $C_{20}H_{24}O_2N_2 + 3H_2O$.—This alkaloid has been made official, as have its sulphate, bisulphate, hydrobromide, hydrochloride, salicylate, and sulphate, and they will be treated under separate heads. (See Index.)

The following additional substances have been found in Cinchona bark: *Quinic* or *Kinic*, *Quinovic* or *Kinovic*, *Quinotannic* or *Cinchotannic acids*, *Quinovin* or *Kinovin*, *Cinchonic red*, volatile butyraceous oil, in small quantity,

and red and yellow coloring matter. These constituents, arranged alphabetically, will now be considered in detail.

CINCHOCEROTIN, $C_{27}H_{48}O_2$.—This substance was discovered by Kerner in flat Calisaya bark from South America. He obtained it in white, very light, crystalline scales. It is not soluble in boiling water, nor in hydrochloric, diluted sulphuric, or glacial acetic acid, but dissolves readily in ether, chloroform, and alcohol. (*A. J. P.*, 1883, p. 357.)

CINCHOFULVIC ACID.—The *cinchonic red* of Reuss, identical with the *insoluble red coloring matter* of Pelletier and Caventou, $C_{12}H_{14}O_7$, is reddish brown, insipid, inodorous, largely soluble in alcohol, especially when hot, and almost insoluble in ether or water, though the latter dissolves a little at the boiling temperature. The acids promote its solubility in water. It precipitates tartar emetic, but not gelatin; but if treated with a cold solution of potassium or sodium hydroxide, or with ammonia, lime, or baryta with heat, and then precipitated by an acid, it acquires the property of forming an insoluble compound with gelatin. It yields protocatechuic acid, $C_7H_6O_4$, when fused with potassium hydroxide. It is most abundant in the red bark (over 10 per cent.), and least so in the pale.

CINCHOTANNIC ACID. *Cinchotannin*, $C_{14}H_{16}O_9$.—*Tannic acid, tannin*, or *soluble red coloring matter* of Pelletier and Caventou, has been considered as possessing all the properties which characterize the proximate vegetable principles associated together under the name cinchotannic acid. It is a glucoside existing in cinchona barks in the proportion of 3 to 4 per cent. It has a brownish-red color and an austere taste, is soluble in water and alcohol, combines with metallic oxides, and produces precipitates with the salts of iron, which vary in color according to the variety of bark, being deep green with the pale bark, blackish-brown with the yellow, and reddish-brown with the red. It also forms white precipitates with tartar emetic and gelatin, and readily combines with atmospheric oxygen, becoming insoluble. It must, however, differ materially from the tannic acid of galls, which could not exist in aqueous solutions containing cinchonine and quinine without forming insoluble compounds with them. Rembold has shown that when cinchotannic acid is boiled with diluted sulphuric acid, cinchonic red is produced, sugar being formed at the same time.

FATTY MATTER.—This was first obtained pure by Laubert, and is of a greenish color as obtained from the pale bark, orange yellow from the yellow. It is insoluble in water, soluble in boiling alcohol, which deposits a part of it on cooling, very soluble in ether, even cold, and saponifiable with the alkalies.

QUINIC ACID (*Hexahydrotetraoxybenzoic acid*), $C_7H_{12}O_6$.—This acid was isolated as early as 1790 by Hofmann, an apothecary of Leer, who obtained it from the calcium salt from cinchona. It exists in a number of important plants—ivy, oak, elm, ash, coffee, etc. It may be desirable to procure the alkaloids in the state of saline combination in which they exist in the bark, since it is possible that they may exert an influence over the system in this state somewhat different from that produced by their combinations with sulphuric or other mineral acids. As it is impossible to procure the quinates immediately from the bark in a pure state, it becomes necessary first to obtain the quinic acid separately, which may thus become of some practical importance. We shall, therefore, briefly describe the mode of procuring it, and its characteristic properties. It is usually prepared from calcium quinate, the residue obtained in the manufacture of quinine sulphate (see *Quininæ Sulphas*) by decomposing an aqueous solution of calcium quinate with oxalic acid, filtering out the precipitated calcium oxalate, and evaporating the filtrate to the crystallizing point; or by evaporating the infusion of bark to a solid consistence, and treating the extract with alcohol, we have in the residue a viscid matter consisting chiefly of mucilage with calcium quinate, which is insoluble in alcohol. If an aqueous solution of this substance be formed, and allowed to evaporate at a gentle heat, crystals of the quinate will be deposited, which may be purified by a second crystallization. The salt thus obtained, being dissolved in water, is decomposed by means of oxalic acid, which precipitates the lime and leaves the *quinic acid* in solution. This may be procured in the crystalline state by spontaneous evaporation, though as usually prepared it is in the form of a thick syrupy liquid. The crystals are transparent and colorless, sour to the taste, soluble in 2 parts of water, but less soluble in alcohol, and almost insoluble in ether. By heating quinic acid or a quinate with manganese dioxide and sulphuric acid, we get yellow crystals of *kinone*, better known as *quinone*, $C_6H_4O_2$, a reaction which may be used for ascertaining the presence of quinic acid. The cinchonine and quinine quinates may be obtained either by the direct combination of their constituents, or by the mutual decomposition of the sulphates of those alkaloids and calcium quinate. *Cinchonine quinate* has a bitter and astringent taste, is very soluble in water, is soluble also in alcohol, and is crystallized with difficulty. *Quinine quinate* is also very soluble in water, but less so in rectified alcohol. Its taste is very bitter, resembling that of yellow bark. It crystallizes in beautiful stellate groups, which are opaque or semi-transparent. The salt is with difficulty obtained free from color, and only by employing the ingredients in a state of extreme purity. (*Ann. Ch. Phys.*, Juillet, 1829.) Lautemann found, in experiments upon himself, that quinic acid, when taken into the system, undergoes a conversion into hippuric acid and in this state escapes with the urine. (*Ann. Ch. Ph.*, cxxv, 9.) Rabuteau has investigated the physiological properties of quinic acid, and has found it closely to resemble the

ordinary vegetable acids, being harmless in its effects on the system, and forming with water a refreshing drink like lemonade. Like other vegetable acids, also, it is decomposed in the system, forming, when taken in the state of an alkaline salt, a carbonate of the alkali in the blood, and rendering that fluid alkaline. (*A. J. M. S.*, Oct., 1872, p. 524.) Quinic acid is said by Zwenger to have been found in the leaves of *Vaccinium Myrtillus* L. (*A. J. P.*, March, 1861, p. 128.) Several esters of quinic acid and compounds with synthetic bases have been introduced into medicine, viz.—*chinotropin, sidonal, new sidonal, urosin,* and *ural.* (See Part II.)

Quinovin, *Kinovin,* or *Chinovin. Kinovic bitter,* $C_{36}H_{62}O_{11}$.—Originally discovered in the false bark called *quinquina nova,* or new bark, this substance has since been found in Calisaya bark, and probably exists, in greater or less proportion, in all the Cinchona barks. It was detected by De Vrij not only in the bark but also in the wood and leaves of *C. Calisaya* and *C. lucumæfolia.* (*J. P. C.*, April, 1860, pp. 225, 258.) It is white, uncrystallizable, almost insoluble in water, but readily dissolved by alcohol and ether. It is very bitter, and, as it is asserted to have no febrifuge virtues, may on this account mislead the judgment in relation to the activity of the bark in which it may be found. Some barks are said to owe their bitterness mainly to this ingredient. Winckler gives, as a certain test of its presence in any bark, copper sulphate, which is indifferent to infusion of bark containing none of this principle, but detects the smallest proportion of it by producing a dirty-green color, soon followed by the deposition of a fine similarly colored powder. This is a salt of copper, and has a very bitter and metallic taste. (See *A. J. P.*, xxv, 343.)

Quinovin in alcoholic solution was shown in 1859 by Hlasiwetz to be resolved by means of hydrochloric acid gas into quinovic acid, $C_{24}H_{38}O_4$, and an uncrystallizable sugar, *mannitan,* $C_6H_{12}O_5$, by assimilation of H_2O. The formation of quinovic acid takes place more easily if kinovin is placed in contact with sodium amalgam and spirit of wine, when after 12 hours mannitan and sodium quinovate are formed. (*Pharmacographia,* 2d ed., p. 364.)

Liebermann and Giesel (*Ber. d. Chem. Ges.*, xvi, 987) believe that two modifications exist, *α-quinovin and β-quinovin,* the former in Cinchona, the latter in Cuprea bark: α-quinovin is a white crystalline powder, nearly insoluble in cold and hot water, but soluble in caustic alkalies, lime water, ammonia water, and glacial acetic acid, soluble with difficulty in chloroform, ether, and petroleum benzin; it dissolves in 57 parts of nearly absolute alcohol. β-quinovin closely resembles α-quinovin, but is not soluble in ether, and crystallizes readily from diluted alcohol.

De Vrij proposes the following method of isolating quinovin. Macerate powdered cinchona with a very weak solution of potassium or sodium hydroxides, precipitate the filtered liquid with an acid, redissolve the precipitate in milk of lime to separate the cinchonic red, filter and precipitate the solution boiling hot with hydrochloric acid, separate the precipitate, wash it, express as much as possible, and lastly dry it on porous stones, and powder it. For a process for preparing quinovin from by-products, see Allen's *Organic Analysis,* 1892, vol. iii, Part II, p. 443. Thus prepared, the quinovic bitter forms soluble compounds with magnesia and lime, and has been employed, in this mode of combination, as a tonic. (*J. P. C.*, April, 1860, p. 258.)

Quinovic Acid (*Kinovic Acid*).—Resulting from the decomposition of quinovin, and possessing the formula $C_{32}H_{48}O_6$; in white, rhomboidal crystals, insoluble in water, but slightly soluble in ether, somewhat more so in boiling alcohol, but very soluble in ammonia and the fixed alkalies, the solutions frothing like soap water. On adding an acid to an alkaline solution of quinovic acid, a hydrate of quinovic acid is thrown down as a very voluminous jelly, the whole contents of the vessel gelatinizing. Kerner (*Deutsche Klin.*, xx, 81) recommends quinovic acid as an excellent tonic, which produces no narcotic symptoms. He prefers it in the form of calcium quinovate, of which forty grains (2.6 Gm.) is the average dose. (*Am. J. M. S.*, Oct., 1869, 543.)

By the experiments of Henry, Jr., and Plisson, it may be considered as established that the alkaloids of the different varieties of bark are combined at the same time with quinic acid and with one or more of the coloring matters which, in relation to these substances, appear to act the part of acids. This idea was originally suggested by Robiquet. (*J. P. C.*, xii, 282, 369.) The compounds of quinine, cinchonine, etc., with the coloring matter are scarcely soluble in water, while their quinates are very soluble.

The odor of bark appears to depend on a *volatile oil,* which Fabroni and Trommsdorff obtained by distillation with water. The oil floated on the surface of the water, was of a thick consistence, and had a bitterish, acrid taste, with the odor of bark.

Yellow Coloring Matter.—This has little taste, is soluble in water, alcohol, and ether, precipitates neither gelatin nor tartar emetic, and is itself precipitated by lead subacetate.

Incompatibles.—Of the relations of bark to the several solvents employed in pharmacy we shall speak hereafter, under the heads of its tincture and other preparations, where we shall also have an opportunity of mentioning some of the more prominent substances which afford precipitates with its liquid preparations. It is sufficient at present to state that all the substances which precipitate the infusion of bark do not by any means necessarily affect its virtues, as it contains several inert ingredients which form insoluble compounds with bodies that do not disturb its active principles.

As *tannic acid* forms with the alkaloids compounds insoluble in water, it is desirable that substances containing this acid in a free state should not be prescribed in connection with the infusion or decoction of bark; for, though these insoluble tannates might be found efficacious if administered, yet, being precipitated from the liquid, they would be likely to be thrown away as dregs, or at any rate would communicate, if agitated, an unpleasant turbidity. The same may be said of the *tincture* and *compound solution of iodine,* which form insoluble compounds with all the cinchona alkaloids, and of the *alkalies, alkaline carbonates,* and *alkaline earths,* which precipitate them from their aqueous solution.

Estimation of Value.—*Grahe's Test.*—A test of the cinchona barks containing one or more of their characteristic alkaloids has been proposed by Grahe. It is founded on the fact that when these barks are exposed to destructive distillation a product is obtained of a bright carmine color, which is yielded by no other bark under the same circumstances, and not by cinchona unless it contain one or more of its peculiar alkaloids. Nor do the pure alkaloids afford it; but, if mixed with a little acetic, quinic, tannic, citric, or tartaric acid, they exhibit the reaction, showing that in the bark it takes place between the alkaloids and organic acids contained in it. Grahe applies the test by heating a piece of the bark weighing from five to ten grains in an ordinary test tube, and gradually increasing the heat to redness. Whitish smoke, and aqueous vapor condensing on the surface of the tube, are first given off, which are soon followed by the appearance of redness in the fumes, and by the deposition, an inch above the heated part, of a red pulverulent film, which is gradually changed into a thick, oily liquid, running down the glass in drops or streaks of a fine carmine color. (*Ch. Cb.,* Feb. 17, 1858, p. 97.)

It is impossible to state with accuracy the relative proportion of the active ingredients in the different varieties of cinchona, as the quantity is by no means uniform in different specimens of the same variety. The results of the most recent experiments have been already stated under the head of the several varieties of bark described. But the medicinal efficiency is measured by the quantity of the peculiar cinchona alkaloids it may contain. In 1880 the U. S. Pharmacopœia for the first time in its history gave a process for assaying cinchona bark; this was deemed necessary because of the impossibility of judging of the quality of the bark by its physical appearances.

Assay.—The Pharmacopœial assay for cinchona is as follows: "Introduce 5 Gm. of Cinchona, in No. 40 powder, into a 500 mil flask and add 200 mils of a mixture of chloroform, 1 volume, and ether, 2 volumes. Stopper the flask, shake it well, and let it stand ten minutes. Then add 5 mils of ammonia water, shake the flask frequently for one hour, and let it stand from eight to ten hours. Now add 10 mils of distilled water, shake the mixture vigorously and when the drug has settled, decant 160 mils of the solution, representing 4 Gm. of Cinchona. Filter it through a pledget of purified cotton into a separator, and rinse both cylinder and cotton with ether. Completely extract the alkaloids from the chloroform-ether solution by shaking out repeatedly with weak sulphuric acid. Collect the acid solutions in a separator, add ammonia water until the solution is distinctly alkaline to litmus, and completely extract the alkaloids by shaking out repeatedly with chloroform. Filter each portion of chloroform as it comes from the separator through a pledget of purified cotton into a tared flask, and wash the funnel and cotton with chloroform. Evaporate the chloroform on a water bath, add 5 mils of alcohol to the residue, and again evaporate. Repeat the evaporation with alcohol and dry the residue at 100° C. (212° F.) to constant weight. The weight will be the amount of total alkaloids from 4 Gm. of Cinchona. (See Proximate Assays, Part III.)" *U. S.*

Under Red Cinchona the U. S. requirements are: "Proceed as directed under *Cinchona,* using 5 Gm. of Red Cinchona;" the British directions are as follows:

Test.—"Red Cinchona Bark when used for official purposes other than the preparation of alkaloids or their salts, is required to yield from 5 to 6 per cent. of total alkaloids, of which not less than one-half consists of quinine and cinchonidine, as determined by the following process: Mix 10 grammes of Red Cinchona Bark, in No. 60 powder, with 6 grammes of *calcium hydroxide;* add 22 millilitres of *water,* mix intimately in a small porcelain dish or mortar, and set aside for an hour or two. Transfer this mixture to a suitable flask fitted with a reflux condenser, add 130 millilitres of *benzolated amylic alcohol,* boil for about half an hour, and then decant the liquid on to a filter, leaving the sediment in the flask; add more of the *benzolated amylic alcohol* to the sediment, and boil and decant as before; repeat this operation a third time; then transfer the contents of the flask to the filter, and wash by percolation with more of the *benzolated amylic alcohol* until the Bark is exhausted. Introduce the collected filtrate, while still warm, into a stoppered glass separator; add to it 2 millilitres of *diluted hydrochloric acid,* mixed with 12 millilitres of *water;* shake well together, and allow the liquids to separate; draw off the acid liquid, and repeat the process with *water* slightly acidified with *hydrochloric acid,* until the alkaloids have been completely removed. Carefully and exactly neutralise the acid liquid, while warm, with *solution of ammonia,* and concentrate by evaporation to the bulk of 16 millilitres. To the concentrated solution add about 1.5 grammes of *sodium potassium tartrate,* dissolved in twice its weight of *water,* stirring with a glass rod; after about one hour collect the precipitate, wash dry at 100° C. (212° F.)

and weigh; the weight in grammes multiplied by 8 gives the percentage of quinine and cinchonidine in the Bark. To the mother-liquor and washings from the preceding process add *solution of ammonia* in slight excess and shake with three successive portions of 10 millilitres of *chloroform;* evaporate the mixed chloroformic solutions to dryness, dry the residue at 110° C. (230° F.) and weigh. The weight in grammes multiplied by 10 and added to the percentage of the quinine and cinchonidine, gives the percentage of total alkaloids." *Br.*

The German Pharmacopœia gives the following method: "The powdered bark is assayed as follows: Shake 20 Gm. of it strongly and repeatedly with a mixture of 10 Gm. of water of ammonia, 20 Gm. of alcohol, and 170 Gm. of ether, and, after a day, decant 120 Gm. of the clear liquid. To this liquid add 3 Cc. of volumetric hydrochloric acid, remove the ether by distillation or evaporation, and again add, if necessary, enough hydrochloric acid to render the solution acid. Then filter, and mix the cold filtrate with 3.5 Cc. of volumetric solution of potassa. When the alkaloids have subsided, drop more of the solution of potassa into the clear supernatant liquid, until nothing more is thrown down. Finally, collect the whole of the precipitate on a filter, and wash it repeatedly with small portions of water, until drops of the wash water allowed to come in contact with the surface of a cold, aqueous, neutral, saturated solution of sulphate of quinine no longer produce a turbidity. When the alkaloids have drained, press them gently between bibulous paper, and, having dried them sufficiently in the air to permit their being removed to a watch-glass, dry them completely, first over sulphuric acid, and, finally, by means of a water-bath. The weight of alkaloids procured by this method should not be less than 0.42 Gm. When a small portion of the same is boiled with 300 parts of water, the filtrate, after cooling, should yield flakes of quinine. When to 5 parts of this solution, after being cooled and decanted, 1 part of chlorine water is added, and water of ammonia immediately dropped in, the liquid should acquire a beautiful green color." For E. R. Squibb's method of assay, see *U. S. D.*, 18th ed., p. 412.

It is usually sufficient to ascertain the quantity of total alkaloids in bark, for this is really a test of the efficacy of the bark for pharmaceutical purposes, since all the organic alkaline principles contained in it are efficient as medicines, and in all probability in a nearly equal degree. But for manufacturing purposes it is necessary to push the investigation further, and ascertain the proportion of the several alkaloids in the mixture.

De Vrij obtained from bark of *C. officinalis* grown at Ootacamund total alkaloids as high as 11.96 per cent. (9.1 per cent. of which was quinine). The highest yield yet recorded was obtained by De Vrij from Ootacamund bark, 13.5 per cent., the great part of which was quinine. Between these and the barks of lowest value there is every grade of productiveness, down to a mere trace of alkaloidal matter. Under the name of *quinetum* a compound is produced in India and other Eastern countries, which consists of the mixed alkaloids of Red Bark, the object being to produce a cheap febrifuge which will answer all practical purposes and save the cost of refining. (See U. S. Dispensatory, 19th edition, p. 359.) *Febrifuge.*—Under this name, the British Indian government introduced a manufactured product, designed to furnish a cheap but valuable substitute for quinine sulphate. It is largely produced at Sikkim, India, by a modification of Dubreuil's process, which consists in extracting the powdered mixed barks with hydrochloric acid, precipitating the alkaloids by the addition of solution of sodium hydroxide, and shaking out with petroleum, adding to the petroleum solution a calculated quantity of diluted sulphuric acid, evaporating and crystallizing.

Uses.—This valuable remedy was unknown to the civilized world until about the middle of the seventeenth century, though the natives of Peru are generally supposed to have been long previously acquainted with its febrifuge powers. Humboldt, however, is of a different opinion. In his memoir on the Cinchona forests, he states that it is unknown as a remedy to the Indians inhabiting the country where it grows, and, as these people adhere pertinaciously to the habits of their ancestors, he concludes that it never was employed by them. They have generally the most violent prejudices against it, considering it poisonous, and in the treatment of fever prefer the milder indigenous remedies. Ruiz and Pavon, however, ascribe the discovery to the Indians; and Tschudi states, in his *"Travels in Peru"* (Am. ed., ii, 280), that the inhabitants of the Peruvian forests drink an infusion of the green bark as a remedy in intermittent fever. On the other hand, the statements of Humboldt have been confirmed by the travellers Markham and Spence, the former remarking that the native Indian doctors did not use the bark, and the latter that the Cascarilleros of Ecuador believed that their red bark is used solely for dyeing. It is uncertain whether, as Jussieu stated in 1739, the Jesuit fathers received their knowledge from the Indians, or, as Humboldt believes, discovered the virtues of the drug for themselves, having been led to make trial of it by its extreme bitterness. The Countess Chinchon, wife of the Viceroy of Peru, having in her own person experienced the beneficial effects of the bark is said, on her return to Spain in the year 1640, to have first introduced the remedy into Europe. Hence the name of *pulvis Comitissæ*, by which it was first known. After its introduction it was distributed and sold by the Jesuits, who are said to have obtained for it the price of its weight in silver. From this circumstance it was called *Jesuits' powder*, a title which it long retained. In 1653, Chifflet, physician to the Archduke Leopold, directed

the attention of all Europe to the bark by his work entitled *Pulvis Febrifugus Orbis Americani.* This gave rise to a very active controversy, the high price of the drug aiding very greatly those who opposed its introduction. According to Sturm, twenty doses in 1658 cost sixty florins. It seems first to have been advertised in England for sale in 1658 by a James Thomson, and by 1660 it was much employed. It still, however, encountered much prejudice and ignorance, and was not made official in the London Pharmacopœia until 1677. Sir Robert Talbot (or Talbor) used it as a secret remedy with so much address and success that in 1679 he cured Charles II of a tertian, and subsequently sold his secret to Louis XIV of France, who published it in 1681.

When taken into the stomach, the bark usually excites in a short time a sense of warmth in the epigastrium, which often diffuses itself over the abdomen and even the breast, and is sometimes attended with considerable gastric and intestinal irritation. Nausea and vomiting are sometimes produced, especially if the stomach was previously in an inflamed or irritated state; and its action is not unfrequently accompanied by purging. If the dose of the cinchona bark has been large enough, the symptoms of cinchonism may result. (See *Quinina.*) At one time cinchona bark and its preparations were used as antiperiodics, but at present for such purpose one of its alkaloids is always selected. The best preparation for use as a tonic is the compound tincture.

Dose, ten grains to one drachm (0.65–3.9 Gm.).

Off. Prep.—*Cinchona.*—Fluidextractum Cinchonæ, *U. S.;* Tinctura Cinchonæ, *U. S.;* Extractum Cinchonæ, *N. F.*

Red cinchona.—Extractum Cinchonæ Liquidum, *Br.;* Infusum Cinchonæ Acidum, *Br.;* Tinctura Cinchonæ, *Br.;* Tinctura Cinchonæ Composita, *U. S.* (*Br.,* from Tincture); Fluidextractum Cinchonæ Aquosum, *N. F.;* Gargarisma Guaiaci Compositum (from Compound Tincture of Cinchona), *N. F.*

CINCHONIDINÆ SULPHAS. U. S.

CINCHONIDINE SULPHATE Cinchonid. Sulph.

(cĭn-ĉhǫ-nĭ-dĭ'næ sŭl'phās)

"The sulphate [$(C_{19}H_{22}ON_2)_2.H_2SO_4 + 3H_2O = 740.53$] of an alkaloid obtained from the bark of several species of cinchona. Preserve it in well-closed containers protected from light." *U. S.*

Cinchonidinum sulfuricum; Sulphate of Cinchonidine; Schwefelsaures Cinchonidin, Cinchonidinsulfat, *G.;* Sulfate de Cinchonidine basique, *Fr.;* Solfato di cinconidina, *It.*

This salt is prepared from the mother liquors obtained in the manufacture of quinine sulphate, and is separated from the sulphates of the other alkaloids by fractional crystallization. The British-India and Javanese cultivated red barks usually contain large quantities of cinchonidine. Of the South American barks, probably the Colombian varieties yield the largest proportion of cinchonidine. Owing to some confusion in naming cinchonidine and quinidine, this alkaloid is sometimes incorrectly called in Germany *chinidine.* Skraup's researches on the composition of cinchonine and cinchonidine (1879) established the correctness of the formula $C_{19}H_{22}ON_2$, instead of the long-accepted formula of Pasteur (1853), $C_{20}H_{24}ON_2$. Skraup's formula has been confirmed by Hesse, and is generally accepted by chemists.

Properties.—Cinchonidine sulphate occurs in "white, glistening, silky needles or prisms; odorless and having a very bitter taste; permanent in the air. One Gm. of Cinchonidine Sulphate dissolves in 65 mils of water, 90 mils of alcohol, and in 620 mils of chloroform at 25° C. (77° F.); also in 22 mils of water at 80° C. (176° F.), and in 41 mils of alcohol at 60° C. (140° F.); nearly insoluble in ether. A saturated aqueous solution of the salt is neutral or faintly alkaline to litmus and is lævorotatory. When anhydrous it melts at about 200° C. (392° F.) with partial decomposition. An aqueous solution of Cinchonidine Sulphate yields with barium chloride T.S., a white precipitate, insoluble in hydrochloric acid. Add ammonia water to 25 mils of an aqueous solution of the salt, 1 in 80; a white precipitate (*cinchonidine*) is produced, which is but slightly soluble in ammonia water, but which, when freshly precipitated, dissolves in 5 mils of ether, the greater part afterwards separating in crystals. When dried to constant weight at 100° C. (212° F.), Cinchonidine Sulphate loses not more than 12 per cent. of its weight. Incinerate about 1 Gm. of Cinchonidine Sulphate; not more than 0.1 per cent. of ash remains. Add 2 mils of sulphuric acid to about 0.1 Gm. of the salt; not more than a faint, yellow color is developed (*readily carbonizable impurities*). Ten mils of a solution of the salt (1 in 1000) in diluted sulphuric acid exhibits only a faint, blue fluorescence. Macerate 0.5 Gm. of Cinchonidine Sulphate, with frequent agitation, at the ordinary temperature, with 20 mils of distilled water, then add 0.5 Gm. of potassium and sodium tartrate and continue the maceration with repeated agitation for one hour at 15° C. (59° F.), and filter the mixture. The addition of 1 drop of ammonia water to the filtrate produces not more than a slight turbidity (*cinchonine or quinidine sulphate*).

Cinchonidine.—The alkaloid itself is not official; as usually seen it is in white, light, pulverulent masses. It is crystallizable, soluble in 1680 parts of cold and in a somewhat smaller quantity of hot water, in about 20 parts of alcohol, and in 70 parts of ether. It melts at 206.5° C. (404° F.), and on cooling becomes a solid mass of crystals at 190° C. (374° F.). The *acid sulphate* (sometimes called *bisulphate*) is much more soluble in water than the official sulphate. *Cinchonidine salicylate* is neutral and crystalline, insoluble in cold water, sparingly

in hot water, easily soluble in alcohol and diluted alcohol. It may be prepared by the direct combination of salicylic acid with the alkaloid. The *hydrobromide* has been employed by Gubler hypodermically. Königs and Husmann having claimed to have converted cinchonine into cinchonidine by the long-continued action of boiling amyl alcohol and solution of potassium hydroxide, Paul and Cownley have investigated this treatment. They failed to get such conversion, and consider that the cinchonine used by Königs and Husmann must have been impure. (*P. J.*, Feb. 20, 1897.)

Uses.—So far as our knowledge goes, this alkaloid influences the system similarly to quinine, the only difference being that it is less powerful. It may be given in doses one-third greater than those of quinine, but should not be relied on in severe cases.

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Elixir Cinchonæ Alkaloidorum and in other Elixirs containing Cinchona Alkaloids in combination with Iron, Bismuth, etc., *N. F.*

CINCHONINÆ SULPHAS. U. S.

CINCHONINE SULPHATE Cinchonin. Sulph.

(cĭn-ĉhŏ-nī'næ sŭl'phăs)

"The sulphate [$(C_{19}H_{22}ON_2)_2.H_2SO_4 + 2H_2O = 722.51$] of an alkaloid obtained from the bark of several species of cinchona. Preserve it in well-closed containers protected from light." *U. S.*

Cinchoniæ Sulphas, *Pharm.* 1870; Sulfate de Cinchonine basique, *Fr. Cod.*; Schwefelsaures Cinchonin, Cinchoninum Sulfuricum, Cinchoninsulfat, *G.*; Solfato cinchonico, *It.*; Sulfato de cinconina, *Sp.*

The U. S. P. 1870 process for making Cinchonine Sulphate was as follows: "Take of the mother-water, remaining after the crystallization of Sulphate of Quinine, in the process for preparing that salt, a *convenient quantity;* Solution of Soda, Alcohol, Diluted Sulphuric Acid, Animal Charcoal, in fine powder, each *a sufficient quantity.* To the mother-water add gradually, with constant stirring, Solution of Soda, until the liquid becomes alkaline. Collect on a filter the precipitate formed, wash it with water, and dry it. Then wash it with successive small portions of alcohol, to remove other alkaloids which may be present. Mix the residue with eight times its weight of water, and, having heated the mixture, add gradually Diluted Sulphuric Acid until it is saturated and becomes clear. Then boil the liquid with Animal Charcoal, filter it while hot, and set it aside to crystallize. Lastly, drain the crystals, and dry them on bibulous paper. By evaporating the mother-liquid, more crystals may be obtained." *U. S.* 1870.

In consequence of its greater solubility, cinchonine sulphate remains behind in the mother water, when quinine sulphate crystallizes, in the process for preparing the latter salt. To separate it from other substances contained in the mother water, it is decomposed by solution of soda, which is preferable to potassa, as it forms a very soluble salt with sulphuric acid, whereas the potassium sulphate, being of difficult solubility, might fall with the precipitated cinchonine. The precipitate may be safely washed with small portions of alcohol, as the alkaloid is almost insoluble in that liquid when cold. It is next reconverted into the sulphate, and the solution, having been boiled with *unpurified* animal charcoal to decolorize it, and at the same time neutralize any possible excess of sulphuric acid which might interfere with the crystallization of the salt, is filtered while hot, and then allowed to stand. It is particularly important that there should be no excess of sulphuric acid while the solution is exposed to heat, as under this influence the alkaloid is much disposed to become uncrystallizable. Hence the advantage of using unpurified animal charcoal or bone black, as the calcium carbonate contained in it neutralizes any excess of the acid. The cinchonine sulphate, held in solution by the liquid while hot, is deposited by it, upon cooling, in crystals.

It may be also prepared by first obtaining cinchonine directly from one of the barks, treating this with water acidulated with sulphuric acid, added gradually until the alkaloid is dissolved, then boiling with purified animal charcoal, filtering the solution while hot, and setting it aside to crystallize.

There are two cinchonine sulphates, the neutral and the acid sulphate. The official salt is the neutral sulphate. It is in "white, lustrous prismatic crystals; odorless, and having a very bitter taste; permanent in the air. One Gm. of Cinchonine Sulphate dissolves in 60 mils of water, 12.5 mils of alcohol, 47 mils of chloroform, and in 3230 mils of ether at 25° C. (77° F.); also in 33 mils of water at 80° C. (176° F.), and in 7 mils of alcohol at 60° C. (140° F.). A saturated aqueous solution of the salt is neutral or slightly alkaline to litmus and is dextrorotatory. An aqueous solution of Cinchonine Sulphate (1 in 100) yields with barium chloride T.S. a white precipitate insoluble in hydrochloric acid. Dried to constant weight at 100° C. (212° F.) Cinchonine Sulphate loses not more than 5 per cent. of its weight. Incinerate about 1 Gm. of Cinchonine Sulphate; not more than 0.1 per cent. of ash remains. Ten mils of a solution of the salt (1 in 1000) in diluted sulphuric acid exhibits only a slight, blue fluorescence. One-tenth Gm. of the powdered salt dissolves completely or nearly so when shaken with 10 mils of chloroform at ordinary temperatures (*quinine or cinchonidine sulphate*). Add 0.1 Gm. of the salt to 2 mils of sulphuric acid; it imparts not more than a faint, yellow tinge to the acid (*readily carbonizable, organic impurities*)." *U. S.* The *acid sulphate*, or *bisulphate*, $C_{19}H_{22}ON_2.H_2SO_4.3H_2O$, is prepared by adding sulphuric acid to the neutral sulphate. According to Baup, 100 parts are soluble in 45 parts of absolute alcohol; it is insoluble in ether. It crystallizes in rhombic octohedrons.

Cinchonine (Cinchonina *U. S.*, 1890), $C_{19}H_{22}ON_2 = 294.20$, was introduced into the U. S. P., 1880, but not admitted in the 8th or 9th Revisions. Several processes have been employed for the preparation of cinchonine. One of the simplest is the following: Powdered pale bark is submitted to the action of sulphuric or hydrochloric acid very much diluted, and the solution obtained is precipitated by an excess of lime. The precipitate is collected on a filter, washed with water, and treated with boiling alcohol. The alcoholic solution is filtered while hot, and deposits the cinchonine when it cools. A further quantity is obtained by evaporation. If not perfectly white, it may be made so by converting it into a sulphate with diluted sulphuric acid, then treating the solution with animal charcoal, filtering, precipitating by an alkali, and redissolving in alcohol in the manner already mentioned. It may also be obtained from the mother waters of quinine sulphate by diluting them with water, precipitating with ammonia, collecting the precipitate on a filter, washing and drying it, and then dissolving it in boiling alcohol, which deposits the cinchonine in a crystalline form upon cooling. It may be still further purified by a second solution and crystallization. Its formula is now generally accepted as $C_{19}H_{22}ON_2$, the molecular weight of which is 292.03, as proposed by Skraup, instead of the older formula, $C_{20}H_{24}ON_2$, of Pasteur. This alkaloid occurs in "white, lustrous prisms or needles, without odor, at first almost tasteless, but soon developing a bitter after-taste; permanent in the air. Soluble, at 15° C. (59° F.), in 3760 parts of water, and in 116 parts of alcohol; in 3500 parts of boiling water, and in 26.5 parts of boiling alcohol. Also soluble in 526 parts of ether, and in 163 parts of chloroform. At 240° C. (464° F.) the crystals fuse together, and at 258° C. (496.4° F.) they melt, forming a brown liquid. When ignited, they are consumed without leaving a residue. When placed on moistened, red litmus paper, Cinchonine shows an alkaline reaction. On adding to a neutral or not more than faintly acid solution of Cinchonine, or of any of its salts, enough potassium ferrocyanide test-solution to redissolve the precipitate first formed, and afterwards an acid, a golden-yellow precipitate will be formed, which, when redissolved by gently warming the liquid, will separate, on cooling, in minute scales or needles. On adding an excess of ammonia water to a solution of Cinchonine in a diluted acid, the alkaloid will be precipitated. The precipitate is but feebly soluble in ammonia, and should require not less than 300 parts of ether for solution. A solution of Cinchonine (1 in 1000) in diluted sulphuric acid should not exhibit more than a faint blue fluorescence (absence of more than traces of *quinine* or *quinidine*). Cinchonine should not impart more than a faintly yellowish tinge to concentrated sulphuric acid (limit of *readily carbonizable, organic impurities*)." *U. S.* 1890. Waddington found it to sublime readily, without change, in perfectly characteristic crystals. (*P. J.*, March, 1868, p. 414.) Its alkaline character is very decided, as it neutralizes the strongest acids. Of the salts of cinchonine, the sulphate, nitrate, hydrochloride, phosphate, and acetate are soluble in water. The neutral tartrate, oxalate, and gallate are insoluble in cold water, but soluble in hot water, alcohol, or an excess of acid. Winckler has shown that cinchonine is rendered uncrystallizable or amorphous by sulphuric acid in excess, aided by heat, a fact of importance in the preparation of the sulphate of this alkaloid. Cinchonine is but little more soluble in carbonic acid water than in pure water, and does not, like quinine, yield crystals of the carbonate on exposure of its carbonic acid solution. It differs from quinine by its rotating the plane of polarization to the right, by the want of fluorescence in its solutions, and by its failing to respond to the thalleioquin test.

Exposed to the air, cinchonine does not suffer decomposition, but very slowly absorbs carbonic acid gas, and acquires the property of effervescing slightly with acids. It is precipitated sulphur yellow by gold trichloride. Chlorine water dissolves it or any of its salts without change; but if ammonia be now added, a white precipitate is produced. It is thus distinguishable from quinine. (See *Quinina.*) J. W. Bill, U. S. A., proposed potassium, ferrocyanide as a very delicate test of cinchonine. If added to the solution of a salt of this alkaloid, it produces a yellowish-white curdy precipitate, which is dissolved upon the application of a gentle heat, but is again deposited, when the liquid cools, as an abundant crop of golden-yellow crystals. No other alkaloid exhibits the same reaction. A cloudy precipitate is produced by the same reagent with a salt of quinine; but this does not happen when the ferrocyanide is in excess; and, if the precipitate be dissolved by heat, no subsidence takes place on cooling. Hence, in the application of this test to cinchonine, a slight excess of the ferrocyanide should be added.

By the action of potassium permanganate cinchonine is decomposed, with the effect of producing, at first, an entirely distinct neutral principle, *cinchotenine*, $C_{18}H_{20}O_3N_2 + 3H_2O$, and an alkaloid, which the authors named *hydrocinchonine*, $C_{19}H_{24}ON_2$, as it differs from cinchonine (cinchonia) only in having two additional atoms of hydrogen. The cinchotenine, when further oxidized by the same reagent, yields quinoline and pyridine derivatives (see Part II), as *cinchonic* (quinoline-carboxylic) *acid*, $C_9H_6N(COOH)$, and *cinchomeronic* (pyridine-dicarboxylic) *acid*, $C_5H_3N(COOH)_2$.

Uses.—Cinchonine sulphate has the same remedial properties as quinine sulphate, but must be given in somewhat larger dose. It may be taken in pill, or in solution made by the addition of diluted sulphuric acid in the proportion of a minim or two drops for each grain of the salt. To lessen the bitterness in taste, it may

be given suspended in syrup, without the use of any acid or with a few grains of powdered licorice added to the mixture.

Dose, tonic, a grain or two (0.065–0.13 Gm.) three or four times a day; antiperiodic dose, fifteen to forty grains (1.0–2.6 Gm.) between the paroxysms.

Off. Prep.—Elixir Cinchonæ Alkaloidorum and in other Elixirs containing Cinchona Alkaloids in combination with Iron, Bismuth, etc., *N. F.*

CINNAMOMUM SAIGONICUM. U. S.

SAIGON CINNAMON Cinnam. Saigon.

(cĭn-nā-mō'mŭm sä-ĭ-gŏn'ĭ-cŭm)

"The dried bark of an undetermined species of *Cinnamomum* (Fam. *Lauraceæ*)." *U. S.*

Annam cinnamon, China cinnamon, God's cinnamon; Cannelle de Saigon, *Fr.*; Saigonzimmt, *G.*

CINNAMOMUM ZEYLANICUM. U. S. (Br.)

CEYLON CINNAMON Cinnam. Zeylan.

(cĭn-nā-mō'mŭm zĕy-lăn'ĭ-cŭm)

"The dried bark of cultivated trees of *Cinnamomum zeylanicum Breyne* (Fam. *Lauraceæ*), without the presence or admixture of more than 3 per cent. of the outer bark or other foreign matter." *U. S.* "Cinnamon Bark is the dried inner bark of shoots from the truncated stocks of Cinnamomum zeylanicum, *Breyn.* Obtained from cultivated trees. Imported from Ceylon, and distinguished in commerce as Ceylon cinnamon." *Br.*

Cinnamomi Cortex, *Br.*; Cinnamomum, *U. S.* 1880; Cinnamon Bark; Cortex Cinnamomi Zeylanici; Cinnamomum Acutum, s. Verum; Cannelle de Ceylan, *Fr. Cod.*; Cannelle, *Fr.*; Brauner Kaneel, Zeylonzimmt, Zimmt, *G.*; Cannella, *It.*; Canela, *Sp.*; Kurundu, *Cingalese*; Karua puttay, *Tamil.*

Both *cinnamomum* and *cassia* were terms employed by the ancients, but whether exactly as now understood it is impossible to determine. The term *cassia*, or *cassia lignea*, has been generally used in modern times to designate the commoner barks of *Cinnamomum Cassia* (Nees) Blume. The barks sold as cinnamon and cassia in different parts of the world are derived from various species of Cinnamomum.

Cinnamomum zeylanicum is a tree about 20 or 30 feet high, covered with a thick, scabrous bark. The branches are numerous, strong, horizontal, and declining, and the young shoots are beautifully speckled with dark green and light orange colors. The leaves are petiolate, opposite for the most part, coriaceous, entire, ovate or ovate-oblong, obtusely pointed, and three-nerved, with the lateral nerves vanishing as they approach the point. There are also two less obvious nerves, one on each side arising from the base, proceeding towards the border of the leaf, and then quickly vanishing. In one variety the leaves are very broad and somewhat cordate. When mature, they are of a shining green upon their upper surface, and lighter-colored beneath. The flowers are small, white, and arranged in axillary and terminal panicles. The fruit is an oval berry, which adheres like the acorn to the receptacle, is larger than the black currant, and when ripe has a bluish-brown surface, diversified with numerous white spots. The tree emits no odor perceptible at any distance. The bark of the root has the odor of cinnamon with the pungency of camphor, and yields this principle upon distillation. The leaves have a spicy odor when rubbed, and a hot taste. A volatile oil has been distilled from them. The petiole has the flavor of cinnamon. It is a singular fact that the odor of the flowers is to most persons disagreeable, being compared by some to the scent exhaled from newly-sawed bones. The fruit has a terebinthinate odor when opened, and a taste in some degree like that of juniper berries. A fatty substance, called *cinnamon-suet*, is obtained from it when ripe, by bruising it and then boiling it in water, and removing the oleaginous matter which rises to the surface, and concretes upon cooling. It is the prepared bark that constitutes the genuine cinnamon.

This species is a native of Ceylon, where it has long been cultivated. It is said also to be a native of the Malabar Coast, and has at various periods been introduced into Java, the Isle of France, Bourbon, the Cape Verds, Brazil, Cayenne, several of the West India islands, and Egypt, and in some of these places is at this time highly productive, especially in Cayenne, where the plant was flourishing so early as 1755. It is exceedingly influenced, as regards the aromatic character of its bark, by the circumstances of soil, climate, and mode of culture. Thus, we are told by Marshall that in Ceylon, beyond the limits of Negombo and Matura, in the western and southern parts of the island, the bark is never of good quality, being greatly deficient in the aromatic flavor of the cinnamon, and that even within these limits it is of unequal value, from the various influences of exposure, soil, shade, and other circumstances. Cinnamon closely resembling Ceylon cinnamon is said to have been sent to Europe from Brazil.

Cassia Cinnamon which was formerly official is the product of *Cinnamomum Cassia* (Nees) Blume, a tree resembling *C. Zeylanicum* but distinguished by the hairiness of the young twigs, petioles and under surfaces of the leaves. The tree is indigenous to and cultivated in southern China, Annam and Cochin-China. It is also cultivated in Sumatra, Ceylon, Japan, Mexico and South America. The bark is known in commerce as *China* or *Canton Cassia* and the commonest or cheapest grade as "*Cassia lignea.*"

Besides the two species above described, others have been thought to contribute to the cinnamon and cassia of commerce. In 1839 (*Madras Journ. Lit. and Sci.*, No. 22), Wight stated that in his belief cinnamon was derived from 12 to 18 specifically distinct trees. *C. inners*, Reinw., is distinguished from *C. zeylanicum* by the nervation of its leaves, which are also paler and thinner than those of the official plant, of which, however, it is probably only a variety.

It yields the so-called *wild cinnamon* of Japan. *C. obtusifolium* Nees, growing in Ceylon, Java, and on the mainland of India, is said to have been the chief source of the drug known formerly by the name of *Folia Malabathri* and consisting of the leaves of different species of Cinnamomum mixed together. *C. Culilawan* Blume of the Moluccas yields the aromatic bark called culilawan, noticed in Part II of this work; and similar barks are obtained from *C. Sintoc* of Java. *Massoy bark,* from which an aromatic volatile oil is obtained called *oil of massoy,* is the product of *Sassafras Goesianum* Leijom. In the mountains of Eastern Bengal, at a height of 1000 to 4000 feet, flourish *C. obtusifolium* Nees, *C. pauciflorum* Nees, and *C. Tamala* Nees et Ebern, and these, with other unknown species, afford quantities of bark which are shipped from Calcutta, Java, Timor, etc., to Europe under the name of *wild cassia.* The bark of the *C. pedatinervium* Meissn, a tree indigenous to Fiji, yields nearly one per cent. of a white aromatic volatile oil, with a pungent spicy taste. For constitution, etc., see *Proc. Chem. Soc.,* xix. These barks are mostly highly aromatic, resembling cinnamon more or less closely in flavor, and are distinguished by yielding to cold water an abundant mucilage. Holmes described the bark of *C. pedativum* Meis., and concludes that it might be of value as a source of safrol and linalool in *P. J.,* 1904, p. 892.

Cassia Buds.—This spice consists of the calyx of *Cinnamomum Cassia* (Nees) Blume, surrounding the young ovary, and, as stated by Martius, on the authority of the elder Nees, about one-quarter of the normal size. It is produced in China; and Reeves states that great quantities of it are brought to Canton from the province which affords cassia. Cassia buds have some resemblance to cloves, and are compared to small nails with round heads. The enclosed ovary is sometimes removed, and they are then cup-shaped at top. They have a brown color, with the flavor of cinnamon, and yield an essential oil upon distillation. They may be used for the same purposes as the bark.

Culture, Collection, Commerce, etc.—In Ceylon, cinnamon bark was originally collected exclusively from the tree in a wild state; but the Dutch introduced the practice of cultivating it, which has been continued since the British came into possession of the island. The principal cinnamon gardens are in the vicinity of Colombo, but the plant is grown from the sea-level up to a considerable elevation, giving the finest product, however, on the sandy soil of the coast line. The seeds are planted in a prepared soil at certain distances, and, as four or five are placed in a spot, the plants usually grow in clusters like the hazel-bush. In favorable situations they attain the height of five or six feet in six or seven years; and a healthy bush will then afford two or three shoots fit for peeling, and every second year afterwards from four to seven shoots in a good soil. The cinnamon harvest commences in May and continues until late in October. The first object is to select shoots proper for decortication, and those are seldom cut which are less than half an inch or more than two or three inches in diameter. Before decortication these shoots are trimmed up, and the small pieces, when dried, constitute *cinnamon chips.* The bark is divided by longitudinal incisions, of which two are made in the smaller shoots, several in the larger, and is then removed in strips by means of a suitable instrument. The pieces are next collected in bundles, and allowed to remain in this state for a short time, so as to undergo a degree of fermentation, which facilitates the separation of the epidermis. This, with the green matter beneath it, is removed by placing the strip of bark upon a convex piece of wood and scraping its external surface with a curved knife. The bark now dries and contracts, assuming the appearance of a quill. The peeler introduces the smaller tubes into the larger, and connects them also endwise, thus forming a congeries of quills which is about forty inches long. When sufficiently dry, these cylinders are collected into bundles weighing about thirty pounds and bound together by pieces of split bamboo. The commerce in Ceylon cinnamon was formerly monopolized by the East India Company; but the cultivation is now unrestricted, and the bark may be freely exported upon the payment of a fixed duty. It is assorted in the island into three qualities, distinguished by the designations of *first, second,* and *third.* The inferior kinds, which are of insufficient value to pay the duty, are used for preparing oil of cinnamon.

The importations of *cassia buds* into the United States in 1916 amounted to 197,056 pounds, and of *cassia* and *cassia leaves* to 7,487,156 pounds, valued at $493,161. Immense quantities of cinnamon barks are exported from China, the finest of which is little inferior to that of Ceylon, though the mass of it is much coarser. It passes in commerce under the name of *cassia,* was formerly official, and is said by Reeves to be brought to Canton from the province of Kwangse, where the tree producing it grows very abundantly. It is, indeed, asserted that true cinnamon of very fine grade occurs in China, although it never enters foreign commerce, because of the high price which it commands at home. (*P. J.,* xxi, 1890.) These fine cinnamons are said to be produced in the mountainous district of Annam, or Cochin-China. Cinnamon of good quality is said to be collected in Java, and considerable quantities of inferior quality have been thrown into commerce, as *cassia lignea,* from the Malabar Coast. Manila and the Isle of France are also mentioned as sources whence this drug is supplied. Little, however, reaches the United States from these places. The island of Martinique, Cayenne, and several of the West India islands yield to commerce considerable quantities of cinnamon of various qualities. That of Cayenne is of two kinds, one of which closely resembles, though it does not quite equal, the aroma of Ceylon, the other resembles the Chi-

nese. The former is supposed to be derived from plants propagated from a Ceylonese stock, the latter from plants which have sprung from a tree introduced from Sumatra. By far the greater proportion of cinnamon brought to this country is imported from China. It is entered as *cassia* and *Saigon cassia* at the custom house.

From what source the ancients derived their cinnamon and cassia is not certainly known. Neither the plants nor their localities, as described by Dioscorides, Pliny, and Theophrastus, correspond precisely with our present knowledge; but in this respect much allowance must be made for the inaccurate geography of the ancients. It is probable that the Arabian navigators at a very early period conveyed this spice within the limits of the Phenician and Grecian and subsequently of Roman commerce.

Properties.—*Saigon cinnamon* takes its name from Saigon, the capital of French Cochin China. It is a thick cassia bark, which has come into European commerce, and was recognized for the first time by the U. S. P., 1890. It is officially described as "in quills attaining a length of 30 cm., and from 3 to 30 mm. in diameter; the bark from 0.5 to 3 mm. in thickness; outer surface light brown to dark purplish-brown with grayish patches of foliaceous lichens and numerous bud-scars; finely wrinkled, especially the bark of younger twigs, otherwise more or less rough from corky patches surrounding the lenticels; inner surface reddish-brown to dark brown, granular, and slightly striate; fracture short; inner bark porous, owing to the presence of large oil cells and mucilage cells, and separated by a continuous layer of stone cells from the outer bark; odor aromatic; taste sweetish, aromatic and pungent. Under the microscope, sections of the older bark of Saigon Cinnamon show a thin layer of more or less lignified cork cells; a narrow layer of starch-bearing parenchyma with scattered stone cells; a nearly continuous zone, several layers wide, of stone cells, among which are small groups of bast-fibers with thickened and slightly lignified walls; a wide inner bark with medullary rays 1 to 3 cells in width, isolated bast-fibers, mucilage cells, oil cells and parenchyma, the cells of the latter either filled with starch grains or containing very small raphides of calcium oxalate; the lumina of parenchyma cells, stone cells and bast-fibers frequently filled with an amorphous reddish-brown substance, which is for the most part insoluble in the ordinary reagents. In the bark of young twigs there is an epidermal layer with a thick yellowish cuticle, fewer stone cells in the zone associated with bast-fibers, and the inner bark is narrower and with fewer secretion cells than in the older bark. The powder is yellowish- or reddish-brown; starch grains numerous, single or compound, the individual grains being somewhat ellipsoidal or polygonal and from 0.003 to 0.02 mm. in diameter; fragments, with colorless stone cells, rather prominent, the cells being very irregular in shape and the lumina containing either air or a reddish-brown amorphous substance; bast-fibers from 0.3 to 1.5 mm. in length and usually in groups of from 2 to 20 with very thick and scarcely lignified walls; numerous cellular, reddish-brown fragments in which the oil cells are not readily distinguishable. Saigon Cinnamon yields not less than 2 per cent. of volatile extractive, soluble in ether. (See Part III, Test No. 12.) Saigon Cinnamon yields not more than 6 per cent. of ash. The amount of ash insoluble in diluted hydrochloric acid does not exceed 2 per cent. of the weight of Saigon Cinnamon taken." *U. S.*

"In closely rolled quills, each about nine millimetres in diameter, and containing numerous smaller quills or channelled pieces. Dull, pale yellowish-brown, darker on the inner surface; thin, brittle and splintery; entirely free from cork; marked with small scars or holes and with faint, shining, wavy longitudinal lines. The powdered Bark exhibits abundant parenchymatous tissue with brown cell-walls, isolated bast-fibers not more than 30 microns in diameter, small simple or compound starch grains and thick-walled sclerenchymatous cells, but no cork or fragments of wood. Fragrant odor; taste warm, sweet and aromatic. Ash not more than 5 per cent." *Br.*

The odor of this cinnamon is fragrant, the taste is highly aromatic, markedly that of cinnamon, and, in the specimens that we have seen, only slightly astringent. It also occurs in commerce much broken, in which state it commands a somewhat smaller price than in quills. The Saigon buds also are brought into the port of New York. The quality of Saigon cassia, as it is commonly termed in trade journals, is distinctly superior to that of other cassias, and the price which it commands much higher. It is obtained from an undetermined species of Cinnamomum but is sometimes ascribed to *Cinnamomum Loureirii* of Nees, the *Laurus Cinnamomum* of Loureiro, a tree which grows in Cochin-China and Japan. According to Siebold, the bark of the large branches is of inferior quality and is rejected; that from the smallest branches resembles the Ceylon cinnamon in thickness, but has a very pungent taste and odor, and is little esteemed, while the intermediate branches yield an excellent bark, about 2 mm. in thickness, which is even more highly valued than the cinnamon of Ceylon, and yields a sweeter and less pungent oil. It yields about 2 per cent. of a volatile oil, *the oil of Nikkei*, having an odor resembling that of cinnamon and consisting of citral, having a specific gravity at 15° C. (59° F.) of 0.9005, and containing about 27 per cent. of aldehyde, chiefly citral.

Ceylon cinnamon occurs "in closely rolled double quills, composed of from 7 to 12 thin layers of separate pieces of bark, from 30 to 50 cm. in length and from 8 to 13 mm. in diameter; the bark attaining a thickness of 1 mm.; outer surface pale yellowish-brown, smooth, longitudinally striate with narrow yellowish groups of bast-fibers, and showing circular

or irregular brownish patches, occasionally with perforations marking the nodes; inner surface light brown, with faint, longitudinal striations; fracture short with projecting bast-fibers; odor agreeably aromatic; taste sweetish and warmly aromatic. Under the microscope, sections of Ceylon Cinnamon usually show no cork but an almost continuous outer layer of stone cells, among which are small groups of bast-fibers resembling those found in *Saigon Cinnamon;* in the inner bark occur numerous bast-fibers singly or in small groups, medullary rays 1 to 2 cells in width, usually with raphides of calcium oxalate; parenchyma with either reddish-brown contents or more or less filled with starch grains; scattered throughout the parenchyma occur oil secretion cells and mucilage cells. The powder is light brown or yellowish-brown; starch grains numerous, varying from spherical to polygonal, from 0.003 to 0.02 mm. in diameter, frequently in small aggregates; bast-fibers from 0.3 to 0.8 mm. in length, usually single, spindle-shaped, with attenuated ends, the walls being very thick and but slightly lignified; colorless stone cells resembling those of *Saigon Cinnamon;* numerous cellular fragments with yellowish-brown walls or contents; cork cells few or none; calcium oxalate in raphides, from 0.005 to 0.008 mm. in length. Ceylon Cinnamon yields not less than 0.5 per cent. of volatile extractive, soluble in ether. (See Part III, Test No. 12.) Ceylon Cinnamon yields not more than 6 per cent. of ash. The amount of ash insoluble in diluted hydrochloric acid does not exceed 2 per cent. of the weight of Ceylon Cinnamon taken." *U. S.*

When distilled Ceylon Cinnamon affords but a small quantity of essential oil, which, however, has an exceedingly grateful flavor. It is brought to this country from England, but it is costly. The inferior sorts are browner, thicker, less splintery, and of a less agreeable flavor, and are little if at all superior to the best Chinese. The finer variety of *Cayenne cinnamon* approaches in character that above described, but is paler and in thicker pieces, being usually collected from older branches. That which is gathered very young is scarcely distinguishable from the cinnamon of Ceylon.

Chinese cinnamon, or *Cassia* (*Cinnamomum Cassia, Cassia Cinnamon,* U. S., 1890), occurs in quills, usually single, sometimes double, very rarely more than double, from 30 to 60 cm. long, 2 to 5 cm. wide, and 0.2 to 3 mm. thick. In some instances the bark is rolled very much upon itself, in others is not even completely quilled, forming segments more or less extensive of a hollow cylinder. It is of a redder or darker color than the finest Ceylon cinnamon, thicker, rougher, denser, and breaks with a shorter fracture. It has a stronger, more pungent and astringent but less sweet and grateful taste, and though of a similar odor, is less agreeably fragrant. It is the kind almost universally kept in our shops. Of a similar character is the cinnamon imported directly from various parts of the East Indies. But under the name of cassia have also been brought to us very inferior kinds of cinnamon, collected from the trunks or large branches of the trees, or injured by want of care in keeping, or perhaps derived from inferior species. It is said that cinnamon from which the oil has been distilled is sometimes fraudulently mixed with the genuine. These inferior kinds are detected, independently of their greater thickness and coarseness of fracture, by their deficiency in the peculiar sensible properties of the spice. Chinese cinnamon is "in quills of varying length and about 1 mm. or more in thickness; nearly deprived of the corky layer; yellowish-brown; outer surface somewhat rough; fracture nearly smooth; odor fragrant; taste sweet, and warmly aromatic." *U. S.* 1890. Cassia is no longer official in the U. S. P., it having been dropped at the 8th Revision.

Powdered cinnamon is often grossly adulterated with sugar, ground walnut shells, galanga rhizome and various other substances. Galanga, according to Schmitz-Dumont, may be detected by the presence of small club-shaped, rod-shaped, partly bent, microscopic pieces of resinotannol. (*Zeit. oeff. Chem.,* 1903, No. 2.) Powdered cassia buds are frequently added to the inferior cinnamon powders, but can hardly be looked upon as an adulterant, as they contain a larger proportion of volatile oil than the lower grades of cinnamon.

The *Pharmacographia* gives the following tests for distinguishing powdered cassia from powdered cinnamon, and for recognizing the inferior varieties of cassia. Make a decoction of powdered cinnamon of known genuineness, and one of similar strength of the suspected powder; when cool and strained, test a fluidounce of each with one or two drops of tincture of iodine. A decoction of cinnamon is but little affected, but in that of cassia a deep blue-black tint is immediately produced. The cheap kinds of cassia known as *cassia vera* may be distinguished from the more valuable Chinese cassia as well as from cinnamon by their richness in mucilage; this can be extracted by cold water; it is a thick glairy liquid, giving dense ropy precipitates with corrosive sublimate or neutral lead acetate, but not with alcohol.

Microscopic Structure.—Ceylon cinnamon usually consists simply of the inner bark, the outer coatings having been stripped off during its preparation for market. Three layers are distinguishable in the liber. "1. The external surface, which is composed of one to three rows of large thick-walled cells, forming a coherent ring; it is only interrupted by bundles of bast fibres, which are obvious even to the unaided eye. 2. The middle layer is built up of about 10 rows of parenchymatous thin-walled cells, interrupted by much larger cells containing deposits of mucilage, while other cells not larger than those of the parenchyma itself are filled with essential oil. 3. The innermost layer exhibits the same thin-walled but smaller cells, yet inter-

sected by narrow somewhat darker medullary rays, and likewise interrupted by cells containing either mucilage or essential oil, instead of bundles of bast fibres. Fibres mostly isolated are scattered through the two inner layers, the parenchyma of which abounds in small starch granules accompanied by tannic and on a longitudinal section the length of the liber fibres becomes more evident, as well as the oil-cells and mucilage cells." (*Pharmacographia.*)

The coarser cassia bark, or *cassia lignea,* usually has some of the external or corky layer adherent to it, and always the parenchymatous mesophlœum or middle bark, but the inner bark constitutes the chief mass. Isolated bast fibers and thick-walled stone cells are scattered even through the outer layers of a transverse section. In the middle zone they are numerous, but do not form a coherent sclerenchymatous ring as in Ceylon cinnamon. The innermost part of the bast shares the structural character of cinnamon, with differences due to age, as, for instance, the greater development of the medullary rays. Oil cells and mucilage cells are likewise distributed among the parenchyma of the former. The finest cassia or Chinese cinnamon has the three layers described in Ceylon cinnamon, but is distinguished by the adherent outer parenchymatous and suberous layer. For an excellent description of the microscopical structure of the commercial cinnamon see Winton and Moeller, "*The Microscopy of Vegetable Foods.*" Spaeth gives the microscopical characteristics of the several kinds of cinnamon, discusses the adulterants of powdered cinnamon and the means of detection in *Ph. Centralh.*, 1908, pp. 724, 729. Rosenthaler and Reis give an excellent pharmacognostical study of Seychelles Cinnamon in *Ber. d. pharm. Gesellsch.*, Berl., 1909, p. 490.

Chemical Composition.—According to the analysis of Vauquelin, cinnamon contains a peculiar volatile oil, tannin, mucilage, a coloring matter, an acid, and lignin. The tannin is of the variety which yields a greenish-black precipitate with the salts of iron. Thos. R. Thornton (*A. J. P.*, 1895, 400) has examined the tannin of *C. Cassia.* He found it to amount to about 3.90 per cent., as an average of three different determinations on different samples. He found it impossible to extract the tannin by any one of several methods tried, and concludes that it either has the phlobophene (anhydride) character as it exists in the drug or acquires such character when brought into contact with water. Jas. A. Ferguson (1887), in the laboratory of the Philadelphia College of Pharmacy, determined the ash of several samples of Ceylon cinnamon, finding an average of 4 per cent., while in powdered *cassia cinnamon* he found 2.8 and 2.5 per cent. (*A. J. P.*, 1887, 278, 279.) The oil obtained from the Cayenne cinnamon was found to be more biting than that from the Ceylon. Bucholz found in 100 parts of *cassia lignea* 0.8 of volatile oil, 4.0 of resin, 14.6 of gummy extractive (probably including tannin), 64.3 of lignin and bassorin, and 16.3 of water, including loss.

This aromatic yields its virtues wholly to alcohol, and less readily to water. At the temperature of boiling alcohol very little of the oil rises, and an extract prepared from the tincture retains, therefore, the aromatic properties. For an account of the volatile oil, see *Oleum Cinnamomi.*

Uses.—Cinnamon is among the most grateful and efficient of the aromatics. It is warm and cordial to the stomach, carminative, distinctly astringent, and, like most other substances of this class, more powerful as a local than as a general stimulant. It is seldom prescribed alone, though, when given in powder or infusion, it will sometimes allay *nausea,* check *vomiting,* and relieve *flatulence.* It is chiefly used as an adjuvant, and enters into a great number of official preparations. It is often employed in *diarrhea,* in connection with chalk and astringents.

Dose, of powder, ten to twenty grains (0.65 to 1.3 Gm.).

Off. Prep.—*Ceylon cinnamon.*—Aqua Cinnamomi, *Br.;* Pulvis Cinnamomi Compositus, *Br.;* Pulvis Cretæ Aromaticus, *Br.;* Tinctura Cardamomi Composita, *Br.;* Tinctura Cinnamomi, *Br.;* Tinctura Lavandulæ Composita, *Br.*

Off. Prep.—*Saigon cinnamon.*—Pulvis Aromaticus, *U. S.;* Fluidextractum Aromaticum (from Aromatic Powder), *U. S.;* Tinctura Cardamomi Composita, *U. S.;* Tinctura Cinnamomi, *U. S.;* Tinctura Lavandulæ Composita, *U. S.;* Cordiale Rubi Fructus, *N. F.;* Elixir Rubi Compositum, *N. F.;* Elixir Taraxaci Composita (from Tincture), *N. F.;* Pulvis Aromaticus Rubefaciens, *N. F.;* Pulvis Cretæ Aromaticus, *N. F.;* Syrupus Cinnamomi, *N. F.;* Tincture Aromatica, *N. F.;* Vinum Aurantii Compositum, *N. F.*

COCAINA. U. S., Br.

COCAINE Cocain.

(cō-cą-ĭ'ną)

"An alkaloid [$C_{17}H_{21}O_4N$ or $C_6H_{11}(C_6H_5CO)ON.COOCH_3$=303.18] obtained from *Erythroxylon Coca* Lamarck and its varieties (Fam. *Erythroxylaceæ*). Preserve it in well-closed containers protected from light." *U. S.* "Cocaine, $C_{17}H_{21}NO_4$, is an alkaloid obtained from the leaves of Erythroxylum Coca, *Lam.*, and its varieties." *Br.*

Benzoyl-ecgonine-methyl-ester; Benzoyl-methyl-ecgonine Cocainum; Cocaïne, *Fr. Cod.;* Cocain, Kokain, *G.*

Owing to the small yield, it is found more profitable to manufacture cocaine in South America and export it, thus saving the expense of transporting the bulky coca leaves.

Properties.—It is officially described as in "large, colorless, four-sided, or six-sided monoclinic prisms, or as a white crystalline powder; odorless. One Gm. of Cocaine dissolves in about 600 mils of water, 6.5 mils of alcohol, 0.7 mil of chloroform, 3.5 mils of ether and in 12 mils of olive oil at 25° C. (77° F.), also in

270 mils of water at 80° C. (176° F.); very soluble in warm alcohol; slightly soluble in liquid petrolatum. It melts between 96° and 98° C. (204.8° and 208.4° F.). On neutralizing carefully an alcoholic solution of Cocaine with diluted hydrochloric acid and evaporating the solution to dryness, the residue responds to the tests for identity and purity under *Cocainæ Hydrochloridum.*" *U. S.*

The British Pharmacopœia gives the following description and tests: "In colorless monoclinic prisms. No odor; taste bitter, followed by a sensation of tingling and numbness. Soluble in 10 parts of *alcohol* (90 per cent.), in 4 parts of *ether,* in 0.5 part of *chloroform,* and in 24 parts of *olive oil;* almost insoluble in *water.* Melting point 98° C. (208.4° F.). The dry salt obtained by dissolving Cocaine in *water* acidified with *hydrochloric acid,* and evaporating the solution, responds to the tests described under 'Cocainæ Hydrochloridum.'" *Br.*

The following was Niemann's process for making cocaine: The leaves were exhausted with 85 per cent. alcohol acidulated with 2 per cent. of sulphuric acid; the tincture was treated with milk of lime and filtered; the filtrate was neutralized with sulphuric acid, and the alcohol distilled off. The syrupy residue was treated with water to separate resin, and then precipitated by sodium carbonate. The deposited matter was exhausted by ether, and the ethereal solution, after most of the ether had been distilled, was allowed to evaporate spontaneously. The cocaine was thus obtained in colorless crystals, mixed with a yellowish-brown matter of a disagreeable odor, which was separated by washing with cold alcohol. E. R. Squibb's process for cocaine and its hydrochloride is as follows: Coarsely ground coca leaves are repercolated with an aqueous five per cent. solution of sulphuric acid, and a very dense, slightly acid percolate is obtained; this is thoroughly agitated with pure coal oil and an excess of sodium carbonate; the liberated alkaloid is retained by the coal oil, and is nearly free from coloring matter; the oily solution is then agitated with acidulated water, and again precipitated by sodium carbonate in the presence of ether. The ethereal solution of cocaine is treated with diluted hydrochloric acid fractionally, and the nearly colorless solutions of cocaine hydrochloride are cautiously evaporated in shallow porcelain pans almost to dryness. The product is in the form of a white, crystalline, granular powder, and is a nearly pure anhydrous salt. (*Ephem.,* 1887, 906.) For Henrique's process see *Proc. A. Ph. A.,* 1895, 999. Pure cocaine is in colorless, transparent prisms, inodorous, of a bitterish taste, soluble in 704 parts of cold water, more soluble in alcohol, and freely so in ether. The solution has an alkaline reaction and a bitterish taste, leaving a peculiar numbness on the tongue. The alkaloid melts at 98° C. (208.4° F.), and on cooling congeals into a transparent mass, which gradually becomes crystalline. Heated above this point it changes color, and is decomposed. It is inflammable, burning with a bright flame, and leaving charcoal. With the acids it forms soluble and crystallizable salts, which are more bitter than the alkaloid itself. The formula is $C_{17}H_{21}NO_4$. (See *Cocainæ Hydrochloridum,* p. 361.) Niemann also obtained wax, a variety of tannic acid (*cocatannic acid*), and a concrete volatile odorous substance. The presence of *hygrine* in coca leaves is not confirmed. A considerable number of closely allied alkaloids, all of which appear to be derivatives of ecgonine, are found in the leaves of *Erythroxylon Coca.* The following list is given in Allen (*Com. Org. Anal.,* 2d ed., vol. iii, Part II, 271), on the authority of Paul and Cownley:

$C_9H_{13}NO_2$, *Anhydro-ecgonine.*
$C_9H_{15}NO_3$, *Ecgonine.*
$C_{16}H_{19}NO_4$, *Benzoyl-ecgonine.*
$C_{17}H_{21}NO_4$, *Benzoyl-ecgonine methyl ester* (*cocaine*).
$C_{18}H_{21}NO_4$, *Cinnamyl-ecgonine.*
$C_{19}H_{23}NO_4$, *Cinnamyl-ecgonine methyl ester.*
$C_{38}H_{46}N_2O_8$, *Cocayl-ecgonine methyl ester* (*cocamine*).
$C_{40}H_{50}N_2O_8$, *Homo-cocamine.*
$C_{17}H_{19}NO_2$, *Benzoyl-pseudotropine* (*tropacocaine*).

With the exception of ecgonine and anhydroecgonine, all of the bodies in the foregoing list are saponifiable, splitting up when heated to from 80° to 100° C. (176°–212° F.) with hydrochloric acid, or when boiled with alcoholic potassium hydroxide.

As the separation of cocaine from the accompanying alkaloids and products of hydrolysis is difficult, Liebermann (*Ber. d. Chem. Ges.,* xxi, 3196) has proposed a synthetic method which avoids these difficulties and at the same time utilizes the amorphous by-products. The mixed bases are boiled with hydrochloric acid, whereby they all suffer hydrolysis with formation of ecgonine; then, by passing dry hydrochloric acid into a solution of ecgonine hydrochloride in methyl alcohol, the hydrochloride of ecgonine methyl ester is formed, which on concentrating the alcoholic solution crystallizes out in prisms. Cocaine is formed when this compound is heated on the water bath with an equal weight of benzoyl chloride until the mixture becomes homogeneous and the evolution of hydrochloric acid ceases. The melted mass is poured into water and separated from the insoluble benzoic acid, when the cocaine is precipitated by ammonia and recrystallized from alcohol. Hesse investigated addition products of ecgonine and produced a crystalline compound of ecgonine and methyl iodide, $C_9H_{15}NO_3$, $CH_3I + H_2O$, and a methyl chloride compound, $C_9H_{15}NO_3,CH_3Cl + H_2O$. (*P. J.,* 1902, 275.) He also extracted four definite compounds, not alkaloids, from the leaves of coca obtained from Java. These bodies are 1. *Cocacitrin,* $C_{23}H_{32}O_{17}$, a yellow crystalline compound with three molecules of water, melting at 186° C. (366.8° F.). This appears to be a glucoside,

yielding a sugar, *cocaose,* which may be identical with *dextrotalose,* since its *osazone* melts at 180° C. (356° F.). 2. *Cocaeetin,* $C_{16}H_{12}O_7$, forming yellow needles with three molecules of water of crystallization. This melts at 260° to 265° C. (500°–509° F.). 3. *Cocaflavin,* $C_{34}H_{38}O_{19}$, which forms yellow crystals with four molecules of water. It yields dextrose and galactose on hydrolysis with diluted sulphuric acid, and is, therefore, probably a glucoside. 4. *Cocaflavetin,* containing two methoxy groups, forms greenish-yellow needles with three molecules of water and melts at 230° C. (446° F.). (*P. J.,* April, 1903, 585.) The tannin of coca leaves strikes a green-black with ferric salts, and has received the name of *cocatannic acid.* Romburgh detected traces of *methyl salicylate* in the distillate from coca. (*Chem. Ztg.,* 1895, 130.)

Uses.—(See p. 362.) For ordinary purposes cocaine hydrochloride is almost universally preferred, other salts of cocaine, however, have been used in medicine. *Cocaine borate* has been recommended for ophthalmological uses. *Cocaine hydriodide* which occurs in colorless crystals moderately soluble in water, has been recommended by R. Marcus as being especially suitable for use by cataphoresis for the production of anesthesia. For medicinal uses, see *Cocaine Hydrochloride.*

Dose, one-eighth to one-fourth grain (0.008–0.016 Gm.).

Off. Prep.—Oleatum Cocainæ, *N. F.;* Unguentum Cocainæ, *Br.*

COCAINÆ HYDROCHLORIDUM. U. S., Br.

COCAINE HYDROCHLORIDE Cocain. Hydrochl. [Cocainæ Hydrochloras, U. S. 1890, Cocaine Hydrochlorate, Cocaine Chloride, Cocainum Hydrochloricum P. I.]

(cō-cą-ī′næ hȳ-drǫ-ȼhlō′rį-dūm)

"The hydrochloride [$C_{17}H_{21}O_4N.HCl$ = 339.65] of the alkaloid cocaine." *U. S.* "Cocaine Hydrochloride, $C_{17}H_{21}NO_4,HCl$, is the hydrochloride of the alkaloid cocaine." *Br.*

Hydrochlorate of Cocaine; Chlorhydrate de Cocaine, *Fr. Cod.;* Cocainum hydrochloricum, *P. G.;* Cocainhydrochlorid, *G.;* Cloridrato di cocaina, *It.*

Preparation.—Cocaine hydrochloride may be made "by agitating with ether an aqueous solution of an acidulated alcoholic extract of coca made alkaline with sodium carbonate; separating and evaporating the ethereal liquid; purifying the product by repeating the treatment with acidulated water, sodium carbonate, and ether; decolorizing; neutralizing with hydrochloric acid, and recrystallizing." *Br.* 1885. It is also made by dissolving cocaine in ether or petroleum benzin, and passing dry hydrochloric acid gas into the solution, when the hydrochloride will separate, this may then be dissolved in alcohol and recrystallized.

Properties.—It is officially described as: "Cocaine Hydrochloride occurs in colorless, transparent, monoclinic prisms; in flaky, lustrous leaflets or as a white, crystalline powder; odorless; permanent in the air. One Gm. of Cocaine Hydrochloride dissolves in 0.4 mil of water, 3.2 mils of alcohol, and in 12.5 mils of chloroform at 25° C. (77° F.); also in 2 mils of alcohol at 60° C. (140° F.); soluble in glycerin, insoluble in ether. An aqueous solution of the salt (1 in 20) is neutral to litmus and is lævorotatory. It melts between 183° and 191° C. (361.4° and 375.8° F.), the higher melting point indicating greater purity. Silver nitrate T.S. produces in an aqueous solution of the salt (1 in 100), a white precipitate insoluble in nitric acid. Add 5 drops of a solution of chromium trioxide (1 in 20) to 5 mils of a solution of Cocaine Hydrochloride (1 in 50); a yellow precipitate is produced which redissolves on shaking the mixture; on now adding 1 mil of hydrochloric acid, a permanent, orange-colored, crystalline precipitate is formed. Dissolve about 0.1 Gm. of the salt in 1 mil of sulphuric acid; not more than a slight yellow tint is produced (*readily carbonizable impurities*). Keep this solution at a temperature of 100° C. (212° F.) for five minutes, then cautiously mix it with 2 mils of distilled water; the aromatic odor of methyl benzoate is noticeable and, on cooling, crystals of benzoic acid form, which dissolve on the careful addition of alcohol. A solution of about 0.01 Gm. of Cocaine Hydrochloride in 1 mil of distilled water yields, on the addition of 2 mils of tenth-normal potassium permanganate V.S., a violet, crystalline precipitate which appears brownish-violet when collected on a filter, and shows characteristic, crystalline aggregates under a low power microscope. Incinerate 0.5 Gm. of Cocaine Hydrochloride; no weighable ash remains. Mix 5 mils of an aqueous solution of the salt (1 in 50) with 0.3 mil of normal sulphuric acid V.S. and 0.1 mil of tenth-normal potassium permanganate V.S.; a violet tint is produced which does not disappear entirely within half an hour (*cinnamyl-cocaine*). Dilute 5 mils of an aqueous solution of the salt (1 in 50), in a beaker, with distilled water to make 85 mils, add 0.2 mil of ammonia water and stir the solution vigorously during five minutes, with occasional rubbing of the sides of the beaker with a stirring rod. A crystalline precipitate of cocaine is formed and the supernatant liquid is clear (*isatropyl-cocaine*). The presence of 0.5 per cent. of isatropyl-cocaine will prevent the formation of nearly all of the precipitate, and will cause the supernatant liquid to be milky." *U. S.*

"In colorless prismatic crystals, or a crystalline powder. No odor; taste bitter, followed by a sensation of tingling and numbness. Soluble in 0.5 part of *water,* and in 3 parts of *alcohol* (90 per cent.); insoluble in *olive oil.* Melting point 182° to 186° C. (359.6°–366.8° F.). Yields the *reactions* characteristic of chlorides. An aqueous solution is neutral to *litmus,* and when applied to the eye dilates the pupil. When moistened with *nitric acid,* the mixture evaporated to dryness, and 1 millilitre of *alcoholic solution of potassium hydroxide* added, a characteristic odor is evolved, recalling pepper-

mint. The addition of 3 drops of *N/10 solution of potassium permanganate* to a solution of 0.1 gramme of the salt in 5 millilitres of *water* to which 3 drops of *diluted sulphuric acid* have been added, gives a violet color, which, if dust is excluded, does not fade in half an hour (absence of cinnamyl-cocaine and certain other coca alkaloids). If 0.1 gramme is dissolved in 100 millilitres of water in a glass beaker, 0.25 millilitre of *solution of ammonia* stirred in, and the mixture set aside for fifteen minutes, the sides of the beaker being occasionally and not too vigorously rubbed with a glass rod, a crystalline deposit separates, leaving the supernatant liquid clear (limit of amorphous alkaloid). 0.05 gramme dissolves in 1 millilitre of cold *sulphuric acid* or cold *nitric acid* without coloration, but with hot *sulphuric acid* the salt chars, evolving an agreeable odor and yielding a sublimate of benzoic acid. Loses not more than 1 per cent. of its weight when dried at 100° C. (212° F.). No appreciable ash." *Br.*

D. Scherbatschew recommends for differentiating cocaine and several of its commoner substitutes placing three drops of the aqueous solution of the suspected substance on a glass slide and adding one drop, respectively, of each of the following reagents: (1) Ten per cent. solution of NH_3. (2) Ten per cent. solution of KOH. (3) A saturated solution of $NaHCO_3$. Stovaine and holocaine give precipitates with all three reagents; betaeucaine gives only a slight precipitate with KOH and none with the other two; nirvanine gives a precipitate with NH_3 and a slight one with KOH but none with $NaHCO_3$; alypine precipitates decidedly with NH_3 and KOH, but not with $NaHCO_3$; novocaine precipitates with KOH but not with the other two. Cocaine and tropacocaine are identified by Hankin's $KMnO_4$ test.

Uses.—It is necessary to distinguish clearly between the local and systemic effects of cocaine. When locally applied cocaine is a paralyzant to the peripheral ends of the sensory nerves, and to a lesser degree to the motor nerves, and stimulating to the muscular coats of the blood vessels. As a result of these actions when painted over mucous membranes it causes a blanching of the part and diminished sensation. It produces not only lessened sensibility to pain and touch but also of the acuity of the special senses, thus it diminishes in the mouth the power of taste and in the nose that of smell.

Systemically it is a stimulant to all parts of the central nervous system including the brain, the spinal cord, and the medulla. Its effects upon the brain are shown by an exaltation of the intellectual faculties similar to that which is produced by caffeine. In overdose it produces a delirium somewhat suggesting that of atropine to which it is chemically related. Its action upon the spinal cord is shown by increased activity of the reflexes but the convulsions which are seen in cocaine poisoning both in the lower animals and in man seem to be due to an action upon the motor area of the brain, rather than to its effect on the cord. The effects on the medullary centers are shown by an increased rapidity of the respiration and sometimes also of its depth. After toxic doses the primary stimulation is followed by a depression of the respiratory center. The blood pressure is elevated chiefly through an action upon the vasomotor center, although there is some evidence that it also stimulates the heart. Concerning the changes in the pulse rate there is difference of opinion. According to Reichert (*P. M. J.*, 1902) small doses slow the pulse rate by stimulating the cardio-inhibitory center, moderate quantities increase the rate by depressing the inhibitory mechanism, while after large toxic doses there may be a second slowing of the heart through depression of its motor ganglia. Cocaine in moderate quantities also stimulates both the voluntary and involuntary muscle fibers. It appears also to have some effect upon the nutritive processes since it causes a marked rise in the bodily temperature. Whether this increase in temperature is due to a direct action upon the thermogenic centers or is simply the result of muscular activity, is as yet not definitely settled. When instilled into the eye it causes dilatation of the pupil, usually without paralysis of accommodation. The widening of the pupil seems to be the result of an action upon the peripheral ends of the sympathetic nerve and can be further increased by the instillation of atropine.

Cocaine is used in medicine both as a local and a systemic remedy. Internally it is of value as a circulatory and respiratory stimulant and is occasionally of use as a cerebral stimulant or as a tonic. Its employment, however, in any condition which requires prolonged administration of the drug is fraught with so great danger of formation of a habit that it is rarely justifiable. In *narcotic poisonings* the simultaneous stimulation of the respiration, circulation, and cerebrum makes it a remedy of particular value.

The most important use of cocaine is as a local application to mucous membranes either for the purpose of contracting the blood vessels or lessening sensation. For the former reason it is useful to relieve congestions such as *hay fever, coryza,* or *laryngitis,* and to control or prevent *hemorrhage* from the nose and throat. There are two great drawbacks to cocaine in this use, the first that the primary contraction of the blood vessels is liable to be followed by a reactive relaxation, and the second is the ever present peril of habit-formation. As a local anesthetic it is useful in operations on the eye, nose, throat, etc., in painful *hemorrhoids, fissure in ano, vomiting, gastralgia,* and other painful diseases of the mucous membranes. While cocaine passes through all mucous membranes with greater or less ease, the unbroken skin offers a practically impassable barrier. Nevertheless, the drug is often used as a local anesthetic, especially for operative purposes, in all parts of the body. To obtain its action it is

necessary that the drug be introduced beneath the skin in some manner; it may be either simply injected hypodermically or introduced into the vicinity of the large nerve trunks, or even injected into the spinal canal. The methods of using cocaine as a local anesthetic are too numerous and complex for consideration in this work and the reader is referred to treatises on Surgery. There is a widespread belief among both pharmacists and physicians that solutions of cocaine cannot be sterilized by heat without danger of decomposition, but a number of chemists have shown that if the solution is not allowed to become alkaline the degree of hydrolysis is insignificant.

Cocaine is also useful for the purpose of dilating the pupil, where paralysis of accommodation is not desired, as for example in ophthalmoscopy.

For local application to mucous membranes an aqueous solution of one of the salts of cocaine, ordinarily the hydrochloride, is usually preferred; Gross, however (*A. E. P. P.*, 1910, lxiii, p. 80) presents evidence that the basic cocaine is a much more powerful anesthetic than its salt and some authorities give preference to oily solutions of basic cocaine.

Toxicology.—As has been pointed out by Kamenzove (*A. I. P. T.*, 1911, xxi, p. 5) there are two distinct types of cocaine poisoning, one characterized by circulatory failure and the other by neurotoxic symptoms. The first type is usually seen after relatively small doses of the drug in persons who possess an idiosyncrasy against it. The prominent symptoms are pallor of the face, vertigo, nausea, failure of the pulse, and usually more or less complete loss of consciousness. The treatment of this type of poisoning is to place the patient in a horizontal position, give rapidly acting stimulants such as hypodermic injections of ammonia or camphor. If the theory of Kamenzove that these symptoms are due to arterial spasm causing anemia of the brain is correct, then the use of amyl nitrite or nitroglycerin would be a rational procedure. The other group of cocaine poisonings is characterized by delirium, increased reflexes, more or less violent convulsions, the pulse usually being rapid and fairly strong but later may become weak, and syncope and cyanosis may intervene. The delirium is frequently associated with hallucinations and at times the patient may develop a violent mania of even homicidal character, as in a case reported by Mattison. In this type of poisoning morphine may be used cautiously to quiet the delirium and chloral or chloroform to quiet the convulsions, and stimulants as indicated. As the cocaine rarely enters the system through the alimentary canal, emptying the stomach and the use of chemical antidotes is generally not indicated.

The habitual use of cocaine as a narcotic stimulant seems to be approaching an extent of sociological importance. In the United States the conditions under which it may be prescribed or dispensed are strictly limited both by Federal, and in many states, by state laws. Koch (*Midland Druggist*, 1911, xlv, p. 211) estimates that there is 130,000 ounces of cocaine used annually by its victims. The cocaine habit is not only one of the most seductive but also one of the most rapidly injurious and difficult of eradication of all drug habits. The characteristic symptoms are changes in the mental and moral qualities, especially characterized by alternate periods of exaltation and depression, loss of appetite and of weight, peculiar pallor of the skin, insomnia, and general failure of health. A symptom which is seen in many cases and is said to be characteristic of chronic cocaine poisoning, is a sensory hallucination, as of some foreign body under the skin or of insects crawling over the person.

Dose, of the salts of cocaine, from one-fourth to one-half grain (0.016–0.03 Gm.).

Off. Prep.—Injectio Cocainæ Hypodermica, *Br.;* Lamellæ Cocainæ, *Br.;* Trochiscus Krameriæ et Cocainæ, *Br.*

COCCUS. U. S., Br.

COCHINEAL

(cŏc′cŭs)

"The dried female of the insect *Coccus cacti* Linné (Fam. *Coccidæ*), enclosing the young larvæ." *U. S.* "Cochineal is the dried fecundated insect, Coccus cacti, *Linn.*" *Br.*

Coccionella; Cochenille, *Fr. Cod.;* Scharlachwurm, *G.;* Cochinilla, *Sp.*

The Cochineal insect is indigenous to Mexico and Central America and in general appearance resembles a wood louse. It is usually found growing upon certain flat-stemmed forms of the Cactus family, chiefly species of Nopalea. The red dye found in the remains of the female insect has been long esteemed by the old races in these sub-tropical countries. Indeed, not only did they appreciate its value, but in order to increase the supplies, the cacti with the insects were successfully cultivated many years before even Cortez landed in Mexico in the early part of the sixteenth century.

The cochineal insect belongs to the order *Hemipteræ*, suborder *Homoptera*, family *Coccidæ*. The latter includes the scale-like insects which are characterized by the fact that the wingless female dies shortly after producing her eggs, the latter being covered up by her dead scale-like body. In the case of the cochineal insect the larvæ are found, as will be shown later on, within her inflated body. In the group of the *Coccidæ* we find a number of interesting scale insects. Here we find the lac insect from which stick-lac of commerce is produced, the latter being a resinous substance excreted by a species of *Coccus* (*Carteria*) *lacca* which inhabit the branches of several tropical trees. From the bodies of these insects also certain coloring agents known as "lac dyes" are produced. China wax, the excretion of an

insect known as "Pela" (*Ericerus pela*) is also the product of a scale insect belonging to this family. Comstock states that there are many species of the *Coccidæ* which excrete wax in considerable quantity.

The cochineal insect was first described by Hernandez in 1651. It is ordinarily in scientific works referred to as *Coccus Cacti* Linné. In the eighth edition of the U. S. Pharmacopœia the name was changed to *Pseudococcus Cacti* (Linné) Burmeister. In a "Catalogue of The Coccidæ of the World," Maria E. Fernaldo gives preference to the name *Dactylopius Coccus* Costa. In Pharmacopœial work we are justified, however, in using the Latin title that has been given precedent by usage, namely *Coccus Cacti*, as otherwise we might change the name with each revision as our knowledge of these insects is extended.

The cochineal insect feeds upon various species of the *Cactaceæ*, more especially the Nopal plant, *Nopalea* (*Opuntia*) *coccinellifera* (Mill.) S.-Dyck, a native of Mexico and Peru. It has spread into other parts of South and Central America and has been introduced into the West Indies, East Indies, Canary Islands, Southern Spain, Algeria, and is said to be found in Florida and California.

The cultivation of cochineal is rather simple in a tropical climate, all that is necessary is to have the cochineal insects and the proper cacti. Senor Santiago da Cruz e Goncalves, a surgeon established in Teneriffe over seventy years ago, and who was appointed by the Spanish Government to superintend the cultivation of cochineal in that island, wrote an interesting article on "The Cultivation of Cochineal." This was translated with some additional notes by G. J. de Nobrega in the *P. J.*, 1848–9, pp. 342–348. Roxburgh has described the cochineal culture in India (*A. J. P.*, 1842, p. 137) and C. J. Sage the cultivation in the Canary Islands, from which most of our commercial supplies are now obtained. Probably the most complete work on the distribution and cultivation of the cochineal insect is by de Ruuscher which was translated into German by Mylius in 1751 and is included in his work entitled "Physikalische Belustigungen." In speaking of the culture of cochineal insects he says, all that is necessary is for one to raise small nests upon potted Nopal plants growing in the house. Then when they are ready to propagate, the insects are transferred to the Nopal plants growing in the fields. In a few days the female lays her eggs, dying shortly thereafter. The young develop under the mother and when mature they creep up the Nopal stems seeking always the juiciest and greenest parts. Recently there has been published by Leon Diquet an article on "The History of The Cochineal Insect of Mexico," and which contains a number of illustrations of the Nopal plantations as well as very much information concerning the cultivation of cochineal in that country.

Kraemer has written an extended monograph on the nature and structure of cochineal (*A. J. P.*, 1913, p. 444), and gives the following facts concerning the life history of the cochineal insect. The female insect is without wings, about 2 mm. in length and consists of from 9 to 12 segments. It is somewhat globular, becoming later distinctly ovoid. In general appearance, as it creeps over the cactus stems, it is convex on the upper, that is the dorsal surface, and somewhat flattened or concave below, that is, on the ventral surface. It is covered with glaucous dust being a coat of wax. This wax is a protective secretion and is formed as a glandular secretion by the "wax pores" and wax hairs, the anatomy of which has been worked out by Mayer. The antennæ are rather short, consisting of 8 parts. The threadlike beak or proboscis, forming a sucking apparatus, is very fully developed. There are 3 pairs of legs which in the commercial article do not show more than 3 joints. Projecting from the posterior portion of the abdomen there are 2 short hairs or bristles, which are wanting in the commercial article.

The male is more elongated and ellipsoidal in outline and is provided with 2 transparent wings which reach beyond the extremity of the abdomen and cross each other longitudinally on the back. The head is distinguished from that of the female in being furnished with a rudimentary beak and with 2 long feathery antennæ. It is said that the male insect is reproduced in large numbers; the larvæ in the commercial cochineal does not show this to be the case. As a matter of fact, actually only one male is necessary for about 300 females. Upon performing their functions the male insects die and are blown away. They are therefore never seen in the commercial article.

The female insect after fecundation grows larger as the young larvæ develop, becoming eventually about twice her original size. She meanwhile attaches herself to the surface of the stems of the cacti, her body penetrating into the upper layer of cells. The upper dorsal surface becomes more or less cartilaginous in structure and more or less convex in shape. The lower surface is drawn toward the upper surface and in this membranous cradle the larvæ are developed. It requires about eight days for the larvæ to become full grown, when they are said to resemble the parents with the exception that they are covered with a short hairy coating. In another week they attain maturity and the females of the new generation are ready to form broods in their turn. The life history of the cochineal insect is completed in about six weeks, two weeks being required for the development of the mature insect from the egg; during the next two weeks the female crawls over the fleshy stems of the cacti, the male in the meanwhile being able to fly about; then the female attaches herself to the tissues of the Nopal plants, her body becoming a membranous cradle for the larvæ of the next generation,

and after which she dies. From three to five generations of the cochineal insect may be produced in a single year. The first generation usually is richer in coloring matter and is considered the most valuable. It is estimated that from an area of about an acre of Nopal plants approximately 100 kilos of cochineal may be gathered; this would represent about 14,000,000 of the membranous cradles with larvæ, or the dried insects of commerce.

Cochineal is defined in the U. S. Pharmacopœia as follows: "Somewhat ovate in outline, convex above, concave beneath, from 3.5 to 5 mm. in length, consisting of from 9 to 12 segments; externally grayish-purple or grayish; in the shell-like, somewhat horny abdomen lie numerous larvæ less than 1 mm. in diameter; the mature larvæ with antennæ consisting of eight joints, 3 pairs of legs, the lower having from 6 to 8 segments, and a characteristic beak or rostrum composed of 4 thread-like parts which pair off into two coils. Cochineal is easily pulverizable and yields a dark red powder, with a characteristic odor and slightly bitter taste. When masticated it colors the saliva red, due to the coloring principle, carminic acid, which is soluble in water, alcohol, or alkalies and slightly soluble in ether, but insoluble in fixed or volatile oils. Alkalies change the color of solutions of Cochineal to purple, while acids change it to reddish-yellow. When Cochineal is macerated in water no insoluble powder separates. Cochineal yields not more than 6 per cent. of ash." *U. S.*

"About five millimetres long; somewhat oval in outline, flat or concave beneath, convex above, transversely wrinkled, purplish-black or purplish-grey; easily reduced to powder, which is dark-red or puce-colored. Macerated in *water*, no insoluble powder is separated. Ash not more than 6 per cent." *Br.*

As found in commerce, the finer cochineal, *grana fina* of Spanish commerce, is in irregularly circular or oval, somewhat angular grains, about one-eighth of an inch in diameter, convex on one side, concave or flat on the other, and marked with several transverse wrinkles. Two varieties of this kind of cochineal are known to the druggist, distinguished by their external appearance. One is of a reddish-gray color, formed by an intermixture of the dark color of the insect with the whiteness of a powder by which it is almost covered, and with patches of a rosy tinge irregularly interspersed. From its diversified appearance, it is called by the Spaniards *cochinilla jaspeada.* It is the variety commonly found in commerce. The other, *cochinilla renegrida,* or *grana nigra,* is dark-colored, almost black, with only a minute quantity of the whitish powder between the wrinkles. The two are distinguished in our markets by the names of *silver grains* and *black grains.* Some suppose the difference to arise from the mode of preparation, the gray cochineal consisting of the insects destroyed by a dry heat; the black, of those destroyed by hot water, which removes the external whitish powder; it is also said that cochineal is blackened by placing the insects with black sand in a bag and swinging backward and forward until some of the juice exudes. According to Faber, who derived his information from a merchant residing in the neighborhood where the cochineal is collected, the silver grains consist of the impregnated female just before she has laid her eggs; the black, of the female after the eggs have been laid and hatched. (*A. J. P.,* xviii, 47.) There is little or no difference in their quality. *Cake cochineal* is the name given to a variety of the drug produced in Argentina. A specimen examined by Stark was in flat cakes about one-fourth of an inch thick, and, under the microscope, was seen to consist chiefly of the cochineal insect, mixed with small portions of the thorns and epidermis of the cactus, in consequence of careless gathering. It is inferior for dyeing purposes to the ordinary variety. (*P. J.,* xiv, 346.) Another and much inferior variety is the *grana sylvestra,* or wild cochineal, consisting partly of very small separate insects, partly of roundish or oval masses, which exhibit, under the microscope, minute and apparently new-born insects, enclosed in a white or reddish cotton-like substance. It is scarcely known in our drug market.

Cochineal has a faint heavy odor and a bitter, slightly acidulous taste.. Its powder is of a purplish-carmine color, tingeing the saliva intensely red. According to Pelletier and Caventou, it consists of a peculiar coloring principle, a peculiar animal matter constituting the skeleton of the insect, stearin, olein, an odorous fatty acid, and various salts. Tyrosin has also been found by De la Rue, and its presence in cochineal confirmed later on by von Miller and Rohde. (*Ber. d. Chem. Ges.,* xxvi, 2660.) It was also analyzed by John, who called the coloring principle *cochinilin.* It is, however, universally known now as *carminic acid.* Hlasiwetz and Grabowski (*Ann. Ch. Ph.,* 141, 329) gave it the formula $C_{17}H_{18}O_{10}$, and considered it to be a glucoside, which was decomposed by boiling with diluted sulphuric acid into a non-fermentable sugar and *carmine red,* $C_{11}H_{12}O_7$. The incorrectness of this view has, however, been demonstrated by von Miller and Rohde (*loc. cit.*), who have shown that the purified carminic acid is a dioxymethyl-*a*-naphthoquinone of the formula $C_{12}H_{11}O_7$, or the double formula $C_{24}H_{22}O_{14}$, and that the carmine red is identical with it. Schunk and Marchlewski (*Ber. d. Chem. Ges.,* xxvii, 2979) have confirmed these results of von Miller and Rohde, and have shown that the reason that the carminic acid as freshly extracted from the cochineal gave the apparent glucoside reaction was that it is impure. They prepared the pure crystallized carminic acid, its anilide, and identified its character as a naphthoquinone derivative. (Recent writers, without modifying the formula above given, have classified carminic acid as a derivative of *hydri-*

odene, C_9H_{10}.) It shows no sharp melting point, beginning to decompose at 130° C. (266° F.). Carminic acid is of a brilliant purple-red color, unalterable in dry air, is very soluble in water, soluble in cold and more so in boiling alcohol, insoluble in ether, and without nitrogen. It is obtained by macerating cochineal in ether, and treating the residue with successive portions of boiling alcohol, which on cooling deposits a part of the carminic acid, and yields the remainder by spontaneous evaporation. It may be freed from a small proportion of adhering fatty matter by dissolving it in official alcohol and then adding an equal quantity of ether. The pure carminic acid is deposited in the course of a few days. Chlorine readily destroys the carminic acid, and nascent hydrogen reduces it to a leuco body, which again becomes red on exposure to the air. Liebermann found that the coating of the silver cochineal consisted of a peculiar wax, which he named *coccerin,* $C_{30}H_{60}(C_{31}H_{61}O_3)_2$; this is soluble in benzene, but nearly insoluble in ether. (*P. J.,* 1885, 186; from *Ber. d. Chem. Ges.*) The aqueous infusion of cochineal is of a violet-crimson color, which is brightened by the acids and deepened by the alkalies. The coloring matter is readily precipitated. The salts of zinc, bismuth, and nickel produce a lilac precipitate, and those of iron a dark purple approaching to black. The salts of tin, especially the nitrate and the chloride, precipitate the coloring matter of a brilliant scarlet, and form the basis of those splendid scarlet and crimson dyes which have rendered cochineal so valuable in the arts. With alumina the coloring matter forms the pigment called *lake.* The finest lakes are obtained by mixing the decoction of cochineal with fresh gelatinous alumina.

The pigment called *carmine* is the coloring matter of cochineal precipitated from the decoction by acids, the salts of tin, etc., or by animal gelatin, and when properly made is of the most intense and brilliant scarlet. Cochineal-carmine requires for its production a decoction of cochineal itself, and not of carminic acid, the nitrogenized matters being essential to its formation. Liebermann (*Ber. d. Chem. Ges.,* xviii, p. 1971) considers cochineal carmine to be no ordinary compound of a coloring matter with alumina, but to be an alumina albuminate of the carmine coloring matter comparable in some respects to the product from alizarin and alumina with "Turkey-red oil." (See *C. D.,* 1893, 199; *Zeit. angew. Chem.,* 1894.) J. J. Hess proved that if fatty matters found in cochineal were removed by treatment with alcohol, a much more brilliant carmine could be produced. (Dingler, *P. J.,* 235, 88; *N. R.,* 1880, 338.) The degree of coloring power in cochineal may be approximately measured by the decolorizing effect produced by solution of potassium permanganate. For a method of applying this process, the reader is referred to a paper by J. M. Merrick, of Boston, in *A. J. P.,* 1871, 263; from *Amer. Chem.,* April, 1871. The Pharmacopœias require that when cochineal is macerated in water no insoluble powder shall be separated, and that when incinerated with free access of air it shall yield not more than 6 per cent. of ash.

Cochineal has been adulterated by causing certain heavy substances, such as powdered talc, lead carbonate, and barium sulphate, by shaking in a bag or otherwise, to adhere, by means of some glutinous material, to the surface of the insects, and thus increase their weight. Cochineal yields 1.5 per cent. of ash. Five specimens of the drug have been examined, which left in their ashes respectively 8, 12, 16, 18, and 25 per cent. of the salt of barium. (*A. J. P.,* 1870, p. 220.) The fraud may be detected by the absence, under the microscope, of a woolly appearance which characterizes the white powder upon the surface of the unadulterated insect. Metallic lead, which is said frequently to exist in fine particles in the artificial coating, may be discovered by powdering the cochineal and suspending it in water, when the metal will remain behind. Grains of a substance artificially prepared to imitate the dried insect have been mixed with the genuine in France. A close inspection will serve to detect the difference. (*J. P. C.,* 3e sér., ix, 110.) Vermilion and chrome-red (lead dichromate) are said also to have been largely used in the adulteration of carmine, to the extent sometimes of 60 or even 70 per cent. (*P. J.,* 1860, p. 547.) There can be no difficulty in detecting them by the appropriate tests. Starch has been used, according to Maisch, for the same purpose in the United States, and in one specimen he found 57.14 per cent. (*A. J. P.,* xxxiii, 18.) Artificial cochineal, prepared by coloring exhausted cochineal powder with rosaniline and forming it into grains has been found in commerce. It may be recognized by the facility with which it forms a paste with water.

The importations of cochineal have diminished, owing to the gradual replacement of this dye by the newer azo colors. In 1889, 550,000 lbs. were brought into the United States; in 1902, 1903, and 1904, the importations were 140,756 lbs., 114,326 lbs., and 162,395 lbs., respectively. The reduction in price has been such that at present the production in the Canaries is said not to be remunerative.

Uses.—Cochineal is supposed by some to possess anodyne properties, but is probably useless. In pharmacy it is employed to color tinctures and tooth powders. To infants with *whooping cough,* cochineal in substance is given in the *dose* of about one-third of a grain (0.021 Gm.) three times a day. The *dose,* of a tincture (one part in ten parts of diluted alcohol), is for an adult from twenty to thirty minims (1.3–2.0 mils). In *neuralgia,* Sauter gave half a tablespoonful (7.5 mils) with asserted cure.

Off. Prep.—Tinctura Cardamomi Composita, *U. S., Br.;* Tinctura Cocci, *Br.;* Liquor Cocci, *N. F.*

CODEINA. U. S., Br.

CODEINE Codein. [Methylmorphine]

(cō-dē-ī'nȧ)

"An alkaloid [$C_{18}H_{21}O_3N + H_2O$ or $C_{17}H_{18}(CH_3)O_3N + H_2O = 317.19$] obtained from opium, or prepared from morphine by methylation. Preserve it in well-closed containers protected from light." *U. S.* "Codeine, $C_{18}H_{21}NO_3,H_2O$, is an alkaloid obtained from opium or prepared from morphine." *Br.*

Codeia, Methylmorphine; Codeinum, Codéine, *Fr. Cod.*; Codein, Kodein, *G.*; Codeina, *It., Sp.*

Preparation.—*Codeine* was discovered in 1832 by Robiquet in morphine hydrochloride prepared according to the process of Gregory. It exists in opium combined like morphine with meconic acid, and is extracted along with that alkaloid in the preparation of the hydrochloride. (See *Morphina.*) When the solution of the mixed morphine and codeine hydrochlorides is treated with ammonia, the former alkaloid is precipitated, and the codeine, remaining in solution, may be obtained by evaporation and crystallization. It may be purified by treating the crystals with hot ether, which dissolves them and yields the codeine in colorless crystals on spontaneous evaporation. Codeine is the methyl derivative of morphine, as shown in the formula $C_{17}H_{18}(CH_3)NO_3$. It may be formed artificially from morphine by treating this latter successively with methyl iodide and fixed alkali. (Grimaux, 1881, *J. Chem. S.*, xliv, 358.) Codeine may be made synthetically by the following process: Morphine, 285 Gm., and nitrosomethylurethane, 132 Gm., are dissolved in 1 kilo. of methyl alcohol. With the solution is mixed, constantly stirring, a solution made by mixing 50 Gm. of potassium hydroxide in 800 Gm. of methyl alcohol. When the reaction is complete, the methyl alcohol is distilled off, and codeine is extracted from the residue with benzene, from which it afterwards separates in characteristic crystals. (*C. D.*, 1898, 237.)

Properties.—Codeine occurs in "colorless, translucent, rhombic prisms, or as a crystalline powder; odorless and slightly efflorescent in warm air. One Gm. of Codeine dissolves in 120 mils of water, 2 mils of alcohol, 0.5 mil of chloroform, and in 18 mils of ether at 25° C. (77° F.); also in 1.2 mils of alcohol at 60° C. (140° F.). A saturated aqueous solution of Codeine is alkaline to litmus and is lævorotatory. Codeine, rendered anhydrous, melts between 154° and 156° C. (309.2° and 312.8° F.). When heated in an insufficient amount of water for complete solution, it melts to oily drops, which crystallize on cooling. Sulphuric acid containing 0.005 Gm. of selenous acid in each mil produces with Codeine a green color, changing rapidly to blue, then slowly back to grass-green. About 0.01 Gm. of Codeine dissolves in 5 mils of sulphuric acid (free from nitrous compounds) without showing other than a transient, pinkish tint; on the addition of a drop of ferric chloride T.S., the solution becomes blue when warmed and changes to red on the further addition of a drop of nitric acid. When dried to constant weight at 80° C. (176° F.), Codeine loses not more than 6 per cent. of its weight. No weighable ash remains on incinerating 0.5 Gm. of Codeine. Dissolve about 0.05 Gm. of potassium ferricyanide in 10 mils of distilled water, add 1 drop of ferric chloride T.S., and then 1 mil of a neutral or slightly acid aqueous solution of Codeine (1 in 100), made with the aid of sulphuric acid; no blue color is produced at once (*morphine*)." *U. S.*

"Colorless or nearly colorless crystals. Soluble in 80 parts of *water*, and in 80 parts of *solution of ammonia*, readily soluble in *alcohol* (90 per cent.), and in *chloroform*. The aqueous solution has a bitter taste and an alkaline reaction. Melting point 155° to 156° C. (311°–312.8° F.). 0.1 gramme dissolves in 1 millilitre of cold *sulphuric acid* without coloration or with the production at most of a faint pink tinge; but when the solution is gently warmed with a trace of *ammonium molybdate* or of *ferric chloride* a deep bluish-violet color is developed which, on the addition of a drop of *diluted nitric acid*, changes to scarlet and finally orange. When a little of the powdered alkaloid is sprinkled on *nitric acid* the liquid becomes yellow but not red (distinction from morphine). A saturated aqueous solution, acidified with *hydrochloric acid*, gives no blue color, but only gradually a dull green, on the addition of diluted *T. Sol. of ferric chloride* and very dilute *solution of potassium ferricyanide* (absence of morphine). A solution (1 in 50) in *water* acidified with *hydrochloric acid* yields a white precipitate with *solution of sodium hydroxide*, but not with *solution of ammonia*." *Br.*

When added in excess to boiling water, the undissolved portion melts and sinks to the bottom, having the appearance of an oil. It may be separated from morphine by a solution of potassium or sodium hydroxide, which dissolves the morphine and leaves the codeine. It has an alkaline reaction on test paper, and combines with acids to form salts, some of which are crystallizable, particularly the nitrate. Its capacity of saturation is almost identical with that of morphine. According to Robiquet, 1 part of hydrochloric acid is saturated by 7.837 of codeine, and by 7.88 of morphine. It is distinguishable, however, from the latter principle by the different form of the crystals, which are octahedral, by its solubility in boiling ether, greater solubility in water, and insolubility in alkaline solutions, and by not assuming a red color with nitric acid, or a blue one with ferric salts. Tincture of galls precipitates from its solutions a codeine tannate. Crystallized from an aqueous solution, it contains about 6 per cent. of water, which is driven off at 100° C. (212° F.). The crystals obtained from a solution in ether contain no water.

Uses.—Codeine produces in the lower animals marked convulsive symptoms, with heightened

reflexes, disturbances of the respiration and rarely tendency to coma. In man the therapeutic dose acts as an uncertain and feeble analgesic and hypnotic, and in large doses may produce marked restlessness. The symptoms of poisoning by it have been vascular excitement, exhilaration, then depression with great anxiety, nausea and vomiting, pale, cool, clammy skin, slight contraction of pupil, and sleeplessness, with slight delirium. In some cases convulsions have been present. In regard to the toxic dose, there is the greatest difference of statement by physicians. Severe poisoning has been reported from the use of four grains, but according to some practitioners five grains have had no effect, and we have frequently given codeine in doses of from six to eight grains without the production of distinct symptoms. It has been highly lauded in the treatment of *diabetes mellitus*, and cases of recovery under its use reported. In the grave form of this disorder we have seen it fail to exert any perceptible influence, but the evidence is sufficient to demand a fair trial of the remedy in any individual case. Medical practitioners often use it to quiet *cough*, to allay *intestinal pain*, and to fulfil various other of the minor narcotic indications for which opium is commonly administered. Although less efficient than morphine it has the advantage of being less constipating and less liable to habit formation. On account of its frequent contamination with morphine, care should be exercised as to the commencing dose, but no effect at all is to be expected, if the alkaloid be pure, from less than one grain (0.065 Gm.), and this dose may be rapidly increased until some symptoms are produced. It may be given in pill or in syrupy solution.

Dose, one-fourth to two grains (0.015–0.13 Gm.).

Off. Prep.—Elixir Terpini Hydratis et Codeinæ, *N. F.*

CODEINÆ PHOSPHAS. U. S., Br.

CODEINE PHOSPHATE Codein. Phos.

(cō-dē-ĭ'næ phŏs'phās)

"The phosphate [$C_{18}H_{21}O_3N.H_3PO_4 + 2H_2O$ or $C_{17}H_{18}(CH_3)O_3N.H_3PO_4 + 2H_2O = 433.27$] of the alkaloid codeine. It yields not less than 67 per cent. of anhydrous codeine ($C_{18}H_{21}O_3N$). Preserve it in well-closed containers, protected from light." *U. S.* "Codeine Phosphate, $C_{18}H_{21}NO_3,H_3PO_4,2H_2O$, is the phosphate of the alkaloid codeine." *Br.*

Phosphate de Codéine, *Fr.*; Codeinum phosphoricum, *P. G.*; Kodeinphosphat, Phosphorsaures Kodein, *G.*

This salt was official for the first time in the U. S. VIII and Br. Pharmacopœia, 1898; it has been introduced because of its easy solubility and stability; it may be made by dissolving 1 part of codeine in 1.25 parts of 25 per cent. phosphoric acid (the solution should be slightly acid in reaction); sufficient alcohol is added to precipitate the codeine phosphate. On account of its large percentage of codeine (about 70 per cent.) it is well fitted for hypodermic injections. It occurs in "fine, white, needle-shaped crystals, or as a crystalline powder; odorless and very efflorescent. One Gm. of Codeine Phosphate dissolves in 2.3 mils of water, 325 mils of alcohol, 4500 mils of chloroform, and in 1875 mils of ether at 25° C. (77° F.); also in 0.5 mil of water at 80° C. (176° F.), and in 125 mils of boiling alcohol. Its aqueous solution (1 in 20) is acid to litmus. Silver nitrate T.S. produces in an aqueous solution of the salt, previously neutralized with ammonia water, a yellow precipitate which is soluble in diluted nitric acid and in ammonia water. Separate portions of 10 mils each of an aqueous solution of Codeine Phosphate (1 in 100), acidulated with nitric acid, are not rendered turbid at once on the addition of a few drops of barium chloride T.S. (*sulphates*), or opalescent by a few drops of silver nitrate T.S. (*chlorides*).

"**Assay.**—Dissolve about 0.5 Gm. of Codeine Phosphate, accurately weighed, in 10 mils of distilled water, add 10 mils of potassium hydroxide T.S. and shake the mixture with three successive portions of 15 mils each of chloroform, or a sufficient quantity to complete the extraction. The combined chloroform solutions, carefully evaporated to dryness on a water bath, yield, after drying to a constant weight at 110° C. (230° F.), not less than 67 per cent. of anhydrous codeine. In other respects Codeine Phosphate responds to the tests of identity and purity under *Codeina*, omitting the melting point and ash test." *U. S.*

"White efflorescent crystals. Taste slightly bitter. Soluble in 3.5 parts of *water*. An aqueous solution (1 in 20) has a slightly acid reaction and yields a white precipitate with *solution of sodium hydroxide*, but not with *solution of ammonia*. Loses its water of crystallisation at 100° C. (212° F.). Yields the *reactions* characteristic of phosphates, and responds to the color-tests described under 'Codeina.'" *Br.*

Uses.—The medicinal properties of codeine phosphate are the same as those of codeine.

Dose, one-fourth to two grains (0.015–0.13 Gm.).

Off. Prep.—Syrupus Codeinæ Phosphatis, *Br.*

CODEINÆ SULPHAS. U. S.

CODEINE SULPHATE Codein. Sulph.

(cō-dē-ĭ'næ sŭl'phās)

"The sulphate [$(C_{18}H_{21}O_3N)_2.H_2SO_4 + 5H_2O$ or $(C_{17}H_{18}(CH_3)O_3N)_2.H_2SO_4 + 5H_2O = 786.52$] of the alkaloid codeine. Preserve it in well-closed containers, protected from light." *U. S.*

Codeinum sulfuricum; Sulfate de Codéine, *Fr.*; Kodein sulfat, Schwefelsaures Kodein, *G.*

Preparation.—Codeine sulphate may be made by dissolving codeine in warm water, adding sufficient sulphuric acid to neutralize, evaporating and crystallizing; 16.71 Gm. of sulphuric acid of official strength will be required to neutralize 100 Gm. of codeine.

Properties.—Codeine sulphate is officially described as in "long, glistening, white, needle-shaped crystals or rhombic prisms, or as a crystalline powder; odorless and efflorescent in the air. One Gm. of Codeine Sulphate dissolves in 30 mils of water and in 1280 mils of alcohol at 25° C. (77° F.); also in 6.5 mils of water at 80° C. (176° F.), and in 440 mils of alcohol at 60° C. (140° F.); insoluble in chloroform or ether. Its aqueous solution (1 in 40) is neutral or not more than faintly acid to litmus. Barium chloride T.S. produces, in an aqueous solution of the salt, a white precipitate which is insoluble in hydrochloric acid. When dried to constant weight at 100° C. (212° F.), Codeine Sulphate loses not more than 12 per cent. of its weight. In other respects the salt responds to the tests for identity and purity under *Codeina*, omitting the melting point." *U. S.*

Uses.—The medicinal properties of this salt are those of the alkaloid codeine.

Dose, one-fourth to two grains (0.015–0.13 Gm.).

Off. Prep.—Syrupus Codeinæ, *N. F.*

COLCHICI CORMUS. U. S., Br.

COLCHICUM CORM Colch. Corm. [Colchici Radix, U. S. 1890, Colchicum Root]

(cŏl'ɕhĭ-cī cŏr'mŭs)

"The dried corm of *Colchicum autumnale* Linné (Fam. *Liliaceæ*), yielding not less than 0.35 per cent. of colchicine." *U. S.* "Colchicum Corm is the fresh corm of Colchicum autumnale, *Linn.*, collected in early summer; or the same deprived of its coats, sliced transversely, and dried at a temperature not exceeding 65° C. (149° F.)." *Br.*

Bulbus s. Tuber Colchici; Meadow-Saffron Root; Bulbe de Colchique, *Fr. Cod.*; Bulbe de Colchique, de Safran bâtard, *Fr.*; Zeitlosenknollen, *G.*; Bulbo di colchico, *It.*; Bulbo de colquico, *Sp.*

COLCHICI SEMEN. U. S. (Br.)

COLCHICUM SEED Colch. Sem. [Colchici Semen P. I.]

(cŏl'ɕhĭ-cī sē'mĕn)

"The dried seeds of *Colchicum autumnale* Linné (Fam. *Liliaceæ*), yielding not less than 0.45 per cent. of colchicine." *U. S.* "Colchicum Seeds are the dried ripe seeds of Colchicum autumnale, *Linn.*" *Br.*

Colchici Semina. *Br.*; Colchicum Seeds; Semences de Colchique, *Fr. Cod.*; Semence de Colchique, *Fr.*; Semen Colchici, *P. G.*; Zeitlosensamen, *G.*; Semi di colchico, *It.*; Semilla de colquico, *Sp.*

Colchicum autumnale, often called *meadow saffron*, is a perennial bulbous plant, the leaves of which appear in spring, and the flowers in autumn. Its manner of growth is peculiar, and deserves notice as connected in some measure with its medicinal efficacy. In the latter part of summer, a new bulb, or *corm*, as the part is now called, begins to form at the lateral inferior portion of the old one, which receives the young offshoot in its bosom and embraces it half round. The new plant sends out roots from its base, and is furnished with a radical spathe, which is cylindrical, tubular, cloven at top on one side, and half under ground. In September, from two to six flowers, of a lilac or pale-purple color, emerge from the spathe, unaccompanied by leaves. The corolla consists of a tube from 10 to 12 cm. long, concealed for two-thirds of its length in the ground, and of a limb divided into six segments. The flowers perish by the end of October, and the rudiments of the fruit remain under ground until the following spring, when they rise upon a stem above the surface, in the form of a three-lobed three-celled capsule. The leaves of the new plant appear at the same time, so that in fact they follow the flower instead of preceding it, as might be inferred from the order of the seasons in which they respectively show themselves. The leaves are radical, spear-shaped, erect, numerous, about 12 cm. long, and 2.5 cm. broad at the base. In the meantime, the new corm has been increasing at the expense of the old one, which, having performed its appointed office, perishes; while the former, after attaining its full growth, sends forth shoots, and in its turn decays. The old corm in its second spring, and a little before it perishes, sometimes puts forth one or more small corms, which are the sources of new plants. The usual method of propagating colchicum is by planting the bulbs about August or September in deep rich soil, about 2 or 3 inches below the surface and about 3 inches apart in the row. (*D. C.*, 1912, p. 134.)

C. autumnale is a native of the temperate parts of Europe and of Northern Africa, growing in moist pastures and meadows. Attempts have been made to introduce its culture into this country, but with no great success, though small quantities of the corm, of apparently good quality, have entered commerce. The flowers possess virtues similar to those of the corm and are recognized by the French Codex.

Colchici Cormus.—The medicinal virtue of the corm depends much upon the season at which it is collected. Early in the spring it is too young to have fully developed its peculiar properties, and late in the fall it has become exhausted by the nourishment afforded to the new plant. The proper period for its collection is from the early part of June, when it has usually attained perfection, to the middle of August, when the offset appears. It may be owing, in part, to this inequality at different seasons that entirely opposite reports have been given of its powers. Krapf ate whole corms without inconvenience; Haller found them entirely void of taste and acrimony, and we are told that in Carniola the peasants use them as food with impunity in the autumn. On the other hand, there can be no doubt of its highly irritating and poisonous nature, when fully developed, under ordinary circumstances. Perhaps soil and climate may have some influence in modifying its character.

Christison found the roots collected in April to be more bitter than those gathered in

July, and conjectures that the common opinion of their superior efficacy at the latter season may not be well founded. Schroff states, as the result of his observation, that the autumnal root is much stronger than that dug in the summer. (See *A. J. P.*, xxix, 324.)

The corm is often used in the fresh state in the countries where it grows, as it is apt to be injured in drying, unless the process is carefully conducted. The usual plan is to cut the corm, as soon as possible after it has been dug up, into thin transverse slices, which are spread out separately upon paper or perforated trays and dried with a moderate heat. The reason for drying it quickly after removal from the ground is that it otherwise begins to vegetate, and a change in its chemical nature takes place; and such is its retentiveness of life that, if not cut in slices, it is liable to undergo a partial vegetation even during the drying process. Houlton recommends that the corm be stripped of its dry coating, carefully deprived of the bud or young bulb, and then dried whole. It is owing to the high vitality of the bud that the corm is so apt to vegetate. During desiccation there is great loss of weight, 70 per cent. being the average for a number of years in the laboratory of Allen & Hanburys, in London.

The recent bulb or corm of *C. autumnale* resembles that of the tulip in shape and size, and is covered with a brown membranous coat. Internally it is solid, white and fleshy, and, when cut transversely, yields, if mature, an acrid milky juice. There is often a small lateral projection from its base, which is the bud for the development of a new plant; this bud is frequently broken off in drying. When dried, and deprived of its external membranous covering, the corm is of an ash-brown color, convex on one side, and somewhat flattened on the other, where it is marked by a deep groove extending from the base to the summit. As found in commerce, it is always in the dried state, sometimes in segments made by vertical sections of the bulb, but generally in transverse circular slices. The U. S. Pharmacopœia describes the corm as follows: "Usually in reniform, transverse or in ovate, longitudinal slices; from 2 to 5 mm. in thickness; flat surfaces whitish, slightly roughened, and of a crystalline appearance under a hand lens; epidermis thin, light brown and finely wrinkled; fracture short and mealy, odor slight; taste bitter and somewhat acrid. The powder is light brown or grayish-brown; starch grains numerous, single or 2- to 6-compound, the individual grains varying from spherical or ovoid to polygonal, and marked with a triangular or star-shaped, central cleft, the grains being from 0.003 to 0.03 mm. in diameter; tracheæ few and with spiral or scalariform thickenings; occasional fragments of epidermal cells with thin, reddish-brown walls. Colchicum Corm yields not more than 6 per cent. of ash.

"**Assay.**—Proceed as directed under *Colchici Semen*, using 15 Gm. of Colchicum Corm." *U. S.*

"Fresh corm about thirty-five millimetres long and twenty-five millimetres broad, somewhat conical, hollowed on one side where a new corm is in process of development, and rounded on the other; covered with a thin brown membranous outer coat, and an inner reddish-yellow one; internally white and solid, and when cut yielding a whitish, turbid juice of a disagreeable odor and bitter taste. Dried slices two or three millimetres thick, yellowish at their circumference, somewhat reniform in outline; firm, whitish, amylaceous; breaking readily with a short fracture. No odor; taste bitter." *Br.*

The cut surface is white and of an amylaceous aspect. Examined with the microscope, the corm is seen to be composed of large irregular cells, full of ovoid, angular, sometimes compound, starch grains, and interspersed with spiral vessels in vascular bundles. The odor of the recent corm is said to be hircine. It is diminished, but not lost, by drying. The taste is bitter, hot, and acrid.

Colchicum corm contains the alkaloid *colchicine*, $C_{22}H_{25}NO_6$, which was made official in the U. S. P.; see *Colchicina*. Colchicine is the active principle and as much as 0.4 per cent. is found in good specimens of the corm; the official requirement is that not less than 0.35 per cent. shall be present, to be determined by assay. See *Assay for Colchicum Seed*, p. 371.

A. T. Thompson states that the milky juice of fresh colchicum produces a fine blue color if rubbed with the tincture of guaiac, and that the same effect is obtained from an acetic solution of the dried corm. He considered the appearance of this color, when the slices were rubbed with a little distilled vinegar and tincture of guaiac, a proof that the drug was good and had been well dried. J. M. Maclagan has shown that this change of color is produced with the albumen, which is not affected if previously coagulated; so that the value of the test consists simply in proving that the drying has not been effected at a heat above 82.3° C. (180° F.), or the temperature at which albumen coagulates. It is probable that this color reaction is not due to the albumen itself, but to an oxidizing enzyme or oxydase which would be susceptible to the same decomposing influences as albumen. A very deep or large notch in the circumference of the slices is an unfavorable sign, as it indicates that the bulb has been somewhat exhausted in the nourishment of the offset. The decoction yields a deep blue precipitate with solution of iodine, white precipitates with lead acetate and subacetate, mercurous nitrate, and silver nitrate, and a slight precipitate with tincture of galls. The value of colchicum is best tested by its bitterness. For method of assaying colchicum, by K. Schwickerath, see *Ph. Rund.*, 1893, 282. Important improvements have been made in the assay by Bredemann. (*Ap. Ztg.*, 1903, 18, Nos. 93, 94, 95.)

Colchici Semen.—The seeds of the meadow-saffron ripen in summer, and should be col-

lected about the end of July or beginning of August. They never arrive at maturity in plants cultivated in a dry soil or in confined gardens. (Williams.) They are officially described as follows: "Ovoid or irregularly globular, more or less pointed at the hilum; from 2 to 3 mm. in diameter; when fresh, several seeds cohering; externally dark brown, finely pitted; tough and of almost bony hardness; internally whitish or light brown; nearly inodorous; taste bitter and somewhat acrid. Under the microscope, transverse sections of Colchicum seed show a seed-coat of a few more or less collapsed cells with thin reddish-brown walls; an endosperm, making up most of the seed, consisting of cells with rather thick, porous walls, the lumina containing oil globules and aleurone grains, the latter being from 0.003 to 0.015 mm. in diameter; a small embryo, the beaked portion, or caruncle, containing numerous, somewhat ovoid, ellipsoidal or polygonal starch grains, from 0.005 to 0.016 mm. in diameter. Colchicum Seed yields not more than 8 per cent. of ash." *U. S.*

"About two and a half millimetres in diameter, subglobular, slightly pointed at the hilum, rough and of a dull reddish-brown color, minutely pitted, very hard and tough. Endosperm oily; its cells with thickened walls and large pits. No odor; taste bitter and acrid." *Br.*

They are chiefly composed of a gray horny endosperm constituted of very thick-walled cells, and surrounded by a closely adherent testa. The leafless embryo is very small, and is situated close to the surface opposite the strophiole. Williams, of Ipswich, England, first brought them into notice in 1820 as superior to the corm. Schroff, however, has found that their activity is inferior to that of the dried corm dug in autumn. (*A. J. P.*, xxix, 324.) A fluidextract and tincture of the seeds are directed in the U. S. Pharmacopœia. Their dose is slightly less than that of the similar preparations made from the corm. The seeds and powder are very seldom adulterated. Judd, however, reports examining a powder which contained fully 50 per cent. of powdered fœnugreek seed. (*Bull. A. Ph. A.*, 1909, p. 193.)

The U. S. Pharmacopœia IX directs that colchicum seed should contain not less than 0.45 per cent. of colchicine, to be determined by the following process:

Assay of Colchicum Seed.—"Introduce 15 Gm. of Colchicum Seed, in No. 60 powder, into a 500 mil flask, and add 10 mils of solution of lead subacetate and 290 mils of distilled water. Weigh the flask and contents, and digest the mixture at from 60° to 70° C. (140°–158° F.) for three hours, with occasional agitation. Cool, add distilled water to restore the original weight and filter off 200 mils. Add 0.75 Gm. of sodium phosphate to the clear filtrate, shake the mixture frequently during half an hour, and filter off 100 mils representing 5 Gm. of Colchicum Seed. Shake out the alkaloid from the filtrate with chloroform until completely extracted, as shown by testing with iodine T.S. (in place of the usual mercuric potassium iodide T.S.), and evaporate the chloroform solution; add about 1 mil of alcohol and again evaporate. Repeat this operation once more and dry the residue to constant weight at 100° C. (212° F.). To this weighed residue contained in a flask add 5 mils of tenth-normal sulphuric acid V.S. and 5 mils of distilled water and heat the mixture for ten minutes at 70° C. (158° F.). Now filter the liquid through a pledget of purified cotton, wash the flask and cotton with distilled water, reject the filtrate and washings and remove as much of the water from the cotton as possible. Dissolve any insoluble residue that may remain on the cotton by washing it first with a little alcohol and then with ether; collect the alcohol-ether washings in the flask, evaporate, and dry the residue to constant weight at 100° C. (212° F.). Deduct this weight from the weight of residue previously obtained. The difference will be the weight of colchicine obtained from 5 Gm. of Colchicum Seed (see Proximate Assays, Part III)." *U. S.*

Uses.—The investigations into the physiological action of colchicum have not as yet yielded a very clear explanation of its therapeutic effects. Dixon and Malden (*J. P.*, 1908, xxxviii, p. 50) have found that it is an active stimulant to the unstriped muscle, increasing intestinal and uterine contractions and bronchial tonus. After large doses it depresses the vasomotor system, causing a marked fall in the blood pressure. When injected subcutaneously in somewhat smaller doses it produces a transient decrease in the number of leukocytes followed after twenty-four hours by an enormous increase, the alterations being especially notable in the number of polymorphonuclear corpuscles. These effects appear to be the result of an action upon the bone marrow. Jackson and Blackfan (*J. A. M. A.*, 1906, xlvii) find an increased output of uric acid under its influence, but they believe this is due rather to an increased formation than a more active elimination, but Denis (*J. P. Ex. T.*, 1915, vii, 609) was unable to detect any change in the amount of uric acid either in the urine or blood.

The poisonous properties of colchicum were known to the ancients, but, while it is generally supposed that the hermodactyls were derived from some species of the genus, the use of meadow-saffron cannot be certainly traced back further than the sixteenth century. Although it has from time to time been recommended for various complaints, it is used to-day only in the treatment of *gout*. There is considerable clinical evidence that full doses of colchicum administered during the acute attack of a *podagra* will often abort it. The treatment, however, is not without serious danger and most clinicians urge caution in the use of colchicum during the attack. It appears also to be of service in those more chronic conditions of disturbed metabolism known variously as uric acid diathesis or *lithemia*.

In preparing colchicum pharmaceutically, if

it be desired to retain the colchicine unchanged, both acids and alkalies should be avoided and as far as possible also heat. As pointed out below, under various conditions colchicine may be decomposed into colcheiceine, colchicinic acid, and various allied products. Whether these derivatives of colchicine possess the therapeutic virtues of the natural alkaloid is uncertain, but Fuehner (*A. E. P. P.*, 1913, lxxii, p. 228) has shown that colcheiceine is very much less toxic than colchicine.

When taken internally in therapeutic dose, colchicum usually produces no other symptoms than intestinal pains and looseness of the bowels. In some rare cases it is said to give rise to copious diuresis or diaphoresis instead of purging. When larger amounts are exhibited, the purging is more pronounced, and there may be also vomiting. With these symptoms there may be some depression, which seems to be due to the gastro-intestinal irritation rather than to the direct action of the poison. In an overdose, it may produce dangerous and even fatal effects. Excessive nausea and vomiting, abdominal pains, purging and tenesmus, great thirst, sinking of the pulse, coldness of the extremities, and general prostration, with occasional symptoms of nervous derangement, such as headache, delirium, and stupor, are among the results of its poisonous action. A peculiarity of its influence is that when its dose is increased beyond a certain point there is not a corresponding increase in the rapidity of the fatal issue. This is probably because it kills not by a direct influence upon the heart or the nervous system, but by causing gastro-enteritis. On post-mortem examination the alimentary mucous membrane is found much inflamed.

Dose, of the dried corm and seed, from two to eight grains (0.13–0.52 Gm.), which may be repeated every four or six hours until its effects are obtained.

Off. Prep.—*Colchicum corm.*—Extractum Colchici Cormi, *U. S.* (*Br.*); Vinum Colchici, *Br.;* Fluidextractum Colchici Cormi, *N. F.;* Vinum Colchici Cormi, *N. F.*

Off. Prep.—*Colchicum seed.*—Fluidextractum Colchici Seminis, *U. S.;* Tinctura Colchici Seminis, *U. S.* (*Br.*); Vinum Colchici Seminis (from Fluidextract), *N. F.*

COLCHICINA. U. S.

COLCHICINE

(cŏl-çhĭ-cĭ'nȧ)

"An alkaloid [$C_{22}H_{25}O_6N = 399.21$] obtained from colchicum. Preserve it in well-closed containers, protected from light." *U. S.*

Colchicine, *Fr.;* Colchicin, *G.*

The alkaloid *colchicine,* whose nature was first precisely made out by Geiger and Hesse, has been the subject of much controversy, for an account of which the reader is referred to the seventeenth edition of the U. S. Dispensatory, page 427, foot-note. It is now recognized to be the *methyl ester* of *acetyl-trimethyl colchicinic acid,* and has the formula $C_{22}H_{25}O_6N$. When colchicine is heated with 3 parts of hydrochloric acid for two hours on the water bath, it is decomposed, with the formation of *colchicinic acid,* $C_{18}H_{15}O_5N$, and *dimethyl colchicinic acid,* $C_{18}H_{19}O_5N$. When colchicine is boiled with water containing sulphuric acid, it is decomposed thus:

$$C_{22}H_{25}O_6N + H_2O = C_{21}H_{23}O_6N + CH_3OH$$

the products formed being *colcheiceine* and methyl alcohol. The colcheiceine is formed so readily that some of the reactions commonly attributed to colchicine itself are probably due to its decomposition product. Colcheiceine, which is *aceto-trimethyl colchicinic acid,* can also be made synthetically by heating *trimethyl colchicinic acid* with acetic anhydride to 100° C. (212° F.). Colchicine has also been built up synthetically from colcheiceine, sodium methylate, and methyl iodide, which are heated together to 100° C. (212° F.). (Johanny, *Monatshefte,* 9, 868.) It forms precipitates with the usual alkaloidal reagents.

Properties.—The U. S. Pharm. IX officially describes colchicine as in "pale yellow, amorphous scales, or as a pale yellow, amorphous powder, turning darker on exposure to light; odorless or nearly so. *Great caution must be used in tasting it and then only in very dilute solutions.* One Gm. of Colchicine dissolves in 22 mils of water, 220 mils of ether, and in 100 mils of benzene at 25° C. (77° F.); also in 21 mils of water at 80° C. (176° F.); freely soluble in alcohol or chloroform; insoluble in petroleum benzin. Its aqueous solution (1 in 30) is neutral to litmus, lævorotatory, and of a yellow color, which is intensified by the addition of mineral acids. It melts between 142° and 146° C. (287.6° and 294.8° F.). Stir about 0.001 Gm. of Colchicine with a few drops of sulphuric acid; a lemon-yellow color is produced, which, on the addition of a drop of nitric acid, changes to greenish-blue, then to red and finally to yellow. On adding an excess of potassium hydroxide T.S., the color is changed to red. The addition of 2 drops of ferric chloride T.S. to 5 mils of an aqueous solution of Colchicine (1 in 100) produces no color (*colcheiceine*), but, on heating, a brownish-red color is developed, which changes to brownish-black; 1 drop of ferric chloride T.S. added to 1 mil of an alcoholic solution of Colchicine (1 in 20) produces a garnet-red color at once. No weighable ash remains on incinerating 0.1 Gm. of Colchicine. Heat a mixture of about 0.01 Gm. of Colchicine, 2 mils of potassium hydroxide T.S., and 1 drop of aniline; no odor of phenylisocyanide develops (*chloroform*)." *U. S.*

Vanderkleed and E'we (*Proc. P. Ph. A.*, 1916, p. 279) point out that commercial samples of colchicine contain chloroform in comparatively

stable form, which might be called chloroform of crystallization. This not only interferes with the melting point determination, but inasmuch as the amount of chloroform present is sometimes over 20 per cent. it becomes a fraud as well.

Uses.—The alkaloid colchicine acts like colchicum, according to Maret and Combemale, in doses of one-twelfth of a grain (0.005 Gm.) producing violent diarrhea, with diminished urinary secretion; in doses of one thirty-second of a grain (0.002 Gm.) causing some abdominal disturbance, with increased diuresis. According to J. Sprega, three grains (0.2 Gm.), repeated in three hours, caused violent gastro-enteritis, ending in death in thirty-one hours. (*Gazz. d. Ospitali*, Oct., 1890.) *Colchicine salicylate* is a yellow amorphous powder, soluble in water, alcohol, and ether, the dose being one-hundredth of a grain (0.0006 Gm.) every four hours.

Dose, one one-hundred and fiftieth to one one-hundredth of a grain (0.0004–0.0006 Gm.).

COLLODIUM. U. S., Br.

COLLODION Collod.

(cŏl-lō′dĭ-ŭm)

Collodion, *Fr. Cod.*; Collodium, *P. G.*; Kollodium, *G.*; Collodio, *It.*; Colodion, *Sp.*

* "Pyroxylin, *forty grammes* [or 1 ounce av., 180 grains]; Ether, *seven hundred and fifty mils* [or 25 fluidounces, 173 minims]; Alcohol, *two hundred and fifty mils* [or 8 fluidounces, 218 minims]. To make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Add the alcohol to the pyroxylin contained in a suitable bottle, shake the mixture thoroughly, then introduce the ether, and again shake the mixture until the pyroxylin is dissolved. Cork the bottle well and set it aside until the liquid becomes clear. Finally decant the clear portion from any sediment which may have deposited, and transfer it to containers which must be well closed. Keep the Collodion in a cool place remote from fire." *U. S.*

"Pyroxylin, 21 grammes; Ether, 750 millilitres; Alcohol (90 per cent), 250 millilitres. Immerse the Pyroxylin in the Alcohol; add the Ether, shake occasionally until dissolved; set aside for a few days; decant if necessary." *Br.*

Collodion is a solution of gun cotton. On account of the facility with which ether evaporates, it is the better menstruum for remedial purposes, but gun cotton will not dissolve in that liquid when quite pure, and the addition of strong alcohol is necessary. Formerly the U. S. Pharmacopœia directed that the gun cotton be prepared at the time of making the collodion, giving directions for the purpose, but at the revision of 1870 the process of the British Pharmacopœia was substantially adopted, a formula for the preparation of pyroxylin being given separately in the Pharmacopœia. A process for the preparation of pyroxylin was not introduced into the U. S. Pharmacopœia IX, but the British Pharmacopœia still retains a process. (See *Pyroxylinum*.) A change has been made, however, in directing the collodion to be decanted from the sediment. In the U. S. P., 1870, the sediment was directed to be re-incorporated with the clear collodion, and the result was the making of a tougher film. This sediment consists of undecomposed filaments of cotton, and these become partially felted as the ethereal liquid evaporates and the film is forming; this direction of the former Pharmacopœia was usually disregarded, although for many purposes the cloudy film is to be preferred.

Acetone has been used as a solvent for pyroxylin and collodion so prepared is on the market.

Properties.—"Collodion is a clear, or slightly opalescent, syrupy liquid; colorless, or slightly yellowish and having the odor of ether. It is highly inflammable. When exposed to the air in a thin layer it leaves a transparent, tenacious film. Specific gravity: 0.765 to 0.775 at 25° C. (77° F.). When mixed with an equal volume of distilled water, a viscid, stringy mass separates; the aqueous liquid is not acid to litmus.

"**Assay.**—Introduce about 10 mils of Collodion into a flask; stopper and weigh accurately, then warm it on a water bath and add 10 mils of distilled water, drop by drop, with constant stirring. Evaporate the mixture on a water bath and dry the residue to constant weight at 110° C. (230° F.). The pyroxylin so obtained corresponds to not less than 5.1 per cent. of the Collodion taken, equal to about 4 Gm. of pyroxylin in 100 mils of Collodion at 25° C. (77° F.). The pyroxylin obtained burns rapidly, with a yellow flame." *U. S.*

"A colorless, highly inflammable liquid of syrupy consistence and ethereal odor. Dries quickly upon exposure to the air, and leaves a thin transparent film, which contracts rapidly on drying and is insoluble in *water* or *alcohol* (90 per cent.)." *Br.*

When applied to a dry surface, the ether quickly evaporates, and a transparent film is left, having remarkable adhesiveness and contractility. On account of the great volatility of ether, collodion must be kept in bottles well stoppered. When insecurely kept, the liquid thickens and becomes less fit for the use of the surgeon. The thickened liquid sometimes contains acicular crystals. The addition of a mixture of 3 volumes of ether and 1 volume of alcohol will generally restore the collodion to its original condition.

Uses.—Collodion was first applied to the purposes of surgery by J. Parker Maynard, of Boston, when a student of medicine, in January, 1847, although, as pointed out by Kahlbaum, Schoenbein, the discoverer of gun cotton, suggested the surgical use of an ethereal solution in 1846. (*Nat. Drug.*, 1902, 8.) It is employed for holding together the edges of incised *wounds*, for covering *ulcers*, abraded or diseased surfaces, *chilblains, chapped nipples*, etc., with an impervious film not acted upon by water, and for encasing parts which require to be kept without relative motion. It should be remembered

that while it protects the underlying tissues from external contamination, it also prevents the escape of any toxic materials already present; to hermetically close an infected wound, as with collodion, is an invitation to blood-poisoning. It is applied brushed over the part, or by means of strips of muslin. In whatever way applied, the solvent quickly evaporates, and leaves the solid adhesive material, which is soluble neither in water nor in alcohol. The rigid film thus formed contracts with a good deal of force. This property adapts collodion for certain purposes, such as drawing together the edges of wounds, exciting pressure on buboes, etc. When, however, the surgeon desires simply to protect a surface, a flexible, non-contracting film is preferable, and the official flexible collodion should be used. Collodion has been variously medicated, and thus made the vehicle of several important medicines for external application. *Iodized collodion* has been proposed by C. Fleming, for the purpose of obtaining the specific effects of iodine in a rapid manner, especially on *tumors*. See *Collodium Iodi*, N. F., Part III. Aran has proposed a *ferruginous collodion*, made of equal parts of collodion and tincture of ferric chloride, as a remedy in *erysipelas*. A *caustic collodion* may be prepared by dissolving 4 parts of corrosive sublimate in 30 of collodion. Macke, of Sorau, has used this preparation for destroying *nævi materni*. The eschar formed is one or two lines in thickness, and separates in from three to six days, leaving but a trifling cicatrix. (For formulas in which collodion is made the vehicle of croton oil, iodoform, salicylic acid, tannin, etc., see National Formulary, Part III.) All these medicated collodions are best applied by means of a camel's-hair brush.

Off. Prep.—Collodium Flexile, *U. S., Br.;* Collodium Stypticum, *N. F.*

COLLODIUM CANTHARIDATUM. U. S. (Br.)

CANTHARIDAL COLLODION Collod. Canth.
[Blistering Collodion Vesicating Collodion]

(cŏl-lō'dĭ-ŭm cạn-thăr-ị-dā'tŭm)

Collodium Vesicans, *Br.;* Blistering Collodion; Collodium Cantharidale, s. Vesicans; Collodion vésicant (cantharidé), *Fr.;* Collodium Cantharidatum, *P. G.;* Spanischfliegen-Kollodium, Blasenziehendes Collodium, *G.*

* "Cantharides, in fine powder, *sixty grammes* [or 2 ounces av., 51 grains]; Glacial Acetic Acid, *five mils* [or 81 minims]; Flexible Collodion, *eighty-five grammes* [or 3 ounces av.]; Acetone, *a sufficient quantity,* to make *one hundred grammes* [or 3 ounces av., 231 grains]. Mix the cantharides with *fifty-five mils* of acetone, to which the glacial acetic acid has been added, and set the mixture aside in a closely-covered container for twenty-four hours. Then transfer it to a percolator and continue the percolation with acetone until the drug is practically exhausted. Reduce the percolate by distillation on a water bath, in a tared flask, to *fifteen grammes* [or 231 grains] and, when cold, dissolve this concentrated extract in *eighty-five grammes* [or 3 ounces av.] of flexible collodion. Finally allow the solution to stand for several hours, and decant the clear liquid from any sediment which may have deposited, and transfer the product to containers, which must be well-closed. Keep Cantharidal Collodion in a cool place, remote from fire." *U. S.*

"Pyroxylin, 25 *grammes;* Cochineal, in powder, 10 *grammes;* Blistering Liquid sufficient to produce 1000 *millilitres.* Shake together until the Pyroxylin is dissolved, set aside till clear, and decant the clear liquid." *Br.*

The official process differs materially from that of the U. S. P. VIII. Acetone and glacial acetic acid are used to extract the cantharidin from the powdered cantharides, by percolation instead of chloroform; the acetone is afterwards recovered by distillation, and the oily residue containing the vesicant is dissolved in the collodion. The original process of Ilisch was to exhaust, by percolation, a pound of cantharides, with a mixture consisting of a pound of ether and three ounces of acetic ether, and in two ounces of this liquid to dissolve 25 grains of gun cotton. Procter stated that it had been found more advantageous to exhaust the flies with ether, distil off the ether, and mix the oily residue with collodion already prepared of the proper consistence (*A. J. P.,* xxiv, 303); but at the present time owing to the cheapness of acetone and its advantage over the very inflammable and dangerous ether the official process is greatly preferred. In the British Pharm., 1914, cochineal is used to color the film "flesh color." Charles S. Rand (*A. J. P.,* xxii, 18) states that Ilisch's preparation, made with double the proportion of ether, vesicates equally well, and proposes the addition of about 1 per cent. of Venice turpentine, which he has found to prevent the disagreeable and sometimes painful contraction of the collodion upon drying. The preparation may be kept indefinitely, without change, in an opaque glass stoppered bottle, but on exposure to the light, the greenish coloring matter of the flies bleaches, and the liquid becomes yellowish. *Cantharidized collodion* may be made from cantharidin by dissolving four grains of cantharidin in one thousand grains of flexible collodion.

Cantharidal collodion is a convenient but uncertain epispastic. It may be applied to the surface by means of a camel's-hair brush, and after the evaporation of the ether, which takes place in less than a minute, may be reapplied if the surface should not be well covered. It produces a blister in about the same time as the ordinary cerate, and has the advantages that it is applied with greater facility, is better adapted to cover uneven surfaces, and retains its place more certainly. According to Rand, if the evaporation of the ether be restrained by a piece of oiled silk immediately after its application, it will act much more speedily.

COLLODIUM FLEXILE. U. S., Br.

FLEXIBLE COLLODION Collod. Flex.

(cŏl-lō'dĭ-ŭm flĕx'ĭ-lē)

Collodion élastique, *Fr.;* Collodium elasticum, *P. G.;* Elastiches Collodium, Kollodium, *G.;* Collodio elastico, *It.;* Colodion elastico, *Sp.*

* "Collodion, *nine hundred and fifty grammes* [or 33 ounces av., 223 grains]; Camphor, *twenty grammes* [or 308.6 grains]; Castor Oil, *thirty grammes* [or 1 ounce av., 25 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Weigh the ingredients, successively, into a tared bottle and shake the mixture until the camphor is dissolved. Keep the product in well-closed containers, in a cool place, remote from fire." *U. S.*

"Collodion, 940 *millilitres;* Canada Turpentine, 40 *grammes;* Castor Oil, 20 *grammes.* Mix." *Br.*

The contractility of the collodion film has long been felt as a drawback to its use simply for the purposes of protection. C. S. Rand proposed to obviate this by dissolving one part of gun cotton and three of Venice turpentine in twenty parts of ether. To give more flexibility to the film, Sourisseau, of Kaiserberg, suggested the addition of one part of elemi to twelve of collodion. According to Startin, of London, opacity and elasticity may be imparted at the same time by adding from half a drachm to a drachm of lard, or some similar fatty matter, previously dissolved in ether, to an ounce of collodion. The qualities of softness and elasticity may also be given by combining collodion with castor oil, in the proportion of thirty parts to two, agreeably to the plan of Guersant, who found it useful, thus modified, in *erysipelas;* and the proportion of castor oil may be increased if thought desirable. This is the method preferred by the French Codex. An elastic collodion, somewhat similar, in which, besides castor oil, Venice turpentine and white wax are ingredients, has been proposed by E. Lauras. (*P. J.*, xii, 303.) According to Cap and Garot, the most successful way for obtaining an elastic collodion is to mix two parts of glycerin with one hundred of collodion. *Glycerized collodion* is exceedingly supple, does not crack and scale off from the skin, and accommodates itself to the motions of the part. In order to imitate the color of the skin, an ethereal tincture of turmeric or saffron may be added, so as to produce the desired tint. Meller has proposed a solution of shellac in highly rectified alcohol, so as to have a gelatinous consistence, as a substitute for collodion. Of all these plans, probably that followed in the official directions is the best. Tournie recommends, in superficial *cervical adenitis* with redness, painting the part with several layers of flexible collodion every two days. (*M. T. G.*, 1874, p. 540.)

Off. Prep.—Collodium Cantharidatum, *U. S.;* Collodium Iodi, *N. F.;* Collodium Iodoformi, *N. F.;* Collodium Salicylici Compositum, *N. F.;* Collodium Stypticum, *N. F.;* Collodium Tiglii, *N. F.*

COLOCYNTHIS. U. S. (Br.)

COLOCYNTH Colocyn. [Bitter Apple, Colocynth Apple]

(cŏl-ŏ-cȳn'thĭs)

"The dried pulp of the fruit of *Citrullus Colocynthis* (Linné) Schrader (Fam. *Cucurbitaceæ*), without the presence or admixture of more than 5 per cent. of seeds or more than 2 per cent. of epicarp." *U. S.* "Colocynth Pulp is the dried pulp of the fruit of Citrullus Colocynthis, *Schrad.*, freed from seeds." *Br.*

Colocynthidis Pulpa, *Br.,* Colocynth Pulp, Bitter Gourd, Apple, or Cucumber, Poma Colocynthidis; Coloquinte, *Fr. Cod.;* Pulpe de Coloquinte, *Fr.;* Fructus Colocynthidis, *P. G.;* Coloquintenapfel, Koloquintenmark, Koloquinten, *G.;* Coloquintide, *It.;* Coloquintida, *Sp.*

Colocynth is another one of those drugs which has given a great amount of trouble to manufacturers because the definition of the U. S. Pharmacopœia, in previous revisions, simply stated that it was the "peeled dried fruit." Notwithstanding the fact that at the end of the description there was a statement that "the seeds should be separated and rejected" the powdered drug consisted frequently of the seeds as well as pulp. In order to avoid any misunderstanding the U. S. Pharmacopœia has followed the British authority and defined Colocynth as the dried pulp. As it is not commercially possible to exclude the seeds entirely, a few being imbedded in the pulp itself, the Pharmacopœia wisely allows a minimum of 5 per cent. of seeds. It is estimated that every 100 pounds of colocynth fruit will yield 30 pounds of pulp and about 70 pounds of seeds. Tunmann (*Suedd. Apoth. Zeit.*, 1907, p. 503) states that the seeds do not contain medicinally active constituents. Francis (*Proc. A. Ph. A.*, 1906, p. 336), on the other hand, says that if the seeds are first deprived of their fixed oil with benzin, dried and then extracted with 75 per cent. alcohol, the extract is almost as active as the U. S. P. product.

Citrullus Colocynthis, or *bitter cucumber,* is an annual plant, bearing considerable resemblance to the common watermelon. The stems, which are herbaceous and beset with rough hairs, trail upon the ground, or rise upon neighboring bodies, to which they attach themselves by their numerous tendrils. The leaves, which stand alternately on long petioles, are triangular, many-cleft, variously sinuated; obtuse, hairy, of a fine green color on the upper surface, rough and pale on the under. The flowers are yellow, and appear singly at the axils of the leaves. The fruit is a globular pepo, of the size of a small orange, yellow and smooth when ripe, and contains, within a hard, coriaceous rind, a white, spongy pulp, enclosing numerous ovate, compressed, white or brownish seeds.

The plant is a native of Turkey, and abounds in the islands of the Archipelago. It grows also in various parts of Africa and Asia. Burckhardt, in his travels across Nubia, found the country covered with it; Thunberg met with it at the Cape of Good Hope, and Ainslie says that it grows in many parts of Lower India, particularly in sandy places near the sea. It is said to

be cultivated in Spain, the island of Cypress, Morocco and in the neighboring countries, and even to have been collected in Japan. Colocynth from the maritime plain between the mountains of Palestine and the Mediterranean is chiefly shipped from Jaffa, and is known as *Turkish colocynth.* It is said to be of superior quality. The fruit is gathered in autumn, when it begins to become yellow, and, having been peeled, is dried quickly in a stove or in the sunshine. Thus prepared, it is imported from the Levant. Small quantities are said to be imported into England from Mogador in the form of brown, unpeeled globular gourds. The so-called *Persian colocynth* of the London markets is very small, and has apparently been compressed in a fresh state, so that the position of the seeds is perceptible through the dry pulp. The microscopic structure and the proportion of the pulp to the seed appear to be the same as in other colocynths. (*P. J.*, xvi, 107.) Colocynth has been grown in New Mexico, but, according to Sayre, the American colocynth possesses only about two-thirds the cathartic action of the Trieste variety.

Properties.—As found in commerce, colocynth is in whitish, globular berries, from 6 to 7 cm. in diameter, very light and spongy, and abounding in seeds which constitute three-fourths of their weight. The seeds are somewhat bitter, but possess little activity, and, according to Captain Lyon, are even used as food in the north of Africa. Nachtigal confirms this statement of Captain Lyon's, but with the qualification that, before being eaten, the seeds are deprived of their coating by some mechanical means, and the kernels are heated to the boiling point, then washed with cold water, dried, and powdered. Flückiger found a bitter principle in the testa, which accounts for its rejection as food, though rendering improper the rejection of the seed in preparing the extract. He found in the kernels about 45 per cent. of fixed oil and 18 per cent. of albumen. (*A. J. P.*, 1872, 538.) They should be separated and rejected, the pulpy matter only being employed. The U. S. Pharmacopœia thus describes colocynth: "Fruits, before the removal of the seeds, nearly globular, from 4 to 7 cm. in diameter, usually more or less crushed and in broken pieces, with occasional patches of the nearly smooth epicarp; yellowish-white or brownish; light, spongy; separable longitudinally when entire into three carpels, each containing, near the outer surface, the ovoid, compressed, yellowish seeds; odor slight; taste intensely bitter. The powder is yellowish-white or buff, consisting chiefly of fragments of parenchyma cells and an occasional fragment with tracheæ; very few lignified tissues of the seed-coat, showing the characteristic stone cells which are nearly isodiametric, irregular, with either straight or undulate walls that are strongly lignified and possess simple pores; globules of fixed oil and aleurone grains very few. Powdered Colocynth must be made from colocynth pulp containing not more than 5 per cent. of seeds and, upon extraction with purified petroleum benzin, yields not more than 2 per cent. of fixed oil. Colocynth yields not more than 15 per cent. of ash." *U. S.*

"White, spongy, light fragments. The powdered Pulp exhibits abundant débris of large, thin-walled parenchymatous cells but no starch, and not more than an occasional sclerenchymatous cell or group of such cells. No odor; taste intensely bitter. Yields not more than 2 per cent. of fixed oil to *petroleum spirit.* Ash not less than 9 per cent." *Br.*

Barclay considers the estimation of ash in powdered colocynth useful in proving its freedom from seeds. The pulp yields from 8.6 to 14 per cent. of ash, the seeds from 2 to 4 per cent., the whole apple 4.6 per cent. (*Am. Drug.*, 1896, 152.) Water and alcohol extract the virtues of colocynth. It is a matter of importance to be able to determine whether the drug miller who usually powders colocynth is careful to reject the seeds. If the seeds have been ground with the dried pulp, the microscope will show the presence of numerous albuminous granules derived from the cotyledons. (W. T. Clark, *P. J.*, vii, 509.) These are best found by putting a small amount of the powder on the glass slide, adding a drop of water, and gently rubbing the cover glass over it; fragments of the double-walled embryo sac show on the outer side elongated, more or less hexagonal, thin-walled cells, and on the inner side irregular, tabular, thick-walled cells. If powdered colocynth contains a large number of starch granules it has probably been adulterated. Power and Moore (*Tr. Chem. Soc.*, xcvii, p. 99) have separated from colocynth an alkaloidal principle which has a violent purgative effect, but this is not the only active principle of the crude drug, because both ether and chloroform extracts of the resin, when free from the alkaloidal principle, were still purgative. They find also alpha-elaterin, but none of the active beta-elaterin. (See *Elaterinum.*) Vauquelin obtained the bitter principle of colocynth in a separate state, and called it *colocynthin.* According to Meissner, 100 parts of the dry pulp of colocynth contain 14.4 parts of colocynthin, 10.0 of extractive, 4.2 of fixed oil, 13.2 of a resinous substance insoluble in ether, 9.5 of gum, 3.0 of pectic acid (pectin), 17.6 of gummy extract derived from the lignin by means of potassium hydroxide, 2.7 of calcium phosphate, 3.0 of magnesium phosphate, and 19.0 of lignin, besides water. Walz supposed that he had found another peculiar principle, *colocynthitin.* It was obtained by treating with ether the alcoholic extract previously exhausted by water, decolorizing the ethereal solution with animal charcoal, evaporating to dryness, and dissolving the residue in anhydrous alcohol, which deposited it in crystals on spontaneous evaporation. It is white and tasteless, and is probably a resin. (*N. Jahrbuch der Pharm.*, xvi, 10.) Colocynthin is obtained by boiling the pulp in water, evaporating the decoction, treating the extract thus procured with alcohol, evaporating the alcoholic solution, and

submitting the residue, which consists of the bitter principle and potassium acetate, to the action of a little cold water, which dissolves the latter and leaves the greater part of the former untouched. Bastick obtained it by exhausting the pulp with cold water, heating the solution to ebullition, adding lead subacetate so long as a precipitate was produced, filtering the liquor when cold, adding diluted sulphuric acid gradually until it no longer occasioned a precipitate, boiling to expel free acetic acid, filtering to separate lead sulphate, evaporating cautiously nearly to dryness, extracting the colocynthin from the residue by strong alcohol, which left the salts, and finally evaporating the alcoholic solution.

The following process, employed by Walz, yields it in a purer state. Colocynth is exhausted by alcohol of sp. gr. 0.84, the tincture evaporated to dryness, the residue treated with water, and the solution precipitated first with lead acetate and afterwards with lead subacetate. The yellow filtered liquor is then treated with hydrogen sulphide to separate the lead, and, after filtration, with solution of tannic acid, which throws down a compound of tannic acid and colocynthin. This is dissolved in alcohol, the tannin thrown down by lead subacetate, the excess of lead separated, and the liquid digested with animal charcoal, filtered, and evaporated. The residue, washed with anhydrous ether, is pure colocynthin. This is yellowish, somewhat translucent, brittle and friable, fusible by a heat below 100° C. (212° F.), inflammable, more soluble in alcohol than in water, but capable of rendering the latter intensely bitter. Mouchon states that it is insoluble in ether. It is neither acid nor alkaline; but its aqueous solution gives with infusion of galls a copious white precipitate. Ahrends (*Neue Arzneimittel*, 1909) gives the synonym of this principle as *citrullin* and gives the formula as $C_{56}H_{84}O_{23}$. Its formula, according to Walz, is $C_{56}H_{42}O_{23}$. Upon the same authority it is a glucoside, being resolved by the action of sulphuric acid into sugar and a peculiar resinous substance termed *colocyntheïn*, to which he gives the formula $C_{44}H_{32}O_{13}$. Henke doubts the probability of colocynthin being a glucoside, and states that it is uncrystallizable; he reviews the methods of previous investigators, and obtained by his own process but 0.66 per cent. of colocynthin. (*A. Pharm.*, 1883, p. 200; *A. J. P.*, 1883, p. 301.) According to Johannson, colocynthin, when heated with diluted sulphuric acid, yields colocyntheïn, elaterin, and bryonin. (*A. J. P.*, 1885, p. 451.) An infusion of colocynth, made with boiling water, gelatinizes upon cooling. Neumann obtained from 768 parts of the pulp, treated first with alcohol and then with water, 168 parts of alcoholic and 216 of aqueous extract. (See also paper by George Wagner, *Proc. A. Ph. A.*, 1893, 179.)

Uses.—The pulp of colocynth is a powerful drastic, hydragogue cathartic, producing, when given in large doses, violent griping, and sometimes bloody discharges, with dangerous inflammation of the bowels. Death has resulted from a teaspoonful and a half of the powder. (Christison.) Even in moderate doses it sometimes acts with much harshness, and it is therefore seldom prescribed alone. By some writers it is said to be diuretic. It was frequently employed by the ancient Greeks and the Arabians, though its drastic nature was not unknown to them. Among the moderns it is occasionally used in obstinate dropsy, and in various affections depending on disordered action of the brain. In combination with other cathartics it loses much of its violence, but retains its purgative energy, and in this form is extensively employed. The compound extract of colocynth is a favorite preparation with many practitioners, and, combined with calomel, extract of jalap, and gamboge, it forms a highly efficient and safe cathartic, especially useful in congestion of the portal circle and torpidity of the liver. (See *Pilulæ Catharticæ Compositæ.*) It is best administered in minute division, effected by trituration with gum or farinaceous matter. The active principle has sometimes been employed, and, in the impure state in which it is prepared by the process of Emile Mouchon, may be given in the dose of a grain (0.065 Gm.).

Thunberg states that the fruit of *C. Colocynthis*, at the Cape of Good Hope, is rendered so mild by being properly pickled that it is eaten both by the natives and by the colonists; but, as it is thus employed before attaining perfect maturity, it is possible that the drastic principle may not have been developed.

Dose, one to five grains (0.065–0.32 Gm.).

Off. Prep.—Extractum Colocynthidis, *U. S.*; Extractum Colocynthidis Compositum (from Extract), *U. S., Br.*; Pilula Colocynthidis Composita, *Br.*; Pilula Colocynthidis et Hyoscyami (from Compound Pill), *Br.*, (from Extract), *N. F.*; Pilulæ Antidyspepticæ (from Compound Extract), *N. F.*; Pilulæ Catharticæ Vegetabiles (from Compound Extract), *N. F.*; Pilulæ Colocynthidis Compositæ (from Extract), *N. F.*; Pilulæ Colocynthidis et Podophylli (from Compound Extract), *N. F.*; Pilulæ Laxativæ Post Partum (from Compound Extract), *N. F.*

CONFECTIO PIPERIS. Br.

(cŏn-fĕc'tĭ-ō pĭp'ĕ-rĭs)

Electuarium Piperis; Electuaire de Poivre, *Fr.*; Pfefferlatwerge, *G.*

"Black pepper of commerce, in powder, 100 *grammes;* Caraway Fruit, in powder, 150 *grammes;* Purified Honey, 750 *grammes.* Mix." *Br.*

This preparation was intended as a substitute for *Ward's Paste*, which acquired some reputation in Great Britain as a remedy in *piles* and ulcers of the rectum. To be of service, it must be continued, according to Brodie, for two, three, or four months. Its stimulating properties render it inapplicable to cases attended with much inflammation.

Dose, from one to two drachms (3.9–7.7 Gm.), repeated two or three times a day.

CONFECTIO ROSÆ GALLICÆ. Br.

CONFECTION OF ROSES

(cŏn-fĕc'tĭ-ō rō'şæ găl'lĭ-cæ)

Conserva Rosarum; Conserve de Rose, *Fr. Cod.*; Conserve de Rose rouge, *Fr.*; Rosen-Conserve, *G.*

Confection of Rose was unfortunately dropped from the U. S. P. IX, but was introduced into the National Formulary IV. (See Part III.)

"Fresh Red-Rose Petals, 250 *grammes;* Refined Sugar, 750 *grammes.* Beat together in a stone mortar," *Br.*

* "Red Rose, in No. 60 powder, *eighty grammes* [or 2 ounces av., 360 grains]; Sugar, in fine powder, *six hundred and forty grammes* [or 22 ounces av., 252 grains]; Clarified Honey, *one hundred and twenty grammes* [or 4 ounces av., 102 grains]; Stronger Rose Water, *one hundred and sixty cubic centimeters* [or 5 fluidounces, 197 minims], to make about *one thousand grammes* [or 35 ounces av., 120 grains]. Rub the Red Rose with the Stronger Rose Water previously heated to 65° C. (149° F.), then gradually add the Sugar and Clarified Honey, and beat the whole together until a uniform mass results." *U. S. VIII.*

In the British process the unblown petals only are used, and these should be deprived of their claws; in other words, the rose-buds should be cut off a short distance above their base, and the lower portion rejected. In the last four editions of the U. S. Pharmacopœia, dried roses have been substituted for the fresh, as the latter are not brought to our market. The process is very similar to that of the French Codex. We have been informed, however, that confection of rose is still made in Philadelphia on a large scale from the fresh petals of the *R. centifolia* and others, by beating them into a pulp with sugar, as in the British process. An excuse for this deviation from the official formula is, that the confection thus made has greater adhesiveness than the official, and is therefore better fitted for the formation of pills. Confection of Rose is slightly astringent; it is used almost exclusively as a vehicle, and is admirably adapted as an excipient and to impart consistence to the pilular mass.

Off. Prep.—Pilula Hydrargyri, *Br*

CONFECTIO SENNÆ. Br.

CONFECTION OF SENNA

(cŏn-fĕc'tĭ-ō sĕn'næ)

Electuarium Sennæ Compositum, Electuarium Lenitivum; Electuaire de Séné composé, *Fr. Cod.*; Electuaire lenitif, *Fr.*; Electuarium e Senna, *P. G.*; Sennalatwerge, *G.*; Elettuario lenitivo, *It.*

Confection of Senna was improperly dropped from the U. S. P. IX, but the National Formulary IV introduced the U. S. P. VIII preparation. (See Part III.)

"Senna Leaves, in powder, 100 *grammes;* Coriander Fruit, in powder, 40 *grammes;* Figs of commerce, 160 *grammes;* Tamarinds, 120 *grammes;* Cassia Pulp, 120 *grammes;* Prunes of commerce, 80 *grammes;* Extract of Liquorice, 15 *grammes;* Refined Sugar, 400 *grammes;* Distilled Water sufficient to produce 1000 *grammes.* Boil the figs and prunes gently with three hundred and fifty grammes of Distilled Water in a covered vessel for four hours; add more Distilled Water to make up the quantity to its original weight, and then incorporate the Tamarinds and Cassia Pulp; digest for two hours; rub the softened pulp of the fruits through a hair sieve, rejecting the seeds and other hard parts; to the pulp thus obtained add the Refined Sugar and Extract of Liquorice, dissolving them by the aid of gentle heat; while the mixture is still warm, add to it gradually the mixed Senna and Coriander powders; mix the whole thoroughly; make the weight of the resulting Confection one thousand grammes, either by evaporation or by the addition of more Distilled Water." *Br.*

* "Senna, in No. 60 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Cassia Fistula, bruised, *one hundred and sixty grammes* [or 5 ounces av., 282 grains]; Tamarind, *one hundred grammes* [or 3 ounces av., 231 grains]; Prune, sliced, *seventy grammes* [or 2 ounces av., 205 grains]; Fig, bruised, *one hundred and twenty grammes* [or 4 ounces av., 102 grains]; Sugar, in fine powder, *five hundred and fifty-five grammes* [or 19 ounces av., 252 grains]; Oil of Coriander, *five grammes* [or 77 grains]; Water, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Digest the Cassia Fistula, Tamarind, Prune and Fig with *five hundred cubic centimeters* [or 17 fluidounces] of Water in a covered vessel, by means of a water-bath, for three hours. Separate the coarser portions and rub the pulpy mass, first through a coarse hair sieve, and then through a muslin cloth. Mix the residue with *one hundred and fifty cubic centimeters* [or 5 fluidounces] of Water, and, having digested the mixture for a short time, treat it as before, and add the product to the pulpy mass first obtained. Then, by means of a water-bath, dissolve the Sugar in the pulpy liquid, and evaporate the whole in a tared vessel, until it weighs *eight hundred and ninety-five grammes* [or 31 ounces av., 250 grains]. Lastly, add the Senna and the Oil of Coriander, and incorporate them thoroughly with the other ingredients while they are yet warm." *U. S. VIII.*

Confection of Senna, when correctly made, is an elegant preparation, and keeps well if properly protected. The U. S. P. VIII process differed from that of 1860 in preparing the pulps, as suggested in former editions of this Dispensatory, instead of taking them already prepared. An improvement was made in the process of the U. S. P. 1890 by replacing the coriander seed of the former Pharmacopœias with oil of coriander; it is almost impossible to powder coriander fine enough to avoid hard particles except by drying it to such an extent as to deprive it injuriously of its volatile oil, and the plan of using the oil directly has therefore been adopted. The oil of coriander should be dropped upon a

portion of the powdered senna contained in a mortar or suitable vessel and this lightly triturated with the rest of the powdered senna so as to distribute it uniformly; the mixture should then be added to the pulpy mass and the official directions then carried out. It was formerly not uncommon to omit the cassia pulp in this preparation, as the pods were not always to be found in the market; but, as this is next to the senna the most active ingredient, the omission was to be regretted. Cassia fistula is now readily procured in commerce, and there can be no excuse for its omission. It has also been proposed to substitute the fluidextract of senna for the crude drug (*A. J. P.*, xliii, 123); but, as the fluidextract is of such uncertain quality, the leaves themselves are preferable.

A very good, pleasant laxative, admirably adapted to cases of habitual costiveness, especially in pregnant women, and in persons affected with *piles*.

Dose, one to two drachms (3.9–7.7 Gm.), at bedtime.

CONFECTIO SULPHURIS. Br.

CONFECTION OF SULPHUR

(cŏn-fĕc'tĭ-ō sŭl'phŭ-rĭs)

Electuarium Sulphuris; Electuaire de Soufre, *Fr.*; Schwefellatwerge, *G.*

"Precipitated Sulphur, 450 *grammes;* Acid Potassium Tartrate, in powder, 110 *grammes;* Tragacanth, in powder, 5 *grammes;* Syrup, 210 *millilitres;* Tincture of Orange, 55 *millilitres;* Glycerin, 170 *millilitres.* Mix." *Br.*

This is merely a mode of administering the two laxatives, sulphur and potassium bitartrate, and the relative proportion of the latter is so small that it can have little effect. The addition of tragacanth is due to a suggestion of Peter Boa, who found that without it a syrupy layer of liquid formed on top of the confection. (*P. J.*, 1882, 682.) The syrup of orange peel, formerly directed, has been replaced in the last two Editions by syrup and tincture of orange, evidently because the syrup of orange peel did not keep well, while the glycerin serves to retain the proper consistence of the confection.

Dose, one to two drachms (3.9–7.7 Gm.) or more.

CONFECTIONES

CONFECTIONS

(cŏn-fĕc-tĭ-ō'nēs)

Electuaries; Conserves, Électuaires, Saccharolés mous, *Fr.*; Conserven, Latwergen, *G.*; Elettuario, *It.*; Electuario, *Sp.*

Under the general title of Confections, the Pharmacopœias include all those preparations having the form of a soft solid, in which one or more medicinal substances are incorporated with saccharine matter, with a view either to their preservation or more convenient administration. But two confections, Rose and Senna, were retained in the Eighth Revision of the U. S. Pharmacopœia and in the Ninth Revision both were dropped and relegated to the National Formulary IV. The old division into Conserves and Electuaries has been abandoned; but, as there is some ground for the distinction, we shall make a few general remarks upon each division before proceeding to the consideration of the individual preparations.

Conserves consist of undried vegetable substances and refined sugar beaten into a uniform mass. By means of the sugar, the vegetable matter is enabled to resist for some time the decomposition to which it would otherwise be exposed in the undried state, and the properties of the recent plant are thus retained to a certain extent unaltered. But, as active medicines even thus treated undergo some change, and those which lose their virtues by desiccation cannot be long preserved, the few conserves now used are intended rather as convenient vehicles of other substances than for separate exhibition. The sugar used in their preparation should be in fine powder.

Electuaries are mixtures consisting of medicinal substances, especially dry powders, combined with syrup or honey, in order to render them less unpleasant to the taste, and more convenient for internal use. They are usually prepared extemporaneously; and it is only when their complex nature renders it convenient to keep them ready made, or some peculiarity in the mode of mixing the ingredients requires attention, that they become proper objects for official direction. Their consistence should not be so soft, on the one hand, as to allow the ingredients to separate, nor so firm, on the other, as to prevent them from being swallowed without mastication. Different substances require different proportions of syrup. Light vegetable powders usually require twice their weight, gum-resins two-thirds of their weight, resins somewhat less, mineral substances about half their weight, and deliquescent salts not more than one-tenth. Should the electuary become dry and hard, more syrup should be added, so as to give it the requisite consistence. If the dryness result from the mere evaporation of the aqueous part, water should be added instead of syrup, and the same remark is applicable to the conserves. To prevent the hardening of electuaries, the French writers recommend the use of syrup prepared from brown sugar, which is less apt to crystallize than that made from the refined. Molasses would answer the same purpose, but its taste might be objectionable. Some employ honey, but this is not always acceptable to the stomach. Glycerin and syrupy glucose might sometimes be used with advantage.

Confectio Aromatica, Aromatic Confection, Electuarium Aromaticum; Electuaire (Confection) aromatique, *Fr.;* Aromatische Latwerge, Getwürzlatwerge, *G.*—"Take of Aromatic Powder *four troyounces;* Clarified Honey, *four troyounces,* or *a sufficient quantity.* Rub the Aromatic Powder with Clarified Honey until a uniform mass of the proper consistence is obtained." *U. S.*, 1870.

This confection affords a convenient means of administering the spices contained in it, and an agreeable vehicle for other medicines. The confection is given in debilitated states of the stomach. The *dose* is from ten to sixty grains (0.65–3.9 Gm.).

Confectio Aurantii Corticis, Confection of Orange Peel, Conserva Aurantii; Conserve d'Ecorce d'Orange, *Fr.;* Apfelsinenschalen-Conserve, *G.*—"Take of Sweet Orange Peel, recently separated from the fruit by grating, *twelve troyounces;* Sugar [refined], *thirty-six troyounces.* Beat the Orange Peel with the Sugar, gradually added, until they are thoroughly mixed." *U. S.,* 1870.

This confection is not used as frequently as it deserves to be. It is, when well made, a grateful aromatic vehicle or adjuvant for tonic and purgative powders.

Confectio Opii, Confection of Opium, which was the modern substitute for the mediæval preparations known as *theriaca* and *mithridate,* has been finally dropped from both Pharmacopœias. One grain of opium was contained in about thirty-six grains of the former United States confection, and in about forty grains of the British. The following is the U. S. Pharmacopœia (1870) formula: "Take of Opium, in fine powder, *two hundred and seventy grains;* Aromatic Powder, *six troyounces;* Clarified Honey, *fourteen troyounces.* Rub the Opium with the Aromatic Powder, then add the Honey, and beat the whole together until thoroughly mixed." *U. S.,* 1870.

COPAIBA. U. S., Br.

COPAIBA Copaib. [Balsam of Copaiba, Copaiva]

(cō-pā'ĭ-bą)

"An oleoresin derived from South American species of *Copaiba* (Fam. *Leguminosæ*)." *U. S.* "Copaiba is the oleo-resin obtained by incision from the trunk of various species of Copaifera, *Linn.*" *Br.*

Balsamum Copaiferarum; Balsam Copaiba, Balsam Capivi; Copahu, *Fr. Cod.;* Oléo-résine (Baume) de Copahu, *Fr.;* Balsamum Copaivæ, *P. G.;* Copaiva; Copaivabalsam, *G.;* Balsamo di Copaive, *It.;* Copaiba, Balsamo de Copaiva, *Sp.*

Copaiba was first noticed in a work published by Purchas, in England, in 1625. The next reference to it was by Cristoval d'Acuña, in 1638. In 1648, Marcgraf and Piso gave a detailed account of the tree which produces it, and the methods of gathering it. Jacquin in 1763 described a species of Copaifera, growing in Martinique, which he named *C. officinalis.* As this was believed to be the same plant with the one observed by Marcgraf in Brazil, it was adopted in the Pharmacopœias, but their identity was denied; and Desfontaines proposed for Jacquin's species the title of *C. Jacquini,* in honor of that botanist. It is now known that many species of *Copaiba* (*Copaifera*) exist in South America, and all of them, according to Martius, yield copaiba. Besides *C. officinalis* (L.) Jacquin, the following yield Copaiba: *C. guianensis* (Desf.) O. Kuntze, *C. Langsdorffii* (Desf.) O. Kuntze, and *C. coriacea* (Mart.) O. Kuntze.

The juice is obtained by making a square chamber in the stems of the trees, reaching to the very center; and the operation is said to be repeated several times during the same season. It is asserted that a single tree will yield about forty liters. As it flows from the wound, it is clear, colorless, and very thin, but it soon acquires a thicker consistence, and a yellowish tinge. It is most largely collected in the provinces of Para and Maranham, in Brazil, and is brought to this country from the port of Para, in small casks or barrels. Large quantities of it come from Maracaibo, in Venezuela, and from other ports on the Caribbean Sea, whence it is brought in casks, demijohns, cans, jugs, etc. The drug is also exported from Angostura, Cayenne, Rio Janeiro, and some of the West India islands.

C. officinalis is a native of Venezuela, and grows in the province of Carthagena, mingled with the trees which afford the balsam of Tolu. It grows also in some of the West India islands, particularly Trinidad and Martinique. This is the source of the Maracaibo or Venezuela Copaiba, which is also obtained in part from *C. guianensis.* This variety of Copaiba is distinguished by being dextrogyrate, more viscid and darker in color.

Numerous varieties of true South American copaiba exist in commerce, known under the name of the various ports of shipment. The most important of these varieties besides Maracaibo is the Para or Maranham Copaibo, which is derived from *C. Langsdorffii* and *C. coriacea,* which is characterized by being optically lævogyrate. The other varieties are Bahia, Carthagena, Maranham, and Cayenne. Each one of these varieties has been referred (see *P. J.,* 1901, lxvi, 325) to a special species of the genus Copaiba, but there is little reason for supposing that this reference is accurate, and there is much reason for believing that various trees contribute to a single variety of copaiba. The following table, according to the researches of Umney and Bennett, shows the specific gravities and percentage of oil of the five most important of these copaibas:

Name.	Sp. gr.	Per cent. of oil.	Resin.
Bahia	0.938	49.7	Soft.
Carthagena	0.970	41.3	Brittle.
Maracaibo	0.969	42.5	Firm, but not easily pulverized.
Maranham	0.990	41.8	Brittle.
Para	0.920	62.4	Very soft.

All of the above varieties answered to the solubility and Gurjun balsam tests.

It will be noticed that the Para and Bahia specimens examined by Umney failed to comply with the tests of the U. S. Pharmacopœia (1890), and yet, supposing that the oil represents the chief therapeutic principle of copaiba, these varieties lead all the others. The German

Pharmacopœia requires that the specific gravity shall be 0.98 to 0.99, and that the acid number shall fall between 75.6 and 84, and the ester number be not more than 8.4. Dieterich. (*P. J.*, April, 1899, and March, 1900.) *Surinam copaiba* is a yellowish or brownish-yellow liquid, of varying consistence; it may be distinguished from Maracaibo copaiba by the fact that one drop of it dissolved in 1 mil of acetic anhydride gives a fine blue color on the addition of a drop of sulphuric acid. (*P. J.*, Nov., 1904.)

According to E. Keto, copaiba of Maracaibo has a density of 0.999; a coefficient of acidity of 85.4; of etherification of 6.7; while that of Para has a density of 0.92; a coefficient of acidity of 19.4; of etherification of 7.4.

Properties.—Copaiba is a clear, transparent liquid, usually of the consistence of olive oil, of a pale yellow color, a peculiar not unpleasant odor, and a bitterish, hot, nauseous taste. Its sp. gr. varies ordinarily from 0.950 to 1.000, but has been known to be as low as 0.916. (Procter, *A. J. P.*, xxii, 292.) It is insoluble in water, but entirely soluble in absolute alcohol, ether, and the fixed and volatile oils. Strong alkaline solutions dissolve it perfectly; but the resulting solution becomes turbid when largely diluted with water. With the alkalies and alkaline earths it forms compounds, in which the resin of the copaiba acts the part of an acid. It dissolves magnesia, especially with the aid of heat, and even disengages carbon dioxide from the magnesium carbonate. If triturated with a sixteenth of its weight of magnesium oxide and a little water and set aside, it gradually assumes a solid consistence, and a similar change is produced with calcium hydroxide. *Solid Copaiba* or *Mass of Copaiba* was official in the U. S. P., 1890, and is now official in the National Formulary IV, Part III. See also U. S. Dispensatory, 19th edition, p. 398. The essential consituents of copaiba are volatile oil and resin, with at times small quantities of acids. As it contains no benzoic acid, it cannot properly be called *balsam of copaiba.* The substances which it most closely resembles, both in composition and in properties, are the turpentines. (See *Oleum Copaibæ.*) For a description of an apparatus for distilling the volatile oil, see a paper by R. A. Cripps in *C. D.*, 1892, 282. Cripps found commercial copaiba to contain the following percentages of volatile oil: 40.95, 45, 45.3, 46.4, 47.8, 48.2, 49.6, 50.4, 50.8, 53.3, 59.6. J. C. Umney (*A. J. P.*, 1893, 544) found in African copaiba 39 per cent. of an oil of 0.918 specific gravity and with a rotation of + 20° 42′, the last character distinguishing it from the other varieties which yield lævorotatory oils.

The official description of Copaiba is as follows: "A pale yellow to brownish-yellow, more or less viscid liquid, either without fluorescence or with only a slightly greenish fluorescence; having a peculiar, aromatic odor, and a persistent, bitter, and acrid taste. It is insoluble in water and partly soluble in alcohol. Soluble, showing not more than a slight opalescence, in dehydrated alcohol, carbon disulphide, or in fixed or volatile oils; completely soluble in chloroform or ether and also soluble in an equal volume of petroleum benzin, a further addition of the solvent producing a flocculent precipitate. Specific gravity: 0.940 to 0.995 at 25° C. (77° F.). When heated on a water bath, no odor of oil of turpentine is evolved; and when all of the volatile oil has been driven off, a hard and brittle resin remains, weighing not less than 36 per cent. of the original weight of the Copaiba taken (*paraffin or fatty oils*). To about 1 Gm. of Copaiba, accurately weighed, add 50 mils of alcohol and 1 mil of phenolphthalein T.S., then titrate the solution with half-normal potassium hydroxide V.S. It shows an acid value of not less than 28 nor more than 95. Dissolve 3 or 4 drops of the volatile oil separated from Copaiba by distillation with steam, in 3 mils of glacial acetic acid, mix the solution with 1 drop of a freshly prepared aqueous solution of sodium nitrite (1 in 10), and carefully underlay this with 2 mils of sulphuric acid. The acetic layer is not colored pink (*gurjun balsam*). Shake 5 mils of Copaiba with 15 mils of alcohol and then heat the mixture to boiling for one minute; no oil separates after cooling and allowing it to stand for one hour (*paraffin oils*). The volatile oil separated from Copaiba by distillation with steam does not boil below 250° C. (482° F.), and shows an angle of rotation in a 100 mm. tube of not less than –7° at 25° C. (77° F.). (*African Copaiba*)." *U. S.*

"A more or less viscous liquid, generally transparent and occasionally fluorescent, yellow to golden brown. Specific gravity 0.975 to 0.995. Entirely soluble in *absolute alcohol*; soluble in four times its volume of *petroleum spirit*, the solution yielding only a slight filmy deposit on standing. Aromatic, characteristic odor; taste acrid, somewhat bitter, persistent. Loses about 45 per cent. of its weight when heated for forty-eight hours to 100° C. (212° F.). Forms a transparent solution with one-third of its volume of *solution of ammonia.* Four drops carefully added to a mixture of 5 millilitres of *glacial acetic acid* with four drops of *nitric acid* do not yield a purplish or violet color (absence of gurjun balsam). 1 gramme dissolved in 25 millilitres of *absolute alcohol* requires for neutralisation not less than 2.7 millilitres of *N/2 alcoholic solution of potassium hydroxide, solution of phenolphthalein* being used as indicator (presence of a due proportion of acid resins). The volatile oil distilled from it responds to the tests described under 'Oleum Copaibæ.'" *Br.*

The *resinous* mass which remains after the distillation of the oil is hard, brittle, translucent, greenish-brown, and nearly destitute of odor and taste. By mixing it with the oil in proper proportion, we may obtain a liquid identical or nearly so with the original juice. This resinous mass is of an acid character, and yields a series of amorphous salts; it may be obtained pure by exposing a mixture of 9 parts of copaiba and 2 parts of aqueous ammonia (sp.

gr. 0.95) to a temperature of 10° C. (50° F.). In this way crystals of *copaivic acid,* $C_{20}H_{30}O_2$, are obtained. This acid agrees with the *abietic acid* of rosin in composition, but not in properties. Copaivic acid is readily soluble in alcohol, and especially in warmed copaiba itself; much less soluble in ether. When recrystallized from alcohol, copaivic acid fuses at 116° to 117° C. (241°–242.6° F.). (*A. J. P.,* 1879, p. 305.)

An analogous substance, *oxycopaivic acid,* $C_{20}H_{28}O_3$, was found in 1841 by H. von Fehling in Para copaiba, and Strauss, in 1865, extracted *meta-copaivic acid,* $C_{20}H_{34}O_4$, from Maracaibo copaiba. Copaivic acid forms crystallizable salts with alkalies, and *sodium copaivate,* $NaC_{20}H_{29}O_2$, made by combining molecular quantities of the acid and soda, is asserted by Zlamál and Roquette to be more efficient than any other preparation of copaiba. Tschirch (*Harze und Harzbehälter,* 1900, p. 297) obtained from Maracaibo balsam a crystalline resin acid corresponding in many respects with Strauss's metacopaivic acid, to which, however, he gave the formula $C_{11}H_{16}O_2$, finding a melting point 89° to 90° C. (192.2°–194° F.) as against 205° to 206° C. (401°–402.8° F.) for Strauss's acid. Para balsam was found by Tschirch to contain two crystallizable resin acids together with several uncrystallizable ones. African copaiba balsam he found to contain a characteristic acid to which he gave the name *illurinic acid* and the formula $C_{14}H_{20}O_2$ or possibly $C_{21}H_{30}O_3$. Keto, who worked out the preceding results jointly with Tschirch, has since published some additional results. (*J. P. C.,* 1902, p. 381.) He finds in Para balsam the two crystallizable acids referred to above, one of which he names *paracopaibic acid* with the formula $C_{20}H_{32}O_3$ and fusing point 142° to 145° C. (287.6°–293° F.), and the other *homoparacopaibic acid,* $C_{18}H_{28}O_3$, fusing at 111° to 112° C. (231.8°–233.6° F.). To *illurinic acid* mentioned by Tschirch he gives the formula $C_{20}H_{28}O_3$ and the melting point 128° C. (262.4° F.).

Copaiba, upon exposure to the air, acquires a deep color, a thicker consistence, and greater density, and, if spread out upon an extended surface, ultimately becomes dry and brittle. This change is owing partly to the volatilization and partly to the oxidation of the essential oil. As it is the soft resin that results from the oxidation of the oil, it follows that the proportion of this resin increases with age. Considerable diversity must, therefore, exist in the drug, and in its physical properties and in the proportions of its ingredients, according to its age and degree of exposure. Similar differences also exist in the copaiba procured from different sources. Thus, that of the *West Indies,* when compared with the *Brazilian,* which is the variety above described, and in common use, is of a thicker consistence, of a deeper or darker yellow color, less transparent, and of a less agreeable, more terebinthinate odor. They differ also, as observed by Buignet, in their action on polarized light, in which they differ not only in degree, but sometimes also even in direction. (*J. P. C.,* Oct., 1861, pp. 266–7.) It is not impossible that differences may exist in the drug according to the circumstances of its collection. The species of Copaifera from which the oleoresin is collected, as well as the age of the tree, its position, and the season of collection, must also have influence over the product. It is highly probable that the resinous matter results from the oxidation of the oil in the cells of the plant, and that the less elaborated the oleoresin may be, the larger proportion it will contain of the oil. It is said that a volatile oil flows abundantly from a tree near Bogota, which is employed to adulterate the copaiba collected in that vicinity and shipped from Maracaibo and other neighboring ports. *African Copaiba,* or *Balsam of Illurine,* which reached the London market first in 1891, from West Africa, is a brownish substance, having a consistency similar to the Maracaibo copaiba, and a greenish fluorescence. Its aromatic odor is entirely different from that of copaiba; its taste is biting, with an after-taste of bitterness. According to Keto (*J. P. C.,* 1902, 381), its density is 0.9905; its coefficient of acidity 55.5; of etherification 8.3. It is soluble in chloroform and petroleum benzin, also in ether, with which it makes an opalescent liquid. Its solution in absolute alcohol, or alcohol of 95 per cent. is not limpid. From it Keto separated *illurinic acid.* Its volatile oil is of a pale yellow color, with a strong odor entirely different from that of copaiba. The residue which remains after the distillation consists of two resins, one soluble, the other insoluble, in alcohol. This oleoresin probably shares the medicinal properties of true copaiba, and is the product of *Hardwickia Mannii* Oliver, a tree closely allied to the true copaibas. (See *Apoth. Zeit.,* 1894, p. 9.)

Adulterations.—Copaiba is often adulterated with a fixed oil, especially castor oil, which, in consequence of its solubility, cannot, like the others, be detected by alcohol. Various plans have been proposed for recognizing the castor oil. The simplest is to boil a drachm of the copaiba in a pint of water until the liquid is wholly evaporated. If the copaiba contains a fixed oil, the residue will be more or less soft, according to the quantity present; otherwise it will be hard. Magnesium carbonate, potassium hydroxide, and sulphuric acid have also been proposed as tests. In the old Edinburgh Pharmacopœia it was stated that copaiba "dissolves a fourth part of its weight of magnesium carbonate, with the aid of a gentle heat, and continues translucent." The presence of a small proportion of any fixed oil renders the mixture opaque. One part of potassium hydroxide dissolved in two of water forms a clear solution with nine parts of pure copaiba, and the liquid continues clear when moderately diluted with water or alcohol; but the presence of one-sixth of fixed oil in the copaiba occasions more or less opacity in the liquid, and half the quantity causes the precipitation of white flakes in

a few hours. (Stolze.) Turpentine, which is said to be sometimes added to copaiba, may be detected by its odor, especially if the copaiba be heated. According to Redwood, most of the proposed tests of the purity of copaiba are liable to fallacy, and the best measure of its activity is the quantity of volatile oil it affords by distillation. Castor oil, Venice turpentine, linseed oil, or gurjun balsam may be detected by means of petroleum benzin, which makes a clear solution with pure copaiba, but if either of the substances mentioned be present a milky mixture, which soon settles into two layers, is formed, the copaiba solution being on top. (*A. J. P.*, July, 1873; *Proc. A. Ph. A.*, xxiv, 191, xxvi, 286.) Maisch has found that *ten* volumes of petroleum benzin, instead of *three* as proposed by Wayne, must be added to one of copaiba to get the best results from this test. Indeed, it has been shown that pure copaiba will sometimes show turbidity when mixed with petroleum benzin. (*A. J. P.*, 1877, p. 131.) Some years since, a substance was imported into New York, under the name of *red copaiba,* which did not possess a single characteristic of the genuine drug. It was of a thick, semi-fluid consistence, not unlike that of balsam of Tolu, as it often reaches us, of a brown color similar to that of the same balsam, though darker, and of an unpleasant yet somewhat aromatic odor, recalling that of liquidambar, but less agreeable. Its origin is unknown. Hager recommends the use of absolute alcohol, which he says completely dissolves, without turbidity, all the varieties of copaiba except the Para, whose solution on standing clears itself by the deposition of a few white flakes. J. M. Fulton asserts that some pure copaibas are not entirely dissolved by absolute alcohol. (*A. J. P.*, 1877.) For additional tests and criticisms by Beckurts and Brueche, see *A. Pharm.*, 1891, p. 90; also *Proc. A. Ph. A.*, 1892, 635. For Hager's test, see *C. D.*, 1894, 740. Dodge and Olcott (*Am. Drug.*, 1895, 5) describe a test to detect gurjun balsam in copaiba, which Kebler regards as the most reliable yet proposed; it is as follows. Four drops of the suspected sample, dissolved in half a fluidounce of glacial acetic acid, will, if pure, remain colorless and clear, or but slightly cloudy, if from four to six drops of pure nitric acid be dropped into the solution. If the sample be pure gurjun balsam, the mixture will have a deep purple color; if a mixture of the two balsams, the depth of color will vary according to the amount of the adulterant, as small a proportion as 2 per cent. being discoverable; a modification of this test is now official. (See also *A. J. P.*, 1896, 143, and 1897, 394.) For a valuable paper on Copaiba by A. R. L. Dohme, see *Proc. A. Ph. A.*, 1904, 322.

Uses.—Copaiba is gently stimulant, diuretic, laxative, and in very large doses often actively purgative. It produces, when swallowed, a sense of heat in the throat and stomach, and extends an irritant action not only throughout the alimentary canal, but also to the urinary passages, and in fact, in a greater or less degree, to the whole mucous membrane, for which it appears to have a strong affinity. The urine acquires a peculiar odor during its use, and its odor may be detected in the breath. It sometimes occasions an eruption upon the skin resembling that of measles, and attended with disagreeable itching and tingling, or even violent pemphigus. (*N. Y. M. J.*, Jan., 1873, p. 416.) Nausea and vomiting, painful purgation, strangury and bloody urine, and a general state of fever are caused by excessive doses. As a remedy it has been found useful in *catarrhs,* particularly those of a chronic character. Thus, it is given with occasional advantage in *leucorrhea, chronic cystitis, chronic diarrhea, hemorrhoids,* and *chronic bronchitis.* The complaint, however, in which it is most employed is *gonorrhea.* It should not be administered in the first stages, when the inflammation is severe and acute, nor is it applicable to very chronic forms of the disorder, such as gleet. It was formerly much esteemed as a vulnerary and as an application to *ulcers,* but it is now seldom used externally. Ruschenberger recommends it locally in *chilblains.* (*Med. Examiner,* i, 77.)

Both the volatile oil and the resin are eliminated by the kidneys in an altered condition; if to the urine of a person taking the drug, nitric acid be added, a precipitate is thrown down, which may be mistaken for albumin. The volatile oil is more active than is the resin, which is not, however, inert. Wilks, of Guy's Hospital, London, speaks of the resin with great confidence as a hydragogue diuretic in obstinate *dropsy,* given in the dose of fifteen or twenty grains three times a day.

It may be given dropped on sugar, but in this form is often so exceedingly offensive as to render some concealment of its nauseous qualities necessary. A less disagreeable form is that of emulsion, prepared by rubbing the copaiba first with mucilage, or the yolk of an egg, and sugar, and afterwards with some aromatic water, as that of mint or cinnamon. The *volatile oil,* which is official in the British Pharmacopœia, may be given in the dose of ten or fifteen minims (0.6–0.9 mil) in emulsion, or, as is almost universally preferred, in capsules.

Dose, of copaiba, from fifteen minims to a fluidrachm (1.0–3.75 mils) three times a day, or a smaller quantity repeated more frequently.

Off. Prep.—Massa Copaibæ, *N. F.;* Mistura Copaibæ, *N. F.;* Mistura Copaibæ et Opii, *N. F.;* Oleum Copaibæ, *Br.*

CORIANDRUM. U. S. (Br.)

CORIANDER Coriand. [Coriander Seed]

(cō-rĭ-ăn'drum)

"The dried ripe fruit of *Coriandrum sativum* Linné (Fam. *Umbelliferæ*), without the presence or admixture of more than 5 per cent. of other fruits, seeds, or foreign matter." *U. S.* "Coriander Fruit is the dried ripe fruit of Coriandrum sativum, *Linn.*" *Br.*

Coriandri Fructus, *Br.;* Coriander Fruit; Coriandre, *Fr. Cod.;* Koriander, *G.;* Coriandro, *It.;* Cilantro, *Sp.*

Coriandrum sativum is an annual plant, with an erect branching stem rising about two feet, and furnished with compound leaves, of which the upper are thrice ternate, with linear pointed leaflets, the lower pinnate, with the pinnæ cut into irregular serrated lobes like those of parsley. The flowers are white or rose-colored, and in compound terminal umbels; the fruit globular, and composed of two concavo-convex mericarps. *C. sativum* is a native of Italy, but at present grows wild in most parts of Europe, having become naturalized in consequence of its extended cultivation. The flowers appear in June, and the fruit ripens in August. It is a singular fact that all parts of the fresh plant are extremely fetid when bruised, while the fruit becomes fragrant by drying. This is the official portion. The chief supplies come from Russia, Morocco, Holland, and Hungary. Attempts have been made to cultivate the plant in Vermont. The amount annually imported into the United States is over 1,000,000 pounds. The drug not infrequently contains a large admixture of earthy and stony substances as well as stems and similar inert matter. Blome reports finding a sample of Coriander that contained 20 per cent. of flaxseed. LaWall has found leguminous starch in a specimen of powdered Coriander, probably from vetch seed which is sometimes accidentally present.

The fruit is officially described as follows: "Mericarps usually coherent; cremocarp nearly globular, from 3 to 5 mm. in diameter; externally light brown or rose colored; summit with 5 calyx teeth and a short stylopodium, each mericarp with 5 prominent, straight, longitudinal, primary ribs and 4 indistinct, undulate secondary ribs; mericarps easily separated, deeply concave on the inner or commissural surface and showing in transverse section 2 vittæ (oil tubes) on the inner surface of each. Under the microscope, sections of Coriander show an epidermis of small cells with thick walls; a layer of several rows of thin-walled more or less collapsed parenchyma separated from a broad zone of strongly lignified, sclerenchymatous fibers which extend as a continuous ring in the mesocarp of each of the mericarps; 2 or 3 layers of large, tangentially elongated, thin-walled parenchyma cells, frequently with numerous large lysigenous intercellular spaces; inner epidermis of large tabular cells, the inner yellowish walls being considerably thickened and closely coherent to the brownish cells of the seed-coat; commissural surface with 2 large, elliptical vittæ; the cells of the pericarp separated from the seed-coat and forming a large elliptical cavity; endosperm distinctly reniform in outline and consisting of tabular or polygonal thick-walled cells containing numerous large aleurone grains each with a rosette aggregate or prism of calcium oxalate. The powder is light brown, consisting chiefly of fragments of endosperm and lignified tissues of the pericarp; calcium oxalate crystals numerous, from 0.003 to 0.01 mm. in diameter, mostly in rosette aggregates, either isolated or in aleurone grains; sclerenchymatous fibers irregularly curved, having thick, yellowish, lignified walls and numerous simple pores; numerous globules of fixed oil; fragments of light yellow vittæ few, associated with elongated polygonal epidermal cells. Coriander yields not less than 0.5 per cent. of volatile extractive, soluble in ether (see Part II, Test No. 12). Coriander yields not more than 7 per cent. of ash." *U. S.*

"Nearly globular, about five millimetres in diameter, uniform brownish-yellow in color, and glabrous. Mericarps usually closely united, and crowned by the calyx teeth and stylopod. Primary ridges wavy and inconspicuous; secondary ridges straight and more prominent. In transverse section, two vittæ on the commissural surface of each mericarp. Aromatic odor, especially when bruised; taste agreeable." *Br.*

The aromatic taste and odor of coriander depend on a *volatile oil,* which may be obtained separate by distillation. One pound of the seeds yields forty-two grains of the oil. (Zeller.) This is colorless or pale yellow, with an agreeable odor of coriander, a mild aromatic taste, and a sp. gr. varying from 0.87 to 0.88. Its main constituent, according to Semmler (*Ber. d. Chem. Ges.,* xxiv, 206), is what was first called *coriandrol,* but is now recognized as right rotatory *linalool,* $C_{10}H_{18}O$, boiling between 194° and 198° C. (381.2°–388.4° F.). Besides this, about 5 per cent. of *dextro-pinene* was isolated, boiling between 156° and 160° C. (312.8°–320° F.). It is one of the most permanent volatile oils, long resisting oxidation. The fruit's virtues are imparted to alcohol by maceration, and less readily to water.

Uses.—Coriander is a rather feeble aromatic. It is almost exclusively employed in combination with other medicines, either to cover their taste, to render them acceptable to the stomach, or to correct their griping qualities. It was well known to the ancients.

Dose, twenty to sixty grains (1.3–3.9 Gm.).

Off. Prep.—Confectio Sennæ, *Br., N. F.;* Syrupus Rhei, *Br.;* Syrupus Sennæ (from Oil), *U. S.;* Tinctura Rhei Composita, *Br.;* Tinctura Sennæ Composita, *Br.;* Fluidextractum Stillingiæ Compositum, *N. F.;* Infusum Gentianæ Compositum, *N. F.*

COTARNINÆ HYDROCHLORIDUM. U. S.

COTARNINE HYDROCHLORIDE Cotarn. Hydrochl. [Cotarnine Chloride]

(cō-tär-nī'næ hȳ-drǫ-ȼhlō'rī-dŭm)

"Quarternary oxymethyl-oxymethylene-dihydro-isoquinoline chloride [$C_{12}H_{14}O_3NCl$ or $(CH_3O)(CH_2O_2).C_9H_6N(CH_3)Cl = 255.58$] obtained by hydrolyzing narcotine, and treating the resulting cotarnine [$(CH_3O)(CH_2O_2)C_8H_5(CHO).NH(CH_3)$] with hydrochloric acid." *U. S.*

This compound was introduced into the U. S. P. IX and is officially described as follows: "Cotarnine Hydrochloride occurs as a yellow, crystal-

line powder; odorless and deliquescent in moist air. It is very soluble in water and alcohol, yielding yellow solutions. Its aqueous solution (1 in 20) is neutral to litmus. Silver nitrate T.S. when added to an aqueous solution of Cotarnine Hydrochloride produces a white precipitate insoluble in nitric acid. About 0.2 Gm. of Cotarnine Hydrochloride, dissolved in 10 mils of distilled water, yields a brown precipitate of cotarnine periodide on the addition of 10 mils of tenth-normal iodine V.S. When this precipitate is collected on a filter and dried to constant weight over sulphuric acid, it melts between 142° and 144° C. (287.6° and 291.2° F.). Heat gradually 0.1 Gm. of Cotarnine Hydrochloride over a Bunsen burner; it is decomposed, evolving characteristic, disagreeable vapors and yielding a reddish-brown liquid, which gradually changes to a hard charred mass. No weighable ash remains on the incineration of this mass. Dissolve about 0.5 Gm. of Cotarnine Hydrochloride in 10 mils of distilled water and add 2 mils of an aqueous solution of sodium hydroxide (15 per cent.). A milk-white precipitate is produced which dissolves on agitation, but is reprecipitated from the solution after standing for some time, leaving the supernatant liquid clear and but faintly yellow." *U. S.*

Uses.—The fact that the only chemical difference between hydrastinine and cotarnine is that in the latter OCH_3 is substituted for one atom of hydrogen led Freund to suggest the substitution of cotarnine for hydrastinine. It has been physiologically studied by Falk (*Th. M.*, 1896, x), Kehrer (*Monat. fur Geburts. und Gynakol.*, 1907, xxvi, p. 709), Laidlaw (*Bio-Chem. J.*, 1910, v, p. 243), and others. It differs in its action from hydrastinine, in that it has practically no influence upon the circulation, but resembles it in its depressant action upon the spinal cord, and in its stimulant effect upon the uterine muscle, and according to Laidlaw, also in the fact that it does not increase the coagulability of the blood.

Under the trade names of *stypticin* and *styptol* the hydrochloride and phthalate of cotarnine, respectively, have been extensively used in the treatment of various forms of *hemorrhage*, especially those from the uterus. Of their value in *menorrhagia* and *metrorrhagia* there is hardly any room for doubt, but that they are equally successful in hemorrhages from other parts of the body, may be questioned, although there is some clinical evidence as to their utility. Each of these preparations is marketed in the form of tablets, containing five-sixths of a grain (0.05 Gm.), of which one to two may be given at a dose, and repeated several times daily. Single doses may be given hypodermically in cases of emergency, as high as three or four grains (0.2–0.26 Gm.).

A double salt of cotarnine hydrochloride and ferric chloride appears on the market under the trade name of *cotargit* and is alleged to contain still better styptic properties than cotarnine. It occurs as a ruby-red crystalline powder freely soluble in water.

Dose, three-fourths of a grain to three grains (0.048–0.2 Gm.).

CREOSOTI CARBONAS. U. S.

CREOSOTE CARBONATE Creosot. Carb.

(crē-o-sō'tī cär'bo-năs)

"A mixture of the carbonates of various constituents of creosote, chiefly guaiacol and creosol." *U. S.*

Creosote carbonate is known also by the trade names of *creosotal* and *creosotal-Heyden;* it is made by treating a solution of creosote and sodium hydroxide with carbonyl chloride. It is officially described as follows: "Creosote Carbonate is a clear, colorless or yellowish, viscid liquid, odorless, and tasteless, or having a slight odor and taste of creosote. On prolonged exposure to a low temperature, crystals of guaiacol carbonate separate, which redissolve on warming. Creosote Carbonate is insoluble in water and freely soluble in alcohol, soluble in petroleum benzin or fixed oils; it is miscible with chloroform or benzene. Specific gravity: 1.145 to 1.170 at 25° C. (77° F.). Heat about 0.5 mil of Creosote Carbonate for a few minutes with 10 mils of alcoholic potassium hydroxide T.S., and cool the mixture; a crystalline precipitate forms, which effervesces with acids. Incinerate about 1 Gm. of Creosote Carbonate; not more than 0.1 per cent. of ash remains. A saturated alcoholic solution of Creosote Carbonate is neutral to moistened litmus paper, and acquires only a yellow color on the addition of ferric chloride T.S. (*creosote*). Heat 25 mils of Creosote Carbonate on a water bath for half an hour with a solution of 15 Gm. of potassium hydroxide in 100 mils of alcohol, then evaporate the alcohol and mix the residue with an excess of hydrochloric acid; a liquid composed of two layers is obtained. On now separating the dark layer of creosote and shaking it with successive portions of 10 mils each of distilled water until the washings are only slightly acid to litmus, it has the boiling point given under *Creosotum;* the distillate, after separation of adhering water, responds to the remaining tests of identity and purity under *Creosotum.*" *U. S.*

Uses.—It is used in the treatment of *tuberculosis, pneumonia* and *bronchitis,* and is recommended as an intestinal antiseptic. It is reputed to be less irritant than is creosote. It is asserted to have an equally beneficial effect upon the bronchial mucosa and much less tendency to disturb digestion.

Dose, from five to thirty minims (0.3–1.8 mils) preferably in emulsion or capsules.

CREOSOTUM. U. S., Br.

CREOSOTE Creosot. [Creasote]

(crē-o-sō'tŭm)

"A mixture of phenols and phenol derivatives, chiefly guaiacol and creosol, obtained during the distillation of wood-tar. Preserve it in

tightly-stoppered, dark amber-colored bottles." *U. S.* "Creosote is a mixture of phenols which may be obtained by the distillation of beech tar, and consists chiefly of guaiacol and creosol." *Br.*

Creasotum, *Br.* (1885); Créosote du Goudron de Bois, *Fr. Cod.*; Créosote, *Fr.*; Kreosotum, *P. G.*; Kreosot, Buchenholstheerkreosot, *G.*; Creosoto, *It.*; Creosota, *Sp.*

This is a substance discovered in 1830 by Reichenbach in the products of the distillation of wood. This distillation of wood yields products very analogous to one fraction of the coal tar obtained by the destructive distillation of bituminous coal. This fraction is the heavy oil of coal tar, which comes over between 165° C. (329° F.) and 200° C. (392° F.): it is often called "*coal tar creosote,*" and contains a group of phenols, including carbolic acid, now known officially as *phenol,* C_6H_6O, boiling at a temperature not higher than 188° C. (370.4° F.), *cresylic acid,* or *cresol,* C_7H_8O, boiling at from 195° to 205° C. (383°–401° F.), and *xylenol,* or *dimethyl phenol,* $C_8H_{10}O$, boiling at 211° C. (411.8° F.). Wood tar is a complex mixture of phenoloid bodies. These are chiefly the acid methylic ethers of catechol (or pyrocatechin) and its homologues.

Preparation.—Creosote is obtained either from wood tar or from crude pyroligneous acid. When wood tar is used, it is distilled until it has attained the consistence of pitch. The distilled liquid divides itself into three layers, an aqueous between two oily layers. The inferior oily layer, which alone contains the creosote, is separated, and saturated with sodium carbonate to remove acetic acid. The liquid is allowed to rest, and the new oil which separates is decanted from it. This oil is distilled and yields products lighter than water, and a liquid heavier. The latter alone is preserved, and, after having been agitated repeatedly with weak phosphoric acid to neutralize ammonia, is allowed to remain at rest for some time. It is next washed until it is free from acidity, and then distilled with a fresh portion of weak phosphoric acid, care being taken to cohobate from time to time. The oily liquid thus rectified is colorless, and contains much creosote, but also a portion of light oil distillate. To separate the latter, the liquid is mixed with a solution of sodium hydroxide of the density 1.12, which dissolves the creosote, but not the light oil. The oil, which floats from its levity, is then separated, and the alkaline solution of the creosote is exposed to the air, until it becomes brown in consequence of the decomposition of a foreign matter, and is then saturated with sulphuric acid. This sets free the creosote, which is decanted and again distilled. The treatment by solution of soda, sulphuric acid, etc., is to be repeated until the creosote no longer becomes brown by exposure to the air, but only slightly reddish. It is then dissolved in a stronger solution of soda, and distilled again, and finally redistilled for the last time, rejecting the first portion which comes over, on account of its containing much water, and collecting the next portion; care being taken not to push the distillation too far. The product collected is creosote.

When creosote is extracted from pyroligneous acid, the first step is to dissolve sodium sulphate in the acid to saturation. The oil which separates and floats above is decanted, and, having been allowed to remain at rest for a few days, is saturated with potassium carbonate with the assistance of heat, and distilled with water. The oily liquid obtained is of a pale yellow color, and is to be treated as above detailed, in relation to the treatment of the corresponding oil obtained from wood tar.

Properties.—Creosote, when pure, is a colorless oleaginous liquid, of the consistence of oil of almonds, slightly greasy to the touch, volatilizable by heat, and having a caustic, burning taste, and a penetrating, disagreeable odor, like that of smoked meat, and analogous to, yet different from, that of phenol. As met with in commerce, it has frequently a brownish tinge. It burns with a sooty flame. Applied in a concentrated state to the skin, it corrugates and then destroys the cuticle, causing a white spot. On paper it leaves a greasy stain, which disappears in a few hours, or in ten minutes if heated to 100° C. (212° F.). It is a non-conductor of electricity, and refracts light strongly. It is devoid of acid or alkaline reaction. Mixed with water, it forms two layers, one consisting of one part of creosote and about eighty of water, the other, of one part of water and ten of creosote. It dissolves a large proportion of iodine and phosphorus, and a considerable amount of sulphur, especially when assisted by heat. Allen states that in Rhenish creosote guaiacol predominates, while a sample of Morson's creosote from "Stockholm tar," examined by him, boiled at about 217° C. (422.6° F.), and consisted chiefly of creosol.

The U. S. Pharm. describes creosote as "an almost colorless or yellowish, highly refractive, oily liquid, having a penetrating, smoky odor, and a burning, caustic taste; it does not readily become brown on exposure to light. Creosote is slightly soluble in water; it is miscible with alcohol, ether, or fixed or volatile oils. It is neutral or faintly acid to litmus. Specific gravity; not below 1.073 at 25° C. (77° F.). It begins to distil between 195° and 200° C. (383°–392° F.) and not less than 80 per cent. by volume distils between 200° and 220° C. (392°–428° F.). Creosote is inflammable, burning with a luminous, smoky flame. Add 1 drop of ferric chloride T.S. to 10 mils of a saturated aqueous solution of Creosote; the liquid develops a violet-blue color, which is very transient; it then clouds almost instantly, the color passing rapidly from a grayish-green to a muddy brown, with finally the formation of a brown precipitate. Mix equal volumes of Creosote and collodion in a dry test tube; no permanent coagulum is produced (*phenol and so-called "coal-tar creosote"*). Mix 4 mils of Creosote with 4 mils of glycerin; a clear mixture results, from which

a creosotic layer, equal to or greater in volume than the Creosote taken, separates on the addition of 1 mil of water (*"coal-tar creosote"*). Two mils of Creosote requires not less than 10 mils nor more than 18 mils of normal sodium hydroxide V.S. to produce a clear liquid. This liquid remains unclouded on diluting with 50 mils of distilled water (*hydrocarbons and bases*). Shake gently 1 mil of Creosote with 2 mils of petroleum benzin and 2 mils of freshly prepared barium hydroxide T.S., until a uniform mixture is produced. Upon complete separation three distinct layers are visible; a middle layer containing the Creosote, a benzin layer which is neither blue nor muddy, and an aqueous layer which does not acquire a red tint (*cœrulignol and some other high-boiling constituents of wood-tar*)." *U. S.*

The British Pharm. describes Creosote as "a colorless or pale yellow, highly refractive liquid, neutral or faintly acid to *litmus*. Freely soluble in *alcohol* (90 per cent.), in *ether*, in *chloroform*, and in *glacial acetic acid*. Specific gravity not below 1.080. Commences to boil below 200° C. (392° F.). Not less than 75 per cent. distils between 200° and 220° C. (392°–428° F.). A solution (1 in 100) in *alcohol* (90 per cent.) produces with a drop of *T. Sol. of ferric chloride* a green coloration rapidly changing to reddish brown. Dropped on white filter paper and exposed to a temperature of 100° C. (212° F.), it leaves no translucent stain (absence of less volatile liquids)." *Br.*

Creosote dissolves in ammonia. Strong nitric and sulphuric acids decompose it, the former giving rise to reddish vapors, the latter to a red color, which becomes black on the addition of more of the acid. Diluted nitric acid converts it into a brown resin, which, treated with ammonia, and then dissolved in boiling alcohol, gives, by evaporation, certain salts of ammonia, two of which contain new acids, discovered by Laurent. Hydrochloric acid produces no change in it. Morson, of London, gives a test based on the solvent power of glycerin over phenol, which is dissolved by it in all proportions, while pure creosote is insoluble or nearly so, and, consequently, if any liquid assumed to be creosote dissolves largely in glycerin, it probably consists in the whole, or in large part, of phenol. Subsequent experiments appear to show that this test succeeds best with Morson's creosote; beechwood creosote, although pure, sometimes mixes with glycerin without turbidity. Hager modified Morson's test by using a mixture of three parts absolute glycerin and one part water, and this is the basis of the present official test for distinguishing creosote from phenol. With this fairly good results are obtained, according to Allen. A still better test, according to John A. Clark, is an alcoholic solution of iron perchloride (*Tinct. Ferri Perchlor.*, Br.), which with an alcoholic solution of creosote produces a deep greenish-blue color, but with phenol a light brown. (*A. J. P.*, June, 1873, 269.) Creosote dissolves a large number of metallic salts, and reduces some of them to the metallic state, as, for example, silver nitrate and acetate. ***Froehde's reagent*** (a solution of 0.1 Gm. of sodium molybdate in 100 mils of concentrated sulphuric acid) is recommended by E. W. Davy as a distinguishing test for phenol. A drop or two of the doubtful liquid is to be agitated with two fluidrachms of distilled water, the whole filtered, and a drop or two of the test solution added. Pure creosote gives a brown or reddish-brown reaction on standing or slight warming, passing to a light yellowish-brown; with phenol, the brown passing to a maroon soon develops a more or less intense purple. The name creosote refers to its antiseptic properties, being derived from *κρέας, flesh,* and *σώζω, I preserve.*

Impurities and Adulterations.—Creosote is sometimes adulterated with rectified oil of tar and the fixed and volatile oils. All these substances are detected by strong acetic acid, which dissolves the creosote, and leaves them behind, floating above the creosote solution. Creosote from beechwood tar, however, is only partially dissolved by hot acetic acid of ordinary strength. Fixed oils are also discovered by a stain on paper not discharged by heat. Any trace of the matter which produces the brownish tinge is detected by the liquid becoming discolored by exposure to sunshine. Commercial creosote sometimes contains phenol and cresol, from coal tar; and, indeed, much of what has been sold for creosote was nothing more than impure phenol. (See *Phenol.*) It has been already stated that phenol strongly resembles creosote; but, as the effects of the two on the system are very different, it is highly desirable to be able to distinguish between them. Tests for this purpose have been given above, and, with those quoted from the Pharmacopœia, are sufficient for the purpose. The large doses in which creosote is now sometimes given makes the sale of the so-called "coal tar creosote" dangerous, for there would be a strong probability that a patient might be given a large dose of phenol with disastrous effects; all pharmaceutical manufacturers have ceased to label or market "coal tar creosote."

Uses.—The constitution of even genuine beechwood creosote varies very greatly in the proportion of guaiacol and creosol and in the amount of monophenols, and it would seem impossible to get under the name of creosote a fixed medicament. Nevertheless, for practical therapeutic purposes creosote is sufficiently constant in its composition, the physiological and therapeutic action of its various constituents being apparently so closely allied as to make variability in the proportion of these constituents of little importance.

The physiological effects produced by creosote have not been closely studied, but it would appear in many of its properties to resemble phenol. It is, however, much less poisonous and doses as high as thirty to sixty minims have been administered three times a day without harmful results. Freudenthal (*N. Y. M. R.*, April, 1892)

reports a case of a woman who took six hundred drops of creosote in a very short time the ingestion being followed almost immediately by unconsciousness with intense trismus, contracted immobile pupil, and general cyanosis, but recovery was made practically without administration of remedies; subsequently this same patient by graduating the dose was able to take five hundred drops daily without ill effect. Creosote is absorbed readily from the intestinal tract and its elimination is fairly rapid. It escapes chiefly through the kidneys in combination with sulphuric and glycuronic acids, but appears also to be in part eliminated by the lungs. Like phenol, it is, when locally applied, a paralyzant to the sensory nerves. Creosote is distinctly superior to phenol in its anti-bacterial properties, especially in dilute solutions. According to Guttmann (*Z. K. M.*, 1887, xiii) one part of creosote to three thousand completely inhibits the growth of bacteria.

Creosote was originally introduced in the treatment of *phthisis* with the idea that it would exercise an antiseptic action in the lungs. It is, however, extremely questionable whether the drug can reach the pulmonic tissue in sufficient concentration to have any direct antibacterial properties. Its beneficial influence in this disease can be ascribed to its stimulating effect upon the bronchial mucous membrane. For this action it is also a very valuable drug in the treatment of all types of *chronic bronchitis,* especially when there is over-secretion. In tubercular conditions it is generally necessary to give the drug in large doses. The secret of doing this successfully is to see that it is well diluted before ingestion. When being used freely it should never be given in the form of capsules but dissolved in either water or milk. A good rule is that the patient should take at least one-half an ounce of fluid for every drop of creosote; thus if ten minims were to be administered it would require five ounces of water. Perom has recommended the hypodermic administration in *phthisis.* For this purpose he uses a ten per cent. solution in oil of sweet almonds, two injections of eighty minims being given daily. Dor employed intratracheal injections of five per cent. solution in sterile olive oil.

Creosote is also a valuable gastro-intestinal antiseptic in the treatment of *fermentative gastritis* and *enteritis.* It is of service in *nausea* and *vomiting* for its local anesthetic action upon the gastric mucosa. Externally it has been used as a surgical disinfectant, but because of its stronger odor and greater cost is inferior to phenol, but when there is foul discharge, as in fetid *leukorrhea, otorrhea, empyema* or *gangrene,* is by many preferred. It is also useful in various *skin diseases,* both for its local anesthetic and antibacterial properties and has been recommended in *chilblains.* In capillary *hemorrhages* it has some power as a hemostatic but is not capable of arresting bleeding from large vessels. For this effect it has been used locally in the milder types of *uterine hemorrhage* and to stop the bleeding from *leech bites.* As a local application it may be employed in strengths of from one to ten per cent., according to the purpose for which it is used. On account of its local anesthetic and antiseptic influence, it is much employed by dentists for the obtunding of sensitive dentine and as an ingredient of pastes for the destruction of nerves. One or two drops of the pure substance must be carefully introduced into the hollow of the tooth on a little cotton, avoiding contact with the tongue or cheek. To render it effectual, the hollow of the tooth must be well cleansed before it is applied. A mixture of fifteen parts of creosote and ten of collodion is said to have a jelly-like consistence, and to be usefully applied to carious teeth, which it protects from the air; but, as pure creosote does not coagulate collodion, this remark applies properly to the impure phenol before stated to be commonly sold under the same name.

In an overdose creosote acts as a poison, producing giddiness, obscurity of vision, depressed action of the heart, convulsions, and coma. Medicinal treatment consists in evacuation of the poisons and administration of ammonia and other stimulants.

Under the name of *Vapor Creasoti* (*Inhalation of Creasote*), the British Pharmacopœia (1885) directed a preparation consisting of 12 minims of creosote and 8 fluidounces of boiling water, which were directed to be mixed in an inhaling apparatus, so arranged that the air should be made to pass through the solution, and then inhaled. It may be used in chronic inflammation of the air passages.

Mistura Creosoti, Br. Pharm., 1898, is no longer official, it was made by shaking 16 minims each of creosote and spirit of juniper with 1 fluidounce of syrup and enough distilled water to make 16 fluidounces of the mixture.

Dose, of creosote, five to ten minims (0.3–0.6 mil), which may be gradually increased.

Off. Prep.—Aqua Creosoti, *U. S.;* Unguentum Creosoti, *Br.;* Mulla Creosoti Salicylata, *N. F.;* Petroxolinum Creosoti, *N. F.*

CRESOL. U. S., Br.

CRESOL

(crēs′ōl)

"A mixture of isomeric cresols [C_7H_8O or $C_6H_4.CH_3.OH = 108.06$] obtained from coal tar. Preserve it in well-closed containers protected from light." *U. S.* "Cresol is a mixture of isomers of the formula C_7H_7OH, obtained from coal tar. Should be preserved in stoppered amber-colored bottles." *Br.*

Cresolum, Cresolum Purum; Cresylic Acid, Tricresol, Methylphenol, Oxytoluene; Cresol, *Fr.;* Enterol, Trikresoll Kresol, *G.*

Preparation.—Cresol was introduced into the U. S. P. (VIII and IX) mainly for use in making the official compound solution of cresol (*Liquor Cresolis Compositus*), an antiseptic solution well adapted for external uses because

of its miscibility with water. Crude carbolic acid is an impure form of cresol. Cresol is prepared from coal tar by collecting the distillates coming over between 140° C. (284° F.) and 220° C. (428° F.), and purifying these by treatment with solution of sodium hydroxide and hydrochloric acid.

Properties.—These are three isomeric cresols: *orthocresol,* melting at 31° C. (87.8° F.) and boiling at 188° C. (370.4° F.); *metacresol,* a liquid boiling at 201° C. (393.8° F.), but not solidifying even at -80° C. (-112° F.); and *paracresol,* forming colorless prisms, melting at 36° C. (96.8° F.) and boiling at 198° C. (388.4° F.). These cresols are all obtainable by fractional distillation from that portion of coal tar boiling between 190° and 210° C. (374°–410° F.). Cresol of the U. S. P. is "a colorless or yellowish to brown-yellow, highly refractive liquid, becoming darker or assuming a reddish tint with age and on exposure to light, and having a phenol-like, sometimes empyreumatic odor. One mil of Cresol dissolves in about 50 mils of water, usually forming a cloudy solution; it is miscible with alcohol, ether, benzene, petroleum benzin, or glycerin; it is dissolved by solutions of the fixed alkali hydroxides. Specific gravity: 1.030 to 1.038 at 25° C. (77° F.). Not less than 90 per cent. by volume of Cresol distils between 195° and 205° C. (383°–401° F.). A saturated aqueous solution of Cresol is neutral or slightly acid to litmus, and becomes blue-violet on the addition of ferric chloride T.S. A solution of 1 mil of Cresol in 60 mils of water is not more than slightly turbid (*hydrocarbons*)." *U. S.*

"A straw-colored liquid, becoming brown on keeping or on exposure to light. Soluble in 50 parts of *water,* the solution being neutral to *litmus;* freely soluble in *alcohol* (90 per cent.), in *ether,* in *chloroform,* in *glycerin,* and in the fixed and volatile oils. Specific gravity 1.040 to 1.050. When 0.5 millilitre is shaken with 300 millilitres of *water* and filtered, the filtrate gives a transient bluish color on the addition of *T. Sol. of ferric chloride.* Not less than 90 per cent. distils between 195° and 205° C. (383°–401° F.). 10 millilitres shaken with 10 millilitres of an aqueous solution (1 in 10) of *sodium hydroxide* form an almost clear liquid, from which no appreciable oily layer separates on standing for twenty-four hours (limit of hydrocarbon oils). 5 millilitres mixed with 5 millilitres of *glycerin* form a clear solution from which, on the addition of 5 millilitres of *water,* the cresol completely separates (absence of phenol)." *Br.*

Uses.—Cresol is used in medicine solely for its disinfectant properties. It far surpasses phenol in power, both as a germicide and antiseptic. Reed (*Trans. of the Association of Military Surgeons,* U. S., 1894, iv), finds that a one-half per cent. solution of cresol is sufficient to destroy the staphylococcus in less than twenty minutes; a one per cent. solution killed in thirty seconds and is equivalent to a four or five per cent. solution of phenol. Because of the sparing solubility of cresol in water it is generally employed in the form of a soapy solution or emulsion (see *Liquor Cresolis Compositus*). This solution retains the germicidal properties of the cresol, thus Fox (*Report of the Commissioner of Health of the State of Pennsylvania,* 1907, p. 123), finds that one per cent. of the official compound solution of cresol kills non-sporulating bacteria after two minutes' exposure and is superior to a one per cent. solution of phenol. McClintock (*U. S. Hygienic Laboratory Bulletin,* No. 82, April, 1912), gives the phenol coefficient of compound solution of cresol without organic matter 3.0, with organic matter 1.87. (For a list of some of the proprietary preparations of cresol, see p. 1347.) There is probably some difference in the germicidal powers of the various cresols so that the mixture which is known officially as cresol varies more or less in activity. According to Sage (*P. J.,* 1908, lxxx, p. 730) the compound solution of cresol of the British Pharmacopœia has a phenol coefficient varying from 1.25 to 3.75 according to the value of the cresylic acid from which it is made. Other authorities, however, do not find so great a variation.

The statement has been made that cresol is practically non-poisonous, but such is certainly incorrect. It is perhaps somewhat less toxic than phenol, but the difference is not very great, and there have been a number of fatal cases of cresol poisoning reported, as well from its use as a douche as from swallowing. The symptoms have been nausea and vomiting, general depression with a tendency towards stupor, gradually developing into coma, smoking albuminous urine, fall of bodily temperature, and collapse. Friedlander (*Th. M.,* 1907) recommends as antidotes large quantities of oil or the white of egg, which he believes act by preventing absorption; milk and watery fluids are to be avoided.

Cresol is used chiefly as a surgical disinfectant, both for the purposes of sterilizing instruments and as a wound dressing. For the former three to five per cent. of the compound solution should be employed, while for application to wounds one per cent. of the compound solution (representing one-half per cent. of cresol) is generally recommended. Cresol is also employed to a limited extent as a gastro-intestinal antiseptic in various types of *enteritis* and *gastritis.* For this purpose one or two minims (0.06–0.12 mil) of the cresol, well diluted, may be given.

Dose, from two to three minims (0.12–0.2 mil).

Off. Prep.—Liquor Cresolis Compositus, *U. S.* (*Br.*).

CRETA PRÆPARATA. U. S., Br.

PREPARED CHALK Cret. Præp. [Drop Chalk]

(crē'tą præ-pą-rā-tą)

"A native form of calcium carbonate freed from most of its impurities by elutriation and

containing, when dried to constant weight at 200° C. (392° F.), not less than 97 per cent. of $CaCO_3$ (100.07)." *U. S.* "Prepared Chalk is native calcium carbonate, freed from most of its impurities by elutriation." *Br.*

Creta Lævigata; Craie lavée, Craie préparée, *Fr.;* Präparirte Kreide, Schlämmkreide, *G.;* Creta preparada, *Sp.*

Preparation.—Calcium carbonate, in the extended meaning of the term, is the most abundant of simple minerals, constituting, according to its state of aggregation and other peculiarities, the different varieties of calcareous spar, common and shell limestone marble, marl, and chalk. It occurs also in the animal kingdom, forming the principal part of shells, and a small proportion of the bones of the higher orders of animals. It is present in small quantity in most natural waters, being held in solution as the bicarbonate, $Ca(HCO_3)_2$, by the carbon dioxide which they contain. In the waters of limestone districts it is a very common impregnation, and causes purging in those not accustomed to its use. In all such cases, boiling the water, by expelling the carbon dioxide, causes the carbonate to be deposited. It has been shown, however, that calcium carbonate is itself in a slight degree soluble in water; so that a small proportion remains in limestone water which has been long exposed to boiling. That the carbonate is not held in solution by free carbon dioxide is shown by the fact that lime water causes no precipitation. (*J. P. C.,* 4e sér., iii, 147.)

Chalk occurs abundantly in the south of England and the north of France. It exists in massive beds, and very frequently contains nodules of flint, and fossil remains of land and marine animals. According to F. V. Hayden, chalk beds identical with those of Europe extend for 400 miles along the Missouri River in Dakota. Chalk is an insipid, inodorous, insoluble, opaque, soft solid, generally white, but grayish-white when impure. It is rough to the touch, easily pulverized, and breaks with an earthy fracture. It soils the fingers, yields a white trace when drawn across an unyielding surface, and when applied to the tongue adheres slightly. Its sp. gr. varies from 2.3 to 2.6. It is never a perfectly pure calcium carbonate, but contains besides gritty silicious particles, small portions of alumina and ferric oxide. If pure, it is entirely soluble in hydrochloric acid, but usually a little silica is left. If this solution be not precipitated by ammonia, it is free from alumina and iron. Chalk, on account of the gritty particles which it contains, is unfit for medicinal use until it has been reduced to a very fine powder.

Having been thus very minutely divided, it is agitated with water, which upon standing a short time deposits the coarser particles, and, being then poured off, slowly lets fall the remainder in an impalpable state. The former part of the process is called *levigation* the latter *elutriation.* The soft mass which remains after the decanting of the clear liquor is made to fall upon an absorbent surface in small portions, which when dried have a conical shape. Practically, prepared chalk is made on the large scale from *whiting* by the manufacturer.

Properties.—"Prepared Chalk occurs as a white to grayish-white, very fine, amorphous powder, often formed into "conical drops"; odorless and tasteless; permanent in the air. Prepared Chalk is almost insoluble in water; insoluble in alcohol; decomposed and dissolved by diluted acetic, hydrochloric, or nitric acid, with copious effervescence. When a weighed amount of Prepared Chalk is dissolved in diluted hydrochloric acid not more than 2 per cent. of residue remains. Dissolve about 0.1 Gm. of Prepared Chalk in 5 mils of diluted acetic acid and filter the solution; the addition of ammonium oxalate T.S. to the filtrate yields a white precipitate, insoluble in acetic acid but soluble in hydrochloric acid. When heated to full redness, Prepared Chalk gradually loses carbon dioxide and is converted into calcium oxide.

"**Assay.**—Proceed as directed under *Calcii Carbonas Præcipitatus.* It shows, in the dried salt, not less than 97 per cent. of $CaCO_3$. Each gramme of dried Prepared Chalk corresponds to not less than 193.9 mils of tenth-normal oxalic acid V.S." *U. S.*

"White friable masses or a white powder. Yields the *reactions* characteristic of calcium and of carbonates. Yields not more than the slightest characteristic *reactions* for iron, aluminium, magnesium, phosphates, sulphates, or silica. *Arsenic limit* 5 parts per million. A solution of Prepared Chalk in *diluted acetic acid* yields no precipitate with *solution of potassium chromate* (absence of barium carbonate)." *Br.*

Uses.—This is the only form in which chalk is used in medicine. It is an excellent antacid; and, as the salts which it forms in the stomach and bowels, if not astringent, are at least not purgative, it is admirably adapted to *diarrhea* accompanied with acidity. It is also sometimes used in acidity of stomach attending *dyspepsia* and *gout,* when a laxative effect is to be avoided, and it is one of the best antidotes for oxalic acid. It has been employed as an application to *burns* and *ulcers,* which it moderately stimulates, while it absorbs the ichorous discharge and thus prevents it from irritating the diseased surface or the sound skin. It is given internally in the form of powder, or suspended in water by the intervention of gum arabic and sugar. (See *Mistura Cretæ.*) Lozenges of chalk were also official under the name of *Trochisci Cretæ* in the U. S. P. 1890. Prepared chalk is better fitted for chalk mixture than the precipitated calcium carbonate, in consequence of its more impalpable character and greater powers of adhesion.

Dose, from ten to forty grains (0.65–2.6 Gm.).

Off. Prep.—Mistura Cretæ, *U. S.* (from Compound Chalk Powder), *Br.;* Pulvis Cretæ Compositus, *U. S.;* Pulvis Cretæ Aromaticus, *Br., N. F.;* Pulvis Cretæ Aromaticus cum Opio (from Aromatic Chalk Powder), *Br., N. F.*

CUBEBA. U. S. (Br.)

CUBEB Cubeb. [Cubebs]

(cū-bē'bą)

"The dried, full-grown, unripe fruits of *Piper Cubeba* Linné filius (Fam. *Piperaceæ*), without the presence or admixture of more than 5 per cent. of stems or other foreign matter." *U. S.* "Cubebs are the dried full-grown unripe fruits of Piper Cubeba, *Linn. fil.*" *Br.*

Cubebæ Fructus, *Br.*; Fructus (s. Baccæ) Cubebæ, Piper Caudatum; Cubebs, Tailed Pepper; Cubèbe, Cubèbe ou Poivre à Queue, *Fr. Cod.*; Cubebæ, *P. G.*; Kubeben, *G.*; Pepe Cubebe, Cubebe, *It.*; Cubeba, *Sp.*; Kebabeh, *Ar.*

Piper Cubeba is a climbing perennial plant, with a smooth, flexuous, jointed stem, and entire, petiolate, oblong or ovate-oblong, acuminate leaves, rounded or obliquely cordate at the base, strongly nerved, coriaceous, and very smooth. The flowers are diœcious and in spikes, with peduncles about as long as the petioles. The fruit is a globose, pedicelled drupe. This species of Piper is a native of Java, Penang, and probably other parts of the East Indies. It is extensively grown in the coffee plantations, supported by the trees which are used for shade, and has been introduced into Ceylon. The dried unripe fruit is the official portion. Our knowledge of the false cubeb of commerce up to 1894 was epitomized in the 17th edition of the U. S. D., p. 457. To this account the reader is referred for historical details. (See also *U. S. D.*, 19th ed., p. 410.)

Properties.—Cubeb is officially described as follows: "Upper portion globular, from 3 to 6 mm. in diameter, with a straight, slender stem-like portion, from 5 to 7 mm. in length; pericarp externally grayish, brownish, or bluish-black; coarsely reticulate; about 0.3 mm. in thickness, easily cut, 1-locular, 1-seeded; the immature seed attached at the base of the pericarp; odor aromatic, characteristic; taste strongly aromatic and pungent. Under the microscope, sections of Cubeb show an epidermal layer of tabular cells with thickened, undulate outer walls, the contents being olive-green; 1 or 2 rows of parenchyma cells, the contents resembling those of the epidermal cells; a continuous layer of radiately elongated, thick-walled stone cells having numerous pores; a few layers of collapsed cells near which may occur an occasional small group of bast-fibers; a middle layer of 10 rows of cells composed chiefly of parenchyma, scattered among which are numerous secretions cells containing a volatile oil and occasionally crystals in the form of short rods, the contents of the secretion cells being colored a deep crimson upon the addition of sulphuric acid; an endocarp of small, somewhat isodiametric or polygonal stone cells with very thick porous walls; seed-coat of several rows of reddish-brown, tangentially elongated, more or less collapsed cells; perisperm of numerous thin-walled parenchyma, the cells being more or less polygonal in shape and containing either small compound starch grains, or globules of a fixed oil or occasionally a crystal of calcium oxalate. The powder is light brown to blackish-brown, consisting of a more or less even distribution of starch-bearing cells of the perisperm and fragments of the pericarp with stone cells; starch grains numerous, single or compound, from 0.002 to 0.012 mm. in diameter; stone cells numerous in palisade-like groups, in surface view rounded or polygonal with rather prominent dark lumina and yellowish porous walls; secretion cells with a yellowish, oily content, becoming reddish on the addition of sulphuric acid; fragments of stalk few, with spiral tracheæ and groups of sclerenchymatous fibers from 0.05 to 1 mm. in length with blunt, rounded, or very much attenuated ends, the walls strongly lignified and with numerous oblique pores. Cubeb yields not less than 10 per cent. of volatile extractive, soluble in ether (see Part III, Test No. 12). Cubeb yields not more than 8 per cent. of ash." *U. S.*

"Nearly globular, about four millimetres in diameter, greyish-brown or nearly black. Pericarp reticulately wrinkled, thin, brittle, and abruptly prolonged at the base into a slender, rounded stalk about one and a half times as long as the globular portion. Seed almost spherical, sometimes much shrivelled, attached by the base. In the transverse section of the pericarp two layers of sclerenchymatous cells, one near the outer, the other near the inner surface, those of the latter being radially elongated and usually arranged in a single row. Strong, aromatic, and characteristic odor; taste warm, aromatic, and somewhat bitter. When 2 grammes of powdered Cubebs are macerated with 20 millilitres of *ether* for twenty-four hours, and shaken occasionally, 10 millilitres of the clear ethereal solution, allowed to evaporate in a flat-bottomed dish, yield a residue which, dried for one hour in a desiccator over *sulphuric acid*, weighs not less than 0.200 gramme. Crushed Cubebs impart a crimson color to *sulphuric acid*. Ash not more than 8 per cent." *Br.*

Commercial cubebs are not infrequently admixed with and entirely substituted by other fruits, some of which contain volatile oils which possess very different properties from the genuine oil of cubeb, being in some instances highly toxic. Hartwich (*Arch. d. Pharm.*, 1898, Heft 3; also p. 172) gives the following classification for the identification of spurious fruits:

I. *Fruits of the Piperaceæ having slender stalks.*

A. STONE CELLS IN EPICARP, ENDOCARP AND DISTRIBUTED IN THE MESOCARP:

Piper ribesioides Wallich (identical with *Padang Cubeb*). Fruits not colored red with sulphuric acid.

B. STONE CELLS ONLY PRESENT IN THE EPICARP AND ENDOCARP:

(*a*) Stone cells of the endocarp radially elongated.

Piper Cubeba L.f. Seed attached only at the base of the pericarp.

α Rinoe Katoentjor, the official variety, which is colored red with sulphuric acid.

β *Rinoe badak,* distinguished by not being colored red with sulphuric acid.

(*b*) Stone cells of the endocarp of isodiametric form.

Piper crassipes Korthals. Sections not colored red with sulphuric acid.

(*c*) Stone cells of the endocarp thickened like a horseshoe.

Piper à court pédicelle. Origin unknown.

C. STONE CELLS PRESENT ONLY IN THE EPICARP:

(*a*) Fruit with stem 3 cm. in length, the stem-like portion being alone 17 mm. long.

Piper mollissimum Blume (*Keboe Cubeb. Karbauw berries*) sections not colored red with sulphuric acid.

(*b*) The fruits and stems much smaller, but distinguished by having radially elongated stone cells.

Piper venosum DC. colored red with sulphuric acid.

D. STONE CELLS ABSENT IN THE PERICARP:

(*a*) African varieties:

1. Fruit without stem 5 to 6 mm. long, stem-like portion equally long.

α *Piper clussi* DC., sections colored red with sulphuric acid.

β *Piper guineense* Schum. sections not colored red with sulphuric acid.

2. Fruits 4 mm. long, 2 to 3 mm. thick and stems 6 mm. long.

Piper borbonense DC. (*Cubèbe du pays*) sections not colored red with sulphuric acid.

(*b*) Indian varieties: None of which are colored red with sulphuric acid.

α Stems flattened.

Piper Lowong Blume. Secretion cells colored bluish-green with sulphuric acid.

Ceylon pepper. Secretion cells colored yellow with sulphuric acid.

β Stem-like portion cylindrical.

Piper canium Blume and *P. phyllostitum* DC.

II. *Fruits of the Piperaceæ without stalks.*

A. STONE CELLS PRESENT IN EPICARP AND ENDOCARP:

1. *Piper nigrum* L. Stone cells of epicarp radially elongated and sections colored red with sulphuric acid.

2. *Cubèbe de Jaba sauvage.* Stone cells of the epicarp not radially elongated.

B. STONE CELLS ONLY IN THE EPICARP:

Dangdang boeroeng. A fruit obtained from Java, the origin of which is unknown.

C. STONE CELLS ABSENT IN PERICARP.

Cubeb from Bangil, origin unknown. Sections at first colored red with sulphuric acid, then becoming brown.

III. *Fruits obtained from plants belonging to other families than the Piperaceæ.*

1. *Xanthoxylum Budrunga* Wall. (*Fagara Budrunga* Roxb.) (*Rutaceæ*).

2. *Bridelia tomentosa* Bl. (*Euphorbiaceæ*).

3. *Tetranthera citrata* N. v. Esenbeck (*Litsea citrata* Bl.) (*Lauraceæ*).

4. *Daphnidium Cubeba* Nees. (*Lauraceæ*).

5. *Pericampylus incanus* Miers. (*Menispermaceæ*).

6. *Xylopia frutescens* Gaertner. (*Anonaceæ*).

7. *Helicteres hirsuta* Bl. (*Steruliaceæ*).

8. *Grewia tomentosa* Juss. (*Tiliaceæ*).

Constituents.—The most obvious constituent of cubeb is the volatile oil, the proportion of which yielded by the drug varies from 4 to 13 per cent. It is, as shown by Oglialoro, a mixture of a terpene, $C_{10}H_{16}$, boiling at 158° to 163° C. (316.4°–325.4° F.), which is present in very small amount, and is probably pinene or camphene, some dipentene, and two oils of the formula $C_{15}H_{24}$, boiling at 262° to 265° C. (503.6°–509° F.). One of these, known as *cadinene,* is strongly lævogyrate, and yields a crystallized compound having the formula, $C_{15}H_{24}2HCl$, and melting at 118° C. (244.4° F.), while the other is less lævogyrate, and does not combine with HCl.

The oil distilled from old cubeb on cooling at length deposits large transparent inodorous octahedra of *camphor of cubeb,* $C_{15}H_{26}O$. E. Schmidt found that this camphor melts at 66.5° C. (152° F.); simply by standing over sulphuric acid, more rapidly on heating, it gave up water and passed into that fraction of cubeb oil which boils at 260° C. (500° F.), of which it is, therefore, simply the hydroxide. Another constituent of cubeb is *cubebin.* This is an inodorous substance, crystallizing in small needles or scales, melting at 125° C. (257° F.), having a bitter taste in alcoholic solution, it dissolves freely in boiling alcohol, but deposits on cooling, and is abundantly soluble in chloroform. Its composition, according to Weidel (1877), is $C_{10}H_{10}O_3$, and its structural formula,

$$C_6H_3\begin{cases} O \\ O>CH_2 \\ C_3H_4OH \end{cases},$$

shows a close relationship to safrol, $C_6H_3\begin{cases} O \\ O>CH_2 \\ C_3H_5 \end{cases}$. Fused with potassium hydroxide it yields proto-catechuic acid. The resin extracted from cubeb consists of an indifferent portion, nearly 3 per cent., and of *cubebic acid,* $C_{13}H_{14}O_7$, amounting to about 1 per cent. (*Pharmacographia,* 2d ed., p. 587.)

The formula of cubebic acid as just given is that of Schmidt. Schultze (*Jahresbericht,* 1873, p. 863), on the other hand, gives to it the formula $C_{26}H_{30}O_7 + H_2O$. According to Capitaine and Soubeiran, *cubebin* is best obtained by expressing cubeb from which the oil has been distilled, preparing from the marc an alcoholic extract, treating this with a solution of potassium hydroxide, washing the residue with water, and purifying it by repeated crystallizations in alcohol. In the official oleoresin of cubeb a deposit takes place consisting chiefly of cubebin, which may be obtained by washing the deposit with a small quantity of cold alcohol to remove adhering resin and oil, and then dissolving repeatedly in boiling alcohol, and crystallizing until the

product is white. E. Schaer calls attention to the similarity in reaction between cubebin and veratrine, aconitine, morphine, and digitalin. (*A. Pharm.*, 1887, p. 531.) The volatile oil is official. (See *Oleum Cubebæ.*) By practical trial Bernatzik has satisfied himself that the peculiar virtues of cubeb as a remedy in *gonorrhea* depend not on the cubebin or the volatile oil, but on the cubebic acid. When the ethereal extract of cubeb is deprived of its volatile oil by evaporation on a water bath, and of cubebin and wax by deposition, a soft resin is left, the *cubebic acid* of Bernatzik, in which, according to F. V. Heydenreich, who experimented with it as a physiological agent, the diuretic properties reside, the cubebin being without apparent effect, and the volatile oil, though stimulant and carminative, having no diuretic action. The soft resin, which was of the consistence of honey, of a dark olive-green color, and some remaining odor of cubeb, when taken in the dose of ten grains every two hours for six hours, acted as a laxative, and gave the urine a peculiar odor, without increasing its quantity; but in the dose of a drachm, once repeated at an interval of three hours, while it produced the same effects as the smaller dose, it considerably augmented the urine. In still larger doses it produced decided irritation of the urinary passages. (*A. J. P.*, Jan., 1868.) Heydenreich's experiments are confirmatory of Bernatzik's conclusion as to the peculiar active principles of cubeb. Cubeb gradually deteriorates by age, and in powder becomes rapidly weaker, in consequence of the escape of its volatile oil. It should be kept whole, and pulverized when dispensed. The powder is said to be sometimes adulterated with that of pimenta.

Uses.—Cubeb is generally stimulant, with a special direction to the urinary organs. In considerable quantities it excites the circulation, increases the heat of the body, and sometimes occasions headache and giddiness. At the same time it frequently produces an augmented flow of the urine, to which it imparts a peculiar odor. Among its effects are also occasionally nausea and moderate purging, and it is said to cause a sense of coolness in the rectum during the passage of the fæces. We have no evidence that it was known to the ancients. It was probably first brought into Europe by the Arabians, and was formerly employed for similar purposes as black pepper, but it was found much less powerful and fell into disuse. In India it has long been used in *gonorrhea* and *gleet*, and as a grateful stomachic and carminative in disorders of the digestive organs, and it is at present very frequently given both in this country and in Europe in *gonorrhea*, after the subsidence of the first active inflammatory symptoms. It has been given also in *leucorrhea*, *cystorrhea*, the *urethritis* of women and female children, *abscess of the prostate gland*, *piles*, and *chronic bronchitis*. In connection with copaiba it has been especially recommended in affections of the neck of the bladder and the prostatic portion of the urethra. It is best administered in powder, of which the dose in *gonorrhea* is from one to three drachms (3.9–11.6 Gm.) three or four times a day. The volatile oil may be substituted, in the dose of ten or twelve minims (0.6–0.7 mil), suspended in water by means of sugar, although the oleoresin is generally preferred. (See *Oleoresina Cubebæ.*) An infusion, made in the proportion of an ounce of cubeb to a pint of water, has been employed as an injection in discharges from the vagina.

Dose, of powdered cubeb, ten grains to one drachm (0.65–3.9 Gm.).

Off. Prep.—Fluidextractum Cubebæ, *N. F.;* Oleoresina Cubebæ, *U. S.;* Tinctura Cubebæ, *Br.;* Trochisci Cubebæ (from Oleoresin), *U. S.;* Elixir Buchu Compositum (from Compound Fluidextract of Buchu), *N. F.;* Fluidextractum Buchu Compositum, *N. F.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodicæ sine Aloes, *N. F ;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloes, *N. F.;* Tinctura Cubebæ, *N. F.*

CUPRI SULPHAS. U. S., Br.

COPPER SULPHATE Cupr. Sulph. [Cupric Sulphate]

(cū'prī sŭl'phăs)

"It contains not less than 62.97 per cent. nor more than 66.79 per cent. of anhydrous copper sulphate corresponding to not less than 98.5 per cent. of the crystallized salt [$CuSO_4 + 5H_2O = 249.72$]. Preserve it in well-closed containers." *U. S.* "Copper Sulphate, $CuSO_4,5H_2O$, may be obtained by the interaction of sulphuric acid, copper or copper oxide, and water." *Br.*

Cuprum Vitriolatum; Blue Vitriol, Roman Vitriol, Blue Stone; Sulfate de Cuivre, *Fr. Cod.;* Vitriol bleu, Couperose bleu, *Fr.;* Cuprum Sulfuricum, *P.G.;* Schwefelsaures Kupfer, Kupfersulfat, Kupfervitriol, Blauervitriol, Blauer Galitzenstein, *G.;* Solfato di rame, Vitriolo di rame, *It.;* Sulfato cuprico, Vitrolo azul, *Sp.*

Preparation.—Copper sulphate occasionally exists in nature, in solution in the water which flows through copper mines. In this case the salt is procured by merely evaporating the waters which naturally contain it. Another method of obtaining it is to roast the native sulphide in a reverberatory furnace, whereby it is made to pass, by absorbing oxygen, into the state of sulphate. Too high a temperature must be avoided during the roasting process to avoid the production of hard masses from which the copper is extracted with great difficulty. The roasted mass is lixiviated, and the solution obtained evaporated that crystals may form. The salt procured by either of these methods contains a little ferric sulphate, from which it may be freed by adding either an excess of cuprous oxide, which precipitates ferric oxide, or recently precipitated copper subcarbonate, which causes the deposition of the iron as a carbonate. (*A. J. P.*, xxxiv, 507.) A third method is to dissolve copper scales to saturation in sulphuric acid contained in a wooden vessel lined with

sheet lead. The scales consist of metallic copper mixed with oxide, and are produced in the process for annealing sheet copper.

Most of the copper sulphate produced at present is obtained as a by-product by the gold, silver, and copper refiners. The production of copper sulphate in the United States is very large, and there is a considerable exportation; this amounted in 1916 to 17,978,242 pounds.

In the U. S. Pharmacopœia copper sulphate is presumed to be obtained pure from the manufacturer; the British Pharmacopœia suggests the method in which it may be prepared, without entering into the details of the process. The German Pharmacopœia has two kinds official, *Cuprum sulfuricum,* which corresponds with the former *Cuprum sulfuricum purum,* and *Cuprum sulfuricum crudum,* or commercial sulphate.

Properties.—Copper sulphate "occurs as deep blue, triclinic crystals, or as blue, granular powder; odorless, of a nauseous, metallic taste; slowly efflorescent in dry air. One Gm. of Copper Sulphate dissolves in 2.5 mils of water, 500 mils of alcohol, and in 2.8 mils of glycerin at 25° C. (77° F.); also in 0.5 mil of boiling water. An aqueous solution of the salt (1 in 20) has a blue color, and is acid to litmus. When heated to 30° C. (86° F.) the salt loses part of its water of crystallization and is converted into a pale blue, amorphous powder. More water is lost at 100° C. (212° F.), and finally at 200° C. (392° F.) a white, anhydrous powder remains. At a still higher temperature, sulphur dioxide and oxygen are given off, and a residue of black cupric oxide remains. Place a drop of an aqueous solution of the salt (1 in 20) on a bright piece of iron; a red film of metallic copper is deposited. Barium chloride T.S. produces a white precipitate, insoluble in hydrochloric acid, in an aqueous solution of the salt (1 in 10). Add ammonia water to an aqueous solution of Copper Sulphate (1 in 10), drop by drop; a pale blue precipitate of cupric hydroxide forms, which redissolves in an excess of ammonia water, producing a deep azure-blue solution. Dissolve 1 Gm. of the salt in 50 mils of distilled water, add 1 mil of diluted hydrochloric acid and pass hydrogen sulphide gas through the solution until all of the copper is precipitated. Upon evaporating the filtrate and igniting, the weight of the residue does not exceed 0.003 Gm. (*other metals*).

"**Assay.**—Dissolve about 1 Gm. of Copper Sulphate, accurately weighed, in 50 mils of distilled water and add 4 mils of acetic acid and 3 Gm. of potassium iodide and titrate the liberated iodine with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 62.97 per cent. nor more than 66.79 per cent. of $CuSO_4$.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.015964 Gm. of $CuSO_4$. Each gramme of Copper Sulphate corresponds to not less than 39.44 mils nor more than 41.83 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

"Blue triclinic prisms. Soluble in 3.5 parts of *water,* very soluble in *glycerin,* almost insoluble in *alcohol* (90 per cent.). The aqueous solution is acid to *litmus.* Yields the *reactions* characteristic of copper and of sulphates. Yields no characteristic *reactions* for lead, zinc or aluminium. *Arsenic limit* 10 parts per million. Contains not more than 0.1 per cent. of iron, calculated as iron, Fe, when tested by the following process:—Dissolve 5 grammes in 25 millilitres of *water,* add 2 millilitres of *nitric acid,* heat to boiling, cool, and add *strong solution of ammonia* until the precipitate which first forms is redissolved and the liquid has a distinct odor of ammonia. Filter. Wash the filter paper thoroughly with *water* made alkaline with *solution of ammonia,* redissolve in *hydrochloric acid* any precipitate that has been collected, reprecipitate with *solution of ammonia,* collect, wash, dry, ignite, and weigh the residue. It weighs not more than 0.007 gramme." *Br.*

When heated, copper sulphate first melts in its water of crystallization, and then dries and becomes white. If the heat is increased, it next undergoes the igneous fusion, and finally, at a high temperature, loses its acid, cupric oxide being left. Four of the molecules of water of crystallization can be driven off at 100° C. (212° F.); but the fifth goes off only at a temperature of from 220° C. (428° F.) to 240° C. (464° F.), when the anhydrous salt remains. Potassium hydroxide, sodium hydroxide, and ammonia throw down from it a bluish-white precipitate of hydrated cupric oxide, which is immediately dissolved by an excess of the last mentioned alkali, forming a rich deep blue solution, called *aqua sappharina.* It is decomposed by the alkaline carbonates, and by borax, lead acetate and subacetate, ferric acetate, silver nitrate, mercuric chloride, potassium tartrate, and calcium chloride, and it is precipitated by all astringent vegetable infusions. If it becomes very green on the surface by the action of the air, it contains ferric oxide. This oxide may also be detected by ammonia, which will throw it down along with the copper oxide, without taking it up when added in excess. When copper sulphate is obtained from the *dipping liquid* of manufacturers of brass or German silver ware, it is always contaminated with zinc sulphate, as pointed out by S Piesse. This liquid is at first a mixture of sulphuric and nitric acids, but becomes, at last, nearly saturated with copper. When zinc is present in copper sulphate, it will be taken up by solution of potassium hydroxide added in excess, from which it may be thrown down, after filtration, in white flocks, by a solution of bicarbonated alkali.

Copper sulphate is incompatible with alkalies and liberates iodine from iodides.

Uses.—Copper sulphate is irritant or mildly escharotic, and when in diluted solution, stimulant and astringent. At one time it was given in *epilepsy* and other nervous diseases, but at present it is never used internally, except for

its influence upon the gastro-intestinal mucous membrane. In *chronic diarrhea* with ulceration it is often a useful remedy. In doses of 5 grains it acts as a powerful, prompt emetic, without causing general depression or much nausea, but is too irritant to be used freely; it is useful as an emetic in *phosphorus poisoning* because it not only empties the stomach but acts also as a chemical antidote to the phosphorus. Externally it is employed in solution as a stimulant to ill-conditioned *ulcers,* as an escharotic for destroying *warts,* fungous *granulations,* and callous edges, and as a styptic to bleeding surfaces. It is found, in not a few instances, to promote the cicatrization of ulcers, and is not infrequently employed, with that view, as a wash for *chancres.* Bevan (*S. M.,* 1905, p. 558) has used copper sulphate successfully in *actinomycosis.* He gave from one to three grains (0.065–0.2 Gm.) daily and applied a 1 per cent. solution to the ulcerated area.

Copper sulphate is highly poisonous to certain of the lower forms of vegetable life, thus it has been found serviceable for destroying the algæ in ponds. While in general its antibacterial properties are not very powerful it seems to be especially poisonous towards the *Bacillus typhosus,* Gildersleeve (*A. J. M. S.,* 1905, cxxxix, p. 757) having shown that as little as one part to a million is sufficient to destroy this bacterium in a period of three hours. It was at one time suggested as a means for purifying drinking water but is not practically available because the presence of various impurities destroys its action.

The preparation called *cuprum aluminatum* (*lapis divinus—pierre divine*) is made, according to the French Codex, by mixing, in powder, three ounces, each, of copper sulphate, potassium nitrate, and alum, heating the mixture in a crucible, so as to produce aqueous fusion, then mixing in a drachm of powdered camphor, and, finally, pouring out the whole on an oiled stone to congeal. The mass, when cold, is broken into pieces, and kept in a well-stoppered bottle. It is often desirable to employ copper sulphate, as a caustic, in the form of pencil. Its tendency to effloresce interferes with its use in this way in the pure state. Llovet recommends for the purpose a mixture of one part of potassa-alum and two of copper sulphate, which are to be first powdered, and then gradually melted together in a porcelain vessel, and poured into moulds made of bronze. (*Gaz. des Hôp.,* Juillet 28, 1863.) Another mode of preparing *pencils of copper sulphate* is to rub briskly together four parts of that salt and one of borax, and to mould the plastic mass which results, into the desired form. (*A. J. P.,* March, 1864, p. 106.) An elongated cone is the best form, made by selecting suitable crystals and turning them in a lathe to the desired form; or they may be made by filing the crystals, and finishing with sand-paper.

Dose, of copper sulphate, as an astringent, one-fourth of a grain (0.016 Gm.); as an emetic, five grains (0.32 Gm.), repeated in fifteen minutes if necessary, but not oftener than once. As a stimulant wash, the solution may be made of the strength of two, four, or eight grains to the fluidounce of water. For its effects as a poison, see *Cuprum.*

Off. Prep.—Liquor Zinci et Ferri Compositus, *N. F.;* Mistura Adstringens, *N. F.*

CUPRUM.

COPPER

(cū'prŭm)

Cu = 63.57

"Fine Copper wire, about No. 25 wire gauge or about 0.02 inch." *Br.,* 1885.

Cupreum Filum: Fil de Cuivre, Cuivre, *Fr.;* Kupfer, Kupferdraht, *G.;* Rame, *It.;* Cobre, *Sp.*

This metal is very generally diffused in nature, and exists principally in four states; as native copper, as an oxide, as a sulphide, and as a salt. Its principal native salts are the silicate, carbonate, arsenate, and phosphate. In the United States it occurs in various localities, but especially in the neighborhood of Lake Superior, in Montana, Arizona, Alaska and East Tennessee. The principal producing copper mines of Europe are those of Spain and Portugal and of Mansfeld in Germany. Chili and Japan are also relatively large producers at present.

The total production of copper in the United States has increased very rapidly in recent years, and now is more than two-thirds of the world's annual production. It was for 1915, 1,424,649,565 pounds, and in 1916 nearly 2,000,000,000 pounds. The three most productive states are Arizona, Montana, and Michigan, in the order named. The consumption of copper in the United States for 1915 was 1,043,461,982 pounds, and exports for the same year 681,953,301 pounds.

Properties.—Copper is a brilliant, sonorous metal, of a reddish color, and very ductile, malleable, and tenacious. It has a slightly nauseous taste, and emits a disagreeable odor when rubbed. Its texture is granular, and its fracture hackly. Its sp. gr. is 8.92 to 8.95, and its fusing point 1080° C. (1976° F.). Exposed to the air it undergoes a slight tarnish. Its combinations are numerous and important. With oxygen it forms two well characterized oxides, a red suboxide, better known as *cuprous* oxide, Cu_2O, and a black oxide, known as *cupric* oxide, CuO. While a cuprous chloride, iodide, and sulphide are known, it is the cupric oxide chiefly that unites with the several acids to form the copper salts. With metals copper forms numerous alloys, of which that with zinc, called *brass,* and that with tin, called *bronze,* are the most useful. *Bell metal, gun metal,* and *German silver* are other alloys in frequent use in which copper is the predominating constituent.

Characteristics.—Copper is recognized by its

color, and the effects of tests on its solution in nitric acid. This solution, with potassium hydroxide, sodium hydroxide, and ammonia, yields a blue precipitate, soluble in excess of the latter alkali, with which it forms a deep azure-blue liquid. Potassium ferrocyanide occasions a brown precipitate of copper ferrocyanide, and a bright plate of iron immersed in the solution immediately becomes covered with a film of metallic copper. Thoms (*Zeit. An. Chem.*, 94, 464) asserts that if to a solution, too dilute to give a sensible reaction with potassium ferrocyanide, be added a solution of potassium iodide, a yellow coloration is produced which becomes violet with starch paste. This test, in absence of deoxidizing agents, will show as little as 1 to 500,000. Potassium ferrocyanide is a very delicate test for minute portions of copper in solution. Another test, proposed by Verguin, is to precipitate the copper in the metallic state on platinum by electrochemical action. For this purpose a drop of the (acid) liquid to be examined is placed on a slip of platinum foil, and a slip of bright iron is brought in contact with the platinum and the liquid. If copper be present it will be instantly precipitated on the surface of the platinum. Copper compounds when present in food or drug products in appreciable amounts may be detected by the simple test of immersing a bright piece of steel or iron (as a knitting needle, spatula) into the material which has been brought to a pasty condition and acidulated with hydrochloric acid. The copper will be deposited upon the iron or steel in the form of a very thin easily perceptible film.

Action on the Animal Economy.—Copper in its pure state is nearly inert, but in combination it is highly deleterious. Nevertheless, a minute portion of the metal has been found in the human body. Wackenroder found copper in the blood of man, but does not consider it a constant and normal constituent. He also detected this metal in the blood of domestic animals living on a mixed diet, but not in their blood when nourished on vegetable food only. It has been found in the feathers of certain birds, as of a grass-green paroquet from Australia, which is said to frequent districts of the country where copper is found.

The soluble combinations of copper, when taken in poisonous doses, produce a coppery taste in the mouth; nausea and vomiting; violent pain in the stomach and bowels; frequent black and bloody stools; small, irregular, sharp, and frequent pulse; faintings; burning thirst; difficulty of breathing; cold sweats; paucity of urine, and burning pain in voiding it; violent headache; cramps, convulsions, and finally death. The best antidote is potassium ferrocyanide, given freely, which forms with the poison the insoluble copper ferrocyanide. Soap and alkalies are also antidotal. Before the antidote can be procured, large quantities of albuminous substance of milk or white of eggs should be given mixed with water, which act favorably by forming copper caseinate and copper albuminate, respectively, but these compounds should be evacuated as soon as possible by vomiting and purging. Should vomiting not take place, the stomach tube may be employed. The symptoms of slow poisoning by copper are, according to Corrigan, of Dublin, a cachetic appearance, emaciation, loss of muscular strength, colicky pains, cough without physical signs, and retraction of the gum, with a persistent purple edge, quite distinct from the blue edge produced by lead. (*Braithwaite's Retrospect*, Am. ed., xxx, 303.) But there is much doubt whether these symptoms can be produced by the metal.

In medico-legal examinations, where cuprous poisoning is suspected, Orfila recommends that the viscera be boiled in distilled water for an hour, and that the matter obtained by evaporating the filtered decoction to dryness be carbonized by nitric acid. The carbonized product will contain the copper. By proceeding in this way there is no risk of obtaining the copper which may happen to pre-exist in the animal tissues. This method of search is preferable to that of examining the contents of the stomach and intestines, from which copper may be absent, while it may have penetrated the different organs by absorption, especially the abdominal viscera.

Vessels of copper which are not coated with tin should not be used in pharmaceutical or culinary operations, for, although the metal uncombined is inert, yet the risk is great that the vessels may be acted on and a poisonous salt formed.

CUSSO. Br.

KOUSSO [Brayera]

(cūs'sō)

"Kousso consists of the dried panicles of pistillate flowers of Brayera anthelmintica, *Kunth.*" *Br.* "The dried panicles of the pistillate flowers of *Hagenia abyssinica* (Bruce) Gmelin (Fam. *Rosaceæ*), without the presence of more than 10 per cent. of the staminate flowers, other parts of the tree, or other foreign matter. Reject any portions of the stems over 3 mm. in diameter and any binding material, before the drug is powdered or used." *N. F.*

Brayera, *N. F.*; Kooso; Kusso; Cousso, *Fr. Cod.*; Kousso, *Fr.*; Flores Koso, *P. G.*; Kosoblüthen, Koso, Kusso, Cusso, *G.*; Kousso, Cosso, *It.*; Couso, *Sp.*

Kousso was dropped from the U. S. P. IX but has been introduced into the N. F. IV and is retained in the Br. Pharm., 1914.

Hagenia abyssinica Willd. (Syn. *Brayera anthelmintica* Kunth) is a beautiful tree about twenty feet high, growing on the table-land of Abyssinia, at an elevation of from three thousand to eight thousand feet. The branches exhibit circular cicatrices, left by the fallen leaves. The latter are crowded near the ends of the branches, are large, pinnate, sheathing at the base, with opposite, lanceolate, serrate, leaflets, villose at the margin, and nerved beneath. The

unisexual flowers are tinged with purple, pedicelled, with an involucre of four roundish, oblong, obtuse, membranous bracts, and are arranged in fours, upon hairy, flexuous, bracteate peduncles, with alternate branches. They are small and of a greenish color, becoming purple. These and the unripe fruit are the parts of the plant employed. The petals are apt to be wanting in the dried flowers. They are brought from Abyssinia packed in boxes, reaching Europe chiefly by way of Aden and Bombay. The Abyssinian name of the medicine has been variously spelled by European writers kosso, koosso, cusso, cosso, etc. The fruit of the tree is said to be used as an anthelmintic in Abyssinia, but Dragendorff failed to detect any active principle in it. It is stated that in Abyssinia, honey gathered directly after the flowering season from beehives in gardens planted with kousso plants, is used in doses of a teaspoonful as a very effective tenicide.

Properties.—The dried flowers are in unbroken though compressed clusters. The male flowers are usually collected, so that ordinarily the general color of the mass is greenish-yellow or light brown; sometimes the female flowers constitute the bulk of the drug, which then has a distinct reddish tint, and is often known in commerce as *red kousso*. In accordance with our Pharmacopœia, this commercial variety should alone be used. The male flowers are often found mixed with the female flowers, when loose (not in bundles), as high as 12 per cent. of this adulteration having been noticed by Meyer and Sandlund. (*Ph. Ztg.*, 1893, No. 99.) The description in the Br. Pharm. is as follows: "Usually in more or less cylindrical rolls from three to six decimetres long, composed of reddish panicles of pistillate flowers. Panicles much branched, the branches arising from the axils of large sheathing bracts; more or less covered with hairs and glands. Flowers numerous, small, shortly stalked, mostly unisexual, with two roundish, membranous, veined bracts at the base of each. Calyx with reddish veins, hairy externally, and consisting of two alternating whorls each of five segments, the inner whorl being curved inwards over the young fruit and shrivelled. No marked odor; taste bitter and acrid." *Br.*

The N. F. describes the drug as "usually in rolls or flattened bundles from 25 to 50 cm. in length, reddish-brown, or occurring more or less loose and stripped from the larger portions of the panicles. Panicle branches cylindrical, somewhat flattened, longitudinally furrowed or wrinkled, externally light brown to yellowish, tomentose, glandular; internally, cork brownish, bast- and wood-fibers yellow, fibro-vascular bundles in wedges, pith large and yellowish-brown; nodes distinct, each with a scar or branch and subtended by a sheathing bract; internodes mostly from 1 to 2 cm. in length; flowers subtended by two ovate, reddish, pubescent and glandular bracts; pedicel short; calyx turbinate, pubescent below, subtended by four or five rigid, spreading, obovate, purple-veined bractlets which are persistent and elongated in fruit, alternating with and larger than the five usually shriveled, reflexed calyx lobes; petals five, caducous, and usually absent in the drug; carpels two; styles exserted, stigmas broad and hairy with prominent papillæ; fruit an ovoid akene about 2 mm. in diameter, enclosed by the remains of the calyx. The staminate flowers are greenish-yellow, with about twenty fertile stamens. Odor slight; taste bitter. The powdered drug is light brown or reddish-brown and, when examined under the microscope, exhibits numerous simple, non-glandular, straight or curved hairs, up to about 1 mm. in length, with thick, strongly lignified walls, usually enlarged at the base; glandular hairs with one- to three-celled stalks, the glandular head unicellular or consisting of one or two pairs of cells; tracheæ spiral, annular, scalariform, or with bordered pores, up to 0.05 mm. in width; sclerenchymatous fibers long, thick-walled, strongly lignified and with numerous, simple, oblique pores; parenchyma of pith more or less lignified and with large simple pores; fragments of epidermal tissue from the bracts and calyx with elliptical stomata up to 0.03 mm. in length; groups of thin-walled, somewhat branching parenchyma cells with large intercellular spaces; tissue from the inner surface of the pericarp consisting of numerous, elongated, porous, strongly lignified cells; calcium oxalate in rosette aggregates up to 0.04 mm. in diameter; occasionally fragments of tissue containing prisms of calcium oxalate, the latter about 0.014 mm. in length; pollen grains few, nearly spherical, from 0.025 to 0.04 mm. in diameter, with three pores. The larger branches of the panicles exhibit simple, non-glandular hairs up to about 5 mm. in length; tracheæ up to 0.125 mm. in width and rosette aggregates of calcium oxalate up to about 0.075 mm. in diameter. Brayera yields not more than 9 per cent. of ash." *N. F.*

As the medicine, from its high price, is apt to be adulterated, it should be procured in the unpowdered state, in which the botanical characters of the flower will sufficiently test its genuineness. It has a fragrant balsamic odor, and the taste, slightly perceptible at first, becomes in a short time somewhat acrid and disagreeable. Analyzed by Wittstein, it was found to contain, in 100 parts, 1.44 of fatty matter and chlorophyll, 2.02 of wax, 6.25 of bitter acrid resin, 0.77 of tasteless resin, 1.08 of sugar, 7.22 of gum, 24.40 of tannic acid, 40.97 of lignin, 15.71 of ashes, with 0.14 part of loss. It has also been studied by Clemens Willing (*Ch. Cb.*, 1855, 224), and by Pavesi (*Viertelj. f. Prak. Pharm.*, 1858, viii, 505) but we are chiefly indebted to Bedall, of Munich, for determining that the bitter acrid resin of Wittstein is equivalent to the *tæniin* of Pavesi, and for the name of *kosin*. This may be obtained by treating kousso repeatedly with alcohol to which calcium hydroxide has been added; the residue is boiled with water, the liquids are mixed, filtered, and dis-

tilled, and the residue treated with acetic acid, which precipitates the kosin in a white flocculent form, soon becoming denser and resin-like, and, on drying, yellowish, or, at a higher temperature, brown. The product is 3 per cent. In bulk, kosin has an odor like that of Russian leather, a persistent bitter and acrid taste, a yellowish or yellowish-white color, and an indistinct crystalline appearance under the microscope. It is very sparingly soluble in water, but freely so in alcohol, ether, and alkaline solutions. (*A. J. P.*, 1872, 394.) Its formula, according to Flückiger, is $C_{31}H_{38}O_{10}$. It fuses at 142° C. (287.6° F.), and remains after cooling an amorphous yellow mass, but if touched with alcohol it immediately assumes the form of stellate tufts of crystals. This may be repeated at pleasure, kosin not being altered by cautious fusion. (*Pharmacog.*, 2d ed., 258.) Leichsenring (*A. Pharm.*, 1894, 50) has re-examined kousso, and finds an inactive crystalline principle to which he gives the name *protokosine*, and an amorphous substance, *kossotoxine*, which he considers the active principle of the drug; the latter is a yellowish powder, fusing at 80° C. (176° F.), and not obtainable in a crystalline state. It is easily soluble in alcohol, ether, benzene, carbon disulphide, and insoluble in water.

Sodium kosinate has been recommended by Pavesi as a very eligible preparation for obtaining the virtues of kosin; a process is given in *Am. Drug.*, 1884, 96; *A. J. P.*, 1885.

Uses.—Kousso is highly valued in Abyssinia as a vermifuge. Bruce speaks of it in his travels, and gives a figure of the plant. Brayer, a French physician practising in Constantinople, published a treatise on it at Paris in 1823. It was in his honor that Kunth adopted the generic title of the plant. Much attention has been attracted to this valuable medicine, and trials made with it have proved its efficacy in the destruction and expulsion of the *tape-worm*. Its effects when taken internally are not very striking. In the ordinary dose it sometimes produces heat of stomach, nausea, and even vomiting, and shows a tendency to act on the bowels, though this effect is not always produced. It appears to act exclusively as a poison to the worms, and has been found equally effectual in both kinds of *tape-worm*. The medicine is taken in the morning upon an empty stomach, a light meal having been made the preceding evening. A previous evacuation of the bowels is also recommended. The flowers are given in the form of powder, mixed with half a pint of warm water, the mixture being allowed to stand for fifteen minutes, then stirred up, and taken in two or three draughts at short intervals. The medicine may be preceded and followed by lemonade. The medium dose for an adult is half an ounce (15.5 Gm.), which may be diminished one-third for a child of twelve years, one-half for one of six years, and two-thirds for one of three years. Should the medicine not act on the bowels in three or four hours, a brisk cathartic should be administered. One dose is said to be sufficient to destroy the worm. Should the quantity mentioned not prove effectual, it may be increased to an ounce (31 Gm.).

Pure kosin has been considerably used in Germany in doses of thirty grains (2 Gm.), taken in two or four powders; but Buchheim found *pure* kosin less powerful as an anthelmintic than that which was not pure, while Arena (*Ph. Z. R.*, 1879, 655) believes that kosin is not the active principle at all, but that the activity of kousso resides exclusively in the green, slightly bitter resin, which is soluble in alcohol and ether. If this view be correct, it explains the greater efficacy of freshly powdered kousso, for the green resin turns yellow by age and loses its power, and Arena's investigations further indicate that the amorphous kosin of commerce is preferable to the pure principle. It is a yellowish-brown mass, which may be given in doses of from seven to fifteen grains (0.45–1.0 Gm.), repeated every half hour until four doses are taken, to be followed in an hour by a full dose of castor oil. So far as we know, no cases of poisoning by kousso or its active principle are on record, but it has been found by Rochebrune to be capable of causing centric convulsions in the lower animals.

Dose, of kousso, half an ounce (15.5 Gm.); of kosin, seven to fifteen grains (0.45–1.0 Gm.).

DATURÆ FOLIA. Br.

DATURA LEAVES

(dą-tū'ræ fō'lĭ-ą)

"Datura Leaves are the dried leaves of Datura fastuosa, *Linn.*, var. alba, *Nees* and also of Datura Metel, *Linn.*" *Br.*

DATURÆ SEMINA. Br.

DATURA SEEDS

(dą-tū'ræ sĕm'ĭ-ną)

"Datura Seeds are the dried seeds of Datura fastuosa, *Linn.* var. alba, *Nees.*" *Br.*

The genus Datura consists of fifteen species, which are distributed throughout the warmer portions of the whole world, the greatest number being found in Central America. Nearly all of them are used locally in medicine. The plants vary from herbs to shrubs and even trees. The leaves of *Datura Stramonium* are official in the U. S. Pharmacopœia. (See *Stramonium*.) The leaves and seeds of *Datura fastuosa alba* are used in India and the Eastern and West Indian Colonies as an equivalent of Belladonna and Stramonium leaves. A tincture of *Datura seeds* is used in India as an equivalent of Stramonium seeds.

Datura fastuosa is a small shrub, indigenous to tropical India. There is said to be several varieties of this species and it is very generally conceded to be the most toxic of the Indian Daturas. The leaves are ovate and more or less angular, the flowers being white or purplish. *Datura Metel* is also an Indian plant and re-

sembles *D. fastuosa.* It differs in that the leaves are cordate, almost entire, and pubescent. The flowers being white. Pyman and Reynolds (*P. J.*, 1908, lxxxi) have found in the *D. meteloides* a new alkaloid, which they call *meteloidine.*

Of the varieties of *D. fastuosa,* the British Pharmacopœia recognizes that known as *alba.* From it the Thugs prepared the poison Dhât (whence is derived the generic name), which they used to stupefy their victims. The leaves and seeds are recognized by the Br. Pharm. 1914, and the leaves are described as "Brownish or yellowish-green, attaining twenty centimetres in length and thirteen centimetres in breadth; ovate, acuminate, with sinuate-dentate margins and long petioles; often unequal at the base; bearing scattered glandular or simple hairs. Characteristic odor; taste bitter." *Br.*

The trumpet-shaped corolla, together with the stamens, is sometimes found mixed with the leaves. The drug has a slight unpleasant odor, and a bitter taste.

The seeds are "yellowish-brown, somewhat wedge-shaped, flattened, with rounded, thickened, furrowed, wavy margins; from four to five millimetres broad and about one millimetre thick. Hilum large, extending from about the middle to the acute end of the seed. Surface finely pitted and reticulated. Endosperm narrow and translucent, enclosing a curved embryo. No odor; taste slightly bitter." *Br.*

They contain the alkaloid hyoscine, a resin, a fixed oil and traces of hyoscyamine and atropine.

Uses.—While this drug produces effects more or less similar to those of belladonna its precise action has not been clearly determined. It is used in India to a considerable extent as a criminal poison. Banerja (*Indian Med. Gaz.*, 1885, xx, p. 209) has reported 32 cases. The symptoms are not given in sufficient detail to allow of definite statement but seem to differ somewhat from those of either atropine or scopolamine. Gimlette (*B. M. J.*, 1903, i, p. 1137) also records several cases of poisoning and states that the nature of the active principle of the drug has not been determined. In India the *Datura fastuosa* leaves have been used for the same purposes as the stramonium leaves.

Off. Prep.—Tinctura Daturæ Seminum, *Br.*

DECOCTA. U. S.

DECOCTIONS

(dẹ-cŏc'tạ)

Tisanes par décoction, Décoctions, *Fr.*; Abkochungen, *G.*; Decotti, *It.*; Cocimiento, *Sp.*

Decoctions are solutions of vegetable principles, obtained by *boiling* the substances containing these principles in water. Vegetable tissues generally yield their soluble ingredients more readily, and in larger proportion, to water maintained at the point of ebullition, than to the same liquid at a lower temperature. Hence decoction is occasionally preferred to infusion as a mode of extracting the virtues of plants, when the call for the remedy is urgent, and the greatest possible activity in the preparation is desirable. The process should be conducted in a covered vessel, so as to confine the vapor over the surface of the liquid, and thus prevent the access of atmospheric air, which sometimes exerts an injurious agency upon the active principle. The boiling, moreover, should not, as a rule, be long continued, as the ingredients are apt to react on one another, and thus lose, to a greater or less extent, their original character. The substance submitted to decoction should if dry be either powdered or well bruised, if fresh should be sliced, so that it may present an extensive surface to the action of the solvent; and previous maceration for some time in water is occasionally useful by overcoming the cohesion of the vegetable fiber. Should the physican not happen to prescribe this preliminary comminution, the pharmacist should not omit it.

All vegetable substances are not proper objects for decoction. In many the active principle is volatile at a boiling heat, in others it undergoes some change unfavorable to its activity, and in a third set is associated with inefficient or nauseous principles, which, though insoluble or but slightly soluble in cold water, are abundantly extracted by that liquid at the boiling temperature, and thus encumber, if they do not positively injure, the preparation. In all these instances, infusion is preferable to decoction. Besides, by the latter process more matter is often dissolved than the water can retain, so that upon cooling a precipitation takes place and the liquid is rendered turbid, and this constitutes the greatest objection to this class of preparations. When the active principle is thus dissolved in excess, the decoction should always be strained while hot, so that the matter which separates on cooling may be mixed again with the fluid by agitation at the time of administering the remedy. In compound decoctions, the ingredients may be advantageously added at different periods of the process, according to the length of boiling requisite for extracting their virtues; and, should one of them owe its activity to a volatile principle, the proper plan is, at the close of the process, to pour upon it the boiling decoction, and allow the liquor to cool in a covered vessel.

As a rule, glass or earthenware vessels should be preferred, as those made of metal are sometimes corroded by the ingredients of the decoction, which thus become contaminated. Vessels of clean cast-iron or common tin, or of block tin, are preferable to those made of copper, brass, or zinc; but iron pots should not be used where astringent vegetable substances are concerned.

Decoctions, from the mutual reaction of their constituents, as well as from the influence of the air, are apt to spoil in a short time. Hence they should be prepared only when wanted for use, and should not be kept, when the weather is warm, for a longer period than forty-eight hours.

The tendency of modern medicine and phar-

macy has been decidedly against the employment of decoctions; their nauseous taste, bulky dose, repulsive appearance, and non-permanent character have been powerful reasons for causing their retirement, while the use of tinctures and fluidextracts has largely increased. In the 1880 revision of the U. S. Pharmacopœia the number of official decoctions was reduced to two, and a general formula was appended for the guidance of the pharmacist. The U. S. P., 1890, reduced the strength of the general formula for decoctions from 10 per cent. to 5 per cent., and this strength was retained in the U. S. P. VIII and IX, as will be seen from the following: "Decoctions must be *freshly made from the drugs,* and, when the strength of decoctions is not otherwise directed, they are to be prepared by the following general formula: * The Drug, coarsely comminuted, *fifty grammes* [or 1 ounce av., 334 grains]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Introduce the drug into a suitable vessel provided with a cover, pour upon it *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of cold water, cover it well, and boil for fifteen minutes. Then allow it to cool to about 40° C. (104° F.), express, strain the expressed liquid, and pass enough cold water through the strainer to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms].

"*Caution.*—The strength of decoctions of energetic or powerful substances should be specially directed by the physician." *U. S.*

The two decoctions of the U. S. P., 1890, *Decoctum Cetrariæ* and *Decoctum Sarsaparillæ Compositum,* were both dismissed in the Eighth Revision and only the general formula for decoctions retained. See *Decoction of Cetraria* Part II, and *Zittman's Decoction,* Part II.

DECOCTUM ACACIÆ CORTICIS. Br.

DECOCTION OF ACACIA BARK

(dẹ-cŏc'tŭm ą-cā'cĭ-æ cŏr'tį-cĭs)

"Acacia Bark, bruised, 60 *grammes;* Distilled Water sufficient to produce 1000 *millilitres.* Boil the Acacia Bark with twelve hundred *millilitres* of Distilled Water, in a suitable vessel, for ten minutes; strain; if necessary pour sufficient Distilled Water over the contents of the strainer to produce the required volume." *Br.*

This decoction was transferred from the British Addendum (1900) to the British Pharm. (1914). It is used in India as an astringent gargle, lotion, or injection. The *dose* is from four fluidrachms to two fluidounces (15–60 mils).

DECOCTUM AGROPYRI. Br.

DECOCTION OF COUCH GRASS [Decoction of Triticum]

(dẹ-cŏc'tŭm ąg-rō-pī'rī)

"Couch Grass, cut small, 50 *grammes;* Distilled Water sufficient to produce 1000 *millilitres.* Boil the Couch Grass with twelve hundred *millilitres* of Distilled Water, in a suitable vessel, for ten minutes; strain; if necessary pour sufficient Distilled Water over the contents of the strainer to produce the required volume." *Br.*

This decoction was transferred from the British Addendum (1900) to the British Pharm. (1914). It is used in *cystitis* and *urinary diseases. Dose,* four fluidrachms to two fluidounces (15–60 mils).

DECOCTUM GOSSYPII RADICIS CORTICIS. Br.

DECOCTION OF COTTON ROOT BARK

(dẹ-cŏc'tŭm gọs-sĭp'ī-ī rą'dį-cīs cŏr'tį-cīs)

"Cotton Root Bark, bruised, 200 *grammes;* Distilled Water sufficient to produce 1000 *millilitres.* Boil the Cotton Root Bark with two thousand *millilitres* of the Distilled Water, in a suitable vessel, until the volume is reduced to one thousand *millilitres;* strain; if necessary pour sufficient Distilled Water over the contents of the strainer to produce the required volume." *Br.*

This decoction was transferred from the British Addendum (1900) to the British Pharm. (1914). It is used as an emmenagogue and in *uterine hemorrhage. Dose,* from four fluidrachms to two fluidounces (15–60 mils).

DECOCTUM ALOES COMPOSITUM. Br.

COMPOUND DECOCTION OF ALOES

(dẹ-cŏc'tŭm ăl'ọ-ēs cọm-pŏs'į-tŭm)

Tisane (Décocté) d'Aloès composée, *Fr.;* Zusammengesetztes Aloëdecoct, *G.*

"Extract of Aloes, 10 *grammes;* Myrrh, Potassium Carbonate, of each, 5 *grammes;* Extract of Liquorice, 40 *grammes;* Compound Tincture of Cardamoms, 300 *millilitres;* Distilled Water sufficient to produce 1000 *millilitres.* Reduce the Extract of Aloes and the Myrrh to coarse powder, and boil them and the Potassium Carbonate and the Extract of Liquorice with four hundred *millilitres* of Distilled Water in a covered vessel for five minutes; cool; add the Tincture of Cardamoms; set aside for two hours; strain through flannel; pass sufficient Distilled Water through the strainer to produce the required volume." *Br.*

This is essentially the former process of the British Colleges. The effect of the alkaline carbonate is, by combining with the resin of the myrrh and the insoluble portion of the aloes, to render them more soluble in water, while the licorice assists in the suspension of the portion not actually dissolved. The tincture of cardamom is useful not only by its cordial property, but also by preventing spontaneous decomposition. This decoction is said not to filter clear when first made, but, if kept for some time, to deposit insoluble matter, and then to become bright and clear on filtering. (*P. J.,* xiv, 491.) J. F. Brown proposes to prepare a concentrated

decoction which keeps for a long time unchanged. (*C. D.*, 1896, 425.)

Long boiling impairs the purgative property of aloes, and the same effect is thought to be produced, to a certain extent, by the alkalies, which certainly qualify its operation and render it less apt to irritate the rectum. This decoction, therefore, is milder as a cathartic than aloes itself; it is also more tonic and cordial, from the presence of the myrrh, saffron, and cardamom, and derives antacid properties from the potassium carbonate. It is given as a gentle cathartic, tonic, and emmenagogue, and is especially useful in *dyspepsia, habitual constipation,* and atonic *amenorrhea.* The decoction should not be combined in prescription with acids, acidulous salts, or other bodies incompatible with the alkaline carbonate.

Dose, from one-half to two fluidounces (15–60 mils).

DECOCTUM HÆMATOXYLI. Br.

DECOCTION OF LOGWOOD

(dę-cŏc'tŭm hæ-mą-tŏx'y-lī)

Tisane (Décocté) de Bois de Campêche, *Fr.;* Blauholz-Abkochung, *G.*

"Logwood, in chips, 50 *grammes;* Cinnamon Bark, bruised, 10 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Boil the Logwood with twelve hundred *millilitres* of Distilled Water in a suitable vessel for ten minutes, adding the Cinnamon Bark towards the end of the time; strain; if necessary pour sufficient Distilled Water over the contents of the strainer to produce the required volume." *Br.*

We prefer the old U. S. formula, which ordered an ounce of the logwood to be boiled with two pints down to a pint, and doubt much whether the wood is exhausted by a boiling of ten or fifteen minutes. The cinnamon of the Br. formula is in general a very suitable addition, but there might be circumstances under which it would be better omitted, and in this case, as in others, any addition to the simple decoction might be left to the judgment of the prescriber.

This is an excellent astringent in *diarrheas* of relaxation.

Dose, for an adult, two fluidounces (60 mils); for a child about two years old, two or three fluidrachms (7.5–11.25 mils).

DECOCTUM ISPAGHULÆ. Br.

DECOCTION OF ISPAGHULA

(dę-cŏc'tŭm ĭs-pąg'hū-lą)

"Ispaghula, bruised, 15 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Boil the Ispaghula with twelve hundred *millilitres* of Distilled Water, in a suitable vessel, for ten minutes; strain; if necessary pour sufficient Distilled Water over the contents of the strainer to produce the required volume." *Br.*

This decoction was transferred from the British Addendum (1900) to the British Pharm. (1914). It is used as a demulcent drink in India for *diarrhea.* *Dose,* four fluidrachms to two fluidounces (15–60 mils).

DECOCTUM SAPPAN. Br.

DECOCTION OF SAPPAN

(dę-çŏc'tŭm săp'păn)

"Sappan, in chips, 50 *grammes;* Cinnamon Bark, bruised, 10 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Boil the Sappan with twelve hundred *millilitres* of Distilled Water, in a suitable vessel, for ten minutes, adding the Cinnamon Bark towards the end of the time; strain; if necessary pour sufficient Distilled Water over the contents of the strainer to produce the required volume." *Br.*

This decoction was transferred from the British Addendum (1900) to the British Pharm. (1914). It is used like logwood decoction in India as an astringent in *diarrhea* in *doses* of four fluidrachms to two fluidounces (15–60 mils).

DIACETYLMORPHINA. U. S.

DIACETYLMORPHINE Diacetylmorph.

(dī-ą-cēt'ŷl-mŏr-phī'ną)

"An alkaloid [$C_{21}H_{23}O_5N$ or $C_{17}H_{17}(O.C_2H_3O)_2ON = 369.19$] prepared from morphine by acetylization. Preserve it in well-closed containers, protected from light." *U. S.*

This alkaloid was introduced under the trade-name of *Heroin.* It is made by treating morphine with acetyl chloride, washing the product with a dilute alkaline solution and crystallizing from alcoholic solution. It is officially described as follows: "Diacetylmorphine occurs as a white, crystalline powder without odor. One Gm. of Diacetylmorphine dissolves in about 1700 mils of water, 31 mils of alcohol, 1.4 mils of chloroform, and in 100 mils of ether at 25° C. (77° F.). Its saturated alcoholic solution is alkaline to moistened litmus paper. It melts between 171.5° and 173.5° C. (340.7° and 344.3° F.). Dissolve about 0.01 Gm. of Diacetylmorphine in a few drops of nitric acid; a yellow color is produced, which gradually changes to greenish-blue. Heat about 0.1 Gm. of Diacetylmorphine with 1 mil of alcohol and 1 mil of sulphuric acid; ethyl acetate is produced, recognizable by its odor. No weighable ash remains on incinerating 0.5 Gm. of Diacetylmorphine. Dissolve 0.2 Gm. of Diacetylmorphine in 5 mils of distilled water with the aid of a few drops of hydrochloric acid, and pour this solution slowly into 5 mils of potassium hydroxide T.S., shaking the test tube occasionally; a white precipitate forms, which quickly redissolves, yielding a clear solution (*other alkaloids*). On heating this solution no odor of ammonia is noticeable (*ammonium salts*). A solution of about 0.02 Gm. of Diacetylmorphine in 2 mils of sulphuric acid is colorless (*readily carbonizable organic impurities*). Dissolve about 0.05 Gm. of potassium ferricyanide in 10 mils of distilled water, add

one drop of ferric chloride T.S. and then 1 mil of an alcoholic solution of Diacetylmorphine (1 in 100); no greenish or blue color is produced at once (*morphine*). Dissolve 1 Gm. of Diacetylmorphine in 10 mils of distilled water and 5 mils of diluted hydrochloric acid in a porcelain dish and evaporate the solution on a water bath to a syrupy consistence (about 2 mils). Transfer this residue to a separatory funnel with the aid of 25 mils of distilled water, render it alkaline with sodium hydroxide solution (10 per cent.) and then shake it out with 3 successive portions of 15, 10 and 5 mils of chloroform, passing the chloroform solutions through a small filter previously moistened with chloroform. Carefully evaporate the combined chloroform solutions to dryness on a water bath, dissolve the residue in 10 mils of fiftieth-normal sulphuric acid V.S., add a few drops of methyl red T.S. and titrate the excess of acid with fiftieth-normal potassium hydroxide V.S. Not less than 7.5 mils of the latter is required (*foreign alkaloids*)." *U. S.*

A method for the rapid and satisfactory separation of morphine from heroin has been described by J. M. Duran. (*J. A. Ph. A.*, 1916, p. 163.) It is based upon the use of carbon tetrachloride as a shaking out solvent, which has the property of dissolving heroin but not morphine.

For uses, see *Diacetylmorphinæ Hydrochloridum.*

DIACETYLMORPHINÆ HYDROCHLORIDUM. U. S. (Br.)

DIACETYLMORPHINE HYDROCHLORIDE Diacetylmorph. Hydrochl. [Diacetylmorphine Chloride]

(dī-ą-cēt'ȳl-mör-phī'næ hȳ-drǫ-ȼhlō'rį-dŭm)

"The hydrochloride [$C_{21}H_{23}O_5N.HCl + H_2O$ or $C_{17}H_{17}(O.C_2H_3O)_2ON.HCl + H_2O = 423.68$] of the alkaloid diacetylmorphine. Preserve it in well-closed containers, protected from light." *U. S.* "Diamorphine Hydrochloride, $C_{21}H_{23}NO_5$,HCl,H_2O, is the hydrochloride of an alkaloid obtainable by the action of acetic anhydride on morphine." *Br.*

Diamorphinæ Hydrochloridum, *Br.*; Diamorphine Hydrochloride; Heroin Hydrochloride.

The British Pharmacopœia (1914) abbreviated the name of this compound to "Diamorphine Hydrochloride" when it was introduced. It is made by dissolving diacetylmorphine in diluted hydrochloric acid, evaporating and crystallizing the product. (See *Diacetylmorphina.*) It is officially described as follows: "Diacetylmorphine Hydrochloride is a white, crystalline powder without odor. One Gm. of Diacetylmorphine Hydrochloride dissolves in 2 mils of water at 25° C. (77° F.); soluble in alcohol; insoluble in chloroform or ether at 25° C. (77° F.). An aqueous solution of Diacetylmorphine Hydrochloride (1 in 20) is neutral or only faintly acid to litmus. It melts at about 230° C. (446° F.) with decomposition. An aqueous solution of the salt with silver nitrate T.S. yields a white precipitate insoluble in nitric acid. In other respects the salt responds to the tests for identity and purity under *Diacetylmorphina,* omitting the melting point." *U. S.*

"A white, crystalline powder; taste bitter. Melting point from 231° to 232° C. (447.8°–449.6° F.). Soluble in 3 parts of *water* and in 11 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of chlorides. 0.1 gramme dissolved in 2 millilitres of *alcohol* (90 per cent.), mixed with 1 millilitre of *sulphuric acid* and warmed, develops an odor of acetic ether. A solution of 0.1 gramme in 1 millilitre of *sulphuric acid* heated on a water bath, cooled and diluted with 6 millilitres of *water,* gives a deep blue color on the addition of an aqueous solution (0.5 in 100) of *potassium ferricyanide* to which 1 drop of *T. Sol. of ferric chloride* has been added. Treated with a few drops of *nitric acid* a yellow color is produced, which changes to greenish-blue on warming, and finally becomes yellow again. 0.02 gramme added to 5 millilitres of an aqueous solution (0.5 in 100) of *potassium ferricyanide,* to which 1 drop of *T. Sol. of ferric chloride* has been added, produces a greenish color and not a deep blue (absence of morphine)." *Br.*

The hydrochloride has the advantage over the alkaloid *diacetylmorphine* because of its much greater solubility in water.

A method for the rapid determination of small quantities of heroin or its salts, especially adapted for revenue officers who are required to give testimony concerning seizures under the Harrison Narcotic Act, was devised by Reginald Miller and is described in *A. J. P.*, 1915, p. 248. It is a colorimetric method, using the formaldehyde sulphuric acid reagent.

Uses.—In its general physiological action *diacetylmorphine* acts much like morphine except that, according to Ott, it is depressant to the spinal cord. It is, however, about twice as powerful in its depressant action upon the respiratory center. For this reason it is greatly inferior to morphine as an analgesic. Its most important use in medicine is as a sedative to the respiratory center; thus it is employed to allay *cough* whether due to *bronchitis* or of nervous origin, to relax the *asthmatic* paroxysm, in *whooping cough, cardiac dyspnea,* and similar conditions. According to Impens (*A. G. P.*, 1899, lxviii, p. 527), although actually more poisonous to the respiratory center it is relatively safer than morphine as disproportionally smaller quantities are needed to exercise therapeutic sedation.

Diacetylmorphine has been employed by physicians in cases in which formation of the drug habit is feared but it is fully as dangerous a drug in this regard as morphine itself, indeed, the diacetylmorphine habit is apparently the more rebellious addiction of the two. Cases of acute poisoning are not very numerous but Trawick (*Kentucky Med. Journ.*, 1911) reports a case, following a dose of one-half a grain, with serious symptoms of the opium type—marked

slowing of the respiration, and contracted pupils. In some cases there is also a semi-delirious condition somewhat resembling that seen in hyoscine poisoning.

Dose, one-sixteenth to one-sixth of a grain (0.004–0.01 Gm.).

Off. Prep.—Elixir Terpini Hydratis et Diacetylmorphinæ, *N. F.*

DIASTASUM. U. S.

DIASTASE

(dī-ăs-tās'ŭm)

"A mixture containing amylolytic enzymes obtained from an infusion of malt. It converts not less than 50 times its weight of potato starch into sugars. Preserve it in well-closed containers, protected from light, heat and moisture." *U. S.*

In germinating grains there is present an enzyme which is capable of converting the starches of the grain into sugar whereby the young plant may be nourished. This diastatic ferment appears to act very much like the ptyalin of the saliva. The substance recognized by the Pharmacopœia under the name of *diastase* is not a pure principle but is a mixture of various inert substances containing the active ferments of malt. It is officially described as follows: "Diastase occurs as a yellowish-white, amorphous powder or in translucent scales; odorless and tasteless. It converts starch into dextrin and maltose. Diastase gradually loses its amylolytic power on keeping; this power is destroyed by heating its solutions above 85° C. (185° F.), or by the addition of much acid and is diminished by the presence of acids or alkalies. Diastase is soluble in water, the solutions being more or less turbid; almost insoluble in alcohol.

"**Assay.**—Mix a quantity of potato starch, purified as directed under *Pancreatinum,* equivalent to 5 Gm. of dry starch, in a beaker with 10 mils of cold distilled water. Add 140 mils of boiling distilled water, and heat the mixture on a water bath with constant stirring for two minutes, or until a translucent, uniform paste is obtained. Cool the paste to 40° C. (104° F.) in a water bath previously adjusted to this temperature. Prepare a fresh solution of 0.1 Gm. of Diastase in 10 mils of distilled water at 40° C. (104° F.) and add it to the paste. Mix them well and maintain the same temperature for exactly thirty minutes, stirring frequently; a thin, nearly clear liquid is produced. Add at once 0.1 mil of this liquid to a previously made mixture of 0.2 mil of tenth-normal iodine V.S. and 60 mils of distilled water; no blue or reddish color is produced." *U. S.*

Diastase being one of the newer enzymes produced commercially is frequently found upon the market in an impure or adulterated condition, samples having been observed containing as much as 60 per cent. of starch. Much of the commercial diastase is variable in strength and frequently it is almost inert. *Takadiastase* is the name of a proprietary form of diastase which is not produced from malt but is produced by the growth of certain species of *aspergillus* upon rice hulls or bran. In Japan takadiastase is used in the brewing industry as malt is used in other countries.

Uses.—Diastase was introduced into medicine with the idea that by virtue of its power of digesting starches it would be useful in *fermentative dyspepsia.* In those rare cases where there is an organic deficiency of saliva, or in the more frequent condition where the patient is too lazy to masticate his food, it may be of service but as its action upon the starch is similar to that of the ptyalin of saliva its range of usefulness as a digestant is certainly not very wide.

The *dose* is five to fifteen grains (0.32–1.0 Gm.).

DIGITALIS. U. S. (Br.)

DIGITALIS Digit. [Foxglove, Digitalis Folium P. I.]

(dĭj-ĭ-tā'lĭs)

"The carefully dried leaves of *Digitalis purpurea* Linné (Fam. *Scrophulariaceæ*), without the presence or admixture of more than 2 per cent. of stems, flowers or other foreign matter. If made into the official tincture and assayed biologically the minimum lethal dose should not be greater than 0.006 mil of tincture, or the equivalent in tincture of 0.0000005 Gm. of ouabain, for each gramme of body weight of frog. Digitalis should be preserved in tightly-closed containers protected from light." *U. S.* "Digitalis Leaves are the dried leaves of Digitalis purpurea, *Linn.,* collected from plants commencing to flower, thoroughly dried at a low temperature, and kept dry in well-filled air-tight containers. When powdered no portion should be rejected." *Br.*

Digitalis Folia, *Br.,* Digitalis Leaf; Digitalis Leaves, Foxglove Leaves; Fairy Cap, Fingers, Thimbles, or Bells, Lady's Glove, Purple Foxglove, Flop-dock, Throatwort, Cottagers; Digitale, *Fr. Cod.;* Feuilles de Digitale Pourprée (de grande Digitale), Digitale Pourprée, Doigtier, *Fr.;* Folia Digitalis, *P. G.;* Purpurrother Fingerhut, Fingerhutkraut, Fingerhut blätter, *G.;* Digitale, *It.;* Digital (Hoja de), Dedalera, *Sp.*

The foxglove is a beautiful plant, with a biennial or perennial fibrous root, which in the first year sends forth large tufted leaves, and in the following summer a single erect, downy, and leafy stem, rising from two to five feet, and terminating in an elegant spike of purple flowers. The lower leaves are ovate, pointed, about eight inches in length and three in breadth, and stand upon short, winged foot-stalks; the upper are alternate, sparse, and lanceolate; both are obtusely serrate, and have wrinkled velvety surfaces, of which the upper is a fine deep green, the under paler and more downy. The flowers are numerous, and attached to the upper part of the stem by short peduncles, in such a manner as generally to hang down upon one side. At the base of each peduncle is a floral leaf, which is sessile, ovate, and pointed. The calyx is divided into five segments, of which the uppermost is narrower than the others. The corolla is monopetalous, bell-form, swelling on

the lower side, irregularly divided at the margin into short obtuse lobes, and in shape and size not unlike the end of the finger of a glove, a circumstance which has suggested most of the names by which the plant is designated in different languages. Its mouth is guarded by long soft hairs. Externally, it is in general of a bright purple; internally, it is sprinkled with black spots upon a white ground. There are numerous garden varieties, one having white flowers. The filaments are white, curved, and surmounted by large yellow anthers. The style is simple, and supports a bifid stigma. The seeds are numerous, very small, grayish-brown, and contained in a pyramidal two-celled capsule. All of the species of the genus *Digitalis* seem to have similar effects upon the system. Miller and Baker (*J. A. Ph. A.*, March, 1914) examined 23 different species or varieties of *Digitalis* and found that one or two, indeed, surpassed the *D. purpurea* in power.

Foxglove grows wild in the temperate parts of Europe, where it flowers in the middle of summer. In this country it is cultivated both for ornament and for medicinal use. (For methods of cultivation in the United States, see Newcomb, *A. J. P.*, 1911, p. 529; Borneman, *A. J. P.*, 1912, p. 547; Miller, *A. J. P.*, 1913, p. 297.) The leaves are the part generally employed. The U. S. Pharmacopœia IX departed from the ancient requirement, and in our opinion properly so, that digitalis should be collected only in the second year. Modern investigators, such as Sharp (*P. J.*, lxxxix, 131), Miller and Baker (*J. A. Ph. A.*, 1913, ii, 198), and Carr (*A. J. P.*, 1913, lxxxv, 297) are unanimous that the first year's leaves are fully as powerful as those collected just before flowering. Hale (*Proc. A. Ph. A.*, 1910, 294), as well as Miller and Baker, finds that there is no difference between the wild and cultivated plants; indeed, the latter say even if grown in hot houses. Likewise the formerly accepted view that digitalis leaves deteriorate rapidly has been shown to be erroneous. Hatcher and Eggleston (*A. J. P.*, 1913, 203) have found that the loss of potency in properly dried leaves was not more than 2 per cent. a year, and Haskell and Miller (*J. A. Ph. A.*, 1914, iii, 306) were unable to detect any change after 12 months. In drying the leaves should not be exposed to a temperature of more than 120° C. (248° F.) for the last named investigators found that, although this temperature had no effect on the quality of the drug, 140° C. (284° F.) was distinctly injurious.

The seeds contain more of the active principle than the leaves, are less likely to suffer in drying, and keep better, but are nevertheless little used. So far as the relative strength of these two parts can be determined from that of their alcoholic extracts, it would appear, from the experiments of Hirtz, that the seeds are ten times stronger than the leaves. (See *A. J. P.*, xxxiii.)

Properties.—Fresh digitalis leaves are without odor but acquire a faint odor when dried. The color of the dried leaf is a dull pale green, modified by the whitish down upon the under surface; that of the powder is a fine deep green. They are officially described as: "Leaves, when entire, attaining a length of 30 cm. and a breadth of 15 cm., ovate to oval, abruptly contracted into winged petioles, the latter from 5 to 10 cm. in length or, in the smaller leaves, nearly absent; margin crenate, irregular (the commercial article usually more or less crumpled and broken), thin, dull, pale green or gray and densely pubescent on the lower surfaces; upper surfaces wrinkled, sparsely hairy; the venation conspicuously reticulated; the midribs and principal veins broad and flat, often purplish, the lower veins continued into the wings of the petioles; odor slight, characteristic; taste strongly bitter. The powder is dark green; with numerous fragments of non-glandular hairs consisting of from 2- to 8-cells (usually 2- to 5-cells), varying in length from 0.145 to 0.435 mm., some of the cells being frequently collapsed; glandular hairs few, small, with a 1- or 2-celled stalk and a 1- or 2-celled glandular head; numerous irregular fragments of lamina showing stomata and occasional waterpores and elongated fragments of veins and petioles showing fibro-vascular tissues. Digitalis yields not more than 15 per cent. of ash." *U. S.*

The British Pharmacopœia description is as follows: "Hairs of two kinds, either simple, mostly 3–5 celled and bluntly pointed, or glandular and consisting of a short pedicel bearing a unicellular or bicellular gland. In transverse section, no sclerenchymatous cells or fibres, and no crystals of calcium oxalate. In the powdered Leaves, groups of epidermal cells with more or less sinuous walls, numerous fragments of multicellular hairs with thin, granular walls; but no sclerenchymatous cells or fibres, or crystals of calcium oxalate. No marked odor; taste very bitter." *Br.*

For a comprehensive description of the morphology and anatomy of the leaves of *Digitalis purpurea* and the adulterants of this drug, see Bohny's article in *Bot. Centralbl.*, 1906, p. 267. Collin reviews the pharmacognosy of Digitalis (*J. P. C.*, 1905, p. 56), showing the characteristics of the powder and the detection of the principal leaf adulterants, such as *Inula Conyza, Verbascum phlomoides, Artanthe elongata,* and *Salvia Sclarea.* Kraemer (*A. J. P.*, 1912, p. 35) discusses the morphology of digitalis leaves and shows the variation and the forms of hairs in different commercial specimens.

Digitalis yields its virtues both to water and to alcohol. It contains, besides active principles, a volatile oil, a fatty matter, a red coloring substance analogous to extractive, chlorophyll, albumen, starch, sugar, gum, lignin, and salts of potassium and lime, among which, according to Rein and Haase, is acid potassium oxalate. Morin, of Geneva, discovered in the leaves two acids: one fixed, called *digitalic acid,* the other volatile and resembling valerianic acid, which he proposed to name *antirrhinic acid* (*P. J.*,

vii, 294). England (*A. J. P.*, 1892, 361) found about 5 per cent. of fixed oil in digitalis leaves. Morries obtained a narcotic empyreumatic oil by the destructive distillation of the leaves. The yield of ash from digitalis leaves is usually put down at from 7 to 10 per cent., and this is in accord with the result reached by F. H. Alcot with British leaves. (*P. J.*, Jan., 1903.) On the other hand, M. Greshoff (*P. J.*, Dec., 1902) has obtained in various samples of German digitalis, after the leaves have been freed from sand and the leaf-stalks removed, a yield of from 16.4 to 25 per cent. of ash.

Under the name of *digitalin* there have long been in commerce two distinct substances obtained from digitalis, both of them crude mixtures of the glucosidal principles. The *French* digitalin was that originally prepared by Homolle. It is a whitish powder, of a neutral reaction, soluble in 2000 parts of cold and in 1000 parts of hot water. It is this digitalin which was formerly recognized by the U. S. and Br. Pharmacopœias. See *U. S. Dispensatory*, 19th edition, p. 424. The so-called *German* digitalin is distinguished from the French by being, in great part or entirely, freely soluble in water.

In 1871, Nativelle received from the French Academy the prize of Orfila for the discovery of the active principle of digitalis. The method of preparation, as finally improved and modified by himself, and published in the *J. P. C.*, xx, 1874, p. 81, and also a process which has the advantage of being far shorter and more readily carried out, devised by Tanret (*Ibid.*, Oct., 1875), may be found on p. 1143, 14th ed., *U. S. D.*

According to the researches of Schmiedeberg (*P. J.*, (3) v, 741), confirmed by Kiliani (*P. J.*, (3) xxii, 1061, and (4) i, 29), the seeds and leaves of *Digitalis purpurea* contain a preponderating amount of a glucoside, *digitonin*. They contain in addition three other substances which possess the power of acting on the heart, namely, crystallizable *digitoxin* and two amorphous glucosides, *digitalin* and *digitalein*.

Digitonin forms fully one-half of the mixed glucosides from the digitalis seed and the principal portion of German "digitalin," from which it may be prepared by extraction with and crystallization from 85 per cent. alcohol. Digitonin softens at 225° C. (437° F.), and melts completely at 235° C. (455° F.). The crystals dissolve sparingly in cold water, more readily in hot, to an opalescent solution which froths on agitation. It cannot be crystallized from water. The aqueous solution is lævorotatory ($[a]_D$ = — 49 at 25° C. [77° F.]), and is precipitated by tannin, ammoniacal lead acetate, and baryta water. Digitonin is only slightly soluble in absolute alcohol, and still less so in ether, chloroform, or petroleum benzin. It forms a crystalline compound with amyl alcohol. According to Kiliani, digitonin has the formula $C_{27}H_{46}O_{14} + 5H_2O$, and when boiled with strong alcohol and hydrochloric acid splits up into *dextrose*, *galactose*, and *digitogenin*, the last body separating in warty masses on cooling. Digitonin does not possess the characteristic physiological properties of digitalis; its action is similar to that of the saponins.

Digitoxin is characterized by its free solubility in alcohol and chloroform, slight solubility in ether, and insolubility in petroleum benzin. It crystallizes from alcohol in pearly scales or needles which melt at 240° C. (464° F.). It is quite insoluble in water, to which it does not impart even a bitter taste. Warmed with strong hydrochloric acid, it gives a yellow or greenish coloration, which is one of the reactions ascribed to the "digitaline crystallisée" of the French Codex. Schmiedeberg states that it is not a glucoside, but Kiliani asserts that upon heating its alcoholic solution with hydrochloric acid it splits up into *digitoxigenin* and a sugar, *digitoxose*. The reaction for this is now considered to be:

$$C_{34}H_{54}O_{11} + H_2O = C_{22}H_{32}O_4 + C_6H_{12}O_4$$

Digitoxin is found mainly in the leaves (Kiliani stating that it is not found in the seeds at all), but Keller (*P. J.*, July 24, 1897) finds it also in the seeds in smaller amount. It is the most poisonous of the constituents of digitalis.

Digitalin (*Digitalinum verum* of Kiliani) forms a white amorphous powder or soft white grains which remain unchanged when heated to 200° C. (392° F.), at 210° C. (410° F.) begin to aggregate, and towards 217° C. (422.6° F.) melt, becoming yellow. When treated with water the particles of digitalin swell up and dissolve slightly, giving a solution which foams strongly on agitation. It is dissolved sparingly (1 to 100) by cold proof spirit, but in considerable amount by hot rectified spirit or absolute alcohol. When a minimum of alcohol is used, the solution on cooling becomes almost solid from the separation of a thick magma of granules, which are, however, destitute of crystalline structure. This peculiar behavior affords a valuable means of testing its purity, as only a small percentage of the other glucosides with the digitalin prevents the formation of the granules. The minutest admixture of amorphous glucosides also rapidly causes an intense yellow coloration. Digitalin is very sparingly soluble in ether or chloroform. When digitalin is heated with diluted hydrochloric acid, an insoluble resinous substance almost immediately separates out; Schmiedeberg termed this *digitaliresin*. By operating in alcoholic solution, Kiliani avoids the separation of resin, and finds that digitalin splits up as a glucoside into *digitaligenin*, *glucose*, and *digitalose*, thus:

$$C_{29}H_{46}O_{12} + H_2O = C_{16}H_{22}O_2 + C_6H_{12}O_6 + C_7H_{14}O_5$$

Kiliani found that commercial *digitalinum purum* contained but 5.5 per cent. of true digitalin.

Digitalein is considered to be a distinct glucoside by Schmiedeberg, but Kiliani, who

worked over it later, regards its independent existence as questionable.

GITALIN has been described by Kraft (*S. W. P.*, 1911, xlix), who believes that digitalein is an impure form of gitalin. The latter is an amorphous white powder soluble in 600 parts of water. It can be obtained also as a crystalline hydrate.

DIGITIN of Schmiedeberg is also considered by Kiliani to be simply digitonin.

The above résumé of our present knowledge clearly shows that the chemistry of digitalis cannot be considered as settled; but it also clearly shows that no "digitalin" completely represents digitalis. Moreover, the digitalin of commerce varies greatly. (See *A. Pharm.*, 1895, 299; also 1895, 698.)

Assay.—Three animals have been suggested as reagents for the biological standardization of digitalis, the frog, the guinea-pig, and the cat. The most commonly used is the frog. Although a number of writers had employed physiological tests to determine the relative potency of different digitalis bodies, the first to use the biological assay in a systematic manner was Houghton, who used what is now known as the "twelve hour frog method."

The U. S. P. recommends the frog method for the biological assay of digitalis and describes it as follows: "For the members of the digitalis series the so-called "one hour frog" method is recommended. This method consists essentially in ascertaining the dose of a drug or preparation which will bring the heart of a standard sized frog to systolic standstill in one hour's time. The method is carried out as described below; all measurements being performed with the same degree of accuracy used in ordinary quantitative chemical estimations.

"*Frogs.*—The frogs to be employed in an assay should be in a healthy condition and of the same species. Those most commonly obtainable in this country are the common grass frogs (*Rana viridis* or *Rana pipiens*). While the dose for a frog is estimated according to its weight, it is best to use frogs of a fairly uniform size, the most convenient weight for such work being between 15 and 25 Gm.

"*Storage.*—Before use the frogs should be stored in tanks kept in a cool room, preferably where the temperature does not rise above 15° C. (59° F.). The bottom of the tanks should be covered with running water or, if running water is not convenient, standing water may be used if it is changed from two to four times daily. An hour before the frogs are to be used for an assay a sufficient number should be taken to the operating room, each one carefully weighed to within 0.1 Gm. and placed in an individual wire cage or container, these are then placed in a tank containing water to the depth to about 1 cm. (½ inch), which is kept during the process of assay at a uniform temperature of 20° C. (68° F.). The maintaining of a uniform temperature at which all assays of the members of this group should be carried out is important, as the susceptibility of frogs differs very considerably at different temperatures.

"*Dosage.*—After the frogs have been weighed as described, the doses to be given are calculated according to their weights and are measured into small conical glasses by means of a finely graduated pipette. The doses of the preparation which are to be injected should be as uniform in quantity as possible and should not exceed 0.015 mil for each gramme of body weight of frog. The members of the digitalis series may be assayed in either fluidextract or tincture strength, being diluted with water as may be necessary to get the volume dose. In case the alcohol content in any preparation after dilution is higher than 20 per cent., the preparation may be subject to careful evaporation and subsequent dilution with an aqueous solution containing 0.7 per cent. of sodium chloride until the original volume is restored and the alcohol content is not above the per cent. named. It is always best to have the alcohol content of different preparations uniform. In case there is a precipitate the preparation to be assayed should be shaken each time a dose is measured out. When the doses are ready, they may be injected into the anterior lymph sac of the animal. This is done by means of a glass pipette which is drawn out to a fine point. The frog is held on its back in one hand and the pipette with the contained drug in the other, the mouth of the frog is operated with the point of the pipette and, carefully avoiding the tongue, the floor of the mouth is punctured and the point of the pipette is then seen to enter the anterior lymph sac of the frog. The contents of the pipette are now forced into the sac either by gravity or by gently blowing, if necessary. In the latter case, care should be taken not to introduce air into the sac. Care should also be taken not to puncture the skin. The animal is then replaced in its cage in the tank, the temperature of which is maintained as stated at 20° C. (68° F.). At the end of one hour from the time of injection each frog is pithed, both brain and cord, the heart is exposed and its condition examined. For the correct end reaction the ventricle should be in systolic standstill while the auricles should be widely dilated. Following mechanical stimulation feeble contractions may be allowed in the auricles and localized contractions in the ventricle, but no general contraction is allowable. If when the heart of an animal is being exposed for examination, remains of the injected drug are found in the lymph sac unabsorbed, such an animal should be discarded and not considered in the results obtained. It happens sometimes that one frog out of a large series may prove a decided exception to the others in the way of increased or decreased susceptibility to the drug. Such an animal should also be discarded. After the primary or trial assay has been carried out and the approximate strength of the preparation ascertained, a second series of frogs is injected in like manner, using doses the limits of which are considerably narrower than the first series. A third or even fourth series of injections may be necessary to

confirm the earlier results. The dose thus found is then compared with the dose of a standard which is similarly ascertained upon another series of frogs of the same lot. From such a comparison the strength of the unknown preparation can be suitably adjusted. The use of a standard is made necessary by the fact that frogs differ in their susceptibility to the members of the digitalis series at different seasons of the year. The condition of susceptibility is ascertained and allowed for by the use of a solution of ouabain (see Part III) as a standard which in appropriate doses is injected into a series of frogs and their resistance thus determined. The necessary strength of an unknown preparation may be calculated from the dose actually found by the ratio of the standard dose of ouabain to the dose of ouabain found necessary to kill. Thus:

"Standard dose of ouabain : Found dose of ouabain :: Standard dose of drug being assayed : Necessary dose of unknown.

"The standard dose of ouabain is 0.0000005 Gm. per gramme of body weight of frog. The standard dose of Tincture of Digitalis to correspond is 0.006 mil per gramme of body weight of frog. If, therefore, in a certain series of frogs the resistance to ouabain is found to be increased so that a dose of 0.00000075 Gm. is necessary to stop the heart in systole in one hour, the dose of Tincture of Digitalis would also have to be increased to 0.009 mil, and the actual dose found calculated against this, instead of against the standard dose of 0.006 mil. For example, in frogs showing the increased resistance as indicated above, if the Tincture being examined assays 0.018 mil per gramme of body weight it is one-half strength.

"*Standards.*—The standards adopted are as follows:

	Gramme or mil for each gramme of body weight of frog
Standard dose of ouabain.....	0.0000005
Digitalis	
Leaves (in the form of tincture)	0.0006
Fluidextract	0.0006
Tincture	0.006." *U.S.*

Houghton prefers that the observation be made at the end of 14 or 15 hours, instead of one hour. Focke (*A. Pharm.*, 1907) modifies the frog's heart method by using a constant dose, the time of arrest being the variant which furnishes the index to relative potency. Because of the variation in the susceptibility of frogs at different times of the year, it has been suggested that the frogs be standardized by testing the susceptibility representatives of each batch of frogs being tested with strophanthin.

The "guinea-pig method" consists in simply finding the minimum lethal dose for a guinea-pig. To a series of previously weighed guinea-pigs is administered hypodermically ascending doses of a tincture of the sample to be tested. The end-point of the test is the smallest dose which will kill the guinea-pig within twenty-four hours. The method is essentially similar to that employed for aconite. (See *Aconitum.*)

A much more elaborate method has been suggested by Hatcher. He has found that the lethal dose of crystalline strophanthin (ouabain) for the cat is very constant, being almost exactly 0.1 milligramme per kilogramme of body weight when administered intravenously. The method of assay is to give a quantity of the sample to be tested, of about two-thirds of the expected fatal dose for the cat, and then run in slowly a solution of strophanthin until death is caused. The difference between the ordinary fatal dose of the glucoside and the quantity used in the test represents the amount of strophanthin to which the digitalis being tested is equivalent; that is, the larger amount of strophanthin which has been used, the weaker is the preparation. It is at present hardly possible to decide which of these methods for the biological testing of digitalis is the most reliable. The cat-method of Hatcher is practically out of the question for any commercial purpose, not merely because of the technical difficulties, but chiefly because of the limited supply of cats. Each of the other methods has its advocates.

Among the most important objections to the frog methods of standardizing are the facts that not only is there great difference in susceptibility between different species of frogs, but also in the same species at different seasons of the year. Focke, for instance, has found that the frog in the spring was twice as resistent to digitalis as in the fall. (*A. Pharm.*, 1907.) This variation is due in part to the difference in temperature at various seasons of the year but also in part to the nutritional condition of the batrachian. For this reason the U. S. P. recommends that the frogs be standardized by testing their resistance against crystalline strophanthin. It is doubtful, however, whether this standardization of a frog is of any great usefulness for the reason that the relative toxicity of various members of the digitalis series to the cold blooded animal bears little correspondence to their relative power in man. The question of whether or not the guinea-pigs show seasonal variation in susceptibility to digitalis is still open for difference of opinion. See Haskell (*A. J. P.*, 1914, lxxvi, p. 7).

After all none of these methods of biological standardization of digitalis and its congeners can be regarded as an accurate method for the assay in the same sense that chemical standardization is; their chief utility is in preventing inert preparations of digitalis from being placed upon the market. An interesting fact was brought out in Bulletin No. 48 of the United States Hygienic Laboratory by Edmunds and Hale. It is that if two samples be tested by different methods, one may be found to be more toxic in the frog, and the other more toxic to the guinea-pig.

For a discussion of the various details of the methods for the assay of digitalis, see Haskell (*A. J. P.*, 1914, lxxxvi, p. 7); Focke (*Z. E. P. T.*, 1909, vii, p. 1); Edmunds and Hale (*U. S. Hygienic Laboratory Bulletin* No. 48, 1909);

Hatcher (*J. A. M. A.*, 1910, lv, p. 746); Houghton and Hamilton (*A. J. P.*, 1909, li); Hamilton and Rowe (*J. A. Ph. A.*, 1915, iv, p. 108); Vanderkleed and Pittenger (*J. A. Ph. A.*, 1914, iii, 815).

No satisfactory chemical assay process has yet been devised for digitalis and hence the U. S. P. contains no process. The amount of digitoxin present in digitalis has been proposed by several investigators as a means of standardizing it, but it is by no means clear that this is a reliable criterion. Several attempts have been made to estimate the practical usefulness of the assay for digitoxin by comparing the results with the physiological tests of digitalis. While some experimenters have found a fairly close agreement between them, the great majority of those who have studied the question incline to the opinion that the two methods of assay do not run at all parallel. There are three possible reasons for this variation and each one of them seems to be operative. These are, first, inaccuracies in the chemical method for assaying digitalis; second, the unavoidable inaccuracy of the biological assay; third, the fact that the relative quantity of digitoxin to the other constituents of digitalis may vary from one sample to another.

While digitoxin is the most important constituent of digitalis it is by no means the only important one. The experiments of Lutzkaga (*A. J. P. T.*, 1908, xviii) and those of Barger and Shaw demonstrate that between 60 and 70 per cent. of the activity of digitalis leaf is due to its digitoxin, and that the proportion of digitoxin cannot be relied upon as a criterion of the quality of the drug. (See *Ber. d. Chem. Ges.*, 1897; *Pharm. Rev.*, 1901, 514; *D. C.*, 1902, 223; *P. J.*, 1902, 663; *Chem. News*, 1903, 123; *A. Pharm.*, 1903, 358.) J. Gordon Sharp proposed a test for digitalis based upon the fact that the leaves contain an enzyme, which acts on amygdalin producing an odor like that of bitter almond with hydrocyanic acid. (*P. J.*, 1902, 236.)

Uses.—Although digitalis appears to have been used by the inhabitants of Britain as far back as the tenth century of the Christian Era, it was introduced into regular medical practice by William Withering in 1775, who obtained his knowledge of the value of foxglove in dropsy from an old woman of Shropshire.

The opinion of the medical profession as to the mode of action of digitalis and the class of cases in which it is useful has undergone many changes. Recent studies have led to another one of these revisions of the accepted belief concerning the effects of this drug upon the system, especially upon the circulation.

When given in small dose, that is, in quantities barely sufficient to cause any visible change, the only marked effect of digitalis upon the circulation is a slowing of the pulse, which is due to a stimulation of the inhibitory mechanism of the heart. After somewhat larger quantities the heart-beat becomes extremely slow, the size of the wave very large, and the vigor of the contraction of the heart perhaps a little increased, but the blood pressure is not materially affected because of the great reduction in pulse rate.

Despite the fact that there is no increase in arterial pressure it is probable that even at this stage of the action of the drug there is more or less stimulant effect upon the vasomotor mechanism, the pressor effect of the vascular constriction being overcome by the great reduction in the pulse rate. When toxic doses are administered the blood pressure is distinctly, and sometimes greatly, elevated. This is brought about partially by an increased vigor of the heart's contraction, but probably in greatest part by constriction of the blood vessels. Often at this stage there appear various forms of cardiac irregularities, the most common of which is that which is known as an "extra-systole"; the irritability of the heart muscle is so greatly increased that before the completion of the diastolic period a new contraction interrupts the relaxation. Sometimes these extra-systoles occur regularly with every alternate beat of the pulse, producing the so-called *pulsus bigeminus* (sometimes incorrectly called a dicrotic pulse). Later on in the poisoning the cardiac contractions become extremely rapid, more or less irregular, and the diastole never complete. Eventually in the frog the ventricle passes into a condition of permanent contraction, or, as it is more frequently called, systolic spasm. In the warm-blooded animal, however, the heart relaxes immediately before death and passes into a state of fibrillation.

Under certain conditions digitalis produces a marked increase in the flow of urine. Apparently in normal health it has little or no diuretic action. Its effect upon the kidney appears to be the result of the reaction of the renal artery. Joseph (*A. E. P. P.*, 1913, lxxiii, p. 81) has shown that the contraction of the renal artery by digitalis is less than that in the rest of the body and that after small doses there may even be an actual dilatation of the blood vessels of the kidney. This, of course, means that a larger proportion of the blood is driven to these organs and consequently there will be a freer secretion.

Digitalis is used in practical medicine for three purposes, as a stimulant in acute circulatory failure, as a diuretic, and as a cardiac tonic in chronic heart disease.

As a circulatory stimulant digitalis is a remedy of only secondary importance. In the first place, in the acuter forms of *circulatory failure*, such as *surgical shock*, when given by the mouth it is so slow in its action that the condition will have terminated one way or the other before it begins to influence the circulation. When given hypodermically it is intensely irritant and even by this channel its effects are too slow to be of much service, and although certain proprietary preparations are upon the market which are suitable for intravenous injection, there is no

reason to believe them superior for this purpose to strophanthin. In *infectious fevers* the weakness of the heart manifests itself sufficiently gradually that there is usually time enough for the action of the drug, but unfortunately clinical experience has shown that in this condition its power is much diminished.

As a diuretic digitalis is of service whenever there is *dropsical accumulation.* How far the beneficial effects are the result of improvement in the circulation and how far from a direct action upon the kidney is somewhat doubtful.

The most important use of this drug is in the treatment of various forms of *chronic heart disease,* including those due to *valvular lesions,* various types of *myocarditis,* and the *cardiac neuroses.* Its beneficial influence in these states is probably the result of several factors: the stimulation of inhibition gives the heart more time to rest, the increased force of the contraction improves the nutrition of the heart muscle, the diuresis, which occurs if there be edema, lessens the burden upon the diseased heart. Although this drug is, in a large number of cardiac conditions, the most important remedy we possess it must not be regarded as a panacea for all forms of chronic heart disease. A discussion of the various forms of cardiac weakness in which this drug is indicated or contra-indicated can scarcely be undertaken in this place, and the interested reader is referred to H. C. Wood, Jr.'s *Text-book of Pharmacology* for further information.

The active principles of digitalis are absorbable through the skin and the external application of digitalis poultices was formerly used to a considerable extent in the treatment of dropsies.

When given by the mouth digitalis acts very slowly, its effects often not being manifest for twenty-four or forty-eight hours after its administration. Its action, however, when once it begins is equally persistent. At times when the drug is being used continuously no evidence of its action may be manifest for several days and then suddenly symptoms of toxic effects come on. This is what is meant by the term "cumulative action."

Preparations of digitalis vary so much in their potency, and the conditions in which it is used so frequently demand the full actions of the drug, that the therapeutist should be guided in his dosage only by the degree of effect. The two most important symptoms indicating that the patient is taking as much as he can stand are great reduction in the rate of the pulse—say below sixty per minute—or the occurrence of nausea.

The symptoms of digitalis poisoning are nausea and vomiting, with muscular weakness, the pulse is at first very slow, may fall to thirty or forty a minute, and in severe cases later becomes very rapid and irregular. In some instances the pulse may be slow as long as the patient remains in a recumbent posture but becomes rapid if he assumes an upright position. Outside of the evacuation of the stomach and keeping the patient lying down there is no treatment of the poisoning which is known to be efficacious, although Zugsmith has reported favorable results from the external application of heat.

Preparations.—Because of the variability of the official preparation of digitalis and of their liability to produce gastric disturbances, a large number of proprietary preparations of the drug have been placed upon the market. It may be pointed out in connection with these substances that Hatcher and Eggleston (*J. P. Ex. T.,* 1912, iv, 113) has shown that the nauseating action of digitalis is due chiefly to the effects of its active principles upon the vomiting center in the medulla, and that any preparation, therefore, which does not nauseate is therapeutically useless. In the second place, it is not probable that any single principle of the drug has exactly the same influence upon the circulation as the whole leaf. The following are some of the more important preparations of digitalis.

Digitalinum Gallicum, French digitaline, also known as *digitaline chloroformique* and as *Homolle's digitaline.* This is official in the French and Belgian Pharmacopœias, is almost insoluble in water, and is said to consist largely of a glucoside allied to, or identical with, digitoxin. (See *P. J.,* 1898, 506.) The dose of the commercial article may be put down as about one two-hundred and sixtieth of a grain (0.00025 Gm.), to be repeated several times per day, the maximum daily dose being one-fortieth of a grain (0.0016 Gm.). The granules of Homolle, which were formerly used in Europe, each contained a milligramme, or about one-sixtieth of a grain, probably equivalent, on the average, to a grain and a half of digitalis of medium strength. One of these globules is usually given as a commencing dose. Forty of them taken with a view to suicide, though followed by copious vomiting, produced the most alarming prostration, with a weak pulse, from 46 to 48 in a minute, intermittent, and at times scarcely perceptible. The patient, however, ultimately recovered. (*Ann. Thér.,* 1858, 103.)

Digitoxin has been used to a certain extent clinically. According to the experiments of Fraenkel, however, it is more liable to give rise to cumulative effects than is the crude drug. It is almost insoluble in water and is locally irritant. *Dose,* one two-hundredth to one one-hundredth of a grain (0.0003–0.0006 Gm.).

Digitalinum Germanicum, also known as *Merck's digitalin* or *German digitalin.* This is practically a concentrated extract of the digitalis seeds. It probably contains true digitalin, and digitalein, as well as digitonin. The dose is from one-tenth to one-half a grain (0.005–0.03 Gm.).

Digalen is claimed to be a *soluble digitoxin,* but such a statement is manifestly impossible. The claim of its discoverer Cloetta that it is isomeric with digitoxin but has twice the molecular weight of digitoxin, would seem to disprove

its identity. According to Kiliani (*M. M. W.*, 1907), it is identical with digitalein.

Digipuratum is a yellowish powder which is asserted to contain all the active glucosides of digitalis leaves in the form of tannates without various objectionable constituents. It is physiologically standardized by tests upon frogs. The dose is the same as that of the leaves.

Of the various pure principles of digitalis the doses are as follows: *Digitalein,* one-sixtieth to one-thirtieth of a grain (0.0011–0.002 Gm.); *digitoxin,* one two-hundredth to one one-hundredth of a grain (0.0003–0.0006 Gm.); *Kiliani's digitalinum verum* has not been used enough clinically to determine the proper dose.

There are two substances known as *crystallized digitaline,* one of which, the *digitaline crystallisée* of the French Codex also known as *Nativelle's digitalin,* is probably identical with digitoxin. Merck's *crystallized digitaline* appears to be largely composed of digitonin and does not therefore represent the physiological properties of digitalis.

Digifolin is asserted to contain the cardiac principles without the saponins of digitalis. It is marketed in the form of tablets and of ampoulæ, each of which represents one-sixth of a grain (0.01 Gm.) of digitalis leaves. *Digipan* is a preparation of the same nature which is issued both in tablets and in solution, the dose of the tablets being one or two and of the solution fifteen drops (0.9 mil). *Adigan* is also a saponin free preparation but does not seem to have been proven clinically. *Digitol* is standardized tincture made from leaves freed of their fatty matters by treating with benzin. The *dose* is the same as of the official tincture.

Dose, of digitalis leaves, one to two grains (0.065–0.13 Gm.).

Off. Prep.—Fluidextractum Digitalis, *U. S.;* Infusum Digitalis, *U. S., Br.;* Tinctura Digitalis, *U. S., Br.;* Pilulæ Digitalis, Scillæ et Hydrargyri, *N. F.*

ELATERINUM. U. S.

ELATERIN Elaterin.

(ĕl-ă-tẹ-rĭ′nŭm)

"A principle obtained from elaterium, a substance deposited by the juice of the fruit of *Ecballium Elaterium* (Linné) A. Richard (Fam. *Cucurbitaceæ*)." *U. S.*

Elaterine, Elatine, *Fr.;* Elaterin, *G;* Elaterina, *Sp.*

Preparation.—Elaterin was introduced into the U. S. Pharmacopœia on account of the well-known variability in quality of commercial elaterium. (See *Elaterium,* Part II.) Care must be taken to examine the elaterin, which is itself liable to be adulterated. It may be procured by evaporating an alcoholic tincture of elaterium to the consistence of thin oil, and throwing the residue while yet warm into a weak boiling solution of potassium hydroxide, this holds the green resin in solution, and the elaterin crystallizes as the liquor cools. Hennell obtained it by treating with ether the alcoholic extract procured by the spontaneous evaporation of the tincture. This consists of elaterin and the green resin, the latter of which, being much more soluble in ether than the former, is completely extracted by this fluid, leaving the elaterin pure. But, as elaterin is also slightly soluble in ether, a portion of this principle is wasted by Hennell's method. By evaporating the ethereal solution, the green resin is obtained separate. Hennell says that this was found to possess the purgative property of elaterium, as it acted powerfully in a dose of less than one-third of a grain. But the effect was probably owing to the presence of a portion of elaterin which had been dissolved by the ether. Flückiger prefers to exhaust elaterium with chloroform, and add to the percolate ether, which precipitates elaterin. The precipitate may be dissolved in chloroform and recrystallized. This process was adopted by the Br. Pharm., 1885.

Properties.—It is in "minute, white, hexagonal scales or prismatic crystals; odorless, and having a slightly acrid, bitter taste; permanent in the air. One Gm. of Elaterin dissolves in 325 mils of alcohol, 15.5 mils of chloroform, 450 mils of ether, and in 310 mils of benzene at 25° C. (77° F.); also in 100 mils of boiling alcohol; it is insoluble in either cold or hot water. Its alcoholic solution is neutral to moistened litmus paper. Mix about 0.01 Gm. of Elaterin with 1 mil of sulphuric acid; only a yellow color is produced (*readily carbonizable impurities*). On the addition of a drop of solution of formaldehyde the mixture becomes brown. A solution of about 0.01 Gm. of Elaterin in 5 mils of melted phenol becomes crimson on the addition of a few drops of sulphuric acid and rapidly changes to scarlet. No weighable ash remains on incinerating 0.1 Gm. of Elaterin. Shake about 0.1 Gm. of Elaterin with a mixture of 9 mils of distilled water and 1 mil of diluted hydrochloric acid and filter; separate portions of the filtrate yield no turbidity with 0.5 mil of mercuric potassium iodide T.S. or with iodine T.S. (*alkaloids*)." *U. S.*

Ernst Johannson (*In. Dis.,* Dorpat, 1884) gives the following reactions for elaterin besides those mentioned in the Pharmacopœia. In all of them elaterin is held in alcoholic solution. Froehde's reagent gives a green color passing into brown which fades away. Vanadin sulphuric acid with the fortieth of a milligramme produced a splendid blue color passing into a clear green, finally into reddish-brown. After mixing with selenic acid and an addition of sulphuric acid, in a few minutes a red-brown color develops, which is not so deep as that which is produced by sulphuric acid. Kohler's reaction is produced by dissolving elaterin in a few drops of concentrated hydrochloric acid, evaporating the acid in a water bath, washing the white, amorphous residue with boiling water, and adding some concentrated sulphuric acid, when an

amaranth-red color develops. By means of these reactions Johannson has been able to find elaterin in large quantities in the fæces of animals poisoned by it, but no trace in the blood or urine or any part of the organism.

Morries obtained 26 per cent. from the best British elaterium, 15 per cent. from the worst, and only 5 or 6 per cent. from the French, while a portion procured according to the directions of the London College yielded to Hennell upwards of 40 per cent. The Br. Pharmacopœia directs that the proportion of elaterin should not be less than 20 per cent. Experiments by John Williams satisfactorily prove that the fruit, exhausted of the free juice from which elaterium is obtained, contains very little if any elaterin, certainly not enough to compensate for the cost of its extraction. (*Chem. News*, 1860, p. 124.) According to Power and Moore (*Tr. Ch. Soc.*, xcvii, p. 99), elaterin consists of two isomeric substances, one lævorotary and physiologically inert, the active compound being dextrorotary. These they designate respectively as *alpha-* and *beta-elaterin*.

Uses.—Elaterin represents all the activities of elaterium; to which it is preferable on account of the greater uniformity of its effects.

Dose, one-twentieth to one-tenth of a grain (0.003–0.006 Gm.).

Off. Prep.—Trituratio Elaterini, *U. S.*

ELIXIR AROMATICUM. U. S.

AROMATIC ELIXIR Elix. Arom. [Simple Elixir]

(ēlĭx'ĭr ăr-ǫ-măt'ĭ-cŭm)

Elixir aromatique, *Fr.*; Aromatisches Elixir, *G.*

* "Compound Spirit of Orange, *twelve mils* [or 195 minims]; Syrup, *three hundred and seventy-five mils* [or 12 fluidounces, 326 minims]; Purified Talc, *thirty grammes* [or 1 ounce av., 25 grains]; Alcohol, Distilled Water, each, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. To the Compound Spirit of Orange add enough Alcohol to make *two hundred and fifty mils* [or 8 fluidounces, 218 minims]. To this solution, add the Syrup in several portions, agitating after each addition, and afterwards add, in the same manner, *three hundred and seventy-five mils* [or 12 fluidounces, 326 minims] of Distilled Water. Mix the Purified Talc intimately with the liquid, and then filter through a wetted filter, returning the first portions of the filtrate until a transparent liquid is obtained. Lastly, wash the filter with a mixture of *one volume* of Alcohol and *three volumes* of Distilled Water, until the product measures *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

This is justly one of the most popular vehicles of the Pharmacopœia. The flavor which is agreeable to nearly all palates is enhanced by its sweetness. If desired it can be colored with cochineal or caramel.

Off. Prep.—Elixir Aromaticum Rubrum, *N. F.*

ELIXIR GLYCYRRHIZÆ. U. S.

ELIXIR OF GLYCYRRHIZA Elix. Glycyrrh. [Elixir Adjuvans, U. S. VIII Elixir of Licorice]

(ēlĭx'ĭr glĭç-ĭr-rhī'zæ)

Adjuvant Elixir, Elixir adjuvant, *Fr.*; Gewürzhaftes Lakritzenelixir, *G.*

* "Fluidextract of Glycyrrhiza, *one hundred and twenty-five mils* [or 4 fluidounces, 109 minims]; Aromatic Elixir, *eight hundred and seventy-five millilitres* [or 29 fluidounces, 282 minims], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix and filter." *U. S.*

Uses.—This elixir is used as a vehicle for the administration of various medicinal preparations; it was introduced into the U. S. Pharmacopœia (8th Rev.) mainly to furnish an alternative elixir to aromatic elixir which is similarly used. The presence of the glycyrrhiza aids in disguising or obtunding the taste of bitter or disagreeable substances and the proportion might advantageously be increased.

ELIXIRIA

ELIXIRS

(ēl-ĭx-ĭr'ĭ-ą)

Cordials; Elixirs, *Fr.*; Elixire, *G.*

Elixirs as they are known in modern American pharmacy are aromatic, sweetened, spirituous preparations, containing small quantities of active medicinal substances. They differ greatly from the liquids formerly termed elixirs, from the fact that the first object sought for in the modern elixir is an agreeable taste, and usually this is attained only by such sacrifices as to render the effect of the medicine almost *nil*, while the principal activity is due to the alcohol, which has proved in many cases very injurious. These considerations have prevented an extensive official recognition of elixirs, and the U. S. Pharm., 1890, recognized but two, one of which, the Aromatic Elixir, has been introduced merely as a vehicle. In the U. S. P. (8th Rev.) two elixirs were introduced, Adjuvant Elixir and Elixir of Iron, Quinine and Strychnine Phosphates. In the U. S. P. IX Elixir of Iron, Quinine and Strychnine Phosphates was dropped and Aromatic Elixir and Elixir of Glycyrrhiza (formerly named Adjuvant Elixir) were alone retained.

A number are, however, included in the N. F. IV. Elixir of Orange, official in the U. S. Pharm., 1880, may be made by the formula on page 435, *U. S. Dispensatory*, 19th edition.

EMBELIA. Br.

EMBELIA

(ĕm-bē'lĭ-ą)

"*Embelia* is the dried fruit of Embelia Ribes, *Burm. fil.*, and also of Embelia robusta, *Roxb.*" *Br.*

Embelia was introduced into the Br. Pharm. (1914) from the British Addendum (1900). It is officially described as "globular, about four

millimetres in diameter, varying in color from dull red to nearly black; warty or striated longitudinally; superior, minutely beaked and often attached to a 5-partite calyx and slender pedicel. Pericarp brittle, enclosing a single seed surrounded by a delicate membrane. Seed reddish, marked with lighter spots. Endosperm horny and slightly ruminated. Taste slightly astringent and aromatic." *Br.*

The genus *Embelia* (Fam. *Myrsinaceæ*) includes a large number of creeping or almost climbing tropical shrubs. They possess petiolate leaves, small white flowers and are especially abundant in tropical Asia, *Embelia Ribes* extending as far as southern China. The fruits of this plant somewhat resemble pepper and have been used as an adulterant of it.

Embelia contains 2.5 per cent. of *embelic acid*, $C_9H_{14}O_2$, which occurs in golden yellow crystals, which are insoluble in water and soluble in alcohol, ether, chloroform and benzene.

Uses.—Embelia, under the names of *viranga, vayvirang* or *birang-i-kabuli*, has long been employed in India as an anthelmintic and has found its way into European commerce. It has but slight laxative properties, so that it is better to follow it by a purgative. It is especially tenicidal, the *tape worm* being expelled dead. The powdered drug may be given in milk early in the morning. Warden has found that *ammonium embelate* is an effective tenicide in dose of three grains (0.2 Gm.) for children and six grains (0.4 Gm.) or more for adults. As it is nearly tasteless and soluble it may be readily administered in syrup.

Dose, of embelia, one to four drachms (3.9–15.5 Gm.).

EMETINÆ HYDROCHLORIDUM. U. S.

EMETINE HYDROCHLORIDE Emet. Hydrochl.

(ĕm'ē-tī-næ hȳ-drọ-ghlō'rī-dŭm)

"The hydrochloride [$C_{30}H_{44}O_4N_2.2HCl = 569.31$] of the alkaloid emetine, obtained from ipecac. It contains variable amounts of water of crystallization. Preserve it in dark amber-colored vials protected from light." *U. S.*

This alkaloidal salt was introduced into the U. S. P. IX. It is made by dissolving emetine in diluted hydrochloric acid, concentrating the solution and separating the crystals. It should be free from cephaeline. It is officially described as follows: "Emetine Hydrochloride occurs as a white or very slightly yellowish crystalline powder, without odor. On exposure to light it gradually darkens. Emetine Hydrochloride is freely soluble in water or alcohol. Its aqueous solution (1 in 20) is slightly acid to litmus. Separate portions of an aqueous solution of the salt (1 in 100) yield precipitates with iodine T.S., mercuric potassium iodide T.S., and with platinic chloride T.S. Sulphuric acid, containing in each mil about 0.005 Gm. of molybdic acid, when added to Emetine Hydrochloride produces a bright green color. Silver nitrate T.S. produces in an aqueous solution of the salt (1 in 20) a white precipitate insoluble in nitric acid. Dried to constant weight at 100° C. (212° F.), it loses not more than 19 per cent. of its weight. No weighable ash remains on incinerating 0.2 Gm. of Emetine Hydrochloride. One-tenth of 1 Gm. of the salt dissolves in 2 mils of sulphuric acid without producing more than a faintly yellow color (*readily carbonizable impurities*). Dissolve 0.1 Gm. of Emetine Hydrochloride in 5 mils of distilled water in a separatory funnel, add to the solution 3 mils of sodium hydroxide T.S. and shake it out with 10 mil portions of ether until the residue obtained by evaporating 1 mil of the ethereal liquid, when dissolved in 1 drop of diluted hydrochloric acid and 1 mil of distilled water, no longer yields a turbidity with iodine T.S. Now acidulate the aqueous liquid with diluted sulphuric acid, then add ammonia water until alkaline and shake it with 10 mils of ether. Evaporate this ethereal liquid and add to the residue 1 mil of sulphuric acid containing about 0.005 Gm. of molybdic acid; no purple color is produced (*cephaeline*)." *U. S.*

For further discussion of the properties see *Ipecacuanha.*

Uses.—Emetine hydrochloride is used, hypodermically, in the treatment of amebic *dysentery* and similar disorders in which ipecac is useful (see *Ipecacuanha*).

Dose, one-fourth to one-half grain (0.015–0.03 Gm.)

EMPLASTRA

PLASTERS

(ĕm-plăs'trą)

Emplâtres, *Fr.*; Pflaster, *G.*; Empiastri, *It.*; Emplastos, *Sp.*

Plasters are solid compounds intended for external application, adhesive at the temperature of the human body, and of such a consistence as to render the aid of heat necessary in spreading them. Spread plasters having rubber in their composition are most largely used; they are usually perforated. Some plasters have as their basis a compound of olive oil and litharge, constituting the Emplastrum Plumbi of the Pharmacopœias. Others owe their consistence and adhesiveness to resinous substances, or to a mixture of these with wax and fats.

In the preparation of the plasters, care is requisite that the heat employed be not sufficiently elevated to produce decomposition, nor so long continued as to drive off any volatile ingredient upon which the virtues of the preparation may in any degree depend. After having been prepared, they are usually shaped into cylindrical rolls, and wrapped in paper to exclude the air. Plasters should be firm at ordinary temperatures, should spread easily when heated, and, after being spread, should remain soft, pliable, and adhesive, without melting, at the heat of the human body. When long kept, they are apt to change color and to become hard and brittle, and, as this alteration is most observable upon their surface, it must depend chiefly upon the action of the air, which should therefore be excluded as much as possible. The defect may

usually be remedied by melting the plaster with a moderate heat and adding a sufficient quantity of oil to give it the due consistence.

Plasters are prepared for use by spreading them upon leather, linen, or muslin, according to the particular purposes they are intended to answer. Leather is most convenient when the application is made to the sound skin, linen or muslin when the plaster is used as a dressing to ulcerated or abraded surfaces, or with the view of bringing and retaining together the sides of wounds. The leather usually preferred is white sheepskin, or the kind known commercially as "hemlock splits." A margin about one-fourth or half an inch broad should usually be left uncovered, in order to facilitate the removal of the plaster, and to prevent the clothing in contact with its edges from being soiled. An accurate outline may be obtained by pasting upon the leather a piece of paper so cut as to leave in the center a vacant space of the required dimensions, and removing the paper when no longer needed. The spreading of the plaster is most conveniently accomplished by the use of a spatula or plaster iron. This may be heated by means of a spirit lamp or gas jet. Care must be taken that the instrument be not so hot as to discolor or decompose the plaster, and special care is requisite in the case of those plasters which contain a volatile ingredient. A sufficient portion of the plaster should first be melted by the heated instrument, and, having been received on a piece of coarse stiff paper, or in a shallow tin tray open on one side, should, when nearly cool, be transferred to the leather, and applied quickly and evenly over its surface. By this plan the melted plaster is prevented from penetrating the leather, as it is apt to do when applied too hot. Before removing the paper from the edge of the plaster, if this has become so hard as to crack, the iron should be drawn over the line of junction.

The spreading of plasters has become to a great extent a lost art to the pharmacists of this country, owing to the introduction of machine-spread plasters, which contain India-rubber in the adhesive composition. These are reasonably permanent, and do not require the application of heat. When made by reliable manufacturers they are in many cases to be preferred, but the introduction of immense quantities of worthless ones by unscrupulous makers has caused many practitioners to direct plasters to be spread by the pharmacist from official plaster. The perforation, or "porousing," of plasters is usually accomplished on a large scale by expensive apparatus. J. J. Edmondson read a paper before the Pennsylvania Pharmaceutical Association in 1887 giving the process for manufacturing rubber-mass plasters as carried on by Johnson & Johnson, of New York. It is as follows: The ingredients employed are—rubber, two parts; Burgundy pitch, one part, gum olibanum, one part. This may vary with some special plasters, but they constitute the component parts of the mass used for the majority.

The crude rubber is at first steeped in hot water, to cleanse and soften it, then the rubber is passed through the washer and crusher, where it is subjected to severe pressure between two corrugated rolls, eight inches in diameter and one foot wide, while a stream of water falling continually washes it thoroughly, and it comes out in sheets somewhat softened. After these sheets are dried, which requires a number of days, they are passed through the grinder, where they are crushed between two smooth rollers, fourteen inches in diameter and thirty-six inches across. This thoroughly softens the rubber and makes it plastic, so that it can be readily worked up with the other ingredients. The principal operation, the mixing, then takes place. The medication must be carefully combined, and the whole manipulation so managed that the plaster will be uniform, so that age or varying temperature shall not affect it. This operation is performed by means of rollers, sixteen inches in diameter, arranged so that one revolves at twice the speed of the other. Between these large rollers the mass is passed with whatever medication is required: *e.g.*, when a belladonna mass is to be made, a certain amount of the stock mass is taken and extract of belladonna in the proportions corresponding to the formula in the Pharmacopœia. These are repeatedly passed through the rollers until the extract of belladonna is thoroughly mixed with the mass, care being taken to keep the temperature from rising high enough to decompose or affect the alkaloids. The spreading is also done by rollers, into which the thoroughly mixed mass is fed at the same time that the cloth is fed, the thickness of the plasters being governed by the adjusting of screws on the side of the machine.

The rubber base is pliable, adhesive, it will not become too hard or too soft, but will yield up the medication to the absorbents of the skin, and its properties will be retained indefinitely. For formulas for plasters of former Pharmacopœias, see *U. S. D.*, 19th edition, p. 436.

EMPLASTRUM BELLADONNÆ. U. S., Br.

BELLADONNA PLASTER Emp. Bellad.

(ĕm-plăs'trŭm bĕl-la-dŏn'næ)

"An adhesive plaster containing 30 per cent. of extract of belladonna leaves and yielding not less than 0.35 per cent. nor more than 0.40 per cent. of the alkaloids from belladonna leaves." *U. S.*

Emplâtre de Belladone, *Fr.*; Belladonna-Pflaster, *G.*; Emplasto de belladonna, *Sp.*

"Liquid Extract of Belladonna, 50.0 *millilitres;* Resin Plaster, 137.5 *grammes.* Concentrate the Liquid Extract of Belladonna by evaporation at a low temperature until it is reduced in weight to *twelve and a half grammes;* add the Resin Plaster, previously melted; mix. This Plaster contains 0.25 per cent. of the alkaloids of Belladonna Root, and is of one-half the strength of the Emplastrum Belladonnæ of the British Pharmacopœia, 1898." *Br.*

No process is given in the U. S. P. IX for

making Belladonna plaster. It is now made almost exclusively with a rubber base by manufacturers on a large scale.

Assay of Belladonna Plaster. U. S. IX. —"Introduce 10 Gm. of Belladonna Plaster into a 100 mil flask. (If the plaster is spread on fabric, cut the portion to be assayed into strips, weigh it accurately, and introduce it into the flask.) Now add 50 mils of chloroform, and shake the mixture until the plaster is dissolved. Pour the chloroform solution into a 250 mil beaker and wash the cloth upon which the plaster was spread with two portions of 25 mils each of chloroform, adding the washings to the chloroform solution in the beaker. Then wash this cloth with 80 mils of alcohol containing 1 mil of ammonia water and pour the washings into the chloroform solution in the beaker. Stir the mixture gently and allow it to stand until the rubber has separated into a compact mass. Dry the cloth upon which the plaster was spread, weigh it and subtract its weight from the original weight of the plaster. Pour the chloroform-alcohol solution into a 350 mil separator, rinse the beaker and rubber with 10 mils of alcohol and add the rinsing to the separator. Then add to the separator 100 mils of distilled water, rotate until thoroughly mixed and allow it to stand until the liquids separate. Then draw off the chloroform into a second separator containing 50 mils of distilled water, shake it thoroughly and after separation draw off the chloroform into a beaker and pour the aqueous solution into the first separator. Return the chloroform solution to the second separator and shake out the contents of the first separator with two portions of 10 and 5 mils, respectively, of chloroform, adding them to the chloroform in the second separator. Completely extract the alkaloids from the chloroform solution by shaking it out repeatedly with weak sulphuric acid. Collect the acid washings in a separator and add ammonia water until the solution is decidedly alkaline to litmus, and completely extract the alkaloids by shaking out repeatedly with chloroform. Filter the chloroform solution through a pledget of cotton, evaporate it to dryness and dissolve the alkaloids from the residue in exactly 5 mils of tenth-normal sulphuric acid V.S., and titrate the excess of acid with fiftieth-normal potassium hydroxide V.S., using cochineal T.S. as indicator (see Proximate Assays, Part III). Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 28.92 milligrammes of the alkaloids from belladonna leaves." *U. S.*

This plaster was formerly prepared, in both Pharmacopœias, with the extract made from the inspissated juice of the leaves, but in the U. S. P., 1880, an alcoholic extract of the root was substituted, with the effect of rendering the plaster easier to be spread and more adhesive, and giving it a light yellowish-brown color, without a shade of green. The official preparation is now of a brownish-green color, due to the extract of belladonna leaves. It is a useful anodyne application in *neuralgic* and *rheumatic pains*. We have seen the constitutional effects of belladonna result from its external use. T. W. Worthington proposed a formula for making belladonna plaster with caoutchouc in the *A. J. P.*, xliii, 153. Machine-spread belladonna plasters have been found in the market which were admitted by a representative of the manufacturer to contain no extract of belladonna whatever. For methods of assaying belladonna plasters, see *A. J. P.*, 1898, 182, 293. *Extract of scopola* has been largely used by manufacturers in making rubber base belladonna plaster.

EMPLASTRUM CALEFACIENS. Br.

WARMING PLASTER

(ĕm-plăs'trŭm căl-ę-fā'cį-ĕns)

Emplastrum Picis Cantharidatum, *U. S.* 1890; Warm Plaster; Emplâtre de Poix cantharide, *Fr.*; Pechpflaster mit Canthariden, *G.*

"Cantharidin, 0.2 *gramme;* Chloroform, 20.0 *millilitres;* Olive Oil, 40.0 *millilitres;* Resin Plaster, 940.0 *grammes.* Dissolve the Cantharidin in the Chloroform, add the Olive Oil, and mix with the Resin Plaster, previously melted on a water bath. This Plaster contains 0.02 per cent. of Cantharidin, which is approximately the proportion contained in the Emplastrum Calefaciens of the British Pharmacopœia, 1898." *Br.*

Cantharidal pitch plaster or warming plaster is not official in the U. S. P. IX; the process of the U. S. P., 1890, will be found on p. 439, *U. S. D.*, 19th edition. The use of the blistering principle cantharidin dissolved in chloroform and olive oil will undoubtedly prove to be an improvement over the older process.

This plaster is an excellent rubefacient, more active than Burgundy pitch, yet in general not sufficiently so to produce vesication.

Warming plaster is employed in *chronic rheumatism,* and in chronic internal diseases attended with inflammation, such as *catarrh, asthma, pertussis, phthisis, hepatitis,* and the sequelæ of *pleurisy* and *pneumonia.*

EMPLASTRUM CANTHARIDIS. U. S. (Br.)

CANTHARIDES PLASTER Emp. Canthar.

(ĕm-plăs'trŭm cạn-thăr'į-dīs)

Emplastrum Cantharidini, *Br.;* Cantharidin Plaster; Emplastrum Epispasticum, s. Vesicatorium, s. Vesicans, Emplastrum Lyttæ; Blistering Cerate or Plaster; Emplâtre Vesicatoire, *Fr. Cod.;* Pommade Épispastique, Emplâtre de Cantharides, *Fr.;* Emplastrum Cantharidum Ordinarium, *P. G.;* Spanischfliegen Pflaster, Blasenpflaster, *G.;* Pomata di cantaridi, *It.;* Unguento de cantharidas, *Sp.*

In the British Pharm., 1914, the name of this plaster was changed to "cantharidin plaster" because it is now made from the blistering principle instead of from the powdered flies or the cerate.

* "Cantharides Cerate, Rosin Plaster, spread on fabric, each, *a sufficient quantity.* Spread cantharides cerate upon rosin plaster, leaving a margin around the edges. It may also be spread on muslin, paper, or other suitable material. This plaster should not be dispensed unless it has been recently prepared. Each square centi-

meter of spread plaster contains 0.1 Gm. of cantharides cerate." *U. S.*

"Cantharidin, 2 *grammes;* Chloroform, 100 *millilitres;* Yellow Beeswax, 450 *grammes;* Wool Fat sufficient to produce 1000 *grammes.* Dissolve the Cantharidin in the Chloroform by the aid of heat, add to the other ingredients previously melted on a water-bath, and stir until cold. This Plaster contains 0.2 per cent. of Cantharidin, which is approximately the proportion contained in the Emplastrum Cantharidis of the British Pharmacopœia, 1898." *Br.*

Uses.—See *Ceratum Cantharidis* (page 313) and *Cantharis* (page 285).

EMPLASTRUM CAPSICI. U. S.

CAPSICUM PLASTER Emp. Capsic.

(ĕm-plăs'trŭm căp'sĭ-cī)

Sparadrapum Capsici; Sparadrap de Capsique, *Fr.;* Capsicumpflaster, *G.*

* "Oleoresin of Capsicum, Rubber Plaster, spread on fabric, each, *a sufficient quantity.* Apply oleoresin of capsicum to the surface of rubber plaster so as to form a thin, even coating, leaving a margin around the edges. Each fifteen square centimeters of spread plaster contains 0.25 Gm. of oleoresin of capsicum." *U. S.*

The oleoresin should be laid on very evenly with a camel's-hair brush.

This affords a convenient way of obtaining the rubefacient effects of capsicum; of course, the practice will be for the pharmacist to employ machine-spread adhesive plaster as the base; although, with a little experience, very good work can be done by hand.

EMPLASTRUM ELASTICUM. U. S.

RUBBER PLASTER Emp. Elast. [Rubber Adhesive Plaster]

(ĕm-plăs'trŭm ę-lăs'tĭ-cŭm)

"A mixture of rubber, resins and waxes, with a filler of an absorbent powder, such as orris root or starch, mechanically mixed and spread upon cotton cloth or other fabric." *U. S.*

Rubber Plaster as above defined is used throughout the world and is made by special machinery on a large scale. It has superseded hand spread adhesive plaster.

EMPLASTRUM HYDRARGYRI. Br.

MERCURIAL PLASTER

(ĕm-plăs'trŭm hȳ-drär'gy-rī)

Emplastrum Mercuriale; Emplâtre mercurial, *Fr. Cod.;* Emplastrum Hydrargyri, *P. G.;* Quecksilberpflaster, *G.;* Empiastro mercuriale, *It.*

"Mercury, 328 *grammes;* Olive Oil, 18 *grammes;* Sublimed Sulphur, 2 *grammes;* Lead Plaster, 652 *grammes.* Heat the Olive Oil with the Sulphur until a reddish-brown liquid is obtained; with this solution triturate the Mercury until metallic globules are no longer visible; add the Lead Plaster, previously melted; mix." *Br.*

Mercurial plaster is no longer official in the U. S. P. IX. The U. S. Pharm. VIII employed oleate of mercury and hydrous wool-fat for the purpose of extinguishing the mercury; this it does effectually, and at the same time increases the efficiency of the mercurial constituent. The quantity of mercury was 30 per cent. The British preparation is stronger, containing 32.8 per cent.

The former U. S. and British processes may be considered identical in their results. Thomas Blunt has found it almost impossible to divide the mercury sufficiently by trituration with oil and rosin, and the resulting plaster was so crumbly that it could not be formed into rolls; but on substituting a weight of Venice turpentine equal to that of the oil and rosin combined, he found it to answer completely. An objection, however, to the turpentine is, that it might render the plaster too irritant for susceptible skins. (*P. J.*, 1864, p. 56.) For methods of assaying this plaster, see *A. J. P.*, 1911, p. 314; *C. D.*, 1911, p. 631; *P. J.*, 1911, p. 654.

Uses.—This plaster is employed to produce the local effects of mercury upon *syphilitic* lesions of the skin and other chronic tumefactions of the bones or soft parts, dependent on a syphilitic taint. It occasionally affects the gums.

From observations made in France by Serres and others, it appears that the mercurial plaster of the Codex (*Emplastrum* (*Emplâtre*) *de Vigo cum Mercurio*), see *U. S. D.*, 19th edition, p. 440, has the power, when applied over the eruption of *small pox,* before the end of the third day from its first appearance, to check its progress and prevent suppuration and pitting. This operation of the plaster, so far from being attended with an increase of the general symptoms, seems to relieve them in proportion to the diminution of the local affection. That the local effect is not ascribable to the mere exclusion of the air is proved by the fact that the use of lead plaster was not followed by the same results. It is probable that other mercurial preparations would answer the same purpose.

EMPLASTRUM MENTHOL. Br.

MENTHOL PLASTER

(ĕm-plăs'trŭm mĕn'thŏl)

Emplâtre de Menthol, *Fr.;* Mentholpflaster, *G.*

"Menthol, 150 *grammes;* Yellow Beeswax, 100 *grammes;* Resin, 750 *grammes.* Melt the Beeswax and Resin together; when the mixture has cooled to about 70° C. (158° F.), add the Menthol, and stir until dissolved." *Br.*

This is an official plaster of the British Pharmacopœia, having been introduced in the additions in 1885. It is a mild counter-irritant, intended especially for relief in localized *neuralgia* and *rheumatic pains.*

EMPLASTRUM PLUMBI. U. S., Br.

LEAD PLASTER Emp. Plumb. [Diachylon Plaster]

(ĕm-plăs'trŭm plŭm'bī)

Emplastrum Lithargyri, *Br.* 1864; Emplastrum Diachylon Simplex, Emplastrum Album Coctum; Litharge Plaster; Emplâtre simple, *Fr. Cod.;* Emplâtre de Plomb (de Litharge), Emplastrum simplex, *Fr.;* Emplastrum Lithargyri (simplex), *P. G.;* Emplastrum Cerussæ, Froschlaichpflaster; Bleipflaster, Diachylonpflaster, *G.;* Empiastro diachilon, *It.;* Emplasto de plomo simple, Emplasto simple, *Sp.*

* "Lead Oxide, *one thousand grammes* [or 35 ounces av., 120 grains]; Olive Oil, *one thousand grammes* [or 35 ounces av., 120 grains]; Lard, *one thousand grammes* [or 35 ounces av., 120 grains]; Boiling Water, *a sufficient quantity.* Heat the olive oil and lard by a gentle heat until liquefied in a bright copper or other suitable vessel of a capacity of not less than four times the bulk of the ingredients, sift the lead oxide, through a No. 80 sieve, upon the surface of the hot liquid and mix thoroughly. Then gradually add *three hundred and fifty mils* [or 11 fluid-ounces, 401 minims] of boiling water, and boil the mixture, constantly stirring, with a wooden spatula, and adding sufficient boiling water, from time to time, to replace that lost by evaporation, until the mass is homogeneous and a small portion removed and dipped into cold water is found to be pliable and tenacious. Then remove it from the fire and wash several times with warm water to remove the glycerin. Finally knead the mass until it is free from water, roll it into cylinders of suitable size, and wrap them in paper." *U. S.*

"Lead Oxide, 400 *grammes;* Olive Oil, 800 *grammes;* Distilled Water, 400 *millilitres,* or *a sufficient quantity.* Boil gently together in a steam-bath, stirring constantly until combination has been effected. When cool remove the plaster-like mass produced; knead it thoroughly with hot water, and allow it to dry." *Br.*

The importance of this plaster, as the basis of many other plasters, requires a somewhat detailed account of the principles and manner of its preparation. A very important change was made in the process for lead plaster in the U. S. Pharmacopœia VIII. The method of boiling litharge, olive oil, and water together, which is still official in the British Pharmacopœia, was discarded and the precipitation method introduced. The resulting product was chemically nearly identical with that made by the boiling process and is much whiter in color, while the adhesiveness of the present plaster seemed to be superior to that of the U. S. P., 1890, but experience has proved that the precipitation method produces a plaster which does not keep as well as did the plaster made in the old way, hence the U. S. P. IX has returned to the former process, although the olive oil is partially replaced by lard.

The reaction in the U. S. P. VIII process, disregarding the palmitin present, was as follows:

$$\underset{\text{Sodium oleate}}{2NaC_{18}H_{33}O_2} + \underset{\text{Lead acetate}}{Pb(C_2H_3O_2)_2} = \underset{\text{Lead oleate}}{Pb(C_{18}H_{33}O_2)_2} + \underset{\text{Sodium acetate}}{2NaC_2H_3O_2}$$

In the U. S. P. IX and the British process a reaction takes place between the oil and water, resulting in the development of glycerin, and of two acid bodies, oleic and palmitic acids, to which, when animal fat is employed instead of olive oil, a third is added—namely, stearic acid. The plaster is formed by a union of these acids with the oxide, and, prepared according to the directions of the Pharmacopœias, is in fact a lead oleo-palmitate, and if the olive oil contained stearin it would be a lead oleo-stearo-palmitate. The glycerin remains dissolved in the water, or mechanically mixed with the plaster. That such is the correct view of the nature of this compound is evinced by the fact that, if the lead oxide be separated from the plaster by digestion at a moderate heat in very dilute nitric acid, the fatty matter which remains will unite with litharge with the greatest facility, without the intervention of water. The fixed or fatty oils are compounds of the free fatty acids mentioned and the radical glyceryl. When boiled with the lead oxide and water, the fatty acids combine with the metallic oxide to form the plaster, and the glyceryl unites with the hydroxyl and becomes glycerin. The British process does not provide for the separation of the glycerin and the plaster is not kneaded to separate the water, both of which, in our opinion, are necessary to produce the best result and which form part of the U. S. P. IX process.

The reaction between olein and lead oxide is as follows:

$$\underset{\text{Olein}}{2C_3H_5(C_{18}H_{33}O_2)_3} + \underset{\text{Litharge}}{3PbO} + \underset{\text{Water}}{3H_2O} = \underset{\text{Lead oleate}}{3Pb(C_{18}H_{33}O_2)_2} + \underset{\text{Glycerin}}{2C_3H_5(OH)_3}$$

Other oleaginous substances and other metallic oxides are susceptible of the same combination, and some of them form compounds having the consistence of a plaster; but, according to Henry, of Paris, no oily matter except animal fat can properly be substituted for olive oil, and no metallic oxide, not even one of the other oxides of lead, for litharge. He ascertained, moreover, that the English litharge is preferable for the formation of lead plaster to the German. From experiments of Soubeiran, it appears that yellow lead oxide or even red lead oxide may be substituted for litharge, and a plaster of good consistence be obtained, but that a much longer time is required for completing the process than when the official formula is followed. Owing to the necessity for its partial deoxidation, the use of yellow lead oxide requires a longer continuance of the process than when litharge is employed. According to Davallon, it is important that the olive oil employed should be pure, for when adulterated, as it frequently is, it yields an imperfect product.

N. S. Thomas prepared a good plaster by substituting lard for olive oil, in the proportion of eight pounds of lard to five of litharge (*A. J. P.,* xix, 175), and we are told that it is a common practice in this country to make lead plaster with a mixture of lard oil and olive oil. Mueller uses equal parts of lard, olive oil, and litharge, having previously heated the litharge until a small sample causes no effervescence when dropped into nitric acid, showing the absence of carbonate. (*Ph. Ztg.,* 1879, p. 70; *A. J. P.,* 1879, p. 190.) It is said that the Eng-

lish plaster makers rarely follow the Br. Pharm. direction, preferring the recipe of the old London Pharmacopœia, which contains more litharge and yields a much firmer and less adhesive product. (*P. J.*, 3d ser., p. 701, 716.)

Zinc Plaster.—De Mussey, having witnessed inconveniences from lead plaster in consequence of the absorption of the lead, substituted for it a plaster with a basis of zinc oxide, which he has found to answer very well in practice. It cannot be made by direct combination of the oxide, and it is necessary to have recourse to the method of double decomposition. Solutions of white olive oil soap and of zinc sulphate being mixed, a copious precipitate takes place of zinc oleopalmitate, which, after being washed and dried, may be combined with resins, oil, and wax, to give it the necessary consistence.

The process of the United States Pharmacopœia VIII by precipitation is well adapted for making comparatively small quantities of lead plaster, but manufacturers prefer the boiling process when large quantities are to be made, and the following details are retained: The vessel in which the lead plaster is prepared should be of such a size that the materials will not occupy more than two-thirds of its capacity. The oil should be first introduced, and the litharge then sprinkled in by means of a sieve, the mixture being constantly stirred with a spatula. The particles of the oxide are thus prevented from coalescing in small masses, which the oil would not easily penetrate, and which would, therefore, delay the process. While the water exerts an important chemical agency in the changes which occur, it is also useful by preventing too high a temperature, which would decompose the oil, and cause the reduction of the oxide. The waste must, therefore, be supplied by fresh additions as directed in the process, and the water added for this purpose should be previously heated, as otherwise it would not only delay the operation, but by producing explosion might endanger the operator.

During the continuance of the boiling, the material should be constantly stirred, and the spatula should be repeatedly passed along the bottom of the vessel, from side to side so as to prevent any of the oxide, which is disposed by its greater density to sink to the bottom, from remaining in that situation. The materials swell up considerably, in consequence partly of the vaporization of the water, partly of the escape of carbon dioxide, which is liberated by the oily acids from some lead carbonate usually contained in the litharge. The process should not be continued longer than is sufficient to produce complete union of the ingredients, and this may be known by the color and consistence of the mass. The color of the litharge gradually becomes paler, and at length almost white when the plaster is fully formed. The consistence increases with the progress of the boiling, and is sufficiently thick when a portion of the plaster, taken out and allowed to cool upon the end of a spatula, or thrown into cold water, becomes solid, without adhering in this state to the fingers. The portion thus solidified should not present, when broken, any red spots, which would indicate the presence of a portion of uncombined litharge. When the plaster is formed, it should be removed from the fire, and after a short time cold water should be poured upon it. Portions should then be detached from the mass, and, having been well kneaded under water, in order to separate the viscid solution of glycerin contained in the interior, should be formed into cylindrical rolls, and wrapped in paper. Such, at least, has been the course of proceeding usually recommended. But Davallon maintains that the presence of glycerin in the plaster is useful by keeping it in a plastic state, and that washing and kneading are injurious, the former by removing the glycerin, the latter by introducing particles of air and moisture into the mass, which is thus rendered more disposed to rancidity. (*A. J. P.*, xv, 274; from *Journ. de Chim. Méd.*) By employing steam heat in the preparation of this plaster, the risk of burning it is avoided. Bernbeck found that lead plaster could be preserved from hardening and oxidation if kept in air tight canisters. (*Ph. Ztg.*, 1881, p. 589.)

Uses.—This plaster, which has long been known under the name of *diachylon,* is used as an application to excoriated surfaces and to slight wounds, which it serves to protect from the action of the air. It may also be beneficial by the sedative influence of the lead which enters into its composition. A case is on record in which lead colic resulted from its long continued application to a large ulcer of the leg. (*Am. J. M. S.*, xxiii, 246.) J. M. Bigelow reports a case of excessive sweating of the feet cured by putting the patient in bed for thirteen days and keeping the feet enveloped in strips of lead plaster. (*N. R.*, Oct., 1875.) Its chief use is in the preparation of other plasters. See *Logan's Plaster, Mahy's Plaster, U. S. D.*, 19th edition, p. 443.

Off. Prep.—Emplastrum Resinæ, *U. S., Br.;* Emplastrum Hydrargyri, *Br.;* Emplastrum Saponis, *N. F., Br.;* Unguentum Diachylon, *U. S.*

EMPLASTRUM RESINÆ. U. S., Br.

ROSIN PLASTER Emp. Res. [Rosin Adhesive Plaster, Adhesive Plaster]

(ĕm-plăs'trŭm rẹ-sĭn'æ)

Resin Plaster, *Br.;* Emplâtre Adhésif, Emplâtre Résineux, *Fr.;* Emplastrum adhæsivum, *P. G.;* Heftpflaster, *G.;* Emplastro adesivo, *It.*

* "Rosin, in fine powder, *one hundred and forty grammes* [or 4 ounces av., 411 grains]; Lead Plaster, *eight hundred grammes* [or 28 ounces av., 96 grains]; Yellow Wax, *sixty grammes* [or 2 ounces av., 51 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Melt the lead plaster and yellow wax together with a gentle heat, then add the rosin and, when melted, mix thoroughly, strain, and

allow the product to cool, stirring until it stiffens." *U. S.*

"Resin, 100 *grammes;* Lead Plaster, 850 *grammes;* Hard Soap, 50 *grammes.* Melt each ingredient separately at as low a temperature as possible; mix." *Br.*

The name of this plaster was changed in the U. S. P. IX to rosin plaster, it was formerly termed adhesive plaster. It differs from lead plaster in being more adhesive and somewhat more stimulating. It resembles the common adhesive plaster of commerce, and is much employed for retaining the sides of wounds in contact, and for dressing ulcers according to the method of Baynton, by which the edges are drawn towards each other and a firm support is given to the granulations. The U. S. P. IX formula differs from that official in U. S. P. VIII in that the use of rubber and petrolatum in place of yellow wax and rosin was abandoned and the old process has been restored. As prepared by the Dublin College it contained soap, which gave it greater pliability, and rendered it less liable to crack in cold weather, without impairing its adhesiveness, and the process of that College has been adopted in the British Pharmacopœia. It is usually spread upon muslin, and the spreading is best accomplished, on a large scale, by means of a machine, as described in the general observations upon plasters. It is kept ready spread by the pharmacist; but, as the plaster becomes less adhesive by long exposure to the air, the supply should be frequently renewed. Adhesive plaster originally employed by Baynton contained only six drachms of rosin to the pound of lead plaster. To obviate the possibility of irritating the skin, Herpin recommends the addition of lead tannate, the proportion of which, when adhesiveness is required in the plaster, should not exceed one-twentieth, but under other circumstances may be increased to one-twelfth.

The addition of Burgundy pitch or turpentine is objectionable, as they greatly increase the liability of the plaster to irritate the skin, and thus materially interfere with the purposes for which the preparation was chiefly intended.

The most popular and widely used forms of adhesive plaster used at the present time are those containing zinc oxide as one of the constituents.

EMPLASTRUM SINAPIS. U. S.

MUSTARD PLASTER Emp. Sinap. [Charta Sinapis, U. S. VIII, Mustard Paper]

(ĕm-plăs'trŭm sĭ-nā'pĭs)

"A uniform mixture of powdered black mustard (deprived of its fixed oil), and a solution of rubber, spread on paper, cotton cloth or other fabric. Preserve it in tightly-closed containers. A square of 100 square centimeters contains not less than 2.5 Gm. of black mustard deprived of its fixed oil. When moistened thoroughly with tepid water and applied to the skin, the Plaster produces a decided warmth and reddening of the skin within five minutes. Before Mustard Plaster is applied, moisten it thoroughly with tepid water." *U. S.*

Sinapisme en feuille, *Fr. Cod.;* Papier Moutarde, Papier Sinapisé, *Fr.;* Charta sinapisata, *P. G.;* Senf-papier, *G.;* Carta senapata, *It.;* Papel sinapico, Charta sinapica, *Sp.*

* "Black Mustard, in No. 60 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Rubber, *ten grammes* [or 154 grains]; Petroleum Benzin, Carbon Disulphide, each, *a sufficient quantity.* Pack the Black Mustard in a conical percolator, and gradually pour Petroleum Benzin upon it until the percolate ceases to produce a permanent, greasy stain upon blotting paper. Remove the powder from the percolator, and dry it by exposure to the air. Having meanwhile dissolved the Rubber in a mixture of *one hundred cubic centimeters* [or 3 fluidounces, 183 minims], each, of Petroleum Benzin and Carbon Disulphide, mix the purified Mustard with a sufficient quantity of the solution to produce a semi-liquid magma, and apply this, by means of a suitable brush, to one side of a piece of rather thick, well-sized paper, so as to cover it completely, and then allow the surface to dry. A surface of sixty square centimeters should contain about 4 Gm. of Black Mustard deprived of oil. Before it is applied to the skin, Mustard Paper should be dipped in warm water for about fifteen seconds." *U. S. VIII.*

"Black and White Mustard Seeds, equal proportions by weight; Benzol, Solution of India-rubber, of each, a sufficient quantity. Bruise the Mustard Seeds and extract the fixed oil by percolation with the Benzol. Dry the residue by exposure to the air in a warm closet, and reduce to No. 60 powder. Mix seventy-five grains (or five grammes) of the purified mustard with five fluid drachms (or eighteen cubic centimetres) of Solution of India-rubber, and spread by means of a suitable brush over about 30 square inches (or about two square decimetres) of one side of a piece of cartridge paper. Allow it to dry by exposure to the air." *Br.,* 1898.

The name of this preparation was changed in the U. S. P. IX from mustard paper to mustard plaster; from a pharmaceutical point of view this was a mistake, for *mustard leaves* as they are often called are very different from either mustard plasters or mustard poultices. The U. S. P. IX and the British Pharm. (1914) no longer admit a process for making *Charta Sinapis,* the U. S. P. IX merely describing the preparation as found in commerce. The U. S. P. VIII and the Br. Pharm., 1898, processes are given above.

The formula for this preparation was greatly improved by the U. S. P. in 1890 and Br., 1898. The British preparation (1885) was at fault in not providing for the extraction of the fixed oil by previously percolating with petroleum benzin or carbon disulphide; otherwise the paper will be greasy, giving to the plaster an untidy appearance and soiling the linen of the patient. Solution of gutta-percha is unsuited for use in this preparation, on account of want

of adhesiveness, and the tendency of the mixture, when dry, to crack and peel off. We have used instead a solution of 1 part of pure rubber in 30 of equal parts of carbon disulphide and petroleum benzin. On the large scale, by means of a plaster spreading apparatus a uniform coat of this solution may be applied to paper. As the latter passes out from under the apparatus, a sieve containing the powdered mustard is shaken over it; this is fixed by the adhesive coat and firmly retained after the evaporation of the volatile liquids in a warm place. The application of the powdered mustard must be properly regulated according to the speed with which the machine delivers the coated paper. The paper is cut into pieces of convenient size, and needs only to be wetted with tepid water to be ready for use. Owing to the fact that the large manufacturers can put mustard paper upon the market at such low rates that it pays the apothecary better to buy than to prepare it, Charta Sinapis, so far as we can learn, is rarely made in the retail stores.

Uses.—For the uses of the mustard plaster, see *Sinapis*, p. 1010.

Experience has shown that the ready-made mustard papers err rather from too much than from too little activity. Moreover, their action cannot be regulated with the same nicety as can that of the mustard poultice. Unless in the case of travellers, and of others who must wait upon themselves, the domestic application is preferable. The *mustard leaves* can rarely be borne for more than ten or fifteen minutes. Care should be observed to protect the leaves, as they are popularly called, from the action of moist air by keeping them in well closed containers.

EMPLASTRUM SAPONIS. Br.

SOAP PLASTER

(ĕm-plăs'trŭm sa-pō'nĭs)

Emplâtre de Savon, *Fr. Cod.;* Emplastrum cum Sapone, *Fr.;* Emplastrum Saponatum, *P. G.;* Seifenpflaster, *G.;* Emplasto de jabon, *Sp.*

"Hard Soap, 140 *grammes;* Lead Plaster, 835 *grammes;* Resin, 25 *grammes.* Melt each ingredient separately at a low temperature; mix; evaporate, with constant stirring, to a proper consistence." *Br.*

* "Soap, dried, and in coarse powder, *ten grammes* [or 154 grains]; Lead Plaster, *ninety grammes* [or 3 ounces av., 76 grains]; Water, *a sufficient quantity,* to make about *one hundred grammes* [or 3 ounces av., 231 grains]. Rub the Soap with enough Water to reduce it to a semi-liquid state; then mix it with the Lead Plaster previously melted, incorporate thoroughly by stirring, and evaporate to the proper consistence." *U. S. VIII.* (See also *N. F. IV,* Part III.)

Soap plaster was not retained in the U. S. P. IX; it was transferred to the National Formulary IV. Soap plaster is considered discutient, and is sometimes used as an application to tumors, where a dressing is required. Somewhat softer in its character, the *soap cerate,* formerly official, may be found useful. This was made as follows: *Ceratum Saponis.* "Take of Soap Plaster *two troyounces;* White Wax *two troyounces and a half;* Olive Oil *four troyounces.* Melt together the Plaster and Wax, add the Oil, and, after continuing the heat a short time, stir the mixture until cool." *U. S.,* 1870.

EMULSA.

EMULSIONS

(ę-mŭl'sa)

Emulsions, *Fr.;* Emulsiones, *G.;* Emulsiones *It., Sp*

Under this head are included in the U. S. Pharmacopœia liquid preparations in which oleaginous substances are suspended in aqueous fluids by the intervention of gum or other viscid matter. The preparations forming the present class of emulsions were termed Mixtures in earlier pharmacopœias, and it is to be regretted that under this indefinite term are still grouped liquids of many kinds; the separation of these into proper classes is only a question of time, and the introduction of this new class into the Pharmacopœia of 1890 marked the first step in the direction of greater accuracy in defining pharmaceutical preparations, and more system in classification. The object of emulsions is usually to facilitate the administration, to conceal the taste, or to obviate the nauseating effects of unpleasant medicines, and their perfection depends upon the intimacy with which the ingredients are blended. Some skill and care are requisite for the production of uniform and perfect emulsions. As a rule, the body to be suspended should be thoroughly mixed by trituration with the substance intended to act as the intermedium, before the aqueous vehicle is added. In the case of the liquid balsams and oils, if gum arabic is employed as the intermedium it should be previously brought to the state of mucilage of the consistence directed in the U. S. Pharmacopœia. When a fixed oil, oleoresin, or balsam is to be made into an emulsion, the method most employed abroad is to add one part of gum to two or three of the oil, in a mortar, triturate until the mixture is complete, and then add at once twice as much water as gum used, and triturate rapidly until the oil is completely emulsified, then gradually add the remainder of the vehicle with constant trituration. Agitation in a bottle is sometimes substituted for trituration. The plan most largely used in this country is to make the emulsion with mucilage. Having a broad flat pestle and a mortar perfectly free from grease, put in a little mucilage, rub it around the mortar, add about half as much oil, triturate from the center so as to emulsify this, then add more mucilage, then oil, and so on until the operation is completed. Care is required never to get the oil in excess of the mucilage. This plan seems to accord with the principle laid down by R. Rother, that the most perfect and rapid emulsifier is a perfect emul-

sion. The proportion of gum and water necessary to make a good emulsion with the fixed oils varies with the oil. Thus, while castor oil requires only two drachms of the gum and three drachms of water to the ounce, most other fixed oils require half their weight of gum, and a weight of water equal to half that of the oil and gum united. These quantities being well rubbed together, any desirable amount of water may afterwards be gradually added, and will readily incorporate with the other ingredients. The white of egg has been frequently ordered by physicians as the suspending substance, but it is inferior for this purpose to the yolk, or to gum arabic. When the white is used it should be well beaten, and incorporated with the oleaginous or balsamic substances before the water is added. When volatile oils are to be emulsified they should be mixed with an equal volume of inert fixed oil to promote stability. Quillaja, saponin, and other substances having similar properties have been proposed as emulsifying agents, but they are objectionable on account of their medicinal activity. Emulsifying agents should be inert.

Leo Roon (*J. A. Ph. A.*, 1916, v, 496) gives an extensive review of the literature on emulsification and Roon and Oesper have made an important contribution to the theory of emulsification (*J. I. & E. C.* 1917, p. 156). The authors agree with Fischer (*Science* 1916, p. 468) that emulsification is due to, or accompanied by, the formation of a hydrated colloid compound. Both the English and Continental methods of emulsification were studied carefully. The unsatisfactory results obtained by the majority of workers with the English method, are alleged to be due to the fact that the hydration of the emulsifying agent occurs progressively and not all at one time and for the greater part is not accomplished in the presence of the internal phase (oil). In the Continental method all of the emulsifying agent (colloid) is hydrated at one time and in the presence of the internal phase (oil). After experimenting with various proportions of materials, it is stated by the authors that the best and quickest results are obtained by the use of the following proportions in the preparation of the original nucleus: oil 4, water 3, gum 2.

Experimental emulsions were produced of the following substances: hexane, sp. gr. 0.691; chloroform, sp. gr. 1.526; carbon tetrachloride, sp. gr. 1.597; benzene, sp. gr. 0.877; oil of turpentine, sp. gr. 0.85; mineral oil, sp. gr. 0.853; cottonseed oil, sp. gr. 0.921. Gum emulsions and soap emulsions were made of all these and the conclusions, in part, were as follows: 1. The presence of a hydrated colloid is necessary for emulsification. 2. This hydration compound is most efficiently used if formed at the moment of dispersion of the internal phase—in other words, the three constituents, internal phase, emulsifier and water, in critical proportions, must all be mixed at one time in order to form a properly hydrated nucleus. 3. Slight variations from the proper procedure or from the critical proportions yield either less stable emulsions or none at all. 4. No emulsion results if the emulsifier is diluted before the dispersion of the internal phase.

EMULSUM AMYGDALÆ. U. S. (Br.)

EMULSION OF ALMOND Emuls. Amygd.

[Milk of Almond]

(ę-mŭl'sŭm ą-mŷg'dą-læ)

Mistura Amygdalæ, *Br.*; Almond Mixture; Mistura Amygdalæ, U. S. P. 1880; Emulsio Amygdalæ, s. Amygdalarum, Emulsio Simplex; Milk of Almonds; Simple Emulsion; Emulsion d'Amande, *Fr. Cod.*; Lait d'Amande, *Fr.*; Mandelemulsion, Mandelmilch, *G.*; Emulsione di mandorle dolci, *It.*; Emulsion comun, *Sp.*

• "Sweet Almond, *sixty grammes* [or 2 ounces av., 51 grains]; Acacia, in fine powder, *ten grammes* [or 154 grains]; Sugar, *thirty grammes* [or 1 ounce av., 25 grains]; Water, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Having blanched the almonds, add the acacia and sugar, and beat them, in a mortar, until they are thoroughly mixed. Then rub the mass with *nine hundred mils* [or 30 fluidounces] of water, at first very gradually added, until a uniform mixture results. Strain this into a graduated vessel, and wash the mortar and strainer with enough water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the whole thoroughly. This preparation must not be dispensed unless it has been recently prepared." *U. S.*

"Compound Powder of Almonds, 125 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres*. Triturate the Powder with a little of the Distilled Water so as to form a thin paste; gradually add the remainder of the Distilled Water; strain through fine muslin." *Br.*

These preparations are essentially the same, the gum and sugar which enter into the U. S. formula directly being ingredients of the compound powder of almonds of the British. The gum arabic in these formulas is introduced not so much for its demulcent properties as to assist in the suspension of the insoluble ingredients of the almonds. The same formula will answer for the preparation of an *emulsion of bitter almonds* from bitter almond or peach kernels. The oleaginous matter of the almonds is suspended in the water by means of their albumen, gum, and sugar, forming a milky emulsion. When the almonds themselves are employed, as in the U. S. process, care should be taken to reduce them to the consistence of a paste previously to the addition of the water, and with each successive portion of fluid a uniform mixture should be formed before another portion is added. Common water, when pure, may be properly substituted for the distilled. Great care should be taken to select the almonds perfectly free from rancidity. The emulsion is not permanent and compound powder of almonds often has a taint of rancidity when kept too long. Upon standing, the oil rises like thick cream to the surface, and

the separation is effected more quickly by heat, alcohol, and the acids, which coagulate the albumen. The preparation is closely analogous to milk in chemical relations and appearance. In warm weather it soon becomes sour.

Uses.—Emulsion of almond has a bland taste, and may be used as an agreeable, nutritive demulcent in *catarrhal* and *dysenteric affections* and irritation of the urinary passages. To be of service it must be freely employed. It is occasionally employed as an emollient lotion, and as a vehicle for less agreeable medicines, but should not be used with any considerable quantity of tinctures, acidulous salts, or other acid substances.

Dose, two to eight fluidounces (60–240 mils).

EMULSUM ASAFŒTIDÆ. U. S.

EMULSION OF ASAFETIDA Emuls. Asafœt.
[Milk of Asafœtida]

(ę-mŭl'sŭm ăs-ą-fœt'ĭ-dæ)

Asafetida Mixture; Mistura (Lac) Asafœtidæ, Mistura Asafœtida, U. S. P. 1880; Mixture (Lait) d'Asafœtida, *Fr.;* Asafœtidaemulsion, Stinkasantmilch, *G.*

* "Asafetida, in tears or selected masses, *forty grammes* [or 1 ounce av., 180 grains]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Rub the Asafetida, in a warmed mortar, with *nine hundred mils* [or 30 fluidounces] of Water, at first very gradually added, until a uniform emulsion results. Then strain the mixture into a graduated vessel, and rinse the mortar and strainer with enough Water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the whole thoroughly." *U. S.*

The present 4 per cent. official emulsion slightly exceeds in strength the mixture of the U. S. P., 1870, which contained but 3 per cent. of asafetida. This emulsion is less stimulant than the tincture, and more prompt in its action than the pill. Its excessively disagreeable odor and taste are, however, objections, which induce a frequent preference for the last mentioned preparation. It is very often employed as an enema. From two to four fluidounces (60–120 mils) may be given by the rectum. D. Ackerman prepares a concentrated *emulsion of asafetida,* which will keep if excluded from the light, by using a mixture of three-fourths of pure water and one-fourth of diluted acetic acid as the menstruum. For cleaning mortars in which asafetida has been rubbed, he recommends solution of potassium hydroxide, followed by soap and water.

Dose, one-half to one fluidounce (15–30 mils).

EMULSUM OLEI MORRHUÆ. U. S.

EMULSION OF COD LIVER OIL Emuls. Ol. Morrh.

(ę-mŭl'sŭm ō'lę-ī mör'rhŭ-æ)

Emulsion de Huile de Foie de Morue, *Fr.;* Leberthranemulsion, *G.*

* "Cod Liver Oil, *five hundred mils* [or 16 fluidounces, 435 minims]; Acacia, in fine powder, *one hundred and twenty-five grammes* [or 4 ounces av., 179 grains]; Syrup, *one hundred mils* [or 3 fluidounces, 183 minims]; Methyl Salicylate, *four mils* [or 65 minims]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Thoroughly mix the acacia with the cod liver oil in a dry mortar or other suitable vessel, then add at once *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of water, and complete the emulsification by trituration or by the aid of a suitable mechanical device. When a thick, white, homogeneous mixture is obtained, add the methyl salicylate and the syrup with sufficient water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms], and mix thoroughly.

"NOTE.—The methyl salicylate may be replaced by a suitable quantity of any other flavoring." *U. S.*

This emulsion was introduced into the U. S.P. VIII for the purpose of affording a simple process for making a reasonably palatable and permanent preparation of cod liver oil. The continental method employed is best adapted for stock emulsions; to those who object to the taste of a combination of syrup and an oil with a fishy taste, the emulsion may be flavored with bruised celery seed and salt and then strained. A very palatable preparation of this type has been prepared in which the flavoring agents used were Worcestershire sauce and mustard. See *Emulsum Olei Morrhuæ cum Hypophosphitibus,* N. F. A comparison of various flavors for this emulsion was made by G. M. Beringer, Jr. (*Proc. N. J. Ph. A.,* 1914, p. 81), in which it is asserted that the best disguising flavors are those of coriander and geranium. Next came anise and cardamom, then bitter almond, clove, pimenta and vanilla. Of inferior value in this respect were peppermint, spearmint, lemon, orange and cinnamon and least valuable of all were caraway, sassafras, wintergreen and nutmeg.

Under the name of *Black Bottle,* there has long been used in New England an emulsion of cod liver oil flavored with licorice and aromatic oils, the following formula for which was contributed to the *Apothecary,* 1913, p. 24, by R. A. Newton: Powdered Acacia, 13 dr.; cod liver oil, 6½ fl. oz.; flavoring oils, 15 min.; pure extract of licorice, 5 dr.; glycerin, 2½ fl. oz.; water, to make 1 pint. Prepare an emulsion.

The flavoring oil mixture in made as follows: Oil of cassia, 1 fl. oz.; oil of lavender, ½ fl. oz.; oil of clove, 1 fl. dr.; oil of peppermint, ½ fl. dr.; Mix.

Dose, two to four fluidrachms (7.5–15 mils).

EMULSUM OLEI TEREBINTHINÆ. U. S.

EMULSION OF OIL OF TURPENTINE
Emuls. Ol. Tereb.

(ę-mŭl'sŭm ō'lę-ī tęr-ę-bĭn'thĭ-næ)

Emulsion d'Essence de Térébenthine, *Fr.;* Terpentinölemulsion, *G.*

* "Rectified Oil of Turpentine, *fifteen mils* [or 243 minims]; Expressed Oil of Almond, *five mils* [or 81 minims]; Syrup, *twenty-five mils*

[or 406 minims]; Acacia, in fine powder, *fifteen grammes* [or 231 grains]; Water, *a sufficient quantity,* to make *one hundred mils* [or 3 fluidounces, 183 minims]. Introduce the acacia into a perfectly dry bottle of sufficient capacity, add the rectified oil of turpentine and the expressed oil of almond and shake the bottle thoroughly. Then add *thirty mils* [or 1 fluidounce, 7 minims] of water and incorporate it by vigorous shaking. When the oil has been completely emulsified add first the syrup, in several portions, shaking after each addition, and then enough water, in divided portions, shaking after each addition, to make the product measure *one hundred mils* [or 3 fluidounces, 183 minims]." *U. S.*

The U. S. P. VIII introduced this emulsion with the view of providing a simple and fairly permanent preparation. Rectified oil of turpentine should be used exclusively. The process is much like the one recommended by J. Winchell Forbes, and a mortar and pestle are not needed to produce a perfect emulsion.

Dose, one-half to one fluidrachm (1.9–3.75 mils).

ERGOTA. U. S., Br.

ERGOT Ergot. [Secale Cornutum, P. I., Ergot of Rye, Spurred Rye]

(ẹr'gọ-tạ)

"The carefully dried sclerotium of *Claviceps purpurea* (Fries) Tulasne (Fam. *Hypocreaceæ*), replacing the grain of rye, *Secale cereale* Linné (Fam. *Gramineæ*), without the presence or admixture of more than 5 per cent. of seeds, fruits or other foreign matter. Before storing, dry Ergot at a temperature not exceeding 70° C. (158° F.), and preserve it, protected from light, in tightly-closed containers to which a few drops of chloroform or carbon tetrachloride are added from time to time to prevent attacks by insects." *U. S.* "Ergot is the sclerotium of Claviceps purpurea, *Tulasne,* originating in the ovary of Secale cereale, *Linn.* Ergot should be thoroughly dried and kept entire in air-tight containers; it should not be used if more than one year old." *Br.*

Secale Clavatum, Mater Secalis, Clavus Secalinus; Rye Smut, Mother of Rye, Cockspur Rye; Ergot de Seigle, *Fr. Cod.;* Ergot, Seigle Ergoté (noir), Blé Cornu, *Fr.;* Secale Cornutum, *P. G.;* Mutterkorn, Kornmutter, Rogenmutter, Zapfenkorn, Hungkorn, *G.;* Segala cornuta, Grano speronato, *It.;* Cornezuelo de centeno, *Sp.*

In all the Gramineæ, or grass family, and in some of the Cyperaceæ, the place of the grains or fruits is sometimes occupied by a morbid growth which, from its resemblance to the spur of a cock, has received the name of *ergot,* adapted from the French. This product is most frequent in the rye, *Secale cereale,* and from that grain was adopted in the first edition of the U. S. Pharmacopœia, under the name of *secale cornutum,* or *spurred rye.* In the edition of 1840 the name was changed to *ergota.* It is probable that this morbid growth has similar properties from whatever plant derived, and the fact has been proved in relation to the ergot of wheat. Tulasne found that dissimilar sclerotia collected from twelve species of grasses, produced fructification identical with that of the ergot of rye, so that it is probable that many apparently dissimilar ergots are specifically identical, their appearance being modified by the species of grass which they inhabit. It is further probable that all ergots have medicinal properties which agree in character though not in intensity. The short thick ergot which gathers upon the wild rice of Minnesota, *Zizania aquatica* L., has long been used as an abortifacient and oxytocic by the Indian women, and it is said that the wild ergot growing on various species of *Agropyrum* and *Elymus* in the Western United States, is fully equal medicinally to the official plant. M. Leperdriel, Jr., affirms that the *ergot of wheat* is destitute of the poisonous properties of that of rye, and is less liable to change. Bentley, of London, found that of two specimens, one of the ergot of rye, the other of wheat, which had been kept under similar circumstances for ten years, the former was quite destroyed, while the latter was apparently unchanged. Ergot is rarer in wheat than in rye, and in the head of the former there is generally but one and very rarely more than two of the diseased grains. It is produced usually in wheat in wet seasons, and on that side of the head most exposed to the dampness. It is shorter and much thicker than the ergot of rye, being about half an inch long and three-quarters of an inch or more in circumference, and cleft into two or three divisions. In color and odor it resembles spurred rye.

The *ergot of oats* is said to be of a black color, measuring from ten to twelve millimeters in length and three to four in thickness, and to have been used in Algeria as a substitute for rye ergot. (*L. M. R.,* March, 1888.) Warburton (*Bot. Gaz.,* 1911, p. 64) reports the occurrence of ergot on oats grown in the oat breeding nursery at Ames, Iowa. The *ergot of diss,* an Algerian reed, *Ampelodesma tenax,* has appeared in commerce to some extent. It is, when small, slightly curved, but when long (6 to 9 centimeters) it takes a spiral turn from right to left, the longitudinal furrows being present on the inner face. It is thinner, dryer, and more brittle than the ergot of rye, and has been used for the preparation of an ergotine or extract closely resembling the official one, but said to be of a more translucent red or brown color. Lallemand asserts that the ergot of diss is twice as strong as the ergot of rye, and states that it is abundant and readily collected. It is also stated to be less hygroscopic and less apt to be attacked by acari than is the official article. (*P. J.,* xvi, 684, 1886.)

Investigations of Tulasne have shown that ergot is not the diseased grain of the rye, but the *sclerotium* of a fungus, the *Claviceps purpurea* Tulasne. This fungus has three stages in its life history. The development of the *sphacelia,* or first stage, commences with that of the pistil, which serves as a soil for it. The ovary

of the rye consists of a cellular membrane made up of two coats, the outer of which has thick-walled cells; the inner being very delicate and green. The sphacelia, when it takes possession of the ovary, identifies itself with the outer layer, and in some measure replaces it, being as it were borne by the inner membrane. It rapidly increases, taking the form of the ovary, and almost obliterating its cavity. The ovule is either entirely wanting, or may be seen, on a careful examination, in an imperfect form. For some time the parasite is represented entirely by the sphacelia, which is an oblong, fungous mass, almost homogeneous, soft and tender, marked on its surface by numerous sinuous furrows, and having within many irregular cavities, which, as well as the outer coat, are uniformly covered with linear parallel cells. From the summits of these peripheric fruit bodies, internal as well as external, issue oval spores, from 0.005 to 0.007 mm. in length, which spread upon neighboring objects, and especially the glumes of the flowers they inhabit. They are a kind of reproductive cells, called conidia, which are produced by many fungi long before the perfect plant is developed. Tulasne calls them "*spermatie.*" The conidia, according to Rufmann and Maben (*P. J.*, 1908, lxxx, p. 247), are carried by a weevil from one ear of rye to another. In the early stage the sphacelia does not affect the top of the ovary, or the attached stigmas. The stamens often abort, but the filaments and anthers may sometimes be seen buried in the tissue of the sphacelia, and are altered by its action. Sometimes the ovule is not completely aborted, but it is certainly never developed into a normal grain. In all ergotized plants the pistils and stigmas, when they remain, are often covered with a mouldiness, consisting of spores and entangled filaments, which end by covering the parts with an abundant ashy or sooty powder. This is a different fungus, and was confounded by Quekett with the ergot plant. It is found as well in the non-ergotized as in the ergotized flowers, and in those of plants which do not bear ergot. At a somewhat advanced period of the development of the sphacelia, there exudes, especially from the summit, a very adhesive juice, which spreads over that structure, bearing along with it an immense number of the spores or "*spermaties.*" These leave on the surface when dry an oily appearance, and afterwards the spots, where they remain, become brownish or blackish. But this exudation does not appear until the sphacelia has ceased to constitute the whole plant.

At the base of the sphacelia is produced a compact body, violet-black without and white within, which is the ergot in a rudimentary state. With this commences the second stage in the development of the fungus. The young ergot is everywhere invested by the tissue of the sphacelia (which Tulasne calls also *spermagonia*, from its office); but, as it increases, it seems to be placed below the spermatopherous apparatus, and raises it steadily out of the floral bracts which conceal it, ending by supporting it wholly at its summit. Sometimes it carries with it the atrophied ovary, which still shows the hairs that crowned it, and some remains of the stigmas. It results that the ergot, which is technically the *sclerotium* of the fungus, remains for some time concealed in the sphacelia, so that this seems to constitute the whole plant; but, when the function belonging to this has been fulfilled, it begins to dry, and is much deformed. The ergot, on the contrary, increases in all directions, and soon appears above the glume. As it augments, the thin coating which it has received from the spermatopherous tissue, especially below, gradually becomes thinner, and seems to disappear, so that its surface, instead of being uniformly violet-black, is only here and there covered with the remains of the tissue, or with a deposit of the conidia or "*spermatie.*" Nevertheless, the sphacelia, deformed, shrunken, and worn away by rains and other causes, remains long at the top of the ergot, along with the abortive ovary, etc., and may even continue to adhere when the ergot is detached from the plant. The time required for full development of the sphacelia and the ergot or sclerotium varies. In an example under the observation of Tulasne, at least a month elapsed after the appearance of the sphacelia before the growth was completed.

Ergot has absolutely nothing in common with normal grain. The anatomical structure and all the physical characters of ergot are those of the mushrooms, or rather of a sclerotic mycelium. The parenchyma, which is whitish, dry, and brittle, consists in all its parts of irregular, globular, or polyhedric thick-walled cells, intimately united, and filled with a limpid oil, but feebly colored by iodine. The superficial utricles, which alone are colored, have an outer wall thicker than the inner, and the color of these is what gives its characteristic hue to ergot. Not the least trace of starch is to be detected. If ergot is planted in a suitable soil, evidences of germination are seen in about three months. Little globular prominences appear on its surface, which gradually enlarge, and raise themselves upon cylindrical stems, and finally become perfect pilei or fruiting fungi, producing elongated, rod-like spores in flask-shaped cavities which open by a little pore. These little fungi belong to the genus *Sphæria*. As they increase, the interior of the ergot becomes exhausted, by contributing to their growth. Falling to the ground, in its natural course, the ergot in the soil germinates, and produces pilei, the spores of which, carried up with the juices of rye, become lodged in the ovary, where they begin the course of life and progress which has been described. Different grains are probably infested with different species of Claviceps, but there is no reason to think that any other species is concerned in the product of any official variety of ergot. (*Annales des Sciences Naturelles*, 3e sér., xx, 5, 1853.) The ergot usually projects out of the glume or husk beyond the ordinary outline of the spike or ear. In some spikes the

place of the seeds is wholly occupied by the ergot in others only two or three spurs are observed. It is said to be much more energetic when collected before than after harvest. Rye has generally been thought to be most subject to the disease in poor and wet soils, and in rainy seasons, and intense heat succeeding continued rains has been said to favor its development, especially if these circumstances occur at the time the flower is forming. It is now, however, asserted that moisture has little or nothing to do with its production. It should not be collected until some days after it has begun to form, as, according to Bonjean, if gathered on the first day it does not possess the poisonous properties which it exhibits when taken on the sixth day. (See *P. J.*, Jan., 1842.) Ergot enters commerce chiefly from Russia, Germany, and Spain. Of the three varieties the Spanish ergot is considered the best, yielding usually from 13 to 15, sometimes as high as 18, per cent. of extractive. It is somewhat darker colored, rather shorter, and more uniform than is the German ergot. An ergot of excellent quality has been sent from the Canary Islands to England. The average annual import of ergot into the United States is about 120,000 pounds. The exports from Russia in 1906 were 430,000 pounds.

Properties.—The official description is as follows: "Cylindraceous, obscurely three-angled, tapering towards both ends, obtuse, somewhat curved, from 1 to 4.5 cm. in length and from 3 to 5 mm. in thickness; externally purplish-black, or brownish-black, longitudinally furrowed; fracture short, pinkish or reddish-white, sometimes grayish-white; odor peculiar, disagreeable, free from mustiness; taste oily and disagreeable. Pour hot water on bruised Ergot; no ammoniacal or rancid odor develops. The powder is grayish-brown, consisting chiefly of whitish fragments composed of false parenchyma of compacted hyphæ and a few purplish colored fragments of the outer layer of the sclerotium; mounts made in hydrated chloral T.S. or in sulphuric acid show the separation of numerous globules of a fixed oil, and many of the fragments are colored yellowish, reddish or rose-purple. Shake 1 Gm. of the powdered drug with a mixture of 20 mils of water and one drop of hydrochloric acid, filter the mixture, make 4 mils of the filtrate alkaline with ammonia water and shake out with 10 mils of ether. Underlay 5 mils of this ethereal solution with 2 mils of sulphuric acid; a blue ring is formed at the zone of contact of the two liquids. Ergot yields not more than 5 per cent. of ash." *U. S.*

"Subcylindrical or somewhat triangular, tapering towards the ends, generally curved; from one and a half to four centimetres long; longitudinally furrowed on each side, but more especially on that which is concave; often irregularly cracked; very dark violet-black externally, whitish or pinkish-white within; fracture short. Odor characteristic and disagreeable, especially when triturated with *solution of sodium hydroxide;* taste disagreeable." *Br.*

The aqueous infusion or decoction is claret-colored, and has an acid reaction. It is precipitated by lead acetate and subacetate, silver nitrate, and tincture of galls, but affords with iodine no evidence of the presence of starch. Long boiling impairs the virtues of ergot. The U. S. P. VIII and the British Pharm., 1914, state that ergot should not be kept for more than a year, but the U. S. P. IX revision has omitted this statement. While there is not sufficient data to allow of positive conclusions, Wood and Hofer (*A. In. M.*, 1910, vi, 388) found that in a sample carefully dried and sealed the activity was not perceptibly diminished after six months, and Eberhardt and Eldred (*J. A. Ph. A.*, 1914, iii, 38) quote Moss as having shown that freed from its oil ergot will retain its virtues unimpaired for two and even five years. (For discussion of the deterioration of the *Fluidextract of Ergot,* see p. 490). The germinating test has been utilized in determining a good quality of ergot and Zimmermann (*Ztschr. f. Pflanzenkrankheiten,* 1907, p. 129) concludes that the sclerotium of *Claviceps purpurea* is capable of germinating even after keeping for two years. Ergot sometimes contains small stones and cereal grains, implying that it has not been carefully garbled. Many samples are "wormy," some really being alive with insects. Old ergot is sometimes brightened by the use of a fixed oil; the revisers of Vienna Pharmacies (*Pharm. Prax.*, 1905, p. 38) reported finding one sample of powdered ergot which contained flour as an adulterant.

Ergot, when perfectly dry and kept in well-stoppered bottles, will retain its virtues for a considerable time, but exposed to air and moisture it speedily undergoes chemical change and deteriorates. It is, moreover, apt to be attacked by a minute worm, which consumes the interior of the grain, leaving the exterior shell and an excrementitious powder. This insect is sometimes found in the ergot before removal from the plant. In the state of powder the medicine more readily deteriorates, but Dragendorff believes that the decay is due to oxidization of the fatty principles of the ergot, and can be prevented by depriving the ergot of its oil before powdering. (*A. P. S.*, XXV.) Camphor and powdered benzoin are said to prevent injury from worms. Aymoiner immerses fresh ergot in an ethereal solution of tolu, dries it, and preserves in tightly closed bottles.

Ergot has been analyzed by Vauquelin, Winckler, Wiggers, Wright, Legrip, Wenzell, Tanret, Dragendorff, and several others. Wright supposed the virtues of ergot to reside in the fixed oil, which he therefore recommended as a substitute for the medicine. The *oil of ergot,* when obtained from grains recently collected, is, according to Wright, often quite free from color, but as usually prepared it is reddish-brown. It has a disagreeable, somewhat acrid taste, is lighter than water, and is soluble in alcohol and alkaline solutions. It is prepared by forming an ethereal tincture of ergot by the process of

percolation, and evaporating the ether with a gentle heat. It may be more cheaply prepared by substituting petroleum benzin for ether. Experience has shown that, though the oil thus prepared with ether may have produced effects analogous to those of ergot, they were to be ascribed rather to some principle extracted along with the oil by the menstruum than to the oil itself, for, when procured by expression, this has been found to be inactive. According to T. R. Baker, the oil has a taste and odor similar to those of castor oil, with which it also agrees in ultimate composition, and yields analogous results in saponification. T. C. Herrmann investigated specially the chemical constitution of the oil of ergot. As obtained by means of ether, it was brownish-yellow, of an aromatic odor and acrid taste, viscid, of the sp. gr. 0.9249, and without the drying property. It consists of 22.703 per cent. of palmitic acid, 69.205 of oleic acid, and 8.091 of glycerin. (*N. R.*, 1872, p. 238; from *Buchner's Repertorium*, 1871, p. 283.) The *sugar of ergot* was found by Mitscherlich to be *mycose*, $C_{12}H_{22}O_{11}$. According to Wenzell (*A. J. P.*, May, 1864), ergot of rye contains two peculiar alkaloids, which he designated *ecboline* and *ergotine*, and claimed to be the active principles of the drug. The two bases of ergot are, according to Wenzell, combined with *ergotic acid*, the existence of which has been further admitted by Ganser. It is said to be a volatile body yielding crystallizable salts.

A crystallizable, colorless alkaloid, *ergotinine*, $C_{35}H_{40}N_4O_6$, which is probably identical with Wenzell's ergotine, was isolated (1877–1878) by Tanret. He obtained it to the amount of 0.04 per cent., some amorphous ergotine, moreover, being present. The solutions of ergotinine turn greenish and red very soon; they are fluorescent. Sulphuric acid imparts to it a red, violet, and finally blue hue.

Tanret also observed in ergot of rye a volatile *camphoraceous* substance.

Voswinkel obtained from ergot a brown amorphous substance, which he proved by hydrolysis to yield *mannose*. The body is a semi-cellulose, and the name *mannan* has been given to it. He states that Dragendorff's *sclerotic acid* and *scleromucin* are identical with mannan. (*Ph. Centralh.*, 1891, p. 531.)

Kobert (*Ph. Centralh.*, 1884, p. 607; All, *Das Mutterkorns*, Leipzig, 1884) found three physiologically active principles: 1st, *ergotic acid*, which he considers the principal constituent of the sclerotic acid of Dragendorff and Podwissotzky, and which is isolated by precipitation with ammoniacal lead subacetate; 2d, *sphacelic acid*, which can be isolated by taking advantage of the insolubility of the free acid in water and its solubility in alcohol; 3d, the alkaloid *cornutine*, which is not identical with the crystalline or with the amorphous ergotinine of Tanret; it is readily soluble in alcohol, and is obtained from an alkaline aqueous solution by agitation with ether. This alkaloid is said to be very poisonous. Kobert's conclusions were questioned by Tanret (*P. J.*, 1885, p. 889), but the former reaffirms his statements and believes that ergotinine is worthless, and that the activity of fresh ergot is due to sphacelic acid and cornutine as above described (*A. Pharm.*, 1886, p. 597). At present (1917) the activity of ergot seems to be due to the presence of (1) a characteristic alkaloid discovered almost simultaneously by Barger and Walpole, and by Kraft (*Pharm.*, 1906), the former calling it *ergotoxine* and the latter *hydro-ergotinine* to show its relation to the *ergotinine* of Tanret which is inert; (2) to certain amines which are common to various putrefying materials. Of these amines there have been so far separated *para-phenyl-hydroxylamine* (also known as *tyramine* or *uteramine*), and *beta-iminazolethylamine* (*histamine, ergamine, imidazol*). Besides these Ewins (*Biochem. J.*, 1914, viii, p. 44) has shown the occurrence in certain specimens of ergot of *acetyl-choline* which is a powerful circulatory depressant, and more or less antagonistic to the other principles of ergot. Cornutine of Kobert apparently does not occur in ergot but is an artefact. (The cornutine of Keller is a very different substance and appears to represent all of the alkaloidal bodies present in the crude drug.) *Sphacelotoxin*, described by Jacoby, is a substance having acid properties contaminated with ergotoxin; Wood and Hofer believe that the acid and the alkaloid are in chemical combination. Barger and Ewins (*Tr. Chem. Soc.*, 1910, xcvii, p. 284) have shown that ergotoxine has the formula $C_{35}H_{41}O_6N_5$. Tanret's ergotinine has $C_{35}H_{39}O_5N_5$, so that it is the anhydride of ergotoxin. Ergotoxine may be changed into ergotonine by boiling with methyl alcohol or acetic anhydride.

Carr and Dale (*W. Br. Ph. Conf.*, 1913, 505) presented a comprehensive and critical review of the preparations of ergot with especial reference, of course, to the B. P., but containing much that is of value in connection with our own official preparations. They state that as *ergotoxine* is the recognized active principle of ergot the value of ergot and its preparations should be judged by the content of that principle. They also recognize the supplementary value of the amines, such as *ergamine*, and state that, given equal ergotoxine values, the sample which is higher in amines will be therapeutically superior. They commend the U. S. P. VIII fluidextract as being a preparation of great value.

Assay.—The great variation in the potency of different samples of ergot, as well as its practical importance, has led to a number of attempts to develop means of determining the quality of the drug. These efforts have included both the chemical and the biological assay.

The earliest systematic use of the biological reaction for determining the quality of ergot were the experiments of Grünfeld in 1895. His method was based upon the quantity of the sample which was necessary to cause gangrene in the combs and wattles of roosters, and is commonly spoken of as the *cock's comb method.*

This test was later utilized by Houghton (*T. G.*, 1898) on a commercial scale.

The criterion of the cock's comb method is the dose of a sample of ergot which is required to cause a bluing of the comb. It is important that the same breed of chickens be used throughout any series of experiments; white Leghorns are generally preferred. The method is carried out as follows: A rooster is weighed, and then a dose of the fluidextract to be tested, equivalent to about 1 mil (16 minims) per kilogramme, is injected into the muscle of the breast. An hour later the bird is examined. If the specimen has been an active one, there will be a bluish or cyanotic appearance around the edge of the comb. The extent and degree of this discoloration is noted. The same rooster may be used over and over again, and the experimenter soon learns the degree of bluing which is the characteristic reaction of that individual chicken for a standard dose of the active drug. If, however, no bluing occurs, the drug is below the standard.

The idea of using the elevation of blood pressure for the assay of ergot seems to have been first suggested by Dixon (*P. J.*, 1905), and was elaborated by Wood and Hofer. (*A. In. M.*, 1910, vi, 388.) The method as employed by the latter is as follows: A dog is anesthetized with morphine and ether, and the carotid artery connected with a mercurial manometer. The normal blood pressure is observed, and then a dose of the sample equivalent to 0.15 Gm. of ergot for each kilo of body weight is injected intravenously, and the blood pressure noted (1) at its highest point after the injection, (2) five minutes after, and (3) ten minutes after the injection, the average elevation above the norm of these three observations represents the physiological activity of the specimen. In order to obviate peculiar susceptibility in individual dogs, it is necessary that experiments be made upon three animals with each sample. Edmunds and Hale modified the method by previously administering atropine for the purpose of avoiding the stimulant action upon the vagus, but their results were less consistent than those who have worked on the normal animal. The two objections which have been urged against this method are, in the first place, the assertion that because the drug is used chiefly as a uterine stimulant, a blood pressure test does not give satisfactory criterion of the therapeutic activity of the drug, and secondly, the possibility of a marked abnormality in the reaction of one of the experimental animals creating a false idea of the activity of the drug. An attempt has been made to obviate this last objection by comparing the effects of a standard specimen upon the same animal.

The most important objection which has been urged against this measure is that since the drug is used chiefly as a uterine stimulant the blood pressure test is not a satisfactory criterion of its therapeutic activity. This objection, however, must not be given too great stress because, in the first place, since ergot is widely used for its vasomotor effect it is important to know its action on the circulation, and in the second place, Stewart and Pittinger (*Trans. of the Amer. Therap. Soc.*, 1914) have shown that there is a close parallelism between the degree of action of various samples of ergot upon the blood pressure and upon the uterus.

Two methods in which the uterine muscle is used as an indicator of ergot have been suggested, that of Kehrer (*A. E. P. P.*, 1908, lviii) in which the uterus is removed from the body and either strips of the isolated muscle or the whole organ are employed, and that of Edmunds in which the uterus *in situ* furnishes the test reaction.

In the first of these the uterus of the guinea-pig is cut out of the body and placed in Locke's solution (see *Liquor Sodii Chloridi Physiologicus*) which is kept at the body temperature and through which oxygen is constantly bubbling. One end of the uterus is fixed and the other attached to a muscle lever which records on a slowly moving drum. The lever is weighted sufficiently to reduce the normal contractions to small size. After waiting a sufficient length of time for the disturbance of function caused by the operation to have subsided, various strengths of a standard solution are added to the Locke fluid in which the uterus is immersed until the amount which is required to produce a barely submaximal contraction has been determined: between the tests with each strength of solution the uterus is washed with normal Locke fluid. After determination of the strength of the standard preparation for the individual uterus being employed, the solution to be tested is added in corresponding strength and then in higher or lower concentration until the amount is found which produces the same degree of contraction as the standard solution.

As a comparison either a standard solution of ergot or of hypophysis may be used. Pittinger and Vanderkleed (*J. A. Ph. A.*, 1914, iii, p. 925) have modified this method by adding weights until the uterus is barely able to move the lever and testing the strength of the muscle against this added resistance.

The method employed by Edmunds (*Hygienic Lab. Bul.*, No. 76, July, 1911) is most satisfactorily performed upon cats. The anesthetized animal, which is kept alive by artificial respiration throughout the experiment, is immersed in a bath of physiological salt solution at a temperature of 39° C. (102.2° F.), the abdomen is then opened by a medium incision, the bladder and intestines drawn aside; one horn of the exposed uterus freed by tearing away the peritoneal attachments and two fine silk threads passed through this horn at a distance of about two centimeters apart. These threads are then connected to a light muscle lever. To obtain the proper degree of tension weights may be added to the muscle lever. The ergot to be tested is then injected intravenously alternating with a standard solution. As in this method there is no definite end reaction it is often difficult to

judge of the relative potency of the two preparations. Edmunds and Hale themselves say of it: "It is not an unusual experience to carry on such an experiment for two or three hours and . . . . to know very little more about the relative strengths of the two specimens at the end than at the beginning of the experiment."

There are several practical objections to all the uterine methods of assay. In the first place, they require a greater degree of technical skill in carrying out than either the blood pressure or cock's comb methods; in the second place, there is no definite end-point of the reaction so that it is difficult to make quantitative comparisons; and in the third place, the uteri of different species of animals do not respond in the same way to the drug, and even in the same species the effect may vary. Thus Dale finds that isolated strips of uterine muscle from the guinea-pig respond to ergotoxine but similar strips from the cat do not, although the intact uterus from the latter animal is excited by this alkaloid; tyramine causes contraction of the uterus in the pregnant and relaxation in the virgin cat.

There has been much discussion as to which method is the most useful for standardizing ergot. For commercial purposes at least the choice lies between the cock's comb and the blood pressure method. The former has the great advantage of its simplicity, but it has the disadvantage of the absence of a sharp end reaction, for the change in the color of the comb may vary anywhere from an almost imperceptible darkening of the tip to a deep cyanotic color of the whole appendage—and hence leaves a wider range for possible personal error. As the different principles of ergot produce different physiological effects, it is evident that the two tests may give very different results for the same specimen of ergot; thus ergotoxine causes both bluing of the comb and rise in blood pressure; while tyramine causes rise in blood pressure but no bluing, while histamine causes no rise in blood pressure but, according to Crawford and Crawford (*J. A. M. A.*, 1913, lxi), it does cause bluing of the comb. For reasons pointed out by Crawford and Crawford, it is improbable that the fluidextract of ergot, prepared according to the U. S. P. will contain any considerable proportion of histamine, and it would seem, therefore, that a blood pressure method would furnish more accurate information concerning the American fluidextract than the test upon the rooster. But it must be remembered that the proper performance of the blood pressure test requires more technical skill than that upon the rooster, and in the hands of the unpractised it is probable that the cock's comb method would yield more favorable results.

The reader who is interested in this subject may find extensive references to the literature in the paper of Wood and Hofer (*A. In. M.*, 1910, iv, p. 388) and of Edmunds and Hale (*U. S. Hygienic Laboratory Bull.*, No. 76, 1911).

Pearson (*J. A. Ph. A.*, 1913, ii, p. 1453) reports upon the tests of the Activity of Ergot by the Blood Pressure Method. One of the first evidences of deterioration of preparations of ergot is the loss of the power to sustain the blood pressure; a good preparation will keep the blood pressure up for about two hours. Heated on a water bath for thirty minutes the fluidextract of ergot loses almost completely its power of raising the blood pressure. Evaporating at room temperature by a current of air does not destroy its activity. Extract of ergot (U. S. P.) had practically no effect on blood pressure. Bonjean's ergotin produced no rise and usually a decided fall in pressure. A powdered extract (method of manufacture not given) produced a temporary rise but the increased pressure was not sustained.

Uses.—Ergot is a stimulant to all forms of involuntary muscle fibers, the most important being the heart, the arteries, and the uterus. When a dose of ergot is injected intravenously there occurs a rise in the blood pressure, sometimes preceded by a transient fall, and accompanied with a reduction in the rate of the pulse. The elevation of the pressure is due in part to a contraction of the blood vessels, the result of a direct stimulant action upon their muscular coats, but also in part to a stimulating effect upon the cardiac muscle. The effect of a small dose of ergot upon the uterus is to increase both the vigor of its contraction, and its muscular tone. If the dose is larger, the increase in muscle tone becomes relatively more and more pronounced, until eventually the organ may be thrown into a permanent spasmodic contraction. Other evidences of the stimulating effect of ergot upon unstriped muscle are seen in increased intestinal peristalsis, contraction of the pupil, and of the bladder.

On the continent of Europe ergot has long been empirically employed by midwives for promoting contraction of the uterus, and its German name "Mutterkorn" implies the popular acceptance of its peculiar powers, but it was first introduced to the regular medical profession as the result of the writings of Stearns (*N. Y. Medical Repository*, 1807.) While a remedy of undoubted utility in properly selected cases of *labor*, its injudicious use may do much harm, and even prove fatal to either the mother or the child. When used freely, ergot is liable to transform the normal intermittent contractions of the parturient uterus into one violent spasm. If this spasmodic contraction occurs too early in the course of the birth process it may lead to asphyxiation of the child, to wide lacerations of the birth canal, or even to rupture of the uterus. In the third stage of labor, however, no such accidents can occur, and many obstetricians recommend the routine use of ergot at this time, as a prophylactic against *post partum hemorrhage*. Ergot is also used as a stimulant to the non-pregnant uterus to check bleeding in *menorrhagias* and *metrorrhagias*.

As a circulatory stimulant, ergot deserves more popularity than it has received. Although certain authors have found it a serviceable remedy in acute circulatory failure, such as *surgical shock,* the slowness of its action interferes with its utility in this condition, and its most important field of usefulness is in chronic vasomotor relaxations. Thus, it is useful in cerebral or *spinal congestion,* in *colliquative sweats,* in relaxing *diarrhea,* and similar conditions in which there are local passive congestions. Because of its success in hemorrhage from the uterus, ergot has been widely employed in various other internal *hemorrhages,* but its value under these circumstances is doubtful. Probably because of the effects of ergot on the circulation it is a very valuable remedy in the treatment of *delirium tremens.* (See Ranson and Scott, *A. J. M. S.,* 1911, cxli, p. 673.) Osborne (*N. Y. M. R.,* July 14, 1906) says that it has a powerful sedative effect upon the central nervous system and is useful in certain types of *asthma,* in *Graves's disease, hysteria,* and especially for the nervousness in the withdrawal of morphine.

Under the name of ergotin, usually with the name of the maker attached, a number of more or less purified extracts of ergot are upon the market. The doses of these range from one to ten grains according to their purity. *Bonjean's Ergotin* is made by exhausting ergot with water, evaporating to the consistency of syrup, precipitating the albumen, gum, etc., with alcohol, decanting the clear liquid and evaporating to the consistency of the soft extract. It is to be remembered in this connection that no aqueous extract of ergot can thoroughly represent the crude drug. *Ergotoxine* is marketed in the form of a crystalline phosphate, the dose of which is from one one-hundredth to one-fiftieth of a grain (0.0006–0.0013 Gm.). The hydrochloride of para-hydroxyphenylethylamine is sold under the trade name of *tyramine.* Its dose is from one-twelfth to one-half of a grain (0.005–0.032 Gm.).

The most widely used unofficial preparations of ergot are as follows:

Ergotin Bonjean (see *Extractum Ergotæ Aquosum,* Part III).—*Dose,* three to eight grains (0.2–0.5 Gm.).

Ergotin Wernich Merck.—Purified, dried, dialyzed aqueous extract of ergot. *Dose,* twenty grains (1.3 Gm.).

Ergotin Wiggers.—*Dose,* ten to fifteen minims (0.6–0.9 mil).

Ergotole.—*Dose,* five to twenty minims (0.3–1.3 mils).

Ernutin.—*Dose,* five to ten minims (0.3–0.6 mil).

Ergone.—*Dose,* fifteen to thirty minims (0.9–1.8 mils).

Cornutol (*Liquid Extractum Ergotæ*).—*Dose,* ten to thirty minims (0.6–1.8 mils).

Clavin.—*Dose,* one-third of a grain (0.02 Gm.).

Toxicology.—Ergot can scarcely be considered as a poison, since an ounce of the fluidextract rarely produces, except in the pregnant, any obvious symptoms unless it be nausea. Large doses are liable, it is true, to produce abortion in pregnant women, but even this result is uncertain. We know of but one instance of fatal poisoning by it, unless the death was produced by the abortion. The symptoms of the recorded cases of poisoning have been paleness, and, as most characteristic, an especial coldness of the surface, partial paralysis with numbness and tingling in the limbs, feebleness of the pulse, restlessness, and finally stupor or delirium.

On the other hand, the long continued and free use of ergot is highly dangerous, even when no immediate effects are perceptible. Fatal epidemics in different parts of the continent of Europe, particularly in certain provinces of France, have long been ascribed to the use of bread made from rye contaminated with this fungus. Dry gangrene, and disorder of the nervous system attended with convulsions, are the forms of disease which have followed the use of this unwholesome food. It is true that ergot has been denied to be the cause, but accurate investigations made by competent men upon the spot where the epidemics have prevailed, together with experiments upon inferior animals, leave no room for reasonable doubt that at least the gangrenous affection alluded to has resulted from it.

Dose, of ergot, fifteen to sixty grains (1–3.9 Gm.).

Off. Prep.—Extractum Ergotæ, *U. S., Br.;* Extractum Ergotæ Aquosum, *N. F.;* Fluidextractum Ergotæ, *U. S.* (*Br.*); Infusum Ergotæ, *Br.;* Injectio Ergotæ Hypodermica (from Extract), *Br.;* Tinctura Ergotæ Ammoniata, *Br., N. F.*

ERIODICTYON. U. S.

ERIODICTYON Eriodict. [Yerba Santa]

(ĕr-ī-o-dĭc'tŷ-ŏn)

"The dried leaves of *Eriodictyon californicum* (Hooker and Arnott) Greene (Fam. *Hydrophyllaceæ*), without the presence or admixture of more than 5 per cent. of stems or other foreign matter." *U. S.*

Mountain Balm, Consumptive's Weed, Bear's Weed, Gum Bush.

Eriodictyon californicum is a low evergreen shrub growing abundantly upon dry hills in California. It is glabrous, resinous, having short petiolate, long lanceolate leaves, irregularly more or less serrate, sometimes entire, whitened beneath, between the reticulations, by a minute and close tomentum, above glabrous. The corolla is tubular funnel-form; the calyx being sparsely hirsute. The leaf structure has been studied by F. W. Ritter. (See *A. J. P.,* 1895, 565.)

E. tomentosum, which grows often along with *E. californicum,* especially in the southern part of California, is readily distinguished by its dense coat of short villous hairs, whitish or rusty-colored with age. It is also a larger shrub than *E. californicum,* has its corolla somewhat salver-

form, and its leaves oblong or oval, and obtuse.

Properties.—The leaves of eriodictyon are characterized by the U. S. Pharmacopœia as "Usually in fragments; when entire, laminæ lanceolate, from 5 to 15 cm. in length, and from 1 to 3 cm. in breadth; summits acute; bases slightly tapering into short petioles; margins irregularly serrate or crenate-dentate; upper surfaces yellowish-brown, covered with a more or less glistening resin; under surfaces grayish or yellowish-white, conspicuously reticulate with greenish-yellow veins; minutely tomentose between the reticulations; thick, brittle; odor aromatic; taste balsamic, bitter, becoming sweetish. Under the microscope, transverse sections of the laminæ of Eriodictyon show upon the upper surface large epidermal cells, the outer walls being very uneven, owing to indentations which appear as striations in surface view; glandular hairs numerous, with short 1-celled stalks and 6- to 8-celled glandular heads; palisade cells very narrow, from 2 to 6 rows deep, containing numerous chloroplastids; cells of dorsal-pneumatic tissue (loose mesophyll) very few; fibro-vascular tissues not strongly developed except in the midrib and more prominent veins; numerous 1-celled, much twisted, thick-walled, non-glandular hairs occurring on the lower surface between the veins. Under the microscope, sections of the stems of Eriodictyon show the epidermis usually replaced by strongly lignified cork; cortex of from 10 to 20 rows of more or less rounded cells; bast-fibers deep-seated with thick, more or less strongly lignified walls and occurring in small groups forming a more or less interrupted circle; sieve tissues in a narrow zone; wood-wedges consisting of tracheæ with spiral thickenings, simple or bordered pores and numerous strongly lignified wood-fibers, separated by medullary rays 1-cell in width; pith very large, the walls of the cells being strongly lignified and with numerous simple pores." *U. S.*

Tunmann (*Ph. Centralh.*, 1908, p. 159) describes and illustrates the pharmacognostic and microscopic characteristics of *Eriodictyon californicum*, and discusses the morphological importance of the oil glands of eriodictyon. H. S. Wellcome (*The Pharmacist*, 1876, p. 33) found the drug to contain two aromatic resins, while an aqueous infusion of leaves which had been exhausted by alcohol yielded an intensely bitter extract. According to the analysis of Chas. Mohr (*A. J. P.*, 1879, 549), it contains tannic acid and 8 per cent. of an acrid, bitter, resin, upon which its activity is believed to depend, also a minute quantity of volatile oil. R. Rother describes (*A. J. P.*, 1887, p. 225) an acid resin which forms with bases quite soluble salts. The acid resin was obtained at the conclusion of the spontaneous volatilization of the several solvents as a green-yellow transparent mass. Thal (*Ph. Z. R.*, 1883, p. 209) affirmed the presence of *ericolin*, $C_{34}H_{56}O_{21}$. Power and Tutin deny that ericolin is present but find besides volatile oil and resin, *triacontane*, $C_{30}H_{62}$, *penta triacontane*, $C_{35}H_{72}$, *eriodictyol*, $C_{15}H_{12}O_6$, *homoeriodictyol*, $C_{16}H_{14}O_6$, and a phenol, $C_{16}H_{42}O_6$.

Uses.—Eriodictyon has long been used in California as a bitter tonic, and also as a stimulant balsamic expectorant. There is considerable testimony to its usefulness in *asthma, chronic bronchitis*, and allied conditions; also in chronic inflammation of the genito-urinary tract. Attention has been called by Kier to its remarkable power of disguising the taste of quinine, and Meyer (*Ph. Ztg.*, 1905) found that it will also mitigate the unpleasantness of hydrastis or aspidium. It is best exhibited in the form of the official fluidextract, the dose of which is one-half to one fluidrachm (1.8–3.75 mils); a solid extract has been made, which may be given in doses of from five to fifteen grains (0.32–1.0 Gm.). In cases of asthma, eriodictyon is often used by smoking. The aromatic syrup is well adapted as a vehicle for quinine.

Dose, fifteen to sixty grains (1.0–3.9 Gm.).

Off. Prep.—Fluidextractum Eriodictyi, *U. S.*; Elixir Eriodictyi Aromaticum (from Fluidextract), *N. F.*; Syrupus Eriodictyi Aromaticus (from Fluidextract), *N. F.*

EUCALYPTOL. U. S.

EUCALYPTOL [Cineol]

(eū-ca-lyp'tŏl)

"An organic compound [$C_{10}H_{18}O = 154.14$] obtained from the volatile oil of *Eucalyptus Globulus* Labillardière (Fam. *Myrtaceæ*) and from other sources. Preserve it in well-closed containers, in a cool place, protected from light." *U. S.*

Eucalyptol, *Fr. Cod.*; Cinéol, Terpane, Cajeputol, *Fr.*; Terpan, *G.*; Eucaliptol, *Sp.*

In the distillation of eucalyptus leaves, the portion which comes over between 170° C. (338° F.) and 178° C. (352.4° F.) is set aside as crude eucalyptol. To obtain it pure a redistillation from potassium hydroxide or calcium chloride is necessary. It is very liquid, nearly colorless, with a strong, aromatic, camphoraceous odor, is slightly soluble in water, but very freely soluble in alcohol. Nitric acid produces with it a crystallizable acid; by the action of phosphoric anhydride (*J. P. C.*, 4e sér., xii, 204) it is converted into *eucalyptene*, $C_{10}H_{16}$, a substance allied to cymene, and *eucalyptolen*.

C. Jahns (*A. J. P.*, 1885, p. 237) gave the formula $C_{10}H_{18}O$ to eucalyptol, and showed it to be identical with cajuputol, or, as it is now generally known, *cineol*. Wallach (*Ann. Ch. Ph.*, 248, pp. 278 to 283) showed that the oil from *E. Globulus* contained cineol (eucalyptol) and *dextro-pinene*, while that from *E. amygdalina* Labill., contained cineol and *lævo-phellandrene*. (For the nearer study of oil of eucalyptus and for consideration of other eucalyptol bearing oils, see under *Oleum Eucalypti.*)

The U. S. P. describes it as "a colorless liquid, having a characteristic, aromatic and distinctly camphoraceous odor, and a pungent, spicy taste;

it produces a cooling sensation in the mouth. Eucalyptol is very slightly soluble in water, miscible with alcohol, chloroform, ether, glacial acetic acid, or fixed or volatile oils. Specific gravity: 0.921 to 0.923 at 25° C. (77° F.). It boils between 174° and 177° C. (345.2° and 350.6° F.). Congealing point: not below 0° C. (32° F.). Eucalyptol is optically inactive (distinction from *oil of eucalyptus and many other volatile oils*). Place 1 mil of Eucalyptol in a freezing mixture and gradually add to it an equal volume of phosphoric acid; a solid, white, crystalline mass of cineol-phosphoric acid results, and if warm water is then added the Eucalyptol separates. Shake 5 mils of Eucalyptol with 5 mils of sodium hydroxide T.S.; the volume of the Eucalyptol is not diminished (*saponifiable oils*). Its alcoholic solution (1 in 10) is neutral to moistened litmus paper, and, on adding a drop of ferric chloride T.S. to 5 mils of this solution, no brown or violet color is produced (*phenols*)." *U. S.*

Uses.—Eucalyptol has to a considerable extent replaced the oil of eucalyptus especially as a stimulant expectorant in *chronic bronchitis* and *bronchorrhea*, etc. Berliner (*B. K. W.*, 1913, p. 1703) injected hypodermically an oily solution of menthol and eucalyptol in the treatment of *tuberculosis of the lungs* with asserted great benefit. Eucalyptol is also widely employed as a vermifuge. Locally it is a popular addition to various washes and sprays to be used in the nose and throat, because of its antiseptic action. Brownscomb (*Chemist and Druggist*, 1910), however, asserts that eucalyptol is a less powerful antiseptic than the other ingredients of the oil of eucalyptus.

Dose, five to ten minims (0.3–0.6 mil), four to six times a day.

Off. Prep.—Liquor Antisepticus, *N. F.;* Liquor Antisepticus Alkalinus, *N. F.;* Liquor Pepsini Antisepticus, *N. F.;* Nebula Aromatica, *N. F.;* Nebula Eucalyptolis, *N. F.;* Nebula Mentholis Composita, *N. F.;* Petroxolinum Eucalyptolis, *N. F.;* Petroxolinum Iodoformi, *N. F.;* Petroxolinum Sulphuratum Compositum, *N. F.;* Pulvis Antisepticus, *N. F.*

EUCALYPTUS. U. S.

EUCALYPTUS Eucalypt. [Blue Gum Leaves]

(eū-ca-lȳp'tŭs)

"The dried leaves of *Eucalyptus Globulus* Labillardière (Fam. *Myrtaceæ*), collected from the older parts of the tree, without the presence or admixture of more than 3 per cent. of the stems, fruits or other foreign matter." *U. S.*

Blue Gum-tree Leaves, Australian Fever-tree Leaves, Eucalyptus Leaves; Eucalyptus, *Fr. Cod.;* Feuilles d'Eucalyptus, *Fr.;* Eucalyptusblätter, *G.;* Eucalitto, *It.;* Eucalipto (Hoja de), *Sp.*

The genus *Eucalyptus* was named by L'Heritier in 1788, from the two Greek words meaning "I cover well," "in allusion to the operculum or lid which covers the calyx until the stamens are fully formed." The plants, which are known as *Gum trees, Woolly butts, Iron barks*, etc., by the natives of Australia and Tasmania, are evergreen and vary from shrubs to trees of enormous height, some of them probably being the highest trees known. Kerner gives the height as 140 to 152 meters. They form, it is stated, about three-fourths of the whole vegetation of those countries. At least one hundred and forty species have been described. The leaves frequently vary in shape and in position on both young and mature trees; they are fixed vertically, and not horizontally as the leaves of our trees, the petiole being twisted. The leaves furthermore contain large oil-secreting reservoirs. The flowers are arranged in cymes or axillary umbels and are devoid of petals; the usually whitish stamens are inflexed in the bud and expand when the operculum is removed, giving the name as already stated to the genus. The fruit is a 3- to 6-celled truncated capsule, or pyxis. The seeds are small and very numerous, the sterile ones predominating; this is no doubt one reason why there has been so much difficulty in producing seedlings.

Most of the species do not require excessive heat for their perfecting, and some of them are able to resist moderate frosts. Over forty species are being grown successfully in the United States, and in the neighborhood of Los Angeles and other points in California a pure oil is said to be commercially produced. On account of the rapidity of their growth and the hardness and indestructibility of their timber, many of the species are very valuable for economic purposes. A number of the species are said to be cultivated in the Southwest as a source of honey. (See *Bulletin No. 35 of the U. S. Bureau of Forestry.*)

With a genus of so many species and numerous varieties it was to be expected that there would be considerable confusion in regard to the accurate determination of its members. Tate and Luehman give prominence to the fruit for purposes of classification. Maiden, however, says that all of its characters display a puzzling amount of variation, and concludes that for herbarium work the best characters are afforded by the anthers and fruits; whereas the scientific forester will be largely guided by the nature of the bark and timber. Baker and Smith, in addition to morphological characters, base their deductions on the chemical properties and physical characters of oils, dyes, kinos, etc. See Bentham, *Flora Australiensis;* Baron F. von Mueller's *Eucalyptographia*, 1879 to 1884. Baker and Smith (*A Research on the Eucalypts*, Sydney, 1902), arrange the species in seven different groups, according to the chemical characteristics of the oils which they produce. It is stated that the leaves of the *E. rebaudianum*, of Paraguay, are used in that country in place of sugar, which they exceed in sweetening power.

Eucalyptus globulus is one of the largest known trees, attaining sometimes a height of 300 or even 350 feet, with a smooth, ash-colored

bark. The leaves attain a foot in length, and vary, according to age, from a glaucous white to a bluish-green color. The flowers are large, pinkish-white, axillary, occurring singly, or in clusters. Although its wood is very resinous, hard, and durable, the tree is remarkable for the rapidity of its growth, reaching, under favorable circumstances, fifty feet of height in five or six years. It flourishes best in valleys having a rich, moist soil, and has very largely been naturalized in semi-tropical countries, partly on account of its economic value, but chiefly because of the reputation it enjoys as a means of overcoming malaria. Its sanitary powers appear to be established, numerous notoriously miasmatic stations and districts having been rendered healthful by its growth. It is probable that the destruction of the miasma is due not so much to emanations from the tree as to the fact that it evaporates water so rapidly from its innumerable large leaves as to drain the swamps and marshes in which it is planted. It is possible, however, that the large amount of volatile oil which must escape from it has some effect, and it is even affirmed (*A. J. P.*, 1875, p. 423) that the parasitic phylloxera will not attack grape-vines growing near it.

The eucalyptus oil of commerce is, indeed, composed chiefly of the oils of *E. amygdalina* and *E. dumosa*, which yield a very much larger product than does the official species. The oils of *E. piperita* and *E. hæmastoma* have a peppermint odor, and that of *E. citriodora* a citron-like odor, while the oil of *E. staigeriana* exactly resembles the oil of verbena; it is probable that these oils will come into commerce for the purposes of the perfumer.

Properties.—The leaves are the official portion of the plant and are officially described as follows: "Laminæ lanceolately scythe-shaped, from 8 to 30 cm. in length and from 2 to 7.5 cm. in breadth; summits when present acute or acuminate; bases unequal, obtuse or more or less rounded and connected with a twisted petiole from 5 to 35 mm. in length; margins slightly uneven, revolute; coriaceous; both surfaces varying from pale yellowish-green to grayish-green and more or less glaucous, glabrous, glandular-punctate and with numerous small, circular, brown dots of cork; veins of the first order anastomosing with each other and forming a line nearly parallel with the margin; odor slightly aromatic; taste aromatic, bitter, and cooling. Under the microscope sections of Eucalyptus show the upper and lower surfaces with nearly similar cells, the outer walls being strongly cuticularized; stomata occur on both surfaces, a region of palisade cells made up of from 3 to 4 rows of cells occurring beneath each surface; among the palisade cells occur large oil-secretion reservoirs, with a yellowish or orange colored oily content; calcium oxalate crystals in cells of the loose mesophyll in the form of rosette aggregates or monoclinic prisms varying from 0.015 to 0.025 mm. in diameter. At the periphery of the fibro-vascular bundles of the midrib and petiole occurs a more or less interrupted circle of small groups of slightly lignified bast-fibers." *U. S.*

Hans Kramer (*B. P. G.*, 1907, p. 319) presents an anatomical study of Eucalyptus with the characteristics of the drug in a powdered form.

In March, 1870, Cloez (*J. P. C.*, 4e sér., xii, 201) reported an elaborate chemical study of the eucalyptus leaves, and his results have been substantially confirmed by Debray (*De l'Eucalyptus Globulus*, Paris, 1872), Rabuteau (*Mém. de l'Académie*, Nov., 1872), and Broughton (*P. J.*, 3d ser., iii, 463). Cloez found, besides chlorophyll, resin, tannin, and inert substances, an essential oil, upon which the virtues of the drug appear to depend. Of this oil the fresh leaves afforded 2.75 parts per hundred, the recently dried leaves 6 parts; leaves which had been kept some time yielded a much smaller percentage. In the distillation, the oil for a time comes over freely at from 170° C. (338° F.) to 178° C. (352.4° F.); subsequently another portion of oil distils at 188° C. (370.4° F.) to 190° C. (374° F.), and finally a very minute portion does not volatilize until the temperature reaches 200° C. (392° F.). Cloez believes the oil to be composed of two camphors, differing in their volatility. The bulk of the oil yielded is the portion first distilled; to this Cloez has given the name of *eucalyptol*, or, as it is now also called, *cineol*, $C_{10}H_{18}O$. (See previous article.) Gildemeister and Hoffmann (*Aetherische Oele*, 1899, p. 690) divide the eucalyptus oils into 5 groups according to their constituents, viz.: Group 1, Cineol (or Eucalyptol) containing oils, of which group *Eucalyptus Globulus* is the most important; Group 2, Citronellal containing oils, of which group *Eucalyptus maculata* is the most important; Group 3, Citral containing oils, of which *E. staigeriana* F. von Muell., is the typical example; Group 4, Peppermint smelling oils, of which *Eucalyptus piperita* is an example; and Group 5, Less known oils of varying odor.

Schimmel & Co. (*Semi-Annual Report*, April, 1897) gave a list of some fifteen varieties of eucalyptus oils from the different Eucalyptus species. In their report for October, 1904, they give the sources and state the properties and components of 109 different eucalyptus oils obtained by them from Baker and Smith, Curators of the Technological Museum of Sydney, N. S. W.

According to Duquesnel, the oil of eucalyptus is adulterated—with alcohol, to be detected by means of fuchsin, which is insoluble in the pure oil but soluble in that containing even a very small percentage of alcohol; with fixed oil, to be detected by boiling with water, when the fixed oil remains on the surface; with volatile oil of copaiba or turpentine, to be detected by means of the boiling point, that of eucalyptol being 170° C. (338° F.), that of oil of turpentine 155° C. (311° F.), that of oil of copaiba 260° C. (500° F.). (*J. P. C.*, 4e sér., xvi, 45.)

Uses.—Whatever medicinal virtue eucalyptus possesses beyond a slight astringency is due to its volatile oil. Preparations of the crude drug are rarely used in this country. The leaves are occasionally rolled into cigarettes to be smoked for the relief of *bronchitis* or *asthma*. For therapeutic properties of the oil of eucalyptus, see page 762.

Dose, of eucalyptus, ten to thirty grains (0.65–2 Gm.); of the oil, five to ten minims (0.3–0.6 mil).

Off. Prep.—Fluidextractum Eucalypti, *U. S.*

EUGENOL. U. S.

EUGENOL

(eū′ǧe-nōl)

"An unsaturated, aromatic phenol [$C_{10}H_{12}O_2$ or $C_6H_3.C_3H_5.OCH_3.OH$ 1:3:4 = 164.10] obtained from oil of clove and from other sources. Preserve it in well-closed containers, in a cool place, protected from light." *U. S.*

Allylguaiacol, Allylmethylpyrocatechol; Eugenol, *Fr.;* Oleum Caryophyllorum, *P. G.;* Eugenol, *G.*

Eugenol is extracted on a large scale from oil of cloves and utilized as the starting point in the manufacture of artificial vanillin. (See *Vanillinum.*) It is also found in pimenta, cinnamon leaves, sassafras, canella, bay and other plants. It is officially described as "a colorless or pale yellow, thin liquid, having a strongly aromatic odor of clove, and a pungent and spicy taste. Exposure to air causes it to become darker and thicker. Eugenol is miscible with alcohol, chloroform, ether or fixed oils; it is soluble in twice its volume of 70 per cent. alcohol. A mixture of 1 part of Eugenol and 20 parts of hot distilled water is only very slightly acid to litmus. Specific gravity: 1.064 to 1.070 at 25° C. (77° F.). It boils between 250° and 255° C. (482° and 491° F.). It is optically inactive and strongly refractive. Dissolve 1 mil of Eugenol in 12 mils of sodium hydroxide T.S. and add 18 mils of distilled water; a clear solution results, which becomes turbid when exposed to air. Shake 1 mil of Eugenol with 20 mils of distilled water and filter; 5 mils of the clear filtrate, upon the addition of 1 drop of ferric chloride T.S., shows a transient, grayish-green color, but not a blue or violet color (*phenol*)." *U. S.*

Uses.—Eugenol may be used for flavoring purposes as oil of cloves.

Dose, two to five minims (0.12–0.3 mil).

Off. Prep.—Mistura Olea Balsamica, *N. F.*

EUONYMI CORTEX. Br.

EUONYMUS BARK

(eū-ŏn′y-mī cŏr′tĕx)

"The dried root bark of Euonymus atropurpureus, *Jacq.*" *Br.* "The dried bark of the root of *Euonymus atropurpureus* Jacquin (Fam. *Celastraceæ*), without the presence of more than 3 per cent. of wood or other foreign matter." *N. F.*

Euonymus, *N. F. IV,* Wahoo; Cortex Euonymi; American Indian Arrow-wood; Ecorce d'Evonymus, *Fr. Cod.:* Spindlebaum, Pfaffenhütchen, Spillbaumrinde, *G.*

Euonymus (*Evonymus*) ***atropurpureus,*** named variously ***wahoo, spindle-tree,*** and ***burning-bush,*** is a tall, erect shrub, with quadrangular branchlets, and opposite, petiolate, oval-oblong, pointed, serrate leaves. The flowers, which stand in loose cymes on axillary peduncles, are small and dark purple, with sepals and petals commonly in fours. The capsule or pod is smooth and deeply lobed. The plant is indigenous, growing throughout the Northern and Western States, and sometimes cultivated for the beauty of its crimson fruit.

The plants belonging to this genus are shrubs or small trees, presenting in the autumn a striking appearance from the rich red color of their fruit, which has obtained for them the name of *burning-bush. E. americanus* L. and *E. europæus* L. have been cultivated in gardens as ornamental plants. Two or more of the species have been used in medicine. Their properties are probably similar, if not identical. Grundner, who experimented with the fruit of *E. europæus,* found it to have no other effect than that of a diuretic. (*Ph. Cb.,* 1847, p. 873.) An oil expressed from the seeds is used in Europe for the destruction of vermin in the hair, and sometimes also as an application to old sores. (*Ibid.,* 1851, p. 641.) Griffith says that the seeds of this and other species are purgative and emetic, and that the leaves are poisonous to sheep and other animals feeding on them. He states also that the inner bark of *E. tingens* Wall. is beautifully yellow, and used in India for dyeing, and in diseases of the eye. (*Med. Bot.,* p. 220.) It is probable that much of the wahoo of our drug stores has been obtained from *E. americanus,* which is distinguished from *E. atropurpureus* by its rough, warty, depressed pods, and almost sessile, thickish leaves.

Properties.—The dried bark is described in the National Formulary as follows: "Usually in transversely curved pieces, occasionally in single quills from 2 to 7 cm. in length; bark from 1 to 2.5 mm. in thickness; very light in weight; outer surface grayish or light brown, somewhat wrinkled, occasionally transversely fissured from the lenticels and with scale-patches of soft cork; inner surface grayish-white, longitudinally striate and somewhat porous; fracture short with silky, projecting elastic fibers. Odor distinct· taste bitter and acrid. The powder is light brown, and when examined under the microscope shows numerous starch grains, nearly spherical, from 0.003 to 0.012 mm. in diameter; fragments of cork with nearly colorless, thin walls; secretion cells with yellowish or brownish amorphous contents; bast fibers very long, with thin, non-lignified walls possessing numerous small, more

or less oblique pores; numerous fragments of starch-bearing parenchyma; calcium oxalate in rosette aggregates from 0.015 to 0.035 mm. in diameter, the amount in different specimens showing some variation. Euonymus yields not more than 12 per cent. of ash." *N. F.*

"In quilled or curved pieces, from two to four millimetres thick. Outer layer a soft, friable, greyish cork, marked with dark patches. Inner surface pale tawny-white and smooth. Fracture short, the fractured surface yellowish in color. Transverse section free from sclerenchymatous cells and fibres, and exhibiting, in the secondary bast, laticiferous cells filled with a granular, elastic substance. Faint but characteristic odor; taste somewhat mucilaginous, afterwards bitter and slightly acrid." *Br.*

The drug frequently has as much as 25 per cent. of adhering wood. The amount of the latter with other foreign matter should not exceed 3 per cent. Holm (*Merck's Rep.*, 1909, p. 169) illustrates the structural characteristics of *E. atropurpureus* and *E. americanus*. Holmes (*P. J.*, 1905) describes the bark of *Alstonia scholaris* which has been used as an adulterant of Euonymus. The name of Wahoo or Waahoo (pronounced *Wawhoo*) was given to it by the Indians. The same name has also been applied to *Ulmus alata*, of the Southern States, and has thus led to mistakes.

It imparts its virtues to water and alcohol. Analyzed by Wm. T. Wenzell, it was found to contain a bitter principle which he named *euonymin*, asparagin, a soft resin, a crystallizable resin, a yellow resin, a brown resin, fixed oil, wax, starch, albumen glucose pectin, and various salts of organic and inorganic acids. Euonymin was obtained by agitating with chloroform a tincture made with diluted alcohol, separating the chloroformic solution and allowing it to evaporate spontaneously, treating the residue with ether, dissolving what was left in alcohol, adding lead acetate to the solution, filtering, precipitating the lead with hydrogen sulphide, and evaporating. The euonymin obtained was uncrystallizable, intensely bitter, soluble in water and alcohol, and neutral in its reactions. It was abundantly precipitated from its solution by lead subacetate and phosphomolybdic acid. For an examination of commercial *euonymin* (the eclectic resinoid) by Paul Thibault, see *N. R.*, 1883, 294. W. P. Clothier found the bark to yield no volatile oil on distillation. According to the same writer, if a concentrated tincture be poured into water, a dark yellow substance will be thrown down, containing resin and fixed oil, which is the *euonymin* of the eclectics, very improperly so named, as, though it contains a portion of the active principle, it is a very complex substance. Clothier found the bark to purge actively without griping. (*Ibid.*, 1861, p. 491.) Frank V. Cassaday (*A. J. P.*, 1889, p. 284) found 1.30 per cent. of volatile oil and resin, 1.48 per cent. of *euonic acid* and resin, 2.10 per cent. of euonymin and resin, together with the usual plant constituents. Kubel has discovered in the fresh inner bark of *E. europæus* a saccharine, crystallizable substance, closely resembling mannite, but differing in its crystalline form and in its melting point. He calls it *euonymite*. (*J. P. C.*, Dec., 1862, 523.)

H. Rogerson (*Ph. J.*, 1912, p. 687) has made a complete chemical examination of this bark with the result that the following definite constituents are reported present: *dulcitol; furan B carboxylic acid*, $C_5H_4O_3$; *euonymol*, $C_{21}H_{30}O_4$ (a new crystalline alcohol, having a melting point of 248° C. [478.4° F.]); a sugar which yielded *d-phenyl glucozazone; euonosteryl*, $C_{31}H_{51}O.OH$; *homoeuonosteryl*, $C_{40}H_{69}O.OH$; *atropurol*, $C_{27}H_{44}(OH)_2$; *citrullol*, $C_{32}H_{36}O_2(OH)_2$; and a mixture of palmitic, cerotic, oleic and linoleic acids. No glucoside was found nor could any product corresponding to the *euonymin* of Wenzell or of Schmiedeberg be found.

Uses.—This bark was first introduced into notice, as a remedy for *dropsy*, under the name of Wahoo, by George W. Carpenter. It exerts a digitalis-like action on the heart, but because of the irregularity of its absorption should not be employed as a systemic remedy. By virtue of its local irritant effects on the intestines it usually exerts a laxative effect but is not to be recommended because of its liability to nauseate and the possibility of circulatory effects. It was formerly used as a diaphoretic in *muscular rheumatism, influenza, acute coryza*, and similar conditions but it does not appear to have any advantage for this purpose over the other nauseating drugs and has been largely abandoned. The fluidextract may be given in doses of eight minims (0.5 mil).

Dose, of euonymus, five to fifteen grains (0.32–1.0 Gm.).

"*Caution.*—It has been stated that the absorption of Euonymus in the gastro-intestinal tract is uncertain and irregular. To avoid an accumulation of the drug or toxic action, the physician should carefully guard the dosage and determine in each case the tolerance of the patient." *N. F.*

Off. Prep.—Extractum Euonymi, *Br., N. F.;* Fluidextractum Euonymi, *N. F.*

EXTRACTA

EXTRACTS

(ęx-trăc'tą)

Extraits, *Fr.;* Extrakte, *G.;* Estratti, *It.;* Extractos, *Sp.*

Extracts, as the term is employed in the Pharmacopœias, are solid preparations, resulting from the evaporation of the solutions of vegetable principles, obtained either by exposing a dried drug to the action of a solvent, or by expressing the juice from a fresh plant. A distinction was formerly made between those prepared from the infusions, decoctions, or tinctures, and those from the expressed juices of plants, the former being called *Extracta*, the latter *Succi Spissati*, but the distinction has

been generally abandoned. There is no such essential difference between these two sets of preparations as to require that tney should be separately classed, and something is gained in the simplicity of nomenclature, as well as of arrangement, which results from their union.

The composition of extracts varies with the nature of the vegetable, the character of the solvent, and the mode of preparation. The object is generally to obtain as much of the active principle of the plant with as little of the inert matter as possible, though sometimes it may be desirable to separate two active ingredients from each other when their effects upon the system are materially different; this may be accomplished by employing a menstruum which, while it dissolves one, leaves the other untouched. The proximate principles most commonly present in extracts are gum, sugar, starch, tannin, extractive, coloring matter, salts, and the peculiar principles of plants, to which, when an alcoholic solvent is employed, may usually be added resinous substances, fatty matter, and frequently more or less essential oil, gum and starch being excluded when the menstruum is pure alcohol. Of these substances, as well as of others which, being soluble, are sometimes necessarily present in extracts, we have taken occasion to treat under various heads in this commentary. There is one, however, which from its supposed almost uniform presence in this class of preparations, and from the influence it is thought to exert upon their character, deserves particular consideration in this place. We allude to *extractive*, or, as it is sometimes called, *extractive matter*.

It has long been observed that in most vegetables there is a substance, soluble both in water and alcohol, which, in the preparation of extracts, undergoes chemical change during the process of evaporation, imparting to the liquid even if originally limpid, first a greenish, then a yellowish-brown, and ultimately a deep brown color, and becoming itself insoluble. This substance, originally called *saponaceous matter* by Scheele, afterwards received the more expressive name of *extractive*, derived from its frequent presence in extracts. Its existence as a distinct principle is denied, or at least doubted, by some chemists, who consider the phenomena supposed to result from its presence as depending upon the mutual reaction of other principles. The most important property of extractive is its disposition to pass, by the influence of atmospheric air at a high temperature, into an insoluble substance. If a vegetable infusion or decoction be evaporated in the open air to the consistence of an extract, then diluted, filtered, and again evaporated, and the process repeated so long as any insoluble matter is formed, the whole of the extractive will be separated from the liquid, while the other ingredients may remain. The name of oxidized extractive which has been given to it is incorrect, and Berzelius proposed to substitute for it that of *apothem*, synonymous with deposit. According to Berzelius, apothem is not completely insoluble in water, but imparts a slight color to that liquid when cold, and is rather more soluble in boiling water, which becomes turbid upon cooling. It is still more soluble in alcohol, and is freely dissolved by solutions of the alkalies and alkaline carbonates, from which it is precipitated by acids. It has a great tendency, when precipitated from solutions, to unite with other principles, and to carry them along with it, thus acquiring properties somewhat different according to the source from which it is obtained. In this way also, even when the extractive of a plant is itself medicinally inert, its conversion into apothem may be injurious by causing a precipitation of a portion of the active principle, and in practical pharmaceutical operations this change should always, if possible, be avoided. We shall treat of the subject under the several heads of (1) the extraction of the soluble principles from the plant; (2) the method of conducting the evaporation; (3) the proper condition of extracts, the changes they are liable to undergo, and the best method of preserving them.

1. *Extraction of the Soluble Principles.*

There are two distinct modes of obtaining, in a liquid state, the principles which we wish to extract: (1) by expression alone; (2) by the agency of a solvent, with or without expression.

1. By Expression.—This method is applicable to recent vegetable substances. All plants cannot be usefully treated in this way, as many have too little juice to afford an appreciable quantity upon pressure, and of the succulent a considerable portion do not yield all their active principles with their juice. Succulent fruits, and various acrid and narcotic plants, are proper subjects for this treatment. The plants should be operated upon, if possible, immediately after collection. Battley, of London, recommended that, if not entirely fresh, they should be revived by the immersion of the stalks in water for twelve or eighteen hours, and those only used which recover their freshness by this management. They should then be cut into pieces, and bruised in a stone mortar till brought to a pulpy consistence. When the plant is not very succulent, it is necessary to add a little water during this part of the process, in order to dilute the juice. After sufficient contusion, the pulp is introduced into a linen or canvas bag, and the liquid parts expressed. Brande states that light pressure only should be employed, as the extract is thus procured greener, of a less glutinous or viscid consistence, and, in his opinion, more active than when considerable force is used in the expression. (See Remington's *Practice of Pharmacy*.) The juice thus obtained is opaque, and usually green, in consequence of the presence of green wax or chlorophyll, and of a portion of the undissolved vegetable fiber in minute division. By heating the juice to about 71.1° C. (160° F.) the albumen contained in it

coagulates, and, involving the chlorophyll and vegetable fiber, forms a greenish precipitate. If the liquid be now filtered, it becomes limpid and nearly colorless, and is prepared for evaporation. The clarification, however, is not absolutely necessary, and is generally neglected. Sometimes the precipitate carries with it a considerable portion of the active principle, in which case it should be subsequently incorporated with the juice, when reduced by evaporation to the consistence of syrup. Ether added to the expressed juices of plants enables them to be kept long without injurious change. Lepage, of Gisors, France, has kept the juice of belladonna in this way more than ten years, and found it, at the end of that time, to yield an extract identical in physical, chemical, and physiological properties with that obtained from the fresh juice. If this fact is found to be of general applicability, it will be of considerable importance, as enabling the pharmacist to supply himself at pleasure with extracts to be relied on, without reference to the season.

2. By Solution.—The active principles of dried vegetable substances can be extracted only by means of a liquid solvent. The menstruum usually employed is either water or alcohol, or a mixture of the two. Water, on account of its cheapness, is always preferred, when circumstances do not strongly call for the use of alcohol. It has the advantage, moreover, that it may be assisted in its action if necessary by a higher degree of heat than the latter. Tap water is often unfit for the purpose, in consequence of the quantity of its saline matter, which in some instances may exert an unfavorable influence on the active principle, and must always be left in the extract. Rain, or distilled water should be preferred. Alcohol is employed when the principles to be extracted are insoluble or but slightly soluble in water, as in the case of the resins; when it is desirable to avoid in the extract inert substances, such as gum and starch, which are dissolved by water and not by alcohol; when the heat required to evaporate the aqueous solution would dissipate or decompose the active ingredients of the plant, as the volatile oils; when the reaction of the water itself upon the vegetable principles is injurious; and, finally, when the nature of the substance to be exhausted requires so long a maceration in water as to endanger spontaneous decomposition. The aqueous solution requires to be quickly evaporated, as this fluid rather promotes than counteracts chemical changes, while an alcoholic tincture may be preserved unaltered for an indefinite period. An addition of alcohol to water is sufficient to answer some of the purposes for which the former is preferable, and the employment of both fluids is essential, when the virtues of the plant reside in two or more principles, all of which are not soluble in either of these menstrua. In this case it is usually better to submit the vegetable to the action of the two fluids successively than of both united. Extracts obtained by the agency of water are called *aqueous extracts;* those by means of alcohol, undiluted or diluted, *alcoholic* or *spirituous extracts.* Sometimes the term *hydro-alcoholic* is applied to extracts obtained by the joint agency of alcohol and water.

Chloroform is frequently used to saturate the water used in making aqueous extracts to prevent fermentation during percolation.

The method of preparing the solution is not a matter of indifference. The drug should be thoroughly bruised, or reduced to a coarse powder, so as to allow the access of the solvent to all its parts, and yet not so finely pulverized as to prevent a ready precipitation of the undissolved or inactive portion. When water is alone employed, it has been customary to boil the medicine for a considerable time, and, if the first portion of liquid does not completely exhaust it, to repeat the operation with successive portions until the whole of the active matter is extracted. This may be known by the sensible properties of the liquid, and by its influence upon reagents. But the boiling temperature produces the decomposition of many vegetable principles, or at least so modifies them as to render them inert, and the extracts prepared by decoction are usually less efficient than those made with a less degree of heat. From numerous experiments upon extracts, Orfila concluded that their virtues were less in proportion to the heat employed. It has, therefore, been recommended to substitute for decoction the process of maceration, digestion, or hot infusion, in the first of which the liquid acts without heat, in the second is assisted by a moderately increased temperature sustained for a considerable time, and in the third is poured boiling hot upon the vegetable matter and allowed to stand for a short period in a covered vessel. When the active principles are readily soluble in cold water, *maceration* is often preferable to the other modes, as starch, which is inert, is thus left behind; but in many instances the preparation would spoil before the extraction would be completed. By *digestion,* though the solvent power of water is moderately increased, the advantage is often more than counterbalanced by the increased disposition to spontaneous decomposition. *Hot infusion,* therefore, is to be preferred where the vegetable substance does not readily yield its virtues to cold water. It has the advantage, moreover, in the case of albuminous substances, that the albumen is coagulated, and thus prevented from increasing the bulk of the extract, without adding to its virtues. A convenient mode of performing this process is to introduce the solid material into a vessel with an opening near the bottom temporarily closed, or into a funnel having a notched cork in its mouth, then to pour on the boiling water, and, having allowed it to remain a sufficient length of time, to draw it off through the opening. This operation may be repeated until the water comes away without any obvious impregnation.

It is always desirable to obtain the solution in

the first place as concentrated as possible, so as to prevent the necessity of long continued evaporation, which injures the extract. It is better, therefore, to incur the risk, both when decoction and infusion are employed, of leaving a portion of the active matter behind, than to obtain a very weak solution. When successive portions of water are employed, those which are least impregnated should be brought by evaporation to the strength of that first obtained before being mixed with it.

Sometimes filtering a turbid infusion or decoction, before evaporation, causes the resulting extract to keep better by removing substances which, beside undergoing decomposition, may act as a ferment, and occasion the decomposition of the active matter of the extract.

When alcohol is employed as a menstruum, the vegetable substance should be macerated in it for one or two weeks, and care should be taken that the tincture be as nearly saturated as possible. The extraction may be hastened by substituting digestion for maceration, as the moderate heat employed, while it facilitates the action of the alcohol, has in this case no effect in promoting decomposition, and the influence of the atmospheric air may be excluded by performing the process in close vessels.

Acetic acid has been introduced into use as a menstruum in the preparation of extracts. It is supposed to be a better solvent of the active principles of certain substances than either water or alcohol alone. According to Girolamo Ferrari, the acrid narcotics, such as aconite, hemlock, hyoscyamus, and stramonium, yield much stronger extracts with distilled vinegar than with water, and still stronger with alcohol to which strong acetic acid has been added. (*J. P. C.*, 3e sér., i, 239.) Experiments have shown that strong acetic acid (60 per cent.) is a powerful solvent for the active properties of various drugs, particularly those which contain volatile oils, and in many cases a 10 per cent. acetic acid is an excellent menstruum for making extracts; for these the name *acetract* has been proposed. (*Proc. A. Ph. A.*, 1897, 416.) E. R. Squibb has used acetic acid largely for extracts. (*West. Drug.*, 1897, 123.)

Ether also is now used to a considerable extent in the preparation of certain extracts. Having the property of dissolving volatile oil and resin, and of evaporating at a temperature insufficient to volatilize the oil, it is admirably adapted for the preparation of extracts from those substances the virtues of which reside in the two principles referred to. An ethereal tincture is first prepared by the process of percolation, and the ether is then allowed to escape by spontaneous evaporation, or distilled off at a very moderate heat. The oleo resinous extracts thus obtained are usually of a thick fluid or semi-fluid consistence. Several of them now rank among the official preparations, in the U. S. P., under *Oleoresinæ*. Acetone is another solvent used much for the same purpose as ether.

The process of *percolation* has in this country been very advantageously applied to the preparation of extracts, both with water and spirituous menstrua. It has the following great advantages: (1) that it enables the soluble principles to be sufficiently extracted by cold water, thereby avoiding the injury resulting from heat in decoction and hot infusion (2) that it effects the extraction much more quickly than can be done by maceration, thereby not only saving time, but also obviating the risk of spontaneous decomposition; and (3) that it affords the opportunity of obtaining highly concentrated solutions, thus diminishing the injurious effects of the subsequent evaporation. While thus advantageous, it is less liable in this particular case than in others to the objection of yielding imperfect results if not well performed, for, though an inexpert or careless operator may incur loss by an incomplete exhaustion of the substance acted on, and the extract may be deficient in quantity, it may still be of the intended strength and quality, which is not the case with infusions or tinctures unskilfully prepared upon this plan. In the process of percolation the drug must first be reduced to the proper degree of fineness. The U. S. P. (8th Rev.) gives the following directions.

Fineness of Powder.—The fineness of powder is expressed, in the Pharmacopœia, either by descriptive words (generally so in the case of brittle or easily pulverizable substances), or in terms expressing the number of meshes to a linear inch of the sieve through which the powder will pass. The corresponding values, in terms of metric measures of length, are added below in parentheses, but it has not been deemed advisable, in this revision, to substitute them in the text of the Pharmacopœia for those at present in use. The diameter of the wire (gauge number) used in making sieve cloth has an important influence upon the size of the mesh, and it is necessary to specify in each case the thickness of the wire, and it was so specified in the U. S. P. VIII but the U. S. Bureau of Standards, owing to the different standards in use by manufacturers of wire gauze determined to standardize the diameter of the particles of the powders, and the U. S. P. IX provides the following statement: "The fineness of powders and granular substances is expressed, in the Pharmacopœia, by numbers which originally represented only the meshes per inch of the sieve through which the powders would pass. Fineness, so used, has been redefined below in terms of the maximum diameter of the particles of the powder as measured by the width of the opening of the meshes of the sieves from which they receive their designating numbers. A powder of a specified number must meet the requirements given below for that number of powder, but the larger proportion of it must not pass through a sieve of a lower degree of fineness.

Number of Powder.		Diameter of Particles
No. 100	Powder has a fineness, in diameter of particles, less than	0.14 millimeter.
No. 80 Very fine powder	Powder has a fineness, in diameter of particles, less than	0.17 millimeter.
No. 60 Fine powder	Powder has a fineness, in diameter of particles, less than	0.23 millimeter.
No. 50 Moderately fine powder	Powder has a fineness, in diameter of particles, less than	0.28 millimeter.
No. 40 Moderately coarse powder	Powder has a fineness, in diameter of particles, less than	0.38 millimeter.
No. 30	Powder has a fineness, in diameter of particles, less than	0.54 millimeter.
No. 20 Coarse powder	Powder has a fineness, in diameter of particles, less than	0.85 millimeter
No. 12 Very coarse powder	Powder has a fineness, in diameter of particles, less than	1.47 millimeters.
No. 6	Powder has a fineness, in diameter of particles, less than	3.00 millimeters.

The degree of fineness defined above shall be such as are determined by sieving tests made with sieves of the Standard Screen Scale recommended by the Bureau of Standards." *U. S.*

Percolation, as directed in the U. S. Pharmacopœia IX "consists in subjecting a comminuted substance or a mixture of substances, contained in a vessel called a percolator, to the solvent action of successive portions of a liquid termed the menstruum in such a manner that the liquid, as it traverses the powder in its descent to the receiver, shall extract the soluble constituents, and pass from the percolator free from insoluble matter.

"When the process is successfully conducted, the first portion of the liquid, or percolate, passing through the percolator will be nearly saturated with the soluble constituents of the substance treated; and if the quantity of menstruum be sufficient for its exhaustion, the last portion of the percolate will be nearly free from color, odor, and taste, other than those of the menstruum itself.

"In preparations which direct the process of percolation, wherever the expression 'until the drug is exhausted' or a similar phrase occurs, it is to be understood that the term 'exhausted' means the point at which the valuable constituents have been as completely extracted as is possible or practical, and this must be determined by the judgment and experience of the operator.

"*Percolators.*—The following statement with regard to percolators and the process of percolation is given in order to illustrate a method of percolation. It is not intended as compulsory and it is permissible for manufacturers and others to modify the process to suit their needs. The percolator most suitable for the quantities contemplated by this Pharmacopœia should be nearly cylindrical, or slightly conical, with a funnel-shaped termination at the smaller end. The neck of this funnel-end should be rather short, and should gradually and regularly become wider toward the orifice, so that a perforated cork, bearing a short glass tube, may be tightly wedged into it. The glass tube, which must not project above the inner surface of the cork, should extend from 3 to 4 cm. beyond the outer surface of the cork, and should be provided with a closely fitting rubber tube, at least one-fourth longer than the percolator itself, and ending in another short glass tube, whereby (when it is desired to interrupt the percolation) the rubber tube may be so suspended that its orifice shall be above the surface of the menstruum in the percolator, a rubber band holding the tube in position.

"The shape of a percolator should be adapted to the nature of the drug to be operated upon. For drugs which are apt to swell, particularly when a feebly alcoholic or an aqueous menstruum is employed, a *conical* percolator is preferable. A *cylindrical* or only slightly tapering percolator may be used for drugs which are not liable to swell, particularly if difficult to exhaust, also when the menstruum is strongly alcoholic, or when ether or some other volatile liquid is used for extraction. The size of the percolator selected should be in proportion to

the quantity of drug extracted. When properly packed in the percolator, the drug should not occupy more than two-thirds of its height. The percolator is best constructed of glass, but, unless otherwise directed, may be made of any suitable material not affected by the drug or menstruum. For hot percolation glass percolators are unsuited, as they are liable to fracture. Metallic percolators in such cases are required.

"The percolator is prepared for percolation by gently pressing a small tuft of purified cotton into the neck, and this may then be moistened by pouring a few drops of menstruum upon the cotton, to facilitate the passage of the first portion of percolate, which is often very dense.

"*The Process.*—The powdered substance to be percolated (which should be uniformly of the fineness directed in the formula, and should be perfectly air-dry before it is weighed) is put into a suitable dish, sufficient menstruum is poured on, and the powder thoroughly stirred until it is uniformly moistened. The moist powder is then passed through a coarse sieve—No. 40 powders, and those which are finer, requiring a No. 20 sieve, and No. 30 powders require a No. 15 sieve for this purpose. Powders of a less degree of fineness usually do not require this additional treatment after the moistening. The moist powder is now transferred to a sheet of thick paper and the whole quantity poured from this into the percolator. It is then shaken down lightly and allowed to remain in that condition for a period varying from fifteen minutes to several hours, unless otherwise directed; after which the powder is pressed, by the aid of a plunger of suitable dimensions, more or less firmly, in proportion to the character of the powdered substance and the alcoholic strength of the menstruum, strongly alcoholic menstrua, as a rule, permitting firmer packing of the powder than the weaker. The percolator is now placed in position for percolation, and, the rubber tube having been fastened at a suitable height, the surface of the powder is covered by an accurately fitting disk of filtering paper, held in place by a glass stopper or percolator weight, and a sufficient quantity of the menstruum poured on through a funnel reaching nearly to the surface of the paper. If these conditions are accurately observed, the menstruum will penetrate the powder equally until it has passed into the rubber tube and has reached, in this, a height corresponding to its level in the percolator, which is now closely covered to prevent evaporation. The apparatus is then allowed to stand at rest for the time for maceration specified in the formula.

"To begin percolation, the rubber tube is lowered and its glass end introduced into the neck of a bottle previously marked for a quantity of liquid to be received, if the percolate is to be measured, or of a tared bottle, if the percolate is to be weighed; and by raising or lowering this receiver the rapidity of percolation may be increased or decreased as may be desirable. A layer of menstruum must constantly be maintained above the powder, so as to prevent the access of air to its interstices, until all has been added, or the requisite quantity of percolate has been obtained. This is conveniently accomplished, if the space above the powder will admit of it, by inverting a bottle containing the entire quantity of menstruum over the percolator in such a manner that its mouth may dip beneath the surface of the liquid, the bottle being of such shape that its shoulder will serve as a cover for the percolator.

"Unless otherwise directed when the dregs of a tincture, or of a similar preparation, are to be subjected to percolation, after maceration with all or with the greater portion of the menstruum, the liquid portion should be drained off as completely as possible, the solid portion packed in a percolator, as before described, and the liquid poured on, until all has passed from the surface, when immediately a sufficient quantity of the directed menstruum should be poured on to displace the retained liquid, until the prescribed quantity has been obtained.

"*Repercolation or Fractional Percolation.*—Authority is given to employ, where it may be applicable, the process of repercolation, without change of the initial menstruum. This process is used in Type Process C for fluidextracts (see page 484).

"*Rate of Flow.*—It is obvious that the success of the process of percolation largely depends upon the regulation of the flow of the percolate; if this should be too rapid, incomplete exhaustion will result, but if too slow, valuable time may be wasted. The rate of flow for fluidextracts for 1000 Gm. of powder should not exceed ten drops a minute; for official quantities of tinctures and preparations of about the same strength twenty drops a minute, and the word 'slowly' throughout the text is understood to mean a rate of flow corresponding to this; it is evident that the proper rate of flow should vary with the quantity and character of the drug employed and the density of the menstruum.

"*Maceration.*—Percolation is not suitable for exhausting some drugs, and the process of maceration is employed for some of the tinctures (Aloes, Asafetida, Sweet Orange Peel, Tolu, etc.). Specific directions will be found in the text, and maceration should be conducted preferably at a temperature of from 15° to 20° C. (59°–68° F.)." *U. S.*

For an account of E. R. Squibb's process of repercolation, see *Fluidextracta.*

Some prefer the mode of expression to that of percolation. This also is applicable both to aqueous and to alcoholic menstrua. The substance to be acted upon is mixed with the menstruum, cold or hot according to circumstances, and the mixture is allowed to stand from twelve to twenty-four hours. The liquid part is then filtered off, and the remainder submitted to strong pressure, in a linen bag, by means of a common screw press, or other convenient apparatus. Another portion of the men-

struum may then be added, and pressure again applied, and, if the substance is not sufficiently exhausted, the same operation may be performed a third time. Frequently only a single expression is required, and very seldom a third. The quantity of menstruum added must vary with the solubility of the principles to be extracted. According to Mohr, the method of expression has the advantages over that of the percolation, that it yields solutions of more uniform concentration, that it does not require the materials to be so carefully powdered, or otherwise so skilfully managed, in order to insure favorable results, and, finally, that it occupies less time.

2. *Mode of Conducting the Evaporation.*

In evaporating the solutions obtained in the modes above described, attention should always be paid to the fact that the extractive matter is constantly becoming insoluble at high temperatures with the access of air, and that other chemical changes are going on, sometimes not less injurious than this, while the volatile principles are expelled with the vapor. The operator should, therefore, observe two rules: (1) to conduct the evaporation at as low a temperature as is consistent with other objects; (2) to exclude atmospheric air as much as possible, and, when this cannot be accomplished, to expose the liquid the shortest possible time to its action. The injurious influence of atmospheric air is much greater at the boiling point of water than at a less heat, even allowing for the longer exposure in the latter case, and therefore a slow evaporation at a moderate heat is preferable to the more rapid effects of ebullition. Bearing these principles in mind, we shall proceed to examine the different modes in practice. First, however, it is proper to observe that decoctions generally let fall, upon cooling, a portion of insoluble matter, and it is a question whether this should be rejected, or retained so as to form a part of the extract. Though it is undoubtedly in many instances inert, as in that of the insoluble substance formed during the decoction of certain vegetable substances, yet, as it frequently also contains a portion of the active principle which a boiling saturated solution necessarily deposits on cooling, and as it is difficult to decide with certainty when it is active and when otherwise, the safest plan, as a rule, is to allow it to remain.

The method of evaporation formerly resorted to in the case of aqueous solutions is rapid boiling over a fire. The more quickly the process is conducted, the better, provided the liquid is to be brought to the boiling point, for the temperature cannot exceed this, and the length of exposure is diminished. But, where this method is employed, it should never be continued until the completion of the evaporation, for when most of the water has escaped, the temperature can no longer be kept down to the boiling point, and the extract is burnt. The caution, therefore, should always be observed of removing the preparation from the fire before it has attained the consistence of thick syrup, and completing the evaporation, either by means of a water bath, or in shallow vessels at a moderate heat. When large quantities of liquid are to be evaporated, it is best to divide them into portions and evaporate each separately, for, as each portion requires less time for evaporation than the whole, it will thus be a shorter time exposed to heat. But the mode of evaporation by boiling is always objectionable, and should be employed only in cases where the principles of the plant are so fixed and unchangeable as to authorize their extraction by the method of decoction.

Evaporation by means of a water bath, from the commencement of the process, is safer than the plan just mentioned, as it obviates all danger of burning the extract; but, as the heat is not supplied directly from the fire, the volatilization of the water cannot go on so rapidly, and, the temperature being nearly the same, when the water bath is kept boiling, there is greater risk of injurious action from the air. The liquid should be stirred during the process. The use of the steam bath has become very general in this country, as it requires a smaller consumption of fuel, and the heat imparted to the liquid, while sufficient to evaporate it, may be less than 100° C. (212° F.). The apparatus consists of an ordinary boiler, containing water, the vapor of which is conducted through a pipe into the evaporating vessels, communicating with each other by means of iron steam pipes. These vessels have the form of an ordinary copper basin, to the inside of which is riveted a shallow tinned copper evaporating basin, intended to contain the liquid to be evaporated. The vapor from the boiler circulates between these vessels, and the water into which it condenses is allowed to escape through a steam valve attached to the bottom of each vessel. The liquid to be evaporated is first distributed in two or three basins, but when considerably concentrated, is transferred to a single one, where it is stirred towards the close of the process to hasten the evaporation. The heat applied to the liquid can be easily regulated by the steam valves.

As the heat capable of being applied by boiling water to the evaporating liquid does not exceed 93.3° C. (200° F.), while that by steam can, by a moderate pressure, be increased to the boiling point or beyond it, the evaporation by the latter agency may be much more rapid than by the former, when the pressure is from ten to twenty pounds to the square inch; so that there is a temptation to raise the heat to a degree seriously injurious to the product. Evaporation, therefore, by steam heat always requires caution and a stirring device should be used. The water bath is much less liable to be abused. In this respect the latter method has the advantage.

A good plan of evaporation, though slow, is to place the liquid in a broad, shallow vessel, exposed in a stove or drying room to a temperature of about 37.8° C. (100° F.), or a little higher, taking care that the air have free

access in order to facilitate the evaporation. This mode is particularly applicable to those cases in which maceration or infusion is preferred to decoction for extracting the active principles. Berzelius says that we may thus usually obtain the extract in the form of a yellowish transparent mass, while extracts prepared in the ordinary way are almost black, and are opaque even in very thin layers. Even when the liquid is boiled at first, the process may often be advantageously completed in this manner. It has been proposed to effect the evaporation at the common temperature, by directing a strong current of air, by means of a pair of smith's bellows, over the surface of the liquid, and in reference to substances which are injured by heat and not by atmospheric air the plan will be found useful.

Plans have been proposed and carried into execution for performing evaporation without the admission of atmospheric air. The apparatus for *evaporation in vacuo,* now largely used by manufacturing pharmacists, is well calculated to meet this object, at the same time that, by removing the atmospheric pressure, it enables the water to rise in vapor more rapidly, and at a comparatively low temperature.

A convenient plan of excluding the air, though it does not at the same time meet the object of reducing the degree of heat, is to distil off the water in close vessels. Berzelius says that this is the best mode of concentration next to that *in vacuo.* Care, however, must be taken that the fire be not too long applied, lest the extract should be burnt. The process should, therefore, be completed by means of the water bath.

In the concentration of alcoholic solutions, distillation should always be performed, as not only is the atmospheric air thus excluded, but the alcohol is recovered, if not absolutely pure, certainly fit for the purpose to which it was originally applied. Here also the water bath should be employed, to obviate any possible risk of injury from the fire. When the decoction or infusion and the tincture of the same vegetable have been made separately, they should be separately evaporated to the consistence of syrup, and then mixed together while they are of such a consistence as to incorporate without difficulty. The object of this separate evaporation is that the spirituous extract may not be exposed to the degree of heat, or lengthened action of the air, which is necessary in the ordinary mode of concentrating the infusion or decoction.

In every instance, care should be taken to prevent any portion of the extract from becoming dry and hard on the sides of the evaporating vessel, as in this state it will not readily incorporate with the remaining mass. The heat therefore, should be applied to the bottom and not to the sides of the vessel.

Inasmuch as the yield of extracts is largely dependent on the character of the menstruum used in the percolation, it follows that there must necessarily be a great variation in the strength of commercial extracts. C. H. LaWall has prepared a valuable table giving the yield of extract by various drugs. (*Proc. A. Ph. A.,* 1897, 414.) For methods of assay, see various official processes.

"**Pilular Extracts** are solid or semi-solid products prepared by exhausting drugs with appropriate solvents and carefully evaporating the solutions to the proper consistence. These extracts preserve the useful constituents of the drug in a concentrated, relatively uniform and permanent condition, and in a form suitable for medication.

"The solvents or menstrua employed in the preparation of pilular extracts are water, alcohol, or mixtures of these in the proportions stated in the formulas. A few drugs require for their extraction the addition of an acid or an alkali to the solvent. Where alcohol is used in the extraction it may be recovered by distillation.

"In the preparation of pilular extracts the concentration of the solutions should be completed without delay, and undue exposure to heat must be avoided. The limit of temperature for the evaporation, as stated in the formulas, should not be exceeded. In the manufacture of these extracts on a large scale an apparatus for distilling and evaporating under reduced pressure should be used. It is also important that the residue be frequently stirred so as to hasten the evaporation and to obtain a uniform product.

"Pilular extracts are extensively used in pill masses and in ointments and, to facilitate their use in these preparations, the degree of concentration is commonly directed to be that of a 'pilular consistence.'

"Pilular extracts should be protected from exposure to sunlight and air by being kept in tightly-covered glass or earthen-ware containers.

"**Powdered Extracts** differ from pilular extracts in that they are dry, fine powders. Powdered extracts are often preferred to pilular extracts for general use, because they can be more accurately weighed, more easily dispensed, and more conveniently preserved in tightly-stoppered bottles.

"In the preparation of powdered extracts, it is necessary to use solvents that will extract the active principles of the drugs, and only a minimum amount of the inert substances. Where the drug contains an oily constituent that would be extracted by the menstruum directed, it becomes necessary to adopt in the process of manufacture a method for the separation of this oil so that the product will retain a satisfactory, pulverulent form.

"The concentration of the liquids containing the extractive should be completed without delay and undue exposure to heat must be avoided.

"The limit of temperature as stated in the formulas should not be exceeded, and the use of apparatus for concentrating under reduced pressure is recommended. The final drying of the soft extract can be greatly facilitated by spreading it upon plates of glass or tinned metal

and exposing it to currents of warm, dry air. Powdered extracts must be thoroughly dried, powdered and mixed with the diluent and preserved in tightly-stoppered, small, wide-mouthed, amber-colored bottles, and stored in a cool and dry place.

"Alkaloidal standards have been adopted for Extracts that can be reliably assayed. Assay methods are directed for the determination of their strength, and to provide for standardization. When necessary, an inert diluent is directed to reduce the product to the standard. In the official formulas glucose is directed for the diluent in pilular extracts and dried starch and magnesium oxide are directed for powdered extracts, but it is permissible for the manufacturer to use as inert diluents for the latter, sugar, sugar of milk, powdered glycyrrhiza, magnesium carbonate or the finely powdered drug or marc from which the respective extract was made. For the convenience of the prescriber, the standards of strength for the Extracts have been adjusted, wherever possible, so that each bears a definite relation to that of the respective drug of average strength, and a statement of the standard precedes the formula," *U. S.*

3. *Condition and Preservation of Extracts.*

Extracts may be prepared of three different degrees of consistence: soft, so that they may be readily made into pills, hard, in order that they may be pulverized, and in a fine, dry powder. The soft extracts always contain a notable percentage of water. In astringent extracts, the evaporation should be carried to dryness. Those obtained from the expressed juices of plants are apt to attract moisture from the air, in consequence of the deliquescent nature of the salts existing in the juice. They are thus rendered softer, and more liable to become mouldy upon the surface. Others, especially such as contain much chlorophyll, harden by time, in consequence of the escape of their moisture, and it not unfrequently happens that small crystals of saline matter are formed in their substance; sodium chloride in small cubes is sometimes found in certain old extracts, having slowly crystallized as they hardened. John Attfield of London, has made a chemical examination of the crystals found in numerous extracts, and ascertained that in a large number they consisted of potassium chloride, and in a comparatively few of potassium nitrate. Potassium chloride was detected in the extracts of belladonna, hemlock, sarsaparilla (compound), colchicum seed, stramonium seed, and aconite; potassium nitrate in the extracts of belladonna, hyoscyamus, and lettuce; and sodium sulphate in extract of stramonium seed. (*P. J.*, March, 1862, p. 448.) The air, moreover, exercises an unfavorable chemical influence over the softer extracts, which are enfeebled, and ultimately become nearly inert, by the same changes which they undergo more rapidly in the liquid state at an elevated temperature. If an extract be dissolved in water, and the liquid be saturated with common salt or any other very soluble salt of difficult decomposition, the greater part of it will be precipitated, in consequence of the insolubility of this class of substances in saline solutions. The precipitate may be again dissolved in pure water.

Abstracts, which were official in the U. S. P., 1880, were not re-introduced in the U. S. P. (8th Rev.), as they did not come into general use; this is unfortunate, as they had many advantages, and are used in certain sections of the country. A description and a typical formula, with comments, will be found in the U. S. Dispensatory, 19th edition, p. 466.

Extracts, in order that they may keep well, should be placed in glazed earthenware, glass, or porcelain jars, and completely protected from the access of the air. This may be effected by covering their surface with a layer of melted wax, or with a piece of paper moistened with strong spirit, then closing the mouth of the vessel with a cork, spreading wax or rosin over this, and covering the whole with leather or a piece of bladder. The application of alcohol to the surface has a tendency to prevent mouldiness. Should the extract become too moist, it may be dried by means of a water bath; should it, on the contrary, be too dry, the proper consistence may be restored by softening it in the same manner and incorporating with it a little distilled water. Martin proposes to preserve extracts in a soft condition by surrounding the vessel containing the extract by another of larger diameter, which is furnished with a tight cover, the space between the two vessels being filled with crystallized sodium sulphate, which gradually parts with its water of crystallization and prevents the extract from becoming hard and dry.

When extracts which are too soft are subjected to a moderate temperature, fermentation may set in; E. Cocardas describes the various forms of "Penicillium-ferment" which are found in such extracts, and concludes that the ferment causes them to undergo changes similar to those effected by heat—*viz.*, the absorption of oxygen and the disengagement of carbon dioxide. (*P. J.*, 1886, p. 590.)

It is preferable to add a definite weight of the glycerin to the percolate. If it were added to the menstruum, owing to the variation in the yield of extracts from plants, some would be too soft, and at another time, in the case of a large yield of extract, the quantity of glycerin would be insignificant.

Extracts from recent plants should be prepared at the season when the plant is medicinally most active; a good rule is to prepare them once a year; but the demand for extracts from fresh drugs has declined rapidly of late, as it has been found that properly dried drugs yield extracts of uniform strength.

Powdered Extracts.—These extracts are largely superseding soft extracts for reasons given in preceding paragraphs; the difficulty of making them arises from the injurious in-

fluence of heat upon concentrated percolates of organic substances, but by the use of vacuum apparatus, suitable absorptive diluents and care, they should be made successfully.

Some extracts when powdered have a tendency to cohere. According to Geiseler, this may be obviated by the addition of sugar of milk or powdered licorice root, two or three parts of the former and one part of the latter to one of the extract being sufficient for the purpose. (*Ph. Cb.*, 1850, p. 238.) Mohr recommends the following plan of drying and preserving extracts. Take equal parts of powdered licorice-root and of the extract, rub them well together in a mortar, put the resulting paste into an earthen vessel with a flat bottom, place this in another of iron, a little deeper, containing calcium chloride thoroughly dried by heat insufficient to melt it; then enclose the whole with a cover fitted to the iron vessel, and allow them to stand for a day or more. When the mixture is quite dry, powder it, and add so much of the powdered root as to make the weight double that of the original extract. This process was substantially adopted in the German Pharmacopœia (1882). The old process of using dextrin as a diluent was found very objectionable, principally on account of the tendency of the extracts to reabsorb moisture. Four parts of extract are now mixed with three parts of finely powdered licorice-root, and dried in a porcelain dish at 40° to 50° C. (104°–122° F.) until the mixture ceases to lose weight. The mass is then rubbed to powder, and sufficient powdered licorice-root added to make the whole weigh eight parts, or double the weight of extract used. In our opinion, this method is not so good as that formerly adopted for abstracts. The German powdered extracts are always half the strength of the extracts, no relation whatever with the drug is established, and the variations in the yield of extract from different drugs have been repeatedly shown to be great. Kirchmann proposes exsiccated sodium sulphate as a diluent instead of dextrin, licorice-root, etc. (*Ph. Ztg.*, 1881, 116.) A. B. Lyons, of Detroit (1898), has introduced *scale extracts*. These do not, as a class, bear a definite relation to the drug; they are assayed, however, and acacia is used as a means of preserving their dry condition; they are easily pulverized, and are very convenient for dispensing.

The plan of incorporating a little glycerin with extracts has been recommended for such extracts as require it, 10 per cent. of glycerin being added to the liquid extract before evaporating to a pilular consistence. By its unchangeable liquid character, glycerin keeps the extract soft, so that it can be readily made into pills, and it also exercises a favorable influence through its chemical properties. The U. S. P. (8th Rev.) directs the use of glycerin for this purpose as follows: "When it is desired to preserve a solid extract (for instance, of Gentian, Taraxacum, etc.) in a plastic condition, suitable for making pills, or for other purposes, it is recommended that there be incorporated with it, after it has been evaporated to the proper consistence, and while it is still warm, 10 per cent. of its weight of glycerin." *U. S.*

Eight extracts were dismissed at the last revision of the U. S. Pharmacopœia, these were as follows: Aloes, digitalis, euonymus hæmatoxylon, krameria, leptandra, quassia, and scopola; five extracts were added as follows: Aconite, oxgall, gelsemium, hydrastis, viburnum prunifolium.

EXTRACTUM ACONITI. U. S.

EXTRACT OF ACONITE Ext. Aconit. [Powdered Extract of Aconite]

(ĕx-trăc'tŭm ăc-o-nī'tī)

"Extract of Aconite yields not less than 1.8 per cent. nor more than 2.2 per cent. of the ether-soluble alkaloids of aconite and, if assayed biologically, the minimum lethal dose should not be greater than 0.00001 Gm. for each gramme of body weight of guinea-pig. *One gramme* of the Extract represents about *four grammes* of aconite." *U. S.*

* "Aconite, in No. 60 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Tartaric Acid, *five grammes* [or 77 grains]; Purified Petroleum Benzin, Starch, dried at 100° C. (212° F.), Alcohol, each, *a sufficient quantity.* Dissolve the tartaric acid in *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol, moisten the drug with this solution and pack it in a cylindrical glass percolator; then add sufficient alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed very slowly, adding alcohol as required. Reserve the first *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of percolate and continue the percolation, until the second percolate measures *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] or until the drug is exhausted. Transfer this second percolate to a suitable apparatus and distil off the alcohol at as low a temperature as practicable, until a residue measuring about *one hundred mils* remains then add the reserved percolate and continue distillation until the residue in the still is of syrupy consistence. Transfer this syrupy residue to a flask, using a little warm alcohol to rinse the still, and adding the rinsing to the flask. When it has cooled, add *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of purified petroleum benzin and shake the mixture thoroughly for several minutes. Allow the liquids to separate and decant the benzin layer as closely as possible; add again to the residue *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of purified petroleum benzin, agitate and decant the benzin layer as before. Transfer the syrupy residue to a shallow evaporating dish, rinse the flask with *twenty mils* [or 325 minims] of warm alcohol, adding the rins-

ings to the residue in the dish, and then incorporate *fifty grammes* [or 1 ounce av., 334 grains] of the thoroughly dried starch. Evaporate the mixture by a very gentle heat on a water bath, frequently stirring, and, when the mass has become thick, spread it on glass plates and continue the drying in an air bath at a temperature not exceeding 70° C. (158° F.) until thoroughly dry. Reduce the product to a fine powder and weigh it. Assay a portion of this product as directed below, and, from the alkaloidal content thus determined, ascertain by calculation the amount of alkaloids in the remainder of the powder and add to this enough of the dried starch to make the finished Extract contain 2 per cent. of the ether-soluble alkaloids of aconite. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly.

"**Assay.**—Introduce 3 Gm. of Extract of Aconite into a 250 mil flask, add 10 Gm. of washed sand and mix thoroughly. Then add 150 mils of ether and 2 mils of ammonia water, shake the mixture vigorously every few minutes during a half hour, and when the dregs have settled decant 100 mils of the clear liquid, representing *two grammes* of the Extract. Proceed as directed under *Belladonnæ Radix*, page 222, twelfth line of the Assay, beginning with the word "Filter," modifying the process there given by using ether instead of chloroform for the final shaking out of the alkaloids.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 64.539 milligrammes of the ether-soluble alkaloids of aconite." *U. S.*

For a biological method of assaying Extract of Aconite, see *Aconitum.*

This extract is an undesirable addition to the U. S. P. IX and requires the utmost care in its preparation, for notwithstanding the addition of both a chemical and biological assay it is often variable in strength as found in commerce.

Dose, one-eighth to one-fourth grain (0.008–0.015 Gm.).

EXTRACTUM ALOES. Br.

EXTRACT OF ALOES

(ĕx-trăc'tŭm ăl'ō-ēs)

Extrait d'Aloès, *Fr.*; Extractum Aloës, *P. G.*; Aloeextract, *G.*; Estratto di aloe acquoso, *It.*

"Aloes, in small fragments, 1000 *grammes;* Distilled Water, boiling, 10,000 *millilitres.* Add the Aloes to the Distilled Water and stir well until they are thoroughly mixed; set aside the mixture for twenty-four hours; decant; strain; evaporate the strained liquid to dryness at a temperature not exceeding 60° C. (140° F.)." *Br.*

The object of this preparation is to afford an aloes purified from mechanical impurities. The process is based upon the British formulas for extracts of Barbados aloes and Socotrine aloes, formerly official. With an official purified aloes, the necessity for this preparation is not obvious. The U. S. P. IX dismissed Extract of Aloes and Aloe Purificata, but added tests for Aloes which exclude inorganic impurities, gum, etc. See *Aloe*, page 115. A powdered extract is official in the N. F. IV. (See Part III.) An extract made with cold distilled water was formerly official in the German Pharmacopœia, as was also the vitriolated extract, "*Extractum Aloes Acido Sulfurico Correctum,*" made by suspending eight parts of extract of aloes in thirty-two parts of distilled water, adding drop by drop one part of pure sulphuric acid, and evaporating in a porcelain vessel to dryness.

Dose, one to five grains (0.06–0.3 Gm.).

Off. Prep.—Decoctum Aloes Compositum, *Br.;* Extractum Colocynthidis Compositum, *Br.;* Pilulæ Antiperiodicæ, *N. F.;* Tinctura Antiperiodica, *N. F.*

EXTRACTUM BELLADONNÆ FOLIORUM. U. S. (Br.)

EXTRACT OF BELLADONNA LEAVES Ext. Bellad. Fol. [Extractum Belladonnæ Foliorum Alcoholicum, Pharm. 1890]

(ĕx-trăc'tŭm bĕl-lą-dŏn'næ fō-lĭ-ō'rŭm)

"Extract of Belladonna Leaves yields not less than 1.18 per cent. nor more than 1.32 per cent. of the alkaloids of belladonna leaves. *One gramme* of the Extract represents about *four grammes* of belladonna leaves." *U. S.* "Dry Extract of Belladonna contains in 100 grammes 1 gramme of the alkaloids of Belladonna Leaves." *Br.*

Extractum Belladonnæ Siccum, *Br.*, Dry Extract of Belladonna; Extractum Belladonnæ Alcoholicum; Extractum Belladonnæ; Extrait de Belladone (Racine), *Fr. Cod.;* Spirituöses Tollkirschenextrakt, *G.;* Estratto di belladonna idroalcoolico, *It.;* Extracto alcoholico de belladona, *Sp.*

The alcoholic extracts of belladonna of the U. S. P., 1880 and 1890, were made from the leaves, in deference to a prejudice which seems to have a strong following. The British Pharmacopœia introduced in the 1885 revision for the first time an alcoholic extract of belladonna, but it differed from the U. S. extract in being made from the root instead of the leaves. The British alcoholic (root) extract (1898) was 66 per cent. weaker than the Br. Pharm., 1885, extract; it now contains 1 per cent. of the alkaloids of belladonna leaves, and is called dry extract of belladonna. The green extract of belladonna made from the juice of fresh leaves and branches is no longer official. (See *U. S. D.*, 19th edition, p. 471.) The absence of chlorophyll in an extract made from the root would cause ointments, cerates, plasters, etc., made from it to be deficient in the characteristic green color so much prized, but there can be no question of the greater uniformity in strength of the root.

The U. S. P. IX introduced this extract in two forms, Pilular Extract and Powdered Extract, so that the pharmacist might select the form that was best suited for dispensing. The

pilular extract is used officially in the ointment. Both forms of the extract, however, are of the same strength.

Pilular Extract of Belladonna Leaves

* "Belladonna Leaves, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Glucose, Alcohol, Water, each, *a sufficient quantity*. Moisten the powder with sufficient of a mixture of *three volumes* of alcohol and *one volume* of water and pack it firmly in a cylindrical percolator, then add enough menstruum, using the same proportion of alcohol and water as before, to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding menstruum of the same strength, until the percolate measures *three thousand mils* [or 101 fluidounces, 212 minims], or until the belladonna leaves are exhausted. Recover the alcohol from the percolate by distillation and evaporate the residue with frequent stirring, at a temperature not exceeding 70° C. (158° F.), to a pilular consistence. Mix the mass thoroughly and weigh it. Assay a portion of this extract, as directed below, and, from the alkaloidal content thus determined, ascertain by calculation the amount of alkaloids in the remainder of the mass, and to this add enough glucose to make the finished Extract contain 1.25 per cent. of the alkaloids of belladonna leaves. Mix thoroughly.

"**Assay.**—Dissolve 2 Gm. of Pilular Extract of Belladonna Leaves in 10 mils of diluted alcohol, transfer the solution to a separator and wash the vessel in which the extract was dissolved with 2 mils of ammonia water previously diluted with 10 mils of distilled water, in divided portions, adding the rinsings to the separator, then proceed as directed under *Fluidextractum Belladonnæ Radicis*, page 486, fourth line of the Assay, beginning with the word "Completely," modifying the process there given by treating the residue twice with 5 mils of ether and evaporating to dryness each time before titration.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 28.92 milligrammes of the alkaloids of belladonna leaves.

Powdered Extract of Belladonna Leaves

* "Belladonna Leaves, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Magnesium Oxide, *twenty grammes* [or 309 grains]; Starch, dried at 100° C. (212° F.), Alcohol, each, *a sufficient quantity*. Moisten the drug with sufficient alcohol and pack it in a cylindrical percolator; then add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed very slowly, adding alcohol as required. Reserve the first *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of percolate and continue the percolation until the second percolate measures *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] or until the drug is exhausted. Transfer the second percolate to a suitable apparatus and distil off the alcohol at as low a temperature as practicable, until a residue measuring about *one hundred mils* [or 3 fluidounces, 183 minims] remains, then add the reserved percolate and continue distillation until the residue in the still is of syrupy consistence. Transfer this syrupy residue to a shallow evaporating dish, rinse the flask or still with a small quantity of warm alcohol, adding the rinsing to the residue in the dish. Evaporate this extract to a pilular consistence, at a temperature not exceeding 70° C. (158° F.), then add *fifty grammes* [or 1 ounce av., 334 grains] of the dried starch and continue the heating, with frequent stirring, until the mass is nearly dry. Now add the magnesium oxide, thoroughly incorporate it and set the product aside in a current of warm air, until thoroughly dry. Reduce the product to a fine powder and weigh it. Assay a portion of this product as directed below, and, from the alkaloidal content thus determined, ascertain by calculation the amount of alkaloids in the remainder of the powder and add to this enough of the dried starch to make the finished Extract contain 1.25 per cent. of the alkaloids of belladonna leaves. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly.

"**Assay.**—Introduce 3 Gm. of Powdered Extract of Belladonna Leaves into a 250 mil flask, add 10 Gm. of washed sand and mix thoroughly. Then add 150 mils of a mixture of chloroform, 1 volume, and ether, 2 volumes, followed by 5 mils of ammonia water. Shake the mixture vigorously every ten minutes during a half hour and when the dregs have settled decant 100 mils of the clear liquid, representing *two grammes* of the Extract; now proceed as directed under *Belladonnæ Radix*, eleventh line of the Assay, beginning with the word "Filter," modifying the process there given by treating the residue twice with ether, and evaporating to dryness each time before titration.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 28.92 milligrammes of the alkaloids of belladonna leaves." *U. S.*

"Belladonna Leaves, in No. 40 powder, Alcohol (70 per cent.), of each, *a sufficient quantity*. Reduce ten grammes of the Belladonna Leaves to No. 60 powder and determine the proportion of alkaloids present by the process described under 'Belladonnæ Folia.' Moisten one thousand grammes of the Belladonna Leaves with two hundred and fifty millilitres of the Alcohol, pack firmly in a percolator and percolate with more of the Alcohol until four thousand millilitres of percolate have been obtained. Determine the proportion of total solids in the

percolate by evaporating twenty millilitres, drying the residue at 80° C. (176° F.), and weighing. Determine also the proportion of alkaloids in the percolate, by the process described under 'Tinctura Belladonnæ,' employing forty millilitres of the percolate in the place of one hundred millilitres of the Tincture. Having thus determined the proportion of total solids and of alkaloids in the percolate, calculate the amount of each the remainder of the percolate will yield, and also the amount of the powdered Belladonna Leaves, the alkaloidal strength of which has also been determined, that must be added to afford a dry extract containing 1 per cent. of alkaloids. Add to the percolate a somewhat smaller amount of the powdered Leaves than calculation has shown to be necessary, recover the alcohol by distillation, and dry the residue in a shallow, flat, tared dish, first on a water-bath, and finally in a current of air at 60° to 80° C. (140°–176° F.). Weigh the dish with its contents, calculate the additional amount of powdered Leaves that will be necessary, add this to the product of evaporation, transfer the whole to a dry, slightly warmed mortar and triturate carefully until thoroughly mixed. Pass the powdered Extract through a No. 20 sieve, transfer to a bottle which can be securely closed, and preserve in a cool dry place. Slightly moisten 5 grammes of the Extract with a mixture of 1 volume of *acetic acid* and 9 volumes of *alcohol* (70 per cent.), pack in a small percolator and percolate with the same menstruum, if necessary under increased air-pressure, until 50 millilitres of percolate have been collected. Then proceed as described under 'Tinctura Belladonnæ,' using 50 millilitres of percolate in the place of 100 millilitres of the Tincture. Examined by the foregoing process, Dry Extract of Belladonna is found to contain in 100 grammes 1 gramme of the alkaloids of Belladonna Leaves. *Limit of error* 0.05 gramme in excess or defect. This Dry Extract contains 1 per cent. of the alkaloids of Belladonna Leaves." *Br.*

Uses.—There is no physiological difference between the pilular and powdered extracts of belladonna. The former may be used in the preparation of pills or ointments the latter wherever the action of belladonna is wished in the form of a powder or compressed tablet. For the conditions in which these extracts are useful, see under *Atropina*.

Dose, internally, from one-sixth to one-third of a grain (0.010–0.021 Gm.).

Off. Prep.—Emplastrum Belladonnæ, *U. S., Br.;* Suppositoria Belladonnæ, *Br.;* Unguentum Belladonnæ, *U. S.;* Pilulæ Aloes et Podophylli Compositæ (from Pilular Extract), *N. F.;* Pilulæ Aloini Compositæ (from Pilular Extract), *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ (from Pilular Extract), *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ Compositæ (from Pilular Extract), *N. F.;* Pilulæ Antidyspepticæ (from Pilular Extract), *N. F.;* Pilulæ Laxativæ Compositæ (from Pilular Extract), *N. F.*

EXTRACTUM CANNABIS. U. S. (Br.)

EXTRACT OF CANNABIS Ext. Cannab. [Extractum Cannabis Indicæ, U. S. P. VIII]

(ĕx-trăc'tŭm căn'nȧ-bĭs ĭn'dĭ-cæ)

"Extract of Cannabis, when assayed biologically, produces incoördination when administered to dogs in a dose of not more than 0.004 Gm. of Extract per kilogramme of body weight." *U. S.*

Extractum Cannabis Indicæ, *Br.;* Extract of Indian Hemp: *Br.;* Extrait de Chanvre de l'Inde, *Fr. Cod.;* Indischer Hanfextrakt, *G.*

* "Cannabis, in No. 20 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, *a sufficient quantity*. Moisten the powder with sufficient alcohol, pack it firmly in a cylindrical percolator and add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding alcohol, until the drug is exhausted. Recover the alcohol from the percolate by distillation and evaporate the residue with frequent stirring, at a temperature not exceeding 70° C. (158° F.), to a pilular consistence. Mix the mass thoroughly and weigh it. Assay a portion of this extract, and from the result thus obtained adjust the weight of the finished Extract, by the addition of glucose, to conform to the required biological standard.

"**Assay.**—Proceed as directed under Biological Assays." *U. S.* (See under *Cannabis* and Part III.)

"Exhaust Indian Hemp, in coarse powder, with Alcohol (90 per cent.) by the *percolation process;* recover the alcohol by distillation, and evaporate the residue to a soft extract." *Br.*

The continuation in the Br. Pharm. of the name of Indian Hemp is unfortunate because of the possibility of its being mistaken for the root of *Apocynum cannabinum*, which is also called Indian Hemp. Several mistakes have occurred through this unfortunate confusion of nomenclature.

Although there is some difference in the details of the two processes, the preparations of the U. S. and Br. Pharmacopœias are practically identical. The U. S. P. IX provides a biological test. (See Part III.)

Great care is necessary in the manufacture of this extract not only in the selection of the crude drug, but also there is reason to believe that excessive heat in evaporating may have an injurious effect on the quality of the preparation. The only means of ascertaining its activity is by means of the biological test. (See p. 279.) The preparation varies exceedingly in strength, so that it is wisest to begin with a small dose, one-quarter of a grain (0.016 Gm.), and rapidly increase the amount given until some effect is produced.

Dose, one-fourth to three-fourths of a grain (0.015–0.045 Gm.).

Off. Prep.—Tinctura Cannabis Indicæ, *Br.;* Mistura Chlorali et Potassii Bromidi Composita, *N. F.*

EXTRACTUM CASCARÆ SAGRADÆ. U. S. (Br.)

EXTRACT OF CASCARA SAGRADA Ext. Casc. Sagr. [Extractum Rhamni Purshianæ, U. S. VIII, Powdered Extract of Cascara Sagrada]

(ĕx-trăc'tŭm căs-căr'æ să-grăd'æ)

"*One gramme* of the Extract represents *three grammes* of cascara sagrada." *U. S.*

Extractum Cascaræ Sagradæ Siccum, *Br.;* Dry Extract of Cascara Sagrada; Extrait de Cascara Sagrada, *Fr. Cod.;* Cascara Sagrada-Extrakt, Amerikanisches Faulbaumrindenextrakt, *G.;* Extracto alcoholico de cascara sagrada, *Sp.*

* "Cascara Sagrada, in No. 20 powder, *nine hundred grammes* [or 31 ounces av., 327 grains]; Magnesium Oxide, *twenty-five grammes* [or 386 grains]; Starch, dried at 100° C. (212° F.), Boiling Water, each, *a sufficient quantity,* to make *three hundred grammes* [or 10 ounces av., 255 grains]. Mix the cascara sagrada with *four thousand mils* [or 135 fluidounces, 122 minims] of boiling water and macerate the mixture during three hours. Then transfer it to a metallic percolator, allow it to drain and pour on boiling water until the percolate measures *five thousand mils* [or 169 fluidounces, 33 minims], or the drug is exhausted. Evaporate the percolate to dryness on a water bath or steam bath, reduce the extract to a fine powder, weigh it, add the magnesium oxide and enough of the dried starch to make the product weigh *three hundred grammes* [or 10 ounces av., 255 grains]. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

"Exhaust Cascara Sagrada, in No. 20 powder, with Distilled Water by the *percolation process;* evaporate the percolate to dryness on a water-bath." *Br.*

This powdered extract was made official in the U. S. P. VIII for the first time; 1 part of the extract represented 4 parts of the drug; in the U. S. P. IX 1 part represents 3 parts of the drug.

The British preparation (1914) is a dry extract. It well represents the virtues of the bark, and furnishes a good means of administering this purgative in pilular form.

Dose, from two to eight grains (0.13–0.5 Gm.).

Off. Prep.—Pilulæ Aloini, Strychninæ et Belladonnæ Compositæ, *N. F.*

EXTRACTUM CIMICIFUGÆ. U. S.

EXTRACT OF CIMICIFUGA Ext. Cimicif. [Powdered Extract of Cimicifuga]

(ĕx-trăc'tŭm cĭm-ĭ-cĭf'ŭ-gæ)

"*One gramme* of the Extract represents *four grammes* of cimicifuga." *U. S.*

Extract of Black Cohosh; Extrait d'Actée à grappes, *Fr.;* Cimicifugaextrakt, *G.*

* "Cimicifuga, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, Starch, dried at 100° C. (212° F.), each, *a sufficient quantity,* to make *two hundred and fifty grammes* [or 8 ounces av., 358 grains]. Moisten the drug with sufficient alcohol, pack it in a cylindrical percolator, and add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, adding alcohol as required until the drug is exhausted. Recover the alcohol from the percolate by distillation and evaporate the residue to dryness, with frequent stirring, at a temperature not exceeding 70° C. (158° F.). Weigh the residue and add sufficient of the dried starch to make the product weigh *two hundred and fifty grammes* [or 8 ounces av., 358 grains]. Reduce the mixture to a fine powder, mix thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

In the U. S. P. VIII this extract was made from the fluidextract, but the U. S. P. IX gives a process. This extract was introduced for the reason that although the fluidextract and tincture represent the virtues of cimicifuga, the alcohol present in both may be therapeutically contra-indicated, and the exceedingly disagreeable taste of the drug is entirely masked if the extract be prescribed in the form of a pill, with proper additions, such as extract of licorice, or if the pill be coated or enclosed in a capsule. It is used in the treatment of *chorea.*

Dose, of the extract, from three to ten grains (0.2–0.65 Gm.).

EXTRACTUM COLCHICI CORMI. U. S. (Br.)

EXTRACT OF COLCHICUM CORM Ext. Colch. Corm. [Powdered Extract of Colchicum Corm]

(ĕx-trăc'tŭm cŏl'chĭ-cī cŏr'mī)

"Extract of Colchicum Corm yields not less than 1.25 per cent. nor more than 1.55 per cent. of colchicine. *One gramme* of the Extract represents about *four grammes* of colchicum corm." *U. S.*

Extractum Colchici, *Br.;* Extractum Colchici Radicis, *U. S.,* 1890; Extrait de Colchique acetique, *Fr.;* Zeitlosen Essigextrakt, *G.*

* "Colchicum Corm, in No. 60 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, Purified Petroleum Benzin, Starch, dried at 100° C. (212° F.), each, *a sufficient quantity.* Moisten the drug with sufficient alcohol, pack it in a cylindrical percolator and add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then

allow the percolation to proceed slowly, adding alcohol as required, until the percolate measures *two thousand mils* or until the drug is exhausted. Recover the alcohol from the percolate by distillation at as low a temperature as practicable until a residue measuring about *one hundred and fifty mils* [or 5 fluidounces, 35 minims] remains in the still. Transfer this residue to a flask, using a little warm alcohol to rinse the still, and add the rinsings to the flask. When it has cooled, add *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of purified petroleum benzin and shake the mixture thoroughly for several minutes. Allow the liquids to separate and decant the benzin layer as closely as possible; again add to the residue *one hundred and fifty mils* [or 5 fluidounces, 35 minims] of purified petroleum benzin, agitate and decant the benzin layer as before, repeat the washing with *one hundred mils* [or 3 fluidounces, 183 minims] of purified petroleum benzin and reject the benzin washings. Transfer the residue to a shallow evaporating dish, rinse the flask with a little warm alcohol, adding the rinsings to the residue in the dish, and evaporate it on a water bath to a thick extract. To this add *fifty grammes* [or 1 ounce av., 334 grains] of the dried starch, mix well, spread the mixture on glass plates and continue the drying in an air bath at a temperature not exceeding 70° C. (158° F.) until thoroughly dry. Reduce the product to a fine powder and weigh it. Assay a portion of this product as directed below, and, from the alkaloidal content thus determined, ascertain by calculation the amount of alkaloid in the remainder of the powder and add to this enough of the dried starch to make the finished Extract contain 1.4 per cent. of colchicine. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small wide-mouthed bottles and stopper them tightly." *U. S.*

"Crush fresh Colchicum Corms, deprived of their coats; press out the juice; allow the feculence to subside, decant; heat the clear liquid to 100° C. (212° F.); strain through flannel, and evaporate at a temperature not exceeding 70° C. (158° F.) to a soft extract." *Br.*

The U. S. VIII extract was an acetic extract of the corm, but in the U. S. P. IX process the acetic acid was omitted. The British extract is made by evaporating the juice of fresh corms.

In Great Britain a preparation called *preserved juice of colchicum* is given in the dose of five minims (0.3 mil) or more. It is made by expressing the fresh corm, allowing the juice to stand for forty-eight hours that the starchy matter may subside, then adding one-fourth of its bulk of alcohol, allowing it again to stand for a short period, and ultimately filtering.

"**Assay.**—Proceed as directed under *Colchici Semen*, page 371, modifying the process there given by using 6 Gm. of the Extract of Colchicum Corm instead of 15 Gm. of colchicum seed. The final weight will be the amount of colchicine from *two grammes* of Extract of Colchicum Corm." *U. S.*

As the fresh colchicum corm is rarely to be had in this country, the U. S. Pharmacopœia employs the dried corm; its process, if properly conducted, will afford a very efficient extract. In preparing this extract according to the British process, by expression from the recent corm, there will be experienced some inconveniences, which would seem to render the U. S. process under all circumstances preferable. (*P. J.*, xiii, 62.) The acetic extract of colchicum made from fresh corms was abandoned by the Br. Ph., 1898, and by the U. S. P. IX, but the acetic acid menstruum is a good solvent for colchicine.

Dose, from one-fourth to one grain (0.016–0.065 Gm.).

EXTRACTUM COLOCYNTHIDIS. U. S.

EXTRACT OF COLOCYNTH Ext. Colocynth. [Powdered Extract of Colocynth]

(ĕx-trăc'tŭm cŏl-o-cŷn'thĭ-dĭs)

"*One gramme* of the Extract represents *four grammes* of colocynth." *U. S.*

Extractum Colocynthidis Alcoholicum; Extrait de Coloquinte, *Fr. Cod.*; Extractum Colocynthidis, *P. G.*; Koloquintenextrakt, *G.*; Estratto di coloquintide idroalcoolico, *It.*

* "Colocynth, in No. 20 powder, *one thousand grammes* (freed from the seeds) [or 35 ounces av., 120 grains]; Diluted Alcohol, Starch, dried at 100° C. (212° F.) each, *a sufficient quantity*, to make *two hundred and fifty grammes* [or 8 ounces av., 358 grains]. Moisten the drug with *two thousand mils* [or 67 fluidounces, 301 minims] of diluted alcohol and macerate it in a closed vessel for twenty-four hours, then transfer the moist drug to a cylindrical percolator, shake it down evenly without packing, and gradually pour diluted alcohol upon it, allowing the percolation to proceed slowly, until the percolate measures *five thousand mils* [or 169 fluidounces, 33 minims]. Recover the alcohol from the percolate by distillation and evaporate the residue to dryness on a water bath or steam bath. Reduce the extract to a fine powder, weigh it, and add sufficient of the dried starch to make the product weigh *two hundred and fifty grammes* [or 8 ounces av., 358 grains]. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

The colocynth should always be deprived of its seeds, following the directions of the U. S. Pharmacopœia, before being submitted to the action of the menstruum. Boiling water extracts such a large amount of pectin and mucilage from colocynth that either the decoction or the hot infusion gelatinizes on cooling, and the extract made by means of it is therefore loaded with inert matter, and, besides, is liable to become mouldy, or so tough and hard as to resist trituration and formation into pills. Hence many years ago the London College, following

in this respect the old French Codex, directed, in the last edition of its Pharmacopœia, maceration with cold water; but diluted alcohol has been found to be a much better menstruum, and has accordingly been adopted in the U. S. Pharmacopœia process, while in the British Pharmacopœia the simple extract has been discarded altogether. The chief, if not exclusive, use of the alcoholic extract is in the preparation of the compound extract.

This preparation should never be substituted for an extract prepared with a menstruum containing a larger percentage of water, because the water extracts a large quantity of mucilaginous and inert matter. Commercial extract of colocynth may be often found in the market made with an aqueous menstruum.

Dose, one-half grain (0.032 Gm.).

Off. Prep.—Extractum Colocynthidis Compositum, *U. S.;* Pilulæ Colocynthidis Compositæ, *N. F.;* Pilulæ Colocynthidis et Hyoscyami, *N. F.*

EXTRACTUM COLOCYNTHIDIS COMPOSITUM. U. S., Br.

COMPOUND EXTRACT OF COLOCYNTH Ext. Colocynth. Co. [Powdered Compound Extract of Colocynth]

(ĕx-trăc'tŭm cŏl-o-cŷn'thĭ-dĭs cŏm-pŏs'ĭ-tŭm)

Extrait de Coloquinte composé, *Fr.;* Zusammengesetztes Koloquintenextrakt, *G.*

• "Extract of Colocynth, *one hundred and sixty grammes* [or 5 ounces av., 282 grains]; Aloes, *five hundred grammes* [or 17 ounces av., 279 grains]; Cardamom Seed, in No. 60 powder, *fifty grammes* [or 1 ounce av., 334 grains]; Resin of Scammony, in No. 60 powder, *one hundred and forty grammes* [or 4 ounces av., 411 grains]; Soap, dried and in powder, *one hundred and fifty grammes* [or 5 ounces av., 127 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Triturate the ingredients until the product is reduced to a No. 60 powder. Pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

"Colocynth Pulp, 150 *grammes;* Extract of Aloes, 300 *grammes;* Scammony Resin, 100 *grammes;* Curd Soap, in powder, 75 *grammes;* Cardamom Seeds, in powder, 25 *grammes;* Alcohol (60 per cent.), 4000 *millilitres*. Macerate the Colocynth Pulp in the Alcohol for four days; press out the tincture; recover the alcohol by distillation; evaporate to dryness; add the Extract of Aloes, Scammony Resin, and powdered Cardamom Seeds; powder; mix the powder with the Curd Soap." *Br.*

The Br. Pharm. (1914) directs Extract of Aloes instead of Barbados Aloes, and decreased the proportion of soap from four to three ounces. The object of the soap is to improve the consistence of the mass, which, when hardened by time, it renders more soluble in the gastric juices. It may possibly also serve the purpose of modifying the action of the aloes. In the U. S. process the extract is in the form of powder, which is very convenient for admixture with other substances; while if given uncombined, it may be readily made into pills by suitable additions. The alternative of using the scammony or its resin, in the first British formula, which appeared to us very objectionable, has been abandoned in the present edition, and the resin only directed. The plan of having the powders simply mixed was liable to the objection that the mixture was not likely to be so thoroughly effected as to obtain a uniform result, and hence the U. S. Pharm., 1880, adopted Squibb's suggestion, to melt together all the ingredients unpowdered, except the cardamom, add a little alcohol, and, when the mixture is thoroughly made, to stir in the powdered aromatic, and finally to reduce the whole to a fine powder. The U. S. P. IX, however, relies upon trituration as an assurance of thorough commingling.

This extract is an energetic and safe cathartic, possessing the activity of its three purgative ingredients, with comparatively little of the drastic character of the colocynth and scammony. It may be still further and advantageously modified by combination with rhubarb, jalap, calomel, etc., with one or more of which it is often united in prescription.

Dose, as a laxative, one to two grains (0.065–0.13 Gm.); as a purgative, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Pilulæ Catharticæ Compositæ, *U. S.;* Pilulæ Catharticæ Vegetabiles, *N. F.;* Pilulæ Antidyspepticæ, *N. F.;* Pilulæ Colocynthidis et Podophylli, *N. F.;* Pilulæ Laxativæ Post Partum, *N. F.*

EXTRACTUM ERGOTÆ. U. S., Br.

EXTRACT OF ERGOT Ext. Ergot.

(ĕx-trăc'tŭm ẹr'gọ-tæ)

Extractum Hæmostaticum; Ergotin, *Br.* (1898); Extrait de Seigle Ergoté, *Fr. Cod.;* Extractum Secalis cornuti, *P. G.;* Mutterkornextrakt, *G.;* Estratto di segala cornutta, *It.*

• "Ergot, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Hydrochloric Acid, *ten mils* [or 162 minims]; Purified Petroleum Benzin, Alcohol, Water, each, *a sufficient quantity*. Pack the ergot in a percolator and slowly percolate it with purified petroleum benzin until a few drops of the percolate, evaporated on filter paper leave no greasy stain. Reject the benzin percolate remove the ergot from the percolator and dry it by exposure to the air. Mix *eight hundred and fifty mils* [or 28 fluidounces, 356 minims] of alcohol with *one hundred and fifty mils* [or 5 fluidounces, 35 minims] of water add the hydrochloric acid to *four hundred mils* [or 13 fluidounces, 252 minims] of this mixture, and moisten the ergot with the acid mixture. Pack it in a cylindrical percolator and macerate for six hours, then add enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the

lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding menstruum, using the same proportion of alcohol and water as before, until the drug is exhausted. Recover the alcohol from the percolate by distillation and evaporate the residue with frequent stirring, at a temperature not exceeding 70° C. (158° F.), to a pilular consistence." *U. S.*

"Ergot, crushed, 1000 *grammes;* Distilled Water, 7500 *millilitres;* Alcohol (90 per cent.), 650 *millilitres.* Macerate the Ergot with *five thousand millilitres* of the Distilled Water for twelve hours; strain; repeat the maceration with the remainder of the Distilled Water; strain; press; evaporate the mixed liquids to *five hundred millilitres;* add the Alcohol; set aside for three days, stirring occasionally; filter; evaporate the filtrate to a soft extract." *Br.*

The menstruum for this extract in the U. S. P. IX is a great improvement over the previous revision in that the percentage of alcohol is increased. The Br. extract is inferior because it is an aqueous extract. Great care is needed in the evaporation as excessive heat destroys the activity of ergot. Pearson (*J. A. Ph. A.*, 1913, ii, 1453) found that after heating for thirty minutes on the water bath fluidextract of ergot was practically inert.

Dose, from five to fifteen grains (0.32 to 1.0 Gm.).

Off. Prep.—Injectio Ergotæ Hypodermica, *Br.*

EXTRACTUM EUONYMI. Br.

EXTRACT OF EUONYMUS

(ĕx-trăc'tŭm eū-ŏn'y-mī)

Dry Extract of Euonymus; Extract of Wahoo; Extrait d'Evonymus atropurpureus, *Fr. Cod.;* Extrait de Fusain Américaine, *Fr.;* Spindelbaumextrakt, Spillbaumrindenextrakt, *G.*

"Exhaust Euonymus Bark in No. 20 powder with Alcohol (45 per cent.) by the *percolation process.* Evaporate the percolate and thoroughly dry the residue. Powder the product as far as possible and mix it with one-fourth of its weight of Calcium Phosphate, continuing the drying and powdering until a sufficiently dry preparation is obtained; transfer this to a well-closed bottle." *Br.*

This extract was not admitted to the U. S. P. IX, but was retained in the Br. Pharm. (1914) and introduced into the National Formulary IV (see Part III) which directs the percolation of euonymus in No. 40 powder with alcohol 4 volumes and water 1 volume. The percolate is evaporated or distilled and the residue dried and mixed with dried starch so that .1 Gm. of the extract represents 4 Gm. of euonymus. On account of the reports of physicians of cumulative effects the following note was inserted: "CAUTION—It has been stated that the absorption of Euonymus in the gastro-intestinal tract is uncertain and irregular. To avoid an accumulation of the drug or toxic action, the physician should carefully guard the dosage and determine in each case the tolerance of the patient." *N. F. IV.* Dry and powdered extract of euonymus is frequently but erroneously termed *"euonymin."*

Dose, one to three grains (0.065 to 0.2 Gm.).

EXTRACTUM FELLIS BOVIS. U. S. (Br.)

EXTRACT OF OXGALL. Ext. Fel. Bov. [Powdered Extract of Oxgall]

(ĕx-trăc'tŭm fĕl'lĭs bōv'ĭs)

"*One gramme* of the Extract represents *eight grammes* of oxgall." U. S.

Fel Bovinum Purificatum, *Br.;* Purified Ox Bile; Fel Tauri Depuratum; Extractum Fellis Bovini; Extrait de Fiel de Bœuf, *Fr. Cod.;* Gereinigte Ochsengalle (Rindsgalle), *G.;* Bile cristallizzata di platner, *It.;* Hiel de toro preparada, *Sp.*

* "Oxgall, *eight hundred grammes* [or 28 ounces av., 96 grains]; Alcohol, *fifteen hundred mils* [or 50 fluidounces, 5 fluidrachms, 45 minims]; Starch, dried at 100° C. (212° F.), *a sufficient quantity,* to make *one hundred grammes* [or 5 ounces av., 231 grains]. Add *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of alcohol slowly and with agitation to the oxgall contained in a bottle of sufficient size. Allow the mixture to stand for two days and then decant the liquid portion. Wash the residue in the bottle with an additional *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol, decant the liquid portion, mix it with the liquid first separated and filter the mixture. Recover the alcohol from the filtrate by distillation, transfer the residue to a shallow dish and evaporate it to a thick extract at a temperature between 75° and 80° C. (167° and 176° F.). Spread this extract on glass plates and continue the drying by exposure to warm air, at a temperature not exceeding 70° C. (158° F.), until thoroughly dry. Reduce the extract to a fine powder, weigh it and add sufficient of the dried starch to make the product weigh *one hundred grammes* [or 3 ounces av., 231 grains]. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

"Evaporate five hundred *millilitres* of fresh ox bile to one-fourth of its volume; shake this liquid with twice its volume of Alcohol (90 per cent.); set the mixture aside until the solid matter has subsided; decant the clear solution, and filter the remainder, washing the filter and contents with a little more Alcohol (90 per cent.). Distil off most of the alcohol from the mixed liquids, and evaporate the residue in a porcelain dish, on a water-bath, to the consistence of a firm extract." *Br.*

The object of this preparation is to furnish purified concentrated Oxgall in a condition in which it can be satisfactorily prescribed for internal administration. The addition of alcohol

to the concentrated liquid is made for the purpose of separating albuminous matter.

Properties.—"A yellowish-green hygroscopic substance, having a taste partly sweet and partly bitter, soluble in *water* and in *alcohol* (90 per cent.). 1 millilitre of an aqueous solution (1 in 100) in which 0.1 gramme of *refined sugar* has been dissolved, gradually acquires a deep violet color when mixed with 10 millilitres of *syrupy phosphoric acid* and heated in a water-bath. Its aqueous solution on the addition of twice its volume of *alcohol* (90 per cent.) gives no precipitate (absence of unpurified ox bile)." *Br.*

Refined oxgall, much used by painters, is prepared, according to Gray, in the following manner. Take of "fresh oxgall, one pint; boil, skim, and add one ounce of alum, and keep it on the fire for some time; to another pint, add one ounce of common salt in the same manner; keep them bottled up for three months; then decant off the clear; mix them in an equal proportion; a thick yellow coagulum is immediately formed, leaving the refined gall clear and colorless."

This extract replaces in the U. S. P. IX the *Fel Bovis Purificatum* of the former revision over which it has the advantage of being more concentrated. The British title is yet retained as Purified Ox Bile. It represents practically a mixture of sodium glycocholate and sodium taurocholate contaminated with traces of fatty and soapy matters. (See *Fel Bovis.*) The directions to add starch in sufficient quantity in this extract is unfortunate. The therapeutic activity of bile resides in its solid matters and as the proportion of these varies greatly it is manifest that the extract should be standardized, not as it is at present, to represent a certain amount of fresh bile, but to represent a proportion of dried bile, *i.e.,* of the biliary solids.

Uses.—By the ancients bile was a very highly esteemed remedy and was used in a great variety of conditions. It, however, fell into desuetude and for many years was rarely employed. Recently it has again come largely into favor but for a very different class of disorders. Its most frequent use to-day is to replace or augment the hepatic secretions when these for any reason are lacking. While the exact rôle that the bile plays in the intestinal tract is not clearly understood, it is well established that it plays an important part in digestion, especially of the fatty foods.

When introduced into the circulation bile has a depressant effect upon the heart muscle leading to a reduction in the blood pressure and slowing of the pulse. Whether or not the slowing of the pulse is partly indicative of inhibitory stimulation is at present under dispute, but it seems well established that after large doses, at least, the slowing of the pulse is the result of a direct action upon the heart muscle. According to Meltzer and Salant (*J. Ex. M.,* viii) there are present in the bile both an excito-motor and depresso-motor principle. Bile has long been recognized as the most powerful stimulant to the secretory activity of the liver which we possess, but according to Shaffer (*A. J. Phys.,* 1907, xvii, p. 389) this is not indicative of a true excitation of the hepatic cells but is simply that, after its injection, the blood contains the preformed material for excretion and that the increase in the output of the bile solids does not exceed the dose which was injected. The presence of bile in the intestinal tract has by some been held to diminish the multiplication of bacteria, but there is no convincing evidence of such an action. It increases peristaltic movements in the large intestines but appears to diminish those of the upper bowel.

Oxgall has been found useful in a variety of conditions in which there is a diminution in the amount of bile in the intestinal tract, as for instance in *catarrhal cholangitis,* and *hepatic torpor.* In *gall stones* while it may improve the digestion by offering a necessary ferment there is no sufficient reason to believe that it will aid the solution of the stones. It is also a valuable agent in the treatment of certain forms of *chronic constipation,* not solely because of its own action in increasing the peristalsis of the colon, but because its presence in the intestines is essential for the action of many of the cathartics. Cholesterin, which is one of the ingredients of bile, has the power of neutralizing certain poisons such as tetanotoxin, sapotoxin, and snake venom, and may perhaps prove clinically useful for this purpose. It should be noted, however, that as cholesterin is scarcely soluble in cold alcohol, the extract will contain not more than traces of it.

The daily amount of bile secreted by an ordinary man varies between two hundred and four hundred mils (6.7–13.3 fluidounces), containing from 1 to 3 per cent. of solids. If there is a marked reduction in the secretion of bile it is evident that the pharmacopœial dose is far too small to have any effect. Because of a supposed injurious action upon gastric digestion various recommendations have been made for administering bile in the form that it will pass through the stomach; among these may be mentioned the use of keratin coated or salol coated pills, and by mixing with spermaceti. We think, however, that the liability of disturbance of the stomach by this agent has been over-estimated.

Among the proprietary preparations of bile may be mentioned: *bilein,* which is marketed in pills ranging from one-twelfth to one-fourth of a grain (0.005–0.016 Gm.); *cholalin,* a yellow powder, dose one-fourth to one-half grain (0.016–0.032 Gm.); *glycotauro,* dose five to ten grains (0.32–0.65 Gm.); *ovogall,* a yellowish powder said to consist of a combination with egg albumen, dose eight to fifteen grains (0.5–1 Gm.); *sodium choleinate,* dose eight to fifteen grains (0.5–1 Gm.); *cholesterin* may be given in doses of fifteen to twenty-five grains (1.0–1.7 Gm.).

Dose, of extract of bile two to eight grains (0.12–0.5 Gm.).

EXTRACTUM GELSEMII. U. S.

EXTRACT OF GELSEMIUM Ext. Gelsem. [Powdered Extract of Gelsemium]

(ĕx-trăc'tŭm ję̆l-sĕm'ĭ-ī)

"*One gramme* of the Extract represents *four grammes* of gelsemium." *U. S.*

* "Gelsemium, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, Magnesium Oxide, Starch dried at 100° C. (212° F.), each, *a sufficient quantity,* to make *two hundred and fifty grammes* [or 8 ounces av., 358 grains]. Moisten the drug with sufficient alcohol, pack it in a cylindrical percolator and add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, adding alcohol as required, until the drug is exhausted. Recover the alcohol from the percolate, by distillation at as low a temperature as practicable, until a residue measuring about *five hundred mils* [or 16 fluidounces, 435 minims] remains in the still. Transfer this residue to a shallow dish, and evaporate it to a soft extract with frequent stirring, at a temperature not exceeding 70° C. (158° F.). Then add *fifty grammes* [or 1 ounce av., 334 grains] of a mixture of *one part* of magnesium oxide and *three parts* of the dried starch, mix well, spread the mass in a thin layer on glass or tinned-metal plates or in a porcelain dish and continue the drying in an air bath, at a temperature not exceeding 70° C. (158° F.), until thoroughly dry. Reduce the extract to a fine powder, weigh it, and add sufficient of the mixture of magnesium oxide and dried starch, made in the same proportion as before, to make the finished product weigh *two hundred and fifty grammes* [or 8 ounces av., 358 grains]. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

Dose, one-eighth to one-fourth of a grain (0.008-0.016 Gm.).

EXTRACTUM GENTIANÆ. U. S., Br.

EXTRACT OF GENTIAN Ext. Gentian.

(ĕx-trăc'tŭm gĕn-tī-ā'næ)

Extrait de Gentiane, *Fr. Cod.;* **Extractum Gentianæ,** *P. G.;* **Enzianextrakt,** *G.;* **Estratto di genzian acquoso,** *It.;* **Extracto acuoso de genciana,** *Sp.*

* "Gentian, in No. 20 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Water, *a sufficient quantity.* Moisten the powder with sufficient water, and allow it to macerate for twenty-four hours; then pack it in a conical percolator, and gradually pour water upon it until the drug is exhausted. Reduce the liquid to *two thousand mils* [or 67 fluidounces, 301 minims] by boiling, strain it, and then evaporate it to a pilular consistence on a water bath." *U. S.*

"Infuse Gentian Root in ten times its weight of Distilled Water for two hours; boil for fifteen minutes; pour off; press; strain; evaporate the liquid to a soft extract." *Br.*

The plan of percolation with cold water is admirably adapted to the extraction of the active principles of gentian. By the use of cold water, starch and pectic acid are left behind, while any albumen that may be taken up is disposed of by the subsequent boiling and straining.

The extract, however, may be advantageously made by macerating the root in two parts of water for thirty-six hours, then expressing in a powerful press, again macerating with additional water, and in like manner expressing, and evaporating the united expressed liquors. Guibourt and Cadet de Vaux obtained by maceration in cold water an extract not only greater in amount, but also more transparent, more bitter, and possessing more of the color and odor of the root, than that prepared by decoction. Guibourt attributes this result to the circumstance that, as gentian contains little if any starch, it yields nothing to boiling which it will not also yield to cold water, while decoction favors the combination of a portion of the coloring matter with the lignin. But this opinion requires modification, now that it is understood that gentian contains pectic acid, which water will extract when boiling hot, but not when cold. Gentian, according to Brande, yields half its weight of extract by decoction.

As ordinarily procured, the extract of gentian has an agreeable odor, is very bitter, and of a dark brown color approaching to black, shining, and tenacious. It is frequently used as a tonic, in the form of pill, either alone or in connection with metallic preparations; but the practice of some pharmacists of using it indiscriminately as a pill excipient is deserving of severe censure.

Dose, from two to eight grains (0.12–0.5 Gm.).

Off. Prep.—Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Ferri, Quininæ, Aloes, et Nucis Vomicæ, *N. F.*

EXTRACTUM GLYCYRRHIZÆ. U. S.

EXTRACT OF GLYCYRRHIZA Ext. Glycyrrh. [Extract of Licorice]

(ĕx-trăc'tŭm glĭ̆ç-ĭr-rhī'zæ)

"The commercial Extract of Glycyrrhiza." *U. S.*

Extractum Liquiritiæ; Liquorice, Licorice; Extrait de Réglisse, *Fr. Cod.;* **Suc de Réglisse, Sucre noir,** *Fr.;* **Succus Liquiritiæ,** *P. G.;* **Lakriz, Lakritzensaft, Süssholzsaft,** *G.;* **Estratto di liquirizia, Sugo di liquirizia,** *It.;* **Extracto acuoso de regaliz, Regaliza en ballos,** *Sp.*

Licorice is an article of export from the north of Spain, particularly Catalonia, where it is obtained in the following manner. The roots of

the *G. glabra,* having been dug up, thoroughly cleansed, and half dried by exposure to the air, are cut into small pieces, and boiled in water until the liquor is saturated. The decoction is then allowed to rest, and, after the dregs have subsided, is decanted, and evaporated to the proper consistence. The extract, thus prepared, is formed into rolls from five to six inches long by an inch in diameter, which are dried in the air, and wrapped in laurel leaves.

The British Pharmacopœia gives a process for making extract of licorice. (See page 453.) The U. S. Pharmacopœia directs that not less than 60 per cent. of it should be soluble in cold water.

Much licorice is prepared in Calabria, according to Fée, from the *G. echinata,* which abounds in that country. The process is essentially the same as that just described, but conducted with greater care, and the Italian licorice is purer and more valuable than the Spanish. It is in cylinders, generally somewhat smaller than the Spanish, and usually stamped with the manufacturer's brand. Most of the extract brought to this country comes from Messina and Catania in Sicily and Naples, from Seville and Saragossa in Spain, and from Smyrna in Turkey. Perhaps in no other part of the world is more licorice consumed than in the United States, from four to five thousand tons having been imported annually before 1860; but the article is now made on an extensive scale in this country, very successfully, with the best modern appliances, and of such good quality as to have almost driven the foreign article out of the market. The principal use of Extract of Licorice is in the manufacture of chewing tobacco, that in the form of rolls as sold by the druggists being a comparatively small portion of the whole amount consumed.

Crude Licorice, Licorice Paste, or Licorice Mass, as it is variously termed, is found in the market in cases ranging from two hundred and fifty to four hundred pounds, of a hard pilular consistence and, as its name implies, in a mass, which has been run into the case while hot and then allowed to cool.

Licorice is usually in cylindrical rolls, somewhat flattened, and often covered with bay-leaves. We have seen it abroad and in this market in large cubical masses. When good, it is black, dry, brittle, breaking with a shining fracture, of a peculiar sweet and slightly acrid or bitterish taste, and almost entirely soluble, when pure, in boiling water.

It is described officially as "in flattened cylindrical rolls or in masses, of a glossy black color externally; fracture brittle, sharp, smooth, conchoidal; taste characteristic and sweet. When pulverized it yields a brown powder. Not less than 60 per cent. of Extract of Glycyrrhiza is soluble in cold water. The yield of ash does not exceed 6 per cent." *U. S.* Neumann obtained 460 parts of aqueous extract from 480 parts of Spanish licorice. It is, however, considerably less soluble in cold water. It is often impure from accidental or fraudulent addition or careless preparation. Starch, sand, the juice of prunes, etc., are sometimes added, and carbonaceous matter, and even particles of copper, are found in it, the latter arising from the boilers in which the decoction is evaporated. In different commercial specimens examined by Chevallier he found from 9 to 50 per cent. of insoluble matter. (*J. P. C.,* xxx, 429.) This is by no means, however, always impurity. In the preparation of the extract by decoction, a portion of matter originally insoluble, or rendered so by decoction, is taken up, and is, in fact, necessary to the proper constitution of the licorice. When this is prepared with cold water, or even with hot water by simple displacement, the extract attracts moisture from the air, becomes soft, and loses the characteristic brittleness of the drug. The additional substances taken up in decoction serve to protect the extract against this change. Delondre has obtained the same result by using steam as the solvent. He prepares from the root an excellent licorice, having all the requisite qualities of color, taste, and permanence, by passing steam, in suitable vessels, through the coarse powder of the root. The vapor thoroughly penetrates the powder, and is drawn off as it condenses. With about 500 lbs. of the root, this treatment is continued for twelve hours, and repeated at the end of five days. The liquors are collected, decanted, clarified with about 4 lbs. of gelatin, and quickly evaporated. After being put into the form of cylinders, the extract is kept for ten days in a drying room, at a temperature of 25° C. (77° F.). A bitter or empyreumatic taste is a sign of inferior quality in licorice. As ordinarily found in commerce, it requires to be purified. (See *Extractum Glycyrrhizæ Purum;* also *Glycyrrhizinum Ammoniatum.*)

Licorice contains *glycyrrhizin,* $C_{24}H_{36}O_9$, a glucoside, partly free and partly in combination with ammonia, to which combination the characteristic sweet taste of licorice is due. The glycyrrhizin when boiled with dilute acids decomposes into *glycyrrhetin,* $C_{18}H_{36}O_4$, and a fermentable sugar.

According to Mellor (*A. J. P.,* 1898, 23, 54, 136) the best process for estimating glycyrrhizin is as follows: The best menstruum with which to treat the commercial powdered extract is a mixture of 40 mils ammonia water, 240 mils of alcohol, and sufficient water to make a liter. After extraction, filter, and precipitate with diluted sulphuric acid. Of twelve samples examined, the highest was a Greek licorice with 27.78 per cent., and the lowest a Spanish with 5.28 per cent. of glycyrrhizin. Of insoluble matter, the highest was a Spanish with 36.52 per cent., and the lowest a Greek with 5.95 per cent. The average yield, however, was strongly in favor of American licorice. In determining the per cent. of glycyrrhizin in the commercial

extract, the tobacco manufacturers dissolve 10 Gm. in 100 mils of water, add 200 mils of alcohol, and allow it to stand over night. The insoluble matter will then have mostly settled; the filtrate may be acidulated with sulphuric acid, and the precipitated glycyrrhizin dried and weighed. For an improvement on the foregoing method see Dwier's article in the *Analyst* for 1913, p. 367, translated from *Ann. Falsif.*, 1913, p. 252; Also Evans' Sons, Lescher and Webb method. *Proc. A. Ph. A.*, 1911, 57 from *Chem. Ztg.*, 1911, No. 92.

The so called *refined licorice*, found in commerce in small cylindrical pieces not thicker than a pipestem, is prepared by dissolving the impure extract in water without boiling, straining the solution, and evaporating. The object of this process is to separate not only the insoluble impurities, but also the acrid oleoresinous substance which is extracted from the licorice root and is necessarily mixed with the unrefined extract. It is customary to add, during the process, a portion of sugar, gum, flour, starch, or perhaps glue. These additions, or something equivalent, are necessary to obviate the deliquescent property of the pure licorice. According to Delondre, 15 per cent. of gum is the proper proportion, when this substance is used; Geiseler has found sugar of milk to lessen the disposition of the extract to absorb moisture; but he considers the best addition, on the whole, to be very finely powdered licorice root, which should be used in the proportion of 1 part to 16 of the purified extract. (*A. J. P.*, xxviii. 225.) The preparation is sometimes attacked by small worms, probably in consequence of the farinaceous additions. Excellent licorice is prepared in some parts of England, from the root cultivated in that country. The *Pontefract cakes* are small lozenges of licorice made in the vicinity of Pontefract, England. For methods of assaying extract of licorice, see *A. J. P.*, 1896, 663; also 1898, 23, 136.

Uses.—Licorice has some demulcent property and is a popular addition to various lozenges. In large quantities it is somewhat laxative. Its most important rôle in medicine, however, is for the purpose of disguising the taste or covering the acrimony of various drugs such as quinine or ammonium chloride. It is also used to impart consistency to pills and troches.

Off. Prep.—Trochisci Ammonii Chloridi, *U. S.*; Trochisci Cubebæ, *U. S.*

EXTRACTUM GLYCYRRHIZÆ PURUM. U. S. (Br.)

PURE EXTRACT OF GLYCYRRHIZA Ext. Glycyrrh. Pur.

(ĕx-trăc'tŭm glўç-yr-rhī'zæ pū'rŭm)

Extractum Glycyrrhizæ, *Br.;* Extract of Liquorice; Extractum Glycyrrhizæ Depuratum, Succus Liquiritiæ, Depuratus; Extrait de Réglisse pur, *Fr.;* Succus Liquiritiæ depuratus, *P. G.;* Gereinigter Süssholzsaft, Reines Lakriz, *G.*

* "Glycyrrhiza, in No. 20 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Ammonia Water, *one hundred and fifty mils* [or 5 fluidounces, 35 minims]; Water, Chloroform Water, each, *a sufficient quantity.* Mix the ammonia water with *three thousand mils* [or 101 fluidounces, 212 minims] of water, and, having moistened the powder with *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of the mixture, allow it to macerate in a closed vessel for twenty-four hours. Then pack it lightly in a cylindrical percolator, and gradually pour upon it, first the remainder of the menstruum, and then chloroform water, until the glycyrrhiza is exhausted. Evaporate the liquid in a porcelain dish on a water bath, to a pilular consistence." *U. S.*

"Licorice Root, in No. 20 powder, 1000 *grammes;* Chloroform Water, 5000 *millilitres.* Mix the Liquorice Root with one-half of the Chloroform Water; set aside for twenty-four hours; strain; press; to the pressed marc add the remainder of the Chloroform Water and set aside for six hours; strain; press; mix the strained liquids; heat to 100° C. (212° F.); strain through flannel; evaporate to a soft extract." *Br.*

The necessity for a pure extract of licorice must be apparent to every pharmacist; the very variable quality of the commercial extract has frequently led to disappointment. The official process affords a preparation which is unexceptionable, the ammonia rendering the glycyrrhizin soluble, yet care must be taken in its evaporation, as it is very easily injured by too much heat, which gives it an empyreumatic taste, destroying at once its usefulness as an agreeable adjuvant. Extract of licorice is incompatible with acids of all kinds which precipitate the glycyrrhizin.

Off. Prep.—Mistura Glycyrrhizæ Composita, *U. S.;* Mistura Ammonii Chloridi, *N. F.*

EXTRACTUM HYDRASTIS. U. S.

EXTRACT OF HYDRASTIS Ext. Hydrast. [Extract of Golden Seal, Powdered Extract of Hydrastis]

(ĕx-trăc'tŭm hў-drăs'tĭs)

"Extract of Hydrastis yields not less than 9 per cent. nor more than 11 per cent. of the ether-soluble alkaloids of hydrastis. *One gramme* of the Extract represents about *four grammes* of hydrastis." *U. S.*

* "Hydrastis, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Tartaric Acid, *five grammes* [or 77 grains]; Alcohol, Magnesium Oxide, Starch, dried at 100° C. (212° F.), each, *a sufficient quantity.* Dissolve the tartaric acid in *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of alcohol, moisten the drug with sufficient of this solution and pack in a cylindrical percolator; then add enough of the acidified alcohol, followed by alcohol if necessary, to saturate the powder and leave a stratum above it. When the liquid begins to

drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, adding alcohol as required, until the drug is exhausted. Recover the alcohol from the percolate by distillation, and evaporate the residue to a soft extract, with frequent stirring, at a temperature not exceeding 70° C. (158° F.). Add *fifty grammes* [or 1 ounce av., 334 grains] of a mixture of *one part* of magnesium oxide and *three parts* of the dried starch, mix thoroughly and spread the mass in a thin layer on glass or tinned-metal plates or in a porcelain dish and continue the drying in an air bath at a temperature not exceeding 70° C. (158° F.), until thoroughly dry. Then reduce the extract to a fine powder and weigh it. Assay a portion of this product as directed below, and, from the alkaloidal content thus determined, ascertain by calculation the amount of alkaloids in the remainder of the powder and add to this enough of the mixture of magnesium oxide and dried starch, made in the same proportion as before, to make the finished Extract contain 10 per cent. of the ether-soluble alkaloids of hydrastis. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

" **Assay.**—Introduce 3 Gm. of Extract of Hydrastis into a 250 mil flask, add 10 Gm. of washed sand and mix thoroughly. Then add 150 mils of ether and 5 mils of ammonia water. Shake the mixture vigorously every ten minutes during a half hour, and when the dregs have settled decant 100 mils of the clear liquid, representing *two grammes* of the Extract. Proceed as directed under *Belladonnæ Radix,* eleventh line of the Assay, beginning with the word " Filter," modifying the process there given by using ether instead of chloroform for the final shaking out of the alkaloids, and drying the residue to constant weight at 100° C. (212° F.), instead of titrating it. The weight will be the amount of ether-soluble alkaloids from *two grammes* of Extract of Hydrastis," *U. S.*

Uses.—This extract was introduced into the U. S. P. IX to furnish a convenient method of administering hydrastis (see *Hydrastis*).

Dose, five to ten grains (0.3–0.6 Gm.).

EXTRACTUM HYOSCYAMI. U. S., Br.

EXTRACT OF HYOSCYAMUS Ext. Hyosc.

(ĕx-trăc'tŭm hȳ-o̤s-cȳ'a̤-mī)

"Extract of Hyoscyamus yields not less than 0.22 per cent. nor more than 0.28 per cent. of the alkaloids of hyoscyamus. *One gramme* of the Extract represents about *four grammes* of hyoscyamus." *U. S.* " Extract of Hyoscyamus contains in 100 grammes 0.3 gramme of the alkaloids of Hyoscyamus Leaves." *Br.*

Extract of Henbane; Extrait de Jusquiame (feuille), *Fr. Cod.;* Extractum Hyoscyami, *P. G.;* Bilsenkrautextrakt, *G.;* Estratto di giusquiamo idroalcoolico, *It.;* Extracto alcohólico de beleno, *Sp.*

* " Hyoscyamus, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Glucose, Alcohol, Water, each, *a sufficient quantity.* Moisten the powder with sufficient of a mixture of *three volumes* of alcohol and *one volume* of water, pack it firmly in a cylindrical percolator and add enough menstruum, using the same proportion of alcohol and water as before, to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding menstruum of the same strength until the drug is exhausted. Recover the alcohol by distillation and evaporate the residue, with frequent stirring, at a temperature not exceeding 70° C. (158° F.), until it is reduced to a pilular consistence. Mix the mass thoroughly and weigh it. Assay a portion of this extract as directed below, and, from the alkaloidal content thus determined, ascertain by calculation the amount of alkaloids in the remainder of the mass and to this add enough glucose to make the finished Extract contain 0.25 per cent. of the alkaloids of hyoscyamus. Mix thoroughly." *U. S.*

" Hyoscyamus Leaves, in No. 40 powder, Alcohol (70 per cent.) of each, *a sufficient quantity.* Reduce ten grammes of the Hyoscyamus Leaves to No. 60 powder, and determine the proportion of alkaloids present by the process described under 'Belladonnæ Folia.' Moisten one thousand grammes of the Hyoscyamus Leaves with two hundred and fifty millilitres of the Alcohol, pack firmly in a percolator, and percolate with more of the Alcohol until four thousand millilitres of percolate have been obtained. Determine the proportion of total solids in the percolate by evaporating twenty millilitres, drying the residue at 80° C. (176° F.), and weighing. Determine also the proportion of alkaloids in the percolate by the process described under ' Tinctura Belladonnæ.' Having thus determined the proportion of total solids and of alkaloids in the percolate, proceed as directed under ' Extractum Belladonnæ Siccum ' to prepare a dry Extract of Hyoscyamus containing 0.3 per cent. of alkaloids. Examined by the process described under ' Extractum Belladonnæ Siccum,' Extract of Hyoscyamus is found to contain in 100 grammes 0.3 gramme of the alkaloids of Hyoscyamus Leaves. *Limit of error* 0.015 gramme in excess or defect." *Br.*

" This Extract may be used when the Extractum Hyoscyami of the International Agreement is required. It contains 0.3 per cent. of the alkaloids of Hyoscyamus Leaves." *Br.*

" **Assay.**—Proceed as directed under *Extractum Belladonnæ Foliorum* (Pilular), page 444, modifying the process there given by using 5 Gm. of Extract of Hyoscyamus instead of 2 Gm. of extract of belladonna leaves. Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 28.92 milligrammes of the alkaloids of hyoscyamus." *U. S.*

The U. S. P. IX introduced a special process for this extract, instead of evaporating the fluid extract as did the U. S. P. VIII. The British Pharm., 1914, discarded the process for making the extract from the fresh leaves and adopted percolation and evaporation of the percolate of dried leaves so that both pharmacopœias are practically in accord. The strength is not quite the same, the U. S. P. IX requires not less than 0.22 per cent. nor more than 0.28 per cent. of alkaloids while the Br. Pharm., 1914, requires not less than 0.3 per cent. of alkaloids. For an account of the disadvantages of the extract from the fresh leaves see U. S. Dispensatory, 19th ed., p. 478.

Dose, from one to two grains (0.065–0.13 Gm.).

Off. Prep.—Pilulæ Cartharticæ Vegetabiles, *N. F.;* Pilula Colocynthidis et Hyoscyami, *Br.* (*N. F.*); Pilulæ Laxativæ Post Partum, *N. F.*

EXTRACTUM KRAMERIÆ. Br.

EXTRACT OF KRAMERIA

(ĕx-trăc'tŭm krą-mē'rĭ-æ)

Extract of Rhatany; Extractum Ratanhæ; Extrait de Ratanhia, *Fr. Cod.;* Ratanhæxtrakt, *G.;* Estratto di ratania acquoso, *It.;* Extracto acuoso de ratania, *Sp.*

"Exhaust Krameria Root, in No. 10 powder, with Distilled Water by the *percolation process;* evaporate the percolate to dryness." *Br.*

This extract was deleted from the U. S. P. IX, but has been introduced in the N. F. IV as a powdered extract (see Part III). In the U. S. P. VIII it was made by percolating the drug with water and evaporating the liquid as in the British process above. The wood of the root yielded to Procter only 6.8 per cent. of extract, while the bark separated from the wood yielded 33 per cent. As the wood is of difficult pulverization, the inference is obvious that, in powdering the roots, the ligneous portion may be rejected with advantage. (*A. J. P.,* xiv, 270.) As a prolonged exposure of the infusion to the air is attended with the absorption of oxygen and the production of insoluble apothem, it is desirable that the evaporation should be conducted rapidly, or in a vacuum. There scarcely appears to be occasion, in the case of rhatany, for heating and filtering the infusion before evaporation as required by the U. S. P. VIII process as the only use of which is to get rid of albumen, and this is not among the recognized ingredients of the root.

Very inferior extracts of rhatany are often sold. Such is the South American extract, which has been occasionally imported. As the product obtained by decoction is greater than that afforded by the official plan, the temptation to substitute the former is not always resisted, although it has been shown to contain nearly 50 per cent. of insoluble matter. Some druggists prepare the extract with an alcoholic menstruum, with a view to the greater product, but the extract thus prepared has from 20 to 30 per cent. less of the active principle than the official.

Extract of krameria should have a reddish-brown color, a smooth shining fracture, and a very astringent taste, and should be almost entirely soluble in water. Its virtues may be considered as in proportion to its solubility. It is much used for all the purposes for which the astringent extracts are employed.

Dose, from five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Trochiscus Krameriæ, *Br.;* Trochiscus Krameriæ et Cocainæ, *Br.*

EXTRACTUM MALTI. U. S.

EXTRACT OF MALT Ext. Malt.

(ĕx-trăc'tŭm mâl'tī)

Essence (Extrait) de Malt, *Fr.;* Malzextrakt, *G.*

* "Malt, in coarse powder, not finer than No. 12, *one thousand grammes* [or 35 ounces av., 120 grains]; Water, *a sufficient quantity.* Pour *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of water upon the powder contained in a suitable vessel and macerate for six hours, then add *four thousand mils* [or 135 fluidounces, 122 minims] of water, heated to 60° C. (140° F.), and digest the mixture for one hour on a water bath at a temperature not exceeding 60° C. (140° F.). Strain the mixture, express, filter the strained liquid, and, by means of a water bath or vacuum apparatus, evaporate the liquid, at a temperature not exceeding 60° C. (140° F.), until it has a specific gravity of not less than 1.350 nor more than 1.400 at 25° C. (77° F.)." *U. S.*

Under the name of extract of malt, two distinct preparations have been put upon the market, the one being a liquid similar to beer, the other, the official extract prepared from malt, composed chiefly of dextrin and glucose, with some albumen and phosphates. The object of the U. S. process is to obtain all of the soluble principles of malt in a permanent form. To secure this, strict attention to the details of the process is necessary. Good extract of malt should contain no starch, have the consistence of thick honey, a brown color, and should be free from empyreumatic taste. A great deal of commercial extract of malt is adulterated with glucose to a surprising extent. A *dry extract of malt* has come into extensive use as an infant's food, made by artificially drying the thick syrupy extract. It is in the form of a straw-colored, coarse powder, and is given dissolved in milk or water.

O. F. Romer and H. R. Randoll of Brooklyn, have patented several improvements in the process of making extract of malt,—namely, 1, the properly ground malt is treated with an alkaline solution, in order to neutralize the fatty acids which usually impart a bad taste to the product; 2, the extract is separated from the solid matters by pressing in press cloths, whereby it is obtained as a clear liquid with scarcely any loss. (*N. R.,* 1880, 179.) Pharmaceutically, extract of malt has been used as an emulsifying agent; it makes

a good basis for a cod liver oil emulsion, for which purpose it is admirably adapted therapeutically. For therapeutic properties see *Maltum.*

Dose, from one to four fluidrachms (3.75 to 15 mils).

Off. Prep.—Emulsum Olei Morrhuæ cum Malto, *N. F.*

EXTRACTUM NUCIS VOMICÆ.
U. S., (Br.)

EXTRACT OF NUX VOMICA Ext. Nuc. Vom.
[Powdered Extract of Nux Vomica, Nucis Vomicæ Extractum, P. I.]

(ĕx-trăc'tŭm nū'cĭs vŏm'ĭ-cæ)

"Extract of Nux Vomica yields not less than 15.2 per cent. nor more than 16.8 per cent. of the alkaloids of nux vomica." *U. S.*

"Dry Extract of Nux Vomica contains in 100 grammes 5 grammes of strychnine." *Br.*

Extractum Nucis Vomicæ Siccum, *Br.;* Dry Extract of Nux Vomica; Extractum Nucum Vomicarum Spirituosum (vel Alcoholicum); Extrait de Noix Vomique, *Fr. Cod.;* Extractum Strychni, *P. G.;* Weingeistiges Krähenaugenextrakt, Brechnussextrakt, Strychnossamenextrakt, *G.;* Estratto di noce vomica alcoolico, *It.;* Extracto alcoholico de nuez vomica, *Sp.*

* "Nux Vomica, in No. 20 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, Water, Purified Petroleum Benzin, Diluted Sulphuric Acid, Ammonia Water, Chloroform, Magnesium Oxide, Starch, dried at 100° C. (212° F.), each, *a sufficient quantity.* Moisten the drug with sufficient of a mixture of *three volumes* of alcohol and *one volume* of water, pack it firmly in a cylindrical percolator, and add enough of the menstruum, using the same proportion of alcohol and water as before, to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding the menstruum as required, until the percolate passes but faintly imbued with bitterness, and the drug is exhausted. Recover the alcohol from the percolate by distillation at as low a temperature as practicable and concentrate the liquid until the residue measures about *two hundred mils* [or 6 fluidrachms, 366 minims]. Transfer this residue to a flask or separator, using a little warm menstruum made of the same proportion of alcohol and water originally used, to rinse the still, and add the rinsing to the separator. Then add *one hundred and fifty mils* [or 5 fluidounces, 35 minims] of water and *two hundred mils* [or 6 fluidounces, 366 minims] of purified petroleum benzin and shake the mixture thoroughly for several minutes. Allow the liquids to separate and decant the benzin layer as closely as possible; again add to the residue *one hundred mils* [or 3 fluidounces, 183 minims] of purified petroleum benzin, agitate, and decant the benzin as before. Wash the mixed benzin solutions, in a separator, with a mixture of *one hundred mils* [or 3 fluidounces, 183 minims] of water and *ten mils* [or 162 minims] of diluted sulphuric acid, separate the aqueous layer and repeat the washing twice with fresh portions, *one hundred mils* [or 3 fluidounces, 183 minims] each, of water and acid made in the same proportion as before. Collect the aqueous solutions in a separator, render the liquid alkaline by the addition of ammonia water and shake it out with three portions of chloroform, *twenty mils* [or 325 minims], *ten mils* [or 162 minims], and *ten mils* [or 162 minims], respectively. Add the combined chloroform solutions to the extract and evaporate the mixture to dryness on a water bath with frequent stirring. Assay a portion of this product as directed below, and, from the alkaloidal content thus determined, ascertain by calculation the amount of alkaloids in the remainder of the product and add to this enough of a mixture of magnesium oxide, *one part,* and of the dried starch, *three parts,* to make the finished Extract contain 16 per cent. of the alkaloids of nux vomica. Reduce the mixture to a fine powder, mix thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

"Liquid Extract of Nux Vomica, Calcium Phosphate, of each, *a sufficient quantity.* Evaporate ten millilitres of the Liquid Extract in a flat-bottomed dish and dry at 100° C. (212° F.). The weight of the dry extract thus obtained deducted from three grammes gives the weight of Calcium Phosphate to be added to each ten millilitres of the Liquid Extract. Take one hundred parts by volume of the Liquid Extract; recover the alcohol by distillation; add sufficient of the Calcium Phosphate, as indicated by the above determination, to produce, when dried at 100° C. (212° F.), and reduced to a fine powder, thirty parts by weight of the Dry Extract." *Br.*

"3 grammes of Dry Extract of Nux Vomica, when exhausted with *alcohol* (70 per cent.), afford a liquid which when tested by the process described under 'Extractum Nucis Vomicæ Liquidum' yield 0.15 gramme of strychnine, representing in 100 grammes of the Dry Extract 5 grammes of strychnine. *Limit of error* 0.2 gramme in excess or defect. This Dry Extract contains 5 per cent. of strychnine." *Br.*

"**Assay.**—Introduce 3 Gm. of Extract of Nux Vomica into a 250 mil flask, add 10 Gm. of washed sand and mix thoroughly. Then add 150 mils of a mixture of ether, 2 *volumes,* and chloroform, 1 *volume,* followed by 5 mils of ammonia water. Shake the mixture vigorously every ten minutes during half an hour, and when the dregs have settled decant 100 mils of the clear liquid, representing *two grammes* of the Extract. Proceed as directed under *Belladonnæ Radix,* twelfth line of the Assay, beginning with the word "Filter," *modifying the process* there given by dissolving the alkaloidal residue in 10 mils of tenth-normal sulphuric acid V.S. instead of 5 mils.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 36.4 milligrammes of the alkaloids of nux vomica." *U. S.*

Extract of Nux Vomica, U. S. P. IX, is a powdered extract containing 16 per cent. of total alkaloids. This alkaloidal strength is the standard adopted by The Brussels Protocol. The U. S. P. VIII standard was 5 per cent. of strychnine and the British Pharm. (1914) retained its former standard of 5 per cent. of strychnine and directed the evaporation of the standardized liquid extract of nux vomica.

Extract of nux vomica (U. S. P. VIII) differed from that of the U. S. Pharm. 1890 in its mode of preparation. Acetic acid is the most effective menstruum for nux vomica, but it has the disadvantage of also extracting inert constituents; it leaves the fixed oil in the marc and this is a great point in its favor, but acetic acid was discarded by the U. S. P. IX. and a menstruum of 3 volumes of alcohol and 1 volume of water substituted; in addition the fixed oil is separated and the dissolved alkaloids washed out and incorporated with the extract.

Dose, one-fourth to one-half of a grain (0.016–0.032 Gm.).

Off. Prep.—Pilulæ Aloes et Podophylli Compositæ, *N. F.;* Pilulæ Ferri, Quininæ Aloes et Nucis Vomicæ, *N. F.;* Pilulæ Laxativæ Post Partum, *N. F.*

EXTRACTUM OPII. U. S. (Br.)

EXTRACT OF OPIUM Ext. Opii [Powdered Extract of Opium, Opii Extractum P. I.]

(ĕx-trăc'tŭm ō'pĭ-ī)

"Extract of Opium yields not less than 19.5 per cent. nor more than 20.5 per cent. of anhydrous morphine. *One gramme* of the Extract represents about *two grammes* of opium." *U. S.*

"Dry Extract of Opium contains in 100 grammes 20 grammes of morphine, calculated as anhydrous." *Br.*

Extractum Opii Siccum, *Br.*; Dry Extract of Opium; Extractum Thebaicum; Extrait d'Opium, *Fr. Cod.;* Extrait Thébaique, *Fr.;* Extractum Opii, *P. G.;* Opiumextrakt, *G.;* Estratto di oppio acquoso, *It.;* Extracto acuoso de opio, *Sp.*

* "Opium, cut in small pieces, *one hundred grammes* [or 3 ounces av., 231 grains]; Starch, dried at 100° C. (212° F.), Water, each, *a sufficient quantity.* Macerate the opium with *three hundred mils* [or 10 fluidounces, 69 minims] of hot water until softened, then rub to a smooth paste. Add to this *one hundred grammes* [or 3 ounces av., 231 grains] of clean, white sand and mix thoroughly. Transfer the mixture to a percolator and allow the percolation to proceed, gradually adding water until the opium is exhausted. Evaporate the percolate to dryness in a shallow evaporating dish, on a water bath, reduce the product to a fine powder and weigh it. Assay a portion of this product as directed below, and, from the alkaloidal content thus determined, ascertain by calculation the amount of anhydrous morphine in the remainder of the powder and add to this enough of the dried starch to make the finished Extract contain 20 per cent. of anhydrous morphine. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

"Exhaust sliced Opium with about five times its weight of Distilled Water; strain the liquid through flannel; cool and ascertain its volume. Determine the percentage of morphine present in forty millilitres of this liquid by the process described under 'Tinctura Opii,' and determine also the percentage of total solids dried at 100° C. (212° F.). Add to the remainder of the liquid sufficient Calcium Phosphate to yield an extract which, when dried at 100° C. (212° F.), contains 20 per cent. of morphine; evaporate to dryness, powder, and finally dry at 100° C. (212° F.). Examined by the process described under 'Opium,' Dry Extract of Opium is found to contain in 100 grammes 20 grammes of morphine, calculated as anhydrous. *Limit of error* 1 gramme in excess or defect. This Dry Extract contains 20 per cent. of morphine." *Br.*

"**Assay.**—Dissolve 4 Gm. of Extract of Opium in 5 mils of distilled water, add gradually, with constant stirring, 25 mils of distilled water, filter, and wash the filter and residue with sufficient distilled water to make the solution measure exactly 50 mils. Then proceed as directed under *Opium,* twenty-seventh line of the Assay, beginning with the word "Place." The morphine obtained represents *two grammes* of Extract of Opium." U. S.

The process for the U. S. P. extract differs from that formerly official in several particulars, opium being used instead of powdered opium, and the extract is assayed, and the percentage of morphine adjusted to 20 per cent., so that the extract of opium can now be depended upon to contain slightly more than twice as much morphine as opium of the minimum official strength.

The U. S. P. process is an improvement over those formerly official; in addition to definite strength of the extract, its reduction to pulverulent form will enable pharmacists to dispense it more accurately and conveniently.

As purely aqueous preparations of opium have been found to agree better with certain individuals than opium alone or its alcoholic preparations, there is reason to believe that there are in the crude drug one or more principles, which are capable of causing nausea, headache, nervous disturbances, etc., and which are insoluble in water, though extracted by alcohol or ether. (See *Opium Deodoratum.*)

Dose, one-sixth to one grain (0.01–0.06 Gm.).

Off. Prep.—Extractum Opii Liquidum, *Br.*

EXTRACTUM OPII LIQUIDUM. Br.

LIQUID EXTRACT OF OPIUM

(ĕx-trăc'tŭm ō'pĭ-ī lĭq'uĭ-dŭm)

"Liquid Extract of Opium contains in 100 millilitres 0.75 gramme of morphine, calculated as anhydrous." *Br.*

"Dry Extract of Opium, 37.5 *grammes;* Alcohol (90 per cent.), 200.0 *millilitres;* Distilled

Water sufficient to produce 1000.0 *millilitres*. Mix the Extract with seven hundred *millilitres* of the Distilled Water; set aside in a cool place for twenty-four hours, stirring frequently; add the Alcohol; set aside again for twenty-four hours; filter; wash the filter with sufficient Distilled Water to produce the required volume." *Br.*

"Examined by the process described under 'Tinctura Opii,' Liquid Extract of Opium is found to contain in 100 millilitres 0.75 gramme of morphine, calculated as anhydrous. *Limit of error* 0.05 gramme in excess or defect. This Liquid Extract contains 0.75 gramme of morphine in 100 millilitres; 110 minims contains ¾ grain." *Br.*

It is a good preparation, one which has long been needed; because of its absence from the Pharmacopœia empirical preparations have obtained a certain vogue. It is well known that in opium there are principles soluble in alcohol but not in water, which often produce various disagreeable effects not experienced from the aqueous extract; what was wanted was a liquid preparation meeting this demand. All that was required was to make an aqueous solution of solid extract, and to add something to preserve it. The British Pharmacopœia uses alcohol for the purpose, and in the original formula employed it in such proportion that an Imperial pint of the liquid should contain three fluidounces of the spirit, or between one-sixth and one-seventh by measure. But this amount of alcohol, according to Squire, is insufficient for its preservation, and should be doubled. In the Br. Pharmacopœia (1898) the spirit was increased; but even with this increase the spirit constitutes only one-fifth, which is considerably short of the proportion recommended by Squire. A preparation similar to the British was made some years since by Eugene Dupuy, of New York. (See *Opium.*) In the *Deodorized Tincture of Opium* of the U. S. Pharmacopœia the advantages of the preparation have, we think, been still better secured.

Dose, five to thirty minims (0.3–1.8 mils).

EXTRACTUM PHYSOSTIGMATIS. U. S.

EXTRACT OF PHYSOSTIGMA [Ext. Physostig. [Powdered Extract of Physostigma]

(ĕx-trăc'tŭm phȳ-sǫ-stĭg'mą-tĭs)

"Extract of Physostigma yields not less than 1.7 per cent. nor more than 2.3 per cent. of the alkaloids of physostigma. *One gramme* of the Extract represents about *thirteen grammes* of physostigma." *U. S.*

Extract of Calabar Bean; Extractum Fabæ Calabaricæ; Extrait de Fève de Calabar, *Fr. Cod.*; Kalabarbohnenextrakt, Physostigmaextrakt, *G.*

* "Physostigma, in No. 60 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Tartaric Acid, *five grammes* [or 77 grains]; Purified Petroleum Benzin, Starch, dried at 100° C. (212° F.), Alcohol, Water, each, *a sufficient quantity*. Dissolve the tartaric acid in *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of a mixture of *three volumes* of alcohol and *one volume* of water, moisten the drug with sufficient of this solution, and pack it in a cylindrical percolator; then add enough of the acidified alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding the remainder of the prepared menstruum and then a mixture of *three volumes* of alcohol and *one volume* of water until the drug is exhausted. Recover the alcohol from the percolate by distillation at as low a temperature as practicable and concentrate the remaining liquid at a temperature not exceeding 70° C. (158° F.) until the residue measures about *two hundred mils* [or 6 fluidounces, 366 minims]. Transfer the residue to a flask, using a little warm menstruum, made of the same proportion of alcohol and water as before, to rinse the still, and add the rinsing to the residue in the flask. Then add *one hundred mils* [or 3 fluidounces, 183 minims] of water and *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of purified petroleum benzin and shake the mixture thoroughly for several minutes. Allow the liquids to separate and decant the benzin layer as closely as possible; again add to the residue *two hundred mils* [or 6 fluidounces, 366 minims] of purified petroleum benzin, agitate, and, after allowing the liquids to separate, decant the benzin layer as before and reject the benzin solutions. Transfer the residue to a shallow evaporating dish, rinse the separator with a little of the warm menstruum, add the rinsings to the residue in the dish and evaporate it to pilular consistence at a temperature not exceeding 70° C. (158° F.). Now add *twenty grammes* [or 309 grains] of the dried starch, thoroughly incorporate it, set the extract aside in a current of warm air until dry, then reduce the product to a fine powder and weigh it. Assay a portion of this product as directed below, and, from the alkaloidal content thus determined, ascertain by calculation the amount of alkaloids in the remainder of the powder and add to this enough of the dried starch to make the finished Extract contain 2 per cent. of the alkaloids of physostigma. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

"**Assay.**—Introduce 3 Gm. of Extract of Physostigma into a 250 mil flask, add 10 Gm. of washed sand and mix thoroughly. Then add 150 mils of ether and proceed as directed under *Physostigma*, third line of the Assay, beginning with the word "stopper."

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 27.52 milligrammes of the alkaloids of physostigma." *U. S.*

This extract was formerly official in the British Pharmacopœia but has not been admitted to the 1914 Edition.

As alcohol is the best solvent for the active principles of the bean, it is preferred in making the extract, while the addition of tartaric acid is to facilitate the solution of the alkaloids.

Dose, from one-sixth to one-half of a grain (0.01–0.032 Gm.).

EXTRACTUM RHEI. U. S., Br.

EXTRACT OF RHUBARB Ext. Rhei [Powdered Extract of Rhubarb]

(ĕx-trăc'tŭm rhē'ī)

"*One gramme* of the Extract represents *two grammes* of rhubarb." *U. S.*

Extractum Rhei Alcoholicum; Extrait de Rhubarbe, *Fr. Cod.;* Extractum Rhei, *P. G.;* Rhabarberextrakt, *G.;* Estratto di rabarbaro acquoso, *It.;* Extracto acuoso de ruibarbo, *Sp.*

* "Rhubarb, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Magnesium Oxide, *fifty grammes* [or 1 ounce av., 334 grains]; Starch, dried at 100° C. (212° F.), Alcohol, Water, each, *a sufficient quantity,* to make *five hundred grammes* [or 17 ounces av., 279 grains]. Moisten the drug with sufficient of a mixture of *four volumes* of alcohol and *one volume* of water, pack it in a cylindrical percolator and add enough of this menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding menstruum of the same proportion of alcohol and water as before until the drug is exhausted. Recover the alcohol from the percolate by distillation at as low a temperature as practicable, and continue distillation until a residue of syrupy consistence remains in the still. Transfer this to a shallow dish, rinse the still with a little warm menstruum, add the rinsings to the residue in the dish, and evaporate the mixture to dryness, with frequent stirring, at a temperature not exceeding 70° C. (158° F.). Weigh the dry extract and add the magnesium oxide and sufficient of the dried starch to make the product weigh *five hundred grammes* [or 17 ounces av., 279 grains]. Reduce the mixture to a fine powder, mix thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

"Exhaust Rhubarb, in No. 20 powder, with Alcohol (60 per cent.) by the *percolation process.* Recover most of the alcohol from the percolate by distillation, and evaporate the residual liquid to dryness." *Br.*

The British extract (1914) is now nearly identical with the U. S. preparation; the menstruum used for the former is, however, slightly more aqueous. Rhubarb yields all its active matter to water and alcohol; but, unless the evaporation be performed with great care and with a moderate heat, it is certain that the purgative principle is to a greater or less extent injured or dissipated in the process, and the extract may thus become even less efficient than the root. When properly prepared, the extract has decidedly the peculiar odor of rhubarb.

Dose, from two to ten grains (0.13–0.65 Gm.).

EXTRACTUM STRAMONII. U. S.

EXTRACT OF STRAMONIUM Ext. Stramon.

(ĕx-trăc'tŭm strą-mō'nĭ-ī)

"Extract of Stramonium yields not less than 0.9 per cent. nor more than 1.1 per cent. of the alkaloids of stramonium. One gramme of the Extract represents about *four grammes* of stramonium." *U. S.*

Extrait de Stramoine (feuille), *Fr. Cod.;* Stechapfelblätterextrakt, *G.*

Pilular Extract of Stramonium

* "Stramonium, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains] Glucose, Alcohol, Water, each, *a sufficient quantity.* Moisten the powder with sufficient of a mixture of *three volumes* of alcohol and *one volume* of water and pack it in a cylindrical percolator; then add enough of this menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed gradually adding menstruum of the same strength, until the drug is exhausted. Recover the alcohol from the percolate by distillation, and evaporate the residue with frequent stirring, at a temperature not exceeding 70° C. (158° F.), to a pilular consistence. Mix the mass thoroughly and weigh it. Assay a portion of this extract as directed below, and, from the alkaloidal content thus determined, ascertain by calculation the amount of alkaloids in the remainder of the mass and to this add enough glucose to make the finished Extract contain 1 per cent. of the alkaloids of stramonium. Mix thoroughly." *U. S.*

"**Assay.**—Proceed as directed under *Extractum Belladonnæ Foliorum* (Pilular), page 444, using 2 Gm. of Pilular Extract of Stramonium.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 28.92 milligrammes of the alkaloids of stramonium." *U. S.*

Powdered Extract of Stramonium

* "Stramonium, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Magnesium Oxide, *twenty grammes* [or 309 grains]; Starch, dried at 100° C. (212° F.), Alcohol, each, *a sufficient quantity.* Moisten the drug with sufficient alcohol and pack it in a cylindrical percolator; then add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed very slowly, adding alcohol as required. Reserve the first *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of percolate and continue the percolation until the second percolate measures *one thousand mils* [or 33

fluidounces, 6½ fluidrachms], or until the drug is exhausted. Transfer the second percolate to a suitable apparatus and distil off the alcohol, at as low a temperature as practicable, until a residue measuring about *one hundred mils* [or 3 fluidounces, 183 minims] remains, then add the reserved percolate and continue distillation until the residue in the still is of syrupy consistence. Transfer this residue to a shallow evaporating dish, rinse the flask or still with a small quantity of warm alcohol, and add the rinsing to the contents of the dish. Evaporate this to a soft extract, with frequent stirring, at a temperature not exceeding 70° C. (158° F.). Then add *fifty grammes* [or 1 ounce av., 334 grains] of the dried starch and continue the heating at the same temperature, with frequent stirring, until the mass is nearly dry. Now add the magnesium oxide, thoroughly incorporate it, and set the product aside in a current of warm air, until thoroughly dry. Reduce the product to a fine powder and weigh it. Assay a portion of this product as directed below, and, from the alkaloidal content thus determined, ascertain by calculation the amount of alkaloids in the remainder of the powder and add to this enough dried starch to make the finished Extract contain 1 per cent. of the alkaloids of stramonium. Mix the powders thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

E'we and Vanderkleed report specimens of extract of stramonium which contain a green coal tar color to simulate the chlorophyll present in extracts made from high grade leaf. This coloring matter interferes with the alkaloidal assay and must be removed by shaking out with chloroform in the acid solution. (*J. A. P. A.*, 1914, 1683.)

"**Assay.**—Proceed as directed under *Extractum Belladonnæ Foliorum* (Powdered), page 444, using 3 Gm. of Powdered Extract of Stramonium.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 28.92 milligrammes of the alkaloids of stramonium." *U. S.*

Dose, from one-eighth to one-fourth of a grain (0.008–0.016 Gm.).

Off. Prep.—Unguentum Stramonii (from Pilular Extract), *U. S.*

EXTRACTUM STROPHANTHI. Br.

EXTRACT OF STROPHANTHUS

(ĕx-trăc'tŭm strŏ-phăn'thī)

Extrait de Strophantus Kombé (Semence), *Fr. Cod.*; Strophantusextrakt, *G.*

"Strophanthus Seeds, reduced to No. 30 powder, and dried at 45° C. (113° F.), 25 *grammes;* Ether, Alcohol (90 per cent.), Milk Sugar, in powder, of each, *a sufficient quantity.* Pack the Strophanthus Seeds in a percolator; moisten with the Ether, and macerate for twenty-four hours; then allow percolation to proceed, continuing the addition of the Ether until the liquid passes through colorless. Remove the marc from the percolator, and dry it, gradually heating it to 50° C. (122° F.). Again reduce it to powder, repack in the percolator, and moisten with the Alcohol. Macerate for forty-eight hours, then pour on successive quantities of the Alcohol, percolating slowly, until two hundred and fifty *millilitres* of liquid are obtained. Evaporate most of the alcohol; transfer the residual liquid to a tared dish; concentrate until the liquid begins to thicken; then add sufficient of the Milk Sugar to produce fifty *grammes* of Extract, in powder." *Br.*

This preparation of the British Pharmacopœia closely resembles an "abstract" of the U. S. P., 1880; an important detail, in our opinion, has been neglected in not washing the fatty matter extracted by the ether with diluted alcohol to remove active constituents held by the fatty substances, then evaporating the solution and incorporating the residue with the extract.

This extract fills a very decided want of a solid preparation of strophanthus that can be administered in pill and capsule, and is without doubt efficient. A grain of it may be considered to represent five minims of the U. S. tincture of strophanthus.

Dose, as given in the British Pharmacopœia, from one-fourth to one grain (0.016–0.065 Gm.).

EXTRACTUM SUMBUL. U.S.

EXTRACT OF SUMBUL Ext. Sumbul

(ĕx-trăc'tŭm sŭm'bŭl)

Extract of Muskroot; Extrait de Racine de Sumbul, *Fr.*; Sumbulwurzelextrakt, Moschuswurzelextrakt, *G.*

* "Sumbul, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, Water, each, *a sufficient quantity.* Moisten the powder with sufficient of a mixture of *four volumes* of alcohol and *one volume* of water and pack it in a cylindrical percolator; then add enough of this menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding menstruum of the same strength until the drug is exhausted. Recover the alcohol from the percolate by distillation and evaporate the residue with frequent stirring, at a temperature not exceeding 70° C. (158° F.), to a pilular consistence." *U. S.*

Dose, two to five grains (0.13–0.32 Gm.).

EXTRACTUM TARAXACI. U. S., Br.

EXTRACT OF TARAXACUM Ext. Tarax.

(ĕx-trăc'tŭm tą-răx'ą-cī)

Extract of Dandelion; Extrait de Dent-de-lion, *Fr.*; Löwenzahnextrakt, *G.*; Estratto di tarassaco acquoso, *It.*

* "Taraxacum, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, Water, each, *a sufficient quantity.* Mix *one hundred and twenty-five mils* [or 4 fluid-

ounces, 109 minims] of alcohol with *eight hundred and seventy-five mils* [or 29 fluidounces, 282 minims] of water, and, having moistened the powder with a portion of the mixture, pack it in a cylindrical percolator, then add enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for twenty-four hours. Then allow the percolation to proceed, gradually adding menstruum of the same strength until the drug is exhausted. Recover the alcohol from the percolate by distillation and evaporate the residue with frequent stirring, on a water bath, to a pilular consistence." *U. S.*

"Crush Taraxacum Root; press out the juice; allow the starchy matter to subside; decant; heat the liquid to 100° C. (212° F.), and maintain the temperature for ten minutes; strain; evaporate to a soft extract." *Br.*

The inspissated taraxacum juice of the former U. S. Pharmacopœias has been superseded by the present hydro-alcoholic extract, because of the very variable quality of the former; if the root is of good quality a better extract can be made by percolation and evaporation in the usual way.

The extract made from the juice is undoubtedly stronger when prepared from the root alone than from the whole plant. It is important that the root should be collected at the right season. The juice expressed from it in the spring is thin, watery, and of a feeble flavor; in the latter part of the summer, and in autumn, thick, opaque, cream-colored, very bitter, and abundant, amounting to one-third or one-half its weight. It may be collected in August, and afterwards until severe frost. According to Squire, frost has the effect of diminishing the bitterness and increasing the sweetness of the root. An extract prepared by inspissating the juice is more efficient than that prepared in the old way by decoction. The inspissation should be effected by exposing the juice in shallow vessels to a current of warm dry air, or by evaporation in a vacuum, and should not be unnecessarily protracted. Long exposure during evaporation changes the bitterness of the juice into sweetness, which is a sign of inferiority. In the British process it is wisely directed that before the evaporation of the juice it shall be exposed for a short time to a heat sufficient to coagulate the albumen, which is then separated and rejected as useless; it is indeed injurious, by favoring decomposition. As often found in the shops, the extract is dark-colored, sweet, and in all probability nearly inert. Houlton took more than an ounce of it in a day, without any sensible effect. (*P. J.*, i, 421.) When prepared from the root and leaves together, it has a greenish color. Brande states that one cwt. of the fresh root affords from twenty to twenty-five pounds of extract by decoction in water. The expressed juice yields from 11 to 25 per cent. of extract, the greatest product being obtained from plants collected in November, and the least in April and May. This extract deteriorates by keeping. It is conveniently given in an aromatic water.

Dose, from fifteen grains to a drachm (1–3.9 Gm.) three times a day.

EXTRACTUM VIBURNI PRUNIFOLII. U. S.

EXTRACT OF VIBURNUM PRUNIFOLIUM Ext. Viburn. Prun. [Powdered Extract of Viburnum Prunifolium]

(ĕx-trăc'tŭm vī-bŭr'nī pru-nĭ-fō'lĭ-ī)

"*One gramme* of the Extract represents *five grammes* of viburnum prunifolium." *U. S.*

* "Virburnum Prunifolium, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Magnesium Oxide, *five grammes* [or 77 grains]; Starch, dried at 100° C. (212° F.), Diluted Alcohol, each, *a sufficient quantity,* to make *two hundred grammes* [or 7 ounces av., 24 grains]. Moisten the powder with sufficient diluted alcohol and pack it in a cylindrical percolator; then add enough diluted alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, adding diluted alcohol as required until the viburnum prunifolium is exhausted. Recover the alcohol from the percolate by distillation at as low a temperature as practicable and evaporate the residue to a soft extract in a shallow dish on a water bath, at a temperature not exceeding 70° C. (158° F.). Add the magnesium oxide, incorporate it thoroughly, spread the extract on glass plates and dry it by exposure to currents of warm air. Reduce the extract to a fine powder, weigh it, and add sufficient of the dried starch to make the finished product weigh *two hundred grammes* [or 7 ounces av., 24 grains]. Mix the powder thoroughly, pass the Extract through a fine sieve, transfer it to small, wide-mouthed bottles and stopper them tightly." *U. S.*

Dose, five to ten grains (0.3–0.65 Gm.).

FEL BOVIS. U. S.

OXGALL

(fĕl bō'vĭs)

"The fresh bile of the ox, *Bos taurus* Linné (Fam. *Bovidæ*)." *U. S.*

Fel Bovinum, Fel Tauri, Bilis Bubula, Ox Bile; Bile de Bœuf, *Fr. Cod.*; Ochsengalle, Rindsgalle, *G.*; Hiel de toro, *Sp.*

Crude oxgall is rarely used for medical purposes. It is, however, frequently employed for various technical purposes, especially for cleaning cloth.

Chemical researches of a very thorough character have thrown much light on the subject of the constituents of gall. The most characteristic constituents of all galls, of whatever origin, are, first, the sodium or potassium salts of certain resinous acids known collectively as the "gall

acids," and, secondly, certain coloring matters known as "gall pigments." The gall acids thus far made known as *glycocholic acid,* $C_{26}H_{43}NO_6$; *taurocholic acid,* $C_{26}H_{45}NSO_7$; *hyoglycocholic acid,* $C_{27}H_{43}NO_5$; *hyotaurocholic acid,* $C_{27}H_{45}NSO_6$; and *chenotaurocholic acid,* $C_{29}H_{49}NSO_6$. Of these, the first two occur in oxgall as sodium salts, although sometimes (in green gall) the first one is absent. The solutions of these gall acids, as well as their alkaline salts, give on addition of sugar and a drop of sulphuric acid a clear and strong purplish-red color. (*Pettenkofer's bile test.*) Drechsel modifies Pettenkofer's test as follows. Add to the concentrated alkaline solution of the biliary salts syrupy phosphoric acid. Next add a little cane sugar, and heat the test tube by setting it in the neck of a flask containing boiling water. After a short heating a characteristic red or reddish-violet color will make its appearance, even if only traces of biliary acids are present. (*N. R.,* 1882, p. 120.)

The gall pigments are such unstable organic coloring matters that their individuality cannot be said to be thoroughly established. The researches of Staedeler (*Verhand. d. Naturf. Ges. in Zürich,* 8) and R. Maly (*Ann. Ch. Ph.,* 132, 129) have, however, given us a better knowledge of them. They are *bilirubin,* $C_{32}H_{36}N_4O_6$; *biliverdin,* $C_{32}H_{36}N_4O_9$; *bilifuscin,* $C_{16}H_{20}N_2O_4$; and *biliprasin,* $C_{16}H_{22}N_2O_6$. Of these, the first two seem to exist originally in the gall, and the others are probably derived from them. Hoppe-Seyler (*Ber. d. Chem. Ges.,* vii, p. 1065) has shown that the hemoglobin and hematin of the blood can be changed into hydrobilirubin, a derivative of bilirubin, so that the origin of these gall pigments seems to be clearly shown. Oxgall contains, in addition, cholesterin, choline, urea, fats, which are the glycerides of acetic and propionic acids, mucus and some inorganic salts, such as sodium and potassium chlorides, and sodium, potassium, calcium, and magnesium phosphates. Bile as secreted from the liver has a specific gravity of about 1.010, and contains from 1 to 3 per cent. of solid matters; in the gall-bladder, however, it becomes more concentrated and has approximately the following composition: Specific gravity, 1.025 to 1.040; total solids, 14 to 29 per cent.; glycocholates and taurocholates, 9 to 12 per cent.; cholesterin, 1.5 to 4 per cent.; lecithin and fats, 1 to 5 per cent.; soaps, 0.2 to 3 per cent.; mucin and protein matters, 2 to 4 per cent.; bile pigments, bilirubin, biliverdine, small amounts. The *sodium glycocholate* and *taurocholate* may be separated in the following manner. Dry ox bile is treated with absolute alcohol, and the tincture precipitated by ether in excess. Both salts are deposited, and the glycocholate crystallizes upon standing, the taurocholate remaining in an amorphous form, resembling oily or resinous matter. They may be separated more completely by taking advantage of their different relations to lead acetate and subacetate. Both the acids are precipitated by the subacetate, the glycocholate only by the acetate. If the deposit above referred to be dissolved in water, solution of lead acetate will throw down a lead glycocholate, while the addition of the lead subacetate to the remainder will precipitate the taurocholate. The acids may be separated from the salts of lead by sulphuric acid, and then recombined with soda.

Properties.—"A brownish-green or dark green, somewhat viscid liquid, having a characteristic odor, and a disagreeable, bitter taste. When Oxgall is shaken with water a frothy mixture is produced. Specific gravity: 1.015 to 1.025 at 25° C. (77° F.). It is neutral or faintly alkaline to litmus. A mixture of 2 drops of Oxgall and 10 mils of water, when treated, first with a drop of a freshly prepared solution of 1 part of sugar in 4 parts of water, and afterwards with sulphuric acid, cautiously added, until the precipitate first formed is redissolved, gradually acquires a brownish-red color, changing successively to carmine, purple, and violet." *U. S.*

For uses see *Extractum Fellis Bovis,* p. 450.

Off. Prep.—Extractum Fellis Bovis, *U. S.;* Fel Bovinum Purificatum, *Br.*

FERRI CARBONAS SACCHARATUS.

U. S., Br.

SACCHARATED FERROUS CARBONATE
Ferr. Carb. Sacch.

(fĕr'rī căr'bo̤-năs săc-ca̤ha̤-rā'tŭs)

"Saccharated Ferrous Carbonate contains not less than 15 per cent. of $FeCO_3$ (115.84). Preserve it in small, well-stoppered bottles, exposed to light." *U. S.* "Saccharated Iron Carbonate is ferrous carbonate, more or less oxidised, mixed with glucose. Contains not less than 50 per cent. of ferrous salts calculated as ferrous carbonate, $FeCO_3$." *Br.*

Saccharated Iron Carbonate; Saccharated Carbonate of Iron; Carbonas Ferrosus Saccharatus; Saccharure de Carbonate Ferreux, *Fr.;* Ferrum Carbonicum Saccharatum, *P. G.;* Zuckerhaltiges Kohlensaures Eisen, Zuckerhaltiges Ferrocarbonat, *G.*

* "Ferrous Sulphate, *fifty grammes* [or 1 ounce av., 334 grains]; Sodium Bicarbonate, *thirty-five grammes* [or 1 ounce av., 103 grains]; Sugar of Milk, *ten grammes* [or 154 grains]; Sugar, in fine powder, Diluted Sulphuric Acid, Distilled Water, each, *a sufficient quantity,* to make, *one hundred grammes* [or 3 ounces av., 231 grains]. Dissolve the ferrous sulphate in *two hundred mils* [or 6 fluidounces, 366 minims] of hot distilled water, add a few drops of diluted sulphuric acid and filter. Dissolve the sodium bicarbonate in *five hundred mils* [or 16 fluidounces, 435 minims] of distilled water at a temperature not exceeding 50° C. (122° F.), and filter. To the solution of sodium bicarbonate, contained in a flask having a capacity of about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] gradually add the solution of ferrous sulphate, and mix thoroughly by rotating the flask. Fill the flask with boiling distilled water, cork it loosely, and set the mixture aside. When the precipitate has subsided, draw off the clear supernatant liquid by means of a siphon; fill the

flask again with hot distilled water and shake it. Again draw off the clear liquid, and repeat the washing with hot distilled water, in the same manner, until the decanted liquid gives merely a slight cloudiness with barium chloride T.S. Drain the precipitate, and transfer it to a porcelain dish containing *seventy grammes* [or 2 ounces av., 205 grains] of sugar and *ten grammes* [or 154 grains] of sugar of milk and mix intimately. Evaporate the mixture to dryness on a water bath, reduce it to powder, weigh, and mix intimately with it, if necessary, enough well-dried sugar to make the product weigh *one hundred grammes* [or 3 ounces av., 231 grains]. To minimize oxidation make this preparation in the shortest possible time." *U. S.*

"Ferrous Sulphate, 97.5 *grammes;* Glucose, 30.0 *grammes;* Sodium Carbonate, 105.0 *grammes;* Distilled Water, boiling, *a sufficient quantity.* Dissolve fifteen *grammes* of the Glucose in three hundred *millilitres* of the Distilled Water, and dissolve the Ferrous Sulphate in the solution. Dissolve the Sodium Carbonate in one hundred and fifty *millilitres* of the Distilled Water, and to this add the solution of the Ferrous Sulphate, stirring constantly. Then add four hundred *millilitres* of the Distilled Water, mix thoroughly, and allow the precipitate to subside. Decant the supernatant liquid, and wash the precipitate with two successive quantities, each of four hundred *millilitres,* of the Distilled Water. Mix the washed precipitate with the remainder of the Glucose, and dry at a temperature not exceeding 100° C. (212° F.). Powder the product, and preserve it in a stoppered bottle." *Br.*

This was introduced into the U. S. P. in 1880; the process is identical with that of the former German Pharmacopœia. When solutions of ferrous sulphate and sodium carbonate are mixed together, there are formed, by double decomposition, sodium sulphate which remains in solution, and ferrous carbonate which falls as a pale-blue precipitate. This precipitate begins immediately to alter in nature by the absorption of oxygen, and, if washed and dried in the ordinary way, becomes ferric oxide, associated with a small quantity of the ferrous carbonate, which has escaped change. As the preparations of iron containing ferrous oxide are the most esteemed, the change which this precipitate undergoes has always been a matter of regret, and various attempts have been made to prevent it. Saccharine matter has been ascertained to possess the required preservative properties, and in the preparation under consideration it is used to prevent the ferrous carbonate as first precipitated from passing into the ferric hydroxide.

Becker, a German physician, was the first to suggest the use of saccharine matter as a means of protection against the absorption of oxygen, and the idea was carried out by Klauer, a German chemist, who first made the saccharated ferrous carbonate. The use of boiling distilled water in the process is to avoid the action of the air contained in unboiled water. The washed precipitate is pressed so as to free it from water as far as possible, and then incorporated with the sugar in fine powder. The mode of treating the precipitate unnecessarily exposes it to the action of the air, and the late London method of incorporating it with the sugar immediately after washing was on this account preferable. The final drying temperature should not exceed 54.5° C. (130° F.).

Properties.—"Saccharated Ferrous Carbonate is a greenish-brown powder, gradually becoming oxidized by contact with air; odorless, and having at first a sweetish, afterwards slightly ferruginous, taste. Saccharated Ferrous Carbonate is only partially soluble in water, but is completely dissolved on the addition of hydrochloric acid, with copious evolution of carbon dioxide, forming a clear, greenish-yellow liquid. Dissolve 1 Gm. of Saccharated Ferrous Carbonate in 5 mils of hydrochloric acid, and dilute the solution with distilled water until it measures 100 mils. Portions of this solution yield a blue precipitate with either potassium ferrocyanide T.S. or potassium ferricyanide T.S.; another 10 mil portion of the solution shows not more than a slight turbidity with barium chloride T.S. (*sulphate*).

"**Assay.**—Dissolve about 2 Gm. of Saccharated Ferrous Carbonate, accurately weighed, in 15 mils of diluted sulphuric acid, and dilute the solution with distilled water to about 100 mils. Titrate immediately with tenth-normal potassium dichromate V.S., potassium ferricyanide T.S being used as indicator. It shows not less than 15 per cent. of $FeCO_3$.

"Each mil of tenth-normal potassium dichromate V.S used corresponds to 0.011584 Gm. of $FeCO_3$. Each gramme of Saccharated Ferrous Carbonate corresponds to not less than 13 mils of tenth-normal potassium dichromate V.S." *U. S.*

"A greenish-brown powder, with a feebly chalybeate taste. Soluble with effervescence in *hydrochloric acid* diluted with half its volume of *water.* 1 gramme, dissolved in excess of warm *concentrated phosphoric acid* and diluted with *water,* does not cease to yield a blue precipitate with *solution of potassium ferricyanide* until 43.1 millilitres of *N/10 solution of potassium bichromate* have been added. *Arsenic limit* 5 parts per million." *Br.*

Saccharated ferrous carbonate is sometimes seen in small coherent lumps, usually of a grayish-brown color, permanent in the air, having a sweet, styptic taste, and wholly and readily soluble in warm hydrochloric acid, diluted with half its volume of water, with effervescence. The presence of ferric oxide is a defect, which is avoided in Vallet's ferruginous mass.

Uses.—This preparation is an excellent chalybeate, possessing the advantages of having nearly all the iron in it in the ferrous state, and of being readily soluble in acids. Originally introduced into the official list by the Edinburgh College, it appeared for the first time in the Dublin and London Pharmacopœias

of 1850 and 1851. It is undoubtedly more active than the ferric subcarbonate, and must be used in a smaller dose. It is, however, inferior to Vallet's ferruginous mass, in the preparation of which the anti-oxidizing influence of saccharine matter is much more fully applied.

Dose, of the saccharated ferrous carbonate, from five to fifteen grains (0.32–1.0 Gm.), given in pills.

FERRI CHLORIDUM. U. S.

FERRIC CHLORIDE Ferr. Chlor. [Iron Perchloride, Sesquichloride of Iron]

(fĕr'rī ȼhlō'rī-dŭm)

"It contains $FeCl_3$ (162.22) in a hydrated form corresponding to not less than 20 per cent. of Fe. Preserve it in well-closed glass containers." *U. S.*

Perchloride of Iron, Chloride of Iron; Ferrum Muriaticum Oxydatum, Chloridum vel Chloruretum Ferricum, Ferri Perchloridum; Chlorure ferrique, *Fr. Cod.*; Perchlorure de Fer, *Fr.*; Ferrum Sesquichloratum, *P. G.*; Eisenchlorid, *G.*; Cloruro ferrico, *Sp.*

The U. S. P. IX does not give a process for preparing ferric chloride; the U. S. P. VIII process is appended.

* "Solution of Ferric Chloride, *one hundred grammes* [or 3 ounces av., 231 grains], to make *forty grammes* [or 1 ounce av., 180 grains]. Evaporate the Solution of Ferric Chloride on a water-bath until it weighs *forty grammes* [or 1 ounce av., 180 grains]; then set it aside in a glass-covered vessel, until it forms a crystalline mass. Lastly, break the salt into pieces, and keep it in glass-stoppered bottles, protected from light." *U. S. VIII.*

The U. S. P. VIII did not give a process for making this salt directly from metallic iron, but simply evaporated the official solution of ferric chloride. The former U. S. P. directed a process which had been adopted with but little alteration from that of Wittstein. When iron is heated with hydrochloric acid, water is decomposed, the hydrogen escapes with effervescence, and the oxygen uniting with the iron forms ferrous oxide, which reacts with the hydrochloric acid to form water and ferrous chloride. The next step of the process is to convert the ferrous chloride into the ferric salt. This is effected by treating it with hydrochloric and nitric acids and heating until red fumes no longer escape. The following reaction explains this:

$$6FeCl_2 + 2HNO_3 + 6HCl = 6FeCl_3 + 2NO + 4H_2O$$

The solution is then evaporated, and, on cooling, concretes into a crystalline mass. The relative proportions of iron and the two acids are adjusted very nearly to the production of these results. There are two crystallized chlorides, one, $FeCl_3 + 3H_2O$, which is very deliquescent, the other, $FeCl_3 + 6H_2O$, which is less so, but which, when allowed to stand over sulphuric acid, liquefies and slowly deposits crystals of the first chloride, $FeCl_3 + 3H_2O$, losing half of its water of hydration.

Properties.—"Ferric Chloride occurs in orange-yellow, crystalline pieces, odorless, or with a faint odor of hydrochloric acid, and having a strongly styptic taste. It is very deliquescent in air. One Gm. of Ferric Chloride dissolves in 0.2 mil of water at 25° C. (77° F.); freely soluble in alcohol and soluble in glycerin or ether. At about 35.5° C. (95.9° F.) the salt fuses to a reddish-brown liquid. When strongly heated, it decomposes, losing some ferric chloride, water and hydrochloric acid, and leaving a residue of ferric oxide. An aqueous solution of Ferric Chloride, made by dissolving 10 Gm. of the salt in 15 mils of distilled water, responds to the tests for identity and purity under *Liquor Ferri Chloridi,* omitting the test for hydrochloric acid.

"**Assay.**—Dissolve about 1 Gm. of Ferric Chloride, accurately weighed in a stoppered weighing-bottle, in 25 mils of distilled water, add 3 mils of hydrochloric acid and 4 Gm. of potassium iodide, and allow the mixture to stand in a glass-stoppered flask or bottle for thirty minutes at a temperature of 40° C. (104° F.). Cool this solution, then dilute it with 100 mils of distilled water and titrate with tenth-normal sodium thiosulphate V.S., using starch T.S. as indicator. It shows not less than 20 per cent. of Fe.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.005584 Gm. of Fe. Each gramme of Ferric Chloride corresponds to not less than 35.8 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

It contains a variable proportion of water according to the crystalline forms it is made to assume, having about 40 per cent., or six molecules, when in fine acicular crystals, and only 22 per cent., or two and a half molecules, when in the form of larger tables.

Syrup of Ferrous Chloride.—Dissolve 5 grammes of dry ferrous chloride in 20 grammes of orange-flower water, and add 800 grammes syrup of gum and 175 grammes syrup of orange-flower. (See *Syrupus Ferri Protochloridi,* N. F. IV, Part III.)

Pills of Ferrous Chloride.—Dry ferrous chloride, powdered marshmallow-root, each 10 grammes, mucilage sufficient. Make into 100 pills, which are to be silvered.

Syrupus Ferri Chloridi (Edel). *Syrup of Iron Chloride.*—Take of Solution of Chloride of Iron (U. S. P.), 208 minims; Potassium Citrate, 224 grains; Citric Acid, 60 grains; Water, 8 fluidounces; Glycerin, 5 fluidounces; Syrup, 16 fluidounces. Dissolve the potassium citrate and citric acid in the water, add the iron solution, and when the reaction ceases filter the solution, then add the glycerin and syrup. (*D. C.,* 1894, 246.)

Tasteless Iron Chloride is made by adding an alkaline citrate in solution to a solution of iron sesquichloride, in such proportion that there shall be two molecules of the former and three molecules of chlorine. Usually from 120 to 140 grains of citric acid saturated with sodium hy-

droxide, potassium hydroxide, or ammonium hydroxide are required for the preparation of an ounce of a tincture of corresponding strength to the official tincture. The addition should be made to the liquor, and the final solution must not contain more than 40 per cent. of alcohol. R. Rother affirms that these so-called salts are mere mixtures of iron citrate and iodide or chloride of the alkali used. (See *Tinctura Ferri Citro-Chloridi*, N. F., Part III.)

Ferric chloride is incompatible with alkalies and with iodides and bromides from which it liberates the halogen elements.

Uses.—Ferric chloride is used almost exclusively in the form of tincture or liquor, and in reference to its effect and application we refer to *Tinctura Ferri Chloridi* and *Liquor Ferri Chloridi*. Excepting deliquescence, it keeps without change. When used, it may be dissolved in water in such proportions as may be required. Six, three, two, and one and a half drachms to a fluidounce of water have been recommended, the stronger solutions being used in the treatment of *varices*, the weaker for injection into *aneurisms*, and for application to *bleeding surfaces*, etc. J. Z. Lawrence, of England, has used it as a styptic in a semi-deliquescent state, and found it extremely efficient. He keeps it in a bottle, in which it gradually deliquesces, and applies the thick liquid portion, with a brush of spun glass, to the bleeding surface.

Dose, one grain (0.065 Gm.).

FERRI ET AMMONII CITRAS. U. S., Br.

IRON AND AMMONIUM CITRATE Ferr. et Ammon. Cit. [Ammonio-Ferric Citrate, Soluble Ferric Citrate]

(fĕr′rī ĕt ăm-mō′nī-ī cī′trās)

"Ferric citrate rendered more readily soluble by the presence of ammonium citrate and containing not less than 16 per cent. nor more than 18 per cent. of Fe. Preserve it in well-closed containers, protected from light." *U. S.*

Citrate of Iron and Ammonia; Ferri et Ammoniæ Citras, *Br.* 1867; Ferrum Citricum Ammoniatum, Ferri Ammonio-Citras, Ferro-Ammonium Citricum; Ammonio-Citrate of Iron, Soluble Citrate of Iron; Citrate de Fer et d'Ammoniaque (de Fer ammoniacal), *Fr. Cod.*; Citrate Ferrique Ammoniacal, *Fr.*; Citronensaures Eisenoxyd-Ammonium (Ammoniak), Ferriammoniumcitrat, *G.*; Citrato ferricoammonico, *Sp.*

No process is given in the U. S. P. IX for Iron and Ammonium Citrate. The British Pharm., 1914, process is as follows: "Solution of Ferric Sulphate, 200 *millilitres;* Solution of Ammonia, 460 *millilitres*, or *a sufficient quantity;* Citric Acid, 80 *grammes;* Distilled Water, *a sufficient quantity*. Prepare ferric hydroxide as follows:—Mix three hundred and twenty millilitres of the Solution of Ammonia with eight hundred millilitres of Distilled Water; gradually add to this the Solution of Ferric Sulphate, previously diluted with eight hundred millilitres of Distilled Water; stir constantly and briskly, taking care that ammonia is, finally, in slight excess as indicated by the odor; set aside the mixture for two hours, stirring it occasionally; pour it on a calico filter; when the liquid has drained away, wash the precipitated ferric hydroxide with Distilled Water until free from sulphates. Dissolve the Citric Acid in its own weight of Distilled Water; warm the mixture on a water-bath; add the ferric hydroxide, previously well drained; stir them together until nearly the whole of the hydroxide has dissolved, or until the Citric Acid is saturated with ferric hydroxide (prepared, if necessary, from more of the Solution of Ferric Sulphate); let the solution cool; add one hundred and ten millilitres of Solution of Ammonia; filter through flannel, adding some Distilled Water if necessary, evaporate to the consistence of syrup, the presence of a very slight excess of ammonia being maintained; dry in thin layers on flat porcelain or glass plates at a temperature not exceeding 40° C. (104° F.); remove the dry flakes of Iron and Ammonium Citrate." *Br.*

In the U. S. Pharmacopœia, 1890, the process consisted simply in evaporating a mixture of solution of ferric citrate and ammonia water. In the British, ferric hydroxide is first precipitated from a solution of the ferric sulphate, then digested at a moderate heat with a solution of citric acid, and lastly neutralized by ammonia. It has, however, been found by E. R. Squibb that a heat above 82.1° C. (180° F.) acts injuriously in the preparation of the ferric citrate, and the boiling heat directed in the British Pharmacopœia of 1864 was, therefore, improper. (*A. J. P.*, xxvii, 297.) This error has been corrected in the present Br. Pharmacopœia, which directs that the salt should be dried at a heat not above 38° C. (100.4° F.). In the U. S., 1890, formula the ferric citrate was used already prepared, in the British it is prepared in the process. The solution should be concentrated to a syrupy consistence before being poured out on porcelain or glass to dry, and it is important that the heat employed in the concentration should not exceed that indicated. Like most of the scaled iron salts, this preparation is not a true chemical compound, the ammonia not being in the proportion to form a double salt.

J. U. Lloyd (*N. R.*, 1879, 323) states that it is usually difficult to adjust accurately the quantity of the ammonia in this process, and proposes to use a definite quantity of a fixed salt, like ammonium citrate, instead. Thus: Prepare a solution of ammonium citrate from citric acid, 8 oz. av., and ammonia water q. s. Add the ammonia water to the citric acid until in slight excess, then evaporate the solution until it measures sixteen fluidounces. Then take of solution of iron tersulphate 16 fluidounces; citric acid 4 ounces av.; distilled water and ammonia water, each, a sufficient quantity; solution of ammonium citrate 5 fluidounces. Prepare hydrated ferric oxide from the solution of iron tersulphate. Having drained it, place in an evaporating dish and add the citric acid, warm upon a steam or water bath, and stir until the citric

acid is dissolved, then add the solution of ammonium citrate and stir until the hydrated oxide is dissolved, filter and evaporate to the consistence of thick syrup, spread upon glass with a brush, and dry. The yield will be 4234 grains.

R. Rother recommends the following method: Dissolve 272 parts of ferric citrate in three or four times its weight of water with heat, add 79 parts of ammonium carbonate, evaporate, and scale in the usual manner. (*A. J. P.*, 1887, p. 166.)

Properties.—Iron and ammonium citrate is more soluble than the ferric citrate. It is in "thin, transparent, garnet-red scales, odorless and having a saline, mildly ferruginous taste. It is deliquescent in moist air. Iron and Ammonium Citrate is readily and completely soluble in water; insoluble in alcohol. An aqueous solution (1 in 20) is neutral or but slightly acid or alkaline to litmus. When strongly heated, it chars, and finally leaves a residue of ferric oxide. Heat Iron and Ammonium Citrate with potassium hydroxide T.S.; it yields a brownish-red precipitate, and ammonia is evolved. Ammonia water, added to an aqueous solution, produces no precipitate, but darkens the solution. Remove the iron from 10 mils of an aqueous solution of Iron and Ammonium Citrate (1 in 10) by boiling it with an excess of potassium hydroxide T.S., filter, and then slightly acidulate the filtrate with acetic acid. A portion of the cooled filtrate, when mixed with 2 mils of calcium chloride T.S., and again heated to boiling, gradually deposits a white crystalline precipitate. Another portion of the filtrate, when acidulated more strongly with acetic acid and allowed to stand for twenty-four hours, does not yield a white crystalline precipitate (*tartrate*). An aqueous solution of Iron and Ammonium Citrate (1 in 100) does not yield a blue precipitate with potassium ferrocyanide T.S. unless it is acidulated with hydrochloric acid (difference from *ferric citrate*).

"**Assay.**—Dissolve about 1 Gm. of Iron and Ammonium Citrate, accurately weighed, in 25 mils of distilled water and 7 mils of hydrochloric acid, in a glass-stoppered flask or bottle, add 4 Gm. of potassium iodide, stopper the bottle securely and keep it at a temperature of 40° C. (104° F.) for thirty minutes. Then cool, and titrate with tenth-normal sodium thiosulphate V.S., using starch T.S. as indicator. It shows not less than 16 per cent. nor more than 18 per cent. of Fe.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.005584 Gm. of Fe. Each gramme of Iron and Ammonium Citrate corresponds to not less than 28.6 mils nor more than 32.2 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

"In thin, dark red, transparent scales. Taste slightly sweet and astringent. Soluble in 0.5 part of *water;* almost insoluble in *alcohol* (90 per cent.). Aqueous solution slightly acid to *litmus.* Yields from 31 to 32 per cent. of ash, which, when moistened with *water,* is not alkaline to *litmus* (absence of fixed alkali). When a solution of 1 gramme in 10 millilitres of *water* is heated with a slight excess of *solution of potassium hydroxide,* ammonia is evolved and ferric hydroxide is precipitated; the filtrate from this, acidified with *acetic acid,* does not yield any crystalline precipitate (absence of tartrates). Yields not more than the slightest characteristic *reaction* for sulphates. *Arsenic limit* 5 parts per million." *Br.*

Its precise chemical constitution is not determined; but Méhu (*Jahresb.*, 1873, 570), on evaporating a solution of ferrous citrate in ammonia to dryness, obtained a salt of the formula $Fe_2(NH_4)_2.(C_6H_5O_7)_2 + 3H_2O$.

Uses.—This salt is a pleasant chalybeate, in doses of five grains (0.32 Gm.). According to Paris, it may be mixed with the carbonated alkalies without decomposition, and given in a state of effervescence with citric acid. It should be prescribed only in solution, as it is not suited for administration in the form of pills, owing to the presence of ammonia, which renders it too soluble, and causes the pills to flatten after they have been made, and frequently to cohere in one solid mass. The official ferric citrate should always be used for pills, as it is more slowly dissolved.

Dose, from three to eight grains (0.2–0.5 Gm.).

Off. Prep.—Vinum Ferri Citratis, *Br.;* Vinum Carnis et Ferri, *N. F.;* Vinum Ferri, *N. F.*

FERRI ET POTASSII TARTRAS. Br.

IRON AND POTASSIUM TARTRATE

(fĕr'rī ĕt pǫ-tăs'sĭ-ī tăr'trăs)

Ferrum Tartaratum, *Br.;* Tartarated Iron; Potassio-Ferric Tartrate; Ferri Potassio-Tartras, Ferrum Tartarizatum, Tartras Ferrico-Potassicus, s. Potassico-Ferricus, s. Ferrico-Kalicus, Ferri-Kalium Tartaricum; Tartarated (tartarized) Iron, Ferro-Tartrate of Potassium; Tartrate Ferrico-potassique, *Fr. Cod.;* Tartrate de Fer et de Potasse, Tartare Chalybé, Tartre martial, *Fr.;* Kaliumferritartrat, Weinsäures Eisenoxyd-Kali, Eisenweinstein, *G.;* Tartrato ferrico-potasico, *It.;* Tartrato ferrico-potasico, *Sp.*

The U. S. P. IX does not recognize this salt; the process of the 1890 Pharmacopœia will be found in the *U. S. Dispensatory,* 19th edition, page 499. The rubric requirement of the U. S. P. VIII is as follows: "It should contain Iron and Potassium Tartrate corresponding in amount to not less than 15 per cent. of metallic iron, and should be kept in well-stoppered bottles, protected from light." *U. S. VIII.*

The British process is as follows: "Solution of Ferric Sulphate, 200.0 *millilitres;* Solution of Ammonia, 320.0 *millilitres,* or *a sufficient quantity;* Acid Potassium Tartrate in powder, 66.5 *grammes;* Distilled Water, *a sufficient quantity.* From the Solution of Ferric Sulphate prepare ferric hydroxide as directed under 'Ferri et Ammonii Citras,' page 465. Mix the ferric hydroxide intimately with the Acid Potassium Tartrate in a porcelain dish; let the mixture stand for twenty-four hours; heat to a temperature not exceeding 60° C. (140° F.), add gradually six hundred *millilitres* of Distilled Water;

stir constantly until nothing more will dissolve; filter; evaporate at a temperature not exceeding 60° C. (140° F.) to the consistence of syrup; dry in thin layers on flat porcelain or glass plates at a temperature not exceeding 40° C. (104° F.); remove the dry flakes of Iron and Potassium Tartrate." *Br.*

The object of this process was to combine the excess of acid in the potassium bitartrate with ferric hydroxide. The plan of Soubeiran in the main was adopted—namely, that of dissolving the moist ferric hydroxide to saturation in a mixture of the bitartrate and water, aided by a moderate heat. The oxide is obtained from the solution of ferric sulphate, which is precipitated by ammonia. Potassium hydroxide, which was used in the former British process, is not a good precipitant, because the alkali adheres obstinately to the precipitated oxide, and cannot be completely separated even by repeated washings. The oxide should be gradually added to the bitartrate and water, heated to 60° C. (140° F.), as recommended by Soubeiran, at which temperature the oxide dissolves more readily and in larger quantity than when a higher temperature is employed. Besides, in the latter case, a portion of the ferric oxide is converted into ferrous oxide. In the U. S., 1890, process the addition of ammonia water to the cooled filtrate dissolves the precipitated insoluble ferric tartrate, and is in accordance with the recommendation of J. U. Lloyd, who asserts that this modification renders the salt more soluble without interfering with its stability. G. H. Chas. Klie suggested this improvement in *A. J. P.*, 1876, p. 170. (See also *N. R.*, 1878, p. 21.) In both formulas the liquid is poured out on a plane surface so as to dry in scales. When duly carried into effect, they yield a product at all times identical, and having all the required qualities of the salt. W. Lyon (*P. J.*, 1902, 530) proposes to substitute potassium and sodium tartrate for the acid potassium tartrate used in the British Pharm. process, believing that the resulting scaled salt will retain its ready solubility for a much longer time than will the official preparation; he uses the following proportions: Solution of ferric sulphate 300 mils; solution of ammonia 480 mils or a sufficient quantity; potassium and sodium tartrate 176 Gm. The official process and directions are otherwise followed. For Roger's process for this salt and the manufacture of *Boules de Mars* (balls of iron and potassium tartrate), see *U. S. D.*, 17th ed., 611.

Ure proposed *ferrous tartrate* for medicinal use. He made it by acting on clean iron filings, or bits of iron wire, with a solution of tartaric acid. It is a pulverulent salt, insoluble in water, and possessing a mild chalybeate taste.

Properties.—Iron and potassium tartrate, according to the U. S. P. VIII, is in "thin, transparent scales, varying in color from garnet-red to reddish-brown, without odor, and having a sweetish, ferruginous taste; slightly deliquescent in the air. Very soluble in water; insoluble in alcohol. When strongly heated, the salt chars, emits fumes having an odor resembling that of burning sugar, and finally leaves a dark brown residue, having a strongly alkaline reaction, and effervescing with acids (distinction from *iron and ammonium tartrate*). An aqueous solution of Iron and Potassium Tartrate should be neutral to litmus paper, and is not precipitated, but rendered darker in color, by ammonia water. With potassium ferrocyanide T.S. the solution does not afford a blue color or precipitate, unless it be acidulated with hydrochloric acid. When heated with potassium hydroxide T.S., the salt yields a brownish-red precipitate. If an aqueous solution of the salt (1 in 10) be deprived of its iron by boiling with an excess of potassium hydroxide T.S., the filtrate, when slightly acidulated with acetic acid, will gradually deposit a white, crystalline precipitate. If 0.555 Gm. of the dry salt be dissolved in 15 Cc. of water and 2 Cc. of hydrochloric acid, in a glass-stoppered flask having a capacity of about 100 Cc., and if, after the addition of 1 Gm. of potassium iodide, and securely closing the flask, the mixture be kept for half an hour at 40° C. (104° F.), and then cooled, it should require not less than 15 Cc. of tenth-normal sodium thiosulphate V.S. to discharge the color of the liquid, starch T.S. being used as indicator (each Cc. of tenth-normal sodium thiosulphate V.S. indicating 1 percent. of metallic iron)." *U. S. VIII.*

"In thin transparent scales of a deep garnet color; taste somewhat sweetish and astringent. Soluble in *water,* sparingly soluble in *alcohol* (90 per cent.). *Arsenic limit* 5 parts per million. The aqueous solution, acidified with *hydrochloric acid,* yields a copious blue precipitate with *solution of potassium ferrocyanide.* When a solution of 1 gramme in 10 millilitres of *water* is boiled with a slight excess of *solution of potassium hydroxide,* a reddish-brown precipitate separates, and the filtered solution, slightly acidified with *acetic acid,* yields, as it cools, a crystalline deposit. Yields not less than 30 per cent. of ferric oxide when incinerated with free access of air, the ash being washed with *water* and again incinerated." *Br.*

According to the view of its nature taken in the U. S. Pharmacopœia VIII, it is a double salt, consisting of one molecule of ferric tartrate and one of potassium tartrate:

$$Fe_2(C_4H_4O_6)_3 + K_2C_4H_4O_6 + H_2O$$

Flückiger (*Pharmaceutische Chemie,* 2d ed., 573, 188), on the other hand, considers the salt formed to be one in which Fe_2O_2 is present as a bivalent group, and gives it the formula:

$$C_4H_4O_6K_2 + C_4H_4O_6(Fe_2O_2) + 4H_2O$$

The salt is incompatible with astringent vegetable infusions, which give rise to a dark-colored precipitate.

Uses.—Iron and potassium tartrate is a mild, agreeable chalybeate, with but little astringency. It is well borne by the stomach, taken fasting or with the food. Its slight taste and ready

solubility make it one of the best ferruginous preparations for children.

Dose, for an adult, five to ten grains (0.32–0.65 Gm.), given preferably in solution.

FERRI ET QUININÆ CITRAS. U. S., Br.

IRON AND QUININE CITRATE Ferr. et Quin. Cit. [Ferri et Quininæ Citras Solubilis, U. S. P. VIII, Soluble Iron and Quinine Citrate]

(fĕr'ri ĕt quĭ-nī'næ cī'trăs)

"Iron citrate and quinine citrate rendered more soluble by the presence of ammonium citrate and containing not less than 11.5 per cent. of anhydrous quinine ($C_{20}H_{24}O_2N_2$) and not less than 13 per cent. of Fe. Preserve it in amber-colored, well-stoppered bottles, protected from light." *U. S.*

Ferri et Quiniæ Citras, *Br.* 1867, *U. S.* 1870; Citrate of Iron and Quinia; Citrate de Fer et de Quinine, *Fr.*; Chininum Ferro-Citricum, *P. G.*; Eisenchinincitrat, Citronensaures Eisen-Chinin, *G.*

The U. S. P. VIII contained two forms of iron and quinine citrate, one of which had the word "Solubilis" in the title; the U. S. P. IX abandoned the use of this word and dropped the less soluble compound entirely, retaining the soluble form under the title "Ferri et Quininæ Citras," which now corresponds with the same preparation of the British Pharm., 1914.

"Solution of Ferric Sulphate, 180 *millilitres;* Quinine Sulphate, 40 *grammes;* Diluted Sulphuric Acid, 60 *millilitres;* Citric Acid, 123 *grammes;* Solution of Ammonia, Distilled Water, of each, *a sufficient quantity.* From the Solution of Ferric Sulphate prepare ferric hydroxide as directed under 'Ferri et Ammonii Citras,' page 465. Mix the Quinine Sulphate with eight times its weight of Distilled Water; add the Diluted Sulphuric Acid; when the salt is dissolved precipitate the quinine with a slight excess of Solution of Ammonia; collect the precipitate on a filter; wash it with twelve hundred *millilitres* of Distilled Water. Dissolve the Citric Acid in its own weight of Distilled Water; warm the solution on a water-bath; add the ferric hydroxide, previously well drained; stir them together; when the hydroxide has dissolved, add the precipitated quinine; continue the stirring until this also has dissolved; let the solution cool; add, in small quantities at a time, sixty *millilitres* of Solution of Ammonia, diluted with eighty *millilitres* of Distilled Water; stir briskly, allowing the quinine which separates with each addition of ammonia to dissolve before the next addition is made; filter the solution; evaporate it to the consistence of a thin syrup; dry the latter in thin layers on flat porcelain or glass plates at a temperature not exceeding 40° C. (104° F.); remove the dry flakes of Iron and Quinine Citrate." *Br.*

The U. S. P. IX does not contain a process for soluble iron and quinine citrate; the U. S. P., 1890, process was as follows: "Ferric Citrate, *eighty-five grammes* [or 2 ounces av., 436 grains]; Quinine, dried at 100° C. (212° F.) to a constant weight, *twelve grammes* [or 186 grains]; Citric Acid, *three grammes* [or 46 grains]; Ammonia Water, Distilled Water, each, *a sufficient quantity,* to make *one hundred grammes* [or 3 ounces av., 231 grains]. Dissolve the Ferric Citrate in *one hundred and sixty cubic centimeters* [or 5 fluidounces, 197 minims] of Distilled Water, by heating on a water-bath at a temperature not exceeding 60° C. (140° F.). To this solution add the Quinine and Citric Acid previously triturated with *twenty cubic centimeters* [or 325 minims] of Distilled Water, and stir constantly until the Quinine and Citric Acid are dissolved. Then add gradually, and with constant stirring, *fifty cubic centimeters* [or 1 fluidounce, 331 minims], or *a sufficient quantity,* of Ammonia Water, so that, after the addition of each portion of the latter, the precipitated Quinine will be redissolved and the liquid acquire a greenish-yellow tint. Lastly, evaporate the solution on a water-bath, at a temperature not exceeding 60° C. (140° F.), to the consistence of syrup, and spread it on plates of glass, so that, when dry, the salt may be obtained in scales. Keep the product in well-stoppered bottles, protected from light." *U. S.*, 1890.

This official preparation was first added to the list in 1890, in answer to a demand which was very persistent. The iron and quinine citrate formerly official was comparatively insoluble and better adapted for use in pills; but the combination of iron, quinine, and citric acid is wanted more frequently in solution, and hence a salt which can be quickly dissolved is necessary.

The use of ferrous sulphate by the former British process was abandoned, and the solution of ferric sulphate retained. From this the freshly precipitated ferric hydroxide is obtained by precipitation with ammonia. The next step is to separate quinine from the sulphate, by simply dissolving the salt in water with the aid of sulphuric acid, and then precipitating by ammonia. Thirdly, the hydroxide and quinine are dissolved successively, aided by the heat of a water bath, in solution of citric acid, whereby an iron and quinine citrate is obtained. The ammonia is added in order to render the iron and quinine citrate more soluble by the agency of a portion of ammonium citrate. It is important that the ammonia should not be added in excess; on the contrary, the solution should retain a slight acid reaction. (Fleurot.) After evaporation, the salt is dried, as in the other process, on glass or porcelain, so as to be obtained in thin scales.

No analysis has been made that determines precisely the chemical composition of this "scaled salt." It is undoubtedly a mere mixture of the iron and quinine citrates, containing ammonium citrate.

Owing to the comparative cheapness of the alkaloid quinine at the present time the tendency to substitute other cinchona alkaloids has greatly diminished, and the introduction of an

official assay process furnishes an excellent check to these practices.

Amorphous quinine or chinoidine was sometimes substituted for the crystallizable alkaloid. For the detection of this fraud, de Vrij proposed a method which depended upon the fact that oxalic acid forms with crystallizable quinine, in a chloroformic solution, white crystals of quinine oxalate without discoloration. (See *N. R.*, 1881, 10.)

When dissolved by the aid of an acid, it forms a solution which, decolorized by a little purified animal charcoal, turns the plane of polarization strongly to the left—a character of quinine, cinchonine turning it to the right. (Squire.) The salt is said to be sometimes adulterated by cinchonine, which would be at once detected by the test of solubility in ether and the effect on polarized light, above given. Oscar Zinn (*A. J. P.*, 1877, 550), examined six commercial samples, two of which contained no quinine, but cinchonine. H. G. Drueding found three out of six samples deficient in quinine. As it occurs in the British market, it is of exceedingly variable composition, containing, according to J. C. Braithwaite, who examined thirty-five different specimens, a proportion of quinine varying from 1.5 to 17 per cent. (*P. J.*, 1868, 157.) The proportion of alkaloid appears to be usually below the standard. (A. W. Gerrard, *P. J.*, March, 1873, 763.) According to C. H. Wood (*P. J.*, 2d ser., x, 644), this salt undergoes a rapid change of composition when exposed to the influence of the direct rays of the sun.

The official process of assay will doubtless bring to light all shortcomings. (See results of examination of commercial iron and quinine citrate by E. C. Federer, *Proc. Mich. Pharm. Assoc.*, 1887, or *Ph. Era*, 1887, p. 357.)

Properties.—The U. S. Pharmacopœia IX describes it as in "thin, transparent scales, of a greenish or golden-yellow color, odorless, and having a bitter, mildly ferruginous taste. It is deliquescent. Iron and Quinine Citrate is rapidly and completely soluble in cold water, partly soluble in alcohol. An aqueous solution (1 in 10) is acid to litmus. When strongly heated, Iron and Quinine Citrate chars, and finally leaves a residue of ferric oxide. When heated with potassium hydroxide T.S., a brown precipitate is produced and ammonia is evolved. On the addition of a slight excess of ammonia water to an aqueous solution of Iron and Quinine Citrate (1 in 10), the color of the liquid is deepened, and a white, curdy precipitate is produced. A portion of the filtrate from this precipitate does not yield a blue color or precipitate with potassium ferrocyanide T.S. unless it is acidulated with hydrochloric acid. Boil an aqueous solution of Iron and Quinine Citrate (1 in 10) with an excess of potassium hydroxide T.S. until completely precipitated, and slightly acidulate the filtrate with acetic acid. A portion of the cooled filtrate, mixed with 2 mils of calcium chloride T.S. and again heated to boiling, gradually deposits a white, crystalline precipitate. Another portion of the filtrate, more strongly acidulated with acetic acid and allowed to stand for twenty-four hours, does not yield a white, crystalline precipitate (*tartrate*).

"**Assay for Quinine.**—Dissolve about 1 Gm. of Iron and Quinine Citrate, accurately weighed, in 20 mils of distilled water in a separator, add 5 mils of ammonia water and 10 mils of chloroform, and shake the separator for one minute. Allow the liquids to separate, draw off the chloroform layer through a small filter moistened with chloroform, into a tared dish, and shake the residuary liquid a second and a third time with portions of 10 mils each of chloroform, passing the chloroform through the filter each time and finally washing the filter with 5 mils of chloroform. Evaporate the combined chloroform solutions, redissolve the residue in 3 mils of alcohol, again evaporate and then dry the residue to constant weight at 100° C. (212° F.). This residue corresponds to not less than 11.5 per cent. of the amount of Iron and Quinine Citrate taken for the assay and conforms to the identity tests under *Quinina*.

"**Assay for Iron.**—Heat the aqueous liquid, from which the quinine has been removed in the manner just described, on a water bath, until the odors of chloroform and of ammonia have disappeared, allow to cool and dilute with distilled water to a volume of 25 mils. Transfer the liquid to a glass-stoppered bottle, add 15 mils of hydrochloric acid and 3 Gm. of potassium iodide, and, after securely closing the bottle, allow the mixture to stand for thirty minutes at 40° C. (104° F.). Then cool and titrate with sodium thiosulphate V.S., using starch T.S. as indicator. It shows not less than 13 per cent. of Fe.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.005584 Gm. of Fe. Each gramme of Iron and Quinine Citrate corresponds to not less than 23.3 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

The British Pharm., 1914, describes it as "in thin scales of a greenish-yellow color, somewhat deliquescent; taste bitter, chalybeate. Soluble in 0.5 part of *water*. The solution is very slightly acid, and yields precipitates which are reddish-brown with *solution of potassium hydroxide*, white with *solution of ammonia*, blue with *solution of potassium ferrocyanide*, and with *solution of potassium ferricyanide*. *Arsenic limit* 5 parts per million. Ash, when moistened with *water*, not alkaline to *litmus* (absence of fixed alkali). 5 grammes, dissolved in 45 millilitres of *water* and treated with excess of *solution of ammonia*, yield a white precipitate, which, when dissolved out by repeated treatment of the liquid with *chloroform*, the latter evaporated, and the residue dried at 110° C. (230° F.), weighs not less than 0.75 gramme. This precipitate is almost entirely soluble in a little *ether;* on incineration it leaves not more than a minute residue; neutralised with *diluted*

sulphuric acid and crystallised, it possesses the characters of and responds to the tests described under 'Quininæ Sulphas.'" *Br.*

See modification of process by F. A. Sieker (*Ph. Rund.*, 1895, 36).

Uses.—Preparations of this character are therapeutically irrational; if the hematinic effects of iron and the tonic action of quinine are desired simultaneously, it is far better to compose an extemporaneous mixture in which the proportion of each shall be regulated to the needs of the individual patient than resort to a fixed combination. Each five grains (0.3 Gm.) of the salt represents approximately one-half grain (0.032 Gm.) of quinine and two-thirds of a grain (0.036 Gm.) of iron.

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Vinum Ferri Amarum, *N. F.*

FERRI HYDROXIDUM CUM MAGNESII OXIDO. U. S.

FERRIC HYDROXIDE WITH MAGNESIUM OXIDE Ferr. Hydrox. cum Mag. Oxid.

(fĕr'rī hȳ-drŏx'ĭ-dŭm cŭm măg-nē'şī-ī ŏx'ĭ-dō)

Ferri Oxidum Hydratum cum Magnesia, *U. S.* 1890, Arsenic Antidote, Ferric Hydrate with Magnesia; Antidotum Arsenici; Antidote to Arsenious Acid; Hydrated Oxide of Iron with Magnesia; Contre-poison de l'arsenic, *Fr.*; Gegengift des Arseniks, Gegengift der Arsenigensaure, *G.*; Hidrato ferrico magnesico, *Sp.*

* "Solution of Ferric Sulphate, *forty millilitres* [or 1 fluidounce, 169 minims]; Magnesium Oxide, *ten grammes* [or 154 grains]; Water, *a sufficient quantity.* Mix the solution of ferric sulphate with *one hundred and twenty-five mils* [or 4 fluidounces, 109 minims] of water, and keep the liquid in a large, well-stoppered bottle. Rub the magnesium oxide with cold water to a smooth and thin mixture, transfer this to a bottle capable of holding about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] fill it with water to about three-fourths of its capacity, and keep it tightly stoppered. When the preparation is wanted for use, shake the magnesium oxide mixture until of a thin, creamy consistence, slowly add to it the diluted solution of ferric sulphate, and shake them together until a uniformly smooth mixture results.

"NOTE.—In this process the 10 Gm. [or 154 grains] of magnesium oxide may be replaced by 300 mils [or 10 fluidounces, 69 minims] of magnesia magma, diluting it with sufficient water to make the required volume.

"Always keep the diluted solution of ferric sulphate and the magnesia mixture on hand in separate bottles, ready for immediate use, so that the antidote may be quickly prepared." *U. S*

Ferric hydroxide was dropped from the U. S. P. IX and ferric hydroxide with magnesium oxide retained. This is a preparation which has been introduced for the purpose of furnishing a ready and efficient antidote against arsenic trioxide or arsenous acid. It is almost identical with the *Antidotum Arsenici* of the German Pharmacopœia, and experience has shown its effectiveness. Ferric hydroxide is produced when to the mixture of magnesia is added the diluted solution of ferric sulphate, and, as the magnesia is in excess and acidity thus prevented, no harm can result from not separating the by-products of the reaction. When mixed as officially directed, and ready for use, it contains ferric hydroxide with magnesium sulphate and hydroxide. It has been shown that no soluble compound with arsenic is formed when it is used as an antidote, and the presence of the magnesium salt, from a therapeutical point of view, is not at all objectionable. (See *Arseni Trioxidum,* p. 195.)

Dose, four fluidounces (120 mils).

FERRI PHOSPHAS. U. S.

FERRIC PHOSPHATE Ferr. Phos. [Ferri Phosphas Solubilis, U.S. VIII, Soluble Ferric Phosphate]

(fĕr'rī phŏs'phās)

"Ferric Phosphate rendered soluble by the presence of sodium citrate. It contains not less than 12 per cent. of Fe. Preserve it in amber-colored, well-stoppered bottles, protected from light." *U. S.*

Ferri et Sodii Citro-phosphas; Ferrum Phosphoricum cum Natrio Citrico; Soluble Phosphate of Iron, Sodio-ferric Citrophosphate; Citro-phosphate de Fer et de Soude, *Fr.*; Natriumferricitro-phosphat, *G.*

This compound must not be confused with the iron phosphate official in the former U. S. and British Pharmacopœias which was an insoluble slate-colored powder. The word "solubilis" was dropped in the title of the U. S. P. IX, and this compound is in thin bright green scales, and the old slate-colored powder is no longer official. (See *Ferri Phosphas Saccharatus.*)

No process is given for this preparation in the U. S. P. IX. That of the U. S. P., 1890, is as follows: "Ferric Citrate, *fifty grammes* [or 1 ounce av., 334 grains]; Sodium Phosphate, unefflouresced, *fifty-five grammes* [or 1 ounce av., 411 grains]; Distilled Water, *one hundred cubic centimeters* [or 3 fluidounces, 183 minims]. Dissolve the Ferric Citrate in the Distilled Water by heating on a water-bath. To this solution add the Sodium Phosphate, and stir constantly until it is dissolved. Evaporate the solution on a water-bath, at a temperature not exceeding 60° C. (140° F.), to the consistence of thick syrup, and spread it on plates of glass, so that, when dry, the salt may be obtained in scales. Keep the product in dark amber-colored, well-stoppered bottles." *U. S.*, 1890. (See preceding article.)

W. A. Puckner (*Proc. A. Ph. A.*, 1897, 231) proposes the following process, preferring potassium chlorate to nitric acid as an oxidizing agent.

Ferrous sulphate, in clear crystals, 156 Gm.; sulphuric acid, 20 mils; potassium chlorate, 12 Gm.; ammonia water, 340 mils; citric acid, 120 Gm.; sodium phosphate, unefflouresced, 200 Gm.; water, a sufficient quantity. Add the sulphuric acid to 240 mils of water, contained in a glass or porcelain vessel, to this add the ferrous sulphate, warm gently until all is dissolved, then

add the potassium chlorate and continue the heat for one-half hour, or until a drop of the solution added to potassium ferricyanide test solution no longer produces a distinct green or bluish-green color. Add this solution, slowly and with constant agitation, to the ammonia water contained in a suitable vessel; to this mixture add hot water, 4000 mils, and allow to subside, and, after one-half hour, decant or siphon off the clear supernatant liquid. To the residue add 2000 mils of hot water, allow to subside, and decant; repeat this washing with six portions of hot water, allowing the last portion to subside for at least six hours or over night. Decant or siphon off the clear liquid as closely as possible, then add to the remaining magma the citric acid and the sodium phosphate, warm gently until solution results, and then evaporate on a water bath at a temperature not exceeding 60° C. (140° F.) until the solution weighs 500 Gm., and spread it on plates of glass, so that, when dry, the salt may be obtained in scales.

Solution of Ferric Phosphate (50 per cent.).—By evaporating the solution made by Puckner's method (see above) on a water bath until it measures 500 mils, a solution is made containing 50 per cent. of ferric phosphate.

Properties.—It is officially described as in "thin, bright green, transparent scales, without odor, and having an acidulous, slightly saline taste. The salt is permanent in dry air when excluded from light, but when unprotected, soon becomes discolored. Ferric Phosphate is freely and completely soluble in water; insoluble in alcohol. An aqueous solution of Ferric Phosphate (1 in 10) is slightly acid to litmus. The addition of ammonia water to an aqueous solution of Ferric Phosphate gives a reddish-brown color, but does not produce a precipitate. Ferric Phosphate, when boiled with potassium hydroxide T.S., produces a brownish-red precipitate without evolving ammonia. Boil an aqueous solution of Ferric Phosphate (1 in 10) with an excess of potassium hydroxide T.S. until deprived of its iron, strongly acidulate the filtrate with hydrochloric acid and cool a portion of the liquid. When mixed with an equal volume of magnesia mixture T.S., followed by a slight excess of ammonia water, this liquid affords an abundant, white, crystalline precipitate. This precipitate turns yellow when washed and treated with a few drops of silver nitrate T.S. (distinction from *pyrophosphate*).

"**Assay.**—Dissolve about 1 Gm. of Ferric Phosphate, accurately weighed, in 25 mils of distilled water, and 15 mils of hydrochloric acid in a glass-stoppered bottle, then add 3 Gm. of potassium iodide, securely stopper the bottle, keep it at a temperature of 40° C. (104° F.) for thirty minutes, then cool and titrate with tenth-normal sodium thiosulphate V.S., using starch T.S. as indicator. It shows not less than 12 per cent. of Fe.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.005584 Gm. of Fe. Each gramme of Ferric Phosphate corresponds to not less than 21.5 mils of tenth-normal sodium thiosulphate V. S." *U. S.*

Uses.—Ferric phosphate is one of the best preparations to use when it is desired to exhibit iron in solution. It is as free from astringency as any of the official salts of iron, has little tendency to disturb the digestion and is an active chalybeate.

The *dose* is from five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Elixir Cinchonæ Alkaloidorum et Ferri, *N. F.;* Elixir Ferri Phosphatis, *N. F.;* Elixir Gentianæ et Ferri Phosphatum, *N. F.;* Liquor Phosphatum Compositus, *N. F.;* Syrupus Ferri, Quininæ et Strychninæ Phosphatum, *N. F.*

FERRI PHOSPHAS SACCHARATUS. Br.

SACCHARATED IRON PHOSPHATE

(fĕr'rī phŏs'phăs săc'ȼha-rā-tŭs)

"Saccharated Iron Phosphate is ferrous phosphate, more or less oxidised, mixed with glucose. It contains not less than 60 per cent. of ferrous salts calculated as ferrous phosphate, $Fe_3(PO_4)_2,8H_2O$." *Br.*

This preparation was introduced into the British Pharmacopœia, 1914, to replace the former "Ferri Phosphas" which was an insoluble slate-colored powder. The process is as follows: "Ferrous Sulphate, 120 *grammes;* Sodium Phosphate, 110 *grammes;* Sodium Carbonate, 50 *grammes;* Glucose, 40 *grammes;* Distilled Water, boiling, *a sufficient quantity.* Dissolve twenty *grammes* of the Glucose in four hundred *millilitres* of the Distilled Water, and dissolve the Ferrous Sulphate in the solution. Dissolve the Sodium Phosphate in four hundred *millilitres* of the Distilled Water, and to this add the solution of the Ferrous Sulphate, stirring constantly. Then add the Sodium Carbonate previously dissolved in four hundred *millilitres* of the Distilled Water. Mix thoroughly, and allow the precipitate to subside. Decant the supernatant liquid, wash the precipitate with two successive quantities, each of two thousand *millilitres* of the Distilled Water, mix it with the remainder of the Glucose, and dry at a temperature not exceeding 100° C. (212° F.). Powder the product and preserve it in a stoppered bottle. A slate-blue, amorphous powder. Taste sweetish, chalybeate. Partially soluble in *water,* soluble in *hydrochloric acid.* The acid solution yields blue precipitates with *solution of potassium ferrocyanide* and *solution of potassium ferricyanide;* when treated with *tartaric acid* and excess of *solution of ammonia,* and subsequently with *solution of magnesium ammonio-sulphate,* it yields a white granular precipitate. 1 gramme dissolved in excess of warm *concentrated phosphoric acid* does not cease to yield a blue precipitate with *solution of potassium ferricyanide* until 35.9 millilitres of *N/10 solution of potassium bichromate* have been added. *Arsenic limit* 5 parts per million." *Br.*

Glucose is used to protect the ferrous phosphate from oxidation, which it does only partially. This iron phosphate must not be confounded with the soluble ferric phosphate of the U. S. P. IX, which is in green transparent scales. As obtained by the present process, this U. S. preparation is not a definite chemical compound, but a mixture, which should probably be called sodio-ferric citro-phosphate, and bears a resemblance to the pyrophosphate, which is now usually made by a similar process. (See *Ferri Phosphas.*)

The British iron phosphate, 1898, was a very different salt. By double decomposition ferrous phosphate and sodium sulphate are produced, the former precipitating as a white bulky powder, which soon changes on exposure to a greenish-blue, and ultimately to a slate color; since the sodium phosphate is chemically an acid salt (Na_2HPO_4) a portion of phosphoric acid is liberated during the reaction, and this, retaining in solution some of the ferrous phosphate, requires the addition of the solution of sodium bicarbonate to neutralize it and set free the remainder of the ferrous phosphate. This salt, when first formed, is represented by the formula $Fe_3(PO_4)_2$; but its strong affinity for oxygen causes the gradual production of a sesquisalt, which, therefore, to a certain extent, always exists in the preparation; hence the former British authority required it to contain at least 47 per cent. of ferrous phosphate, $Fe_3(PO_4)_2.8H_2O$.

Ferric phosphate, dissolved to saturation in a boiling solution of metaphosphoric acid (HPO_3), under the name of *superphosphate of iron*, was proposed as a remedy, in 1851, by Routh, of London. Thomas Greenish of the same city, states that the solution of the salt, on cooling, hardens into a mass of pilular consistence, soluble in water in all proportions, and free from any disagreeable or inky taste.

Uses.—Ferric phosphate possesses the general properties of the ferruginous preparations, and has been given with advantage in *amenorrhea* and *dyspepsia.*

Dose, from five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Syrupus Ferri Phosphatis, *Br.;* Syrupus Ferri Phosphatis cum Quinina et Strychnina, *Br.*

FERRI SULPHAS. U. S., Br.

FERROUS SULPHATE Ferr. Sulph. [Iron Protosulphate]

(fĕr'rī sŭl'phăs)

"It contains not less than 54.36 nor more than 57.07 per cent. of anhydrous ferrous sulphate, corresponding to about 99.5 per cent. of the crystallized salt [$FeSO_4 + 7H_2O = 278.02$]. Preserve it in well-closed containers." *U. S.*

"Ferrous Sulphate may be prepared by the interaction of diluted sulphuric acid and iron. It contains not less than 97.5 per cent. of pure ferrous sulphate, $FeSO_4,7H_2O$." *Br.*

Sulphate of Iron, Green Vitriol, Iron Vitriol, Sulfas Ferrosus, Ferrum Vitriolatum Purum, Vitriolum Martis Purum; Sulfate Ferreux Officinal, *Fr. Cod.;* Sulfate (protosulfate) de Fer, *Fr.;* Ferrum Sulfuricum, *P. G.;* Ferrosulfat, Schwefelsaures Eisenoxydul, *G.;* Solfato ferroso, *It.;* Sulfato ferroso, *Sp.*

The British Pharmacopœia (1885) contained the following process for this salt: "Take of Iron Wire *four ounces* [avoirdupois]; Sulphuric Acid *four fluidounces* [Imperial measure]; Distilled Water *one pint and a half* [Imp. meas.]. Pour the water on the Iron placed in a porcelain dish, and add the Sulphuric Acid, and, when the disengagement of gas has nearly ceased, boil for ten minutes. Filter now through paper, and, after the lapse of twenty-four hours, separate the crystals which have been deposited from the solution. Let these be dried on filtering paper placed on porous bricks, and preserved in a stoppered bottle." *Br.,* 1885.

The object of this process is to make a pure ferrous sulphate by direct combination. Sulphuric acid, in a concentrated state, acts but imperfectly on iron, but when diluted, a vigorous action takes place. The theoretical quantities for mutual reaction are 56 of iron to 98 of acid. This proportion is one part of iron to one and three-quarters of acid. The British Council uses an excess of acid, the weight of acid being 7.38 avoirdupois ounces, instead of 7. An excess of iron, however, is desirable, as it tends to secure the production of a perfect ferrous sulphate. A process for this salt was given in the U. S. P., 1870, which was based upon the method of Bonsdorff. This chemist found that, when a perfect ferrous sulphate was formed in solution by heating diluted sulphuric acid with an excess of iron, it might be crystallized free from sesquioxide, provided a little excess of sulphuric acid were added to the liquid before filtration, in order to prevent the formation of any sesquioxide during the process, at the same time avoiding, as much as possible, contact with the air. Hence the directions in the former U. S. Pharmacopœia formula to acidulate with sulphuric acid, to cause the funnel to touch the bottom of the receiving vessel, which avoids the dropping of the liquid through the air, and to cover the vessel containing the concentrated liquid when it is set aside to crystallize.

Commercial Ferrous Sulphate or *Copperas* is manufactured on a large scale for the purposes of the arts, from the native ferric sulphide or iron pyrites, by roasting, oxidation by exposure to air and moisture, and lixiviation. The constituents of the mineral become sulphuric acid and ferrous and ferric oxides, which, by their union, form the salt. Ferrous sulphate is also obtained in many chemical processes as a collateral or by-product, as in the manufacture of alum, in the precipitation of copper from solutions of copper sulphate by scraps of iron, in the manufacture of hydrogen, etc.

Commercial ferrous sulphate is far from being pure. Besides containing some ferric sulphate, it is generally contaminated with metallic and

earthy salts, such as those of copper, zinc, aluminum, and magnesium. Two principal kinds occur in the market, one in large grass-green crystals, the surface of which is studded with yellow spots; the other of a bluish-green color, and ordinarily mixed with the powder of the effloresced salt. Commercial sulphate should never be dispensed by the pharmacist until it has undergone purification by recrystallization from a slightly acid solution, and brought into compliance with the official requirements.

Properties.—Ferrous sulphate is in the form of "pale bluish-green, monoclinic prisms, without odor, and having a saline, styptic taste; efflorescent in dry air. On exposure to moist air, the crystals rapidly oxidize, and become coated with brownish-yellow, basic ferric sulphate. When it has thus deteriorated the salt must not be used for any official purpose. One Gm. of Ferrous Sulphate dissolves in 1.4 mils of water at 25° C. (77° F.); in 0.4 mil of boiling water; insoluble in alcohol. An aqueous solution of the salt (1 in 20) is acid to litmus. When slowly heated to 115° C. (239° F.) the crystals disintegrate, and the salt loses the greater part of its water of crystallization. An aqueous solution of the salt, even when highly diluted, gives with potassium ferricyanide T.S. a blue color or precipitate, and with barium chloride T.S. a white precipitate insoluble in hydrochloric acid. Dissolve 1 Gm. of the salt in about 50 mils of distilled water containing 1 mil of diluted sulphuric acid, heat the solution to boiling, oxidize it with nitric acid and then mix it with a slight excess of ammonia water and filter. The filtrate is colorless, and, after acidulating with hydrochloric acid, it does not respond to the Test for heavy metals (see Part III, Test No. 3). Agitate 1 Gm. of Ferrous Sulphate in small fragments during four or five minutes, with 10 mils of alcohol, and filter the mixture; the filtrate does not immediately redden moistened blue litmus paper (*free acid*).

"**Assay.**—Dissolve about 1 Gm. of Ferrous Sulphate, accurately weighed, in about 25 mils of diluted sulphuric acid and titrate with tenth-normal potassium permanganate V.S until a permanent pink color is produced. It shows not less than 54.36 per cent. nor more than 57.07 per cent. of $FeSO_4$.

"Each mil of tenth-normal potassium permanganate V.S. used corresponds to 0.015191 Gm. of $FeSO_4$. Each gramme of Ferrous Sulphate corresponds to not less than 35.78 mils nor more than 37.57 mils of tenth-normal potassium permanganate V.S." *U. S.*

"Oblique rhombic prisms of a greenish color, or a crystalline powder of a pale bluish-green color; taste astringent. Insoluble in *alcohol* (90 per cent.), soluble in less than 2 parts of *water* previously boiled and cooled, giving a clear solution (absence of oxysulphate). Yields the *reactions* characteristic of ferrous salts and of sulphates. 1 gramme dissolved in 20 millilitres of *diluted sulphuric acid* decolorises not less than 35 millilitres of *N/10 solution of potassium permanganate.* Yields no characteristic *reactions* for copper or zinc. *Arsenic limit* 2 parts per million." *Br.*

As prepared by Bonsdorff's method, ferrous sulphate is blue, verging upon green. When it becomes more green than blue, or entirely green, an indication is afforded that it contains some sesquioxide. By exposure to the air the crystals absorb oxygen, and become first green, and ultimately covered with a yellow efflorescence of subsulphate, insoluble in water. Sometimes the crystals are quite permanent when made by Bonsdorff's method, owing to the slight excess of acid which they contain. The aqueous solution is bluish green, but by standing it attracts oxygen, and becomes first green and then reddish depositing in the meantime a portion of sesquisulphate, having the composition:

$$Fe_2(SO_4)_3 + Fe_2O_3 + 8H_2O$$

At a red heat it loses its acid, and is converted into the anhydrous ferric oxide called *colcothar.* It is incompatible with the alkalies and their carbonates, soaps, lime water, calcium and barium chlorides, sodium borate and phosphate, silver nitrate, and lead acetate and subacetate. It is decomposed also by astringent vegetable infusions, the tannic and gallic acids of which form, if any sesquioxide be present, a black compound of the nature of ink. The extent to which this change lessens the activity of the salt is not well ascertained. Ferrous sulphate, as found in commerce, is often the impure commercial sulphate, which is not fit for medicinal use. The perfectly pure salt is precipitated white by potassium ferrocyanide, but that of ordinary purity gives a greenish precipitate, more or less deep, with this test, owing to the presence of some ferric salt. Copper may be detected by immersing in the solution a bright piece of iron, on which a cuprous film will be deposited. Both copper and zinc may be detected by oxidizing the iron by boiling the solution of the salt with nitric acid and then precipitating the iron by an excess of ammonia. If the filtered solution be blue, copper is present, and if it contain zinc, this will be separated in flakes of white oxide on expelling the excess of ammonia by ebullition.

It is often desirable to protect ferrous sulphate against the oxidation to which it is liable on exposure. Sugar acts as a preservative in the case of this salt, as in that of ferrous iodide. It may be added to the solution, or incorporated with the sulphate in substance. E. Latour has given a formula for crystallizing the salt with sugar. Geo. Welborn has found that a small lump of camphor, wrapped in tissue paper, and placed in the bottle with the sulphate, prevents its oxidation. (*P. J.*, May, 1868, p. 537.) Pavesi, of Mortara, effects the same object by incorporating it with an equal weight of gum arabic, by evaporating a joint solution of the two substances with a gentle heat. (*J. P. C.*, 4e sér., iii, 49.)

Uses.—Ferrous sulphate is an active local irritant and astringent. In overdoses it pro-

duces nausea, vomiting, griping, and purging, and other evidences of gastro-enteric irritation. Because of this action it is not to be recommended as an internal remedy. Externally, the solution has been used in chronic *ophthalmia, leucorrhea,* and *gleet,* made of various strengths, from one or two to eight or ten grains of the salt to the fluidounce of water. Velpeau has recommended in *erysipelas* the local use of a three per cent. solution applied by compresses kept constantly wet. An ointment made of one or two parts of the sulphate to sixty of lard was found by Devergie to be particularly efficacious in certain skin diseases, especially in *eczema.* In scaly affections it had no effect. (See *Ferri Sulphas Exsiccatus.*)

Ferrous sulphate, usually in the form of the impure salt or commercial copperas, is a disinfectant and deodorant as it unites with both hydrogen sulphide and ammonia. It is asserted that ferric sulphate unites with organic substances to form definite stable compounds, and that animal substances kept in a 3 per cent. solution of neutral ferric sulphate for some time and then removed, mummify without decomposition. (*N. R.,* Dec., 1883, 685.) Ferrous sulphate is incompatible with alkalies and also with even feeble oxidizing agents which quickly convert it into ferric sulphate or subsulphate.

Dose, two to five grains (0.13–0.32 Gm.).

Off. Prep.—Ferri Carbonas Saccharatus, *U. S., Br.;* Ferri Phosphas Saccharatus, *Br.;* Ferri Sulphas Exsiccatus, *U. S., Br.;* Ferri Sulphas Granulatus, *U. S.;* Liquor Ferri Subsulphatis, *U. S.;* Liquor Ferri Tersulphatis, *U. S., Br.;* Massa Ferri Carbonatis, *U. S.;* Mistura Ferri Composita, *Br., N. F.;* Liquor Ferri Oxysulphatis, *N. F.;* Liquor Zinci et Ferri Compositus, *N. F.*

FERRI SULPHAS EXSICCATUS. U. S., Br.

EXSICCATED FERROUS SULPHATE Ferr. Sulph. Exsic. [Dried Ferrous Sulphate]

(fĕr′rī sŭl′phăs ĕx-sĭc-cā′tŭs)

"Exsiccated Ferrous Sulphate contains the equivalent of not less than 80 per cent. of the anhydrous salt [$FeSO_4 = 151.91$]." *U. S.* "Exsiccated Ferrous Sulphate is Ferrous Sulphate deprived of part of its water of crystallization. It contains not less than 77 per cent. of pure anhydrous ferrous sulphate, $FeSO_4$." *Br.*

Ferri Sulphas Exsiccata, *Br.* 1885; Dried Sulphate of Iron Sulfate Ferreux desséché, *Fr.;* Ferrum Sulfuricum Siccum *P. G.;* Getrochnetes Ferrosulfat, Entwässertes Schwefel saures Eisenoxydul, *G.;* Sulfato ferroso desecado, *Sp.*

* "Ferrous Sulphate, in coarse powder, *one hundred grammes* [or 3 ounces av., 231 grains]. Allow the salt to effloresce at a temperature of about 40° C. (104° F.), in dry air, and then heat it in a porcelain dish, on a water-bath, constantly stirring, until the product weighs from *sixty-four* to *sixty-five grammes* [or 2 ounces av., 113 grains to 2 ounces av., 128 grains]. Lastly, reduce the residue to a fine powder, and transfer it at once to dry, well-stoppered bottles." *U. S.*

No process is given in the British Pharmacopœia, 1914. The 1898 process was as follows:

"Expose Ferrous Sulphate, $FeSO_4,7H_2O$, in a porcelain or iron dish to a temperature of 100° C. (212° F.), stirring occasionally until aqueous vapor ceases to be given off; reduce the residue, which should weigh about 60 per cent. of the original salt, to a fine powder."

Properties.—"Exsiccated Ferrous Sulphate is a grayish-white powder, slowly soluble in water. A solution of the salt (1 in 20) in distilled water which has been recently boiled and cooled is not more than slightly turbid, and conforms to the reactions and tests under *Ferri Sulphas,* except the test for free acid, when taken in proportionate amount.

"**Assay.**—Dissolve about 0.8 Gm. of Exsiccated Ferrous Sulphate, accurately weighed in a stoppered weighing-bottle, in about 25 mils of diluted sulphuric acid and titrate with tenth-normal potassium permanganate V.S. until a permanent pink color is produced. It shows not less than 80 per cent. of $FeSO_4$.

"Each mil of tenth-normal potassium permanganate V.S. used corresponds to 0.015191 Gm. of $FeSO_4$. Each gramme of Exsiccated Ferrous Sulphate corresponds to not less than 52.7 mils of tenth-normal potassium permanganate V.S." *U. S.*

"A nearly white powder, slowly but entirely soluble in *water.* 0.5 gramme dissolved in *water* and acidified with *sulphuric acid* decolorises not less than 25.3 millilitres of *N/10 solution of potassium permanganate. Arsenic limit* 5 parts per million." *Br.*

In this process about six molecules out of seven, of the water of crystallization of the salt, are driven off. The heat should not exceed 149° C. (300° F.), otherwise the salt itself would suffer decomposition. If the heat has been excessive, the color of the salt will be brownish instead of grayish-white. Dried ferrous sulphate is used for making pills, the crystallized sulphate not being adapted to that purpose. In prescribing the dried sulphate it is necessary to recollect that about three grains of it are equivalent to five grains of the crystallized salt.

Dose, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Pilulæ Aloes et Ferri, *Br., N. F.;* Pilula Ferri, *Br.;* Pilulæ Ferri, Quininæ, Aloes et Nucis Vomicæ, *N. F.*

FERRI SULPHAS GRANULATUS. U. S.

GRANULATED FERROUS SULPHATE Ferr. Sulph. Gran. [Precipitated Ferrous Sulphate]

(fĕr′rī sŭl′phăs grăn-ū-lā′tŭs)

Granulated Sulphate of Iron; Ferri Sulphas Præcipitatus, *U. S. P.* 1880; Precipitated Sulphate of Iron; Sulfate Ferreux précipité, *Fr.;* Präcipitirtes Ferrosulfat, *G.*

* "Ferrous Sulphate, *one hundred grammes* [or 3 ounces av., 231 grains]; Distilled Water, *one hundred mils* [or 3 fluidounces, 183 minims]; Diluted Sulphuric Acid, *five mils* [or 81 minims]; Alcohol, *twenty-five mils* [or 406

minims]. Dissolve the Ferrous Sulphate in the Distilled Water previously heated to boiling, add the Diluted Sulphuric Acid, and filter the solution while hot. Evaporate the solution immediately in a tared porcelain dish, on a sand-bath, until it weighs *one hundred and fifty grammes* [or 5 ounces av., 127 grains], and then cool it quickly, with constant stirring. Transfer the product to a glass funnel stopped with a plug of purified cotton, and, when it has thoroughly drained, pour the Alcohol upon it. When this has also drained, spread the crystalline powder on bibulous paper, dry it quickly at room temperature, and transfer it at once to dry, well-stoppered bottles. Granulated Ferrous Sulphate is a very pale bluish-green, crystalline powder, which conforms in every respect to the reactions and tests for purity under *Ferri Sulphas.*" *U. S.*

The process of the U. S. P. (1890), retained by the U. S. P., differs radically in manipulation from that of 1880; instead of pouring the filtered solution of ferrous sulphate into alcohol and collecting the precipitate which falls, the solution is granulated by heat with constant stirring (not quite to dryness), and this salt is then washed with alcohol, which displaces impurities and facilitates the rapid drying of the granular powder.

The product is practically identical with the granulated sulphate of iron of the British Pharmacopœia (1885). The British Pharmacopœia (1898) omitted the granulated salt entirely. The process of the U. S. Pharmacopœia of 1880 had the advantage of being more manageable and convenient, ferrous sulphate being used directly instead of being made by the action of sulphuric acid on the metal. The directions given in the first part of the former British process are precisely the same as those laid down by the British Council for making ferrous sulphate; but the hot solution of the iron in the sulphuric acid, instead of being allowed to filter into an empty vessel, is made to drop into a portion of alcohol, the mixture being stirred while it cools. The acid directed is in excess, and the filtrate is consequently an acid solution of ferrous sulphate mixed with alcohol. The stirring as the mixture cools, finely granulates the salt, which separates perfectly pure, the alcohol holding in solution any ferric sulphate which may have been formed, and the excess of acid dissolving any free sesquioxide. This process, in its main features, is that of Berthemot. (See 8th ed., U. S. D.)

Properties.—Barckhauser, Salzer, and others have stated that ferrous sulphate precipitated by alcohol did not always contain seven molecules of water, and it could not be relied upon for making volumetric solutions because of this lack of uniformity in composition. Caro (*Ann. Ch. Ph.,* clxv, 29) and Schlickum (*Ph. Ztg.,* No. 49), on the other hand, maintain that precipitated ferrous sulphate is constant in composition, and Schlickum proved that if the precipitation took place in the cold it always contained seven molecules of water, but *boiling* with strong alcohol diminished the proportion of water of crystallization. This salt is less liable to oxidation on exposure than is the sulphate in its ordinary form, and experience has shown that it is admirably adapted for dispensing.

Dose, two to five grains (0.13–0.32 Gm.).

Off. Prep.—Pilulæ Ferri Carbonatis, *U. S.*

FERRUM. U. S., Br.

IRON Ferr.

(fĕr'rŭm)

"Metallic iron [Fe = 55.84] in the form of fine, bright wire." *U. S.* "Iron is annealed iron wire, having a diameter of about 0.1 millimetre (about No. 35 wire gauge), or wrought-iron nails, free from oxide. *Arsenic limit* 200 parts per million." *Br.*

Fer, Mars, Fer métallique, *Fr. Cod.;* Fil de Fer, *Fr.;* Eisen, Eisendraht, *G.;* Ferro, Limatura di ferro, *It.;* Hierro, *Sp.*

In the U. S. Pharmacopœia, this metal is employed in different preparations in the form of wire; it was official in 1850 as *Ferri Ramenta, Iron Filings.* See *U. S. Dispensatory,* 19th edition, p. 514.

Iron is the most abundant and useful of the metals, and so interwoven with the wants of mankind that the extent of its consumption by a nation may be taken as an index of progress in civilization. It is universally diffused in nature, not only in the mineral but also in the vegetable and animal kingdoms. There are very few minerals in which traces of it are not to be found, and it is an essential constituent in many parts of animals, but particularly in the blood. It is one of the few metals which are not deleterious to the animal economy. Iron occurs: (1) native (almost exclusively, however, of meteoric origin); (2) as a sulphide, in the minerals *pyrites, pyrrotine,* or *magnetic pyrites,* and *arsenopyrite* or *mispickel* (a sulph-arsenide of iron); (3) oxidized, embracing the magnetic, specular, red, brown, and argillaceous iron oxides, also *chromite* (mixed iron, chromium, and magnesium oxides) and *franklinite* (mixed iron, manganese, and zinc oxides); (4) in saline combination, forming ferrous carbonate, sulphate, phosphate and arsenate. Those minerals of iron which admit of being worked to advantage are called *iron ores.* These include the different native oxides and the carbonate (spathic iron). The best iron is obtained from the ferroso-ferric oxide usually called magnetic iron ore, and the anhydrous sesquioxide, known as specular iron ore. These occur abundantly in Sweden, and furnish the superior iron of that country. The upper peninsula of Michigan and the borders of Lake Champlain in New York yield similar ores. As a rule, those ores yield the best iron which occurs in primitive formations.

Extraction.—The mode of extracting iron from its ores varies somewhat with the nature

of the ore; but the general principles of the operation are the same for all. The ore, previously broken into small pieces and roasted, is exposed to the action of an intense heat, urged by an air blast, in contact with carbonaceous matter, such as charcoal, coke, or anthracite, and in connection with some flux capable of fusing with the impurities of the ore. The flux varies with the nature of the ore, and is generally limestone. Fluorspar is occasionally used, but is not often found in sufficiently large deposits to be available. The flux, whatever it may be, enters into fusion with the impurities, and forms what is called the slag, which is a fusible lime silicate chiefly, while the carbon monoxide formed from the carbonaceous matter, acting on the ferric oxide, reduces it to the metallic state. The reduced metal, from its density, occupies the lower part of the furnace, and is protected from the action of the air by the melted slag which floats on its surface. When the reduction is completed, the slag is allowed to run out by a hole in the side of the furnace, and the melted metal by an aperture at the bottom, the latter being received into a series of sand moulds, where it solidifies in masses, known in commerce by the name of *pig* or *cast iron*. In this state the metal is brittle and far from being pure, as it contains from 3 to 6 per cent. of carbon, with silicon, phosphorus, sulphur, and manganese. It is purified, and brought to the state of *malleable iron*, by being fused and subjected, while stirred, to the action of a current of air on its surface. By these means the carbon is nearly burnt out, and the other impurities are oxidized and made to rise to the surface as a slag. Instead of this process, called "refining," usage in this country and in England substitutes what is called "pig boiling"—that is, the pig iron is at once submitted to the operation of puddling without previous refining. The "puddling" process consists in heating the charge of pig iron on the hearth of a reverberatory furnace in contact with ferric oxide and in a reducing flame. The silicon is first burnt out, and then the carbon gradually disappears; the phosphorus goes into the "tap cinder" as phosphide and phosphate; the sulphur in part disappears as sulphur dioxide and in part remains in the cinder as ferrous sulphide. As the metal approaches to purity, it becomes tough and less liquid, and its particles agglutinate so as to form semi-fused lumps, though the temperature of the furnace continues the same. These lumps are then taken out of the furnace, and their particles, by means of ponderous hammers moved by steam or water power, or by great pressure, are forced together so as to form one tenacious mass. The metal is finally rolled out into bars of a convenient size, when it constitutes *wrought iron* of commerce.

The third form of commercial iron, known as "steel," is made either by the *cementation* process, the *Bessemer* process, the *open hearth* process, or by *electrical* processes. In the first case, wrought iron is packed with charcoal and heated until combination takes place, and the resulting steel is cast into ingots. In the second case, cast iron is melted in large vessels called converters, when a blast of air is blown through the mass, burning out the requisite amount of carbon, and then, after addition of a small amount of *spiegeleisen*, or manganiferous cast iron, the finished product is run into moulds; while in the third or open hearth process, a mixture of pig iron and ore is heated with a reverberatory flame, as in the puddling process, or bars and blooms of wrought iron are heated with the pig iron, and steel is made by the combination of the two. Steel contains from ½ to 1 per cent. of carbon.

Iron mines occur in most countries, but more particularly in northern ones. In Spain the principal mines furnish spathic iron and the red oxide. The chief iron ores of France are the spathic iron, and the specular, brown, and argillaceous oxides; of Germany, the spathic iron and brown oxide. The island of Elba is celebrated for its rich and abundant specular iron ore. In the United States iron is abundant. The principal ores that are worked are the magnetic, red, and brown oxides. The magnetic oxide is found in large beds in Essex County, N. Y., on the borders of Lake Champlain, and in the Lake Superior district; the red oxide in New York, New Jersey, Pennsylvania, Alabama, and especially in a very pure state in Missouri, at Iron Mountain and Pilot Knob; the brown oxide in Eastern Pennsylvania.

Properties.—Iron is a hard, malleable, ductile, and tenacious metal, of a grayish-white color and fibrous texture, a characteristic taste, and a sensible odor when rubbed. In tenacity it yields only to nickel and cobalt. (Deville.) Its sp. gr. is about 7.7, and its fusing point very high, about 1510° C. (2750° F.). It possesses magnetic properties and is very malleable. It is combustible, and, when heated to whiteness, burns in atmospheric air, and with brilliant scintillations in oxygen gas. At a red heat, its surface is converted into black oxide, and at common temperatures, by the combined agency of air and moisture, it becomes covered with a yellowish-brown matter, called *rust*, which is the hydrated sesquioxide. It combines with all the non-metallic elements, except hydrogen and nitrogen, and with most of the metals. It forms three compounds with oxygen, a ferrous oxide and a ferric oxide, which by their union form the native magnetic oxide, hence often termed ferroso-ferric oxide, and a trioxide, which forms an acid called ferric acid. The *monoxide*, or ferrous oxide, is of a dark blue color, attracted by the magnet, and spontaneously combustible in the air, being converted into sesquioxide or ferric oxide. It is the base of ferrous sulphate, and the green salts of iron generally. It is very prone to absorb oxygen, and hence the salts which contain it are soon partially converted, when in solution, into salts of the ferric oxide.

Its formula is FeO, consisting of one atom of iron, Fe, and one of oxygen, O. The *sesquioxide*, or ferric oxide, is readily obtained by dissolving iron in nitrohydrochloric acid, precipitating by ammonia, and igniting the precipitate. It is of a red color, not attracted by the magnet, and forms salts which for the most part have a reddish color. Its formula is Fe_2O_3, consisting of two atoms of iron, Fe, and three atoms of oxygen, O. An allotropic variety of the sesquioxide, soluble in water, and not responding to the ordinary tests of iron, has been discovered by Péan de Saint-Gilles. The *native black oxide*, the magnetic oxide of mineralogists, consists of one molecule of FeO and one molecule of Fe_2O_3.

Under the name of *Ferri Oxidum Magneticum*, the British Pharmacopœia formerly had a preparation consisting of this oxide with three molecules of water. *Ferric acid*, discovered by Frémy, may be obtained, in union with potassium hydroxide, by passing chlorine through a very concentrated solution of the alkali, holding the hydrated ferric oxide in suspension, or by fusing iron filings with potassium nitrate. The acid anhydride consists of one atom of iron and three of oxygen, FeO_3. Iron forms a number of important salts.

Iron is readily detected, even in minute quantities, by bringing it to the state of ferric salt in solution, and adding potassium ferrocyanide or tincture of galls, the former of which will strike a deep blue, the latter a black color. Bringing it to the state of a ferric salt is readily effected by boiling the solution containing it with a little nitric acid. F. B. Power prefers the *iodometric method* for estimating the quantity of iron in scaled salts. It is based on the liberation of iodine by ferric iron, and the subsequent estimation of the liberated iodine by a tenth-normal volumetric solution of sodium thiosulphate. (*Ph. Rund.*, 1891, 205.)

Uses.—The only condition in which the value of iron, as an internal remedy, has been proven beyond cavil is in certain types of *anemia*. The conditions of the blood which are characterized by a reduction in the percentage of hemoglobin may be divided into three groups, those in which the number of corpuscles is reduced to a greater extent than the percentage of hemoglobin—each individual corpuscle, therefore, being richer than normal in coloring matter—second, those in which the reduction in the number of corpuscles and the quantity of hemoglobin is approximately equal, and thirdly, those in which the number of corpuscles is not reduced as much as the percentage of hemoglobin—each corpuscle being poor in coloring matter. The first condition is seen typically in cases of pernicious anemia; the second in the so-called accidental anemias, those which are due to hemorrhage, wasting diseases, etc.; and the third is seen in chlorosis. The value of iron in any individual case of impoverishment of the blood is in proportion as the condition approaches the chlorotic type. In true *pernicious anemia*, iron is probably of no value at all, in the accidental or secondary anemia, it is often of considerable service, and in true *chlorosis* it almost reaches the height of a specific.

Some years ago, certain chemists, failing to find any increase in the amount of iron in the urine after the administration of the inorganic salts of iron by the mouth, were led to believe that these forms of iron were not absorbable from the intestinal tract, and the theory had at one time a considerable number of adherents. It would carry us beyond the proper bounds of an article for the Dispensatory to go into all the evidence for and against the absorbability of iron, and the reader interested in the details is referred to H. C. Wood, Jr.'s *Pharmacology*. The subject may be summed up for the present purposes with the statement that it has been as firmly established as any fact in pharmacology, that the inorganic salts of iron are absorbed through the intestinal walls, and exercise a direct influence upon the blood making organs. That the amount of iron in the urine is not increased is owing to the fact that the great bulk of the metal is eliminated through the intestinal glands; this is true whether the drug be given by the mouth or hypodermically. Because of the former vogue for the theory of the non-absorption of iron, various chemists were led to place upon the market preparations which are spoken of as "organic iron" or "masked iron," supposed to be in a more assimilable form than the pharmacopœial salts. There is no convincing evidence that any of these preparations has any advantage over the inorganic salts, except, perhaps, a little less liability to disturb digestion. Indeed, the experiments of Abderhalden (*Z. B.*, 1900, xxxix) indicate that the iron in organic combination is of less value for the treatment of anemia than when in the inorganic form. Because iron is an essential constituent of the hemoglobin, it was formerly almost universally believed, and still is to a considerable extent, that it acted in anemia as a food-stuff; but this belief has for its base mere assumption, and the infinitesimal amount of iron which is consumed in the human body, as well as the fact that patients with chlorosis are not cured by feeding upon the foods rich in iron, throws great doubt upon this ancient legend, and the experiments of Abderhalden, quoted above, furnish almost conclusive proof of its error. It is far more probable that the action of iron is due to a stimulating effect upon the blood making organs analogous to the stimulant action of caffeine upon the kidneys, or strychnine upon the spinal cord.

The question of the selection of a preparation of iron for an individual case is often one of great importance. If it be simply desired to combat anemia, a preparation should be selected which is free as may be from astringency. Most of the liquid preparations of iron are more or less injurious to the teeth, so that

commonly it is preferable to give a solid salt in pill or capsule rather than one of the liquid forms, unless the latter be especially indicated.

It would be much better if the U. S. P. recognized only a fraction of the present official preparations. All that can be accomplished with any preparation in simple anemia can be done with reduced iron or pill of the carbonate for exhibition in solid form and the ammonio-citrate or soluble phosphate for liquids. No compounds in which iron is combined with an alkaloid should be recognized by the Pharmacopœia or used by the practitioner. Of course, such combinations are to a greater or less extent effective, but the proportionate amount of the alkaloid and the iron required in individual cases varies indefinitely, and the habitual use of a fixed proportion, such as is demanded by the pharmacopœial combinations, strongly inclines the practitioner of medicine to careless and routine practice. The official alkaloidal-ferruginous preparations have no advantage whatever over extemporaneous prescriptions combining iron and the alkaloid.

Certain salts of iron are extremely astringent and more or less irritant. The most important of these are the sulphates and the chlorides. These salts should never be employed as chalybeates, except in those cases in which, for some reason, astringency is desired. In some cases some laxative should be combined with iron to overcome its constipating influence.

Iron has been employed hypodermically to some extent. It has been asserted by the chemists working under Kobert, of Dorpat, that when a solution of iron and sodium citrate is injected subcutaneously in man, 40 per cent. of the iron escapes in the urine unaltered, the elimination of the iron usually being accompanied by pronounced renal irritation. The hypodermic use of some of the organic compounds of iron has been strongly recommended by investigators. The latest researches seem, however, to show that the iron citrate is as good a preparation for the hypodermic administration of iron as any other, the iron appearing in the urine half an hour after its injection and being present for twenty-four hours. According to Gloevecke, 1 mil of a 10 per cent. solution, thrown into the muscles of the back, causes an enduring sharp pain, but Lepine asserts that 2.5 mils of a 4 per cent. solution produces little or no disturbance. It is stated that after the hypodermic injection of large doses the irritation of the alimentary canal is more severe than when the drug is given by the mouth—a statement which finds confirmation in the experiments of Gottlieb, who found that when he injected iron subcutaneously into a dog he was able to obtain nearly 97 per cent. of it from the fæces. The effort at intestinal elimination is evidently accompanied by irritation if the amount of iron to be eliminated is large.

Off. Prep.—Liquor Ferri Chloridi, *U. S.* (*Br.*); Liquor Ferri Pernitratis, *Br.;* Syrupus Ferri Iodidi, *U. S., Br.;* Syrupus Ferri Phosphatis, *Br.;* Syrupus Ferri Phosphatis cum Quinina et Strychnina, *Br.;* Vinum Ferri, *Br.;* Liquor Ferri Protochloridi, *N. F.;* Syrupus Calcii Iodidi, *N. F.;* Syrupus Ferri et Mangani Iodidi, *N. F.*

FERRUM REDUCTUM. U. S. (Br.)

REDUCED IRON Ferr. Reduct. [Iron by Hydrogen, Quevenne's Iron]

(fĕr'rŭm rę-dŭc'tŭm)

"Iron reduced to the metallic state by the action of hydrogen upon ferric oxide. It contains not less than 90 per cent. of metallic iron [Fe = 55.84]. Preserve it in well-closed containers." *U. S.* "Reduced Iron may be obtained by reducing ferric hydroxide, heated to dull redness, by means of a stream of dry hydrogen. It contains not less than 80 per cent. of metallic iron, with a variable amount of iron oxide." *Br.*

Ferrum Redactum, *Br., U. S.* 1870; Ferri Pulvis, *U. S.* 1850; Powder of Iron; Ferrum Hydrogenio Reductum, Ferrum Ope Hydrogenii Paratum; Iron reduced by Hydrogen; Fer réduit par l'Hydrogène, *Fr. Cod.;* Ferrum reductum, *P. G.;* Reduzirtes Eisen, *G.;* Ferro ridotto dall' idrogeno, *It.;* Hierro reducido por el hidrogeno, *Sp.*

A process for this form of iron is no longer given in the United States Pharmacopœia. (See *U. S. Dispensatory,* 19th edition, page 518.)

This preparation was introduced into the United States and Dublin Pharmacopœias of 1850, and is retained in the present edition of our own, although the process for it has been abandoned. It consists of metallic iron in fine powder, obtained by reducing the ferric oxide by hydrogen at a dull red heat. The subcarbonate of the U. S. Pharm., 1870, which is essentially the ferric oxide, is deprived of water by calcination, and then subjected to the reducing influence of a stream of hydrogen, purified from hydrogen sulphide and acid compounds by passing successively through a solution of lead subacetate and milk of lime. The hydrogen unites with the oxygen of the ferric oxide to form water, and leaves the iron in the metallic state. The ferric oxide should be perfectly free from sodium sulphate, which it is likely to contain when imperfectly washed. If this salt be present, it will be reduced by the hydrogen to the state of sodium sulphide, which will contaminate and spoil the metallic iron formed, and cause the preparation, when taken internally to give rise to unpleasant eructations. The heat should be carefully regulated, for if it fall below dull redness, part of the oxide will escape reduction, and if it exceed that point considerably, the particles of reduced iron will agglutinate, and the preparation will be heavy and not readily pulverizable. The 1885 British process is not so well fitted for practical purposes as is that of the U. S. Pharm., 1870. In the 1885 revision of the British Pharmacopœia, instead of directing a certain quantity of hydrated ferric oxide, a process is given in the formula for making the ferric oxyhydrate by precipitating a solution of ferric chloride. The direction to dry the hydrogen is unnecessary. On the subject of powder of iron, manufac-

turing chemists will find it useful to consult the paper of Soubeiran and Dublanc, in which full directions are given for purifying the hydrogen, constructing the furnace, regulating the heat, and avoiding explosions. (*A. J. P.*, xviii, 303.) For improvements by Procter, see *A. J. P.*, xix, 11. The necessity for purification of the hydrogen by passing it successively through concentrated potassium permanganate solution, lead acetate solution, and sulphuric acid has been proved by T. Appel. (*Oest. Zeit. f. Pharm.*, 1892, 395.)

Various processes have been proposed for obtaining powder of iron. Arthur Morgan, of Dublin, recommended the use of dried potassium ferrocyanide, thoroughly mixed with anhydrous ferric oxide, and calcined with pure potassium carbonate at a low red heat. The product contains all the iron in a reduced state, mixed with soluble matters, which are carefully washed away. (See *A. J. P.*, 1854, p. 450.) A similar process to the above has been proposed by a German chemist, named Zängerle, iron oxalate being substituted for the ferric oxide. (See *P. J.*, 1857, p. 565.) Wöhler recommended the use of the same oxalate, not in connection with potassium ferrocyanide, but as a suitable compound of iron for reduction by hydrogen. W. Müller found that ferric oxide obtained by heating the metal in the air is reduced when moist at 293° C. (559.4° F.); when quite dry, at 305° to 339° C. (581°–642.2° F.); the oxalate moist, at 278° C. (532.4° F.). Another eligible compound for reduction is the crystalline powder of ferric oxide, prepared by fusing, in a clay crucible, pure dried ferrous sulphate with three times its weight of sodium chloride, and then washing the melted mass when cold, until everything soluble is removed. (Wöhler.) Crolas prepares a pure ferric oxide by adding barium chloride to the solution of ferric chloride to precipitate the contaminating sulphate, getting rid of the barium chloride by crystallization and precipitating by solution of ammonia. The ammonium chloride is driven off by heat. (*J. P. C.*, 4e sér., xx, 30.) The process of Eugène Fegueux consists in reducing the ferric oxide by carbonic oxide, formed by passing a stream of carbon dioxide over a red hot charcoal in the reduction tube, before it reaches the ferric oxide. The carbon dioxide, thus reduced to carbonic oxide, is formed again by the deoxidizing of the ferruginous oxide.

Under the name of "*alcoholized iron*," a powdered iron was at one time sold in this country, said to be prepared, in the eastern parts of Germany, by attrition of iron filings with honey, by some cheap method, as by attachment to a saw mill or steam machinery. It had the appearance of powdered plumbago, but under the magnifying glass was seen to contain particles with metallic luster and rounded as if by friction. It was soluble in diluted sulphuric acid, with the escape of hydrogen, free, or nearly so, from sulphur, but a small quantity of black powder remained undissolved. (*A. J. P.*, 1867, p. 11.) The relation of the epithet "alcoholized" to this powder is an example of an unusual use of the word alcohol, which in the Arabic means "very finely divided." The word alcoholize, therefore, simply means to reduce to an impalpable powder and has been so used since its first use by Phillips in 1706. It is not much inferior to reduced iron, and is better than some preparations sold by that name.

Properties.—Reduced iron is a light, tasteless powder, soft to the touch, of an iron-gray color, and without metallic luster. If black, the preparation is to be rejected as not being fully deoxidized. When thrown into a diluted acid, it causes a lively effervescence of hydrogen without odor. A small portion of it, struck on an anvil with a smooth hammer, forms a scale having a brilliant metallic luster. It takes fire upon the application of a flame. On account of its great liability to oxidation, it should be kept in a dry bottle, well stoppered. A black powder, having a composition corresponding with that of the magnetic oxide of iron, was formerly sold under the name of Quevenne's iron. This synonym is now applied to the official product. The spurious powder may be known by its having a black instead of an iron-gray color, and by its effervescing but slightly with acids. In the process for making reduced iron, part of the oxide almost always escapes full deoxidation, and comes out of the tube having a black color. This part should be rejected, instead of being sold as reduced iron, as appears to have been done by some manufacturing chemists. If the preparation has been very badly made, its solution in diluted sulphuric acid will produce an intensely red color with potassium sulphocyanate. It is officially described as "a very fine, grayish-black, lusterless powder, without odor or taste; permanent in dry air. Reduced Iron is insoluble in water or alcohol. When ignited in contact with air, it glows and is converted into black ferroso-ferric oxide. Shake 1 Gm. of Reduced Iron with 5 mils of distilled water and filter; the liquid does not change the color of litmus. One Gm. of Reduced Iron, when treated with 20 mils of diluted sulphuric acid in a flask, causes the evolution of nearly odorless hydrogen gas, which does not affect paper moistened with lead acetate T.S. within two minutes (*sulphide*), and, on applying a gentle heat, the Iron dissolves in the acid without leaving more than 1 per cent. of residue. Add 20 mils of diluted sulphuric acid to 0.5 Gm. of Reduced Iron contained in a small, covered beaker, and, after the reaction has somewhat subsided, warm the liquid on a water bath until the reaction ceases. Collect any minute, undissolved residue upon a very small filter, rinse the beaker with distilled water, add the rinsings to the filter, and then wash the residue with distilled water until free from acid reaction. Transfer the residue to the beaker by rinsing it back, and, after adding about 0.25 Gm. of potassium chlorate and 5 mils of hydrochloric acid, slowly evaporate the

solution to dryness on a water bath. Dissolve the residue in sufficient distilled water to measure 50 mils, and add 5 mils of this solution to 5 mils of a saturated solution of sulphurous acid and heat the liquid on a water bath for fifteen minutes, or until all traces of sulphurous acid have been removed. The resulting solution meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"**Assay.**—Introduce into a 100 mil flask about 1 Gm. of Reduced Iron, previously well triturated and accurately weighed, and add 10 Gm. of fine powdered mercuric chloride and 50 mils of boiling distilled water. Boil the mixture for five minutes, shaking it frequently, then fill the flask to the 100 mil mark with distilled water, recently boiled and cooled, and cool it to room temperature. Again fill the flask to the mark with distilled water, stopper, agitate the contents well, and allow it to stand for a few minutes. Now filter the contents of the flask and immediately titrate 20 mils of the filtrate to which has been added 20 mils of diluted sulphuric acid, with tenth-normal potassium permanganate V.S. until a permanent pink color is produced. It shows not less than 90 per cent. of Fe when calculated from the original weight of Reduced Iron taken.

"Each mil of tenth-normal potassium permanganate V.S. used corresponds to 0.005584 Gm. of Fe. Each gramme of Reduced Iron corresponds to not less than 161.2 mils of tenth-normal potassium permanganate V.S." *U. S.*

"A fine greyish-black powder, strongly attracted by the magnet, and producing metallic streaks when rubbed with firm pressure in a mortar. Dissolves in *hydrochloric acid* with evolution of hydrogen, and without any odor of hydrogen sulphide, the solution giving a light-blue precipitate with *solution of potassium ferrocyanide.* When 0.25 gramme, in very fine powder, is added to a hot solution of 1.25 grammes of *copper sulphate* in 20 millilitres of *water,* the mixture kept hot and occasionally well shaken during ten minutes, and then rapidly filtered with the minimum of exposure to air, the filtrate decolorises not less than 35.8 millilitres of *N/10 solution of potassium permanganate.* Not more than 1 per cent. is insoluble in *hydrochloric acid. Arsenic limit* 200 parts per million." *Br.*

O. E. Winter (*J. A. P. A.*, 1913, p. 296) presents a critical review of the methods and requirements in all existing pharmacopœias and compares the efficiency of the various official methods for the determination of the iron. He favors the mercuric chloride method adopted in the U. S. P. IX, when accompanied by a limiting test for sulphides, which when present in large amounts, interferes with the accuracy of the method.

Uses.—Powder of iron, reduced from the oxide by hydrogen, was first prepared for medicinal purposes by Quevenne and Miquelard, of Paris. It is one of the best of the chalybeate tonics, nearly free from astringency. Observations to determine its therapeutic value, compared with that of the other ferruginous preparations, were made by Costes, for nearly four years, at the Saint-André hospital of Bordeaux, with the results highly favorable to it. It is sometimes prepared with chocolate in the form of lozenges.

Dose, one to three grains (0.065–0.20 Gm.) several times a day, given in powder or in pill.

Off. Prep.—Pilulæ Ferri Iodidi, *U. S.;* Trochiscus Ferri Redacti, *Br.;* Extractum Ferri Pomatum, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arsenii Fortiores, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arsenii Mites, *N. F.*

FLUIDEXTRACTA. U. S. (Br.)

FLUIDEXTRACTS

(flū-id-ĕx-trăc'tă)

Extracta Liquida, *Br.;* Fluid Extracts; Extraits liquides, *Fr.;* Extracta fluida, *P. G.;* Fluidextrakte, Flüssige Extrakt, *G.*

"Fluidextracts are concentrated liquid preparations of vegetable drugs, containing alcohol either as a solvent or as a preservative, and bearing a uniform relation to the drug used so that *one mil* of the fluidextract closely represents the activity of *one gramme* of the air-dried and powdered drug of standard quality." *U. S.*

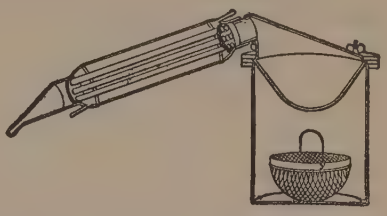
The Latin title Extractum —— Fluidum formerly used for Fluid Extracts was dropped by the U. S. P. VIII because of the confusion which resulted from the necessary bringing together of the extracts and fluid extracts due to a strict alphabetical arrangement; the name "fluidextractum" is now used for "fluidextract" and the latter made one word; this, of course, brings the fluidextract under the letter F instead of the letter E under which extracts and fluidextracts were formerly both classed.

Fluidextracts were first introduced into the U. S. P. of 1850 as a distinct class of preparations, the fluidextract of sarsaparilla being the only one previously directed, either in our own official code or by the British Colleges. Now we have one hundred and fifty-seven that are official in the U. S. P. IX, British Pharm., 1914, and National Formulary IV, besides large quantities of non-official fluidextracts annually produced. They are now perhaps the most important class of liquid preparations in use. Their distinctive character is the concentration of the active ingredients of medicinal substances into a small bulk, in the liquid form, a cubic centimeter, mil, or fluidgramme of any one of them now representing a gramme of the crude drug. In addition to convenience of administration, the advantage of these preparations is that, evaporation not being carried so far as in ordinary extracts, the active principles are less liable to be injured by heat. Formerly their main difficulty was the liability of substances in the liquid state to undergo spontaneous decomposition. In the U. S. P. of 1850 this was counteracted by means of sugar and of alcohol, but in 1865 (*A. J. P.*, 1865, p. 50) Taylor proposed the use of glycerin,

which was adopted in the U. S. P., 1870, revision. Glycerin, while it exerts a powerful preservative influence, possesses the valuable property of dissolving matters deposited by some of the fluidextracts when made with sugar, as in the old official recipes. Consequently these fluidextracts were much clearer and better preparations than were the old ones. Subsequent experience with these fluidextracts showed that the use of glycerin should be circumscribed, and that it had been employed too freely in the U. S. P., 1870, formulas. The solvent powers of glycerin are so great that the fluidextracts were frequently loaded with many inert principles, which it dissolved, giving them a dense, rich appearance, without increasing their activity. As the primary object of fluidextracts is concentration, suitable menstrua should in each case be selected with the single object of dissolving and retaining permanently the active constituents of the drug.

The present fluidextracts are of the same strength as those formerly official, and the formulas are based upon the theory that from a given weight of drug an amount of fluidextract shall be made equal in measure to the bulk of the same weight of distilled water; in other words, upon the relation of gramme to millilitre. Although the metric system is admirable in practice, some may prefer to use ordinary weights and measures; in such cases, to make 20 *fluidounces* of a fluidextract 19 *troyounces* of drug will be required, while if avoirdupois weight is preferred, the most convenient relation to recollect will be that 50 *avoirdupois ounces* are required to make 48 *fluidounces,* or *three pints,* of a fluidextract. It has been repeatedly proposed to make 50 *per cent. tinctures* or half-strength fluidextracts, the main object being to secure more representative preparations when made on the small scale. Experiments by Sayre, Gregory, Patch, and others prove that half-strength fluidextracts possess no advantages over those of official strength. (*D. C.*, 1897, 119, 147.) The precipitation experienced heretofore, when the evaporated weak percolate was added to the reserved portion, is considerably diminished by causing the former to be evaporated to a soft extract. This precipitation, formerly noticed more particularly in alcoholic fluidextracts, was due to the greater volatility of the alcohol in the weak percolates, which, when evaporated, left the residue to a great extent aqueous; when this was added to the strongly alcoholic reserved portion, a precipitation of resinous and frequently active matter took place, which necessitated the storing of the fluidextract until precipitation ceased, and subsequent filtration. This is not altogether avoided by evaporating to a soft extract, but the loss of activity through precipitation is thus greatly diminished. Fluidextracts invariably deposit insoluble matter upon standing, and those made in warm weather, owing to the greater solvent powers of the menstrua (due to the elevated temperature) are found to deposit more freely than the same kind of fluidextracts if made in the winter time with menstrua correspondingly reduced in temperature.

A useful distillatory apparatus has been contrived by Joseph P. Remington for recovering alcohol from weak percolates, and for general pharmaceutical uses. The still shown in the cut is the new form. It is made of tinned copper, the still body holding about three gallons; the condenser has seven straight tubes surrounded



with the cold water introduced by a rubber tube from a hydrant or bucket of water placed higher than the still, and carried off as it becomes warmed by the tube shown at the upper part of the condenser. By a siphon arrangement not shown in the cut, the still can be fed from a reservoir while distillation is in progress, thus using a three gallon still where otherwise a much larger one would have been necessary. The joints are carefully ground, and troublesome lutes and water joints are entirely superseded. The condenser, having straight tubes instead of a spiral one, is easily cleaned, and is powerful enough to condense a gallon of alcohol in thirty minutes. The still may be set into a kettle partly filled with water and thus used as a water bath, or a shallow tinned copper dish with flat rim, which accompanies the still, may be placed between the two brass ring bands and clamped securely. (*A. J. P.*, May, 1879.) Remington's *Practice of Pharmacy,* Fourth ed., page 158.

For valuable papers on percolation and fluidextracts, by William Procter, E. R. Squibb, Alonzo Robbins, and others, see *Proc. A. Ph. A.*, 1859, p. 265; 1863, p. 222; *A. J. P.*, 1878, pp. 209, 329; 1873, pp. 85, 189.

Several methods have been suggested for preparing fluidextracts more economically. The use of acetic acid as a menstruum to replace alcohol or diluted alcohol has the merit of economy. (See *Extracta,* also *A. J. P.*, 1899, 1–14; *Proc. Pennsylvania Pharm. Assoc.*, 1898, 116; *A. J. P.*, 1898, 543; *A. J. P.*, 1899, 67; *Ph. Era,* 1898, 796; *Proc. Minnesota Pharm. Assoc.*, 1902, 103; *West. Drug.*, 1903, 652.)

The most important modification is the plan of repercolation, as proposed by E. R. Squibb, for this class of preparations as well as the dry extracts.

Repercolation.—In consequence of the existing high price of alcohol, it is important to adopt some plan by which, while the ends aimed at are attained, the consumption of the men-

struum used in percolation may be diminished. This object has been accomplished, to a considerable extent, by E. R. Squibb, of Brooklyn, N. Y., by a modification of the process of percolation to which he has given the name at the head of the present paragraph. As defined by the author, repercolation consists in the successive application of the same percolating menstruum to fresh portions of the substances to be percolated. The result is that the same menstruum, acting repeatedly on unexhausted portions of the substance, becomes concentrated to the greatest possible extent, so that much of the menstruum is saved, while subsequent evaporation is avoided, which is itself an object of great importance in the preparation of extracts. It is obvious that repercolation is not applicable to the preparation of infusions, decoctions, tinctures, etc., in which the object in general is less a high degree of concentration than precision in the strength of the preparation, and consequently in the dose. It is to the extracts and fluidextracts that the process is peculiarly adapted, and there now remains no doubt whatever of the great value of the improvement. One of its disadvantages is that the substance treated is less completely exhausted than when the proceeding is inverted, and fresh portions of menstruum are made to act on the same material until the latter is deprived of all its soluble matter. But the loss in this way is trifling, compared with the gain when a menstruum as high-priced as alcohol is employed.

Another practical disadvantage is the inconvenience of keeping the weak percolates, as these have to be labelled, numbered, and stored away for use until the same operation is repeated. In deciding when to adopt it, the operator will, of course, be influenced by the relative value of the drug and the menstruum. In order to secure the most favorable results in repercolation, certain methods of proceeding are advisable in various steps of the process, differing with the character of the substance to be acted on; and these can be determined only by a careful study, confirmed by repeated experiment. Squibb used repercolation exclusively on the large scale in the manufacture of extracts and fluidextracts, and applied it especially to the preparation of fluidextracts of cinchona; and since his first paper, which was reproduced in the 14th revision of the U. S. Dispensatory, p. 1164, he introduced several improvements, which are intended to make the process useful to the apothecary in his every-day work. See Type Process C, page 484.

The plan of N. Spencer Thomas consists in exposing the substance to be acted on to successive expressions, by means of a press, with the menstruum divided into different portions, so that fresh portions of liquid are brought to act on the same solid body in different stages of exhaustion, and then mixing the expressed liquids. The due proportion between the weight of the medicine and the bulk of the ultimate fluidextract is secured by regulating the measure of the last added portion of menstruum, which, in the process as described by Thomas, is the third. Whatever may be the advantages of this method—and it is not without its recommendations—it is liable to the objection of loss of alcohol through exposure during expression. Another method of limiting the quantity of alcohol used has been proposed by S. P. Duffield, of Detroit. It consists in macerating, for from six to ten days, the medicine to be acted on, previously deprived, by means of a vacuum apparatus, of all the air, and of all readily volatilizable matter contained in its pores, with a certain volume of the menstruum, which is forced through a tube into the vacuum pan by atmospheric pressure, and thus brought into the most intimate contact with all parts of the powder. The process is completed by submitting the mass thus impregnated to hydraulic pressure, and, after allowing the liquid to settle in glass carboys, drawing off the clear liquid into bottles. It is obviously inapplicable to substances whose virtues depend in any considerable degree upon readily volatilizable constituents. Campbell (*A. J. P.*, xlii, 17) proposed a method for doing away with the use of heat, which, however, although in some cases it may do well, cannot be relied upon for the complete exhaustion of all drugs. Sixteen troyounces of the powder are moistened with four to six fluidounces of the menstruum (usually alcohol), and packed in a glass funnel, a piece of sponge having previously been put in the beak of the funnel; the surface of the powder is covered with a disk of paper, and twelve fluidounces of menstruum poured on. When the sponge becomes saturated, the beak of the funnel is corked tightly and the whole set aside for four days, at the end of which time the percolation may be allowed to proceed without further addition of menstruum. J. W. Mill has called attention to the advantage of separating the powder into fine and coarse parts by means of sieves and packing the finer powder at the bottom.

H. Biroth (*Pharm.*, April, 1877) proposes the method which he termed "*insuccation*," for making non-alcoholic fluidextracts; the advantages claimed for it are simplicity and economy. Colaz prepared fluidextracts from fresh plants by bruising and crushing them, and placing the mass in a dialyzer suspended in 90 per cent. alcohol; when the dialysis is completed, the liquid is evaporated to free it from alcohol, the remaining aqueous liquid retaining the active constituents in the proportions in which they are found in the plant. (*Ph. Post*, xxix, 271.) Haussmann (*A. J. P.*, 1895, 291), after examining a large number of commercial fluidextracts, recorded his results in tabular form, and considered that there is great variation in the quality, due to deviation from pharmacopœial processes.

J. U. Lloyd proposes to recover the alcohol which remains absorbed by the residue after percolation, by mixing the wet residues with an equal bulk or less of dry sawdust, and then

percolating this with water. (*A. J. P.*, June, 1877.) Wm. M. Thomson, of Philadelphia, devised a very complete method of preparing fluidextracts on a large scale; the principles of his process are maceration and percolation *in vacuo*, and although the principles which have been applied have long been known, and similar apparatus used by Duffield and others, there are many useful practical points which merit a notice in detail. The percolators are egg-shaped, and made of tinned copper; they are capable of being tightly covered, and communicate by means of stopcocks above and below, and iron and stout rubber tubing, with a very efficient double acting air pump. The moistened powder is packed tightly in the percolator, and the cover securely bolted on. The stopcock in the cover is now opened, which communicates with the air pump and a partial vacuum created in the space above the moistened drug; the stopcock is now closed and another stopcock in the cover opened, which communicates by a tube with the reservoir containing the menstruum. The menstruum, of course, quickly penetrates the powder, taking the place of the interstitial air, and when the powder is saturated it is permitted to macerate *in vacuo* a sufficient length of time. To start percolation, a receiver is connected with the beak of the percolator, and, the air being exhausted from it, the percolate at once makes its appearance. When the flow slackens, air may be forced by the pump in the space above the powder, if desired, and the receiver again exhausted below. In this way, it can be seen, entire control of these powerful physical forces may be secured. The advantages are very apparent in preventing the loss of volatile principles and alcohol, while protecting from chemical change caused by exposure to the air. It is quite possible to make official fluidextracts without recourse to subsequent evaporation of weak percolate. For a cut of this apparatus, see *A. J. P.*, 1882.

Assaying Fluidextracts.—The number of assay processes for fluidextracts was materially increased in the U. S. P. (9th Rev.) for preparations made from alkaloidal drugs. The process in each case differs but slightly from the process used for the corresponding drug; they will be found in the succeeding pages under their appropriate headings.

A new method of assay for alkaloidal fluidextracts, especially adapted to the mydriatic leaf drugs in that the interfering chlorophyll is removed, making only one shaking out operation necessary, was proposed by LaWall (*J. A. Ph. A.*, 1912, 29), as follows: Place 25 Gm. of sodium chloride in a 100 mil graduated cylinder, with water sufficient to make 85 mils. Agitate well for 1 minute, then pour upon a dry filter and collect 50 mils of clear filtrate, which can be shaken out as directed in the final shake out of the ordinary assay process, using the solvent directed for the particular drug which is being assayed. The method does not work with cinchona, guarana or other drugs containing large amounts of alkaloids in the form of cinchotannates.

Fluidextracts U. S. P. IX.

* "The fluidextracts of this Pharmacopœia, with few exceptions, may be classified according to the menstrua used in the extraction of the drugs and the processes of manufacture employed. Several drugs require special manipulation to obtain satisfactory fluidextracts, and for these appropriate formulas have been devised and are printed in full in the text. The following type processes are described, and in each formula the process to be used is designated by reference to the type process:

"**Type Process A**—In this class are included those fluidextracts that are made with a menstruum of alcohol or a mixture of alcohol and water by the usual process of percolation. Moisten *one thousand grammes* [or 35 ounces av., 120 grains] of the powdered drug directed with a sufficient quantity of the prescribed menstruum to render it evenly and distinctly damp and to maintain it so, after macerating for six hours in a tightly-covered container. Then pack it in a cylindrical percolator and add enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding more menstruum until the drug is exhausted. Reserve the first *eight hundred and fifty mils* [or 28 fluidounces, 356 minims] of the percolate (unless otherwise specified in the formula); recover the alcohol from the remainder and concentrate the residue to a soft extract at a temperature not exceeding 60° C. (140° F.); dissolve this in the reserved portion, mix thoroughly, and finally add a sufficient quantity of the menstruum to obtain *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] or the volume determined by calculation from the assay.

"**Type Process B**—In this class are included those fluidextracts in which glycerin or an acid is used in the extraction and two menstrua are successively employed. Menstruum I contains the glycerin or acid in definite proportion to the amount of the drug, and Menstruum II, a mixture of alcohol and water intended for completing the exhaustion of the drug. Moisten *one thousand grammes* [or 35 ounces av. 120 grains] of the powdered drug directed with a sufficient quantity of the prescribed Menstruum I, to render it evenly and distinctly damp and to maintain it so after macerating for six hours in a tightly-covered container. Then pack it in a cylindrical percolator, add the remainder of Menstruum I, and, when this has just disappeared from the surface, gradually add Menstruum II, constantly maintaining a stratum of liquid above the drug. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours, and then allow the percolation to proceed slowly, gradu-

ally adding Menstruum II until the drug is exhausted. Reserve the first *eight hundred and fifty mils* [or 28 fluidounces, 356 minims] of the percolate (unless otherwise specified in the formula); recover the alcohol from the remainder and concentrate the residue to a soft extract at a temperature not exceeding 60° C. (140° F.); dissolve this in the reserved portion, mix thoroughly, and finally add a sufficient quantity of Menstruum II to obtain *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] or the volume determined by calculation from the assay.

"**Type Process C**—The process of *fractional* or *divided percolation.* This is especially recommended for drugs containing volatile ingredients or constituents injured by exposure to heat. This process may likewise be used as an alternative process in the formulas in which Type Process A is directed. Divide *one thousand grammes* [or 35 ounces av., 120 grains] of the powdered drug directed into three portions of *five hundred grammes* [or 17 ounces av. 279 grains] *three hundred grammes* [or 10 ounces av. 255 grains] and *two hundred grammes* [or 7 ounces av. 24 grains] respectively. Moisten the first portion of the drug (500 Gm.) [or 17 ounces av., 279 grains] with a sufficient quantity of the prescribed menstruum to render it evenly and distinctly damp and to maintain it so after macerating for six hours in a tightly-covered container. Then pack it in a cylindrical percolator and add enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours and then allow the percolation to proceed slowly, gradually adding more of the menstruum. Reserve the first *two hundred mils* [or 6 fluidounces, 366 minims] of percolate and continue the process until the additional percolate measures *fifteen hundred mils* [or 50 fluidounces, 345 minims], the latter being collected in successive portions of *three hundred mils* [or 10 fluidounces, 69 minims] each.

"Moisten the second portion of the powdered drug (300 Gm.) [or 10 ounces av. 255 grains] with a sufficient quantity of the percolate collected in the preceding operation immediately after the reserved portion, to render it evenly and distinctly damp and to maintain it so after macerating for six hours in a tightly-covered container. Then pack it in a cylindrical percolator and macerate and percolate as directed for the first part of the drug, using as menstruum the several portions of percolate from the preceding operation in the order in which they have been collected, and, if this be insufficient, follow with some of the original menstruum. Reserve the first *three hundred mils* [or 10 fluidounces, 69 minims] of percolate and continue the process until the additional percolate measures *eight hundred mils* [or 27 fluidounces, 24 minims] collecting the weaker percolate in successive portions of *two hundred mils* [or 6 fluidounces, 366 minims] each.

"Moisten the third portion of the powdered drug (200 Gm. [or 7 ounces av. 24 grains]) with a sufficient quantity of the percolate collected in the preceding operation immediately after the reserved portion, to render it evenly and distinctly damp and to maintain it so after macerating for six hours in a tightly-covered container. Then pack it in a cylindrical percolator and macerate and percolate as before, using as menstruum the several portions of percolate from the preceding operation in the order in which they have been collected, and, if this be insufficient, follow with more of the original menstruum. Collect *five hundred mils* [or 16 fluidounces, 435 minims] of percolate and mix this with the two portions previously reserved so as to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of finished fluidextract.

"When Type Process C is directed for fluidextracts which are adjusted by assay to a definite alkaloidal standard, collect only *four hundred and twenty mils* [or 14 fluidounces, 97 minims] of percolate from the third portion of drug instead of the *five hundred mils* [or 16 fluidounces, 435 minims] directed above. Mix this percolate with the two portions previously reserved, assay a portion of the mixture and then adjust its volume, by the addition of the menstruum directed, so that each *one hundred mils* [or 3 fluidounces, 183 minims] of finished fluidextract will contain the prescribed amount of alkaloid.

"**Type Process D**—In this class are included those fluidextracts in which extraction is effected by infusion and percolation with boiling water, alcohol being added to the concentrated liquid as a preservative.

"In the preparation of fluidextracts by either Process A, B, or C, the rate of percolation must be carefully controlled and, for the quantities directed in the formulas of the Pharmacopœia, the flow should not exceed ten drops per minute until the reserved percolate is collected, and twenty drops per minute thereafter. As a rule *one thousand grammes* [or 35 ounces av., 120 grains] of powdered drug may be exhausted by percolation with sufficient menstruum to yield *three thousand mils* [or 101 fluidounces, 212 minims] of percolate.

"Fluidextracts should be kept in tightly-stoppered containers for one month and then, if perfectly clear, they should be stored in amber-colored bottles protected from sunlight and extremes of temperature. If sedimentation has occurred the clear portion should be decanted, the remainder filtered and the liquids thoroughly mixed before storing.

"The percentage of alcohol in fluidextracts made by type processes A, B, or C is variable and always less than that in the menstruum employed, due, among other causes, to loss of alcohol by evaporation during manufacture, to the presence of a variable proportion of water in the air-dried drug, and to the extraction from the drug of its soluble constituents, which also often vary greatly in different lots of the same drug. The percentage of alcohol in the finished

product can therefore only be ascertained by an actual determination (see Determination of Alcohol in Official Preparations, Part III, No. 14). To *one thousand grammes* [or 35 ounces av., 120 grains] of the ground drug add *five thousand mils* [or 169 fluidounces, 33 minims] of boiling water, mix thoroughly and allow it to macerate in a covered container for two hours in a warm place. Then transfer the moist drug to a tinned or enameled metallic percolator and allow percolation to proceed, gradually adding boiling water until the drug is exhausted. Evaporate the percolate on a water bath or steam bath to the volume specified and when cold add the alcohol directed and mix thoroughly." *U. S.*

FLUIDEXTRACTUM ACONITI. U. S.

FLUIDEXTRACT OF ACONITE Fldext. Aconit.

(flū-ĭd-ĕx-trăc'tŭm ăc-ō-nī'tī)

" *One hundred mils* of Fluidextract of Aconite yields not less than 0.45 Gm. nor more than 0.55 Gm. of the ether-soluble alkaloids of aconite. If assayed biologically the minimum lethal dose should not be greater than 0.00004 mil for each gramme of body weight of guinea-pig." *U. S.*

Fluid Extract of Aconite Root; Extrait liquide de Racine d'Aconit, *Fr.*; Flüssiges Eisenhutknollenextrakt, *G.*

* " Aconite, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains].

" Prepare a Fluidextract by Type Process C, as modified for alkaloidal drugs (see page 484), using a mixture of *three volumes* of alcohol and *one volume* of water as the menstruum and adjusting the volume of the finished Fluidextract so that each *one hundred mils* contains 0.5 Gm. of the ether-soluble alkaloids of aconite." *U. S.*

" **Assay.**—From a pipette drop 15 mils of Fluidextract of Aconite evenly over the surface of 15 Gm. of purified sawdust (see Part III) and evaporate to dryness at a temperature not exceeding 75° C. (167° F.). Transfer the mixture to a 250 mil flask, add 150 mils of ether, and proceed as directed under *Belladonnæ Radix,* page 222, fifth line of the Assay, modifying the process there given by using the ammonia water with a small quantity of distilled water to rinse the dish in which the mixture was evaporated, and ether only in the final shaking out of the alkaloids.

" Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 64.539 milligrammes of the ether-soluble alkaloids of aconite.

" For an alternative method of assaying Fluidextract of Aconite see Biological Assays (Part III)." *U. S.* (See *Aconitum.*)

This preparation of aconite root was found useful by Procter as a basis for making the other preparations of aconite,—the plaster, extract, tincture, or liniment. The fluidextract is of a bright deep reddish-brown color. It will doubtless be frequently employed as an addition to liniments for obtaining the peculiar effects of aconite.

Dose, one-half to one minim (0.03–0.06 mil), but on account of its very powerful character it should always be used with caution, beginning with the smallest dose.

Off. Prep.—Linimentum Aconiti et Chloroformi, *N. F.*

FLUIDEXTRACTUM AROMATICUM. U. S.

AROMATIC FLUIDEXTRACT Fldext. Aromat.

(flū-ĭd-ĕx-trăc'tŭm ăr-ō-măt'ĭ-cŭm)

Extrait liquide aromatique, *Fr.*; Flüssiges Aromatisches Extrakt, *G.*

* " Aromatic Powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process C (see page 484), using alcohol as the menstruum." *U. S.*

This is a valuable fluidextract; it is an excellent aromatic in concentrated form, and will be found very useful not only as an addition to liquids when an aromatic is desired, but its concentrated form permits its use in small quantities with dry powders, like pepsin, bismuth subnitrate, etc., when desired for administration. It is rarely used alone.

Dose, from ten to twenty minims (0.6–1.3 mils), diluted with water, or dropped on sugar.

FLUIDEXTRACTUM ASPIDOSPERMATIS. U. S.

FLUIDEXTRACT OF ASPIDOSPERMA Fldext. Aspidosp. [Fluidextract of Quebracho]

(flū-ĭd-ĕx-trăc'tŭm ăs-pĭ-dō-spēr-mā'tĭs)

* "Aspidosperma, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process B (see page 483), using a mixture of *one hundred and ten mils* [or 3 fluidounces, 345 minims] of glycerin, *six hundred and seventy mils* [or 22 fluidounces, 315 minims] of alcohol and *two hundred and twenty mils* [or 7 fluidounces, 211 minims] of water as Menstruum I, and a mixture of *two volumes* of alcohol and *one volume* of water as Menstruum II." *U. S.* (See *Aspidosperma,* page 204.)

Dose, one fluidrachm (3.75 mils).

FLUIDEXTRACTUM AURANTII AMARI. U. S.

FLUIDEXTRACT OF BITTER ORANGE PEEL Fldext. Aurant. Amar.

(flū-ĭd-ĕx-trăc'tŭm âu-răn'tĭ-ī ă-mā'rī)

Extrait liquide d'Ecorce d'Orange amére, *Fr.*; Flüssiges Pomeranzenschalenextrakt, *G.*

* "Bitter Orange Peel, in No. 20 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process C (see page 484), using a mixture of *three volumes* of alcohol and *one volume* of water as the menstruum." *U. S.*

This fluidextract is useful as a tonic; when dry, the bitter orange peel having very little oil present, there is necessarily little agreeable orange flavor to the fluidextract. Monroe Bond recommends a *Fluidextract of Sweet Orange*

Peel, made with a menstruum of seven parts of alcohol and one of glycerin. (*A. J. P.,* 1873, p. 482.)

Dose, fifteen to thirty minims (0.9–1.8 mils).

Off. Prep.—Vinum Rhei Compositum, *N. F.*

EXTRACTUM BELÆ LIQUIDUM. Br.

LIQUID EXTRACT OF BAEL

(ĕx-trăc'tŭm bē'læ lĭq'uĭ-dŭm)

"Bael Fruit, bruised, 1000 *grammes;* Chloroform Water, 15000 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Macerate the bruised Bael Fruit for twelve hours in five thousand *millilitres* of the Chloroform Water; pour off and reserve the clear liquid; repeat the maceration a second and a third time for one hour in each case, using for each maceration five thousand *millilitres* of the Chloroform Water; press the marc; strain the mixed liquids through flannel. Evaporate to seven hundred and fifty *millilitres;* cool; add sufficient of the Alcohol to produce the required volume; filter." *Br.*

This represents whatever therapeutic virtues may reside in Bael Fruit. (See *Belæ Fructus,* page 219.)

Dose, one to two fluidrachms (3.75–7.5 mils).

FLUIDEXTRACTUM BELLADONNÆ RADICIS. U. S. (Br.)

FLUIDEXTRACT OF BELLADONNA ROOT

Fldext. Bellad. Rad.

(flŭ-ĭd-ĕx-trăc'tŭm bĕl-lą-dŏn'næ rą'dĭ-cīs)

"*One hundred mils* of Fluidextract of Belladonna Root yields not less than 0.405 Gm. nor more than 0.495 Gm. of the alkaloids of belladonna root." *U. S.*

"Liquid Extract of Belladonna contains in 100 millilitres, 0.75 gramme of the alkaloids of Belladonna Root." *Br.*

Extractum Belladonnæ Liquidum, *Br.,* Liquid Extract of Belladonna; Extrait liquide de Racine de Belladone, *Fr.;* Flüssiges Tollkirschenwurzelextrakt, *G.*

* "Belladonna Root, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]." *U. S.*

* "Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *five volumes* of alcohol and *one volume* of water as the menstruum, and reserving the first *eight hundred mils* [or 27 fluidounces, 24 minims] of the percolate.

"After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and, from the result thus obtained, ascertain by calculation the amount of alkaloids in the remainder of the liquid and dilute this with enough menstruum to make *one hundred mils* of the finished Fluidextract contain 0.45 Gm. of the alkaloids of belladonna root." *U. S.*

"Belladonna Root, in No. 20 powder, 1000 *grammes;* Alcohol (90 per cent.), Distilled Water, of each *a sufficient quantity.* Exhaust the Belladonna Root with a mixture of seven volumes of the Alcohol and one volume of Distilled Water by the *repercolation process* until from every three *grammes* of the Root one *millilitre* of strong percolate has been obtained." *Br.*

"**Assay.**—Introduce 10 mils of Fluidextract of Belladonna Root into a separator and add 10 mils of distilled water and 2 mils of ammonia water. Completely extract the alkaloids by shaking out repeatedly with chloroform and then extract the alkaloids from the chloroform solution by shaking out repeatedly with weak sulphuric acid until the alkaloids are completely removed. Collect the acid washings in a separator, add ammonia water until the solution is decidedly alkaline to litmus, and completely extract the alkaloids by shaking out repeatedly with chloroform. Evaporate the combined chloroform washings to dryness, dissolve the alkaloids from the residue in exactly 5 mils of tenth-normal sulphuric acid V.S. and titrate the excess of acid with fiftieth-normal potassium hydroxide V.S., using cochineal T.S. as indicator.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 28.92 milligrammes of the alkaloids of belladonna root (see Proximate Assays, Part III)." *U. S.*

"Determine the proportion of alkaloids in this strong percolate by the following process: Introduce into a separator 10 *millilitres* of the strong percolate, 50 *millilitres* of *water,* 2 *millilitres* of *diluted sulphuric acid,* and 10 *millilitres* of *chloroform.* Shake vigorously, set aside until complete separation has taken place, draw off the lower layer, and wash it with two successive portions, each of 10 *millilitres,* of *water* acidified with *diluted sulphuric acid.* Add the washings to the upper layer left in the separator. Make the mixture distinctly alkaline with *solution of ammonia,* and extract the alkaloids by shaking with three successive portions, each of 10 *millilitres* of *chloroform.* Mix the chloroformic solutions, shake with 10 *millilitres* of *water,* allow separation to take place, draw off the lower layer into a beaker, and set aside for the chloroform to evaporate. Heat the residue on a water-bath for thirty minutes, add 10 *millilitres* of *N/20 solution of sulphuric acid,* warm gently until dissolved, and titrate back with *N/20 solution of sodium hydroxide, tincture of cochineal* being used as indicator. Deduct the number of *millilitres* of alkaline solution required from 10; the remainder, multiplied by 0.01446, gives the number of *grammes* of the alkaloids contained in 10 *millilitres* of the strong percolate. To the remainder of the strong percolate add sufficient of the alcoholic menstruum to produce a Liquid Extract of Belladonna containing 0.75 *gramme* of the alkaloids of Belladonna Root in 100 *millilitres.* Examined by the foregoing process, Liquid Extract of Belladonna is found to contain in 100 millilitres 0.75 gramme of the alkaloids of Belladonna Root. *Limit of error* 0.05 gramme in excess or defect. This Liquid Extract contains 0.75 gramme of the alkaloids of Belladonna Root in 100 millilitres; 110 minims contains ¾ grain." *Br.*

The British liquid extract, 1914, represented several radical improvements in British pharmacy,—*i.e.*, the use of repercolation with absence of heat in the process, and standardization, thus making the end product bear a definite relation towards the quantity of active constituents found in the root (0.75 per cent.). It is based upon the formula proposed by R. A. Cripps. (*P. J.*, 1895, 795.) It will be observed that the alkaloidal standards of the U. S. and Br. Pharmacopœias are not identical; the U. S. fluidextract is made from the standardized drug (belladonna root) (0.45 per cent.); the British liquid extract is made from the *unstandardized* drug and hence the standard for the liquid extract can be made stronger (0.75 per cent.). The fluidextract of the root is a good preparation, of reddish-brown color, very different in appearance from the deep-green fluidextract of the leaves which is often seen in the market.

Dose, from one to two minims (0.06–0.12 mil) of the British liquid extract, not more than one minim (0.06 mil).

Off. Prep.—Emplastrum Belladonnæ, *Br.;* Extractum Belladonnæ Siccum, *Br.;* Linimentum Belladonnæ, *U. S., Br.;* Unguentum Belladonnæ, *Br.*

FLUIDEXTRACTUM BUCHU. U. S.

FLUIDEXTRACT OF BUCHU Fldext. Buchu.

(flū-ĭd-ĕx-trăc'tŭm bū'chū)

Extrait liquide de Bucco, *Fr.;* Flüssiges Buccoextrakt, *G.*

* "Buchu, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using alcohol as the menstruum." *U. S.*

The menstruum selected for this fluidextract has been alcohol, although experience has shown that with the weaker alcohol used in the U. S. P. VIII formula it was possible to percolate buchu leaves satisfactorily. We prefer as a menstruum that of the U. S. P. VIII, *i.e.*, alcohol 3, water 1.

This fluidextract is of a dark green color, and shows in a high degree the sensible properties of the leaves. It acquires the odor of mint when long kept, showing that some change takes place in its volatile oil. This fluidextract affords the best means at our command for the exhibition of buchu.

Dose, thirty minims to a fluidrachm (1.8–3.75 mils), three to five times a day.

Off. Prep.—Elixir Buchu, *N. F.*

FLUIDEXTRACTUM CANNABIS. U. S.

FLUIDEXTRACT OF CANNABIS Fldext. Cannab. [Fluidextractum Cannabis Indicæ, U. S. P. VIII]

(flū-ĭd-ĕx-trăc'tŭm căn'nă-bĭs)

"When assayed biologically Fluidextract of cannabis produces incoördination when administered to dogs in a dose of not more than 0.03 mil per kilogramme of body weight." *U. S.*

Extrait liquide de Chanvre Indien, *Fr.;* Flüssiges Indisch-Hanfextrakt, *G.*

* "Cannabis, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using alcohol as the menstruum. After dissolving the soft extract in the reserve liquid, assay a portion as directed below and from the result thus obtained adjust the volume of the finished Fluidextract to conform to the above biological standard.

"**Assay.**—Proceed as directed under *Cannabis* and also under Biological Assays, Part III." *U. S.*

Uses.—The fluidextract of cannabis represents the therapeutic virtues of that drug in a convenient form. The smallness of the dose is an advantage over the tincture and many believe that the extract is injured by the evaporation. Unfortunately the fluidextract, even when properly made, does not retain its powers and after a year is almost worthless. For this reason the commercial samples vary so greatly in power that it is impossible to assign the proper dose. The only satisfactory way to use it is to start in with doses of one or two minims, increasing each day until some effect is obtained.

Dose, one to four minims (0.06–0.25 mil).

Off. Prep.—Collodium Salicylici Compositum, *N. F.*

FLUIDEXTRACTUM CASCARÆ SAGRADÆ. U. S. (Br.)

FLUIDEXTRACT OF CASCARA SAGRADA Fldext. Casc. Sagr. [Fluidextractum Rhamni Purshianæ, U. S. VIII]

(flū-ĭd-ĕx-trăc'tŭm căs-căr'æ są-grăd'æ)

Extractum Cascaræ Sagradæ Liquidum, *Br.;* Liquid Extract of Cascara Sagrada; Extrait liquide de Cascara Sagrada, *Fr.;* Flüssiges Cascara-Sagrada-extrakt, *G.*

* "Cascara Sagrada, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, *two hundred and fifty mils* [or 8 fluidounces, 218 minims]. Prepare a Fluidextract by Type Process D (see page 484). Evaporate the aqueous percolate to *seven hundred and fifty mils* [or 25 fluidounces, 173 minims] and when cold gradually add the alcohol and, if necessary, sufficient water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.* "Cascara Sagrada, in No. 20 powder, 1000 *grammes;* Alcohol (90 per cent.), 250 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Exhaust the Cascara Sagrada with the Distilled Water by the *percolation process;* evaporate the percolate to six hundred *millilitres;* add the Alcohol previously mixed with one hundred and fifty *millilitres* of the Distilled Water, or with sufficient to produce the required volume." *Br.*

This fluidextract is a good preparation, but the aromatic fluidextract is more largely used.

The emodin strength of this and similar preparations of cascara, which has been arbitrarily set by most manufacturers at 1.50 grammes in each 100 mils of the fluidextract, may be estimated by the method of Vanderkleed and Ewe (*Proc. Pa. Pharm. Assoc.*, 1913, p. 325.)

Dose, fifteen minims to one fluidrachm (0.9–3.75 mils).

Off. Prep.—Extractum Cascaræ Sagradæ Siccum, *Br.;* Syrupus Cascaræ Aromaticus, *Br.*

FLUIDEXTRACTUM CASCARÆ SAGRADÆ AROMATICUM. U. S.

AROMATIC FLUIDEXTRACT OF CASCARA SAGRADA
Fldext. Casc. Sagr. Arom. [Fluidextractum Rhamni Purshianæ Aromaticum, U. S. VIII]

(flū-ĭd-ĕx-trăc'tŭm căs-căr'æ są-grăd'æ ăr-ō-măt'ĭ-cŭm)

Tasteless Fluidextract of Cascara Sagrada; Extrait liquid Aromatique de Cascara Sagrada, *Fr.;* Bitterloses flüssiges Cascara-Sagradaextrakt, *G.*

* "Cascara Sagrada, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Magnesium Oxide, *one hundred and twenty-five grammes* [or 4 ounces av., 179 grains]; Pure Extract of Glycyrrhiza, *forty grammes* [or 1 ounce av., 180 grains]; Glycerin, *two hundred mils* [or 6 fluidounces, 366 minims]; Alcohol, *two hundred and fifty mils* [or 8 fluidounces, 218 minims]; Benzosulphinide, *one gramme* [or 15 grains]; Oil of Anise, *two and five-tenths mils* [or 40 minims]; Oil of Cinnamon, *two-tenths of a mil* [or 3 minims]; Oil of Coriander, *one-tenth of a mil* [or 1½ minims]; Methyl Salicylate, *two-tenths of a mil* [or 3 minims]; Boiling Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Thoroughly mix the cascara sagrada with the magnesium oxide, moisten the mixture with *two thousand mils* [or 67 fluidounces, 301 minims] of boiling water, set it aside for two hours, stirring occasionally, and then pack it in a percolator. Now pour on boiling water and allow the percolation to proceed until the drug is exhausted. Evaporate the percolate to *five hundred mils* [or 16 fluidounces, 435 minims] and while yet warm dissolve in it the extract of glycyrrhiza. When cold, add the glycerin, then the alcohol in which the benzosulphinide and the oils have been dissolved, and finally sufficient water to make the Fluidextract measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

An aromatic fluidextract was introduced into the U. S. P. VIII for the first time. It is given as a laxative, the object of the addition of magnesium oxide is to destroy the bitter taste of the cascara sagrada. Lime is sometimes used instead of magnesia but it has been shown that lime acts injuriously upon the laxative principles of cascara sagrada.

Dose, fifteen minims to one fluidrachm (0.9–3.75 mils).

Off. Prep.—Elixir Cascaræ Sagradæ, *N. F.;* Elixir Cascaræ Sagradæ Compositum, *N. F.*

FLUIDEXTRACTUM CIMICIFUGÆ. U. S.

FLUIDEXTRACT OF CIMICIFUGA
Fldext. Cimicif. [Fluidextract of Black Cohosh, Fluidextract of Black Snakeroot]

(flū-ĭd-ĕx-trăc'tŭm cĭm-ĭ-cĭf'ŭ-gæ)

Extractum Cimicifugæ Liquidum, *Br.* 1898, Liquid Extract of Cimicifuga; Liquid Extract of Actæa Racemosa; Extrait liquide d'Actée à Grappes, *Fr.;* Flussiges Cimicifugaextrakt, *G.*

* "Cimicifuga, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using alcohol as the menstruum." *U. S.*

There probably cannot be two opinions about the menstruum, although it has been asserted that a good fluidextract can be made with a menstruum of three parts alcohol and one part water. The probabilities are, however, that a portion of the resinous principle would precipitate on standing. This fluidextract is of a deep reddish-brown color, and thoroughly represents the drug.

Dose, from ten to thirty minims (0.6–1.9 mils).

Off. Prep.—Elixir Sodii Salicylatis Compositum, *N. F.;* Syrupus Cimicifugæ Compositus, *N. F.*

FLUIDEXTRACTUM CINCHONÆ. U. S. (Br.)

FLUIDEXTRACT OF CINCHONA Fldext. Cinchon. [Fluidextract of Calisaya Bark]

(flū-ĭd-ĕx-trăc'tŭm cĭn-chō'næ)

"*One hundred mils* of Fluidextract of Cinchona yields not less than 4 Gm. nor more than 5 Gm. of the alkaloids of cinchona." *U. S.* "Liquid Extract of Cinchona contains in 100 millilitres 5 grammes of the alkaloids of Red Cinchona Bark." *Br.*

Extractum Cinchonæ Liquidum, *Br.,* Liquid Extract of Cinchona; Extractum Chinæ Calisayæ Fluidum; Extrait liquide de Quinquina jaune, *Fr.;* Flüssiges Kalisayarinden extrakt, Flüssiges Chinaextrakt, *G.*

* "Cinchona, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process B (see page 483), using a mixture of *one hundred mils* [or 3 fluidounces, 183 minims] of glycerin, *one hundred mils* [or 3 fluidounces, 183 minims] of diluted hydrochloric acid and *eight hundred mils* [or 27 fluidounces, 24 minims] of alcohol as Menstruum I and a mixture of *four volumes* of alcohol and *one volume* of water as Menstruum II. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and, from the result thus obtained, ascertain by calculation the amount of alkaloids in the remainder of the liquid, and dilute this with enough of Menstruum II to make each *one hundred mils* of the finished Fluidextract contain 4.5 Gm. of the total alkaloids of cinchona." *U. S.*

"Red Cinchona Bark, in No. 60 powder, 1000 *grammes;* Hydrochloric Acid, 31 *millilitres;* Glycerin, 125 *millilitres;* Alcohol (90 per cent.), Distilled Water, of each *a sufficient quantity.* Mix the Red Cinchona Bark with five thousand *millilitres* of the Distilled Water, to which the Hydrochloric Acid and Glycerin have been added; set aside in a covered vessel for forty-eight hours, stirring frequently; transfer to a percolator; when the liquid ceases to pass continue the percolation with Distilled Water until the percolate ceases to give a precipitate with excess of *solution of sodium hydroxide.* Evaporate the percolate in a porcelain or enamelled

iron vessel at a temperature not exceeding 85° C. (185° F.), until it is reduced to one thousand *millilitres.*" *Br.*

Assay of Fluidextract of Cinchona.—"From a pipette drop 5 mils of Fluidextract of Cinchona evenly over the surface of 10 Gm. of purified sawdust (see Part III) and evaporate it to dryness at a temperature not exceeding 80° C. (176° F.). Transfer the mixture to a 500 mil flask, and proceed as directed under *Cinchona,* third line of the Assay, beginning with the words 'and add,' modifying the process there given by increasing the amount of ammonia water to 10 mils, using this in divided portions to rinse the dish in which the mixture was evaporated, and adding the rinsings to the flask.

"The weight of the residue is the amount of total alkaloids from 4 mils of Fluidextract of Cinchona." *U. S.*

British Assay.—"Determine the proportion of alkaloids in the liquid product by the following process: Transfer 5 *millilitres* to a stoppered glass separator; add 15 *millilitres* of *benzolated amylic alcohol* and 10 *millilitres* of *N/1 alcoholic solution of potassium hydroxide;* shake well, set aside in a warm place for a few minutes, shaking occasionally, and then allow the liquids to separate; pour off the clear upper layer into a second separator and repeat the shaking with two further portions of 15 and 10 *millilitres* of *benzolated amylic alcohol.* Shake the mixed alcoholic liquids with two portions, each of 5 *millilitres,* of *water,* and reject the aqueous liquid; then shake vigorously with a warm mixture of 12 *millilitres* of *diluted hydrochloric acid* and 60 *millilitres* of *water,* using three successive portions of 30, 30, and 12 *millilitres,* and drawing off the acid liquids into a separator. To this acid liquid add 15 *millilitres* of *chloroform* and distinct excess of *solution of ammonia,* shake vigorously, allow the liquids to separate and draw off the chloroformic layer into a tared dish; repeat the shaking and separating with further portions, each of 10 *millilitres,* of *chloroform* until the aqueous liquid, after acidification with *diluted sulphuric acid,* gives no further precipitate with *solution of potassio-mercuric iodide.* Add the chloroformic solutions to that in the dish, allow the chloroform to evaporate slowly; dry the residue in the dish at a temperature of about 110° C. (230° F.) and weigh. The weight of the residue is that of the total alkaloids in 5 *millilitres* of the liquid product. Having thus ascertained the alkaloidal strength of the liquid product, bring every volume of it containing 5 *grammes* of total alkaloids to eighty-five *millilitres,* either by evaporation or by dilution with Distilled Water as may be necessary, add twelve and a half *millilitres* of the Alcohol, and finally sufficient Distilled Water to produce one hundred *millilitres* of the Liquid Extract. Examined by the foregoing process, Liquid Extract of Cinchona is found to contain in 100 *millilitres* 5 grammes of the alkaloids of Red Cinchona Bark. *Limit of error* 0.2 gramme in excess or defect. This Liquid Extract contains 5 grammes of the alkaloids of Red Cinchona Bark in 100 millilitres; 110 minims contain 5 grains." *Br.*

The process for this fluidextract was changed in the U. S. P. IX by the addition of diluted hydrochloric acid to the menstruum of alcohol, glycerin and water.

The U. S. fluidextract of cinchona is a moderately thin, dark reddish-brown, translucent fluid, of a bitter, astringent taste.

Dose, five to twenty minims (0.3–1.3 mils).

FLUIDEXTRACTUM COLCHICI SEMINIS. U. S.

FLUIDEXTRACT OF COLCHICUM SEED
Fldext. Colch. Sem.

(flŭ-ĭd-ĕx-trăc'tŭm cŏl'çhĭ-cī sĕm'ĭ-nĭs)

"*One hundred mils* of Fluidextract of Colchicum Seed yields not less than 0.36 Gm. nor more than 0.44 Gm. of colchicine." *U. S.*

Extrait liquide de Semences de Colchique, *Fr.;* Flüssiges Zeitlosensamenextrakt, *G.*

* "Colchicum Seed, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Purified Petroleum Benzin, *a sufficient quantity.* Pack the colchicum seed in a cylindrical percolator and slowly percolate with purified petroleum benzin until a few drops of the percolate leave no greasy stain when evaporated on a piece of filter paper. Reject the benzin solution, remove the powder from the percolator and dry it by exposure to the air. Then proceed to make the Fluidextract by Type Process A (see page 483), using a mixture of *two volumes* of alcohol and *one volume* of water as the menstruum. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and, from the result thus obtained, ascertain by calculation the amount of alkaloids in the remainder of the liquid, and dilute this with enough menstruum to make each *one hundred mils* of the finished Fluidextract contain 0.4 Gm. of colchicine." *U. S.*

"Assay of Fluidextract of Colchicum Seed.—Introduce 15 mils of Fluidextract of Colchicum Seed into a 500 mil flask, add 10 mils of solution of lead subacetate, previously diluted with 35 mils of distilled water, shake the mixture thoroughly, then add 240 mils of distilled water, again agitate the mixture and proceed as directed under *Colchici Semen,* page 371, ninth line of the Assay." *U. S.*

The use of glycerin in the former U. S. fluidextract was objectionable, as the fixed oil contained in the seeds was always thrown out of solution, and was usually found floating on the fluidextract, rendering the preparation unsightly. The present formula, U. S. P. IX, is an improvement, as the fixed oil is removed by the benzin treatment. L. I. Morris (*A. J. P.,* 1881, 7) believes that it is unnecessary to grind the colchicum seeds, and that if the whole seeds are digested with diluted alcohol at 80° C. (176° F.) the colchicine is easily extracted.

Dose, two to eight minims (0.12–0.5 mil).

Off. Prep.—Vinum Colchici Seminis. *N. F.*

FLUIDEXTRACTUM DIGITALIS. U. S.

FLUIDEXTRACT OF DIGITALIS Fldext. Digital.

(flū-ĭd-ĕx-trăc'tŭm dĭg-ĭ-tă'lĭs)

"If assayed biologically the minimum lethal dose should not be greater than 0.0006 mil of the Fluidextract, or the equivalent in Fluidextract of 0.0000005 Gm. of ouabain, for each gramme of body weight of frog." *U. S.*

Extrait liquide de Digitale, *Fr.;* Flüssiges Fingerhutkrautextrakt, Flüssiges Digitalisextrakt, *G.*

* "Digitalis, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *five volumes* of alcohol and *one volume* of water as the menstruum."

Assay.—For a method of assaying Fluidextract of Digitalis, see *Digitalis,* and also Biological Assays, Part III.

The increase in the proportion of alcohol in this fluidextract as compared to that of the U. S. VIII is a great advantage. Not only does this menstruum extract the activities of the drug more thoroughly, but with the low percentage of alcohol in the former fluidextract there was marked deterioration of the preparation when kept. (See Hamilton, *A. J. P.,* Feb., 1914.)

Dose, one-half to two minims (0.03–0.12 mil).

FLUIDEXTRACTUM ERGOTÆ. U. S. (Br.)

FLUIDEXTRACT OF ERGOT Fldext. Ergot.
[Secalis Cornuti Extractum Fluidum P. I.]

(flū-ĭd-ĕx-trăc'tŭm ẹr'gọ-tæ)

Extractum Ergotæ Liquidum, *Br.;* Liquid Extract of Ergot; Extrait liquide de Seigle ergoté, *Fr.;* Extractum Secalis Cornuti fluidum, *P. G.;* Mutterkorn-Fluidextrakt, Flüssiges Mutterkornextrakt, *G.*

* "Ergot, recently ground and in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process B (see page 483), using a mixture of *twenty mils* [or 325 minims] of hydrochloric acid and *nine hundred and eighty mils* [or 33 fluidounces, 66 minims] of diluted alcohol as Menstruum I, and diluted alcohol as Menstruum II." *U. S.* "Ergot, crushed, 1000 *grammes* Distilled Water, 7500 *millilitres;* Alcohol (90 per cent.), 375 *millilitres.* Macerate the crushed Ergot with five thousand *millilitres* of the Distilled Water for twelve hours; strain; repeat the maceration with the remainder of the Distilled Water; press; strain; evaporate the mixed liquids to seven hundred *millilitres;* when cold, add the Alcohol; set aside for an hour; filter. The product measures about one thousand *millilitres.*" *Br.*

The Br. preparation is greatly inferior to the U. S. because of the use of an aqueous menstruum. It has been shown by Barger and Dale (*Biochem. J.,* 1907, ii, p. 286) that the Br. liquid extract is almost completely lacking in the characteristic alkaloid, ergotoxin.

Uses.—An increase in the percentage of alcohol used in this fluidextract would have been an advantage, as some of the active principles of ergot are practically insoluble in water. Great care should be observed in the evaporation of the second portion of the percolate not to exceed the official temperature, 60° C. (140° F.) as the activity of ergot is seriously lessened by heating.

The U. S. fluidextract, when fresh, well represents the activity of ergot and is probably the best preparation of ergot on the market. Unfortunately, however, as shown by H. C. Wood, Jr. (*A. J. P.,* 1911, 172), it is subject to rapid deterioration. (For literature on this subject, see Eberhardt and Eldred, *J. A. Ph. A.,* 1914, iii, 38.) This loss of potency is accelerated by exposure to the air and the preparation should be stored in small containers which are kept tightly corked until used. Pittenger and Vanderkleed assert that by keeping the fluidextract in hermetically sealed vacuum tubes it will retain its activity almost indefinitely; but the figures they give do not entirely confirm their claim. Certainly the common custom of buying fluidextract of ergot, for retail dispensing, and pouring out a little now and then as it may be called for, on prescriptions, can not be too severely condemned. Under such conditions the preparation may lose 50 per cent. of its power in less than six months.

Dose, from half a fluidrachm to two fluidrachms (1.8–8.0 mils).

FLUIDEXTRACTUM ERIODICTYI. U. S.

FLUIDEXTRACT OF ERIODICTYON Fldext. Eriodict.
[Fluidextract of Yerba Santa]

(flū-ĭd-ĕx-trăc'tŭm ĕr-ĭ-ō-dĭc'tỹ-ī)

Extrait liquide d'Eriodictyon, *Fr.;* Flüssiges Eriodictyonextrakt, *G.*

* "Eriodictyon, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *four volumes* of alcohol and *one volume* of water as the menstruum, and reserving the first *eight hundred mils* [or 27 fluidounces, 24 minims] of percolate." *U. S.*

For a process for Aromatic Fluidextract of Yerba Santa, see *U. S. D.,* 19th ed., p. 539.

This fluidextract has a dark brownish-green color, and has proven a valuable addition.

Dose, from fifteen minims to a fluidrachm (0.9–3.75 mils).

Off. Prep.—Elixir Eriodictyi Aromaticum, *N. F.;* Syrupus Eriodictyi Aromaticus, *N. F.*

FLUIDEXTRACTUM EUCALYPTI. U. S.

FLUIDEXTRACT OF EUCALYPTUS
Fldext. Eucalypt.

(flū-ĭd-ĕx-trăc'tŭm eū-cạ-lỹp'tī)

Extrait liquide d'Eucalyptus, *Fr.;* Flüssiges Eucalyptusextrakt, *G.*

* "Eucalyptus, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see

page 483), using a mixture of *three volumes* of alcohol and *one volume* of water as the menstruum, and reserving the first *eight hundred mils* [or 27 fluidounces, 24 minims] of percolate." *U. S.*

This fluidextract well represents the drug, and is of a dark greenish-brown color, having the peculiar odor and taste of eucalyptus very strongly developed, but in effectiveness it is much inferior to the volatile oil.

Dose, from ten to thirty minims (0.6–1.8 mils).

FLUIDEXTRACTUM FRANGULÆ. U. S.

FLUIDEXTRACT OF FRANGULA Fldext. Frangul. [Fluidextract of Buckthorn Bark]

(flū-ĭd-ĕx-trăc'tŭm frăn'gū-læ)

Extrait liquide d'Ecorce de Bourdaine, *Fr.;* **Extractum Frangulæ fluidum,** *P. G.;* **Faulbaum-Fluidextrakt, Flüssiges Faulbaumrindenextrakt,** *G.*

* " Frangula, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, *two hundred and fifty mils* [or 8 fluidounces, 218 minims]. Prepare a Fluidextract by Type Process D (see page 484). Evaporate the aqueous percolate to *seven hundred and fifty mils* [or 25 fluidounces, 173 minims] and, when cold, add the alcohol and, if necessary, sufficient water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

This is a fluidextract which has been quite largely used in this country. It is intended to be a laxative, but it is frequently disappointing, as the drug is rarely to be obtained of uniformly good quality. The fluidextract is of a dark reddish-brown color. For a process for Sweet Fluidextract of Buckthorn, see *U. S. D.,* 19th ed., p. 540.

Dose, ten to twenty minims (0.6–1.3 mils).

Off. Prep.—Elixir Catharticum Compositum, *N. F.;* Syrupus Sennæ Compositus, *N. F.*

FLUIDEXTRACTUM GELSEMII. U. S.

FLUIDEXTRACT OF GELSEMIUM Fldext. Gelsem.

(flū-ĭd-ĕx-trăc'tŭm gĕl-sĕm'ĭ-ī)

Extrait liquide de Jasmin jaune ou Gelsemium, *Fr.;* **Flüssiges Gelber Jasminextrakt, Flüssiges Gelsemiumextrakt,** *G.*

* " Gelsemium, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *four volumes* of alcohol and *one volume* of water as the menstruum." *U. S.*

In this fluidextract the former menstruum of alcohol has been replaced in the U. S. P. IX with alcohol, 4 volumes, and water, 1 volume. It is of a dark reddish-brown color.

Dose, from one to three minims (0.06–0.2 mil).

Off. Prep.—Elixir Sodii Salicylatis Compositum, *N. F.*

FLUIDEXTRACTUM GENTIANÆ. U. S.

FLUIDEXTRACT OF GENTIAN Fldext. Gentian.

(flū-ĭd-ĕx-trăc'tŭm jĕn-tī-ā'næ)

Extrait liquide de Gentiane, *Fr.;* **Flüssiges Enzianextrakt,** *G.*

* " Gentian, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using diluted alcohol as the menstruum." *U. S.*

This is a translucent, reddish-brown fluid, with the odor and taste of the root. It may be questionable whether it is needed, though it has the advantage that we may obtain from it the tonic effects of the drug with less alcohol than in an equivalent quantity of the tincture, and pharmaceutically it affords a convenient method of giving to mixtures the tonic properties of gentian when required.

Dose, from ten to thirty minims (0.6–1.8 mils).

Off. Prep.—Elixir Gentianæ, *N. F.;* Elixir Gentianæ et Ferri, *N. F.;* Elixir Gentianæ et Ferri Phosphatis, *N. F.;* Elixir Gentianæ Glycerinatum, *N. F.*

FLUIDEXTRACTUM GLYCYRRHIZÆ. U. S. (Br.)

FLUIDEXTRACT OF GLYCYRRHIZA Fldext. Glycyrrh.

(flū-ĭd-ĕx-trăc'tŭm glĭç-ĭr-rhī'zæ)

Extractum Glycyrrhizæ Liquidum, *Br.;* **Liquid Extract of Liquorice; Fluidextract of Licorice or Liquorice; Extrait liquide de Réglisse,** *Fr.;* **Flüssiges Süssholzwurzelextrakt,** *G.*

* " Glycyrrhiza, in No. 20 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, *two hundred and fifty mils* [or 8 fluidounces, 218 minims]; Ammonia Water, Chloroform Water, Water, each, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix *three hundred mils* [or 10 fluidounces, 69 minims] of ammonia water with *twenty-seven hundred mils* [or 91 fluidounces, 142 minims] of chloroform water and moisten the glycyrrhiza with a sufficient quantity of the mixture; pack it in a cylindrical percolator and add enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding more of the same menstruum until the glycyrrhiza is exhausted. Reserve the first *five hundred mils* [or 16 fluidounces, 435 minims] of the percolate and evaporate the remainder on a water bath to a soft extract; dissolve this in the reserve portion and add enough water to make the product measure *seven hundred and fifty mils* [or 25 fluidounces, 173 minims]. A few drops of ammonia water may be added if necessary to facilitate solution. Now gradually add the alcohol, allow the product to stand for seven days in a stoppered container, then decant the clear liquid, filter the remainder and wash the residue on the filter with enough of a mixture of *one volume* of alcohol and *three volumes* of water to make the Fluidextract measure *one*

thousand mils [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

"Liquorice Root, in No. 20 powder, 1000 *grammes;* Chloroform Water, 5000 *millilitres;* Alcohol (90 per cent.), *a sufficient quantity.* Mix the Liquorice Root with one-half of the Chloroform Water; set aside for twenty-four hours; strain; press; to the pressed marc add the remainder of the Chloroform Water, and set aside for six hours; strain; press; mix the strained liquids; heat to 100° C. (212° F.); strain through flannel; evaporate until the liquid has acquired, when cold, a specific gravity of 1.200; add to this one-fourth of its volume of the Alcohol; let the mixture stand for twelve hours; filter." *Br.*

The process for this fluidextract was materially changed in the U. S. P. VIII. The former processes, while making stable fluidextracts of good appearance, were deficient in not providing for the removal of the acrid, oily constituent found in licorice root; the U. S. P. VIII process overcame this difficulty by exhausting the coarsely powdered root with boiling water, concentrating the infusions, adding alcohol to precipitate inert constituents, and filtering; the filtrate was distilled to recover the excess of alcohol, and glycerin, ammonia water and alcohol added to bring the measure to the required standard. This process was essentially that recommended by A. R. L. Dohme. The U. S. P. IX process differs materially. Chloroform water is used to exhaust the licorice root with ammonia water to dissolve the glycyrrhizin, alcohol is added finally to preserve the fluidextract. The object of using chloroform water in the U. S. and British processes is to prevent decomposition in the aqueous liquids. The British formula for the liquid extract has several inconvenient manipulative features, such as the repeated macerations and expressions, evaporating to a certain specific gravity, etc. (See *Mont. Pharm. Journ.*, 1893, 147; *P. J.*, 1898, 188.) This preparation is now very largely used as an adjuvant, and for disguising the bitter taste of quinine, which should be added to the preparation of licorice just before the dose is taken. It is a very convenient form for using licorice, as the ammonia renders the glycyrrhizin soluble, thus materially adding to the power and sweetness of the fluidextract, and it also greatly lessens the acridity. It is a very dark reddish-brown liquid, having the well known sweet taste of licorice, and froths when shaken with water. A *syrup of licorice* may be made by adding two parts of fluidextract to fourteen parts of simple syrup. (See also N. F., Part III.) An elixir containing licorice (*Elixir Adjuvans*) was made official in the U. S. P. VIII and introduced into the U. S. P. IX under the name of *Elixir of Glycyrrhiza.*

Used as a vehicle only.

Off. Prep.—Elixir Glycyrrhizæ, *U. S.;* Mistura Sennæ Composita, *Br.;* Syrupus Sarsaparillæ Compositus, *U. S.;* Elixir Glycyrrhizæ Aquosum, *N. F.;* Elixir Glycyrrhizæ Aromaticum, *N. F.;* Elixir Taraxaci Compositum, *N. F.;* Syrupus Cimicifugæ Compositum, *N. F.*

EXTRACTUM GOSSYPII RADICIS CORTICIS LIQUIDUM. Br.

LIQUID EXTRACT OF COTTON ROOT BARK

(ĕx-trăc'tŭm gŏs-sĭp'ĭ-ī rạd'ĭ-cīs cŏr'tĭ-cīs lĭq'uĭ-dŭm)

"Cotton Root Bark, in No. 30 powder, 1000 *grammes;* Glycerin, 250 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Mix the Glycerin with seven hundred and fifty *millilitres* of the Alcohol; moisten the Cotton Root Bark with this mixture and continue the *percolation process,* using as menstruum first the remainder of the mixture of Glycerin and Alcohol, and afterwards sufficient of the Alcohol to produce the required volume." *Br.*

The fluidextract of cotton root bark (U. S. P. 1890) was not retained in the U. S. P. VIII or IX, but the National Formulary IV introduced a fluidextract made from the recently-gathered air-dried bark of the root, using alcohol for the menstruum. (See Part III.) The British process requires the use of glycerin which may have a tendency to prevent gelatinization.

Uses.—There is reason to believe that cotton-root bark loses some of its activity in drying. For this reason the preparation of the N. F. IV is to be preferred to the Br. For therapeutic properties of cotton root, see *Gossypii Radicis Cortex.*

Dose, one-half to one fluidrachm (1.8–3.75 mils).

FLUIDEXTRACTUM GRANATI. U. S.

FLUIDEXTRACT OF POMEGRANATE

Fldext. Granat.

(flû-ĭd-ĕx-trăc'tŭm grạ-nā'tī)

Fluidextract of Pomegranate Root Bark; Extrait liquide d'Ecorce de Balaustier, Extrait liquide d'Ecorce de Grenadier, *Fr.;* Flüssiges Granatwurzelrindenextrakt, *G.*

* "Pomegranate, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process B (see page 483), using a mixture of *one hundred mils* [or 3 fluidounces, 183 minims] of glycerin, *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol and *four hundred mils* [or 13 fluidounces, 252 minims] of water as Menstruum I, and diluted alcohol as Menstruum II." *U. S.*

This fluidextract was admitted to the U. S. Pharmacopœia (8th Revision) for the first time; it well represents the virtues of pomegranate.

Dose, from one-half to one fluidrachm (1.8–3.75 mils).

FLUIDEXTRACTUM GRINDELIÆ. U. S. (Br.)

FLUIDEXTRACT OF GRINDELIA

Fldext. Grindel.

(flû-ĭd-ĕx-trăc'tŭm grĭn-dē'lĭ-æ)

Extractum Grindeliæ Liquidum, *Br.,* Liquid Extract of Grindelia; Extrait liquide de Grindélia, *Fr.;* Flüssiges Grindelienextrakt, *G.*

* "Grindelia, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *three volumes*

of alcohol and *one volume* of water as the menstruum." *U. S.* "Grindelia, in No. 40 powder, 1000 *grammes;* Sodium Bicarbonate, 100 *grammes;* Distilled Water, 500 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Exhaust the Grindelia by *percolation* with the Alcohol. Recover the alcohol from the percolate by distillation, and dissolve the residue in the Distilled Water, to which the Sodium Bicarbonate has previously been added; after effervescence has ceased, add sufficient Distilled Water to produce seven hundred and fifty *millilitres,* and then sufficient of the Alcohol to produce the required volume." *Br.*

This is a fluidextract which well represents the drug; owing to the large quantity of resinous matter present, it does not mix well with aqueous liquids. The so-called "*alkaline fluid extract of grindelia*" may be made by evaporating one pint of official fluidextract until reduced to twelve fluidounces, making a solution of 180 grains of sodium bicarbonate in four fluidounces of water, adding it slowly to the evaporated fluidextract, and filtering; the British liquid extract is made upon this principle. The fluidextract is a dark brown liquid having the peculiar odor of grindelia.

For medical properties and uses, see *Grindelia.*

Dose, from one-half to one fluidrachm (1.8–3.75 mils).

FLUIDEXTRACTUM GUARANÆ. U. S.

FLUIDEXTRACT OF GUARANA Fldext. Guaran.

(flū-ĭd-ĕx-trăc'tŭm guą-rā'næ)

"*One hundred mils* of Fluidextract of Guarana yields not less than 3.6 Gm. nor more than 4.4 Gm. of caffeine." *U. S.*

Extrait liquide de Guarana, *Fr.;* Flüssiges Guaranaextrakt, *G.*

* "Guarana, in No. 60 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *three volumes* of alcohol and *one volume* of water as the menstruum, and reserving the first *eight hundred mils* [or 27 fluidounces, 24 minims] of percolate. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and, from the result thus obtained, ascertain by calculation the amount of alkaloid in the remainder of the liquid and dilute this with enough menstruum to make each *one hundred mils* of the finished Fluidextract contain 4 Gm. of caffeine." *U. S.*

Assay.—Introduce 5 mils of Fluidextract of Guarana into a separator, add 1 mil of ammonia water, and shake out the alkaloid with chloroform until completely extracted, as shown by testing with iodine T.S. Evaporate the combined chloroform solutions to dryness and dissolve the residue in 20 mils of distilled water with the aid of heat. Allow this to cool, filter it into a separator and wash the container and filter with several small portions of distilled water, adding the rinsings to the liquid in the separator. Then shake out the alkaloid with chloroform until completely extracted, as shown by testing with iodine T.S., evaporate the combined chloroform solutions and dry the residue to constant weight at 80° C. (176° F.). The weight represents the alkaloid in 5 mils of Fluidextract of Guarana (see Proximate Assays, Part III)." *U. S.*

The menstruum for this fluidextract, U. S. P. IX (alcohol 3, water 1), is stronger than that of the U. S. P. VIII (diluted alcohol).

This fluidextract is of doubtful utility. The powdered drug itself is portable, not unpleasant to the taste, and is efficient when given suspended in water; nothing is gained by making it into a fluidextract. The fluidextract is of a deep reddish-brown color. (See *Proc. A. Ph. A.,* 1897, 423.)

Dose, one to two fluidrachms (3.75–7.5 mils).

Off. Prep.—Elixir Guaranæ, *N. F.*

EXTRACTUM HAMAMELIDIS LIQUIDUM. Br.

LIQUIDEXTRACT OF HAMAMELIS

(ĕx-trăc'tŭm hăm-ą-mĕl'ĭ-dĭs lĭq'uĭ-dŭm)

Fluidextractum Hamamelis Foliorum, Fluidextract of Hamamelis Leaves; Fluidextract of Witch-hazel Leaves; Extrait liquide de Hamamélis, *Fr.;* Flüssiges Hamamelisextrakt, *G.;* Extracto fluido de hamamelis, *Sp.*

"Hamamelis Leaves, dried, in No. 40 powder, 1000 *grammes;* Alcohol (45 per cent.), sufficient to produce 1000 *millilitres.* Exhaust the Hamamelis Leaves by *percolation* with the Alcohol. Reserve the first eight hundred and fifty *millilitres* of the percolate; recover the alcohol from the remainder by distillation; evaporate the residue to a soft extract; dissolve this in the reserved portion; add sufficient of the Alcohol to produce the required volume." *Br.*

This liquid extract well represents the virtues of witchhazel. The fluidextract of hamamelis leaves of the U. S. P. VIII was not retained in the U. S. P. IX, but will be found in the N. F. (See Part III.) It has a dark reddish-brown color.

Dose, ten to thirty minims (0.6–1.8 mils).

Off. Prep.—Unguentum Hamamelidis, *Br.*

FLUIDEXTRACTUM HYDRASTIS. U. S. (Br.)

FLUIDEXTRACT OF HYDRASTIS Fldext. Hydrast. [Fluidextract of Golden Seal]

(flū-ĭd-ęx-trăc'tŭm hȳ-drăs'tĭs)

"*One hundred mils* of Fluidextract of Hydrastis yields not less than 1.8 Gm. nor more than 2.2 Gm. of the ether-soluble alkaloids of hydrastis." *U. S.* "Liquid Extract of Hydrastis contains in 100 millilitres 2 grammes of hydrastine." *Br.*

Extractum Hydrastis Liquidum, *Br.;* Liquid Extract of Hydrastis; Extrait liquide de Hydrastis, *Fr.;* Extractum Hydrastis fluidum, *P. G.;* Hydrastis-Fluidextrakt; Flüssiges Hydrastisextrakt, *G.;* Estratto di idraste liquido, *It.;* Extracto fluido de hidrastis, *Sp.*

* "Hydrastis, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process B (see

page 483), using a mixture of *one hundred mils* [or 3 fluidounces, 183 minims] of glycerin, *six hundred mils* [or 20 fluidounces, 138 minims] of alcohol and *two hundred mils* [or 6 fluidounces, 366 minims] of water as Menstruum I, and a mixture of *two volumes* of alcohol and *one volume* of water as Menstruum II. Reserve the first *seven hundred and fifty mils* [or 25 fluidounces, 173 minims] of percolate. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and, from the result thus obtained, ascertain by calculation the amount of alkaloids in the remainder of the liquid and dilute this with enough of Menstruum II to make each *one hundred mils* of the finished Fluidextract contain 2 Gm. of the ether-soluble alkaloids of hydrastis.

"Hydrastis Rhizome, in No. 60 powder, 1000 *grammes;* Alcohol (60 per cent.), *a sufficient quantity.* Exhaust the Hydrastis Rhizome with the Alcohol by the *percolation process;* reserve the first eight hundred and fifty *millilitres* of the percolate; recover the alcohol from the remainder by distillation; evaporate to a soft extract and dissolve in the reserved portion.

"**Assay.**—Proceed as directed under *Fluidextractum Belladonnæ Radicis,* page 486), modifying the process there given by using 5 mils of Fluidextract of Hydrastis instead of 10 mils of the fluidextract of belladonna root and using only ether as the immiscible solvent throughout the assay. Dry the residue to constant weight at 100° C. (212° F.), instead of titrating it. The weight represents the amount of ether-soluble alkaloids in 5 mils of the Fluidextract of Hydrastis." *U. S.*

"Determine the proportion of hydrastine in the liquid extract thus obtained by the following process: Transfer 10 millilitres of the liquid extract to a 100 millilitre graduated flask, add 20 millilitres of *solution of potassium iodide* diluted with 60 millilitres of *water,* and then sufficient *water* to produce 100 millilitres. Shake the mixture for several minutes and filter. Transfer 50 millilitres of the filtrate to a separator, render alkaline with *solution of ammonia,* add 30 millilitres of *ether,* and shake at intervals during several minutes. Allow the liquids to separate, draw off the aqueous solution into a beaker and the ethereal solution into a tared beaker. Return the aqueous solution to the separator and repeat the operation with two successive portions, each of 20 millilitres, of *ether* for one minute. Draw off and reject the aqueous layer; transfer the ethereal solutions to the tared beaker and evaporate at a gentle heat; dry the residue on a water-bath and weigh. The weight is that of the hydrastine in 5 millilitres of the liquid extract examined. To the remainder of the liquid extract add sufficient of the menstruum to produce a Liquid Extract of Hydrastis containing 2 grammes of hydrastine in 100 millilitres. Examined by the foregoing process Liquid Extract of Hydrastis is found to contain in 100 millilitres 2 grammes of hydrastine. *Limit of error* 0.1 gramme in excess or defect. This Liquid Extract contains 2 grammes of hydrastine in 100 millilitres; 110 minims contain 2 grains." *Br.*

The fluidextract thoroughly represents the drug. It is of a deep brownish-yellow color.

Dose, from fifteen minims to one fluidrachm (0.9–3.75 mils).

Off. Prep.—Tinctura Hydrastis, *Br.;* Mistura Rhei Alkalina, *N. F.*

FLUIDEXTRACTUM HYOSCYAMI. U. S.

FLUIDEXTRACT OF HYOSCYAMUS Fldext. Hyosc. [Fluidextract of Henbane]

(flū-ĭd-ĕx-trăc'tŭm hȳ-ŏs-cȳ'ă-mī)

"*One hundred mils* of Fluidextract of Hyoscyamus yields not less than 0.055 Gm. nor more than 0.075 Gm. of the alkaloids of hyoscyamus." *U. S.*

Extrait liquide de Jusquiame, *Fr.;* Flüssiges Bilsenkrautextrakt, *G.*

* "Hyoscyamus, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *three volumes* of alcohol and *one volume* of water as the menstruum. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and, from the result thus obtained, ascertain by calculation the amount of alkaloids in the remainder of the liquid and dilute this with enough menstruum to make each *one hundred mils* of the finished Fluidextract contain 0.065 Gm. of the alkaloids of hyoscyamus." *U. S.*

"**Assay.**—Proceed as directed under *Fluidextractum Belladonnæ Radicis,* page 486, modifying the process there given by using 25 mils of the Fluidextract of Hyoscyamus in place of 10 mils of fluidextract of belladonna root, and before titrating treating the residue twice with 5 mils of ether and evaporating to dryness each time.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 28.92 milligrammes of the total alkaloids of hyoscyamus." *U. S.*

The menstruum for this fluidextract was improved in the revision of the U. S. Pharmacopœia IX by increasing the alcoholic strength to alcohol 3, water 1. It is of a very dark greenish-brown color. For the medicinal properties, see *Hyoscyamus.*

Dose, from three to ten minims (0.2–0.6 mil).

FLUIDEXTRACTUM IPECACUANHÆ. U. S. (Br.)

FLUIDEXTRACT OF IPECAC Fldext. Ipecac.

(flū-ĭd-ĕx-trăc'tŭm ĭp-ĕ-căc-ū-ăn'hæ)

"*One hundred mils* of Fluidextract of Ipecac yields not less than 1.8 Gm. nor more than 2.2 Gm. of the ether-soluble alkaloids of ipecac." *U. S.* "Liquid Extract of Ipecacuanha contains in 100 millilitres 2 grammes of the alkaloids of Ipecacuanha Root." *Br.*

Extractum Ipecacuanhæ Liquidum, *Br.;* Liquid Extract of Ipecacuanha; Extrait liquide d'Ipécacuanha, *Fr.;* Flüssiges Ipecacuanhaextrakt, *G.*

* "Ipecac, in No. 60 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process B (see page 483), using a mixture of *one hundred mils* [or 3 fluidounces, 183 minims] of diluted hydrochloric acid, *two hundred mils* [or 6 fluidounces, 366 minims] of alcohol and *two hundred mils* [or 6 fluidounces, 366 minims] of water as Menstruum I, and a mixture of *two volumes* of alcohol and *three volumes* of water as Menstruum II. Reserve the first *eight hundred mils* [or 27 fluidounces, 24 minims] of percolate. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and, from the result thus obtained, ascertain by calculation the amount of alkaloids in the remainder of the liquid and dilute this with enough of Menstruum II to make each *one hundred mils* of the finished Fluidextract contain 2 Gm. of the ether-soluble alkaloids of ipecac." *U. S.*

"Ipecacuanha Root, in No. 120 powder, 1000 *grammes;* Alcohol (90 per cent.), *a sufficient quantity.* Pack the Ipecacuanha Root uniformly in a conical percolator, add two hundred *millilitres* of the Alcohol, and set aside for twelve hours; then percolate with successive portions, each of two hundred *millilitres,* of the Alcohol, added at intervals of twelve hours, until the liquid begins to drop from the orifice of the percolator. Continue the percolation with more of the Alcohol until seven hundred and fifty *millilitres* of percolate have been collected. Reserve this portion. Then percolate until exhaustion is complete; recover the alcohol from this percolate by distillation, and dissolve the residual extract in the reserved portion." *Br.*

Assay of Fluidextract of Ipecac.—"From a pipette drop 10 mils of Fluidextract of Ipecac evenly over the surface of 10 Gm. of purified sawdust (see Part III), and evaporate it to dryness at a temperature not exceeding 80° C. (176° F.). Transfer the impregnated sawdust to a 250 mil flask and add 100 mils of ether. Rinse the dish in which the mixture was evaporated with 6 mils of ammonia water, previously diluted with an equal volume of water, used in several portions, and add the rinsings to the flask. Stopper the flask and shake in vigorously every few minutes, during two hours. Now add 15 mils of distilled water, again shake the flask well, and when the sawdust has subsided decant 50 mils of the ether solution, representing 5 mils of the Fluidextract. Completely extract the alkaloids from this solution by shaking out with weak sulphuric acid. Collect the acid washings in a separator; add ammonia water until the solution is decidedly alkaline to litmus, and completely extract the alkaloids by shaking out repeatedly with ether. Evaporate the combined ether washings to dryness, dissolve the alkaloid from the residue in exactly 10 mils of tenth-normal sulphuric acid V.S. and titrate the excess of acid with fiftieth-normal potassium hydroxide V.S., cochineal T.S. being used as indicator (see Proximate Assays, Part III).

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 24 milligrammes of the ether-soluble alkaloids of ipecac." *U. S.*

"Determine the proportion of alkaloids in the liquid extract thus obtained by the following process: Introduce 5 *millilitres* of the liquid extract into a separator and add 4 *millilitres* of *water,* 1 *millilitre* of *diluted sulphuric acid,* and 10 *millilitres* of *ether.* Shake, and separate the ethereal solution. Repeat the shaking with 5 *millilitres* of *ether* and again separate. Wash the mixed ethereal solutions in a second separator with two successive portions, each of 5 *millilitres,* of *water,* and add the washings to the contents of the first separator. Shake this aqueous liquid with 10 *millilitres* of *chloroform* and excess of *solution of ammonia.* Separate the chloroformic solution and filter it through a small filter-paper into a tared dish. Repeat the shaking with *chloroform,* separation, and filtration, twice, finally washing the filter-paper with a little *chloroform.* Evaporate the mixed chloroformic solutions to about 2 *millilitres,* add 5 *millilitres* of *ether,* evaporate, dry at a temperature not exceeding 80° C. (176° F.) and weigh the residual alkaloids. To the remainder of the liquid extract add sufficient of the Alcohol to produce a Liquid Extract of Ipecacuanha containing in 100 *millilitres* 2 grammes of the alkaloids of Ipecacuanha Root. Examined by the foregoing process Liquid Extract of Ipecacuanha is found to contain in 100 millilitres 2 grammes of the alkaloids of Ipecacuanha Root. *Limit of error* 0.1 gramme in excess or defect. This Liquid Extract contains 2 grammes of the alkaloids of Ipecacuanha Root in 100 millilitres; 110 minims contains 2 grains." *Br.*

The menstruum for the U. S. fluidextract was altered in the U. S. P. IX by the addition of hydrochloric acid, which combines with the alkaloids and more thoroughly exhausts the ipecac. It was proved by J. U. Lloyd that when alcohol alone is used a portion of emetine escapes solution. On the other hand, it is known that when the menstruum is more aqueous large amounts of the pectinous principles are taken up, and it is very desirable to separate these in order to prevent their appearance as a flocculent precipitate in syrup of ipecac; but efficiency is to be sought for as the first desideratum, and hence a menstruum which will extract the activity and make a fluidextract that will not let fall a bulky precipitate of inert matter has been secured; usually this will not mix with syrup without slight precipitation, but the improved official process for syrup of ipecac should effectually separate any precipitate resulting from the presence of apotheme in the fluidextract. The British liquid extract (1914) is standardized; the excellent researches of Paul and Cownley on ipecac, and the assay work of Kremel, Keller, and others, undoubtedly prompted the introduction of the process for the liquid extract. (See *Ipecacuanha.*) It will probably be found, however, that the U. S. menstruum is preferable. An *acetic extract of ipecac* (dry) is used in Great Britain; it has been shown that the heating necessary to dry it is injurious to its emetic properties. (*P. J.,* 1895, 158.)

This fluidextract is a thin, dark reddish-brown, transparent liquid, of a bitterish, slightly acrid taste, but without the nauseous flavor of the root. It is a convenient preparation for adding to expectorant and diaphoretic mixtures, and is used officially in preparing the syrup of ipecac, and other preparations named below.

Dose, as emetic, fifteen to thirty minims (0.9–1.8 mils); as an expectorant, one to two minims (0.06–0.12 mil).

Off. Prep.—Syrupus Ipecacuanhæ, *U. S.;* Tinctura Ipecacuanhæ et Opii, *N. F.;* Vinum Ipecacuanhæ, *Br., N. F.;* Mistura Rhei Composita, *N. F.;* Syrupus Asari Compositus, *N. F.;* Syrupus Cimicifugæ Compositus, *N. F.*

EXTRACTUM KAVÆ LIQUIDUM. Br.

LIQUID EXTRACT OF KAVA

(ĕx-trăc'tŭm kāv'æ lĭq'uĭ-dŭm)

"Kava Rhizome, in No. 20 powder, 1000 *grammes;* Alcohol (90 per cent.), *a sufficient quantity;* Alcohol (45 per cent.), *a sufficient quantity.* Mix the powdered Kava Rhizome with two thousand *millilitres* of the Alcohol (90 per cent.); set aside in a closed vessel for forty-eight hours; transfer to a percolator and percolate slowly, reserving the first seven hundred and fifty *millilitres* of the percolate. Continue the percolation, adding the Alcohol (45 per cent.) until the powder is exhausted; recover most of the alcohol from this percolate by distillation; evaporate the residue at a temperature below 80° C. (176° F.) to a soft extract, and dissolve this in the reserved percolate; add sufficient of the Alcohol (90 per cent.) to produce one thousand *millilitres* of the Liquid Extract." *Br.*

This fluidextract was introduced into the British Pharm. (1914), and is also official in the N. F. IV. (See Part III.) It represents kava and may be given in the *dose* of thirty minims to one fluidrachm (1.8–3.75 mils).

FLUIDEXTRACTUM LOBELIÆ. U. S.

FLUIDEXTRACT OF LOBELIA Fldext. Lobel.

(flû-ĭd-ęx-trăc'tŭm lo-bē'lĭ-æ)

Extrait liquide de Lobélie enflée, *Fr.;* Flüssiges Lobelienkrautextrakt, Flüssiges Lobelienextrakt, *G.*

* "Lobelia, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process B (see page 483), using a mixture of *fifty mils* [or 1 fluidounce, 331 minims] of acetic acid, *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol and *four hundred and fifty mils* [or 15 fluidounces, 104 minims] of water as Menstruum I, and diluted alcohol as Menstruum II." *U. S.*

This fluidextract differs from that of the U. S. P. VIII in that the menstruum is acetic acid 1, alcohol 10, water 9 parts. The acetic menstruum is well adapted for exhausting the drug.

This is a valuable fluidextract. It is of a dark olive color, having the acrid taste of lobelia in a very marked degree.

Dose, as an expectorant, from one to five minims (0.06–0.3 mil); as an emetic, from ten to twenty minims (0.6–1.3 mils).

FLUIDEXTRACTUM NUCIS VOMICÆ. U. S. (Br.)

FLUIDEXTRACT OF NUX VOMICA Fldext. Nuc. Vom.

(flû-ĭd-ęx-trăc'tŭm nū'cĭs vŏm'ĭ-cæ)

"*One hundred mils* of Fluidextract of Nux Vomica yields not less than 2.37 Gm. nor more than 2.63 Gm. of the alkaloids of nux vomica." *U. S.* "Liquid Extract of Nux Vomica contains in 100 millilitres 1.5 grammes of strychnine." *Br.*

Extractum Nucis Vomicæ Liquidum, *Br.;* Liquid Extract of Nux Vomica; Extrait liquide de Noix-Vomique, *Fr.;* Flüssiges Krähenaugen-Extrakt, Brechnussextrakt, Strychnossamenextrakt, *G.*

* "Nux Vomica, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *three volumes* of alcohol and *one volume* of water as the menstruum, and reserving the first *eight hundred mils* [or 27 fluidounces, 24 minims] of percolate. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and, from the result thus obtained, ascertain by calculation the amount of alkaloids in the remainder of the liquid and dilute this with enough menstruum to make each *one hundred mils* of the finished Fluidextract contain 2.5 Gm. of the alkaloids of nux vomica.

"Nux Vomica, in No. 20 powder, 1000 *grammes;* Alcohol (70 per cent.), *a sufficient quantity.* Exhaust the Nux Vomica with the Alcohol by the *repercolation process* until five hundred millilitres of percolate have been obtained. Place this percolate in a closed vessel with fifteen grammes of Hard Paraffin and heat to 60° C. (140° F.) for a few minutes, shaking vigorously. Allow the contents of the vessel to cool and the layer of paraffin which will have separated to solidify. Pour off the percolate thus freed from fat; filter." *Br.*

Assay.—"Proceed as directed under *Fluidextractum Belladonnæ Radicis,* page 486, using 10 mils of Fluidextract of Nux Vomica, modifying the process there given by dissolving the alkaloidal residue in 10 mils of tenth-normal sulphuric acid V.S. instead of 5 mils.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 36.42 milligrammes of the alkaloids of nux vomica." *U. S.*

"Determine the proportion of strychnine in it by the following process: Evaporate 10 *millilitres* on a water-bath to a syrupy extract; dissolve the residue in 10 *millilitres* of warm *water* and transfer to a separator, washing the dish with a further 10 *millilitres* of *water.* Add 10 *millilitres* of *chloroform* and a solution of 5 *grammes* of *sodium carbonate* in 25 *millilitres* of *water.* Shake vigorously; set aside and separate the chloroformic solution. Repeat the extraction with *chloroform* twice. Mix the three chloro-

formic solutions, and extract the alkaloids by shaking with three successive portions, each of 10 *millilitres*, of *N/1 solution of sulphuric acid*, transferring the acid solutions to a second separator. Make the acid solutions alkaline with *solution of ammonia*, and again extract the alkaloids by shaking successively with 10, 5, and 5 *millilitres* of *chloroform*, drawing off the chloroformic solutions into a small flask. Remove the chloroform by distillation, dissolve the residue in 15 *millilitres* of *water* containing 3 per cent. by weight of *sulphuric acid*, heat the solution to 50° C. (122° F.), add 3 *millilitres* of a mixture of equal volumes of *nitric acid* and *water*, and set aside for ten minutes. Transfer the solution to a separator, rinsing the flask with a little *water*, make alkaline with *solution of sodium hydroxide*, and extract the alkaloid by shaking successively with 10, 5, and 5 *millilitres* of *chloroform*. Wash the mixed chloroformic solutions in a separator with 5 *millilitres* of *water*, transfer to a tared dish and allow the chloroform to evaporate, adding towards the end 5 *millilitres* of *alcohol* (90 per cent.). Evaporate to dryness, dry the residue at 100° C. (212° F.) and weigh. The weight is the weight in *grammes* of the strychnine contained in 10 *millilitres* of percolate. To the remainder of the percolate add sufficient Alcohol (70 per cent.) to produce a Liquid Extract of Nux Vomica containing in 100 *millilitres* 1.5 *grammes* of strychnine. Examined by the foregoing process Liquid Extract of Nux Vomica is found to contain in 100 *millilitres* 1.5 *grammes* of strychnine. *Limit of error* 0.05 *gramme* in excess or defect. This Liquid Extract contains 1.5 grammes of strychnine in 100 *millilitres;* 110 minims contain 1.5 grains." *Br.*

This fluidextract has been retained principally with the view of giving the pharmacist an accurately adjusted liquid preparation of nux vomica which is more concentrated than the tincture. The process of assay is practically the same as that for the extract. The British assay process is based on that recommended by Dunstan and Short. (*P. J.*, 1884, 623.) The menstruum has been carefully selected so that the alkaloids shall be extracted and as much of the oil left in the residue as possible. In order to make a dry powdered extract it would be necessary to separate the fixed oil before assaying it, and then to make up the weight, if necessary, with sugar of milk or some inert, soluble powder. (See *Extractum Nucis Vomicæ.*) An important advantage, aside from that of securing uniformity and safety, is that the operator need not carry the percolation beyond the point at which it ceases to be profitable (on account of the waste of alcohol), because the extract must be brought to a definite alkaloidal strength. Such an extract can be used with great advantage to make tincture or nux vomica of definite alkaloidal strength.

Dose, one to three minims (0.06–0.2 mil).

Off. Prep.—Tinctura Nucis Vomicæ, *Br.;* Extractum Nucis Vomicæ Siccum, *Br.*

EXTRACTUM PICRORHIZÆ LIQUIDUM. Br.

LIQUID EXTRACT OF PICRORHIZA

(ẹx-trăc'tŭm pĭc-rō-rhīz'æ lĭq'uị-dŭm)

"Picrorhiza, in No. 60 powder, 1000 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres*. Exhaust the Picrorhiza with the Alcohol by the *percolation process*. Reserve the first eight hundred and fifty *millilitres* of the percolate; recover the alcohol from the remainder by distillation; evaporate the residue to a soft extract; dissolve this in the reserved portion; add sufficient of the Alcohol to produce the required volume." *Br.*

This fluidextract was transferred from the British and Colonial Addendum to the British Pharm. (1914). (See *Picrorhiza.*)

Dose, fifteen to sixty minims (0.9–3.75 mils).

FLUIDEXTRACTUM PILOCARPI. U. S.

FLUIDEXTRACT OF PILOCARPUS Fldext. Pilocarp. [Fluidextract of Jaborandi]

(flū-ịd-ẹx-trăc'tŭm pī-lọ-căr'pī)

"*One hundred mils* of Fluidextract of Pilocarpus yields not less than 0.55 Gm. nor more than 0.65 Gm. of the alkaloids of pilocarpus." *U. S.*

Extractum Jaborandi Liquidum, *Br.*, 1898; Liquid Extract of Jaborandi; Extrait liquide de Jaborandi, *Fr.;* Flüssiges Jaborandiextrakt, *G.*

* "Pilocarpus, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *two volumes* of alcohol and *one volume* of water as the menstruum, and reserving the first *eight hundred mils* [or 27 fluidounces, 24 minims] of percolate. After dissolving the soft extract in the reserve liquid, assay a portion as directed below, and from the result thus obtained, ascertain by calculation the amount of alkaloids in the remainder of the liquid and dilute this with enough menstruum to make each *one hundred mils* of the finished Fluidextract contain 0.6 Gm. of the alkaloids of pilocarpus."

"**Assay.**—From a pipette drop 15 mils of Fluidextract of Pilocarpus evenly over the surface of 15 Gm. of purified sawdust (see Part III), and evaporate it to dryness on a water bath. Transfer the mixture to a 250 mil flask, add 150 mils of chloroform, and proceed as directed under *Belladonnæ Radix*, page 222, fifth line of the Assay, beginning with the word 'Stopper,' modifying the process there given by increasing the amount of ammonia water to 6 mils, mixed with 5 mils of distilled water, which is to be used, in divided portions, to rinse the dish in which the mixture was evaporated, the rinsings being added to the mixture in the flask; the 100 mils of chloroform solution must be drawn off from the bottom of the flask.

"Each mil of tenth-normal sulphuric acid V.S. corresponds to 20.815 milligrammes of the alkaloids of pilocarpus." *U. S.*

This fluidextract represents jaborandi leaves

thoroughly. Of the liquid preparations of the drug, the infusion and tincture are both open to objection, the former on account of the bulkiness of the dose, and the latter because of the amount of alcohol it contains. Liquid abstract of jaborandi was deleted from the Br. Pharm. (1914).

Dose, from fifteen minims to half a fluidrachm (0.9–1.8 mils).

FLUIDEXTRACTUM PODOPHYLLI. U. S.

FLUIDEXTRACT OF PODOPHYLLUM Fldext. Podophyll.

(flū-ĭd-ĕx-trăc'tŭm pŏd-ō-phĭl'lī)

Fluidextract of May Apple or Mandrake; Extrait liquide de Podophylle, *Fr.;* Flüssiges Fussblattwurzelextrakt, Flüssiges Podophyllumextrakt, *G.*

* "Podophyllum, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using alcohol as the menstruum." U. S.

The menstruum of the U. S. P. VIII fluidextract which was alcohol 4, water 1, was changed to alcohol in the U. S. P. IX. This is a fluidextract which well represents the root, but is of very little use, since podophyllum is much better administered in other forms.

Dose, from five to fifteen minims (0.3–0.9 mil).

FLUIDEXTRACTUM RHEI. U. S.

FLUIDEXTRACT OF RHUBARB Fldext. Rhei

(flū-ĭd-ĕx-trăc'tŭm rhē'ī)

Extrait liquide de Rhubarbe, *Fr.;* Flüssiges Rhabarberextrakt, *G.*

* "Rhubarb, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *four volumes* of alcohol and *one volume* of water as the menstruum." *U. S.*

The present process affords a fluidextract which thoroughly represents the root, but when mixed with syrups and water, it loses its transparency. An alkali or an alkaline carbonate dissolves this precipitate, but the use of the fluidextract is limited. The British Pharm. (1898) "Liquor Rhei Concentratus" is made with alcohol (20 per cent.) as a menstruum and is one-half the strength of the U. S. fluidextract of rhubarb.

Dose, for an adult, as a purgative, twenty to thirty minims (1.3–1.8 mils); as a laxative, from five to ten minims (0.3–0.6 mil).

Off. Prep.—Syrupus Rhei, *U. S.;* Mistura Rhei Alkalina, *N. F.;* Mistura Rhei Composita, *N. F.;* Syrupus Sennæ Compositus, *N. F.;* Vinum Rhei Compositum, *N. F.*

FLUIDEXTRACTUM ROSÆ. U. S.

FLUIDEXTRACT OF ROSE Fldext. Rosæ

(flū-ĭd-ĕx-trăc'tŭm rō'sæ)

Fluidextract of Red Rose; Extrait liquide de Rose rouge, *Fr.;* Flüssiges Essigrosenblumenblätterextrakt, *G.*

* "Red Rose, in No. 20 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process B (see page 483), using a mixture of *one hundred mils* [or 3 fluidounces, 183 minims] of glycerin, *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol and *four hundred mils* [or 13 fluidounces, 252 minims] of water as Menstruum I, and diluted alcohol as Menstruum II." *U. S.*

This fluidextract is a useful adjuvant and an excellent astringent. It is of a deep red color, with the agreeable flavor of rose. Wm. C. Alpers prefers repercolation for this fluidextract, stating that even a moderate heat imparts an unpleasant odor to the finished product. (*Proc. A. Ph. A.*, 1897, 425.)

Dose, from one to two fluidrachms (3.75–7.5 mils).

Off. Prep.—Mel Rosæ, *U. S.;* Syrupus Rosæ, *N. F.*

FLUIDEXTRACTUM SABAL. U. S.

FLUIDEXTRACT OF SABAL Fldext. Sabal [Fluidextract of Saw Palmetto]

(flū-ĭd-ĕx-trăc'tŭm sā'bąl)

* "Sabal, in No. 20 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *four volumes* of alcohol and *one volume* of water as the menstruum." *U. S.*

This fluidextract was introduced into the U. S. P. IX. It represents the virtues of saw palmetto berries.

Dose, fifteen minims (0.9 mil).

FLUIDEXTRACTUM SARSAPARILLÆ. U. S.

FLUIDEXTRACT OF SARSAPARILLA Fldext. Sarsap.

(flū-ĭd-ĕx-trăc'tŭm sär-są-pą-rĭl'læ)

Extractum Sarsæ Liquidum., *Br.* 1898; Liquid Extract of Sarsaparilla; Liquor Sarsæ; Extrait liquide de Salsepareille, *Fr.;* Flüssiges Sarsaparillaextrakt, *G.*

* "Sarsaparilla, in No. 20 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using diluted alcohol as the menstruum." *U. S.*

The British Pharm. (1914) deleted Extractum Sarsæ Liquidum. The process will be found in the 19th ed., U. S. Dispensatory, page 559.

The introduction of a simple fluidextract of sarsaparilla into our Pharmacopœias was judicious, as it enables the physician to associate this medicine with others at his pleasure, and in such proportions as he may deem expedient. He may rely upon the efficiency of the preparation, if made with sufficient care and skill and from good parcels of the root. The U. S. fluidextract is a somewhat dense, scarcely translucent liquid, of a very dark reddish-brown color, and of a sweetish and a slightly acrid taste.

Dose, thirty to sixty minims (1.8–3.75 mils).

Off. Prep.—Syrupus Sarsaparillæ Compositus, *U. S.*

FLUIDEXTRACTUM SARSAPARILLÆ COMPOSITUM. U. S.

COMPOUND FLUIDEXTRACT OF SARSAPARILLA Fldext. Sarsap. Co.

(flū-ĭd-ĕx-trăc'tŭm săr-să-pă-rĭl'læ cŏm-pŏs'ĭ-tŭm)

Extrait liquide de Salsepareille composé, *Fr.;* Zusammengesetztes flüssiges Sarsaparillaextrakt, *G.*

* "Sarsaparilla, in No. 20 powder, *seven hundred and fifty grammes* [or 26 ounces av., 199 grains]; Glycyrrhiza, in No. 20 powder, *one hundred and twenty grammes* [or 4 ounces av., 102 grains]; Sassafras, in No. 30 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Mezereum, in No. 30 powder, *thirty grammes* [or 1 ounce av., 25 grains]. Mix the powders and prepare a Fluidextract by Type Process B (see page 483), using a mixture of *one hundred mils* [or 3 fluidounces, 183 minims] of glycerin, *five hundred mils* [or 16 fluidounces, , 435 minims] of alcohol and *four hundred mils* [or 13 fluidounces, 252 minims] of water as Menstruum I, and diluted alcohol as Menstruum II." *U. S.*

The compound fluidextract is intended to represent, in a concentrated state, the compound decoction of sarsaparilla, having all its ingredients with the exception of the guaiacum wood, which probably adds little to the efficacy of the decoction. It was originally proposed by Wm. Hodgson, Jr. (*A. J. P.*, ii, 285), and the official process differs from his mainly in the omission of the guaiacum wood, the resin of which, separating during the evaporation, somewhat embarrassed the process, without adding to the virtues of the extract. The British Pharm. (1898) "Liquor Sarsæ Compositus Concentratus" is of the same strength as the fluidextract of the U. S. Pharmacopœia, and is made with a menstruum of distilled water with 225 mils of alcohol as a preservative in 1000 mils of finished solution.

Dose, from thirty minims to one fluidrachm (1.8–3.75 mils).

FLUIDEXTRACTUM SCILLÆ. U. S.

FLUIDEXTRACT OF SQUILL Fldext. Scill.

(flū-ĭd-ĕx-trăc'tŭm sçĭl'læ)

"If assayed biologically the minimum lethal dose should not be greater than 0.0006 mil of Fluidextract, or the equivalent in Fluidextract of 0.0000005 Gm. of ouabain, for each gramme of body weight of frog." *U. S.*

Extrait liquide de Scille, *Fr.;* Flüssiges Meerzwiebelextrakt, *G.*

* "Squill, in No. 20 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Diluted Alcohol, Alcohol, Water, each, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix *two thousand mils* [or 67 fluidounces, 301 minims] of alcohol with *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of water, moisten the squill thoroughly with sufficient of the mixture and allow it to macerate for two hours in a tightly-covered container. Then transfer it to a percolator, shake it down evenly without packing, and pour on enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding more menstruum composed of *two volumes* of alcohol and *one volume* of water. When the percolate measures *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] close the lower orifice and macerate the drug twelve hours before continuing the percolation. Then collect a second *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of percolate, again interrupt the percolation, macerate for twelve hours and then continue the percolation until the total percolate measures *five thousand mils* [or 169 fluidounces, 33 minims]. Recover the alcohol from the percolate at as low a temperature as possible and then concentrate the residue to a volume measuring *eight hundred mils* [or 27 fluidounces, 24 minims]. When the residue is cold, add slowly, with continuous agitation, *two thousand mils* [or 67 fluidounces, 301 minims] of alcohol and set the mixture aside in a tightly-stoppered container for twelve hours. Decant the supernatant liquid from the syrupy layer, filter the decanted liquid and wash the syrupy residue with two portions of *three hundred mils* [or 10 fluidounces, 69 minims] each of a mixture of *four volumes* of alcohol and *one volume* of water, passing the washings through the filter into the previously collected alcoholic liquid. Reduce the combined alcoholic liquids to *eight hundred mils* [or 27 fluidounces, 24 minims] by distillation and finally add enough diluted alcohol to make the finished Fluidextract measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

"**Assay.**—For a method of assaying Fluidextract of Squill, see *Digitalis,* and also Biological Assays (Part III)." *U. S.*

The U. S. P. has very properly returned to an alcoholic instead of an acetic acid menstruum for this preparation, as Houghton has shown that the fluidextract of the U. S. P. VIII did not represent the activity of squills, but it is doubtful whether the complicated process of the U. S. P. IX will be employed for such a rarely used fluidextract.

Dose, from one to three minims (0.06–0.2 mil).

Off. Prep.—Syrupus Scillæ Compositus, *U. S.;* Mistura Pectoralis, Stokes, *N. F.*

FLUIDEXTRACTUM SENEGÆ. U. S.

FLUIDEXTRACT OF SENEGA Fldext. Seneg.

(flū-ĭd-ĕx-trăc'tŭm sĕn'ę-gæ)

Extrait liquide de Polygale de Virginie, Extrait liquide de Sénéca, *Fr.;* Flüssiges Senegaextrakt, G.

* "Senega, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Ammonia Water, Alcohol, Water, each, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix *two thousand mils* [or 67 fluidounces, 301 minims] of alcohol

with *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of water, and, having moistened the powder with sufficient of this mixture, pack it in a cylindrical percolator and add enough menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding menstruum, composed of a mixture of *two volumes* of alcohol and *one volume* of water, until the drug is exhausted. Reserve the first *eight hundred mils* [or 27 fluidounces, 24 minims] of the percolate and evaporate the remainder to a soft extract; dissolve this in the reserved liquid and then gradually add ammonia water until the product is faintly alkaline and possesses a slight odor of ammonia. Finally add enough of the menstruum to make the Fluidextract measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

Formerly, Fluidextract of Senega was very frequently the cause of annoyance to the pharmacist through gelatinization. This was due to the presence of pectinous bodies in the root. The addition of an alkali to the menstruum effectually prevents this, and in this respect the present preparation is a great improvement over the 1890 fluidextract. We prefer, however, solution of sodium hydroxide, as the alkaline liquid, to ammonia water, as the latter is rarely uniform in quality as found in commerce. This fluidextract is a blackish-brown, moderately thin liquid. For other processes, see *N. R.*, 1883, pp. 195, 196. The British Pharm. (1898) "Liquor Senegæ Concentratus" was made half the strength of the U. S. fluidextract with a menstruum composed of 2 parts of 20 per cent. alcohol and 1 part of 45 per cent. alcohol.

Dose, five to twenty minims (0.3–1.3 mils).

Off. Prep.—Syrupus Scillæ Compositus, *U. S.;* Syrupus Senegæ, *U. S.;* Mistura Pectoralis, Stokes, *N. F.;* Syrupus Cimicifugæ Compositus, *N. F.*

FLUIDEXTRACTUM SENNÆ. U. S.

FLUIDEXTRACT OF SENNA Fldext. Senn.

(flū-ĭd-ĕx-trăc'tŭm sĕn'næ)

Extrait liquide de Séné, *Fr.;* Flüssiges Sennaextrakt, *G.*

* "Alexandria Senna, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *one volume* of alcohol and *two volumes* of water as the menstruum, and reserving the first *eight hundred mils* [or 27 fluidounces, 24 minims] of percolate." *U. S.*

The U. S. P. VIII process provided for the elimination of the griping principles by the previous percolation of the powdered senna with alcohol; diluted alcohol was then used to exhaust the drug of the purgative principles. This previous treatment of the senna was deleted from the U. S. P. IX process and the menstruum was made less alcoholic. The fluidextract is a dark, blackish, thick, and somewhat turbid liquid, with a strong flavor of senna. It is well adapted for exhibition with saline cathartics, such as Epsom salt or cream of tartar, which also obviate its griping. In this case not more than one-half of the full dose of the fluidextract should be given at once.

The British Pharm. (1898) "Liquor Sennæ Concentratus" was more like a concentrated infusion than a fluidextract, but had the same strength of the latter, the menstruum is distilled water; tincture of ginger and alcohol being added.

Dose, from one-half to two fluidrachms (1.8–7.5 mils), for an adult.

Off. Prep.—Syrupus Sarsaparillæ Compositus, *U. S.;* Syrupus Sennæ, *U. S.;* Elixir Cascaræ Compositum, *N. F.;* Elixir Catharticum Compositum, *N. F.;* Syrupus Ficorum Compositus, *N. F.;* Syrupus Sennæ Aromaticus, *N. F.;* Syrupus Sennæ Compositus, *N. F.*

FLUIDEXTRACTUM SPIGELIÆ. U. S.

FLUIDEXTRACT OF SPIGELIA Fldext. Spigel. [Fluidextract of Pink Root]

(flū-ĭd-ĕx-trăc'tŭm spĭ-gē'lĭ-æ)

Extrait liquide de Spigélie, *Fr.;* Flüssiges Spigelienextrakt, *G.*

* "Spigelia, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using diluted alcohol as the menstruum." *U. S.*

This preparation differs from that official prior to 1890 in having no glycerin in the menstruum; the U. S. P., 1870, fluidextract contained 50 per cent. of glycerin. Diluted alcohol is an excellent menstruum.

The fluidextract of spigelia is a dark-brown translucent liquid, with the flavor of the root. The dose may be repeated morning and evening for three or four days, and then followed by a brisk cathartic. It is, however, most used in connection with the fluidextract of senna, the fluidextract of spigelia and senna formerly official being an excellent combination, which should not have been dropped from the Pharmacopœia. The formula is as follows:

Extractum Spigeliæ et Sennæ Fluidum, U. S. 1870. *Fluid Extract of Spigelia and Senna.*—"Take of Fluid Extract of Spigelia *ten fluidounces;* Fluid Extract of Senna, *six fluidounces;* Oil of Anise, Oil of Caraway, each, *twenty minims.* Mix the Fluid Extracts, and dissolve the Oils in the mixture." *U. S.* 1870.

Dose, for an adult, from one to two fluidrachms (3.75–7.5 mils); for a child of two or three years, from ten to twenty minims (0.6–1.3 mils).

FLUIDEXTRACTUM STAPHISAGRIÆ. U. S.

FLUIDEXTRACT OF STAPHISAGRIA Fldext. Staphisag. [Fluidextract of Stavesacre]

(flū-ĭd-ĕx-trăc'tŭm stăph-ĭ-sā'grĭ-æ)

Fluidextract of Stavesacre Seed; Extrait liquide des Semences de Staphisaigre, *Fr.;* Flüssiges Stephanskörnerextrakt, *G.*

* " Staphisagria, in No. 20 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using alcohol as the menstruum. The oil which separates in the freshly prepared Fluidextract may be removed by chilling and filtering the cold Fluidextract through a filter moistened with alcohol." *U. S.*

This fluidextract was first made official in the U. S. P. VIII. Mixed with two or three parts of alcohol and ether, it is used as an external application to destroy lice.

FLUIDEXTRACTUM STILLINGIÆ. U. S.

FLUIDEXTRACT OF STILLINGIA Fldext. Stilling.

(flū-id-ĕx-trăc'tŭm stĭl-lĭn'jĭ-æ)

Extrait liquide de Stillingie, *Fr.;* **Flüssiges Stillingiaextrakt,** *G.*

* " Stillingia, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using diluted alcohol as the menstruum." *U. S.*

The glycerin in the menstruum has been abandoned in this fluidextract, which is of a dark reddish-brown color.

Dose, from fifteen to forty-five minims (0.9–2.8 mils).

Off. Prep.—Elixir Corydalis Compositum, *N. F.*

FLUIDEXTRACTUM SUMBUL. U. S.

FLUIDEXTRACT OF SUMBUL Fldext. Sumbul [Fluidextract of Musk Root]

(flū-id-ĕx-trăc'tŭm sŭm'bŭl)

Extrait liquide de Sumbul, *Fr.;* **Flüssiges Sumbulwurzelextrakt oder Moschuswurzelextrakt,** *G.*

* " Sumbul, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *four volumes* of alcohol and *one volume* of water as the menstruum." *U. S.*

This fluidextract was made official for the first time in the U. S. P. VIII, superseding the tincture of sumbul, to which it is superior.

Dose, half a fluidrachm to one fluidrachm (1.8–3.75 mils).

FLUIDEXTRACTUM TARAXACI. U. S.

FLUIDEXTRACT OF TARAXACUM Fldext. Tarax. [Fluidextract of Dandelion]

(flū-id-ĕx-trăc'tŭm tą-răx'ą-cī)

Extractum Taraxaci Liquidum, *Br.* 1898; **Liquid Extract of Taraxacum; Fluidextract of Dandelion; Extrait liquide de Pissenlit,** *Fr.;* **Flüssiges Löwenzahnwurzelextrakt,** *G.*

* " Taraxacum, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process B (see page 483), using a mixture of *one hundred mils* [or 3 fluidounces, 183 minims] of glycerin, *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol and *four hundred mils* [or 13 fluidounces, 252 minims] of water as Menstruum I, and diluted alcohol as Menstruum II." *U. S.*

The activity depends more upon the proper selection of the root than upon anything else. The addition of solution of sodium hydroxide to the menstruum in the U. S. P. VIII revision was dropped in the U. S. P. IX. The process of exhausting the drug is not difficult, and one of the best tests of this fluidextract is its bitter taste. It is a blackish, moderately thick liquid.

Dose, from one to three fluidrachms (3.75–11.25 mils).

Off. Prep.—Elixir Gentianæ Glycerinatum, *N. F.;* Elixir Taraxaci Compositum, *N. F.*

FLUIDEXTRACTUM TRITICI. U. S. (Br.)

FLUIDEXTRACT OF TRITICUM Fldext. Tritic. [Fluidextract of Couch Grass]

(flū-id-ĕx-trăc'tŭm trĭt'ĭ-cī)

Extractum Agropyri Liquidum, *Br.;* **Liquid Extract of Couch Grass; Liquid Extract of Triticum; Fluidextract of Couch-grass Root; Extrait liquide de petit Chiendent,** *Fr.;* **Flüssiges Queckenwurzelextrakt,** *G.*

* " Triticum, finely cut, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, *two hundred mils* [or 6 fluidounces, 366 minims], Prepare a Fluidextract by Type Process D (see page 484), evaporate the aqueous percolate to *eight hundred mils* [or 27 fluidounces, 24 minims] and when cold add the alcohol and, if necessary, sufficient water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

" Couch Grass, cut small, 1000 *grammes;* Distilled Water, boiling, 10,000 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Boil the Couch Grass with the Distilled Water for thirty minutes; strain; evaporate to seven hundred and fifty *millilitres;* cool, and add sufficient of the Alcohol to produce the required volume; filter." *Br.*

For therapeutic uses, see *Triticum* and *Agropyrum.*

In making this fluidextract in warm weather, it is advisable to commence evaporating the percolate before the drug is exhausted, or fermentation may set in; triticum contains fermentable sugars, and diluted aqueous solutions do not keep well.

This fluidextract represents whatever virtues triticum possesses. The German Pharmacopœia formerly directed an *Extractum Graminis,* by digesting 1 part of Triticum with 6 parts of hot water, for six hours, straining, evaporating to a syrup, mixing 1 part of this extract with 4 parts of cold distilled water, filtering, and evaporating to an extract. The fluidextract is preferable, as the excessive use of heat is avoided.

Dose, from three to six fluidrachms (11.25–22.5 mils).

FLUIDEXTRACTUM UVÆ URSI. U. S.

FLUIDEXTRACT OF UVA URSI Fldext. Uvæ Ursi

(flū-id-ĕx-trăc'tŭm ū'væ ûr'sī)

Extrait liquide de Busserole, *Fr.;* **Flüssiges Bärentraubenblätterextrakt,** *G.*

* " Uva Ursi, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process B (see

page 483), using a mixture of *one hundred mils* [or 3 fluidounces, 183 minims] of glycerin, *three hundred mils* [or 10 fluidounces, 69 minims] of alcohol and *five hundred mils* [or 16 fluidounces, 435 minims] of water as Menstruum I, and a mixture of *one volume* of alcohol and *two volumes* of water as Menstruum II. Reserve the first *eight hundred mils* [or 27 fluidounces, 24 minims] of percolate." *U. S.*

This preparation is a dense, black liquid, of a sweet, bitterish, astringent, but not very disagreeable taste.

Dose, from thirty minims to a fluidrachm (1.8–3.75 mils).

FLUIDEXTRACTUM VERATRI VIRIDIS. U. S.

FLUIDEXTRACT OF VERATRUM VIRIDE Fldext. Verat. Vir. [Fluidextract of Green Hellebore]

(flū-ĭd-ĕx-trăc'tŭm vē-rā'trī vĭr'ĭ-dīs)

Fluidextract of American Hellebore; Extrait liquide de Vératre américain, *Fr.;* Flüssiges Grüngermerextrakt, *G.*

* "Veratrum Viride, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using alcohol as the menstruum." *U. S.*

This is the best preparation of veratrum and thoroughly represents the drug.

Dose, one to four minims (0.06–0.24 mil).

FLUIDEXTRACTUM VIBURNI PRUNIFOLII. U. S. (Br.)

FLUIDEXTRACT OF VIBURNUM PRUNIFOLIUM Fldext. Viburn. Prun. [Fluidextract of Black Haw]

(flū-ĭd-ĕx-trăc'tŭm vī-bŭr'nī prū-nĭ-fō'lĭ-ī)

Extractum Viburni Liquidum, *Br.;* Liquid Extract of Black Haw; Extrait liquide de Viburne, *Fr.;* Flüssiges Viburnumextrakt, *G.*

* "Viburnum Prunifolium, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *two volumes* of alcohol and *one volume* of water as the menstruum." *U. S.*

"Black Haw, in No. 60 powder, 1000 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Exhaust the Black Haw with the Alcohol by the *percolation process.* Reserve the first eight hundred and fifty *millilitres* of the percolate; recover the alcohol from the remainder by distillation; evaporate the residue to a soft extract; dissolve this in the reserved portion; add sufficient of the Alcohol to produce the required volume." *Br.*

This is a fluidextract which well represents the drug. It is of a dark reddish-brown color.

Dose, from one-half to one fluidrachm (1.8–3.75 mils).

Off. Prep.—Elixir Viburni Prunifolii, *N. F.*

FLUIDEXTRACTUM XANTHOXYLI. U. S.

FLUIDEXTRACT OF XANTHOXYLUM Fldext. Xanthox. [Fluidextract of Prickly Ash]

(flū-ĭd-ĕx-trăc'tŭm xăn-thŏx'ȳ-lī)

Extrait liquide d'Ecorce de Clavalier, *Fr.;* Flüssiges Zahnwehrindenextrakt, *G.*

* "Xanthoxylum, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using a mixture of *three volumes* of alcohol and *one volume* of water as the menstruum." *U. S.*

This fluidextract thoroughly represents the virtues of the drug. (See *Xanthoxylum.*)

Dose, from one-half to one fluidrachm (1.8–3.75 mils).

Off. Prep.—Elixir Corydalis Compositum, *N. F.*

FLUIDEXTRACTUM ZINGIBERIS. U. S.

FLUIDEXTRACT OF GINGER Fldext. Zingib.

(flū-ĭd-ĕx-trăc'tŭm zĭn-gĭb'ĕ-rĭs)

Extrait liquide de Gingembre, *Fr.;* Flüssiges Ingwerextrakt, *G.*

* "Jamaica Ginger, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]. Prepare a Fluidextract by Type Process A (see page 483), using alcohol as the menstruum." *U. S.*

This fluidextract is a highly concentrated alcoholic solution of the active principles of ginger. It is transparent, and of a reddish color.

Dose, from five to twenty minims (0.3–1.3 mils).

Off Prep.—Syrupus Zingiberis, *U. S.*

FŒNICULUM. U. S. (Br.)

FENNEL Fœnic. [Fennel Seed]

(fœ-nĭc'ū-lŭm)

"The dried, ripe fruit of cultivated varieties of *Fœniculum vulgare* Miller (Fam. *Umbelliferæ*), without the presence or admixture of more than 4 per cent. of foreign matter." *U. S.* "Fennel Fruit is the ripe fruit of Fœniculum vulgare, *Mill.,* collected from cultivated plants, and dried." *Br.*

Fœniculi Fructus, *Br.;* Semen Fœniculi, Fennel Fruit (Seed), Sweet Fennel Fruit; Fenouil doux (Fruit), *Fr. Cod.;* Fruits (Semences) de Fenouil, *Fr.;* Fructus Fœniculi, *P. G.;* Fenchel, Fenchelsamen, *G.;* Finocchio, *It.;* Hinojo, *Sp.*

The plant producing fennel seed was attached by Linnæus to the genus *Anethum,* but was separated from it by De Candolle, and placed, with three or four others, in a new genus styled *Fœniculum,* which has been generally adopted by botanists. The *Anethum Fœniculum* of Linnæus embraced two varieties, the *common* or *wild fennel,* and the *sweet fennel,* the latter being the plant usually cultivated in the gardens of Europe. These are considered by De Candolle as distinct species, and named respectively *Fœniculum vulgare* and *Fœniculum dulce,* but the correctness of the opinion of the great Swedish botanist is now generally admitted.

Fœniculum vulgare is a stout, glabrous biennial or perennial, aromatic herb, with leaves dissected into numerous filiform segments. The flowers are in large, flat, terminal umbels, with from thirteen to twenty rays, and destitute both of general and partial involucres. The

corolla consists of five petals, which, as well as the stamens, are golden yellow. The fruit is ovate, and of a dark color, especially in the grooves. The plant is a native of Europe, growing wild upon sandy and chalky ground throughout the continent, and is also abundant in Asia, possibly extending as far as China. It is extensively cultivated in Europe as well as in this country. It has escaped from gardens and is somewhat naturalized in Maryland and Virginia. In India fennel is said to be obtained from *F. panmorium* DC., which is probably, however, only a variety of the official plant. Sicilian fennel is affirmed to be the fruit of *F. piperitum.*

F. dulce De Cand., *Sweet Fennel* bears a general resemblance to *F. vulgare,* but differs in having its stem somewhat compressed at the base, its radical leaves somewhat distichous, and the number of rays in the umbel only from 6 to 8. It is also a much smaller plant, being only about a foot high; its flowers appear earlier, and its young sweet shoots or turiones are eaten in Italy boiled or as a salad. According to Index Kewensis it is identical with *F. vulgare.*

Properties.—The roots of fennel were formerly employed in medicine, but are generally inferior in virtues to the fruit, which is now the only portion recognized by any of the pharmacopœias. It is stated that manufacturers of the oil usually distil the whole plant.

The official description is as follows: "Mericarps usually separate, each being broadly elliptical, more or less curved, from 4 to 10 mm. in length and from 1 to 3.5 mm. in breadth, some having a slender stalk from 2 to 10 mm. in length; dorsal surface convex, yellowish-green to grayish-brown, with three prominent, longitudinal primary ribs and at the summit a short, conical stylopodium; commissural surface with three narrow, light brown, longitudinal areas separated by two dark brown or brownish-black areas containing the vittæ or oil-tubes; odor and taste aromatic and characteristic. Under the microscope, transverse sections of Fennel show a pentagonal mericarp, four of the edges being nearly equal and slightly concave, the other or commissural surface being much longer and more or less undulate; cells of the seed-coat closely united with those of the pericarp, giving the section two very distinct areas, the inner and larger portion (endosperm) more or less rounded-pentagonal and somewhat reniform, composed of polygonal cells, filled with aleurone grains containing rosette aggregates of calcium oxalate and a thin protoplasmic layer enclosing a fixed oil; the outer or pericarp layer distinguished by large elliptical vittæ with thick, brown walls, occurring singly and alternating with the primary ribs, and two vittæ on the dorsal surface, making usually six vittæ in all, there sometimes being, however, one or two vittæ additional; in the central portion of each of the ribs occurs a nearly circular, fibro-vascular bundle with a few tracheæ and numerous thin-walled, strongly lignified sclerenchymatous fibers. The powder is yellowish-brown consisting of irregular angular fragments; tissues of endosperm, colorless, the cells filled with aleurone grains, each containing a rosette aggregate of calcium oxalate, about 0.002 mm. in diameter; fragments containing yellowish-brown vittæ, from 0.1 to 0.2 mm. in width; sclerenchymatous fibers few, strongly lignified and with numerous, oblique, simple pores; parenchyma cells with more or less thick walls and simple pores and occasionally reticulately thickened; tracheæ few and either spiral or annular; in mounts made with hydrated chloral T.S., numerous globules of a fixed oil separate. Fennel yields not more than 9 per cent. of ash." *U. S.*

Fennel seeds (half fruits) are officially described in the Br. Pharm. as follows:

"Small, oblong, straight or slightly curved, from three to ten millimetres long, and from two to four millimetres in diameter. Greenish or greenish-brown. Each of the two mericarps with five prominent principal ridges and six large vittæ. Aromatic odor; taste strong, sweet and camphoraceous. Ash not more than 11 per cent." *Br.*

There are ten chief varieties of fennel known in commerce, the fruits differing very much in size and considerably in taste. They are as follows: French (sweet); French (bitter); German; Puglis; Indian; Russian; Macedonian; Galician; Persian and Japanese. For histological differences of the different commercial varieties see monograph by Hartwich and Jama in *B. P. G.,* 1909, p. 306. Rosenthaler (*B. P. G.,* 1913, p. 570) has made a pharmacognostical study of a Chinese fennel.

Commercial fennel varies greatly in quality, this being either due to lack of care in harvesting or deliberate adulteration. It may contain sufficient sand, dirt, stem tissues, weed seeds, or other material beyond the 4 per cent. limit prescribed by the Pharmacopœia that it amounts to adulteration. The fruits, especially the powder, may be deficient in volatile oil, inferring that they have been partly exhausted. Exhausted or otherwise inferior fennel is occasionally improved in appearance by the use of a factitious coloring. (See Spaeth, in *Ph. Zentralh.,* 1908, p. 545; and 1913, p. 736.)

Schimmel & Co.'s Semi-Annual Report for April, 1897, gives as additional varieties of fennel—Aleppo, oil amounting to 0.75 per cent.; Macedonian, 3.4 to 3.8 per cent.; Moravian, 3 per cent.; Milanese, 4.2 per cent.; Roumanian, 4.6 per cent.; Spanish, amount not stated; and Syrian (Damascus), 1.6 per cent. Of these, the Syrian may be the same as that called Persian by Umney, and the Roumanian the same as that called Russian. Several additional varieties are also mentioned by Umney (*P. J.,* 1897, lviii, p. 226), who states that the European varieties were almost entirely displaced by the East Indian seed and that the latter would probably be supplanted by the Japanese variety.

The odor of fennel seed is fragrant, its taste warm, sweet, and agreeably aromatic. It yields its virtues to hot water, but more freely to

alcohol. The essential oil may be separated by distillation with water. (See *Oleum Fœniculi.*) From 960 parts of the seed Neumann obtained 20 parts of volatile and 120 of fixed oil.

Uses.—Fennel seed was used by the ancients. It is one of our most grateful aromatics, and in this country is much employed as a carminative, and as a corrigent of other less pleasant medicine, particularly senna and rhubarb. It is recommended for these purposes by the absence of any highly excitant property. An infusion may be prepared by introducing two or three drachms of the seeds into a pint of boiling water. In infants the infusion is frequently employed as an enema for the expulsion of flatus.

Dose, of the bruised or powdered seeds, twenty grains to half a drachm (1.3–2.0 Gm.).

Off. Prep.—Aqua Fœniculi, *U. S.* (from oil), *Br.;* Infusum Sennæ Compositum, *U. S.;* Pulvis Glycyrrhizæ Compositus, *Br.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodicæ sine Aloes, *N. F.;* Species Laxativæ, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.*

FRANGULA. U. S.

FRANGULA Frang. [Buckthorn Bark]

(frăn'gū-lą)

"The dried bark of *Rhamnus Frangula* Linné (Fam. *Rhamnaceæ*)." *U. S.*

Rhamni Frangulæ Cortex, *Br.* (1885); Frangula Bark; Alder Buckthorn; Ecorce de Bourdaine, Bourgène, *Fr.;* Cortex Frangulæ, *P. G.;* Faulbaumrinde, *G.;* Corteccia di frangola, *It.*

R. Frangula or *Alder Buckthorn* is an erect glabrous shrub from ten to fifteen feet high, without thorns, with broadly ovate obtuse leaves, the margins being entire or slightly sinuate, the under side sometimes slightly downy, and the rather numerous lateral veins diverging equally almost from the whole length of the midrib. Flowers all hermaphrodite, two or three together in each axil, with the calyx teeth, petals, and stamens in fives. Fruit dark purple, the size of a pea. This plant grows in hedges and bushy places throughout Europe and Russian Asia, except in the far north. It has become established on Long Island, northern New Jersey and in Ontario.

It is probable that most of the species of the genus *Rhamnus* have cathartic properties. An article upon *R. Purshiana* will be found elsewhere, as it is official in both of the Pharmacopœias. (See *Cascara Sagrada.*) The *R. catharticus* Linn., or common buckthorn, grows in Europe along with the official species, and has become locally naturalized in the Eastern portions of the United States. Its bark is probably often sold for the official article. It is distinguished by its more spreading, thorny habit, and its diœcious flowers, which are thickly clustered in the axils and have their parts in fours. The leaves also are more acute, have their margins finely serrate and their lateral veins mostly proceeding from the proximal half of the midrib. The fruit is purplish-black.

Properties.—This bark is officially described as "in quills varying in length, frequently flattened or crushed; from 0.5 to 1 mm. in thickness; outer surface grayish-brown or purplish-black, with numerous, prominent, lighter-colored, transverse lenticels and occasional patches of foliaceous lichens bearing small, blackish apothecia; inner surface smooth, dark brown with occasional purplish blotches, longitudinally striate, becoming red when moistened with solutions of the alkalies; fracture short, slightly fibrous in the inner layer; odor distinctive; taste slightly bitter. Under the microscope, transverse sections of Frangula show a distinctly undulate corky layer, composed of about 12 rows of reddish-brown cells; parenchyma cells of the primary cortex with numerous rosette aggregates of calcium oxalate, from 0.01 to 0.025 mm. in diameter; inner bark with bast-fibers in narrow, interrupted rows, the groups of fibers being separated radially by the medullary rays; bast-fibers with thick, strongly lignified, yellowish walls and narrow lumina and each group surrounded by a layer of crystal fibers, the prismatic crystals of calcium oxalate varying from 0.007 to 0.015 mm. in diameter, medullary rays one to two cells in width, occasionally three; cells of the parenchyma and medullary rays with numerous starch grains, 0.003 mm. in diameter. The powder is yellowish-brown; stone cells absent (distinguishing it from the powder of *Cascara Sagrada*). Add 0.1 Gm. of powdered Frangula to 10 mils of hot distilled water, shake the mixture occasionally until cold and filter; on the addition of a few drops of ammonia water, the filtrate is colored a deep red. Macerate 0.1 Gm. of powdered Frangula with 10 drops of alcohol, boil with 10 mils of distilled water and filter when cold. Shake this filtrate with 10 mils of ether; a yellow, ethereal solution separates, and 3 mils of this ethereal solution, when shaken with 3 mils of ammonia water, yields an alkaline solution, which, on being diluted with 20 mils of distilled water, still possesses a distinct cherry-red color. Frangula yields not more than 6 per cent. of ash." *U. S.*

As first pointed out by Schrenk (*Am. Drug.,* April, 1887), the bark of *Rhamnus Frangula* can be distinguished from that of *R. Purshiana* (*Cascara Sagrada*) by the absence of the irregular angular sclerenchymatous cells, which in *R. Purshiana* are wedged together in large compact groups, increasing in size and number towards the surface, and causing the short fracture of the outer bark.

Tschirch and Pool (*S. W. P.,* 1908, p. 665) have made a comparative pharmacognostical and chemical study of the barks of *R. Frangula* and *R. Purshiana.* Würffel (*Zeit. Oest. Apoth. Ver.,* 1907, p. 211) and Mitlacher (*Bull. sc. pharmacol.,* 1911, p. 10) report the substitution of Frangula by the bark of an alder (*Alnus glutinosa* Medic). The latter may be detected by not being reddened with solutions of the alkalies. Mitlacher (*Ph. Post,* 1905, p. 751) and

Moser (*A. J. P.*, 1909, p. 580) have found that the official Frangula is either admixed with or entirely substituted by the bark of *R. carniolica* A. Kerw. E'we (*Proc. A. Ph. A.*, 1914, p. 131) obtained a sample of Frangula which proved to be wild-cherry bark.

It is not certainly known which of the several bodies isolated from frangula bark is the purgative principle. The most important body, *frangulin*, the *rhamnoxanthin* ($C_{20}H_{20}O_{10}$) of Buchner and Binswanger, may be obtained by Phipson's process by macerating the bark for three or four days in carbon disulphide, then permitting the liquid to evaporate, exhausting the residue with alcohol, which leaves the fatty matter behind, evaporating the alcoholic liquid to dryness, and recrystallizing from ether. As thus obtained it is in fine yellow crystals, melting at about 226° C. (438.8° F.), and subliming in golden-yellow needles. It is insoluble in water, soluble in 160 parts of warm 80 per cent. alcohol, nearly insoluble in cold alcohol, soluble in hot fixed oils, petroleum benzin, and oil of turpentine. It communicates its color to cotton, silk, and wool. Faust (*A. Pharm.*, clxxxvii, 8) first proved the glucosidal character of frangulin by boiling it in alcoholic solution with hydrochloric acid, obtaining glucose and *frangulinic acid*, $C_{14}H_8O_4$. This forms fine microscopic needles of reddish color, fusing at 248° to 250° C. (478.4°–482° F.). Liebermann and Waldheim (*Ber. d. Chem. Ges.*, 9, p. 1775) obtained in this decomposition instead of frangulinic acid, *emodin*, $C_{15}H_{10}O_5$, trioxymethylanthraquinone. Frangulinic acid, on the other hand, would be a dioxyanthraquinone and an isomer of alizarin. Schwabe, in 1888, also found that *emodin* and *rhamnodulcite* were the decomposition products of *frangulin*, to which latter he gave the formula $C_{21}H_{20}O_9$, instead of that given above by Buchner. (Planchon et Collin, *Drogues Simples* (1896), vol. ii, 590.) E. Amweg has devised a method of separating the glucosides from frangula, cascara and rhubarb by extraction with solvents; he uses, 1, benzene; 2, a mixture of two parts of benzene, and one part of absolute alcohol, and 3, alcohol (60 per cent.) (*Ap. Ztg.*, 1897, 747.) Kubly isolated a crude acid which, when purified, he termed *frangulic acid;* Amweg regards this acid as a decomposition product and calls it *pseudo-frangulin*, this when hydrolyzed becomes *pseudo-emodin*. The emetic action of the green bark is attributed to a hydrolytic ferment, which is destroyed by heating. (*P. J.*, 1898, 24.)

Tschirch and Bromberger state that the bark of *Rhamnus cathartica* was found to contain *rhamnosterin, rhamnofluorin, emodin, chrysophanol* and *d-glucose*. (*S. W. P.*, 1912, v. 50, pp. 193–197.)

Uses.—In its fresh state this drug is very irritant to the gastro-intestinal mucous membrane, producing, when taken in sufficient quantity, violent catharsis, accompanied by vomiting and much pain. During drying it is said to lose much of its irritant power, and the dried bark is affirmed to resemble rhubarb in its action. The U. S. P. VIII required that the bark should be at least one year old, but this requirement does not appear in the U. S. P. IX. A *decoction* (an ounce to the pint) may be used in tablespoonful doses, or a dessertspoonful of an *elixir*, made by mixing four fluidounces of the fluidextract with twelve of elixir of orange, may be employed.

Dose, of frangula, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Fluidextractum Frangulæ, *U. S.;* Elixir Catharticum Compositum (from Fluidextract), *N. F.;* Syrupus Sennæ Compositus (from Fluidextract), *N. F.*

GALLA. U. S., Br.

NUTGALL Gall. [Aleppo Galls, Smyrna Galls]

(găl'la)

"Excrescences on the young twigs of *Quercus infectoria* Olivier and other allied species of *Quercus* (Fam. *Fagaceæ*), induced by the punctures on the leaf-buds and by the deposited ova of *Cynips tinctoria* Hartig (Order *Hymenopteræ*). Not more than 5 per cent. of Galls float in water." *U. S.* "Galls are excrescences on Quercus infectoria, *Olivier*, resulting from the deposition of the eggs of Cynips gallæ tinctoriæ, *Olivier*." *Br.*

Galls, Syrian Galls; Galla Halepensis, s. Turcica, s. Levantica, s. Tinctoria, s. Quercina; Galle de Chêne, d'Alep, *Fr. Cod.;* Noix de Galle, *Fr.;* Gallæ, *P. G.;* Galläpfel, Gallen, *G.;* Noce di galla, *It.;* Agalla, *Sp.*

Many plants, when pierced by certain insects, particularly those of the genus *Cynips*, are affected at the points of puncture with a morbid action, resulting in excrescences, which, as they are derived from the juices of the plant, partake more or less of its chemical character. Most of the oaks are occasionally thus affected, and the resulting excrescences, having in a high degree the astringency of the plant, have been employed for various practical purposes. They are known by the name of *galls*, a term which, as well as their use in medicine, has been handed down from the ancients. *Quercus infectoria, Q. ægilops, Q. excelsa, Q. Ilex, Q. Cerris*, and *Q. Robur* have been particularized as affording this product; but it is now generally admitted, on the authority of Olivier, that the official galls are derived chiefly, if not exclusively, from *Q. infectoria*. Under the name of *Chinese galls*, a product has been brought from China, supposed to be caused by an insect allied to the aphis, as such an insect has been found in the interior of them. They are irregularly spindle-shaped, often more or less bent, with obtusely pointed protuberances, about two inches long by an inch in diameter at the central thickest part, of an ash color and a soft velvety feel, very light, hollow, with translucent walls about a line in thickness, of a slight odor recalling that of ipecac, and a bitter astringent taste. From an examination of fragments of leaves and petioles found among these galls, Schenck concluded that the tree on which they

are found is a species of Rhus; but according to Decaisne, their true source is probably the *Distylium racemosum* of Zuccarini, a large tree of Japan, the leaves of which produce a velvety gall, resembling the one in question. (Guibourt, *Hist. Nat. des Drogues,* 1850, iii, 703.) Daniel Hanbury asserts that this opinion of Decaisne is erroneous (*P. J.,* Feb., 1862, p. 421), as in his examination of the packages imported from China and Japan he has found remains of different parts of a species of *Rhus,* but never any of a *Distylium.* Besides, the form of the galls of the *Distylium,* as figured by Siebold and Zuccarini, is entirely different. The species of *Rhus* which yields the commercial Chinese galls is the *R. semialata* Murray. The Chinese make great use of this product both in dyeing and as a medicine. L. A. Buchner, Jr., has found it to contain 65 per cent. of tannic acid identical with that of the official galls. (*Ph. Cb.,* July, 1851, p. 526.) It is recommended by Stenhouse for the manufacture of gallic acid, being preferable for this purpose to the official galls, in consequence of its less amount of coloring matter. (*P. J.,* Dec., 1862.) An inferior kind of galls is produced in great quantities in England, by the attack of the *Cynips kollari* of Hartig, upon the common English oak; but they have been ascertained to contain little tannic acid, and are of little value.

Quercus infectoria, or the so-called *dyer's oak,* is a small tree or shrub, with a crooked stem, seldom exceeding six feet in height. The leaves are petiolate, obtusely toothed, smooth and of a bright-green color on both sides. The acorn is elongated, smooth, two or three times longer than the cup, which is sessile, somewhat downy, and scaly. This species of Quercus grows, according to Olivier, throughout Asia Minor, from the Archipelago to the confines of Persia. M. Kinnier found it also in Armenia and Kurdistan; Hardwicke observed it growing in the neighborhood of Adwanie, and it probably pervades the middle latitudes of Asia.

The gall originates from the puncture of the *Cynips tinctoria* Hartig, a hymenopterous insect or fly, with a fawn-colored body, dark antennæ, and the upper part of its abdomen shining brown. The insect pierces the shoots and young boughs, and deposits its egg in the wound. This irritates the part, and a small tumor quickly rises, which is the result of a morbid growth, exhibiting various cells under the microscope, but no proper vegetable fiber. The egg grows with the gall, and is soon converted into a larva, which feeds upon the vegetable matter around it, and thus form a cavity in the center of the excrescence. The insect at length becomes a fly, and escapes by eating its way out. The galls are in perfection when fully developed, before the egg has been hatched or the fly has escaped. Collected at this period, they are called, from their dark color, *blue, green,* or *black galls,* and are most highly esteemed. Those which are gathered later and have been injured by the insect are *white galls.* They are usually larger, less heavy and compact, and of a lighter color than the former.

The galls collected in Syria and Asia Minor are brought to this country chiefly from the ports of Smyrna and Trieste, or from London. As they are produced abundantly near Aleppo, it has been customary to designate them by the name of that town, though the designation, however correct it may formerly have been, is now wholly inapplicable, as they are obtained from many other places, and the product of different parts of Asiatic Turkey is not capable of being discriminated, at least in our markets. Great quantities of galls, very closely resembling those from the Mediterranean, have been brought to the United States from Calcutta. Royle states that they are taken to Bombay from Bussorah through the Persian Gulf. We are, nevertheless, informed that galls are among the products of Moultan. Those of France and other southern countries of Europe have a smooth, shining reddish surface, are little esteemed, on account of their small yield of tannin, and are seldom brought to the United States.

Properties.—Galls are "nearly globular, from 0.8 to 2.2 cm. in diameter; externally blackish-olive-green or blackish-gray, more or less tuberculated on the upper portion, the basal portion being nearly smooth and contracted into a short stalk; heavy, sinking in water, excepting the smaller galls; fracture short-horny; internally grayish or dark brown, consisting of a central portion slightly radiating and resinous, occasionally hollow and traversed by a narrow radial canal extending to the exterior as shown by the perforation in the whole gall; odor slight; taste strongly astringent. The powder consists of numerous fragments of thick-walled starch-bearing parenchyma; starch grains numerous; more or less free in the powder and varying in shape from spherical or ellipsoidal to polygonal, and from 0.005 to 0.03 mm. in diameter; stone-cells few, resembling those found in fruits and seeds, varying considerably in shape and size, and from 0.025 to 0.3 mm. in length; occasional fragments with spiral or reticulate tracheæ; fragments mounted in dilute ferric chloride T.S. assume a deep blue or greenish-blue color. Macerate 0.5 Gm. of the powdered Nutgall with 2 mils of alcohol for a few minutes, add 500 mils of water, stir the mixture well for five minutes and filter. Take 1 mil of the light yellowish-brown solution, and dilute it with 10 mils of water; it shows a distinct blue or violet-blue color upon the addition of a drop of ferric chloride T.S." *U. S.*

"Hard, heavy, subglobular, from twelve to eighteen millimetres or more in diameter, tuberculated on the surface, the tubercles and intervening spaces being smooth; dark bluish-green or dark olive-green externally, yellowish or brownish-white within, with a small central cavity. Galls sink in water and exhibit no perforation. No odor; taste intensely astringent." *Br.*

The best are externally of a dark bluish or lead color, sometimes with a greenish tinge,

internally whitish or brownish, hard, solid, brittle, with a flinty fracture, a striated texture, and a small spot or cavity in the centre, indicating the presence of the undeveloped or decayed insect. Their powder is of a light yellowish-gray. Those of inferior quality are of a lighter color, sometimes reddish or nearly white, of a loose texture, with a large cavity in the centre, communicating externally by a small hole through which the fly has escaped.

Kraemer (*Bot. Gaz.*, 1900, p. 275) made a microchemical study of American galls. These closely resemble the Aleppo variety and are formed on *Quercus coccinea* Muench and *Q. imbricaria* Michx. by *Cynips aciculata*. Kraemer found the chemical constituents to vary with the development of the insects. At the chrysalis stage gallic acid is more abundant than when the winged insect is developed. Texas galls are formed on the live oak (*Q. vireus*), California oak balls are formed on *Q. lobata*.

Galls are formed on a number of trees and shrubs, including oaks, rhus, rhododendron, juniper, eucalyptus and sage. Hartwich (*Arch. d. Pharm.*, 1905, p. 584) illustrates these several varieties and discusses their composition. Richter gives minute descriptions of the origin, structural characteristics and microscopical appearance of galls in *Ph. Zentralh.*, 1912, p. 533. Feist and Haun have published (*A. Pharm.*, 1913, v. 251, p. 468) an article on the constitution of the tannin in Turkish and Chinese galls.

Galls have a bitter, very astringent taste, and when whole are inodorous or nearly so, but bruised or in powder they have a decided and peculiar though not very strong odor. The tannin of galls, usually known as *gallo-tannic acid*, appears to exist in the galls, in part at least, as a glucoside, but one very easily broken up by ferments like pectase into glucose and *di-gallic acid*, $C_{14}H_{10}O_9$, which is the material, therefore, extracted from the galls. This digallic acid may be considered as the anhydride of *gallic acid*, $C_7H_6O_5$, formed from two molecules of this latter by the elimination of one molecule of water. Commercial tannin yields from 0 to 22 per cent. of glucose, showing the presence of varying amounts of the unaltered glucoside. Galls yield, on an average, from 65 to 77 per cent. of tannin. (See *Acidum Tannicum* and *Acidum Gallicum*, see also "The Tannins," by Henry Trimble, J. B. Lippincott Co., 1894.) All the soluble matter of galls is taken up by forty times their weight of boiling water, and the residue is tasteless. Alcohol dissolves seven parts in ten, ether five parts. A saturated decoction deposits upon cooling a copious pale-yellow precipitate. The infusion or tincture affords precipitates with sulphuric and hydrochloric acids, lime water, and ammonium and potassium carbonates, with solutions of lead acetate and subacetate, copper and iron sulphates, silver and mercuric nitrates, and potassio-antimonyl tartrate; with solution of gelatin; and with the infusions of Peruvian bark, calumba, opium, and many other vegetables, especially those containing alkaloids, with most of which tannic acid forms insoluble compounds. The infusion of galls reddens litmus paper, is rendered orange by nitric acid, milky by mercuric chloride, and has its color deepened by ammonia, but yields no precipitate with either of these reagents. Zinc sulphate was said by A. T. Thomson to slowly occasion a precipitate, but this result was not obtained by Duncan. Infusion of galls is rendered more permanent by the addition of 10 per cent. of glycerin.

A variety of galls was imported into Germany, which was said to be derived from Central Asia, especially from the provinces of Khokan, Khiva, and Bokhara, where they are used in dyeing. They are of various forms, some being long, others round, cylindrical, or angular, and sometimes they are grouped upon a single stalk, and covered with little elevations. They differ from all other galls by their color, being on one side yellow, and on the other of a fine red. Most of them present a little opening, and in the interior are eggs and larvæ of a peculiar species of aphis. They have yielded, on analysis, 43.10 per cent. of tannin, 3.03 of a green wax, 16 of cellulose, and an undetermined quantity of fecula and volatile oil. (R. Palne, *J. P. C.*, April, 1873.)

From the so-called gall-wax of certain kinds of galls, M. Nierenstein obtained a nitrogenous constituent, $C_{13}H_{17}O_6N$, which is probably a lævorotatory *galloleucin*. (*Z. Phys. Ch.*, 92, 53.)

Uses.—Galls have a powerfully astringent action, but are no longer prescribed internally. *Aromatic Syrup of Galls* is sometimes prescribed. For a process, see U. S. Dispensatory, 19th ed., p. 574. Nutgalls may be used externally for the same purposes as tannic acid.

Dose, five to fifteen grains (0.3–0.9 Gm.).

Off. Prep.—Tinctura Gallæ, *N. F.;* Unguentum Gallæ, *U. S., Br.;* Unguentum Gallæ cum Opio, *Br.;* Elixir Rubi Compositum, *N. F.*

GAMBIR. U. S.

GAMBIR [Pale Catechu]
[To replace Catechu, U. S. 1890]

(găm'bĭr)

"A dried extract prepared from decoctions of the leaves and twigs of *Ourouparia Gambir* (Hunter) Baillon (Fam. *Rubiaceæ*)." *U. S.* (See *Catechu* and *Catechu Nigrum*, page 305.)

Catechu Pallidum, Terra Japonica, Gambier, Cutch; Gambir Cubique, *Fr.;* Catechu, *P. G.;* Katechu, Gambir-Catechu, *G.;* Catecu, *It., Sp.*

Ourouparia Gambir (Hunter) Baillon (*Uncaria Gambier* Roxb.) This is a climbing shrub with slender stems somewhat thickened at the nodes; leaves ovate or oblong, entire, rounded at the base but abruptly attenuated at the summit, opposite and stipulated, smooth on both sides. The flowers are small, crowded into a dense globular head on a hairy receptacle; the flower heads are borne on long axillary peduncles which bear in the middle a whorl of bracts. At the point where these bracts occur

the peduncle breaks after the falling of the inflorescence and the remainder of the peduncle becomes elongated and curved into hooks by means of which the plant climbs. Corolla gamopetalous, trumpet-shaped, tube slender; fruit one inch long, pericarp dry, dehiscing vertically into two valves; seeds very numerous.

It is a native of Malacca, Sumatra, Cochin-China, and other parts of Eastern Asia, and is largely cultivated in the islands of Bintang, Singapore, and Prince of Wales. The gambir is prepared by lopping off the leaves, shoots, and twigs of the plant, chopping them into pieces, and throwing them into an iron pot filled with boiling water. When the leaves are exhausted and the liquid sufficiently thick, it is poured into small wooden tubs, and so soon as sufficiently cool, a half-closed hand is plunged into the semi-fluid mass and a piece of light wood shaped like an elongated dice box rapidly worked up and down in the hollow formed by the hand. The extract begins to thicken by a process which is compared to crystallization. The mass is finally turned out, and cut into cubes, which are put upon trays and smoke-dried. (See also *P. J.*, 1892, 1003.) This extract, which is known by the native Malays as *pinang* or *siren* was first brought to the attention of the profession by Campbell.

The amount of gambir exported from the Straits Settlements in 1910 amounted to 40,000,000 pounds, of which about 15,000,000 pounds was shipped to the United States.

Most of the commercial article is shipped from Singapore to London and Hamburg. The natives of Malay distinguish four different kinds: 1. *Gambir bulat* or *round Gambir*, which occurs in biscuit-like pieces and is mostly used for chewing. 2. *Gambir papan* or *table Gambir* which occurs in yellowish-brown thin tablets and is also used in chewing. 3. *Gambir paku* (*nail* or *finger Gambir*) which occurs in long black sticks resembling licorice extract. 4. *Gambir dutoor* or *cube Gambir*. The latter is the form in which it is usually found in commerce. Gambir is also imported in large blocks, being used in this form for dyeing and tanning.

Properties.—Gambir is "usually in cubical or rectangular pieces from 20 to 30 mm. in diameter; externally pale grayish-brown to reddish-brown, more or less dull and porous; friable; internally of a light brown or dull earthy color; inodorous; taste bitterish and very astringent. Upon scraping a piece of Gambir and mounting the separated fragments in hydrated chloral T.S. and examining them under the microscope, numerous acicular crystals, from 0.01 to 0.03 mm. in length, separate at the edges of the fragments and gradually dissolve, leaving a few, thick-walled, non-glandular hairs which, when entire, may be 0.35 mm. in length; a few fragments of leaves may also be present showing either epidermal cells or small narrow tracheæ with spiral or annular markings; a few starch grains either single or compound, of variable shapes and from 0.005 to 0.015 mm. in diameter; a number of bacteria may also be present. Macerate 1 Gm. of Gambir with 50 mils of water, and filter; the pale yellowish-brown solution obtained gives an intense, green color with dilute ferric chloride T.S.; but yields no precipitate with copper sulphate T.S. Not less than 65 per cent. of Gambir is soluble in water and not less than 60 per cent. is soluble in alcohol. Gambir yields not more than 9 per cent. of ash." *U. S.*

The microscopical appearance of gambir is very characteristic and Brumwell (*J. S. C. Ind.*, 1911, p. 475) illustrates the appearance of commercial specimens. Gambir is light and porous, so that it floats when thrown in water. It is partially soluble in cold water, and almost wholly so in boiling water, which deposits a portion upon cooling. Duhamel, Ecky, and Procter dissolved 87.5 per cent. of it in cold water by means of percolation. (*A. J. P.*, xvi, 166.) Nees von Esenbeck found it to consist of from 36 to 40 per cent. of *catechutannic acid*, a peculiar principle called *catechuin*, *catechin*, or *catechuic acid*, gum or gummy extractive, a deposit like cinchonic red, and 2.5 per cent. of lignin. *Catechin*, when perfectly pure, is snow-white, of a silky appearance, crystallizable in fine needles, melting at 217° C. (422.6° F.), unalterable in the air if dry, fusible by heat, very slightly soluble in cold water, with which it softens and swells up, soluble in boiling water, which deposits it on cooling, and soluble also in alcohol and ether. It very slightly reddens litmus paper, and, though coloring solution of chloride of iron green, and producing with it a grayish-green precipitate, differs from tannic acid in not affecting a solution of gelatin. The very great discordance of different authors as to its formula seems to be explained by some experiments of Etti (*Ann. Ch. Ph.*, 186, p. 327), who showed that *catechin*, $C_{15}H_{18}O_8$, readily gives at 100° C. (212° F.), or even when kept for some time over sulphuric acid, an anhydride, $C_{30}H_{34}O_{15}$, and at 160° C.(320° F.) a second anhydride, $C_{30}H_{32}O_{14}$, which, mixed in varying proportions, explain the varying results. Gautier (*Bull. Soc. Chim.*, 30, 567) finds three different catechins separable by their different solubility in water, all of them crystallizable. These are: *a-catechin*, $C_{40}H_{38}O_{18} + 2H_2O$, melting at from 204° to 205° C. (399.2°–401° F.), and present in gambir to the amount of 12 per cent.; *b-catechin*, $C_{47}H_{38}O_{16} + H_2O$, melting at from 176° to 177° C. (348.8°–350.6° F.), and 2 per cent. present in gambir; and *c-catechin*, $C_{40}H_{38}O_{18} + H_2O$, melting at 163° C. (325.4° F.), and present in gambir to the amount of 6.5 per cent.

Perkin and Yoshitako (*P. J.*, 1902, p. 530) have made an elaborate investigation of gambir and acacia catechus. They find three catechins, designated respectively as (*a*), (*b*), and (*c*). Catechin (*b*), $C_{15}H_{14}O_6 + 4H_2O$, occurs in air dried, colorless needles, melting at 175° to 177° C. (347°–350.6° F.), and gives on fusion with alkali, phloroglucinol, protocatechuic acid, and an acid resembling acetic acid. Catechin (*c*), $C_{15}H_{14}O_6$, air dried, contains no water of

crystallization and forms colorless prisms, melting at 235° to 237° C. (455°–458.6° F.). Catechin (*a*), $C_{15}H_{14}O_6 + 3H_2O$ (or less probably $C_{14}H_{14}O_6 + 3H_2O$), air dried, forms colorless needles, melting at 204° to 205° C. (399.2°–401° F.).

Good gambir should occur in a hard compact mass, breaking up, when the adhering mat is removed, into distinct cubes of a brownish-black color externally, and a deep mahogany-red with an occasional streak of yellow internally. It should not steam when the mat is opened. From this quality it grades down to a stuff which has been prepared by mixing the material obtained by reboiling the exhausted leaves with various mixtures. This lowest grade is not in cubes, steams when opened, frequently shows large patches of black or dirty blue color, and often has a sour fetid odor; its color varies from black to light-brown.

The varieties between the two extremes are very great; sometimes gambir occurs in solid mass of fair quality; sometimes the cubes are of extraordinary size, and of a color varying from a dirty white to a very pale yellow. At the Edinburgh Forestry Exhibition in 1885 the Maharajah of Johore exhibited specimens labelled "gambir produced in Johore." The first quality, which was "*makan*" (for eating), was in regular cubes, externally cassia-brown color, internally pale cinnamon brown, and yielded 32 per cent. of tannic acid; the second quality was in badly formed cubes, externally brown and black, internally cinnamon, and yielded 30 per cent. of tannic acid; the third quality was in dull-brown, well-shaped cubes, internally pale brown, and yielded 19 per cent. of tannic acid. The oblong or *parallelopiped gambir* was of a uniform dull brown, very hard and strong, and yielded only 2 per cent. of tannic acid. MacEwan believes that the low percentage of tannin was due to the decoction not having been subjected to prolonged boiling, which favors the decomposition of catechin, with the formation of catechu-tannic acid. None of the finest varieties of gambir, such as are used by the natives for chewing, occur to any extent in American commerce. Prebble records his examination of a cube gambir of fine appearance which contained a large percentage of starch. (*P. J.*, 1893, 21.)

Enormous quantities of gambir are used both in Europe and America in tanning, calico printing, dyeing, as an ingredient in boiler compounds for preventing the hard scaly incrustation caused by certain kinds of water, and other art processes requiring tannic acid.

Vanderkleed and E'we call attention to the fact that the apparent alcohol soluble content of gambir may be unduly raised by the high moisture content of some of the commercial varieties, which they report as containing over 21 per cent. of moisture, all of which would be calculated in the alcohol soluble extractive by the ordinary methods in which no allowance is made for water. (*J. A. Ph. A.*, 1914, 1685.)

Uses.—Gambir is a serviceable remedy in those cases where astringents are indicated. The complaints to which it is best adapted are *diarrhea* dependent on debility or relaxation of the intestinal mucous membrane, and *passive hemorrhages*, particularly from the uterus. A small piece held in the mouth and allowed slowly to dissolve is an excellent remedy in *relaxation of the uvula* and the *irritation of the fauces* and *troublesome cough* which depend upon it. Applied to *spongy gums*, in the state of powder, it sometimes proves useful; and it has been recommended as a dentifrice in combination with powdered charcoal, Peruvian bark, myrrh, etc.

Dose, from ten grains to half a drachm (0.65–2.0 Gm.), which should be frequently repeated, and is best given with sugar, gum arabic, and water.

Off. Prep.—Tinctura Gambir Composita, *U. S.* (*Br.*); Trochisci Gambir, *N. F.*; Pulvis Gambir Compositus, *N. F.*; Tinctura Pectoralis (from Compound Tincture), *N. F.*

GELATINUM. U. S., Br.

GELATIN Gelat.

(ǧe-lăt'ĭ-nŭm)

"The purified product obtained from animal tissues, as skin, ligaments, and bones, by treatment with boiling water." *U. S.* "Gelatin is the air-dried product obtained by the action of boiling water on animal tissues such as skin, tendons, ligaments, and bones." *Br.*

Gelatine; Gélatine animale, *Fr. Cod.*; Colle de Flandre purifiée, *Fr.*; Gelatina alba, *P. G.*; Weisser Leim, Gelatine, Gallerte, *G.*; Gelatina, *Sp.*

Gelatin is the term applied to purified forms of the substance ordinarily known as *glue*, and the bones and animal matter from which the best qualities of gelatin are prepared are carefully selected so as to be free from decomposed products and odorous substances. The hot solution of gelatin must be thoroughly clarified if the so-called sparkling gelatin is to be made.

The *collagens* are a class of albuminoids abundant in bones, skin, tendons, cartilage and similar tissues of animals. These collagens unite with water at high temperatures, producing the compounds known respectively as glue and gelatin which differ from each other mainly in the character of the raw stock from which they are manufactured and also in the relative amounts of *glutin* and *chondrin* which they contain; glutin being present in higher proportions in glue, to which it imparts its great adhesive power and chondrin giving to gelatin its greater gelatinizing power. Among the commercial varieties of these substances may be mentioned *hide glue* and *bone glue*, which are commercially the most important.

On account of the tendency to decompose during the process of manufacture it is sometimes the practice to employ preservatives such as sulphurous acid, which, being frequently used in excessive amounts, remain in the finished product as contaminating substances. Sometimes metallic impurities, as lead, copper, zinc, and arsenic, are present from the apparatus or

substances used during the manufacture of the gelatin.

After the gelatin solution has been purified by the use of animal charcoal or other appropriate means, it is brought to the proper degree of concentration and is then allowed to solidify or gelatinize. It is now cut up into slabs which are rapidly dried in long, continuous mechanical drying machines where it is supported upon netting to allow free access of the warm, dry air currents which pass over it.

The surface of sheet gelatin is covered with lozenge-shaped marks, due to impressions left by the knotted netting upon which it is dried. Shred gelatin is made by cutting sheet gelatin into very narrow shreds by a shearing-machine. (See *Nat. Drug.*, 1894, 134.) *Gelatose* and *paragelatose* are terms used by Dastre and Floresco to define gelatin which has lost its power of "gelatinization" through the action of ferments or microbes, saline solutions, or the prolonged action of boiling water. (*P. J.*, 1895, 454.)

Properties.—It is officially described as "an amorphous solid, in sheets or flakes or in ground, powdered or shredded form, colorless or slightly yellowish, and having a very slight, characteristic odor and taste; unalterable in the air when dry, but decomposing when moist or in solution. Gelatin is insoluble in cold water but swells and softens when immersed in it, gradually absorbing from 5 to 10 times its own weight of water; soluble in hot water, acetic acid or glycerin; insoluble in alcohol, chloroform, ether, benzene, carbon disulphide or fixed or volatile oils. An aqueous solution of Gelatin (1 in 5000) is at once rendered turbid by the addition of tannic acid T.S. A hot solution of Gelatin in distilled water (1 in 40) is free from putrid odor, and is not more than slightly acid to litmus; it appears not more than slightly opalescent in a stratum 2 cm. in thickness, and, on cooling to 6° C. (42.8° F.) and standing for several hours, it forms a firm, transparent or translucent jelly. Incinerate about 0.5 Gm. of Gelatin; not more than 2 per cent. of ash remains. A solution of the ash in 25 mils of distilled water, made with the aid of heat and a few drops of hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3). Heat 1.5 Gm. of Gelatin with 30 mils of hydrochloric acid (1 in 4) in a 150 mil Erlenmeyer flask on a water bath, and, when the Gelatin has dissolved, add 3 mils of saturated bromine water and heat it on a water bath for fifteen minutes, shaking the flask occasionally. Then add 0.5 Gm. of potassium iodide and follow it immediately with 0.5 mil of a 25 per cent. solution of stannous chloride. Heat the solution for five minutes on a water bath, cool and subject it to the Test for arsenic (see Part III, Text No. 1). The stain produced, if any, is not greater than that produced in a test made with the same quantities of the reagents to which 2 mils of the standard arsenic test solution (see Part III, Test No. 1) has been added. Dissolve 20 Gm. of Gelatin in 150 mils of hot distilled water in a flask having a round bottom and a long neck, add 5 mils of phosphoric acid and 1 Gm. of sodium bicarbonate, and at once connect the flask with a condenser. Distil 50 mils, receiving the distillate under the surface of 50 mils of tenth-normal iodine V.S. Acidulate the distillate with a few drops of hydrochloric acid, add 2 mils of barium chloride T.S., and heat on a water bath, until the liquid is nearly colorless. The precipitate of barium sulphate, if any, when filtered, washed and ignited, weighs not more than 0.0015 Gm., corresponding to not more than 0.002 per cent. of *sulphur dioxide* in the Gelatin, correction being made for any sulphate which may be present in 50 mils of the tenth-normal iodine V.S.

"NOTE.—Gelatin used for making capsules for medicines contains not more than 0.15 per cent. of sulphur dioxide." *U. S.*

"In almost colorless, translucent sheets or shreds. Insoluble in *alcohol* (90 per cent.) and in *ether;* soluble in *acetic acid.* A solution in hot *water* (1 in 50) is inodorous and solidifies to a jelly on cooling. An aqueous solution yields a precipitate with *solution of tannic acid,* but not with solutions of other acids, or with dilute solution of *alum, solution of lead acetate,* or *T. Sol. of ferric chloride.* Ash not more than 2 per cent." *Br.*

Gelatin is largely used for making *capsules.* Certain medicines are so offensive to the taste, and consequently so likely to cause nausea, that it is highly desirable to administer them in such a way as to prevent their contact with the tongue and palate. This object is fully accomplished, so far as regards many disagreeable liquid medicines, by the use of the capsules of gelatin. A polished bulb of iron, ivory, or bone, of the size and shape of the capsules required, and connected by a slender rod with a handle, is first greased by rubbing with an oiled cloth, and then dipped into a solution of gelatin made by heating six parts of pure gelatin with one of sweetened water. Upon being withdrawn, it is held for a short time so as to allow the excess of the solution to run off, and then fixed with the handle in a board, the coated bulb being upward, until the coating becomes cold and firm. The capsule is now removed by the fingers, and further dried by exposure on a tray. A number of capsules having been prepared, they are placed each in a small cell upon a board, with their mouths upward, and the liquid they are to contain is introduced by means of a syringe with a fine point. Their mouths are then closed with a drop of the solution of gelatin applied by means of a stick or glass rod, which is afterwards strengthened by an additional coating, given by dipping the mouth of the capsule into the solution diluted with a little water. The capsules may be made of such a capacity as to contain from ten to fifteen grains of copaiba or other liquid. Capsules are now largely used for enclosing dry powders like quinine, etc. These are ovoid in shape, and after being filled with the powder by the pharmacist, are closed by putting upon

the open end a rounded gelatin cap and pressing it down tightly. When so-called *soft capsules* are desired, a small quantity of glycerin is introduced into the gelatin mass; this makes the film elastic by preventing its drying completely. Gelatin capsules are now made in enormous quantities by machinery.

Formalized gelatin is but very slightly or not at all affected by the gastric juice, but is slowly dissolved in the intestines. Advantage has been taken of this fact to manufacture capsules for the administration of drugs which it is desirable should not come in contact with the gastric mucous membrane. A special brand of such capsules is on the market under the name of *glutoid capsules.* These are called *enteric capsules.*

Scoville (*J. A. Ph. A.*, 1915, p. 1243) recommends that the sealed capsules be immersed in a 1 per cent. aqueous formaldehyde solution for thirty seconds, then dried quickly and allowed to stand two weeks before use. Capsules so treated will remain enteric for about one year, but if stronger formaldehyde solutions are used or the time of treatment extended, the capsules, after standing for a few days, become insoluble in the intestines.

Uses.—In 1896 Dastre and Floresco (*C. R. S. B.*, 1896, ii, iii), while engaged in a research of the physical properties of gelatin, made the observation that, after a solution of gelatin had been injected into a vein, the blood of a dog coagulated almost instantaneously. This observation has led to an immense amount of study concerning the effect of gelatin administered by various channels upon the coagulability of the blood. It is well established that solutions of gelatin injected either intravenously or subcutaneously cause a great reduction in the time required for the blood to clot. Unfortunately, because of the liability of gelatin to contamination with tetanus, these injections are not permissible in human medicine. Two methods have been suggested to obviate the difficulty, one is to sterilize the gelatin, by subjecting to relatively high temperatures on repeated occasions, and the other to exhibit it by the mouth. When gelatin is eaten it undergoes a process of digestion similar to that of the protein foods, being finally converted into a substance known as *gelatose,* which differs from gelatin in that solutions of it do not gelatinize on cooling. When boiled for a long period of time a somewhat analogous change in gelatin takes place. There has been some difference of opinion as to whether the loss of its gelatinizing power is accompanied by a loss of its therapeutic virtue. While the matter cannot be considered as finally settled the evidence is very strong that a solution of gelatin may be perfectly sterilized without losing its power of hastening coagulation. Although less firmly supported there is still strong reason for believing that the administration of gelatin by the mouth influences clotting of the blood in the same way. To what change in the blood is due the increased coagulability under the influence of gelatin is at present undetermined. The theory at one time advanced that the effects were due to the lime in the gelatin is too absurd to require contradiction. The most probable explanation is that of Moll (*W. K. W.*, 1903) that it increases the amount of fibrinogen.

Gelatin is used in medicine in all cases where increased coagulability of the blood is desirable, thus in various forms of internal *hemorrhage* as *hemoptysis, hematemesis,* or *menorrhagia,* it is one of the most valuable agents we possess; in various dyscrasias of the blood, such as *hemophilia* or *purpura hemorrhagica,* it has been employed with apparent great benefit. In certain types of *aneurism* it will apparently encourage the deposit of clot in the aneurismal sac. It has also been employed in the treatment of *diarrhea* and *mucous colitis* with asserted benefit.

The method of exhibiting the gelatin will vary greatly according to the condition for which it is employed. In local hemorrhages, as *epistaxis,* a warm 10 per cent. solution may be applied directly to the bleeding point; in *gastric ulcer* the administration by the mouth is probably the preferable method as a local action may be obtained in this manner. In internal hemorrhages when the bleeding is copious, the drug should generally be given hypodermically, as the absorption from the intestinal tract is too slow to be of service. The intravenous injection has in several instances caused fatal embolism and should, under no circumstances, ever be resorted to. For hypodermic administrations it is usually necessary to obtain one of the specially prepared sterilized forms of gelatin. These are generally marketed in the form of 10 per cent. solutions. Of this 10 per cent. solution from one to three fluidounces (30–90 mils) may be injected subcutaneously. In the slower forms of hemorrhage administration by the mouth should be tried first for obvious reasons. For this purpose from a half to two ounces (15.5–62 Gm.) of commercial gelatin may be dissolved in four or five times as much water, suitably flavored and seasoned, and allowed to cool and eaten in the same manner as ordinary table gelatin.

Dose, one-half to one ounce (15.5–31 Gm.).

Off. Prep.—Gelatinum Glycerinatum, *U. S.;* Suppositoria Glycerini, *Br.* (Vehicle for lamellæ in Br.)

GELATINUM GLYCERINATUM. U. S.

GLYCERINATED GELATIN Gelat. Glycerin.

(ge-lăt'i-nŭm glĭç-e-ri-nā'tŭm)

Gelatina Glycerinata, Gelatinum Glycerini; Glycerin Jelly; Gelée Glycérinée, *Fr.;* Glycerinleim, *G.*

* "Gelatin, *one hundred grammes* [or 3 ounces av., 231 grains]; Glycerin, *one hundred grammes* [or 3 ounces av., 231 grains], Water, *a sufficient quantity,* to make *two hundred grammes* [or 7 ounces av., 24 grains]. Pour upon the Gelatin sufficient Water, which has been previously boiled and cooled, to cover it; allow it to stand one hour; pour off the Water and allow the Gelatin to drain for a few minutes; then transfer it to a dish, add the Glycerin,

and heat it on a water-bath until the gelatin is dissolved. Strain the solution while hot, and transfer it to a tared dish, continue to heat on the water-bath until the product weighs *two hundred grammes* [or 7 ounces av., 24 grains]. When cold, cut the mass into pieces, and preserve them in well-closed containers." *U. S.*

This preparation was made official for the first time in the U. S. Pharm. VIII.

Uses.—Glycerinated gelatin is used as a vehicle in making gelatin suppositories, bougies, etc. The National Formulary IV introduced a class of preparations termed "*Glycerogelatins*," to be used in dermatological practice. (See Part III.)

Off. Prep.—Glycerogelatinum Acidi Salicylici, *N. F.;* Glycerogelatinum Iodoformi, *N. F.;* Glycerogelatinum Zinci Durum, *N. F.;* Glycerogelatinum Zinci Molle, *N. F.;* Suppositoria Boroglycerini, *N. F.*

GELSEMIUM. U. S. (Br.)

GELSEMIUM Gelsem. [Yellow Jasmine Root, Yellow Jessamine]

(ğĕl-sĕm'ĭ-ŭm)

"The dried rhizome and roots of *Gelsemium sempervirens* (Linné) Aiton filius (Fam. *Loganiaceæ*)." *U. S.* "Gelsemium Root is the dried rhizome and root of Gelsemium nitidum, *Michaux*." *Br.*

Gelsemii Radix, *Br.;* Gelsemium Root, Yellow Jasmine, Yellow Jessamine, Carolina or American Yellow Jessamine, Yellow or Evening Trumpet Flower; Gelsemium, *Fr. Cod.;* Jasmin sauvage, *Fr.;* Gelsemie, Giftjasmin, *G.;* Gelsemio, *Sp.*

The *yellow* or *Carolina Jessamine* (*Gelsemium sempervirens*) is one of the most beautiful climbing plants of our Southern States, ascending lofty trees, and forming festoons from one tree to another, and during its flowering season, in the early spring, scenting the atmosphere with its delicious odor. The stem is twining, smooth, and shining; the leaves perennial, opposite, nearly persistent, short, petiolate, lanceolate, entire, dark green above, and paler beneath; the flowers in axillary clusters, large, of a deep-yellow color, and fragrant, with a very small, five-leaved calyx, and a funnel-shaped corolla, having a spreading, five-lobed, nearly equal border. The fruit is a flat, compressed capsule, divisible into two parts, two-locular, and furnished with flat seeds, which adhere to the margins of the valves. The plant grows in rich, moist soils along the sea-coast from Virginia to the south of Florida and Texas. The flowers are said to be poisonous. *Gelsemium elegans* Benth., of upper Burma, is an extremely poisonous creeper which contains gelsemine or an allied alkaloid.

This official plant must not be confounded with the true yellow jasmine of Madeira, often planted in the Southern States, which is the *Jasminum odoratissimum* L., which also has very fragrant yellow flowers.

Properties.—It is officially described as: "Rhizome cylindrical, usually in pieces from 3 to 20 cm. in length and from 3 to 30 mm. in diameter; externally light yellowish-brown, longitudinally wrinkled, with purplish-brown longitudinal lines and transverse fissures; the upper surface with a few stem-scars, the under and side portions with numerous roots and root-scars; fracture tough, splintery; internally light brown or pale yellow, bark thin, wood distinctly radiate, excentral, pith disintegrated; odor slight; taste bitter. Roots light brown; fracture one-half transverse, the other oblique or splintery. Under the microscope, sections of the rhizome of Gelsemium show a strong development of cork, the walls being grayish or yellowish-brown and more or less lignified; a cortex made up chiefly of parenchyma containing starch and having in the outer portion small scattered groups of stone cells or sclerenchymatous fibers, and in the inner portion in the region of the medullary ray prisms of calcium oxalate; woody portion made up of broad wedges consisting of large tracheæ and fiber-tracheids separated by starch-bearing medullary rays, the innermost cells, or those nearer the pith, being strongly lignified, while the outermost layers, or those nearer the cortex, are non-lignified and may contain prisms of calcium oxalate; an internal phloem or sieve, the cells forming distinct, more or less rounded groups, the latter being partly surrounded by a thin-walled starch-bearing pith. The powder is dark yellow, tracheæ with bordered pores numerous, and conspicuous; spiral tracheæ few; bast-fibers and fiber-tracheids long and narrow, strongly lignified; starch grains spherical, from 0.004 to 0.008 mm. in diameter; calcium oxalate in monoclinic prisms from 0.015 to 0.03 mm. in length; occasional groups of stone cells or sclerenchymatous fibers, the walls being very thick, porous, and strongly lignified." *U. S.*

"In nearly cylindrical pieces about fifteen centimetres or more long, and usually from six to eighteen millimetres thick; occasionally with fibrous rootlets attached. Fracture splintery. In transverse section, a thin cortex, and a porous, yellowish, distinctly radiate wood with numerous, conspicuous, straight medullary rays. Rhizome usually with a brown or dark brownish-violet cork, often much fissured; nearly straight, and exhibiting silky fibres in the bast. Root yellowish-brown, finely wrinkled, and somewhat tortuous. Slightly aromatic odor; taste bitter." *Br.*

A microscopic character, said by Rothrock to be diagnostic, is the more or less complete division of the pith into four parts by plates of large thin-walled cells. (*A. J. P.*, 1884.) For elaborate study of structure of gelsemium, see *A. J. P.*, 1898, 398; *A. J. P.*, 1899, 422; *D. C.*, 1901, 244. Holm has contributed an article on the morphology of the overground portion of *Gelsemium sempervirens*. (*Merck's Rep.*, 1908, p. 86.) Tunmann (*Ph. Zentralh.*, 1907, p. 679) has made a pharmacognostic study of gelsemium and has proposed its identification through the microsublimation of æsculin. (See *Ap. Ztg.*, xxvi, p. 812.) Tutin (*P. J.*, Feb. 10, 1912) has shown that the sublimate ob-

tained by Tunmann from gelsemium root must have consisted of scopoletin. Tutin further states that "The detection of scopoletin in gelsemium may prove to be a valuable means of distinguishing this drug from others of a similar appearance, such as that derived from *Gelsemium elegans* Benth., but it is doubtful whether the sublimation method is the most convenient one. If 0.5 gramme of ground gelsemium be heated in a test tube with chloroform, the mixture filtered, and the filtrate shaken with water to which a few drops of dilute ammonia have been added, the aqueous layer, on separation, will be found to show a distinct, blue fluorescence, thus indicating the presence of scopoletin."

Sayre (*A. J. P.*, 1897, 8) found specimens of the root mixed with considerable proportions of the stem. Ingham (*A. J. P.*, 1897, 234) found that there was not much difference between the root and rhizome in alkaloidal value, but the stem does not appear to contain either gelsemine or gelsemic acid. (See also *A. J. P.*, 1897, 140.) Gelsemium yields its virtues to water, and readily to diluted alcohol. Analyzed by Henry Kollock, it was found to contain gum, starch, pectic acid, albumen, gallic acid, fixed oil, a fatty resin, a dry acrid resin, yellow coloring matter, volatile oil, extractive, lignin, a peculiar alkaloid called *gelsemine*, potassium, calcium, and magnesium salts, iron, and silica. The alkaloid, however, was not obtained sufficiently pure to admit of a full investigation of its properties. (*A. J. P.*, xxvii.) After Kollock's experiments, the alkaloid was obtained in a crystalline form, but still impure, by Maisch, from a tincture of the root, by a process of which a very brief abstract is given in *A. J. P.*, 1869, by C. L. Eberle, who in the same paper publishes the results of his own investigation. Eberle not only extracted gelsemine, but also satisfactorily established its alkaline properties, and proved that it was not contained in the wood of the root. Soon afterwards, the chemistry of yellow jasmine was more thoroughly investigated by Theo. G. Wormley. (*A. J. P.*, 1870.) He obtained pure gelsemine from the root and a peculiar acid, which he called *gelseminic* (gelsemic) *acid.*

Wormley obtained the acid by acidulating a concentrated aqueous solution of the drug and extracting with ether. (For details of his method, see *U. S. D.*, 19th ed., p. 578.) The acid, when pure, is colorless, inodorous, almost tasteless, and readily crystallizable, usually in groups or tufts of fine needles. The action of concentrated nitric acid upon gelsemic acid or any of its salts, produces a yellow, reddish, or red solution, which, if treated with ammonia in excess, becomes of a deep blood-red color, lasting for hours. The one-thousandth of a grain will exhibit these changes. Potassium, sodium, or ammonium hydroxide, added to the acid, cause it to become intensely yellow, and form with it highly fluorescent solutions. The acid is fusible, and, at a high heat, volatilizable without change. Robbins (*Deut. Chem. Ges.*, 1876, 1182), stated that it was identical with *æsculin* (the glucoside of the horse-chestnut), and gave it the formula $C_{15}H_{16}O_9 + 1\frac{1}{2}H_2O$.

But Coblentz (*Proc. A. Ph. A.*, 1897, 225) showed that it differs from æsculin in several particulars, and gave for its formula $C_{13}H_{11}O_5$, which melts at 206° C. (402.8° F.). E. Schmidt believes that Wormley's gelsemic acid is identical with *scopoletin* derived from scopola root, and gives the name as *β-methylæsculetin*, $C_9H_5(CH_3)O_4$.

Gelsemine was obtained by Wormley, from the concentrated extract from which gelsemic acid has been separated by ether, by rendering it slightly alkaline, then shaking out repeatedly with chloroform. It is a brittle, transparent solid, crystallizing with difficulty from alcohol. Boiling water sparingly dissolves it. It softens at 38° C. (100.4° F.), and fuses at 45° C. (113° F.). The pure base gives no color reaction with strong nitric acid, and the mixture is scarcely changed in color by heating. Strong sulphuric acid has no apparent action upon it; but if to the mixture a little manganic oxide be added and then rubbed with a glass rod, a deep crimson-red is obtained, passing to green. This reaction is so delicate, that it can be demonstrated with a solution of 1 in 100,000. If this reaction be performed upon the pure alkaloid, the color may be sufficiently intense to cause it to be mistaken for strychnine, but if a parallel experiment be carried on with strychnine, the two alkaloids cannot be mistaken, for the strychnine gives an intense purple, passing to red. Gerrard analyzed the alkaloid with care, and gives the formula $C_{12}H_{14}NO_2$ as its correct composition. F. A. Thompson (*Ph. Era*, 1887, p. 3) announced the presence of a second alkaloid, which he called *gelseminine*. After obtaining a solution of the alkaloids as sulphates he agitates it with an alkali and ether; the ethereal solution is shaken with water acidulated with hydrochloric acid, and the alkaloids are converted into hydrochlorides; gelseminine hydrochloride being easily soluble, and gelsemine hydrochloride less soluble, the latter is deposited on standing, and may be obtained pure by repeated crystallizations. He asserts that gelseminine differs greatly in physical and chemical properties from gelsemine, but, as he did not succeed in obtaining it absolutely pure, did not give the differences.

Sayre (*J. A. Ph. A.*, 1912, p. 458; 1913, p. 436; 1914, p. 314, and 1915, p. 60) has made a series of investigations of the principles of gelsemium based partly upon the work of C. W. Moore (*J. Ch. Soc.*, 1910, p. 2223), who reported gelseminine to consist of two amorphous alkaloids. Sayre found two alkaloids differing in physiological activity and color reactions, the one of which he called gelseminine (the former name for the combination of the two), and the other *gelsemoidine*, which was later changed to *sempervirine*. This latter alkaloid is similar in some of its properties to cinchonamine, par-

ticularly in the matter of the insolubility of its salts in water. Sayre also calls attention to the fact that the alkaloid commercially supplied under the name gelseminine is usually the crystalline alkaloid gelsemine. He states that the principles obtained by him show the following color reactions with sulphuric acid and manganic oxide: *Gelsemine,* at first crimson, then green, and finally yellow; *gelseminine,* at first brown, then pink, and finally yellow; *gelsemoidine,* at first purple and finally blue.

Uses.—According to the researches of Cushny (*A. E. P. P.,* 1892, xxxi, 49) gelseminine is so much more powerful than gelsemine that it is improbable that the latter alkaloid plays any part in the effect of the whole drug in mammals. Gelseminine is a depressant to the centers in the spinal cord and, in large doses, also paralyzes the peripheral motor nerves. Gelsemine acts, in the frog, much like strychnine, causing convulsions, by stimulating the spinal cord, which are followed by paralysis due to an effect on the motor nerves. In toxic quantities gelsemium lowers the blood pressure, probably by a direct action on the heart, but death is usually brought about through respiratory failure. When locally applied, or if given internally in poisonous dose, it causes dilatation of the pupil with loss of accommodation.

Formerly gelsemium was used as an arterial sedative and febrifuge in various sthenic *fevers,* but is probably useless for this purpose. Barthlow (*Pract.,* 1870, v, 200) has recommended it in spasmodic disorders, as *asthma* and *whooping cough.* It is, at present, rarely used except in the treatment of *neuralgias,* especially those involving the facial nerves. The mode of its action in these cases is obscure, but there is considerable clinical evidence of its utility.

The symptoms of gelsemium poisoning are: dizziness, dimness of vision, dilated pupil, general muscular debility, and universal prostration, reducing the frequency and force of the pulse, and the frequency of respiration. After very pronounced poisonous doses the symptoms which have just been enumerated are intensified: double or impaired vision, ptosis, dilated insensible pupils, falling of the lower jaw, loss of power of enunciation, and excessive muscular relaxation are associated with slow, labored breathing, which in some cases is interrupted by violent spells of dyspnœa; consciousness is long unimpaired, but is apt to be lost before death, and in rare cases unconsciousness has been present, even although recovery followed. Of the various symptoms of gelsemium poisoning the most characteristic are the dropping of the jaw and the ocular manifestations, combined with general muscular relaxation. The effects usually begin in half an hour, but sometimes almost immediately. According to Wormley, death has occurred at periods which vary from one to seven and a half hours. Twelve minims of the fluidextract are said to have proved fatal to a boy three years old, and thirty-five drops of a tincture of the bark have caused death in one hour and a half. In several instances a drachm of the fluidextract has, under treatment, been recovered from.

The treatment of poisoning by gelsemium should consist in evacuating the stomach, maintaining absolute rest in the horizontal position, keeping up the bodily temperature, if required, by external warmth, and administering spinal and arterial stimulants. We have very little experimental data as to the physiological antidotes to gelsemium. Our general knowledge indicates that ammonia, strychnine, and digitalis given hypodermically should be of service in the treatment of the poisoning.

Gelsemium should be administered in the form either of the tincture or of the fluidextract, the dose of the tincture being ten minims (0.6 mil), that of the fluidextract two minims (0.12 mil); to be repeated, if necessary, every 2, 4, or 6 hours, and gradually increased until the object is obtained, or some obvious effect is produced on the system.

Dose, of gelsemium, one to two grains (0.065–0.13 Gm.).

Off. Prep.—Extractum Gelsemii, *U. S.;* Fluidextractum Gelsemii, *U. S.;* Tinctura Gelsemii, *U. S., Br.;* Elixir Sodii Salicylatis Compositum (from Fluidextract), *N. F.*

GENTIANA. U. S. (Br.)

GENTIAN Gentian. [Yellow Gentian Root]

(ǧĕn-tī-ā′nạ)

"The dried rhizome and roots of *Gentiana lutea* Linné (Fam. *Gentianaceæ*)." *U. S.*
"Gentian Root is the dried rhizome and root of Gentiana lutea, *Linn.*" *Br.*

Gentianæ Radix, *Br.;* Gentian Root, Bitter Root, Fel Root; Radix Gentianæ Rubræ (vel Luteæ vel Majoris); Gentiane (Racine), *Fr. Cod.;* Racine de Gentiane (de Gentiane jaune), Gentiane jaune, *Fr.;* Radix Gentianæ, *P. G.;* Enzian, Enzianwurzel, Bitterwurzel, Rother Enzian, *G.;* Genziana, *It.;* Genciana (Raiz de), *Sp.*

Gentiana lutea or *Yellow Gentian* is among the most remarkable of the species which compose this genus, both for its beauty and great comparative size. From its thick, long, branching, perennial rhizome, an erect, round stem rises to the height of three or four feet, bearing opposite, sessile, ovate, acute, five-nerved leaves of a bright-green color, and somewhat glaucous. The lower leaves, which spring from the root, are narrowed at their base into the form of a petiole. The flowers are large and beautiful, of a yellow color, peduncled, and placed in whorls at the axils of the upper leaves. The calyx is monophyllous, membranous, yellowish, and semi-transparent, splitting when the flower opens, and reflected when it is fully expanded; the corolla is rotate, and deeply divided into five or six lanceolate, acute segments; the stamens are five or six, and shorter than the corolla. The plant grows among the Apennines, the Alps, the Pyrenees, and in other mountainous or elevated regions of Europe. It is stated by Bourquelot and Hérissey that in order to develop the deep colored fracture preferred by many druggists the root is frequently submitted to fermentation by heaping it up into a mass which becomes

heated. Gentian root which has thus been treated is said to yield 27 per cent. less extractive than does that which has been properly dried. Further, even in the best commercial dried root the *sucrose, gentianose* and *gentiopicrin* of the fresh root are present only in extremely small amounts. (*J. P. C.*, 6, 16, 513.)

Several other species possess analogous virtues, and are used for similar purposes. The roots of *G. purpurea* L. and *G. punctata* L., inhabiting the same regions as *G. lutea*, and of *G. pannonica* Scopoli, growing in Austria, are said to be often mingled with the official, from which they are scarcely distinguishable. In fact the German Pharmacopœia permits the use of the rhizome and roots of these three species. The *G. macrophylla* of Pallas is used in Siberia.

G. quinquefolia L. (*G. quinqueflora* Lam.), growing throughout the Northern and Northwestern States, is said to be much used in domestic practice. In Europe the rhizome of the *G. asclepiadea* L. is often admixed with the official rhizome. According to Vogl, they can be detected by the abundance of lignified prosenchymatous elements and stone cells, the genuine powder containing scarcely any lignified elements other than large reticulated vessels. (*O. Z.*, 1903, 141.)

One indigenous species *G. Catesbæi* (now *G. Elliottii* Chapm.), growing in the Southern States, formerly had a place in the secondary catalogue of the U. S. Pharmacopœia, and is reputed to be but little inferior to the official species.

This plant, popularly called *blue gentian*, has a perennial, branching, somewhat fleshy root, and a simple, erect, rough stem, rising eight or ten inches in height, and bearing opposite leaves, which are ovate-lanceolate, acute, and rough on their margin. The flowers are of a palish-blue color, crowded, nearly sessile, and axillary or terminal. The divisions of the calyx are linear-lanceolate, and longer than the tube. The corolla is large, ventricose, plaited, and divided at its border into ten segments, of which the five outer are more or less acute, the five inner bifid and fringed. The number of stamens is five, and the stigmas are bifid. The capsule is oblong, acuminate, with two valves, and a single cell. *G. Elliottii* Chapm. grows in the grassy swamps from Virginia to Florida, where it flowers from September to December. It may be given in powder in the dose of from fifteen to thirty grains, or in the form of extract, infusion, wine or tincture.

Powdered gentian is not infrequently adulterated with ground olive stones, ground peanut shells, and even quassia root. These are all readily detected by means of their lignified tissues, which may be seen through the use of the microscope. Gadd and Gadd assert (*P. J.*, 1905, xxi, p. 439) that adulterations of Gentian are most readily detected by means of the microscope, but that good evidence of quality is also furnished by the yield of extract, which should be about 40 per cent.

Properties.—As found in commerce, gentian is in pieces of various dimensions and shapes, usually of considerable length, consisting sometimes of longitudinal slices, sometimes of the rhizome and root cut transversely. They are twisted, wrinkled externally, sometimes marked with close transverse rings of a grayish-brown color on the outside, yellowish or reddish within, and of a soft, spongy texture. It is officially described as occurring "in nearly cylindrical, sometimes branching pieces, of variable length, from 5 to 35 mm. in thickness; externally yellowish-brown, the rhizome portion annulate, the roots longitudinally wrinkled; fracture short and uneven when dry, but tough and flexible when damp; internally yellowish-brown, the bark from 0.5 to 2 mm. in thickness, separated from the somewhat spongy, woody portion by a dark brown cambium zone; odor strong, characteristic; taste slightly sweetish, then strongly and persistently bitter. The powder is light brown or yellowish-brown, consisting chiefly of parenchymatous cells with fragments of scalariform or reticulate tracheæ; starch grains few or none. Stone cells and sclerenchymatous fibers are absent. Gentian yields not more than 6 per cent. of ash." *U. S.*

"Parenchymatous tissue of rhizome and root abundant, containing small oil globules and minute crystals of calcium oxalate but not more than an occasional starch grain; vessels reticulated; no sclerenchymatous cells or fibres. Characteristic odor; taste at first slightly sweet but afterwards bitter. When 5 grammes of the powdered Root are macerated with 100 millilitres of *water* for twenty-four hours, shaken occasionally and filtered, 10 millilitres of the filtrate yield on evaporation in a flat-bottomed dish not less than 0.165 gramme of residue dried at 100° C. (212° F.). Ash not more than 6 per cent." *Br.*

Kromayer, in 1862, first obtained the bitter principle of gentian in a state of purity, and gave it the name of *gentiopicrin*, and the formula $C_{20}H_{30}O_{12}$. This principle has been found in many other species of the genus *Gentiana* and seems to be a characteristic principle of the genus. It is a glucoside, crystallizing in colorless needles, which readily dissolve in water. It is soluble in 95 per cent. alcohol, but in absolute alcohol only when aided by heat; it does not dissolve in ether. A solution of sodium hydroxide forms with it a yellow solution. Under the influence of diluted acids, gentiopicrin is resolved into glucose and an amorphous yellowish-brown neutral substance named *gentiogenin*. Fresh gentian roots yield about one-tenth per cent. of gentiopicrin. Another constituent is *gentianin* or *gentisin*, $C_{14}H_{10}O_5$. It forms tasteless, yellowish prisms, subliming with partial decomposition at a temperature over 300° C. (572° F.) sparingly soluble in alcohol, and with alkalies yields intensely yellow, crystallizable compounds, easily decomposed by carbon dioxide. Von Kostanecki (*A. J. P.*, 1891, p. 192), by boiling gentisin with hydriodic acid, succeeded in demethylating

it, and so obtained *gentisein*, $C_{13}H_8O_5$, which crystallizes with $2H_2O$ in fine straw-colored needles; these become anhydrous at 100° C. (212° F.). A triacetyl derivative was then formed from this gentisein. Gentisin is therefore the methyl ether of gentisein, and can be written $C_{13}H_5O_2\begin{cases}OCH_3\\OH\\OH\end{cases}$. Hlasiwetz and Habermann showed, in 1875, that when *gentianin* was melted with potassium hydroxide it yielded phloroglucin, $C_6H_3(OH)_3$, and dioxybenzoic acid, $C_6H_3.(OH)_2COOH$. The latter was at first called *gentianic* or *gentisinic acid*. Maisch believed that tannin is absent from gentian root, and states that the dark olive-green coloration observed when ferric chloride is added to its preparations is due to gentisic acid. (*A. J. P.*, 1876.) Ville (*A. J. P.*, 1877) and Davies (*P. J.*, 1879) maintain that there is a small quantity of tannin in gentian root. Patch (*A. J. P.*, 1876) found that an alcoholic solution of an ethereal extract of gentian yielded a dark-green coloration with ferric salts, but if the alcoholic solution were diluted with water it yielded no precipitate with gelatin. Subsequently (*Proc. A. Ph. A.*, 1881) he showed that there was a principle associated with the resinous matter in gentian (but which was not isolated in a state of purity) that produced the reactions of a tannin, viz., a greenish-black color with ferric chloride, and precipitates with tartar emetic, cinchonidine sulphate, and gelatin. Louis Magnes found in the root, when perfectly dried at 100° C. (212° F.), 15 per cent. of glucose. When gentian is macerated in cold water, it undergoes the vinous fermentation, in consequence of the presence of this saccharine principle. From the fermented infusion a spirituous liquor is obtained by distillation, which, though bitter, and having an unpleasant odor, is said to be relished by the Swiss and Tyrolese. A. Meyer (*Ph. Cb.*, May, 1882) obtained a sweet principle, which he called *gentianose*, $C_{18}H_{32}O_{31}$, by precipitation of the filtered juice with alcohol, treatment with ether, and crystallization from alcohol. It does not reduce Fehling's solution. Infusion of gentian is precipitated by tannic acid and the soluble salts of lead, but is compatible with the salts of iron. Pectin, so frequently found in fleshy roots, exists in gentian. (Bourquelot and Herissey, *Répert de Pharm.*, 1898.) The yellow coloring matter of the root was investigated by E. V. Howell, who concludes that it is quercitrin. Tanret (*P. J.*, lxxvi, p. 87) found two glucosides, *gentiamarin* and *gentiin*. He also states (*B. G. T.*, 1905, p. 730) that in fresh roots the amount of gentiopicrin is about 1.5 per cent., but that it is destroyed in the process of drying so that dried roots contain only 0.1 per cent.

Uses.—Gentian has been known from the highest antiquity and is said to have derived its name from Gentius, a king of Illyria. Many of the complex preparations handed down from the Greeks and Arabians contain it among their ingredients. The ordinary preparations of gentian are, however, almost without physiological properties except their local effects on the mucous membrane of the alimentary tract. Moorhead (*J. P. Ex. T.*, 1915, vii) has given a scientific rationale for the ancient empirical belief in the bitters, by showing that gentian markedly increased the gastric secretions in cachectic dogs. As a stimulant to gastric digestion gentian is perhaps the most popular of all bitters in the treatment of *atonic dyspepsia, anorexia,* and similar complaints. In overdose it acts as a local irritant and may occasion nausea or vomiting. The porous property of the root causes it to expand with moisture and it has been employed as a substitute for the sponge tent to enlarge strictured passages. According to Tanret (*B. G. T.*, 1905, p. 730) gentiopicrin is highly poisonous to the plasmodium and in doses of twenty to thirty grains (1.3–2.0 Gm.) is a useful remedy in *malarial fevers;* it might be pointed out in this connection that it would require between four and five pounds of dried gentian root to produce one dose of gentiopicrin.

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Extractum Gentianæ, *U. S., Br.;* Fluidextractum Gentianæ, *U. S.;* Infusum Gentianæ Compositum, *Br.;* Tinctura Gentianæ Composita, *U. S., Br.;* Elixir Gentianæ (from Fluidextract), *N. F.;* Elixir Gentianæ et Ferri (from Fluidextract), *N. F.;* Elixir Gentianæ et Ferri Phosphatis (from Fluidextract), *N. F.;* Elixir Gentianæ Glycerinatum (from Fluidextract), *N. F.;* Infusum Gentianæ Compositum, *N. F.;* Pilulæ Antiperiodicæ (from Extract), *N. F.;* Pilulæ Ferri, Quininæ, Aloes et Nucis Vomicæ (from Extract), *N. F.;* Pilulæ Antiperiodicæ sine Aloe (from Extract), *N. F.;* Tinctura Amara, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.;* Tinctura Rhei et Gentianæ, *N. F.;* Tinctura Zedoariæ Amara, *N. F;* Vinum Aurantii Compositum, *N. F.*

GLUCOSUM. U. S., Br.

GLUCOSE Glucos. [Syrupy Glucose, Liquid Glucose]
(glū-cō′sŭm)

"A syrupy product obtained by the incomplete hydrolysis of starch, consisting chiefly of dextrose (d-glucose) [$C_6H_{12}O_6 = 180.10$] and dextrins." *U. S.* "Glucose is a mixture of dextrose and other analogous substances, and is obtained by the hydrolysis of starch." *Br.*

Saccharum amylaceum; Saccharum uveum; Grape-sugar; Starch-sugar; Dextrose, *E.;* Stärkezucker; Traubenzucker; Kartoffelzucker, Glukose, Glykose, *G.*

Glucose was introduced into the U. S. P. IX and British Pharm., 1914, for the first time.

Glucose and syrupy glucose are commercial designations of the liquid or semi-solid product of the hydrolysis of starch by diluted acids in the presence of moisture and heat. Formerly the conversion was accomplished by the use of sulphuric acid, the excess of which was subsequently removed by neutralization with milk of lime and crystallizing out the difficultly soluble calcium sul-

phate, enough of which remained in solution, however, to render the detection of glucose in honey or cane sugar syrup indirectly possible by testing for calcium sulphate. (For details, see *U. S. D.*, 19th ed., p. 1071.) The conversion at the present time is accomplished by the use of hydrochloric acid which is ultimately volatilized by raising the temperature in open vessels, so that modern glucose contains no calcium sulphate and the older tests for its detection therefore are not applicable. The straw or amber color of the crude product was formerly removed by bleaching with sulphur dioxide, which sometimes was allowed to remain in the finished product in appreciable amounts. As many state food laws specifically prohibit sulphur dioxide or sulphites in most food products in which glucose was largely used as an ingredient, the modern method of decolorizing it is analogous to that for cane sugar and consists in the use of animal charcoal filters. The composition of commercial glucose varies. Theoretically the reaction is as follows:

$$\underset{\text{Starch}}{C_6H_{10}O_5} + H_2O = \underset{\text{Dextrose}}{C_6H_{12}O_6}.$$

In practice, however, the reaction is much more complex when a syrupy liquid is desired as is the case in commercial glucose and besides the dextrose which is the predominating constituent, maltose, and dextrin, which is the constituent that prevents glucose from crystallizing. Another carbohydrate, which is unfermentable, named *gallisin*, $C_{12}H_{24}O_{10}$, is also present in varying amounts.

Syrupy glucose is also known commercially as *corn syrup*, although a better name would be *starch syrup*, as it is only in the United States where corn is the cheapest raw material that it is made exclusively from corn starch. In Germany it is made from potato starch and it certainly would not be proper to term such a product "corn syrup."

On account of the preponderance of dextrose which is a powerful reducing sugar and directly capable of alcoholic fermentation glucose is much used in the industries where these properties are desirable as in brewing and in reducing indigo to its leuco derivative, indigo-white, in the dye vat. It is extensively used as an adulterant in dyewood extracts, sole leather, etc. It is a frequent ingredient in the manufacture of confectionary, jellies, etc. Formerly some discredit attached to its use in food products under the mistaken popular belief that its manufacture was in some way connected with that of glue. The question of its healthfulness is no longer in doubt for when properly made and free from impurities it may be considered as predigested starch.

It is theoretically possible, but not practicable at present, to make glucose not only from starch but also from any carbohydrate having the same formula, as cellulose (saw-dust).

The product of the complete hydrolysis or conversion of the starch by acids is commercially produced as a white or nearly white crystalline or waxy solid known as "*grape sugar*" or "*bread sugar*," the former name being applied because dextrose is also found in grapes and the latter name because it is used in bread baking on the large scale as a yeast food. It is also sometimes known as "*corn sugar*."

Glucose is not so sweet as cane sugar and is more slowly soluble in cold water.

Pure dextrose, $C_6H_{12}O_6$, which is sometimes improperly called glucose in chemical literature, may be obtained from commercial grape sugar by recrystallization and is in use as an ingredient in culture media in bacteriological work. It usually occurs in a hydrated form, $C_6H_{12}O_6 + H_2O$, and is in colorless crystals of a less sweet taste than sucrose, soluble in from 1 to 2 parts of cold water. It melts at 146° C. (294.8° F.), and at higher temperatures decomposes with the production of caramel. It is very strongly dextrorotatory from which fact it takes the name of dextrose. Nitric acid oxidizes it and forms a number of decomposition products of which *saccharic acid*, $H_2C_6H_8O_8$, is the most important. Saccharic acid is an amorphous, deliquescent solid easily soluble in water and forming salts with metallic bases.

Dextrose has strong reducing properties and is estimated quantitatively by means of Fehling's solution.

Glucose is officially described as follows: "A colorless or slightly colored, thick, syrupy liquid. It is odorless or nearly so and has a sweet taste. It is very soluble in water, sparingly soluble in alcohol. An aqueous solution of Glucose is neutral or slightly acid to litmus. Add a few drops of an aqueous solution of Glucose (1 in 20) to 5 mils of hot alkaline cupric tartrate T.S.; a copious red precipitate of cuprous oxide is produced (*distinction from cane sugar*). Introduce about 0.5 Gm. of Glucose into a wide-mouthed, tared weighing-bottle, weigh accurately, add 2 mils of distilled water, evaporate the water at about 70° C. (158° F.), and dry the residue to constant weight at 90° C. (194° F.). The loss in weight of the Glucose does not exceed 21 per cent. (*water*). Incinerate Glucose at a temperature not exceeding a low red heat; not more than 1 per cent. of ash remains. A solution of 5 Gm. of Glucose in 15 mils of distilled water, mixed with 5 drops of phenolphthalein T.S., requires not more than 0.6 mil of tenth-normal potassium hydroxide V.S. to produce a pink color (*free acid*). Dissolve about 2 Gm. of Glucose in 50 mils of distilled water, boil the solution for one minute and cool; the addition of one drop of tenth-normal iodine V.S. to this solution produces no blue color (*starch*). On now adding a few drops of starch T.S. to the solution a blue color is produced (*limit of sulphur dioxide*). An aqueous solution of Glucose does not respond to the Test for heavy metals (see Part III, Test No. 3). If the solution of Glucose is not colorless, comparison must be made with 10 mils of the same solution, to which a volume of distilled water, equal to that of the hydrogen sulphide T.S., has been added. Dissolve 1.5 Gm. of Glucose in 5 mils of distilled water; add 5

mils of diluted sulphuric acid and 1 mil of bromine water and heat for five minutes on a water bath. Then add 0.5 Gm. of potassium iodide, follow it with 5 drops of stannous chloride T.S., cool and subject the solution to the Test for arsenic (see Part III, Test No. 1). The stain produced, if any, is not greater than that produced in a test made with the same quantities of the reagents to which 2 mils of the standard arsenic test solution (see Part III, Test No. 1) has been added." *U. S.*

"A very viscous syrup, almost colorless. No odor; taste sweetish. Freely soluble in *water,* the solution being dextrorotatory and yielding a red precipitate when warmed with *solution of potassio-cupric tartrate.* 2 grammes dried at 100° C. (212° F.) in a thin film in a flat-bottomed dish do not lose more than 0.4 gramme (limit of moisture). When 10 grammes are dissolved in 100 millilitres of *water,* to which 10 millilitres of *N/10 solution of iodine* have previously been added, on shaking the mixture and immediately titrating with *N/10 solution of sodium thiosulphate,* not less than 6.8 millilitres of the latter solution are required for decolorisation (limit of sulphites). *Arsenic limit* 2 parts per million. Ash not more than 0.5 per cent." *Br.*

Uses.—As pointed out in the article on *saccharum* it is generally believed that the sugars must be converted into glucose before they are utilized by the body cells. At any rate it seems to be well established that glucose may be directly oxidized in the body and furnish energy to the various tissues. Thus Dixon (*J. P.,* 1907, xxxv, p. 346) has found that the injection of glucose into the blood stream may cause an immediate increase in the force of the cardiac contractions presumably by furnishing an easily oxidizable food stuff. In cases of severe malnutrition glucose may be used either hypodermically or intravenously to furnish an immediate fuel material to the body. For this purpose it is employed in the strengths of from one to five per cent. dissolved in physiological salt solution; one quart (1 liter) of the solution may be injected either directly into the vein or into the subcutaneous tissues. In cases of *gastric ulcer* or other conditions in which it is undesirable to administer food by the stomach, rectal enemata of six to eight fluidounces (180–240 mils) of a ten per cent. solution of glucose, every four hours, is often of assistance in aiding the maintenance of the nutritive condition. In *acidosis,* especially that type seen after prolonged *anesthesia,* the administration of large amounts of carbohydrates usually exercise a most beneficial action. The administration of glucose immediately before the production of anesthesia has been highly recommended as a preventative for vomiting, especially in children. (See *B. M. J.,* 1911, ii, p. 505.)

Locally glucose has been used for its dehydrating effect, especially in the treatment of gun-shot wounds. For this purpose gauze may be saturated with solutions of glucose, either with or without the addition of some antiseptic, and placed over the wounds. It is claimed that this treatment encourages the flow of lymph and thereby tends to diminish the severity of infection. (See *L. L.,* 1915, i, p. 851.) Pharmaceutically glucose is used in solid extracts and other preparations where a uniform, moist consistence is desired and as a diluent.

Off. Prep.—Used in making extracts U. S. P. and N. R., and in Br. Pharm. for pill masses. Ferri Carbonas Saccharatus, *Br.;* Ferri Phosphas Saccharatus, *Br.;* Mistura Ferri Composita, *Br.;* Syrupus Ferri Iodidi, *Br.;* Syrupus Glucosi, *Br.*

GLYCERINUM. U. S., Br.

GLYCERIN Glycerin. [Glycerol]

(glĭç-ĕ-rĭn'nŭm)

"A liquid obtained by the hydrolysis of vegetable or animal fats, or fixed oils, purified by distillation, and containing not less than 95 per cent. of the trihydric alcohol $C_3H_5(OH)_3$ or $CH_2OH.CHOH.CH_2OH$ (92.06). Preserve it in well-closed containers." *U. S.* "Glycerin, or glycerol, is a trihydric alcohol, $C_3H_5(OH)_3$, associated with a small percentage of water; it is obtained by the hydrolysis of fats and fixed oils by means of alkalies or of superheated steam." *Br.*

Glycerina, *U. S.* 1870; Glycerine; Glycerine officinale, *Fr. Cod.;* Glycerinum, *P. G.;* Glycerin, Glyceryloxyhydrat, Oelsüss, Scheelesches Süss, *G.;* Glicerina, *It., Sp.*

Litharge, olive oil, and water are boiled together in the 1890 process for making lead plaster; the olein of the oil is decomposed by the lead oxide, according to the following reaction:

$$2(C_3H_5(OC_{18}H_{33}O)_3) + 3PbO + 3H_2O = 2(C_3H_5(OH)_3) + 3(Pb(OC_{18}H_{33}O)_2)$$

by which lead oleate or plaster and free glycerin are obtained. (See *Emplastrum Plumbi.*) It follows, therefore, that the plaster, while still hot and in the liquid state, contained glycerin diffused through it. It was this process that was used for preparing glycerin in the formula of U. S. P., 1850. In accordance with this, when the liquid plaster is mixed with an equal measure of boiling water, and the mixture stirred briskly, a solution of glycerin is obtained, which, after having been decanted, and evaporated to a limited extent, is freed from lead by hydrogen sulphide. The liquid is then filtered to separate lead sulphide, heated to free it from hydrogen sulphide, and finally evaporated to expel the water, which is known to be all removed when the mass ceases to lose weight.

Glycerin was discovered in 1789 by Scheele, by whom it was called the *sweet principle of oils.* It is produced not only during the saponification of the fats and oils by lead oxide in forming lead plaster, but also during the same process when effected by potassium and sodium hydroxides in the manufacture of soap, the alkalies uniting with the fatty acids and setting the glycerin free. Soap-maker's waste is an abundant source of glycerin; but when thus obtained it is apt to have more or less odor, which even

percolation through animal charcoal does not always remove. The recovery of glycerin from spent soap lyes is effected very generally by the Van Ruymbeke process. The lye is settled and drawn off from the sludge, treated with a "persulphate of iron" containing about 50 per cent. of sulphuric acid, which forms a copious precipitate of ferric hydroxide and iron soaps and carries down all other insoluble impurities. After filtration, the lye, which is nearly water-white, is evaporated in vacuo. Some sodium sulphate and sodium chloride crystallize out, after which the glycerin is concentrated and distilled under a high vacuum. The two methods of saponification by which glycerin has been obtained on a large scale are the process of Wilson and Payne, of decomposing the fats by superheated steam and subsequent distillation, and the lime autoclave process of Milly. The process of Richard A. Tilghman, of Philadelphia (the patent for which was obtained in 1854, and, after years of litigation, was at last sustained in 1888), consists in subjecting fatty bodies to the action of water at a high temperature under pressure, whereby the fats, which are *glycerides* or *esters* of the fatty acids, are broken up into free glycerin and free fatty acids, the water supplying the elements of hydrogen and oxygen necessary for that change. The reaction is as follows for the case of a fat like stearin:

$$C_3H_5(OC_{18}H_{35}O)_3 + 3H.OH = C_3H_5(OH)_3 + 3C_{18}H_{35}O.OH$$

More recent processes are the hydrolysis of fats in the presence of the Twitchell reagents (a sulphonated fatty acid), and the Connstein ferment process. The former especially is now in general use in all modern soap factories. Ordinary impure glycerin may be purified by distillation with steam under pressure. Though, when distilled alone, it is partially decomposed, giving off pungent vapors of *acrolein*, yet in a current of superheated steam it passes over unchanged at temperatures between 204.4° and 260° C. (400° and 500° F.). A better grade of glycerin made by distillation is known as *dynamite glycerin*. A still purer product is made by maintaining it at 0° C. (32° F.) for some time and then inducing crystallization by introducing a few crystals previously prepared by cooling to a much lower temperature. It crystallizes in large massive crystals of a high degree of purity. Glycerin is now being made by synthetic processes. A recent English patent starts with propylene which is first converted into dichlor-propane, which subsequently is converted into allyl chloride and then into trichlor-propane, $CH_2Cl.CHCl.CH_2Cl$, which when heated with water to 150° C. (302° F.) splits up into glycerin and water according to the following reaction:

$$\underset{\text{Trichlor propane}}{CH_2Cl.CHCl.CH_2Cl} + 3H_2O = \underset{\text{Glycerin}}{CH_2OH.CHOH.CH_2OH} + 3HCl.$$

Glycerin is always produced to a limited extent during alcoholic fermentation, the amount of glycerin present in certain liquids produced originally by alcoholic fermentation as wine, vinegar, etc., being so constant as to constitute a valuable aid in proving identification or freedom from adulteration. Various attempts have been made to economically recover the glycerin from the waste liquors of distilleries but without practical results as yet, although there is little doubt of its ultimate accomplishment. In 1909 the United States production of glycerin was given as 81,885,536 pounds, and the present production is estimated to be 100,000,000 pounds.

Properties.—"Glycerin is a clear, colorless liquid, of a thick, syrupy consistence, having not more than a slight, characteristic odor which is neither harsh nor disagreeable, sweet to the taste and producing a sensation of warmth in the mouth; when exposed to the air, it absorbs moisture. Glycerin is miscible with water or alcohol; insoluble in chloroform, ether, benzene, petroleum benzin, carbon disulphide or fixed or volatile oils. An aqueous solution of Glycerin (1 in 20) is neutral to litmus. Specific gravity: not below 1.249 at 25° C. (77° F.). Glycerin does not appreciably volatilize from weak aqueous solutions. When of a strength between 70 and 100 per cent., it rapidly volatilizes at 100° C. (212° F.). Heat a few drops of Glycerin with about 0.5 Gm. of potassium bisulphate; pungent vapors of acrolein are evolved. Glycerin is colorless when viewed transversely in a tube of colorless glass about 30 mm. in diameter, held in a vertical position. Heat 50 Gm. of Glycerin in an open, shallow, 100 mil porcelain or platinum dish until it ignites, then allow it to burn without further application of heat in a place free from draught; not more than 0.015 per cent. of carbonaceous and mineral residue remains. Subject this residue to a low red heat, until combustion is complete; not more than 0.007 per cent. of mineral ash remains. This ash, when dissolved in 10 mils of distilled water and titrated with hundredth-normal silver nitrate V.S., using potassium chromate T.S. as indicator, shows, in the original 50 Gm. of Glycerin, not more than 0.001 per cent. of chlorides calculated as sodium chloride. Each mil of hundredth-normal silver nitrate V.S. consumed corresponds to 0.0005846 Gm. of NaCl. Mix 5 mils of Glycerin by vigorous shaking with an equal volume of sulphuric acid in a glass-stoppered cylinder; the liquid does not become darker than yellow on standing for one hour (*readily carbonizable impurities*). Mix 50 Gm. of Glycerin with 50 mils of freshly boiled distilled water and 5 mils of half-normal potassium hydroxide V.S., and boil the mixture for five minutes. When cold, it requires not less than 4 mils of half-normal hydrochloric acid V.S. for neutralization, using phenolphthalein T.S. as indicator (*fatty acids and esters*). An aqueous solution of Glycerin (1 in 10) remains clear on the addition of calcium chloride T.S. (*oxalic acid*); another portion of

the solution is not affected by barium chloride T.S. after acidulation with a few drops of diluted hydrochloric acid (*sulphate*). An aqueous solution of Glycerin does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of Glycerin meets the requirements of the Test for arsenic (see Part III, Test No. 1). A mixture of 5 mils of Glycerin and 5 mils of an aqueous solution of potassium hydroxide (1 in 10) does not become yellow when kept for five minutes at 60° C. (140° F.) (*acrolein, glucose*), nor emit an odor of ammonia (*ammonium compounds*)." *U. S.*

"A clear, colorless, hygroscopic, syrupy liquid. No odor; taste sweet, followed by a sensation of warmth. Miscible with *water,* and with *alcohol* (90 per cent.). Insoluble in *ether,* in *chloroform,* and in fixed oils. Specific gravity 1.260. When strongly heated decomposes with evolution of irritating vapors. Neutral to *litmus.* An aqueous solution (1 in 10) yields no characteristic *reactions* for ammonium, chlorides, or sulphates. Assumes, when heated, not more than a faint yellow but no pink coloration, and yields not more than a very slight charred residue and no odor of burnt sugar (absence of sugar). Undergoes no darkening in color when mixed with an equal volume of *solution of ammonia* and a few drops of *solution of silver nitrate,* the mixture being kept protected from light and the observation being made after a lapse of five minutes (absence of formic acid, acrolein). Gently warmed with an equal volume of *diluted sulphuric acid,* the mixture being vigorously shaken, not more than a faint odor is noticeable (absence of fatty acids). Shaken with an equal volume of *sulphuric acid,* the mixture being kept cool, not more than a very slight straw coloration is produced (absence of extraneous organic matter). A mixture of 10 millilitres of Glycerin with 40 millilitres of *water,* 1 drop of *solution of ammonia,* and 1 drop of *solution of tannic acid,* assumes not more than a faint and transient pink or purple coloration (limit of iron). When tested for lead according to the quantitative test described in Appendix V, but using 10 grammes in each Nessler glass, no difference is observed upon the addition of the *solution of sodium sulphide* to one of the solutions (absence of lead). When the foregoing test is repeated, but omitting the addition of *solution of ammonia* and of *solution of potassium cyanide,* and adding to each solution 1 millilitre of *diluted hydrochloric acid,* no difference in color is observed upon the addition of *solution of hydrogen sulphide* to one of the solutions (absence of copper). *Arsenic limit* 4 parts per million. No appreciable ash." *Br.*

When exposed to the air glycerin gradually absorbs moisture. As already stated, though decomposed by a high heat in its unmixed state, yet with water under pressure it is volatilizable unchanged at a temperature between 204.4° and 260° C. (400° and 500° F.). Cooled down rapidly, it only becomes more viscid, without congealing, even when a temperature of –40° C. (–40° F.) is attained; but, if kept for some time at a temperature of about 0° C. (32° F.), it gradually forms hard but deliquescent crystals, which melt only at about 22° C. (71.6° F.). This fact is now utilized as a means of concentrating and purifying glycerin. According to G. F. Wilson, glycerin, when of the density 1.24, contains 94 per cent. of anhydrous glycerin; when of the density 1.26, 98 per cent. A table by Wilhelm Lenz (*Zeit. An. Chem.,* 1880), showing the percentage of absolute glycerin in mixtures of glycerin and water, which was obtained by a quantitative determination of the carbon in the various dilutions by ultimate analysis, will be found in the U. S. D., 15th ed., p. 712. The table below by W. W. J. Nicol of England, has been constructed after careful determinations, aided by A. B. Lyons's data on expansion of glycerin solutions. (*Ph. Era.,* 1888.)

Glycerin has been formed artificially from

Per cent. Glycerin.	Sp. Gr. at 15° C. = 59° F.	Per cent. Glycerin.	Sp. Gr. at 15° C. = 59° F.	Per cent. Glycerin.	Sp. Gr. at 15° C. = 59° F.	Per cent. Glycerin.	Sp. Gr. at 15° C. = 59° F.
1	1.00236	26	1.06500	51	1.13265	76	1.20131
2	1.00473	27	1.06765	52	1.13539	77	1.20404
3	1.00711	28	1.07031	53	1.13814	78	1.20677
4	1.00949	29	1.07297	54	1.14088	79	1.20949
5	1.01189	30	1.07564	55	1.14362	80	1.21221
6	1.01430	31	1.07832	56	1.14637	81	1.21493
7	1.01673	32	1.08100	57	1.14912	82	1.21766
8	1.01917	33	1.08370	58	1.15187	83	1.22038
9	1.02163	34	1.08639	59	1.15462	84	1.22310
10	1.02409	35	1.08908	60	1.15737	85	1.22583
11	1.02656	36	1.09176	61	1.16011	86	1.22855
12	1.02904	37	1.09445	62	1.16286	87	1.23128
13	1.03153	38	1.09713	63	1.16561	88	1.23400
14	1.03403	39	1.09983	64	1.16837	89	1.23673
15	1.03653	40	1.10253	65	1.17113	90	1.23945
16	1.03905	41	1.10525	66	1.17387	91	1.24217
17	1.04160	42	1.10798	67	1.17662	92	1.24487
18	1.04416	43	1.11071	68	1.17937	93	1.24756
19	1.04672	44	1.11345	69	1.18212	94	1.25021
20	1.04930	45	1.11618	70	1.18487	95	1.25285
21	1.05189	46	1.11893	71	1.18761	96	1.25547
22	1.05449	47	1.12167	72	1.19035	97	1.25809
23	1.05712	48	1.12441	73	1.19309	98	1.26072
24	1.05973	49	1.12716	74	1.19583	99	1.26335
25	1.06236	50	1.12990	75	1.19857	100	1.26596

tribromallyl, by Wurtz, and from trichlorhydrin, by Friedel and Silva.

Glycerin possesses extensive powers as a solvent, and is an excellent excipient for many medicinal substances. It dissolves bromine and iodine, sulphur iodide, potassium and sodium chlorides, the fixed alkalies, some of the alkaline earths, lime, for example, for which it increases the solvent powers of water (*J. P. C.*, June, 1874), and a large number of neutral salts. It also dissolves the vegetable acids, particularly tannic acid. It is a good solvent of pepsin, and is used for the extraction of this principle from the mucus of the stomach. Two parts and a half of glycerin dissolve one of sugar, and three and a half parts, one of gum. When starch paste and glycerin are heated together, a turbid liquid is formed, which deposits on cooling, the supernatant liquid holding starch in solution. (*J. P. C.*, Nov., 1868, pp. 361–362.) J. S. Blockley of London, has ascertained that certain glucosides are far more soluble in glycerin than in water. Thus, salicin dissolves in eight parts of cold glycerin, and santonin in eighteen parts when boiling. The latter solution, when of half this strength, forms on cooling an almost solid mass. Glycerin, next to alcohol, is the best solvent of iodine. Iodine and potassium iodide, when dissolved in it, form *iodized glycerin*, the medicinal applications of which are given under iodine. (See *Iodum.*) It combines with a number of alkalies, and also with sulphuric acid. Glycerin does not evaporate rapidly when exposed to the air, although it vaporizes to such an extent as to make it necessary to avoid a water-bath temperature to the concentrated article during its quantitative estimation. It can not be distilled without decomposition, unless in the presence of water or steam. When decomposed by heat, it emits extremely irritating vapors of acrolein, which is allylaldehyde, $CH_2.CH.CHO$. At a full red heat it takes fire, and burns with a blue flame. In consequence of the high temperature required for its volatilization, it has been proposed to use it for an evaporating bath, in which a heat beyond that of boiling water is required. Glycerin is antiseptic, and has been recommended by Warington and Demarquay to preserve alimentary substances and objects of natural history, and to inject bodies for dissection. According to W. Frazer, it does not answer for preserving pathological preparations, as they are completely softened by its action. Berthelot of Paris, succeeded in combining glycerin with a number of acids, both mineral and organic, forming three distinct series of neutral compounds. Among others, he has united it with the fatty acids, producing, by synthesis, the organic fatty substances stearin, palmitin, olein, etc.

By Pasteur it was ascertained to be one of the products of the vinous fermentation. Glycerin is a triatomic alcohol, being a compound of the triad radical (C_3H_5) with 3(OH) groups. In the natural fats, the three H atoms of these OH groups are replaced by fatty acid radicals like stearyl, $C_{18}H_{35}O$, palmityl, $C_{16}H_{33}O$, and oleyl, $C_{18}H_{33}O$. The natural fats are, therefore, compounds of an alcohol radical with an organic acid, and are true esters, which are known as *glycerides*.

The solvent and preservative properties as well as agreeable taste and permanent consistence of glycerin render it very useful as a menstruum in pharmacy, and a class of preparations consisting of medicinal substances dissolved in it has come into extensive use. The British Pharm. (1885) adopted such a class, under the name of *Glycerina*, or *glycerins*. The title "glycerines" is not now available because the termination "ine" is reserved for alkaloids, while the term *glyceroles*, adopted from the French, is objectionable, as the termination "ole" has been used to designate certain proximate principles; but the U. S. Pharmacopœia title, *Glycerita*, or *glycerites*, is satisfactory. (See *Glycerita*, p. 523.) G. M. Beringer proposed a class of preparations made with glycerin. (See *Fluidglycerates*, in the National Formulary IV.)

Impurities and Tests.—Glycerin is occasionally deficient in density and consistency. According to Dalpiaz, it is sometimes perfectly colorless from being bleached by chlorine, when it is apt to contain calcium chloride, as well as free chlorine. The latter may be detected by rendering the suspected sample slightly blue by a few drops of an acid solution of indigo in sulphuric acid, when, if free chlorine be present the blue color will disappear. Starch paste containing a little potassium iodide is a better test, however; if a blue color appears when this is added to glycerin, free chlorine is indicated. (See U. S. P. and Br. tests, page 519.)

Glycerin, on account of its high price (1917), has been substituted industrially by a number of cheaper products, among which was a commercial invert sugar of about the same consistency as glycerin, but slightly higher in specific gravity. (Jos. Feil, *J. A. Ph. A.*, 1914, 1648.)

In the quantitative determination of glycerin when in a state of purity, the specific gravity test is important. In crude glycerin and in other products where it may only exist in small amounts, various processes are in use. One of the best known of these is the Hehner, Richardson, Jaffe, method, which depends upon the oxidation of potassium dichromate, or it may be determined by its acetylization with acetic anhydride, the so-called acetin method.

The official method of the A. O. A. C. given in Bulletin No. 107, of the Bureau of Chemistry of the U. S. Department of Agriculture, is used for the determination of glycerin in wines, etc. Leroy Forman (*J. A. Ph. A.*, 1914, 1644) shows this method to give low results when applied to the analysis of tablets, confections, etc. He overcomes this difficulty by the use of milk of lime during the evaporation.

For a method of extracting glycerin from mixtures containing sugar and glucose, see a paper by Prescott, *N. R.*, 1878. For methods of determining glycerin in mixtures or its detection in wines, etc., see *Chem. News*, 1882; *A. J. P.*, 1882; *S. W. P.*, 1881; *Chem. News*, 1886; *Am. Drug.*, 1886.

Uses.—Glycerin is valuable as a vehicle not only because of the solvent properties noted on page 521, but because of its sweetness, having the great advantage over syrup of non-fermentability. It has been recommended as a preservative for galenicals in which alcohol is undesirable, but its antiseptic action is so slight that its usefulness for this purpose is very questionable. When injected intravenously in large doses it is capable of causing severe and even fatal poisoning, but the amount required to produce this effect is so large as to suggest that it acts rather by altering the physical condition of the blood than by any true physiological properties. It is absorbable from the alimentary tract and although partly eliminated unchanged, a portion seems to be oxidized in the body and is apparently capable of furnishing energy to the system. (See Catillon, *A. G. P.*, 1889–1890, xlvi.) It is, however, of no practical value as a food-stuff and although it was at one time suggested as a substitute for cod liver oil in *phthisis* it has been shown to be worthless. Faust and Tallquist (*A. E. P. P.*, 1907, lvii, p. 366), on the theory that the hemolytic poison in *pernicious anemia* is oleic acid, suggested the use of glycerin as a remedy and the theory has received some clinical confirmation. As a local application glycerin is often of service. Many believe that beneficial effects of the cataplasm of kaolin are largely due to the glycerin it contains, and pure glycerin has been recommended as an application in *burns, wounds, furuncles,* and similar local inflammatory diseases. Its beneficial effects in these conditions are commonly attributed to its hygroscopic properties. In a diluted form it is often of great value for its emollient properties in various forms of *skin diseases;* pure glycerin may irritate a delicate skin.

It has recently been extensively employed in habitual *constipation* in the form of suppositories. (See *Suppositoria Glycerini.*)

To collodion it gives a valuable plasticity. Incorporated in very small proportion with extracts and pills, it keeps them soft and free from mouldiness. Glycerin may be used in the form of an ointment, and is also used in the menstruum of official extracts, fluidextracts, glycerites, infusions, syrups, tinctures, etc., and in making pills.

Dose, one fluidrachm (3.75 mils).

Off. Prep.—Gelatinum Glycerinatum, *U. S.;* Suppositoria Glycerini, *U. S., Br.;* Cataplasma Kaolini, *N. F.;* Glycerites, *U. S.* (*Br.*), Fluidextracts, *U. S., N. F.;* Tinctures, *U. S., N. F.;* and as solvent and preservative in other preparations; Glycerites, *N. F.;* Fluidglycerates, *N. F.*

GLYCERINUM ALUMINIS. Br.

GLYCERIN OF ALUM

(glĭç-ẹ-rī′nŭm ạ-lū′mĭ-nĭs)

Glycéré d'Alun, *Fr.;* Alaun-Glycerit, *G.*

"Purified Alum, 20.0 *grammes;* Distilled Water, 7.5 *millilitres;* Glycerin sufficient to produce 120.0 *millilitres.* Powder the Alum, triturate with the Distilled Water and Glycerin until solution is effected, warming slightly if necessary; set aside; pour off the clear liquid from any deposit that may be formed." *Br.*

This has an astringency similar to glycerite of tannin without the tendency to soil the linen or blacken in contact with iron, but it is much more irritating.

GLYCERINUM BORACIS. Br.

GLYCERIN OF BORAX

(glĭç-ẹ-rī′nŭm bọ-rā′cĭs)

Glycéré de Borax, *Fr.;* Borax-Glycerit, *G.*

"Purified Borax, 20 *grammes;* Glycerin, 120 *millilitres.* Powder the Borax, and triturate with the Glycerin in a warmed mortar until solution is effected." *Br.*

The demulcent properties and sweet taste of this preparation render it a useful and convenient method of applying borax to the infantile *thrush* and other forms of sore mouth in children. It has been highly commended in *erysipelas* by D. M. Salazar of Madrid. The part should be freely painted with it and then covered with raw cotton. (*N. Y. M. R.*, viii 311.)

GLYCERINUM PEPSINI. Br.

GLYCERIN OF PEPSIN

(glĭç-ẹ-rī′nŭm pĕp-sī′nī)

Glycéré de Pepsine, *Fr.;* Pepsin-Glycerit, *G.*

"Pepsin, 100.0 *grammes;* Hydrochloric Acid, 11.5 *millilitres;* Glycerin, 600.0 *millilitres;* Distilled Water, sufficient to produce 1000.0 *millilitres.* Mix the Hydrochloric Acid, Glycerin, and two hundred and sixty *millilitres* of the Distilled Water; add the Pepsin; dissolve; add sufficient Distilled Water to produce the required volume; set aside for twenty minutes; filter. Ten mils of this preparation contain 1 gramme of Pepsin; 1 fluidrachm contains about 5.5 grains." *Br.*

This preparation is practically identical with the glycerite of pepsin of the National Formulary. (See Part III.)

Dose, one fluidrachm (3.75 mils), equivalent to five grains of pepsin.

GLYCERINUM PLUMBI SUBACETATIS. Br.

GLYCERIN OF SUBACETATE OF LEAD

(glĭç-ẹ-rī′nŭm plŭm′bī sŭb-ăç-ẹ-tā′tĭs)

Glycéré de Sousacétate de Plomb, *Fr.;* Bleiessigglycerit, *G.*

"Strong Solution of Lead Subacetate, 500 *millilitres;* Glycerin, 500 *millilitres;* Distilled

Water, a sufficient quantity. Evaporate the Strong Solution of Lead Subacetate to dryness on a water-bath; add the Glycerin; warm gently until dissolved; cool; add Distilled Water till the specific gravity of the mixture is 1.48; filter, if necessary." *Br.*

This glycerite originated with Balmanno Squire of London, but the process made official in the Br. Pharm. (1898) was that recommended by R. W. Parker. (See *A. J. P.*, 1886, 296.) The official process (1914) is a simpler one and more convenient for the pharmacist. It is a powerful sedative astringent, and may be employed as a local application in external inflammation.

GLYCERINUM TRAGACANTHÆ. Br.

GLYCERIN OF TRAGACANTH

(glĭç-ĕ-rĭ'nŭm trăg-ă-căn'thæ)

Glycéré de Gomme Adragante, *Fr.;* Traganth-Glycerit, *G.*

"Tragacanth, in powder, 10 *grammes;* Glycerin, 30 *millilitres;* Distilled Water, 10 *millilitres.* Mix the Glycerin with the Tragacanth; add the Distilled Water; triturate until a homogeneous paste is produced." *Br.*

This preparation has been introduced into the British Pharmacopœia mainly to serve as an excipient for pills.

GLYCERITA

GLYCERITES

(glĭç-ĕ-rĭ'tă)

Glycerinum, *Br.;* Glycerins; Glycerata, Glycerolata, Glycerols; Glycérés, *Fr. Cod.;* Glycérats, Glycérolés, *Fr.;* Glycerit, Glycerolat, *G.*

These are solutions of medicinal substances in glycerin. In the thirteenth edition of the Dispensatory various reasons were adduced for preferring the name glycerates for these preparations, but, as the revisers of the U. S. Pharmacopœia have adopted that of glycerites, these reasons are omitted. The U. S. name is certainly much better than the British name glycerin (*Glycerinum*) for this does not distinguish a *class* of preparations from the *solvent* used in making them. (See preceding articles.)

Glycerin has valuable properties as a solvent and vehicle for medicinal substances. Such are its not unpleasant taste and bland character, its wide range of solvent power, which adapts it sometimes as a menstruum where neither water nor alcohol could be advantageously used, and enables it to retain in solution otherwise insoluble substances so frequently found in infusions and decoctions, and its preservative influence, which often protects against oxidation, and, by a destructive agency upon all of the lowest forms of vegetable and animal life, prevents the various fermentative processes so destructive to organic bodies. Another important property, as a vehicle for external remedies, is the permanence of its liquid character, so that it does not, like water and alcohol, dry up when applied to the skin, resembling in this respect, as well as in its demulcent quality, the fixed oils, without their tendency to rancidity. Hence it has of late come into extensive use in the preparation of medicinal solutions, which, under the name of *Glycérés* found admission into the French Codex of 1866, and are now recognized by both the United States and British Pharmacopœias.

GLYCERITUM ACIDI TANNICI. U. S. (Br.)

GLYCERITE OF TANNIC ACID Glycer. Acid. Tann. [Glycerite of Tannin]

(glĭç-ĕ-rĭ'tŭm ăç'ĭ-dī tăn'nĭ-cī)

Glycerinum Acidi Tannici, *Br.;* Glycerin of Tannic Acid (of Tannin); Glycéré de Tannin, *Fr. Cod.;* Glycérole de Tannin, Glycérine tannique, *Fr.;* Tannin-Glycerit, Tannin-Glycerol, *G.*

* "Tannic Acid, *twenty grammes* [or 308.6 grains]; Glycerin, *eighty grammes* [or 2 ounces av., 360 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Weigh the glycerin into a tared, wide-mouthed bottle with a capacity of about *one hundred and twenty-five mils.* Place the bottle and contents in a water bath, heat the water until it boils, and continue the heat for a few minutes; add the tannic acid to the hot glycerin in small, successive portions, agitate the mixture until the tannic acid is dissolved and strain the solution while warm through purified cotton." *U. S.*

"Tannic Acid, 20 *grammes;* Glycerin, sufficient to produce 100 *millilitres.* Triturate the Tannic Acid with the Glycerin in a warmed mortar until solution is effected." *Br.*

The U. S. preparation is a 20 per cent. solution by weight; the strength of the British preparation is somewhat weaker, being a 20 per cent. solution by measure. H. F. Meier found that the greenish scum usually seen on the surface of the preparation is chlorophyll from the tannin.

This preparation may be used, both internally and externally, for most of the purposes to which tannic acid is applied. On the whole, it is the most useful preparation of tannic acid for external use; as circumstances require it the official strength may be altered by direction of the physician; a very concentrated solution, two parts of glycerin to one of tannin, may be made by the aid of a moderate heat. This applied daily to nipples, during the later months of pregnancy, will usually prevent the occurrence of *sore nipples* during suckling.

Dose, from ten to forty minims (0.65–2.6 mil). (See *Acidum Tannicum.*)

GLYCERITUM AMYLI. U. S. (Br.)

GLYCERITE OF STARCH Glycer. Amyl.

(glĭç-ĕ-rĭ'tŭm ăm'y-lī)

Glycerinum Amyli, *Br.,* Glycerin of Starch, Glycamyl, Plasma; Glycéré d'Amidon, *Fr. Cod.;* Glycérate simple (d'Amidon), *Fr.;* Unguentum Glycerini, *P. G.;* Glycerinsalbe, Stärke-Glycerit, *G.;* Glicerolato di amido, *It.;* Glicerolado de almidon, *Sp.*

* "Starch, *ten grammes* [or 154 grains]; Water, *ten mils* [or 162 minims]; Glycerin,

eighty grammes [or 2 ounces av., 360 grains]. Triturate the starch with the water, until a homogeneous mixture is produced. Then gradually add this to the glycerin, contained in a porcelain dish, and heated to about 140° C. (284° F.). Continue the heat, with constant stirring, keeping it below 144° C. (291.2° F.), until a translucent jelly is formed. Transfer the product to suitable vessels, provided with well-fitting covers." *U. S.*

"Starch, 20 *grammes;* Glycerin, 130 *millilitres;* Distilled Water, 30 *millilitres.* Mix; heat, stirring constantly, until a translucent jelly is formed." *Br.*

Of these preparations it is only necessary to say that, with the exception of an inconsiderable difference in the proportions, they are the same as that brought into notice in 1858 by G. F. Schacht under the name of *plasma,* as a substitute for ointments, the emollient and demulcent properties of which they possess, without their inconvenience, whether used simply, or as a vehicle for other substances to be employed locally. Schacht prepared plasma by mixing 70 grains of starch in powder, and a fluidounce of glycerin, heating to 115.6° C. (240° F.) until the union is effected, and stirring constantly. The stirring should be continued moderately, during the cooling, to secure a proper consistence. As the plasma is liable to absorb moisture, it should be kept in well closed vessels. (*P. J.,* Oct., 1866, 210.) J. H. Pearson (*P. J.,* 1897, 201) recommends the addition of one grain of powdered tragacanth to the ounce of finished product, to prevent the separation of the glycerin and water from the mass, on standing.

GLYCERITUM BOROGLYCERINI. U. S. (Br.)

GLYCERITE OF BOROGLYCERIN Glycer. Boroglyc. [Solution of Boroglyceride]

(glĭç-ĕ-rī'tŭm bō-rō-glĭç-ĕ-rī'nī)

Glycerinum Acidi Borici, *Br.;* Glycerin of Boric Acid; Glycerite of Glyceryl Borate; Glycéré de boroglycéride, *Fr.* Boroglyceridlösung, *G.*

* "Boric Acid, in fine powder, *three hundred and ten grammes* [or 10 ounces av., 409 grains]; Glycerin, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Heat *four hundred and sixty grammes* [or 16 ounces av., 99 grains] of Glycerin, in a tared porcelain dish on a sand bath, to a temperature between 140° and 150° C. (284° and 302° F.), and add the boric acid in portions, constantly stirring. When all is added and dissolved, continue the heat at the same temperature, frequently stirring, and breaking up the film which forms on the surface until the mixture has been reduced to the weight of *five hundred grammes* [or 17 ounces av., 279 grains] then add to it *five hundred grammes* [or 17 ounces av., 279 grains] of glycerin, mix thoroughly, and immediately transfer it to bottles and stopper them tightly." *U. S.*

"Boric Acid, 300 *grammes;* Glycerin, sufficient to produce 1000 *grammes.* Add the Boric Acid to four hundred and fifty *grammes* of the Glycerin, boil until dissolved, constantly stirring; evaporate at a temperature rising to but not exceeding 150° C. (302° F.) until the weight of the mixture has been reduced to five hundred grammes, the stirring being continued. Add sufficient Glycerin to produce the required weight; mix thoroughly." *Br.*

This solution was first introduced into the U. S. P. 1890 from the National Formulary. It is a thick, sweet, viscid, colorless liquid, and has the advantage of offering the antiseptic, boric acid, in a very soluble form. It may be made more rapidly than by the above process if one ounce av. of boroglyceride be dissolved in one ounce av. of glycerin with the aid of a gentle heat. (See *Boroglyceride,* Part II.)

GLYCERITUM HYDRASTIS. U. S.

GLYCERITE OF HYDRASTIS Glycer. Hydrast. [Glycerite of Goldeh Seal]

(glĭç-ĕ-rī'tŭm hȳ-drăs'tĭs)

"*One hundred mils* of Glycerite of Hydrastis yields not less than 1.12 Gm. nor more than 1.37 Gm. of the ether-soluble alkaloids of hydrastis." *U. S.*

Glycéréd'Hydrastis du Canada, *Fr.;* Gelbwurzel-Glycerit, *G.*

* "Hydrastis, in No. 60 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Glycerin, Alcohol, Water, each, *a sufficient quantity,* to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Moisten the Hydrastis with *three hundred and fifty mils* [or 11 fluidounces, 401 minims] of Alcohol, pack it firmly in a cylindrical percolator; and add enough Alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding Alcohol, until the drug is exhausted. Remove nearly all of the Alcohol, by distillation or evaporation, pour the thick concentrated liquid into *four hundred and fifty mils* [or 15 fluidounces, 104 minims] of ice-cold Water, and set it aside, in a cold place, for twenty-four hours. Then filter and assay a portion of this filtrate by the process given below, and, from the result thus obtained, ascertain by calculation the amount of ether-soluble alkaloids in the remainder of the liquid. Add to this enough cold water to make each *one hundred mils* of the product contain 2.5 Gm. of the ether-soluble alkaloids of hydrastis. Finally add an equal volume of glycerin, and mix." *U. S.*

"Assay.—Proceed as directed under *Fluidextractum Belladonnæ Radicis,* page 486, first line of the Assay, modifying the process there given by using 5 mils of Glycerite of Hydrastis instead of 10 mils of fluidextract of belladonna root and using only ether as the immiscible solvent throughout the assay. Wash the final ether extractions with 10 mils of distilled water, draw off the water and discard it. Then filter the ether solution through a pledget of purified cotton, wash the cotton with ether, evaporate

the filtrate and washings, and dry the residue at 100° C. (212° F.) to constant weight instead of titrating it. The weight represents the amount of ether-soluble alkaloids in 5 mils of the Glycerite of Hydrastis." *U. S.*

The process for this glycerite has been improved by adopting J. U. Lloyd's suggestion to concentrate the alcoholic tincture by distillation or evaporation and pouring the thick liquid into ice-cold water, for the purpose of separating the oily and resinous matter which is useless. F. A. Sieker found that glycerite of hydrastis as made by the former U. S. process varies greatly in strength. (See *Proc. A. Ph. A.*, 1893, 691; also *Ph. Rund.*, 1895, 236, and *Proc. A. Ph. A.*, 1894, 668.) Its medicinal properties are those of hydrastis.

Dose, from one-half to one fluidrachm (1.8–3.75 mils).

GLYCERITUM PHENOLIS. U. S. (Br.)

GLYCERITE OF PHENOL Glycer. Phenol. [Glyceritum Acidi Carbolici, Pharm. 1890, Glycerite of Carbolic Acid]

(glĭç-ẹ-rī'tŭm phẹn-ō'lĭs)

Glycerinum Acidi Carbolici, *Br.;* Glycerin of Phenol; Glycérole d'Acide Phénique, Glycéré de Phenol, Glycérine Phénique, *Fr.;* Phenol-Glycerit, *G.;* Glycerina con acido fenico, *Sp.*

* "Liquefied Phenol, *twenty mils* [or 325 minims]; Glycerin, *eighty mils* [or 2 fluidounces, 338 minims], to make *one hundred mils* [or 3 fluidounces, 183 minims]. Add the Liquefied Phenol to the Glycerin, and thoroughly mix." *U. S.*

"Phenol, 20 *grammes;* Glycerin, sufficient to produce 100 *millilitres.* Triturate the Phenol with the Glycerin in a warmed mortar until solution is effected." *Br.*

Uses.—For the uses of this preparation, see *Phenol.* The U. S. P. IX glycerite is a 20 per cent. by volume solution of liquefied phenol; the British preparation is slightly stronger, being a 20 per cent. by volume solution of crystallized phenol. It may be used internally or locally, and for both purposes should in general be diluted with water.

Dose, from five to ten minims (0.32–0.65 mil).

GLYCYRRHIZA. U. S. (Br.)

GLYCYRRHIZA Glycyrrh. [Licorice Root Licorice Liquorice Root]

(glĭç-ŷr-rhī'zạ)

"The dried rhizome and roots of *Glycyrrhiza glabra typica* Regel et Herder, known in commerce as Spanish Licorice, or of *Glycyrrhiza glabra glandulifera* Regel et Herder, known in commerce as Russian Licorice (Fam. *Leguminosæ*). Preserve powdered and whole Glycyrrhiza in tightly-closed containers to which a few drops of chloroform or carbon tetrachloride are added from time to time to prevent attack by insects." *U. S.* "Liquorice Root is the peeled root and peeled subterranean stem of Glycyrrhiza glabra, *Linn.*, and other species of Glycyrrhiza." *Br.*

Glycyrrhizæ Radix, *Br.;* Radix Glycyrrhizæ Hispanicæ, Spanish Licorice Root; Réglisse, *Fr. Cod.;* Racine de Réglisse, Bois doux, Racine douce, Bois de Réglisse, *Fr.;* Radix Liquiritiæ, *P. G.;* Spanisches Süssholz, Spanische Süssholzwurzel, Süssholzwurzel, *G.;* Liquirizia, *It.;* Regaliz (Raiz de), Orozuz, Palo dulce, *Sp.*

Glycyrrhiza glabra has a perennial root, which is round, succulent, tough, and pliable, furnished with sparse fibers, rapid in its growth, and in a sandy soil penetrates deeply into the ground. The stems are herbaceous, erect, slightly branching, and usually four or five feet in height. The leaves are alternate, pinnate, consisting of several pairs of ovate, blunt, petiolate leaflets, with a single leaflet at the end, of a pale-green color, and clammy on their under surface. The flowers are violet or purple, formed like those of the pea, and arranged in axillary spikes supported on long peduncles. The calyx is tubular and persistent. The fruit is a compressed, smooth, acute, one-celled legume, containing from one to six small kidney-shaped seeds. There are two very distinct varieties of the plant yielding the root: in the typical form, or var. *typica*, the underground portion is spreading, producing slender rhizomes. This plant grows best on sandy soil near streams, usually not being found more than fifty meters from a body of water. It is indigenous to southern Europe and southwestern Asia, and is cultivated in England, Germany and Austria and has been grown on an experimental scale in the United States. The second variety, var. *glandulifera*, has been sometimes designated as a distinct species, because the entire plant is pubescent or roughly glandular. The underground portions are not spreading and it produces a large fusiform root. This variety is indigenous to southeastern Europe and in western Asia. It is also cultivated to some extent in Russia. Asiatic licorice, known as "*Chuntschir*," is obtained from *G. uralensis* Fisch. The plant is found in Siberia, Turkestan and Mongolia, and it is claimed that the root is of better quality and is but little inferior to the best Russian licorice. (*Pharm. Journ. Russ.*, 1908, p. 1063; also *P. J.*, 1908, lxxxi, 164.)

It is probable that a portion of the root from Italy and Sicily is the product of *G. echinata*, which grows wild in Apulia. This species is also abundant in the south of Russia, where, according to Hayne, sufficient extract is prepared from it to supply the whole Russian empire. Large quantities of licorice root are now imported for the purpose of making the extract. The annual imports of licorice root in the United States is enormous. Between 75,000,000 and 100,000,000 pounds are annually imported from Turkey and about half of this quantity from Russia. The U. S. Department of Agriculture has had Spanish licorice under cultivation in South Carolina and the plant thrives in various localities in this country. It is said that the soil and climatic conditions in the Coachella Valley of California are ideal for the growing of the licorice plant. Ozmun describes the plantation of licorice in Turkey and the Levant and the manner of harvesting and

handling this article. The licorice plant has been cultivated according to precedence of date in Spain, Italy, Greece, The Ottoman Empire, Russia, China, Turkestan and Persia. (See *Proc. A. Ph. A.*, 1905, p. 273; *A. J. P.*, 1907, p. 39; *Oil, Paint and Drug Rep.*, 1906, p. 37, and 1908, p. 22.)

A species of Glycyrrhiza, *G. lepidota* Pursh., grows abundantly about St. Louis, in the State of Missouri, and flourishes from Colorado to New Mexico, westward into Nevada and Northern California and northward to Washington. It is probably the same as the licorice plant mentioned by Mackenzie as growing on the northern coast of this continent. Nuttall states that its root possesses in no inconsiderable degree the taste of licorice, and M. L. McCullough found it to contain 6.39 per cent. of crude glycyrrhizin, in contrast with 7.18 per cent. in the official species. (*A. J. P.*, 1890.) Schneider reports that *G. lepidota glutinosa* Pursh., a native of California, is much like *G. glabra* and can no doubt be substituted for the true licorice. (*Pacific Pharm.*, II, p. 144.)

Properties.—The two varieties are described in the U. S. Pharmacopœia as follows:

"*Spanish Licorice* (also known as Italian, Levant, Persia, Turkish, or Arabian Licorice)—Nearly cylindrical, upper portion more or less knotty; usually in pieces from 14 to 20 cm. or more in length and from 5 to 20 mm. in thickness; externally yellowish-brown or dark brown, longitudinally wrinkled, the thinner rhizomes often having prominent alternate buds, the thicker rhizomes having distinct corky patches; fracture coarsely fibrous; internally lemon-yellow, radiate; bark from 1 to 3 mm. in thickness; wood porous, in narrow wedges, rhizome with small pith; odor distinctive; taste sweetish and slightly acrid. Under the microscope, transverse sections of pieces of the older rhizome of Spanish Licorice show a periderm of numerous layers of yellowish-brown cork cells, a phellogen and one or more rows of cells of the phelloderm, the cells showing a tendency to collenchymatous thickenings and with occasional monoclinic prisms of calcium oxalate; a middle bark of starch-bearing parenchyma and whitish groups of bast-fibers surrounded with crystal-fibers; inner bark with a very characteristic radial arrangement of phloem and medullary rays, the phloem consisting of wedges of small groups of bast-fibers and parenchyma, separated by an almost continuous, obliterated sieve tissue, the cells of the latter being very irregular in outline and with thick, highly refracting walls; medullary rays from 1 to 8 cells wide; wood characterized by broad wedges consisting of large tracheæ with yellowish walls, small compact groups of wood-fibers and starch-bearing parenchyma alternating with the broad medullary rays; pith composed of parenchyma, the cells being large, more or less polygonal in outline and containing numerous starch grains, or prisms of calcium oxalate. In sections of roots the pith is absent.

"*Russian Licorice.*—Nearly cylindrical, somewhat tapering, sometimes split longitudinally, from 15 to 30 cm. in length and from 1 to 5 cm. in diameter; when deprived of the outer corky layer, it is externally pale-yellow; fracture coarsely fibrous; internally lemon-yellow; wood radially cleft; odor distinct; taste sweetish. Under the microscope, transverse sections of the rhizome and roots of Russian Licorice somewhat resemble those of Spanish Licorice, but the cork cells are absent.

Powdered Glycyrrhiza is pale brownish-yellow (Spanish Licorice) or pale yellow (Russian Licorice); starch grains numerous, mostly single and elliptical or oval, and from 0.002 to 0.02 mm. in diameter; tracheæ mostly with bordered pores; wood- and bast-fibers numerous, strongly lignified, very long, much attenuated at the ends and about 0.01 mm. in width; crystal-fibers with monoclinic prisms of calcium oxalate, the latter from 0.01 to 0.02 mm. in diameter, occasional fragments of red-dish-brown cork cells occur in Spanish Licorice, but are practically absent in the Russian Licorice. Add 10 Gm. of powdered Glycyrrhiza to 100 mils of distilled water, allow the mixture to macerate for fifteen minutes with occasional stirring; and then heat it for one-half hour on a water bath. Filter the mixture and add through the filter enough water to make the filtrate measure 100 mils; not less than 0.2 Gm. of residue remains on evaporating 10 mils of this filtrate and drying it at 100° C. (212° F.). Glycyrrhiza yields not more than 7 per cent. of ash." *U. S.*

"When 5 grammes are macerated with 50 millilitres of *chloroform water* for twenty-four hours, shaken occasionally and filtered, 10 millilitres of the filtrate evaporated in a flat-bottomed dish yield not less than 0.200 gramme of residue dried at 100° C. (212° F.). Ash not more than 6 per cent." *Br.*

Formerly commerce was chiefly supplied with licorice root by Italy and Spain, but the amount coming from these sources is at present probably not more than 10 per cent. of the whole, the greater portion coming from Southern Russia, a large amount from Anatolia and Syria, and a little from Turkey and Persia. The Spanish variety has been most esteemed, but, according to H. N. Rittenhouse, the peeled Russian licorice is richer in glycyrrhizin and extractives than is any other variety, and is in fact the most valuable. Russian licorice is usually very large, quite sweet, but at the same time rather more bitter and acrid than is the Spanish variety. Licorice root is often worm eaten and more or less decayed; such root should be rejected, as should also the small fibrous roots often shipped from Spain. The best pieces are large, bright yellow internally, and have the layers and the bark distinct. Rusby has stated that he has seen ground licorice imported which apparently consisted of the peelings of Russian licorice. (*Ph. Era*, 1909, p. 634.)

A character said by Rothrock (*A. J. P.*,

1884) to be diagnostic is the occurrence of crystal fibers adjoining the wood and bast fibers. These are recognized in the official description of the powdered drug. In the Russian root the parenchymatous wood-cells are larger than in the Spanish. The powder is of a grayish-yellow color, when the root is pulverized without being deprived of its epidermis; of a pale sulphur-yellow, when the epidermis has been removed. Robiquet found the following ingredients in licorice root: (1) a peculiar transparent yellow substance, called *glycyrrhizin*, of a sweet taste, scarcely soluble in cold water, very soluble in boiling water, with which it gelatinizes on cooling, thrown down from its aqueous solution by acids, readily soluble in cold alcohol, insusceptible of the vinous fermentation, yielding no oxalic acid by the action of nitric acid, and therefore wholly distinct from sugar; (2) a crystallizable principle named *agedoïte* by Robiquet, but subsequently proved to be identical with *asparagin;* (3) starch; (4) albumen; (5) a brown acrid resin; (6) a brown nitrogenous extractive matter; (7) lignin; (8) salts of calcium and magnesium, with phosphoric, sulphuric, and malic acids. Flückiger states that a small amount of tannin is also always contained in the root, or rather its bark. The chief constituent, *glycyrrhizin,* $C_{44}H_{68}NO_{18}$, Gorup-Besanez (*Ann. Ch. Ph.,* 118) considered to be a glucoside, as on boiling with diluted acids it breaks up into *glycyrrhetin* and an uncrystallizable sugar capable of fermentation. Roussin (*J. P. C.,* July, 1875) found that the sweet taste of the root was not owing to the free glucoside, but to its compound with ammonia.

Habermann (*Ann. Ch. Ph.,* 197) found that glycyrrhizin-ammonia was the acid ammonium salt of glycyrrhizic acid, a nitrogenous acid, and gave the formula $C_{44}H_{62}NO_{18}.NH_4$ for it. (See *Glycyrrhizinum Ammoniatum.*) He succeeded in extracting from the commercial "ammoniacal glycyrrhizin," *glycyrrhizic acid,* which may be considered to be the active constituent of licorice. It was obtained by dissolving the crude glycyrrhizin in glacial acetic acid at a boiling temperature, rapidly filtering, again treating the crystalline parts of the filtrate in the same manner, and finally purifying by repeated crystallizations from 90 per cent. alcohol. Its properties are peculiar, and account to a great extent for the singular behavior of liquid licorice preparations. With water, in which the substance is but little soluble at ordinary temperature, it forms a transparent, faintly yellow jelly. On mixing 1 Gm. of the body with 100 mils of water, the mixture after a few hours becomes so jelly-like that the open vessel may be inverted without losing any substance. It is insoluble in ether, but slightly soluble in absolute alcohol (even boiling), more so in alcohol of 90 per cent., and especially so when hot. Its solubility increases with the decrease of the percentage of alcohol. The apparent glucosidal character of glycyrrhizic acid Habermann explains by the fact that it breaks up on boiling with diluted sulphuric acid into *glycyrrhetin* and *parasaccharic acid,* according to the reaction:

$$C_{44}H_{68}NO_{18} + 2H_2O = C_{32}H_{47}NO_4 + 2C_6H_{10}O_5.$$

(*Ann. Ch. Ph.,* cxcvii; *N. R.,* Sept., 1879.) By fusing glycyrrhizin with potassium hydroxide, Weselsky and Benedikt (*Ber. d. Chem. Ges.,* 1876) obtained *paraoxybenzoic acid.*

For methods of quantitatively determining glycyrrhizin, see *Ext. Glycyrrh.,* p. 452.

Uses.—Powdered licorice root is used for various pharmaceutical purposes as in the preparation of pills, either to give due consistence or to cover their surface and prevent them from cohering, and as a diluent of powdered extracts, etc. As a remedial agent it has been almost entirely replaced by the extract.

Off. Prep.—Extractum Glycyrrhizæ, *U. S., Br.;* Extractum Glycyrrhizæ Purum, *U. S.;* Fluidextractum Glycyrrhizæ, *U. S.* (*Br.*); Mistura Glycyrrhizæ Compositus (from Extract), *U. S.;* Pulvis Glycyrrhizæ Compositus, *U. S., Br.;* Elixir Glycyrrhizæ Aquosum (from Fluidextract), *N. F.;* Elixir Glycyrrhizæ Aromaticum (from Fluidextract), *N. F.;* Fluidglyceratum Glycyrrhizæ, *N. F.;* Mistura Ammonii Chloridi (from Pure Extract), *N. F.;* Syrupus Glycyrrhizæ (from Fluidglycerate), *N. F.*

GLYCYRRHIZINUM AMMONIATUM. U. S.

AMMONIATED GLYCYRRHIZIN Glycyrrh. Ammon.

(glĭç-ŷr-rhī-zī'nŭm ąm-mō-nī-ā'tŭm)

"A sweet principle combined with ammonia obtained from glycyrrhiza." *U. S.*

Glycyrhizine Ammoniacale, *Fr. Cod.;* Glyzina, Glyzine, *Fr.;* Ammoniak-Glycyrrhizin, *G.*

The process for making this preparation was omitted from the U. S. P. IX. That of the U. S. P. VIII is appended.

"Glycyrrhiza, in No. 20 powder, *five hundred grammes* [or 17 ounces av., 279 grains]; Water, Ammonia Water, Sulphuric Acid, each, *a sufficient quantity.* Mix *four hundred and seventy-five mils* [or 16 fluidounces, 29 minims] of Water with *twenty-five mils* [or 406 minims] of Ammonia Water, and, having moistened the powder with the mixture, macerate for twenty-four hours. Then pack it moderately in a conical glass percolator, and gradually pour water upon it until *five hundred mils* [or 16 fluidounces, 435 minims] of percolate are obtained. Add Sulphuric Acid slowly to the percolate, with constant stirring, so long as a precipitate is produced. Collect this on a strainer, wash it with cold Water until the washings no longer have an acid reaction, redissolve it in Water with the aid of Ammonia Water, filter, if necessary, and again add Sulphuric Acid so long as a precipitate is produced. Collect this, wash it, dissolve it in a sufficient quantity of Ammonia Water previously diluted with an equal volume of Water, and spread the clear solution upon plates of glass, so that, when dry, the product may be obtained in scales." *U. S. P. VIII.*

The U. S. P. IX describes it as follows: "Ammoniated Glycyrrhizin occurs in dark brown or brownish-red scales, without odor, and having a very sweet taste. It is freely soluble in water and soluble in alcohol. Its aqueous solution when heated with potassium hydroxide T.S. evolves ammonia. Supersaturate an aqueous solution of Ammoniated Glycyrrhizin with an acid; a precipitate is produced (consisting essentially of *glycyrrhizin*), which, when dissolved in hot water, forms a jelly on cooling. This substance, after being washed with diluted alcohol and dried, appears as an amorphous, yellow powder, having a strong, bitter-sweet taste, and an acid reaction. Incinerate 0.5 Gm. of Ammoniated Glycyrrhizin; not more than 0.5 per cent. of ash remains." *U. S.*

This is a preparation whose introduction is a result of the researches of Z. Roussin, communicated to the Société de Pharmacie of Paris, June 2, 1875. This investigator noticed that *glycyrrhizin*, the sweet principle of licorice root, is insipid when compared with the root itself, and suspected that it existed in a modified form in the root. Experiment showed that alkalies developed the sweet taste, and he ultimately proved that the alkali with which it was combined in the root was ammonia, and that glycyrrhizin played the part of an acid. He named the compound *ammonium glycyrrhizate*, and called attention to the fact that licorice root which had lost a portion of its sweetness through fermentation and the development of acetic acid and precipitation of insoluble glycyrrhizin could be restored to its former sweetness if allowed to remain a sufficient length of time in an ammoniacal atmosphere. The U. S. P. VIII process for ammoniated glycyrrhizin is closely modelled after Roussin's, with the exception of the substitution of percolation by a slightly ammoniated menstruum for maceration and expression with cold water. Roussin purified his product by redissolving it in alcohol and precipitating with ether; this is deemed unnecessary for a preparation which is intended to be useful without being expensive. (See *Proc. A. Ph. A.*, 1876, p. 544.)

Connerade proposed some modification of Roussin's method; his process is as follows: "Macerate ground liquorice root with one and a half parts by weight of water, strain, wash the residue with a very small quantity of water, heat the mixed liquids to boiling to coagulate albumen, strain again, and then add diluted sulphuric acid (1 in 10), as long as a precipitate is produced. Let this settle, decant the liquid, and dissolve the precipitate in solution of ammonia, diluted with nine parts of water. Filter the latter and evaporate it to dryness. The compound then remains as a brown, friable varnish, unaltered by air, of a pure, sweet taste, easily soluble in cold water, and imparting to the latter, even when diluted to 1 in 1000 parts, an amber color. The yield is about 10 per cent. of the weight of the root." (*N. R.*, March, 1881.)

Uses.—This substance appears to possess the medicinal properties of licorice, and may be used as an elegant substitute for it in mixtures which are neither acid nor alkaline. It is incompatible with acids which destroy its sweetness by throwing down the insoluble glycyrrhizic acid.

Dose, from five to fifteen grains (0.32–1.0 Gm.).

GOSSYPII RADICIS CORTEX. Br.

COTTON ROOT BARK

(gŏs-sĭp'I-I răd'ĭ-cĭs cŏr'tĕx)

"Cotton Root Bark is the dried root-bark of Gossypium herbaceum, *Linn.*, and of other cultivated species of Gossypium." *Br.*

"The recently-gathered air-dried bark of the root of one or more of the cultivated varieties of *Gossypium herbaceum* Linné, *Gossypium Barbadense* Linné, or *Gossypium arboreum* Linné (Fam. *Malvaceæ*), without the presence of more than 5 per cent. of wood or other foreign matter." *N. F.*

Gossypii Cortex, *N.F.*; Ecorce de la Racine de Cottonnier *Fr.*; Baumwoll-Wurzelrinde, *G.*; Corteza de la raiz d'algodon, *Sp.*

In consequence of changes produced in the plants of this genus by cultivation, botanists have found great difficulty in determining which are distinct species and which are merely varieties. By some taxonomists more than fifty species of *Gossypium* are recognized. There are only 5 or 6 species which yield useful products and the bulk of the cotton is the product of two species: *G. herbaceum* L., which furnishes the Upland or short staple cotton, and *G. barbadense* L., the source of the Sea Island or long staple cotton. All of the species are of tropical origin. The Upland cotton has been cultivated in East India and Arabia since ancient times. The Sea Island cotton is indigenous to America and is of the type observed by Columbus.

Gossypium herbaceum is a biennial or triennial plant, with a branching stem from two to six feet high, and palmate hoary leaves, the lobes of which are somewhat lanceolate and acute. The flowers possess yellow petals, having a purple spot near the claw. The leaves of the involucre or outer calyx are serrate. The capsule opens when ripe, and displays a loose white tuft of long slender filaments, which surround the seeds and adhere firmly to the outer coating. The plant is a native of Asia, but is cultivated in most tropical countries. It requires a certain duration of warm weather to perfect its seeds, and, in the United States, does not mature north of Virginia.

The herbaceous part of the plant contains much mucilage, and has been used as a demulcent. The seeds yield by expression a fixed oil of the semi-drying kind, which is employed for making soap and for other purposes. (See *Oleum Gossypii.*) The bark of the root has been supposed to possess medicinal virtues, and is recognized by the National Formulary IV. Another portion, for which the plant is cultivated, is the filamentous substance surrounding the seeds. This, when separated, constitutes the cotton of commerce, and when purified, is

official as *Purified Cotton.* Cotton seeds have been employed in our Southern States with great asserted success in the treatment of intermittents, but are at present seldom, if ever used. (For details, see *U. S. D.*, 16th ed.) For an account of a microscopical and microchemical examination of cotton root bark by F. W. Morgan, see *A. J. P.*, 1898, p. 427. Farwell has made a histological study of the root and stem barks. (See *Merck's Rep.*, 1914, p. 133.) The drug of commerce frequently contains a considerable woody material. It is said it deteriorates with age and therefore only recently gathered bark should be used.

Properties.—Cotton Root Bark is described as: "In strips or quilled pieces; thin, tough and fibrous. Cork thin, pale brown, longitudinally striated; removed in places and then disclosing the orange-brown cortex. Inner surface whitish, silky and finely striated. Secondary bast readily separable into thin fibrous laminæ. No odor; taste slightly acrid and astringent." *Br.*

The N. F. describes the bark as follows: "In flexible bands or quilled pieces, attaining a length of 30 cm. and a thickness of about 1 mm.; outer surface orange-brown, smooth, slightly wrinkled, with small circular lenticels, the outer corky layer frequently exfoliated and showing the more or less fissured and fibrous middle bark; inner surface light brown, longitudinally striate; fracture tough, fibrous, the inner bark readily separable into fibrous layers. Odor slight; taste very slightly acrid. Under the microscope, sections of Cotton Root Bark show an outer layer of cork composed of four to six layers of tabular, thin-walled, yellowish-brown, non-lignified cells; a thin primary cortex, consisting of starch-bearing parenchyma and an occasional large secretion reservoir with yellowish-brown contents; inner bark with large groups of bast fibers arranged in interrupted, concentric circles, separated radially by medullary rays and tangentially by the leptome or sieve tissue; bast fibers from 0.3 to 1 mm. in length and about 0.015 mm. in width, the walls being about 0.005 mm. in thickness, strongly lignified and with very few pores, the ends being acute and markedly attenuate; medullary rays one to six cells wide, the cells usually filled with starch grains; the latter from 0.003 to 0.02 mm. in diameter; occasional cells containing rosette aggregates of calcium oxalate from 0.009 to 0.025 mm. in diameter. Cotton Root Bark yields not more than 7 per cent. of ash." *N. F.*

E. S. Wayne, of Cincinnati, found in it a peculiar acid resin, colorless and soluble in water, when pure, but absorbing oxygen on exposure, and then becoming red and insoluble in water. It is deposited from the fluidextract on standing. He suggests that this may be the active principle of the root; but the fact has not been determined. (*A. J. P.*, 1872.) William C. Staehle (*A. J. P.*, 1875) made an examination of this resin, and obtained results somewhat different from those of Wayne. Staehle's percolate was of a dark reddish-brown color, while Wayne's was pale amber. This is accounted for, however, by the presence of a principle which is colorless in the fresh bark, but of a dark red in bark which has been exposed to air and light. W. A. Taylor noticed that the change in color from pale amber to dark red took place in an alcoholic tincture. (*A. J. P.*, 1876.) Staehle found the resin soluble in 14 parts of alcohol, 15 parts of chloroform, 23 parts of ether, and 122 parts of benzene.

Power and Browning (*P. J.*, 1914, xciii, 420) found in an investigation of cotton root bark the following constituents: acetovanillone (in the steam distillate), a phenolic acid (probably two-thirds dihydroxybenzoic acid), salicylic acid, a new colorless phenolic substance, $C_9H_{10}O_3$, a new yellow phenolic substance, $C_{13}H_{18}O_5$, betaine, a fatty alcohol, $C_{20}H_{42}O$, a phytosterol, $C_{27}H_{46}O$, triacontane, ceryl alcohol, oleic and palmitic acids, and a sugar. Almost all of these constituents were separated from the resinous extractive which constituted between 10 and 11 per cent. of the air dried bark. No tannin was present and no alkaloids were detected.

Uses.—Cotton root bark was introduced into medicine by Bouchelle (*A. J. M. S.*, August, 1840), who stated that it was habitually resorted to by the slaves of the south as an abortifacient. His favorable opinion has been confirmed by various southern practitioners, and Scott (*T. G.*, 1911) has shown experimentally that cotton root bark increases the contractions and tonus of the uterus in the lower animals, although it is somewhat less powerful than ergot. It is used not only to strengthen the contractions in uterine inertia during *labor,* but also in the treatment of *metrorrhagias,* especially when dependent on *fibroids.* Bellany, of Georgia, asserts that the root should be gathered as late as possible in the fall before frost. Bouchelle used a decoction made by boiling four ounces of the inner bark of the root in a quart of water down to a pint, of which he gave a wine glass full (60 mils) every twenty or thirty minutes. The U. S. P., 1890, recognized a fluidextract (see *U. S. Dispensatory,* 19th edition, p. 525); for the N. F. IV fluidextract, see Part III.

Dose, thirty to sixty grains (2.0–3.9 Gm.).

Off. Prep.—Decoctum Gossypii Radicis Corticis, *Br.;* Extractum Gossypii Radicis Corticis Liquidum, *Br.;* Fluidextractum Gossypii Corticis, *N. F.*

GOSSYPIUM PURIFICATUM. U. S. (Br.)

PURIFIED COTTON Gossyp. Purif.
[Absorbent Cotton]
(gŏs-sȳp'ĭ-ŭm pū-rĭ-fĭ-cā'tŭm)

"The hairs of the seed from one or more of the cultivated varieties of *Gossypium herbaceum* Linné (Fam. *Malvaceæ*), freed from adhering impurities and linters and deprived of fatty matter." *U. S.* "Cotton consists of the hairs of the seed of Gossypium herbaceum, *Linn.,* and of other cultivated species of Gossypium, freed from fatty matter." *Br.*

Gossypium, *Br.;* Cotton Wool; Lana (Lanugo, s. Pili) Gossypii; Coton Hydrophile, *Fr. Cod.;* Coton absorbant, Xylum præparatum, *Fr.;* Gossypium depuratum, *P. G.;* Gereinigte Baumwolle, Baumwolle, *G.;* Cotone assorbente, C. idrofilo, *It.;* Algodon hidrofilo, Algodon absorbente, *Sp.*

There is considerable difference in the capsules or so-called bolls, the seeds, as well as the lint of the several species of Gossypium. The bolls of Sea Island (*G. barbadense*) cotton are uniformly smaller, more sharply pointed, contain fewer and smaller seeds and longer lint than the Upland bolls. The Sea Island cotton has small black seeds from which the lint separates readily. The Upland cottons have large seeds which are greenish in color, and surrounded by a short, dense hair beneath the longer and more valuable lint. The lint of the Sea Island cotton is from 3.5 to 6.5 cm. in length, while the Upland cotton seldom exceeds 3.5 cm. in length, usually being much shorter. There are numerous hybrids between these two types, *G. herbaceum* and *G. barbadense.* The long and extra long fiber produced in the United States are all obtained from varieties of *G. barbadense* and their hybrids, the shorter fibers being usually Upland cottons of the *G. herbaceum* type. The commercial grading of cotton by the New York Cotton Exchange is as follows: Samples the average fiber of which is under 25 mm. in length are called "short staple"; those between 25 to 30 mm. are called "medium" and from 30 to 40 mm. are called "long staple." What are known as "full grades" are designated by the words "fair," "middling fair," "good middling," "middling," "low middling," "good ordinary" and "ordinary."

Properties.—"Purified Cotton occurs in white, soft, fine filaments, appearing under the microscope as hollow, flattened and twisted bands, spirally striate, and slightly thickened at the edges; inodorous and almost tasteless; insoluble in ordinary solvents, but soluble in an ammonia solution of cupric oxide. When Purified Cotton, previously compressed in the hand, is thrown on the surface of cold water, it readily absorbs the latter and sinks. Incinerate 5 Gm. of Purified Cotton; not more than 0.2 per cent. of ash remains. Thoroughly saturate about 10 Gm. of Purified Cotton with 100 mils of distilled water, then with the aid of a glass rod press out two portions of the water, 25 mils each, into white porcelain dishes. Add to one portion 3 drops of phenolphthalein T.S. and to the other portion 1 drop of methyl orange T.S.; no pink color develops in either portion (*alkali or acid*). Extract 5 Gm. of Purified Cotton, tightly packed in a narrow percolator, with ether, until the percolate measures 20 mils, and evaporate this to dryness; the residue does not exceed 0.6 per cent. (*fatty matter*). Extract 10 Gm. of Purified Cotton, in a narrow percolator, with alcohol, until the percolate measures 100 mils. When observed downward through a column 20 cm. in depth, the percolate may show a yellowish color, but no blue or green tint (*dyes*); and, on evaporating this percolate to dryness, the weight of the residue does not exceed 0.5 per cent. (*resins and soap*)." *U. S.*

"In long, white, soft filaments, each consisting of an elongated cell, appearing, when seen under the microscope, as a flattened, twisted band with slightly thickened rounded edges. Inodorous and tasteless. Soluble in *ammoniacal solution of copper oxide.* Readily wetted by *water,* and not imparting to it either an alkaline or an acid reaction. Ash not more than 0.5 per cent." *Br.*

It is without odor or taste, soluble in strong alkaline solutions, and decomposed by the concentrated mineral acids. In chemical character it is related to but not identical with lignin, the latter being a very different product and called *lignocellulose.* By nitric acid it is converted into gun cotton, for an account of which see *Pyroxylinum* and *Collodium.* *Mercerized cotton* is made by treating woven cotton fabrics with concentrated sodium hydroxide solution which so modifies the fiber that a sheen-like silk is produced. This must not be confused, however, with artificial silk which is made by several processes in which cotton or cellulose is taken as the starting point. In one of these the cellulose is converted into a nitroderivative which, after dissolving in suitable solvents to make a thick solution, is drawn out into threads which are subsequently denitrated and made less inflammable by immersing them in alkaline sulphide solution. In another method the cellulose is treated with alkali and carbon disulphide which forms cellulose thiocarbonate or xanthate which when treated with water yields "*viscose,*" a thick tenacious substance capable of being drawn into glossy threads, which is sold as *artificial silk,* and also used as bottle caps.

In the process of purifying cotton a soap is formed through the union of the fatty matter with the alkali, and this is subsequently dissolved out by repeated washings. F. L. Slocum published in 1881 a process for preparing it as follows: Take of the best quality of carded cotton batting any desired quantity, and boil it with a 5 per cent. solution of potassium or sodium hydroxide for one-half hour, or until the cotton is entirely saturated with the solution, and the alkali has saponified all oily matter. Then wash thoroughly, to remove all soap, and nearly all alkali; press out the excess of water, and immerse in a 5 per cent. solution of chlorinated lime for 15 or 20 minutes; again wash, first with a little water, then dip in water acidulated with hydrochloric acid, and thoroughly wash with water; press out the excess of water, and again boil for 15 or 20 minutes in a 5 per cent. solution of potassium or sodium hydroxide; now wash well, dipping in the acidulated water and washing thoroughly with pure water. Afterwards press out and dry quickly.

The amount of loss by this process is practically 10 per cent. A sample of 360 gr. lost, on boiling with alkali and bleaching, 15 gr., or 4.17 per cent., and 270 gr. of this bleached sample lost, on again boiling with an alkali, 14 gr., or

5.18 per cent., a total loss of 9.35 per cent. (*A. J. P.*, 1881, p. 53. See also *Ph. Era.*, 1890, 22.)

Wood Wool.—Under this name Bruns has introduced finely grained, purified wood fiber, such as is used in making paper. It may be medicated like cotton.

The first U. S. P. IX test proves the absence of fatty matter, for if even a small quantity be present the cotton will float in water. Repeated experiments have proved that cotton will take fire and burn spontaneously if impregnated with linseed oil, or some of the other fixed oils, and allowed to stand, whereby the heat of the oxidation of the oil suffices to ignite the matted fibers of the cotton. Raw cotton, analyzed by M. Schunck, was found, independently of cellulose ($C_6H_{10}O_5$)n, of which it chiefly consists, to contain vegetable wax, a fatty acid, coloring matter, pectic acid, and a little of an albuminoid substance. (*J. P. C.*, Sept., 1868, 233.) For medicinal use it should be carded into thin sheets. Air passed through cotton becomes sterile on account of the microscopic organisms being strained out of it; and this fact has been utilized in preserving infusions by placing them in bottles containing corks armed with tubes loosely filled with cotton, and drawing the infusion from a stopcock near the bottom.

Uses.—The use of cotton as a filtering medium and in the preparation of medicated waters has already been alluded to. It is much used in surgery as a dressing for *burns, scalds, blisters,* and *wounds,* in order to prevent the access of pathogenetic germs and to absorb discharges. Cotton batting is often employed to maintain a uniform temperature in parts affected with *acute rheumatic inflammation.* Absorbent cotton has been medicated in various ways and come largely into use. (For *Iodized Cotton,* see page 593.) *Picric Cotton* is prepared by dissolving 0.25 Gm. of picric acid in 25 Gm. of ether, or of 94 per cent. alcohol, and immersing in the solution 10 Gm. of clean cotton, and drying. *Salicylic Cotton* (5 per cent.) may be prepared by Brun's process, by saturating one kilogramme of cotton with 4 liters of a solution of 50 Gm. of salicylic acid, and 20 Gm. of castor oil in 3.930 liters of alcohol. *Benzoic Cotton* is made in the same way, substituting benzoic for salicylic acid. *Chlorinated Cotton.* Pavesi subjects cotton moistened with glycerin, and suspended at the top of a large wide-mouthed bottle, to the action of chlorine vapor, generated by adding sulphuric acid to chlorinated lime. (*N. R.*, July, 1880.) Joseph W. England communicates in *A. J. P.*, 1887, p. 173, practical formulas for preparing the following medicated cottons and gauzes: *Borated Cotton, Benzoated Cotton, Salicylated Cotton, Naphthalinated Cotton, Iodoformized Cotton, Carbolized Cotton, Sublimated Cotton, Carbolized Gauze, Sublimated Gauze, Absorbent Canton Flannel.* For methods of assay of medicated cottons, gauzes, etc., see *Proc. A. Ph. A.*, 1897, 457, 458, 459. See also formulas for the extemporaneous preparation of medicated gauzes, by George M. Beringer, Jr., *A. J. P.*, 1911, p. 178.

Off. Prep.—Pyroxylinum, *Br.;* Gossypium Stypticum, *N. F.*

GRANATUM. U. S.

POMEGRANATE Granat. [Pomegranate Bark]

(grą-nā'tŭm)

"The dried bark of the stems and roots of *Punica Granatum* Linné (Fam. *Punicaceæ*), without the presence or admixture of more than 2 per cent. of wood or other foreign matter. Preserve it in tightly-closed containers." *U. S.*

Granati Cortex, *Br.*, 1898; Pomegranate Bark; Grenadier, *Fr. Cod.;* Ecorce de la Racine de Grenadier (de Balaustier), Ecorce de Granade, *Fr.;* Cortex Granati, *P. G.;* Granatrinde, Granatwurzelrinde, *G.;* Melograno to, Malicorio, Scorza del Melograno ti, *It.;* Granada (Corteza de), *Sp.*

The *pomegranate* is a small tree, attaining in favorable situations the height of twenty feet, with a very unequal trunk, and numerous branches which sometimes bear thorns. The leaves are opposite, petiolate, entire, oblong or lance-shaped, pointed at each end, smooth, shining, and of a bright-green color. The flowers are large, of a rich scarlet color, and stand at the end of the young branches. The petals are roundish and wrinkled, and are inserted into the upper part of the tube of the calyx, which is red, thick, and fleshy. The fruit is a globular berry, about the size of an orange, crowned with the calyx, covered with a reddish-yellow, thick, coriaceous rind, and divided internally into many loculi, which contain an acidulous pulp, and numerous oblong, angular seeds.

This tree grows wild upon both shores of the Mediterranean, in Arabia, Persia, Bengal, China, and Japan, has been introduced into the East and West Indies, and is cultivated in all civilized countries where the climate is sufficiently warm to allow the fruit to ripen. In higher latitudes, where it does not bear fruit, it is raised in gardens and hot houses for the beauty of its flowers, which become double and acquire increased splendor of coloring by cultivation. Doubts have been entertained as to its original country. The name of *Punicum Malum,* applied by the ancients to its fruit, implies that it was abundant at an early age in the vicinity of Carthage. The fruit, for which the plant is cultivated, varies much in size and flavor. It is said to attain greater perfection in the West Indies than in its native country. The edible pulp is red, succulent, pleasantly acid, and sweetish. The flowers were recognized by the Dublin College, and the seeds are official in France. See a paper by J. U. Lloyd in *West. Drug.*, 1897, 202.

The pomegranate may be grown in the United States as far north as Virginia. It is cultivated to some extent in California, and the Gulf States as a garden and hedge plant. The seeds are utilized in the south in making cooling drinks. There are several varieties of the pomegranate. The typical having an acid pulp, and others having a sweet and sub-acid character. There is an East Indian variety which is seedless and is highly prized in India. There are several double-

flowered varieties which do not bear fruit and are largely cultivated in the south and in greenhouses for ornamental purposes.

The *rind of the fruit* is seen in commerce in the form of irregular fragments, hard, dry, brittle, of a yellowish or reddish-brown color externally, paler within, without odor, and of an astringent, slightly bitter taste. It contains a large proportion of tannin, and in countries where the tree abounds, has been employed for tanning leather.

The flowers, sometimes called *balaustines,* are inodorous, have a bitterish, astringent taste, and impart a violet-red color to the saliva. They contain tannic and gallic acids, and were used by the ancients in dyeing.

Properties.—"The stem bark is mostly in somewhat flattened or transversely curved pieces, to some extent in quills, from 2 to 8 cm. in length; bark from 0.5 to 3.5 mm. in thickness; outer surface yellowish to grayish-brown, with grayish patches of foliaceous lichens with their brownish-black apothecia, longitudinally wrinkled, also marked with small, broadly elliptical lenticels and with more or less abraded patches of cork; inner surface light yellow or yellowish-brown, finely striate; fracture short, smooth, inner bark yellowish-green; odor slight; taste astringent, somewhat bitter and nauseous. The root bark is in transversely curved pieces; externally brownish-yellow to dark brown with irregular patches of cork; internally dark yellow, the medullary rays extending nearly to the outer surface. The powder is yellowish-brown to dark brown; calcium oxalate crystals in rosette aggregates, monoclinic prisms or crystal fibers, the individual crystals from 0.01 to 0.018 mm. in diameter; starch grains numerous, spherical, ellipsoidal biconvex, polygonal or irregular, and single or compound, from 0.002 to 0.01 mm. in diameter; fragments of whitish cork with strongly lignified walls; stone cells mostly single, occasionally in small groups, the individual cells from 0.05 to 0.18 mm. in length, the walls being very thick and strongly lamellated; occasional fragments of wood with long wood-fibers from 0.015 to 0.02 mm. in width, the walls being slightly lignified and from 0.003 to 0.008 mm. in thickness and associated with tracheæ possessing simple and bordered pores. Mix 1 Gm. of powdered Pomegranate with 100 mils of distilled water, macerate it with occasional agitation for about an hour and filter; a light yellow filtrate is obtained. Upon the addition of a drop of ferric chloride T.S. to 10 mils of this filtrate a bluish-black precipitate is produced. Upon the addition of from 40 to 50 mils of lime water to another portion of 10 mils of the filtrate, an orange-brown, flocculent precipitate is produced. Pomegranate yields not more than 16 per cent. of ash." *U. S.*

The roots of the pomegranate are hard, heavy, knotty, ligneous, and covered with a bark which is yellowish-gray or ash-gray on the outer surface, and yellow on the inner. The *root bark* occurs in quills or fragments similar to but differing from those of the stem as shown in the official characterization. "The transverse section exhibits numerous fine radial and tangential lines." *Br.* (1898). It has little or no odor, colors the saliva yellow when chewed, and leaves in the mouth an astringent taste without disagreeable bitterness. There is considerable question as to the relative value of the root and stem barks of *granatum.* The drug of commerce usually consists of a mixture of stem and root bark, the former commonly predominating. Granatum is sometimes substituted by the barks of other plants. The principal of these being *Berberis vulgaris,* which is bitter and not astringent; *Buxus sempervirens,* which is also bitter and free from tannin; and *Strychnos Nux Vomica* or false Angostura bark which has a dark inner surface and a very bitter taste. None of these barks have the characteristic checkered appearance of the transverse surface of genuine Granatum.

The bark of the stem of the pomegranate is sold as root bark: for microscopic diagnosis, see *P. J.,* 1873. As the activity of the barks of different portions of the plant is important, represented by the alkaloids the analyses of Stoeder are of interest. His results are: stem and branch bark, in thin quills, 0.612 per cent.; average quills, 0.350 per cent.; thick quills, 0.498 per cent.; root bark from south of Europe, in thick quills, 1.010 per cent.; shaved root bark from Java, 1.326 per cent.; exfoliated bark from dry thick roots of unknown age, 1.240 per cent.; finely rasped wood from these roots, 0.218 per cent. According to the same authority (*Nederl. Tijd. Pharm.,* 1890), of the bark of three varieties of the wild pomegranate recognized and used by the natives of Java, the red-flowered "merah," yielded 2.43 per cent.; the white-flowered, "poetih," yielded 3.75 per cent.; the black-flowered, "hitam," yielded 1.71 per cent.

The infusion of granatum yields a deep-blue precipitate with salts of iron, and a yellowish-white precipitate with solution of gelatin. The inner surface of the bark, steeped in water and then rubbed on paper, produces a yellow stain, which by the contact of ferrous sulphate is rendered blue, and by that of nitric acid acquires a slight rose tint, which soon vanishes. These properties serve to distinguish this bark from those of the box root and barberry. When used, it should be separated from the ligneous portion of the root, as the latter is inert. The bark contains more than 22 per cent. of tannic acid, which Rembold (*Ann. Ch. Ph.,* 143, 285) found to consist for the most part of a peculiar variety, *punico-tannic acid,* $C_{30}H_{16}O_{13}$; when boiled with diluted sulphuric acid it is resolved into *ellagic acid,* $C_{14}H_8O_9$, and sugar. Punico-tannic acid is accompanied by common tannic acid, yielding by means of sulphuric acid, gallic acid, which appears sometimes to pre-exist in the bark. Henry Trimble, however (*A. J. P.,* 1897, 636), as the result of an ultimate analysis of the purified tannin and a study of its reactions, pronounced it to be identical with gallo-

tannic acid. Pomegranate bark also yields a considerable quantity of *mannite,* which was formerly described under the names of *punicin* or *granatin.* The medicinal value of the root, however, is due, according to Tanret (*C. R. A. S.,* lxxxvi, 1270, and lxxxvii, 358), to an alkaloid *pelletierine,* $C_8H_{15}NO$, a dextrogyrate liquid boiling at 195° C. (383° F.), easily soluble in water, alcohol, and ether, and specially so in chloroform. It has strong basic properties and precipitates many metallic salts: 1000 parts of dry bark yielded 4 parts of it.

Tanret (*C. R. A. S.,* lxxxviii, p. 716) announced that he had found three additional volatile bases in the bark, a liquid left-rotating one, a liquid optically inactive one, and a crystallizable inactive one, to which the names of *methylpelletierine,* $C_9H_{17}NO$, and *pseudopelletierine* (*granatonine*), $C_9H_{15}NO$, and *isopelletierine,* have been given. Carl J. Bender (*Ph. Centralh.,* 1885, p. 6) found three bases in pomegranate bark, one crystallizable and two amorphous. He objects to the name pelletierine, and substitutes *punicine.* Wm. F. Junkunz analyzed pomegranate bark, and believed that the alkaloid exists in the bark as a tannate. (*A. J. P.,* 1884.) The old idea that the bark loses activity when kept seems to be negatived by the analysis of De Vrij. (*P. J.,* xxi.) Piccinni isolated a tertiary alkaloid, $C_{10}H_{13}NO$, from pomegranate root bark. (*P. J.,* 1900, 249.) Flückiger stated that methyl pelletierine predominates in the bark of the root and pelletierine in the bark of the overground portions of the plant. For Leger's method of determining total alkaloids, see *P. J.,* 1904, 581. Assay processes for granatum are given in most of the foreign pharmacopœias and these were critically reviewed by Dichgans (*Ph. Ztg.,* 1914, 852), who finds the one in the Swiss Pharmacopœia to be the best.

Uses.—The rind of the pomegranate fruit was formerly recognized by the U. S. Pharmacopœia. It is astringent, and in the form of decoction is sometimes employed in *diarrhea* and *colliquative sweats,* and, more frequently, as an injection in *leucorrhea,* and as a gargle in *sore throat* in the earlier stages, or after the inflammatory action has in some measure subsided. The powdered rind has also been recommended in *intermittent fever.* The flowers have the same medicinal properties and are used for the same purposes. The bark of the root was used by the ancients as a vermifuge, and is recommended in the writings of Avicenna, but was unknown in modern practice until brought into notice by F. Buchanan, who learned its powers in India. The Mahometan physicians of Hindostan consider it a specific against *tænia.* One of these practitioners, having relieved an English gentleman in 1804, was induced to disclose his secret, which was then made public. The French writers prefer the product of the wild pomegranate, growing on the borders of the Mediterranean, to that of the plant cultivated in gardens for ornamental purposes. The bark may be administered in powder or decoction, but the latter form is usually preferred. The decoction is prepared by macerating two ounces of the bruised bark in two pints of water for twenty-four hours, and then boiling to a pint. Of this a wineglassful may be given every half hour, hour, or two hours, until the whole is taken. It often nauseates and vomits, and usually purges. Portions of the worm often come away soon after the last dose. It is recommended to give a dose of castor oil and to diet the patient strictly on the day preceding the administration of the remedy, and, if it should not operate on the bowels, to follow it by castor oil, or an enema. If not successful on the first trial, it should be repeated daily for three or four days, until the worm is discharged. It appears to have been used by the negroes of San Domingo before its introduction into Europe.

Pomegranate owes its anthelmintic powers to the alkaloids, pelletierine and isopelletierine, the mixture of which is official. The efficacy of these tænicides has been abundantly confirmed, and it appears to be established that the tannate is the most effective and the least dangerous form of the remedy,—probably because its insolubility prevents its rapid absorption and enables it to come in prolonged contact with the worm. The experiments of Dujardin-Beaumetz have shown that the alkaloids from pomegranate act upon the higher animals like curare, causing paralysis of the motor nerves without affecting sensation. The same authority asserts that hypodermic injections of six grains produce in man severe vertigo, muscular weakness, and great retinal congestion. Double vision has also been noted, and Galezowski has been led by it to prescribe pelletierine in paralysis of the third and sixth pairs of nerves; he affirms that he has succeeded in affording relief after the failure of potassium iodide and blisters. The proper dose of pelletierine tannate is variously given by authorities. It has been stated to be from one-half to three-quarters of a grain (0.032–0.048 Gm.) (*B. G. T.,* xcvi, xcvii), but others place it as high as eight grains (0.5 Gm.). Commercially, it occurs almost exclusively as a syrupy solution, put up, we believe, under the supervision of its discoverer, each bottle containing a single dose, it is stated, of about five grains (0.32 Gm.). We have seen pronounced temporary general palsy produced in a female adult by this dose. The dose of pomegranate rind and flowers in powder is from twenty to thirty grains (1.3–2.0 Gm.). *Decoctum Granati Corticis* was formerly official in the British Pharm. (1898). The decoction may be prepared in the proportion of four ounces of the bark to twenty fluidounces of water, and given in the dose of half a fluidounce (15 mils). The remedy should always be given after a twelve hours' fast, and be followed in two hours by a brisk cathartic. The seeds are demulcent.

Dose, twenty to thirty grains (1.3–2.0 Gm.).

Off. Prep.—Fluidextractum Granati, *U. S.*

GRINDELIA. U. S., Br.

GRINDELIA Grindel.

(grĭn-dē'lĭ-ą)

"The dried leaves and flowering tops of *Grindelia camporum* Greene, or *Grindelia cuneifolia* Nuttall, or *Grindelia squarrosa* (Pursh.) Dunal (Fam. *Compositæ*), without the presence or admixture of more than 10 per cent. of stems or other foreign matter." *U. S.* "Grindelia consists of the dried leaves and flowering tops of Grindelia camporum, *Greene*." *Br.*

California Gum-plant; Grindelia, *Fr.*; Grindelie, *G.*

The genus Grindelia includes some twenty-five species, six or eight of which are found in South America and the remainder occurring in the United States west of the Mississippi. They are coarse perennial or biennial herbs, being occasionally shrub-like. Most, if not all, of the species produce a resinous exudation on the stem and leaves and especially on the flower-heads. The leaves are alternate, sessile or clasping and spinulose-dentate. The flowers occur in large terminal heads composed of both discoid and radiate yellow flowers. The ray flowers are pistillate and the involucre is more or less hemispherical, the bracts being imbricated, in several series, being usually subulate-tipped. The drug of the market appears to be derived in large part from *G. camporum* Greene, which is the common "*gum plant*" of California. It occurs abundantly in the inner coast ranges, where it has been collected in quantity in Lake and Napa Counties. It is also common in the foot hills of the Sierra Nevada and is almost the only plant found on the plains in certain regions of the Sacramento Valley. The leaves are oblong or spatulate, sessile or clasping, coarsely serrate and of a pale-green color. The flower-heads are yellow and the involucre consists of several rows of lanceolate acuminate recurved bracts. The achenes are distinctive in this species and are usually biauriculate or more rarely unidentate at the summit.

G. cuneifolia closely resembles *G. camporum*. The leaves are cuneate oblong or linear oblong and either sessile or amplexicaul. It is a marsh plant and is not as glutinous as *G. camporum*. The leaves of this species, in addition to their being cuneiform in shape, are darker green and not so thick as in *G. camporum*. The achenes are compressed and closely resemble those of *G. camporum*.

G. squarrosa is a common plant on the prairies and dry banks of the West. It has been reported as occurring from the Saskatchewan to Minnesota, Texas and California. It is a glabrous, erect, branching herb having linear-oblong or spatulate leaves, which are more or less clasping at the base and sharply spinulose-dentate. It is especially characterized by the bracts of the involucre being linear-lanceolate, subulate tipped and spreading or squarrose at the summit, giving the species its name. The achenes are truncate, those of the outer flowers being usually thicker. The pappus consists of two or three awns.

It was formerly supposed that the drug of commerce was derived from *G. robusta*. The studies of Perrédès (*Proc. A. Ph. A.*, 1906, 370) showed this not to be the case. *G. robusta* is apparently not a very common plant and is distinguished by having cordate-oblong, amplexicaul, coarsely serrate leaves. The involucre is squarrose and leafy at the base. The pappus consists of two awns. At one time both *G. cuneifolia* and *G. camporum* were considered merely as varieties of *G. robusta*.

According to Joseph Beauvais (*A. J. P.*, Feb., 1889), the resin of the leaf of *G. robusta* is contained in epidermal glands, and also in rather large resin-ducts situated in an interior collenchymatous layer.

Properties.—The official description of grindelia is as follows: "Stems with attached branches terminated with resinous flower-buds; stems cylindrical, not exceeding 2 mm. in diameter; light yellow or rose-colored, with alternate leaf-scars, occasionally with basal portions of leaves, sometimes more or less irregularly flexuous and coated with resin, especially at the nodes; leaves usually separate and more or less broken and varying in shape when entire from oblong and lanceolate to oblanceolate-spatulate and cuneate-spatulate, from 1 to 7 cm. in length, mostly sessile or amplexicaul and more or less sharply serrate or evenly spinosely-toothed, pale yellow to yellowish-green, very resinous, somewhat coriaceous and brittle; bracts of flowering branches almost entire and usually more or less spreading; heads more or less resinous, viscid, many-flowered, either conical-urceolate or depressed-urceolate, involucres from 5 to 20 mm. in breadth, composed of numerous imbricated bracts with more or less recurved tips; ray flowers yellow, ligulate and pistillate; disk florets yellow, tubular and perfect; pappus of two or three mostly unequal linear awns about the length of the disk florets; disk achenes more or less ovoid or oblong; more or less compressed or triquetrous, and either biauriculate or broadly unidentate or with a broad truncate corky, thickened summit; odor balsamic; taste aromatic and bitter, resinous. The powder is yellowish-brown; consisting of numerous fibrous fragments made up of tissues of the stem, the most prominent being the tracheæ with annular and spiral thickenings or marked with simple or bordered pores, associated with numerous, narrow, strongly lignified wood-fibers; pith cells more or less tabular and containing a layer of protoplasm in which are embedded numerous spheroidal granules; fragments of epidermis of leaves very characteristic and showing more or less polygonal areas containing large chloroplastids, and the large, colorless, basal cells of the multicellular glandular hairs; pollen grains spherical, about 0.035 mm. in diameter, spinose, and in section showing three pores." *U. S.*

"Stems slender, yellow, smooth. Leaves three to five centimetres long, oblong or spatulate, sessile or amplexicaul, pale green, rigid, brittle, smooth, glabrous; surface minutely dotted; margin coarsely serrate. Flower-heads yellow, hard,

resinous, with several rows of lanceolate-acuminate, recurved bracts. Fruits bi-auriculate or unidentate at the summit, with a pappus consisting of two thick, stiff bristles. All parts more or less resinous. Slightly aromatic odor; taste aromatic and bitter." *Br.*

As it occurs in commerce, grindelia is in the form of the whole dried herb; the stems are about eighteen inches in length, light brownish, very frequently stripped of their leaves, but with some of the floral heads adherent. The brittle leaves are much broken, and, with separate floral heads, are mixed with the stem. The taste is warm, peculiar, and very persistent. Tunmann (*Ph. Zentralh.*, 1908, p. 457) has made an excellent pharmacognostical study of *G. robusta*. Wohn (*Merck's Rep.*, 1910, p. 310) presents the results of a morphological study of *G. squarrosa*. Farwell (*D. C.*, 1907, p. 460) reports having received one of the California "tar weeds," *Hemizouella minima* Gray, for grindelia. The plant is very diminutive in size, but the inflorescence is very glutinous. Perrédès (*P. J.*, 1909, xxix, pp. 596 and 604) gives the results of some experiments in the cultivation of *G. camporum*. The activity of the drug probably resides in the resinous exudation. C. J. Rademaker obtained from it an oil, the odor of which closely resembled that of oil of turpentine, resin, and a crystalline body having an alkaline reaction. (*N. R.*, 1876, p. 205.) W. H. Clark and John L. Fischer (*A. J. P.*, 1888, p. 433) failed to verify all of Rademaker's results, but obtained an alkaline principle to which the name of *grindeline* was given. A. Schneegans (*A. J. P.*, 1892, 369) found in *Grindelia robusta, saponin*, which, he states, is composed of two glucosides; he also found indications of an alkaloid, but believes that its presence is not yet certainly proved. See also *M. R.*, 1898, 394. *Grindelia robusta* is said to contain 0.28 per cent. of a dark-brown essential oil, having a specific gravity of 0.9582 at 15° C. (59° F.), and the optical rotation in alcoholic solution of −8° 08′. It is soluble in ether, amyl alcohol, and chloroform. (*Ph. Ztg.*, 48, 574.)

Uses.—Grindelia is possessed of only feeble physiologic powers, but according to Buffington, when given to the lower animals in very large doses produces narcosis, with dilated pupils, slowing of the action of the heart from stimulation of the inhibitory nerves, and elevation of the blood pressure from stimulation of the vasomotor center. Dobroklowsky has found that it had a primary stimulating and later depressant effect on the isolated frog's heart. He further states that it acts chiefly upon the motor nerves and muscles, but Buffington asserts that it paralyzes first the sensory nerve-trunks, then the sensory side of the spinal cord, and afterwards involves the motor nerve-trunks and cord. Grindelia is used almost solely in the treatment of *bronchial catarrhs*, especially when there is a tendency to *asthma*. Its action is probably simply that of a stimulating expectorant, but some believe it exerts also an antispasmodic influence. It is frequently used in conjunction with stramonium leaves in the preparation of "Asthma powders" or cigarettes. It has been employed with asserted success in *whooping cough*. Its active principles appear to be excreted from the kidneys; hence, after large doses, there are sometimes evidences of renal irritation, and in chronic *catarrh of the bladder* good has been effected by its stimulant influence upon the mucous membrane of the viscus. As a local application, grindelia has been employed with asserted advantage in *burns, vaginitis, genito-urinary catarrh*, etc., applied either in the form of a poultice or in solution. It has considerable use also as a local application in the treatment of *rhus poisoning*. The fluidextract, diluted with water, is employed.

Dose, thirty to forty grains (2.0–2.6 Gm.).

Off. Prep.—Fluidextractum Grindeliæ, *U. S.* (*Br.*).

GUAIACI LIGNUM. Br.

GUAIACUM WOOD

(gwī′ă-cī lĭg′nŭm)

"Guaiacum Wood is the heart-wood of Guaiacum officinale, *Linn.*, or of Guaiacum sanctum, *Linn.*" *Br.* "The heart-wood of *Guaiacum officinale* Linné or of *Guaiacum sanctum* Linné (Fam. *Zygophyllaceæ*)." *N. F.*

Lignum Sanctum (vel Benedictum); Lignum Vitæ; Gayac, *Fr. Cod.*; Bois de Gayac, *Fr.*; Lignum Guajaci, *P. G.*; Guajakholz, Franzosenholz, Pockholz, *G.*; Guajaco, Legno guajaco, *It.*; Guayaco (Leño de), *Sp.*

Guaiacum officinale is a large tree, of a very slow growth. When of full size it is from forty to sixty feet high, with a trunk four or five feet in circumference. The branches are knotted, and covered with an ash-colored striated bark. That of the stem is of a dark-gray color, variegated with greenish or purplish spots. The leaves are opposite, and abruptly pinnate, consisting of two, three, and sometimes four pairs of leaflets, which are obovate, veined, smooth, shining, dark green, from an inch to an inch and a half long, and almost sessile. The flowers are of a rich blue color, stand on long peduncles, and grow to the number of eight or ten at the axils of the upper leaves. The seeds are solitary, hard, and of an oblong shape.

G. sanctum L. is distinguished from *G. officinale* by its five-celled fruit and its oblong or obliquely obovate or sometimes rhomboid-ovate leaflets, six to eight to each leaf. It grows in Cuba, the Bahama Islands and Florida. Its wood is smaller than that of *G. officinale*, and is said by Fée to be paler and less dense.

The commercial supplies are shipped from the Bahama Islands and Florida to London, Hamburg and Havre.

G. officinale grows throughout tropical America, particularly in the Lesser and Greater Antilles, also in Brazil, Venezuela and Colombia. The commercial drug is exported from Port au Prince, Puerto Plata and St. Domingo, also Savanilla (Colombia) and Puerto Cabello (Venezuela). *G. arboreum* of De Candolle has been said to furnish some of the guaiacum wood of commerce.

As imported, guaiac wood is in the shape of logs or billets, covered with thick gray bark, which presents on its inner surface, and upon its edges, when broken, numerous shining crystalline particles. These were supposed by Guibourt to be benzoic acid, by others a resinous exudation from the vessels of the plant; but Otto Berg has determined that they are crystals of calcium sulphate. The billets are used by turners for the fabrication of various instruments and utensils, for which the wood is well adapted by its extreme hardness and density. It is sometimes kept by pharmacists in the state of shavings or raspings, which they obtain from the turners. It is commonly called *lignum vitæ*, a name which obviously originated from its durable properties.

Properties.—Guaiacum wood is hard and heavy. The color of the sap-wood is yellow, that of the older and central layers greenish-brown, that of the shavings a mixture of the two. It is said that when the wood is brought into a state of minute division its color is rendered green by exposure to the air, and bluish-green by the action of nitric acid fumes, and the latter change may be considered as a test of its genuineness. (Duncan.) An easier test is a solution of corrosive sublimate, which, added to the shavings and slightly heated, causes a bluish-green color in the genuine wood. Guaiacum wood is almost without odor unless rubbed or heated, when it becomes odorous. When burned, it emits an agreeable odor. It is bitterish and slightly pungent, but requires to be chewed for some time before the taste is developed.

"Dark greenish-brown, dense, hard; heavier than water. In transverse section, abundant sclerenchymatous fibres, scattered, isolated vessels, and medullary rays one cell wide. Odor, on warming, somewhat aromatic; taste slightly acrid. An alcoholic tincture prepared from the Wood assumes a blue color on the addition of diluted *T. Sol. of ferric chloride.*" *Br.*

The N. F. IV describes it as follows: "Usually in the form of shavings, chips or raspings of a greenish-brown color, heavier than water, entirely free from adhering bark and containing only a few chips or shavings of a whitish color (*sap wood*). Almost odorless except when heated; taste bitter and acrid when chewed for some time. The powder, when examined under the microscope, exhibits numerous fragments of more or less lignified, thick-walled wood fibers, up to 0.028 mm. in width, some with simple, oblique pores; tracheæ from 0.09 to 0.16 mm. in width, some filled with resin; numerous small masses of resin; wood parenchyma and medullary ray cells up to 0.02 mm. in width, with lignified, porous walls and usually containing resin; occasionally tangential views of the medullary rays show an elliptical group of from three to six cells; the resin masses and resinous tissue become bluish-green on the addition of iodine T.S. Place powdered Guaiac Wood in a solution of sodium chloride (1 in 3); the blackish-brown part only will sink and this does not exceed in amount the portion which floats. Shake 10 mils of alcohol with 0.5 Gm. of ground Guaiac Wood for a few seconds and filter the mixture; the filtrate yields a deep blue color with one drop of a solution of ferric chloride (1 in 10). Guaiac Wood yields to alcohol not less than 15 per cent. of extractive. Guaiac Wood yields not more than 3 per cent. of ash." *N. F.*

Guaiac wood contains, according to Trommsdorf, 26 per cent. of resin, and 0.8 of bitter pungent extractive, upon both of which, probably, though chiefly on the former, its medicinal virtues depend. (See *Guaiacum.*) Paetzold (*Schim. Rep.*, 1902, 43) states that the bark of the guaiac tree yields 1 per cent. of a volatile oil, having an exquisite odor. The wood yields its virtues but slightly to water. One pound of the wood afforded to Geiger two ounces of extract.

Uses.—Guaiacum wood possesses no therapeutic powers which are not contained in its resin and the latter is always to be preferred.

Dose, thirty to sixty grains (2.0–3.9 Gm.).

Off. Prep.—Decoctum Sarsaparillæ Compositum, *N. F.*

GUAIACOL. U. S., Br.

GUAIACOL

(guaĭ'ą-cŏl)

"The monomethyl ether [$C_7H_8O_2$ or $C_6H_4(OH)(OCH_3)$ 1:2 = 124.06] of ortho-dihydroxybenzene, obtained from wood-tar creosote or prepared synthetically. Preserve it in well-closed containers, protected from light." *U. S.*

"Guaiacol, $C_7H_8O_2$, may be prepared synthetically or obtained by the fractional distillation of beech tar creosote." *Br.*

Ortho-dioxybenzene-methyl-ester, Methyl-orthodioxybenzene, Methyl-pyrocatechin, Catechol-monomethyl-ether; Gaïacol, *Fr. Cod.*; Guajakol, Brenzcatechin-monomethyl-ester, *G.*; Guajocolo, *It.*; Guayacol, *Sp.*

Preparation.—Guaiacol is the monomethyl ester of the ortho-dioxybenzene known as catechol (pyrocatechin), and can be readily made from this diatomic phenol by methylating with the aid of methyl-sulphuric acid. It is, however, largely obtained from beechwood creosote, of which it constitutes from 60 to 90 per cent. The separation of the diatomic phenols and phenol-ethers from monatomic phenols in a mixture like creosote, is effected in several ways. The compounds formed by baryta with the former are much less soluble than those with the latter, and this is also true of magnesia compounds. Another method is to rub up the creosote with potassium carbonate. Guaiacol and creosol combine to form solid addition compounds, from which the other phenols are washed out with ether or petroleum benzin, when the crystalline mass is decomposed with water and the phenols separated.

Properties.—It is officially described in the United States Pharmacopœia as "a colorless or yellowish, strongly refractive liquid, or a colorless or yellowish, crystalline solid, having an agreeable, aromatic odor. It becomes darker on exposure to light and air. The solid form

when liquefied may remain so for some time, even at a low temperature. One Gm. of Guaiacol dissolves in 53 mils of water and in 0.8 mil of glycerin at 25° C. (77° F.), but separates from the glycerin on the addition of water; miscible with alcohol, chloroform, ether or acetic acid. The specific gravity of liquid Guaiacol is between 1.110 and 1.114 at 25° C. (77° F.). Solid Guaiacol melts at about 28° C. (82.4° F.). Not less than 85 per cent. of Guaiacol distils between 200° and 210° C. (392° and 410° F.). The addition of a drop of ferric chloride T.S. to 10 mils of an alcoholic solution of Guaiacol (1 in 100) produces an immediate blue color, changing to emerald-green, and finally becoming yellowish. Incinerate about 1 Gm. of Guaiacol; not more than 0.1 per cent. of ash remains. Shake 2 mils of liquefied Guaiacol with 4 mils of purified petroleum benzin; the mixture separates on standing into two distinct, clear layers. Permanent turbidity or failure to separate into layers indicates the presence of impurities. One mil of liquefied Guaiacol dissolves in 2 mils of potassium hydroxide solution (15 per cent.), when heated for one minute in boiling water; on cooling, it congeals to a nearly white mass. Much coloration or failure to congeal indicates the presence of impurities. The mass thus obtained forms a clear solution with 20 volumes of distilled water (turbidity indicates *oily hydrocarbons*)." *U. S.*

"A colorless liquid, or colorless crystals melting at about 28° C. (82.4° F.). Characteristic, tarry odor; taste caustic, very pungent. Soluble in 80 parts of *water;* freely soluble in *alcohol* (90 per cent.), in *ether,* in *glycerin,* and in fixed oils. Liquid Guaiacol optically inactive; specific gravity 1.16 to 1.20. Distils between 200° and 205° C. (392°–401° F.). A trace of *T. Sol. of ferric chloride* added to 25 millilitres of a solution (1 in 100) of Guaiacol in *alcohol* (90 per cent.) immediately produces a blue color which changes to emerald-green on the addition of more of the test-solution, and finally becomes yellowish. When liquid Guaiacol is shaken with twice its volume of *petroleum spirit* and allowed to stand, the mixture separates into well-defined layers which do not exhibit permanent turbidity. 1 millilitre of liquid Guaiacol dissolves when warmed with 2 millilitres of an aqueous solution (15 in 100) of *sodium hydroxide;* the nearly white mass which results on cooling yields a clear solution with 25 millilitres of *water* (absence of oily hydrocarbons)." *Br.*

S. Vreven recommended the following method for distinguishing between guaiacol and creosote: A drop of the liquid to be examined, 2 to 3 drops of ether, and 1 or 2 drops each of concentrated nitric and hydrochloric acids are well shaken together in a test tube. The mixture assumes at first a red-brown color, which is particularly evident in the ether layer; but upon spontaneous evaporation, well-formed needle-shaped crystals will separate out if guaiacol is present, the formation of these crystals being facilitated by occasional shaking, whereas in the presence of creosote oily globules only separate. While phenol gives a reaction similar to that of guaiacol, the crystals formed are easily distinguished from the needles produced by the latter. (*Zeit. Oest. Apoth. Ver.,* 1896, 711.)

Uses.—Guaiacol is locally irritant and somewhat anesthetic. Its germicidal power, although inferior to that of creosote, equals or perhaps surpasses phenol. It is absorbed readily, not only from the alimentary canal, but also through the skin. It is eliminated chiefly through the kidneys in combination with sulphuric and glycuronic acids. Although its general physiological action has not been carefully studied, it seems to resemble phenol, although less poisonous. Guaiacol is used internally chiefly as a stimulating expectorant in *phthisis* and *bronchitis.* It has been also largely used by endermic administration as an antipyretic in *pneumonia* and other *fevers,* but is liable to produce dangerous collapse. Locally it is employed for its anesthetic effects in *herpes zoster, eczema, furunculosis,* and similar conditions, and as an antiseptic in *old ulcers,* especially when *tubercular* or *leprous.*

For percutaneous administration from ten to twenty drops are gently rubbed on the abdomen and the surface covered with oiled silk.

Dose, from five to ten minims (0.3–0.6 mil).

Off. Prep.—Petroxolinum Guaiacolis, *N. F.*

GUAIACOLIS CARBONAS. U. S. (Br.)

GUAIACOL CARBONATE Guaiacol. Carb.

(guaĭ'ą-cō-lĭs cär'bo-năs)

"A guaiacol derivative [$(C_7H_7O)_2CO_3$ or $(C_6H_4(OCH_3)O)_2.CO = 274.11$]." *U. S.* "Guaiacol Carbonate, $(C_7H_7O)_2CO_3$, is the carbonic ester of guaiacol. It may be obtained by the interaction of carbonyl chloride with sodium guaiacolate." *Br.*

Guaiacol Carbonas, *Br.,* Duotal; Carbonate de Gaïacol, *Fr.;* Guajacolkarbonat, Kohlensaure-Gaujacyläther, *G.;* Carbonato de guayacol, *Sp.*

Guaiacol carbonate was introduced into the British Pharmacopœia (1914) for the first time.

Properties.—It is officially described as "a crystalline powder, odorless and tasteless or having a slight, aromatic odor and taste. Guaiacol Carbonate is insoluble in water; 1 Gm. dissolves in 60 mils of alcohol, 1 mil of chloroform, and in 18 mils of ether at 25° C. (77° F.); freely soluble in benzene and slightly soluble in glycerin or fixed oils; freely soluble in boiling alcohol. It melts between 83° and 87° C. (181.4° and 188.6° F.). Incinerate 1 Gm. of Guaiacol Carbonate; not more than 0.1 per cent. of ash remains. A saturated alcoholic solution of Guaiacol Carbonate yields no bluish-green color on the addition of ferric chloride T.S. (*free guaiacol*), and is not acid to litmus paper which has been previously moistened with distilled water. One-tenth Gm. of Guaiacol Carbonate dissolves in 2 mils of sulphuric acid without producing more than a faint yellow color (*readily carbonizable impurities*). Heat about 0.5 Gm. of Guaiacol Carbonate for a few minutes with 10 mils of alcoholic potassium hy-

droxide T.S. and cool the mixture; a crystalline precipitate is formed, which effervesces with acids. If the alcohol is evaporated from the filtered liquid, the residue supersaturated with diluted sulphuric acid and shaken out with ether, the separated ether layer, upon spontaneous evaporation of the ether, leaves a residue which responds to the tests for identity under *Guaiacol." U. S.*

"A white crystalline powder, inodorous and almost tasteless. Insoluble in *water;* sparingly soluble in *alcohol* (90 per cent.), the solution being neutral to *litmus.* Melting point 85° to 88° C. (185°–190.4° F.). When the liquid obtained by heating Guaiacol Carbonate with *N/20 solution of sodium hydroxide* is acidified, carbon dioxide is evolved and guaiacol is liberated. A saturated solution in *alcohol* (90 per cent.) does not assume a greenish or bluish color on the addition of *T. Sol. of ferric chloride* (absence of free guaiacol). No appreciable ash." *Br.*

Uses.—Guaiacol carbonate is much used as a substitute for guaiacol on account of its comparative tastelessness and its lack of irritant properties. It is, however, much less active and less effective than is guaiacol, both as a local and systemic drug. The experiments of W. Hesse indicate that when taken internally much of it passes through the alimentary canal unabsorbed.

Dose, from ten to twenty grains (0.65–1.3 Gm.).

GUAIACUM. U. S. (Br.)

GUAIAC Guaiac. [Guaiaci Resina, Pharm. 1890, Guaiac Resin]

(guaĭ'ạ-cŭm)

"The resin of the wood of *Guaiacum officinale* Linné, or of *Guaiacum sanctum* Linné (Fam. *Zygophyllaceæ*)." *U. S.* "Guaiacum Resin is the resin obtained from the stem of Guaiacum officinale, *Linn.,* or of Guaiacum sanctum, *Linn.*" *Br.*

Guaiaci Resina, *Br.,* Guaiacum Resin; Résine de Gayac. *Fr. Cod.;* Resina Guajaci, *P. G.;* Guajak, Guajakharz, *G.;* Resina de guajaco, *It.;* Resina de guayaco, *Sp.*

For a description of *Guaiacum officinale,* see *Guaiaci Lignum,* p. 535.

Guaiac resin was introduced into the London Pharmacopœia in 1677. It exists in the tree as a physiological product filling up the tissues of the wood. It is obtained in several different modes. The most simple is by spontaneous exudation, or by incisions made into the trunk. Another method is by sawing the wood into billets about three feet long, boring them longitudinally with an auger, then placing one end of the billet on the fire, and receiving in a calabash the melted guaiac, which flows out through the hole at the opposite extremity. But the plan probably most frequently pursued is to boil the wood, in the state of chips or sawdust, in a solution of common salt, and skim off the substance which arises to the surface. Guaiac is chiefly produced in the eastern portion of the Island of Haiti, being exported from Port au Prince and Gonaïves. (*Ap.-Ztg.,* xxv, p. 556.) It is estimated that in 1912 about 6000 pounds of guaiac resin were exported to the United States. It is usually in large irregular pieces of various sizes, in which small fragments of bark, sand, and other impurities are mixed with the genuine guaiac, so as to give to the mass a diversified appearance. Sometimes it is found in small roundish homogeneous portions, separate or agglutinated; sometimes in homogeneous masses, prepared by melting and straining the drug in its impure state. It is probable that the guaiac obtained from the billets in the manner above described is of uniform consistence.

Properties.—The masses are irregular or somewhat globular, of a glassy luster and resinous fracture. They are of a deep greenish-brown or dark-olive color on their external surface, and internally wherever the air can penetrate. The predominant hue of those parts not exposed to the air is reddish-brown or hyacinthine, diversified, however, with shades of various colors. The odor is feeble but fragrant, and is rendered stronger by heat. The taste, which is at first scarcely perceptible, becomes acrid after a short period, and a permanent sense of warmth and pungency is left in the mouth and fauces. Guaiac is brittle, and when broken presents a shining glass-like surface, conchoidal or splintery, with smaller fragments more or less translucent. It is readily pulverized, and the powder, at first of a light-gray color, becomes green on exposure to the light. Its sp. gr. varies from 1.2 to 1.23. It softens in the mouth, and melts with a moderate heat. Water dissolves a small proportion of guaiac, not exceeding nine parts in 100, forming an infusion of a greenish-brown color and sweetish taste, which upon evaporation yields a brown substance soluble in hot water and alcohol, but scarcely so in ether. Alcohol takes up the whole, with the exception of impurities. The official requirements are as follows: "In irregular fragments or in large, nearly homogeneous masses, occasionally in more or less rounded or ovoid tears, enclosing fragments of vegetable tissues; externally brown, becoming greenish-gray-brown on exposure, the fractured surface having a glassy luster, the thin pieces being translucent and varying in color from reddish to yellowish-brown; odor balsamic; taste slightly acrid. Guaiac melts between 85° and 90° C. (185° and 194° F.). It is readily soluble in alcohol, ether, chloroform, creosote, and in solutions of the alkalies or in hydrated chloral T.S. It is sparingly soluble in carbon disulphide or benzene and not more than 15 per cent. is insoluble in alcohol; the alcoholic solution, on the addition of an excess of chlorine water or tincture of ferric chloride, becomes blue, changing quickly to green, the color being best seen when the solutions are diluted with an equal volume of water. Macerate the crushed or powdered Guaiac with 4 or 5 times its weight of purified petroleum benzin for three hours and then filter; the filtrate

is colorless, and does not give a green color on the addition of an equal volume of cupric acetate T.S. (*rosin*). The powder is grayish, becoming green on exposure to the air. Guaiac yields not more than 4 per cent. of ash." *U. S.*

"In masses, or sometimes in large more or less rounded tears. Brittle; fracture vitreous; thin splinters transparent, from yellowish-green to reddish-brown. Powdered Resin greyish, but becoming green on exposure to light and air. Odor, on warming, somewhat aromatic; taste slightly acrid. A solution in *alcohol* (90 per cent.) is colored blue by diluted *T. Sol. of ferric chloride.* 1 gramme of the powdered Resin, shaken for five minutes with 5 millilitres of *petroleum spirit,* yields a colorless filtrate which does not become green when shaken with an equal volume of *diluted solution of copper acetate* (absence of colophony). Not more than 10 per cent. insoluble in *alcohol* (90 per cent.). Ash not more than 4 per cent." *Br.*

The tincture is of a deep-brown color, is decomposed by water, and affords blue, green, and brown precipitates with the mineral acids. It is colored blue by nitric acid, by chlorine, and by tincture of ferric chloride, and usually by spirit of nitrous ether, and is similarly changed when treated successively by diluted hydrocyanic acid and solution of copper sulphate. Either in substance or tincture, guaiac gives a blue color to gluten and substances containing it, to mucilage of gum arabic, to milk, and to various freshly cut roots, as to the potato, carrot, and horseradish. This is on account of the fact that oxidizing enzymes or oxidases are present in all of these substances and guaiac resin is one of the most delicate reagents for detecting this class of enzymes. It is soluble also in ether, alkaline solutions, and sulphuric acid. The solution in sulphuric acid is of a rich claret color, deposits, when diluted with water, a lilac precipitate, and, when heated, yields charcoal. Exposed to air and light, guaiac absorbs oxygen and becomes green, and the change takes place rapidly in the sunshine. Schaer states that a good natural guaiac resin is preferable to a resin purified by alcoholic treatment as a reagent, but a solution of resin extracted by chloroform from the wood is the most sensitive of all. Tincture of guaiac has been used for the detection of blood stains, which it does by the blue color produced by it, when in contact with the red coloring matter of blood, in connection with some ozonized substance, especially hydrogen dioxide. R. M. Bertolet (*Am. J. M. S.,* Jan., 1874) has used it to distinguish between the blood of man and other mammals, in which the corpuscles are non-nucleated, from that of other classes, as birds, fishes, and reptiles, which have nucleated corpuscles.

Lücker (*Proc. A. Ph. A.,* 1894, 953), finds in guaiac three acids,—viz., *guaiacic,* $C_{20}H_{24}O_4$, occurring in crystals melting at 86° C. (186.8° F.); *guaiaconic,* $C_{20}H_{24}O_5$, an amorphous body melting at from 81° to 83° C. (177.8°–181.4° F.); and *guaiacinic,* $C_{21}H_{22}O_7$. He considers all three of them to be probably condensation products from tiglic aldehyde with creosol and guaiacol. Döbner has also determined that these three acids form a series of hydroxyl-containing acids which may be represented by the formulas: $C_{20}H_{23}O_3(OH)$, $C_{20}H_{22}O_3(OH)_2$ and $C_{21}H_{19}O_4(OH)_3$. (Tschirch, *Harze und Harzbehälter,* 1900, p. 300.) *Guaiac yellow,* the coloring matter of guaiac resin, was first observed by Pelletier. It crystallizes in pale yellow quadratic octahedra having a bitter taste, but is not a glucoside. Guaiac resin also yields interesting products on dry distillation. First, according to Hlasiwetz, is obtained *guaiacene,* C_5H_8O, at 118° C. (244.4° F.), next *guaiacol,* $C_6H_4\begin{cases}OCH_3\\OH\end{cases}$, being the methyl ether of pyrocatechin, at 205° to 210° C. (401°–410° F.), and with it *kreosol,* $C_6H_3(CH_3)_2OH$, and finally *pyroguaiacin,* $C_{33}H_{44}O_6$ (according to Wiesner, $C_{18}H_{18}O_3$), in pearly scales, melting at 180° C. (356° F.). According to Lieben and Zeisel (*Ber. d. Chem. Ges.,* xiv, p. 932), guaiacene is the aldehyde of tiglic acid, $C_5H_8O_2$, and can be made synthetically from a mixture of acetaldehyde and propionaldehyde. When distilled with zinc dust there is obtained *creosol* (50 per cent. in the case of resin purified by alcohol) and 30 per cent. of a mixture of *toluene, meta-* and *paraxylene,* with a little *pseudocumene* and *guaion,* $C_{12}H_{12}$.

Saponin has been found by E. Paetzold in the bark, the wood, and the natural resin of guaiacum. (*Bull. des Sciences Pharm.,* iii, 407.) According to the experiments of W. Frieboes (*In. Dis.,* Rostock, 1903), this saponin (1 to 1000) forms a frothing solution which is persistent, is an excellent emulsifier, has the power to maintain in solution large proportions of sparingly soluble substances and is innocuous and non-irritant.

The mineral acids are incompatible with the solutions of guaiac.

Adulterations.—This drug is sometimes adulterated with the rosin of the pine. The fraud may be detected by the terebinthinate odor exhaled when the sophisticated guaiac is thrown upon burning coals, as well as by its partial solubility in hot oil of turpentine. This liquid dissolves rosin, but leaves pure guaiac untouched. Amber was said to be another adulterant at one time. Nitric acid affords an excellent test of guaiac. If paper moistened with the tincture be exposed to the fumes of this acid, it speedily becomes blue. Purgotti proposed guaiac resin as a test for copper. (See *A. J. P.,* June, 1880.)

Uses.—Guaiac, like many other resinous substances, is stimulant and alterative. If given to a patient when covered warm in bed, and accompanied with hot drinks, may assist in exciting perspiration, and hence it has been ranked among the diaphoretics. In large doses it purges, and it has been especially commended as a laxative in *chronic rheumatism,* and it is thought by some practitioners to be possessed of emmenagogue powers. It has been given in *chronic rheumatism, gouty affections,* secondary *syphilis, scrofulous diseases,* and *cutaneous eruptions,* but is

of doubtful service. The medicine is given in substance or tincture. The dose of the powder is from ten to thirty grains (0.65–2.0 Gm.), which may be exhibited in pill or bolus, in the shape of an emulsion formed with gum arabic, sugar, and water, or as a syrup. An objection to the form of powder is that it quickly aggregates. Guaiac is sometimes administered in combination with alkalies, with which it readily unites. The ammoniated tincture of guaiac is a preparation of this kind. Several European Pharmacopœias direct a *soap of guaiac,* under the name of *sapo guaiacinus,* to be prepared by diluting solution of potassium hydroxide with twice its weight of water, boiling lightly, then adding guaiac gradually, with continued agitation, so long as it continues to be dissolved, and finally filtering, which was followed by evaporating to the pilular consistence.

T. C. Craig (*A. J. P.,* July, 1880) recommends a *Syrup of Guaiac* made as follows: Powd. Guaiac Resin, 640 grains; Caustic Potassa, 58 grains; White Sugar, 1 lb. (av.); Water, q. s. Dissolve the Potassa in 8 fluidounces of water; moisten the Guaiac with this solution; pack it in a percolator, and gradually pour on the remainder of the solution; when this ceases dropping, add sufficient water to make the percolate measure 8 fluidounces; add the sugar, and dissolve.

Dose, from ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Mistura Guaiaci, *Br.;* Pilula Hydrargyri Subchloridi Composita, *Br.;* Tinctura Guaiaci, *U. S.;* Tinctura Guaiaci Ammoniata, *U. S., Br.;* Trochiscus Guaiaci Resinæ, *Br.;* Gargarisma Guaiaci Compositum, *N. F.;* Glyceritum Guaiaci, *N. F.;* Mistura Guaiaci (from Tincture), *N. F.;* Pilulæ Antimonii Compositæ, *N. F.;* Tinctura Guaiaci Composita, *N. F.*

GUARANA. U. S.

GUARANA

(guạ-rā′nạ)

"A dried paste consisting chiefly of the crushed seeds of *Paullinia Cupana* Kunth (Fam. *Sapindaceæ*), yielding not less than 4 per cent. of caffeine." *U. S.*

Paullinia, Brazilian Cocoa, Guarana Bread; Guarana, *Fr. Cod.;* Pasta Guaranæ; Guarana, *G., It.;* Paulinia, Guarana, *Sp.*

There are described of the genus *Paullinia* 121 species, all of them confined in their geographical range to tropical and subtropical South America, except one, which has strayed to Eastern and Western Africa, and two others which are found in Mexico and in the gardens of the Sandwich Islands. The name of the genus was given in honor of Christ. Fred. Paullini, a German medico-botanical writer, who died in 1712.

The *Paullinia Cupana* Kunth is a climbing shrub with alternate compound impari-pinnate leaves, which is native to the Northwestern provinces of Brazil. The flowers are of yellowish color, growing in spicate panicles. The leaves are long petioled, the leaflets being 5 to 6 inches long by 2 or 3 inches wide, and sinuate dentate on the margins. The fruit is ovoid or pyriform and about the size of a grape, and contains 1 to 3 seeds which resemble small horse chestnuts.

It is probable that in the preparation of guarana the seeds of the allied species *P. sorbilis* Martius, are used interchangeably with those of the official species.

The seeds, which look like small horse-chestnuts, are lenticular and almost thorny, and invested with a flesh-colored arillus, which is easily separable when dry. *Guarana* is made exclusively by the Guaranis, a tribe of South America Indians, and probably varies in the details of its preparation, as it certainly does in appearance and quality. The drug appears to be produced almost exclusively from plants cultivated in the region of the lower Madeira and southward. After the seeds are shelled and thoroughly washed they are roasted for about six hours, and their external papery shells are then removed by placing them in sacks and beating them with clubs; or, after the seeds have been broken in a mortar, the coarse powder is mixed with a little water, and then kneaded into a paste, which is shaped into cylindrical or globular masses. The latter are dried, sometimes in the sun, or more usually by the heat of a slow fire so arranged as to avoid smoke. When finished, the masses are of a reddish-brown color, rugose on the surface, very hard, with an irregular fracture, and of a marbled appearance when broken, due to the fragments of the seeds and their black testa embedded in the mass.

Guarana occurs in a number of molded forms, and an excellent collection of these can be found in the Philadelphia Commercial Museum. Stockman (*P. J.,* liii; *P. J.,* lxxxix, p. 685) describes and illustrates some of these interesting forms.

Properties.—It is officially described as follows: "Usually in cylindrical sticks, about 3 to 5 cm. in diameter, externally dark reddish-brown; hard and heavy; fracture uneven, often fissured in the center; internally pale reddish-brown, showing more or less coarse fragments of seeds and occasionally their blackish-brown integuments; odor slight; taste slightly astringent and bitter. The powder is light pinkish-brown; consisting mostly of irregular masses of parenchyma containing more or less altered starch grains; unaltered starch grains occasional, varying from spherical and polygonal to ellipsoidal and broadly ovoid, 0.01 to 0.025 mm. in diameter; occasional fragments with narrow, elongated sclerenchymatous cells; the walls being thick, yellowish and non-lignified. Place on a slide a drop of hydrochloric acid, add about 0.001 Gm. of powdered Guarana, then add a drop of gold chloride T.S. and allow the mixture to stand for a few minutes; beginning at the edge of the mount, crystals of caffeine and gold chloride separate in the form of orthorhombic plates and needles, the latter usually occurring in spheroidal aggregates and finally forming branching groups.

"**Assay.**—Introduce 6 Gm. of Guarana, in No. 60 powder, into a flask and add 120 mils of chloroform and 6 mils of ammonia water. Stopper the flask, shake it frequently for half an hour, then let it stand four hours. Again shake the flask vigorously and when the drug has settled, filter the liquid rapidly through a pledget of purified cotton and collect 100 mils of the filtrate, representing 5 Gm. of Guarana. Evaporate the clear filtrate to dryness and dissolve the residue in weak sulphuric acid with the aid of a gentle heat. When the liquid has cooled, filter it into a separator and wash the container and filter with several small portions of distilled water. Now add ammonia water until the liquid is distinctly alkaline to litmus and shake out the caffeine with chloroform until completely extracted, as shown by testing with iodine T.S. in place of the usual mercuric potassium iodide T.S. Evaporate the united chloroform solutions and dry the residue to constant weight at 80° C. (176° F.). The weight is the amount of caffeine from 5 Gm. of Guarana (see Proximate Assays, Part III)." *U. S.*

Guarana is of a somewhat astringent and bitterish taste, and in this, as well as in its odor, bears some resemblance to chocolate, though not oleaginous. It swells up and softens in water, which partially dissolves it. It is also partly soluble in alcohol. Martius found in it a crystallizable principle, which he named *guaranine*, but which was later proved by Berthemot and Dechastelus to be identical with *caffeine*. Alexander Bennett, in an elaborate series of physiological experiments, confirmed this identity Caffeine may be obtained by microsublimation and Rosenthaler (*B. P. G.*, xxi, p. 532) describes the crystals obtained from guarana by means of pyroanalysis. According to Berthemot and Dechastelus, the caffeine exists in the seeds united with tannic acid, with which it appears to form two compounds, one crystallizable and soluble in water, the other of a resinoid appearance and insoluble. Besides these ingredients the seeds contain free tannic acid, gum, albumen, starch, and a greenish fixed oil. (*J. P. C.*, xxvi, 514.)

M. I. Wilbert (*J. A. Ph. A.*, 1914, 1286) reported a compilation of analyses of guarana comprising 41 samples in which the caffeine content varied from 3.72 to 5.16 per cent.

Rochefontaine and Gusset prepared caffeine by mixing one part of calcined magnesia with five parts of powdered guarana, moistening with water, and, after standing twenty-four hours, exhausting the mass with boiling chloroform, evaporating the chloroform, treating the residue with boiling water, filtering, and evaporating over sulphuric acid. (*A. J. P.*, 1886, p. 248.) F. V. Greene (United States Navy) prefers a process for obtaining caffeine from guarana similar to one proposed by Wayne for its extraction from tea and coffee. See *U. S. D.*, 19th ed., p. 606.

F. V. Greene has shown that the tannic acid from guarana has different properties from that found in other plants, and proposes to call it *paullinitannic acid*. (*A. J. P.*, 1877, 390.) Fournier has found in guarana, besides caffeine tannate, the following principles: gum, starch, an acrid green fixed oil, a concrete volatile oil, an aromatic liquid volatile oil soluble in water with a little alcohol, another liquid volatile oil scarcely soluble in water, a peculiar principle not precisely determined, and tannic acid. (*J. P. C.*, April, 1861, 291.) E. R. Squibb examined commercial guarana, and obtained 4.38 per cent. of alkaloid from good specimens. On account of the uncertainty of the composition of guarana, he recommended physicians to prescribe fluidextract of green coffee in its place. (See *Ephem.*, 1884, 612.)

Uses.—The effects of guarana upon the system are chiefly those of its alkaloid, although it contains enough tannin to have an appreciable influence. It is habitually employed by the Indians, either mixed with articles of diet, as with cassava or chocolate, or in the form of drink, prepared by scraping it, and suspending the powder in sweetened water, precisely as other nations use teas, coffees, etc. It is also considered by the Indians useful in the prevention and cure of bowel complaints. Gavrelle, who was at one time physician to Dom Pedro, in Brazil, and there became acquainted with the virtues of this medicine, called the attention of the profession to it some years since in France. It is now used in medicine almost exclusively to give relief during the paroxysm of *migraine*, and in atonic *chronic diarrhea*, taken three or four times a day.

Dose, of the powder, twenty to sixty grains (1.3–3.9 Gm.); of the fluidextract, twenty to sixty minims (1.3–3.75 mils).

Off. Prep.—Fluidextractum Guaranæ, *U. S.*; Elixir Guaranæ (from Fluidextract), *N. F.*

GUMMI INDICUM. Br.

INDIAN GUM [Ghatti Gum]

(gŭm'mī ĭn'dĭ-cŭm)

"Indian Gum is a gummy exudation from the stem of Anogeissus latifolia, *Wall.*" *Br.*

The genus *Anogeissus* (Fam. *Combretaceæ*) includes four or five different species of tropical trees. Of these *A. latifolia* is widely distributed in Farther India. The tree is large and handsome, and one of the most useful of tropical India. The leaves are broadly elliptical, obtuse at the base and summit. They contain large amounts of tannin and are used in Bombay for tanning. The flowers are axillary and the fruit is 2-winged, being arranged horizontally into dense heads. The gum from this tree is collected in April and is used extensively in calico printing, especially in Lucknow. It is less adhesive than Acacia and is usually used in connection with turmeric with which there is some specific combination.

"In vermiform or rounded tears of varying size, colorless or pale yellow; surface dull, fracture vitreous. Slight odor; taste insipid and

mucilaginous. Entirely soluble in *water,* forming a viscous, adhesive mucilage. Insoluble in *alcohol* (90 per cent.). The aqueous solution is gelatinised by the addition of *alcohol* (90 per cent.), or *solution of lead subacetate;* but it is unaffected by the addition of *T. Sol. of ferric chloride* or of *solution of lead acetate* (distinction from Amrad and certain other gums). It is not colored blue or brown by a small quantity of *N/10 solution of iodine* (absence of starch or commercial dextrin). Ash not more than 4 per cent. In India and the Eastern Divisions of the Empire, Indian Gum may be employed in making the official preparations for which Gum Acacia is directed to be used, one part of the former being taken for every two parts ordered of the latter (see 'Mucilago Gummi Indici')." *Br.*

Uses.—Indian gum is used for the same purposes in pharmacy as acacia. It must not be confounded with the so-called *India Gum* which is only slightly soluble in water. (See p. 3.)

Off. Prep.—Mucilago Gummi Indici, *Br.*

HÆMATOXYLI LIGNUM. Br.

LOGWOOD

(hæ'mą-tŏx'ȳl-ī lĭg'nŭm)

"Logwood is the heart-wood of Hæmatoxylon campecheanum, *Linn." Br.* "The heart-wood of *Hæmatoxylon campechianum* Linné (Fam. *Leguminosæ*) that has not undergone fermentation." *N. F.*

Hæmatoxylon, *N. F.*; Lignum Campechianum, Lignum Cœruleum; Bois de Campêche ou Bois d'Inde, *Fr. Cod.*; Bois de Sang, *Fr.*; Blauholz, Campecheholz, Blutholz, Kampeschenholz, *G.*

Hæmatoxylon campechianum is a tree of middle size, usually not more than twenty-four feet high, though, under favorable circumstances, it sometimes rises forty or fifty feet. The trunk is often very crooked, and is covered with a dark rough bark. The branches are beset with sharp spines. The sap-wood is yellowish, but the interior layers are of a deep-red color. The leaves are alternate, abruptly pinnate, and composed of three or four pairs of sessile, nearly obcordate, obliquely nerved leaflets. The flowers, which are in axillary spikes or racemes near the ends of the branches, have a brownish-purple calyx and lemon-yellow petals. They exhale an agreeable odor, said to resemble that of the jonquil.

The tree is a native of Campeche, the shores of Honduras Bay, and other parts of tropical America, and has become naturalized in Jamaica. It is cultivated in tropical America and Asia. The wood, which is the part used in medicine, is a valuable article of commerce, and largely employed in dyeing. It comes to us in logs deprived of the sap-wood and having a blackish-brown color externally. It has been estimated that about 400,000,000 pounds of logwood are annually consumed. In 1912 Haiti exported about 83,000,000 pounds of logwood to the United States. (See *A. J. P.,* 1912, p. 86.) According to Louis Siebold, the ground or chipped logwood of commerce is unfit for use as a medicinal agent, because it has been prepared as a dyestuff by being exposed in large moist heaps until its hematoxylin has been converted by oxidation into hematein. As a coloring agent, for commercial purposes, this fermented logwood, according to Siebold, is much superior to the natural wood. An inferior variety of logwood which contains little or no hematoxylin, but a pure yellowish-gray dye is that known as *bastard logwood.* According to the researches of E. S. Earl this bastard logwood is produced by a variety of the species, which, when growing, cannot be distinguished from the ordinary form. (*B. D. A. J.,* i, 31.)

Properties.—Logwood is hard, compact, heavy, of a deep-red color, becoming purplish-black by exposure, internally brown-red, and marked with irregular, concentric circles, splitting irregularly, of a slight peculiar odor, and a sweet, somewhat astringent taste. Logwood is officially described as "Hard, heavy, dull orange to purplish-red externally and reddish-brown internally. In transverse section, alternating yellowish-brown and dark brown wavy tangential lines. In the form of chips or coarse powder, it is free from signs of fermentation, and from green metallic lustre. Slight, agreeable odor; taste sweetish, astringent. Readily imparts a reddish-violet color to *water* made slightly alkaline with *solution of sodium hydroxide." Br.*

The N. F. IV description is as follows: "Usually in small chips, reddish-brown, the freshly cut surface dark yellowish-red; a transverse section of the wood shows medullary rays which are up to four cells wide. Odor faint, agreeable; taste sweetish, astringent. Hematoxylon imparts a yellowish color to water containing a little acid, the color being changed to purple or violet-red by alkalies. The powder is reddish-brown and, when examined under the microscope, exhibits medullary ray cells in one to seven rows; wood fibers, long, with thickened walls; wood parenchyma with occasional crystals of calcium oxalate; tracheæ from 0.09 to 0.17 mm. in width; walls of the cells colored brownish-red, the inner cells containing resin masses. Hematoxylon yields not more than 3.5 per cent. of ash." *N. F.*

Its solution affords precipitates with sulphuric, nitric, hydrochloric, and acetic acids, alum, copper sulphate, lead acetate, and ferrous sulphate, striking a bluish-black color with the last mentioned salt. Precipitates are also produced with it by lime water and gelatin. Chevreul found in logwood a volatile oil, an oleaginous or resinous matter, a brown substance the solution of which is precipitated by gelatin (*tannin*), another brown substance soluble in alcohol but insoluble in water or ether, a nitrogenous substance resembling gluten, free acetic acid, various salts, and a peculiar principle called *hæmatoxylin* or *hæmatin* (which must not be confused with the hæmatin of the blood), on which the coloring properties of the wood depend. This is ob-

tained by digesting the aqueous extract in alcohol, evaporating the tincture until it thickens, then adding a little water, and submitting the liquid to a new but gentle evaporation. Upon allowing it to rest, hematoxylin is deposited in crystals, which may be purified by washing with alcohol and drying. Thus procured, the crystals are shining, of a yellowish-rose color, bitterish, acrid, and slightly astringent to the taste, readily soluble in boiling water, forming an orange-red solution which becomes yellow on cooling, and soluble also in alcohol and ether. According to Erdmann, who obtained hematoxylin by the process of Chevreul, substituting ether for alcohol, its crystals, when quite pure, are colorless, without a tinge of redness; its taste is sweet, like that of licorice, without bitterness or astringency; and it is not of itself a coloring substance, but affords beautiful red, blue, and purple colors, by the joint action of an alkaline base and the oxygen of the air. He obtained from logwood 9 to 12 per cent. of crystallized hematoxylin, to which he gave the formula $C_{16}H_{14}O_6$. It crystallizes with 1 or with 3 molecules of water, and is readily soluble in hot water or alcohol, but sparingly in cold water or in ether. (*J. Pr. Chem.*, xxxvi, p. 205.) By the combined action of ammonia and oxygen dark violet crystalline scales of *hematein*, $C_{16}H_{12}O_6 + 3H_2O$, are produced. They show a fine green hue, which is also very commonly observable on the surface of the logwood chips of commerce. Hematein may again be transformed into hematoxylin by means of nascent hydrogen or of sulphurous acid. Commercial extract of logwood extracted from the wood by boiling water contains both hematoxylin and hematein. Hematoxylin, in alcoholic solution, is used as an indicator in the U. S. P. IX. (See Hematoxylin Test-solution, Part III.)

Uses.—Logwood is a mild astringent, devoid of irritating properties, and well adapted to the treatment of that relaxed condition of bowels which is apt to succeed *cholera infantum*. It is also occasionally used with advantage in ordinary *chronic diarrhea* and *chronic dysentery*. *Hematoxylin* was found by Combemale (*B. M. N.*, xxxiii, 1894) to be very feebly antiseptic, but capable in large doses of producing fatal gastro-enteritis in the lower animals. It is used not only as a dye-stuff but also as a microscopical stain.

Dose, from ten to thirty grains (0.65–1.9 Gm.).

Off. Prep.—Decoctum Hæmatoxyli, *Br.*

HAMAMELIDIS CORTEX. Br.

HAMAMELIS BARK [Witchhazel Bark]

(hăm-ą-mĕl'ĭ-dĭs cŏr'tĕx)

"Hamamelis Bark is the dried bark of Hamamelis virginiana, *Linn.*" *Br.*

Hamamelidis Cortex, *U. S. VIII*, Witchhazel, Spotted Hazel, Snapping Hazel, Winterbloom; Ecorce de Hamamelis, *Fr. Cod.*; Hamamelis, Zauberhasel, *G.*; Hamamelis, *Sp.*

This bark was deleted from the U. S. P. IX, but retained by the British Pharm., 1914. The U. S. P. VIII definition was as follows: "The bark and twigs of *Hamamelis virginiana* Linné (Fam. *Hamameliadaceæ*)."

Witchhazel is an indigenous shrub, from five to fifteen feet high, growing in almost all sections of the United States, usually on hills or in stony places, and often on the banks of streams. It is the only species of the genus found in Eastern North America, occurring from New Brunswick to Minnesota and southward to Florida and Texas. Schneider asserts that it has been introduced into California and that it is extensively cultivated in this locality. It is specifically characterized by its leaves being obovate or oval, wavy-toothed, and somewhat downy when young. The seeds are black and shining externally, white, oily, and farinaceous within, and edible like the hazelnut. It is remarkable for the late appearance of its yellow flowers, which expand in September or October, and continue until the weather becomes very cold in winter. The fruit, which is a nut-like capsule not unlike the hazelnut, ripens in the following summer, and is often mingled on the same plant with the new blossoms.

Properties.—The bark occurs "in curved or channelled pieces about one and a half millimetres thick, and from one-half to two decimetres long, sometimes covered with a silvery-grey or dark-grey scaly cork marked with transverse lenticels, but frequently freed from the cork, and then exhibiting a nearly smooth reddish-brown outer surface. Inner surface pale reddish-pink, and finely striated longitudinally; fracture laminated and coarsely fibrous. In transverse section, a cortex containing prismatic crystals of calcium oxalate, a complete ring of sclerenchymatous cells, and numerous tangentially elongated groups of bast fibres. No marked odor; taste astringent." *Br.*

The twigs are "flexible and tough, of irregular length, not more than 6 Mm. in diameter, branching, or bearing nodes at intervals of 2 to 5 Cm.; externally varying from yellowish-brown to deep purplish-brown, lightly longitudinally wrinkled, and having scattered small circular whitish or pale lenticels; bark occupying about one-fifth of the radius; wood greenish-white, lightly radiate, and exhibiting one to three annual rings; pith centric, small." *U. S. VIII.*

Holm (*Merck's Rep.*, xxi, p. 5) has written an illustrated paper on the morphology of hamamelis.

Walter B. Cheney examined witchhazel bark, and found tannin, resin, extractive, but no indication of an alkaloid or other crystalline principle. (*A. J. P.*, 1886, p. 418.) It contains a trace of volatile oil, however. John Marshall, of the University of Pennsylvania, also found that hamamelis root contains tannic acid and a trace of volatile oil, but no other active substance. (*T. G.*, ii, 295.)

Uses.—The bark of the witchhazel is said to have first attracted attention on account of its

use by the North American Indians as a sedative application to external inflammations. It was many years ago recommended by James Fountain and N. S. Davis (*N. Y. M. J.*, x, 208; *Trans. Amer. Med. Assoc.*, i, 350) in *hemorrhage* of the *lungs* and *stomach*. Professional attention was strongly directed to the remedy on account of the enormous sale of a much vaunted proprietary remedy said to be made by distilling the bark with very dilute alcohol (six per cent.), and used externally for *sprains* and *bruises*, and internally for most of the diseases to which flesh is heir. The pecuniary success of this remedy probably depended in very small part upon the virtues of the witchhazel, which seems to possess no active physiological properties. At least we have injected a very concentrated distillate in large quantities into frogs and into mammals without perceiving any more effects than would be produced by the injection of similar quantities of distilled water, and Guy, in Paris, has reached similar conclusions. This preparation has been so largely used that it has been widely replaced by a similar preparation officially known as *Aqua Hamamelidis*, which see. The fluidextract of the drug is a mild astringent and has been especially recommended in *varicose veins* and *hemorrhoids*. The dose of the fluidextract given ordinarily is a teaspoonful (3.75 mils) four times a day. It may, however, be given in double the quantity with impunity and probably in such doses is an advantageous astringent.

Dose, of leaves or of bark, thirty grains (2 Gm.).

Off. Prep.—Aqua Hamamelidis, *U. S.*; Tinctura Hamamelidis, *Br.*

HAMAMELIDIS FOLIA. Br.

HAMAMELIS LEAVES [Hamamelis, U. S. 1890 Witchhazel Leaves]

(hăm-ą-mēl'ĭ-dĭs fō'lĭ-ą)

"Hamamelis Leaves are the fresh or dried leaves of Hamamelis virginiana, *Linn.*" *Br.* "The dried leaves of *Hamamelis virginiana* Linné (Fam. *Hamamelidaceæ*), collected in autumn before the flowering of the plants, and without the presence of more than 10 per cent. of stems or other foreign matter." *N. F.*

Hamamelidis Folia, *N. F.*; Feuilles de Hamamelis, *Fr. Cod.*; Witchhazel, Witch Hazel Leaves.

These leaves were deleted from the U. S. P. IX, but were retained in the British Pharm., 1914, and National Formulary IV.

The National Formulary IV added the following to the U. S. P. VIII definition: "Before the flowering of the plants and without the presence of more than 10 per cent. of stems or other foreign matter."

The British Pharm., 1914, describes the leaves as follows: "Broadly oval in outline, from seven to fifteen centimeters long. Upper surface dark green or brownish-green, under surface paler; apex obtuse, margin sinuate; narrowed towards the base, oblique, slightly cordate, and shortly petiolate. Veins pinnate and prominent on the under surface, where they are furnished with stellate hairs. No marked odor; taste astringent and slightly bitter." *Br.*

The N. F. IV description is as follows: "Petioles from 1 to 1.5 cm. in length; laminæ when entire broadly elliptical or rhomboid-ovate, usually inequilateral, mostly from 8 to 12 cm. in length; summits usually acute, sometimes rounded or acuminate; bases slightly heart-shaped and oblique; margins sinuate or sinuate-dentate; upper surfaces pale or brownish-green, occasionally dark brown with a few stiff, straight hairs; lower surfaces lighter in color, somewhat hairy, midrib and veins prominent. Odor slight; taste astringent, slightly aromatic and bitter. Transverse sections show in addition to the epidermal layers, a palisade layer consisting of a single row of cells and a dorsal pneumatic tissue made up of three to six rows of strongly branching cells; large collateral, fibro-vascular bundles occur in the midrib and petiole, the tracheæ narrow, mostly spiral and associated with numerous narrow, strongly lignified and porous wood fibers; around the phloem occurs a nearly continuous circle of bast fibers, possessing strongly lignified walls; calcium oxalate in monoclinic prisms, from 0.01 to 0.035 mm. in diameter, either in the cells of the mesophyll or in crystal fibers associated with the bast fibers. Under the microscope, surface sections of Hamamelis Leaves show upon the lower surface narrow elliptical stomata, about 0.015 mm. in length and with two to four neighboring cells; from both surfaces, but especially from the under surface, arise stellate hairs composed of from four to twelve cells united at the base, the individual cells being from 0.02 to 0.075 mm. in length, either straight or more or less bent and with very thick walls and narrow lumina, the latter sometimes only apparent in the lower portion of the cells. Hamamelis Leaves yield not more than 6 per cent. of ash." *N. F.*

The microscopical characteristics of the hamamelis leaves have been described by Hans Kramer in *B. P. G.*, xvii, p. 323.

See *Hamamelidis Cortex*.

Off. Prep.—Fluidextractum Hamamelidis Foliorum, *N. F.* (*Br.*); Liquor Hamamelidis, *Br.*; Unguentum Hamamelidis (from Liquid Extract), *Br.*

HEXAMETHYLENAMINA. U. S. (Br.)

HEXAMETHYLENAMINE Hexam. [Hexamethylenetetramine]

(hĕx-ą-mĕ-thȳl-ēn-ą-mī'nȧ)

"A condensation product of ammonia and formaldehyde, hexamethylene-tetramine [$(CH_2)_6N_4 = 140.14$]. Preserve it in well-closed containers." *U. S.* "Hexamine may be obtained by the interaction of ammonia with formic aldehyde. It contains not less than 98 per cent. of pure hexamethylenetetramine, $C_6H_{12}N_4$." *Br.*

Hexamina, *Br.*; Urotropine, Urotropin, Cystogen, Formin, Aminoform, Cystamine, Uritone.

The full name of this compound is hexamethylenetetramine, which was originally used by Nicolaier; the Latin title was shortened upon its admission to the U. S. P. VIII to *Hexamethylenamina,* and in U. S. P. IX abbreviated to "Hexam."; the British Pharm. (1914) adopted the name "Hexamina."

Preparation.—Hexamethylenamine may be made by the gradual addition of 70 parts of stronger ammonia water to 100 parts of a forty per cent. solution of formaldehyde which must be kept well cooled. The ammonia water must be added carefully in small quantities until in slight excess, which is indicated by its odor remaining after the liquid has stood several hours; then ten parts of ammonia water are added and the solution allowed to stand until crystallization is completed. The hexamethylenamine is purified by treatment with animal charcoal and recrystallization.

Properties.—It is officially described as in "colorless, lustrous, odorless crystals, or as a white, crystalline powder. One Gm. of Hexamethylenamine dissolves in 1.5 mils of water, 12.5 mils of alcohol and in 320 mils of ether at 25° C. (77° F.); soluble in chloroform. Its aqueous solution is alkaline to litmus. At about 263° C. (505.4° F.) it sublimes without melting and with partial decomposition, emitting a disagreeable odor. Heat an aqueous solution (1 in 10) with diluted sulphuric acid; it decomposes with the liberation of formaldehyde (recognized by its poor or by its darkening paper moistened with silver ammonium nitrate T.S.). When an aqueous solution (1 in 10) is heated with diluted sulphuric acid and then supersaturated with solution of sodium hydroxide, ammonia is liberated. Incinerate 2 Gm. of Hexamethylenamine; not more than 0.05 per cent. of ash remains. An aqueous solution of Hexamethylenamine (1 in 50) does not become colored or turbid when mixed with an equal volume of hydrogen sulphide T.S. (*heavy metals*). Separate portions of 10 mils each of an aqueous solution of Hexamethylenamine (1 in 50), acidulated with 5 drops of nitric acid, are not rendered turbid by a few drops of barium chloride T.S. (*sulphate*) nor more than slightly opalescent by a few drops of silver nitrate T.S. (*chloride*). Add 1 mil of alkaline mercuric potassium iodide T.S. to 10 mils of an aqueous solution of Hexamethylenamine (1 in 20); no other color is produced than that which results from the addition of the same amount of the reagent to 10 mils of distilled water (*ammonium salts*)." *U. S.*

"Colorless crystals or crystalline powder. Inodorous; taste at first sweetish, afterwards bitter. Soluble in 1.5 parts of *water,* and in 8 parts of *alcohol* (90 per cent.). The aqueous solution is alkaline to *litmus.* When heated to 263° C. (505.4° F.), it sublimes without fusing, and partially decomposes. When heated with *diluted sulphuric acid* formic aldehyde is evolved, and when the solution is cooled and made alkaline with *solution of sodium hydroxide* ammonia is liberated. 0.1 gramme warmed with 5 millilitres of *sulphuric acid* and 0.1 gramme of *salicylic acid* develops a carmine color. A solution of 1 gramme in *water,* mixed with 35 millilitres of *N/1 solution of sulphuric acid,* evaporated on a water-bath until the odor of formaldehyde has disappeared, requires for neutralisation not more than 7 millilitres of *N/1 solution of sodium hydroxide, solution of methyl orange* being used as indicator. No appreciable ash." *Br.*

Hexamethylenamine is slightly hydrolyzed, even by water, with the liberation of ammonia by the following reaction:

$$(CH_2)_6N_4 + 6H_2O = 4NH_3 + 6CH_2O.$$

This decomposition is prevented or diminished by the presence of alkalies and is increased by the presence of acids. Being a rather strong base hexamethylenamine combines with acids to form salts and it has the effect of decomposing salts of alkalies weaker than itself and thus liberates NH_3 from ammonium salts.

It frequently becomes necessary to test for the presence of hexamethylamine in differentiation from formaldehyde. The best test for this purpose is bromine water which gives an orange precipitate when added to aqueous solutions containing even minute traces of hexamethylamine. No precipitate or reaction is produced under these conditions with formaldehyde. This test is applicable directly to urine, but not to body fluids, because of the interfering effect of the proteins therein contained.

If the bromine water test is not directly applicable the fluid is tested for formaldehyde before and after distillation with sulphuric acid. The best test for formaldehyde under such conditions is that of Rimini (*Ann. di Farm.,* 1891, xvii, 97) and is applied as follows: To 10 mils of the fluid to be tested are added in rapid succession, agitating after each addition, the following reagents in the prescribed amounts: 3 drops of a 0.5 per cent. aqueous solution of phenylhydrazine hydrochloride, 2 drops of a 0.5 per cent. aqueous solution of sodium nitroprusside and 3 drops (or a slight excess) of a 15 per cent. aqueous solution of sodium hydroxide. In the presence of formaldehyde even in amounts as small as 1 in 1,000,000, a fugitive green or blue color is produced which quickly changes to yellow and finally to yellowish-red. In the absence of formaldehyde no shade of green or blue is observed when the sodium hydroxide is added.

Uses.—Locally hexamethylenamine is mildly irritant and feebly antiseptic. It is absorbed rapidly from the alimentary tract and circulates in the blood unchanged. Although the greater part is eliminated through the kidneys it has been detected in practically every secretion of the body. After it has passed through the kidney if the urine be, as it normally is, acid in reaction, the hexamethylenamine is slowly broken up with the liberation of formaldehyde. The rapidity of its decomposition appears to be in direct proportion to the degree of acidity

and there is strong evidence that when the urine is alkaline it remains in the bladder unchanged. Although originally introduced as a solvent for uric acid, hexamethylenamine is today used almost exclusively for its antiseptic action, especially in *cystitis.* When the bladder is infected by organisms which cause alkalization of the urine the drug is of little influence —since its effects depend almost entirely on the liberation of formaldehyde—unless the urine can be rendered acid. On the other hand in the cystitis due to typhoid bacillus or whenever the urine is acid, it is probably the most efficient urinary antiseptic we possess. It has also been employed with apparent benefit to prevent infections of the kidney in *scarlatina* and other infectious diseases, although its mode of action in these conditions is not evident.

In 1908 Crowe (*A. I. P. T.,* 1908, xviii, p. 315) demonstrated the appearance of hexamethylenamine in the bile and reported three cases of *cholecystitis* in which the bile became practically sterile after its administration. Although Hanzlik (*J. A. M. A.,* 1914, lxii, p. 295) disputes these conclusions and asserts that on account of the alkalinity of the bile the drug cannot act as an antiseptic in the gall bladder, there is considerable evidence as to its value as a preventative against *gall-stones* and curative of various infections of the bile passages. Miller, in 1911, used it with good results in the treatment of *acute coryza,* and Eisenberg (*J. A. M. A.,* 1912, June 29), in *acute bronchitis.* Despite the theoretical objections which have been urged against this treatment the clinical evidence of its value in those various respiratory infections commonly called *colds,* is too strong to be denied. In our experience, if used within twenty-four hours after the onset of symptoms, about 75 per cent. of the cases can be completely aborted. It has also been suggested for its influence in preventing the growth of germs in the cerebro-spinal fluid, as in *meningitis* and *poliomyelitis,* but its usefulness in these conditions has not been established.

If, as seems at present probable, the value of hexamethylenamine depends upon the liberation of formaldehyde, it is evident that it must be used in sufficiently large doses to form an antiseptic quantity of this reagent. Hinman (*J. A. M. A.,* 1913, lxi, p. 1601), as the result of experimental studies, reaches the conclusion that on account of the fact that some of the drug escapes decomposition, at least forty-five grains (3 Gm.) a day are required in *cystitis.* There are a number of persons who are unable to take such doses on account of the local irritant effect of the drug on the genito-urinary tract. A number of cases of hemorrhagic cystitis have been reported from the use of too large doses of hexamethylenamine.

Not only are there a large number of compounds of hexamethylenamine upon the market, but the official drug is sold under an almost innumerable number of trade names. The compounds of hexamethylenamine are considered in Part II.

An interesting and novel use of hexamethylenamine is afforded by its ready inflammability, and the fact that it burns with a smokeless flame. In the absence of a bunsen burner or an alcohol lamp, a five grain tablet of hexamethylenamine placed upon a metal or other non-inflammable surface and ignited will develop enough heat and for a long enough time to boil a test tube full of liquid, as in making a test for albumen in urine.

Dose, five to twenty grains (0.32–1.3 Gm.).

HIRUDO. Br.

LEECHES

(hĭ-rū′dō)

"Leeches are (1) Hirudo medicinalis, *Linn.,* the Speckled Leech, and (2) Hirudo quinquestriata, *Schmarda,* the Five-striped or Australian Leech." *Br.*

Sangsue médicinale, *Fr. Cod.;* Hirudines, *P. G.;* Blutegel, *G.* Sanguisuga, Mignatta, *It.;* Sanguijuela, *Sp.*

Leeches are highly specialized *Annelides.* This class contains the worms with red blood, having soft retractile bodies composed of numerous segments or rings, breathing generally by means of branchiæ, with a nervous system consisting in a double knotted cord, destitute of feet, and supplying their place by the contractile power of their segments or rings. There are three classes of leeches, depending upon their habits. (1) Temporary parasites which include most of this group of animals and are found in cold seas. (2) A class of nearly permanent parasites which are found in both temperate and tropical regions. (3) A class of of predatory hunters or scavengers which are confined to warm regions. These classes may change from one mode of life to another. Four families are usually distinguished and commonly designated as fish leeches; tortoise and snail leeches; worm leeches; and jawed leeches. The latter include the *Hirudinidæ,* which are distinguished in that they have no proboscis and generally possess three-toothed jaws. The true blood-sucking leeches, the medicinal leech of Europe, belong to this group.

The leech is an aquatic worm with a flattened body, tapering towards each end, and terminating in circular flattened disks, the hinder one being the larger of the two. It swims with a vertical undulating motion, and moves when out of the water by means of these disks or suckers, fastening itself first by one and then by the other, and alternately stretching out and contracting its body. The mouth is placed in the center of the anterior disk, and is furnished with three cartilaginous jaws at the entrance of the alimentary canal. These jaws are lined at their edges with fine sharp teeth, and meet so as to make a triangular incision in the flesh. The head is furnished with small raised points, supposed by some to be eyes. Respiration is carried on through small apertures ranged along the inferior surface. The nervous system consists of a cord extending the whole length, furnished with numerous gan-

glions. The intestinal canal is straight, and terminates in the anus, near the posterior disk. Leeches are hermaphrodite, and mutually impregnate each other. They are oviparous; and the eggs, varying from six to fifteen, are contained in a sort of spongy, slimy cocoon, from half an inch to an inch in diameter. These are deposited near the edge of the water, and hatched by the heat of the sun. The leech is torpid during the winter, and casts off from time to time a thick slimy coating from its skin. It can live a considerable time in sphagnous moss or in moistened earth, and is frequently transported in this manner to great distances without injury.

Savigny has divided the genus *Hirudo* of Linnæus into several genera. The true leech is the *Sanguisuga* of this author, and is characterized by its three lenticular jaws, each armed with two rows of teeth, and by having ten ocular points. Several species are used for medicinal purposes, of which the most common are the gray and the green leech of Europe, both of which are varieties of the *Hirudo medicinalis* of Linnæus, and the *Hirudo decora* of this country.

The British Pharm. (1914) gives the following description: "Body soft, smooth, five centimetres or more long, tapering to each extremity, plano-convex, marked with from ninety to one hundred fine annulations. Anterior extremity terminated by a small sucker surrounding the tri-radiate jaws, the posterior extremity by a large sucker. (1) Speckled Leech: dorsal surface olive-green, with six longitudinal stripes; ventral surface greenish-yellow, with black spots. (2) Five-striped Leech: dorsal surface greenish-brown, with five longitudinal stripes; ventral surface greenish-yellow, not spotted." *Br.*

1. *Hirudo medicinalis* Linn. (*Sanguisuga officinalis* Savigny). *The green* or *gray leech.*—This leech is marked with six longitudinal dorsal ferruginous stripes, the four lateral ones being interrupted or tessellated with black spots. The color of the back varies from a blackish to a grayish-green. The belly in the one variety is of a yellowish-green color, free from spots, and bordered with longitudinal black stripes. In the second variety it is of a green color, bordered and maculated with black. This leech varies from two to four inches in length. It inhabits marshes and running streams, and is abundant throughout Europe. A variety of the leech has come into use in Europe, called in commerce, *African leeches.* They are of a beautiful light-green color, varying to a deep green, and often inclining to red, with black points on the back, and broad streaks of a bright orange yellow, which are black towards the abdomen. They correspond perfectly with the *Sanguisuga interrupta* of Moquin-Tandon. These leeches draw very well. (*P. J.*, x, 38.) The leeches from Algiers, called in French commerce, *dragons* (*Sanguisuga troctena* of Moquin-Tandon), of which considerable numbers have been taken to France, are said by M. A. de Quatrefages, contrary to former opinion, to be quite equal to the European. (*J. P. C.*, 3e sér., xxxiii.)

2. *Macrobdella* (*Hirudo*) *decora* Say, the medicinal leech of America, has a back of a deep pistachio-green color, with three longitudinal rows of square spots. These spots are placed on every fifth ring, and are twenty-two in number. The lateral rows of spots are black, and the middle range of a light brownish-orange color. The belly is of the latter color, variously and irregularly spotted with black. The American leech sometimes attains the length of four or five inches, although its usual length is from two to three. It does not make so large and deep an incision as the European leech, and draws less blood. *Hirudo quinquestriata* Schmarda (*Hirudo australis* Bosisto; *Limnobdella quinquestriata* R. Blanch), the *five-striped* or *Australian leech,* has a dorsal surface greenish-yellow-brown, with five longitudinal stripes, the ventral surface being greenish-yellow and not spotted. The jaws are large, with forty-eight to fifty teeth, the inner being the larger.

The great use made of leeches in the practice of medicine has occasioned them to become a considerable article of commerce. They are collected in Spain, France, Italy, Germany, and Sweden, and carried in large numbers to London and Paris. They are also frequently brought to this country, as the practitioners in some of our large cities use only the foreign leeches, although our own waters furnish an inexhaustible supply. The indigenous leech was formerly much used in the city of Philadelphia.

Attempts were made, in France, on a large scale, to propagate leeches for sale. This was done by means of natural meadows, in which numerous small ponds were made, where the leeches, with certain cautions as to nourishment and preservation, multiplied and grew so rapidly as to become a source of profit. In order that they may propagate, it is necessary that they should be fed on blood, which is given them either by causing animals, as horses, cows, etc., to be driven into the meadows, or by obtaining blood from slaughter houses, and, after depriving it of fibrin by agitation, immersing the animals for a time in it while the blood is yet warm.

The proper preservation of leeches is an object of importance, as they are liable to a great and sudden mortality. They are usually kept in jars, in clear, soft water, which should be changed twice a week in winter and every other day in summer. The jar must be covered with a linen cloth, and placed in a situation not liable to sudden changes of temperature. They will live a long time and continue active and healthy without any other attention than that of frequently changing the water in which they are kept. Derheims has proposed the following excellent method of preserving them. In the bottom of a large basin or trough of marble he places a bed, six or seven inches deep, of a mixture of moss, turf, and fragments of wood. He strews pebbles above, so as to retain them in their place without compressing them

too much or preventing the water from freely penetrating them. At one end of the trough, and about midway of its height, is placed a thin slab of marble or earthenware, pierced with numerous holes, and covered with a bed of moss, which is compressed by a thick layer of pebbles. The reservoir being thus disposed is half filled with water, so that the moss and pebbles on the shelf shall be kept constantly moist. The basin is protected from the light by a linen cover stretched over it. By this arrangement the natural habits of the leech are not counteracted. One of these habits, essential to its health, is that of drawing itself through the moss and roots to clear its body from the slimy coat which forms on its skin and is a principal cause of its disease and death. James Banes recommends that when kept in jars they should be cleansed by means of a whisk of very fine broom or willow, when the water is changed. Lahache, an apothecary at Bruyères, strongly recommends carrageen, or Irish moss (*Chondrus crispus*), as admirably adapted to the habits and wants of the leech, furnishing the animal, he supposes, with nutriment, as it does not die of inanition when thus kept. The water should be renewed in the jars daily. (*J. P. C.*, 4e sér., iii, 128.) Alfred Allchin keeps them in aquaria with growing water-plants and snails, which keep the water pure. For other methods of keeping leeches, also of raising them, see *U. S. D.*, 14th ed., 472.

Uses.—Leeches afford the least painful and in many instances the most effectual means for the local abstraction of blood. They are often applicable to parts which, either from their situation or from their great tenderness when inflamed, do not admit of the use of cups, and in the case of infants are under all circumstances preferable to that instrument. They are indeed a powerful therapeutic agent, and give to the physician, in many instances, a control over disease which he could obtain in no other way.

In applying leeches to the skin, care should be taken to shave off the hair, if there be any, and to have the part well cleansed with soap and water, and afterwards with pure water. If the leech does not bite readily, the skin should be moistened with a little blood, or milk and water. It is said to bite more freely if the skin has been previously reddened by a sinapism and then washed perfectly clean. Sometimes the leech is put into a large quill open at both ends, and applied with the head to the skin until it fastens itself, when the quill is withdrawn. If it be desirable that the leech shall bite in a particular spot, this end may be attained by cutting a small hole in a piece of blotting paper, and then applying this moistened to the skin, so that the hole shall be immediately over the spot from which the blood is to be taken. Leeches continue to draw blood until they are gorged, when they drop off. The quantity of blood which they draw varies with the part to which they are applied, and the degree of inflammation existing in it. From the loose and vascular textures they will abstract more than from those which are firm and compact, and more from an inflamed than from a healthy part. As a very efficient mode of applying leeches, it is recommended, after having moistened the skin with pure warm water, to put the leeches into a tumbler half full of cold water, and by an adroit movement invert it upon the part. The leeches are said to attach themselves so rapidly that it seems to the patient as though they made but a single bite. When they are all attached, the glass is to be carefully removed, the water being absorbed, as it runs off on one side, by a sponge or linen cloths. As a rule, our leechers apply six for every fluidounce of blood. A single European leech will draw from half an ounce to an ounce. The quantity may often be much increased by bathing the wound with warm water. Leeches will continue to suck after their tails are cut off, which is sometimes done, although it is a barbarous practice. They may be separated from the skin at any time by sprinkling a little salt upon them. After they drop off, the same application will make them disgorge the blood they have swallowed. Under the name of *bdellotomy*, a practice has been introduced into Germany, of making a small incision in the side of the leech while drawing. The blood escapes through the wound, and the animal will continue to suck for a long time, so that one will perform the office of many in the quantity of blood taken. The practice of using over again leeches which have been made to disgorge the blood they have sucked is to be condemned on account of the danger of carrying infection from one patient to another. In cases where the bleeding from leech bites continues longer than is desirable, it may be stopped by continued pressure, with the application of lint, by the use of collodium, or by touching the wounds with lunar caustic. A little cotton, impregnated with a saturated solution of alum in boiling hot water, and, after it has become sufficiently cool, but before the alum has begun to crystallize, pressed upon the wound, will often prove effectual. If lunar caustic be applied, the stick must first be brought to a fine point, which is to be inserted in the wound hot. When the part wounded is without a bony basis, pressure may be made by pinching the wound between the fingers. It may sometimes be necessary, in the case of a deep bite, to sew the wound, which is readily done with a single stitch of the needle, that need not penetrate deeper than the cutis.

In 1884 Haycraft showed that the saliva of the leech prevented the coagulation of the blood. This is due to the action of a secondary albumose known as *herudin* (*hirudin* is a commercial name for a preparation manufactured from leech heads the precise nature of which is not revealed). Although Rimann and Wolff found that it required twenty milligrammes to render one hundred grammes of human blood non-coagulable, Satterlee and Hooker found that as small an amount as three and a half milli-

grammes per hundred grammes, caused perceptible retardation of clotting. The anticoagulant properties of leech extract, or its active principle, have been of much value in the physiological laboratory. Leech extract may be prepared according to the following method which is a modification of that suggested by Franz: cut off the leech heads, mince them, rub up with a very fine sand, add to the mass 5 mils of physiological salt solution for each leech head and heat for 20 minutes at a temperature of 100° C. (212° F.), allow to macerate for twelve hours, decant off the liquid, wash the sand several times with physiological salt solution, unite the liquids and filter through cheesecloth. This solution, which is suitable for some laboratory purposes, is not gaged by the quantity of solution, but by the number of leech-heads represented. According to Franz, it requires three leeches per kilo body weight to prevent coagulation of the blood in the dog. Preference to-day, however, is generally given to hirudin. This has been used not only in physiological laboratory, but in clinical medicine for the purpose of preventing clotting during transfusion of blood. Marshall (*J. P. Ex. T.*, 1915, vii, 157) has found that commercial samples of hirudin may be highly toxic, apparently from contamination with some product of putrefaction. (For details of technique and extensive literature on the whole subject see article of Satterlee and Hooker, *J. A. M. A.*, 1914, lxii, p. 1781.) On the theory that *eclampsia* was due to excessive fibrin content of the blood, hirudin has been suggested as a therapeutic measure in this condition.

HOMATROPINÆ HYDROBROMIDUM.

U. S., Br.

HOMATROPINE HYDROBROMIDE Homatrop. Hydrobr. [Homatropine Bromide, Homatropine Hydrobromate]

(hō-măt-rō-pĭ′næ hȳ-drō-brō′mĭ-dŭm)

"The hydrobromide [$C_{16}H_{21}O_3N.HBr = 356.11$] of homatropine, an alkaloid obtained by the condensation of tropine and mandelic acid. Preserve it in well-closed containers, protected from light." *U. S.* "Homatropine Hydrobromide, $C_{16}H_{21}NO_3$,HBr, is the hydrobromide of an alkaloid prepared from tropine." *Br.*

Bromhydrate d'Homatropine, *Fr. Cod.;* Homatropinum hydrobromicum, *P. G.;* Homatropinhydrobromid, Bromwasserstoffsaures Homatropin, Bromwasserstoffsaures Oxytoluyltropein, *G.*

Preparation.—This alkaloidal salt was first admitted to the British Pharmacopœia in the additions of 1890. Homatropine, $C_{16}H_{21}NO_3$, is prepared by evaporating a mixture of tropine, $C_8H_{15}NO$ (obtained through the saponification of hyoscyamine), and *mandelic acid* (phenyl-glycollic), $C_6H_5.CH(OH)COOH$, with diluted hydrochloric acid; mandelic acid may be produced by acting on amygdalin with hydrochloric acid, or synthetically from benzaldehyde and hydrogen cyanide.

Properties.—Homatropine hydrobromide is officially described as follows: "A white, odorless, crystalline powder, or in rhombic prisms. *Great caution must be observed in tasting it, using only very dilute solutions.* Its solution when locally applied dilates the pupil of the eye. One Gm. of Homatropine Hydrobromide dissolves in 6 mils of water, 40 mils of alcohol, and in 420 mils of chloroform at 25° C. (77° F.); also in 12 mils of alcohol at 60° C. (140° F.); insoluble in ether. Its aqueous solution (1 in 20) is neutral to litmus. It melts at about 212° C. (413.6° F.) with partial decomposition. Shake 2 mils of chloroform with 1 mil of an aqueous solution of the salt (1 in 10) to which a few drops of chlorine water have been added; the chloroform assumes a brownish color. When added to solutions of Homatropine Hydrobromide, iodine T.S. produces a brown precipitate; silver nitrate T.S. in similar solutions produces a yellowish-white precipitate insoluble in nitric acid. No weighable ash remains on incinerating 0.1 Gm. of Homatropine Hydrobromide. Separate portions of 1 mil each of an aqueous solution of the salt (1 in 20) are not precipitated by tannic acid T.S.; or, after acidulation with hydrochloric acid, by platinic chloride T.S. (*foreign alkaloids*). Add a slight excess of ammonia water to 1 mil of an aqueous solution of the salt (1 in 100), shake it out with chloroform and evaporate the chloroformic solution to dryness on a water bath. The residue becomes yellow and finally brick-red in color when warmed with about 1.5 mils of a solution made by dissolving 1 Gm. of mercuric chloride in 50 mils of a mixture of 5 volumes of alcohol and 3 volumes of distilled water (distinction from *most other alkaloids except atropine and hyoscyamine*). Evaporate about 0.01 Gm. of Homatropine Hydrobromide, with 5 drops of nitric acid, to dryness in a porcelain dish on a water bath; the residue acquires no violet color on the addition of a few drops of alcoholic potassium hydroxide T.S. (*atropine, hyoscyamine, or hyoscine*)." *U. S.*

"White crystalline powder, or aggregations of minute crystals. Soluble in about 6 parts of *water,* and in about 18 parts of *alcohol* (90 per cent.), the solutions being neutral to *litmus.* Yields the *reactions* characteristic of bromides. An aqueous solution (1 in 100) applied to the eye powerfully dilates the pupil. 1 millilitre of this solution made alkaline with *solution of ammonia,* shaken with *chloroform,* the chloroformic solution being then separated and evaporated, yields a residue which turns first yellow and then brick-red when warmed with 1.5 millilitres of a solution (2 in 100) of *mercuric chloride* in *alcohol* (60 per cent.) When treated with *nitric acid* and *alcoholic solution of potassium hydroxide* as described under 'Atropina,' a reddish-yellow color is produced, not changing to violet (distinction from atropine)." *Br.*

Uses.—Homatropine is used in medicine solely as a mydriatic and cycloplegic. Its effects upon the eye are, like those of atropine, due to a paralyzing action upon the peripheral ending of

the oculo-motor nerve. It has the advantage over atropine in being relatively much less toxic to the general system and of being somewhat quicker in its action. It has in the past been stated that homatropine had no depressant effect upon the pneumogastric nerve, indeed that it slowed the pulse, but Zulick has shown (*J. P. Ex. T.*, 1915, vi, 473) that its effects upon cardiac inhibition are similar in kind to those of atropine, although it requires very large doses to affect the circulation. Occasionally unpleasant symptoms have followed the instillation of homatropine solutions into the eye, but we know of no fatal case of homatropine poisoning.

After the instillation of a 1 per cent. solution the pupil begins to dilate in from seven to twenty minutes and accommodation fails in forty to ninety minutes, while recovery is usually complete in three to four days. For simple dilatation of the pupil a 1 per cent. solution is sufficient, but when it is desired to paralyze accommodation completely a 2 per cent. solution may be employed.

Dose, internally, from one one-hundredth to one-fiftieth of a grain (0.0006–0.0013 Gm.).

Off. Prep.—Lamellæ Homatropinæ, *Br.*

HUMULUS. U. S.

HOPS Humul.

(hū'mŭ-lŭs)

"The carefully dried strobiles of *Humulus Lupulus* Linné (Fam. *Moraceæ*) bearing their glandular trichomes and without the presence or admixture of more than 2 per cent. of stems, leaves or other foreign matter. Preserve it in tightly-closed containers, protected from light." *U. S.*

Lupulus, *Br. Pharm.* 1898; Hop; Strobili Humuli, s. Lupuli; Houblon, *Fr. Cod.*; Hopfen, *G.*; Luppolo, *It.*; Lupulo (Fruto de), Hombrecillo, *Sp.*

Hops, under the title "Lupulus" were deleted from the British Pharm. (1914).

The hop plant is a twining, rough perennial having angular, rough, flexible stems, which twine around neighboring objects in a spiral direction from left to right, and climb to a great height. The leaves are opposite, and stand upon long footstalks. The smaller are sometimes cordate; the larger have three or five lobes; all are serrate, of a deep green color on the upper surface, and, together with the petioles, extremely rough, with minute prickles. At the base of the footstalks are two to four smooth, ovate, reflexed stipules. The flowers are numerous, axillary, and furnished with bracts. The staminate flowers are a yellowish-white, and arranged in panicles; the pistillate, which grow on a separate plant, are pale green, and disposed in solitary, peduncled aments, composed of membranous scales, ovate, acute, and tubular at the base. Each scale bears, near its base, on its inner surface, two flowers, consisting of a roundish compressed ovary, and two styles, with long filiform stigmas. The aments are converted into ovate membranous cones or strobiles, the scales of which contain, each, at its base, two small achenes, surrounded by a yellow, granular powder or the so-called *Lupulin*. Only the pistillate plants are cultivated by the hop growers in Europe, and it is interesting to note that the unfertilized pistillate plants produce strobiles richer in aroma and more plenteous in lupulin. The plants flower in August and the fruits are harvested during September. The hops grown in this country contain a great many achenes, showing that the staminate plants are also cultivated. The strobiles are collected when the scales change from a light golden to a somewhat deeper hue.

The hop plant is a native of North America and Europe. In parts of New England, New York, and Michigan it is extensively cultivated, and most of the hops consumed in the United States is supplied by those districts. England probably produces the largest quantity of hops, with Germany and Austria next in order. The part of the plant used is the fruit or strobiles. These, when fully ripe, are picked, dried by artificial heat, packed in bales, and sent into the market under the name of hops.

By separating the volatile oils and determining its acid and ester value, Rabak (*C. D.*, lxxxv, 376) is able to distinguish American grown from imported hops. He finds that the European hops always show a lower ester value in the volatile oil than do the American.

Hops consists of numerous thin, translucent, veined, leaf-like scales, which are of a pale greenish-yellow color, and contain near the base two small, round, black achenes. They are officially described as follows: "Strobile ovoid-cylindrical, about 3 cm. in length, consisting of a narrow, hairy, flexuous rachis and numerous, imbricated, yellowish-green to pale brown, obliquely-ovate, membranous scales, the base of each with numerous, yellowish-brown, glandular hairs, and frequently infolded on one side, enclosing a subglobular, light brown, very glandular achene; odor strong and characteristic, becoming disagreeable and valerian-like on aging; taste aromatic and bitter. Hops yield not more than 8 per cent. of ash." *U. S.*

Though brittle when quite dry, they are pulverized with great difficulty. Their odor is strong, peculiar and fragrant; their taste very bitter, aromatic, and slightly astringent. Their aroma, bitterness, and astringency are imparted to water by decoction, but the first mentioned property is dissipated by long boiling. The most active part of hops is a substance formed on the surface of the scales, and, in the dried fruit, existing in the state of very small granules. This substance was called *lupulin* by A. W. Ives of New York, by whom its properties were first investigated and made generally known, though it was previously noticed by Sir J. E. Smith of England, and Planche of France. The scales themselves, however, are not destitute of virtues, and contain, as shown by Payen and Chevallier, the same active principles as does lupulin, though in less proportion.

Hops are often subjected in Germany to the fumes of burning sulphur, because of the

supposition that they keep better when thus treated. Besides, by being partially bleached by the process, old hops, which have suffered from time, having become darker, generally spotted, and weaker, assume a brighter appearance, as if fresher, and generally command a better price in the market. To detect the consequent presence of sulphurous acid, the brewers put a silver spoon in a mixture of hops and water, under the impression that it will produce a black stain upon the silver. But this test will answer only when applied within a fortnight after the use of the sulphur. A more delicate method is that of Heidenreich, who puts twenty or thirty strobiles of the hops in a flask with zinc and hydrochloric acid, and passes the hydrogen evolved through solution of lead acetate. If sulphurous acid be present, hydrogen sulphide will be produced, which will occasion a dark precipitate with the solution. But even this plan often fails when the hops have been kept more than three or four weeks. A modification of this test has been proposed by R. Wagner. For the solution of lead acetate used in Heidenreich's method there is to be substituted a solution of sodium nitroprusside, so weak as to have a very light brown color, to which have been added a few drops of solution of potassium hydroxide. If the gas evolved contain the minutest proportion of sulphur, a violet color will be produced when the first bubble passes into the solution; and this will, by a continuance of the process become a magnificent purple. The least trace of sulphurous acid may thus be found, but a few months after the sulphuring of hops none at all can be detected.

Hops are said to be sometimes threshed in order to separate the lupulin, which is sold separately. Their efficiency is thus, no doubt, greatly impaired. Hops thus treated have the scales more or less broken; and any parcel presenting this appearance is to be suspected. Hops often contain a variable quantity of lupulin in consequence of the granules of this substance separating, especially on agitation, and seeking the lower portion of the mass, which thus becomes richer, while the upper is poorer. They should always be examined in reference to the lupulin they contain, and, if nearly or quite destitute of it, should be deemed of inferior value and not be used medicinally.

LUPULIN, N. F. IV (see also Part II).—Lupulin is obtained by rubbing or threshing and sifting the strobiles, of which it constitutes from one-sixth to one-tenth by weight. It is in the state of a yellowish powder, mixed with minute particles of the scales, from which it cannot be entirely freed when procured by a mechanical process. It has the peculiar flavor of hops, and appeared to Lebaillif and Raspail, when examined by the microscope, to consist of glandular hairs filled with a yellow matter. They originate in a cell formed among those of the epidermis, and, when fully developed, secreting a resinous matter. (*J. P. C.*, 3e sér., xxvi.) It is inflammable, and when moderately heated becomes somewhat adhesive. The odor of lupulinic grains resides in the essential oil. This is obtained to the extent of 0.9 per cent. by distilling hops with water. When distilled from the fresh strobiles the oil has a greenish color, but a reddish brown when old hops have been employed. It is devoid of rotatory power, neutral to litmus paper, and gives no remarkable coloration with concentrated sulphuric acid. According to Chapman (*J. Chem. S.*, 1895, 54, 780) the essential oil consists of two terpenes, one $C_{10}H_{16}$, and the other $C_{10}H_{18}$, boiling between 160° and 171° C. (320° and 339.8° F.) and a sesquiterpene called *humulene,* boiling at 263° to 266° C. (505.4°–510.8° F.). This latter makes up almost two-thirds of the oil. There is also a small amount of an oxygenated constituent, probably $C_{10}H_{18}O$. The bitter principle formerly called *lupulin* or *lupulite* was first isolated by Lermer, who called it the *bitter acid of hops* (*Hopfenbittersäure*). It crystallizes in large brittle rhombic prisms, and possesses the peculiar bitter taste of beer. Its composition is $C_{32}H_{50}O_7$. Lupulin consists chiefly of wax (*myricyl palmitate,* according to Lermer) and resins, one of which is crystalline and unites with bases.

Besides the constituents of the glands, hops contain, according to Etti, *lupulo-tannic acid* and *phlobaphene.* The former is a whitish, amorphous mass, soluble in alcohol, hot water, or acetic ether, but not in ether. By heating the *humulo-tannic acid* to 130° C. (266° F.), or by boiling its aqueous or alcoholic solution, it gives off water and is transformed into phlobaphene, a dark-red amorphous substance,

$$2C_{25}H_{24}O_{13} - H_2O = C_{50}H_{46}O_{25}$$

The latter substance, on boiling it with diluted mineral acids, becomes hydrolized, and furnishes glucose and *hop-red,* according to the reaction:

$$C_{50}H_{46}O_{25} + 2H_2O = C_{38}H_{26}O_{15} + 2C_6H_{12}O_6$$

From raw phlobaphene, ether removes the bitter principles of hops, a colorless crystallizable and a brown amorphous resin, besides chlorophyll and essential oil. (*Pharmacographia,* 2d ed.) The existence of a peculiar alkaloid in hops, suggested by Lermer in 1863, and confirmed by Griessmayer, has been denied. A. Chaston Chapman (*P. J.*, 1912, xcii, 878), found cultivated hops to contain from 1.7 to 4 per cent. of nitrogen which is a constituent of the following principles recognized by him in an investigation of the subject: aspartic acid, l-asparagine, choline, betaine, adenine, histidine, hypoxanthine, and arginine, besides an unidentified base, no trace of a morphine-like alkaloid could be detected, although this has been stated by some authorities to be present. Etti found arabic (pectic) acid, phosphates, nitrates, malates, citrates, and also sulphates, chiefly of potassium, to occur in hops. The amount of ash afforded by hops dried at 100° C. (212° F.) would appear to be on an average about 6 to 7 per cent. (U. S. P. IX not more than 8 per cent.) H. Bungener has isolated from hops a bitter crystalline substance, $C_{25}H_{36}O_4$, which is insoluble in water,

but soluble in alcohol and alkaline solutions. He believes it to be identical with Lermer's hop-bitter acid, to be feebly acid, and to possess the character of an aldehyde. (*P. J.*, 1884.)

Uses.—Hops are an aromatic bitter and hence may be useful in *atonic dyspepsia.* By many they are believed to have a sedative effect on the nervous system and are used in *hysteria, restlessness, isomnia,* and the like. Whether this latter action is due to anything more than an effect through the imagination is open to question.

An *infusion* prepared with half an ounce of hops and a pint of boiling water may be given in the dose of four fluidounces (120 mils). The tincture was a British official preparation of hops, but the alcohol probably acts more decidedly upon the system than the hops. The fluidextract of hops of the N. F. IV is superior because of the relatively smaller amount of alcohol. A pillow of hops has proved useful in allaying restlessness and producing sleep in nervous disorders. They should be moistened with water containing a trace of glycerin previously to being placed under the head of the patient, in order to prevent rustling. Fomentations with hops, and cataplasms made by mixing them with some emollient substance, are often beneficial in local pains and tumefactions.

The effects of hops may be obtained conveniently by the use of *lupulin,* which, although at one time much employed as an anaphrodisiac, has fallen into deserved desuetude.

Dose, thirty to ninety grains (2.0–5.8 Gm.).

Off. Prep.—Elixir Humuli (from Fluidextract), *N. F.;* Fluidextractum Humuli, *N. F.;* Tinctura Humuli, *N. F.*

HYDRARGYRI CHLORIDUM CORROSIVUM. U. S. (Br.)

CORROSIVE MERCURIC CHLORIDE Hydrarg. Chlor. Corr. [Bichloride of Mercury, Corrosive Sublimate, Mercuric Chloride Perchloride of Mercury]

(hȳ-drär′gy-rī ȼhlō′rī-dŭm cŏr-rō-sī′vŭm)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99.5 per cent. of $HgCl_2$ (271.52). Preserve it in well-closed containers." *U. S.* "Mercuric Chloride may be obtained as a sublimate by heating a mixture of mercuric sulphate, sodium chloride, and black oxide of manganese. It contains not less than 98.6 per cent. of pure mercuric chloride, $HgCl_2$." *Br.*

Hydrargyri Perchloridum, *Br.,* Perchloride of Mercury, Sublimatus Corrosivus, Chloruretum (Chloretum) Hydrargyricum, Hydrargyrum Corrosivum Sublimatum, Hydrargyri Bichloridum; Hydrargyrum Muriaticum Corrosivum, Sublimatus Corrosivus, Mercurius Sublimatus Corrosivus; Corrosive Chloride of Mercury, Sublimé corrosif, Chlorure mercurique, *Fr. Cod.;* Deutochlorure de Mercure, *Fr.;* Hydrargyrum Bichloratum, *P. G.;* Quecksilberchlorid, Aetzender Quecksilbersublimat, *G.;* Bicloruro di mercurio, *It.;* Cloruro mercurio, *Sp.*

The former official processes for this salt will be found in the U. S. D., 19th ed., p. 617.

The names given in the two Pharmacopœias to this important chloride do not exactly correspond. It is called *Hydrargyri Chloridum Corrosivum* in the U. S. Pharmacopœia, and *Hydrargyri Perchloridum* in the British. We prefer the former, as indicating, beyond any possibility of mistake, the article intended, as well as its corrosive property. Perchloride and subchloride are hardly sufficiently distinctive, when a mistake may be so serious as that of confounding corrosive sublimate and calomel. Indeed, death has at least in one recorded instance occurred in consequence of this confusion of nomenclature, and our official guides should take especial care to guard against such mistakes. The British Pharmacopœia (1898) uses for the English names mercuric chloride for corrosive sublimate and mercurous chloride for calomel, but these names are not used in prescription writing.

Preparation.—Corrosive sublimate may be made by heating sulphuric acid and the metal together, in a chamber so arranged as to carry off the sulphurous oxide, to form mercuric sulphate; the dry salt obtained is then mixed with sodium chloride, and the mixture sublimed. It is usually made on the large scale, by the direct combination of gaseous chlorine with mercury which is heated almost to the volatilizing point. This process was originally patented by A. T. Thomson, of London, England. It is also sometimes manufactured by dissolving mercuric oxide (red precipitate) in hydrochloric acid, evaporating the solution to dryness, dissolving the dry mass in water, and crystallizing. Here a double decomposition takes place, resulting in the formation of water and the chloride. This method may be used in emergencies for making small amounts.

Properties.—Corrosive mercuric chloride is officially described as in "heavy, colorless, rhombic crystals, or crystalline masses, or as a white powder, odorless, permanent in the air, and having a characteristic and persistent metallic taste. *Great caution should be used in tasting it.* One Gm. of Corrosive Mercuric Chloride dissolves in 13.5 mils of water, 3.8 mils of alcohol, about 12 mils of glycerin, and in 22 mils of ether, at 25° C. (77° F.); also in 2.1 mils of boiling water and 1.6 mils of boiling alcohol. The salt fuses to a colorless liquid at 265° C. (509° F.) and at about 300° C. (572° F.) it volatilizes in dense, white vapors, leaving not more than 0.1 per cent. of residue. An aqueous solution of Corrosive Mercuric Chloride (1 in 20) is acid to litmus, but becomes neutral upon the addition of sodium chloride. Separate portions of an aqueous solution of the salt (1 in 20) yield a white precipitate with ammonia water; a black precipitate with an excess of hydrogen sulphide; a red precipitate, soluble in an excess of the reagent, with potassium iodide T.S.; and a white precipitate, insoluble in nitric acid, with silver nitrate T.S. Not more than 0.5 per cent. of residue remains on dissolving finely powdered Corrosive Mercuric Chloride in ether or alcohol.

"**Assay.**—Dissolve about 0.5 Gm. of Corrosive Mercuric Chloride, previously dried to constant weight in a desiccator over sulphuric

acid and accurately weighed, in 300 mils of cold distilled water to which 1 mil of hydrochloric acid has been added. Pass hydrogen sulphide through the cold solution until saturated and the precipitate of mercuric sulphide readily subsides, leaving a clear supernatant liquid. Collect the precipitate on counterpoised filters, wash it well with cold distilled water and finally with three portions of about 10 mils each of alcohol. Then close the tip of the funnel with a cork stopper, add sufficient carbon tetrachloride to cover the precipitate, cover the funnel with a watch-glass, and allow it to stand for about half an hour. Then drain off the solvent and wash the precipitate with further portions of carbon tetrachloride until after evaporating about 1 mil of the filtrate no visible residue remains. Remove the adhering carbon tetrachloride by washing with several portions of 10 mils each of alcohol and, after drying in the air, transfer to an oven and dry to constant weight at about 110° C. (230° F.). The weight of mercuric sulphide obtained, when multiplied by 1.167, indicates its equivalent in $HgCl_2$, which corresponds in the dried salt to not less than 99.5 per cent. of $HgCl_2$.

"Each gramme of Corrosive Mercuric Chloride, previously dried to constant weight, corresponds to 0.8526 Gm. of mercuric sulphide.

"Corrosive Mercuric Chloride, previously dried to constant weight, may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

"Heavy, colorless, crystalline masses, possessing a highly acrid, metallic taste. Soluble in 18 parts of *water,* and in 4 parts of *alcohol* (90 per cent.), or of *ether.* Yields the *reactions* characteristic of mercuric salts and of chlorides. When heated Mercuric Chloride sublimes without decomposition, leaving only a trace of fixed residue. Yields not less than 72.8 or more than 73.8 per cent. of metallic mercury, Hg, when tested by the following process:—Dissolve 0.5 gramme in 20 millilitres of *water* in a tared beaker-flask, add 10 millilitres of *hypophosphorous acid,* or sufficient to reduce the whole of the mercuric chloride present, and heat on a water-bath until the particles of mercury that separate collect at the bottom of the flask. Pour the contents of the flask on a tared filter-paper, wash both the flask and filter-paper successively with *water, alcohol* (90 per cent.), and *ether;* dry over *sulphuric acid,* and weigh the metallic precipitate." *Br.*

Ether is capable of removing corrosive sublimate, to a considerable extent, from its aqueous solution when agitated with it. According to Mialhe, ether will not dissolve it when accompanied by a considerable quantity of mercuric oxide and a chloride of an alkalifiable metal. Sulphuric, nitric, and hydrochloric acids dissolve it without alteration. When heated it melts, and readily sublimes in dense, white, acrid vapors, which condense on cool surfaces, in white, shining needles. Its aqueous solution renders green the syrup of violets, and is precipitated brick-red, becoming yellow, by the fixed alkalies and alkaline earths, and white by ammonia. (See *Hydrargyrum Ammoniatum.*) The former precipitate is mercuric oxide, which has the property of evolving oxygen and of being reduced to metallic globules when exposed to heat. This oxide is formed in the process for preparing *aqua phagedænica,* called also *yellow wash.* (See *Lotio Hydrargyri Flava.*) Corrosive sublimate forms, with ammonium chloride and sodium chloride, compounds which are more soluble than the uncombined mercurial salt. The combination of corrosive sublimate with ammonium chloride was formerly called *sal alembroth,* or *salt of wisdom.* According to F. Hinterberger, corrosive sublimate is capable of combining with quinine and cinchonine. (*Chem. Gaz.,* ix, 211.) By dissolving one part of corrosive sublimate and a hundred parts of sodium chloride in distilled water and evaporating to dryness, a soluble preparation is obtained which does not coagulate albumen. (*A. J. P.,* xliv, 11.) J. F. Brown (*C. D.,* 1896, 425) recommended for dispensing purposes a solution of mercuric chloride of such strength that ten minims contain one grain, made by dissolving ninety-six grains of corrosive sublimate in one and a half ounces avoirdupois of glycerin and six fluidrachms of distilled water by the aid of heat, then cooling the solution and adding distilled water until the solution measures two fluidounces.

Tests.—Pure corrosive chloride of mercury sublimes, when heated, without residue, and its powder is entirely and readily soluble in ether. Consequently, if a portion of any sample should not wholly dissolve in ether, or if it should not evaporate entirely, the presence of some impurity is proved. The U. S. P. IX limiting test is not more than 0.5 per cent. of residue on treatment with ether or alcohol. If calomel be present, and it frequently is, it will not be wholly soluble in water. Arsenic is reported to be a frequent impurity in corrosive sublimate. (See paper by J. Granville Smith, *A. J. P.,* 1877, p. 397.) Corrosive sublimate is incompatible with many of the metals, the alkalies and their carbonates, soap, lime water, tartar emetic, silver nitrate, the lead acetates, the potassium and sodium sulphides, the soluble iodides, and all the sulphydrates. It is decomposed by many vegetable and some animal substances. According to A. T. Thomson, it produces precipitates in infusions or decoctions of chamomile, horseradish, calumba, cinchona, gambir, rhubarb, senna, simaruba, and oak bark. Mialhe and Lepage have shown that corrosive sublimate is slowly converted into calomel by syrup of sarsaparilla and syrup of honey, but is not changed by contact with pure syrup. Samuel Kennedy (*Ph. Rec.,* 1888, p. 201) proved conclusively that when corrosive sublimate was dissolved in compound syrup of sarsaparilla, as frequently prescribed, precipitation invariably occurred. He found that if sodium chloride in quantity equalling that of the mercurial used

were added, precipitation was greatly retarded.

Uses.—Corrosive sublimate is a powerful mercurial and may be used for the various purposes for which the other preparations of this metal are employed. (See page 566.) When administered in large doses it is prone to irritate the stomach and intestines and, therefore, such large quantities of mercury cannot be introduced into the system with this salt as with calomel. It is probably the best of all the preparations of mercury for hypodermic use in *syphilis*. From ten to twenty minims of an 0.5 per cent. solution in distilled water may be thrown deeply into the muscles, preferably of the back. The pain of the injection may be obviated by the previous injection of cocaine. Most careful asepsis is necessary to avoid abscess formation.

It has been employed, especially by intravenous injection with asserted benefit in *septicemia*, especially following child-birth. Stowe (*Chicago Medical Recorder*, 1911, xxxiii, p. 461) injects one-fifth of a grain at a dose.

Externally employed, corrosive sublimate is stimulant, escharotic, and germicidal. The powdered chloride has been used as an escharotic, but is, in general, inferior to silver nitrate or potassium hydroxide. In *onychia maligna*, however, it is employed with great advantage, mixed with an equal weight of zinc sulphate, and sprinkled thickly upon the surface of the ulcer, which is then to be covered with a pledget of lint saturated with tincture of myrrh. The whole diseased surface is thus removed, and the ulcer heals. This practice originated, we believe, with Perkins, of Philadelphia, and was highly recommended by Physick. Geo. B. Wood often employed it with success. A solution of corrosive sublimate in collodion (four parts to thirty) has been used as a caustic, for the destruction of *nævi materni*, and for other purposes. It can be very accurately applied, but its use requires care, as fatal poisoning has followed a single application of the alcoholic solution of corrosive sublimate to a moderate surface of *ringworm*. (*L. L.*, 1871, ii, 413.) It is applied by means of a camel's-hair pencil.

Corrosive sublimate is one of the most powerful of known chemical germicides. Solutions containing one part in twenty thousand are sufficient to destroy the vitality of most non-sporulating bacteria while one in one thousand will kill the most resistant sporulating organisms. According to Koch, one part in three hundred thousand absolutely prevents the multiplication of the *Bacillus anthracis*, while Behring (*D. M. W.*, 1887) finds that as little as one part in a million has a distinctly inhibiting effect. The practical utility of mercuric chloride as a disinfectant is, however, greatly limited by its chemical instability. It has a strong affinity for albumen and, although the precipitate formed is redissolved in an excess of albumen, the disinfectant power of mercury is very much reduced. Moreover, it attacks most metals which are used in surgery and is therefore unsuitable for disinfecting instruments. Nevertheless, because of its convenience as well as its powerful action it is perhaps the most commonly employed germicide for surgical purposes.

The solution of one in one thousand may be used for washing the hands, disinfecting furniture, etc., and is even employed in the disinfecting of *wounds;* usually, however, a much weaker solution than that just mentioned is employed by the surgeon. It is rarely if ever justifiable to use upon a mucous surface or a wound a solution stronger than one in two thousand, and if the solution is to be used freely and continuously, as in washing out the vagina, etc., one in ten thousand is as strong as should be employed; indeed, the employment of a vaginal wash of this strength has been followed by violent poisoning. (See H. C. Wood, Jr., *Am. Med.*, Dec., 1902.) In a number of cases a solution of one part in fifteen hundred used locally by the surgeon has produced death, preceded by constitutional symptoms.

It is essential that the tablets be colored or in some way marked so that the attention may be drawn to their nature, and accidental poisoning prevented. Mercuric chloride tablets are now officially recognized. (See *Toxitabellæ Hydrargyri Chloridi Corrosivi.*)

Poisoning.—Because of the ease with which it is obtained corrosive sublimate is one of the most commonly used poisons for suicidal purposes, and the wide spread employment of tablets of it as antiseptics has led to a number of accidental cases. The symptoms of poisoning by bichloride of mercury generally come on promptly with a metallic taste, burning pain in the gullet and epigastrium, followed by vomiting and purging. The vomitus is first mucous or bilious, but later becomes bloody, the stools also usually contain blood. In many cases there is a profound collapse, as shown by rapid feeble pulse, cold clammy skin, and muscular weakness, even comparatively early in the poisoning. The urine becomes scanty or maybe entirely suppressed, albuminous, and sometimes hemorrhagic. If the patient survives for a few days salivation develops and ulcers appear around the mouth and throat. Death may occur within a few hours of the ingestion of the poison, but may be postponed for nearly a fortnight. On postmortem examination the whole alimentary canal is found the seat of a corrosive inflammation, there is violent nephritis and sometimes protoplasmic degenerations in the internal organs. It is not necessary for the poison to be swallowed in order to produce serious or even fatal results. H. C. Wood, Jr. (*American Medicine*, 1902, iv, p. 1006), has found references to more than 150 cases of poisoning from its use as intra-uterine douches of which a large number ended fatally, and Craig (*J. A. M. A.*, 1906, xlvii, p. 1484) has reported death from the application of an alcoholic solution to the back and arm.

In the treatment of acute poisoning by mercuric chloride, the stomach should be at once evacuated, preferably by means of the stomach

tube or by the hypodermic injection of apomorphine. The most available antidote is some form of albumin, as milk, egg, or hashed meat; according to Taddei, wheat flour may be used, gluten having the same antidotal properties as albumen. As the albuminate of mercury is soluble in an excess of albumen and probably under other conditions, it is important to continue the evacuation of the stomach even after the administration of the antidote. Fantus (*Jour. of Lab. and Clin. Med.*, 1916, i, 879) from an elaborate experimental study reaches the conclusion that the antidotal value of albumin has been greatly overestimated. He recommends a mixture of sodium hypophosphite with sodium acetate. After the evacuation of the stomach and the efforts at neutralizing the local irritant effects of the drug, elimination should be encouraged by the free use of water both by the mouth and hypodermic injection of salt solution. Counter irritation over the kidneys and demulcent drinks are indicated and such other symptoms as arise may be met with appropriate remedies.

Tests for Corrosive Sublimate.—On account of the extreme virulence of this chloride as a poison, the reagents by which it may be detected form a subject of study of the utmost importance, as connected with medico-legal investigations.

If the mixture suspected of containing corrosive sublimate be wholly inorganic the following tests may be used for its detection: A preliminary test for mercury may be made with copper foil and strong hydrochloric acid. (Reinsch's test.) If the foil be darkened or changed it may be dried, placed in a tube of hard glass and heated when mercury will distil and separate in the cooler portions of the tube where it may be recognized by an examination under the microscope which will reveal the characteristic globules of the element. Tests in an aqueous solution of the substance may also be applied with hydrogen sulphide solution, which precipitates black mercuric sulphide; with potassium iodide solution, which cautiously added in just the proper amount precipitates red mercuric iodide; with an alkaline carbonate or hydroxide, which will precipitate the yellow mercuric oxide; and with stannous chloride solution which will reduce mercuric salts to mercurous and will thus give a white precipitate of calomel. The chlorine may be recognized by the customary silver nitrate test.

If any organic matter be present most or all of the foregoing tests will fail and as if ignition be resorted to, the mercury compounds will probably be volatilized, the destruction of the organic matter must be accomplished in the wet way by heating the substance with strong hydrochloric acid, and then cautiously adding powdered potassium chlorate in small portions, continuing the heating until the organic matter is completely destroyed and the dark color which the mixture originally assumed upon heating with the acid, has changed to a clear golden yellow. This solution may then be carefully heated to drive off the free chlorine and the tests as previously described may be applied.

Dose, of corrosive sublimate, from one-fortieth to one-eighth of a grain (0.0015–0.008 Gm.), preferably given after meals, in solution.

Off. Prep.—Liquor Hydrargyri Perchloridi, *Br.;* Toxitabellæ Hydrargyri Chloridi Corrosivi, *U. S.;* Mulla Hydrargyri Chloridi Corrosivi, *N. F.*

HYDRARGYRI CHLORIDUM MITE.
U. S. (Br.)

MILD MERCUROUS CHLORIDE Hydrarg. Chlor. Mit. [Calomel, Mercurous Chloride, Protochloride of Mercury, Subchloride of Mercury]

(hȳ-drär′gy-rī ȼhlō′rī-dŭm mī′tē)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99.6 per cent. of HgCl (236.06). Preserve it in well-closed containers, protected from light." *U. S.* "Mercurous Chloride, HgCl, is obtained as a sublimate by heating a mixture of mercurous sulphate and sodium chloride." *Br.*

Hydrargyri Subchloridum, *Br.*, Calomelas; Hydrargyri Chloridum, Hydrargyrum Chloratum (Muriaticum), Mercurius Dulcis, Chloruretum Hydrargyrosum; Mild Chloride of Mercury, Submuriate of Mercury; Chlorure Mercureux, *Fr. Cod.;* Protochlorure ou Sous-muriate de Mercure, Calomel, *Fr.;* Hydrargyrum Chloratum, *P. G.;* Quecksilberchlorür, *G.;* Protocloruro di mercurio, *It.;* Cloruro mercurioso sublimado, *Sp.*

Very properly, processes for this compound have been omitted from the Pharmacopœias, as it cannot be made by the pharmacist conveniently. For processes of the U. S. P., 1870, and of the Br. Pharm., 1885, with remarks, see *U. S. Dispensatory*, 19th edition, p. 623.

The original method of making calomel was practised at Apothecaries' Hall, London, by taking advantage of the following reaction:

$$HgSO_4 + 2NaCl + Hg = Na_2SO_4 + 2HgCl$$

To bring the calomel into a state of minute division the method of Joseph Jewell, of London, improved by Ossian Henry, is sometimes employed. It consists in causing the calomel in vapor to come in contact with steam in a large receiver, whereby it is condensed into an impalpable powder, and perfectly washed from corrosive sublimate in the same operation. Calomel made by this process, sometimes called Jewell's or Howard's *hydrosublimate of mercury*, is free from all suspicion of containing corrosive sublimate, and is much finer than when obtained by levigation and elutriation. This kind of calomel is included in the French Codex under a distinct name. (*Mercure* (*Protochlorure de*) *par volatilization.*) Soubeiran, of Paris, perfected a process for obtaining calomel as an impalpable powder, by substituting the agency of cold air for that of steam for the purpose of condensing it. A description of his apparatus may be found in the *J. P. C.* (3e sér., ii.), and of the English

apparatus, as described by F. C. Calvert, in the same journal (3e sér., iii). Both these papers were copied into the *A. J. P.* (xv).

Calomel may also be prepared in the dry way by taking four parts of corrosive sublimate and rubbing it up in a mortar with three parts of mercury, after moistening the mass with alcohol. The powder is then dried and sublimed in glass flasks. The powder should be dried quickly before sublimation, so as to drive off any trace of uncombined mercury. A comparative examination of English and American calomel was undertaken separately in 1885 by Bedford and Patch. (See *Proc. A. Ph. A.*, 1885.) While there was no reason for preferring English calomel, none of the samples exhibited more than traces of mercuric chloride. Calomel is also made in the wet way by Wöhler's method by precipitating a solution of corrosive sublimate by a stream of sulphurous acid, taking advantage of a reaction first observed by Vogel. Calomel obtained in the humid way, called *precipitated calomel,* was formerly official with the Dublin College, and was adopted in the French Codex. This form of calomel is a crystalline powder, which is unfit for use until after elaborate levigation and elutriation.

Properties.—When in mass, its form and appearance depend on the shape and temperature of the subliming vessel. In this state it is generally in the form of a white, fibrous, crystalline cake, the interior of which is often studded with shining transparent crystals, having the shape of quadrangular prisms, and a texture somewhat horny and elastic. When the mass is scratched it yields a yellow streak, which is very characteristic. Its sp. gr. is 7.2. Patch found (*Proc. A. Ph. A.*, 1885, p. 477) the sp. gr. of calomel to vary from 6.94 to 7.93, the standard being water at 3.9° C. (39° F.). Powder is the official form of this chloride, in which state it is always kept by pharmacists. The powder has a light buff or ivory color, if obtained by the levigation of sublimed masses; but if condensed at once in the form of an impalpable powder, it is perfectly white. To protect it from the action of the light, it should be kept in a dark place, or in bottles painted black or covered with black paper. By the action of the fixed alkalies or alkaline earths it immediately becomes black, in consequence of the formation of mercurous oxide, reducible by heat to the metallic state. The preparation employed under the name of *lotio nigra,* or *black wash,* as a local application to syphilitic *ulcers,* etc., is made by adding a *drachm* of calomel to a *pint* of lime water. (See *Lotio Nigra.*)

It is officially described as "a white, impalpable powder, becoming yellowish-white on being triturated with strong pressure, and showing only small, isolated crystals when viewed under a lens having a magnifying power of one hundred diameters. It is odorless and tasteless, and permanent in the air. Mild Mercurous Chloride is insoluble in water, alcohol, ether or cold dilute acid. When strongly heated, Mild Mercurous Chloride is volatilized without fusion or the evolution of brown vapors, leaving not more than 0.1 per cent. of residue. The salt is blackened by contact with calcium hydroxide T.S., with solutions of alkali hydroxides or with ammonia water. When heated with an equal weight of dried sodium carbonate (free from chloride) in a dry glass tube, Mild Mercurous Chloride yields a sublimate of metallic mercury. Dissolve the residue in nitric acid and filter; silver nitrate T.S. produces in the filtrate a white, curdy precipitate insoluble in nitric acid. Shake 2 Gm. of the salt with 20 mils of ether, filter, evaporate the filtrate, and add 10 mils of distilled water; not more than a slight opalescence results upon the addition of silver nitrate T.S. to 5 mils of the solution (*mercuric chloride*). Heat 1 Gm. of the salt with potassium hydroxide T.S.; no ammonia is evolved (*ammoniated mercury*).

"**Assay.**—Mix, in a tared flask, about 1 Gm. of Mild Mercurous Chloride, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed, with 10 mils of distilled water, add 50 mils of tenth-normal iodine V.S. and 5 Gm. of potassium iodide, dissolved in 10 mils of distilled water, stopper the flask, allow the mixture to stand, with occasional agitation, until complete solution has taken place and estimate the excess of iodine by titration with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows, in the dried salt, not less than 99.6 per cent. of HgCl.

"Each mil of tenth-normal iodine V.S. used corresponds to 0.023606 Gm. of HgCl. Each gramme of Mild Mercurous Chloride, previously dried to constant weight, corresponds to not less than 42.2 mils of tenth-normal iodine V.S.

"Mild Mercurous Chloride, previously dried to constant weight, may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

"A heavy dull white powder, sometimes rendered yellowish by prolonged trituration; nearly tasteless. Insoluble in *water,* in *alcohol* (90 per cent.), and in *ether;* soluble in a boiling mixture of *nitric acid* and *hydrochloric acid,* the solution, when diluted with *water,* yielding the *reactions* characteristic of mercuric salts. Volatilises when sufficiently heated, leaving not more than a trace of fixed residue. Warmed with *solution of sodium hydroxide* it becomes black, but does not evolve ammonia (absence of mercuric-ammonium chloride). When 1 gramme is well shaken with 10 millilitres of *water* and filtered, the filtrate is not darkened by *hydrogen sulphide* (absence of mercuric chloride)." *Br.*

An easy method of detecting corrosive sublimate, proposed by Bonnewyn, is to put some of the suspected powder upon a well polished surface of iron, and then moisten it with a drop of alcohol or ether. If the calomel be pure the surface will remain quite unaffected.

while it will be blackened by corrosive sublimate if present in the proportion of only 1 to 50,000. (*J. P. C.*, 1865, 4e sér., ii, 79.) The presence of any soluble chloride whatever in the calomel would be detected by the production of a precipitate by silver nitrate with the washing. Soluble salts of mercury may be detected by rubbing the suspected calomel with ether on a bright surface of copper, when the metal will become amalgamated and exhibit a white stain. When this test shows impurity, the soluble salt present is probably corrosive sublimate. Calomel containing corrosive sublimate acts violently on the bowels, and, when the impurity has been present in considerable amount, has been known to cause death. Besides being incompatible with the alkalies and alkaline earths, calomel is also decomposed by the alkaline carbonates, soaps, sulphydrates, and, according to some authorities, by iron, lead, and copper. By boiling with the alkaline formates it is decomposed, and metallic mercury liberated. (H. Rose, *Annal. der Physik und Chem.*, cvi, 500.)

Calomel should not be given at the same time with nitrohydrochloric acid, for fear of generating corrosive sublimate; death is reported to have followed such a combination. According to the experiments of Deschamps, calomel is decomposed by bitter almonds and by hydrocyanic acid. In the former case corrosive sublimate, mercuric cyanide, and ammonium chloride are formed; in the latter, corrosive sublimate and mercuric cyanide only; hence this writer considers it very dangerous to associate calomel with bitter almonds or hydrocyanic acid in prescription. This conclusion has been confirmed by Mialhe and Prenleloup, and more recently it has been shown by E. Riegel that cherry-laurel water has the power of converting calomel into corrosive sublimate. According to Mialhe calomel is in part converted into corrosive sublimate and metallic mercury by ammonium chloride and by sodium and potassium chlorides, even at the temperature of the body; hence he believes that the conversion may take place in the primæ viæ. Diekman (*Pharm. Era*, xxii, 7) experimented upon this subject and showed that the amount of mercuric chloride thus formed is not over 0.6 per cent. of the calomel taken, and consequently must be considered as negligible.

Uses.—As an alterative calomel may be used for the general properties of the mercurials. (See page 566.) It is relatively non-irritant to mucous membranes and may be given in large doses so that it is possible to bring the system under the general influence of the mercury very rapidly.

Aside from its alterative action, mercurous chloride is used as a cathartic, diuretic, and antiseptic. As a laxative it is slow but thorough in its action, affecting both upper and lower bowels. While the former belief that it was a stimulant to hepatic secretion has been shown to be incorrect, it in some way increases the bile in the intestinal tract, perhaps through an action on the bile passages or perhaps through its antiseptic effect preventing the decomposition of the natural bile. It is therefore preferred in cases where there is an absence of this secretion as shown by light colored stools, and in *biliousness*. It is also a valuable agent to cleanse the intestines in *enteritis* both because of the thoroughness of its effect and of its antiseptic action. When used as a purgative better effects may be obtained with less discomfort by giving it in divided doses, thus a quarter of a grain may be given every half hour until three or four grains have been taken. It is usually advisable to follow it the next day with a saline for the reason that if it should fail to operate sufficient calomel may be absorbed to cause salivation.

The mode of action of calomel as a diuretic is not yet positively determined, but there is abundant evidence that it is one of the most powerful stimulants to the kidney which we possess. According to Fleckseder (*W. K. W.*, 1911, p. 1421), it is especially useful in the severe dropsies of heart disease after the failure of other drugs. An old combination with digitalis and squill, frequently but incorrectly spoken of as *Niemeyer's pill*, is widely employed for this purpose. To obtain its diuretic effect it is usually necessary to give it in large doses. Ordinarily from a quarter to half a grain may be given every two hours until beginning ptyalism, but in emergencies where an immediate effect is desired it may be well to give five grains (0.32 Gm.) at once, repeating every two hours until fifteen grains (0.9 Gm.) have been taken. Purgative action may be guarded against by the simultaneous exhibition of opium.

Although calomel has long been used both externally and internally for its disinfectant properties, the studies of Schamberg and Kolmer (*J. A. M. A.*, 1914, lxii, p. 1950) indicate that its germicidal power has been underestimated. According to these investigators, weight for weight it is equal to the corrosive sublimate. Externally it is used for a dusting powder in various infections of the eye, and in *venereal ulcers*. Internally it is used for its antiseptic action in various types of *enteritis* or *dysentery*. Some commercial cosmetic preparations contain calomel in suspension, and it has always been found difficult or impossible to duplicate these smooth suspensions with commercial calomel, which first forms a curd and then rapidly settles out. F. W. Nitardy (*J. A. Ph. A.*, 1914, p. 965) found it possible to communicate the desired suspending qualities to ordinary calomel by first adding 5 per cent. by volume of mucilage of acacia, which produces a fine suspension, then allowing the calomel to settle out, decanting and discarding the supernatant liquid and replacing it with distilled water. By repeating this operation several times the acacia is all removed but the calomel retains its marked suspending quality.

The *dose* of calomel as an alterative is from one-sixth to one-third of a grain (0.01–0.02 Gm.); as a cathartic, from two to five grains (0.12–0.3 Gm.).

Off. Prep.—Pilulæ Catharticæ Compositæ, *U. S.;* Pilula Hydrargyri Subchloridi Composita, *Br.;* Unguentum Hydrargyri Subchloridi, *Br.;* Pilulæ Antimonii Compositæ, *N. F.;* Pulvis Hydrargyri Chloridi Mitis et Jalapæ, *N. F.;* Trochisci Santonini Compositi, *N. F.*

HYDRARGYRI IODIDUM FLAVUM. U. S.

YELLOW MERCUROUS IODIDE Hydrarg. Iod. Flav. [Mercurous Iodide, Protoiodide of Mercury, Yellow Iodide of Mercury]

(hȳ-drär′gy-rī ī-ōd′ī-dŭm flā′vŭm)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99 per cent. of HgI (327.52). Preserve it in well-closed containers, protected from light." *U. S.*

Hydrargyri Iodidum Viride, U. S. P. 1880; Green Iodide of Mercury, Hydrargyri Iodidum, U. S. P. 1850; Iodide of Mercury, Hydrargyrum Iodatum Flavum, Hydrargyri Protoioduretum, Ioduretum Hydrargyrosum; Protiodure de Mercure, Iodure mercureux, *Fr. Cod.;* Gelbes Jodquecksilber, *G.;* Protojoduro di mercurio, *It.;* Yoduro mercurioso, *Sp.*

The U. S. P. IX omitted a process for making yellow mercurous iodide. The U. S. P. VIII process was as follows:

"Mercury, *fifty grammes* [or 1 ounce av., 334 grains]; Nitric Acid, Potassium Iodide, Distilled Water, each, *a sufficient quantity.* Mix *twenty mils* [or 325 minims], each, of Nitric Acid and Distilled Water, and, when the liquid is cold, pour it upon the Mercury contained in a glass beaker. Set the mixture aside in a dark place, and keep it at a temperature between 25° and 30° C. (77° and 86° F.), with occasional agitation, until the reaction ceases and a little mercury still remains undissolved. Separate the crystals of mercurous nitrate, which will have formed, from the mother-liquid, allow them to drain in a glass funnel, and dry them on bibulous paper, in a dark place. When the salt is dry dissolve *forty grammes* [or 1 ounce av., 180 grains] of it in *six hundred and fifty mils* [or 21 fluidounces, 470 minims] of Distilled Water to which *six mils* [or 97 minims] of Nitric Acid have previously been added. Having prepared a solution of *sixteen grammes* [or 247 grains] of Potassium Iodide in *thirty-two mils* [or 1 fluidounce, 39 minims] of Distilled Water, slowly pour the solution of Potassium Iodide into the solution of Mercurous Nitrate, with constant stirring, which should be continued for fifteen minutes, allow the precipitate to subside, decant the supernatant liquid, and wash the precipitate by decantation with ten successive portions of *five hundred mils* [or 16 fluidounces, 435 minims] each of Distilled Water. Finally, transfer the precipitate to a filter, and dry it between sheets of bibulous paper, in a dark place, at a temperature not exceeding 40° C. (104° F.), and keep it in dark amber-colored vials, with the least possible exposure to light. Instead of weighing off *forty grammes* [or 1 ounce av., 180 grains] of the Mercurous Nitrate as above directed, the whole of the crystallized salt may be taken and the amount of Potassium Iodide, etc., adjusted to the proportions given above."

The Br. Pharm. dropped this salt at its 1885 revision, and has not restored it.

The process of the U. S. P. VIII differed from that official in 1880 for green iodide of mercury. (See *U. S. Dispensatory,* 19th ed., p. 627.) It is essentially the process recommended by Edward Soetje (*Proc. A. Ph. A.,* 1888, p. 167), the product is the result of double decomposition between mercurous nitrate and potassium iodide, in solution, *yellow* mercurous iodide and potassium nitrate being formed. This method of making mercurous iodide has long been known, but the disadvantage heretofore has been that some mercuric iodide was formed, which contaminated the product; the thorough washing by ten successive portions of distilled water should remove all traces of this impurity. Several other methods of making mercurous iodide have been proposed. (See *U. S. D.,* 19th ed., p. 627.)

George A. Haffa precipitated a solution of mercurous nitrate with potassium iodide, and obtained mercurous iodide of a yellow or green color according to the density of the solution. The solution of mercurous nitrate is prepared by acting upon 15,000 gr. of mercury with a cold mixture of nitric acid (6000 gr.) and water (4000 gr.), placing the vessel in cold water, and stirring the contents constantly until the reaction has entirely ceased; the white crystalline mass, without being separated from the excess of metallic mercury, is then dissolved in water acidulated with nitric acid (1 oz. to the gallon) until the solution measures four pints. For preparing *green mercurous iodide,* six ounces of a solution of mercurous nitrate are mixed with six pints of water, and there is added in a continuous stream, and with constant stirring, a solution of potassium iodide (3 oz. in 54 oz. of water); the precipitate is washed with water, and dried without the aid of heat. *Yellow mercurous iodide* is prepared in the same manner, except that two ounces of solution of mercurous nitrate diluted with water (8 pints) are used with a solution of potassium iodide (1 oz. in 4 pints of water). This salt darkens much more quickly when exposed to the light than that made by the U. S. P. 1880 process. (*A. J. P.,* 1886.) Stomen practically confirms these results. (*Ber. d. Chem. Ges.,* 1887; see also *Ph. Era,* 1888.) From experiments by H. C. Wood, it appears that the green iodide is a mixture of yellow iodide and metallic mercury. By continuing the trituration, the powders become more and more yellow, and at length have only a tinge of green. He infers that pure mercurous iodide is yellow, and that the green color is owing to an admixture of the blue of the mercury with the yellow of the mercurous iodide. (*P. J.,* 1868.) Flückiger (*Pharmaceutische Chemie,* 2d ed., 1888) agrees with this view, and says that by slow sublimation, at a very gentle heat,

the true mercurous iodide can be obtained in small transparent yellow crystals of the quadratic system which are related to the forms of calomel. (See *J. P. C.*, 1894, 67.) Francois's process is essentially the result of the reducing action of aldehyde on iodomercurammonium iodide. (*J. P. C.*, 1894, 67.)

Properties.—It is officially described as "a bright yellow, amorphous powder, odorless and tasteless. By exposure to light it becomes greenish in proportion as it undergoes decomposition into metallic mercury and mercuric iodide. Yellow Mercurous Iodide is almost insoluble in water and wholly insoluble in alcohol or ether. When slowly and moderately heated, it assumes at first an orange and then a red color, becoming yellow again on cooling. When quickly and strongly heated, it is at first partially decomposed into mercury and mercuric iodide, and finally is volatilized, leaving not more than 0.2 per cent. of residue. When heated with an equal weight of dried sodium carbonate, in a dry glass tube, Yellow Mercurous Iodide yields a sublimate of metallic mercury. When Yellow Mercurous Iodide is heated with sulphuric acid and a little manganese dioxide, the vapor of iodine is evolved. When 0.5 Gm. of the salt is thoroughly shaken with 10 mils of alcohol and the mixture filtered, 5 mils of the perfectly clear filtrate is not affected by an equal volume of hydrogen sulphide T.S. (*mercuric iodide*).

"**Assay.**—Transfer to a flask about 1 Gm. of Yellow Mercurous Iodide, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed, add 50 mils of tenth-normal iodine V.S. and 5 Gm. of potassium iodide, dissolved in 10 mils of distilled water, stopper the flask, and allow the mixture to stand in the tightly-stoppered flask, with occasional agitation, until complete solution has taken place. Then titrate with tenth-normal sodium thiosulphate V.S., using starch T.S. as indicator. It shows, in the dried salt, not less than 99 per cent. of HgI.

"Each mil of tenth-normal iodine V.S. used corresponds to 0.032752 Gm. of HgI. Each gramme of Yellow Mercurous Iodide, previously dried to constant weight, corresponds to not less than 30.2 mils of tenth-normal iodine V.S.

"Yellow Mercurous Iodide, previously dried to constant weight, may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

Its sp. gr. is 7.75. If quickly and cautiously heated, it sublimes in red crystals, which afterwards become yellow. "Gradually heated in a test-tube, it yields a yellow sublimate, which, upon friction, or after cooling, becomes red, while globules of metallic mercury are left in the bottom of the tube." *Br.* 1867.

Uses.—Mercurous iodide is used in advanced *syphilis*. The dose is one-fifth of a grain (0.012 Gm.), gradually increased to two grains (0.13 Gm.). It should never be given at the same time with potassium iodide, which converts it into mercuric iodide and metallic mercury.

Dose, one-fifth of a grain (0.012 Gm.).

HYDRARGYRI IODIDUM RUBRUM
U. S., Br.

RED MERCURIC IODIDE Hydrarg. Iod. Rub. [Biniodide of Mercury, Mercuric Iodide, Red Iodide of Mercury]

(hȳ-drär'gy-rī ī-ōd'ī-dŭm rŭ'brŭm)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99 per cent. of HgI_2 (454.44). Preserve it in well-closed containers, protected from light." *U. S.* "Red Mercuric Iodide, HgI_2, is obtained by the interaction of aqueous solutions of mercuric chloride and potassium iodide." *Br.*

Mercurius Iodatus Ruber, Deutoioduretum Hydrargyri, Hydrargyrum Iodatum Rubrum, Ioduretum Hydrargyricum; Deutoiodide of Mercury; Iodure mercurique, *Fr. Cod.*; Deuto-iodure (Bi-iodure) de Mercure, *Fr.*; Hydrargyrum Bijodatum, *P. G.*; Quecksilberjodid, Rothes Jodquecksilber, *G.*; Bijoduro di mercurio, *It.*; Yoduro mercurico, *Sp.*

No process for preparing this salt is given in the U. S. P. IX, nor British Pharm. (1914). The U. S. P. VIII process is appended.

"Corrosive Mercuric Chloride, *forty grammes* [or 1 ounce av., 180 grains]; Potassium Iodide, *fifty grammes* [or 1 ounce av., 334 grains]; Distilled Water, *a sufficient quantity*. Dissolve the Corrosive Mercuric Chloride and the Potassium Iodide, each, in *eight hundred mils* [or 27 fluidounces, 24 minims] of Distilled Water, and filter the solutions separately. Pour both solutions, simultaneously and in a thin stream, with constant and very active stirring, into *two thousand mils* [or 67 fluidounces, 5 fluidrachms] of Distilled Water. When the precipitate has subsided, decant the supernatant liquid, collect the precipitate on a filter, and wash it with cold Distilled Water, until the washings give not more than a slight opalescence with silver nitrate test solution. Finally, dry it in a dark place, between sheets of bibulous paper, at a temperature not exceeding 40° C. (104° F.), and keep it in well-stoppered bottles, protected from light."

In the above process for forming mercuric iodide a double decomposition takes place between corrosive sublimate and potassium iodide. resulting in the formation of potassium chloride which remains in solution, and mercuric iodide which precipitates. The precipitate is soluble in the reacting salts, and hence a loss of part of it is incurred by an excess of either. It is best, however, to have a slight excess of the potassium iodide, which is furnished by the proportion taken in the formula, as then decomposition of the whole of the corrosive sublimate is insured, and any contamination of the mercuric iodide by it prevented; loss by solution in the supernatant liquid is largely obviated by the improvement which was first introduced in the U. S. P. 1890, whereby separate solutions are poured simultaneously into a large volume of water.

For other methods of preparing this salt see *U. S. D.*, 19th ed., p. 629.

Properties.—As obtained by the old Edinburgh process, it is in splendid crimson acicular

crystals. Köhler has found, however, that it crystallizes better from boiling hydrochloric acid. (*Ber. d. Chem. Ges.*, 1879, p. 608.) It also crystallizes well from hot saturated solutions in acetone, glacial acetic acid, absolute alcohol, amyl alcohol, and nitric acid of 1.2 sp. gr., see also *Chem. News*, 1900, 24. When heated the mass becomes yellow at about 150° C. (302° F.), melting at 254° C. (489.2° F.) to a dark yellow liquid, and sublimes at 349° C. (660.2° F.) in yellow rhombic scales, which become red on cooling. Mercuric iodide is a dimorphous substance, having a different crystalline form in its red and yellow states. According to Schiff, it is only in its yellow form that it is soluble in alcohol; hence it is that, when separated by water from its alcoholic solution, it falls in this condition. (*Ann. Ch. Ph.*, cix, 371.) It forms definite compounds with the iodides of the alkali metals. The compound formed with potassium iodide has been used as a medicine. (See *Mercuric Potassium Iodide* T.S. Part III.)

"Red Mercuric Iodide is a scarlet-red, amorphous powder, odorless, nearly tasteless, and permanent in the air. Red Mercuric Iodide is almost insoluble in water; 1 Gm. dissolves in 115 mils of alcohol, 910 mils of chloroform, and in 120 mils of ether at 25° C. (77° F.); also in 20 mils of boiling alcohol; soluble in solutions of the soluble iodides, mercuric chloride, sodium thiosulphate, and hot solutions of the alkali chlorides. When heated to about 150° C. (302° F.) the salt becomes yellow, but again assumes a red color on cooling; upon further heating, it fuses to a dark yellow liquid which, on cooling, forms a yellow, crystalline mass; at higher temperatures it is finally volatilized, leaving not more than 0.2 per cent. of residue. Heat the salt with potassium hydroxide T.S., and add a little sugar of milk; the compound is reduced and metallic mercury is precipitated. Boil about 0.1 Gm. of the salt with 2 mils of potassium hydroxide T.S., filter and supersaturate the filtrate with nitric acid. The liquid becomes yellow from the liberation of iodine which produces a blue color upon the addition of a few drops of starch T.S. Agitate thoroughly about 0.5 Gm. of Red Mercuric Iodide with 10 mils of distilled water and filter; the filtrate does not become more than slightly colored by hydrogen sulphide T.S. (*soluble mercury salts*). Two Gm. of Red Mercuric Iodide dissolves quickly in 100 mils of distilled water, containing 2 Gm. of potassium iodide, without leaving more than 0.004 Gm. of insoluble matter.

Assay.—Red Mercuric Iodide, when previously dried to constant weight in a desiccator over sulphuric acid and assayed by the Electrolytic method (see Part III, Test No. 4) shows not less than 99 per cent. of HgI_2." *U. S.*

"A crystalline powder of a vermilion color, becoming yellow when heated to about 150° C. (302° F.). Almost insoluble in *water*, sparingly soluble in *alcohol* (90 per cent.), freely and entirely soluble in *ether* (absence of mercurous iodide), and in *solution of potassium iodide*. Yields the *reactions* characteristic of mercuric salts and of iodides. Volatilises at a temperature under redness, leaving not more than a trace of fixed residue. When 0.5 gramme is well shaken with 10 millilitres of *water* and filtered, the filtrate is not colored more than slightly brown by *hydrogen sulphide* (limit of mercuric chloride), and does not become more than opalescent on the addition of *solution of silver nitrate* (limit of chlorides)." *Br.*

Uses.—Mercuric iodide resembles corrosive sublimate in its activities and therapeutic uses. Like the chloride it is an intense local irritant and is capable of giving rise to violent gastro-enteritis. It is also an active germicide, although its sparing solubility has to a large extent prevented its practical employment. The double iodide of potassium and mercury has, however, been recommended as a practical disinfectant. As an internal remedy mercuric iodide is employed especially in old obstinate cases of *syphilis*, and those attended with rheumatoid pains, or *diseases of the bones*.

Cazenave considers mercuric iodide to be the best topical application in *lupus*. He applies it in thin layers, every six or eight days, to small portions of the ulcerated surface at a time, in the form of a caustic ointment, made of equal parts of the iodide, oil, and lard. The application produces severe pain, and gives rise to a sharp inflammation, which soon terminates, leaving the ulcer in an improved condition, with a tendency to cicatrize smoothly and on a level with the surrounding skin. A solution of mercuric iodide in olive oil (1 in 5000), which is to be prescribed as an external application, has been prepared by Delacour. (See *J. P. C.*, 1903, 603; 1904, No. 2.)

Dose, one-twentieth to one-twelfth of a grain (0.003–0.005 Gm.).

Off. Prep.—Liquor Arseni et Hydrargyri Iodidi, *U. S.* (*Br.*); Unguentum Hydrargyri Iodidi Rubri, *Br.*; Liquor Hydrargyri et Potassii Iodidi, *N. F.*

HYDRARGYRI OXIDUM FLAVUM.
U. S., Br.

YELLOW MERCURIC OXIDE **Hydrarg. Oxid. Flav.**

(hȳ-drär′gy-rī ŏx′ĭ-dŭm flā′vŭm)

"It contains, when dried to constant weight at 150° C. (302° F.), not less than 99.5 per cent. of HgO (216.60). Preserve it in well-closed containers, protected from light." *U. S.*

"Yellow Mercuric Oxide may be obtained by the interaction of aqueous solutions of mercuric chloride and sodium hydroxide. It contains not less than 99.3 per cent. of pure mercuric oxide, HgO." *Br.*

Yellow Oxide of Mercury; Hydrargyrum Oxidatum Flavum vel præcipitatum; Precipitated Oxide of Mercury Mercuric Oxide; Oxyde Mercurique jaune, *Fr. Cod.*; Oxide de Mercure jaune ou précipité, *Fr.*; Hydrargyrum oxydatum via humida paratum, *P. G.*; Präcipitirtes (Gelbes) Quecksilberoxyd, *G.*; Ossido mercurico giallo, *It.*; Oxido mercurico amarillo, *Sp.*

No process is given in the U. S. P. IX or

British Pharm. (1914) for this salt. The U. S. P. VIII process was as follows:

"Corrosive Mercuric Chloride, *one hundred grammes* [or 3 ounces av., 231 grains]; Sodium Hydroxide, *forty grammes* [or 1 ounce av., 180 grains]; Distilled Water, *a sufficient quantity.* Dissolve the Corrosive Mercuric Chloride in *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of warm Distilled Water, and filter the solution. Dissolve the Sodium Hydroxide (which should contain at least 90 per cent. of pure, anhydrous sodium hydroxide) in *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of cold Distilled Water, and into this solution pour gradually, and with constant stirring, the solution of Corrosive Mercuric Chloride. Allow the mixture to stand for an hour at a temperature of about 30° C. (86° F.), stirring frequently. Then decant the supernatant, clear liquid from the precipitate, and wash the latter repeatedly by the addition and decantation of portions of Distilled Water, using *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of Water each time. Collect the precipitate on a strainer, and continue the washing with warm Distilled Water, until a small portion of the washings, when poured on a little mercuric chloride test solution, no longer produces a yellowish turbidity at the line of contact of the two liquids. Then allow the precipitate to drain, and dry it between sheets of bibulous paper, in a dark place, at a temperature not exceeding 30° C. (86° F.), and keep it in well-stoppered bottles, protected from light."

The process formerly adopted for this preparation was that of Hoffmann. The United States Pharmacopœia directed the alkaline solution in excess, and the addition of the corrosive sublimate to the alkali. Both these points are important, for if the corrosive sublimate be in excess, brown oxychloride will be formed towards the last of the decomposition, and when the alkali is added to the solution of corrosive sublimate, the same compound will be formed from the first, and is with difficulty decomposed by an excess of alkali. The solution of sodium hydroxide should be as free as possible from carbonate, to prevent the formation of brown mercuric carbonate. The mercuric chloride is precipitated by the sodium hydroxide, sodium chloride being left in solution. The object of the subsequent washing is to remove the sodium chloride and the excess of the alkali. The process was improved in the 1890 revision (and the improvement retained in the 8th Rev.) through the use of a freshly made solution of sodium hydroxide; the official "solution of potassa" used in the U. S. P. 1880 process invariably contained potassium carbonate, except when it was freshly made, and the presence of carbonate gave the mercuric oxide a reddish-brown tint which was very objectionable.

Properties.—The official mercuric oxide is of a yellow color similar to that of the yolk of egg, and is a completely amorphous powder, exhibiting no evidence of crystalline particles even under the microscope. Yellow mercuric oxide differs from the red only by being amorphous and in a much more minute state of division, the red oxide by trituration acquiring an orange and finally a yellow color. In consequence of its different state of aggregation, it is much more quickly acted on by reagents than is the red oxide. Thus, oxalic acid, which acts slowly on the red oxide, combines with the yellow oxide at lower temperatures, producing the white oxalate, and while the latter oxide, in contact with chlorine, gives up oxygen to that element, forming hypochlorous acid and corrosive sublimate, the former exercises scarcely any influence on the gas at common temperatures. It is described in the U. S. Pharmacopœia as "a light orange-yellow, amorphous, heavy, impalpable powder; odorless, and having a somewhat metallic taste; permanent in the air, but turning darker on exposure to light. Yellow Mercuric Oxide is almost insoluble in water; insoluble in alcohol; readily dissolved by diluted hydrochloric or nitric acid, forming colorless solutions. When moistened with hot distilled water, Yellow Mercuric Oxide is not alkaline to litmus. When moderately heated, Yellow Mercuric Oxide assumes a red color. At a red heat it is completely decomposed into oxygen and metallic mercury, and is finally volatilized, leaving not more than 0.2 per cent. of residue. A solution of 0.5 Gm. of Yellow Mercuric Oxide in 25 mils of either diluted hydrochloric or diluted nitric acid is not more than slightly turbid. Heat 0.5 Gm. of Yellow Mercuric Oxide for two hours in a test tube, on a water bath, with a solution of 1 Gm. of oxalic acid in 10 mils of distilled water and 1 mil of ammonia water, replacing from time to time the water lost by evaporation; it is converted into white or yellowish-white mercuric oxalate (distinction from *red mercuric oxide*).

"Assay.—Dissolve about 0.5 Gm. of Yellow Mercuric Oxide, previously dried to constant weight at 150° C. (302° F.) and accurately weighed, in 10 mils of distilled water, and 5 mils of nitric acid, and further dilute the solution with 150 mils of distilled water. Then add 2 mils of ferric ammonium sulphate T.S. and titrate with tenth-normal potassium sulphocyanate V.S. to the production of a permanent yellowish-red color. It shows, in the dried Oxide, not less than 99.5 per cent. of HgO.

"Each mil of tenth-normal potassium sulphocyanate V.S. used corresponds to 0.01083 Gm. of HgO. Each gramme of Yellow Mercuric Oxide, previously dried to constant weight, corresponds to not less than 91.9 mils of tenth-normal potassium sulphocyanate V.S.

"Yellow Mercuric Oxide, previously dried to constant weight, may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

"A yellow powder; insoluble in *water;* readily soluble in *hydrochloric acid,* the solution yielding the *reactions* characteristic of mercuric salts. When 1 gramme is shaken with 5 millilitres of

water for five minutes, the mixture is neutral to *litmus*. When gently heated it assumes a red color. The solution obtained by dissolving 0.5 gramme in 2 millilitres of *nitric acid* and diluting with 20 millilitres of *water* requires not less than 45.8 millilitres of *N/10 solution of ammonium thiocyanate* to produce a permanent pink coloration, *solution of ferric sulphate* being used as indicator. Heated to incipient redness it is resolved into oxygen and the vapor of mercury, leaving not more than 0.5 per cent. of fixed residue." *Br.*

I. Comere explains in a paper in *Répert. de Pharm.*, 1881, 199, the various conditions and modifications in the process necessary to make the oxide vary in color. (*N. R.*, 1882, 149.)

Uses.—The attention which has been paid to the yellow oxide is owing to its peculiar applicability to the local treatment of diseases of the eye, in consequence of its amorphous character. B. Squire of England, was the first to notice publicly this use of the oxide. (*P. J.*, 2d ser., vi, 512.) At present the yellow oxide is very largely used by oculists throughout the world in *conjunctivitis, hordeolum,* and other inflammations of the eye. The red oxide, however carefully it may be triturated, even though in a perfectly impalpable state, still shows under the microscope crystalline particles, which in contact with the conjunctiva cause more or less irritation; it can, therefore, be readily understood that, in the ordinary mode of preparing it for use as an ointment, it may sometimes be productive of serious annoyance. From this objection the yellow oxide is exempt. The yellow oxide is also used largely in various *skin diseases,* notably *eczema* of the external auditory canal.

Off. Prep.—Unguentum Hydrargyri Oxidi Flavi, *U. S., Br.*

HYDRARGYRI OXIDUM RUBRUM. U. S., Br.

RED MERCURIC OXIDE Hydrarg. Oxid. Rub. [Red Precipitate]

(hȳ-drär'gy-rī ŏx'ĭ-dŭm rŭ'brŭm)

"It contains, when dried to constant weight at 150° C. (302° F.), not less than 99.5 per cent. of HgO (216.60). Preserve it in well-closed containers, protected from light." *U. S.* "Red Mercuric Oxide may be obtained by heating mercurous nitrate until acid vapors cease to be evolved. Contains not less than 99.3 per cent. of pure mercuric oxide, HgO." *Br.*

Peroxide of Mercury, Red Oxide of Mercury; Hydrargyri Nitrico-oxydum, Mercurius Corrosivus Ruber vel Præcipitatus, Oxydum Hydrargyricum; Oxyde mercurique rouge, *Fr. Cod.;* Deutoxyde ou Péroxyde de Mercure, Précipité rouge, Poudre de Jean de Vigo, *Fr.;* Hydrargyrum Oxydatum, *P. G.;* Quecksilberoxyd, Rother Praecipitat, Quecksilber Præcipitat, Rothes Quecksilberoxyd, *G.;* Ossido mercurico rosso, *It.;* Oxido mercurico rojo, *Sp.*

Neither Pharmacopœia gives at present an official process for this oxide. The U. S. P. 1870 and the British Pharm. (1885) gave the following processes:

"Take of Mercury *thirty-six troyounces;* Nitric Acid *twenty-four troyounces;* Water *two pints.* Dissolve the Mercury, with the aid of a gentle heat, in the Acid and Water previously mixed, and evaporate to dryness. Rub the dry mass into powder, and heat it in a very shallow vessel until red vapors cease to rise." *U. S.* 1870. "Take of Mercury, by weight, *eight ounces* [avoirdupois]; Nitric Acid *four fluidounces and a half* [Imperial measure]; Water *two fluidounces* [Imp. meas.]. Dissolve half the Mercury in the Nitric Acid diluted with the Water, evaporate the solution to dryness, and with the dry salt thus obtained, triturate the remainder of the Mercury until the two are uniformly blended together. Heat the mixture in a porcelain dish, with repeated stirring, until acid vapors cease to be evolved." *Br.* 1885.

In this process the mercury is dissolved by the nitric acid, forming either mercuric nitrate, or a mixture of this with mercurous nitrate. The resulting mass when exposed to a strong heat is decomposed, giving out red nitrous fumes, and assuming successively a yellow, an orange, and a brilliant purple-red color, which becomes orange-red on cooling. These changes are owing to the gradual separation and decomposition of the nitric acid, by the oxygen of which the mercurous oxide, if any be present, is converted into mercuric oxide, while nitrogen dioxide gas escapes, and becomes nitrogen tetroxide on contact with the air. The mercuric oxide is left behind, but in general not quite free from the nitrate, which cannot be wholly decomposed by heat without endangering the decomposition of the oxide itself, and the volatilization of the metal.

The preparation is still frequently called by its older name, *red precipitate.* The name of *red mercuric oxide* is appropriate and more definite.

In the preparation of this mercurial, various circumstances influence the nature of the product, and must be attended to, if it is desired to procure the oxide with that fine bright orange-red color, and shining scaly appearance, usually considered desirable. Among these circumstances is the condition of the mercuric nitrate submitted to calcination. According to Gay-Lussac, it should be employed in the form of small crystalline grains. If previously pulverized, as directed in some of the official processes, it will yield an orange-yellow powder; if it be in the state of large and dense crystals, the oxide will have a deep orange color. Care must be taken that the mercury and acid be free from impurities. It is highly important that sufficient nitric acid be employed fully to saturate the mercury. According to R. Dufass a mercuric oxide which combines the good properties of both red and yellow oxides, without any of their disadvantages, is obtained as follows: 125 Gm. of potassium carbonate and 500 Gm. of water are heated to boiling, and a solution of 100 Gm. of mercuric chloride in 1875 Gm. of water is slowly added under continued boiling. The resultant precipitate, after washing and drying, is obtained as an orange-

yellow crystalline powder. (*Süddeut. Apoth. Ztg.*, 1902, 836.) Payssé, who paid great attention to the manufacture of red precipitate, recommended 70 parts of nitric acid from 34° to 38° Baumé, to 50 parts of mercury. This, however, is an excess of acid. We have been told by a skilful practical chemist of Philadelphia that he has found, by repeated experiment, 7 parts of nitric acid of 35° Baumé to be sufficient fully to saturate 6 parts of mercury. Less will not answer, and more will be useless. It is not necessary that the salt should be removed from the vessel in which it is formed; it is even asserted that the product is always more beautiful when the calcination is performed in the same vessel. A glass flask may be used with a large flat bottom, so that an extended surface may be exposed and all parts heated equally. The metal and acid having been introduced, the flask should be placed in a sand bath, and covered with sand up to the neck. The solution of the mercury should be favored by a gentle heat, which should afterwards be gradually increased till red vapors appear, then maintained as equably as possible until these vapors cease and at last slightly elevated until oxygen gas begins to escape. This may be known by the increased brilliancy with which a taper will burn if placed in the mouth of the flask, or by its rekindling if partially extinguished. Too high a temperature must be carefully avoided, as it decomposes the oxide and volatilizes the mercury. At the close of the operation, the mouth of the vessel should be stopped, and the heat gradually diminished, the flask being still allowed to remain in the sand bath. These last precautions are said to be essential to the fine red color of the preparation. It is best to operate upon a large quantity of materials, as the heat may be thus more uniformly maintained. The former direction of the Br. Ph., to rub a portion of mercury with the nitrate before decomposing it, renders the process more economical, as the nitric acid, which would otherwise be dissipated, is thus employed in oxidizing an additional quantity of the metal. As the process is ordinarily conducted in laboratories, the mercuric nitrate is decomposed in shallow earthen vessels, several of which are placed upon a bed of sand, in the chamber of an oven or furnace, provided with a flue for the escape of the vapors. Each vessel may convently contain ten pounds of the nitrate. There is always loss in the operation thus conducted. Egeling states that this oxide can be prepared by precipitation so that the resulting product cannot be distinguished from that made by ignition. Into a boiling solution of mercuric chloride (1:5) a boiling concentrated solution of potassium hydroxide is poured, until the dark brown color of the oxychloride is changed to a bright red, and the liquid reacts faintly alkaline; this is poured into 20 volumes of boiling water, and the precipitate collected, washed and drained. (*Ph. Ztg.*, 92, 517.) (For a process for *Hydrargyrum præcipitatum per se, precipitate per se,* or *calcined mercury,* all practically identical with red mercuric oxide, see *U. S. D.*, 17th ed., 704.)

Properties.—Red mercuric oxide, well prepared, has a brilliant red color, with a shade of orange, a shining scaly appearance, and an acrid taste. It is very slightly soluble in water, of which Barker found 1000 parts to take up 0.62 of the oxide. Christison found 1 part of the oxide to be dissolved by about 7000 parts of boiling water, and the solution to give a black precipitate with hydrogen sulphide. Tannic acid precipitates metallic mercury from an aqueous solution of the oxide, especially when heated. (Bullock, *Proc. A. Ph. A.*, 1858, p. 306.) It is insoluble in cold alcohol and ether. (*Ibid.*) Nitric and hydrochloric acids dissolve it without effervescence.

"Red Mercuric Oxide occurs as heavy, orange-red, crystalline scales, or as a crystalline powder, acquiring a yellow color when finely divided; odorless and having a somewhat metallic taste, permanent in the air. Red Mercuric Oxide is almost insoluble in water; insoluble in alcohol; readily dissolved by diluted nitric acid, or by hydrochloric acid. When heated to about 400° C. (752° F.), Red Mercuric Oxide becomes dark violet or almost black, but assumes its original color on cooling. At a red heat it is completely decomposed into oxygen and metallic mercury, and is finally volatilized without leaving more than 0.2 per cent. of residue. A solution of 0.5 Gm. of Red Mercuric Oxide in 25 mils of either hydrochloric or nitric acid is not more than slightly turbid. Heat 0.5 Gm. of Red Mercuric Oxide for two hours, in a test tube on a water bath, with a solution of 1 Gm. of oxalic acid in 10 mils of distilled water and 1 mil of ammonia water, replacing, from time to time, the water lost by evaporation; it will not change color within two hours (distinction from *yellow mercuric oxide*). Mix 1 Gm. of Red Mercuric Oxide with 5 mils of distilled water, add 2 mils of sulphuric acid, cool the mixture and carefully pour upon it 2 mils of ferrous sulphate T.S.; no brown zone develops at the line of contact (*nitrate*).

"Assay.—Dissolve about 0.5 Gm. of Red Mercuric Oxide, previously dried to constant weight at 150° C. (302° F.) and accurately weighed, in 10 mils of distilled water and 5 mils of nitric acid, and further dilute the solution with 150 mils of distilled water. Then add 2 mils of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium sulphocyanate V.S. to the production of a permanent yellowish-red color. It shows, in the dried Oxide, not less than 99.5 per cent. of HgO.

"Each mil of tenth-normal potassium sulphocyanate V.S. used corresponds to 0.01083 Gm. of HgO. Each gramme of Red Mercuric Oxide, previously dried to constant weight, corresponds to not less than 91.9 mils of tenth-normal potassium sulphocyanate V.S.

"Red Mercuric Oxide, previously dried to constant weight, may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

"Orange-red powder, or crystalline scales. Insoluble in *water;* soluble in *hydrochloric acid,* the solution yielding the *reactions* characteristic of mercuric salts. Gently heated it becomes dark violet, but resumes its orange-red color on cooling. Heated in a dry test-tube it does not evolve orange fumes (absence of nitrates). Responds to the quantitative test described under 'Hydrargyri Oxidum Flavum.' Heated to incipient redness it is resolved into oxygen and the vapour of mercury, leaving not more than 0.3 per cent. of fixed residue." *Br.*

Uses.—This preparation is too harsh and irregular in its operation for internal use, but is still employed externally as a stimulant and escharotic in the state either of powder or of ointment, although to a great extent supplanted by the yellow oxide. The powder is sprinkled on the surface of *chancres,* and *indolent, flabby,* or *fungous ulcers.* The powder should be finely levigated.

Hydrargyri Oxidum Nigrum, U. S. 1850. *Black Mercurous Oxide.*—This preparation has been dropped from both Pharmacopœias, and is now very rarely used. For a full account of its preparation, uses, and properties, see *U. S. D.,* 14th ed., 1256.

Off. Prep.—Unguentum Hydrargyri Oxidi Rubri, *N. F., Br.*

HYDRARGYRI SALICYLAS. U. S.

MERCURIC SALICYLATE Hydrarg. Salicyl. [Mercuric Subsalicylate]

(hȳ-drär'gy-rī săl-ĭ-cȳ'lăs)

"A compound of mercury and salicylic acid containing not less than 54 per cent. nor more than 59.5 per cent. of Hg. Preserve it in well-closed containers protected from light." *U. S.*

Mercuric salicylate is a compound of more or less varying chemical composition, having the approximate formula:

$$HgC_6H_4OCOO = 336.63.$$

It is neither a normal salicylate nor a true subsalicylate as will be seen by the above formula which shows the mercury replacing both the phenolic and carboxylic hydrogen.

It is usually prepared by effecting a combination between freshly precipitated yellow mercuric oxide and salicylic acid in the presence of moisture and with gentle heating.

It is readily dissolved by solutions of alkalies which form double salts with it and from which solutions it is reprecipitated upon the addition of acids. It is decomposed by strong mineral acids.

This salt was made official in the U. S. P. IX. It is officially described as follows:

"Mercuric Salicylate is a white, slightly yellowish or slightly pinkish powder; odorless and tasteless. Mercuric Salicylate is nearly insoluble in water or alcohol; dissolved by solutions of the fixed alkalies or their carbonates; dissolved by warm solutions of the alkali halides with the formation of double salts. Heat about 1 Gm. of the salt with 10 mils of hydrochloric acid; a solution is obtained from which salicylic acid separates on cooling. A piece of copper foil added to a portion of the filtered solution, nearly neutralized with ammonia water, immediately becomes coated with metallic mercury. To another portion of this solution add a few drops of ferric chloride T.S.; a violet color is produced. Incinerate about 0.5 Gm. of the salt in a porcelain crucible; not more than 0.2 per cent. of residue remains. The salt does not redden moistened blue litmus paper (*free salicylic acid*). No dark color results at once on shaking about 0.1 Gm. of the salt with 5 mils of hydrogen sulphide T.S. (*foreign mercury compounds*). About 0.2 Gm. of the salt dissolves completely in 4 mils of normal sodium hydroxide V.S.

"**Assay.**—Digest about 0.5 Gm. of Mercuric Salicylate, accurately weighed, in 15 mils of sulphuric acid and 10 mils of nitric acid on a water bath until dissolved. Cool the solution, dilute it with 150 mils of distilled water, add 30 mils of solution of hydrogen dioxide and mix well. Now add gradually, with constant stirring, 5 mils of diluted hypophosphorous acid, then 5 Gm. of sodium chloride, dissolved in 20 mils of distilled water, stir thoroughly and allow the mixture to stand until the precipitate has subsided. Filter and wash the precipitate with distilled water. Transfer the precipitate and filter to a flask, add 50 mils of tenth-normal iodine V.S. and 2 Gm. of potassium iodide, agitate the mixture until all of the precipitate has dissolved and titrate the excess of tenth-normal iodine V.S. with tenth-normal sodium thiosulphate V.S. It shows not less than 54 per cent. nor more than 59.5 per cent. of Hg.

"Each mil of tenth-normal iodine V.S. corresponds to 0.02006 Gm. of Hg. Each Gm. of Mercuric Salicylate corresponds to not less than 26.9 mils nor more than 29.7 mils of tenth-normal iodine V.S.

"Mercuric Salicylate may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

Uses.—Mercuric Salicylate is used chiefly in the treatment of *syphilis,* especially by intramuscular injection. The advantages claimed for it are that it is locally non-irritant and that it does not salivate. The first of these is due to its insolubility and the second is an evidence of its slow absorption. Nelson and Anderson (*J. A. M. A.,* 1915, lxv, 1905) reach the conclusion that, although there may be a subsidence of the objective manifestations of *syphilis* under the use of mercuric salicylate, the drug does not exercise a real curative effect. Mercuric salicylate is also used locally for its germicidal effect either as a dusting powder in the strengths of ten per cent., or as an injection in *gonorrhea,* one part of the drug being suspended in 300 of mucilage. It is also said to be a useful local application in *alopecia* of syphilitic origin.

For intramuscular injection a ten per cent. suspension in sterile liquid petrolatum may be employed. Of this ten minims (0.6 mil) may be injected deeply into the muscles of the back or buttocks, under strict asepsis, two or three

times a week. It has also been used by mixing with an equal part of potassium carbonate and dissolving in distilled water.

Dose by mouth, one-twelfth to one-third grain (0.005–0.021 Gm.).

HYDRARGYRUM. U. S., Br.

MERCURY Hydrarg. [Quicksilver]

(hȳ-drär′gy-rŭm)

"It contains not less than 99.5 per cent. of Hg (200.6). Preserve it in strong, well-closed containers." *U. S.* "Mercury is a liquid metal which may be obtained from native mercuric sulphide." *Br.*

Hydrargyrum Vivum, Mercurius Vivus, Argentum Vivum, Mercure Purifié, *Fr. Cod.*; Vif Argent, *Fr.*; Hydrargyrum, *P. G.*; Quecksilber, *G.*; Mercurio, *It., Sp.*

Mercury is found pure, forming an amalgam with silver, in the form of chloride (native calomel), but most abundantly as the sulphide or native cinnabar. Mines of this metal are found at Almaden in Spain, at Idria in Carniola, in the former duchy of Deux-Ponts, in Belluno, a province of Venetia, in Corsica, in the Philippine Islands and China, near Huancavelica in Peru, near Azogue in Colombia, at Durango in Mexico, at Yulgilbar, New South Wales, at New Almaden, New Idria, and other localities in Santa Clara County, California, about sixty-six miles from San Francisco, and in Brewster and other counties in Texas. The most ancient mine is that of Almaden in Spain, which was worked before the Christian era. This mine, and the mines of California, are the most productive at the present day, the Spanish mine yielding about three and a quarter millions of pounds, and the California mines about two-thirds of this amount annually. The ore in all the mines mentioned is cinnabar. The cinnabar from old Almaden is of a dull-red color in mass, of a dull brick-red color when in fine powder, and of the sp. gr. 3.6. That from New Almaden is of a bright-red color, slightly inclining to purple, not so hard as the Spanish ore, of a brilliant vermilion color in powder, and of the sp. gr. 4.4. The California cinnabar is richer in mercury, because purer, than the Spanish, the former yielding about 70 and the latter about 38 per cent. of mercury, according to the analysis of Adam Bealey. The California mine had been long known to the Indians, but its commercial value was first made known about 1843, by a Mexican, named Castillero, who became its first owner. At present it is in the hands of Americans. Ruschenberger has detected selenium in California cinnabar.

Extraction.—Mercury is obtained almost exclusively from the sulphide or native cinnabar. It is extracted by two principal processes. According to one process, the mineral is picked, pounded, and mixed with lime. The mixture is then introduced into cast iron retorts, which are placed in rows, one above the other, in an oblong furnace, and connected with earthenware receivers one-third full of water. Heat being applied, the lime combines with the sulphur, so as to form calcium sulphide and sulphate, while the mercury distils over, and is condensed in the receivers. The other process is practised at Almaden in Spain. Here a square furnace is employed, the floor of which is pierced with many holes, for the passage of the flame from the fireplace beneath. In the upper and lateral part of the furnace, holes are made, communicating with several rows of *aludels*, formed of adapters passing into one another, which terminate in a small chamber that serves both as condenser and receiver. The mineral, having been picked by hand and pulverized, is kneaded with clay, and formed into small masses, which are placed on the floor of the furnace. Heat being applied, the sulphur burns, and the volatilized mercury passes through the aludels to be condensed in the chamber.

Mercury, as found in commerce, is contained in cylindrical wrought iron bottles, called flasks, each containing 75 pounds. The United States production for 1916 was 28,942 flasks mainly in California, the world's production for 1913 is given as 124,654 flasks, Spain, Italy, Austria-Hungary, and the United States being the chief producers. The world's production at present is about 9,500,000 pounds. The exports are made principally to China, Mexico, Chili, and Peru. The chief uses of the metal are in mining silver and gold, in preparing vermilion, in making thermometers and barometers, in silvering looking glasses, and in forming various pharmaceutical compounds.

Properties.—Mercury is "a shining, silver-white metal; liquid at ordinary temperatures and easily divisible into spherical globules. When cooled to about –40° C. (–40° F.), it forms a ductile, malleable mass. It is without odor or taste. Specific gravity: about 13.5 at 25° C. (77° F.). Mercury is insoluble in the ordinary solvents, also in concentrated hydrochloric acid and, at ordinary temperatures, in sulphuric acid, but it dissolves in the latter when boiled with it, and is readily and completely dissolved by nitric acid. At ordinary temperatures Mercury volatilizes very slowly, but more rapidly as the temperature increases, and at about 358° C. (676.4° F.) it boils and is volatilized, yielding not more than 0.02 per cent. of residue. When globules of Mercury are dropped upon white paper, they roll about freely, retaining their globular form, and leaving no streaks or traces. Mercury must be perfectly dry and present a bright surface even after agitation in contact with air.

" Assay.—Dissolve about 0.4 Gm. of Mercury, accurately weighed, in a mixture of 10 mils of distilled water and 10 mils of nitric acid, warm the solution gently until red fumes cease to be evolved and the solution is colorless, and add 150 mils of distilled water. Then add 2 mils of ferric ammonium sulphate T.S. and titrate with tenth-normal potassium sulphocyanate V.S. to the production of a permanent, yellowish-red

color. It shows not less than 99.5 per cent. of Hg.

"Each mil of tenth-normal potassium sulphocyanate V.S. used corresponds to 0.01003 Gm. of Hg. Each gramme of Mercury corresponds to not less than 99.2 mils of tenth-normal potassium sulphocyanate V.S.

"Mercury may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

"A silver-white, heavy liquid with a metallic lustre; easily divisible into globules. Readily volatilises when heated, leaving no appreciable fixed residue (absence of metallic and other impurities)." *Br.*

When perfectly pure it undergoes no alteration by the action of air or water, but in its ordinary state suffers a slight tarnish. When heated to near the boiling point, it gradually combines with oxygen, and is converted into mercuric oxide; but at the temperature of ebullition it parts with the oxygen with which it had combined, and is reduced again to the metallic state. It boils at 358° C. (676.4° F.), yielding a colorless vapor, and congeals at –39.4° C. (–39° F.), forming a malleable solid of tin-white color. It is a good conductor of heat, and its specific heat is small. It is not attacked by hydrochloric acid, nor by cold sulphuric acid; but boiling sulphuric acid or cold nitric acid dissolves it, producing mercurous sulphate and mercurous nitrate, respectively, with the liberation, in the former case, of sulphurous acid; in the latter, of nitrogen dioxide. Its combinations are numerous, and many of them constitute important medicines. It forms two series of compounds, the *mercurous* compounds containing the atom Hg^{I}, and the *mercuric* compounds containing the atom Hg^{II}.

Mercury, as it occurs in commerce, is in general sufficiently pure for pharmaceutical purposes. Occasionally it contains foreign metals, as lead, tin, zinc, and bismuth. Brande informs us that in examining large quantities of this metal in the London market he found it in only one instance intentionally adulterated. When impure, the metal has a dull appearance, leaves a trace on white paper, is deficient in due fluidity and mobility, as shown by its not forming perfect globules, is not totally dissipated by heat, and when shaken in a glass bottle coats its sides with a pellicle, or if very impure, deposits a black powder. If agitated with strong sulphuric acid, the adulterating metals become oxidized and dissolved, and thus the mercury may to a limited extent be purified. Lead is detected by shaking the suspected metal with equal parts of acetic acid and water, and then testing the acid by sodium sulphate or potassium iodide. The former will produce a white, the latter a yellow, precipitate, if lead be present. Bismuth is detected by dropping a nitric solution of the mercury, prepared without heat, into distilled water, when bismuth subnitrate will be precipitated. The complete solubility of the metal in nitric acid shows that tin is not present, and, if hydrogen sulphide does not act upon hydrochloric acid previously boiled upon the metal, the absence of contaminating metals is shown. Mercury may be purified by digesting it with a small portion of weak nitric acid, or with a solution of mercuric chloride, whereby all the ordinary contaminating metals will be removed. It may also be purified by distillation. For further details regarding the purification of mercury, see *U. S. D.*, 19th edition, p. 635.

Mercury is detected with great delicacy by Smithson's process, which consists in the use of a plate of tin, lined with one of gold, in the form of a spiral. When immersed in a mercurial solution, this galvanic combination causes the precipitation of the mercury on the gold, which consequently contracts a white stain. In order to be sure that the stain is caused by mercury, the metal must be volatilized in a small tube, so as to obtain a characteristic globule. Danger and Flandin have improved on Smithson's process. (See *Chem. Gaz.*, No. 61, p. 191.) A minute portion of any of the preparations of mercury, either in the solid state or in concentrated solution, being placed on a bright plate of copper, and a drop of a strong solution of potassium iodide added, a silvery characteristic stain will immediately appear on the copper.

For further details regarding the detection of mercury in compounds or preparations containing it, see *Hydrargyri Chloridum Corrosivum.*

It is difficult to accurately weigh small specified quantities of metallic mercury. An ingenious method was suggested by H. Kral, which is as follows: It consists of using a goose quill, into which the necessary quantity of mercury has been weighed. A small hole is then cut immediately above the surface of mercury, and the apparatus is ready for use. By simply immersing it into the bottle containing the mercury, it is filled through the opening, and uniform quantities, sufficiently accurate for practical purposes, are thus easily measured. (*Ph. Centralh.*, 1895, 422, 423.) In pharmaceutical operations a medicine dropper may be used to transfer the mercury.

Uses.—Metallic mercury in bulk is not absorbable, but when in a finely divided condition or in combination as a salt, it is taken up from the alimentary tract. In what form it is absorbed is at present uncertain. There are two widely held views, one that it is converted into an albuminate which is soluble in an excess of protein matter, and the other that it forms in the intestinal tract an oxide which is dissolved by the fatty matters. After its absorption it escapes from the system chiefly through the kidneys, although it has been detected in practically every secretion of the body. The elimination is comparatively slow so that when used over long periods of time it tends to accumulate in the system and may be stored up in the body for long periods. When present in the blood in large amounts it acts as a local irritant to vari-

ous glandular structure and leads to an increased secretion. The salivary glands are usually the most sensitive so that ptyalism is an early symptom of chronic mercurial poisoning, but both the kidney and bowels are frequently affected.

The effects of small quantities of mercury on the bodily functions are not positively known but it appears to act somewhat like arsenic, restraining destructive metabolism and thereby causing a tendency to increase in weight. A stimulating effect upon the blood making organs is often manifest by an increase in the number of red blood cells, but after toxic doses anemia may result apparently through destruction of the bone marrow. After large doses there is also a diminution in the fibrin content of the blood. Whether this latter change is caused by therapeutic quantities is at present uncertain, but the clinical effects seen in conditions attended with fibrinous exudate would lead one to believe that it does.

In the form of blue mass (see page 688) and of calomel (see page 557), mercury is used as a cathartic and in the latter form also as a diuretic. All of the soluble salts appear to be more or less actively germicidal, the bichloride being the most widely employed. In this place will be considered the effects of mercury upon the system which are common to all the preparations used internally.

The most marked constitutional effects from mercury are seen in *syphilis*. Its beneficial action in this affection is due to a direct toxic effect upon the spirochetes which are the cause of the disease. Under full mercurialism the obvious lesions of lues may disappear with great rapidity, but some of the germs remain hidden, so to speak, in the internal organs, especially in the central nervous system, and it is usually essential that the administration of mercury be continued for from one to two years. The generally accepted mode of using the metal is to give it in ascending doses until a mild degree of ptyalism is produced, then withdraw the metal for a few days to allow the system to clear itself of the excess and give it in doses just below that which caused salivation. In inflammatory diseases of the serous membranes, as *pleurisy, meningitis,* and *iritis,* especially when there is fibrinous exudate, mercury is often of the utmost value. In similar conditions involving mucous membranes—especially *enteritis*—while it appears to exercise more or less antiphlogistic action, its effects are much less striking.

The first observable signs of mercury inducing ptyalism are a coppery taste in the mouth, a slight soreness of the gums, and an unpleasant sensation in the sockets of the teeth when the jaws are firmly closed. Shortly afterwards the gums begin to swell, a line of whitish matter is seen along their edges, and the breath is infected with a peculiar and very disagreeable odor, called the mercurial fetor. The saliva at the same time becomes increased in quantity and more viscid, and, if the affection proceed, the gums, tongue, throat, and face become much swollen; ulcerations attack the lining membrane of the mouth and fauces; the jaws become excessively painful; the tongue is coated with a thick whitish fur, and the saliva flows in streams from the mouth.

If the use of the metal be persisted in, as was formerly sometimes the custom, the devitalized tissue affording a favorable place for bacterial growth, extensive necrosis may follow. In the treatment of *ptyalism* it should be remembered that the inflammation of the salivary glands is the result of an effort at excretion and those drugs, such as potassium iodide, which tend to hasten the elimination of the metal will aggravate the symptoms. The most important element of the treatment is local cleanliness. Antiseptic and astringent mouth washes should be frequently used and ulcerated spots may be touched with solutions of silver nitrate. If the flow of saliva is excessive full doses of atropine may be given.

In the foregoing observations we have described the ordinary effects of mercury, but occasionally, in peculiar constitutions, its operation is quite different, being productive of a dangerous disturbance of the vital functions. Pearson gave a detailed account of this occasional peculiarity in the operation of mercury, in his work on venereal diseases. The symptoms which characterize it are a small and frequent pulse, anxiety about the præcordia, pale and contracted countenance, great nervous agitation, and alarming debility. Their appearance is the signal for discontinuing the mercury, as a further perseverance with it might be attended with fatal consequences. Mercury occasionally produces a peculiar eruption of the skin, which is described by writers under the various names of *hydrargyria, eczema mercuriale,* and *lepra mercurialis.* Those who work in mercury, and are, therefore, exposed to its vapor, such as looking-glass silverers, and quicksilver miners, are injured seriously in their health, and not unfrequently affected with shaking palsy, attended with vertigo and other cerebral disorders. The miners are often salivated.

Many plants, exposed to the influence of the vapor spontaneously rising from mercury in confined air, perish in a few days, while if sulphur be placed by the side of the metal no effect of the kind is experienced. (Boussingault, *J. P. C.,* Sept., 1867, p. 176.) A probable inference from this fact is that workmen necessarily exposed to the vapor of mercury might be protected by the presence of sulphur in sufficient quantity.

Mercury has in the past been given in the metallic state, in the quantity of a pound or two, in *obstruction of the bowels,* to act by its weight; but the practice is of doubtful advantage.

Off. Prep.—Emplastrum Hydrargyri, *Br.;* Hydrargyrum cum Cretæ, *U. S., Br.;* Linimentum Hydrargyri (from Ointment), *Br.;* Massa Hydrargyri, *U. S.* (*Br.*); Unguentum Hydrar-

gyri, *U. S., Br.;* Unguentum Hydrargyri Compositum, *Br.;* Unguentum Hydrargyri Dilutum, *U. S.;* Petroxolinum Hydrargyri, *N. F.*

HYDRARGYRUM AMMONIATUM.
U. S., Br.

AMMONIATED MERCURY Hydrarg. Ammon. [White Precipitate]

(hȳ-drär′gy-rŭm ąm-mō-nī-ā′tŭm)

"It contains mercurammonium chloride [$HgNH_2Cl = 252.09$] corresponding to not less than 78 per cent. nor more than 80 per cent. of Hg. Preserve it in well-closed containers, protected from light." *U. S.*

Hydrargyri Præcipitatum Album; Hydrargyrum Amidatobichloratum (ammoniato-muriaticum), Mercurius Præcipitatus Albus; Hydrargyri Ammonio-Chloridum; Ammoniochloride of Mercury, Mercuric Ammonium Chloride; Mercuric amido-chloride; Chloramidure de Mercure, Oxychlorure Ammoniacal de Mercure, Lait Mercuriel, Mercure Précipité Blanc, *Fr.;* Hydrargyrum praecipitatum album, *P. G.;* Weisser Quecksilberpräcipitat, Quecksilber-Chloridamid, *G.;* Cloramiduro di mercurio, *It.*

"Mercuric Chloride, 60 *grammes;* Solution of Ammonia, 80 *millilitres;* Distilled Water, *a sufficient quantity.* Dissolve the Mercuric Chloride in *twelve hundred millilitres* of Distilled Water with the aid of heat; pour the liquid into the Solution of Ammonia diluted with *four hundred millilitres* of Distilled Water, constantly stirring; collect the precipitate on a filter; wash it with *two hundred and fifty millilitres* of Distilled Water, and dry at a temperature not exceeding 30° C. (86° F.)." *Br.*

No process was recognized by the U. S. P. IX, but the U. S. P. VIII process was as follows:

"Corrosive Mercuric Chloride, in powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Ammonia Water, Distilled Water, each, *a sufficient quantity.* Dissolve the Corrosive Mercuric Chloride in *two thousand mils* [or 67 fluidounces, 5 fluidrachms] of warm Distilled Water, filter the solution, and allow it to cool. Pour the filtered liquid gradually, and with constant stirring, into *one hundred and fifty mils* [or 5 fluidounces, 35 minims] of Ammonia Water, taking care that the latter shall remain in slight excess. Collect the precipitate on a filter, and, when the liquid has drained from it as much as possible, wash it with a mixture of *four hundred mils* [or 13 fluidounces, 252 minims] of Distilled Water and *twenty mils* [325 minims] of Ammonia Water. Finally, dry the precipitate between sheets of bibulous paper, in a dark place, at a temperature not exceeding 30° C. (86° F.), and keep it in well-stoppered bottles, protected from light."

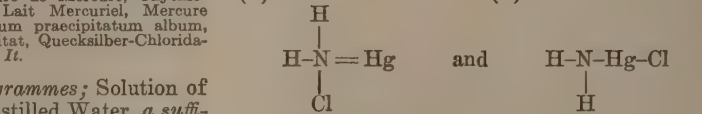
The British Pharmacopœia directs the preparation of white precipitate by precipitating a solution of mercuric chloride by ammonia. When ammonia, in slight excess, is added to a cold solution of mercuric chloride, ammonium chloride is formed in solution, and the white precipitate of the Pharmacopœias thrown down. The precipitate is usually washed with distilled water until the washings cease to give evidence of the presence of a chloride by producing a precipitate with silver nitrate acidulated with nitric acid. The white precipitate forms according to the following reaction:

$$HgCl_2 + 2NH_3 = NH_4Cl + NH_2HgCl$$

In other words, one molecule of the mercuric chloride reacts with two of the ammonia, and yields one molecule of ammonium chloride and one of *mercur-ammonium chloride,* or white precipitate. The commercial varieties have at times differed somewhat from the present official preparation in composition, the formula being $N_2H_5HgCl_2$ (or *Mercur-diammonium chloride*). (See paper by F. X. Moerk, *A. J. P.,* 1888.)

Of the two possible formulas illustrated by the following:

(1) (2)



Saha and Choudberry (*Ztschr. Anorg. Chem.,* 1914, 86, 225) concluded that the second formula is the only tenable one, agreeing with certain experiments by which derivatives were formed.

Properties.—"Ammoniated Mercury occurs as white, pulverulent pieces, or as a white, amorphous powder, without odor, and having an earthy, afterwards styptic and metallic taste; permanent in the air. Ammoniated Mercury is insoluble in water or alcohol. By prolonged washing with water it is gradually decomposed, assuming a yellow color, and becoming converted into a basic salt. Readily dissolved by warm hydrochloric, nitric, or acetic acid, and by a cold solution of ammonium carbonate. Also completely dissolved by a cold solution of sodium thiosulphate, with the evolution of ammonia; when this solution is heated for a short time, red mercuric sulphide is separated, which, on protracted boiling, turns black. At a temperature below a red heat, Ammoniated Mercury is decomposed without fusion, and at a red heat it is volatilized without leaving more than 0.2 per cent. of residue. When heated with potassium hydroxide T.S., the salt turns yellow, and evolves ammonia. A solution of the salt in diluted nitric acid yields with potassium iodide T.S. a red precipitate soluble in an excess of the reagent. With silver nitrate T.S. its nitric acid solution yields a white precipitate. The salt is completely soluble in hydrochloric acid (*mercurous salts*) without effervescence (*carbonates*)." *U. S.*

"**Assay.**—Dissolve about 0.5 Gm. of Ammoniated Mercury, accurately weighed, in 2 mils of hydrochloric acid and 10 mils of distilled water, warming gently until solution is effected, then dilute with 300 mils of distilled water and proceed as directed under *Hydrargyri Chloridum Corrosivum,* page 552, beginning with the word

'Pass' on line 6 of the Assay. The weight of mercuric sulphide obtained when multiplied by 0.862 indicates its equivalent in mercury (Hg) which corresponds to not less than 78 per cent. nor more than 80 per cent. of Hg.

"Each gramme of Ammoniated Mercury corresponds to not less than 0.9047 Gm. nor more than 0.9279 Gm. of mercuric sulphide.

"Ammoniated Mercury may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

"A white, heavy, tasteless powder; insoluble in *alcohol* (90 per cent.) or *ether;* slowly decomposed by *water*. Digested with *solution of sodium hydroxide* it evolves ammonia, acquiring a pale yellow color, and the liquid, filtered and acidified with *nitric acid,* yields a white precipitate with *solution of silver nitrate*. Boiled with *solution of stannous chloride* it becomes grey, and yields globules of metallic mercury. Volatilises without fusing when sufficiently heated, leaving no appreciable fixed residue. When 0.3 gramme is triturated in a glass mortar with a few drops of *water,* and transferred to a flask with the aid of 40 millilitres of *water,* the mortar being finally rinsed with a solution of 2 grammes of *potassium iodide* in 10 millilitres of *water* and the rinsings added to the contents of the flask, then, the flask being securely closed and rotated frequently until solution is complete, the liquid thus obtained requires for neutralisation not less than 22.5 millilitres of *N/10 solution of hydrochloric acid, solution of methyl orange* being used as indicator (presence of not less than 94.5 per cent. of mercuric-ammonium chloride, NH_2HgCl)." *Br.*

Adulteration with white lead, chalk, or calcium sulphate may be detected by exposing a sample to a strong red heat, when these impurities will remain. Should starch be mixed with it, a charred residue will be obtained on the application of heat. Lead or starch may be found by digesting it with acetic acid, and testing the acetic solution with the compound solution of iodine, which will give a yellow precipitate if lead and a blue one if starch be present. The absence of mercurous compounds is shown by its not being blackened when rubbed with lime water.

Uses.—Ammoniated mercury is used only as an external application. It is a valuable remedy in parasitic skin diseases, such as *ringworm* or *favus,* and is also employed for destruction of *lice*. Mercur-diammonium chloride is said to produce an ointment more translucent and less white than the genuine, and more apt to become yellow on being kept. (J. Borland, *P. J.*, Dec., 1867, p. 262.)

Ammoniated mercury has been swallowed by mistake. It is highly poisonous, producing gastric pain, nausea, and purging. For recovery after taking half a drachm, see *L. L.,* July 4, 1857. The remedies employed were an emetic of zinc sulphate and milk.

Off. Prep.—Unguentum Hydrargyri Ammoniati, *U. S., Br.*

HYDRARGYRUM CUM CRETA.
U. S., Br.

MERCURY WITH CHALK Hydrarg. c. Cret.

(hȳ-drär'gy-rŭm cŭm crē'tą)

"It contains not less than 37 per cent. nor more than 39 per cent. of Hg." *U. S.*

Gray Powder; Æthiops Cretaceus; Mercure avec la Craie, Poudre de Mercure crayeux, *Fr.;* Quecksilber mit Kreide, *G.*

* "Mercury, *thirty-eight grammes* [or 1 ounce av., 150 grains]; Clarified Honey, *ten grammes* [or 154 grains]; Prepared Chalk, *fifty-seven grammes* [or 2 ounces av., 5 grains]; Water, *a sufficient quantity,* to make *one hundred grammes* [or 3 ounces av., 231 grains]. Weigh the mercury and clarified honey successively into a strong bottle of the capacity of *one hundred mils* [or 3 fluidounces, 183 minims], and add *two mils* [or 32 minims] of water. Cork the bottle, and shake it for about half an hour at a time, until the aggregate time of shaking reaches ten hours, or until the globules of mercury are no longer visible under a lens magnifying *four diameters*. The shaking may be more conveniently performed by mechanical means. Rub the prepared chalk with water, in a mortar, to a thick, creamy paste, and, having added the contents of the bottle, wash out the last portions with a little water, triturate the whole to a uniform mixture. Finally, dry the mixture, first between ample layers of bibulous paper, and afterwards in a dish at the ordinary temperature, until it weighs *one hundred grammes* [or 3 ounces av., 231 grains]. Then reduce it to a uniform powder, without trituration, and keep it in well-closed containers, protected from light." *U. S.*

"Mercury, 20 *grammes;* Prepared Chalk, 40 *grammes*. Triturate together in a porcelain mortar until the mixture acquires a uniform grey color and metallic globules cease to be visible to the naked eye." *Br.*

Dr. E. R. Squibb suggested the present official method of making mercury with chalk. The process is termed "succussion." When mercury is triturated with certain dry and pulverulent substances, such as chalk or magnesia, it gradually loses its fluidity and metallic luster and becomes a dark-gray powder. A similar change takes place when it is rubbed with viscid or greasy substances, such as honey or lard. The globules disappear, so as in some instances not to be visible even through a good lens, and the mercury is said to be *extinguished*. It was formerly thought that the metal was oxidized in the process. At present the change is generally ascribed to the mechanical division of the metal, which in this state is supposed to be capable of acting on the system with greater energy. There is good reason, however, to believe that in this, as in all the analogous preparations of mercury in which the metal is extinguished by trituration, a very small portion is converted into mercurous oxide, while by far the greater part remains in the metallic state.

Mercury with chalk is officially described in

the U. S. P. IX as "a light gray, rather damp powder, free from grittiness, without odor, and having a slightly sweet taste. Digest 0.1 Gm. of the powder with 20 mils of warm acetic acid; the chalk dissolves with effervescence, and a residue of finely divided mercury is left. On filtering this mixture, the filtrate becomes not more than slightly opalescent on the addition of a few drops of hydrochloric acid (*mercurous oxide*). Digest 0.1 Gm. of the powder with 20 mils of warm diluted hydrochloric acid and filter; the filtrate is not rendered more than slightly brown by hydrogen sulphide T.S. (*mercuric oxide*).

"**Assay.**—Dissolve about 1 Gm. of Mercury with Chalk, accurately weighed, in a mixture of 10 mils of distilled water and 10 mils of nitric acid and heat it on a water bath until red fumes cease to be evolved and the liquid becomes colorless. Then add 150 mils of distilled water and 2 mils of ferric ammonium sulphate T.S. and titrate the solution with tenth-normal potassium sulphocyanate V.S. It shows not less than 37 per cent. nor more than 39 per cent. of Hg.

"Each mil of tenth-normal potassium sulphocyanate V.S. used corresponds to 0.01003 Gm. of Hg. Each gramme of Mercury with Chalk corresponds to not less than 36.9 mils nor more than 38.9 mils of tenth-normal potassium sulphocyanate V.S.

"Mercury with Chalk may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

"A light-grey powder, free from grittiness; tends to aggregate into minute globules. Insoluble in *water;* partially dissolved by *diluted hydrochloric acid,* the residual mercury being left in a finely divided state; the filtered liquid does not yield any white or grey precipitate on the addition of *solution of stannous chloride* (absence of mercuric compounds)." *Br.*

Robert B. Matter suggests an improved process for its preparation whereby labor and time are saved. It is as follows: "Mix twelve parts of finely powdered gum arabic with twelve parts of prepared chalk, triturate with sufficient water to form a rather thin paste, add thirty-eight parts of mercury, and continue the trituration until the globules of mercury have disappeared. Now add thirty-eight parts of finely powdered prepared chalk and sufficient water to form a thin paste, triturate, and when all the globules of mercury have disappeared, place the mortar in a hot water bath. The mixture distributed around the sides of the mortar will dry rapidly, when it can be easily scraped out, powdered in a clean mortar, passed through bolting cloth, or a fine sieve, and finally rubbed lightly in a clean dry mortar; 8 ounces may be made by this process in an hour." (*A. J. P.*, 1886, 119.)

Many modifications of the earlier processes suggested for the manufacture of this important preparation have appeared from time to time (see *U. S. D.*, 19th ed., p. 639), but the present official process is entirely satisfactory.

As found in commerce, mercury with chalk, instead of being the mild preparation intended, sometimes acts very harshly, causing vomiting, gastric pains, etc. This has been ascribed to the presence of antimony or arsenic, which, however, must be rare; the ordinary cause of the harshness is no doubt mercuric oxide, produced in minute proportion either during the trituration, or by the spontaneous change which occurs with time, mercurous oxide becoming mercuric oxide by the influence of light. The only sure method to guard against such results is to test the preparation carefully before dispensing it. (See *A. J. P.*, 1878, p. 325.) If the mercury contained in it be volatilized by heat, and the remaining chalk be dissolved by diluted acetic acid, the solution should not be colored by hydrogen sulphide. The presence of any probable metallic impurity may be detected in this way. To detect mercuric oxide, a portion of the powder may be treated with diluted hydrochloric acid with a moderate heat, and the solution tested by stannous chloride, which, if there be any mercuric oxide present, will cause a precipitation of metallic mercury as a black powder.

Uses.—Mercury with chalk is a very mild mercurial, similar in its properties to the blue mass, but much weaker. It is sometimes used as an alterative, particularly in the complaints of children attended with deficient biliary secretion, indicated by white or clay-colored stools. The chalk is antacid, and, though in small quantity, may sometimes be a useful accompaniment of the mercury in *diarrhea.* Eight grains of the U. S. preparation contain about three grains of mercury. It should not be given in pill with substances which become hard on keeping, as the contraction of the mass presses together the particles of mercury, which in time appear in globules in the interior of the pill.

Dose, as an alterative, one to three grains (0.06–0.2 Gm.); as a laxative, ten to twenty grains (0.65–1.3 Gm.).

HYDRASTINA. U. S.

HYDRASTINE

(hȳ-drăs-tĭ'nạ)

"An alkaloid [$C_{21}H_{21}O_6N = 383.18$] obtained from hydrastis or prepared synthetically. Preserve it in well-closed containers, protected from light." *U. S.*

Hydrastine, *Fr. Cod.;* Hydrastin, *G.*

Hydrastine may be obtained by exhausting the powdered root as far as possible with water by percolation, adding hydrochloric acid to the infusion so as to precipitate the berberine in the form of hydrochloride, and treating the mother liquor with solution of ammonia in slight excess. The hydrastine is precipitated, in an impure state, and may be purified by repeated solution in boiling alcohol, which deposits it in crystals on cooling. A little animal charcoal may be used towards the close of the process, in order to deprive the crystals completely of color. To Mahla, of Chicago, and Perrins, of London, is due the credit of having investigated this alka-

loid. The name hydrastine must not be confused with the similar name of the eclectic preparation called *hydrastin,* which is an almost inert preparation made by collecting, washing, and drying the precipitate produced by pouring a concentrated alcoholic solution of the drug into a large volume of water.

Properties.—"Hydrastine occurs in white to creamy white, glistening prisms or as a white, micro-crystalline powder; permanent in the air. Hydrastine is almost insoluble in water; 1 Gm. is soluble in 170 mils of alcohol, 1.4 mils of chloroform, and in 175 mils of ether at 25° C. (77° F.); also in 22 mils of alcohol at 60° C. (140° F.); freely soluble in benzene. Its saturated alcoholic solution is alkaline to litmus. It melts at about 131° C. (267.8° F.). Sulphuric acid produces a yellow color when added to Hydrastine; on heating the mixture, a purple color develops. Sulphuric acid containing 0.005 Gm. of molybdic acid in each mil gives with Hydrastine a green color, changing to olive-green and then to brown; nitric acid yields a reddish-yellow color; sulphuric acid containing 0.005 Gm. of selenous acid in each mil gives a light green color, changing to brown. No weighable ash remains on incinerating 0.1 Gm. of Hydrastine. A solution of about 0.1 Gm. of Hydrastine in 10 mils of diluted sulphuric acid shows no blue fluorescence (*hydrastinine*), but, on the gradual addition of potassium permanganate T.S., avoiding excess, a blue fluorescence develops. An aqueous solution of Hydrastine (1 in 20), made with the aid of a slight excess of diluted hydrochloric acid, is not reddened by chlorine water (*berberine*)." *U. S.*

Uses.—Hydrastine is an active alkaloid which is slowly absorbed and probably eliminated by the kidneys and lower bowel unchanged. When given to the lower animals it primarily stimulates the spinal motor cord, causing tetanic convulsions, with heightened reflexes, followed, if the dose has been large enough, by loss of reflex activity, and motor paralysis, which are probably in part due to depression of the motor centers, and are certainly, at least in part, the outcome of depression of the motor nerves and also of the muscles themselves. Death may occur in a convulsion from cramp-asphyxia, or later from simultaneous paralysis of the respiratory center and of the peripheral apparatus. The arterial pressure is first elevated and secondarily depressed; the first rise of pressure is probably due to the stimulation of the heart muscle, increasing the output of force, and of both the vasomotor centers and the muscle fibers in the arteriole coats, causing contraction of the blood vessels; the fall of pressure is the result of a direct paralytic action exerted upon the muscle fibers in the heart and in the arterioles. Hydrastine notably increases intestinal peristalsis, and, according to Fellner (*Arch. f. Gyn.,* 1906, lxviii), uterine contractions. It would seem to be a universal muscle poison, which acts upon both striated and non-striated muscle fibers in heart, arterioles, intestines, uterus, and generally throughout the body, its first stimulant action being followed by marked depression. Hydrastine has been shown by Fellner and Slavatinski to have a distinct ecbolic action, and premature labor is asserted to have been caused by its hypodermic administration. In practical medicine it is chiefly employed for the arrest of uterine hemorrhage, and in ordinary *menorrhagia.* When a prompt action is desired, a soluble salt like the hydrochloride should be administered hypodermically.

Dose, of pure hydrastine, one-sixth to one-half grain (0.01–0.032 Gm.).

HYDRASTINÆ HYDROCHLORIDUM. U. S.

HYDRASTINE HYDROCHLORIDE Hydrastin. Hydrochl. [Hydrastine Chloride]

(hȳ-drăs-tī'næ hȳ-drọ-ȼhlō'rī-dŭm)

"The hydrochloride [$C_{21}H_{21}O_6N.HCl$ = 419.65] of the alkaloid hydrastine. Preserve it in well-closed containers, protected from light." *U. S.*

Hydrastine hydrochloride was introduced in the U. S. P. IX to provide a soluble form of the alkaloid hydrastine.

"Hydrastine Hydrochloride occurs as a white to creamy-white powder, odorless, and hygroscopic. Hydrastine Hydrochloride is very soluble in water and in alcohol; slightly soluble in chloroform; very slightly soluble in ether. An aqueous solution of the salt (1 in 20) is neutral or only slightly acid to litmus. An aqueous solution of the salt (1 in 20) yields with silver nitrate T.S. a white precipitate, insoluble in nitric acid. In other respects the salt responds to the tests for identity and purity under *Hydrastina,* omitting the melting point." *U. S.*

Dose, one-sixth to one-half of a grain (0.01–0.03 Gm.).

Off. Prep.—Liquor Hydrastinæ Compositus, *N. F.*

HYDRASTININÆ HYDROCHLORIDUM. U. S.

HYDRASTININE HYDROCHLORIDE Hydrastinin. Hydrochl. [Hydrastininæ Hydrochloras, Pharm. 1890, Hydrastinine Hydrochlorate, Hydrastinine Chloride]

(hȳ-drăs-tī-nī'næ hȳ-drọ-ȼhlō'rī-dŭm)

"The hydrochloride [$C_{11}H_{11}O_2N.HCl$ = 225.57] of hydrastinine, an alkaloid obtained by the oxidation of hydrastine. Preserve it in well-closed containers, protected from light." *U. S.*

Hydrastininum hydrochloridum, *P. G.;* Hydrastininhydrochlorid, Salzsaures Hydrastinin, *G.*

Preparation.—*Hydrastinine* is an artificial alkaloid, produced by acting on hydrastine, the alkaloid from hydrastis, with oxidizing agents. When manganese dioxide and sulphuric acid are used together, or when platinic chloride is employed, hydrastinine and *opianic acid* are the products. Hydrastinine is also manufactured synthetically from berberine, from safrol, and from heliotropine.

Properties.—Hydrastinine hydrochloride is officially described as in "light yellowish needles, or as a yellowish-white, crystalline powder without odor. One Gm. of Hydrastinine Hydrochloride dissolves in 195 mils of chloroform, and in 1820 mils of ether at 25° C. (77° F.); very soluble in water and alcohol. Its aqueous solution (1 in 20) is neutral to litmus and shows a blue fluorescence, especially when highly diluted. It melts at about 210° C. (410° F.) with partial decomposition. In an aqueous solution of the salt (1 in 20), potassium dichromate T.S. produces a precipitate which redissolves if gently heated, but on cooling the solution it separates again in glistening needles. Silver nitrate T.S. produces in an aqueous solution of the salt a white precipitate, insoluble in nitric acid. No weighable ash remains on incinerating 0.1 Gm. of Hydrastinine Hydrochloride. In an aqueous solution of the salt (1 in 20) bromine T.S. produces a yellow precipitate, which is completely soluble in ammonia water, producing an almost colorless solution (*hydrastine*). Add a few drops of ammonia water to 1 mil of an aqueous solution of Hydrastinine Hydrochloride (1 in 20); no turbidity is produced (*foreign alkaloids*). Add slowly 4 or 5 drops of a solution of sodium hydroxide (1 in 7) to a solution of 0.2 Gm. of the salt in 3 mils of distilled water; each drop causes a milky turbidity, which disappears again on shaking (*foreign alkaloids*). From this solution, after standing for some time, pure white hydrastinine separates, and the supernatant fluid is almost colorless." *U. S.*

Uses.—Hydrastinine is, when given in large enough amount, a powerful depressant to the whole motor tract, affecting the psycho-motor centers of the cerebral cortex, the motor nerve, and the muscle itself. In the present state of our knowledge it is uncertain whether the depression is or is not preceded by a brief period of excitation, but it is almost certain that there is a primary stimulation of the muscles. The alkaloid slows the action of the heart but increases the force of the beat, and markedly augments the blood pressure, contracting actively the blood vessels by stimulating both the vasomotor centers and the muscles in the walls of the arterioles. In the toxic dose it finally paralyzes respiration, although there is reason for believing that in the beginning it stimulates the function. Death occurs from asphyxia, to which is usually ascribed the final fall of the arterial pressure.

It has a direct stimulant action upon the uterus. According to Kehrer (*Monatsschr. Geburtsh. u. Gynäk.*, 1907, xvi, p. 709), it rivals in the certainty of its effect the best preparations of ergot. It would seem that it is a universal muscle poison, primarily stimulant in its action, and that in this way it affects the heart, the arterioles, and the uterus. According to von Bunge, it markedly increases peristalsis, so that even the intestines do not escape its muscular action.

Hydrastinine was originally recommended by Falck in the treatment of *menorrhagia, metrorrhagia, dysmenorrhea,* and even *endometritis.* The testimony as to its value in all forms of uterine hemorrhage seems to be conclusive, and it is affirmed by many gynæcologists that it has a pronounced alterative influence upon the mucous membrane of the uterus. From our own experience we are convinced that it has value as a cardiac tonic, not equal in power or certainty of action to digitalis, but often useful as a substitute for that drug, especially in minor cases of heart failure. Its sedative action on the central nervous system, conjoined with its stimulating influence upon the circulation and its pronounced effects upon the genital system, make it a very valuable remedy in the treatment of feeble women of hysterical temperament, with tendency to uterine fluxes.

Dose, usually employed, from three-fourths of a grain to one and a half grains (0.048–0.096 Gm.) every three to six hours, but probably larger doses might often be used with advantage, since no ill effects have been as yet recorded as being produced by it. The salt may be given hypodermically.

HYDRASTIS. U. S. (Br.)

HYDRASTIS [Golden Seal]

(hȳ-drăs'tĭs)

"The dried rhizome and roots of *Hydrastis canadensis* Linné (Fam. *Ranunculaceæ*), without the presence or admixture of more than 2 per cent. of the stems, leaves or other foreign matter and yielding not less than 2.5 per cent. of the ether-soluble alkaloids of Hydrastis." *U. S.* "Hydrastis Rhizome is the dried rhizome and roots of Hydrastis canadensis, *Linn.*" *Br.*

Hydrastis Rhizoma, *Br.;* Hydrastis Rhizome; Rhizoma Hydrastis; Golden Seal, Yellow Root, Yellow Puccoon, Orange Root, Indian Dye, Indian Turmeric, Ohio Turmeric; Indian Paint, Ground Raspberry, Eye Root, Eye balm, Yellow Eye, Jaundice Root; Hydrastis, *Fr. Cod.;* Racine d'Hydrastis du Canada, Sceau d'or, *Fr.;* Canadische Gelbwurzel, Gelbes Blutkraut, *G.;* Idraste, *It.;* Hidrastis del Canada (Rhizoma de), *Sp.*

Hydrastis canadensis is a small, herbaceous, perennial plant, with a thick, fleshy, yellow rhizome, from which numerous long roots arise, and an erect, simple, pubescent stem, from six inches to a foot in height. There are usually but two leaves, which are unequal, one sessile at the top of the stem, the other attached to the stem a short distance below by a thick roundish footstalk, causing the stem to appear as if bifurcate near the summit. The leaves are pubescent, roundish-cordate, with from three to seven, but generally five, lobes, which are pointed and unequally serrate. A solitary flower stands upon a peduncle rising from the basis of the upper leaf. It is without corolla, but with a greenish-white calyx, the sepals of which closely resemble petals, and are very caducous, falling very soon after the flower has expanded. The fruit is a globose, compound, red or crimson berry, half an inch or more in diameter, composed of many fleshy carpels, each tipped with a short curved beak, and containing one or rarely two seeds. The

plant grows in moist, rich woodlands in most parts of the United States, and at one time abundantly in the North and West. The fruit bears a close resemblance to the raspberry, but is not edible. The root is the part used. The Indians employed it for staining and dyeing yellow under the name of *yellow puccoon*, and it is said to impart a rich and permanent yellow, and with indigo a fine green, to wool, silk, and cotton. There is but one other species of *Hydrastis* known—viz., *H. jezoensis* Sieb. et Zucc., which is found in Northern Japan.

Enormous quantities of hydrastis are consumed. It is estimated that between 200,000 and 300,000 pounds of the drug are annually used in medicine. As the natural supplies are becoming limited many experiments in the cultivation of hydrastis have been made. It can be grown from cuttings of the rhizome and from seed. It furthermore can be grown with the natural shade of the woodlands or by means of artificial shade. The important articles on the cultivation of hydrastis are the following: John Uri Lloyd, *Proc. A. Ph. A.*, 1905, p. 307, and in *A. Ph. A.*, vol. i, p. 5; Alice Henkel and G. Fred Klugh, *Circ. No. 6, Bureau of Plant Industry, U. S. Department of Agriculture;* J. C. Baldwin, *A. J. P.*, 1913, p. 147. Most of the commercial supplies are obtained from the Ohio Valley. The States producing hydrastis are West Virginia, Ohio, Kentucky and Indiana. The chief market being Cincinnati.

Properties.—The fresh rhizome is juicy, and loses much of its weight in drying. The drug is officially described as "rhizome horizontal or oblique, sub-cylindrical and usually more or less flexuous, from 1 to 5 cm. in length and from 2 to 7 mm. in diameter, occasionally with stem-bases; externally yellowish or grayish-brown, marked by numerous stem-scars and more or less annulate from scars of bud-scales, otherwise deeply longitudinally wrinkled; on the under and lateral portions arise numerous, long, filiform roots which are easily detached; fracture short, waxy; internally of a deep yellow color and consisting mostly of parenchyma enclosing an interrupted circle of small fibro-vascular bundles; odor distinctive; taste, bitter. Macerate the drug for a short time in water until it is softened, then make sections and mount them directly in sulphuric acid and examine under the microscope; in a short time numerous acicular or rod-shaped crystals separate, some attaining a length of 0.2 mm. The powder is brownish-yellow; starch grains numerous, from 0.002 to 0.015 mm. in diameter, mostly single, nearly spherical, and either free or in the parenchyma cells; fragments with the tissues of the fibro-vascular bundles mostly associated with starch-bearing parenchyma; tracheæ with simple and bordered pores and occasionally spiral thickenings, and associated with short sclerenchymatous fibers possessing thin walls with simple pores; occasional fragments of tabular cork cells with reddish-brown walls." *U. S.*

"Rhizome tortuous, simple or branched, from ten to forty millimetres long and from three to ten millimetres thick; yellowish-brown, becoming darker by age. On the upper surface, short ascending branches usually terminated by cup-shaped scars; on the lower surface and sides numerous thin, brittle roots. Fracture clean, resinous; fractured surface brownish-yellow or greenish-yellow. In transverse section, a ring of bright yellow, somewhat distant, wood-bundles. Slight but characteristic odor; taste bitter. Ash not more than 11 per cent." *Br.*

The color of the rhizome, though yellow in the recent root, becomes a dark yellowish-brown by age; that of the rootlets and the interior of the root is yellow, and that of the powder still more so.

Holm gives a valuable illustrated article on the morphology of the hydrastis plant in *Merck's Rep.*, xxii, p. 202. (See also *Chem. Zeit.*, 1894, p. 134.) Rosenthaler has extended his studies of microsublimates to that of hydrastis and finds that the pyroanalytical sublimate of hydrastis gives general alkaloidal reaction and a characteristic reaction with sulphuric acid. (*Apoth. Zeit.*, xxviii, p. 991.) Owing to the high price of hydrastis the quality of the commercial article has steadily deteriorated in recent years, and Lloyd asserts that every drug native to the soil which resembles this rhizome, either in fiber or in color, has been known to be mixed with it. (*Pharm. Rev.*, xxiii, p. 330.)

"**Assay.**—Introduce 10 Gm. of Hydrastis, in No. 60 powder, into a 250 mil flask and add 100 mils of ether and proceed as directed under *Belladonnæ Radix*, page 222, fourth line of the Assay, beginning with the word "Stopper." Modify the process there given by using 50 mils of the ether solution, representing 5 Gm. of Hydrastis, to complete the assay. Use ether instead of chloroform for the final shaking out of the alkaloids, and dry the residue to constant weight at 100° C. (212° F.) instead of titrating. The weight is the amount of ether-soluble alkaloids from 5 Gm. of Hydrastis." *U. S.*

The medicine imparts its virtues and coloring matters to water and alcohol. Examined by Alfred B. Durand of Philadelphia, it was found to contain albumen, starch, fatty matter, resin, yellow coloring matter, sugar, lignin, and various salts. He also discovered a peculiar nitrogenous, crystallizable substance, for which he proposed the name of *hydrastine*. (*A. J. P.*, 1851, p. 112.) It was also found that the root contained another alkaloid, to which it owes its yellow color. F. Mahla first ascertained that this alkaloid of hydrastis was *berberine*. (*Am. J. S.*, Jan., 1862, p. 43.) It exists in large proportion in hydrastis, constituting, according to Perrins, nearly 4 per cent. For a valuable paper by J. U. Lloyd on the preparation of salts of berberine, see *A. J. P.*, 1879, p. 11. Lerre's process based on Lloyd's for preparing hydrastine and berberine will be found in the *U. S. D.*, 19th ed., p. 643.

Wilhelm (*P. J.*, 1888, 325) furnishes a process for obtaining the alkaloids from hydrastis as follows. The extract obtained by treating the coarsely powdered root with water acidified with acetic acid at 37.8° C. (100° F.) is evap-

orated to a syrup and excess of diluted sulphuric acid added, when berberine sulphate separates. The filtrate neutralized with ammonia water gives a precipitate containing much hydrastine; this is separated, and on adding ammonia water in excess to the filtrate a further precipitate is produced, which contains *canadine.* Both precipitates, boiled with ethyl acetate, give solutions which, on cooling, deposit hydrastine in large crystals, somewhat colored, but rendered pure by recrystallization. The crystals from the second ammonia precipitate are much purer than those from the first; by slow evaporation of the ethyl acetate solution they can be obtained as large as walnuts.

A substance obtained by the precipitation of an infusion of the root by hydrochloric acid has been for some time known and used by the "Eclectics," under the name of *hydrastin;* it consists of a small proportion of hydrastine, with berberine and resin, and the reader must be cautious not to confound this substance with the alkaloid to which the name properly belongs. Perrins obtained 1.5 per cent. of the eclectic principle from the root, and, having given five grains of it to a rabbit without any other effect than a slight uneasiness which soon ceased, concluded justly that it was not poisonous.

Canadine ($C_{20}H_{21}NO_4$) was extracted by E. Schmidt; it occurs in the form of brilliant, small, white nodules, melting at 134° C. (273.2° F.). When canadine is dissolved in alcohol and treated with iodine, berberine hydriodide (which is yellow in color) is formed. Canadine was believed to be identical with dihydromethylberberine (*Ph. Post,* 1892, 230), and the formula $C_{21}H_{21}NO_4$ was given to it. E. Schmidt, however (*A. Pharm.,* 1894, 136–154), has found that its true formula is $C_{20}H_{21}NO_4$, and, owing to the fact that iodine forms with it berberine hydriodide, he believes that canadine is a *tetrahydroberberine.* Schmidt also obtained, as an additional product of the iodine reaction, the hydriodide of another base, which he believes is intermediate between berberine and canadine. For a process for isolating canadine, see *Proc. A. Ph. A.,* 1894, 1103. The alkaloid discovered by A. K. Hale, and obtained later by Burt and by Lerchen, and which was named *xanthopuccine,* is now considered to be identical with canadine. For processes for making hydrastine and berberine, see *D. C.,* 1897, 34. It is probable, from the odor of hydrastis, that besides the two alkaloids here mentioned it contains also an active volatile principle, but this has not yet been isolated.

LaWall (*Proc. Pa. Ph. A.,* 1912, p. 142) made separate assays of the rhizome and rootlets from a 98-pound lot of the drug. There was present 45.5 pounds of rhizome and 48 pounds of rootlets, the balance being dirt and waste. The rhizomes assayed 2.48 per cent. of hydrastine and the rootlets 1.38 per cent. The average of the entire lot was 1.92 per cent.

Uses.—Hydrastis owes its virtues almost entirely to hydrastine, the alkaloid berberine, aside from some effect as a bitter, being practically inert. It has enjoyed a widespread reputation as a local remedy in various forms of *catarrh,* such as *rhinitis, gastritis, vaginitis,* and *urethritis.*

In chronic or subacute *inflammations* of the *colon* and *rectum* injections of hydrastis are often of great service, and it has been used in *hemorrhoids* with asserted excellent results.

The strength of the local application of hydrastis to be used in various diseases of the mucous membrane varies from five to twenty-five per cent. of the fluidextract. In *gonorrhea* from forty to eighty minims (2.5–5.0 mils) of the fluidextract, may be used to the fluidounce (30 mils). In *hemorrhoids* from two to four drachms to the fluidounce may be used. The glycerite is not so useful a local preparation as the fluidextract diluted with water, a deposit of the insoluble resinous substance upon the mucous membrane and its constant prolonged influence being important.

The general action of hydrastis upon the system and internal uses are the same as those of hydrastine (see p. 571).

It is essential to recognize the differences, medicinally, between the preparations of hydrastis. The so-called *hydrastin* of commerce is really an impure body, containing berberine, canadine, hydrastine, and probably some resin. The *dose* of this hydrastin is from five to ten grains (0.32–0.65 Gm.).

There is some reason for believing that *berberine* has a special action upon the gastro-intestinal tract. Marfori has, however, found that even in large therapeutic dose it is without perceptible influence upon the circulation or the nervous system. When, therefore, a preparation of hydrastis is to be used for effects other than a local action on the gastro-intestinal or other mucous membrane, a salt of the pure alkaloid hydrastine should be used.

According to the studies of Falck and Guenste, berberine causes in dogs and rabbits restlessness, convulsive tremblings, hurried respiration, and diarrhea, followed, if the dose has been large enough, by decrease of the breathing rate, widespread paralysis, dyspnea, convulsions, and death. In man as yet no serious symptoms have been recorded as produced by it. Buchner is stated to have taken nearly twenty grains without causing anything more serious than a loose stool. Marek (*W. M. W.,* 1911, 2146) has presented evidence that it possesses valuable oxytocic properties, and is useful in *delayed labor.* It has been employed in internal medicine as a simple bitter, in doses of from two to five grains (0.13–0.32 Gm.).

Hydroberberine (Canadine), whose molecule contains four atoms of hydrogen more than the molecule of berberine, is said by Marfori to differ from berberine physiologically; it produces in moderate dose an increase in the blood pressure by stimulating the vasomotor center in the medulla. *Opianic, hydrastinic,* and *berberinic acids* are said by the same authority to be almost inert physiologically, except that they are feebly antiseptic. (*T. G.,* 1890.)

For a physiological study of the *methylamine* derivatives of hydrastine (*hydrastine methylamine*), see *V. A. P. A.*, cxlii, 1895.

Dose, of hydrastis, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Extractum Hydrastis, *U. S.;* Fluidextractum Hydrastis, *U. S.* (*Br.*); Glyceritum Hydrastis, *U. S.;* Tinctura Hydrastis, *U. S., Br.;* Mistura Rhei Alkalina (from Fluidextract), *N. F.*

HYOSCYAMINÆ HYDROBROMIDUM. U. S.

HYOSCYAMINE HYDROBROMIDE Hyoscyamin. Hydrobr. [Hyoscyaminæ Hydrobromas, Pharm. 1890, Hyoscyamine Hydrobromate, Hyoscyamine Bromide]

(hȳ-ǫs-cȳ-ą-mĭ'næ hȳ-drǫ-brō'mĭ-dŭm)

"The hydrobromide [$C_{17}H_{23}O_3N.HBr = 370.12$] of hyoscyamine, an alkaloid obtained from hyoscyamus and other plants of the *Solanaceæ*. Preserve it in well-closed containers, protected from light." *U. S.*

Hyoscyaminum Hydrobromicum; Bromhydrat d'Hyoscyamine, *Fr.;* Hyoscyaminhydrobromid, Bromwasserstoffsaures Hyoscyamin, *G.*

For discussion of the properties of hyoscyamine, see *Hyoscyaminæ Sulphas.*

Preparation.—This salt may be made by dissolving 10 Gm. of hyoscyamine in 11 Gm. of hydrobromic acid (25 per cent.), evaporating and crystallizing.

Properties.—Hyoscyamine hydrobromide is officially described in the United States Pharmacopœia IX as in "white, prismatic crystals without odor. It is deliquescent on exposure to the air. *Great caution must be observed in tasting it, using only a very dilute solution.* It dilates the pupil of the eye. One Gm. of Hyoscyamine Hydrobromide dissolves in 2.5 mils of alcohol, 1.7 mils of chloroform, and in 2260 mils of ether at 25° C. (77° F.); very soluble in water. Its aqueous solution (1 in 20) is neutral to litmus, and is strongly lævorotatory. It melts at about 152° C. (305.6° F.). Silver nitrate T.S., when added to an aqueous solution of the salt, yields a yellowish-white precipitate which is insoluble in nitric acid. Shake 2 mils of chloroform with 1 mil of an aqueous solution of the salt (1 in 10) to which a few drops of chlorine water have been added; the chloroform assumes a brownish color. Add about 0.01 Gm. of the salt to 5 drops of nitric acid, and evaporate to dryness in a porcelain dish; the residue yields a violet color upon the addition of alcoholic potassium hydroxide T.S. Gold chloride T.S., when added to an aqueous solution of the salt (1 in 20), yields a precipitate which, when recrystallized from a small quantity of boiling distilled water, acidulated with hydrochloric acid, is deposited on cooling in minute, lustrous, golden-yellow scales (difference from *atropine and scopolamine*). Platinic chloride T.S. does not form a precipitate in aqueous solutions of the salt (1 in 20) (difference from *most alkaloids*). No weighable ash remains on incinerating 0.1 Gm. of Hyoscyamine Hydrobromide. About 0.05 Gm. of the salt dissolved in 1 mil of sulphuric acid gives not more than a faint yellow color (*carbonizable impurities*)." *U. S.*

Uses.—The medicinal properties and the dose of this salt of hyoscyamine are precisely those of the sulphate, to which it is preferred by some.

Dose, one two-hundredth to one one-hundredth of a grain (0.0003–0.0006 Gm.).

HYOSCYAMINÆ SULPHAS. Br.

HYOSCYAMINE SULPHATE

(hȳ-ǫs-cȳ-ą-mĭ'næ sŭl'phăs)

"Hyoscyamine Sulphate, $(C_{17}H_{23}O_3N)_2,H_2SO_4,2H_2O$, is the sulphate of an alkaloid, hyoscyamine, obtained from various plants belonging to the natural order Solanaceæ." *Br.*

Sulfate d'Hyoscyamine, *Fr.;* Hyoscyaminum Sulfuricum, Schwefelsaures Hyoscyamin, Hyoscyaminsulfat, *G.*

Hyoscyamine sulphate was deleted from the U. S. P. IX, but retained by the British Pharm. (1914).

Although Brandes announced the existence of an alkaloid in the seeds of *Hyoscyamus niger,* the process which he used to obtain it was not successful in other hands. The credit of first isolating the alkaloid *hyoscyamine* from the plant must be given to Geiger and Hesse, who obtained it as long ago as 1833. Höhn and Reichardt's process, in which the seed is used as the source, is as follows. They treat hyoscyamus seed first with ether to separate fatty matter, then with alcohol acidulated with a few drops of sulphuric acid, and afterwards distil the alcoholic solution. The aqueous residue is to be neutralized with sodium hydroxide, and the liquid precipitated by a solution of tannin. The precipitate, having been placed on a porcelain plate to dry, is mixed while yet moist with an excess of lime, and then exhausted by strong alcohol. The alcoholic solution is treated with sulphuric acid, then with sodium hydroxide, and finally with ether, which dissolves the liberated hyoscyamine. By distilling off the ether a colorless oleaginous liquid is left, which at length solidifies.

These investigators originally gave to hyoscyamine the formula $C_{15}H_{23}O_3N$, but Ladenburg later showed by a study of its decomposition products that it is isomeric with atropine, $C_{17}H_{23}O_3N$. Ladenburg made the most complete study of atropine and hyoscyamine that we have, and has established their relations to each other in a clear light. According to him (*Ber. d. Chem. Ges.,* xiii, pp. 251, 909, and 1549), hyoscyamus contains two alkaloids, a crystalline one, to which the name of *hyoscyamine* is given, and an amorphous one, which remains in the mother liquor after the removal of the crystallizable alkaloid, for which he proposed the name *hyoscine,* but which is now believed to be identical with scopolamine. Hyoscyamine treated with boiling baryta water assimilates a molecule of water and splits up into what were

called *hyoscinic acid,* $C_9H_{10}O_3$, and *hyoscine,* $C_8H_{15}ON$, but which Ladenburg showed to be identical with the decomposition products of atropine, *tropic acid* and *tropine.* Hyoscyamine is to-day regarded as a stereo-isomer of atropine, from which it differs in certain physical properties, notably in that it is lævorotatory to polarized light, while atropine is optically inert.

Hyoscyamine crystallizes in colorless, transparent, silky needles, fusing at 108.5° C. (227.3° F.), is inodorous, of an acrid, disagreeable taste, slightly soluble in water, very soluble in alcohol and ether, and volatilizable with little change if carefully distilled. It is quickly altered by contact with water and an alkali, and when heated with potassium or sodium hydroxide is completely decomposed, with the disengagement of ammonia. It neutralizes the acids, forming crystallizable salts, and is precipitated by infusion of galls. The alkaloid and its salts are very poisonous, and the smallest quantity, introduced into the eye, produces dilatation of the pupil, which continues long.

Hyoscine was first known in commerce as *amorphous hyoscyamine.* The best salts, according to Edlefsen, to prepare and dispense are the *hydrobromide* and *hydriodide,* the former of which is the one most frequently used. Hyoscine hydriodide crystallizes from water, in which it is only moderately soluble, in small, hemihedral prisms, which mostly have a slight yellowish color. (See *Scopolominæ Hydrobromidum.*)

The double gold chloride, $C_{17}H_{21}O_4NHCl + AuCl_3$, is less soluble than the corresponding gold salt of hyoscyamine, and so serves to separate them when together.

Properties.—The British Pharmacopœia describes hyoscyamine sulphate as "a deliquescent crystalline powder. Soluble in 0.5 part of *water.* Melting point from 203° to 204° C. (397.4°–399.2° F.). Yields the *reaction* characteristic of sulphates. When treated with *nitric acid* and *alcoholic solution of potassium hydroxide,* as described under 'Atropina,' a violet coloration is produced. 0.05 gramme, dissolved in 5 millilitres of *water* acidified with *hydrochloric acid,* yields with *solution of auric chloride* a yellow precipitate which, recrystallised from *water* acidified with *hydrochloric acid,* forms brilliant golden-yellow scales melting, when dried, at 165° C. (329° F.). Dissolves in *sulphuric acid* without coloration. No appreciable ash." *Br.*

Uses.—The physiological effects of hyoscyamine are qualitatively the same as those of its isomer atropine, although there is some difference quantitatively. Atropine, as pointed out on page 221, is regarded as a mixture of dextro and lævorotatory alkaloids. Cushny (*J. P.,* 1903, xxx, p. 177) has shown that the lævorotatory substance (hyoscyamine) is relatively more active in its paralyzing effect on nerve endings and less active in its stimulant action upon the central nervous system. Like atropine, hyoscyamine checks secretion by paralyzing the terminals of nerves to the various glands, dilates the pupil by paralyzing the ends of the oculomotor nerve, and increases the pulse rate by paralyzing the pneumogastrics. The rise in blood pressure is comparatively small after hyoscyamine because it exercises but a feeble influence on the vasomotor center, similarly it causes but little increase in the respiration and shows less tendency to cause delirium. The former belief that hyoscyamine possessed narcotic properties was doubtless due to its contamination with scopolamine; there is no convincing evidence that chemically pure hyoscyamine has a depressant action upon the cerebrum. Clinically, hyoscyamine may be substituted for atropine wherever the action on peripheral nerves is desirable, as for instance, to check excessive secretion, to dilate the pupil, or to allay intestinal spasm.

Dose, one two-hundredth to one one-hundredth of a grain (0.0003–0.0006 Gm.).

HYOSCYAMUS. U. S. (Br.)

HYOSCYAMUS Hyosc. [Henbane, Hyoscyami Folium P. I.]

(hȳ-ǫs-cȳ'ą-mŭs)

"The dried leaves or fruiting tops of *Hyoscyamus niger* Linné (Fam. *Solanaceæ*), yielding not less than 0.065 per cent. of the alkaloids of Hyoscyamus." *U. S.* "Hyoscyamus Leaves are the leaves of Hyoscyamus niger, *Linn.,* collected from the flowering plants, and dried." *Br.*

Hyoscyami Folia, *Br.;* Hyoscyamus Leaves, Henbane Leaves, Black Henbane; Stinking Nightshade, Insane Root, Poison Tobacco; Jusquiame noire, *Fr. Cod.;* Belene, Chenile, *Fr.;* Herba Hyoscyami, *P. G.;* Bilsenkraut, Bilsenkrautblätter, *G.;* Giusquiamo, *It.;* Beleno, *Sp.*

There are about eleven species of the genus *Hyoscyamus* known; these are distributed from the Canary Islands over Europe and Northern Africa to Asia.

Hyoscyamus niger, or *henbane,* is usually a biennial plant, with a long, tapering, whitish, fleshy, somewhat branching root, not unlike that of parsley, for which it has been eaten by mistake, with poisonous effects. The stem, which rises in the second year, is erect, branching, from one to four feet high, and thickly furnished with leaves. These are large, oblong-ovate, deeply sinuated with pointed segments, undulated, soft to the touch, and at their base embrace the stem. The upper leaves are generally entire. Both the stem and leaves are hairy, viscid, and of a sea-green color. The flowers form long, one-sided, leafy spikes, which terminate the branches, and hang downward. They are composed of a calyx with five pointed divisions, a funnel-shaped corolla, with five unequal, obtuse segments at the border, five stamens inserted into the tube of the corolla, and a pistil with a blunt, round stigma. The corolla is of an obscure yellow color, beautifully variegated with purple veins. The fruit is a globular two-celled capsule, covered with a lid, invested with the persistent calyx, and contains numerous small seeds, which are discharged by the horizontal separation of the lid. The whole plant has a rank, offensive odor.

H. niger is susceptible of considerable diversity of character, causing varieties which have by some been considered as distinct species. Thus, the plant is sometimes annual, the stem simple, smaller, and less downy than in the biennial plant, the leaves shorter and less hairy and viscid, and the flowers often yellow without the purple streaks.

The plant is found in the northern and eastern sections of the United States, occupying waste grounds in the older settlements, particularly cemeteries, old gardens, and the foundations of ruined houses. It is, not, however, a native of this country, having been introduced from Europe. In Great Britain, and on the continent of Europe, it grows abundantly along the roads, around villages, amidst rubbish, and in uncultivated places. Both varieties were formerly cultivated in England, but at present the biennial is chiefly or solely grown. The annual plant flowers in July or August, the biennial in May or June. For an account of the cultivation of the biennial variety of Hitchin, England, see *P. J.*, Feb., 1860.

Mitlacher, in connection with other plants, has carried on a series of experiments on the cultivation of Hyoscyamus and reports on the results of his work in *Ph. Post*, 1911, p. 390 and *Zeit. Oest. Apoth. Ver.*, 1912, p. 401. Hyoscyamus has been successfully grown in the testing gardens of the Bureau of Plant Industry. There is usually some difficulty in growing hyoscyamus owing to its destruction by insects (*A. J. P.*, 1912, p. 551), but Newcomb was very successful with his experiments in Minneapolis. (*A. J. P.*, 1914, p. 531.) Schneider also has pointed out that henbane thrives well in California and says that it no doubt will do well in the Coast valleys. (*Pac. Pharm.*, iii, p. 192.) Peckolt reports that *Hyoscyamus niger* grows wild in portions of Brazil. (*B. P. G.*, xix, p. 33.) Chevalier has shown that by cultivation the alkaloidal content of hyoscyamus can be increased to 0.286 per cent. of total alkaloids. (*C. R. A. S.*, 1910, p. 344.)

H. albus, so named from the whiteness of its flowers, is used in France indiscriminately with the former species, with which it appears to be identical in medicinal properties. *Hyoscyamus muticus* L., of Egypt, i said to grow luxuriantly in the temperate zone and to produce a very much larger proportion of total alkaloids than does the official English plant, although the relative proportions of hyoscine and hyoscyamine are not the same. It appeared in the London market in the form of broken stalks with a few capsular fruits and traces of leaves and may become an important source of the alkaloids to the manufacturers.

Properties.—All parts of *Hyoscyamus niger* are active. The official description of the plant is as follows: "Usually much wrinkled, with numerous stems and with the flowering or fruiting tops intermixed; leaves when entire attaining a length of 25 cm., a breadth of 10 cm., ovate or ovate-oblong, very inequilateral, the lower with short petioles, the upper sessile, summits acute, margins coarsely and angularly 1- to 4-toothed or lobed; grayish-green, glandular-hairy, particularly on the lower surfaces; flowers nearly sessile with an urn-shaped, unequally 5-toothed calyx and a campanulate corolla which in the fresh state is of a yellowish color; fruit a 2-locular pyxis, and enclosed in a large urn-shaped calyx with 5 acute teeth; odor heavy, distinctive; taste somewhat bitter and acrid. Stems from 3 to 10 cm. in length and from 2 to 5 mm. in thickness, nearly cylindrical or somewhat compressed, longitudinally wrinkled and hairy. The powder is grayish-green; under the microscope, it exhibits calcium oxalate crystals usually in the form of 4- to 6-sided, isolated prisms, sometimes in twins, from 0.015 to 0.025 mm. in length, also occurring in spherical aggregates either isolated or attached to the prismatic crystals, sometimes in rosette aggregates, 0.02 mm. in diameter, and occasionally in sphenoidal micro-crystals; hairs numerous, of two kinds; the non-glandular from 2 to 10 cells in length, the glandular with a 1- to many-celled head and a 1- to 4-celled stalk; fragments of epidermis with broadly elliptical stomata from 0.03 to 0.035 mm. in length and with 3 to 4 neighboring cells; fragments of tracheæ with simple or bordered pores and spiral or reticulate thickenings, also associated with sclerenchymatous fibers having thin porous walls and showing little or no lignification; pollen grains, nearly smooth and from 0.035 to 0.05 mm. in diameter. The presence of the leaves of *Hyoscyamus muticus* Linné in either the crude or powdered Hyoscyamus may be determined by the characteristic, branching, non-glandular hairs occurring on both the stems and leaves of that species. Hyoscyamus yields not more than 30 per cent. of ash." *U. S.*

"Pale green, varying in length but seldom exceeding twenty-five centimetres; mostly sessile; exstipulate, triangular-ovate or ovate-oblong, acute, undulated, irregularly toothed, sinuate or pinnatifid, with conspicuous midrib. On both surfaces, but particularly on the under surface and near the veins, long uniserial hairs terminating in pluricellular glands. In the mesophyll prismatic and cluster-crystals of calcium oxalate." *Br.*

Much of the efficacy of hyoscyamus depends upon the time at which it is gathered. The leaves should be collected soon after the plant has flowered. In the biennial plant, those of the second year are preferred to those of the first. The latter, according to Houlton, are less clammy and fetid, yield less extractive, and are medicinally much less efficient. It is said that the plant is sometimes destroyed by severe winters in England, and that no leaves of the second year's growth are then obtainable. This is, perhaps, one of the causes of the great uncertainty of the medicine as found in commerce. The root also is said to be much more poisonous in the second year than in the first.

"Assay.—Introduce 30 Gm. of Hyoscyamus, in No. 60 powder, into a 500 mil flask and add 300 mils of a mixture of 1 volume of chloroform and 2 volumes of ether. Stopper the flask,

shake it well, and allow it to stand for ten minutes; then add 5 mils of ammonia water and shake the flask vigorously every ten minutes during two hours. Now add 40 mils of distilled water, again shake the flask and when the drug has settled decant 200 mils of the solution, representing 20 Gm. of Hyoscyamus, and proceed as directed under *Belladonnæ Radix*, page 222, beginning with the word 'Filter' on twelfth line of the Assay. Before titration treat the residue twice with 5 mils of ether and evaporate to dryness each time. Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 28.92 milligrammes of the total alkaloids of Hyoscyamus." *U. S. IX.*

The recent leaves have, when bruised, a strong, disagreeable, narcotic odor, somewhat like that of tobacco. Their taste is mucilaginous and very slightly acrid. When dried, they have little odor or taste. Thrown upon the fire, they burn with a crackling noise, as if they contained a nitrate, and at the same time emit a strong odor.

Much of the henbane of commerce is taken from the plant in the first year of its growth. The drug of the market is very variable, frequently containing an excess of sand and the leaves of other species of hyoscyamus. A few years ago, it was admixed with *H. muticus*, a plant growing in Egypt. The latter is readily determined by the presence of characteristic branching non-glandular hairs which are found on both the stems and leaves. (See *A. J. P.*, 1908, p. 361 and Kraemer's *"Scientific and Applied Pharmacognosy."*)

Hyoscyamus is completely extracted by diluted alcohol. The aqueous infusion is of a pale-yellow color, insipid, with the narcotic odor of the plant. The leaves were analyzed by Lindbergsen, who obtained from them a narcotic principle. They contain a large proportion of potassium nitrate, F. Mahla having obtained, as nearly as he could estimate from his experiments, 2 per cent. of that salt. (*A. J. P.*, 1859, p. 402.) The seeds are very small, roundish, compressed, somewhat kidney-shaped, a little wrinkled, of a gray or yellowish-gray color, of the odor of the plant, and of an oleaginous, bitterish taste. Geiger and Hesse (1833) were the first to demonstrate the existence of an alkaloid in hyoscyamus. Ladenburg stated in 1880 that there are two alkaloids in the plant,—one crystallizable, *hyoscyamine*, and the other amorphous, *hyoscine* (scopolamine, p. 985). (See *Hyoscyaminæ Sulphas*, p. 575.) Höhn (*Ann. Ch. Ph.*, 157, 98) obtained from the seeds a bitter principle which proved to be a glucoside. He calls it *hyoscypicrin*, and gives it the formula $C_{27}H_{52}O_{14}$.

From experiments made by Hirtz upon the relative medicinal power of extracts from the seeds and from the leaves, he inferred that the former had ten times the strength of the latter. Henbane leaves yield, by destructive distillation, a very poisonous empyreumatic oil.

Uses.—Hyoscyamus combines the therapeutic actions of its two alkaloids, hyoscyamine and scopolamine. Because of the presence of the former it tends to check secretion and to relax spasm of the involuntary muscles, while through the narcotic effects of its scopolamine it lessens pain and exercises a slight somnifacient action. Its most important use is in relief of painful spasmodic affections of the unstriped muscle, as in *lead colic* and *irritable bladder*. It is also employed to allay nervous irritation, as in various forms of *hysteria* or *irritable cough*, but is inferior to scopolamine for these purposes. Externally cataplasms or fomentations of the fresh leaves have been employed to allay pain in *cancerous ulcers* and *hemorrhoids*, but its employment for this purpose is of doubtful advantage.

Hyoscyamus is preferably given in the form of the fluidextract or tincture. The inspissated juice of the fresh leaves (*Extractum hyoscyami viride*, Br.) is exceedingly variable in its operation and is not to be recommended.

Dose, of the leaves, two to five grains (0.13–0.32 Gm.).

Off. Prep.—Extractum Hyoscyami, *U. S., Br.;* Fluidextractum Hyoscyami, *U. S.;* Pilula Colocynthidis et Hyoscyami (from extract), *Br.;* Tinctura Hyoscyami, *U. S., Br.;* Pilulæ Catharticæ Vegetabiles (from Extract), *N. F.;* Pilulæ Colocynthidis et Hyoscyami (from Extract), *N. F.;* Pilulæ Laxativæ Post Partum (from Extract), *N. F.*

HYPOPHYSIS SICCA. U. S.

DESICCATED HYPOPHYSIS Hypophysis Sic. [Desiccated Pituitary Body]

(hȳ-pŏph'-ȳ-sĭs sĭc'cą)

"The posterior lobe obtained from the pituitary body of cattle, cleaned, dried, and powdered." *U. S.*

The *Hypophysis cerebri*, or *pituitary body*, is a small bean-shaped body found within the skull in the depression known as the *sella turcica* or pituitary fossa. Its longest diameter is in the transverse direction and it consists of two distinct portions enclosed together in a connective-tissue capsule. The smaller, or anterior lobe, is composed of nerve cells similar to the gray matter of the brain and continuous with the *infundibulum* which forms a portion of the floor of the third ventricle of the brain. The *posterior lobe*, which is much larger, is made up of glandular epithelium and contains here and there collections of colloid material homologous to that found in the thyroid body. In the human being the pituitary body measures about 12 mm. transversely, 7 mm. longitudinally and 5 mm. vertically, and weighs from five to twenty grains. In cattle the organ has a weight of two or three drachms (7.7–11.6 Gm.). When dried it loses approximately three-fourths of its weight. In commerce it appears as "a yellowish or grayish, amorphous powder, having a characteristic odor. It is only partially soluble in water." *U. S.*

Because of our ignorance of the active principle of the hypophysis it is at present impossible to devise a process for chemical assay.

Of the various physiological tests which have been suggested, the only one which offers any promise of proving practically useful is that based upon the stimulant action on the uterus. This method has been favorably reported on by Heidelberg, Pittenger and Vanderkleed (*J. A. Ph. A.*, 1914, iii, p. 808), and by Roth (*Hygienic Laboratory Bull.* No. 100, November, 1914.) The method used is precisely the same as the isolated uterus test for ergot. (See p. 426.) For a standard Roth recommends *histamine*, which is generally efficient in the proportions of one to twenty million, but Heidelberg, Pittenger, and Vanderkleed prefer a standard solution of the pituitary body itself.

Uses.—The precise function of this body in normal animals is not known, although its removal causes profound alterations in the bodily function, prominent among which are overgrowth of the bones and deposit of fat. According to Cushny (*J. A. M. A.*, 1909, liii) the destruction of the anterior lobe is accompanied with glycosuria and subnormal temperature. Feeding the pituitary to normal animals causes an increase in the output of nitrogen, phosphorus, and lime. Because of the loss of the last two elements many writers have concluded that it hastens the bony catabolism.

In 1899 Schafer and Vincent (*J. P.*, 1899, xxv, 87) discovered that the injection of an aqueous extract of the hypophysis into the vein caused a rise of blood pressure rivalling that brought about by suprarenal extract in height and surpassing it in duration. The theory which was at one time advanced that the action of pituitary extract was similar to that of the suprarenal extract has been shown to be erroneous. The pressor principle is found only in the posterior lobe of the hypophysis, but the present evidence indicates that the anterior lobe is more important in its nutritive effects than the posterior.

The physiological effects of the posterior lobe of the pituitary body are stimulation of all the unstriped muscles, and increased secretion of the kidney and probably of the mammary glands. Among those muscles affected by the drug which are of importance from the standpoint of its clinical use, may be mentioned the circulatory, uterine, and intestinal muscles. The stimulant action upon the blood vessels is shown by the increase in arterial pressure which is apparently of purely vascular origin (Wiggers, *A. J. M. S.*, 1911, cxli, 142); the heart is not made up of unstriped muscle and does not appear to be stimulated by the drug. Repeated doses, even if intervals of an hour or two are allowed to elapse between their exhibition, do not produce the same degree of rise as the primary injection; indeed after a sufficient number of doses the drug exercises a depressor rather than a pressor influence. As was first shown by Ott and Scott (*Monthly Cyclopedia and Med. Bull.*, August, 1909), the extract of hypophysis is one of the most powerful and certain stimulants for the uterine muscle that we possess. While it does increase the tonus of this muscle it seems to be especially efficient to increase the vigor of individual contractions. The increase in the flow of urine seems to be the result of direct action upon the renal epithelium, for although the renal arteries are generally relatively dilated by the drug, Hoskins and Means (*J. P. Ex. T.*, 1913, iv, p. 435) have shown that there is no constant relation between the dilation of the renal artery and the degree of diuresis. It is probable, therefore, that the local widening of the vessels in the kidney is the result and not the cause of the increased functional activity of this organ, and the diuretic action is of the same type as that of caffeine.

The most common use of the hypophysis at present is as a uterine stimulant especially during *labor*. Although it is a very valuable drug in this condition when used circumspectly, there is no doubt that it is capable of doing great harm and has been greatly abused. While it seems less liable than ergot to cause tetanic spasm of the womb and there is therefore less danger of asphyxiation of the child (see Quigley, *J. A. M. A.*, 1915, lxiv, p. 1222), there have been reported several cases of rupture of the uterus from its injudicious use. Before the head has passed the pelvic outlet its use in general should be avoided, although occasional circumstances may indicate its use at an earlier stage. For the treatment of *postpartum hemorrhage* it has the great disadvantage that its effects last only from one to two hours and there appears to be a tendency towards secondary relaxation. The promptness of its action, however, renders it in some cases superior to ergot; the two drugs may often be exhibited simultaneously, the pituitary for its primary, quick effect and the ergot to maintain the action. It has also been used to control *menorrhagia* and *metrorrhagia*. The effect of the extract of hypophysis on blood pressure suggests its use for the treatment of *surgical shock*. Musser (*A. J. M. S.*, 1913, cxlvi, p. 208) has shown that even when exhibited by the mouth it causes a marked rise in blood pressure in human beings. There have been, however, comparatively few clinical reports of its use as a circulatory stimulant. As an intestinal stimulant it has been highly lauded by many surgeons for the prevention or treatment of post-operative paralysis of the bowel. As a diuretic, although classed by physiologists as one of the most potent stimulants to the kidney, it has failed to achieve wide popularity. The enormous increase in the secretion of milk which has followed its exhibition has naturally suggested its use as a lacteal stimulant both in human beings and also animals, but the present evidence seems to be that the primary stimulation is followed by a compensatory diminution of glandular activity. Among other conditions for which it has been recommended may be mentioned *Graves's disease, hay fever, rickets, acromegaly,* and *tetany*. Its value in these conditions, if it has any, is probably dependent upon its influence over the nutritive processes and the whole gland is preferable. When, however, the effect upon the in-

voluntary muscles is desired, whether of the uterus or arteries, we believe that the extract of the posterior lobe is to be preferred, since the anterior portion of the hypophysis has no effect upon these muscles and may exercise undesirable influences on the metabolism.

Dose, from one-half to three grains (0.032–0.2 Gm.).

Off. Prep.—Liquor Hypophysis, *U. S.*

INFUSA. U. S.

INFUSIONS

(ĭn-fū′ṣą)

Apozèmes, Tisanes, Infusions, *Fr.;* Infusa, *P. G.;* Infusionen, Aufgüsse, *G.;* Infusi, *It.;* Infusiones, *Sp.*

These are aqueous solutions obtained by treating with water (without the aid of ebullition), vegetable products only partially soluble in that liquid. The water employed may be hot or cold, according to the objects to be accomplished. Infusions are generally prepared by pouring boiling water upon the vegetable substance and macerating the mixture in a tightly closed vessel until the liquid cools. The soluble principles are thus extracted more rapidly, and, as a rule, in a larger proportion, than at a lower temperature. Some principles, moreover, are dissolved in this manner which are nearly or quite insoluble in cold water. A prolonged application of heat is in some instances desirable, and this may be effected by placing the vessel near the fire. Cold water is preferred when the active principle is highly volatile, when it is injured by heat, or when any substance of difficult solubility at a low temperature exists in the vegetable, which it is desirable to avoid in the infusion. A longer continuance of the maceration is necessary in this case, and in warm weather there is sometimes danger that spontaneous decomposition may commence before the process is completed. When a strong infusion is required, the process of *percolation* may be advantageously resorted to. The water employed should be free from saline impurities which frequently produce precipitates and render the infusion turbid. Fresh river, rain, or distilled water is usually preferable to water pumped from wells or obtained from springs, except when the latter are known to produce water which will not react with any of the constituents of the infusion.

The substance to be acted on should be sliced or bruised, or in the state of powder, but this last condition is seldom requisite, unless when percolation is employed, and is always inconvenient, as it requires that the infusion should be filtered through paper in order completely to separate the undissolved portion. In other cases it is sufficient to strain it through fine linen or muslin. When percolation is resorted to, the substance should be more or less finely powdered. The United States Pharmacopœia furnishes a general formula for infusions, which is to be used when the proportions are not specified. In the U. S. P., 1880, the strength of such infusions was fixed at 10 per cent. Experience has shown, however, that this was too strong for general purposes, and in the U. S. Pharmacopœia of 1890 and the Eighth and Ninth Revision, 5 per cent. has been chosen as the limit.

General Formula for Infusions, U. S. P. IX.

"Infusions must be *freshly made from the drugs,* and, when the strength of Infusions is not otherwise directed, they are to be prepared by the following general formula: The Drug, coarsely comminuted, *fifty grammes* [or 1 ounce av., 334 grains]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Introduce the substance into a suitable vessel provided with a cover, pour upon it *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of boiling water, cover the vessel tightly, and allow it to stand for half an hour. Then strain with expression, and pass enough water through the strainer to make the Infusion measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. If the activity of the Infusion is affected by heat, cold water only should be used.

"*Caution.*—The strength of Infusions of potent or very active drugs should be specially directed by the physician." *U. S.*

Infusions are usually prepared in glazed earthenware or porcelain vessels fitted with covers. Brande suggests the use of clean metallic vessels, which, when finely polished, retain the heat for a longer time, but they are more liable to chemical alterations, and may sometimes injuriously affect the preparation. Vessels of block-tin are generally well adapted for the purpose.

As infusions do not keep well, especially in warm weather, they should be made extemporaneously and in small quantities. In this country they are usually prepared in the patient's home, and the propriety of their introduction into the Pharmacopœia has been doubted, but it is desirable to have certain fixed standards for the regulation of the medical practitioner, and it is always preferable to direct infusions from the apothecary, for whose guidance official formulas are necessary. Physicians would, indeed, find an advantage in more frequently directing them to be prepared by the pharmacist, instead of leaving their preparation to the carelessness or want of skill of attendants upon the sick. Infusions may be kept during hot weather, and for many months, by straining them *while hot,* and pouring them at once into bottles provided with accurately ground stoppers. The bottle must be brim-full, the stopper being made to displace its bulk of the fluid. A common bottle with a cork stopper may be used, if the softened cork be forced into the full bottle, tied down, and at once dipped into hot sealing wax. The hotter the liquid and the freer from the air the better will the infusion keep. Sterilization of infusions by heating them to the boiling point, then preserving in bottles which have been kept hot to destroy germs, and stoppered with steril-

ized cotton, is effective, particularly if the bottles have a stopcock near the bottom to draw the infusion when wanted. Alméns has proposed a very efficient method of preserving infusions. (*A. J. P.*, April, 1875.) It is as follows: The infusion or decoction is heated for some time in a water bath at 100° C. (212° F.), and the bottle is then fitted with a tight cork, through which a glass tube passes lightly filled with cotton wool. The cork has a second opening, through which a glass tube passes nearly to the bottom of the bottle; this tube is bent at a sharp angle and has fitted to it a piece of india rubber tubing, to which a pinchcock is attached, by means of which the contents may be drawn as wanted. By making very concentrated infusions, as suggested by Donovan, with a mixture of three parts of water and one part of alcohol, they may be long kept, and when used can be diluted with water to the proper strength. Thus, if made four times as strong as the official infusion, they may be diluted with three measures of water. The proportion of alcohol would thus be very small, but it might still be medicinally injurious, and infusions should not be prepared in this way unless with the cognizance of the prescriber.

Battley, of London, introduced a set of preparations, which he called *inspissated infusions*, the advantages of which are that the virtues are extracted by cold water, are not injured by heat used in the evaporation, are in a concentrated state, and are not impaired by time. To prepare them he macerated the material, coarsely powdered, bruised, or finely sliced, in twice its weight of cold distilled water, pressing the solid matter into the liquid repeatedly by a rammer or the hand; then allowed the liquid to drain out, or expressed it in the case of highly absorbent substances, and repeated the process, with an amount of water equal to that which had been separated, until the strength was exhausted. Four or six hours of maceration were usually sufficient. The infusion is then to be concentrated by evaporation, at a temperature not exceeding 71.1° C. (160° F.) to the sp. gr. 1.200, and as much alcohol is to be added as will make its sp. gr. 1.100. These preparations are very analogous to the *fluidextracts* already considered. As a rule, it would probably be preferable to prepare infusions by the process of percolation.

The inspissated infusions must be diluted when administered. The presence of alcohol, though in small quantity, would sometimes be a serious objection. (*P. J.*, x, 129.) *Concentrated infusions* of the strength of 50 per cent. were introduced into the British Pharmacopœia (1898); they are mostly made by percolation, and were termed "Liquors." This certainly led to confusion in nomenclature, and it is difficult to understand why they were not called concentrated infusions, particularly as their almost universal use is for making ordinary infusions by diluting with water. They were dropped from the British Pharm. 1914.

INFUSUM ALSTONIÆ. Br.

INFUSION OF ALSTONIA

(ĭn-fū'sŭm ăl-stōn'ĭ-ą)

"Alstonia, bruised, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for half an hour; strain while hot." *Br.*

See *Alstonia*, page 119.

Dose, one-half to one fluidounce (15–30 mils).

INFUSUM AURANTII. Br.

INFUSION OF ORANGE PEEL

(ĭn-fū'sŭm âu-răn'tĭ-ī)

Tisane d'Ecorce d'Orange, *Fr.;* Pomeranzenschalenaufguss, *G.*

"Dried Bitter-Orange Peel, cut small, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

A grateful stomachic.

Dose, from one-half to one fluidounce (15–30 mils).

INFUSUM AURANTII COMPOSITUM. Br.

COMPOUND INFUSION OF ORANGE PEEL

(ĭn-fū'sŭm âu-răn'tĭ-ī cŏm-pŏs'ĭ-tŭm)

Tisane d'Ecorce d'Orange composée, *Fr.;* Pomeranzen und Citronenschalenaufguss, G.

"Dried Bitter-Orange Peel, cut small, 25 *grammes;* Lemon Peel, cut small, 10 *grammes;* Cloves, bruised, 5 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

A grateful stomachic in the *dose* of from one-half to one fluidounce (15–30 mils).

INFUSUM BUCHU. Br.

INFUSION OF BUCHU

(ĭn-fū'sŭm bū'ȼhū)

Infusum Diosmæ, s. Barosmæ; Tisane de Buchu, *Fr. Cod.;* Buchuaufguss, *G.*

"Buchu Leaves, freshly broken, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

It has the odor, taste, and medicinal virtues of the leaves, and affords a convenient method of administering the medicine.

Dose, from one to two fluidounces (30–60 mils).

INFUSUM CALUMBÆ. Br.

INFUSION OF CALUMBA

(ĭn-fū'sŭm cą-lŭm'bæ)

Infusion of Columbo; Tisane de Columbo, *Fr.;* Kolombo-Infusion, Kolomboaufguss, *G.;* Infusion de Colombo, *Sp.*

"Calumba Root, cut small, 50 *grammes;* Distilled Water, cold, 1000 *millilitres.* Infuse in a covered vessel for half an hour; strain." *Br.*

The *infusion of calumba* is likely to spoil very quickly, especially in warm weather. Ca-

lumba contains starch and albumen. Cold water extracts the latter without the former; hot water the former with comparatively little of the latter, which is partially coagulated by the heat. Both starch and albumen are liable to spontaneous change, but the former is much the more permanent of the two. Hence it is, according to Greenish, that the hot infusion keeps best. Indeed, he ascribes the change which takes place in the starch of the hot infusion chiefly to the agency of a little albumen which has escaped coagulation. According to these views, the best plan of preparing infusion of calumba is to exhaust the root with cold water, by which the starch is left behind, and then to heat the infusion to the boiling point in order to coagulate the albumen. (*A. J. P.*, xviii, 141; from *P. J.*) Upon comparing specimens of the cold and hot infusion, we have not found the results of Greenish fully confirmed. The cold infusion appeared to keep better than the hot. Nevertheless the plan of preparing the infusion above proposed is probably the best. The infusion of calumba is not colored by salts of iron, and may be conveniently administered in connection with them.

Dose, one fluidounce (30 mils), three or four times a day.

INFUSUM CARYOPHYLLI. Br.

INFUSION OF CLOVES

(ĭn-fū'zŭm căr-ŷ-o-phŷl'lī)

Tisane de Girofle, *Fr.;* Gewürznelken-Infusion, Gewürznelkenaufguss, *G.*

"Cloves, bruised, 25 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

The infusion of cloves affords precipitates with lime water, and with the soluble salts of iron, zinc, lead, silver, and antimony. (Phillips.)

Dose, one fluidounce (30 mils).

INFUSUM CASCARILLÆ. Br.

INFUSION OF CASCARILLA

(ĭn-fū'zŭm căs-ca-rĭl'læ)

Tisane de Cascarille, *Fr.;* Kaskarillaufguss, *G.*

"Cascarilla, in No. 10 powder, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

This infusion affords precipitates with lime water, infusion of galls, silver nitrate, lead acetate and subacetate, zinc sulphate, and ferrous sulphate.

Dose, one fluidounce (30 mils).

INFUSUM CHIRATÆ. Br.

INFUSION OF CHIRETTA

(ĭn-fū'zŭm ch-rā'tæ)

Tisane de Chirette, *Fr.;* Chirettaufguss, *G.*

"Chiretta, cut small, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

Dose, from one-half to one fluidounce (15–30 mils).

INFUSUM CINCHONÆ ACIDUM. Br.

ACID INFUSION OF CINCHONA

(ĭn-fū'zŭm cĭn-ch-nō'næ ăc'ĭ-dŭm)

Infusion of Yellow Bark; Infusion of Calisaya Bark; Tisane de Quinquina jaune, *Fr.;* Kalisaya-Rindenaufguss, *G.*

"Red Cinchona Bark, in No. 40 powder, 50.0 *grammes;* Aromatic Sulphuric Acid, 12.5 *millilitres;* Distilled Water, boiling, 1000.0 *millilitres.* Mix the Red Cinchona Bark with the Distilled Water in a covered vessel; add the Aromatic Sulphuric Acid; infuse for one hour; strain while hot." *Br.*

Though the infusion with boiling water is more quickly prepared than the infusion with cold water, and therefore better adapted to cases of emergency, yet the former is a more elegant preparation, not turbid like the latter, and at least equally efficient. We therefore prefer the process of the U. S. Pharmacopœia, 1890, provided it be skilfully conducted. (See *U. S. Dispensatory,* 19th ed., p. 654.)

The U. S., 1890, infusion is an efficient preparation. Water extracts from bark quinine and cinchonine kinates, but leaves behind the compounds which these principles form with the cincho-tannic acid. The simple infusion, therefore, is rather feeble. But the addition of the acid insures the solution of all or nearly all the active matter. It would be best to macerate the bark with the acidulated water some time before it is introduced into the percolator. The infusion of cinchona, made without acid, affords precipitates with the alkalies, alkaline carbonates, and alkaline earths; the soluble salts of iron, zinc, and silver; corrosive mercuric chloride, arsenic trioxide, and tartar emetic; gelatinous solutions; and various vegetable infusions and decoctions, as those of galls, chamomile, calumba, cascarilla, horseradish, cloves, catechu, orange peel, digitalis, senna, rhubarb, valerian, and simaruba. In some instances the precipitate occurs immediately, in others not for several hours. The loss of few, however, of these substances by precipitation diminishes the efficacy of the infusion, as they do not affect the active principles. The alkalies, alkaline earths, and vegetable astringents are really incompatible. As gallic, tartaric, and oxalic acids form salts with quinine of somewhat difficult solubility, the neutral and soluble gallates, tartrates, and oxalates produce in the infusion slight precipitates of corresponding salts of the alkaloids, but these are redissolved by an excess of the acid. Antimony and potassium tartrate does not precipitate the alkaloids. Solutions of iodine are incompatible, forming with the alkaloids insoluble compounds. For an account of the chemical reactions of the infusions of different varieties of cinchona bark, see *A. J. P.*, ix, 128. The simple infusion of cin-

chona may be advantageously administered in cases which require tonic treatment but do not call for the full powers of the bark. The acid infusion has all the powers of cinchona itself.

Dose, one fluidounce (30 mils).

INFUSUM DIGITALIS. U. S., Br.

INFUSION OF DIGITALIS Inf. Digit.

(ĭn-fū'zŭm dĭg-ĭ-tā'lĭs)

Infusion of Foxglove; Tisane de Digitale, *Fr.;* Fingerhutaufguss, Digitalisaufguss, *G.;* Infusion de digital, *Sp.*

* "Digitalis, bruised, *fifteen grammes* [or 231 grains]; Cinnamon Water, *one hundred and fifty mils* [or 5 fluidounces, 35 minims]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Pour *five hundred mils* [or 16 fluidounces, 435 minims] of boiling water upon the digitalis, contained in a suitable vessel, and allow it to macerate for one hour. Then strain, add the cinnamon water to the strained liquid, and pass enough water through the residue on the strainer to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix well. *Infusion of Digitalis must be freshly prepared from the leaves."* *U. S.*

"Digitalis Leaves, in No. 20 powder, 7 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

This infusion is a valuable preparation and has been the subject of much discussion. The U. S. P. IX process has been improved by the deletion of alcohol, which was added for the purpose of preserving the infusion, which it did only partially. The present process, U. S. P. IX, is simple and satisfactory provided that great care is used in the selection of the digitalis.

The *infusion of digitalis* if prepared properly represents thoroughly the therapeutic activities of the drug. There is a belief among many clinicians that it is more actively diuretic than the tincture, but this idea is probably due to the fact that it is usually given in proportionately larger dose. According to Focke (*A. Pharm.,* ccxlix, p. 323) water will extract about 85 per cent. of the activity of digitalis leaves. As the infusion of digitalis deteriorates rapidly it is essential that it be freshly prepared for each order. It should also be made strictly according to the pharmacopœial process, the custom sometimes indulged in by careless pharmacists of diluting the fluidextract cannot be too severely condemned.

Dose of the U. S. infusion, one to four fluidrachms (3.75-15 mils). The British infusion is much weaker and may be given in doses of two to six fluidrachms (7.5–22.5 mils).

INFUSUM ERGOTÆ. Br.

INFUSION OF ERGOT

(ĭn-fū'zŭm ẹr'gọ-tæ)

Tisane de Seigle ergoté, *Fr.;* Mutterkornaufguss, *G.*

"Ergot, freshly crushed, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

Dose, two fluidounces (60 mils).

INFUSUM GENTIANÆ COMPOSITUM. Br.

COMPOUND INFUSION OF GENTIAN

(ĭn-fū'zŭm gĕn-tī-ā'næ cọm-pŏz'ĭ-tŭm)

Tisane de Gentiane composée, *Fr.;* Enzianaufguss, *G.*

"Gentian Root, thinly sliced, 12.5 *grammes;* Dried Bitter-Orange Peel, cut small, 12.5 grammes; Lemon Peel, cut small, 25.0 *grammes;* Distilled Water, boiling, 1000.0 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

The National Formulary IV introduced compound infusion of gentian which differs very slightly from that official in the U. S. P. 1870. (See *N. F.,* Part III.)

It has been the custom with some physicians to prescribe a concentrated infusion made with one-fourth the quantity of menstruum directed by the formula of U. S. P. 1870. This permits the use of a valuable tonic with the presence of but a trifling amount of alcohol. This concentrated preparation keeps well, and it may be diluted with the right quantity of the proper menstruum by the pharmacist to make the infusion of U. S. P. 1870. The use of the alcohol is to assist in dissolving the bitter principle, and at the same time to contribute towards the preservation of the infusion, which, without this addition, is very prone to spoil. The alcohol has, however, been abandoned by the British Pharmacopœia, and lemon peel substituted.

Dose, one fluidounce (30 mils), repeated three or four times a day.

INFUSUM KRAMERIÆ. Br.

INFUSION OF KRAMERIA

(ĭn-fū'zŭm krą-mē'rĭ-æ)

Infusion of Rhatany; Tisane de Ratanhia, *Fr.;* Ratanhiawurzelaufguss, *G.*

"Krameria Root, bruised, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

The *infusion of rhatany* is undoubtedly most efficient when prepared from the root in a state of moderately coarse powder by the mode of percolation with cold water, as directed in the U. S. process of 1870.

Dose, of the infusion, from one to two fluidounces (30–60 mils).

INFUSUM QUASSIÆ. Br.

INFUSION OF QUASSIA

(ĭn-fū'zŭm quäs'sĭ-æ)

Tisane de Quassie, *Fr.;* Quassiaaufguss, *G.;* Infusion de cuasia amarga, *Sp.*

"Quassia Wood, rasped, 10 *grammes;* Distilled Water, cold, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain." *Br.*

Boiling water may be employed when it is desirable to obtain the preparation quickly, but

cold water affords a clearer infusion. The fifteen minutes maceration directed in the British Pharmacopœia, considering that cold water is used, appears to us to be too short for the exhaustion of the wood.

Dose, two fluidounces (60 mils), three or four times a day.

INFUSUM RHEI. Br.

INFUSION OF RHUBARB

(ĭn-fū'zŭm rhē'ī)

Tisane de Rhubarbe, *Fr.;* Rhabarberaufguss, *G.;* Infuso di rabarbaro, *It.;* Infusion de ruibarbo, *Sp.*

"Rhubarb, in thin slices, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

In order that the rhubarb may be exhausted, it should be digested with the water near the source of heat, at a temperature somewhat less than that of boiling water. It is customary to add some aromatic, such as cardamom, fennel seed, or nutmeg, which improves the taste of the infusion and renders it more acceptable to the stomach. One drachm of either of these spices may be digested in connection with the rhubarb.

This infusion may be given as a laxative, and is occasionally used as a vehicle for tonic, antacid, or more active cathartic medicines. The stronger acids and most metallic solutions are incompatible with it.

Dose, one to two fluidounces (30–60 mils).

INFUSUM ROSÆ ACIDUM. Br.

ACID INFUSION OF ROSES

(ĭn-fū'zŭm rō'zæ aç'ĭ-dŭm)

Infusum Rosæ Compositum, *N. F.;* Compound Infusion of Rose; Acid Infusion of Rose; Tisane de Rose composée, *Fr;* Saurer Rosenaufguss, *G.*

"Red-Rose Petals, dried and broken, 25.0 *grammes;* Diluted Sulphuric Acid, 12.5 *millilitres;* Distilled Water, boiling, 1000.0 *millilitres.* Add the Diluted Sulphuric Acid to the Distilled Water; infuse the Red-Rose Petals in the mixture in a covered vessel for fifteen minutes; strain while hot." *Br.*

The formula of the U. S. P. 1870 is preferable to that of the Br. Pharm. on account of the presence of sugar. It is unfortunate, in our opinion, that this elegant infusion was not reinstated at the last revision of the U. S. Pharmacopœia. We append the formula of the U. S. P. 1870: "Take of Red Rose [dried petals] *half a troyounce;* Diluted Sulphuric Acid *three fluidrachms;* Sugar [refined], in coarse powder, *a troyounce and a half;* Boiling Water *two pints and a half.* Pour the Water upon the Rose in a covered glass or porcelain vessel; add the Acid, and macerate for half an hour. Lastly, dissolve the Sugar in the liquid, and strain." *U. S.* The process for this infusion in the N. F. IV is practically the same. (See Part III.)

The red rose serves little other purpose than to impart a fine red color and a slight rose and astringent flavor to the preparation, which owes its medicinal virtues almost exclusively to the sulphuric acid. According to J. B. Barnes, one part of glycerin added to eight or nine parts of infusion of rose increases greatly its brightness and transparency. It is refrigerant and astringent, and affords a useful and not unpleasant drink in *hemorrhages* and *colliquative sweats.* It is much used by British practitioners as a vehicle for saline medicines, particularly magnesium sulphate, the taste of which it serves to cover. It is also employed as a gargle, usually in connection with acids, nitre, alum, or tincture of Cayenne pepper.

Dose, two fluidounces (60 mils).

INFUSUM SCOPARII. Br.

INFUSION OF BROOM

(ĭn-fū'zŭm scǫ-pā'rī-ī)

Tisane de Genêt à balais, *Fr.;* Besenginsteraufguss, *G.*

"Broom Tops, dried and bruised, 100 grammes; Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

This preparation has been introduced in place of the Decoction of Broom of the British Pharmacopœia of 1885. Water thoroughly extracts the virtues of broom, and the large quantity of water in each dose aids the diuretic action.

Dose, from one to two fluidounces (30–60 mils).

INFUSUM SENEGÆ. Br.

INFUSION OF SENEGA

(ĭn-fū'zŭm sĕn'ę-gæ)

Tisane de Polygale de Virginie, *Fr.;* Senegaaufguss, *G.*

"Senega Root, in No. 10 powder, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for half an hour; strain while hot." *Br.*

Dose, one fluidounce (30 mils).

INFUSUM SENNÆ. Br.

INFUSION OF SENNA

(ĭn-fū'zŭm sĕn'næ)

Senna Tea; Tisane de Séné, *Fr.;* Sennaaufguss, *G.*

"Senna Leaves, 100 *grammes;* Ginger, sliced, 5 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

We prefer the coriander of the U. S. P. 1870 to the ginger of the British. The infusion deposits, on exposure to the air, a yellowish precipitate, which is said to aggravate its griping tendency; it should, therefore, not be made in large quantities. It is customary to prescribe with it manna and some one of the saline cathartics, which increase its efficacy and render it less painful in its operation. (See *Infusum Sennæ Compositum.*) The cold infusion, especially if made by percolation from the coarsely powdered leaves, while probably not inferior in strength to that prepared with boil-

ing water, is said to be less unpleasant to the taste.

Dose, two fluidounces (60 mils).

Off. Prep.—Mistura Sennæ Composita, *Br.*

INFUSUM SENNÆ COMPOSITUM. U. S.

COMPOUND INFUSION OF SENNA Inf. Senn. Co.

(ĭn-fū'zŭm sĕn'næ cŏm-pŏz'ĭ-tŭm)

Tisane de Séné composée, *Fr.;* Infusum Sennæ Compositum, *P. G.;* Wiener Trank, Sennaaufguss, *G.;* Infuso di sena con manna, *It.*

* "Senna, *sixty grammes* [or 2 ounces av., 51 grains]; Manna, *one hundred and twenty grammes* [or 4 ounces av., 102 grains]; Magnesium Sulphate, *one hundred and twenty grammes* [or 4 ounces av., 102 grains]; Fennel, bruised, *twenty grammes* [or 309 grains]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Pour *eight hundred mils* [or 27 fluidounces, 24 minims] of boiling water upon the senna, manna, and fennel contained in a suitable vessel, and allow the mixture to macerate for half an hour. Then strain, express and dissolve the magnesium sulphate in the Infusion, and again strain. Lastly, add enough water through the strainer to make the Infusion measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. This preparation must not be dispensed unless it has been recently prepared." *U. S.* (See *Mistura Sennæ Composita, Br.*)

This preparation is used in Europe and to some extent in this country. The synonym, "*Black Draught,*" has been deleted from the U. S. P. IX because of the similarity in name to "*Black Drop*" (Acetum Opii), death having resulted through the confusion in names. The taste is bitter and nauseous and the infusion is now rarely employed.

Dose, four fluidounces (120 mils).

INFUSUM UVÆ URSI. Br.

INFUSION OF BEARBERRY

(ĭn-fū'zŭm ū'væ ûr'sī)

Tisane d'Uva Ursi, *Fr.;* Bärentraubenblätteraufguss, *G.*

"Bearberry Leaves, bruised, 50 *grammes;* Distilled Water, boiling, 1000 *millilitres.* Infuse in a covered vessel for fifteen minutes; strain while hot." *Br.*

Dose, from one to two fluidounces (30–60 mils), three or four times a day.

INJECTIO APOMORPHINÆ HYPODERMICA. Br.

HYPODERMIC INJECTION OF APOMORPHINE

(ĭn-jĕc'tĭ-ō ăp-ọ-mör-fĭn'næ hŷ-pọ-dẹr'mĭ-cą)

Injection hypodermique d'Apomorphine, *Fr.;* Subcutane Apomorphineinspritzung, *G.*

"Apomorphine Hydrochloride, 1 *gramme;* Diluted Hydrochloric Acid, 1 *millilitre;* Distilled Water, recently boiled and cooled, sufficient to produce 100 *millilitres.* Mix the Diluted Hydrochloric Acid with fifty millilitres of the Distilled Water; dissolve the Apomorphine Hydrochloride in the mixture, and add sufficient of the Distilled Water to produce the required volume. This Injection should be recently prepared. 100 millilitres contain 1 gramme of Apomorphine Hydrochloride; 110 minims contain 1 grain." *Br.*

Dose, by subcutaneous injection, from two to eight minims (0.12–0.5 mil).

INJECTIO COCAINÆ HYPODERMICA. Br.

HYPODERMIC INJECTION OF COCAINE

(ĭn-jĕc'tĭ-ō cō-cą-ĭ'næ hŷ-pọ-dẹr'mĭ-cą)

Injection hypodermique de Cocaine, *Fr.;* Subcutane Cocaineinspritzung, *G.*

"Cocaine Hydrochloride, 5.00 *grammes;* Salicylic Acid, 0.15 *gramme;* Distilled Water, 100.0 *millilitres,* or *a sufficient quantity.* Boil the Distilled Water; add the Salicylic Acid; dissolve the Cocaine Hydrochloride in the solution when cool; add, if necessary, sufficient recently boiled and cooled Distilled Water to produce one hundred millilitres of the Injection. This Injection is of one-half the strength of the corresponding preparation of the British Pharmacopœia 1898. It contains 5 grammes of Cocaine Hydrochloride in 100 millilitres; 110 minims contain 5 grains." *Br.*

This injection is half the strength of Br. Pharm. (1898) preparation.

Dose, by subcutaneous injection, from two to ten minims (0.12–0.6 mil).

INJECTIO ERGOTÆ HYPODERMICA. Br.

HYPODERMIC INJECTION OF ERGOT

(ĭn-jĕc'tĭ-ō ẹr'gọ-tæ hŷ-pọ-dẹr'mĭ-cą)

Hypodermic Injection of Ergotin; Injection hypodermique d'Ergot de Seigle, *Fr.;* Subcutane Mutterkorneinspritzung, *G.*

"Extract of Ergot, 33 *grammes;* Phenol, 1 *gramme;* Distilled Water, recently boiled and cooled, sufficient to produce 100 *millilitres.* Dissolve. This Injection should be recently prepared. 100 millilitres contain 33 grammes of Extract of Ergot; 110 minims contain 33 grains." *Br.*

This preparation does not represent ergot. (See *Ergota,* page 428.)

Dose, by subcutaneous injection, from three to ten minims (0.2–0.6 mil).

INJECTIO MORPHINÆ HYPODERMICA. Br.

HYPODERMIC INJECTION OF MORPHINE

(ĭn-jĕc'tĭ-ō mör-fĭn'næ hŷ-pọ-dẹr'mĭ-cą)

Injection hypodermique de Morphine, *Fr.;* Subcutane Morphinespritzung, *G.*

"Morphine Tartrate, 2.5 *grammes;* Distilled Water, recently boiled and cooled, sufficient to produce 100.0 *millilitres.* Dissolve. This Injection is of one-half the strength of the corresponding preparation of the British Pharmacopœia, 1898. It contains 2.5 grammes of Morphine Tartrate in 100 millilitres; 110 minims contain 2.5 grains." *Br.*

This solution is made from morphine tartrate in place of the morphine acetate formerly used; this is a great improvement, as the acetate is the most unstable of all morphine salts. The morphine strength of this injection is one-half that

of the Hypodermic Injection of Morphine of the British Pharmacopœia of 1898.

Dose, by subcutaneous injection, from five to ten minims (0.3–0.6 mil).

INJECTIO STRYCHNINÆ HYPODERMICA. Br.

HYPODERMIC INJECTION OF STRYCHNINE

(ĭn-jĕc'tĭ-ō strȳch-nī'næ hȳ-pō-dẹr'mĭ-cą)

"Strychnine Hydrochloride, 0.75 *gramme;* Distilled Water, recently boiled and cooled, sufficient to produce 100.0 *millilitres.* Dissolve. This Injection contains 0.75 gramme of Strychnine Hydrochloride in 100 millilitres; 110 minims contain ¾ grain." *Br.*

Dose, by subcutaneous injection, five to ten minims (0.3–0.6 mil).

INJECTIONES HYPODERMICÆ

HYPODERMIC INJECTIONS

(ĭn-jĕc-tĭ-ōnēs hȳ-pō-dẹr'mĭ-cæ)

Under this head are classed preparations which are recognized in the British Pharmacopœia for hypodermic application. These preparations are really of very little value, on account of their proneness to undergo decomposition, and the difficulty of maintaining their sterility, and are greatly inferior to the *hypodermic tablets* of various strengths which are now supplied by manufacturing pharmacists—the size of the tablets not varying with the strength, because it is always necessary to use so much diluent in order to make the tablet of sufficient size to handle conveniently. The tablets most used contain apomorphine, morphine, morphine and atropine, atropine, strychnine, pilocarpine, cocaine, hyoscyamine, physostigmine, hyoscine, nitroglycerin, or caffeine; each should be readily soluble in fifteen minims of water. These tablets should be made official, since their convenience, permanence, and accuracy in weight have caused them to come into universal use. The selection of the diluent is an important question; very finely powdered cane sugar has been employed, but is apt to produce local irritation and even abscesses. Sodium chloride has also been recommended, but the best diluent seems to be dried neutral sodium sulphate.

IODOFORMUM. U. S., Br.

IODOFORM Iodof.

(ī-ō-dọ-fôr'mŭm)

"Triiodomethane [$CHI_3 = 393.77$] usually obtained by the action of iodine upon alcohol or acetone, in the presence of an alkali or alkali carbonate. Preserve it in well-closed containers, in a cool place, protected from light." *U. S.*

"Iodoform, CHI_3, may be obtained by the action of iodine on ethylic alcohol in the presence of solution of potassium carbonate." *Br.*

Triiodomethane, Formyltriiodide; Iodoforme, *Fr. Cod.;* Iodure de formyle, *Fr.;* Iodoformium, *P. G.;* Jodoform, Carboneum jodatum, Trijodmethan, *G.;* Jodoformio, Trijodometano, *It.;* Yodoformo, *Sp.*

This compound, discovered by Sérullas about 1828, was later investigated chemically by J. B. Dumas. It was introduced as a remedy, about the year 1837, by R. M. Glover of London, and Bouchardat, of Paris, and was first adopted as official in the U. S. Pharmacopœia of 1870.

Preparation.—Cornélis and Gille published a process in *J. P. C.,* 1852, p. 196. (See *U. S. D.,* 14th ed., 511.) Other chemists have proposed processes, but they all depend upon the interaction of iodine, alcohol, or acetone in the presence of an alkali or alkaline carbonate. (See *U. S. D.,* 19th edition, p. 659.)

Iodoform is now made by electrolysis. An alkaline solution of sodium iodide is electrolyzed in the presence of alcohol, when, iodine being liberated at the anode, iodoform is obtained by the following reaction:

$$CH_3.CH_2OH + 10I + H_2O = CHI_3 + CO_2 + 7HI$$

The hydriodic acid formed combines with the sodium hydroxide present, to make sodium iodate, which, with the carbon dioxide, forms the side products. The temperature is kept at about 70° C. (158° F.) during the reaction and a diaphragm is used. The yield of iodoform is about 70 per cent. M. Otto produces iodoform industrially, direct from alkaline iodides, as follows: 100 kg. of water, 300 kg. of alcohol, 10 kg. of sodium carbonate and 55 kg. of potassium iodide are heated to 50° C. (122° F.) in a suitable vessel, and a current of ozone is passed through the mixture. Iodoform is deposited and crystallizes in a pure condition on the sides of the vessel and throughout the fluid itself. The alcohol may be replaced by acetaldehyde, acetone, etc. (*Ap. Ztg.,* 1900, 166.)

The fact, noticed by Lieben in 1870, that many other compounds besides ethyl alcohol yield iodoform when treated with iodine and alkali, led Krämer (*Ber. d. Chem. Ges.,* 1880, p. 1000) to propose the iodoform formation as an exact quantitative test for the presence of acetone in methyl alcohol. This "iodoform test" is now used in testing the purity of methyl alcohol for use in the manufacture of aniline dye colors, as well as the purity of acetone itself. It is also used as a confirmatory test for the identification of ethyl alcohol in the absence of acetone or aldehyde. (See *Acetonum.*) Heinrich Spindler proposes to make iodoform from the chlorides, bromides, or chloro-bromides of the paraffin series by reaction with an inorganic iodide; thus, if chloroform and *anhydrous* calcium iodide are heated to 120° C. (248° F.) iodoform is produced. (*Am. Drug.,* 1886, p. 67.) F. Günther recommends mixing alcohol containing 25 per cent. of aldehyde with ten times its weight of solution of sodium hydroxide, adding the iodine, and passing a current of carbon dioxide through the mixture. (*A. Pharm.,* 1887, p. 373.)

Properties.—It is in the form of "a fine, lemon-yellow powder, or in lustrous crystals of the hexagonal system, having a peculiar, very

penetrating and persistent odor, and an unpleasant, slightly sweetish taste suggestive of iodine. It is nearly insoluble in water to which it, however, imparts its odor and taste. One Gm. of Iodoform dissolves in 60 mils of alcohol, 80 mils of glycerin, 10 mils of chloroform, 7.5 mils of ether, 2.8 mils of carbon disulphide, and in 34 mils of olive oil at 25° C. (77° F.); also in about 16 mils of boiling alcohol. Its solutions are neutral to litmus.

Iodoform is slightly volatile, even at ordinary temperatures, and in boiling water distils slowly with the vapor of water. At about 115° C. (239° F.) it melts to a brown liquid, and at a higher temperature it decomposes, emitting vapors of iodine. Incinerate about 1 Gm. of Iodoform; not more than 0.2 per cent. of ash remains. Dry about 1 Gm. of Iodoform, accurately weighed, for twenty-four hours over sulphuric acid; the loss in weight does not exceed 1 per cent. Shake about 2 Gm. of Iodoform for one minute with 5 mils of distilled water and filter; the filtrate is colorless and free from bitter taste (*soluble yellow coloring matter, picric acid*), and does not affect the color of litmus (*acids or alkalies*)." *U. S.*

"Shining, lemon-yellow, small, hexagonal crystals, somewhat unctuous to the touch. Odor and taste persistent and disagreeable. Very slightly soluble in *water;* soluble in 100 parts of *alcohol* (90 per cent.), and in 8 parts of *ether,* the solutions being neutral to *litmus;* soluble also in *chloroform,* in *carbon disulphide,* in volatile oils, and in fixed oils; sparingly soluble in *benzene.* When warmed with *alcoholic solution of potassium hydroxide,* the resulting solution, acidified with *nitric acid,* becomes brown, and, when cold, changes to blue on the addition of *mucilage of starch.* 10 millilitres of *water* with which 1 gramme of Iodoform has been shaken are colorless and not bitter (absence of soluble yellow coloring matters and of picric acid), and yield no *reactions* for iodides. No appreciable ash." *Br.*

Iodoform is a volatile substance, soft to the touch, and totally devoid of corrosive properties. With potassium hydroxide in solution, it is decomposed, yielding potassium formate and iodide. Hence these two principles are incompatible in prescriptions. The specific gravity of iodoform, about which there has been a controversy, was determined by J. Percy Remington to be 4.000; the specific gravity of 2.000, as given in the U. S. P. 1890, was undoubtedly due to the operator taking the specific gravity of iodoform in water, and when this is done it is practically impossible to free the crystals from admixed air; the result was reached by using a saturated solution of iodoform in pure kerosene as the liquid, and by a simple calculation obtaining the equivalent in water. Iodoform is sometimes met with in commerce adulterated with water; Vulpius (*Ph. Cb.,* 1894) on examination detected 13 per cent. in one specimen.

Uses.—When applied locally, iodoform exercises a marked anesthetic action. Although of itself it is almost free of antibacterial properties, when brought in contact with the bodily secretions it gradually liberates some compound —perhaps free iodine—which is actively antiseptic. The experiments of Gosselin of Caen indicate that it is especially inimical to the tubercle bacillus. If taken internally it is gradually absorbed and is partially decomposed, liberating inorganic iodine; a part, however, appears to circulate unchanged. When exhibited in large doses, to the lower animals, it produces narcotic effects, and two stages in its operation have been noticed; the first is marked with more or less prostration, with symptoms of intoxication, the animal tottering, inclining to one side with the head falling, with loss of appetite, but without vomiting. The next day, unless a very large dose has been given, complete recovery takes place. A still larger dose induces the second stage, characterized by a remarkably intense excitation, with anxious breathing, strong and short pulse, a true opisthotonos, sometimes very striking, and convulsive movements of the paws, especially the hinder ones. After death fatty degeneration of the heart, liver, and kidneys may be found.

The chief value of iodoform in practical medicine is as an external application. It has long been used in cases of painful *ulcers* and as an antiseptic dressing to *wounds.* The testimony from surgeons is so strong that it is difficult to avoid believing that it is one of the most certain remedies of the class. Its beneficial effects seem to be due partly to absorption of secretions—making an unfavorable soil for bacterial growth—partly to the antiseptic effect of its decomposition products and partly to its local anesthetic effect. Some believe that it exerts some specific influence on cell growth that encourages healing. It is also of much value for its anesthetic powers in *laryngeal tuberculosis* and in *internal hemorrhoids;* in the latter condition it is best applied in the form of a suppository, which may contain from five to ten grains (0.3–0.6 Gm.).

The local application of iodoform in surgical *tuberculosis* has received the highest commendation from numerous surgeons. In the treatment of *tuberculous abscesses,* in tuberculous *empyema,* in *tubercular joints,* in non-suppurating *tuberculous glands,* and even in *tuberculous peritonitis,* numerous cures have been claimed. The manner of application varies with different surgeons. Verneuil, who has had an enormous experience, prefers in the treatment of abscesses and of tuberculous glands, and in most other cases, the injection of a 5 per cent. ether solution. Others prefer glycerin as a vehicle, especially in empyema cases, while others, especially in *peritonitis,* dust the dry powder over the surface which has been laid open.

Internally, iodoform has been used in *syphilis,*

goiter, and *phthisis,* originally with the idea that it would act as an iodide. As pointed out above, however, it is only partly broken up in the system and its action therefore is quite different from the inorganic iodides. Whether it is of any real value as internal remedy is at present open to doubt.

The very free use of iodoform in Germany as an antiseptic dressing to *wounds, ulcers,* etc., has led to many cases of poisoning. In the most characteristic and severe cases the phenomena of iodoform poisoning resemble somewhat those of meningitis; they are headache, somnolence, deepening into stupor, contracted, motionless pupils, abnormal quiet or restlessness ending in active delirium, with, however, a normal temperature and an exceedingly rapid pulse. Burlureaux affirms that if a piece of silver be placed in the mouth of a person suffering from iodoform poisoning, immediately the taste of garlic will be perceived, and if some of the saliva be mixed with calomel, a canary-yellow precipitate of mercurial iodide will be obtained. The most that such a test can accomplish is to show that the patient is under the influence of some compound of iodine. In cases of this character death almost always follows, although the symptoms may have developed abruptly and the dressing has at once been removed. In other cases the principal symptoms are general malaise and depression, faintness, headache, loss of appetite, and a persistent iodoform taste in the mouth. In some cases there is a slight temporary increase of temperature. Mental depression or excitement is especially noticed. Finally the pulse becomes accelerated, soft, and feeble; in some cases the pulse is very rapid—from 150 to 180—while the temperature remains normal or is only slightly elevated. It is asserted by Samter and Retzlaff (*T. G.,* 1889) that potassium bromide is an antidote in iodoform poisoning, its antidotal powers being due to the fact that it exceeds all other salts in its power of dissolving iodine compounds.

Langenstein has attributed a fatal result to the local application of one drachm of the powder. It is advisable that in ordinary cases not more than thirty grains (2 Gm.) be employed at once as a wound dressing, although in cases of tuberculosis the surgeon is warranted in taking the risk of larger amounts. Verneuil sometimes injects at one sitting 75 grains of the iodoform.

Iodoform gauze may be made by saturating surgical gauze with a 5 per cent. solution of iodoform in ether, and allowing it to dry at room temperature.

One of the principle obstacles to its employment is the odor, which, to some patients, is unbearable. Many methods of disguising the odor have been recommended, but in our experience the large quantity required of each deodorizing agent would preclude its employment. Tannin has been recommended, but, as this operates by decomposing the iodoform, it is not to be thought of in this connection. Probably the best class of substances to use are the volatile oils, such as anise, peppermint, fennel, bergamot, almond, etc., tonka, coffee, and balsam of Peru, although the latter acts by forming a compound, and the aim should be not to destroy the odor, but so to modify it as to remove its objectionable features. Olive oil saturated with camphor is said to dissolve 6 per cent. of iodoform, and is preferred by some surgeons.

Dose, one to five grains (0.065–0.32 Gm.).

Off. Prep.—Suppositoria Iodoformi, *Br.;* Unguentum Iodoformi, *U. S., Br.;* Collodium Iodoformi, *N. F.;* Glycerogelatinum Iodoformi, *N. F.;* Iodoformum Aromatisatum, *N. F.;* Petroxolinum Iodoformi, *N. F.*

IODUM. U. S., Br.

IODINE

(ī-ō′dŭm)

"It contains not less than 99.5 per cent. of I (126.92). Preserve it in glass-stoppered bottles, in a cool place." *U. S.* "Iodine may be obtained from the ashes of seaweeds and from native iodides and iodates. It contains not less than 99 per cent. of pure iodine, I." *Br.*

Iodinium, *U. S.* 1870; Iode sublimé, *Fr. Cod.;* Iode, *Fr.;* Jodum, *P. G.;* Jod, *G.;* Jodo, *It.;* Yodo, *Sp.*

Iodine is a non-metallic element, discovered in 1812 by Courtois, a soda manufacturer of Paris. It exists in certain marine vegetables, particularly the fuci or common sea weeds, which have long been its most abundant natural source. It has been reported in some fresh water plants, among which are the water cress, brooklime, and fine-leaved water hemlock; also in the ashes of tobacco, and of Honduras sarsaparilla. (Chatin.) It has been found in the beet-root of the grand duchy of Baden. (Lamy.) Macadam detected a trace of iodine in 100 gallons of water used for domestic purposes in Edinburgh, in several of the domestic animals, and in man. He detected it also in potatoes, beans, peas, wheat, barley and oats. (*P. J.,* Nov. 1854, p. 235.) It is doubtful whether iodine is as widely distributed in land plants as the above statements would indicate, and some allowance must be made for faulty methods used by earlier observers. Iodine has been reported to be present in the animal kingdom, as in the sponge, the oyster, various polypi, cod liver oil, and eggs, and, in the mineral kingdom, in sea water in minute quantity, in certain salt springs, as silver iodide in a rare Mexican mineral, in a zinc ore of Silesia, in native sodium nitrate, and in some kinds of rock salt. It is now obtained commercially from one of these sources—viz., from the native sodium nitrate, or Chili saltpetre, with which it occurs as sodium iodate. The production of the province of Tarapaca (Chili) has assumed large dimensions within recent years, as a result of higher prices established by a combination of Scotch, French,

and South American producers. The importations of iodine into the United States have increased greatly within the past two years, being 631,510 pounds in 1915 and 1,044,525 pounds in 1916 with a value of $2,447,764. Bussy has obtained iodine, in the proportion of one part in five thousand, from the coal gas liquor of the gas works of Paris. It was first discovered in the United States in the water of the Congress Spring, at Saratoga, by William Usher. It was detected in the Kanawha saline waters by Emmet, and it occurs in the bittern of the salt works of Western Pennsylvania, in the amount of about eight grains to the gallon. In sea weeds the iodine exists in the state probably of sodium iodide. In different countries sea weeds are burned for the sake of their ashes, the product being a dark-colored fused mass called *kelp*. This substance, besides sodium carbonate and iodide, contains more or less sodium chloride, potassium chloride, sodium sulphate, etc. The deep sea fuci contain the most iodine, and when these are burned at a low temperature for fuel, as is the case in the island of Guernsey, their ashes furnish more iodine than does ordinary kelp. (Graham.) According to Geo. Kemp, the laminarian species, especially *Laminaria digitata, L. saccharina,* and *L. bulbosa,* which are deep water sea weeds, and contain more potassium than sodium, are particularly rich in iodine.

Preparation.—Although most largely produced in South America, iodine is still obtained from kelp, and in Great Britain is manufactured chiefly at Glasgow. The kelp, which on an average contains 1-224th part of iodine, is lixiviated with water, in which about half dissolves. The solution is concentrated until a pellicle forms and allowed to cool, whereby nearly all the salts, except sodium iodide, are separated, they being less soluble than the iodide. The remaining liquor, which is dense and dark-colored, is made very sour by sulphuric acid, which causes the evolution of carbon dioxide, hydrogen sulphide and sulphurous acid, and the deposition of sulphur. The liquor is then introduced into a leaden still, and distilled with manganese dioxide into a series of glass receivers, inserted into one another, in which the iodine is condensed. In this process the sodium iodide is decomposed, and the iodine evolved according to the reaction:

$$2NaI + 2H_2SO_4 + MnO_2 = MnSO_4 + Na_2SO_4 + 2H_2O + I_2$$

which leaves as residue manganous sulphate and sodium sulphate. In this treatment much care is needed to avoid the liberation of chlorine from chlorides present, which will form volatile iodine trichloride and so occasion loss. This can be avoided by heating the acidified iodide solution with ferric chloride, when iodine is liberated according to the reaction:

$$2NaI + 2FeCl_3 = 2FeCl_2 + 2NaCl + I_2$$

The methods for the separation of the iodine from its combinations in the mother liquors as practised in South America may be divided essentially into three classes. (1) The mother liquors after the crystallization of the saltpetre without further concentration are treated with a solution of sodium sulphite of strength exactly corresponding to the amount of iodine present, for if an excess be used the iodine will be converted into hydriodic acid; the iodine is liberated according to the reaction:

$$2NaIO_3 + 4HNaSO_3 + SO_2 = Na_2SO_4 + 4HNaSO_4 + I_2$$

the iodine thus separated from the sodium iodate is filtered through linen cloth, washed, pressed, and sublimed. (2) The mother liquors are treated with sodium sulphite or bisulphite until the precipitated iodine is converted into HI, and this is precipitated as cuprous iodide by a solution of copper sulphate and sodium sulphite. (3) The amount of iodine is increased by fractional evaporation and crystallization of the mother liquors, and then, after adding the calculated amount of sodium bisulphite, the iodine is distilled off from the acidified liquor.

The methods formerly practised for obtaining iodine from sea weeds were accompanied with great loss. A notable improvement over the old kelp processes are the "char" and "wet" processes of E. C. C. Stanford (*J. Soc. Chem. Ind.*, 1885, p. 518), which show the following results when compared with the old processes. *Kelp process;* per cent. utilized, 18; kelp, 18 tons, yield salts 9 tons and iodine 270 lbs.; residues, kelp waste 18 tons, valueless. *Char process;* per cent. utilized, 36; char, 36 tons, yield salts 15 tons and iodine 600 lbs.; residues, charcoal 36 tons, tar, and ammonia. *Wet process;* per cent. utilized, 70; water extract, 33 tons, yield salts 20 tons and iodine 600 lbs.; residues, algin 20 tons, cellulose 15 tons, dextrin, etc.

Still another improvement was made in Germany (A. James, German Patent No. 95,063, of March 17, 1897), whereby over 91 per cent. of the iodine present in the sea weed has been recovered. Sea weed either wet or dry is immersed in sea water that has previously been treated with quicklime to precipitate the magnesia and give a distinctly alkaline reaction. The sea weed in the proportion of about one ton to the cubic meter of water is left immersed for twelve hours, during which time about 60 per cent. of the iodine is dissolved. It is then leached for six hours, each time in a second and third portion of prepared sea water. The combined extraction waters are then treated with ferrous sulphate, to coagulate mucilaginous matter, neutralized with sulphuric or hydrochloric acid, and the iodine then set free with an oxidizing agent like nitric acid or persulphate of ammonium, 1.5 kilos of nitric acid being required per cubic meter of solution. Iodine thus freed is extracted with petroleum naphtha, this solution being agitated with caustic alkali to form iodide and iodate, which are then treated in the usual manner.

Iodine is purified by sublimation in containers of porcelain, earthenware or glass, taking care to reject any white crystals which may appear in the first portion which comes over, which consists of cyanogen iodide. Moisture which has sometimes been reported to the extent of 15 or 20 per cent. and which may be suspected if the iodine adheres to the inside of the container in which it is kept, may be readily detected by assaying for the iodine content and also by the fact that such iodine will not make a transparent solution with chloroform.

Properties.—Iodine is described by the U. S. Pharmacopœia as "heavy, bluish-black, brittle, rhombic plates, having a metallic luster, a distinctive odor, and a sharp and acrid taste. Specific gravity: about 4.66 at 17° C. (62.6° F.). Iodine imparts a deep brown, evanescent stain to the skin, and slowly destroys vegetable colors. One Gm. of Iodine dissolves in 2950 mils of water, 12.5 mils of alcohol, 80 mils of glycerin, and in 4 mils of carbon disulphide at 25° C. (77° F.); freely soluble in chloroform, ether, or aqueous solutions of iodides; its solution in alcohol or in an aqueous solution of potassium iodide has a reddish-brown color; its diluted solution in chloroform or carbon disulphide has a violet color. Iodine volatilizes slowly at ordinary temperatures. When heated to about 114° C. (237.2° F.) it fuses and is gradually dissipated in the form of a purple vapor, leaving not more than 0.05 per cent. of residue. Add starch T.S. to a saturated aqueous solution of Iodine; a blue color is produced. On boiling the mixture the color is discharged but reappears as it cools, unless it has been subjected to long continued boiling. A solution of Iodine in chloroform is transparent (*moisture*). To determine the presence of cyanogen, chlorine or bromine, proceed as follows: Triturate 0.5 Gm. of finely powdered Iodine with 20 mils of distilled water and filter the solution. To one-half of the filtrate carefully add tenth-normal sodium thiosulphate V.S. until the solution is just decolorized. Then add a few drops of ferrous sulphate T.S., and subsequently a little sodium hydroxide T.S., and heat the mixture gently. On now adding a slight excess of hydrochloric acid, the liquid does not become blue (*cyanogen iodide*). To the other half of the aqueous filtrate, in a test tube, add a slight excess of silver nitrate T.S., shake the liquid actively, allow the precipitate to subside, and, having poured off the clear, supernatant liquid completely, shake the precipitate with a mixture of 1 mil of ammonia water and 9 mils of distilled water, and filter. On adding a slight excess of nitric acid to the filtrate, not more than a slight opalescence makes its appearance (*chlorine or bromine*).

"**Assay.**—Introduce about 0.5 Gm. of powdered Iodine into a tared weighing-bottle, stopper, weigh accurately, and add 1 Gm. of potassium iodide dissolved in 5 mils of distilled water. Dilute this solution with distilled water to about 50 mils and titrate with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 99.5 per cent. of I.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.012692 Gm. of I. Each gramme of Iodine corresponds to not less than 78.4 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

"In rhombic prisms or octahedrons of the trimetric system, of dark color, and metallic lustre. Characteristic odor. Yields, when gently heated, a violet-colored vapor. Very slightly soluble in *water,* more soluble in *alcohol* (90 per cent.); readily soluble in *solution of potassium iodide,* in *ether,* and in *carbon disulphide. Mucilage of starch* colors the aqueous solution deep blue. Sublimes without appreciable residue, the first portion sublimed not including any slender colorless prisms emitting a pungent odor (absence of iodine cyanide). A solution of Iodine in *chloroform* is perfectly clear (absence of moisture). 0.5 gramme, dissolved in 50 millilitres of *water* containing 1 gramme of *potassium iodide,* requires for decolorisation not less than 39 millilitres of *N/10 solution of sodium thiosulphate.*" *Br.*

It is a volatile substance, and evaporates even at common temperatures. Its vapor has the sp. gr. 8.7, being the heaviest gaseous substance known. If inhaled mixed with air, it excites cough and irritates the nostrils. When it comes in contact with cool surfaces, it condenses in brilliant steel-gray crystals. Iodine is freely soluble in alcohol and ether, but requires 3000 times its weight of water to dissolve it. If water stands on iodine for some time, especially in a strong light, it apparently dissolves more iodine, but the result depends upon the formation of hydriodic acid, in a solution of which iodine is more soluble than in water. The solution of iodine in water has a slight disagreeable taste, a feeble odor, and a light-brown color; its solution in alcohol or ether is nearly black. Its solubility in water is very much increased by the addition of certain salts, as sodium chloride, ammonium nitrate, or potassium iodide, and the same effect is produced, to some extent, by tannic acid. Its solution in tannic acid is called *iodo-tannin,* of which Socquet and Guillermond made a syrup for internal and an aqueous solution for external use. It is also soluble in glycerin, as ascertained by Cap in 1854. According to I. Walz, glacial acetic acid is an excellent solvent of iodine, at least equal to alcohol. When the acid is heated to boiling with excess of iodine, and then allowed to cool slowly, it deposits iodine in beautiful large slender crystals, sometimes half an inch long, much larger and more abundant than those formed from other solutions. (*Chem. News,* 1873, p. 233.) In chemical characters iodine resembles chlorine, but its affinities are weaker. It combines with most of the non-metallic and nearly all the metallic elements, forming a class of compounds called iodides. Some of these are official, as the iron, mercury, lead, potassium, sodium, strontium, and sulphur iodides. It

forms with oxygen one oxide, *iodic oxide*, I_2O_5, and two acids, *iodic* and *periodic*, and with hydrogen an acid called *hydriodic acid* which is official as the diluted acid and in the syrup.

Tests.—Iodine, in most cases, may be recognized by its characteristic purple vapor; but, where this cannot be made evident it is detected unerringly by starch, which produces with it a deep-blue color. The test was discovered by Colin and Gaultier de Claubry, and is so delicate that it will indicate the presence of iodine in 450,000 times its weight of water. In order that the test may succeed, the iodine must be free, and the solutions cold. To render it free when in combination, as it always is in the animal fluids, a little chlorine, free from iodine, must be added to the solution suspected to contain it. Thus, in testing urine for iodine, the secretion is mixed with starch, and acidulated with hydrochloric acid and a drop or two of chlorine water added, when, if iodine be present, the color produced will vary from a light purple to a deep indigo blue, according to the amount of the element present. Sometimes in mineral waters the proportion of iodine is so minute that the starch test, in connection with chlorine, gives a doubtful coloration. In such cases a large volume of the water, sometimes as much as 10 liters, must be evaporated to dryness and the residue extracted with a minimum amount of water and the tests applied to the solution thus obtained.

Bargu and Starling (*P. J.*, 1914, xcii, 146) have called attention to the fact that other organic compounds besides starch have the property of showing a blue color with iodine, and have published a list of more than sixty such substances.

The detection and estimation of iodine in small amounts in combinations containing organic matter may be accomplished by methods analogous to the one used for the estimation of iodine in thyroid glands, which see.

One of the most delicate reactions yet devised for the qualitative detection of iodine is that recently discovered by Ciusa and Terni (*Gaz. Ch. It.*, 43, ii, 86) in which a solution composed of 10 grammes of mercuric nitrate, 50 mils of distilled water, 5 mils of nitric acid, and 60 mils of stronger ammonia water, is used. One mil of the reagent is added to 25 mils of the solution to be tested, chlorides give a white precipitate and bromides a yellow precipitate, neither of which are distinctive or interfere in any way. If iodides are present even in minute amounts a yellowish-red or brownish-red color or precipitate is produced.

It has been long known that when a mixture of iodine and starch in water is subjected to heat the blue color disappears, and that, if the heat be not too long continued, so as to volatilize the iodine or convert it into hydriodic acid, the color will return on the cooling of the liquid. Various explanations have been given of this curious fact by Personne and others, but the only one that is quite satisfactory is that by Magnes-Lahens, which he supports by experiment, that during the continuance of the heat the particles of starch and iodine separate, to unite again on refrigeration. (*J. P. C.*, 4e sér., iii, 405.)

Adulterations.—Iodine is said to be occasionally adulterated with mineral coal, charcoal, plumbago, and black manganese oxide. These are easily detected by their fixed nature, while pure iodine is wholly volatilized by heat. Herberger found native antimony sulphide in one sample, and plumbago in another, and Righini has detected as much as 25 per cent. of calcium chloride. The presence of cyanogen iodide and of water has already been referred to, and the modes of detecting and separating them pointed out. (See page 590.) Besides this test the British Pharmacopœia directs that the official iodine should be soluble in alcohol, ether, and a solution of potassium iodide, and should sublime without residue, and that the part which first comes over should contain no colorless prisms of a pungent odor.

Uses.—Iodine was first employed as a medicine in 1819, by Coindet, of Geneva. Iodine, whether taken into the stomach in the form of the element or as one of the salts of hydriodic acid, is absorbed readily and circulates in the blood chiefly in the form of an iodide, although it is probable that a small amount of the iodine is absorbed in the form of a protein compound. Although it can be found in a number of other secretions it is eliminated practically entirely through the kidneys. Elemental iodine is also capable of being absorbed through the skin; Herzfeld and Elin (*B. M. J.*, October 5, 1912) have shown that iodine can be demonstrated in the urine after painting the skin with the tincture. As iodine circulates as an iodide the effects are the same whether it be given in the elemental state or as a salt of hydriodic acid. Although Macht (*J. H. B.*, 1914, xxv) states that the iodine ion is a powerful stimulant when perfused through isolated heart or blood vessels, when introduced into the circulation of the intact mammal it has practically no influence. The common belief that the iodides dilate the arterioles is absolutely without reasonable foundation. The only important physiological effect of iodide is its influence upon metabolism. This action is not clearly understood although it is evident that the continued use of this drug increases the rapidity of nitrogenous breakdown; according to Chistoni (*A. I. P. T.*, xxi, p. 339), the elimination of uric acid and other purin bases is increased disproportionately. It appears to have some influence upon glands—beyond its action as a salt—not only increasing the quantity but changing the character of their secretions, especially diminishing excessive viscidity. In those morbid states attended with fibrinous exudation, the iodides have a similar effect on the exudate. There is a belief among many practitioners that it will even cause the absorption of organized fibroid tissue; this, however, is not well substantiated. In *syphilis* and *tuberculosis* there is often a very rapid breaking

down of the characteristic local lesions. This effect seems to be due to an increased autolysis but whether a specific reaction in certain diseases or merely the manifestations of general effect in the *locum minoris resistentiæ* is uncertain.

In *syphilis* iodine is without a direct curative property, that is, it has no effect upon the growth of the specific micro-organism. Because, however, of its power of causing the breakdown of syphilitic lesions it is a remedy of utmost importance in the tertiary stage, not merely because it lessens the extent of the sequelæ of the luetic affection, but because it drives the spirochetes from their lurking places into the general circulation where they may be reached by direct antisyphilitics. In the early stages iodine is useful because it forms a freely soluble compound with the mercury and thereby tends to prevent the deposit of the metal in internal organs.

Its effect in tuberculosis is analogous to that in *syphilis,* but whether this action in hastening the breakdown of the lesions will be beneficial or otherwise to the tuberculous patient, depends upon the location and character of the infection. Thus in *phthisis* generally the most favorable result is the walling off and ultimate calcification of the local lesion and the iodides by softening the infected area may not only delay the whole process, but may even cause a dissemination of themicro-organisms throughout the lung. On the other hand, in inoperable *lymphadenitis* it will hasten suppuration and may lead to the extrusion of the bacilli. In a somewhat similar way iodine may be useful in *bony tuberculosis.* In *leprosy* it apparently has a somewhat similar type of action, although less marked. It has also a potent effect in *actinomycosis* and even appears to have a direct curative effect. In inflammations of either the serous or mucous membranes attended with fibrinous exudates or viscid secretions, as *pleurisy, pericarditis,* or *bronchitis,* iodine is often of great value because of its liquefying action. In *bronchitic asthma,* while it has no direct influence upon the paroxysms, by its effect in increasing and liquefying the bronchial secretions it proves itself one of the most frequently serviceable drugs we possess. In chronic inflammatory conditions accompanied with a formation of fibroid connective tissue, as in *interstitial nephritis, arteriosclerosis,* and fibroid degenerations of the nervous centers, it is widely employed, not, however, because it is of proven utility but in a kind of despairing hope that it may produce some amelioration of the condition. In degenerative changes occurring as the result of *syphilis,* however, such as *locomotor ataxia,* it often appears to have some beneficial effect. It is habitually employed in *chronic rheumatism* which it probably influences through its action upon metabolism. The experiments of Reid Hunt (*J. P. Ex. T.,* 1910, ii, 15) indicate that iodine is a stimulant to the thyroid gland, which may explain its beneficial influence in simple *goiter* and its harmful effects in exophthalmic goiter. Potassium iodide forms in the body a freely soluble compound with either mercury or lead, and is therefore frequently used in the treatment of *lead poisoning* or in *mercurial* cachexia to hasten the elimination of the metal; it must be remembered, however, that by causing the solution of deposits it may cause an exacerbation of symptoms.

Elemental iodine has two important therapeutic properties which its salts do not share. These are as a local irritant and as a germicide. As a counter-irritant it is used especially in various forms of *arthritis,* notably those due to trauma, but is also of service in *bronchitis* or *glandular enlargement.* Its action in these conditions may be aided by absorption through the skin and consequent systemic effects of the drug. It is also employed for its local irritant effect as an injection for the cure of local effusions, as *ovarian dropsy, hydrocele,* and *ganglion.*

Antiseptic Uses.—Elemental iodine is a powerful germicide. Goebel (*Cb. B.,* 1906, xlii, p. 86) finds that a 1 to 1000 solution killed the *Staphylococci* after one minute's exposure and even the highly resistant anthrax spores if the exposure was prolonged to 15 minutes; Hailer found that as little as 1 part in 8000 was sufficient to destroy the staphylococci in 2 minutes. According to Peck (*P. J.,* 1911, lxxxvii, p. 450), a 1 to 1000 aqueous solution of iodine will kill the typhoid bacillus in one minute, but 1 in 10,000 will not kill it in three minutes. Of great importance in the practical use of iodine in surgery is its power of penetrating the skin. Turner and Catto (*L. L.,* 1911) found that after the external application of a 3 per cent. solution of iodine the whole thickness of the skin was sterile. Bovee (*Am. J. Obstetrics,* July, 1911) found that the application of 5 per cent. of the U. S. P. tincture of iodine completely sterilized the surface of the skin within 15 minutes but that hairy regions, as the pubes, required 50 per cent. of this tincture (representing 3 per cent. of iodine) for complete sterilization.

In 1908 Grossich (*Cb. Chir.,* 1908, p. 1285) suggested painting of the skin with a 10 per cent. tincture of iodine as a means of sterilizing the site of operation. According to his claims no previous washing was necessary because of the penetrating power of the iodine. The method has been widely followed and with more or less modification is now almost universally employed by surgeons. Probably the most commonly employed routine in this country is to cleanse the skin with liniment of soft soap, thoroughly wash away the soap with alcohol, and then paint with the official tincture of iodine. Among the various solutions which have been suggested instead of the tincture, probably the most widely employed is that in benzin originally suggested by Heussner. This author used a solution containing one part of iodine, 750 of benzin, and 250 of liquid petro-

latum. Reich-Brutzkus (*W. K. W.*, 1913) uses a solution containing 3 parts of iodine, 10 parts of alcohol, and 90 of chloroform. From its use in sterilizing the seat of operation iodine has rapidly come into popularity as a surgical disinfectant for a wide variety of purposes. Woodbury (*N. Y. M. J.*, 1912, xcvi, p. 101) recommends it to sterilize the surgeon's hands, instruments, sutures, and dressings. Painting recent wounds with tincture of iodine, it is asserted, is an efficient protection against infection by most of the common pus producing organisms. Magi (*Policlinico*, xxii, 517) highly recommends in *erysipelas* painting the affected part with tincture of iodine. In proper dilutions it is used in various infections of mucous membranes as *conjunctivitis, urethritis, diphtheria, cystitis*, etc. More recently the vapors of nascent iodine have been employed in various local infections. These may be generated by heating iodoform. It is also used locally in various skin diseases both for its antiseptic and alterative effect.

Lugol used aqueous solutions of iodine in which the element is dissolved by double its weight of potassium iodide. These solutions were of varying strength according to the purpose for which they were employed. His *iodine lotion*, used as a wash in scrofulous *ophthalmia*, in *ozena*, etc., contained two grains of iodine and four of potassium iodide in a pint of water. His *rubefacient iodine solution* is formed by dissolving half an ounce of iodine and an ounce of potassium iodide in six fluidounces of water. *Lugol's caustic iodine solution* is made of iodine and potassium iodide, each, an ounce, dissolved in two fluidounces of water. This is used to destroy soft and fungous granulations, and has been employed with decided benefit in *lupus*. Under the name of *iodine paint* an alcoholic solution similar to the official tincture, but of twice the strength, is employed.

A mode of applying iodine locally has been suggested by R. Greenhalgh, of London, which consists in thoroughly impregnating raw cotton with a solution in glycerin of potassium iodide and of iodine, in the proportion of two ounces of the former and one ounce of the latter to eight ounces of the menstruum, and then drying the "*iodized cotton.*" It is intended for application to the cervix or os uteri, which is effected through a speculum. (*L. L.*, May 26, 1866, p. 582.) Méhu's method of making iodized cotton is as follows: Finely divided iodine (5 to 10 parts) is sprinkled between layers of loose cotton (100 parts) introduced into a tall glass vessel, and the latter placed horizontally on a water or sand bath. As soon as vapors of iodine are seen to rise, and the air has been expelled from the vessel, the latter is tightly stoppered. On continuing to apply a moderate and uniform heat, the iodine vapors penetrate the cotton, and color it yellow. After about two hours, the cotton will have assumed the color of burnt coffee, and the operation is finished. Cotton iodized in other ways, as by immersion in concentrated solutions of iodine in ether or carbon disulphide, retains merely traces of iodine. (*N. R.*, April, 1867.)

Iodine, in the state of vapor, has been employed by inhalation, in the treatment of *phthisis* and *chronic bronchitis*, but has failed to fulfil expectations, and is at present very rarely practised. For details as to methods, the reader is referred to the 14th edition of the *U. S. D.*

Under the names of *iodagol* and *iodéol* suspensions asserted to contain 25 per cent. and 20 per cent., respectively, of *colloidal iodine* have been introduced for local applications.

As an internal remedy one of the salts of hydriodic acid is usually preferred as being less prone to disturb digestion although the compound solution is frequently of service. (See page 646.) For endermic absorption the ointment of iodine is the most useful of the official preparations. Although less irritant than iodine the alkaline iodides are still very prone to upset the stomach. This fact has led to the recommendation of a host of compounds and preparations, many of which are noticed in Part II of this work.

In an overdose iodine acts as an irritant poison. From four to six grains (0.26–0.4 Gm.), in man, cause a sense of constriction in the throat, sickness and pain at the stomach, and at length vomiting and colic. Even in medicinal doses it sometimes causes alarming symptoms, such as fever, restlessness, disturbed sleep, palpitations, excessive thirst, acute pain in the stomach, vomiting and purging, violent cramps, frequent pulse, and, finally, progressive emaciation if the medicine be not laid aside. Such violent symptoms are, however, very rare, but where iodine or potassium iodide is given freely a mild *iodism* is not unfrequent. It is usually characterized by pain or heaviness in the region of the frontal sinuses, with or without coryza; in some instances soreness of the mucous membrane of the mouth and throat, or a mild ptyalism, is the prominent symptom, or a papular eruption may be the first manifestation of the constitutional action of the remedy. Absorption of the mammæ and wasting of the testicles have been reported as caused by the long-continued use of the drug, but such results are extremely rare.

In cases of poisoning by iodine, the stomach must be evacuated, and drinks administered containing an amylaceous substance, such as flour, starch, or arrow-root.

Dose, of iodine, one-twelfth to one grain (0.005–0.065 Gm.) well diluted.

Off. Prep.—Liquor Iodi Compositus, *U. S.*; Tinctura Iodi, *U. S.* (*Br.*); Tinctura Iodi Fortis, *Br.*; Tinctura Iodi Mitis, *Br.*; Unguentum Iodi, *U. S.*, *Br.*; Collodium Iodi, *N. F.*; Liquor Iodi Phenolatus (from Compound Solution), *N. F.*; Petroxolinum Iodi, *N. F.*; Petroxolinum Iodi Dilutum, *N. F.*; Phenolum Iodatum, *N. F.*; Syrupus Iodotannicus, *N. F.*; Tinctura Iodi Fortior, *N. F.*; Tinctura Iodi Decolorata, *N. F.*

IPECACUANHA. U. S. (Br.)

IPECAC Ipecac. [Ipecacuanhæ radix P. I.]

(ĭp-ẹ-căc-ŭ-ăn'hạ)

"The dried root of *Cephaelis Ipecacuanha* (Brotero) A. Richard, known in commerce as Rio Ipecac, or of *Cephaelis acuminata* Karsten, known in commerce as Cartagena Ipecac (Fam. *Rubiaceæ*), without the presence or admixture of more than 5 per cent. of stems or other foreign matter and yielding not less than 1.75 per cent. of the ether-soluble alkaloids of Ipecac." *U. S.* "Ipecacuanha Root is the dried root of Psychotria Ipecacuanha, *Stokes*." *Br.*

Ipecacuanhæ Radix, *Br.*, Ipecacuanha Root; Poaya, *Braz.* Ipécacuanha annelé ou officinale, *Fr. Cod.*; Racine brésilienne, *Fr.*; Radix Ipecacuanhæ, *P. G.*; Ruhrwurzel, Brechwurzel, Ipecacuanha, *G.*; Ipecacuana, *It.*; Ipecacuana (Raiz de), *Sp.*

The term *ipecacuanha,* derived from the language of the aborigines of Brazil, has been applied to various emetic roots of South American origin. The botanical character of the ipecac plant of commerce was long unknown. At the present time the plant is well known, but there is considerable conflict regarding the proper botanical name to designate it. The several Pharmacopœias differ from each other in the generic names used, and hence there may be some confusion. The U. S. Pharmacopœia wisely retains the generic name *Cephælis,* this having been recognized for years in this country. The British Pharmacopœia uses the generic name *Psychotria,* which practice has been followed in that country for many years. The Swiss and German Pharmacopœias follow Engler and Prantl, and use the generic name *Uragoga.* The latter is probably correct, but in view of the unstability of this subject, particularly as other generic names have been proposed and may even supersede all of these it is wise to adhere to the old name *Cephælis,* thus causing no confusion.

Cephaëlis Ipecacuanha is a small shrubby plant, with a slender root from four to six inches long, marked with annular rugæ, simple or somewhat branched, descending obliquely into the ground, and here and there sending forth slender fibrils. The stem is two or three feet long, but, being partly under ground, and often procumbent at the base, usually rises less than a foot in height. It is slender; in the lower portion leafless, smooth, brown or ash-colored, and knotted, with radicles frequently proceeding from the nodes; near the summit, pubescent, green, and furnished with leaves seldom exceeding six in number. These are opposite, petiolate, oblong-obovate, acute, entire, from three to four inches long, from one to two broad, obscurely green and somewhat rough on their upper surface, pale, downy, and veined on the under. At the insertion of each pair of leaves are deciduous stipules, embracing the stem, membranous at the base, and separated above into numerous bristle-like divisions. The flowers are small, white, each accompanied with a green bract, and collected in a semi-globular head, supported upon a round, solitary, axillary footstalk, and embraced by a monophyllous involucre. The latter being deeply divided into four, sometimes five or six, obovate, pointed segments. The fruit is an ovate, obtuse berry, which is at first purple, but becomes almost black when ripe, and contains two small plano-convex seeds.

Cephaëlis tomentosa, of Trinidad, has been studied by Francis Ransom, who finds that it contains emetine, but in too small quantity for commercial purposes. For description of the root, etc., see *P. J.*, xix, p. 258.

The Rio ipecac plant of Brazil flourishes in moist, thick, and shady woods, being most abundant within the limits of the eighth and twenty-second degrees of south latitude. It flowers in January and February, and ripens its fruit in May. The root is active in all seasons, but, as it has to be dried rapidly, collection during the rainy season is relaxed. The native collector, or *poayero,* seizes all the stems of a clump, loosens them by a zigzag motion, and then, thrusting a pointed stick under the roots, tears up the whole mass. The roots, freed from dirt by shaking, are then dried. The amount gathered daily varies from 8 to 30 pounds, according to skill and locality. Extirpation does not take place, because, as shown by the Edinburgh gardeners McNab and Lindsay, a very small fragment of the root, or even a petiole of a leaf, will rapidly produce a new plant. Weddell, indeed, many years since, stated that the remains of the root, often purposely left in the ground, serve the purpose of propagation, each fragment giving rise to a new plant. Ipecac of commerce comes chiefly from the interior province of Matto-Grosso, upon the upper waters of the Paraguay (from which in some years as much as 450,000 kilos are shipped), although some is said to be gathered near Philadelphia north of Rio Janeiro. The chief places of export are Rio Janeiro, Bahia, and Pernambuco. It is brought to the United States in large bags or bales. The importation into the United States have increased from 78,654 pounds in 1914 to 203,734 pounds in 1916.

Unofficial Varieties of Ipecac.—From time to time there have been imported into Europe various drugs stated to be ipecac, but differing from the official drug. Of these the most important are White Ipecac; the Larger Striated Ipecac of Planchon (*J. P. C.*, Déc., 1872); and the Lesser Striated Ipecac of Planchon.

Larger Striated Ipecac (Planchon). *Violet Striated Ipecac. Ipecac of St. Martha. Ipecac of Carthagena. Striated Elastic Ipecac* (Attfield).—This variety of ipecac is generally acknowledged to be the product of *Psychotria emetica* L., growing in the deep forests of Colombia. The drug occurs in rather long fragments, sometimes 9 or 10 cm., with a thickness of from 5 to 9 mm. The pieces are for the most part almost straight, sometimes sinuous, more rarely tortuous. At distant intervals they are marked by contractions, or circular fur-

rows. Their whole surface is largely striated longitudinally. To their upper part are often attached one or more remaining portions of the stem, distinguished from the root by their much smoother surface. Their color is a grayish-brown, tending sometimes to reddish-brown. Like other ipecacs, they have an outer cortical and a central ligneous portion. The former is soft, so that it may even be penetrated by the nail. It has a horny aspect, and a variable color, passing from whitish, by shades of rose, violaceous, and blackish violet. Its thickness is at least two-thirds of the root, and becomes still greater when this is immersed in water. The central part is yellowish-white. The root has little odor, and a taste scarcely nauseous, sometimes flat, and often sweetish. As to the microscopic characters, the most striking are probably the total absence of the starch granules, and the relatively very small diameter of the vessels in the central part. Chemically this variety is characterized by the presence of sugar. It also contains 0.027 per cent. of emetine.

Lesser Striated Ipecac (Planchon). *Ipecac des Côtes d'Or* (Pelletier). *Black Ipecac. Black Striated Ipecac. Striated Brittle Ipecac* (Attfield). *False Ipecac* (Holmes).—It is probably obtained from a species of *Richardsonia.* It occurs in very short fragments, 2 or 3 cm. long, and 2 or 3 mm. in thickness; some nearly cylindrical, others narrowly fusiform; others again formed of roundish or pyriform segments, somewhat thicker than the preceding, placed end to end. The color is generally of a gray-brown, darker than that of the other kind. The longitudinal striæ are fine, and regular on the transverse section. The cortical portion is horny, and its consistence firmer than in the larger kind; the wood is yellowish, and porous. The presence of the starch granules is another of the distinguishing characters of this variety. It contains a larger proportion of emetine than the preceding, yielding, according to the analysis of Pelletier, 9 per cent.

White Ipecac is obtained from *Ionidium Ipecacuanha* St. Hil. (fam. *Violaceæ*). It is obtained from Brazil. The root is much branched, free from annulations and of a grayish-white or light brownish-yellow color. The bark is very thin and the wood is light-yellow and porous. It is distinguished by the presence of stone cells and freedom from starch. It contains inulin and no emetine.

According to Pelletier, 100 parts contain 5 of an emetic substance, 35 of gum, 1 of nitrogenous matter, and 37 of lignin. (*Histoire abrégée des Drogues simples,* i, 514.)

The root of a species of *Ionidium* growing in Quito has attracted some attention as a remedy in *elephantiasis,* under the South American name of *cuichunchulli.* The plant received from Bancroft the name of *I. Marcucci;* but Hooker found the specimen received from Bancroft to be the *I. parviflorum* of Ventenat. Lindley thinks a specimen he received under the same name from Quito to be the *I. microphyllum* of Humboldt. If useful in elephantiasis, it is so probably by its emeto-purgative action. (See *A. J. P.,* vii, 186.)

Under the name of *East Indian Ipecac* there has appeared in the London markets a root of a pale pinkish-brown color, tapering rapidly from the base to the apex, and having annulations much closer than in the true ipecac. It is especially distinguished from the latter root by being evidently monocotyledonous—that is, without the central woody column—the vascular bundles appearing under a pocket lens as a more or less irregular ring of brownish dots. R. A. Cripp obtained from it a minute quantity of an alkaloidal substance, certainly distinct from the alkaloids of ipecac. (*P. J.,* lv.) Ranwez and Campion have also described a false ipecac derived from a monocotyledonous plant, *Cryptocoryne spiralis.* (*Ann. Pharm.,* i.)

In 1866 the cultivation of ipecac was introduced into India by King, but it was not until twenty years later (1886), when it was found that ipecac flourished in the Straits Settlements equally as well as in the Province of Minas, Brazil, that its cultivation became successful.

Cephælis acuminata Karsten is the source of the drug of commerce known as *Cartagena, Panama,* or *Savanilla Ipecac.* The plant is indigenous to Colombia. The leaves according to Karsten are elliptical, pointed, the stipules being separated, often almost to their base in a subulate fringe. The root is much larger and the percentage of active constituents is different from that of Rio ipecac. Humboldt considered *C. acuminata* merely as a different geographical form of *C. Ipecacuanha.* Owing to the scarcity of Rio ipecac the importations of the Cartagena variety is considerable, at times being the only form obtainable. It was for this reason that it was included in the U. S. Pharmacopœia. Braun discussed the subject of the cultivation of ipecac (*Der Pflanzer,* Tanga, i, p. 50) and commented on the available varieties to be selected and the best methods for collecting and treating the drug. Derry states (*C. D.,* lxxx, p. 822) that when established it grows well on virgin soils or where there is a depth of vegetable humus and the situation is moist and shady, but the properties of the root deteriorate with continued cultivation.

Properties.—Rio ipecac is in pieces 2.4 to 4 mm. thick, variously bent and contorted, simple or branched, consisting of an interior slender, light straw-colored, ligneous cord, with a thick, brittle, brownish, finely wrinkled, cortical covering, which presents on its surface a succession of circular, unequal, prominent rings or rugæ, separated by very narrow fissures, frequently extending nearly down to the central fiber. This appearance of the surface has given rise to the term *annelé,* or *annulated,* by which the true ipecac is designated by French pharmacists. The cortex is hard, horny, and

semi-transparent, breaks with a resinous fracture, and easily separates from the tougher ligneous fiber, which possesses the medicinal virtues of the root in a much inferior degree. On microscopic examination the very thick bark is seen to be formed of uniform parenchymatous cells, without traces of the medullary rays, which are very distinct in the woody central cylinder. Attached to the root is frequently a smoother and more slender portion, which is the base of the stem, and should be separated before pulverization. Pereira has met, in the English market, with distinct bales composed of these fragments of stems, with occasionally portions of the root attached. Much stress has been laid upon the color of the external surface of the ipecac root, and diversity in this respect has even led to the formation of distinct varieties. Thus, the epidermis is sometimes deep brown or even blackish, sometimes reddish-brown or reddish-gray, and sometimes light gray or ash-colored; hence the varieties of ipecac root which were formerly recognized, the *brown, red* and *gray*. It is now known that the color of the root varies according to the circumstances of growth and soil, so that coloration as the basis of classification has been abandoned, and the ipecacs of commerce are divided according to their geographical sources, into the *Brazilian* or *Rio Ipecac,* the *Cartagena* or *Colombia Ipecac,* and the *Johore* or *Indian Ipecac;* of these, the two varieties which are recognized by the U. S. Pharmacopœia are described as follows: "*Rio Ipecac.*—In cylindrical pieces, curved, and sharply flexuous, occasionally branched, from 3 to 15 cm. in length and from 2.4 to 4 mm. in thickness; externally dark brown, closely annulated, with thickened, incomplete rings, and usually exhibiting transverse fissures with vertical sides; fracture of bark short, of wood tough, bark very thick, light brown, easily separable from the yellowish-white wood; odor very slight, distinctive, the dust sternutatory; taste bitter and nauseous, somewhat acrid. Stems cylindrical, attaining a length of 10 cm. and a thickness of 2 mm., dark brown, finely longitudinally wrinkled and with a few elliptical scars. *Cartagena Ipecac.*—Cylindrical or slenderly fusiform, more or less tortuous, from 3 to 12 cm. in length and from 4 to 6.5 mm. in thickness; externally grayish-brown, the annulations usually not so numerous as in Rio Ipecac, occasionally transversely fissured and with circular scars of roots; bark 2 mm. in thickness, dark brown, smooth, somewhat horny, and easily separable from the light brown wood. Stems attaining a length of 10 cm. and a thickness of from 2 to 3 mm., cylindrical, somewhat zigzag, due to the prominent nodes with their elliptical stem-scars, grayish or dark brown and longitudinally wrinkled; bark thin. The powder from both varieties of Ipecac is light brown; starch grains numerous, single or from 2- to 4- or more compound, the individual grains spherical or polygonal, from 0.003 to 0.017 mm. in diameter; calcium oxalate in raphides, from 0.015 to 0.04 mm. in length, few; tracheids with bordered pores and oblique slit-like pores. The stem bark shows a few, slightly elongated stone cells, from 0.03 to 0.045 mm. in length with thick lignified walls and simple branching pores. Ipecac yields not less than 1.8 per cent. nor more than 4.5 per cent. of ash." *U. S.*

"In somewhat tortuous pieces seldom more than fifteen centimeters long or six millimetres thick; from dark brick-red to very dark brown; closely annulated externally, the annulations not taking the form of narrow ridges partially encircling the root (distinction from Cartagena ipecacuanha). Fracture short, the fractured surface exhibiting a thick greyish bark and small dense wood. Bark consisting of thin-walled parenchymatous cells, some containing slender raphides, but most filled with simple or compound starch grains, the simple seldom exceeding fifteen microns in length; wood consisting chiefly of tracheids and containing no vessels or typical medullary rays. In the powdered Root, thin-walled parenchymatous tissue, abundant simple or compound starch grains, the single grains seldom exceeding 15 microns in diameter, acicular calcium oxalate crystals, fragments of brown cork, lignified tracheids and wood-parenchyma; but not more than a very occasional vessel or strongly thickened sclerenchymatous cell. Slight odor; taste bitter. Ash not more than 5 per cent. Yields not less than 2 per cent. of alkaloids when tested by the following process." *Br.*

"**Assay.**—Introduce 10 Gm. of Ipecac, in No. 80 powder, into a 250 mil flask, add 100 mils of ether and proceed as directed under *Belladonnæ Radix,* page 222, fifth line of the Assay, beginning with the word "Stopper." Modify the process there given by using 50 mils of the ether solution, representing 5 Gm. of Ipecac, to complete the assay. Use ether instead of chloroform for the final shaking out of the alkaloid, and dissolve the alkaloid from the residue in 10 mils of tenth-normal sulphuric acid V.S.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 24 milligrammes of the ether-soluble alkaloids of Ipecac." *U. S.*

"Shake 7 grammes of the Root, in No. 60 powder, frequently during 5 minutes with 70 millilitres of a mixture of 1 volume of *chloroform* and 3 volumes of *ether;* add 5 millilitres of *solution of ammonia* and shake frequently during one hour; then add 5 millilitres of *water* or sufficient to make the powder agglomerate on violently shaking. Separate 50 millilitres of the clear liquid, and shake first with 10 millilitres of *N/10 solution of hydrochloric acid,* and then with three successive portions, each of 3 millilitres, of *water.* Mix the several aqueous solutions, make alkaline with *solution of ammonia,* and shake out first with 10 millilitres and then with three successive portions, each of 5 millilitres, of a mixture of 6 volumes of *ether*

and 1 volume of *chloroform*. Mix the several ethereal solutions, evaporate, dry the residue at 80° C. (176° F.) and weigh. It weighs not less than 0.100 gramme. Powdered Ipecacuanha Root, when used for official purposes other than the production of standardised preparations, must be adjusted, if necessary, by the addition of powdered Milk Sugar to contain in 100 grammes when tested by the foregoing process 2 grammes of the alkaloids of Ipecacuanha Root. *Limit of error* 0.1 gramme in excess or defect." *Br.*

Cartagena ipecac is usually to be distinguished from the Brazilian by its lighter color and the fact that many of its roots are scarcely at all annulated, and some are even smooth. On the other hand, in most specimens of Carthagena ipecac which we have examined, some of the roots could not be distinguished from those of the Brazilian variety. The cultivation of ipecac, which was introduced into India by the British Government, has especially succeeded in the neighborhood of Johore (Straits Settlement). On account of the great local demands in India, only a small amount of this ipecac comes into general commerce, and very little of it reaches the United States. *Johore* or *Indian ipecac* is especially characterized by the excellent appearance, regularity and large size of the roots, which are deeply annulated, somewhat light in color, and having to a marked degree the general physical and microscopical characteristics of the Brazilian root. Beilee asserts that the Indian ipecac is usually inferior to the Brazilian, yielding only 0.54 per cent. of emetine (*Bull. Soc. de Pharm. de Bordeaux*, xlvi, p. 171), but according to Ransom, Paul and Cownley, and to Umney and Swinton, it is very rich in alkaloids, and, like the Brazilian root, has for its dominant alkaloid, emetine. (See *P. J.*, vol. 63, 69, 70.) Many years ago there was imported from Carácas into the United States a large gray ipecac with badly marked rings. This variety disappeared for a time but is probably the *Colombian* or *Cartagena Ipecac* of modern commerce. It is quite common to find in commerce mixtures of Rio and Cartagena ipecac. These are usually distinguished from each other by the larger size of the starch grains and crystals which occur in the Carthagena variety. (See Schneider, *Jour. of Pharmacology* (N. Y. C. P.), 1897, p. 1; and Collin, *J. P. C.*, xx, p. 293.) Hartwich (*Ap. Ztg.*, xxvi, p. 57), however, points out that the size of the starch grains is not sufficient to differentiate these varieties and states that there is a greater difference in the cells of the woody portion of the root.

Ipecac of commerce is occasionally adulterated with the roots of other plants, the following having been recently reported: Mannich and Brandt (*J. P. C.*, xx, p. 276) have found pieces of *Heteropteris pauciflora*, which do not contain either starch or raphides. Farwell (*D. C.*, li, p. 459) obtained a so-called ipecac from South America which contained no alkaloids. Schneider reports (*Pacific Pharm.*, v, p. 177) the presence of *Asclepias* and a *Spurge* or *Euphorbia*. He also states that the drug is adulterated with foreign roots and with roots of related plants, excess of stems, clay, dirt, infusional earth and cereals. Kraemer (*Proc. A. Ph. A.*, 1900, p. 214) has published a note on a so-called ipecac which proved to be derived from *Polygala angulata* D.C. The best work on the differentiation of ipecac; cephaëline hydrobromide crystallizes that of Hartwich. (*A. Pharm.*, 1904, p. 677; 1905, p. 647.) Tunmann (*Gehe and Co., Handelsbericht*, 1912, p. 165) has submitted this drug to pyroanalysis and obtained characteristic sublimate crystals. For elaborately illustrated articles upon the microscopy of ipecac and its adulterations, see Henry G. Greenish, *P. J.*, 1895, 685, and Albert Schneider, *Am. Drug.*, 1897. According to Greenish, the distinctive characteristics of the powder of either Brazilian or Cartagena ipecac are: (a) the form and size of the starch grains; (b) the absence of vessels, presence of perforated trachoides; (c) the acicular raphides; to these may be added (d) the emetine reaction with chlorine. The stem may in either case be distinguished from the root (in powder) by the presence (a) of sclerenchymatous cells; (b) of lignified cells of the pith; (c) of spiral vessels.

According to the researches of A. R. L. Dohme (*A. J. P.*, 1895), the stems adhering to the ipecac roots contain from fifteen to twenty per cent. less of the alkaloids than do the roots themselves. Moreover, it appears to be established that the portions of the stem distinct from the root contain much less of the alkaloids than does the base of the stem, so that the Pharmacopœia very properly directs that not more than 7 cm. of the stems shall be allowed. The bark of ipecac root should make eighty per cent. of the whole. When the bark in either variety of ipecac is opaque, with a dull amylaceous aspect, the root is less active. As the woody part is nearly inert, and much more difficult of pulverization than the cortical it often happens that, when the root is powdered, the portion last remaining in the mortar possesses scarcely any emetic power, and care should be taken to provide against any defect from this cause. The German Pharmacopœia provides for the rejection of the last fourth of the powder.

The alkaloid emetine found in ipecac by Pelletier, in 1817, was shown by Paul and Cownley (*A. J. P.*, 1895, p. 256, and 1901, p. 87) to consist of three alkaloids, *emetine, cephaëline,* and *psychotrine*. J. U. Lloyd reports the presence of another alkaloid which he calls *hyptonine*. More recently, Hesse (*P. J.*, 1914, xciii, p. 425) has found two new bases, *ipecamine* and *hydroipecamine*. Willigk discovered *ipecacuanhic acid*, which was shown by Reich (*A. Pharm.* (2), cxiii, p. 208) to be a glucoside and to have the formula $C_{14}H_{18}O_7$. Finnemore and Braithwaite (*Trans. Br. Ph. Con.*, 1912, p. 496) confirmed the glucosidal nature of this body and suggested the name *ipecacuanhin*.

There has been considerable dispute as to the composition of the ipecac alkaloids, especially of emetine. The United States Pharmacopœia, following Kunz-Krause, gives $C_{30}H_{44}O_4N_2$. The latter considers the structural formula to be $C_{26}H_{27}(OCH_3)_4(OH)N_2$. Carr and Pyman (*Proc. Chem. Soc.*, 1913, xxix, 226), however, believe that the proper formula for emetine is $C_{29}H_{40}O_4N_2$, and Windaus and Herman (*Ap. Ztg.*, 1914, 443) give $C_{30}H_{42}O_4N_2$. Both Hesse, who accepts the formula for emetine of Kunz-Krause, and Carr and Pyman regard emetine as the oxy-methyl ether of cephaëline. Carr and Pyman give for the formula of cephaëline, $C_{28}H_{38}O_4N_2$, but Hesse gives the structural formula of cephaëline, $C_{25}H_{28}(OCH)_3(OH)N_2$, in harmony with his formula for emetine. According to Carr and Pyman, psychotrine has the formula $C_{28}H_{36}O_4N_2$, and yields, on reduction, cephaëline and isocephaëline. According to Paul and Cownley, the melting point of emetine is 60° C. (140° F.), of cephaëline 102° C. (215.6° F.), and of psychotrine 138° C. (260.4° F.). Psychotrine and its salts are rapidly decomposed on exposure to light, in this respect differing from emetine and cephaëline, neither of which are affected by light. It crystallizes from ether, in prisms of lemon-yellow color.

The medicinal virtues of ipecac reside chiefly, if not solely, in the alkaloids emetine and cephaëline. Different samples of ipecac root vary not only in the total percentage of alkaloidal contents, but also in the proportion of the alkaloids, and the question whether Rio and Cartagena ipecac ought to be considered as interchangeable remedies has become one of importance. Paul and Cownley (*A. J. P.*, 1901, lxxiii, 57), as the result of an exhaustive study, found that the two ipecacs do not differ materially in the total amount of alkaloid contained, but that whereas in the Brazilian root emetine is the dominant alkaloid, in the Colombian root cephaëline predominates, and that therefore the two roots cannot be considered as therapeutically identical. This work of Paul and Cownley has been confirmed by Carl Lowin (*A. I. P. T.*, 1902), so that it would appear to be settled that in general terms Rio ipecac contains 1.5 per cent. of emetine and 0.5 of cephaëline; Cartagena contains 0.9 of emetine and 1.2 of cephaëline. The practical accuracy of these researches, however, has been challenged by the large dealers in the products of ipecac. In 1903, as the result of twenty assays of different lots of each drug, Caeser and Loretz, of Halle, report the results given in the following table:

Formerly Brazilian ipecac commanded in the American market a higher price than did the Carthagena variety. At times the Carthagena ipecac has been from ten to fifteen cents a pound higher than the Brazilian, indicating that in some way it especially recommends itself to the manufacturing pharmacists.

W. G. Whiffen patented in Germany in 1898 a process for making emetine, basing it on the separation of emetime hydrobromide from extract of ipecac; cephaëline hydrobromide crystallizes with great difficulty, while emetine hydrobromide is easily crystallized and separated. (*C. D.*, 1898, 694.)

According to the researches of Tokuye Kimura (*A. J. P.*, 1903, 1), ipecacuanhic acid occurs as a brown, hygroscopic, amorphous mass, freely soluble in warm water and alcohol but very slightly soluble in cold water or ether, insoluble in chloroform, having the formula $C_{17}H_{26}O_{10}$ or a multiple of the same. As a glucoside it is allied to the saponin acids but has no hæmolytic action and does not form soapy solutions. Its most characteristic reaction is that its solution strikes with ferric chloride a green alizarin tint, which, by the addition of ammonia or saturated baryta water, changes to violet or blackish, with the final separation of a blackish-brown precipitate. On the addition to the discolored solution of diluted hydrochloric acid the green color returns. According to the experiments of Kimura, ipecacuanhic acid is readily absorbed but is possessed of feeble physiological activity and is not germicidal, so that the value of ipecac in dysentery can scarcely depend upon its presence.

Flückiger (*Ph. Ztg.*, 1886, p. 30) gave a process for assaying ipecac, which consists in exhausting 10 to 15 grammes of the drug in very fine powder with boiling chloroform to which a drop of solution of ammonia has been added; the extraction is continued until the chloroform passing through shows no sign of alkaloid when treated with acidulated water. Upon distilling off the chloroform, the emetine is left in a very pure condition, and may be dried at 100° C. (212° F.) and weighed, or perhaps more conveniently titrated with Mayer's reagent. He found the average quantity of emetine in ipecac root not to exceed 1 per cent. (*P. J.*, 1886, 643.) H. W. Jones approves of this method, and modifies it by treating the residue from the chloroformic solution with water and diluted sulphuric acid, filtering, and recovering the alkaloid by means of chloroform and ammonia. (*P. J.*, 1886, p. 277.) For other methods, see a paper by A. B. Lyons, *A. J. P.*, 1885, pp. 531,

	Total Alkaloids.	Emetine.	Cephaëline.	Ash.
Rio (Mato Grosso Root)	2.73	1.98	0.50	3.34
Rio (Bahia Root)	2.19	1.36	0.63	3.21
Indian from Johore	2.45	1.46	0.62	2.93
Cartagena	2.75	1.47	1.39	6.02

542; also Lyons' *Assay of Drugs,* 1899, 181, 187.

Uses.—Ipecac was employed as an emetic by the natives of Brazil when that country was first settled by the Portuguese, but, though described in the work of Piso, it was not known in Europe until 1672, and did not come into use until some years afterwards. John Helvetius, grandfather of the famous author of that name, having been associated with a merchant who had imported a large quantity of ipecac into Paris, employed it as a secret remedy, and with so much success in dysentery and other bowel affections that general attention was drawn to it, and the fortunate physician received from Louis XIV a large sum of money and public honors on the condition that he should make it public.

Ipecac is in large doses emetic, in smaller doses, diaphoretic and expectorant, and in still smaller, stimulant to the stomach, exciting appetite and facilitating digestion. In quantities not quite sufficient to cause vomiting, it produces nausea, and frequently acts on the bowels. As an emetic it is mild, but tolerably certain, and free from corrosive or narcotic properties. The emetic effect seems to be due partly to the local irritant effect of the drug upon the mucous membrane of the stomach, although the experiments of Hatcher show that there is some direct stimulant action upon the vomiting center in the medulla. Of the two alkaloids to which the drug owes its activity it would seem from the experiments of Wild (*L. L.,* 1895, ii, p. 1274) that cephaëline is much more active as an emetic than emetine, although the latter is capable, in sufficient dose, of causing vomiting. Because of the promptness with which the emesis occurs it is scarcely possible for enough of the active principles to be absorbed from the stomach to produce direct systemic effects. When injected subcutaneously or intravenously in large dose, however, the alkaloids act as depressants to the motor side of the spinal cord and probably also to the respiratory center. It would seem that they have some special predilection for the lungs for after toxic doses alternating areas of pallor and intense hyperemia have been found in the pulmonary tissue.

Originally introduced into Europe as a remedy for *dysentery,* ipecac for centuries was alternately lauded as a specific and condemned as useless in this disease. In 1911 Vedder (*Bull. Manila Med. Soc.,* March, 1911; also *J. A. M. A.,* 1914, lxii, p. 501) showed that an infusion of ipecac representing one part of the drug in ten thousand destroyed the viability of the *Entamœbæ,* and that the alkaloid emetine in a one to one-hundred thousand solution had the same effect. He also showed that the drug was possessed of no bactericidal virtues. Since this research reasons for the diversions of opinion as to the usefulness of ipecac are apparent. There are two types of dysentery, one due to a specific amœba and the other caused by a bacillus. In the latter form of the disease the drug is useless but is probably the most efficacious remedy we possess in the amœbic type of dysentery. The great difficulty in its employment has always been to obviate the emetic effect which sometimes made it almost impossible to get enough of the drug into the intestinal tract to have an effect. In 1912 Rodgers (*B. M. J.,* 1912, i, p. 1424, and ii, p. 405) introduced the hypodermic administration of the alkaloid emetine which has since then become the standard treatment of *amœbic dysentery.* For this purpose from one to three grains of the emetine hydrochloride (0.065–0.2 Gm.) should be injected daily; preferably divided into two or three doses. The treatment is also of value in the various sequelæ of dysentery, such as *abscess of the liver,* although it does not always produce complete cures. In 1914 Smith and Barrett (*J. A. M. A.,* 1914, lxiii, p. 1746) brought forward evidence that *pyorrhea alveolaris,* or *Rigg's disease,* is due to a specific amœba, and suggested the use of emetine in its treatment. Their discovery has been confirmed by Bass and Johns (*J. A. M. A.,* 1915, lxiv, p. 553) and others. Smith and Barrett recommended the direct application of a 1 per cent. solution directly to the pus pockets but Bass and Johns prefer the hypodermic administration.

As an emetic ipecac is rarely used merely for the purpose of evacuating the stomach, but when an action upon the portal circulation is desirable, as in the so-called *biliousness* or *acute alcoholism,* it is often of service. Many clinicians believe that it has a direct influence upon hepatic secretion, but it is more probable that its effects upon the liver are due simply to its emetic action. By virtue of their nauseating effect small doses of ipecac tend to increase various secretions of the body, thus it is widely used as a diaphoretic, especially in combination with opium (see *Pulvis Ipecacuanhæ et Opii*) in the early stages of *acute coryza* and other mild infections. In the same way it acts as an expectorant, and in the early stages of *acute bronchitis* it is one of the most valuable remedies we possess. Many years ago Trousseau affirmed that ipecac possessed valuable hemostatic powers, especially useful in *hemoptysis,* but this use of it failed to receive general recognition. The treatment has been revived by Flandin (*Press. Med.,* 1913) and other French clinicians.

As an emetic ipecac may be given in substance in the dose of twenty to thirty grains (1.3–2.0 Gm.), repeated in fifteen to twenty minutes if necessary. As an expectorant the syrup is generally preferred. If ipecac itself is used in dysentery it should be given in doses of five grains every hour combined with opium to prevent vomiting. To obviate the nauseating effect of emetine when given by the mouth, Bass and Johns have used a combination with Lloyd's reagent.

Under the name of *riopan,* a preparation asserted to contain 50 per cent. of combined cephaëline and emetine has been introduced. This is marketed in the form of tablets each containing one-thirtieth of a grain (0.002 Gm.), which is

stated to be equivalent to about a grain and a half of ipecac (0.096 Gm.).

Dose, emetic, twenty to thirty grains (1.3–2.0 Gm.); nauseating, two grains (0.13 Gm.); diaphoretic, one grain (0.065 Gm.); stomachic, one-fourth to one-half grain (0.016–0.032 Gm.).

Off. Prep.—Fluidextractum Ipecacuanhæ, *U. S.* (*Br.*); Pilula Ipecacuanhæ cum Scilla, *Br.;* Pulvis Ipecacuanhæ et Opii, *U. S.* (*Br.*); Syrupus Ipecacuanhæ, *U. S.;* Trochiscus Ipecacuanhæ, *Br.;* Trochiscus Morphinæ et Ipecacuanhæ, *Br.;* Vinum Ipecacuanhæ (from Fluidextract), *Br., N. F.;* Mistura Rhei Composita (from Fluidextract), *N. F.;* Pilulæ ad Prandium (Chapman's), *N. F.;* Pilulæ Antidyspepticæ, *N. F.;* Pilulæ Laxativæ Compositæ, *N. F.;* Pilulæ Laxativæ Post Partum, *N. F.;* Syrupus Asari Compositus (from Fluidextract), *N. F.;* Syrupus Cimicifugæ Compositus (from Fluidextract), *N. F.;* Syrupus Ipecacuanhæ et Opii (from Tincture), *N. F.;* Tinctura Ipecacuanhæ et Opii (from Fluidextract), *N. F.*

IPOMŒÆ RADIX. Br.

ORIZABA JALAP ROOT [Mexican Scammony Root]

(ī-pō-mœ'æ rā'dix)

"Orizaba Jalap Root is the dried root of Ipomœa orizabensis, *Ledanois.*" *Br.*

Orizaba Root, Male Jalap, Light, Woody, or Fusiform Jalap; Jalap stalks; Purgo Macho (*Mexican*).

The genus *Ipomœa* (Fam. *Convolvulaceæ*) comprises about 300 species of herbs and shrubs, some being erect, others prostrate, but very many climbing. They are remarkable for their showy flowers, as in *I. purpurea,* the common morning glory of the garden. Many of the species produce large tuberous roots which contain a drastic purgative resin. *Orizaba* (also known as *light* or *fusiform*) *Jalap Root* has been recently introduced into the British Pharmacopœia as a source of scammony resin. The plant yielding it (*Ipomœa orizabensis*) is indigenous to Mexico and produces a large, fusiform, more or less branching root attaining a length of 5 dm., yellow on its outer surface, milky-white within. The stem is cylindrical, slightly villous and climbing. The leaves are large, petiolate, cordate, acuminate and villous on the veins. The corolla is campanulate and reddish-purple. The capsule is 2-locular and one seeded.

The drug occurs in transverse slices of the root, or in pieces of irregular shape made by vertical section of these slices. The horizontal cut surface is dark from exposure, unequal from the greater shrinking in desiccation of some parts than others, and presents the extremities of numerous fibers, which are often concentrically arranged. Internally the color is grayish, and the texture, though much less compact than that of jalap, is sometimes almost ligneous.

It is officially described as follows: "In irregular, tough, or fibrous pieces of varying size and shape, but often in portions, three to five centimetres wide and two to four centimetres thick, of transverse slices of large roots. Externally greyish-black and wrinkled, internally greyish or brownish. From the transverse surface coarse fibres protrude in irregular concentric circles. Slight odor; taste faintly acrid. Yields to *alcohol* (90 per cent.) a resin which has the properties enumerated under 'Scammoniæ Resina.'" *Br.*

See also under *Jalap* for further facts concerning these substances.

Ipomœa root has purgative properties similar to those of true jalap, but is less powerful. It is stated (*J. P. C.,* xxiv, 166) that thirty to sixty grains (2–3.9 Gm.) are required to act effectively. It is, however, rarely employed and is official only as a source of scammony resin.

ISPAGHULA. Br.

ISPAGHULA

(is-pag'hū-la)

"Ispaghula consists of the dried seeds of Plantago ovata, *Forsk.*" *Br.*

Ispaghue, Spogel Seeds.

Plantago ovata (*P. Ispaghula* Roxb.) is a herbaceous plant (Fam. *Plantaginaceæ*) growing in India and Persia and extending westward to Spain and the Canary Islands. It is either erect or decumbent and varies in height from 2.5 cm. to 1 dm. The leaves are ovate and either glabrous or shaggy hairy. The flower spikes are either cylindrical or reduced to a globular head. The seeds closely resemble those of other species of *Plantago.*

They are described as follows: "Seeds boat-shaped, somewhat acute at one end, from two to three millimetres long and from one to one and a half millimetres wide; pale greyish-brown, with a darker elongated spot on the convex side; on the concave side the hilum covered with the remains of a thin white membrane. In *water* the testa swells, producing a viscous mucilage. No odor or taste." *Br.*

The seeds of the *Plantago amplexicaulis* Cav. are also sold in the Indian bazaars as Ispaghula. They resemble the official seeds, but are of a darker color.

They yield to water a viscid mucilage. They are used in India as a demulcent in *dysentery* and various intestinal irritations, and are also slightly laxative. On roasting they are said to become astringent, and as such are used for *diarrheas,* especially of children. By European practitioners they have been chiefly employed in *chronic diarrhea.* In India they are also used for their demulcent effect in catarrhal conditions, especially of the genito-urinary tract.

Dose, from one to two and a half drachms (3.9–9.8 Gm.).

Off. Prep.—Decoctum Ispaghulæ, *Br.*

JALAPA. U. S., Br.

JALAP Jalap.

(jạ-lā'pạ)

"The dried tuberous root of *Exogonium Purga* (Wenderoth) Bentham (Fam. *Convolvulaceæ*), yielding not less than 7 per cent. of the total resins of Jalap." *U. S.* "Jalap consists of the dried tubercules of Ipomœa Purga, *Hayne*." *Br.*

Radix Jalapæ, Radix Ipomœarum; Jalap Tubéreux ou officinal, *Fr. Cod.*; Tubera Jalapæ, *P. G.*; Jalape, Jalapenknollen, Jalapenwurzel, *G.*; Gialappa, Sciarappa, *It.*; Jalapa (Raiz de), *Sp.*

The precise botanical origin of jalap remained long unknown. It was at first ascribed by Linnæus to a *Mirabilis*, and afterwards to a new species of *Convolvulus*, to which he gave the name of *C. Jalapa*. The correctness of the latter reference was generally admitted, and, as the *Ipomœa macrorrhiza* of Michaux, growing in Florida and Georgia, was believed to be identical with the *C. Jalapa* of Linnæus, it was thought that this valuable drug, which had been obtained exclusively from Mexico, might be collected within the limits of the United States; but the error of this opinion was soon demonstrated. John R. Coxe, of Philadelphia, received living roots of jalap from Mexico in 1827, and succeeded in producing a perfect flowering plant, of which a description was published by Nuttall (*Am. J. M. S.*, Jan., 1830). The same plant has since been cultivated in various parts of Europe, and has been introduced into the Neilgherry Hills of India, where it grows vigorously. J. H. Balfour (*Curtis's Bot. Mag.*, Feb., 1847) maintains that the plant belongs to the genus Exogonium of Choisy, as defined in De Candolle's *Prodromus*, being distinguished from Ipomœa by its exserted stamens. Bentham and Hooker, however, do not acknowledge the validity of the various genera into which Ipomœa has been broken up by Choisy (*Genera Plantarum*, ii). Engler and Prantl have restored the genus *Exogonium* [*E. Purga* (Wender.) Benth.] for the plant yielding the root called jalap.

The root of *Exogonium Purga* (*Ipomœa Purga* Hayne) is a roundish, somewhat pear-shaped tuber, externally blackish, internally white, with long fibers proceeding from its lower part, as well as from the upper rootstalks. A tuber, produced by Coxe, was, in its third year, between two and three inches in diameter. The stem is round, smooth, much disposed to twist, and rises to a considerable height upon neighboring objects, about which it twines. The leaves are petiolate, heart-shaped, entire, smooth, pointed, deeply sinuated at the base and prominently veined on their under surface. The lower leaves are nearly hastate or with diverging angular points. The flowers, which are large and of a lilac-purple color, stand upon peduncles about as long as the petioles. Each peduncle supports two or, more rarely, three flowers. The calyx is without bracts, five-leaved, obtuse, with two of the divisions external. The corolla is funnel-form. The stamens are five in number, with oblong, white, somewhat exserted anthers. The stigma is simple and capitate.

The jalap plant is a native of Mexico, where it is dug during the whole year, and usually dried over the hearths of the Indian huts. It derives its name from the city of Jalapa, in the state of Vera Cruz, in the neighborhood of which it grows, at the height of about 6000 feet above the ocean. The drug is brought from the port of Vera Cruz in bags containing usually between 100 and 200 pounds. The amount of jalap annually invoiced through the Vera Cruz consulate to the United States is about 200,000 pounds. The jalap plant is now successfully cultivated in the government cinchona plantations in India. Analyses of the Indian tubers show that when grown on fresh soil they contain from 16 to 17 per cent. of resin, and that by manuring the percentage is notably increased, even to 22 per cent. It has also been cultivated in Jamaica, South America and Ceylon. The jalap grows freely in the south of England, but the season is too short for the production of seed by it, although the root has yielded 11.97 per cent. of resin. (*P. J.*, Feb., 1869.) For an account of the cultivation of jalap in Madras, see *Am. Drug.*, 1896, 127.

Properties.—Jalap is officially described as follows: "Fusiform, irregularly ovoid or pyriform, upper end more or less rounded, lower end slightly tapering, the large roots often incised or cut into pieces; from 4 to 15 cm. in length and from 12 to 60 mm. in diameter; externally dark brown, longitudinally wrinkled or furrowed and with numerous lenticels; hard, compact, not fibrous; when broken, internally dark brown, mealy or waxy, bark from 1 to 2 mm. in thickness outer bundles separated from the outer cortical layer by a distinct, brown cambium zone; odor slight but distinctive, smoky; taste somewhat sweet and acrid. The powder is light brown; starch grains numerous, single or 2- to 3-compound, and more or less swollen, ellipsoidal or ovoid with concentric or excentral lamellæ and radiating clefts or fissures, from 0.003 to 0.035 mm. in diameter; calcium oxalate in rosette aggregates from 0.01 to 0.035 mm. in diameter; tracheæ short, wide, with simple or bordered pores; lactiferous vessels with yellowish-brown, resinous masses. Jalap yields not more than 6.5 per cent. of ash." *U. S.*

"Tubercules dark brown, irregularly oblong, napiform or fusiform, three to eight centimetres or more long, the larger being often incised. Hard, compact and heavy; externally wrinkled, and marked with small transverse scars; internally yellowish-grey to dingy brown. In transverse section irregular, dark, concentric lines; examined microscopically numerous compound starch grains, many of which are gelatinised, cluster-crystals of calcium oxalate, and cells containing a resinous emulsion stained yellow by *N/10 solution of iodine;* in the wood, pitted

vessels and tracheids. Characteristic odor; taste at first sweet but afterwards acrid and disagreeable. Ash not more than 6.5 per cent. Yields not less than 9 or more than 11 per cent. of resin having the properties of Jalap Resin, when treated by the process described under 'Jalapæ Resina.'" *Br.*

Jalap is usually kept by pharmacists in the state of powder, which is of a yellowish-gray color, and when inhaled irritates the nostrils and throat, and provokes sneezing and coughing. Jalap yields its active properties partly to water, and completely to diluted alcohol.

"**Assay.**—Pack 10 Gm. of Jalap, in No. 60 powder, in a cylindrical percolator and extract it with alcohol until the percolate measures 100 mils. Transfer 20 mils of the percolate to a separator, add 20 mils of chloroform, mix the liquids, then add 20 mils of distilled water and shake the mixture thoroughly. When the liquids have completely separated, draw off the chloroform into a tared beaker, wash the contents of the separator by rotating with 5 mils of chloroform and draw it off into the beaker. Evaporate the chloroform solution on a water bath, add about 2 mils of alcohol, again evaporate, and then dry the residue to constant weight at 100° C. (212° F.). The weight will be the amount of total resins from 2 Gm. of Jalap." *U. S.*

Buchner and Herberger supposed that they had discovered a basic substance, which they called *jalapin.* G. A. Kayser found that the resin of jalap previously discovered by Cadet de Gassicourt consists of two portions, one of which, amounting to seven parts out of ten, is hard and insoluble in ether, the other is soft and soluble in that menstruum. The hard resin he named *rhodeoretin,* and found to be identical with the jalapin of Buchner and Herberger. By reaction with the alkalies it is converted into an acid, called *rhodeoretinic acid.* Rhodeoretin is slightly soluble in water, freely so in alcohol, and insoluble in ether, chloroform, or benzene, and the alcoholic solution is precipitated both by ether and water. It is dissolved by solutions of the alkalies, more quickly if heated, and is not precipitated by acids, having become soluble by conversion into the acid above referred to. It purges violently in the dose of three or four grains, and is supposed to be the active principle of jalap. Mayer confirmed and extended the observations of Kayser. He gave the name of *convolvulin* to Kayser's rhodeoretin, and stated its formula as $C_{31}H_{50}O_{16}$. This substance is colorless when pure, dissolving easily in ammonia water, and is not reprecipitated by acids, because of its conversion into *convolvulinic acid,* which is a hydroxide of the glucoside convolvulin. This, on being treated with nitric acid, yields *sebacic acid.* Convolvulin possesses in a high degree the purgative properties of jalap. A. Kromer (*Ph. Z. R.,* 1894, Nos. 1–7) also made a study of convolvulin. He finds it to be lævogyrate, and gives it the formula $C_{31}H_{108}O_{27}$, which was later changed (*Die Glykoside,* Van Rijn, 1900, p. 391) and is now given by Hoehnel as $C_{54}H_{96}O_{27}$, which is deduced from its analysis and decomposition products; alkalies decompose it into one molecule of volatile *methylethyl-acetic acid,* $C_5H_{10}O_2$, one molecule of *purginic acid,* $C_{25}H_{46}O_{12}$, and one molecule of *convolvulinic acid,* $C_{45}H_{80}O_{28}$. (See also *A. Pharm.,* 1901, 373.) This latter is amorphous, yielding a white hygroscopic powder soluble in water and alcohol, insoluble in ether; strong sulphuric acid colors it red or brown-red; by the action of acids one molecule of convolvulinic acid yields five molecules of a glucose and one molecule of *convolvulinolic acid,* $C_{15}H_{30}O_3$, which is insoluble in water, melts at 51.5° C. (124.7° F.), is not colored by sulphuric acid, and is isomeric with jalapinolic acid and scammonolic acid, both of which melt at from 63° to 64° C. (145.4°–147.2° F.). Mayer obtained from *Ipomœa orizabensis* a resin which he called *jalapin,* which was afterwards shown by Keller to be identical with the resin of scammony. Mayer's jalapin differs from convolvulin in being soluble in ether. The formula of jalapin, according to Samuelson, is $C_{34}H_{56}$

1. *Action of solvents.*

Solvent.	Jalapin.	Convolvulin.
Chloroform.	Readily soluble.	Slightly soluble.
Ether.	Very soluble.	Insoluble.
Petrol. naphtha.	Slightly soluble.	Insoluble.
Oil of turpentine.	Slightly soluble.	Insoluble.
Benzene.	Slightly soluble.	Insoluble.
Carbon disulph.	Easily soluble.	Insoluble.
Water.	Slightly soluble.	Slightly soluble.
Hydrochloric acid.	Slightly soluble.	Readily soluble.
Sulphuric acid.	Very soluble, with production of maroon color changing to black.	Readily soluble, with production of bright red coloration.
Potassium hydroxide.	Easily soluble.	Easily soluble, with production of odor of whisky when heated.
Ammonia water.	Readily soluble, more so than convolvulin.	Slightly soluble.

2. *Reactions with Oxidizing Agents on convolvulin and jalapin dissolved in concentrated sulphuric acid.*

Agent.	Jalapin.	Convolvulin.
Potassium dichromate.	Produces odor of rancid butter and reddish-brown color.	Produces odor of rancid butter and olive-green color.
Potassium permanganate.	Same reactions.	Same reactions.
Potassium nitrate.	Same reactions, but not so strong.	Same reactions.
Potassium chlorate.	Same reactions, but not so strong.	Same reactions.
Manganese dioxide.	Same odor, and color dark green.	Same odor, and color rose-pink.

O_{16}. Poleck (*A. J. P.*, 1892, p. 465) continued the investigation of the jalapin from *I. orizabensis*, and confirmed the identity of it with scammonin, giving it the formula $C_{34}H_{56}O_{16}$. He suggested that the name of jalapin, which is misleading, should be replaced by *orizabin*. A. F. Stevenson (*N. R.*, 1879, 359) has studied the two resins found in jalap, and furnishes a tabular statement of the differences between the soft resin jalapin and the hard resin convolvulin, which is given in the following table. For the method of obtaining the resin of jalap pure, see *Resina Jalapæ*.

Power and Rogerson report a chemical examination of *Ipomœa purpurea* Roth, known as the common *morning glory*. They conclude that this plant, like many other species of the same genus, contains resins which possess purgative properties, and is thus capable of being used medicinally. (*A. J. P.*, 1908, p. 255.)

Jalap is apt to be attacked by worms, which, however, are said to devour the amylaceous or softer parts, and to leave the resin, so that the worm eaten drug is more powerfully purgative than that which is sound. Thus, out of 397 parts of the former, Henry obtained 72 parts of resin, while from an equal quantity of the latter he procured only 48 parts. Hence, worm eaten jalap should be employed for obtaining the resin, but should not be pulverized, as it would afford a powder of more than the proper strength. The drug is also liable to various adulterations, or fraudulent substitutions, which, however, can usually be detected without difficulty by means of the microscope.

According to Herlant, even in powder it is easy to detect the presence of the root of *Mirabilis Jalapa*, which is sometimes used as an adulterant to jalap, by the presence of raphides of calcium oxalate.

Tampico Jalap (*Purga de Sierra Gorda*, Mexican).—This drug closely resembles in appearance, odor, and taste the true jalap, but the tubers are somewhat smaller, more elongated and shrivelled. According to Ambrose Andouard, it is the *jalap digité majeur* of Guibourt. Through the efforts of Daniel Hanbury, of London, aided by two Prussian officials in Mexico, Hugo Finck, vice-consul at Cordova, and E. Bonecke, consul-general at Mexico, the origin of the drug was traced to the state of Guanajuato, where it grows along the Sierra Gorda, near San Luis de la Paz. In this place it is purchased from the Indians, and conveyed by mules to Tampico, where it enters into commerce. Through the agency of the same gentlemen, Hanbury, after some failures, succeeded in obtaining a living tuber, from which he raised a flourishing plant that proved to be an undescribed species of the genus *Ipomœa*, differing from *I. Purga* by its bell-shaped corolla and pendulous flower-buds. To it Hanbury gave the name *I. simulans*. (*A. J. P.*, July, 1870.) H. Spirgatis, of Königsberg, obtained a resin by preparing a tincture of the Tampico jalap, evaporating, washing, boiling the residue in water, redissolving in alcohol, and decolorizing by charcoal. He gave it the name of *tampicin*. Its physical properties are similar to those of the jalap resin. It is brittle, tasteless, inodorous, insoluble in water, soluble in ether and alcohol, and in solution has a feeble acid reaction. By strong alkalies it is changed into a soluble acid which Spirgatis calls *tampicic acid*. By the action of diluted sulphuric, nitric, or hydrochloric acid, it is converted, slowly if cold, but rapidly with heat, into a peculiar acid called *tampicolic*, with sugar. For the mode of preparing these acids, and their properties, the reader is referred to an article in *N. R.*, July, 1871, p. 50. The melting point of tampicin is 130° C. (266° F.); its formula is $C_{34}H_{54}O_{14}$. The percentage of it yielded by the drug varies from a minimum of 10 per cent. (Hanbury) to a maximum of 15 per cent. (Umney). Andouard states that it is purgative.

The average percentage of resin in Jalap has of late years distinctly lessened; indeed this fact has received official recognition. The U. S. P., 1890, required 12 per cent., and the French Codex, 1884, 16 to 18 per cent. Much of the commercial jalap is far below the lowered official standard, and this appears to be due, not, as believed by Flückiger, to the extraction of the resin from the roots in Mexico, but to the fact that the wild tubers are collected indiscriminately from November to March; the cultivators of India are very careless in their methods. The lowness of the U. S. P. standard (7 per cent.) is to be regretted, especially as the Br. Ph. requires 11 per cent., but it is probably necessary, practically, to meet the commercial conditions. The German Pharmacopœia of 1900, however, requires 9 per cent. From a compilation by M. I. Wilbert (*J. A. Ph. A.*, 1914, 1286) the range of 173 reported analyses of jalap was from 3.67 per cent. to 21.76 per cent. (For various analyses of commercial Jalap, see *U. S. D.*, 18th ed., also *J. P.*, lxxii, p. 152.)

A comparison of various methods of assay was made by Dr. P. Seidler (*Ph. Ztg.*, 1912, No. 2, 15), who recommends the process of the P. G.V., which he says can be still further improved.

The question as to possible substitutes for the official species is also growing in importance. Flückiger pointed out that the seeds of the *Ipomœa hederacea* (see *Kaladana*) yield 8 per cent. of resin identical with that obtained from *Ipomœa Purga*, and the British Pharmacopœia now recognizes *Kaladana* and its resin. Shimoyama, of Tokio, has shown that jalap resin can be obtained from the *Ipomœa triloba* (*Pharbitis triloba*) of Japan. M. K. Hyrano confirms this, and states that the seeds of the plant have long been used in Japan, under the name of "*kengashi*." (For details and method of extracting the resin, see *P. J.*, Oct., 1888.)

Jalap should be rejected when it is light, of a whitish color internally, of a dull fracture, spongy, or friable. Powders of calomel and jalap, taken on long voyages to southern climates, are said, when brought back, to have be-

come consolidated, and so far chemically altered as plainly to exhibit globules of mercury. This change is ascribed by Schacht and Wackenroder to a fungous growth. (*A. Pharm.*, xxxix, 239.)

Uses.—Jalap is an active cathartic, operating briskly and sometimes painfully upon the bowels, and producing copious watery stools. The aqueous extract purges moderately, without much griping, and is said to increase the flow of urine. The portion not taken up by water gripes severely. The aqueous extract obtained from jalap, previously exhausted by rectified spirit, is said to have no cathartic effect. Jalap was introduced into Europe in the latter part of the sixteenth or the beginning of the seventeenth century, and at one time ranked among the purgative medicines most extensively employed. It is applicable to most cases in which an active cathartic is required, and from its hydragogue powers is especially adapted to the treatment of *dropsy*. It is generally given in connection with other medicines, which assist or qualify its operation. In dropsical complaints it is usually combined with potassium bitartrate.

The combination of jalap with calomel has long been popular, in the United States, in *bilious fever* and other complaints attended with *congestion of the liver* or portal circle. In overdoses jalap may produce dangerous hypercatharsis. It is said to purge when applied to a wound. Jalapin when taken internally is probably absorbed, but as yet its presence has never been detected in the urine, and it remains uncertain whether it is eliminated or destroyed. Müller (*In. Dis.*, Dorpat, 1885) found traces of it in the blood, and even in the heart, lungs, and spleen of cats poisoned with it.

The *dose* of jalap, in powder, is from ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Pulvis Jalapæ Compositus, *U. S., Br.;* Pulvis Scammonii Compositus, *Br.;* Resina Jalapæ, *U. S.* (*Br.*); Tinctura Jalapæ, *Br., N. F.;* Tinctura Jalapæ Composita, *Br., N. F.;* Extractum Jalapæ, *N. F.;* Fluidextractum Jalapæ, *N. F.;* Pilulæ ad Prandium (Cole's), *N. F.;* Pilulæ Catharticæ Vegetabiles (from Resin), *N. F.;* Pulvis Hydrargyri Chloridi Mitis et Jalapæ, *N. F.;* Syrupus Sennæ Aromaticus, *N. F.*

KALADANA. Br.

KALADANA [Semen Pharbitidis, Pharbitis Seeds]

(kă-lă-dă'nă)

"Kaladana consists of the dried seeds of Ipomœa hederacea, *Jacq.*" *Br.*

Closely allied to *Ipomœa hederacea* is *I. muricata*, the seeds of which are largely imported into Bombay, from Persia, under the name of *tukm-i-nil*. The juice of this plant is employed to destroy bedbugs, and the seeds are said to be identical in their medicinal properties with those of the official plant.

Ipomœa hederacea Jaeq. (*I. cærulea* Kon.; *Pharbites Nil*, Choissy) is a twining annual plant belonging to the *Convolvulaceæ*. It has large blue flowers whence the specific name *Nil* which signifies in Hindustani *blue*. The leaves are three-lobed and the plant, while common throughout India, is found throughout the tropical regions of both hemispheres. Flückiger found it to contain 8.2 per cent. of resin which corresponded in its various properties to the resin of jalap.

Kaladana seeds are in the form of the segment of a sphere, black, somewhat hairy, weighing from one-half drachm to nearly one drachm.

They are described by the British Pharm., 1914, as follows: "Seeds in the form of a segment of a sphere; usually about five millimetres long, but sometimes much smaller; nearly black. In transverse section, minute dark resin-cells in the plaited cotyledons. Slight odor; taste acrid." *Br.*

From them is prepared *pharbitisin, kaladana resin* (*Kaladanæ Resina,* Br.), by digesting the seed with alcohol until exhaustion, and precipitating with distilled water. (For details, see *Kaladanæ Resina.*)

Uses.—Kaladana seeds were used by the Arabian physicians, under the name of *Habbunnil*, and have been recommended as a safe and active cathartic by various English physicians resident in India. Their action is probably similar to that of jalap.

Dose, thirty to forty-five grains (2–3 Gm.).

Off. Prep.—Kaladanæ Resina, *Br.;* Pulvis Kaladanæ Compositus, *Br.;* Tinctura Kaladanæ, *Br.*

KALADANÆ RESINA. Br.

KALADANA RESIN [Pharbitisin]

(kă-lă-dă'nă rę-sī'nă)

"Kaladana Resin is a mixture of resins obtained from Kaladana." *Br.*

The resin is prepared from Kaladana by a process similar to that employed in isolating the resin from jalap. It is as follows: "Exhaust coarsely powdered Kaladana with Alcohol (90 per cent.). Recover most of the alcohol by distillation; pour the concentrated solution thus obtained into eight times its volume of Distilled Water; allow the resin that separates to subside, wash with Distilled Water, and dry at a gentle heat." *Br.*

It is officially described as "in brownish, opaque fragments, translucent at the edges; brittle, breaking with a resinous fracture; readily reduced to a grey powder. Somewhat disagreeable odor, especially when warmed; taste sweetish, acrid. Readily soluble in *alcohol* (90 per cent.); almost insoluble in *benzene, ether, chloroform,* or *carbon disulphide*. When 1 gramme of the powdered Resin is triturated with 20 millilitres of *water* and filtered, the filtrate is almost colorless. A solution of 0.1 gramme in 10 millilitres of *solution of sodium hydroxide,* boiled for a few moments and cooled, when acidified with *hydrochloric acid,* may become opalescent but not immediately turbid (absence of certain other resins)." *Br.*

This resin appears to be identical with con-

volvulin or at least very closely related to it chemically.

Dose, two to eight grains (0.12–0.5 Gm.).

KAOLINUM. Br.

KAOLIN

(kā-o-lī'nŭm)

"Kaolin is a native aluminium silicate, powdered, and freed from gritty particles by elutriation." *Br.* "A native hydrated aluminum silicate, powdered and freed from gritty particles by elutriation." *N. F.*

Terra porcellanea; Porcelain Clay, Bolus Alba; Terre à porcelaine, *Fr.*; Porcellanerde, Porcellanthon, *G.*

This substance was introduced into the U. S. P. VIII for the purpose of forming the basis of the preparation *Cataplasma Kaolini* which was dropped from the U. S. P. IX, but introduced in the N. F. IV.

Kaolin, $Al_2(SiO_3)_3 + Al_2O(OH)_4$, occurs in abundant deposits as a decomposition product of felspar; the latter is a double silicate of aluminium and alkali, and in its weathering, the alkali is gradually eliminated. A pure kaolin contains approximately 47 per cent. of silica, 40 per cent. of alumina, and 13 per cent. of water.

Pure kaolin is almost infusible, but the presence of impurities, notably undecomposed felspar, increases its fusibility greatly. On the other hand, fire clays which are infusible are kaolins containing a considerable amount of free silica.

Large deposits of kaolin have been recently opened in Florida. It is now used extensively for clarifying oils, such as lard and cotton seed oils and mineral lubricating oils.

The British Pharmacopœia describes it as "a soft whitish powder, insoluble in *water,* or in diluted acids. When the product of its fusion with alkalies is digested with *water,* the filtered solution acidified with *hydrochloric acid,* evaporated to dryness, and the residue digested with *diluted hydrochloric acid,* a deposit of silica is obtained, and the supernatant acid solution yields the *reactions* characteristic of aluminium." *Br.*

It is described in the N. F. IV as "a soft, white or yellowish-white powder, or in lumps, insoluble in water, and in cold dilute acids and solutions of the alkali hydroxides. It has an earthy or clay-like taste. When moistened with water, Kaolin assumes a darker color and develops a marked clay-like odor. Mix 1 Gm. of Kaolin with 10 mils of distilled water and 5 mils of sulphuric acid in a porcelain dish; no effervescence occurs. Evaporate the mixture until the excess of water is removed, and further heat the residue until dense white fumes of sulphuric anhydride appear, then add 20 mils of distilled water, boil for a few minutes and filter; there remains on the filter a gray residue of impure silica. To one-half of the filtrate just obtained add ammonia water; a gelatinous precipitate of aluminum hydroxide is obtained which is insoluble in an excess of the reagent. To the remaining half of the filtrate add sodium hydroxide T.S.; a gelatinous precipitate is produced which is completely or almost completely soluble in an excess of the reagent. Rub 2 Gm. of Kaolin in a mortar with 10 mils of distilled water; the mixture does not acquire more than a slight reddish tint on the addition of 0.5 Gm. of sodium salicylate (*iron*). Ignite Kaolin at a red heat; not less than 85 per cent. of a non-volatile residue remains." *N. F.*

It should not be confused with other silicious earths, such as Kieselguhr, which is now official (see *Terra Silicea Purificata*). It should never be used as a filtering medium on account of its property of removing active constituents from solution by its adsorptive properties. (See Scoville, *J. A. Ph. A.*, 1916, v, 506.)

Thomas J. Keenan, in an interesting article in the *Am. Drug.,* 1914, p. 55, gives a history of kaolin and its uses and points out the uncertainty of the product, due to the loose application of the name and proposes that the name be restricted to a compound having the composition $H_2Al_2Si_2O_8 + H_2O$.

Uses.—Various forms of clay have been used in medicine from time immemorial either as external or internal remedies. The value of these appears to reside in their absorbing properties, although there are some who attribute to them direct antiseptic action. The variety commonly known as *Fuller's earth* has a much higher absorbing power than kaolin. Because of its property of absorbing large amounts of liquid, Fuller's earth is used for many pharmaceutical purposes, especially in the preparation of pills. Not only, however, will it mechanically hold considerable liquid, but further has the property of separating many dissolved substances from solutions. To what this adsorbing power—as it is denominated—is owing is at present somewhat obscure, although it appears to be in part dependent upon the colloidal nature of the earth. It will decolorize fluids by adsorption of the coloring matter, will remove many alkaloids and apparently even certain bacterial toxines. Fantus (*J. A. M. A.*, 1915, lxiv, p. 1838) has shown that there is considerable difference in the adsorbing power of various substances sold under the name of Fuller's earth.

Although kaolin has been asserted to possess antiseptic properties there is no convincing proof of this assertion and its almost complete insolubility renders it highly improbable. It is, however, of service in various local infections, but its value in these conditions is generally explicable on mechanical grounds. It has been used with apparently good results in *suppurating wounds, tuberculous ulcers, weeping eczema, ozena, leucorrhea,* and similar conditions where its absorbent powers make it valuable. The claim is made that in many of these conditions because of its very fine pulverization it penetrates into the infected area and carries with it various antiseptics which may have been added. It has been used internally in *Asiatic cholera, gastro-enteritis,* and *dysentery.*

Its effects in the latter conditions are probably those of a protective to the mucous membrane. Its virtues in these conditions appear to be due in part to the adsorption of the irritant secretions, and in part to its protective influence upon the mucous membrane. According to Hess (*J. A. M. A.*, 1916, lxvi, p. 106), it surpasses either bismuth or chalk in lessening diarrhea. Probably by the formation of colloidal compounds it delays the absorption of toxic alkaloids from the alimentary tract, and Fantus has shown that it is an effective chemical antidote in the treatment of *strychnine poisoning*. While the absorption of some alkaloids is delayed more than others, it probably has a wide field of usefulness in poisoning. Kaolin is also widely used in the form of the cataplasm (see *Cataplasma Kaolini*) as a carrier of heat and moisture in various local inflammations instead of poultices. It is also recommended because of its mechanical properties as an aid in cleansing the hands of the surgeon.

Cimolite is a perfumed powder having similar physical properties to kaolin. Kaolin is not easily affected by most chemical reagents, and it forms a good diluent or excipient for silver nitrate, potassium permanganate, or other salts which are decomposed by organic substances.

Dose, one-half to two ounces (15.5–60 Gm.) several times a day.

Off. Prep.—Cataplasma Kaolini, *N. F.*

KAVÆ RHIZOMA. Br.

KAVA RHIZOME

(kă'væ rhī-zō'mą)

"Kava Rhizome is the peeled, dried, and divided rhizome of Piper methysticum, *Forst. fil.*" *Br.* "The dried rhizome and roots of *Piper methysticum* Forster (Fam. *Piperaceæ*)." *N. F.*

Kava, *N. F.*; Methysticum; Kava-kava.

The genus *Piper* includes a large number of sub-tropical plants, which are mostly shrubs, and rarely herbs or trees. A number of the species are of great economic importance. *Piper methysticum* is a shrub, several feet high, indigneous to many of the South Sea Islands. The plant has cordate, acuminate leaves and very short axillary spikes of flowers. The natives prepare a fermented liquor from the upper portion of the rhizome and the base of the stems.

Kava rhizome occurs "in whitish or light brownish-grey irregularly cuboid or roughly wedge-shaped fragments from which the periderm has been sliced off; from one to five centimetres thick. In transverse section, usually exhibiting a central dense pith, surrounded by a distinct ring of narrow, radiating, vascular bundles separated by relatively broad, paler, medullary rays. Fracture starchy. Slight agreeable odor; taste pungent and bitter." *Br.*

The N. F. description is as follows: "Consisting of a large, irregular knotty crown, often 12 cm. or more in diameter, from which proceed numerous, long, cylindrical, tough, nearly simple roots, which tend to fray out into bare, separated fibro-vascular bundles; the crown soft, light, spongy, and granular and very starchy; externally dark-brown or blackish, the crown frequently partly scraped and light brown to light gray; internally white. Odor faint but characteristic; taste aromatic and pungent, slightly bitter, more or less local anæsthesia resulting. The powdered drug, when examined under the microscope, exhibits numerous, simple, or two- to three-compound starch grains, the individual grains being up to 0.045 mm. in diameter, many with radial clefts or triangular fissures at the center; yellow resin and oil cells; narrow sclerenchymatous fibers with thin, strongly-lignified walls; tracheæ with scalariform or reticulate markings, up to 0.15 mm. in width; few nearly isodiametric wood parenchyma from the remains of the stem. Kava yields not more than 8 per cent. of ash." *N. F.*

The pharmacognosy of this drug has been written up by Semenow in *Ap. Ztg.*, 1890, p. 216, and True, *Ph. Rev.*, xiv, No. 2. Powdered Kava consists of numerous starch grains which are either single or 2- to 3-compound, the individual grains having central radial clefts with triangular fissures varying from 0.006 to 0.035 mm. in diameter. The sclerenchymatous fibers have thin walls which are strongly lignified. The tracheæ have scalariform or reticulate markings. The oil cells frequently contain a yellowish resin. The drug should not yield more than 8 per cent. of ash.

Gobley isolated from kava root a crystalline principle (analogous to piperin), *methysticin*, or *kavahin*, which is without odor and taste, and is probably inert. (*J. P. C.*, Jan., 1860.) It possesses the formula $C_{15}H_{14}O_5$, and is the methyl ester of p-piperonyl acetic acid, and when purified forms silky, lustrous needles melting at 138° to 139° C. (280.4°–282.2° F.). Kavahin differs from piperin and cubebin in being colored red by hydrochloric acid, the red color fading on exposure to air into a bright yellow, and in being colored by strong sulphuric acid a purplish violet, which passes into green. In 1844 Morson discovered an active principle, *kawine*. This is a greenish-yellow, strongly aromatic and acrid resin. It was again studied by Cuzaut in 1860, and by Lewin in 1886. This latter investigator separates it into two resins, of which the β-resin is greasy and of a reddish-brown color, appearing in mass almost black. This is less active than the α-resin, which is yellowish-brown, has the characteristic odor of the drug, is freely soluble in alcohol, and placed upon the tongue produces a burning sensation followed by local anesthesia. (*A. J. P.*, 1886, 450.) *Yangonin* is another glucoside which has been studied by Borsche and Gerhardt. (*Riedels Archives*, 1914, 50.) A volatile oil has also been found in the root. (*J. P. C.*, March, 1862.) Lavialle (*L'Union Pharm.*, Jan., 1889) claims to have obtained an alkaloid, *kavaine*. (See also *Proc. A. Ph. A.*, 1897, 564.)

Uses.—Under the names of *Ava* or *Kava* the natives of the Sandwich Islands have used as an intoxicant a beverage prepared from kava rhizome. The intoxication is wholly unlike that caused by alcohol, being of a silent and drowsy character, accompanied by incoherent dreams, with great loss of muscular power, which is probably due to the action of kava resin upon the spinal cord.

The physiological action of kava and its resin has been investigated by L. Lewin (*Piper Methysticum,* Berlin, 1886), and David Cerna (*T. G.,* 1891). The phenomena which follow the hypodermic injection of the fluidextract of kava or of a solution of its resin are, anesthesia at the point of injection, followed, after absorption, by general paralysis, due to a direct action on the motor side of the spinal cord; the motor nerves and the muscles remain intact. The local anesthesia is due to a paralysis of the sensory nerve filaments, and when the resin is brought in contact with the mucous membranes there is a burning pain, followed in time by a complete loss of sensibility, which is remarkably permanent, since Lewin found that from six to seven minims of a solution of kava injected beneath the skin produced a complete loss of sensibility in the surrounding area, which did not pass away for eight days. (*D. M. Ztg.,* Feb., 1886.) The action of the drug upon the circulation is subordinate to its nervous influence, but according to the experiments of Cerna it does stimulate the heart, although it decreases the number of pulsations by stimulating the inhibitory nerve centers. The same investigator found that at first it stimulates, afterwards depresses, and finally paralyzes the respiratory center. The insolubility and irritant action of kava resin has lessened its use as a practical local anesthetic.

As long ago as 1857 kava root was employed in the treatment of *gonorrhea,* and there is much testimony to its value both in the acute and the chronic form of the disease, as well as in *vaginitis, leucorrhea, nocturnal incontinence,* and similar conditions of the genito-urinary tract.

Under the name of *gonosan* a twenty per cent. solution of kava resin in oil of sandalwood is used internally in the treatment of *gonorrhea.* The advantages claimed for it are that it is much less likely to disturb the stomach than sandalwood oil, that it is locally anesthetic and hence relieves the pain and, apparently, also has some anaphrodisiac action. According to Ganz (*All. M. C. Z.,* 1906, p. 213), while not of itself gonocidal it renders the urine permanently antiseptic and so deprives the gonococci of conditions favorable for their growth. The preparation is marketed in capsules containing 0.3 Gm. of which two to four may be given several times a day. (For the methods of determining kava resins in this and similar preparations, see *Ph. Ztg.,* 1914, 284.)

Dose, of kava rhizome, from fifteen to forty-five grains (1–3 Gm.).

Off. Prep.—Extractum Kavæ Liquidum, *Br.,* (*N. F.*).

KINO. U. S., Br.

KINO

(kī'nō)

"The spontaneously dried juice of *Pterocarpus Marsupium* Roxburgh (Fam. *Leguminosæ*)." *U. S.* "Kino is the juice obtained from incisions in the trunk of Pterocarpus Marsupium, *Roxb.,* heated to boiling and evaporated to dryness. Known in commerce as East Indian, Malabar, Madras, or Cochin kino." *Br.*

Gummi (s. Resina) Kino; Indian Kino, Malabar Kino; Kino de l'Inde, *Fr. Cod.;* Kino, *G.;* Goma quino, *Sp.*

The term kino was originally applied to a vegetable extract or inspissated juice taken to London from the western coast of Africa, and introduced to the notice of the profession by Fothergill. Vegetable products obtained from various other parts of the world, resembling kino in appearance and properties, afterwards received the same name, and some confusion and uncertainty still exist, in relation to the botanical and commercial history of the drug. We shall first consider the general properties of official kino, then the several varieties.

Properties.—The official description is as follows: "In small, brittle angular fragments, usually considerably less than 15 mm. in diameter, varying in color from dark reddish-brown to reddish-black; when crushed upon a slide and examined under the microscope the angular fragments are more or less translucent with a glass-like, conchoidal surface, the thinner pieces having a yellowish-red or deep brownish-red color, the pieces often being marked by nearly parallel, curved and straight lines; inodorous; taste very astringent; when masticated it colors the saliva somewhat pink. The powder is of a dark brick-red color; upon the addition of water, the sharp angular fragments assume a deep rich-red color and become more or less rounded and separate into innumerable, small, granular particles among which are a large number of rod-shaped bacteria. On mounting powdered Kino in alcohol the fragments at first assume a deep red color, then mostly dissolve, leaving a number of small, colorless granules and indistinguishable, cellular fragments. Kino is only partly soluble in cold water, and not less than 40 per cent. is soluble in boiling water. The latter solution, when cooled and filtered, shows a faintly acid reaction, gives a dark green precipitate with ferric chloride T.S. and a reddish-violet color with alkalies. The yield of alcoholic extractive is not less than 45 per cent. Kino contains not more than 12 per cent. of moisture, and yields not more than 3 per cent. of ash." *U. S.*

"In small, angular, glistening, opaque, reddish-black, brittle fragments; transparent and ruby-red in thin laminæ. Inodorous; taste very astringent. Almost entirely soluble in *alcohol* (90 per cent.), slowly and incompletely soluble in cold *water,* not less than 75 per cent.

soluble in boiling *water*, the solutions being deep red in color. Almost entirely insoluble in *ether*. An aqueous solution (1 in 20) yields a voluminous reddish precipitate with dilute mineral acids, and, when largely diluted with *water*, a greenish-black precipitate with *T. Sol. of ferric chloride*. Ash not more than 2.5 per cent. In India and the Eastern Divisions of the Empire, Butea Gum (Buteæ Gummi) may be employed in making the official preparations for which Kino (distinguished in commerce as East Indian, Malabar, Madras, or Cochin kino) is directed to be used." *Br.*

If in large masses, it may be reduced without difficulty into minute fragments. It is without odor, and has a bitter, highly astringent taste, with a somewhat sweetish after-taste. It burns with little flame, and does not soften with heat. It imparts its virtues and a deep red color to water and alcohol, but is nearly insoluble in ether. Cold water forms with it a clear infusion. Boiling water dissolves it more largely, and the saturated decoction becomes turbid on cooling, and deposits a reddish sediment. The tincture is not disturbed by water. When long kept, it often gelatinizes, and loses its astringency. (See *Tinctura Kino.*) Kino undoubtedly consists chiefly of a modification of tannic acid or tannin, which has received the name of *kino-tannic acid*, with extractive, gum, and sometimes probably a little resin, but we need a careful analysis of the different well-ascertained varieties. The aqueous solution is precipitated by gelatin, the soluble salts of iron, silver, lead, and antimony, mercuric chloride, and sulphuric, nitric, and hydrochloric acids. The precipitate with iron is of an olive or greenish-black color. The alkalies favor the solubility of kino in water, but essentially change its nature and destroy its astringency.

1. East India Kino. *Malabar Kino.*—This is the variety at present probably most used and most highly esteemed, and the only one recognized by the British and United States Pharmacopœias. Its origin was long unknown. It is now ascertained, through the researches of Pereira, Royle, Wight, and others, to be the product of *Pterocarpus Marsupium*, a lofty tree growing upon the mountains of the Malabar coast of Hindostan. Kino is the juice of the tree extracted through longitudinal incisions in the bark and afterwards dried in the sun. Upon drying it breaks into small fragments, and is put into wooden boxes for exportation. It is collected near Tellicherry, and exported from Bombay. It is sometimes imported into this country directly from the East Indies, but more commonly from London. From a communication in the *Journal of the Asiatic Society of Bengal*, by F. Mason, it appears that kino is also collected in the Tenasserim provinces, in Farther India, and has been exported from Maulmain to Europe. It is produced by a tree called *Pa-douck*, which Christison recognized from a description furnished to him by Begbie, of Maulmain, as *Pterocarpus Marsupium*, so that this kino has the same origin as that from Malabar. *Pterocarpus indicus*, of the Mauritius Islands, where it is known as *sang-dragon*, also yields a red kino to commerce.

When kino is boiled in water, the decoction deposits, on cooling, a bright red substance, and a similar deposition takes place when a cold filtered aqueous solution is long exposed with a broad surface to the air. According to Hennig, kino consists of tannic acid about 40 per cent., with a trace of gallic acid, kinoic acid, pectin, ulmic acid, and inorganic salts, with excess of earthy bases. (See *A. J. P.*, xv, 544.) C. Etti obtained a new constituent, *kinoin*, by extracting kino with ether. He finally adopted the following method as more practicable. One part of gum kino is added to 2 parts of boiling diluted (1 to 5) hydrochloric acid. Kino-red immediately separates as a soft mass, becoming gradually solid on cooling, while the *kinoin*, mixed with a small quantity of kino-red, remains in solution. The solid residue is once more boiled with water, the liquids are united and shaken with ether. The ethereal solution, on evaporation, leaves a crystalline reddish residue, which is dissolved in hot water, on the cooling of which tolerably pure crystals of *kinoin* are obtained. By continued recrystallization they are obtained colorless. Their formula is $C_{14}H_{12}O_6$, and *kino-red* is the anhydride of this:

$$2C_{14}H_{12}O_6 - H_2O = C_{28}H_{22}O_{11}$$

This kino-red heated to 160° to 170° C. (320°–338° F.), parts with a molecule of water and yields a lower anhydride, $C_{28}H_{20}O_{10}$. Both anhydrides are precipitated by gelatin, but kinoin itself is not. When heated with hydrochloric acid to 120° to 130° C. (248°–266° F.), kinoin yields methyl chloride, gallic acid, and catechol, and hence probably has the constitution of a guaiacol or *methyl-catechol gallate*. Kino contains about 1.5 per cent. of kinoin. (*Ber. d. Chem. Ges.; N. R.*, Feb., 1897.) Kremel found Malabar kino, Butea gum, eucalyptus kino, and the kino from *Coccoloba uvifera* to be free from Etti's kinoin, but to contain a body acquiring, like kinoin, a red color with ferric chloride, which proved to be *pyrocatechuic acid;* this was present either alone or mixed with gallic acid. (*A. J. P.*, 1883, 267.) Some doubt was also thrown upon the value of Etti's conclusions by White (*P. J.*, 1903, p. 676), who failed to find several of the constituents reported by Etti. The true chemistry of kino may therefore be considered to be in a somewhat doubtful state. This is probably due to the fact that many different drugs have appeared in commerce under that name. Kino contains in its natural condition an oxidizing enzyme or oxidase which is the cause of the gelatinization which takes place in preparations of this drug. This enzyme can be destroyed by heat and advantage is taken of this fact in making *Tinctura Kino* (which see). In an examination made by David Hooper of ten varieties of East Indian kino, the proportion of

tannic acid was found, after thoroughly drying the kino, to vary from 80 to 97 per cent. of the whole mass. (*Agricultural Ledger of India*, No. 11, 1901.)

It is said that catechu, broken into small fragments, has sometimes been sold as kino. Genuine kino is sometimes substituted by the extract of krameria. The latter is more brittle and dissolves more quickly in water.

2. West India or Jamaica Kino.—This is believed to be the product of the *Coccoloba uvifera* L., or *sea-side grape*. It grows in the West Indies and neighboring parts of the continent. The kino is said to be obtained by evaporating a decoction of the wood and bark, which are very astringent.

Although it has been many years since any large quantity appeared in our markets, it may occasionally be met. It is contained in large gourds, into which it was evidently poured while in a liquid or semi-liquid state, and then allowed to harden. When taken from the gourd it breaks into fragments of various sizes, upon an average about as large as a hazelnut, and having some tendency to the rectangular form. The consistence of these fragments is uniform, their surface smooth and shining, and their color a dark reddish-brown approaching to black. They are, however, neither so glistening nor so black as the East India kino. In mass they are quite opaque, but in thin splinters are translucent and of a ruby redness. They are readily broken by the fingers into smaller fragments, are easily pulverized, and yield a dull-reddish powder, considerably lighter colored than that of the East Indian variety. The West India kino is without odor, and has a very astringent, bitterish taste, with a scarcely observable sweetish after-taste. It adheres to the teeth when chewed, although rather less than the East Indian variety, and colors the saliva red. The solubility of Jamaica kino was very carefully examined by Robert Bridges, who found that cold water dissolved 89 per cent., and alcohol 94 per cent. The portion dissolved by alcohol and not by water was probably of a resinous nature, as it appeared to be viscid, and very much impeded the filtration of the aqueous solution. Considering the nature of this substance, the form of kino in which it was found is probably, like that from the East Indies, an inspissated juice. Guibourt, who states that Jamaica kino is but slightly dissolved by cold water, must have operated on a different product.

3. South American Kino. *Caraccas Kino.*—In 1839, an astringent extract was described which had been introduced into our market, derived from Caraccas, and known by that name to the druggists. It is probably the same as that described by Guibourt, in the last edition of his *History of Drugs*, as the kino of *Colombia*. As imported, this variety of kino is in large masses, some weighing several pounds, covered with thin leaves, or exhibiting marks of leaves upon their unbroken surface, externally very dark, and internally of a deep reddish-brown or dark port-wine color. Some of the masses are very impure, containing pieces of bark, wood, leaves, etc.; others are more homogeneous, and almost free from impurities. The masses are broken up by means of a mill so as to resemble East India kino, from which, however, this variety differs in being more irregular, less sharply angular, more powdery, and less black. In appearance, taste, odor and other sensible properties this kino closely resembles the West India variety. It is not improbable that they are derived from the same plant, and there is no difficulty in supposing that this may be the *Coccoloba uvifera*, as that tree grows as well upon the continent as in the islands. South American kino was found by Bridges to yield 93.5 per cent. to cold water, and 93 per cent. to alcohol; so that, while it has almost the same solubility as Jamaica kino in alcohol, it is somewhat more soluble in cold water. The aqueous solution in this case was not embarrassed by the adhesive matter which impeded the filtration in the former variety, and the want of a minute proportion of resinous matter in the South American kino is the only apparent difference between the two drugs.

4. African Kino.—The original kino employed by Fothergill was known to be the product of a tree growing in Senegal, and upon the banks of the Gambia, on the western coast of Africa, but the precise character of the tree was not ascertained until a specimen, sent home by Mungo Park during his last journey, enabled the English botanists to decide that it was the *Pterocarpus erinaceus* of Lamarck and Poiret. A particular account of *Pterocarpus erinaceus* and its concrete juice, with a figure, by W. F. Daniell, is contained in the *P. J.* for August, 1854 (vol. xiv, p. 55). The importation of African kino has long ceased. In 1896, however, a consignment of African kino reached London. It was examined by E. M. Holmes, who stated that it was evidently yielded by *P. erinaceus*. (*C. D.*, 1896, 226.) It is said to be still used by the Portuguese of Angola, under the name of *Sangue de Drago*. As described by Fothergill, the African kino, for which he proposed the name of *gummi rubrum astringens Gambinense*, was in lumps of about the size of those of gum Senegal or dragon's blood, and so similar in appearance to the latter that a good judge might easily be deceived. These lumps were hard, brittle, opaque, and almost black, but minute fragments were reddish and transparent like garnet. The drug was inodorous, of a strongly astringent and sweetish taste, and soluble in water to the extent of about five or six parts out of seven, forming a deep red astringent infusion. There can be little doubt that this variety of kino is a concrete juice, which exudes either spontaneously or from wounds in the bark, and hardens in the air. (*Med. Obs. and Inq.*, i, 358.)

Macaranga Kino is obtained from *Macaranga Roxburghii* Wright, of the Deccan peninsula. It occurs in the form of odorless, taste-

less tears or irregular masses. The tears have fibrous fractures and when immersed in water yield unravelling fibers giving the appearance of a sea anemone. According to Hooper, this kino yields from 6 to 15 per cent. of a peculiar tannin and is closely allied to Butea kino, from which it is distinguished by fibrous tears and the fact that it contains so much gum which swells without dissolving in water. (*P. J.*, lxvi, 616.)

MYRISTICA KINO.—There has been produced in Southern India a kino consisting of smaller or larger angular pieces, of deep garnet color, in thin fragments, and having the general characteristics of Malabar kino; according to E. Schaer, it is a product of *Myristica malabarica,* of *M. fragrans,* and probably of other species of the genus. In all important respects these kinos are said to correspond with Malabar kino, but to be distinguishable by containing crystals of calcium tartrate. *Myristica Kino* is probably a distinctive product from the so-called *Syndai varnish,* a rich red fluid obtained from the *Myristica gibbosa* Hook. f., and employed in Assam as a varnish. This varnish is highly astringent and after exposure becomes perfectly impervious, the changes being due to the presence of a ferment or enzyme. As has been shown by D. Hooper (*P. J.*, June 20, 1903), Syndai varnish, if kept in corked bottles, gelatinizes in a few weeks. Edmund White made an investigation into the cause of the gelatinization of tincture of kino (*P. J.*, May, 1903), from which it appeared that this phenomenon was due to the presence in the kino of an enzyme belonging to the oxydases, and this enzyme was subsequently isolated by David Hooper from the fresh juice of *Myristica gibbosa.* (*Proc. A. Ph. A.*, 1903, 733.) It is believed by White that this enzyme may be eliminated from the official as well as other kinos by a judicious method of collection, and considers it probable that the following one, adopted by J. G. F. Marshall and described in the "*Agricultural Ledger*" (1900, No. 11, 381), will accomplish this: "A longitudinal cut is made with an axe or knife, called *acha katti,* through the bark of the trees, down to the cambium, about 1½ feet long, and side cuts are made to lead into this. A bamboo tube is then fixed at the bottom of the main incision in order to catch the juice. In the course of about twenty-four hours the flow of gum ceases and the bamboo is taken down. When several of these bamboo cups are nearly full they are taken to headquarters and emptied into a large cauldron and the juice boiled. During the boiling, the impurities, consisting of pieces of bark, wood and leaves, rise to the surface and are skimmed off. When sufficiently concentrated to the consistence of a thick extract it is exposed to the sun, in thin layers, in shallow vessels until it is dry enough to crumble to pieces. The kino is then weighed and packed away in wooden cases." (*P. J.*, 1903, 702.)

Botany or Blue Mountain kino is obtained from *Angophora lanceolata* Cav. Colombo kino is obtained from a number of species of *Angophora.* Hooper (*P. J.*, 1908, xxvii, 161) reports the occurrence of three new astringent plant juices or kinos. They are derived from *Jatropha Curcas,* from South Salem; *Xylia dolabriformis,* from Burma; and *Parkia insignis* ("*Myauk-tanyet*"), also from Burma.

Uses.—Kino is powerfully astringent, and in this country is much used for the suppression of morbid discharges. In *diarrhea,* not attended with febrile excitement or inflammation, it is often an excellent adjunct to opium and the absorbent medicines, and is a favorite addition to chalk mixture. It is also used in *chronic dysentery* when astringents are admissible; in *leucorrhea* and *diabetes;* and in *passive hemorrhages,* particularly those from the uterus and the intestines. The infusion may be made by pouring eight fluidounces of boiling water on two drachms of the extract, and straining when cool; aromatics may be added, if deemed advisable. The dose of this infusion is a fluidounce (30 mils). The proportion of alcohol in the tincture renders it frequently an unsuitable preparation.

Dose, eight to thirty grains (0.5–2.0 Gm.).

Off. Prep.—Pulvis Catechu Compositus, *Br.;* Pulvis Kino Compositus, *Br.;* Tinctura Kino, *U. S., Br.;* Pulvis Kino et Opii Compositus, *N. F.;* Tinctura Kino et Opii Composita (from Tincture), *N. F.*

KINO EUCALYPTI. Br.

EUCALYPTUS KINO [Eucalyptus Gum Red Gum]

(kī'nō eū-cą-lўp'tī)

"Eucalyptus Kino is an exudation from the stem of various species of Eucalyptus." *Br.*

Eucalypti Gummi, *Br.* 1898; Australian Kino.

Eucalyptus kino is prepared from a number of species of Eucalyptus, but most of the commercial article is prepared from *E. rostrata,* a tree which is very abundant in Western Australia. This tree received its name from the rastrate character of the opercula. Masses of kino are sometimes found in cavities between the wood and the bark, this being due to the evaporation of the sap in these places. It is usually obtained by incising the trees and collecting the exuding liquid which is then dried in the sun. It has been stated that five hundred pounds of the kino are sometimes yielded in a single year by one tree, but this seems to be a great exaggeration. Occasionally the juice reaches England unevaporated. *Kino juice* has a fine deep red color, a slightly aromatic odor, and a decidedly astringent taste, and on evaporation yields a genuine kino in varying amount. It must not be confounded with the so-called *Liquid Kino,* or *apple tree juice,* which is obtained from incisions in the *Angophora intermedia* or *narrow-leaved apple tree* of Australia. This varies from the consistency and colorlessness of water to an orange brown or reddish-brown liquid as thick as molasses. It contains

catechin and tannic acid, and is said to be especially employed for the purposes of tanning nets.

Properties.—Australian kino usually occurs in dark, reddish-brown (not reddish-black) masses or grains, which when sufficiently thin may be translucent and garnet-like. This form of kino is at the present time very largely used and while similar to the official or East Indian Kino in physical and therapeutical properties has not in solution the tendency to gelatinize. For further information concerning it the reader is referred to an elaborate paper on it by J. H. Maiden, in *P. J.*, Oct., 1889; also *A. J. P.*, 1897, 1.

"In very dark reddish-brown grains or small masses. Thin fragments transparent and ruby-red, or garnet-red. Inodorous; taste astringent. Tough and adhering to the teeth when chewed. Not less than 80 per cent. soluble in *water*. Almost entirely soluble in *alcohol* (90 per cent.)." *Br.*

Eucalyptus kino contains catechin, pyrocatechin and kinoin, and in some specimens a volatile oil, giving a slightly aromatic odor to the drug, which is especially developed by hydrochloric acid. J. H. Maiden (*A. J. P.*, 1895, 575) states that Australian kino contains *eudesmin* and *aromadendrin*. The former of these when purified exists as a pure white mass with a luster resembling spermaceti. It is soluble in hot water, but crystallizes out again on cooling. It is soluble in alcohol, ether, acetic ether, and chloroform, but not in benzene, petroleum spirit, or carbon disulphide. It is dissolved by sulphuric acid with a dark color changing to purple, by nitric acid with a beautiful yellow color. Its formula is given as $C_{36}H_{30}O_8$, and its melting point as 99° C. (210.2° F.). The second substance was also obtained crystallized from boiling water, and melted at 162° C. (323.6° F.). No analysis has been made of it.

Uses.—It does not equal kino in astringency. It is used for *diarrheas of relaxation*, and other affections for which kino has been employed, and is also largely employed as the basis of lozenges and gargles for the relief of relaxed conditions of the pharynx.

Dose, from five to twenty grains (0.3–1.3 Gm.).

Off. Prep.—Trochiscus Kino Eucalypti, *Br.*

KRAMERIÆ RADIX. Br.

KRAMERIA ROOT [Rhatany Root]

(krą-mē'rī-æ rā'dīx)

"Krameria Root is the dried root of Krameria triandra, *Ruiz and Pav.* (Peruvian Rhatany), and also of another species of Krameria, probably Krameria argentea, *Mart.* (Pará Rhatany)." *Br.* "The dried root of *Krameria triandra* Ruiz et Pavon, known in commerce as Peruvian Rhatany, or of *Krameria Ixina* Linné, known in commerce as Savanilla Rhatany, or *Krameria argentea* Martius, known in commerce as Para or Brazilian Rhatany (Fam. *Leguminosæ*), without the presence of more than 5 per cent. of stems or other foreign matter." *N. F.*

Krameria, *N. F.*; Rhatany Radix Ratanhæ; Ratanhia, *Fr. Cod.*; Radix Ratanhiæ, *P. G.*; Ratanhiawurzel, *G.*; Ratania, *It.*; Ratania (Raiz de), *Sp.*

The genus *Krameria* was named in honor of J. G. H. Kramer, a physician and botanist of Temesvar, Hungary.

Krameria was dropped from the U. S. P. IX but retained in the British Pharm., 1914, and in the N. F.

Krameria triandra is a shrub, having a long, much-branched, spreading root, of a blackish-red color; with a round, procumbent, very dark colored stem, divided into numerous branches of which the younger are leafy and thickly covered with soft hairs, giving them a white, silky appearance. The leaves are few, sessile, oblong-ovate, pointed, entire, presenting on both surfaces the same silky whiteness of the young branches. The flowers are lake-colored, and stand singly on short peduncles at the axils of the upper leaves. The stamens are three. The nectary is of four leaflets, the two upper spatulate, the lower roundish and shorter. The fruit is globular, of the size of a pea, surrounded by stiff reddish-brown prickles, and having one or two seeds. It is a native of the Peruvian Andes, growing in dry argillaceous and sandy places. It flowers at all seasons, but is at the height of its bloom in October and November. The root is dug up after the rains, and, according to Tschudi, it is especially obtained in the southern provinces of Peru. Closely allied to it is *K. Ixina* L., which yields *Savánilla Rhatany*. It is, however, distinguished by having four stamens, and occurs in Guiana and Northern Brazil. The name *rhatany* is said to express in the tongue of the Peruvian Indians the creeping character of the plant yielding the root.

Para or *Brazilian Rhatany* was described by Berg in 1865, and is believed to be the root of the *K. Argentea*. It closely resembles the Savanilla variety. Two forms of rhatany which Cotton has described as *Black* and *Brown Antilles rhatany* because produced in these islands have been pronounced by Flückiger (*P. J.*, July, 1870, p. 84) to be identical with the Para Rhatany. According to the studies of Dunwoody (*A. J. P.*, 1890) this rhatany contains the same active principles as the root of *K. Triandra*, but in slightly less quantity.

The British Pharmacopœia recognizes two varieties of rhatany, which are described as follows: "Peruvian Rhatany is nearly cylindrical, slightly flexuous, reddish-brown; length variable; thickness not exceeding fifteen millimetres. Cork scaly; fracture splintery; wood yellow. In transverse section, bark bright reddish-brown and occupying about one-third of the radius of the section. Pará Rhatany is cylindrical, nearly straight, dark purplish-brown or almost black, and marked with deep transverse cracks. Fracture short; wood pale reddish-brown. In transverse section, bark dark reddish-brown and occupying about one-half of the radius of the

section. Both varieties inodorous; taste of the bark astringent, of the wood scarcely perceptible. Ash not more than 4 per cent." *Br.*

The N. F. description is as follows:

"**Peruvian Rhatany.**—It consists of a knotty, several to many-headed crown with numerous branching roots, the latter rarely attaining a length of 50 cm. and usually less than 1 cm. in thickness, cylindrical, somewhat tapering, and flexuous or wavy; externally light reddish-brown or brownish-red, more or less marked with dark scaly cork, especially in the upper portion, otherwise nearly smooth, somewhat longitudinally wrinkled and devoid of transverse fissures, fracture of bark slightly fibrous, of wood tough and splintery, the pinkish-brown bark less than one-third of the radius, the wood yellowish or pinkish-white and finely radiate. Inodorous, wood nearly tasteless, bark astringent.

"**Savanilla Rhatany and Para Rhatany.**—Roots usually separate, less flexuous and tapering than those of Peruvian Rhatany, and usually not exceeding 12 mm. in thickness; externally purplish-brown or chocolate-brown and marked with numerous transverse fissures; fracture less tough than that of Peruvian Rhatany; internally the bark and wood darker, the bark about two-fifths or more of the radius and more astringent than that of Peruvian Rhatany. Inodorous, wood nearly tasteless, bark astringent. Powdered Krameria is reddish-brown; starch grains simple or two- to four-compound, the individual grains spherical, ellipsoidal, or plano-convex, and sometimes with a central, radial or star-like cleft, from 0.003 to 0.035 mm. in diameter; bast fibers more or less wavy in outline with very much attenuated ends and with non-lignified walls; tracheæ with simple or bordered pores associated with numerous wood fibers which are narrow-spindle shaped and with thick, porous, slightly lignified walls; numerous cellular fragments with yellowish or reddish-brown walls; calcium oxalate in monoclinic prisms, from 0.01 to 0.1 mm. in length, few or frequently absent. Macerate 2 Gm. of powdered Krameria with 10 mils of alcohol, with occasional stirring for one hour, and filter. The deep reddish colored filtrate obtained yields a dark brownish-red precipitate and a deep orange-red filtrate upon the addition of an excess of alcoholic lead acetate T.S.; this latter filtrate yields no precipitate upon the further addition of a drop or two of alcoholic lead acetate T.S., and yields an olive-brown solution having a purplish fluorescence upon the addition of a drop or two of ferric chloride T.S. Krameria yields not less than 9 per cent. of aqueous extractive and not more than 5 per cent. of ash." *N. F.*

A rhatany appeared not long since in the London market from Guayaquil. It is described as a large woody root from 1 to 5 cm. in diameter. The bark is of a reddish-brown color with blackish streaks, is thin in comparison to the pith, is of a fibrous texture, and is somewhat striated on the surface and dotted over with small warts. It has a very astringent taste, but no marked odor. E. M. Holmes thinks that it is not the product of the genus *Krameria*. According to the analysis of Passmore, *Guayaquil rhatany* contains a larger quantity of tannin than the Peruvian drug, but less than the Para or the Savanilla rhatany. (*P. J.*, 1903, lxxvi, 878.) A spurious rhatany of unknown botanical origin has appeared in the English market coming from Peru. The root is tapering and varies from two to three and a half inches in length, and a quarter to five-eighths of an inch in diameter. The bark is reddish-brown, rough, scaly and longitudinally grooved. The root has a short fracture and a meditullium of about 24 wedge shaped bundles, is odorless and of an astringent taste. For detailed macro- and microscopical descriptions, see P. H. Marsden, *P. J.*, 1901, 618.

According to an analysis made in the University of Wisconsin, the *Krameria lanceolata* Torrey, of North America, yields 34.5 per cent. of extract and 17 per cent. of tannin, and is therefore richer than the official drug. When treated with iron it strikes a deep-purple color, and is thus easily distinguished from Para rhatany, which gives a dirty brown color, and from Savanilla rhatany, which gives a violet color.

As the astringency is much stronger in the cortical than in the ligneous portions, the smallest pieces are preferable, as they contain the largest proportion of the bark. The powder is of a reddish-brown color. The starch grains occur single or two- to four-compound, the individual grains being spherical, ellipsoidal, or plano-convex, and sometimes with a central, radial, or star-like cleft, from 0.003 to 0.035 mm. in diameter. The bast fibers are more or less wavy in outline with very much attenuated ends and with non-lignified walls. The tracheæ possess simple or bordered pores associated with numerous wood fibers which are narrow-spindle shaped and with thick, porous, slightly lignified walls. There are also numerous cellular fragments with yellowish or reddish-brown walls. Calcium oxalate may occur in monoclinic prisms, from 0.01 to 0.1 mm. in length. Macerate 2 Gm. of powdered Krameria with 10 mils of alcohol, with occasional stirring for one hour, and filter. The deep reddish colored filtrate obtained yields a dark brownish-red precipitate and a deep orange-red filtrate upon the addition of an excess of alcoholic lead acetate T.S.; this latter filtrate yields no precipitate upon the further addition of a drop or two of alcoholic lead acetate T.S., and yields an olive-brown solution having a purplish fluorescence upon the addition of a drop or two of ferric chloride T.S. Krameria should yield not less than 9 per cent. of aqueous extract and not more than 5 per cent. of ash.

The virtues of the root are extracted by water and alcohol, to which it imparts a deep reddish-brown color. From the researches of Vogel, Gmelin, Peschier, and Trommsdorff, it appears to contain tannic acid, lignin, and

minute quantities of gum, starch, saccharine matter, and an acid which Peschier considered as peculiar and named *krameric acid.* The tannic acid of rhatany (*krameria-tannic* or *ratanhia-tannic acid*) is separated by treating the ethereal extract of the bark with alcohol, and evaporating the alcoholic solution. It gives a dark-green precipitate with ferric chloride, a flesh-colored one with gelatin, and none with tartar emetic. (Gmelin.) The tannin of rhatany, in the presence of melted potassium hydroxide, is transformed into protocatechuic acid and phloroglucin, and with diluted acids gives glucose and a peculiar red coloring principle called *ratanhia red,* $C_{26}H_{22}O_{11}$. (*J. P. C.,* Jan., 1868, p. 73.) The proportion of red astringent matter obtained by Vogel was 40 per cent. The mineral acids and most of the metallic salts throw down precipitates with the infusion, decoction, and tincture of rhatany, and are incompatible in prescription.

In examining a specimen of extract of rhatany from America, Wittstein discovered an alkaloid, which he thought to be identical with tyrosine. A somewhat different result was obtained by Ruge, who, after an examination, showed that the new alkaloid is not identical with tyrosine, for it has the formula $C_{10}H_{13}NO_3$, while that of tyrosine is $C_9H_{11}NO_3$, but is rather homologous with it. Like tyrosine, it is an amido-acid, and forms salts equally with mineral acids and with strong bases. It was called *ratanhine* by Ruge. Goldschmidt has since shown (*D. C.,* 1914, 17) that the formula of *rhatanin* is $C_{20}H_{43}NO_3$, and that it is a homologue of tyrosine. It is identical with *angelin, geoffrayin,* and *andirin,* which have been described in various plants. He obtained it in crystalline needles, melting at 280° C. (536° F.). (See *A. J. P.,* 1875, p. 266.)

Cold water extracts all the astringency of rhatany, forming a clear deep-red infusion, which upon careful evaporation yields an almost perfectly soluble extract. The root yields its virtues also to boiling water by maceration, but the resulting infusion becomes turbid upon cooling, in consequence of the deposition of apotheme taken up by the water when heated. By boiling with water a still larger proportion of the apotheme is dissolved, and a considerable quantity of the pure tannin becomes insoluble in cold water, and medicinally inert, either by combining with the starch which is also dissolved, or by conversion into apotheme through the agency of the atmosphere. The decoction is, therefore, an ineligible preparation, and the extract resulting from its evaporation, though greater in weight than that from the cold infusion, contains much less soluble and active matter. Alcohol dissolves a larger proportion of the root than water, but this is owing to the solution of apotheme, and the alcoholic extract contains little if any more of the astringent principle than that prepared by cold water, while it is encumbered with much inert matter. (See *Extractum Krameriæ.*)

A very delicate test for the presence of rhatany is given by Glücksmann (*Ph. Post,* 1912, 65), who states that if an extract containing it be diluted with water until almost colorless, the addition of 0.5 Gm. of sodium bicarbonate to 10 mils of the liquid will produce a rose red color.

Uses.—Rhatany is an active astringent, and may be advantageously given in *chronic diarrhea.* It has long been used in Peru as a remedy in bowel complaints, as a corroborant in cases of enfeebled stomach, and as a local application to spongy gums. Ruiz, one of the authors of the Peruvian Flora, first made it known in Europe. In the form of infusion, tincture, or extract, rhatany has been used locally in *fissure of the anus, prolapsus ani,* and *leucorrhea.*

Dose, of the powder, twenty to thirty grains (1.3–2.0 Gm.).

Off. Prep.—Extractum Krameriæ, *Br., N. F.;* Infusum Krameriæ, *Br.;* Pulvis Catechu Compositus, *Br.;* Tinctura Krameriæ, *Br., N. F.;* Trochiscus Krameriæ (from Extract), *Br.;* Trochiscus Krameriæ et Cocainæ (from Extract), *Br.;* Fluidextractum Krameriæ, *N. F.;* Fluidglyceratum Krameriæ, *N. F.;* Pulvis Gambir Compositus, *N. F.;* Syrupus Krameriæ, *N. F.*

LACTUCARIUM. U. S.

LACTUCARIUM Lactucar.

(lăc-tū-cā′rĭ-ŭm)

"The dried milk-juice of *Lactuca virosa* Linné (Fam. *Compositæ*)." *U. S.*

Lactucarium Anglicum, Lactucarium Germanicum; Strong-scented Lettuce, Green Endive; Lactucarium, *Fr. Cod.;* Giftlattichsaft, *G.;* Lactucario, *Sp.*

The plants of this genus yield when wounded a milky-juice, to which, indeed, they owe their generic name. The juice from *L. sativa, L. virosa,* and *L. altissima* Bieberstein has been supposed to possess narcotic properties.

Lactuca sativa or *garden lettuce* is an annual plant. The stem, which rises above two feet, is erect, round, simple below, and branching in its upper part. The lower leaves are obovate, undulate and rounded at the summit; the upper are smaller, sessile, cordate, and toothed; both are shining, and of a yellowish-green color. The flowers are pale yellow, small, and disposed in an irregular terminal corymb. Before the flower-stem begins to shoot, the plant contains a bland pellucid juice, has little taste or odor, and is much used as a salad for the table, but during the period of inflorescence it abounds in a milky juice, which readily escapes from incisions in the stem. The juice is more abundant in the wild than in the cultivated plants. The original native country of the garden lettuce is unknown. The plant has been cultivated from time immemorial, and flourishes equally in hot and temperate latitudes. Some botanists suppose that *L. virosa* of the old continent is the parent of all the varieties of the cultivated plant.

Lactuca virosa, the *acrid* or *strong-scented lettuce*, is biennial, with a stem from two to four feet high, erect, prickly near the base, above smooth and divided into branches. The lower leaves are large, oblong-ovate, undivided, toothed, commonly prickly on the under side of the midrib, sessile, and horizontal; the upper are smaller, clasping, and often lobed; the bracts are cordate and pointed. The flowers are numerous, of a sulphur-yellow color, and disposed in a panicle. The plant is a native of Europe.

It is lactescent, and has a strong disagreeable odor like that of opium, and a bitterish, acrid taste.

Lactucarium is cultivated in Scotland, Germany, Austria and France. According to Fairgrieve (*P. J.*, 1873, iii, p. 972) the plant cultivated in Scotland is the *L. virosa*, var. *montana*. From May to August, or even as late as September, the collectors spread over the field cutting the head of each stalk and scraping the flow into their vessels. This is repeated several times daily until the plants are exhausted. The method of cultivation in the Mosel Valley, Germany, is described by Kieffer (*Ph. Zeit.*, i, p. 143), who states that the drug of Germany is shipped to England and later imported into the United States via San Francisco, where it is supposedly used in the adulteration of opium. The cultivation in France is described by Van Italie (*J. P. C.*, 1913, viii, p. 449).

For various plans which have been suggested for collecting the drug, see 14th ed., *U. S. D.*

Lactucarium, as brought from England, is in small, irregular lumps, about the size of a pea or larger, of a reddish-brown color externally, and of a narcotic odor and bitter taste. As prepared near Edinburgh, it is commonly in roundish, compact, and rather hard masses, weighing several ounces. (Christison.) A variety known in our market as *German lactucarium* is in pieces about 4 cm. long by 2.5 cm. in thickness, four-sided, with one side convex and the three others flat, or slightly concave from shrinking, as if quarter sections of a saucer-shaped cake which had been divided before it was quite dry. The color on the outer or convex surface is darkish brown, that of the cut surfaces light yellowish-brown. From experiments by Parrish and Bakes, the German appears to be inferior to the English, as 44 per cent. of spirituous extract was obtained from the latter, and only 36 per cent. from the former, while the two extracts were about equal in their sensible properties. (*A. J. P.*, 1860, p. 226.) French lactucarium resembles the German, except in being in circular cakes about 4 cm. in diameter. The official description is as follows: "Usually in quarter sections of hemispherical masses, or in irregular, angular pieces; externally dull reddish- or grayish-brown; fracture tough, waxy; internally light brown or yellowish; somewhat porous; odor distinctive, opium-like; taste bitter. Lactucarium is partly soluble in alcohol and ether and, when triturated with water, it yields a turbid mixture. Treat Lactucarium with boiling water and filter; the filtrate is clear while hot; on cooling it becomes turbid but clears upon the addition of ammonia water or alcohol; it is not colored blue by iodine T.S. (*starch*). An alcoholic solution of Lactucarium gives not more than a faint green color upon the addition of a drop of ferric chloride T.S. (*tannin*). The powder is grayish-brown to dark brown, consisting almost entirely of irregular fragments without any cellular structure: when mounted in hydrated chloral T.S., the fragments become clear, showing granular fragments, and from this deposit, numerous rod-shaped crystals and broad monoclinic prisms as well as aggregates of these, all of which polarize light. In the preparation of powdered Lactucarium, dry the crude drug at a temperature not exceeding 70° C. (158° F.). Lactucarium contains not more than 15 per cent. of moisture, and yields not more than 10 per cent. of ash." *U. S.*

The *thridace* of François, at one time supposed to be identical with lactucarium, is in all probability nothing more than the inspissated expressed juice of lettuce, and, indeed, was directed as such in the French Codex of 1837, the leaves being rejected, and the stalks alone, near the flowering period, being subjected to pressure.

The drug of commerce usually has a growth of mold on the surface. If it has penetrated the drug to any extent it reduces its quality. Occasionally specimens are met with that are moldy throughout, and these should be rejected. In color, taste, and odor, lactucarium bears considerable resemblance to opium, and has sometimes been called *lettuce opium*. It does not attract moisture from the air. It yields nearly half its weight to water, with which it forms a deep-brown infusion. It is partly soluble in ether and alcohol. From its resemblance in some of its properties and to opium, it was conjectured to contain morphine, or some analogous principle, but this conjecture is false. There is no doubt as to the complexity of the composition of lactucarium, but so feeble are its properties that it has largely gone out of active use, and its chemistry is of little practical importance. Buchner, Aubergier, and Walz claim severally to have discovered the active principle, which has been named *lactucin*, but the substances obtained by these different chemists are not exactly identical in properties, and the lactucin of Walz and Aubergier is considered by Lenoir as owing its bitterness to impurities, separated from which it is without taste and inert. For a full account of the earlier analyses of lactucarium, see 16th edition, *U. S. D.* Ludwig found, in 100 parts, 48.63 of substances insoluble in water, and 51.37 of substances soluble in water. Of the insoluble matter 42.64 parts were of *lactucerin* or *lactucon*, in snow-white aggregated granules, dissolving in strong hot alcohol which deposits it on cooling, readily soluble in ether but insoluble in water, incapable of saponification by potassium hydroxide, and therefore not properly a fat, and in alcoholic solution faintly reddening litmus paper. On

the other hand, Hesse states that lactucon which, according to Massner, has the composition $C_{28}H_{44}O_2$, is a mixture of esters, of which one, $C_{36}H_{58}O_2(C_2H_3O)_2$, is a diacetyl ester yielding, when saponified, *α-lactucerol,* $C_{36}H_{60}O_2$, and acetic acid, while the other is a mono-acetyl ester, $C_{36}H_{59}O_2(C_2H_3O)$. Of the 51.37 parts soluble in water, 6.98 were albumen, 1.75 lactucerin, held in solution by other substances, 27.68 bitter extract soluble in water and in alcohol, and 14.96 aqueous extract insoluble in alcohol of 0.830. The former of these extracts was found to contain a peculiar acid substance called *lactucic acid,* and the lactucin of Aubergier. *Lactucic acid* is of difficult crystallization, light yellow, strongly bitter, without sour taste, of an acid reaction, and readily soluble in alcohol and water. It has as much claim as any other discovered substance to be considered the active principle of lactucarium.

The assertion sometimes made that *Lactuca virosa* contains a mydriatic alkaloid has been denied by J. C. Braithwaite and H. E. Stevenson, *P. J.*, 1903, 148. Farr and Wright (*P. J.*, 1904, p. 16) claim, however, to have definitely established the presence of a mydriatic alkaloid, giving alkaloidal reactions with Mayer's and Thresh's reagents, and producing a powerful mydriatic effect upon the eye.

Kromayer (*Ann. Ch. Ph.*, cv, p. 3) found also *lactucopikrin,* $C_{44}H_{32}O_{21}$, a brown, amorphous, and very bitter substance of weak acid reaction. It is easily soluble in water and alcohol. Ludwig's lactucic acid Kromayer considers to be an oxidation product of lactucopikrin.

Hesse (*Handwörterbuch,* iv, p. 8) prepared *lactucerin,* and finds it to crystallize in white needles, fusing point 210° C. (410° F.), soluble in hot ligroin, chloroform, and benzene. On fusion with potassium hydroxide it yields acetic acid and *lactuceryl alcohol,* $C_{18}H_{30}O$, which forms white needles, fusing at 162° C. (323.6° F.), and is easily soluble in ether, chloroform, and hot alcohol. Hesse has since (*Ann. Ch. Ph.*, 234, p. 243) determined that lactucarium contains the acetates of *α-* and *β-lactucerol,* $C_{18}H_{30}O$. These compound ethers are saponified with alcoholic potash and water added, which precipitates *α-* and *β-*lactucerol. These are washed, dried in the air, and taken up with boiling alcohol. On cooling, *α-*lactucerol separates out first and can be purified by recrystallization, while the *β-*lactucerol is obtained from the mother liquor. The acetate of *α-*lactucerol fuses at 210° C. (410° F.), while that of *β-*lactucerol fuses at 230° C. (446° F.). For an examination of *Russian lactucarium,* by L. Schiperovitch, see *Ph. Z. R.*, or *D. C.*, 1886.

Uses.—The ancients believed that lettuce had soporific properties, and many years ago J. R. Coxe, of Philadelphia, first proposed the employment of the inspissated milky juice as a medicine. It was chiefly, however, through the recommendation by Duncan, Sr., of Edinburgh, that the medicine came into use and was adopted as official in various pharmacopœias. It is claimed for it that it has, although in a very much inferior degree, the anodyne and calming properties of opium, without its disposition to derange the digestive organs. It has been employed in this country to some extent to allay *cough* and quiet *nervous irritation,* but we believe that the general experience is in accord with our own in finding it to be almost devoid of narcotic properties. We have never been able to obtain any good results from its use. Water distilled from lettuce (*eau de laitue*) is used in France as a mild sedative, in the quantity of from two to four ounces. The fresh leaves boiled in water are sometimes employed in the shape of cataplasm. It is said that in Egypt a mild oil is derived from the seeds, fit for culinary use. (See *Syrupus Lactucarii.*)

Dose, ten to twenty grains (0.65–1.3 Gm.), but much larger quantities may be given without obvious effects.

Off. Prep.—Syrupus Lactucarii (from Tincture), *U. S.;* Tinctura Lactucarii, *U. S.*

LAMELLÆ.

DISCS

(lą-mĕl'læ)

Gelatina Medicata in Lamellis; Medicated Gelatin Disks; Disques de Gélatine, *Fr.;* Gelatinlamellen, Gelatinplättchen, *G.*

Under this head are included in the British Pharmacopœia minute *gelatin discs* which contain traces of alkaloids, and which are designed to be inserted by oculists under the eyelid, in order to produce, through solution in the tears, such effects as they desire. A hot solution of gelatin containing the alkaloid in proper proportion is poured on a slightly greased or waxed glass or porcelain plate, cooled and dried, and then cut into discs, which, by previous calculation, will be found to contain the requisite quantity of medicament. A little glycerin is added to keep them from getting too hard and dry.

In Appendix X, British Pharmacopœia, a general formula is inserted as follows:

"Process for Preparation of Discs (Lamellæ), Br.—Discs are prepared by the following process:—Gelatin, 18 *grammes;* Glycerin, 2 *grammes;* Distilled Water, 88 *grammes.* Mix the Glycerin with the Distilled Water, allow the Gelatin to soak in the mixture till soft, and then dissolve by a gentle heat; cool the basis so produced. Take the prescribed quantity of the above basis, melt it by a gentle heat, add the prescribed quantity of medicament, dissolve and mix. Pour the melted and medicated basis upon a sheet of plate glass 10 centimetres square, previously thinly coated with White Beeswax, in such a manner that the solution is evenly distributed. Dry at a temperature not exceeding 36° C. (96.8° F.), and from the film thus obtained cut discs 3 millimetres (nearly ⅛ inch) in diameter."

LAMELLÆ ATROPINÆ. Br.

DISCS OF ATROPINE

(lą-mĕl'læ ăt-rǫ-pī'næ)

Disques d'Atropine, *Fr.*; Atropinplättchen, *G.*

"Discs of Atropine are discs of Gelatin with Glycerin, each weighing about 1.3 milligrams (1/50 grain) and containing 0.013 milligram (1/5000 grain) of Atropine Sulphate. Prepare as directed in Appendix X, employing 0.016 gramme of Atropine Sulphate and 8.8 grammes of *basis*." *Br.*

LAMELLÆ COCAINÆ. Br.

DISCS OF COCAINE

(lą-mĕl'læ cō-cą-ī'næ)

Disques de Cocaine, *Fr.*; Cocainplättchen, *G.*

"Discs of Cocaine are discs of Gelatin with Glycerin, each weighing about 3.5 milligrams (1/20 grain) and containing 1.3 milligrams (1/50 grain) of Cocaine Hydrochloride. Prepare as directed in Appendix X, employing 1.65 grammes of Cocaine Hydrochloride and 15 grammes of *basis*." *Br.*

LAMELLÆ HOMATROPINÆ. Br.

DISCS OF HOMATROPINE

(lą-mĕl'læ hō-măt-rǫ-pī'næ)

Disques d'Homatropine, *Fr.*; Homatropinplättchen, *G.*

"Discs of Homatropine are discs of Gelatin with Glycerin, each weighing about 2.1 milligrams (1/32 grain) and containing 0.65 milligram (1/100 grain) of Homatropine Hydrobromide. Prepare as directed in Appendix X, employing 0.82 gramme of Homatropine Hydrobromide and 10.1 grammes of *basis*." *Br.*

Lucas (*C. D.*, 1899, 959) furnishes an improved formula for these discs; it is as follows: Gelatin, 30 gr.; Glycerin, 3 gr.; Distilled Water, 150 gr.; Homatropine hydrobromide, 10 gr. Dissolve and pour on to a waxed plate, so as to produce a film exactly 4 inches square. When dry, but still supple, punch out discs 1-7 inch diameter.

The product is about 784 discs, the remainder of the film being wasted. Each disc will weigh rather less than 1-20 gr. No inconvenience has been found in using discs weighing 1-15 gr., as, owing to their extreme tenuity, they soften as soon as they are inserted beneath the eyelid.

LAMELLÆ PHYSOSTIGMINÆ. Br.

DISCS OF PHYSOSTIGMINE [Discs of Eserine]

(lą-mĕl'læ phȳ-sǫ-stĭg-mī'næ)

Disques d'Ésérine, *Fr.*; Physostigminplättchen, *G.*

"Discs of Physostigmine are discs of Gelatin with Glycerin, each weighing about 1.3 milligrams (1/50 grain) and containing 0.065 milligram (1/1000 grain) of Physostigmine Sulphate. Prepare as directed in Appendix X, employing 0.082 gramme of Physostigmine Sulphate and 8.45 grammes of *basis*." *Br.*

LAUROCERASI FOLIA. Br.

CHERRY-LAUREL LEAVES

(lâų'rō-cĕr'ą-sī fō'lĭ-ą)

"Cherry-Laurel Leaves are the fresh leaves of Prunus Laurocerasus, *Linn.*" *Br.*

Cherry Bay; Laurier-cerise, *Fr. Cod.*; Kirschlorbeer, *G.*; Lauroceraso, *It.*; Laurel-cerezo (Hoja de), *Sp.*

Prunus Laurocerasus is a small evergreen tree, rising 15 or 20 feet, with long, spreading branches, which, as well as the trunk, are covered with a smooth, blackish bark. The leaves are oval-oblong, petiolate, from five to seven inches in length, acute, finely toothed, firm, coriaceous, smooth, beautifully green and shining, with oblique nerves, and yellowish glands at the base. The flowers are small, white, strongly odorous, and disposed in simple axillary racemes. The fruit is an oval drupe, very similar in shape and structure to a small black cherry. The cherry-laurel is a native of Asia Minor, but is cultivated in Europe, both for medicinal use and for the beauty of its shining evergreen foliage. Almost all parts of it have more or less of the odor of hydrocyanic acid.

In their recent and entire state cherry-laurel leaves have scarcely any odor; but, when bruised, they emit the characteristic odor of the plant in a high degree. Their taste is somewhat astringent and strongly bitter, with the flavor of the peach kernel. They are officially described as "thick, coriaceous, on short, strong petioles, oblong or somewhat obovate, from twelve to eighteen centimetres long, tapering towards each end, recurved at the apex, distantly but sharply serrate and slightly revolute at the margins; dark green, smooth and shining above, much paler beneath; midrib prominent, with one or two glandular depressions on the under surface near its base. Inodorous, but emitting when bruised an odor resembling that of prussic acid." *Br.*

Cherry-laurel leaves are sometimes substituted by the leaves of other species of *Prunus*. These are readily distinguished in that they do not possess the characteristic glandular hairs which occur on the basal portion of the leaves and petioles of *P. Laurocerasus*. (*B. P. G.*, 1907, p. 325.)

Cherry-laurel leaves yield a volatile oil containing benzaldehyde and hydrocyanic acid by distillation with water, which they strongly impregnate with their flavor. One pound, avoirdupois, of the fresh leaves yields 40.5 grains of the oil. (*Ph. Cb.*, 1855, 205.) The oil resembles that of bitter almonds, for which it is said to be sometimes sold in Europe, where it is employed to flavor liquors and various culinary preparations, but, as the glucoside of cherry-laurel leaves is decomposed more slowly than ordinary crystallized amygdalin, it is liable to hold hydrocyanic acid, and hence to be poisonous. The glucoside referred to has been termed *laurocerasin*, or "amorphous amygdalin." It is decomposed by emulsin into hydrogen cyanide, benzaldehyde, and sugar, but more slowly

than ordinary amygdalin. Its optical activity also differs from that of ordinary amygdalin. (Jacobsen, *Die Glykoside,* 25.) That the oil exists already formed, to a certain extent, in the fresh leaves, is rendered probable by the fact, stated by Winckler, that they yield it in considerable quantity when distilled without water. (*J. P. C.,* xxv, 195.) The fresh leaves are used to flavor milk, cream, etc., and more safely than the oil, though they also are poisonous, when too largely employed.

Uses.—The leaves of the cherry-laurel possess properties similar to those of hydrocyanic acid, and the water distilled from them is much employed in various parts of Europe for the same purposes as that active medicine. But it deteriorates by age, and therefore, as kept by pharmacists, must be of variable strength. J. Bröker, a Dutch pharmacologist, has satisfied himself, by numerous experiments, that the proportion of hydrocyanic acid in the leaves varies with the season, the age of the plant, the character of the soil and of the weather, and thinks that, in consequence of this variability, they are inferior for medicinal use to bitter almonds, which in this respect have a more uniform composition. He found the proportion of the acid in the leaves greatest in July, and least in February. (*B. F. M. R.,* Oct., 1868, p. 517.) It is not, therefore, to be regretted that the want of the plant in this country has prevented the general introduction of so variable a remedy as the distilled water. (See *Aqua Laurocerasi.*)

Off. Prep.—Aqua Laurocerasi, *Br.*

LIMONIS CORTEX. U. S., Br.

LEMON PEEL Limon. Cort.

(lĭ-mō'nĭs cŏr'tĕx)

"The outer rind of the fresh ripe fruit of *Citrus medica Limonum* (Risso) Hooker filius (Fam. *Rutaceæ*)." *U. S.* "Lemon Peel is the fresh outer part of the pericarp of the fruit of Citrus medica, *Linn.,* var. β Limonum, *Hook. f.*" *Br.*

Limonis Pericarpium; Ecorce (Zeste) de Citron, de Limon, *Fr. Cod.;* Cortex Citri Fructus, *P. G.;* Citronenschale, Limonenschale *G.;* Scorza di Limone, *It.*

For some general remarks on the genus *Citrus,* see *Aurantii Cortex.*

Citrus medica, or lemon tree, closely resembles *Citrus Aurantium,* before described. The leaves, however, are larger, slightly indented at the edges, and stand upon footstalks which are destitute of the winged appendages that characterize the other species. The flowers, moreover, have a purplish tinge on their outer surface, and the fruit is different in appearance from the orange. There are several varieties of *Citrus medica,* which some botanists consider as distinct species, but which scarcely differ except in the character of their fruits. Those particularly deserving of notice are the citron, lemon, and lime. 1. In the *citron, C. medica genuina* (*Bentley & Trimen,* p. 53), the fruit is very large, sometimes six inches in length, ovoid, with a double rind, of which the outer layer is yellowish, thin, unequal, rugged, with innumerable vesicles filled with essential oil; the inner is white, very thick and spongy. It is divided in the interior into nine or ten loculi, filled with small oblong vesicles, which contain an acid juice precisely like that of the lemon, and used for the same purposes. The rind is applied to the preparation of conserves to which it is adapted by its thickness. The fruit is called *cédrat* by the French. 2. The *lemon, C. medica,* var. *Limonum* (*Citrus Limonum* of Risso) (*Bentley & Trimen,* p. 54) is smaller than the preceding, with a smoother and thinner rind, a pointed nipple-shaped summit, and a very juicy, acid pulp. In other respects it closely resembles the citron, to which, however, it is usually preferred in consequence of the greater abundance of its juice. 3. The *lime* is still smaller than the lemon, with a smoother and thinner rind, oval, rounded at the extremities, of a pale-yellow or greenish-yellow color, and abounding in a very acid juice, which renders it highly useful for the purposes to which the lemon is applied. It is the product of *C. medica acida.* According to E. M. Holmes the West India limes are much richer in acid than are those produced in the South of Europe; the juice of the spineless variety was found to contain 37.73 grains per ounce; the ordinary West India lime 36.15 grains per ounce; the Sicily lime 30.32 grains per ounce. Lime juice is recognized by the N. F. IV under the name *Succus Citri.*

The *Citrus medica,* like the orange-tree, is a native of Asia. It is now known to grow wild in Northern India, and was introduced into Europe from Persia or Media. It was first cultivated in Greece, afterwards in Italy, as early as the second century, and has now spread over the whole civilized world, being raised by artificial heat where the climate is too cold to admit of its exposure during winter to the open air.

Properties.—The exterior rind of the lemon has a fragrant odor, and a warm, aromatic bitter taste, somewhat similar to that of the orange, though less agreeable. It is usually found in narrow, thin bands, with very little of the spongy, white, inner layer adhering to it, and is officially described as follows: "The outer, lemon-yellow or dark yellow layer, recently separated by grating or paring and consisting of an epidermal layer, numerous parenchyma cells containing yellow chromoplastids, and large oil reservoirs with globules of the volatile oil; odor highly fragrant, distinctive; taste pungent, aromatic. Under the microscope, sections of the rind, mounted in a fixed oil, show an epidermal layer composed of small tabular cells, a hypodermal layer containing numerous plastids, a mesocarp with colorless, thin-walled parenchyma and large, elliptical oil reservoirs; parenchyma cells containing a layer of granular protoplasm adhering to the walls and occasionally membrane crystals of calcium oxalate,

which are irregularly polygonal in shape, and from 0.015 to 0.025 mm. in diameter." *U. S.*

"Outer surface pale yellow and more or less rough; with only a small amount of the white spongy part of the pericarp on the inner surface; in transverse section numerous large oil-glands below the epidermis. Strong, characteristic and fragrant odor; taste aromatic and bitter." *Br.*

It contains a bitter principle, and yields, by expression or distillation, an essential oil, which is much used for its flavor. Both this and the rind itself are recognized in the Pharmacopœias. (See *Oleum Limonis.*) When the white, spongy portion of the rind is boiled in water, and the decoction evaporated, crystals are deposited of a substance called *hesperidin.* This is a glucoside, and has the formula $C_{22}H_{26}O_{12}$, and is decomposed by diluted acids into *hesperetin,* $C_{16}H_{14}O_6$, and glucose, $C_6H_{12}O_6$. It turns dingy black when gently warmed with alcoholic solution of ferric chloride. It is bitter, but as it is found most largely in the spongy and comparatively tasteless part of the rind, it may be doubted whether it is entitled to be considered as the active bitter principle. (See *A. J. P.,* xxvi, 553.) Lemon peel yields its virtues to water, wine, and alcohol. E. G. Clayton (*An.,* xix, 134) calls attention to the distinction between lemon peel and orange peel when moistened by strong hydrochloric acid. Orange peel under these circumstances changes in color from a yellow to a rich dark green color, while lemon peel retains its hue or assumes a dingy yellowish-brown tint.

The German Pharmacopœia under the title of *Cortex Citri Fructus* requires that the lemon peel be derived from the completely developed but not fully ripe fruits of *Citrus medica* L.

Uses.—The rind of the lemon is sometimes used to qualify the taste and increase the power of stomachic infusions and tinctures.

Off. Prep.—Tinctura Limonis Corticis, *U. S.* (*Br.*); Infusum Aurantii Compositum, *Br.;* Syrupus Limonis, *Br.*

LINIMENTA

LINIMENTS

(lĭn-ĭ-mĕn'tą)

Embrocations; Liniments, Embrocations, *Fr.;* Linimenta, Linimente, Einreibungen, *G.*

These are preparations intended for external use, of such a consistence as to render them conveniently applicable to the skin by gentle friction with the hand.

LINIMENTUM ACONITI. Br.

LINIMENT OF ACONITE

(lĭn-ĭ-mĕn'tŭm ăc-ǫ-nī'tī)

"Liniment of Aconite contains in 100 millilitres 0.2 gramme of the ether-soluble alkaloids of Aconite Root." *Br.*

Liniment d'Aconit, *Fr.;* Akonitliniment, *G.*

"Aconite Root, in No. 40 powder, 500 *grammes;* Camphor, Alcohol (90 per cent.), of each, *a sufficient quantity.* Moisten the Aconite Root with part of the Alcohol, pack in a percolator, and percolate with more of the Alcohol until the Root is exhausted. Reserve the first seven hundred and fifty *millilitres* of the percolate; evaporate the remainder to a syrup and add it to the reserved portion. Determine the weight of ether-soluble alkaloids in fifteen *millilitres* of the tincture thus obtained by the process described under 'Aconiti Radix.' Add to the remainder of the tincture sufficient of the Camphor and of the Alcohol to produce a Liniment of Aconite containing in 100 millilitres 0.2 gramme of the ether-soluble alkaloids of Aconite Root and 3 grammes of Camphor. Examined by the foregoing process Liniment of Aconite is found to contain in 100 *millilitres* 0.2 gramme of the ether-soluble alkaloids of Aconite Root. *Limit of error* 0.01 gramme in excess or defect." *Br.*

This preparation of the British Pharm., 1914, is now made of a definite strength through the introduction of an assay process. It is a very strong tincture of aconite root with camphor; that of the U. S. P., 1870, was almost equivalent to a fluidextract of aconite.

Uses.—Either may be applied alone by means of a camel's-hair pencil, or in connection with two parts or more of soap liniment or chloroform liniment, by rubbing it on the part affected. It must be used with caution lest sufficient aconite be absorbed through the skin to cause poisoning.

LINIMENTUM AMMONIÆ. U. S., Br.

AMMONIA LINIMENT Lin. Ammon. [Volatile Liniment, Hartshorn Liniment]

(lĭn-ĭ-mĕn'tŭm ąm-mō'nī-æ)

Liniment of Ammonia, Linimentum volatile, Linimentum ammoniacale; Liniment ammoniacal (volatil), *Fr. Cod.;* Savon ammoniacal, *Fr.;* Linimentum Ammoniatum, *P. G.;* Flüchtiges Liniment, Flüchtige Salbe, *G.;* Linimento ammoniacale, *It.;* Linimento amoniacal, *Sp.*

* "Ammonia Water, *two hundred and fifty mils* [or 8 fluidounces, 218 minims]; Sesame Oil, *seven hundred and fifty mils* [or 25 fluidounces, 173 minims], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Agitate the ammonia water with the sesame oil until a uniform mixture is obtained." *U. S.*

"Solution of Ammonia, 250 *millilitres;* Almond Oil, 250 *millilitres;* Olive Oil, 500 *millilitres.* Shake together." *Br.*

The process of the U. S. Pharmacopœia IX differs from that of the U. S. P. VIII not only in the proportion of ammonia water, which has been slightly reduced, but in the substitution of sesame oil for cottonseed oil. The British preparation is made with almond oil and olive oil with the proviso that "in India, and in the Eastern, African, Australasian, and North American Divisions of the Empire, Arachis Oil or Sesame Oil, but no other oil or fat, may be employed in making the official

Liniments, Plasters, Ointments, and Soaps for which Olive Oil is directed to be used." *Br.*

The U. S. and British Pharmacopœias agree at present very nearly in the strength of this liniment. In the process, the ammonia reacts with the oil to form a soap, which is partly dissolved, partly suspended in the water, producing a white, opaque emulsion. The liniment is an excellent rubefacient, with the added advantage of being relatively inexpensive, in *inflammatory affections of the throat,* in *catarrhal and other pectoral complaints of children,* and in *rheumatic pains.* It is applied by rubbing it, or placing a piece of flannel saturated with it, over the affected part. Should it occasion too much inflammation, it must be diluted with oil.

LINIMENTUM BELLADONNÆ. U. S., Br.

BELLADONNA LINIMENT Lin. Bellad.

(lĭn-ĭ-mĕn'tŭm bĕl-la-dŏn'næ)

Liniment of Belladonna; Liniment de Belladone, *Fr.;* Belladonnaliniment, *G.*

* " Camphor, *fifty grammes* [or 1 ounce av., 334 grains]; Fluidextract of Belladonna Root, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the Camphor in about *eight hundred mils* [or 27 fluidounces, 24 minims] of the Fluidextract, and then add enough of the latter to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly." *U. S.*

" Liquid Extract of Belladonna, 500 *millilitres;* Camphor, 50 *grammes;* Distilled Water, 100 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Dissolve the Camphor in three hundred *millilitres* of the Alcohol; add the Liquid Extract of Belladonna, the Distilled Water, and sufficient of the Alcohol to produce the required volume. Set aside for twenty-four hours; filter." *Br.*

The two liniments are not identical in strength. The U. S. P. fluidextract of belladonna representing in 100 mils 0.45 Gm. of mydriatic alkaloids, while the British Pharm., 1914, requires liquid extract of belladonna to contain 0.75 Gm. of mydriatic alkaloids; but it will be observed that in the British liniment the liquid extract of belladonna is diluted with alcohol and water, so that the difference in strength will not be important for a preparation to be used externally.

The process for this liniment in both Pharmacopœias has been improved by using an assayed fluidextract.

LINIMENTUM CALCIS. U. S., Br.

LIME LINIMENT Lin. Calc. [Carron Oil]

(lĭn-ĭ-mĕn'tŭm căl'cĭs)

Liniment of Lime; Liniment calcaire, *Fr. Cod.;* Savon calcaire, *Fr.;* Kalkliniment, *G.;* Linimento de calce, *It.;* Linimento Oleo-calcareo, *Sp.*

* " Solution of Calcium Hydroxide, *five hundred mils* [or 16 fluidounces, 435 minims]; Linseed Oil, *five hundred mils* [or 16 fluidounces, 435 minims], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix them by agitation." *U. S.*

" Solution of Lime, 500 *millilitres;* Olive Oil, 500 *millilitres.* Shake together." *Br.*

The lime forms a soap with the oil, of which there is a great excess, that separates upon standing. Olive oil, as directed by the British Pharmacopœia, is often substituted for that of flaxseed, which was originally used, but it possesses no other advantage than that of having a less unpleasant odor and of being somewhat less expensive. The use of cottonseed oil in the U. S. P., 1880, did not meet the expectations of those who proposed it, and the U. S. P., 1890, reinstated linseed oil. This is a very useful application in recent *burns* and *scalds,* when smeared thickly upon lint or cotton batting. It is sometimes called *Carron oil,* from having been much employed at the Carron iron works in Scotland. It relieves the pain by excluding the air and restoring alkalinity in the burnt area.

LINIMENTUM CAMPHORÆ. U. S., Br.

CAMPHOR LINIMENT Lin. Camph. [Camphorated Oil]

(lĭn-ĭ-mĕn'tŭm căm'phŏ-ræ)

" *One hundred grammes* of Liniment of Camphor yields not less than 19.5 Gm. nor more than 20.5 Gm. of Camphor. This preparation is not intended for hypodermic use." *U. S.*

Liniment of Camphor, Linimentum Camphoratum; Huile camphrée, *Fr. Cod.;* Liniment camphré, *Fr.;* Kampherliniment, Kampheröl, *G.*

* " Camphor, in coarse powder, *two hundred grammes* [or 7 ounces av., 24 grains]; Cottonseed Oil, *eight hundred grammes* [or 28 ounces av., 96 grains], to make *one thousand grammes* [or about two pints]. Introduce the cottonseed oil into a suitable flask or bottle, heat it on a water bath, introduce the camphor and stopper the container securely. Dissolve the camphor by agitation without the further application of heat.

" **Assay.**—Weigh 25 Gm. of Camphor Liniment into a tared 150 mil flask and connect this flask with a 500 mil distillation flask containing 275 mils of alcohol. Adjust the tube from the distillation flask so that it reaches to within 0.5 cm. of the bottom of the flask containing the Liniment and connect the latter flask with a condenser. Now heat both flasks on sand baths and regulate the temperature so that the alcohol vapors will pass rapidly through the Liniment without condensing. Receive the distillate in a flask graduated to 250 mils and continue the distillation until at 25° C. (77° F.) the distillate measures 250 mils. Fill a 200 mm. polariscope tube with the distillate and take the mean of four or more readings of the rotation, beginning at zero each time. The temperature correction for each degree is half a minute, additive if above, subtractive if below

25° C. (77° F.). Place about 20 Gm. of the Camphor Liniment in an evaporating dish, 9 cm. in diameter, and cover it with an inverted funnel 8 cm. in diameter. Place the dish on wire gauze, 10 cm. above a Bunsen burner having a flame 4 cm. high. When the camphor has all sublimed, dissolve 0.5 Gm. of the sublimate in sufficient alcohol to make exactly 25 mils at 25° C. (77° F.), and take the mean of four or more polariscope readings as before. The minutes of rotation of the distillate divided by the minutes of rotation of the control test just made, and this multiplied by 20, will give the number of grammes of camphor in 100 Gm. of Camphor Liniment." *U. S.*

"Camphor, in flowers, 200 *grammes;* Olive Oil, 800 *grammes.* Dissolve the Camphor in the Olive Oil in a closed vessel." *Br.*

S. D. Wetterstroem prefers cold solution to the official method, thus avoiding any loss of camphor. (*West. Drug.,* 1897, 68.) For methods of assaying camphor liniment, see *C. D.,* 1900, 338; *P. J.,* 1898, 545; *P. J.,* 1902, 106; *Am. Drug.,* 1905, 345.

Uses.—This liniment is a very popular counter-irritant embrocation in *sprains, bruises, rheumatism, acute bronchitis,* and various other inflammatory states. Camphor liniment should not be confounded with camphorated oil of the German Pharmacopœia which is much weaker (1 in 10).

For fatal case of poisoning from swallowing this liniment, see Barker, *B. M. J.,* 1910, ii, p. 921.

The term "camphorated oil" is sometimes applied to the solution of camphor in olive oil intended for hypodermic use; the liniment of camphor must not be used for this purpose.

Off. Prep.—Linimentum Chloroformi, *Br.;* Linimentum Hydrargyri, *Br.;* Linimentum Terebinthinæ Aceticum, *Br.;* Ceratum Camphoræ, *N. F.*

LINIMENTUM CAMPHORÆ AMMONIATUM. Br.

AMMONIATED LINIMENT OF CAMPHOR

(lĭn-ĭ-mĕn'tŭm căm'phŏ-ræ ăm-mŏ-nī'ă-tŭm)

Compound Liniment of Camphor, *Br.;* Liniment ammoniacal camphré, *Fr. Cod.;* Linimentum ammoniato-camphoratum, *P. G.;* Flüchtiges Kampherliniment, Ammoniak- und Kampher-Liniment, *G.;* Linimento ammoniacale canforato, *It.;* Linimento amoniacal alcanforado, *Sp.*

"Camphor, 125 *grammes;* Oil of Lavender, 5 *millilitres;* Strong Solution of Ammonia, 250 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Dissolve the Camphor and Oil of Lavender in six hundred *millilitres* of the Alcohol; add the Strong Solution of Ammonia gradually, shaking frequently; finally add sufficient of the Alcohol to produce the required volume." *Br.*

This is inferior to the camphor liniment because the absence of a lubricant makes rubbing difficult.

LINIMENTUM CHLOROFORMI. U. S., Br.

CHLOROFORM LINIMENT Lin. Chlorof.

(lĭn-ĭ-mĕn'tŭm ȼhlō-rŏ-fōr'mī)

Liniment of Chloroform; Liniment au Chloroforme, *Fr. Cod.;* Chloroformliniment, *G.*

* "Chloroform, *three hundred mils* [or 10 fluidounces, 69 minims]; Soap Liniment, *seven hundred mils* [or 23 fluidounces, 321 minims], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix them by agitation." *U. S.*

"Chloroform, 500 *millilitres;* Liniment of Camphor, 500 *millilitres.* Mix." *Br.*

A very great improvement was made in this preparation by the Committee of Revision of 1880, in the substitution of soap liniment for the olive oil. This change had been proposed in a previous edition of the Dispensatory, and it was desirable on account of the greasy residue which was left on the skin by the old preparation. The British Pharmacopœia has retained the oily vehicle. This is an excellent local application in painful affections. As the chloroform rapidly evaporates, it is desirable, in order to obtain its full counter-irritant effect, to guard against this by using waxed paper, or some other impermeable covering.

An accurate and expeditious method of assaying this liniment for its chloroform content is suggested by Jos. L. Mayer (*Proc. N. Y. S. P. Assn.,* 1912, p. 295), which consists in distilling the chloroform and collecting it in a graduated cylinder containing distilled water. The chloroform is measured when it ceases to come over and the calculation readily made.

LINIMENTUM CROTONIS. Br.

LINIMENT OF CROTON OIL

(lĭn-ĭ-mĕn'tŭm crŏ-tō'nĭs)

Linimentum Tiglii, *N. F. IV;* Liniment crotoné, *Fr.;* Krotonölliniment, *G.*

"Croton Oil, 120 *millilitres;* Oil of Cajuput, 440 *millilitres;* Alcohol (90 per cent.), 440 *millilitres.* Mix." *Br.*

This liniment is slightly weaker than that of the former British Pharmacopœia, but is almost identical with *Linimentum Tiglii* of N. F. IV (see Part III).

This is a pustulating preparation, the irritant influence of which has been increased by the substitution of the oil of cajuput and alcohol for the olive oil of the original formula. From ten to thirty minims (0.6–1.8 mils) may be rubbed upon a limited surface, and repeated twice a day or oftener until an eruption is produced.

LINIMENTUM HYDRARGYRI. Br.

LINIMENT OF MERCURY

(lĭn-ĭ-mĕn'tŭm hȳ-drăr'gy-rī)

Linimentum Mercuriale; Liniment mercuriel, *Fr.;* Quecksilberliniment, *G.*

"Ointment of Mercury, 50 *grammes;* Solution of Ammonia, 40 *millilitres;* Liniment of Camphor, 80 *millilitres.* Shake the Solution of Ammonia with the Liniment of Camphor, and

triturate the Ointment of Mercury with the mixture. This Liniment contains approximately three-fifths of the proportion of Mercury contained in the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

This is a stimulating liniment, employed for both its local and constitutional effects in *syphilitic pains,* in *glandular enlargements, swellings of the joints,* and to promote the absorption of fluid. It is said to be more likely to salivate than is mercurial ointment. One fluidrachm (3.75 mils) may be rubbed upon the affected part night and morning. It should be thoroughly agitated before being applied.

LINIMENTUM OPII. Br.

LINIMENT OF OPIUM

(lĭn-ĭ-mĕn'tŭm ō'pĭ-ī)

Anodyne Liniment; Liniment opiacé, *Fr.;* Opiumliniment, *G.*

"Tincture of Opium, 500 *millilitres;* Liniment of Soap, 500 *millilitres.* Mix; set aside for a few days; filter." *Br.*

We are informed that the preparation which has been commonly used under the name of *anodyne liniment* is that of the late London Pharmacopœia, as given in former editions of the *U. S. Dispensatory,* consisting of one part by measure of tincture of opium and three parts of soap liniment, and consequently having only half the opiate strength of the present British liniment. The use of this class of preparations is founded on error, as opium is not efficient as a local remedy.

LINIMENTUM POTASSII IODIDI CUM SAPONE. Br.

LINIMENT OF POTASSIUM IODIDE WITH SOAP

(lĭn-ĭ-mĕn'tŭm pŏ-tăs'sĭ-ī ī-ŏd'ĭ-dī cŭm sā-pō'nē)

Liniment savonneux ioduré, *Fr.;* Jodkalium-Seifenliniment, *G.*

"Curd Soap, recently prepared and in shavings, 40 *grammes;* Potassium Iodide, 30 *grammes;* Glycerin, 20 *millilitres;* Oil of Lemon, 2 *millilitres;* Distilled Water, 200 *millilitres.* Mix the Curd Soap with the Distilled Water and Glycerin in a tared porcelain dish on a water-bath; when the Soap is dissolved make up to the original weight with Distilled Water; pour the liquid into a mortar containing the Potassium Iodide, previously powdered; mix briskly by trituration; continue the trituration until the mixture is cold, set aside for an hour; then add the Oil of Lemon, and again triturate the gelatinous product." *Br.*

This preparation is apparently intended, by application to the surface, which may be attended with a gentle friction, to produce the absorption of the iodide, and thus to obtain its alterative and deobstruent effects through the circulation. The soap and glycerin act as demulcents, and thus obviate in some measure the local irritation of the salt.

LINIMENTUM SAPONIS. U. S., Br.

SOAP LINIMENT Lin. Sapon. [Liquid Opodeldoc]

(lĭn-ĭ-mĕn'tŭm sā-pō'nĭs)

Tinctura Saponis Camphorata, *U. S.* 1850; Spiritus Nervinus Camphoratus; Camphorated Tincture of Soap; Liniment savonneux camphré, *Fr.;* Linimentum saponato camphoratum, *P. G.;* Flüssiger Opodeldok, *G.;* Linimento di sapone con canfora, *It.*

* "Soap, dried and granulated or powdered, *sixty grammes* [or 2 ounces av., 51 grains]; Camphor, in small pieces, *forty-five grammes* [or 1 ounce av., 257 grains]; Oil of Rosemary, *ten mils* [or 162 minims]; Alcohol, *seven hundred mils* [or 23 fluidounces, 321 minims]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the camphor and the oil of rosemary in the alcohol, add the soap and sufficient water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Agitate the mixture until the soap is dissolved, set it aside in a cool place for twenty-four hours, and then filter." *U. S.*

"Soft Soap, 80 *grammes;* Camphor, 40 *grammes;* Oil of Rosemary, 15 *millilitres;* Distilled Water, 170 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Dissolve the Soap, Camphor, and Oil of Rosemary in six hundred *millilitres* of the Alcohol; add the Distilled Water and sufficient of the Alcohol to produce the required volume; set aside for a week; filter." *Br.*

This process is intended to furnish a saturated solution of Castile soap. The recommendation in the 16th edition of this Dispensatory, that granulated soap be used in preference to soap in shavings in this liniment, was adopted by the U. S. Pharmacopœia, Eighth Revision, for powdered soap does not vary greatly in the proportion of water left in it; the process is one recommended by Geo. W. Sloan, of Indianapolis, and if all the details are carefully followed it is a great improvement over that of the U. S. Pharmacopœia 1880. The improvement was made in the eighth revision of the U. S. P. of making a gelatinous mass of the soap by adding it to sufficient boiling water and heating it until dissolved; the soft mass easily dissolves in the alcoholic solution of the oils, but in the U. S. P. IX process the granulated or powdered soap is added to the alcohol and when the water is introduced solution occurs almost at once. The liquid should be cold before filtration to avoid precipitation in cold weather. The British preparation is now made with soft (potash) soap; this method was recommended by J. T. Hornblower. (*C. D.,* 1894, 571.) The liniment is said to be made more quickly and precipitation is avoided. Although olive oil contains a large percentage of olein, yet it has been proposed to substitute almond oil, for it is still richer. A formula for making almond oil soap on the small scale may be found in *P. J.,* 2d ser., xi, 417. The economy of this is, however, very doubtful. Castor oil has also been suggested. (*A. J. P.,* xliv, 529.) G. W. Barckhausen states that the potassa soaps are per-

fectly soluble in alcohol, and suggests rape seed oil as a good base. (*A. J. P.*, 1873, p. 17.)

Any pharmaceutical difficulty encountered in making a satisfactory preparation by the official formula can usually be attributed to the use of soap which is not in compliance with the official requirements.

The 1850 edition of the U. S. Pharmacopœia recognized under the title *Linimentum Saponis Camphoratum* a semi-solid preparation which had a wide popularity under the name *opodeldoc.* (See *N. F.*, Part III.) Older formulas for this preparation are well represented by the U. S. P., 1850, process as follows:

Opodeldoc.—"Take of Common Soap (made from animal oil), sliced, *three ounces;* Camphor *an ounce;* Oil of Rosemary, Oil of Origanum, each, *a fluidrachm;* Alcohol *a pint.* Digest the Soap with the Alcohol, by means of a sand-bath, till dissolved; then add the Camphor and Oils, and, when they are dissolved, pour the liquid into broad-mouthed bottles. This liniment has, when cold, the consistence of a soft ointment." *U. S. P.*, 1850.

This preparation differs from the official Linimentum Saponis chiefly in being prepared with common white soap, made with animal fat, instead of Castile soap, which is made of olive oil. The former is peculiarly adapted to the purposes of this formula, in consequence of assuming, when its alcoholic solution cools, the consistence characteristic of the liniment. It is customary after the solution of the soap has been effected to pour the liquid into small wide-mouthed glass bottles, containing about four fluidounces, in which it concretes into a soft, translucent, uniform, yellowish-white mass. This liniment melts with the heat of the body.

Soap liniment is much used, as an anodyne and gently rubefacient embrocation, in *sprains, bruises,* and *rheumatic* or *gouty pains.*

Off. Prep.—Linimentum Chloroformi, *U. S.;* Linimentum Opii, *Br.;* Linimentum Aconiti et Chloroformi, *N. F.*

LINIMENTUM SAPONIS MOLLIS. U. S.

LINIMENT OF SOFT SOAP Lin. Sapon. Moll. [Tincture of Green Soap]

(lĭn-ĭ-mĕn'tŭm sā-pō'nĭs mŏl'lĭs)

Tinctura Saponis Virdis, *U. S. P.* 1880; Spiritus Saponis Kalini Hebra; Teinture de Savon vert, *Fr.;* Hebra's Seifenspiritus, *G.*

* "Soft Soap, *six hundred and fifty grammes* [or 22 ounces av., 406 grains]; Oil of Lavender, *twenty mils* [or 325 minims]; Alcohol, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the oil of lavender with *three hundred mils* [or 10 fluidounces, 69 minims] of alcohol, dissolve in this the soft soap by stirring or agitation, and set the solution aside for twenty-four hours. Then filter it through paper, adding sufficient alcohol to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

This is the *tincture of green soap* of Hebra under a new name; it should never have been called Tinctura Saponis Viridis, as it belongs clearly in the class of liniments and is always used externally. C. E. Smith suggested the preparation of this liniment from the fixed oil directly, which has the advantage of convenience as well as of greater uniformity of strength. (See *U. S. D.*, 19th ed., p. 698.) If a green color is desirable in this preparation, it may be obtained by using hemp seed oil or Malaga olive oil. (See *Proc. A. Ph. A.*, 1903, 420.)

LINIMENTUM SINAPIS. Br.

LINIMENT OF MUSTARD

(lĭn-ĭ-mĕn'tŭm sĭ-nā'pĭs)

Linimentum Sinapis Compositus, *N. F.;* Liniment Sinapisé composé, *Fr.;* Zusammengesetztes Senfliniment, Senfliniment, *G.*

"Volatile Oil of Mustard, 35 *millilitres;* Camphor, 55 *grammes;* Castor Oil, 125 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Dissolve the Camphor and the Oils in the Alcohol." *Br.*

The N. F. preparation differs from the Br. in containing fluidextract of mezereum in addition to the mustard oil and camphor (see Part III). It affords a convenient method of applying the volatile oil of mustard, and may often be appropriately used as a substitute for sinapisms. The castor oil seems to be added in order to increase somewhat the consistence of the liniment, and was probably chosen from among oleaginous substances in consequence of its solubility in alcohol. The effect is increased if the liniment be applied on flannel, and volatilization guarded against by covering it with oiled silk.

LINIMENTUM TEREBINTHINÆ. U. S., Br.

TURPENTINE LINIMENT Lin. Terebinth. [Kentish's Ointment]

(lĭn-ĭ-mĕn'tŭm tĕr-ĕ-bĭn'thĭ-næ)

Linimentum Terebinthinatum; Liniment of Turpentine; Liniment térébenthiné, *Fr.;* Terpentinliniment, *G.*

* "Rosin Cerate, *six hundred and fifty grammes* [or 22 ounces av., 406 grains]; Oil of Turpentine, *three hundred and fifty grammes* [or 12 ounces av., 151 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Dissolve the Rosin Cerate, previously melted in a dish on a water-bath, in the Oil of Turpentine, and mix them thoroughly." *U. S.*

"Soft Soap, 75 *grammes;* Camphor, 50 *grammes;* Rectified Oil of Turpentine, 650 *millilitres;* Distilled Water sufficient to produce 1000 *millilitres.* Mix the Soft Soap with one hundred *millilitres* of the Distilled Water; dissolve the Camphor in the Oil of Turpentine; gradually add the latter solution to the former, triturating until the mixture becomes a thick creamy emulsion; add sufficient Distilled Water to produce the required volume." *Br.*

The U. S. preparation is the liniment originally proposed by Kentish, and subsequently so highly lauded as a remedy in *burns* and *scalds.* It should be applied as soon after the occurrence of the accident as possible, and

should be discontinued when the peculiar inflammation excited by the fire is removed. The best mode of application is to cover the burnt or scalded surface with pledgets of gauze saturated with the liniment. It should not be allowed to come in contact with the sound parts. This liniment may also be successfully applied in other cases of cutaneous inflammation requiring stimulation, as in certain conditions of *erysipelas*. The present British preparation, so far as regards its rubefacient operation, may be looked upon as almost undiluted oil of turpentine, the soft soap having little other effect than to give consistence to the liniment, and the camphor acting as an anodyne, and both being too small in bulk to dilute the oil materially.

LINIMENTUM TEREBINTHINÆ ACETICUM. Br.

LINIMENT OF TURPENTINE AND ACETIC ACID

(lĭn-ĭ-mĕn'tŭm tĕr-ĕ-bĭn'thĭ-næ ą-cĕt'ĭ-cŭm)

Linimentum Album; Acetic Turpentine Liniment, Stokes' Liniment; Liniment térébenthiné acétique, *Fr.*; Terpentin- und Essig-liniment, *G.*

"Glacial Acetic Acid, 110 *millilitres;* Liniment of Camphor, 445 *millilitres;* Rectified Oil of Turpentine sufficient to produce 1000 *millilitres.* Mix." *Br.*

Under this name the National Formulary IV (see Part III) contains a formula for *St. John Long's Liniment,* which unfortunately is not identical with the process of the British Pharm., 1914.

This is a powerful rubefacient liniment, combining the irritant properties of the oil of turpentine and acetic acid, though somewhat diluted by the camphor liniment. Glacial acetic acid was substituted for acetic acid in the 1885 revision in equivalent proportion; the change is an improvement pharmaceutically, as it now affords a clear solution.

LINUM. U. S. (Br.)

LINSEED [Flaxseed]

(lī'nŭm)

"The ripe seeds of *Linum usitatissimum* Linné (Fam. *Linaceæ*), without the presence or admixture of more than 3 per cent. of other seeds or foreign matter. Preserve it in tightly-closed containers and add a few drops of carbon tetrachloride or chloroform from time to time to prevent attack by insects." *U. S.* "Linseed consists of the dried ripe seeds of Linum usitatissimum, *Linn.*" *Br.*

Lini Semina, *Br.;* Semence de Lin, *Fr. Cod.;* Grains de Lin, *Fr.;* Semen Lini, *P. G.;* Leinsamen, Flachssamen, *G.;* Lino, Semi di Lino, *It.;* Lino (Semilla de), Linaza, *Sp.*

Off. Prep.—Lini Semina Contusa, *Br.;* Species Emollientes, *N. F.*

LINI SEMINA CONTUSA. Br.

CRUSHED LINSEED

(lī'nī sĕ-mī-ną cŏn-tū'są)

"Crushed Linseed is Linseed reduced to a coarse powder. It should be recently prepared." *Br.*

Linum Contusum, *Br.* 1898; Crushed Flaxseed.

Common *flax* is an annual plant, with an erect, slender, round stem, about two feet in height, branching at top, and, like all other parts of the plant, entirely smooth. The leaves are small, lanceolate, acute, entire, of a pale-green color, sessile, and scattered alternately over the stem and branches. The flowers are terminal, and of a delicate-blue color. The calyx is persistent, and composed of five ovate, sharp-pointed, three-nerved leaflets, which are membranous on their border. The petals are five, obovate, striated, minutely scalloped at their extremities, and spread into funnel-shaped blossoms. The filaments are also five, united at the base, and the germ, which is ovate, supports five slender styles, terminating in obtuse stigmas. The fruit is a globular capsule, about the size of a small pea, having the persistent calyx at the base, crowned with a sharp spine, and containing ten seeds in distinct cells. This highly valuable plant, now almost everywhere cultivated, is said by some to have been originally derived from Egypt, by others from the great elevated plain of Central Asia. It flowers in June and July, and ripens its seed in August.

The flax plant was cultivated for its fiber by the American colonists soon after the landing of Columbus. Soon thereafter it was grown for its seed and already in 1792 the United States exported nearly 300,000 bushels of flaxseed. Very early the linseed oil industry was developed in the United States and in 1810 there were nearly 300 linseed oil mills in the 14 states, more than half of them being in Pennsylvania. It is estimated that at the present time 12,000,000 bushels of seed are crushed annually for the oil. The annual crop of flaxseed in the United States approximates 30,000,000 bushels. A large quantity of seed is annually exported as well as oil-cake, the latter being extensively used as a cattle food.

Properties.—The official description of flaxseed is as follows: "Ovate or oblong-lanceolate, flattened, obliquely pointed at one end, from 3 to 5 mm. in length; externally chestnut-brown, very smooth and shiny, the raphe extending as a distinct, light-yellow ridge along one edge; easily cut with the finger-nail; internally olive-green; oily; odor slight; taste mucilaginous and oily. Under the microscope, transverse sections of Linseed when mounted in hydrated chloral T.S. show an epidermis with a mucilaginous layer from 0.01 to 0.03 mm. in thickness, covered by a very thin layer of cutin which is often more or less broken; two layers of parenchyma which overlie a continuous ring of stone cells having yellowish, porous walls and rather large lumina; a pigment layer, the cells having a reddish-brown content; an endosperm consisting of from 6 to 10 rows of cells surrounding the two large plano-convex cotyledons; the cells of both the endosperm and the cotyledons contain a fixed oil and aleurone grains, the latter being from 0.003 to 0.02 mm. in diameter." *U. S.*

"Seeds small, brown, glossy, nearly flat; from

about four to six millimetres long; ovate, somewhat obliquely pointed; surface glabrous and minutely pitted. Internally yellowish-white, with a narrow oily endosperm and two large oily cotyledons. Epidermal cells filled with mucilage which swells and dissolves in *water*. No odor; taste mucilaginous, oily." *Br.*

The linseeds in commerce have been divided by E. M. Holmes into two groups. The first group, characterized by the seeds being of sufficient size for six or seven to weigh a grain, contains Bombay, Bold Calcutta, Sicilian, and Ionian seed; in the group of small seeds (10 to 12 to the grain) are English, Dutch, Russian, and ordinary Calcutta varieties. An important practical point noticed by Holmes is that much of the drug of commerce is adulterated with weed seeds, which are nearly always smaller than the linseeds, and can therefore be separated by the sieve. When linseed meal is to be made for medicinal use, this separation should always be insisted upon, as many of the weed seeds are from Cruciferæ, and are irritating. For detailed information as to varieties of linseed, weed seeds, etc., the reader is referred to Holmes's paper. (*P. J.*, July, 1881; also *N. R.*, 1881.)

The ground seeds are found in commerce under the name of *flaxseed meal*. This is of a dark-gray color, highly oleaginous, and when mixed with hot water forms a soft adhesive mass, much employed for luting by practical chemists. "The powder of flaxseed is lemon-yellow or light brown, consisting chiefly of large, oily globules and irregular fragments of endosperm and seed-coat; the seed-coat is characterized by the tabular pigment cells filled with a reddish-brown, insoluble content and the somewhat elongated stone cells with yellowish walls; mounts made from material from which the fixed oil has been removed show aleurone grains from 0.003 to 0.02 mm. in diameter, both free and in the cells of the endosperm and embryo. *Linseed Meal* or *Flaxseed Meal* is light olive-brown with reddish-brown fragments; the latter being very coarse and the cellular tissues are the same as those of the powder. Powdered Linseed or Flaxseed and Linseed Meal or Flaxseed Meal must be free from any unpleasant or rancid odor. The powder, upon extraction with purified petroleum benzin, yields not less than 30 per cent. of a fixed oil, at least 98 per cent. of which is saponifiable. Boil 1 Gm. of the fat-free Linseed or Flaxseed Powder or Meal, with 50 mils of water, cool and filter; the filtrate gives not more than a faint blue color, on the addition of iodine T.S. Linseed yields not more than 6 per cent. of ash." *U. S.*

Crushed flaxseed is "a coarse, brownish-yellow powder, with readily visible fragments of the brown seed-coats. Bland, not pungent or rancid, odor when mixed with warm *water*. Yields not less than 30 per cent. of oil when exhausted by *carbon disulphide;* the oil thus obtained responds to the tests described under 'Oleum Lini'; the residual powder exhibits no starch grains when examined under the microscope. Ash not more than 5 per cent." *Br.*

The average composition of linseed oil cake is thus given by Schaedler (*Technologie der Fette und Oele,* 1883): moisture, 10.56 per cent.; oil, 9.83 per cent.; non-nitrogenous fiber, 44.61 per cent.; ash, 6.5 per cent.; proteid matter, 28.5 per cent.

Much of the linseed meal of commerce is simply cake meal, which was, indeed, official in the former Br. Ph., but such meal is unfit for medicinal use, not only because it contains very little oil, but also because the oil which is in it has, through rupture of the cells and partial expression, been so exposed to the air as to become rancid. Linseed meal is sometimes adulterated with corn meal, or other meals containing starch, whose presence is at once revealed by the iodine test. It is sometimes found in the market adulterated with petroleum or other mineral oil, doubtless made by powerfully pressing the pure linseed meal and substituting for the linseed oil the less expensive product, petroleum. (*A. J. P.*, 1902, 31.)

The absolute value of a sample of crushed linseed can be determined by analysis. It should contain from 25 to 35 per cent. of oil, not more than 8 or 8.5 per cent. of husk, and less than 8 per cent. of ash. The following *test* is said to be sufficient for practical purposes: "Put half an ounce of the meal into a glass vessel, pour six ounces of boiling water over it, stir well, and allow it to stand for twelve hours. If first-class, it should absorb all the water, and show a thin scum of white glutinous liquid on the top, which will adhere closely to a glass rod or a wooden pencil dipped into it. If the meal does not absorb nearly all the water, it is of inferior quality. The amount of inferiority must be judged by the amount of water not absorbed, and by the character of the fluid on the top of the solution. If it is thin and non-glutinous, the meal is of inferior quality."

Meyer found in linseed fixed oil, wax, resin, extractive, tannin, gum, nitrogenous mucilage, starch, albumen, gluten, and various salts. Meurein could find no starch, but detected phosphates, which had escaped the notice of Meyer. (*J. P. C.*, 3e sér., xx, 97.) For some years there has been a discussion concerning the reaction for starch which is sometimes ascertained in commercial flaxseed. Apparently starch grains are not usually present, although it is stated that they may occur in appreciable quantities in the unripe seed. (*Ph. Ztg.*, li, p. 658.) Certain tissues of the seed coat beneath the mucilaginous epidermis may give a starch reaction, and it is stated that even the cells may contain starch. (*Proc. A. Ph. A.*, 1907, lv, p. 326.) Their investing coat abounds in a peculiar gummy matter or mucilage, which is readily imparted to hot water, forming a thick viscid fluid, that lets fall white flakes upon the addition of alcohol, and affords a copious dense precipitate with lead subacetate. The viscid mucilage of linseed cannot be filtered until it has been boiled.

It contains in the dry state more than 10 per cent. of mineral substances; when freed from these and dried at 110° C. (230° F.), it has, like althæa mucilage, the formula $C_{12}H_{20}O_{10}$. The seeds by exhaustion with cold or warm water afford about 15 per cent. of this mucilage. By boiling with nitric acid, it yields crystals of mucic acid; by diluted mineral acids, it is broken up into dextrogyrate gum, sugar, and cellulose. (Kirchner and Tollens, *Ann. Ch. Ph.*, clxxv, 215.) For further information on the histology and pharmacognosy of the flaxseed, see Winton and Moeller, "The Microscopy of Vegetable Foods;" Kate B. Winton, *Bot. Gaz.*, lviii, p. 2445; Collin, *J. P. C.*, 1909, xxix, p. 369.

Jorissen and Hairs (*Drogues Simples*, t. ii, 685) obtained from the young plant a glucoside, to which they gave the name of *linamarin*, which crystallizes in colorless needles, melting at 134° C. (273.2° F.), without odor, but possesses a fresh and bitter taste. It differs from amygdalin in not being decomposed by emulsin, but diluted acids decompose it into sugar, hydrocyanic acid, and a third product which is volatile and possesses certain of the characters of the acetones. No benzaldehyde is formed. Linseed contains about 4 per cent. of nitrogen, corresponding to about 25 per cent. of proteid substances. After expression of the oil these substances remain in the cake, so that the latter contains 5 per cent. of nitrogen and constitutes a very important article for feeding cattle and is termed *cake meal*. The interior of the seed, or nucleus, is rich in a peculiar oil, which is separated by expression, and extensively employed in the arts on account of its drying properties. (See *Oleum Lini.*)

Uses.—Flaxseed is demulcent and emollient. The mucilage obtained by infusing the entire seeds in boiling water, in the proportion of half an ounce to the pint, is much and very advantageously employed in *catarrh, dysentery, nephritic* and *calculous complaints, strangury,* and other inflammatory affections of the mucous membrane of the lungs, intestines, and urinary passages. The whole seed is occasionally given in tablespoonful doses as a laxative. By decoction, water extracts a portion of the oleaginous matter, which renders the mucilage less fit for administration by the mouth, but superior as a laxative enema. The meal mixed with hot water forms an excellent emollient poultice.

LIQUOR ACIDI ARSENOSI. U. S. (Br.)

SOLUTION OF ARSENOUS ACID Liq. Acid. Arsen. [Hydrochloric Solution of Arsenic Solution of Arsenic Chloride]

(lĭ'quŏr ăç'ĭ-dī är-sē-nō'sī)

"An aqueous solution, containing arsenous acid equivalent to not less than 0.975 per cent. nor more than 1.025 per cent. of As_2O_3 (197.92)." *U. S.*

Liquor Arsenici Hydrochloricus, *Br.;* Liquor Arsenici Chloridi, *U. S. P.* 1870; Soluté d'Acide Arsénieux, *Fr. Cod.*; Liqueur de Boudin, Liqueur arsénicale hydrochlorique, *Fr.*; Chlorarsenik-Lösung, *G.*

* "Arsenic Trioxide, *ten grammes* [or 154 grains]; Diluted Hydrochloric Acid, *fifty grammes* [or 1 ounce av., 334 grains]; Distilled Water, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Mix the diluted hydrochloric acid with *two hundred and fifty grammes* [or 8 ounces av., 358 grains] of distilled water, in a tared flask, add the arsenic trioxide, and boil until the arsenic trioxide is completely dissolved. Then allow it to cool, add enough distilled water to make the product weigh *one thousand grammes* [or 35 ounces av., 120 grains] and filter." *U. S.*

"Arsenious Anhydride, in powder, 10 *grammes;* Hydrochloric Acid, 12 *millilitres;* Distilled Water sufficient to produce 1000 *millilitres.* Dissolve the Arsenious Anhydride and the Hydrochloric Acid in five hundred *millilitres* of Distilled Water by the aid of heat; cool; add sufficient Distilled Water to produce the required volume." *Br.*

This solution is stronger than the *Liquor Arsenici Chloridi* of the U. S. P., 1870. The name has also been changed, as the former title was a misnomer. The hydrochloric acid does not enter into combination with the arsenic trioxide; it merely aids in its solution. True arsenic chloride, As_2Cl_6, cannot exist in aqueous solution but is immediately hydrolized into arsenous and hydrochloric acids. The British title is, in our opinion, to be preferred, because the U. S. name does not indicate the presence of the hydrochloric acid.

Properties.—"Solution of Arsenous Acid is a clear, colorless liquid, odorless, having an acidulous taste and an acid reaction. Hydrogen sulphide T.S., added to Solution of Arsenous Acid, produces a lemon-yellow precipitate of arsenic trisulphide which is completely soluble in ammonium carbonate T.S.

"**Assay.**—Dilute about 20 mils of Solution of Arsenous Acid, accurately weighed, with about 50 mils of distilled water, dissolve 2 Gm. of sodium bicarbonate in this solution and titrate with tenth-normal iodine V.S., using starch T.S. as indicator. It shows not less than 0.975 per cent. nor more than 1.025 per cent. of As_2O_3.

"Each mil of tenth-normal iodine V.S. used corresponds to 0.004948 Gm. of As_2O_3. Each gramme of Solution of Arsenous Acid corresponds to not less than 1.97 nor more than 2.07 mils of tenth-normal iodine V.S." *U. S.*

According to the British Pharmacopœia, it is "a colorless liquid; acid to *litmus*. 25 millilitres diluted with *water* discharge the color of 50.4 millilitres of *N/10 solution of iodine,* the presence of a slight excess of *sodium bicarbonate* being maintained throughout the operation. This Solution contains 1 gramme of Arsenious Anhydride in 100 millilitres; 110 minims contain 1 grain." *Br.*

Uses.—The medicinal properties of this solution are the same as those of Fowler's solution, with which it corresponds in strength, being

nearly three times as strong as the former London solution of arsenic chloride.

Dose, from two to eight minims (0.12–0.5 mil).

LIQUOR ACIDI CHROMICI. Br.

SOLUTION OF CHROMIC ACID

(lĭ'quŏr ăç'ĭ-dī ȼhrō'mĭ-cī)

Soluté d'Acide Chromique, *Fr. Cod.;* Chromsaurelösung, *G.*

"Chromic Anhydride, 25 *grammes;* Distilled Water sufficient to produce 100 *millilitres.* Dissolve." *Br.*

This was officially described in the British Pharm., 1898, as "an orange-red, inodorous, caustic, strongly acid liquid. Specific gravity, 1.185. It should respond to the tests described under 'Acidum Chromicum.'"

It is simply a definite solution of chromic anhydride (25 per cent.), and will probably be found convenient as a caustic application. (See *Chromii Trioxidum,* p. 330.) It is not used internally.

LIQUOR ADRENALINI HYDROCHLORICUS. Br.

HYDROCHLORIC SOLUTION OF ADRENALIN

(lĭ'quŏr ăd-rĕn-ą-lī'nī hȳ-drọ-ȼhlō'rĭ-cŭs)

Solution of Adrenalin Hydrochloride; Solution of Epinephrine hydrochloride.

"Adrenalin, 1 *gramme;* Chloroform, 5 *millilitres;* Sodium Chloride, 9 *grammes;* Diluted Hydrochloric Acid, 3 *millilitres;* Distilled Water, recently boiled and cooled, sufficient to produce 1000 *millilitres.* Dissolve the Chloroform and the Sodium Chloride in nine hundred *millilitres* of the Distilled Water, add the Diluted Hydrochloric Acid, dissolve the Adrenalin in the mixture, and add sufficient Distilled Water to produce the required volume. Preserve the Solution in amber glass bottles." *Br.*

Solution of adrenalin hydrochloride devised by Dr. Jokichi Takamine is a protected preparation marketed by Parke, Davis & Co., of Detroit, and has had a large sale throughout the world. The U. S. P. IX could not make it official under the name of adrenalin because it is a proprietary preparation. The British Pharmacopœia, 1914, however, with the consent of the firm introduced the "hydrochloric solution of adrenalin." This solution contains free acid and sodium chloride with a little chloroform to act as a preservative. Care should be used to avoid the presence of iron in compounding prescriptions as it is incompatible. Steel spatulas must not be brought in contact with adrenalin solutions. In fact, it is desirable to prescribe the solution without admixture, and in original containers. C. P. Beckwith in the *Bulletin of Pharmacy,* 1915, page 129, gives an excellent résumé of the incompatibilities of adrenalin solution. (See *Adrenalin,* page 94.)

When adrenalin is to be incorporated with ointments or with oily nasal sprays it is recommended that the oily solution known as *adrenalin inhalent* be used; it contains the same per cent. of adrenalin as the solution. The use of metallic spatulas or containers must be avoided in dispensing such ointments.

For uses of this solution, see *Adrenalinum.*

Dose, five to twenty minims (0.3–1.3 mils).

LIQUOR AMMONII ACETATIS. U. S., Br.

SOLUTION OF AMMONIUM ACETATE Liq. Ammon. Acet. [Spirit of Mindererus]

(lĭ'quŏr ąm-mō'nī-ī ăç-ę-tā'tĭs)

"An aqueous solution containing not less than 7 per cent. of $NH_4C_2H_3O_2$ (77.07), with small amounts of acetic and carbonic acids." *U. S.*

Spiritus Mindereri; Liquor Ammoniæ Acetatis; Acétate d'Ammoniaque liquide, *Fr. Cod.;* Esprit de Mindérérus, *Fr.;* Liquor Ammonii Acetici, *P. G.;* Ammoniumacetatlösung, Essigsaure Ammoniumlösung, *G.*

* "Ammonium Carbonate, *five grammes* [or 77 grains]; Diluted Acetic Acid, *one hundred mils* [or 3 fluidounces, 183 minims]. Add the ammonium carbonate (which must be in hard translucent pieces), gradually to the cold diluted acetic acid, and stir until it is dissolved. This preparation must not be dispensed unless it has been recently prepared." *U. S.*

"Acetic Acid, 162.5 *millilitres;* Ammonium Carbonate, 50.0 *grammes,* or a sufficient quantity; Distilled Water sufficient to produce 1000.0 *millilitres.* Mix the Acetic Acid with five hundred *millilitres* of the Distilled Water; neutralise with Ammonium Carbonate; add sufficient Distilled Water to produce the required volume." *Br.*

This preparation is an aqueous solution of ammonium acetate. The U. S. process by which it is formed involves the decomposition of ammonium carbonate by diluted acetic acid. The formula of commercial ammonium carbonate is complex, but the reaction is expressed by the following equation:

$$CO(OH)ONH_4.CO(NH_2)ONH_4 + 3(C_2H_3O_2.H) = 3(C_2H_3O_2.NH_4) + H_2O + 2CO_2$$

Distilled vinegar was formerly used, but it was replaced by diluted acetic acid, which is much to be preferred. The quantity of ammonium carbonate necessary to saturate a given weight of the acid of average strength cannot be laid down with precision, on account of the variable quality of the salt. The preparation, when made with the diluted acetic acid of the U. S. Pharmacopœia, contains about 7 per cent. of ammonium acetate. It is more convenient to add the salt to the acid than to add the acid to the salt, as the point of saturation is thus more easily attained. In ascertaining this point by test paper, the alkaline reaction will begin, though a portion of free acetic acid may still remain, a little of it being insufficient to overcome the natural alkaline reaction of the salt. A complication is caused by the presence of

free carbon dioxide, which may be expelled from the liquid towards the end of the saturation by warming it.

The formula of the U. S. P., 1890, differed from that formerly official in dropping what has been called the "mixed solution process," and the U. S. P. IX has retained the 1890 process without change. It is to be regretted that the official process does not direct the preparation of two solutions, one of acetic acid, the other of ammonium carbonate, these solutions to be mixed in equal volumes to prepare the official solution of ammonium acetate. The separate solutions keep well, and the rapidity and ease with which this preparation can be made by the pharmacist, are advantages which at once recommend its exclusive use, while the physician is more likely to secure a fresh preparation, and one which usually retains a quantity of carbon dioxide to render the preparation grateful to the patient.

As some pharmacists will prefer to make solution of ammonium acetate in this way, the following procedure is suggested: Ammonium Carbonate, *ten grammes* [or 1 ounce av., 293 grains]; Acetic Acid (36 to 37 per cent.), *thirty-four mils* [or 5 fluidounces, 211 minims]; Distilled Water, sufficient to make *two hundred mils* [or two pints]. Dissolve the Ammonium Carbonate in sufficient Distilled Water to make *one hundred mils* [or 1 pint], and filter the solution. Then to the Acetic Acid add enough Distilled Water to make *one hundred mils* [or 1 pint]. Keep the solutions in separate, well-stoppered bottles, and when solution of ammonium acetate is to be dispensed measure equal quantities of each solution and mix them.

The present British process does not differ essentially from ours; in the older Br. Pharmacopœias the strong solution of ammonia was used instead of the carbonate, and the ammonia combined directly with the acetic acid, without other reaction. There was an advantage in this process in the use of ammonia instead of its carbonate, as the difficulty of ascertaining the precise point of saturation arising from carbon dioxide was avoided, but in this solution, as in the neutral mixture, a great benefit remedially is gained by the presence of carbonic acid, which reconciles the stomach to the medicine, and sometimes even allays vomiting in febrile diseases. With this view of the subject it is better to use ammonium carbonate; the change has been made in the present Br. Pharmacopœia, but the advantages are practically lost because the solution is nearly always made in advance of actual use, and official solution of ammonium acetate is rarely sparkling, but as generally dispensed it has a flat, mawkish taste, quite in contrast with that made by the "mixed solution process."

Properties.—Solution of ammonium acetate is "a clear, colorless liquid, free from empyreumatic odor and having a mildly saline, acidulous taste, and an acid reaction. It is volatile when heated. Not more than 0.003 Gm. of ash remains on evaporating 20 mils of the Solution and igniting the residue. When Solution of Ammonium Acetate is heated with potassium hydroxide T.S., ammonia is evolved. Add 1 mil each of sulphuric acid and alcohol to 5 mils of the Solution and boil the mixture; ethyl acetate is formed, recognizable by its odor.

"**Assay.**—Dilute about 25 mils of Solution of Ammonium Acetate, accurately weighed, with 100 mils of distilled water, transfer it to a distilling flask, render it alkaline with potassium hydroxide T.S. and distil the liquid until all of the ammonia has been driven over (about 100 mils of distillate), receiving the distillate under the surface of 50 mils of normal sulphuric acid V.S, contained in a flask. Then titrate with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 7 per cent. of $NH_4C_2H_3O_2$.

"Each mil of normal sulphuric acid V.S. used corresponds to 0.07707 Gm. of $NH_4C_2H_3O_2$. Each gramme of Solution of Ammonium Acetate corresponds to not less than 0.91 mil of normal sulphuric acid V. S." *U. S.*

"Specific gravity 1.016. Mixed with an equal volume of a saturated aqueous solution of *hydrogen sulphide* not more than the slightest darkening in color results (limit of heavy metals). Solution of Ammonium Acetate should be preserved in a vessel free from lead." *Br.*

When it contains an excess of alkali, its taste is bitterish. It should be freshly prepared at short intervals, as its acid becomes decomposed and a portion of ammonium carbonate is generated. When pure it is not precipitated by barium chloride.

Ammonium acetate is a salt of difficult crystallization, and very deliquescent. It may be obtained by sublimation from a mixture of equal parts of dry potassium or calcium acetate and ammonium chloride, or, according to Berthelot, by dissolving glacial acetic acid in ammonia water, keeping the retort cool, and adding enough water to prevent the crystallization of the salt during the neutralization; the solution is then evaporated in a current of dry, gaseous ammonia until the liquid solidifies on cooling. It is then introduced into a large dish, and this placed upon caustic lime, under a large bell glass, into which a considerable quantity of ammonia gas is injected. After a few days the crystalline mass is broken, and the dish replaced as before upon lime in an ammoniacal atmosphere, under the bell glass. When this operation has been repeated several times, a perfectly pure ammonium acetate is obtained, which crystallizes in large needles, like potassium nitrate, and resembles ammonium formate; it is extremely soluble in water, and does not possess an acid reaction. (*A. J. P.*, 1875, p. 25.) It is formed by the union of one molecule of acetic acid, $H.C_2H_3O_2$, with one group, NH_4, from $NH_4.OH$, the hydroxide, or $(NH_4)_2CO_3$, the carbonate. When evaporated to dryness, however, it readily yields an acid salt, $C_2H_3O_2.NH_4 + C_2H_3O_2.H$.

Uses.—Solution of ammonium acetate is used as a saline diaphoretic and diuretic, especially in febrile conditions.

Dose, from half a fluidounce to a fluidounce and a half (15–45 mils) every three or four hours, mixed with water and sweetened with sugar.

Off. Prep.—Liquor Ferri et Ammonii Acetatis, *U. S.*

LIQUOR AMMONII CITRATIS. Br.

SOLUTION OF AMMONIUM CITRATE

(lĭ'quŏr ăm-mō'nĭ-ī cĭ-trā'tĭs)

Citrate d'Ammoniaque liquide, *Fr.;* Ammoniumcitratlösung, Citronensaure Ammoniak-Flüssigkeit, *G.*

"Citric Acid, 125.0 *grammes;* Ammonium Carbonate, 87.5 *grammes,* or a sufficient quantity; Distilled Water sufficient to produce 1000.0 *millilitres.* Dissolve the Citric Acid in five times its weight of Distilled Water; neutralise with Ammonium Carbonate; add sufficient Distilled Water to produce the required volume. Specific gravity, 1.057. Mixed with an equal volume of a saturated aqueous solution of *hydrogen sulphide* not more than the slightest darkening in color results (limit of heavy metals). Solution of Ammonium Citrate should be preserved in a vessel free from lead." *Br.*

This solution is also official in the N. F. IV. (See Part III.)

This solution may be used for the same purposes as *Solution of Ammonium Acetate.*

Dose, from two to six fluidrachms (7.5–22.5 mils).

LIQUOR ARSENI ET HYDRARGYRI IODIDI. U. S. (Br.)

SOLUTION OF ARSENOUS AND MERCURIC IODIDES

Liq. Arsen. et Hydrarg. Iod. [Donovan's Solution]

(lĭ'quŏr ăr'sẹ-nī ĕt hy-drär'gy-rī ī-ŏd'ĭ-dī)

"An aqueous solution containing not less than 0.95 per cent. nor more than 1.05 per cent. of AsIs (455.72) and not less than 0.95 per cent. nor more than 1.05 per cent. of HgI_2 (454.44)." *U. S.*

Liquor Arsenii et Hydrargyri Iodidi, *Br.,* Solution of Arsenious and Mercuric Iodides; Liquor Arsenici et Hydrargyri Iodidi, *Br.* 1867, *U. S.* 1870; Solution of Hydriodate of Arsenic and Mercury; Solutio Donovani; Soluté d'Iodo-arsénite de Mercure, Liqueur de Donovan, *Fr.;* Jodquecksilber Arseniklösung, Donovansche Tropfen, *G.*

* "Arsenous Iodide, *ten grammes* [or 154 grains]; Red Mercuric Iodide, *ten grammes* [or 154 grains]; Distilled Water, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Rub the arsenous iodide and red mercuric iodide together in a mortar, add *one hundred and fifty mils* [or 5 fluidounces, 35 minims] of distilled water, and continue the trituration until solution is effected. Filter the solution, and pass sufficient distilled water through the filter to make the product weigh *one thousand grammes* [or 35 ounces av., 120 grains]. Mix thoroughly. Preserve it in well-filled, amber-colored bottles. It must not be dispensed if darker than pale yellow." *U. S.*

"Arsenious Iodide, 10 *grammes;* Red Mercuric Iodide, 10 *grammes;* Distilled Water sufficient to produce 1000 *millilitres.* Triturate the Arsenious Iodide and Red Mercuric Iodide with two hundred and fifty *millilitres* of the Distilled Water until dissolved; filter; pass through the filter sufficient Distilled Water to produce the required volume. This Solution contains the equivalent of 1 gramme of Arsenious Iodide and 1 gramme of Red Mercuric Iodide in 100 millilitres; 110 minims contain the equivalent of 1 grain of each salt." *Br.*

This solution was introduced to the notice of the medical profession in 1839 by Donovan, of Dublin, as a therapeutic agent combining the medicinal virtues of its three ingredients, and was adopted as an official preparation in the U. S. and Dublin Pharmacopœias of 1850. It was dropped from the British Pharmacopœia of 1867, but reintroduced in the 1885 revision, and fortunately made to correspond in strength with the U. S. preparation—namely, 1 per cent. of each of the active ingredients. The formula of the U. S. Pharmacopœia is the simplified one of Procter, which consists essentially in dissolving equal weights of arsenic triiodide and mercuric iodide (red iodide) in a measured quantity of distilled water.

Properties.—"Solution of Arsenous and Mercuric Iodide is a clear, colorless or pale yellowish liquid, without odor, and having a disagreeable metallic taste. One mil of Solution of Arsenous and Mercuric Iodide, mixed with 10 mils of distilled water, to which a few drops of lead acetate T.S. have been added, produces a bright yellow precipitate. Add a few drops of Solution of Arsenous and Mercuric Iodide to a mixture of about 0.5 Gm. of zinc and 5 mils of diluted hydrochloric acid in a test tube, and cover the mouth of the test tube with a filter paper which has been moistened with mercuric chloride T.S. and dried; a yellow stain appears upon the inner surface of the filter paper within one minute.

"**Assay for Arsenous Iodide.**—Introduce about 25 mils of Solution of Arsenous and Mercuric Iodide into a flask, weigh accurately, dilute with 25 mils of distilled water, then dissolve 2 Gm. of sodium bicarbonate in this solution and titrate it with tenth-normal iodine V.S., using starch T.S. as indicator. It shows not less than 0.95 per cent. nor more than 1.05 per cent. of AsIs.

"Each mil of tenth-normal iodine V.S. used corresponds to 0.022786 Gm. of AsIs. Each gramme of Solution of Arsenous and Mercuric Iodide corresponds to not less than 0.42 mil nor more than 0.46 mil of tenth-normal iodine V.S.

"**Assay for Mercuric Iodide.**—Introduce about 25 mils of Solution of Arsenous and Mercuric Iodide into a flask, weigh accurately, add 5 mils of potassium hydroxide T.S. and 5 mils of solution of formaldehyde, and warm the mix-

ture on a water bath until the mercuric salt has been completely reduced to metallic mercury. Carefully decant the clear, supernatant liquid from the residue of metallic mercury and wash the mercury carefully by decantation, with two successive portions of 25 mils each of distilled water. Dissolve the residue of metallic mercury in 5 mils of nitric acid, dilute the solution with 50 mils of distilled water, add 2 mils of ferric ammonium sulphate T.S. and titrate with tenth-normal potassium sulphocyanate V.S. to the formation of a permanent pink color. It shows not less than 0.95 per cent. nor more than 1.05 per cent. of HgI_2.

"Each mil of tenth-normal potassium sulphocyanate V.S. corresponds to 0.022722 Gm. of HgI_2. Each gramme of Solution of Arsenous and Mercuric Iodide corresponds to not less than 0.42 mil nor more than 0.46 mil of tenth-normal potassium sulphocyanate V. S." *U. S.*

Uses.—This preparation has been found decidedly useful as an alterative in various chronic diseases of the skin, such as in the later stages of *syphilis,* especially with "night pains;" in certain cases of *lymphadenitis* and in some forms of chronic joint disease.

Dose, from one to five minims (0.06–0.3 mil), three times a day, given preferably in distilled water.

LIQUOR ATROPINÆ SULPHATIS. Br.

SOLUTION OF ATROPINE SULPHATE

(lĭ'quŏr ăt-rŏ-pī'næ sŭl-phā'tĭs)

Soluté de Sulfate d'Atropine, *Fr.;* Schwefelsaure Atropin-lösung, *G.*

"Atropine Sulphate, 1 *gramme;* Distilled Water, recently boiled and cooled, sufficient to produce 100 *millilitres.* Dissolve. This Solution should be freshly prepared. It contains 1 gramme of Atropine Sulphate in 100 millilitres; 110 minims contain 1 grain." *Br.*

This solution contains 1 per cent. of atropine sulphate. Camphor water was substituted for distilled water on account of its antiseptic properties at the 1885 revision. Salicylic acid and distilled water were used (1898) with the same object in view, but the British Pharm., 1914, discarded preservatives.

Dose, one-half to one minim (0.03–0.06 mil).

LIQUOR BISMUTHI ET AMMONII CITRATIS. Br.

SOLUTION OF BISMUTH AND AMMONIUM CITRATE

(lĭ'quŏr bĭs-mū'thī ĕt ăm-mō'nī-ī cĭ-trā'tĭs)

Liquor Bismuthi; Solution of Bismuth, Liquid Bismuth; Soluté de Citrate de Bismuth ammoniacal, *Fr.;* Citronensaure Wismuth-Ammoniak-Lösung, Wismuth-Ammoniakcitratlösung, *G.*

"Bismuth Oxynitrate, 70 *grammes;* Citric Acid, 52 *grammes;* Solution of Ammonia, Distilled Water, of each, *a sufficient quantity.* Powder the Citric Acid and mix it in a mortar with the Bismuth Oxynitrate and twenty *millilitres* of Distilled Water. Allow the mixture to stand, with occasional stirring, for half an hour, or until a small portion is completely soluble in Solution of Ammonia. Transfer to a beaker, using four hundred *millilitres* of Distilled Water to rinse the mortar. Allow the precipitate to settle, remove the clear liquid by decantation, and wash the precipitate with three successive quantities, each of four hundred *millilitres,* of Distilled Water. Add to the washed precipitate, while moist, just sufficient Solution of Ammonia to dissolve it, and then add sufficient Distilled Water to produce one thousand *millilitres* of the Solution." *Br.*

Some years since, a secret preparation was made and sold by Schacht, of Clifton, England, under the name of *Liquor Bismuthi,* which was shown by Tichborne (*P. J.,* 1864, 301) to contain bismuth oxide, ammonia, and citric acid. Various formulas for a similar solution have been suggested (see *U. S. D.,* 17th ed., 794, and 19th ed., 706), but that official is probably as good as any.

The British Pharmacopœia describes this preparation as "a colorless liquid, freely miscible with *water;* taste somewhat metallic; slightly alkaline to *litmus.* Evolves ammonia when heated with *solution of sodium hydroxide.* 10 millilitres, evaporated to dryness and the residue ignited, yield not less than 0.5 gramme of bismuth oxide." *Br.*

Bismuth and ammonium citrate, obtained by Bartlett's process, is in fine, glossy, translucent, colorless scales, of a slightly acidulous, somewhat metallic, not disagreeable taste, very soluble in water, but not deliquescent, and of an acid reaction. (See page 236.) From an analysis by Bartlett, it appears to possess the formula $Bi,C_6H_5O_7.NH_3 + 3H_2O$. Rother, however (1876), considers that the formula should be written $C_6H_5O_7(NH_4)_3Bi(OH)_3$.

Uses.—This preparation is much more astringent than are the insoluble salts of bismuth, and is at the same time irritant, and not possessed of the peculiar medicinal properties which grow out of insolubility of the subnitrate or subcarbonate. It is, therefore, not a substitute for these, and is adapted to the treatment of *diarrheas* of relaxation rather than of irritation.

Dose, from one-half to one fluidrachm (1.8–3.75 mils).

LIQUOR CALCIS. U. S., Br.

SOLUTION OF CALCIUM HYDROXIDE Liq. Calc. [Lime Water]

(lĭ'quŏr căl'cĭs)

"An aqueous solution containing not less than 0.14 per cent. of $Ca(OH)_2$ (74.09) at 25° C. (77° F.). Preserve it in well-filled, tightly-stoppered bottles. The percentage of calcium hydroxide varies with the temperature at which the solution is prepared, being about 0.17 per cent. at 15° C. (59° F.), and diminishing as the temperatures rises." *U. S.*

Aqua Calcariæ Ustæ, Calcaria Soluta, Aqua Calcis; Solution of Calcium Hydrate, Solution of Lime; Eau (Solutè) de Chaux, *Fr. Cod.*; Aqua Calcariæ, *P. G.*; Kalkwasser, *G.*; Acqua di calce, *It.*; Agua de cal, *Sp.*

* "Lime, *fifty grammes* [or 1 ounce av., 334 grains]; Distilled Water, *a sufficient quantity.* Slake the lime by the very gradual addition of *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of distilled water, and agitate it occasionally during half an hour. Allow the suspended particles to subside, decant the supernatant liquid and reject it. Transfer the magma of calcium hydroxide to a filter and wash it repeatedly with boiling distilled water, until the washings, after acidulation with nitric acid, show not more than a faint cloudiness with silver nitrate T.S. (*chloride*). Return the magma to a suitable container, add *five thousand mils* [or 169 fluidounces, 33 minims] of distilled water, agitate it thoroughly, allow the mixture to stand for twenty-four hours, agitate again, and, when the coarser particles of solid matter have subsided pour the liquid, holding the undissolved calcium hydroxide in suspension, into a bottle having a tight stopper. From time to time shake the bottle to insure a saturated solution. Pour off the clear liquid when required for use. The undissolved calcium hydroxide must not be used for making additional quantities of Solution of Calcium Hydroxide unless the product is found to be of full strength when assayed." *U. S.*

"Calcium Hydroxide, 50 *grammes;* Distilled Water, *a sufficient quantity.* Wash the Calcium Hydroxide with Distilled Water until free from chlorides; then shake it with five thousand *millilitres* of Distilled Water in a stoppered green glass bottle for two or three minutes; set aside until clear. The clear Solution may be drawn off with a siphon as required for use, and should then be transferred to a green glass bottle." *Br.*

A solution of calcium hydroxide, $Ca(OH)_2$, in water is the result of these processes. By the slaking of the lime it is reduced to powder, and rendered more easily diffusible through the water. According to both Pharmacopœias, the solution is to be kept in bottles with a portion of undissolved hydroxide, which causes it always to be saturated whatever may be the temperature and to whatever extent it may be exposed to the air. If care be taken to have a considerable quantity of the solution in the bottle, and to avoid unnecessary agitation, the upper portion will always remain sufficiently clear for use. The employment of distilled water as the solvent may seem a useless refinement, but in many places the common water is very impure. Water dissolves but a minute proportion of lime, and, contrary to the general law, less when hot than when cold. Hence the propriety of employing cold water in the process. According to Phillips, a pint of water (the wine pint of the U. S. P., 1870) at 100° C. (212° F.) dissolves 5.6 grains of lime, at 15.5° C. (60° F.) 9.7 grains. For Green's automatic device for dispensing lime water in excellent condition, see *Proc. A. Ph. A.*, 1893, 474; see also 1904, 66.

The practice of using the undissolved lime indefinitely by refilling the bottle with water, is reprehensible, as notwithstanding the excess, its tendency to become carbonated and insoluble is great, and lime water is often dispensed deficient in strength; it is much safer to use the lime but once or twice than to run the risk of dispensing a liquid of insufficient strength.

Properties.—Lime water is "a clear, colorless liquid without odor, and having an alkaline taste. It is strongly alkaline to litmus. It absorbs carbon dioxide from the air, a pellicle of calcium carbonate forming on the surface of the liquid. On being heated it becomes turbid, due to the separation of calcium hydroxide which redissolves when the liquid is cooled. The alkaline reaction of the Solution entirely disappears after it has been saturated with carbon dioxide and subsequently boiled (*alkalies and their carbonates*).

"**Assay.**—Titrate 50 mils of Solution of Calcium Hydroxide with tenth-normal sulphuric acid V.S., using phenolphthalein T.S. as indicator; it shows not less than 0.14 per cent. of $Ca(OH)_2$.

"Each mil of tenth-normal sulphuric acid V.S. used corresponds to 0.0037045 Gm. of $Ca(OH)_2$. Each mil of Solution of Calcium Hydroxide corresponds to not less than 0.38 mil of tenth-normal sulphuric acid V.S." *U. S.*

"Twenty-four millilitres require for neutralisation 10 millilitres of *N/10 solution of sulphuric acid.* Yields no characteristic *reactions* for lead or chlorides. This Solution contains the equivalent of rather more than 0.1 gramme of Lime, CaO, in 100 millilitres; 110 minims contain the equivalent of 1/10 grain." *Br.*

Exposed to the air it attracts carbon dioxide, and becomes covered with a pellicle of insoluble calcium carbonate, which, subsiding after a time, is replaced by another, and so on successively until the whole of the lime is precipitated. Hence the necessity of keeping lime water either in closely corked bottles which should be full, or, what is more convenient, in bottles with an excess of lime.

Uses.—Lime water is mildly antacid, and astringent, often useful in *dyspepsia* with acidity of stomach or *diarrhea.* Mixed with from one to three measures of milk, which completely covers its offensive taste, it is of service in *nausea* and *vomiting* dependent on irritability of stomach. It is often added to milk to prevent the formation of hard curds, and thus increase its digestibility. In severe repeated vomiting with loss of digestive power a diet exclusively of lime water and milk (one to six) is often very effectual. Having been found to possess the property of dissolving false membrane, it has naturally been employed as a local remedy in *pseudo-membranous croup.* It may be applied by directing lime water spray, produced by the atomizer, so that it shall be inhaled by the patient. When employed to allay *nausea,* it is

usually given in the dose of a tablespoonful mixed with the same quantity of milk, and repeated at intervals of half an hour, an hour, or two hours.

Dose, one to four fluidounces (30–120 mils).

Off. Prep.—Linimentum Calcis, *U. S., Br.*

LIQUOR CALCIS CHLORINATÆ. Br.

SOLUTION OF CHLORINATED LIME

(lĭ'quŏr căl'cĭs ȼhlō-rĭ-nā'tæ)

Soluté d'Hypochlorite de Chaux, *Fr. Cod.;* Chlorure de Chaux liquide, *Fr.;* Chlorkalklösung, Chlorkalk-Flüssigkeit, *G.*

"Chlorinated Lime, 100 *grammes;* Distilled Water, 1000 *millilitres.* Mix; transfer the mixture to a stoppered bottle; set aside for three hours, shaking occasionally; filter through calico. Preserve the filtrate in a stoppered bottle in a cool dark place." *Br.*

For the properties and uses of this preparation, see *Calx Chlorinata.* The British Pharmacopœia gives the following tests: "If 2 *millilitres* are added to a solution of 1 gramme of *potassium iodide* in 25 *millilitres* of *water,* acidified with 2 *millilitres* of *hydrochloric acid,* a brownish-red solution is obtained which requires for decolorisation not less than 11.7 *millilitres* of *N/10 solution of sodium thiosulphate* (presence of not less than 2 per cent. of available chlorine). When freshly prepared, this Solution yields about 3 per cent. of available chlorine." *Br.*

This determines its strength in chlorine, by ascertaining the quantity of iodine which the chlorine contained in it is capable of separating from potassium iodide. Notwithstanding, however, that a test of its character is thus given by the Pharmacopœia, its strength must vary according to the quality of the chlorinated lime employed. It is one of the best antidotes against poisoning by hydrogen sulphide, ammonium sulphydrate, potassium sulphide, and hydrocyanic acid. For external application the solution may be diluted with twice its bulk of water, or may be used of the full strength in some cutaneous affections.

Dose, for internal use, from ten to thirty minims (0.6–1.9 mils).

LIQUOR CALCIS SACCHARATUS. Br.

SACCHARATED SOLUTION OF LIME

(lĭ'quŏr căl'cĭs săc-ȼhă-rā'tŭs)

Syrupus Calcis (*U. S. VIII*); Syrup of Lime; Syrup of Calcium Hydroxide; Syrupus Calcariæ; Syrup of Calcium Hydroxide; Sirop de Chaux, *Fr.;* Kalksyrup, *G.*

"Calcium Hydroxide, 50 *grammes;* Refined Sugar, in powder, 100 *grammes;* Distilled Water, 1000 *millilitres.* Mix the Calcium Hydroxide with a solution of the Refined Sugar in the Distilled Water. Set aside in a stoppered green glass bottle for a few hours, shaking occasionally; separate the clear Solution by means of a siphon, avoiding unnecessary exposure to air. Specific gravity, 1.055. Twenty millilitres require for neutralisation 13.2 millilitres of *N/1 solution of sulphuric acid.* Yields no characteristic *reactions for lead.* This Solution contains the equivalent of nearly 2 grammes of Lime, CaO, in 100 millilitres; 110 minims contain nearly 2 grains." *Br.*

Properties.—Syrup of Lime is not official in the U. S. P. IX. It was described in the U. S. P. VIII as "a transparent, pale yellow liquid, of alkaline taste and reaction. Specific gravity: about 1.145 at 25° C. (77° F.). The addition of a solution of an alkali carbonate produces a white precipitate, soluble in acids with effervescence. The addition of ammonium oxalate T.S. produces a white precipitate, insoluble in acetic acid, but soluble in hydrochloric acid." *U. S.*

The British saccharated solution of lime differs from the U. S. P. VIII syrup in containing a smaller proportion of sugar and of lime.

Sugar forms with lime certain definite compounds which may be looked upon as sucrates. According to M. S. Benedikt (*J. P. C.,* 4e sér., xix, 96), there are at least four of these combinations. Some, if not all, of them are much more soluble than the lime itself, so that in this way a much stronger solution of lime can be obtained than by the instrumentality of water alone. The syrup remains perfectly transparent, and is in no degree disturbed by dilution with water. It has a decidedly alkaline and even caustic taste, and should always be largely diluted when administered.

Uses.—Syrup of lime is an active antacid and astringent, which may be used as a substitute for lime water in all cases in which that preparation is suitable. Twenty minims of it (1.3 mils) are equal to a fluidounce of lime water.

Dose, fifteen to sixty minims (0.9–3.75 mils).

LIQUOR CRESOLIS COMPOSITUS.

U. S. (Br.)

COMPOUND SOLUTION OF CRESOL Liq. Cresol. Co.

(lĭ'quŏr crẹ-sō'lĭs cọm-pŏs'ĭ-tŭs)

Liquor Cresol Saponatus, *Br.;* Solution of Cresol with Soap; Soluté de Crésol composé, *Fr.;* Liquor Cresoli saponatus, *P. G.;* Kresolseifenlösung, *G.*

* "Cresol, *five hundred grammes* [or 17 ounces av., 279 grains]; Linseed Oil, *three hundred grammes* [or 10 ounces av., 255 grains]; Potassium Hydroxide, *eighty grammes* [or 2 ounces av., 360 grains]; Alcohol, *thirty mils* [or 1 fluidounce, 7 minims]; Water, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Heat the linseed oil in a tared vessel of a capacity equal to about four times the bulk of the ingredients, on a water bath to a temperature of 70° C. (158° F.). Dissolve the potassium hydroxide in 50 mils of water and warm the solution to 70° C. (158° F.), add it to the linseed oil and mix thoroughly; then incorporate the alcohol

and continue to heat the mixture without stirring until a small portion is found to be soluble in boiling water without the separation of oily drops. While yet warm add the cresol and mix thoroughly, maintaining the temperature at about 70° C. (158° F.) until a clear solution is produced. Finally add sufficient water to make the finished product weigh *one thousand grammes* [or 35 ounces av., 120 grains]. Note: In this process the 80 Gm. of potassium hydroxide may be replaced by 54 Gm. of sodium hydroxide." *U. S.*

"Cresol, 500 *grammes;* Castor Oil, 350 *grammes;* Potassium Hydroxide, 80 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Mix the Cresol with the Castor Oil and heat to 80° C. (176° F.). Dissolve the Potassium Hydroxide in seventy *millilitres* of the Distilled Water. Mix the two solutions and heat the mixture until one volume of it forms a clear liquid with ten volumes of Distilled Water. Cool, and add sufficient Distilled Water to produce the required volume." *Br.*

Compound Solution of Cresol was introduced into the U. S. P. (8th Rev.) to supply the demand for an antiseptic solution which mixes freely with water. With some samples of cresol there has been experienced some difficulty in securing immediately a clear solution, showing that combination has not been effected, but by allowing the mixture to stand with occasional stirring, the solution will become clear. LaWall and Cook (*A. J. P.,* 1906, 169) suggested a modification of the manipulation which secures a clear solution immediately. It was adopted by the Committee of Revision of the U. S. P. IX. The official process permits the alternative use of sodium hydroxide, which produces a product identical in appearance and probably of equal value with the one made from potassium hydroxide and at a greatly reduced cost.

Uses.—This solution is intended as a substitute for the many commercial preparations of cresol on the market. Although it forms a clear solution with distilled water, with tap water it becomes cloudy, owing to precipitation of lime soaps. This change, however, does not appear to interfere with its therapeutic properties. It is a powerful germicidal mixture, at least twice as strong as phenol as a destroyer of micro-organisms. It is also less caustic than phenol, but the statement that it is much less poisonous has been shown to be untrue. The *Chemist and Druggist of Australasia* reports in 1911 (vol. xxvi, p. 299) fifty-six deaths from lysol—a widely used proprietary brand of this solution. It is especially useful for sterilizing instruments and the skin, its soapy nature making it peculiarly valuable for the latter purpose. It may be diluted with from 30 to 90 times its bulk of water (3 per cent. to 1 per cent. solution). It has been used to a small extent internally as an antiseptic in *fermentative gastritis.*

Dose, one to two minims (0.06–0.12 mil).

LIQUOR EPISPASTICUS. Br.

BLISTERING LIQUID

(lī'quŏr ĕp-ĭ-spăs'tĭ-cŭs)

Linimentum Cantharidis; Liqueur Vésicant, Huile de Cantharides térébenthinée, *Fr.;* Spanischfliegenliniment, Blasenziehende Flüssigkeit, *G.*

"Cantharidin, 4 *grammes;* Castor Oil, 25 *millilitres;* Resin, 12 *grammes;* Acetone sufficient to produce 1000 *millilitres.* Dissolve. This Blistering Liquid contains approximately the same proportion of Cantharidin as the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

This liquid is used in making the British Blistering Collodion. (See p. 374.) Greenish and Wilson propose that the official blistering liquid be prepared by the following formula: Cantharidin, 1 part; castor oil, 6 parts; rosin, 3 parts; acetic ether, enough to make 300 fluid parts. The castor oil and rosin are added to replace the natural fat of the cantharides, and are necessary to aid the absorption of the cantharides by the skin. (*P. J.,* 1898, 259.)

Off. Prep.—Collodium Vesicans, *Br.*

LIQUOR ETHYL NITRITIS. Br.

SOLUTION OF ETHYL NITRITE

(lī'quŏr ĕ'thĭl nī-trī'tĭs)

"Solution of Ethyl Nitrite contains not less than 2.5 or more than 3 per cent. by weight of ethyl nitrite in a mixture of ninety-five parts by volume of Absolute Alcohol with five parts by volume of Glycerin. The ethyl nitrite may be obtained by the interaction of alcohol (90 per cent.), sodium nitrite, and diluted sulphuric acid, at a low temperature. Solution of Ethyl Nitrite should be stored in small bottles." *Br.*

Soluté de Nitrite d'Ethyle, *Fr.;* Aethylnitritlösung, *G.*

This was a new official preparation in the Br. Ph., 1898; it might be called improved spirit of nitrous ether; it is difficult to explain the reason for its introduction without the dismissal of spirit of nitrous ether; the strength is very slightly greater than that of the British spirit (less than the U. S. spirit of nitrous ether), and a choice should be made between them. The addition of glycerin as a preservative and the substitution of absolute alcohol for rectified spirit, are relied upon to make a permanent solution. This method was proposed by Dunstan and Dymond (*P. J.,* 1888, 861), who believe that ethyl nitrite is the *sole* valuable constituent in spirit of nitrous ether; glycerin prevents loss of the very volatile ethyl nitrite, while the absence of water is secured by the use of absolute alcohol, water in the alcohol being shown to be the principal cause of decomposition and loss of ethyl nitrite. Solution of ethyl nitrite was strongly recommended by Leech, and the advantage claimed for it is that it is free from aldehyde. The increased cost, due to the use of absolute alcohol, will be apt to prevent the extensive use of the solution.

It is described as "a nearly colorless transparent liquid, of characteristic apple-like odor and taste. Specific gravity 0.823 to 0.826. When poured on an acidified strong solution of *ferrous sulphate* contained in a test-tube, a deep olive-brown coloration is produced at the surface of contact of the two liquids. Does not effervesce when shaken with *sodium bicarbonate* (absence of acid). 10 millilitres, mixed with 5 millilitres of *N/1 solution of sodium hydroxide* and 5 millilitres of *water*, do not assume a yellow color (absence of acetaldehyde). 1 volume, shaken briskly at intervals during five minutes in a brine-charged nitrometer with 1 volume of *solution of potassium iodide* and 1 volume of *diluted sulphuric acid*, yields at 15.5° C. (60° F.), and normal pressure, not less than 6.5 or more than 7.8 volumes of nitric oxide gas." *Br.*

This preparation affords a means of giving ethyl nitrite internally.

Dose, from twenty to sixty minims (1.3–3.75 mils). (See *Spiritus Ætheris Nitrosi.*)

LIQUOR FERRI CHLORIDI. U. S. (Br.)

SOLUTION OF FERRIC CHLORIDE Liq. Ferr. Chlor. [Solution of Iron Perchloride]

(lĭ′quŏr fĕr′rī ȼhlō′rı̤-dī)

"An aqueous solution containing ferric chloride [$FeCl_3 = 162.22$], corresponding to not less than 10 per cent. nor more than 11 per cent. of Fe. Preserve it in glass-stoppered bottles protected from light." *U. S.*

"This Solution contains 20 grammes of Iron in 100 millilitres; 110 minims contain 20 grains." *Br.*

Liquor Ferri Perchloridi Fortis, *Br.;* Liquor Ferri Muriatici Oxydati, Strong Solution of Ferric Chloride, Solution of Chloride of Iron; Chlorure Ferrique dissous, *Fr. Cod.;* Soluté de Perchlorure de Fer, Chlorure Ferrique liquide, *Fr.;* Liquo-Ferri Sesquichlorati, *P. G.;* Flüssiges Eisenchlorid, Eisen chloridlösung, *G.;* Solucion de Cloruro Ferrico, *Sp.*

* "Iron, in the form of fine, bright wire, and cut into small pieces, *one hundred and twenty-five grammes* [or 4 ounces av., 179 grains]; Hydrochloric Acid, *six hundred and eighty grammes* [or 23 ounces av., 432 grains]; Nitric Acid, Distilled Water, each, *a sufficient quantity*, to make *one thousand grammes* [or 35 ounces av., 120 grains]. Introduce the iron wire into a flask having a capacity of about *two thousand mils* [or 67 fluidounces, 301 minims], pour upon it a mixture of *four hundred and twenty grammes* [or 14 ounces av., 357 grains] of hydrochloric acid and *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of distilled water, and heat the mixture on a water-bath for not less than one hour and fifteen minutes, or until effervescence ceases; then boil the liquid, filter it through paper, and, having rinsed the flask and iron wire with a little hot distilled water, pass the rinsings through the filter. To the filtered liquid add *two hundred and twenty grammes* [or 7 ounces av., 333 grains] of hydrochloric acid, then add the mixture slowly and gradually, in a stream, to *sixty-five grammes* [or 2 ounces av., 128 grains] of nitric acid contained in a tared capacious porcelain vessel, and warm gently. If the solution has acquired a black color, continue the addition of nitric acid, drop by drop, until red fumes are no longer evolved and the solution assumes a clear, reddish-brown color. After effervescence ceases, heat on a sand bath, stirring occasionally until the liquid is free from nitric acid, as indicated by the test given below. During the heating add distilled water from time to time to maintain about the original volume. Finally, add the remaining *forty grammes* [or 1 ounce av., 180 grains] of hydrochloric acid and enough distilled water to make the solution weigh *one thousand grammes* [or 35 ounces av., 120 grains]." *U. S.*

"Iron, 70 *grammes;* Hydrochloric Acid, 410 *millilitres;* Nitric Acid, 30 *millilitres;* Distilled Water, *a sufficient quantity*. Place the Iron in a flask; add a mixture of two hundred and fifty millilitres of Hydrochloric Acid and one hundred and forty millilitres of Distilled Water; expose to a moderate temperature until effervescence ceases; then boil; filter from undissolved Iron; rinse the flask and contents with a little Distilled Water; pour the rinsings over the filter; add to the filtrate one hundred and forty millilitres of Hydrochloric Acid; mix; pour the solution in a slow continuous stream into the Nitric Acid, chemical action being promoted if necessary by gently warming; evaporate the product until a precipitate begins to form; add twenty millilitres of Hydrochloric Acid, and sufficient Distilled Water to produce three hundred and fifty millilitres, or to make the resulting Solution respond to the following tests." *Br.* (See page 634.)

The strength of solution of ferric chloride U. S. P. (8th Rev.) was reduced from the former standard of 13 per cent. of iron (U. S. P., 1890) to 10 per cent. of iron, which corresponds to the solution of the German Pharmacopœia; this strength is sufficient for all purposes, and is more convenient for calculations. The U. S. P. IX strength is from 10 to 11 per cent. The British preparation contains 15.84 per cent. of iron. By the reaction between the hydrochloric acid and the iron, ferrous chloride is produced, which by the subsequent agency of the hydrochloric and nitric acids is converted into ferric chloride, or, as it is denominated in the British Pharmacopœia, perchloride of iron, this being retained in solution by the water with the excess of acid. This excess of acid is limited by a special test in the U. S. P. IX, because too great excess would complicate other formulas in which the tincture is used, such as the tincture of ferric citro-chloride. This solution was included in the original British Pharmacopœia, but was not official with us until 1870. The original British formula (1864) was defective in several respects. For an account of these, see the 13th edition of this book. The formula for the present British solution has been modelled after that of the U. S. Pharmacopœia.

When iron is treated with hydrochloric acid there is a copious evolution of hydrogen, and an emerald-green solution of ferrous chloride ($FeCl_2$) results. Green crystals having the composition $FeCl_2,4H_2O$ separate if the solution is permitted to rest. In the official process, water is added to the hydrochloric acid in order to retain the crystals in solution, and the mixture is heated while still in contact with the excess of iron, in order to hasten the complete conversion of all the hydrochloric acid into ferrous chloride. The action slackens very materially as the quantity of hydrochloric acid is gradually lessened in the mixture, but when it is brought, as officially directed, to the boiling point, a saturated solution is produced. After filtering from the excess of iron, half the original quantity of hydrochloric acid is added—this for the purpose of supplying the amount which is requisite to form the solution of ferric chloride—and the mixture is then gradually poured into nitric acid, which at once converts the solution of green ferrous chloride into the solution of red ferric chloride. Formerly the nitric acid was added to the solution; now the order is reversed, in accordance with the recommendation of C. L. Diehl, to prevent frothing. (See *A. J. P.*, 1867, p. 140.) The reaction between the acids and the solution may be thus expressed:

$$\underset{\text{Ferrous chloride.}}{6FeCl_2} + \underset{\text{Nitric acid.}}{2HNO_3} + \underset{\text{Hydrochloric acid.}}{6HCl} =$$

$$\underset{\text{Ferric chloride.}}{6FeCl_3} + \underset{\text{Nitrogen dioxide.}}{N_2O_2} + \underset{\text{Water.}}{4H_2O}$$

If the solution should have a black color, and not a clear ruby-red, it is due to the presence of a nitro-compound composed of a portion of ferrous chloride and nitrogen dioxide, $FeCl_2 + N_2O_2$. As this compound is easily decomposed, all that is necessary is to heat the liquid and add a few drops of nitric acid, when the black color soon disappears, nitrogen dioxide is liberated, and a ruby-red solution remains. Any excess of nitric acid is to be evaporated. The final addition of hydrochloric acid is to compensate for any loss which may have been suffered by heating the solution, and to secure an excess of the acid in the finished preparation; otherwise a reddish-brown deposit of oxychloride would gradually form, and precipitation would result upon dilution with alcohol in making the official tincture.

The use of chlorine instead of nitric acid for converting the ferrous chloride to the ferric condition is advocated by C. W. Weiss (*Ph. Ztg.; N. R.*, 1883, p. 247), and J. W. England devised a process, based upon such substitutions. (See *U. S. D.*, 19th ed., p. 714.)

The solution of ferric chloride, properly made, is "a reddish-brown liquid, having a faint odor of hydrochloric acid, an acid, strongly styptic taste, and an acid reaction. Specific gravity: from 1.29 to 1.32 at 25° C. (77° F.). Separate portions of an aqueous dilution of the Solution (1 in 10) yield a brownish-red precipitate with ammonia water, a blue precipitate with potassium ferrocyanide T.S., and a white precipitate, insoluble in nitric acid, with silver nitrate T.S. Precipitate the iron completely from a weighed portion of about 2 mils of the Solution, previously diluted with 50 mils of distilled water, by adding an excess of ammonia water and filter. The filtrate is colorless, and does not yield a precipitate with hydrogen sulphide T.S. (*zinc, lead or copper*); nor does it leave on evaporation and ignition a fixed residue corresponding to more than 0.1 per cent. of the amount taken (*salts of the fixed alkalies*). Add a clear crystal of ferrous sulphate to a cooled mixture of equal volumes of sulphuric acid and an aqueous dilution of the Solution (1 in 10); the crystal does not become brown nor does a brownish-black color develop around it (*nitric acid*). Add a few drops of freshly prepared potassium ferricyanide T.S. to an aqueous dilution of the Solution (about 1 in 20); a brown color is produced which does not at once turn green or greenish-blue (*ferrous salts*). To about 0.5 Gm. of Solution of Ferric Chloride, accurately weighed, add 10 mils of distilled water and 50 mils of tenth-normal silver nitrate V.S., shake it vigorously, then add 2 mils of nitric acid and sufficient distilled water to measure exactly 100 mils, and mix well. Filter the mixture through a dry filter (rejecting the first filtrate) and determine the excess of silver nitrate in 50 mils of the filtrate by titration with tenth-normal potassium sulphocyanate V.S. The percentage of chlorine found is not less than 3 per cent. nor more than 5 per cent. in excess of that required to combine with the iron present as ferric chloride. The percentage of iron found, multiplied by 1.9, gives the percentage of chlorine combined as ferric chloride (*free hydrochloric acid*). Each mil of tenth-normal silver nitrate V.S. corresponds to 0.003546 Gm. of Cl.

"**Assay.**—Transfer about 2 Gm. of Solution of Ferric Chloride to a flask, stopper and weigh accurately, then add 5 mils of hydrochloric acid, 25 mils of distilled water and about 3 Gm. of potassium iodide, securely stopper the flask and allow the mixture to stand for thirty minutes at a temperature of 40° C. (104° F.). Cool the liquid, dilute it with 100 mils of distilled water and then titrate with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 10 per cent. nor more than 11 per cent. of Fe.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.005584 Gm. of Fe. Each gramme of Solution of Ferric Chloride corresponds to not less than 17.9 mils nor more than 19.7 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

"An orange-brown solution with a strong styptic taste. Miscible with *water* and with *alcohol* (90 per cent.) in all proportions. Specific gravity about 1.49. Yields the *reactions* characteristic of ferric salts and of chlorides.

Yields no characteristic *reactions* for lead, copper, zinc, calcium, sodium, potassium, ammonium, or ferrous salts. On adding a clear crystal of *ferrous sulphate* to a cooled mixture of equal volumes of *sulphuric acid* and of the Strong Solution diluted with nine times its volume of *water* the crystal does not become brown, nor does a brownish-black color develop around it (limit of nitrates). *Arsenic limit* 10 parts per million. 5 millilitres diluted with 80 millilitres of *water* yield, upon the addition of an excess of *solution of ammonia,* a reddish-brown precipitate, which, when well washed and incinerated, weighs 1.42 grammes. This Solution contains 20 grammes of Iron in 100 millilitres; 110 minims contain 20 grains." *Br.*

Water and alcohol unite with it in all proportions. The British preparation (*Liquor Ferri Perchloridi Fortis*) is stronger than the U. S. official, the sp. gr. of the former being about 1.49 at 15.5° C. (60° F.), of the latter from 1.29 to 1.32 at 25° C. (77° F.). It should be remembered, however, that there is in the British Pharmacopœia, another solution of ferric chloride which is weaker; it has the sp. gr. 1.110 and is termed *Liquor Ferri Perchloridi.* (See page 636.)

From the experiments of Adrian it appears that sugar has the property when mixed in certain proportions with solution of ferric chloride of converting it partly into ferrous chloride. The alteration commences immediately on the addition of sugar, as shown by the deeper color of the liquid; after some hours potassium ferricyanide will indicate the presence of a ferrous salt, and after twenty-four hours the greater proportion of the ferric salt has undergone the change. (*B. M. S. J.,* March, 1868.)

Uses.—This preparation was brought prominently into notice by Pravaz, a surgeon of Lyons, who found that a few drops of a strong solution, injected into a blood vessel, produced coagulation of all the blood in the vessel for the extent of an inch or more. Its use as a styptic was the natural result of this observation. In arresting *hemorrhages* from cut surfaces or wounded vessels it has proved remarkably successful. It has also been found advantageous as an application to *nasal polypi, erectile tumors,* or *nævi materni* in infants, in *ulcers* about the nails, and in various cutaneous affections. Attempts have been made to cure *nævi materni* by the injection of the solution into the erectile tumor, but this proceeding is hazardous and has caused death. (*Ann. Thér.,* 1867, p. 117.) It has been used externally with asserted success in *varicose veins.* In *post-partum hemorrhage* it has been largely employed, a solution of it, varying in strength from a drachm to a half ounce to the pint, being thrown directly into the relaxed uterus. Garrett (*B. M. J.,* 1913, i) recommends the stronger solution of iron chloride *Br.* as a local application in *ringworm* of the scalp; he states that it must be applied full strength to get good results. Zeissl has used it as a local remedy in *acne rosacea.* Bourget has employed a gelatinized solution of ferric chloride in the treatment of *gastric ulcer.* (*Th. M.,* 1909, p. 353.) His solution consists of 100 grammes each of gelatin, glycerin, and water, and 50 grammes of the *liquor ferri perchloridi,* P. G.

Dose, one to five minims (0.06–0.3 mil).

Off. Prep.—Liquor Ferri Perchloridi, *Br.;* Tinctura Ferri Chloridi, *U. S.* (*Br.*); Gossypium Stypticum, *N. F.;* Tinctura Ferri Chloridi Ætherea, *N. F.;* Tinctura Ferri Citro-chloridi, *N. F.*

LIQUOR FERRI ET AMMONII ACETATIS. U. S.

SOLUTION OF IRON AND AMMONIUM ACETATE
Liq. Ferr. et Ammon. Acet. [Basham's Mixture]

(lĭ'quŏr fĕr'rī ĕt ăm-mō'nī-ī ăç-ē-tā'tĭs)

Mistura Ferri et Ammonii Acetatis, *U. S. P.* 1880.

* "Tincture of Ferric Chloride, *forty mils* [or 1 fluidounce, 169 minims]; Diluted Acetic Acid, *sixty mils* [or 2 fluidounces, 14 minims]; Solution of Ammonium Acetate, *five hundred mils* [or 16 fluidounces, 435 minims]; Aromatic Elixir, *one hundred and twenty mils* [or 4 fluidounces, 28 minims]; Glycerin, *one hundred and twenty mils* [or 4 fluidounces, 28 minims]; Distilled Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. To the solution of ammonium acetate (which must be slightly acid) add, successively, the diluted acetic acid, the tincture of ferric chloride, the aromatic elixir, and the glycerin, and lastly, enough distilled water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. This preparation must not be dispensed unless it has been recently prepared." *U. S.*

The official name of this preparation has been changed to "Liquor" in accordance with the views expressed in the 16th edition of this work, as it belongs to the class of solutions, and is not a mixture in the modern acceptation of the term. It is still, however, frequently prescribed under the old designation "*Mist. Basham.*" The formula has been improved by the addition of glycerin, which enables the solution to remain undecomposed somewhat longer. It should be borne in mind, however, that this was never intended to be a permanent solution, and in time precipitation and decomposition surely set in. Some pharmacists adopt the plan of keeping all the ingredients, except the tincture of ferric chloride and water, mixed together in advance, and when called upon to dispense the solution, to add the proper quantity of tincture and water; this saves time and enables them to dispense a clear solution.

"Solution of Iron and Ammonium Acetate is a clear, reddish-brown liquid, of a sweetish, saline and afterward slightly astringent taste; it possesses an aromatic odor. The Solution is acid to litmus. Specific gravity: about 1.039 at 25° C. (77° F.). The Solution yields a blue precipitate with potassium ferrocyanide T.S., but the addition of ammonia water produces no

precipitate. When Solution of Iron and Ammonium Acetate is heated with potassium hydroxide T.S., ammonia is evolved. Add 1 mil each of sulphuric acid and alcohol to 5 mils of the Solution and boil the mixture; ethyl acetate is formed, recognizable by its odor." *U. S.*

When freshly made, it is a transparent, bright red liquid. When cloudy, the absence of sufficient free acid is indicated. The iron is in the form of an acetate, while there is formed, as one of the products of decomposition, a small quantity of ammonium chloride, the larger proportion of ammonium acetate remaining undecomposed.

Basham's mixture is actively chalybeate, and also astringent, and is very largely used in *chronic Bright's disease.* There has arisen a popular superstition that it exercises a curative effect in nephritis, but its value is probably simply that of a hematinic and not superior to other forms of iron.

Dose, from one-fourth to one-half fluidounce (7.5–15 mils).

LIQUOR FERRI PERCHLORIDI. Br.

SOLUTION OF FERRIC CHLORIDE

(lĭ'quŏr fĕr'rī pĕr-ȼhlō'rĭ-dī)

Solution of Perchloride of Iron.

"Strong Solution of Ferric Chloride, 250 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Mix." *Br.*

This is one-fourth the strength of the *Liquor Ferri Perchloridi* of the Br. Pharmacopœia of 1864, which is the *Liquor Ferri Perchloridi Fortis* of the present edition. (See p. 633.) It is of the same ferruginous strength as the British Tincture of Ferric Chloride. The specific gravity of this solution is 1.110, and it may be substituted for the tincture of ferric chloride when alcohol is objectionable, as it has the same strength; it is very astringent.

Dose, from ten to thirty minims (0.6–1.8 mils), well diluted.

LIQUOR FERRI SUBSULPHATIS. U. S.

SOLUTION OF FERRIC SUBSULPHATE Liq. Ferr. Subsulph. [Solution of Basic Ferric Sulphate, Monsel's Solution]

(lĭ'quŏr fĕr'rī sŭb-sŭl-phā'tĭs)

"An aqueous solution containing basic ferric sulphate corresponding to not less than 13 per cent. nor more than 14 per cent. of Fe." *U. S.*

Solution of Subsulphate of Iron; Solution of Persulphate of Iron; Liquer hémostatique de Monsel, *Fr.;* Basisch-schwefelsaure Eisenoxydlösung, Monsel's Eisenlösung, Monselsche Eisenlösung, *G.*

* "Ferrous Sulphate, *six hundred and seventy-five grammes* [or 23 ounces av., 284 grains]; Sulphuric Acid, *sixty-five grammes* [or 2 ounces av., 128 grains]; Nitric Acid, Distilled Water, each, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Add the sulphuric acid to *five hundred mils* [or 16 fluidounces, 435 minims] of distilled water in a tared capacious porcelain dish, heat the mixture to nearly 100° C. (212° F.), then add *seventy grammes* [or 2 ounces av., 205 grains] of nitric acid, and mix well. Divide the ferrous sulphate, coarsely powdered, into four approximately equal portions, and add these portions, one at a time, to the hot liquid, stirring after each addition until effervescence ceases. If, after the ferrous sulphate has dissolved, the solution is of a black color, add nitric acid, a few drops at a time, with heating and stirring, until red fumes cease to be evolved. Boil the solution until it assumes a red color, and is free from nitric acid, as indicated by the test given below. During the heating add distilled water from time to time to maintain about the original volume. Lastly, add enough distilled water to make the product weigh *one thousand grammes* [or 35 ounces av., 120 grains]. Filter if necessary. Keep it in well-stoppered containers, in a moderately warm place (not under 22° C. or 71.6° F.), protected from light. This solution sometimes crystallizes, forming a semi-solid, whitish mass. When this occurs, the application of a gentle heat will restore the liquid condition." *U. S.*

This process is essentially that of E. R. Squibb. The object is to obtain in solution *Monsel's persulphate of Iron,* improperly so called, as it differs both in composition and in properties from the salt of iron properly named persulphate. The composition of the true persulphate (tersulphate) is $Fe_2(SO_4)_3$, and it is a neutral salt, while Monsel's persulphate has the composition $5Fe_2(SO_4)_3.Fe_2(HO)_6$, and is properly a subsalt, as it is very appropriately designated in the U. S. Pharmacopœia.

In its preparation the ferrous sulphate is converted into ferric sulphate at the expense of the nitric acid; but the sulphuric acid, mixed with the nitric, is in quantity insufficient to form the normal salt. The sesquioxide is therefore but partially saturated, and a subsalt results, having the constitution above mentioned.

J. Creuse offers the following formulas for the preparation of the solutions of *ferric sulphate* and *ferric subsulphate,* holding them to be superior to the official because they require no especial apparatus and generate no noxious vapors:

For the ferric sulphate, take of Ferrous Sulphate, in coarse powder, twelve troyounces; Sulphuric Acid two troyounces and sixty grains; Potassium Chlorate three hundred and forty-eight grains; Boiling Water twelve fluidounces. Dissolve the ferrous sulphate in the boiling water in a glass flask, or in any convenient bottle; add the sulphuric acid gradually, and, while the liquid is hot, add the potassium chlorate by small portions. When all is dissolved, filter, and complete twenty-four fluidounces. The following formula explains the reactions:

$$6FeSO_4 + 3H_2SO_4 + KClO_3 = 3Fe_2(SO_4)_3 + 3H_2O + KCl$$

For the subsulphate, take of the ingredients above enumerated, respectively, twelve troy-

ounces, one troyounce and thirty grains, three hundred and forty grains, ten fluidounces; proceed as before; evaporate to twelve fluidounces; filter. (*A. J. P.*, xliii, 169.) The solutions thus obtained contain some potassium chloride.

Properties.—The solution of ferric subsulphate is "a dark reddish-brown liquid, odorless or nearly so, of an acid, strongly styptic taste, an acid reaction and miscible with water and alcohol without decomposition. Specific gravity: about 1.548 at 25° C. (77° F.). Separate portions of an aqueous dilution of the Solution (1 in 20) yield a brownish-red precipitate with ammonia water, a blue precipitate with potassium ferrocyanide T.S., and a white precipitate, insoluble in hydrochloric acid, with barium chloride T.S. Add a clear crystal of ferrous sulphate to a cooled mixture of equal volumes of sulphuric acid and an aqueous dilution of the Solution (1 in 10); the crystal does not become brown nor does a brownish-black color develop around it (*nitric acid*). Add a few drops of freshly prepared potassium ferricyanide T.S. to 2 mils of an aqueous dilution of the Solution (1 in 20); a brown color is produced without a tinge of green or greenish-blue (*ferrous salt*).

"**Assay.**—Transfer about 1.5 Gm. of Solution of Ferric Subsulphate to a flask, stopper and weigh accurately, then add 5 mils of hydrochloric acid, 25 mils of distilled water, and 2 Gm. of potassium iodide, securely stopper the flask and allow the mixture to stand for thirty minutes at a temperature of 40° C. (104° F.). Cool the liquid, dilute it with 50 mils of distilled water, and then titrate with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 13 per cent., nor more than 14 per cent. of Fe.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.005584 Gm. of Fe. Each gramme of Solution of Ferric Subsulphate corresponds to not less than 23.3 mils nor more than 25.1 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

A little sulphuric acid decolorizes the liquid in a considerable degree, and an excess of the same acid converts it into a white, soft, pasty solid, resembling plaster of Paris which has begun to solidify after mixture with water. This test, according to Squibb, is quite characteristic. (*N. Y. Journ. Med.*, 1860, p. 173.)

By evaporation, upon a glass surface, with a moderate heat, the solution yields ferric subsulphate or *Monsel's salt*, in the form of thin transparent scales, of a light reddish-brown color, deliquescent, and readily soluble in water. Attention was first called to the special styptic virtues of ferric sulphate by Monsel in 1852; but it was not until 1857 that he published the formula for the peculiar salt which now goes by his name, and the solution of which is the subject of the present article. (See *J. P. C.*, Sept., 1857; also *Ibid.*, Juillet, 1859.)

Uses.—In consequence of its deficiency of sulphuric acid, this salt is less irritant than the ferric sulphate, while it has at least equal, if not greater, astringency. It is very efficacious as a styptic, through its power of coagulating the blood. The solution may be applied by means of a small sponge or pencil of spun glass to the bleeding surface or vessel. It is an excellent styptic in *hemorrhage* from the stomach and bowels.

Dose, from two to five minims (0.12–0.3 mil), properly diluted, and repeated as often as necessary.

LIQUOR FERRI TERSULPHATIS. U. S. (Br.)

SOLUTION OF FERRIC SULPHATE Liq. Ferr. Tersulph. [Solution of Iron Tersulphate]

(lĭ'quor fĕr'rī tĕr-sŭl-phā'tĭs)

"An aqueous solution containing normal ferric sulphate [$Fe_2(SO_4)_3 = 399.89$], corresponding to not less than 9.5 per cent. nor more than 10.5 per cent. of Fe." *U. S.*

Liquor Ferri Persulphatis, *Br.;* Solution of Normal Ferric Sulphate, Solution of Tersulphate of Iron; Solution of Persulphate of Iron; Persulfate de Fer liquide, *Fr.;* Ferrisulfatlösung, Schwefelsaure Eisenoxydlösung, Flüssiges Schwefelsaures Eisenoxyd, *G.*

* "Ferrous Sulphate, *five hundred grammes* [or 17 ounces av., 279 grains]; Sulphuric Acid, *ninety-six grammes* [or 3 ounces av., 169 grains]; Nitric Acid, Distilled Water, each, *a sufficient quantity*, to make *one thousand grammes* [or 35 ounces av., 120 grains]. Add the sulphuric acid to about *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of distilled water in a tared capacious porcelain dish, heat the mixture to nearly 100° C. (212° F.), then add *fifty-six grammes* [or 1 ounce av., 427 grains] of nitric acid and mix well. Divide the ferrous sulphate, coarsely powdered, into four approximately equal portions, and add these portions, one at a time, to the hot liquid, stirring after each addition until effervescence ceases. When all of the ferrous sulphate is dissolved, if the solution has acquired a black color add nitric acid, a few drops at a time, heating and stirring until red fumes cease to be evolved, and the Solution assumes a clear reddish-brown color; then boil the liquid until it is free from nitric acid, as indicated by the test given below. During the heating add distilled water from time to time to maintain about the original volume. Lastly, add enough distilled water to make the product weigh *one thousand grammes* [or 35 ounces av., 120 grains]. Filter if necessary." *U. S.*

"Ferrous Sulphate, 400.0 *grammes;* Sulphuric Acid, 37.5 *millilitres;* Nitric Acid, 37.5 *millilitres;* Distilled Water, *a sufficient quantity.* Add the Sulphuric Acid to five hundred *millilitres* of the Distilled Water; dissolve the Ferrous Sulphate in the mixture with the aid of heat; mix the Nitric Acid with one hundred *millilitres* of the Distilled Water; add to this diluted acid, warmed, the solution of Ferrous Sulphate; concentrate by boiling, until, on the sudden disengagement of ruddy vapors, the

liquid ceases to be black and acquires a red color. If any ferrous salt remain in the solution, add a few drops of Nitric Acid, and boil again. When the solution is cold add, if necessary, sufficient Distilled Water to produce five hundred and fifty *millilitres*." *Br.*

The strength of this solution was increased in the U. S. Pharm. VIII. The U. S. P. (1890) required a strength equivalent to 8 per cent. of metallic iron, the present Pharmacopœia requires about 10 per cent. The ferrous sulphate is preferably in clear crystals, meaning by this "not effloresced," because when the crystals are coated with a whitish powder they have lost water of crystallization, and the proportion of iron present is variable. The nitric acid in the process gives up enough of its oxygen to convert it entirely into ferric sulphate, and the effervescence is owing to the escape of nitrogen dioxide; this becomes red nitrogen tetroxide by contact with the air. The conversion of the ferrous salt into ferric salt is incomplete until the effervescence ceases, and the color, instead of black, as it was at first, has become reddish-brown. Indeed, in order to convert the whole into ferric sulphate it is necessary to continue the heat until nitrous odor ceases to be evolved and thus the entire absence of nitric or nitrous acid from the solution is insured. In consequence of the higher oxidation of the iron the sulphuric acid of the sulphate is insufficient to saturate it. Enough sulphuric acid, therefore, is added to meet this demand. The process is completed by adding enough water to make a definite weight. The U. S. and British formulas are the same in principle.

Properties.—The solution, prepared according to the U. S. formula, is "a yellowish-brown liquid, almost odorless, having an acid, strongly styptic taste, and an acid reaction; it is miscible with water and alcohol. Specific gravity: about 1.432 at 25° C. (77° F.). Separate portions of an aqueous dilution of the Solution (1 in 20) yield a brownish-red precipitate with ammonia water, a blue precipitate with potassium ferrocyanide T.S., and a white precipitate, insoluble in hydrochloric acid, with barium chloride T.S. Add a clear crystal of ferrous sulphate to a cooled mixture of equal volumes of sulphuric acid and an aqueous dilution of the Solution (1 in 10); the crystal does not become brown, nor does a brownish-black color develop around it (*nitric acid*). Add a few drops of freshly prepared potassium ferricyanide T.S. to 2 mils of an aqueous dilution of the Solution (1 in 20); a brown color is produced without a tinge of green or greenish-blue (*ferrous salt*).

"**Assay.**—Transfer about 1.5 Gm. of Solution of Ferric Sulphate to a flask, stopper and weigh accurately, then add 5 mils of hydrochloric acid, 25 mils of distilled water, and 2 Gm. of potassium iodide, securely stopper the flask and allow the mixture to stand for thirty minutes at a temperature of 40° C. (104° F.). Cool the liquid, dilute it with 50 mils of distilled water and then titrate with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 9.5 per cent. nor more than 10.5 per cent. of Fe.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.005584 Gm. of Fe. Each gramme of Solution of Ferric Sulphate corresponds to not less than 17 mils nor more than 18.8 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

"A dark-red solution. Inodorous; very astringent. Miscible in all proportions with *alcohol* (90 per cent.) and *water*. Specific gravity about 1.441. Yields the *reactions* characteristic of ferric salts and of sulphates. Yields no characteristic *reactions* for ferrous salts. *Arsenic limit* 5 parts per million. 5 millilitres diluted with 80 millilitres of *water* yield, upon the addition of excess of *solution of ammonia*, a precipitate which, when well washed and incinerated, weighs 1.04 grammes." *Br.*

Procter found that a preparation containing 120 grains of sesquioxide to the fluidounce is apt to deposit the anhydrous sulphate on standing.

Uses.—This solution, though powerfully astringent, is too irritant for general use. The chief employment of it is in making other ferruginous preparations in which the ferric hydroxide is wanted, and it should always be kept on hand for the quick preparation of the antidote to arsenic.

LIQUOR FORMALDEHYDI. U. S., Br.

SOLUTION OF FORMALDEHYDE Liq. Formaldehyd.

(lĭ'quŏr fōrm-ăl-dē-hȳ'dī)

"An aqueous solution containing not less than 37 per cent. by weight of CH_2O or H.CHO (30.02), with varying amounts of methyl alcohol to prevent polymerization. Preserve it in a moderately warm place, protected from light." *U. S.* "Solution of Formaldehyde is an aqueous solution containing in 100 millilitres not less than 36 and not more than 38 grammes of formaldehyde, CH_2O. Formaldehyde may be obtained by the limited oxidation of methyl alcohol." *Br.*

Formol, Formalin; Soluté d'Aldehyde Formique, *Fr.*; Formaldehydum solutum, *P. G.*; Formaldehydlösung, *G.*; Formol, *Sp.*

Preparation.—*Formaldehyde* was first prepared in 1868 by Hofmann by passing a mixture of air and methyl alcohol vapor over heated platinum, and it is still practically obtained only from the oxidation of methyl alcohol. This is accomplished in "formaldehyde lamps," or on a larger scale in forms of apparatus, such as that described by G. L. Taylor (*A. J. P.*, 1898, 195) as follows: The methyl alcohol to be converted is contained in a circular steel tank, capable of resisting heavy pressure; in the bottom of this tank is placed a coil of copper pipe into which steam at a high temperature is admitted; by this means the alcohol in the tank is boiled, and the resulting vapor is confined until a pressure of 75 to 80 pounds is reached, when it is

allowed to escape into an air-mixer. This mixer is so constructed that an exactly determined quantity of air can be intimately combined with the methyl alcohol vapors. From the mixer the combination of air and vapor passes with great force and velocity through a fine tube into the converter, which has been brought to a dull red heat. This converter consists of two concentric copper tubes, the space between which is filled with broken coke or other material of a similar nature. The inner tube is finely perforated with many small holes. The alcohol vapor is admitted into this inner tube, and, escaping through the perforations, is oxidized by coming in contact with the heated coke and the copper surface of the outer tube. The gases so produced pass into the condenser, which consists of a cylindrical tank—which may be of copper; it contains a copper pipe, through which circulates a refrigerating mixture capable of reducing the temperature in the tank to about 0° C. (32° F.), at which temperature formic aldehyde condenses into a clear mobile liquid, which boils at –21° C. (–5.8° F.), and which polymerizes to paraformaldehyde at 20° C. (68° F.). After a certain process of purification, enough water is added to the formaldehyde so obtained to form a 40 per cent. solution; but this solution is not, strictly speaking, a solution of formaldehyde, as the pure formaldehyde polymerizes the moment the temperature rises above 20° C. (68° F.), and it is this property which renders the addition of water or alcohol necessary. Hence the aqueous solution of formaldehyde probably contains some paraformaldehyde and some unconverted methyl alcohol is always present which is allowed to remain because of the preservative effect it has in preventing polymerization. This change which sometimes occurs in commercial solutions of formaldehyde during the winter months is accompanied by the deposition of a white precipitate sometimes occupying a bulk equal to one-half of the original liquid and when it has occurred the only method of restoration is to acidify with sulphuric acid and redistil the liquid. The commercial products are always aqueous solutions, the common strength being the 37 per cent. solution; a 50 per cent. solution is not permanent.

Properties.—Solution of formaldehyde or "formaldehyde," as it is commonly called, is officially described as "a clear, colorless or nearly colorless liquid, having a pungent odor and a caustic taste; its vapor acts as an irritant upon mucous membrane. It is miscible with water or alcohol. On long standing, especially in the cold, Solution of Formaldehyde sometimes loses its transparency, the cloudiness being due to the separation of paraformaldehyde. Dilute 5 mils of Solution of Formaldehyde with 25 mils of distilled water and add 3 mils of silver ammonium nitrate T.S.; metallic silver is produced either in the form of a finely divided gray precipitate or as a bright metallic mirror adhering to the sides of the test tube. Add 2 drops of Solution of Formaldehyde to 5 mils of sulphuric acid in which a little salicylic acid has been dissolved, and warm the liquid very gently; a permanent deep red color appears. Not more than 1 mil of normal potassium hydroxide V.S. is required to neutralize 20 mils of Solution of Formaldehyde, to which 2 drops of phenolphthalein T.S. have been added (*free acids*).

"**Assay.**—Transfer 3 mils of Solution of Formaldehyde to a tared flask containing 10 mils of distilled water, tightly stopper and weigh accurately. Add to the contents of the flask 50 mils of normal potassium hydroxide V.S., and follow this immediately but slowly through a small funnel with 50 mils of solution of hydrogen dioxide which has previously been rendered neutral to litmus with potassium hydroxide. Now heat the mixture cautiously on a water bath for five minutes, shaking occasionally during this time; allow the mixture to cool, rinse the funnel and sides of the flask with distilled water and, after allowing it to stand thirty minutes, titrate with normal sulphuric acid V.S., using litmus T.S. as indicator. It shows not less than 37 per cent. of CH_2O, correction being made for free acid if present.

"Each mil of normal potassium hydroxide V.S. corresponds to 0.03002 Gm. of CH_2O. Each gramme of Solution of Formaldehyde corresponds to not less than 12.3 mils of normal potassium hydroxide V.S." *U. S.*

"A colorless liquid with a characteristic, pungent odor. Neutral or slightly acid to *litmus*. Miscible with *water* and with *alcohol* (90 per cent.) in all proportions. Caustic when applied to the skin. Specific gravity 1.079 to 1.081. Yields, when evaporated to dryness, a whitish, amorphous residue which leaves no appreciable ash on incineration. Yields with *solution of silver ammonio-nitrate* a precipitate of metallic silver. On the addition of 2 drops of the Solution to 5 millilitres of *sulphuric acid*, in which a little *salicylic acid* has been previously dissolved, a deep red coloration is produced. When 1 millilitre is mixed with 10 millilitres of *N/10 solution of iodine*, the mixture nearly decolorised with *solution of sodium hydroxide* and warmed, no yellow, crystalline precipitate is produced (absence of acetone). Diluted with four times its volume of *water* it yields no characteristic *reactions* for iron, copper lead, calcium, chlorides, or sulphates. Contains in 100 millilitres not less than 36 and not more than 38 grammes of formaldehyde, CH_2O, as determined by the following process:—To 50 millilitres of *N/1 solution of sodium hydroxide* add 3 millilitres of Solution of Formaldehyde and 50 millilitres of *solution of hydrogen peroxide* and warm on a water-bath; similarly mix 50 millilitres of *N/1 solution of sodium hydroxide* with 50 millilitres of *solution of hydrogen peroxide* and warm on a water-bath. When the reactions are complete and all effervescence has ceased, add a few drops of *solution of phenolphthalein* to each mixture and titrate with *N/1*

solution of sulphuric acid. The difference between the two titrations is not less than 36 and not more than 38 millilitres." *Br.*

Formaldehyde may be determined in aqueous solutions by treatment with excess of standard ammonia, which converts it into hexamethylenamine. The excess of ammonia may then be titrated with standard acid. The mixture of the formaldehyde solution and ammonia should stand for at least twelve hours. This method, however, has not been found in practice to be as accurate as the hydrogen dioxide method, which was therefore chosen by the Revision Committee as the basis of the official assay process. Because of the use of formaldehyde as a preservative of milk and food products the detection of small amounts of it is a matter of great importance. Several of the tests proposed are primarily applicable to milk only, being based on reactions which take place in the presence of milk proteids, so that if these tests are to be applied in testing other liquids for the presence of formaldehyde, the material must be mixed with an equal quantity of milk which has been shown previously to be free from formaldehyde. The principal tests may be divided into two groups, those in which a colored zone is obtained at the junction of two liquids, one of which has been superimposed upon the other, and those in which a color reaction is obtained in the body of the liquid tested. The first group includes the resorcinol-sulphuric acid test, the phenol-sulphuric acid test, and the sulphuric acid test of Hehner (carried out in the presence of milk). The method of application of the two tests first mentioned is as follows: To 5 mils of the liquid to be tested, one or two drops of a one per cent. aqueous solution of phenol or resorcinol are added, and this liquid is then allowed to flow gently down the inside of the test tube containing 2 or 3 mils of the sulphuric acid so as to form a layer above the acid without mixing. In the presence of formaldehyde a rose-colored zone is produced in extreme dilution, or in more concentrated solutions an opaque pinkish zone above the rose-colored one. In the Hehner test, the liquid to be tested is mixed with an equal volume of formaldehyde-free milk, and this mixture is allowed to flow down the inside of the test tube upon 2 or 3 mils of commercial sulphuric acid containing a trace of ferric chloride. A violet zone is formed in the presence of formaldehyde. The general color tests constituting the second group of tests are the phenylhydrazine test with its modifications, the phloroglucinol test, the resorcinol-soda test, and the hydrochloric acid test. (A full discussion and comparison of these tests by C. H. LaWall will be found in *Am. Drug.*, 1905, vol. xlvii, p. 33.)

The foregoing tests are all group tests for aldehydes and positive results will be obtained in the presence of furfurol, vanillin, and many other aldehydic bodies. The best specific test given by formaldehyde only is that of Rimini, and is carried out as follows: To 10 mils of the clear liquid or distillate is added 0.05 gramme phenylhydrazine hydrochloride followed by 3 drops of a 5 per cent. aqueous solution of sodium nitroprusside, and, finally, by 1 mil (or an excess) of a 10 per cent. sodium hydroxide solution. In the presence of formaldehyde a blue or greenish-blue color is immediately produced which, however, quickly changes to yellow and finally to red.

The test is so sensitive as to detect the substance in a solution containing but one drop of commercial formaldehyde solution in five gallons of water.

A. B. Lyons (*Proc. A. Ph. A.*, 1905, 326) proposes the use of *beef peptone* in place of milk (except when milk is under investigation) in Hehner's test (see above). He also suggests the use of morphine and sulphuric acid as a test for formaldehyde. (*Proc. A. Ph. A.*, 1905, 329.)

Uses.—Formaldehyde was introduced as a disinfectant by Trillat in 1888. It is remarkable among germicidal agents for the fact that its action in solution is less powerful than as a vapor. Its solutions are about equivalent in germicidal activity to those containing the same percentages of phenol. Burgess (*L. L.*, 1900, i, p. 1797) found that a 2 per cent. solution would kill the *B. coli communis* in five minutes and Slater and Rideal found that it required 50 minutes for a one per cent. solution to destroy various non-sporulating micro-organisms. Its action as an antiseptic, however, far exceeds that of phenol. In Slater and Rideal's experiments one part in five thousand absolutely inhibited, and one in twenty thousand greatly restrained the growth of bacteria. As regards the effects of formaldehyde vapor, it has been shown that as little as one part in three thousand parts of air will destroy many bacteria and, according to Kenwood, one or two per cent. will rapidly disinfect all surfaces. It should be remarked in this connection that the penetrating power of formaldehyde has been usually overestimated and that bundles of clothing or similar material are not effectually disinfected by such strengths of the gas.

Formaldehyde is an intense local irritant both to mucous membranes or if in sufficient concentration, to the skin. In strong solution it precipitates albumen or gelatin, but very minute quantities are asserted to prevent the coagulation of albumen by heat. When injected into the circulation in such dilutions as not to precipitate the proteins of the blood, or after its absorption through the gastro-intestinal mucosa, it exercises relatively slight effects on the vital functions. According to McGuigan (*J. A. M. A.*, 1914, lxii, p. 984) large quantities lower the blood pressure by a direct action upon the heart and vessel walls. Fleig states that it causes contraction of the renal vessels. It is rapidly oxidized in the system and appears in the urine as formic acid, so that after the administration of even relatively large doses no formaldehyde can be found in the excretions.

Formaldehyde is used in medicine chiefly for its disinfectant properties. Because of its local irritant influence it is rarely of service as a surgical application to the living body. It is occasionally used for the disinfection of surgical instruments and apparatus. For this purpose the vapor is more efficient than the solution. The most important use of formaldehyde is for the disinfection of rooms and various objects like books which might be injured by steam. Although it has a powerful effect on some forms of organic matter, things which are likely to come in contact with patients suffering from infectious diseases, such as clothing and the decorations in the sick room, are not injured by disinfectant strengths. Because of its affinity for ammonia and for hydrogen sulphide it has strong deodorizing properties. Various methods for the vaporization of formaldehyde are used in room disinfection; these include (1) direct generation by oxidizing methyl alcohol; (2) spontaneous evaporation of a solution sprinkled around the room; (3) evaporation of the official solution by means of heat; (4) vaporization of the official solution by oxidizing agents; and (5) decomposition of its polymer known as paraform. The first of these has been largely abandoned because of its cumbersomeness and the uncertainty of amount, the second because of its inefficiency and injurious effect upon the operators. The decomposition of paraform by heat is a convenient method for disinfecting small spaces, such as boxes containing surgical appliances, or closets, but is too expensive for general use; moreover, the presence of considerable amounts of aqueous vapor in the air is essential for best results with formaldehyde, and in most of the apparatuses using paraform insufficient provision is made for this. The method of evaporating aqueous solutions of formaldehyde with heat is the basis of a number of efficient apparatuses, but it is doubtful whether these have any real advantage over the cheap and handy method of volatilizing by means of oxidizing agents. The substances which have been used for the latter service include potassium permanganate, quick lime, barium peroxide, and sodium dichromate. The method recommended by the Pennsylvania State Board of Health, Dixon (*A. J. P.*, July, 1912) is as follows: For a thousand cubic feet of air space, one pint of the official solution of formaldehyde and eight ounces of potassium permanganate. Place the potassium permanganate in a bucket with at least ten times the capacity of the amount of disinfectant. Pour the formaldehyde on the permanganate. Eighty per cent. of the formaldehyde is liberated in the first five minutes. Doerr recommends the proportion of one part each of potassium permanganate, formaldehyde solution, and water. Hall and Roberts assert that seven parts of potassium permanganate to ten of formaldehyde solution is the most economical; this gives a liberation of 63 per cent. of the total formaldehyde. If water is added the percentage of liberation is lower, but the water is advantageous in aiding the disinfectant properties. It should be remembered that with careless use there is a possibility of setting fire to the room. In 1914, owing to the scarcity of potassium permanganate caused by the European war, a method was devised by LaWall (*J. A. M. A.*, 1914, lxiii, 1025) in which sodium dichromate takes the place of potassium permanganate. Notwithstanding some criticism of this process, as destroying a larger amount of the formaldehyde than the potassium permanganate method, tests made by the Pennsylvania Health Department bacteriologist, working under conditions such as are actually encountered in practical disinfection work, show all bacteria to be killed when the directions are carefully followed.

Inhalations of formaldehyde vapors have been tried in the treatment of pulmonary disorders, notably *phthisis*, with the idea of direct destructive action upon the bacteria, but they are so irritant to mucous membranes that the treatment has done more harm than good. Formaldehyde is also of service for the purpose of hardening the skin and of stopping excessive sweating in various forms of *hyperidrosis*. For this use the official solution should be diluted with from one to three parts of water. It is used in pharmacy for hardening gelatin capsules. (See page 511.)

Although its physiological action is comparatively slight, yet when swallowed it is a dangerous poison on account of its local irritant effects. The symptoms of formaldehyde poisoning are immediate severe abdominal pains with blood-stained vomiting, general collapse often with loss of consciousness, and albuminous, bloody or suppressed urine. Out of ten cases collated by McLoughlin (*Cleveland Med. Journ.*, 1909) three ended fatally. The smallest fatal dose of which we have any knowledge is the case reported by Eli (*J. A. M. A.*, liv) in which "a few drops of a 40 per cent. solution of formaldehyde" killed a three year old child with symptoms of edema of the larynx. The ordinarily fatal dose for an adult is about three fluidounces of the official solution. The diagnosis is usually easy from the odor of formaldehyde in the vomitus. The treatment requires an immediate evacuation of the stomach, the use of dilute ammonia water as an antidote, subsequently demulcents and symptomatic remedies as they may be indicated.

Formaldehyde is also used to harden gelatin capsules. (See p. 511.)

Festiform is a solution of formaldehyde solidified by the addition of soap. *Autan* is a mixture of paraform and barium peroxide which in the presence of water liberates formaldehyde gas. *Formysol* is a formalized soft soap as is also veroform. *Lysoform* is another saponaceous mixture containing formaldehyde.

Off. Prep.—Liquor Formaldehydi Saponatus, *Br.*

LIQUOR FORMALDEHYDI SAPONATUS. Br.

SOLUTION OF FORMALDEHYDE WITH SOAP

(lĭ'quŏr förm-ăl-dē-hī'dī să-pō-nā'tŭs)

"Soft soap, 400 *grammes;* *Alcohol* (90 per cent.), 300 *millilitres;* Solution of Formaldehyde, 200 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Dissolve the Soft Soap in the Alcohol; add the Solution of Formaldehyde and sufficient Distilled Water to produce the required volume." *Br.*

This solution was introduced into the British Pharm., 1914, for the first time. It is intended to be used externally and for surgical cleansing.

LIQUOR HYDRARGYRI NITRATIS ACIDUS. Br.

ACID SOLUTION OF MERCURIC NITRATE

(lĭ'quŏr hȳ-drär'gy-rī nī-trā'tĭs ăç'ĭ-dŭs)

Liquor Hydrargyri Nitratis, *N. F.;* Solution of Mercuric Nitrate; Solution of Nitrate of Mercury; Solution of Pernitrate of Mercury; Liquor Hydrargyri Nitrici Oxydati; Azotate Mercurique liquide, *Fr. Cod.;* Deutazotate (Pernitrate) de Mercure liquide, *Fr.;* Mercurnitratlösung, Quecksilberoxydnitratlösung, Flüssiges Salpetersaures Quecksilberoxyd, *G.*

"Mercury, 120 *grammes;* Nitric Acid, 150 *millilitres;* Distilled Water, 45 *millilitres.* Mix the Nitric Acid with the Distilled Water in a tared flask; dissolve the Mercury in the mixture without the application of heat; then boil gently until the Solution weighs three hundred and sixty *grammes.* Preserve it in a stoppered bottle not exposed to the light." *Br.*

The U. S. P. IX dismissed this solution, but the British Pharm. retained it. The National Formulary IV (see Part III) introduced the solution which was official in the U. S. P. VIII which was as follows:

"Red Mercuric Oxide, *forty grammes* [or 1 ounce av., 180 grains]; Nitric Acid, *forty-five grammes* [or 1 ounce av., 257 grains]; Distilled Water, *fifteen grammes* [or 231 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Mix the Nitric Acid with the Distilled Water, and dissolve the Red Mercuric Oxide in the mixture. Keep the product in glass-stoppered bottles." *U. S. VIII.*

In the British process, mercury is dissolved, with the assistance of heat, in an excess of nitric acid, and there is formed an acid mercuric nitrate, which is brought to a determinate bulk by evaporation. The proportion of nitric acid is sufficient not only to form mercuric nitrate, but also to furnish a large excess of acid.

Properties.—Solution of mercuric nitrate is a clear, nearly colorless, heavy liquid, having a faint odor of nitric acid, and a strongly acid reaction. "Specific gravity about 2.0. Yields no characteristic *reaction* for mercurous salts." *Br.*

Mercuric nitrate, the salt present in this preparation, can be obtained in large crystals of the composition $Hg(NO_3)_2 + 4H_2O$, when its solution is allowed to evaporate slowly over sulphuric acid. The same salt, which is very deliquescent, is obtained as a crystalline magma by adding strong nitric acid to the concentrated solution.

Uses.—This preparation is used as a caustic application to *cancers, lupus, ulcerations* of the *cervix, chancres,* etc. When a very free use is desired, it may be applied to the diseased surface by a camel's-hair brush, or preferably by a brush made of spun glass; usually, however, the application is made with a glass rod, or a match or similar fragment of wood. In *acne* and *boils,* a drop proportioned in size to the pustule applied to the apex is sometimes of service. The parts touched immediately become white, the surrounding parts inflame, and in a few days a yellow scab is formed, which gradually falls off. Sometimes the application produces salivation. When it is desirable to avoid this result, the cauterized part should be washed with water immediately after the application of the caustic. It is not used internally.

LIQUOR HYDRARGYRI PERCHLORIDI. Br.

SOLUTION OF MERCURIC CHLORIDE

(lĭ'quŏr hȳ-drär'gy-rī pĕr-ȼhlō'rĭ-dī)

Liquor Hydrargyri Bichloridi; Solution of Bichloride of Mercury; Solution of Corrosive Sublimate; Sublimatlösung, *G.*

"Mercuric Chloride, 1 *gramme;* Distilled Water, sufficient to produce 1000 *millilitres.* Dissolve. This Solution should be kept protected from light. 100 millilitres contain 0.1 gramme of Mercuric Chloride; 110 minims contain 1/10 grain." *Br.*

This solution may be used as affording a convenient method of exhibiting corrosive sublimate. The ammonium chloride formerly used (Br. Ph., 1885) to aid in dissolving the mercuric chloride has been omitted in the process of the Br. Ph., 1914.

Dose, from one-half to one fluidrachm (1.8–3.75 mils).

LIQUOR HYDROGENII DIOXIDI. U. S. (Br.)

SOLUTION OF HYDROGEN DIOXIDE Liq. Hydrog. Diox. [Solution of Hydrogen Peroxide, Aqua Hydrogenii Dioxidi, U. S. P. VIII]

(lĭ'quŏr hȳ-drŏ-gē'nĭ-ī dī-ŏx'ĭ-dī)

"An aqueous solution containing not less than 3 per cent. by weight of H_2O_2 (34.02), corresponding to not less than 10 volumes of available oxygen. Preserve it in a cool place protected from light. Upon removing the stopper from the bottle, not more than a slight pressure should be observed." *U. S.* "Solution of Hydrogen Peroxide is an aqueous solution of hydrogen peroxide, H_2O_2, prepared by the interaction of water, barium peroxide, and a dilute mineral acid, at a temperature below 10° C. (50° F.)." *Br.*

Liquor Hydrogenii Peroxidi, *Br.,* Solution of Hydrogen Peroxide; Oxygenized Water, Oxygen Hydrate; Péroxide d'Hydrogène; Solutéofficinal d'eau oxygénée au dixiéme, *Fr. Cod.;* Wasserstoffhyperoxyd, Wasserstoffhyperoxidlösung, *G.;* Acqua ossigenata, *It.;* Agua oxigenada, *Sp.*

The extended use of this preparation, which was discovered by Thenard in 1818, has earned for it a place in the U. S. and British Pharmacopœias. It consists of water in which, by the presenting to it of oxygen in a nascent state, an additional atom of this element has combined with the hydrogen, forming the dioxide $(HO)_2$, or H_2O_2.

The U. S. P., 1890, process (see *U. S. D.*, 18th edition, p. 214) consisted in the decomposition of barium dioxide by phosphoric acid, barium phosphate being thrown down as a precipitate, hydrogen dioxide being found dissolved in the supernatant aqueous liquid; the barium phosphate is filtered out, and any trace of barium salt is finally removed by the cautious addition of sulphuric acid, which precipitates it as insoluble barium sulphate; the very fine precipitate which usually passes through the pores of filter paper is caught and held on the filter by the starch, and the clear solution may be adjusted to contain 3 per cent., *by weight*, of absolute hydrogen dioxide by assay.

Commercially it is usually made by a process essentially the same as that given above, the phosphoric acid being regenerated from the precipitate of barium phosphate by the addition of sulphuric acid which converts it into insoluble barium sulphate with the liberation of almost the original amount of phosphoric acid used. Another method is also used in which hydrofluoric acid is employed. This yields the comparatively insoluble barium fluoride as a by-product and the hydrofluoric acid may be regenerated from this also by the use of sulphuric acid. On the large scale it is necessary to reduce the temperature of the reaction by refrigeration of some kind in order to get any where near the full theoretical yield from the barium dioxide used. One of the important points is the preliminary hydration of the barium dioxide which is accomplished by allowing the dioxide to stand in contact with an excess of water until it attains a creamy consistence.

According to Crismer, a pure solution may be made by dissolving barium peroxide in a slight excess of diluted hydrochloric acid (sp. gr. 1.10), and shaking the solution with an equal volume of ether. The ethereal layer is separated and shaken with a little water, which will take up most of the hydrogen peroxide, after the separation of which the ether is again shaken with the above separated solution of barium peroxide, and then with water as before. These operations are repeated five or six times. It is possible in this way to obtain solutions containing from 0.8 to 0.9 per cent. of the peroxide, which are perfectly neutral and free from foreign substances. (*Bull. Soc. Chim.*, 1891, 24.) Horlin (*Zeit. angew. Chem.*, 1902, 600) prepares the solution by adding at a low temperature with caution, sodium dioxide to a solution of hydrofluoric acid; hydrogen dioxide and sodium fluoride are produced, the solution is treated with aluminum fluoride, which results in producing the insoluble double fluoride of aluminum and sodium, which separates out. The official Solution is strong enough for most practical uses, for, although it can readily be made stronger, the difficulties of preserving it largely increase with its increased strength, and hence the Committee of Revision wisely fixed the standard at *ten volumes of available oxygen*. The British Pharmacopœia requires that the Solution shall indicate a yield of from *nine to eleven volumes* of oxygen when tested by the nitrometer test. (See page 644.)

Properties.—Hydrogen dioxide was prepared by Regnault in a nearly pure state. As thus procured, it is a colorless liquid of a fluid consistence, of the sp. gr. 1.452, remaining liquid at zero, beginning to give out oxygen when heated above 15.5° C. (60° F.), and at a higher heat rapidly and sometimes explosively resolved into water and oxygen. But when diluted with water, with which it unites in all proportions, it is not decomposed under 37.7° C. (100° F.). It may be evaporated *in vacuo* at a gradually increasing temperature, a nearly pure hydrogen dioxide coming over at about 84° C. (183.2° F.). Wolffenstein states that he has prepared, after repeated fractioning, hydrogen peroxide (99.1 per cent.). (See *Ber. d. Chem. Ges.*, 1894, 3307. See also Schiloff's process, *Chem. News*, 1896, 38.) Crystallized hydrogen dioxide has been made by W. Staedel by applying a freezing mixture to a very strong solution of the dioxide, and collecting the separated columnar crystals; it is a very active body, being decomposed with explosive violence on coming in contact with manganese dioxide. (*Ph. Centralh.*, 1902, 546.) The great facility with which it parts with oxygen renders it a powerful oxidizer; and the simple contact with various substances, as platinum, gold and silver, causes it to be resolved into oxygen and water. On the contrary, certain other substances, even though ordinarily evincing a strong affinity for oxygen, as phosphorus, for example, are unaffected by it, and there are a number of bodies which have the property not only of being unaffected by it, but of restraining its oxidizing influence on other bodies, while some salts, like silver oxide, are actually reduced by it. Traces of impurities modify the stability of hydrogen dioxide; acids increase, alkalies decrease, its stability. Some manufacturers add a certain proportion of oxalic acid to the solution of hydrogen dioxide to raise the apparent value of the product, as shown by the permanganate assay; for a method of detecting this fraud, see a paper by G. Arth (*D. C.*, 1902, p. 141).

The official solution is described as "a colorless liquid, odorless or having an odor suggesting ozone, slightly acid to the taste and producing a peculiar sensation and froth in the mouth; prone to deteriorate upon keeping or upon protracted agitation, and rapidly decomposed by contact with many oxidizing as well as reducing substances. If the stopper of the bottle is coated with paraffin or replaced by a

pledget of purified cotton, deterioration is retarded. When exposed to the air at the ordinary temperature or when heated on a water bath at a temperature not exceeding 60° C. (140° F.), the solution loses chiefly water. When rapidly heated, it frequently decomposes suddenly. Solution of Hydrogen Dioxide is acid to litmus. Shake 1 mil of Solution of Hydrogen Dioxide with 10 mils of distilled water containing 1 drop of diluted sulphuric acid, and add 2 mils of ether. The subsequent addition of a drop of potassium dichromate T.S. produces a blue color in the aqueous layer. Upon agitation, this blue color passes into the ethereal layer. Not more than 0.03 Gm. of solid residue remains on evaporating 20 mils of the Solution to dryness on a water bath (*non-volatile matter*). It requires not more than 2 mils of tenth-normal potassium hydroxide V.S., phenolphthalein T.S. being used as indicator, to neutralize 25 mils of Solution of Hydrogen Dioxide (*free acid*). Add 1 mil of ammonia water to 1 mil of the Solution and evaporate the liquid to dryness on a water bath; the residue meets the requirements of the Test for arsenic (see Part III, Test No. 1). Evaporate 1 mil of the Solution to dryness on a water bath and dissolve the residue in 10 mils of distilled water containing 1 mil of diluted hydrochloric acid; the liquid does not respond to the Test for heavy metals (see Part III, Test No. 3). Evaporate 50 mils of the Solution, previously rendered alkaline by the addition of sodium hydroxide T.S., to dryness on a water bath and transfer the dry residue to a platinum crucible. Moisten the residue with sulphuric acid, and cover the crucible with a watch glass, the convex side of which is coated with a thin layer of wax which is afterwards scratched so as to expose the glass. Cool the watch glass by placing water in the concave side and standing in this a small beaker which must be kept filled with cold water. Now heat the crucible and contents on a water bath for one hour; the surface of the watch glass after being cleaned shows no sign of corrosion (*hydrofluoric acid*). The addition of 2 drops of diluted sulphuric acid to 10 mils of the Solution produces no turbidity or precipitate within ten minutes (*barium*). Add 4 drops of sodium acetate T.S. to 10 mils of the Solution and follow with 4 drops of calcium chloride T.S.; no turbidity or precipitate is produced within ten minutes (*oxalic acid*). Shake out 100 mils of Solution of Hydrogen Dioxide in a separator with a mixture of three volumes of chloroform and two volumes of ether, using 50 mils, 25 mils, and 25 mils, respectively, and evaporate the combined solutions to dryness at room temperature in a tared glass dish. A residue may be obtained which weighs not more than 0.04 Gm. (*limit of preservative*)." *U. S.*

"A colorless and odorless liquid. Taste slightly acid. Decomposed by heat into water and oxygen. On adding a few drops to 10 millilitres of *water* mixed with a drop of *solution of potassium chromate*, 10 drops of *diluted sulphuric acid*, and 2 millilitres of *ether*, a blue layer appears between the ethereal and the aqueous liquid, and, after shaking, the *ether* also becomes blue. 2 millilitres vigorously shaken in a brine-charged nitrometer with 4 millilitres of *solution of copper ammonio-sulphate* liberate, at 15.5° C. (60° F.), and normal pressure, not less than 18 and not more than 22 millilitres of oxygen, corresponding to about 10 volumes of available oxygen in 1 volume of the Solution. 25 millilitres require for neutralisation not more than 2.5 millilitres of *N/10 solution of sodium hydroxide, solution of methyl orange* being used as indicator (limit of acidity). Yields no characteristic *reactions* for barium. Evaporated to dryness on a water-bath, not more than 1 per cent. of solid residue remains." *Br.*

"**Assay.**—Dilute about 2 Gm. of Solution of Hydrogen Dioxide, accurately weighed, with 20 mils of distilled water, then acidulate it with 20 mils of diluted sulphuric acid and titrate with tenth-normal potassium permanganate V.S. It shows not less than 3 per cent. of H_2O_2.

"Each mil of tenth-normal potassium permanganate V.S. used corresponds to 0.0017008 Gm. of H_2O_2, or to 0.0008 Gm. of oxygen. Each gramme of Solution of Hydrogen Dioxide corresponds to not less than 17.6 mils of tenth-normal potassium permanganate V.S." *U. S.*

Charles Rice suggests improvements in the method of assay which are practical. (See *Am. Drug.*, 1892, 30.) F. X. Moerk has proposed a rapid and effective method of assaying this solution (see *A. J. P.*, 1893, 65); J. F. Brown confirmed the value of Moerk's method (*P. J.*, 1896, 271). *Solution of hydrogen dioxide should be kept in a cool place, and not too tightly stoppered.* (A plug of absorbent cotton is often used.) Neglect of these precautions, particularly in hot weather, will be likely to result in an explosion and fracture of the bottle containing it, due to a brisk evolution of oxygen in a confined space, on account of the increased temperature.

Hydrogen dioxide solution is usually preserved at the present time by the use of acetanilid or some other equally efficacious agent for retarding its decomposition. The presence of acetanilid was first called attention to in pharmaceutical literature by LaWall (*A. J. P.*, 1906, p. 582). Boroglycerin, caffeine, and other substances have also been used for the purpose. When acetanilid is used the solution upon standing for some time occasionally acquires a disagreeable odor due to the formation of nitrobenzol and other decomposition derivatives of the acetanilid. The amount of acetanilid used as a preservative is very small, being about 0.05 per cent. A study of the effect of various preservatives was reported by A. M. Glover (*A. J. P.*, 1913, p. 538), who found acetanilid to be the best of all that were tried.

It has been claimed that its deterioration is often due to the alkalinity of the glass bottles

in which it is stored, and that if alkali-free glass containers be used it will keep for extended periods without a preservative.

Jordan (*J. A. Ph. A.*, 1913, ii, p. 344) finds that solutions of hydrogen dioxide kept in bottles stoppered with cotton, instead of a cork, retain their activity very much better, he believes, on account of the evaporation of the water. He also found that bottles protected from the light retained their activity better than those exposed to the light. Most of the samples examined were below pharmacopœial strength. One contained as little as 0.24 per cent. of H_2O_2, but the majority of them ranged from 2.5 to 3 per cent.

Uses.—Hydrogen peroxide in solution undergoes a slow process of reduction liberating a portion of its oxygen. Certain organic matters, however, among which may be mentioned pus and blood, exercise a powerful catalyzing action so that the oxygen is given off very rapidly. Evidently this nascent oxygen must have a powerful oxidizing effect and thereby destroy many forms of organic matter. It should be noted that in the presence of these reducing agents the antibacterial powers of the drug are greatly reduced. As long as there is effervescence caused by the application of hydrogen dioxide to a wound there is no great destruction of bacteria. Upon the system generally hydrogen peroxide does not, and cannot, exert any physiological action, because it cannot exist in the blood.

The most important use for this agent is as an antibacterial agent. The germicidal activity of hydrogen peroxide is generally greatly overestimated. Although in relatively dilute solution it will eventually destroy many of the pathogenic micro-organisms, its action is extremely slow, unless the solution be fairly concentrated. Gifford (*N. Y. M. R.*, 1888) found that a neutral solution containing 15 per cent. by volume of H_2O_2 (therefore stronger than the official solution) would destroy anthrax spores after five minutes' exposure, and pus cocci in one minute, but that the same solution when diluted with four parts of water did not kill the pus cocci after thirty minutes. Traugott found that 1 per cent. by weight killed typhoid bacilli in five minutes and staphylococci in fifteen to thirty minutes. In the presence of organic matter this compound is so rapidly broken down that it is even less efficient; as pointed out by Gifford, its germicidal action does not depend upon the liberated oxygen, but upon the hydrogen peroxide molecule. On the other hand, if allowed sufficient time relatively small quantities are highly efficient. Heinemann (*J. A. M. A.*, 1913, lx, p. 1603) reaches the conclusion from his experiments that three teaspoonfuls of the official solution after six hours' exposure will destroy 99 per cent. of the bacteria present in a liter of drinking water; this quantity makes about a one to one thousand solution of hydrogen peroxide.

The addition of hydrogen dioxide solution has at times been recommended as an emergency method for the preservation of milk. It effects a partial or complete sterilization of the milk and quickly disappears, being dissociated into H_2O and O. A paper dealing with the length of time during which the H_2O_2 persists in the milk has been published in the *Analyst*, 1915, p. 482, by M. E. Hines.

The solution of hydrogen dioxide is used in medicine as a means of cleansing infected *wounds*, freely suppurating *ulcers*, and the like. Its value in these conditions is probably more in destroying the organic matter which forms a breeding place for the micro-organisms than for its antibacterial action. Its styptic effect—probably due to the activation of the fibrin ferment of the blood and consequent more rapid coagulation—as well as its harmless nature make it a very popular antiseptic for household use. It is sometimes injected into deep cavities for the purpose of determining the presence of pus, which will be signalized by effervescence; the method, however, must be used with caution, as if there be not a free vent for the gas sufficient pressure may be generated within the cavity to cause serious results. Because of its lack of toxicity it is a favorite disinfectant for application to various mucous membranes, especially those of the nose and throat. In *diphtheria* or *tonsillitis* the official solution may be applied pure, either by means of an atomizer or cotton applicator. Diluted with equal parts of water it is often employed as a gargle in *pharyngitis*, or as a mouth wash in *stomatitis*, but it appears frequently to exercise an injurious effect upon the epithelium of the buccal mucous membrane. In slow *hemorrhages* it often exercises a styptic effect, perhaps through activating the specific ferments of the blood which lead to clot formation. Internally the solution of hydrogen dioxide has been used with success by Goodman (*Penna. M. J.*, 1910) and others, in the treatment of *hyperchlorhydria*. It is asserted that it diminishes the acidity of the gastric juice, increases the secretion of mucus and exercises an antiseptic action in the stomach.

One great disadvantage of the solution of hydrogen dioxide is the rapidity with which it deteriorates. The New Hampshire State Board of Health reported in 1912 that more than half of the samples examined were below the Pharmacopœial standard.

Solution of hydrogen dioxide is used in 10 or 15 per cent. aqueous solutions, for various commercial purposes, such as cleaning and bleaching old and stained engravings or oil paintings, or as an auricome for bleaching dark colored hair. It is employed, moreover, in increasing degree in the textile industries for bleaching. Lunge has proposed its use in the ready valuation of chlorinated lime or bleaching powder, which is decomposed by it with the simultaneous liberation of oxygen from both substances in equal amount.

Under the name of *perhydrol* a solution asserted to represent 100 volume per cent. (30 per cent. by weight) of hydrogen dioxide is upon the market.

Dose, one fluidrachm (3.75 mils).

LIQUOR HYPOPHYSIS. U. S.

SOLUTION OF HYPOPHYSIS Liq. Hypophysis [Solution of the Pituitary Body]

(lĭ'quŏr hȳ-pŏph'ȳ-sĭs)

"A solution containing the water-soluble principle or principles from the fresh posterior lobe of the pituitary body of cattle. Extract the finely minced material with slightly acidulated water, boil the solution for ten minutes and filter it. Sterilize this filtrate and preserve it in a sterile condition in glass containers. A transparent liquid, colorless or nearly so, having a faint, characteristic odor. One mil of Solution of Hypophysis, diluted 20,000 times, has the same activity on the isolated uterus of the virgin guinea-pig as a 1 to 20,000,000 solution of beta-iminazolyl-ethylamine hydrochloride when tested as directed by the United States Hygienic Laboratory." *U. S.*

Uses.—The solution of the posterior lobe of the pituitary body possesses the physiological action and therapeutic properties of this organ (see *Hypophysis Sicca*), but has the great advantage of being in a convenient form for administration, especially for hypodermic use. While it is probable that even when given by the mouth the pituitary exerts an effect upon the functions of the body, it is certainly more active when administered hypodermically and is today rarely exhibited orally. As it is impracticable for the retail pharmacist to prepare sterile solutions of the hypophysis of definite activity, the apothecary will ordinarily stock one of the commercial solutions. These preparations—which are sold under various trade names as *pituitrin, hypophysin, pituitary extract,* etc.—vary, however, greatly in their activity and rarely conform to the Pharmacopœial definition. According to Pittenger (*J. A. Ph. A.*, 1917, vi), the commercial solutions of hypophysis are from two to five times as strong as the standard given in the U. S. P.; a fact which it is important that both the physician and the druggist realize, as overdoses of this remedy are capable of much harm. The most frequent use of this drug is as a uterine stimulant, especially in *labor,* although it is sometimes used as a circulatory stimulant in surgical *shock.*

Dose, of the U. S. P. preparation, ten to thirty minims (0.6–1.8 mils).

LIQUOR IODI COMPOSITUS. U. S.

COMPOUND SOLUTION OF IODINE Liq. Iodi Co. [Lugol's Solution]

(lĭ'quŏr ī-ō'dī cŏm-pŏs'ĭ-tŭs)

"An aqueous solution containing not less than 4.8 per cent. nor more than 5.2 per cent. of I and not less than 9.8 per cent. nor more than 10.2 per cent. of KI. Preserve the solution in glass-stoppered bottles, protected from light." *U. S.*

Liquor Iodinii Compositus, *U. S.* 1870; Soluté ioduré de Lugol, *Fr.*; Lugolsche Jodlösung, *G.*

* "Iodine, *five grammes* [or 77 grains]; Potassium Iodide, *ten grammes* [or 154 grains]; Distilled Water, *a sufficient quantity,* to make *one hundred grammes* [or 3 ounces av., 231 grains]. Dissolve the iodine and potassium iodide in a sufficient quantity of distilled water to make the product weigh *one hundred grammes* [or 3 ounces av., 231 grains]." *U. S.*

In this solution iodine is dissolved in water with the assistance of potassium iodide. Iodine dissolves sparingly in water, but freely in a solution of this salt. In using potassium iodide to render iodine more soluble in water, the iodide is generally taken in a quantity twice the weight of the iodine, and this is the proportion adopted in the U. S. formula. The preparation is a *concentrated* solution of iodine with potassium iodide, and is intended to facilitate the administration of the combination in drops. The present formula does not differ in strength from that of 1880. In the Br. Pharmacopœia a solution is directed having much more iodine than the U. S. solution, and weaker in potassium iodide, the former having about fifty grains of iodine and thirty grains of potassium iodide in the fluidounce, while the latter has nearly twenty-six grains of iodine and fifty-two grains of potassium iodide in the fluidounce, the difference in the fluidounce of the two Pharmacopœias being too small to enter into the calculation. Its name was changed in the 1914 revision of the Br. Pharmacopœia to *Tinctura Iodi Fortis.* (See under Tinctures.) The British solution is made with alcohol, and closely resembles the *Liniment of Iodine* of the *Br. Ph.*, 1885. "Compound Solution of Iodine is a transparent liquid of a deep brown color, having an odor of iodine. A drop of Compound Solution of Iodine when added to 1 mil of starch T.S., diluted with 10 mils of water, produces a deep blue color.

"**Assay for Potassium Iodide.**—Evaporate in a tared, porcelain dish on a water bath about 5 mils of Compound Solution of Iodine, accurately weighed in a stoppered weighing-bottle, repeatedly moisten the residue with distilled water and re-evaporate until it becomes white. It leaves a residue of not less than 9.8 per cent. nor more than 10.2 per cent. of a salt which responds to the tests for identity and purity under *Potassii Iodidum.*

"**Assay for Iodine.**—Dilute about 10 mils of Compound Solution of Iodine, accurately weighed in a stoppered weighing-bottle, with 25 mils of distilled water and titrate with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 4.8 per cent. nor more than 5.2 per cent. of I.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.012692 Gm. of I. Each gramme of Compound Solution of Iodine corresponds to not less than 3.8 mils nor more than 4.1 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

Uses.—Lugol's solution is used internally as a means of obtaining the therapeutic effects of

iodine. It is also an efficient chemical antidote to some of the alkaloidal poisons.

Dose, of the U. S. P. solution, from two to five minims (0.12–0.3 mil), three times a day, given in at least four tablespoonfuls of water or of milk, so as to avoid irritation of the stomach.

Off. Prep.—Liquor Iodi Phenolatus, *N. F.*

LIQUOR MAGNESII BICARBONATIS. Br.

SOLUTION OF MAGNESIUM BICARBONATE [Fluid Magnesia]

(lĭ'quŏr măg-nē'shĭ-ī bī-kär-bŏ-nā'tĭs)

Liquor Magnesii Carbonatis, *Br.* 1898; Eau magnésienne, Magnésie liquide, *Fr.;* Kohlensaure Magnesialösung, Magnesiawasser, *G.*

"Magnesium Sulphate, 40 *grammes;* Sodium Carbonate, 50 *grammes;* Distilled Water, *a sufficient quantity.* Dissolve the two salts separately, each in two hundred *millilitres* of the Distilled Water; heat the solution of Magnesium Sulphate to the boiling point; add to it the solution of Sodium Carbonate; boil until carbon dioxide ceases to be evolved; collect the precipitate on a calico filter; wash it with Distilled Water until the filtrate is free from sulphates. Mix the washed precipitate with four hundred *millilitres* of Distilled Water; place the mixture in a suitable apparatus; force into it pure washed carbon dioxide; let the mixture remain in contact with excess of carbon dioxide, retained under a pressure of about three atmospheres, for twenty-four hours or longer; decant the resulting solution, and again pass carbon dioxide into it. Keep the Solution in securely closed bottles." *Br.*

The title of this solution was changed in the British Pharm., 1914, to "Solution of Magnesium *Bicarbonate.* It was formerly solution of Magnesium *Carbonate;* the word bicarbonate more accurately describes the magnesium salt in the finished preparation.

The object of this process is to obtain a solution of magnesium bicarbonate by means of carbon dioxide, the carbonate being insoluble in pure water. The first step is to prepare a freshly precipitated hydrated magnesium carbonate, which is more readily dissolved than is a carbonate which has been kept for some time. As the magnesium carbonate of the Br. Pharmacopœia consists of three molecules of the neutral carbonate and one of magnesium hydroxide with four molecules of water, it follows that, in its preparation from the two salts used in the process, a portion of carbon dioxide escapes, and the boiling is directed to be continued until the escape of the gas ceases, so that the normal composition may be insured, and a longer heat, which might affect the constitution of the carbonate so as to diminish its solubility, avoided. The precipitate is thoroughly washed, in order to remove every trace of sodium sulphate, which may be indicated by the non-action of the test of barium chloride. The next step is to dissolve the precipitated carbonate in water impregnated with carbon dioxide, and, as the solution even thus favored is slowly effected, the carbonate is directed to remain exposed to the action of carbon dioxide, under pressure, for twenty-four hours, and still the whole of the carbonate is not dissolved, and filtration is necessary. According to the Br. Pharm., the solution "effervesces slightly, or not at all, when the containing vessel is first opened. Yields no characteristic *reactions* for sulphates. *Lead limit* 0.5 part per million. *Arsenic limit* 0.2 part per million. 20 millilitres evaporated to dryness yield a white residue, which after calcination weighs not less than 0.16 and not more than 0.19 gramme. This residue is insoluble in *water,* and when dissolved in a dilute acid yields the *reactions* characteristic of magnesium. This Solution contains the equivalent of about 2 grammes of the official Magnesium Carbonate in 100 millilitres; 1 fluid ounce contains the equivalent of about 10 grains." *Br.*

On exposure to the air, some of the carbon dioxide escapes, and a portion of the salt is deposited. According to Muncy, the preparation as it occurs in commerce is usually much below the standard strength.

This solution is but slightly effervescent, is clear, and should be free from bitterness. Nevertheless, its taste is more disagreeable than is that of the undissolved carbonate or hydroxide, over which it has no advantage. (See *Magma Magnesiæ,* page 670.)

Dose, as an antacid laxative, from one to two fluidounces (30–60 mils).

LIQUOR MAGNESII CITRATIS. U. S.

SOLUTION OF MAGNESIUM CITRATE Liq. Mag. Cit.

(lĭ'quŏr măg-nē'shĭ-ī cĭ-trā'tĭs)

"*One hundred mils* of the Solution contains magnesium citrate corresponding to not less than 1.5 Gm. of magnesium oxide (MgO = 40.32)." *U. S.*

Liquor Magnesii Citrici; Solution of Citrate of Magnesium; Limonade purgative au Citrate de Magnésie, *Fr. Cod.;* Flüssige Citronensaure Magnesia, Magnesiumcitratlösung, Magnesiumlimonade, *G.;* Limonata magnesiaca, *It.;* Limonada purgante de citrato magnesico, *Sp.*

* "Magnesium Carbonate, *fifteen grammes* [or 231 grains]; Citric Acid, *thirty-three grammes* [or 1 ounce av., 72 grains]; Syrup, *sixty mils* [or 2 fluidounces, 14 minims]; Purified Talc, *five grammes* [or 77 grains]; Oil of Lemon, *one-tenth of a mil* [or 1½ minims]; Potassium Bicarbonate, *two and five-tenths grammes* [or 39 grains]; Water, *a sufficient quantity.* Dissolve the citric acid in *one hundred and fifty mils* [or 5 fluidounces, 35 minims] of hot water in a suitable dish, and, having added the magnesium carbonate, previously mixed with *one hundred mils* [or 3 fluidounces, 183 minims] of water, stir until it is dissolved. Then add the syrup, heat the mixed liquids to the boiling point, immediately introduce the oil of lemon, previously triturated with the purified talc, and filter the mixture, while hot, into a strong bottle (previously rinsed with

boiling water) of suitable capacity. Introduce enough boiled water to make the product measure *three hundred and fifty mils* [or 11 fluidounces, 401 minims]. Stopper it with purified cotton until cold, then drop in the potassium bicarbonate, and immediately stopper the bottle securely. Lastly, shake the solution occasionally until the potassium bicarbonate is dissolved. Keep the bottle on its side in a cool place, preferably in a refrigerator. *Note.*—In this process the 2.5 Gm. [or 39 grains] of potassium bicarbonate may be replaced by 2.1 Gm. [or 33 grains] of sodium bicarbonate, preferably in tablet form." *U. S.*

This formula first appeared in the second edition of the U. S. Pharmacopœia of 1850. The original formula was soon found to have defects. Four-fifths of the carbonate was dissolved in the citric acid, and the solution filtered into a bottle containing the syrup of citric acid, and then the reserved fifth, mixed with water, was added to the acid citrate, and the bottle tightly corked. The addition of the reserved carbonate was intended to impregnate the preparation with carbon dioxide by its solution in the excess of citric acid. To effect the solution of this reserved carbonate required at least half an hour. But the chief objection to the formula as originally framed was that the magnesium citrate, when the solution was kept for some days, crystallized out in the form of a white granular precipitate, which rendered the solution unfit for medicinal use. This precipitate was found by Procter to be $Mg_3(C_6H_5O_7)_2 + 14H_2O$. This still occurs to some extent, although more slowly, and probably cannot be avoided except by a very great reduction in the amount of magnesia. The U. S. P. (8th Rev.) process improved the formula by increasing the quantity of citric acid, using 33 Gm. instead of 30 Gm. formerly used. The use of potassium bicarbonate introduces potassium citrate, but in too small a proportion to be of any consequence. It is somewhat more convenient to use calcined magnesia in place of the carbonate, and in one of the best processes that we have seen the fifteen grammes of carbonate in the official formula are replaced by five grammes of light calcined magnesia. We prefer a modification in the manipulation of the official process; if instead of the solution being filtered into the bottles containing the syrup it is filtered into a separate vessel, and then the proper quantity poured very carefully down the inside of the bottle, or with the aid of a funnel having only a lateral opening so that the liquid is delivered against the sides of the bottle, so as not to disturb the heavy layer of syrup, if then the crystals of bicarbonate be dropped in, very little loss of carbon dioxide will ensue if the bottle is at once securely stoppered. When the bottle is dispensed, a vigorous shake at once liberates the carbon dioxide, and the patient is sure to have a highly effervescent liquid. Special bottles for this solution can now be procured which have a "patent stopper" attached; they are very convenient. The crown stopper is also frequently seen as devices for applying these are now upon the market in a comparatively inexpensive form. Solid magnesium citrate is best used in the form of the effervescent magnesium citrate of the U. S. P., 1890. (See *U. S. D.*, 19th edition, p. 726.)

The official preparation (U. S. P. IX) differs from that of former pharmacopœias in providing a means for effecting partial sterilization, such as boiling the mixed liquids, rinsing the bottle with boiling water, using boiled water for diluting the mixed liquids, and stoppering the bottle with purified cotton. These measures are helpful in destroying bacteria, but after all has been done the potassium bicarbonate or sodium bicarbonate added at the last may introduce germs which may develop growths. The oil of lemon should be fresh and without terebinthinate odor. The tincture made from fresh lemon peel would probably prove more satisfactory as a flavor.

Properties.—This official solution is founded on a preparation proposed by Roge Delabarre, and improved by Rabourdin, of Paris. It is an aqueous solution of magnesium citrate, containing an excess of citric acid, impregnated with carbon dioxide and sweetened with syrup. When properly prepared, it is a clear liquid, having an agreeable taste like that of lemonade. "Add 1 mil of glacial acetic acid and 3 mils of an aqueous solution of potassium acetate (1 in 2) to 10 mils of Solution of Magnesium Citrate, shake the mixture vigorously, then gently rub the sides of the test tube with a glass rod for a few minutes and allow to stand for one hour; no white crystalline precipitate, soluble in ammonia water, is produced (*tartaric acid*). Dilute 2 mils of the Solution with 8 mils of distilled water and add 5 drops of hydrochloric acid and 1 mil of barium chloride T.S.; no turbidity is produced within one minute (*sulphate*). Dilute 2 mils of the Solution with 8 mils of distilled water and add 5 mils of ammonium oxalate T.S.; not more than a slight turbidity is produced (*calcium*).

"**Assay.**—Transfer 10 mils of Solution of Magnesium Citrate, accurately measured, to a platinum or porcelain dish, evaporate to dryness, and ignite until most of the carbonaceous matter has burned off. Add to the residue 20 mils of diluted hydrochloric acid, heat on a water bath for fifteen minutes, filter if necessary, and wash the residue thoroughly with hot water. To the combined filtrate and washings, which should measure about 100 mils, add an excess of sodium phosphate T.S. (about 20 mils), then add ammonia water gradually, with constant stirring, until slightly alkaline, allow to stand for ten minutes, add 30 mils of ammonia water, and allow to stand for twelve hours. Collect the precipitate on a filter, wash it with dilute ammonia water (1 volume of ammonia water to 3 volumes of water) until 10 mils of the washings, when acidulated with nitric acid, yield not more than an opalescence on the

addition of a few drops of silver nitrate T. S. Dry, and ignite to constant weight. The weight of the magnesium pyrophosphate so obtained is not less than 0.414 Gm., indicating an equivalent of not less than 1.5 Gm. of magnesium oxide in 100 mils of the Solution." *U. S.*

Overlooking the excess of acid which it contains, the salt present is the tribasic citrate, in which the six atoms of hydrogen from two molecules of citric acid are replaced by three atoms of magnesium. Accordingly, it consists of two molecules of citric acid and three atoms of magnesium. It is advisable in preparing the solution to introduce the magnesia in small portions, for if too hastily added it is liable to cause the formation of the neutral citrate, which cannot afterwards be readily dissolved. Dorvault made a solid magnesium citrate which is perfectly and readily soluble, by melting on a sand bath 100 parts of crystallized citric acid in its water of crystallization, and thoroughly incorporating with it 29 parts of calcined magnesia. A pasty mixture is formed, which soon hardens, and may be pulverized for use. Magnesium citrate, thus prepared, is soluble in twice its weight of water. When in saturated solution it soon precipitates as a nearly insoluble hydroxide, but with eight or ten times its weight of water it forms a permanent solution. Simonin found that an insoluble magnesium citrate may be restored to solubility in boiling water by being thoroughly rubbed up with water so as to form a paste. The necessary trituration will be abridged if a little citric acid be added. For other modifications, suggestions, etc., see Kondratowisch, *N. R.*, 1883, p. 246; Neynaber, *A. J. P.*, 1884, p. 472 (the proposed substitution of acetic acid by the latter is not desirable, because of the impossibility of avoiding an empyreumatic taste); also A. B. Stevens, *Proc. Mich. State Pharm. Assoc.*, 1885; and F. W. Sennewald, *Nat. Drug.*, 1887.

Magnesium metatartrate has been proposed, in the place of the citrate, by Léger, who, however, states that as a purgative it is more powerful than the citrate, resembling the sulphate. On account of its pleasant taste it might, perhaps, be substituted for Epsom salt. (See *Metatartaric Acid*, page 81.)

Uses.—This solution is a cooling cathartic, and operates mildly. It has come into extensive use in the United States, on account of the facility with which it may be taken and its acceptability to the stomach.

Dose, as a purge, the whole quantity directed in the formula, or twelve fluidounces (360 mils); as a laxative, half that quantity.

LIQUOR MORPHINÆ ACETATIS. Br.

SOLUTION OF MORPHINE ACETATE

(lĭ'quŏr mŏr-phĭ'næ ăç-ē-tā'tĭs)

Soluté d'Acétate de Morphine, *Fr.;* Essigsaure Morphinlösung, *G.*

"Morphine Acetate, 1 *gramme;* Diluted Acetic Acid, 2 *millilitres;* Alcohol (90 per cent.), 25 *millilitres;* Distilled Water, sufficient to produce 100 *millilitres.* Mix the Alcohol with an equal volume of Distilled Water, adding the Diluted Acetic Acid; dissolve the Morphine Acetate in the mixture, and add sufficient Distilled Water to produce the required volume. This Solution contains 1 gramme of Morphine Acetate in 100 millilitres; 110 minims contain 1 grain." *Br.*

Morphine acetate often contains a little uncombined morphine, in consequence of the escape of a portion of the acid during its evaporation, and especially when this is pushed to dryness. It is on this account apt to be unreliable. Hence the addition of the diluted acetic acid, which at the same time neutralizes the alkaloid in excess and enables the solution to be completely effected. The alcohol is added as a preservative. The present solution contains about 1 per cent. of morphine acetate and is, therefore, about equivalent in strength to tincture of opium.

Dose, from fifteen to thirty minims (0.9–1.8 mils).

LIQUOR MORPHINÆ HYDROCHLORIDI. Br.

SOLUTION OF MORPHINE HYDROCHLORIDE

(lĭ'quŏr mŏr-phĭ'næ hȳ-drŏ-ç̇hlō'rĭ-dī)

Solution of Hydrochlorate of Morphine, *Br.* 1885; Liquor Morphinæ Muriatis, *Dub.;* Solution of Muriate of Morphia; Soluté de Hydrochlorate de Morphine, *Fr.;* Salzsaure Morphinlösung, *G.*

"Morphine Hydrochloride, 1 *gramme;* Diluted Hydrochloric Acid, 2 *millilitres;* Alcohol (90 per cent.), 25 *millilitres;* Distilled Water, sufficient to produce 100 *millilitres.* Mix the Alcohol with an equal volume of Distilled Water, adding the Diluted Hydrochloric Acid; dissolve the Morphine Hydrochloride in the mixture, and add sufficient Distilled Water to produce the required volume. This Solution contains 1 gramme of Morphine Hydrochloride in 100 millilitres; 110 minims contain 1 grain." *Br.*

The use of the alcohol is to prevent spontaneous decomposition, that of the acid probably to assist in the solution of the salt. The solution contains about 1 per cent. of morphine hydrochloride.

Dose, from fifteen to thirty minims (0.9–1.8 mils).

LIQUOR MORPHINÆ TARTRATIS. Br.

SOLUTION OF MORPHINE TARTRATE

(lĭ'quŏr mŏr-phĭ'næ tăr-trā'tĭs)

Soluté de Tartrate de Morphine, *Fr.;* Weinsteinsaure Morphinlösung, *G.*

"Morphine Tartrate, 1 *gramme;* Alcohol (90 per cent.), 25 *millilitres;* Distilled Water, sufficient to produce 100 *millilitres.* Mix the Alcohol with an equal volume of Distilled Water; Dissolve the Morphine Tartrate in the mixture; add sufficient Distilled Water to produce the required volume. This Solution contains 1

gramme of Morphine Tartrate in 100 millilitres; 110 minims contain 1 grain." *Br.*

This solution was introduced into the Br. Ph., 1898, because of the superior solubility and stability of the morphine tartrate, alcohol being used to preserve the liquid. It is of the same strength as the other solutions of morphine, about 1 per cent. It is not intended for hypodermic use and should not be confounded with the *Injectio Morphinæ Hypodermatica.* Various solutions of morphine sulphate have been in vogue, but have been abandoned by the Pharmacopœias on account of their tendency to undergo decomposition. The U. S., 1870, solution (*Liquor Morphinæ Sulphatis*) contained 1 grain of morphine sulphate to the fluidounce; the Br., 1885, solution 4.375 grains in the same quantity. *Magendie's Solution of Morphine* was of the strength of 16 grains to the fluidounce.

Dose, from fifteen to thirty minims (0.9–1.8 mils).

LIQUOR PANCREATIS. Br.

PANCREATIC SOLUTION

(lĭ'quŏr păn-crē'ă-tĭs)

"Pancreatic Solution contains the digestive principles of the fresh pancreas of the pig. Mix two hundred and fifty *millilitres* of Alcohol (90 per cent.) with two hundred *millilitres* of Glycerin and sufficient Distilled Water to produce one thousand *millilitres.* In this mixture macerate for seven days two hundred and fifty *grammes* of the pancreas, freed from fat and external membrane, and finely divided by trituration with washed sand or powdered pumice stone; filter." *Br.*

Liquor Pancreatius; Soluté de Pancréatine, *Fr.;* Pancreatinlösung, Pankreasessenz, *G.*

This official preparation of the Br. Ph., 1898, has been introduced to supply the demand for a liquid digestive solution made from the pancreas; it closely resembles the preparation recommended by Benger. (*Proc. Roy. Soc.,* xxxii, 145; see also *Pancreatinum.*) "When 3 *millilitres* of the Solution together with 0.2 *gramme* of *sodium bicarbonate* and 20 *millilitres* of *water* are added to 80 *millilitres* of milk and the mixture kept at 45° C. (113° F.) for one hour, on placing 5 millilitres of this liquid with 5 *millilitres* of *ether* and 5 drops of *nitric acid* in a stoppered tube and gently inverting the tube three times, no curdy precipitate appears in the lower layer." *Br.*

The solution digests albuminoids, converts starch into sugar in an alkaline solution, albumin and fibrin into peptones, and peptonizes milk. As it acts normally in alkaline solutions, while the gastric juices are strongly acid, its practical value as an internal medicament is doubtful. Its chief value is for the predigestion of foods.

Dose, from one to two fluidrachms (3.75–7.5 mils).

LIQUOR PICIS CARBONIS. Br.

SOLUTION OF COAL TAR

(lĭ'quŏr pī'cĭs căr-bō'nĭs)

Soluté de Goudron de Houille, *Fr.;* Kohlenteerlösung, *G.*

"Prepared Coal Tar, 200 *grammes;* Quillaia Bark, in No. 20 powder, 100 *grammes;* Alcohol (90 per cent.), 1000 *millilitres.* Exhaust the powdered Quillaia Bark with the Alcohol by the *percolation process.* To the resulting tincture add the Prepared Coal Tar, and digest the mixture at 50° C. (122° F.) for two days, stirring occasionally. Cool and decant, or filter." *Br.*

This solution of the Br. Ph., 1898, is practically identical with *Liquor Carbonis Detergens, Coal Tar Saponin,* and the *Liquor Picis Carbonis* of the N. F. IV (see Part III), and similar well-known preparations which have been largely used by dermatologists. The process for solution of coal tar is modelled after that for *compound tincture of coal tar,* proposed by L. A. Duhring. (*Am. J. M. S.*) It owes its virtues largely to phenol and other derivatives of coal tar. (See *Pix Carbonis Præparata.*)

Solution of coal tar is stimulating, and is prescribed, diluted with from ten to fifty parts of water, as a wash in *eczema, psoriasis, pruritus,* and other skin diseases.

LIQUOR PLUMBI SUBACETATIS. U. S. (Br.)

SOLUTION OF LEAD SUBACETATE Liq. Plumb. Subacet. [Goulard's Extract]

(lĭ'quŏr plŭm'bī sŭb-ăç-ē-tā'tĭs)

"An aqueous solution containing lead subacetate approximately $Pb_2O(CH_3.COO)_2 = 548.25$, corresponding to not less than 18 per cent. of Pb. Preserve the Solution in well-stoppered bottles." *U. S.*

Liquor Plumbi Subacetatis Fortis, *Br.,* Strong Solution of Lead Subacetate; Acetum Plumbi, Acetum Saturni, Plumbum Hydrico-Aceticum Solutum; Acétate (sous-) de Plomb liquide, *Fr. Cod.;* Extrait de Goulard, Vinaigre de Plomb (de Saturne), *Fr.;* Liquor Plumbi Subacetici, *P. G.;* Bleiessig, *G.*

* "Lead Acetate, *one hundred and eighty grammes* [or 6 ounces av., 153 grains]; Lead Oxide, finely powdered, *one hundred and ten grammes* [or 3 ounces av., 385 grains]; Distilled Water, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Dissolve the lead acetate in *seven hundred mils* [or 23 fluidounces, 321 minims] of boiling distilled water and add the solution slowly and in portions to the lead oxide, which has previously been rubbed to a smooth paste with *one hundred mils* [or 3 fluidounces, 183 minims] of distilled water, and place in a porcelain dish of about *one liter* [or 33 fluidounces, 6½ fluidrachms] capacity. Boil this mixture during half an hour with occasional stirring, adding distilled water as required to maintain about the original volume. Finally, when cool, filter the solution, protecting it as much as possible from the air, and add sufficient distilled

water, which has previously been boiled and cooled, to make the finished product weigh *one thousand grammes* [or 35 ounces av., 120 grains]." *U. S.*

"Lead Acetate, 250 *grammes;* Lead Oxide, in powder, 175 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Dissolve the Lead Acetate in seven hundred and fifty *millilitres* of the Distilled Water, add the Lead Oxide, set aside for forty-eight hours, shaking occasionally; filter, and pass through the filter sufficient Distilled Water to produce the required volume."

The Br. Pharm., 1914, adopted a "cold process" for making this solution and inserts an assay process as a test. This is necessary to secure uniformity and establish a standard.

The U. S. P. IX process does not differ essentially from that formerly official. Crystallized lead acetate consists of one atom of lead, two acetic acid groups, and three molecules of water. The formula is $Pb(C_2H_3O_2)_2 + 3H_2O = 379.20$. Litharge, as usually found in commerce, is an impure lead oxide. When solution of lead acetate is boiled with lead oxide, a large quantity of the oxide is dissolved, and a lead subacetate is formed which remains in solution. The precise composition of the subacetate varies with the proportion of lead acetate and of litharge employed. Thus, starting with three molecules of normal acetate, $Pb_3(C_2H_3O_2)_6$, we may have $Pb_3O(C_2H_3O_2)_4$, and $Pb_3O_2(C_2H_3O_2)_2$ formed successively. The latter of these oxyacetates is known as Goulard's, and a mixture of the two constitutes the basis of the official solution. In executing the process, the litharge should be employed in very fine powder, and, according to Thénard, should be previously calcined in order to decompose the lead carbonate which it always contains in greater or less proportion, and which is not dissolved by the solution of the acetate. Nevning states that a solution of lead subacetate more permanent than the official one may be prepared by simply allowing litharge to remain for twenty-four hours in a solution of lead acetate, with occasional agitation. This preparation probably contains much less of the lead oxide than does the official solution. Courtonne recommends dissolving seventy-five parts by weight of crystallized lead acetate in one hundred and sixty-five parts of water, and adding eleven parts of ammonia water, sp. gr. 0.923. This quick method has the disadvantage of containing ammonium acetate in small quantity. (*Chem. Ztg.,* 1894.) Several methods have been proposed for making this by a process which will eliminate the necessity of boiling. For Haussmann's method by agitating the lead salts with hot water and subsequently adding the lead oxide and occasionally agitating until cold, see *A. J. P.,* 1897, 559; *A. J. P.,* 1896, 427; *M. R.,* 1896, 329; *Ph. Rev.,* 1896, 250.

In many pharmaceutical manufacturing laboratories when this preparation is made on the large scale, the cold process is always used as it seems to work very well with large quantities, and the final adjustment is then made to the standard strength after assaying the preparation.

Properties.—The solution of lead subacetate of the U. S. Pharmacopœia is "a clear, colorless liquid, odorless and having a very sweet, astringent taste. It is alkaline to litmus but not to phenolphthalein. On exposure to the air it absorbs carbon dioxide, which causes the formation of a white precipitate. Specific gravity: about 1.245 at 25° C. (77° F.). When Solution of Lead Subacetate is added to a solution of acacia, it produces a dense, white precipitate (distinction from *normal lead acetate*). Separate portions of Solution of Lead Subacetate, diluted with 10 volumes of recently boiled distilled water, yield a black precipitate with hydrogen sulphide T.S., a yellow precipitate with potassium iodide T.S., and a white precipitate with diluted sulphuric acid. Solution of Lead Subacetate yields with potassium ferrocyanide T.S. a precipitate which is not perceptibly blue or red (*iron or copper*).

"**Assay.**—Transfer about 1.5 Gm. of Solution of Lead Subacetate, accurately weighed, to a 200 ml measuring flask, dilute with 50 mils of recently boiled distilled water, then add 50 mils of tenth-normal oxalic acid V.S., agitate the mixture thoroughly for five minutes, fill to the mark with distilled water, and filter, rejecting the first 20 mils of the filtrate. Add 5 mils of sulphuric acid to 100 mils of the filtrate (representing one-half of the amount of Solution of Lead Subacetate originally taken), warm to about 70° C. (158° F.), and titrate with tenth-normal potassium permanganate V.S. It shows not less than 18 per cent. of Pb.

"Each mil of tenth-normal oxalic acid V.S. used corresponds to 0.010355 Gm. of Pb. Each gramme of Solution of Lead Subacetate corresponds to not less than 17.4 mils of tenth-normal oxalic acid V.S." *U. S.*

"A clear colorless liquid, with a sweet astringent taste; alkaline to *litmus.* Becomes turbid by exposure to the air. Forms an opaque white jelly with *mucilage of gum acacia.* Yields the *reactions* characteristic of lead and of acetates. Specific gravity 1.275. When 1 gramme is diluted with 20 millilitres of *water* and mixed with excess of *N/1 solution of oxalic acid,* the precipitate collected, washed, transferred to a flask and decomposed with excess of *diluted sulphuric acid,* the mixture thus obtained, heated to 60° C. (140° F.), decolorises not less than 17 millilitres of *N/10 solution of potassium permanganate.*" *Br.*

When concentrated by evaporation, it deposits on cooling crystalline plates, which, according to Barker, are flat, rhomboidal prisms, with dihedral summits. It has an alkaline reaction, tingeing the syrup of violets green, and reddening turmeric paper. One of its most striking properties is the extreme facility with which

it is decomposed. Carbon dioxide throws down a white precipitate of lead carbonate; and this happens by mere exposure to the air, or by mixture even with distilled water, if this has had an opportunity of absorbing carbon dioxide from the atmosphere. It affords precipitates also with the alkalies, alkaline earths, and their carbonates, with sulphuric and hydrochloric acids free or combined, with hydrogen sulphide and the sulphydrates, with the soluble iodides and chlorides, and, according to Thénard, with solutions of nearly all neutral salts. Solutions of gum, tannin, most vegetable coloring principles, and many animal substances, particularly albumin, produce with it precipitates consisting of the substance added and lead oxide. It should be kept in well-stoppered bottles. It is distinguished from the solution of lead acetate by being precipitated by gum arabic. For a method (other than the official) of assaying this solution volumetrically, see *P. J.*, 1886, 656.

Crystallized Lead Subacetate.—Jeannel prepares crystallized lead subacetate in accordance with the following formula. Triturate six parts of neutral lead acetate with two parts of pure litharge, and add one part of water. Heat in a porcelain dish, stirring with a glass rod, until fusion and finally ebullition occur. After two or three minutes of boiling, filter through paper in a funnel heated by a sand bath. Allow to cool and crystallize. (*J. P. C.*, 4e sér., xi, 54.)

Uses.—This solution is astringent and sedative but is employed only as an external application. It is widely used, especially mixed with an equal part of tincture of opium—a mixture commonly known as *lead water and laudanum*—in inflammation arising from *sprains, bruises, burns, blisters,* etc., to which it is applied by means of linen cloths, which should be removed as fast as they become dry. It always, however, requires to be diluted. Blackburn (*J. A. M. A.*, 1906, xlvi, p. 954) reports erythema following the local application of lead water and laudanum, and we have seen blistering apparently resulting from this popular embrocation. From four fluidrachms to a fluidounce (15–30 mils), added to a pint (480 mils) of distilled water, forms a solution sufficiently strong in ordinary cases of external inflammation. When applied to the skin denuded of the cuticle, the solution should be still weaker, as constitutional effects might result from the absorption of the lead. Paralysis is said to have been produced by its local action; and poisoning by its injection for *gonorrhea* has been reported. (*Dublin Journ. Med. Sci.*, 1874.) The solution has the common name of *Goulard's extract,* derived from a surgeon of Montpellier by whom it was introduced into general notice, though previously employed.

Off. Prep.—Liquor Plumbi Subacetatis Dilutus, *U. S., Br.;* Ceratum Plumbi Subacetatis, *N. F.;* Mistura Adstringens, *N. F.;* Glycerinum Plumbi Subacetatis, *Br.;* Unguentum Plumbi Subacetatis, *Br.*

LIQUOR PLUMBI SUBACETATIS DILUTUS. U. S., Br.

DILUTED SOLUTION OF LEAD SUBACETATE Liq. Plumb. Subacet. Dil. [Lead Water]

(lī'quọr plŭm'bī sŭb-ăç-ẹ-tā'tīs dị-lū'tŭs)

Aqua Saturnina; Goulard's Lotion, Goulard's Water, *Br.;* Diluted Solution of Subacetate of Lead; Lotion à l'Acétate de Plomb, *Fr. Cod.;* Eau de Saturne, Eau de Goulard, Eau blanche, *Fr.;* Aqua Plumbi, *P. G.;* Bleiwasser, Kuhlwasser, *G.*

* "Solution of Lead Subacetate, *forty grammes* [or 1 ounce av., 180 grains]; Distilled Water, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Mix the solution of lead subacetate with enough distilled water, previously boiled and cooled to make the product weigh *one thousand grammes* [or 35 ounces av., 120 grains]. This preparation must be preserved in small, well-filled and tightly-stoppered bottles." *U. S.*

"Strong Solution of Lead Subacetate, 12.5 *millilitres;* Distilled Water, recently boiled and cooled, sufficient to produce 1000.0 *millilitres.* Mix." *Br.*

In the edition of the U. S. Pharmacopœia of 1870 the proportion was increased from two to three fluidrachms to the pint, and this proportion has been practically retained in the preparation now official. The direction to dilute the strong solution with distilled water *previously boiled and cooled* is an improvement, as even the small amount of carbon dioxide dissolved in distilled water usually made the lead water cloudy. Owing to the liability to serious results due to the frequent confounding of the name lime water and lead water, it is safer to dispense lead water in a slightly opalescent condition, while lime water should be perfectly transparent. The Br. preparation, though stronger than the old one of the London College, is still feeble. The minute proportion of alcohol in the former British solution can have little effect, and it was omitted from Br. Pharm., 1914. The preparation should be excluded from the air as much as possible.

LIQUOR POTASSII ARSENITIS. U. S. (Br.)

SOLUTION OF POTASSIUM ARSENITE Liq. Pot. Arsen. [Fowler's Solution Liquor arsenicalis Fowleri P. I.]

(lī'quọr pọ-tăs'sī-ī är-sẹ-nī'tīs)

"An aqueous solution containing potassium arsenite, corresponding in amount to not less than 0.975 per cent. nor more than 1.025 per cent. of As_2O_3 (197.92). Preserve the Solution in amber-colored bottles." *U. S.*

Liquor Arsenicalis, *Br.;* Arsenical Solution; Solutio Arsenicalis Fowleri, Kali Arsenicosum Solutum; Soluté d'Arsenite de Potasse, *Fr. Cod.;* Liqueur de Fowler, Liqueur arsénicale de Fowler, *Fr.;* Liquor Kalii arsenicosi, *P. G.;* Fowlersche Tropfen, Fowlersche Lösung, *G.;* Soluzione alcalina di arsenito de potassio, Liquore del Fowler, *It.;* Solucion de arsenito potasico, Licor arsenical de Fowler, *Sp.*

* "Arsenic Trioxide, in fine powder, *ten grammes* [or 154 grains]; Potassium Bicarbonate, *twenty grammes* [or 309 grains]; Compound Tincture of Lavender, *thirty grammes* [or 1

ounce av., 26 grains]; Distilled Water, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Boil the arsenic trioxide and potassium bicarbonate, in a tared flask, with *one hundred grammes* [or 3 ounces av., 231 grains] of distilled water, until solution has been effected. Then add enough distilled water to make the solution weigh *nine hundred and seventy grammes* [or 34 ounces av., 94 grains]; then add the compound tincture of lavender and filter through paper." *U. S.*

"Arsenious Anhydride, in powder, 10 *grammes;* Potassium Carbonate, 10 *grammes;* Compound Tincture of Lavender, 30 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Dissolve the Arsenious Anhydride and the Potassium Carbonate in five hundred *millilitres* of Distilled Water by the aid of heat; cool; add the Compound Tincture of Lavender and sufficient Distilled Water to produce the required volume." *Br.*

This preparation originated with Fowler, of Stafford, England, and was intended as a substitute for the celebrated remedy known under the name of "the *tasteless ague drop.*" It now contains potassium arsenite corresponding in amount to 1 per cent. of arsenic trioxide, and the British solution has been made to correspond with this and the International Proctocol (Part I). It is a potassium arsenite dissolved in water, and is formed by the combination of the arsenic trioxide with the potassium of the bicarbonate or carbonate, carbon dioxide being evolved. In the present U. S. process the bicarbonate has been preferred to the carbonate and in order to expedite the process the quantity has been doubled. As the bicarbonate is decomposed to carbonate by boiling water, there is present in the finished solution some potassium carbonate. According to M. H. Buignet, ebullition disengages the carbon dioxide slowly, so that after four hours' boiling the solution still retains about one-sixth of this gas. The name by which the preparation is designated in the U. S. Pharmacopœia is the more correct. The contact of arsenic trioxide with potassium bicarbonate in the presence of a small quantity of boiling water gives rise to effervescence with decomposition of bicarbonate. It has, however, been denied that potassium carbonate is decomposed by arsenic trioxide, which is supposed to be merely held by it in solution, and, in this view of the nature of the preparation, the British name of *Arsenical Solution* would be appropriate. The compound spirit of lavender is added to give it taste and prevent its being mistaken for water. For Oldberg's process, see *Proc. A. Ph. A.,* 1893, 430; see also *A. J. P.,* 1895, 403.

In making this preparation care should be taken that the arsenic trioxide is pure. This object is best secured by using the form which comes in small pieces, instead of the commercial powder, and powdering the lumps in a mortar. Calcium sulphate is a common impurity in the powdered oxide, and if present will remain undissolved, and cause the solution to be weaker than it should be. Another insoluble impurity in the powdered oxide is calcium arsenite, which is sometimes present to the amount of 25 per cent. (Buignet.) Hence, if the arsenic trioxide does not entirely dissolve, the solution must be rejected. If official arsenious acid is used and the resulting preparation assayed and standardized, these difficulties need cause no fear.

Vanderkleed and E'we (*Proc. P. Ph. A.,* 1916, p. 283) point out that there are substances of widely differing composition offered in the market under the name of potassium arsenite. One of these consists of pure $KAsO_2$, while the other is $KAsO_2.H_3AsO_3$.

Properties.—"Solution of Potassium Arsenite is a clear or faintly opalescent liquid with a pink color and a slight odor of lavender. It is alkaline to litmus. Acidulate strongly 10 mils of the Solution with hydrochloric acid and add an equal volume of hydrogen sulphide T.S.; a yellow precipitate is produced which dissolves in ammonium carbonate T.S. Acidulate 4 mils of Solution of Potassium Arsenite with diluted nitric acid, add 1 mil of silver nitrate T.S. and superimpose a layer of ammonia water upon this liquid; no red or reddish-brown color is observed at the line of contact (*arsenate*).

"**Assay.**—Dilute about 20 mils of Solution of Potassium Arsenite, accurately weighed, with 75 mils of distilled water, acidify the mixture very slightly with diluted hydrochloric acid, then dissolve in the solution 2 Gm. of sodium bicarbonate and titrate the resulting liquid with tenth-normal iodine V.S., starch T.S. being used as indicator. It shows not less than 0.975 per cent. nor more than 1.025 per cent. of As_2O_3.

"Each mil of tenth-normal iodine V.S. used corresponds to 0.004948 Gm. of As_2O_3. Each gramme of Solution of Potassium Arsenite corresponds to not less than 1.97 nor more than 2.07 mils of tenth-normal iodine V.S." *U. S.*

"A reddish liquid, alkaline to *litmus,* and having the odor of lavender. 25 millilitres, neutralised with *hydrochloric acid,* discharge the color of 50.4 millilitres of *N/10 solution of iodine,* the presence of a slight excess of *sodium bicarbonate* being maintained throughout the operation. This Solution contains 1 gramme of Arsenious Anhydride in 100 millilitres; 110 minims contain 1 grain." *Br.*

According to R. Fresenius, solutions of alkaline arsenites slowly absorb oxygen from the air, and are in part converted into arsenates. Hence the propriety of keeping this solution in small bottles well filled. Mohr states that the alkaline reaction of the official solution delays the change, and experience has confirmed this statement. The slight precipitate found in this solution after keeping proved to be silicic acid, caused by the action of the alkaline solution on the glass container.

Uses.—This solution has the general action of the arsenical preparations on the animal economy, already described under the head of *Arseni Trioxidum.* Its liquid form makes it

convenient for exhibition and gradual increase, and it is the preparation generally resorted to when arsenic is given internally. It has been much employed in *intermittent fever, skin diseases,* and the other affections for which arsenic is employed. In *chorea* it is almost a specific, and in *nervous diseases* of debility it is often very useful. In *malarial affections* and *chorea* it should be administered in ascending doses until the puffiness about the eyes or disturbance of the bowels betrays the arsenical impression. For the peculiar effects upon the human organism, see *Arseni Trioxidum.*

Duflos's antidote to the poisonous effects of Fowler's solution, and of the salts of the acids of arsenic generally, is ferric acetate with excess of base, made by dissolving freshly precipitated ferric hydroxide in acetic acid to saturation, adding an equal quantity of the hydroxide to the solution, and diluting the whole with water to the consistence of cream. If the official solution of ferric acetate be used in an emergency, the free acid should first be neutralized with a little ammonia.

Dose, of potassium arsenite solution, three to five minims (0.2–0.3 mil), which may be gradually increased.

LIQUOR POTASSII CITRATIS. U. S.

SOLUTION OF POTASSIUM CITRATE Liq. Pot. Cit. [Neutral Mixture]

(lĭ'quŏr pŏ-tăs'sĭ-ī cĭ-trā'tĭs)

"An aqueous solution containing not less than 8 per cent. of $K_3C_6H_5O_7$ (306.34), with small amounts of citric and carbonic acids." *U. S.*

Mistura Potassii Citratis; Liquor Kalii Citrici; Citrate de Potasse liquide, *Fr.;* Flüssiges Citronensaures Kali, Kaliumcitratlösung, *G.*

* "Potassium Bicarbonate, *eight grammes* [or 123 grains]; Citric Acid, *six grammes* [or 92 grains]; Distilled Water, *a sufficient quantity,* to make *one hundred mils* [or 3 fluidounces, 183 minims]. Dissolve the potassium bicarbonate and the citric acid, each, in *forty mils* [or 1 fluidounce, 169 minims] of distilled water. Filter the solutions separately and wash the filters with enough distilled water to obtain in each case *fifty mils* [or 1 fluidounce, 331 minims]. Mix the two solutions, and, when effervescence has ceased, transfer to a bottle and stopper tightly. This preparation must not be dispensed unless it has been recently prepared." *U. S.*

Solution of potassium citrate has been made identical with the mixture formerly official as *Mistura Potassii Citratis;* nevertheless the mixture made with lemon juice will continue to be preferred by some practitioners; its formula therefore follows:

Mistura Potassii Citratis, U. S., 1880. *Mixture of Citrate of Potassium.* [*Neutral Mixture.*] *Mistura Neutralis; Potion gazeuse (effervescente),* Fr.—"Fresh Lemon Juice, strained, *one hundred parts* [or four fluidounces]; Bicarbonate of Potassium, about *ten parts,* or *a sufficient quantity.* Add the Bicarbonate of Potassium gradually to the Lemon Juice until it is neutralized. This preparation should be freshly made, when wanted for use."

The *official solution* is stronger than the mixture, and is more definite in composition; lemon juice varies in strength, and consequently the amount of potassium citrate in the resulting mixture cannot be uniform. On the other hand, the mixture is much to be preferred on account of its more agreeable taste. An improvement has been made in the present official solution in directing the acid and the alkaline salt to be dissolved separately, and the direction to dispense the preparation in a fresh condition will undoubtedly lead to the keeping of the filtered solutions, by the pharmacist, in separate bottles, and mixing in equal measures or weights when prescribed. The solutions keep well for a considerable length of time, and there is thus greater convenience and a saving of time and labor.

Properties.—The U. S. Pharmacopœia describes the solution as "a clear, colorless liquid, odorless and having a mildly saline taste. It is slightly acid to litmus. It conforms to the reactions and tests for an aqueous solution of the salt as given under *Potassii Citras,* when concentrated to the proper strength.

"**Assay.**—Evaporate to dryness about 15 mils of Solution of Potassium Citrate, accurately weighed, and proceed as directed under the Assay for alkali salts of organic acids (see Part III, Test No. 6). It shows not less than 8 per cent. of $K_3C_6H_5O_7$.

"Each mil of half-normal sulphuric acid V.S. used corresponds to 0.051057 Gm. of $K_3C_6H_5O_7$. Each gramme of Solution of Potassium Citrate, after evaporation and ignition, corresponds to not less than 1.57 mils of half-normal sulphuric acid V.S." *U. S.*

Uses.—The solution of potassium citrate has long been used under the name of *neutral mixture, saline mixture,* or *effervescing draught.* It formerly was much used as a refrigerant diaphoretic, in cases of *fever* with dry skin, but has been largely superseded by the more potent antipyretics. It has the therapeutic virtues of potassium citrate and the presence of the carbonic acid often makes it more acceptable to the stomach.

Dose, of official solution, four fluidrachms (15 mils).

LIQUOR POTASSII HYDROXIDI. U. S. (Br.)

SOLUTION OF POTASSIUM HYDROXIDE Liq. Pot. Hydrox. [Liquor Potassæ, Pharm. 1890, Solution of Potassa]

(lĭ'quŏr pŏ-tăs'sĭ-ī hȳ-drŏx'ĭ-dī)

"An aqueous solution containing not less than 4.5 per cent. of KOH (56.11). Preserve Solution of Potassium Hydroxide in bottles made of hard glass, and provided with rubber

stoppers or with glass stoppers coated with petrolatum." *U. S.* "Solution of Potash is an aqueous solution containing in 100 millilitres 5 grammes of pure potassium hydroxide, KOH. It should be preserved in a green glass bottle furnished with an air-tight stopper." *Br.*

Liquor Potassæ, *Br.;* Kali Hydricum Solutum, Lixivium Causticum; Solution of Potash; Potasse caustique liquide, Lessive caustique, *Fr.;* Liquor Kali Caustici, *P. G.;* Aetzkalilauge, Kalilauge, *G.*

* "Potassium Hydroxide, *sixty grammes* [or 2 ounces av., 51 grains]; Distilled Water, *nine hundred and forty grammes* [or 33 ounces av., 69 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Dissolve the potassium hydroxide in the distilled water." *U. S.*

In the U. S. P. IX the only process for making this solution is the simple one of dissolving potassium hydroxide in sufficient distilled water to make a solution of about 5 per cent. strength (potassium hydroxide not less than 85 per cent., see page 899). The former process of decomposing potassium bicarbonate with lime and mixing with water having been dropped. (See *U. S. D.,* 19th ed., p. 733.)

The British Pharmacopœia, 1914, does not give a detailed process, merely specifying that one hundred millilitres shall contain five grammes of potassium hydroxide.

Properties.—Solution of potassium hydroxide is "a clear, colorless, odorless liquid, having, even when diluted, a very acrid and caustic taste. *It should not be tasted unless largely diluted.* It is strongly alkaline and readily absorbs carbon dioxide from the air. Specific gravity: about 1.046 at 25° C. (77° F.). It conforms to the reactions and tests for an aqueous solution of potassium hydroxide as given under *Potassii Hydroxidum,* when concentrated to the proper strength. Introduce about 20 mils of Solution of Potassium Hydroxide into a flask, stopper, weigh accurately and titrate it directly with normal hydrochloric acid V.S., using methyl orange T.S. as indicator. It shows not more than 5.5 per cent. of alkalinity, calculated as KOH (*carbonate*).

"**Assay.**—Transfer about 50 mils of Solution of Potassium Hydroxide, accurately weighed, to a 250 mil measuring flask, add 20 mils of barium chloride T.S. and fill the flask to the mark with distilled water, which has previously been boiled and cooled. Then thoroughly agitate the liquid, filter it through a dry filter, reject the first 20 mils and titrate 100 mils of the filtrate, representing 20 mils of the solution, with normal hydrochloric acid V.S., using phenolphthalein T.S. as indicator. It shows not less than 4.5 per cent. of KOH, when calculated to the amount of Solution originally taken.

"Each mil of normal hydrochloric acid V.S. used corresponds to 0.05611 Gm. of KOH. Each gramme of Solution of Potassium Hydroxide (after treatment with barium chloride T.S.) corresponds to not less than 0.80 mil of normal hydrochloric acid V.S." *U. S.*

"A colorless, strongly alkaline liquid. Yields no characteristic *reactions* for lead, copper, arsenic, iron, aluminium, calcium, magnesium, sodium, or ammonium, and not more than the slightest *reactions* for carbonates, chlorides, or sulphates. Specific gravity 1.045. 20 millilitres require for neutralisation 17.8 millilitres of *N/1 solution of sulphuric acid.* This Solution contains 5 grammes of Potassium Hydroxide, KOH, in 100 millilitres; 110 minims contain 5 grains." *Br.*

It acts rapidly on animal and vegetable substances, and when rubbed between the fingers produces a soapy feeling, in consequence of a partial solution of the cuticle. It dissolves gum, resins, and extractive matter, and forms soap with oily and fatty bodies. It is incompatible with acids, acidulous salts, and all metallic and earthy salts held in solution by an acid; also with all ammonia salts, and with calomel and corrosive sublimate. The two official solutions of potassium hydroxide are now nearly identical in strength, the U. S. solution having the sp. gr. 1.046 at 25° C. (77° F.), and the Br. 1.045 at 15.5° C. (60° F.). On account of its strong attraction for carbon dioxide, solution of potassium hydroxide should be carefully preserved from contact with the air.

Uses.—Solution of potassium hydroxide is powerfully antacid, and mildly diuretic, and was formerly much used, but, on account of its irritant properties, has been superseded by the carbonated alkalies.

Dose, ten to thirty minims (0.6–1.8 mils).

LIQUOR POTASSII PERMANGANATIS.
Br.

SOLUTION OF POTASSIUM PERMANGANATE

(lĭ'quŏr pŏ-tăs'sĭ-ī pĕr-măn'gă-nā'tĭs)

Soluté, de Permanganate de Potasse, *Fr.;* Kaliumpermanganatlösung, *G.*

"Potassium Permanganate, 10 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Dissolve. This Solution contains 1 gramme of Potassium Permanganate in 100 millilitres; 110 minims contain 1 grain." *Br.*

This is an unstable 1 per cent. solution of potassium permanganate which decomposes upon exposure and deposits manganese oxides.

Dose, of the British Pharmacopœia, from two to four fluidrachms (7.5–15 mils), equivalent to from 1.1 to 2.2 grains of the salt. Very few stomachs will bear more than one grain (0.065 Gm.) of the permanganate.

LIQUOR SODÆ CHLORINATÆ.
U. S., Br.

SOLUTION OF CHLORINATED SODA Liq. Sod. Chlorinat. [Liquor Sodæ Chloratæ, U. S. 1890, Labarraque's Solution]

(lĭ'quŏr sō'dæ ĕhlŏ-rĭ-nā'tæ)

"An aqueous solution of chlorine compounds of sodium, containing not less than 2.5 per cent. of available Cl. Preserve the Solution in well-

stoppered bottles, in a cool place, protected from light." *U. S.*

Liquor Natri Chlorati; Liquor Natri Hypochlorosi; Bleaching Solution; Chlorure de Soude liquide, *Fr. Cod.;* Liqueur de Labarraque, *Fr.;* Chlornatronlösung, Bleichflüssigkeit, *G.;* Solucion de hipoclorito sodico, Licor de Labarraque, *Sp.*

* "Monohydrated Sodium Carbonate, *seventy grammes* [or 2 ounces av., 205 grains]; Chlorinated Lime, *one hundred grammes* [or 3 ounces av., 231 grains]; Water, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Triturate the chlorinated lime with *five hundred mils* [or 16 fluidounces, 435 minims] of water gradually added until a uniform mixture results. Dissolve the monohydrated sodium carbonate in *five hundred mils* [or 16 fluidounces, 435 minims] of hot water, and add this solution to the chlorinated lime mixture contained in a suitable vessel. Stir or shake the mixture thoroughly and if it becomes gelatinous warm the vessel very gently until its contents again liquefy. Then transfer the mixture to a wetted muslin strainer, returning the first portion until the liquid passes through clear, and when no more liquid drains from it, wash the precipitate with enough water to make the product weigh *one thousand grammes* [or 35 ounces av., 120 grains]." *U. S.*

"Chlorinated Lime, 100 *grammes;* Sodium Carbonate, 150 *grammes;* Distilled Water, 1000 *millilitres.* Dissolve the Sodium Carbonate in two hundred and fifty *millilitres* of the Distilled Water; thoroughly triturate the Chlorinated Lime with the remainder of the Distilled Water; mix the two liquids; shake occasionally during three or four hours; filter. This Solution should be freshly prepared." *Br.*

This solution was first brought into notice as a disinfecting agent by Labarraque, an apothecary of Paris. It was afterwards found to possess valuable therapeutic properties. The U. S. process is practically that of Payen, adopted in the French Codex of 1837. It consists in decomposing a solution of monohydrated sodium carbonate by one of chlorinated lime. Calcium carbonate is precipitated and the chlorinated soda remains in solution. The proportion employed gives an excess of sodium carbonate, the presence of which renders the solution more permanent. Sodium bicarbonate has been recommended instead of sodium carbonate, on account of the state of crystalline powder in which the calcium carbonate is precipitated, rendering its separation from the supernatant solution very easy, while the precipitate produced by sodium carbonate is a kind of magma from which the liquor is not readily decanted. It is stated also that a little excess of the bicarbonate is useful in various ways. (*Ann. Thér.,* 1866, 107.)

Properties.—The U. S. solution is "a clear, pale greenish liquid, having a faint odor of chlorine and a disagreeable, alkaline taste. The Solution at first colors red litmus paper blue, and then bleaches it. The addition of hydrochloric acid to the Solution causes an evolution of chlorine and carbon dioxide.

"Assay.—Mix in a flask about 7 mils of Solution of Chlorinated Soda, accurately weighed, with 50 mils of distilled water, add 1 Gm. of potassium iodide and 5 mils of acetic acid and titrate with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 2.5 per cent. of available Cl.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.003546 Gm. of available Cl. Each gramme of Solution of Chlorinated Soda corresponds to not less than 7 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

"A colorless alkaline liquid with a faint odor of chlorine and astringent taste. Decomposed by *hydrochloric acid,* evolving chlorine. Yields not more than slight *reactions* for calcium or carbonates. Specific gravity 1.054. If 5 millilitres are added to a solution of 1 gramme of *potassium iodide* in 100 millilitres of *water* acidified with 5 millilitres of *hydrochloric acid,* a brownish-red solution is obtained, which requires for decolorisation not less than 37.6 millilitres of *N/10 solution of sodium thiosulphate* (presence of not less than 2.5 per cent. by weight of available chlorine)." *Br.*

This test, like that of our own Pharmacopœia, is intended to determine the chlorine strength of the solution. The acetic or hydrochloric acid liberates the chlorine, which then liberates from the potassium iodide an equivalent quantity of iodine, by which the solution is rendered brown, and, the iodine being converted into hydriodic acid by the sodium thiosulphate, the solution again becomes colorless. The quantity of the solution of the latter salt required to bleach the liquid measures the amount of iodine, and this, that of the chlorine which has separated it. The color of turmeric is first rendered brown, and afterwards destroyed. When carefully evaporated, a mass of damp crystals is obtained, which, when redissolved in water, possess the properties of the original liquid. Solution of chlorinated soda, when exposed to the air, absorbs carbon dioxide and slowly evolves chlorine which acts as a disinfectant.

Nature and Composition.—In their chemical nature these solutions are identical. Assuming the chlorinated lime to be essentially calcium hypochlorite with calcium chloride (see page 265), the solutions, after decantation from the precipitated calcium carbonate, will contain *sodium hypochlorite* with *sodium chloride:*

$$Ca(OCl)_2 + CaCl_2 + 2Na_2CO_3 = 2CaCO_3 + 2NaOCl + 2NaCl$$

Besides these there will be present more or less *sodium carbonate,* according as there happens to be in the chlorinated lime less or more chlorine to decompose it. In all cases, however, there will be an excess of sodium carbonate, as the best chlorinated lime does not contain sufficient chlorine to effect its entire decomposition, in the proportion in which it is taken in the formula.

Arny and Dawson (*Proc. A. Ph. A.,* 1908, p. 841) criticized the process for making this

solution and recommended the reduction of the U. S. P. standard for chlorinated lime from 30 per cent. of available chlorine to 25 per cent. largely because it is difficult for pharmacists to procure the drug commercially of this strength.

Uses.—The solution of chlorinated soda possesses the germicidal value of its available chlorine. For the disinfection of large masses of organic matter it is inferior to chlorinated lime, not merely because of its greater cost, but also because of its lower content of chlorine. It is, however, an excellent agent for the disinfection of various utensils which are not injured by its bleaching action, such as clinical thermometers and glass or china ware which has been used by patients with contagious disease. It has also been employed to a considerable extent in the treatment of external infected *wounds* or *ulcers*, as well as in various infected conditions of the vagina, bladder, mouth, or throat. For the latter purposes it is usually well to dilute it with from 15 to 30 parts of water. Where it is used in irrigation, as in washing out the bladder by means of double cannula, half an ounce may be employed in one and one-half pints of water. During the European war a solution of chlorinated soda neutralized with boric acid achieved great notoriety as a germicide in *gun-shot wounds* under the name of *Dakin's solution*. The formula as given by Dakin (*B. M. J.*, 1915, ii, p. 318) is as follows: 140 Gm. of dry sodium carbonate (or 400 Gm. of the crystalline) are dissolved in 10 liters of tap water. Add 200 Gm. of chlorinated lime and shake well. Half an hour later siphon off the clear fluid and filter through cotton. Add 40 Gm. of boric acid, which should yield a solution only faintly alkaline. This solution represents, according to Dakin, between 0.5 to 0.6 per cent. of sodium hypochlorite. Later Dr. A. Carrel submitted a formula for what is called *"Carrel-Dakin Solution"* (Daufresne's technic), giving the following detail for its preparation, and advising its use instead of all previously published formulas:

The requisites of a solution of sodium hypochlorite for surgical use, which have been established by the European war, after numerous tests and a long practical experience are: complete absence of caustic alkali and a concentration of sodium hypochlorite of not less than 0.45, nor more than 0.50 per cent. Three chemical substances are indispensable to Dakin's solution and all should conform to the U. S. P. standards for purity: chlorinated lime, anhydrous sodium carbonate and sodium bicarbonate. Among these three products the latter two are of a practically adequate constancy, but this is not the case with the first. Its content in active chlorine (decoloring chlorine) varies within wide limits, and it is absolutely indispensable to titrate it before using it. Weigh out 20 Gm. of an average sample of chlorinated lime, mix it as completely as possible with 1 liter of ordinary water, and leave it in contact for a few hours, agitating it from time to time. Filter. Measure exactly, with a graduated pipette, 10 mils of the clear fluid; add to it 20 mils of a 1 in 10 solution of potassium iodide and 2 mils of acetic or hydrochloric acid. Drop, a drop at a time, into this mixture a tenth-normal volumetric solution of sodium thiosulphate until decoloration is complete. The number of mils of the hypochlorite solution required for complete decoloration, multiplied by 1.775, gives the weight of the active chlorine contained in 100 Gm. of the chlorinated lime. This figure being known, it is applied to the accompanying table, which will give the quantities of chlorinated lime, of sodium carbonate and of sodium bicarbonate which are to be employed to prepare 10 liters of Carrel-Dakin's solution.

Quantities of Ingredients for Ten Liters of Carrel-Dakin's Solution.

Titer of Chlorinated Lime	Chlorinated Lime, Gm.	Anhydrous Sodium Carbonate, Gm.	Sodium Bicarbonate, Gm.
20	230	115	96
21	220	110	92
22	210	105	88
23	200	100	84
24	192	96	80
25	184	92	76
26	177	89	72
27	170	85	70
28	164	82	68
29	159	80	66
30	154	77	64
31	148	74	62
32	144	72	60
33	140	70	59
34	135	68	57
35	132	66	55
36	128	64	53
37	124	62	52

Example: If it required 16.6 mils of the tenth-normal solution of the sodium thiosulphate for complete decoloration, the titer of the chlorinated lime in active chlorine is:

$$16.6 \times 1.775 = 29.7 \text{ per cent.}$$

The quantities to be employed to prepare 10 liters of the solution will be in this case:

Chlorinated lime	154 Gm.
Dry sodium carbonate	77 Gm.
Sodium bicarbonate	62 Gm.

If crystalline sodium carbonate is being used, then instead of the 80 Gm. of dry carbonate it must be replaced by:

Crystalline sodium carbonate .... 220 Gm.

Preparation of Dakin's Solution.—To prepare 10 liters of the solution: 1. Weigh exactly the quantities of chlorinated lime, sodium carbonate and sodium bicarbonate which have been determined in the course of the preceding trial. 2. Place in a 12-liter jar the chlorinated lime and 5 liters of tap water, agitate

vigorously for a few minutes, and leave in contact for from six to twelve hours, over night, for instance. 3. At the same time dissolve, cold, in the five other liters of water the sodium carbonate and the bicarbonate. 4. Pour the solution of the sodium salts all at once into the jar containing the maceration of chlorinated lime, agitate vigorously for a few moments, and leave it quiet to permit the calcium carbonate to settle as it forms. At the end of half an hour, siphon the liquid and filter it through double paper to obtain an entirely limpid product, which must be protected from light. Exposed to the light solutions of hypochlorite undergo very rapid deterioration and are not fit for use twenty-four hours after their preparation. To guard against this danger, the finished product should be stored in large wicker-covered demijohns of black or amber glass.

Titration of Carrel-Dakin's Solution.—It is a wise precaution to verify, from time to time, the titer of the solution. This titration utilizes the same material and the same chemical substances as are used to determine the active chlorine in the chlorinated lime: Measure out 10 mils of the solution, add 20 mils of 1 in 10 solution of potassium iodide, and 2 mils of acetic or hydrochloric acid. Drop, a drop at a time, into this mixture a tenth-normal solution of sodium thiosulphate until decoloration is complete. The number of mils employed multiplied by 0.03725 will give the weight of the sodium hypochlorite contained in 100 mils of the solution. A solution is correct when, under the conditions given above, from 12 to 13 mils of tenth-normal thiosulphate are required to complete the decoloration:

$$13 \times 0.03725 = 0.485 \text{ per cent. of NaOCl}$$

The Test for the Alkalinity of Carrel-Dakin's Solution.—It is easy to differentiate the solution obtained by this procedure from the commercial hypochlorites and from Labarraque's solution: Pour into a glass about 20 mils of the fluid, and drop on the surface a few centigrams of phenolphthalein in powdered form. Carrel-Dakin's solution, correctly prepared, gives absolutely no change in tint, while in the same conditions Javel water and Labarraque's solution give an intense red coloration which indicates in the latter two solutions the presence of free caustic sodium. (See *J. A. M. A.*, 1916, p. 1777. Also *J. A. Ph. A.*, 1917, p. 458, *Am. Dr.*, 1917, p. 25.)

Another chlorine containing body, known as *Dakin's antiseptic,* is *para-toluene-sodium-sulpho-chloramide,* which is described in *J. A. Ph. A.*, 1917, p. 387. (See also *Chlorazene,* Part II.) *Para-toluene-sulpho-dichloramine,* sold under the name *Dichloramine T,* is soluble in oil and its solution has been called *Dakin's oil* (see *J. A. M. A.*, 1917, vol. lxix, pp. 27, 1076; see also *Dichloramine T,* Part II).

Under the name of *antiformin* an alkaline solution of sodium hypochlorite is largely used in the bacteriological laboratory. This solution contains about 7.5 per cent. of sodium hydroxide and 5.2 per cent. of chlorine. Its especial value lies in its property of liquefying various organic matters and of dissolving most varieties of bacteria. It is especially employed for the purpose of recognizing tubercle bacilli in the sputum; it liquefies the sputum, so that centrifugation is possible, and dissolves other bacteria.

LIQUOR SODII ARSENATIS. U. S., Br.

SOLUTION OF SODIUM ARSENATE Liq. Sod. Arsen.

(lĭ'quŏr sō'dī-ī ăr-sẹ-nā'tĭs)

"An aqueous solution containing not less than 0.975 per cent. nor more than 1.025 per cent. of Na_2HAsO_4 (185.97)." *U. S.*

Liquor Sodii Arseniatis, *Br.* 1885; Solution of Arseniate of Sodium; Soluté d'Arseniate de Soude, *Fr.;* Arsensaure Natronlösung, *G.*

* "Exsiccated Sodium Arsenate, previously dried to constant weight at 150° C. (302° F.), *one gramme* [or 15.4 grains]; Distilled Water, *a sufficient quantity,* to make *one hundred grammes* [or 3 ounces av., 231 grains]. Dissolve the exsiccated sodium arsenate in sufficient distilled water to make the product weigh *one hundred grammes* [or 3 ounces av., 231 grains]." *U. S.*

"Anhydrous Sodium Arsenate, 1 *gramme;* Distilled Water, sufficient to produce 100 *millilitres.* Dissolve. This Solution contains the equivalent of 1 gramme of Anhydrous Sodium Arsenate in 100 millilitres; 110 minims contain the equivalent of 1 grain." *Br.*

This is simply an official form for the administration of sodium arsenate. (See *Sodii Arsenas* and *Sodii Arsenas Exsiccatus.*) "The Solution conforms to the reactions and tests for an aqueous solution of the salt as given under *Sodii Arsenas Exsiccatus,* when concentrated to proper strength.

"**Assay.**—Pour into a tared flask about 30 mils of Solution of Sodium Arsenate, weigh accurately, heat to 80° C. (176° F.) and add 10 mils of hydrochloric acid and 3 Gm. of potassium iodide. Allow the mixture to stand for fifteen minutes at 80° C. (176° F.), in a glass-stoppered flask, cool and then titrate with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 0.975 per cent. nor more than 1.025 per cent. of Na_2HAsO_4.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.0092985 Gm. of Na_2HAsO_4. Each gramme of Solution of Sodium Arsenate corresponds to not less than 1.05 mils nor more than 1.10 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

It now contains 1 per cent. of exsiccated sodium arsenate, where formerly there was present but 0.87 per cent., and the British solution has been made to correspond in strength. The salt is directed to be dried, in order that the solution may be of a uniform strength, as, from the mode in which the sodium arsenate is ordered to be prepared, it is scarcely possible

that it should always contain precisely the same quantity of water of crystallization. It is important in drying it to limit the heat to 150° C. (302° F.), lest a portion of the arsenic should be volatilized.

Dose, from three to five minims (0.2–0.3 mil), to be cautiously increased, if necessary.

LIQUOR SODII CHLORIDI PHYSIOLOGICUS. U. S.

PHYSIOLOGICAL SOLUTION OF SODIUM CHLORIDE
Liq. Sod. Chlor. Physio. [Physiological Salt Solution Normal Salt Solution]

(lī'quŏr sō'dĭ-ī ȼhlō'rĭ-dī phȳs-ĭ-ǫ-lŏ'gĭ-cŭs)

* "Sodium Chloride, *eight and five-tenths grammes* [or 131 grains]; Distilled Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the sodium chloride in sufficient freshly distilled water to measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] and filter. Then sterilize the solution, preferably in an autoclave, under steam pressure, at a temperature of from 115° to 120° C. (239°–248° F.) for fifteen minutes, or by boiling it during at least one hour, and preserve it in a sterile condition. This solution should not be used after it has been made forty-eight hours." *U. S.*

The Pharmacopœia directs that salt solution may be sterilized by boiling for one hour. If this be done a considerable amount of the water may be evaporated and the concentration of the solution materially altered. This should be avoided as far as possible by using a narrow-necked flask, stoppered with cotton and not boiling too vigorously, whether sterilized in the autoclave or by boiling the flask should be stoppered with cotton before sterilization.

Uses.—When pure water is brought in contact with the blood it causes alteration in the red blood corpuscles, allowing the escape of hemoglobin from them into the plasma; this is known as "laking" of the blood. The addition of inorganic salts to the water, in quantities sufficient to make a solution of the same osmotic tension as the blood serum, prevents this action on the corpuscles. When a solution contains just the amount of salt necessary to prevent laking it is said to be isotonic with the blood. Because of its non-toxicity sodium chloride is the salt usually employed for the purpose of preparing an isotonic solution. The amount of salt necessary for this purpose varies in different animals; in the human being it requires an 0.9 per cent. solution of sodium chloride, but an 0.6 per cent. is isotonic with ox blood. This isotonic solution is sometimes spoken of as *normal salt solution,* an unfortunate term, as it is likely to be confused with the normal solution of sodium chloride used by chemists, which is nearly seven times stronger. A much better term is the official name, *physiological salt solution.* In 1882 Ringer showed that after all the blood had been washed out of the heart with an isotonic sodium chloride solution, the addition of small amounts of calcium and potassium would cause that organ again to begin to contract, and that it would continue beating for some time if supplied with these salts. He therefore suggested that calcium and potassium be added to the sodium chloride solution in preparing a physiologically indifferent fluid. Although Ringer originally recommended the addition of calcium phosphate to saturation for the purpose of supplying the needed lime, as at present used in physiological laboratories *Ringer's solution* has the following composition: sodium chloride, 0.7 per cent.; potassium chloride, 0.03 per cent.; calcium chloride, 0.025 per cent. Subsequently it was shown that if this solution was rendered slightly alkaline it offered a still more favorable medium for the heart. In 1895 Locke suggested the addition of dextrose in order to furnish a food stuff to the heart. *Locke's solution,* which is widely used in physiological laboratories, contains: sodium chloride, 0.9 Gm.; calcium chloride, 0.024 Gm.; potassium chloride, 0.042 Gm.; sodium bicarbonate, 0.02 Gm.; dextrose, 0.1 Gm.; water, 100 mils. A still more recent modification known as *Tyrode's solution* has the following combination: sodium chloride, 0.8 per cent.; potassium chloride, 0.02; calcium chloride, 0.02; magnesium chloride, 0.01; sodium phosphate, 0.005; sodium bicarbonate, 0.1 per cent. Although theoretically these solutions are preferable to that of simple sodium chloride, because more nearly approximating the composition of the bodily fluids, yet practically the reserve supply of calcium and potassium in the human body is so large that it is extremely doubtful whether they are ordinarily superior for medical purposes.

Physiological salt solution is used for the purpose of introducing large quantities of water into the system more rapidly than could be done through the alimentary tract. In cases of low blood pressure due either to severe *hemorrhage*—in which the volume of blood is so greatly reduced as to be unable to properly fill the blood vessels—or due to vasomotor paresis, such as *surgical shock*—when the vessels are so dilated that the normal quantity of blood is unable to fill them—the introduction of large amounts of blood into the circulation, as by intravenous injection of physiological salt solution, by filling the vascular system restores a normal resistance and thereby tends to bring the blood pressure back to the normal. In a similar way when large amounts of fluid have been lost from the body—as in the violent purgation of *Asiatic cholera* or *arsenic poisoning*—the administration of a salt solution by increasing the volume of blood is often of much benefit. As is well known, the volume of the urine and of the sweat depends in large measure upon the volume of the blood and the introduction of large quantities of fluid, as by the injection of physiological salt solution, tends to increase these secretions. It is probable that the increased output of water under these circumstances will

carry with it certain toxic substances, and the method of treatment is widely used in certain cases of systemic poisoning, such as *uremia,* with the idea of increasing the elimination of the toxic material. It is more likely, however, that the benefit from the injection of fluids in cases of extraneous poisonings, such as *corrosive sublimate* or *lead poisoning,* is due more to the dilution of the blood than to the actual increase in elimination.

Physiological salt solution may be administered either intravenously, subcutaneously (*hypodermoclysis*), or through the colon (*enteroclysis*). Absorption through the last channel is relatively slow and enteroclysis is employed chiefly in those conditions where it is desirable to avoid the administration of water by the mouth. In either hypodermic or intravenous injection it is essential that the salt solution be absolutely sterile. For this reason it is necessary not only to make the solution with freshly distilled water, but that it should be resterilized after the addition of the sodium chloride. It is, of course, equally essential that the vessels used for the injection, and also the skin of the patient, should also be properly sterilized. From one pint to two quarts (500–1900 mils) of the physiological salt solution may be injected at one dose and repeated again if necessary in a few hours.

LIQUOR SODII GLYCEROPHOSPHATIS. U. S.

SOLUTION OF SODIUM GLYCEROPHOSPHATE Liq. Sod. Glycerophos. [Solution of Sodium Glycerinophosphate]

(lĭ'quŏr sō'dĭ-ī glĭ-cĕr-ō-phŏs-phā'tīs)

"An aqueous solution of sodium glycerophosphate containing not less than 50 per cent. of the anhydrous salt ($Na_2C_3H_7PO_6$ or $Na_2C_3H_5(OH)_2PO_4 = 216.10$)." *U. S.*

"A clear, colorless or yellowish, syrupy liquid. In other respects it conforms to the reactions and tests for purity under *Sodii Glycerophosphas.*

"**Assay.**—Proceed as directed under *Sodii Glycerophosphas.* It shows not less than 50 per cent. of $Na_2C_3H_7PO_6$.

"Each mil of half-normal hydrochloric acid V.S. used corresponds to 0.10805 Gm. of $Na_2C_3H_7PO_6$.

"Each gramme of Solution of Sodium Glycerophosphate corresponds to not less than 4.63 mils of half-normal hydrochloric acid V.S." *U. S.*

This solution was introduced into the U. S. P. IX for the first time; it contains about 50 per cent. of sodium glycerophosphate and is the product which was sold commercially for many years as sodium glycerophosphate. (See *Sodii Glycerophosphas*).

Dose, five to ten minims (0.3–0.6 mil).

Off. Prep.—Elixir Calcii et Sodii Glycerophosphatum, *N. F.;* Elixir Glycerophosphatum Compositum, *N. F.*

LIQUOR SODII HYDROXIDI. U. S.

SOLUTION OF SODIUM HYDROXIDE Liq. Sod. Hydrox. [Liquor Sodæ, U. S 1890, Solution of Soda]

(lĭ'quŏr sō'dĭ-ī hȳ-drŏx'ĭ-dī)

"An aqueous solution containing not less than 4.5 per cent. of NaOH (40.01). Preserve Solution of Sodium Hydroxide in bottles made of hard glass and provided with rubber stoppers or with glass stoppers coated with petrolatum." *U. S.*

Solution of Caustic Soda; Natrium Hydricum Solutum; Soude caustique liquide, *Fr. Cod.;* Lessive des Savonniers, *Fr.;* Liquor Natri Caustici, *P. G.;* Aetznatronlauge, Natronlauge, *G.;* Solucion de sosa caustica, *Sp.*

* "Sodium Hydroxide, *fifty-six grammes* [or 1 ounce av., 427 grains]; Distilled Water, *nine hundred and forty-four grammes* [or 33 ounces av., 131 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Dissolve the sodium hydroxide in the distilled water." *U. S.*

Solution of sodium hydroxide is prepared in the same way as solution of potassium hydroxide. In the U. S. P. VIII and IX the process is that of simple solution of sodium hydroxide in water; in the U. S. P., 1890, process by a double decomposition between sodium carbonate and calcium hydroxide, there are formed sodium hydroxide in solution, and calcium carbonate which precipitates:

$$Na_2CO_3 + Ca(OH)_2 = 2NaOH + CaCO_3$$

In this process an excess of lime is used, which is necessary to insure a full decomposition of the carbonate.

Properties.—Solution of sodium hydroxide, sometimes called solution of caustic soda, is "a clear, colorless, odorless liquid, having, when diluted, a very acrid and caustic taste. *It should not be tasted unless largely diluted.* It is strongly alkaline and readily absorbs carbon dioxide from the air. Specific gravity: about 1.056 at 25° C. (77° F.). It conforms to the reactions and tests for an aqueous solution of sodium hydroxide as given under *Sodii Hydroxidum,* when concentrated to the proper strength. Introduce about 20 mils of Solution of Sodium Hydroxide into a flask, stopper, weigh accurately and titrate it directly with normal hydrochloric acid V.S., using methyl orange T.S. as indicator. It shows not more than 5.5 per cent. of alkalinity, calculated as NaOH (*carbonate*).

"**Assay.**—Transfer about 50 mils of Solution of Sodium Hydroxide, accurately weighed, to a 250 mil measuring-flask, add 20 mils of barium chloride T.S. and fill the flask to the mark with distilled water, which has been previously boiled and cooled. Then thoroughly agitate the liquid, filter it through a dry filter, reject the first 20 mils, and titrate 100 mils of the clear filtrate with normal hydrochloric acid V.S., using phenolphthalein T.S. as indicator. It shows not less than 4.5 per cent. of NaOH when calculated to the amount of solution originally taken.

"Each mil of normal hydrochloric acid V.S. used corresponds to 0.04001 Gm. of NaOH. Each gramme of Solution of Sodium Hydrox-

ide corresponds to not less than 1.12 mils of normal hydrochloric acid V.S." *U. S.*

Its properties and tests are the same as those of solution of potassium hydroxide, with the exception that no precipitate is produced by platinic chloride or tartaric acid. The alkali dissolved must be viewed as sodium hydroxide (Na.OH), of which two molecules are formed by the union of the oxide with water, according to the reaction:

$$Na_2O + H_2O = 2Na.OH$$

Uses.—The solution of sodium hydroxide is mildly caustic and actively antacid. For most of the local uses for which caustic soda is employed it is generally too feeble, while for internal administration it is too irritant to the stomach and is rarely employed as a medicine.

Dose, ten to thirty minims (0.6–1.8 mils).

LIQUOR STRYCHNINÆ HYDROCHLORIDI. Br.

SOLUTION OF STRYCHNINE HYDROCHLORIDE [Solution of Hydrochlorate of Strychnine, Brit. Pharm. 1885]

(lĭ'quŏr strĭ̆ĝh-nĭ'næ hȳ-drŏ-ĉhlō'rĭ-dī)

Liquor Strychniæ; Soluté de Chlorhydrate de Strychnine, *Fr.;* Salzsaure Strychninlösung, *G.*

"Strychnine Hydrochloride, 1 *gramme;* Alcohol (90 per cent.), 25 *millilitres;* Distilled Water, sufficient to produce 100 *millilitres.* Mix the Alcohol with an equal volume of Distilled Water; dissolve the Strychnine Hydrochloride in the mixture, and add sufficient Distilled Water to produce the required volume. This Solution contains 1 gramme of Strychnine Hydrochloride in 100 millilitres; 110 minims contain 1 grain." *Br.*

This is the solution of hydrochloride of strychnine of the British Pharmacopœia which was formerly official as *Liquor Strychniæ;* the name has been made definite, and the strength slightly increased, so as to make it conform with the other active solutions; it contains about 1 per cent. of strychnine. The spirit is added for its preservation. A change was made in the last revision of the Br. Pharm., 1898, whereby strychnine hydrochloride is dissolved directly in water containing a little alcohol. This is said to prevent the tendency of the solution to crystallize in cold weather, a fault of the Br. Ph., 1885, process.

Dose, from three to six minims (0.2–0.4 mil), equal respectively to about one-thirtieth and one-eighteenth of a grain (0.002–0.004 Gm.) of the alkaloid.

LIQUOR ZINCI CHLORIDI. U. S., Br.

SOLUTION OF ZINC CHLORIDE Liq. Zinc. Chlor.

(lĭ'quŏr zĭn'cī ĉhlō'rĭ-dī)

"An aqueous solution containing not less than 48.5 per cent. nor more than 52 per cent. of $ZnCl_2$ (136.29)." *U. S.*

Chlorure de Zinc liquide, Soluté de Burnett, *Fr.;* Flüssiges Chlorzink, Chlorzinklösung, *G.*

* "Zinc, granulated, *two hundred and forty grammes* [or 8 ounces av., 204 grains]; Hydrochloric Acid, *eight hundred and forty grammes* [or 29 ounces av., 276 grains]; Nitric Acid, *twelve grammes* [or 185 grains]; Precipitated Zinc Carbonate, *twelve grammes* [or 185 grains]; Distilled Water, *a sufficient quantity,* to make about *one thousand grammes* [or 35 ounces av., 120 grains]. Add the hydrochloric acid gradually to the zinc and *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of distilled water contained in a glass or porcelain vessel, and allow the mixture to stand until the reaction ceases and the acid is saturated. Then pour off the liquid, add the nitric acid and heat the mixture at a temperature not exceeding 115° C. (239° F.), until a portion, when removed and cooled, solidifies. Allow it to cool, and dissolve the solidified mass in sufficient distilled water to make the product weigh *one thousand grammes* [or 35 ounces av., 120 grains]. Then add the precipitated zinc carbonate, agitate the mixture occasionally during twenty-four hours, and set it aside until it has become clear by subsidence. Separate the clear Solution by decantation or by means of a siphon, and preserve it in tightly stoppered bottles." *U. S.*

"Granulated Zinc, 400 *grammes;* Hydrochloric Acid, 1100 *millilitres;* Distilled Water, *a sufficient quantity.* Mix the Hydrochloric Acid with five hundred *millilitres* of Distilled Water in a porcelain dish; add the Zinc; apply gentle heat until gas is no longer evolved; boil for half an hour, supply the water lost by evaporation; allow the product to cool. Test a few drops of the resulting liquid for iron and lead. If either be present, filter the remainder of the cooled product into a bottle, and add *solution of chlorine* by degrees, with frequent shaking, until the liquid acquires a permanent odor of chlorine; add Zinc Carbonate in small quantities at a time, with renewed shaking until the whole of the iron or lead is precipitated; filter the liquid and evaporate to one thousand millilitres. If no iron or lead be present, filter the remainder of the cooled product, and evaporate it to one thousand millilitres." *Br.*

The zinc chloride is made in the usual way, by dissolving zinc in hydrochloric acid. The nitric acid in the U. S. process is added in order that any iron present shall be converted into ferric chloride, from which it is afterwards precipitated by the zinc carbonate. In the older processes the former object was accomplished by the use of solution of chlorinated lime, the latter by chalk. This is a decided improvement, as the use of the chalk as a precipitant introduced into the preparation some calcium chloride, while the zinc carbonate adds only a little zinc chloride in solution. Hydrogen dioxide has been used instead of nitric acid as an oxidizing agent by Besthorn and others. The preparation is completed by bringing it to a certain weight by the addition of distilled water, and by filtration to separate the pre-

cipitated iron and any excess of the carbonate. On account of the difficulty of freeing zinc from iron contamination, Francis Hemm proposes the simpler process of making this solution from iron-free zinc oxide; he dissolves 300 Gm. of such zinc oxide in 840 Gm. of hydrochloric acid in a porcelain dish, with the aid of heat, cools, filters, and evaporates the filtrate to 1000 Gm. (*Am. Drug.*, 1900, 199.)

Properties.—As procured by the U. S. P. process, solution of zinc chloride is "a clear, colorless, odorless liquid, having a very astringent, metallic taste, and an acid reaction. Specific gravity: about 1.548 at 25° C. (77° F.). It conforms to the identity and purity tests for an aqueous solution of the salt as given under *Zinci Chloridum*, when taken in proportionate amount.

"**Assay.**—Transfer to a tared flask about 0.6 Gm. of Solution of Zinc Chloride, weigh accurately, and proceed as directed under the Assay for chlorides (see Part III, Test No. 5). It shows not less than 48.5 per cent. nor more than 52 per cent. of $ZnCl_2$.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.0068145 Gm. of $ZnCl_2$. Each gramme of Solution of Zinc Chloride corresponds to not less than 71.2 mils nor more than 76.3 mils of tenth-normal silver nitrate V.S." *U. S.*

"A colorless liquid; taste astringent and sweetish. Specific gravity 1.530. Yields no characteristic *reactions* for lead, copper, cadmium, arsenic, iron, aluminium, calcium, magnesium, or sulphates." *Br.*

Uses.—The solution of zinc chloride is actively caustic and a powerful germicide, possessed of deodorant properties. In dilute solution it acts as a stimulating astringent with some antiseptic powers. It has been employed, either in full strength or with equal parts of water, for the destruction of *cancerous ulcers*, especially when there is fetid discharge. It has, however, the disadvantages of destroying healthy as well as diseased tissue and that its action is accompanied with a considerable amount of pain. In dilute solution it is used for its astringent and antiseptic influence in *gleet*, *vaginitis* and, occasionally, in other inflammations of the mucous membranes; for these purposes it may be employed in strengths of from 1 to 5 per cent. Formerly the solution of zinc chloride was largely used as a general disinfectant both for surgical and sanitary purposes, but has been largely replaced by other agents. It is also commonly used for the preservation of bodies for dissection. *Burnett's Disinfecting Fluid* was an aqueous solution of zinc chloride very similar to the present official solution; as originally recommended it was made by dissolving one pound of zinc chloride in five gallons of water, but was commercially often prepared by the natural deliquescence of the crystals.

LIQUORES

SOLUTIONS

(lĭ-quō'rēz)

Solutés, *Fr.*; Liquores, *P. G.*; Lösungen, *G.*; Soluzione, *It.*; Solucion, *Sp.*

The U. S. Pharmacopœia includes in this class of preparations all *aqueous* solutions without sugar in which the substance acted on is wholly soluble in water, excluding those in which the dissolved matter is gaseous or very volatile, as in the Aquæ, or Waters. The British Pharmacopœia does not make this distinction and includes several alcoholic solutions of volatile principles among the liquors.

Although several changes were made in the strength of preparations of this class in the U. S. Pharmacopœia of 1880 for the sake of round numbers and to adjust the relative quantity of solid to the solvent, so as to avoid fractions in the percentages, yet it was a question then whether these were advantages sufficient to overbalance the disadvantage of changing the doses of important preparations. Since the important change was made, which makes the powerful solutions contain one per cent. of active ingredient, it would certainly be a serious mistake to alter this proportion in the future. The standard of 1 per cent. for arsenical solutions was adopted by the Conférence Internationale pour l'Unification de la Formule des Médicaments Héroïques in 1902, and has been accepted by all the Pharmacopœias. The 1 per cent., in this connection, refers not to the substance named in the preparation, but to the substance used in making it. Thus in *Liquor Potassii Arsenitis*, the finished preparation does not contain 1 per cent. of potassium arsenite as might be supposed, but contains 1 per cent. of the arsenic trioxide used in making the preparation.

The Br. Pharm., 1898, introduced ten concentrated infusions, with the object of affording an easy method of making, through dilution, ordinary infusions. The titles were very inappropriate, and the British Pharmacopœia, 1914, dismissed *concentrated infusions*.

LITHII BROMIDUM. U. S.

LITHIUM BROMIDE Lith. Brom.

(lĭth'ĭ-ĭ brō'mĭ-dŭm)

"It contains not less than 85 per cent. of LiBr (86.86). Preserve it in air-tight containers." *U. S.*

Lithium Bromatum; Bromure de Lithium, *Fr. Cod.*; Bromlithium, Lithiumbromid, *G.*

This salt was made official in the U. S. P., 1880. Yvon prepares *lithium bromide* by mixing 37 parts of lithium carbonate, 200 parts of distilled water, and 80 parts of bromine, and passing a current of hydrogen sulphide through the mixture until the color of bromine has disappeared. A slight heat is then applied, to drive off excess of hydrogen sulphide and to

agglutinate the sulphur. After filtration the liquor is concentrated and finally crystallized by desiccating it under a bell glass, over sulphuric acid. It may also be obtained by double decomposition. Lithium sulphate is first formed by treating 37 parts of lithium carbonate with 49 parts of monohydrated sulphuric acid diluted with its own volume of water. Then 119 parts of potassium bromide are dissolved in the smallest possible quantity of water. When the two solutions are mixed, an abundant precipitate of potassium sulphate is produced on the addition of a little alcohol. The whole is evaporated to dryness, the operation finished on a water bath, and the residue is treated with alcohol, which removes only lithium bromide and deposits it again on evaporation. The bromide may then be crystallized from water or kept in solution of known strength. (*P. J.*, Sept. 18, 1876.) No process is given in the Pharmacopœia.

Properties.—It is officially described as "a white, granular salt, odorless and having a sharp, slightly bitter taste; very deliquescent. One Gm. of Lithium Bromide dissolves in 0.6 mil of water at 25° C. (77° F.); also in 0.4 mil of boiling water; freely soluble in alcohol and soluble in ether. An aqueous solution of the salt (1 in 20) is neutral or slightly alkaline to litmus. At a low red heat the salt fuses, and at a higher heat it is slowly volatilized. It imparts a crimson color to a non-luminous flame. Silver nitrate T.S., added to an aqueous solution of the salt (1 in 10), produces a yellowish-white precipitate insoluble in nitric acid or in a moderate excess of ammonia water. Add a few drops of ferric chloride T.S. and 1 mil of chloroform to 10 mils of an aqueous solution of the salt (1 in 20) and shake the mixture. The chloroform does not acquire a violet tint (*iodide*). Drop 1 mil of diluted sulphuric acid on about 1 Gm. of the powdered salt; no yellow color appears at once (*bromate*). Dissolve about 0.1 Gm. of Lithium Bromide in 5 mils of distilled water, add an excess of silver nitrate T.S. and a few drops of nitric acid; filter and wash the precipitate with distilled water, then digest it for ten minutes with 5 mils of ammonium carbonate T.S. and filter. On supersaturating the filtrate with nitric acid, not more than a slight turbidity is produced at once (*chloride*). Five mils of an aqueous solution of the salt (1 in 100) acidulated with 3 drops of hydrochloric acid shows no immediate turbidity with 1 mil of barium chloride T.S. (*sulphate*). Add 5 mils of hydrochloric acid and 5 mils of chlorine T.S. to 0.4 Gm. of Lithium Bromide contained in a flat-bottomed flask of 50 mils capacity, evaporate the mixture almost to dryness on a water bath, add 10 mils of amyl alcohol and cautiously heat the mixture until the lower aqueous layer has evaporated. Then add 3 drops of hydrochloric acid and boil the solution for three minutes; the resulting insoluble residue, if any, when collected on a filter, washed with amyl alcohol and dried at 110° C. (230° F.), weighs not more than 0.002 Gm. (*other alkalies*). The removal of water from the amyl alcohol mixture is facilitated by passing a current of air through the hot solution. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Introduce into a tared weighing-bottle about 0.35 Gm. of Lithium Bromide stopper, weigh accurately, and proceed as directed under the Assay for bromides (see Part III, Test No. 5). It shows not less than 85 per cent. of LiBr.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.008686 Gm. of LiBr. Each gramme of Lithium Bromide corresponds to not less than 97.9 mils of tenth-normal silver nitrate V.S." *U. S.*

Uses.—Lithium bromide was first brought into notice as a remedy by S. Weir Mitchell, who asserts that its action differs from that of the other bromides only in being more hypnotic. Although careful physiological studies of it are wanting, there is little reason for believing that it differs essentially from other bromides in its influence upon the human organism. It should be administered in dilute aqueous solution. Each drachm of it contains fifty-five grains of bromine, and it therefore exceeds potassium bromine in bromine strength.

Dose, ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Elixir Lithii Bromidi, *N. F.*; Syrupus Bromidorum, *N. F.*

LITHII CARBONAS. U. S., Br.

LITHIUM CARBONATE Lith. Carb.

(lĭth'ĭ-ī căr'bŏ-năs)

"It contains, when dried to constant weight at 100° C. (212° F.), not less than 98.5 per cent. of Li_2CO_3 (73.88). Preserve it in well-closed containers." *U. S.* "Lithium Carbonate may be obtained from native silicates of lithium. It contains not less than 98.5 per cent. of pure lithium carbonate, Li_2CO_3." *Br.*

Carbonas Lithicus; Carbonate of Lithia; Carbonate de Lithine, *Fr. Cod.*; Carbonate lithique, *Fr.*; Lithium Carbonicum, *P. G.*; Lithiumcarbonat, Kohlensaures Lithium, *G.*; Carbonato di litio, *It.*; Carbonato de litina o litico, *Sp.*

The alkali *lithia*, so far as has yet been ascertained, is rare in nature, for, though extensively diffused, exists in very small proportion, except in a few scarce minerals. It was discovered by Arfvedson in 1817, in certain minerals from the iron mines of Utö, as *petalite, triphane,* and a variety of *tourmaline.* (Berzelius.) It has since been found in other minerals, as *lepidolite, spodumene, amblygonite,* etc., and in numerous mineral waters, as those of Carlsbad, Salsomaggiore, Pyrmont, Kissingen, Kreuzmach, Aix-la-Chapelle, Vichy, etc., in Europe, and the Gettysburg spring in the United States, in which it exists generally as a carbonate or a bicarbonate. By spectrum analysis it has been detected in the waters of the Atlantic Ocean and of the

Thames, the Delaware, the Potomac and many other rivers; in the ashes of plants grown on a granite soil, and even in milk and human blood. In the mother waters of tartaric acid, in the factories, it has been found in a proportion to justify extraction. It was at one time largely obtained from a *phosphatic triphyline* found in Bavaria, in which it existed as a phosphate, but this source is said to have been exhausted. There are several methods of extracting lithia from the minerals containing it, an account of which may be seen in *Roscoe and Schorlemmer,* vol. ii, Part I, page 158. They contain the alkali in various proportions, from 4.5 per cent. in lepidolite to 11 per cent. in amblygonite. Lithium carbonate is prepared from lepidolite in the following manner. Ten parts of finely powdered lepidolite, 10 parts of barium carbonate, 5 parts of barium sulphate, and 3 parts of potassium sulphate are fused at a very high temperature in a wind furnace. The heavy barium silicate and sulphate sink to the bottom, and a layer of potassium and lithium sulphates is found at the top of the fused mass. These can be extracted by simple lixiviation, and then the carbonate prepared by double decomposition with ammonium carbonate.

In another process the lepidolite is digested with hot sulphuric acid which produces the sulphates of aluminum and lithium principally, and these are separated by crystallization or precipitation operations.

Lithia, Li_2O, is the oxide of the metal lithium, and ranks in chemical properties with the fixed alkalies. In the form of hydroxide, LiOH, it is white and translucent; does not deliquesce in the air, but absorbs carbon dioxide, and becomes opaque; is fusible below ignition, but not volatilizable at a white heat; is soluble in water, but less so than potassium or sodium hydroxides; is sparingly soluble in alcohol, and in solution has an acrid alkaline taste, caustic properties, and a strong alkaline reaction. The salts of lithium are generally freely soluble, with the exception of the neutral carbonate and phosphate, the latter of which is nearly insoluble. *Lithium,* which was first obtained by Bunsen and Matthiessen, in 1855, is silver-white, brilliant, softer than lead, ductile, capable of welding, and the lightest known solid. Its sp. gr. is 0.594, melting point 180° C. (356° F.), atomic weight 6.94, and symbol Li. For a method of making lithium for scientific demonstration on the small scale by electrolysis, see *Ph. Rev.,* 1899, 264.

Lithium carbonate may be prepared directly from one of the lithia minerals, in the manner already described, or from lithium sulphate or chloride in concentrated solution by adding ammonium carbonate. The precipitated salt should be washed with alcohol and dried.

Properties.—It is "a light, white powder, odorless, and having an alkaline taste; permanent in the air. One Gm. of Lithium Carbonate dissolves in 78 mils of water at 25° C. (77° F.); also in 140 mils of boiling water; almost insoluble in alcohol; dissolved by diluted acids with effervescence. At a low red heat the salt fuses; at a higher temperature it loses some of its carbon dioxide, and is partially converted into lithium oxide. It imparts a crimson color to a non-luminous flame. A saturated aqueous solution of the salt is alkaline to litmus. Lithium Carbonate, when dissolved in 40 parts of diluted acetic acid, leaves not more than 0.15 per cent. of insoluble residue. Mix 1 part of Lithium Carbonate with 20 parts of distilled water and add hydrochloric acid, drop by drop, with agitation until solution takes place. The resulting solution, after boiling and cooling, responds to the following tests when applied to separate portions: The addition of ammonia water to 5 mils of this solution until it has an alkaline reaction produces neither turbidity nor precipitation either before or after boiling (*iron, aluminum*). Dilute another portion of 4 mils of this solution with 6 mils of distilled water; it does not respond to the Test for heavy metals (see Part III, Test No. 3). Add a slight excess of diluted hydrochloric acid to 0.2 Gm. of Lithium Carbonate contained in a flat-bottomed flask of 50 mils capacity, evaporate the mixture almost to dryness on a water bath, add 10 mils of amyl alcohol and cautiously heat the mixture until the lower aqueous layer has evaporated. Then add 3 drops of hydrochloric acid and boil the solution for three minutes. The resulting insoluble residue, if any, when collected on a filter, washed with amyl alcohol and dried at 110° C. (230° F.), weighs not more than 0.002 Gm. (*other alkalies*). The removal of the water from the amyl alcohol mixture is facilitated by passing a current of air through the hot solution.

"**Assay.**—Dissolve about 1.5 Gm. of Lithium Carbonate, previously dried to constant weight at 100° C. (212° F.) and accurately weighed, in 50 mils of normal sulphuric acid V.S. and titrate the solution with normal potassium hydroxide V.S., methyl orange T.S. being used as indicator. It shows, in the dried salt, not less than 98.5 per cent. of Li_2CO_3.

"Each mil of normal sulphuric acid V.S. used corresponds to 0.03694 Gm. of Li_2CO_3. Each gramme of Lithium Carbonate, previously dried, corresponds to not less than 26.7 mils of normal sulphuric acid V.S." *U. S.*

"White powder, or minute crystalline grains. Taste slightly alkaline. Soluble in 80 parts of *water;* insoluble in *alcohol* (90 per cent.). Aqueous solution alkaline to *litmus.* Soluble with effervescence in *hydrochloric acid;* the solution evaporated to dryness leaves a residue which communicates a crimson color to flame, and, redissolved in *water,* yields a precipitate with *solution of sodium phosphate.* 1 gramme, diffused in about 50 millilitres of *water,* requires for neutralisation not less than 26.6 or more than 27.1 millilitres of *N/1 solution of sulphuric acid, solution of methyl orange* being used as indicator. Yields no character-

istic *reactions* for copper, iron, aluminium, zinc, magnesium, or chlorides, and not more than the slightest *reactions* for calcium or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

F. A. Flückiger states that lithium carbonate is less soluble in warm water than in cold water. He recommends as a test of purity that it should require for solution 70 parts or a little more of water at 15° C. (59° F.), and states further that its solution saturated at 90° C. (194° F.) has the sp. gr. 1.009 at 15° C. (59° F.); this latter solution contains 1 part of the salt in 111.3 parts of water. (*A Pharm.*, 1887, p. 509.)

Effervescing Lithium Carbonate may be made as follows: Take of citric acid, 40 parts, sodium bicarbonate, 50 parts, and lithium carbonate, 10 parts. Powder and mix well, then introduce into a wide flat-bottomed dish, and heat to about 100° C. (212° F.), stirring constantly until the powder becomes granular. Separate the granules of uniform size by means of appropriate sieves, and preserve them in well-stoppered bottles. (See *Lithii Citras Effervescens.*)

Uses.—In 1843 Alexander Uré called attention to the fact that uric acid was comparatively freely soluble in solutions of lithium carbonate. This observation was confirmed by Garrod in 1857 who recommended the use of the metal in both acute and chronic forms of gout. This recommendation has been blindly followed by a large proportion of the medical profession for more than fifty years without questioning the validity of the scientific basis and without any close analysis of the clinical results. Garrod's experiment, however, as pointed out by H. C. Wood, Jr. (*J. A. M. A.*, 1916, lxvi, p. 1069), involved conditions which are absolutely inapplicable to human medicine; as a matter of fact it has been shown that the addition of lithium carbonate even in fatally large doses does not affect the solubility of sodium urate in the blood. Moreover there is no convincing clinical evidence of the usefulness of lithia in *gout*.

The clinical results which have been achieved with the "Lithia Waters" have been due to the water in them and not to the lithium. It has been shown by the Bureau of Chemistry of the U. S. Department of Agriculture, none of the natural lithia waters contain more than one-twentieth grain per gallon, while most of them contain only spectroscopic traces.

In sufficient quantities lithium acts upon the system very much like potassium, being depressant to the nerve centers and to the circulation. The non-toxic salts of lithium, like those of potassium, have a diuretic effect, and if given in sufficient dose may aid in the elimination of various substances from the blood, and incidentally the poisons of *gout*, but are probably not superior to the potash salts. Lithium carbonate has the properties of the other earthy carbonates but, being less soluble than the sodium and potassium salts, is perhaps somewhat less prone to irritate the stomach.

Dose, five to fifteen grains (0.32–1.0 Gm.).

Off. Prep.—Elixir Formatum Compositum, *N. F.;* Sal Potassii Bromidi Effervescens Compositus, *N. F.*

LITHII CITRAS. U. S., Br.

LITHIUM CITRATE Lith. Cit.

(lĭth'ĭ-ī cī'trăs)

"It contains not less than 98.5 per cent. of $Li_3C_6H_5O_7 + 4H_2O$ (281.92). Preserve it in air-tight containers." *U. S.* "Lithium Citrate may be obtained by the interaction of citric acid and lithium carbonate. It contains not less than 98.5 per cent. of pure lithium citrate, $Li_3C_6H_5O_7,4H_2O$." *Br.*

Lithiæ Citras, Lithium Citricum; Citrate of Lithium, Citrate of Lithia; Citrate de Lithine, *Fr. Cod.;* Citronensaures Lithium, Lithiumcitrat, *G.*

Neither of the Pharmacopœias gives at present a process for this salt; the U. S. Pharmacopœia process of 1870 was as follows: "Take of Carbonate of Lithium, *one hundred grains;* Citric Acid, in crystals, *two hundred grains;* Distilled Water, *two fluidounces.* Dissolve the Citric Acid in the water gently heated, and to the solution gradually add the Carbonate of Lithium until perfectly dissolved, heating the solution so long as effervescence is produced. Evaporate, by means of a steam- or sand-bath, to a viscid consistence, dry the residue in an oven, at a temperature of about 240° C. (464° F.), then rapidly pulverize it, and preserve the powder in a well-stoppered bottle." *U. S.*, 1870.

Properties.—Lithium citrate is in the form of "a white powder, or in the granular form, odorless, and having a cooling, faintly alkaline taste. It is deliquescent on exposure to moist air and loses its water of crystallization when heated to 150° C. (302° F.). One Gm. of Lithium Citrate dissolves in 1.4 mils of water at 25° C. (77° F.); very slightly soluble in alcohol. An aqueous solution of the salt (1 in 20) is faintly alkaline to litmus but is not reddened by one drop of phenolphthalein T.S. At a red heat the salt chars, emits inflammable vapors having a pungent odor, and finally leaves a black residue of lithium carbonate mixed with carbon. It imparts a crimson color to a non-luminous flame. Boil an aqueous solution of Lithium Citrate (1 in 20) with an equal volume of calcium chloride T.S.; a white precipitate forms. Treat the residue obtained by igniting 0.4 Gm. of the salt at a red heat with a slight excess of diluted hydrochloric acid, filter, wash the residue with distilled water, evaporate the filtrate and washings almost to dryness on a water bath, in a flat-bottomed flask of 50 mils capacity, add 10 mils of amyl alcohol and cautiously heat the

mixture until the lower aqueous layer has evaporated. Then add 3 drops of hydrochloric acid and boil the solution for three minutes. The resulting insoluble residue, if any, when collected on a filter, washed with amyl alcohol and dried at 110° C. (230° F.), weighs not more than 0.004 Gm. (*other alkalies*). The removal of the water from the amyl alcohol mixture is facilitated by passing a current of air through the hot solution. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Proceed as directed under the Assay for alkali salts of organic acids (see Part III, Test No. 6). It shows not less than 98.5 per cent. of $Li_3C_6H_5O_7 + 4H_2O$.

"Each mil of half-normal sulphuric acid V.S. used corresponds to 0.04699 Gm. of $Li_3C_6H_5O_7 + 4H_2O$. Each gramme of Lithium Citrate corresponds to not less than 21 mils of half-normal sulphuric acid V.S." *U. S.*

"Small white crystals. Taste saline, cooling. Soluble in 2 parts of *water*. Yields the *reactions* characteristic of citrates. Heated to redness it blackens, evolving inflammable gases; and the residue, neutralised with *hydrochloric acid*, yields with *alcohol* (90 per cent.) a solution which burns with a crimson flame. 1 gramme, heated to redness till gases cease to be evolved, leaves an alkaline residue which, when treated with *water*, filtered, and well washed, yields a clear solution requiring for neutralisation not less than 10.5 millilitres of *N/1 solution of sulphuric acid*. *Lead limit* 5 parts per million. *Arsenic limit* 2 parts per million. Free from the impurities indicated under 'Lithii Carbonas.'" *Br.*

Uses.—Lithium citrate, like the corresponding salts of sodium and potassium, is oxidized in the system and appears in the urine as a carbonate. It may be used for precisely the same purposes as the other citrates (see page 897), but has no real advantage. It is the compound which is employed in making the widely used so-called "lithia tablets."

Dose, from ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Lithii Citras Effervescens, *Br.;* Elixir Lithii Citratis, *N. F.;* Sal Lithii Citras Effervescens, *N. F.;* Sal Vichyanum Factitium Effervescens cum Lithio, *N. F.*

LITHII CITRAS EFFERVESCENS. Br.

EFFERVESCENT LITHIUM CITRATE

(lĭth'ĭ-ī cī'trăs ĕf-fẹr-vĕs'cẹns)

Sal Lithii Citratis Effervescens, *N. F.;* Effervescent Salt of Lithium Citrate; Limonade séche au Citrate de Lithine, *Fr.;* Brauselithiumcitrat, *G.*

This effervescent salt was dropped from the U. S. P. IX, but was introduced into the N. F. IV. (See Part III.)

"Sodium Bicarbonate, in powder, 580 *grammes;* Tartaric Acid, in powder, 310 *grammes;* Citric Acid, in powder, 210 *grammes;* Lithium Citrate, in powder, 50 *grammes*. Mix the Lithium Citrate with the Citric Acid, then add the Tartaric Acid, and, lastly, the Sodium Bicarbonate, triturating thoroughly. Place the mixture in a dish or pan of suitable form heated to between 90° and 105° C. (194° and 221° F.). When the mixture, by the aid of careful manipulation, has assumed a granular character, separate it, by means of suitable sieves, into granules of uniform and convenient size. Dry the granules at a temperature not exceeding 55° C. (131° F.). The product weighs about one thousand *grammes*." *Br.*

Uses.—This effervescent salt forms an agreeable method of administering lithia; its medicinal properties are those of lithium citrate.

Dose, two drachms (7.7 Gm.), given in solution.

LOBELIA. U. S., Br.

LOBELIA Lobel.

(lọ-bē'lĭ-ą)

"The dried leaves and flowering tops of *Lobelia inflata* Linné (Fam. *Lobeliaceæ*), without the presence or admixture of more than 10 per cent. of stems or other foreign matter." *U. S.* "Lobelia is the dried flowering herb of Lobelia inflata, *Linn.*" *Br.*

Indian or Wild Tobacco, Asthma-weed, Puke-weed, Gagroot, Vomitwort, Bladder Pod, Eyebright; Lobélie enflée, *Fr. Cod.;* Herba Lobeliæ, *P. G.;* Lobelienkraut, *G.;* Lobelia, *It.*

Lobelia inflata, often called *Indian tobacco*, is an annual or biennial indigenous plant, usually a foot or more in height, with a fibrous root, and a solitary, erect, angular, very hairy stem, much branched about midway, but rising considerably above the summits of the highest branches. The leaves are scattered, or alternate, petiolate, the upper sessile, ovate, or oblong, about two inches (5 cm.) long, irregularly toothed, pubescent, pale green. The flowers are numerous, small, disposed in leafy terminal racemes, and upon short axillary footstalks. The calyx is five-toothed and much inflated in fruit. The corolla, which is of a delicate blue, has a labiate border, with the upper lip divided into two, the lower into three segments. The united anthers are curved, and enclose the stigma. The fruit is an oval, striated, inflated capsule, crowned with the persistent calyx, and containing, in two cells, numerous very small, oblong, reticulated brown seeds.

Lobelia inflata is a very common weed, growing in the roadsides and in neglected fields throughout the Eastern United States and Canada. Its flowers begin to appear towards the end of July, and continue to expand in succession until the occurrence of frost. All parts of it are medicinal, but, according to Eberle, the root and inflated capsules are most powerful. The plant should be collected in August

or September, when the capsules are numerous, and should be carefully dried. It may be kept whole or in powder. As found in commerce, it is often in oblong compressed cakes, prepared by the Shakers or the herb dealers. Lobelia is grown regularly in the testing gardens of the Bureau of Plant Industry of the U. S. Department of Agriculture. It has been suggested that in cultivating *Lobelia inflata* the seeds should be planted in the autumn. (*Ann. Rep. U. S. Dept. Agric.*, 1905, p. 147.)

Properties.—Dried lobelia has a slightly irritating odor, and when chewed, though at first without much taste, soon produces a burning acrid impression upon the posterior parts of the tongue and palate, very closely resembling that occasioned by tobacco, and attended in like manner with a flow of saliva and a nauseating effect. "Stems cylindrical, coarsely and irregularly furrowed, yellowish-green, occasionally purplish and with numerous spreading hairs; leaves alternate, sessile or narrowing into a short petiole, usually more or less broken; when entire, laminæ ovate or oblong, from 2 to 9 cm. in length, obtusely toothed or irregularly serrate-denticulate, each tooth with a yellowish-brown, gland-like apex; pale green and with scattered, bristly hairs; flowers blue in long, loose racemes with short pedicels, calyx tube ovoid, with 5 subulate teeth, corolla tubular, from 3 to 4 mm. in length, 5-parted, the upper 2-lobed portion cleft nearly to the base; stamens with anthers united above into a curved tube enclosing the bifid stigmas; capsules ovoid or ellipsoidal, from 5 to 8 mm. in length, light brown, wholly inferior and enclosing numerous brownish, oblong and coarsely reticulate seeds; odor slight, taste strongly acrid. The powder is dark green, odor irritating; fragments of seed-coat composed of more or less polygonal cells with thick, yellowish walls; occasionally, non-glandular hairs elongated-conical, from 0.3 to 0.6 mm. in length; fragments of stem with tracheæ showing annular or spiral thickenings or simple pores associated with narrow wood-fibers, the walls of the latter being rather thin, more or less lignified and porous; fragments of epidermis of leaf with elliptical stomata, 0.025 mm. in length, and usually with 3 or 4 neighboring cells; pollen grains nearly spherical, from 0.015 to 0.03 mm. in diameter. Lobelia yields not more than 8 per cent. of ash." *U. S.*

"Stems angular, channelled, and furnished with narrow wings; often of a purplish tint; bearing one-celled hairs and the scars of alternate leaves. Leaves irregularly toothed and hairy. Capsules inflated, two-celled, containing, when ripe, minute, oblong, reticulated, brown seeds. In transverse section of the stem, laticiferous vessels in the bast. Somewhat irritating odor; taste at first not marked, but subsequently burning and acrid. Ash not more than 12 per cent." *Br.*

The morphology of *Lobelia inflata* is described and illustrated by Holm in *Merck's Rep.*, xvi, p. 341. The German Pharmacopœia directs that Lobelia should be gathered at the end of the flowering period. A number of the foreign Pharmacopœias do not permit the inclusion of the fruit. The drug of commerce ofttimes is collected late in the season after most of the leaves have fallen and the plant has gone to seed. At times the commercial drug consists of the entire herb, and again may consist entirely of the thick and inert stems.

The activity of lobelia is dependent upon the presence of a liquid alkaloid first isolated by Procter in 1838 and by him named *lobeline.* He obtained it by the following process:

The seeds were treated with alcohol acidulated with acetic acid, until deprived of acrimony, and the tincture was evaporated; the resulting extract was triturated with magnesia and water, and, after repeated agitation for several hours, the liquor, holding lobeline in solution, was filtered; this was then shaken repeatedly with ether until no longer acrid, and the ethereal solution, having been decanted, was allowed to evaporate spontaneously. The residue which was reddish-brown and of the consistence of honey, was deprived of coloring matter by dissolving it in water, adding a slight excess of sulphuric acid, boiling with animal charcoal, saturating with magnesia, filtering, agitating with ether until this fluid had deprived the water of acrimony, and finally decanting and allowing the ether to evaporate. Thus obtained, *lobeline* is a yellowish liquid, lighter than water, of a somewhat aromatic odor, and a very persistent, acrid taste. It is soluble in water, but much more copiously in alcohol and ether, and the latter fluid readily removes it from its aqueous solution. It has an alkaline reaction, and forms soluble and crystallizable salts with sulphuric, nitric, and hydrochloric acids, and a very soluble but not crystallizable salt with acetic acid. It forms an insoluble compound with tannic acid, which instantly precipitates it from its solution. By a boiling heat it is entirely decomposed, losing all its acridity, but when combined with acids it may be subjected to ebullition with water without change. (*A. J. P.*, ix, 105, xiii, 1; see also a paper by W. D. Richardson, Jr., *A. J. P.*, 1872, p. 293.) Siebert, from a study of the crystallized hydrochloride and chloroplatinate, derived the formula $C_{15}H_{23}O_2N$ for the free alkaloid.

Pereira found a peculiar acid which he named *lobelic acid;* besides gum, resin, chlorophyl, fixed oil, lignin, salts of lime and potassium, with ferric oxide. Enders separated an acrid substance which he called *lobelacrin* (*Pharmacographia* 2d edition, 400), but Lewis (*P. J.*, 1878, viii) considers lobelacrin as a mixture of lobeline lobelate, with lobelic acid. Lloyd has isolated a crystalline neutral principle (*Ph. Rund.*, 1887, 32) which melts at 225° C. (437° F.), to which he gave the name *inflatin.* It does not appear to have any therapeutic value. Ac-

cording to Procter the seeds contain a much higher percentage of lobeline than the rest of the plant; from the whole plant he obtained a yield of one-fifth of one per cent. The alkaloid appears to be a rather unstable body, being decomposed by boiling temperature as well as by the caustic alkalies.

Vanderkleed and E'we (*Proc. P. P. A.*, 1916, p. 276) propose a method for assaying this drug and its preparations.

Uses.—Lobelia is said to have been used as a medicine by the aborigines of America, but was first brought into general professional notice by Cutler, of Massachusetts. The leaves or capsules, chewed for a short time, occasion giddiness, headache, general tremors, and ultimately nausea and vomiting. When swallowed in the full dose, the medicine produces speedy and severe vomiting, attended with continued and distressing nausea, copious sweating, and great general relaxation. When toxic doses are taken, these symptoms are very severe, and have added to them burning pain in the fauces or œsophagus, progressive failure of voluntary motion, rapid, feeble pulse, fall of temperature, and finally collapse with stupor or coma; in some cases convulsions precede death. Death has often resulted from its empirical use. Its poisonous effects are most likely to occur when, as sometimes happens, it is not rejected by vomiting.

In large quantities lobelia has a paralyzant effect on the peripheral motor nerves like that of curare, but this action plays little rôle in its therapeutic usefulness. As has been shown by Edmunds (*A. J. Phys.*, 1904, xi, p. 80), it acts upon the sympathetic ganglia like nicotine, first stimulating and secondarily depressing. During the primary stage of stimulation there is increased flow of saliva, dilatation of the pupil, constriction of the blood vessels, slowing of the pulse, and other evidences of sympathetic excitation. The slowing of the pulse at first more than counterbalances the vascular constriction, and the blood pressure is usually lowered; later, however, the pulse becomes very rapid and the blood pressure high. The vomiting appears to be due to an action upon the emetic center. In the secondary stage of poisoning the pupil is contracted, salivary secretion checked, respirations slow, and the blood pressure falls. According to Muto and Iwakawa (*A. E. P. P.*, 1910, lxii), lobeline is a primary stimulant to the respiratory center, the failure in respiration which occurs after toxic doses being due to its paralytic effect on the phrenic nerve. According to Dixon and Brodie (*J. P.* 1903, xxix), it causes a relaxation of the bronchial muscles which may, however, be preceded by a short stage of constriction.

As an emetic lobelia should never be employed. Its most important use in medicine is as a nauseating expectorant in *bronchitis*, especially when associated with bronchial spasm. Large doses will sometimes cause complete cessation of the *asthmatic* paroxysms, but it is more commonly employed between the paroxysms for its combined expectorant and antispasmodic influence.

By the eclectics lobelia is used in a host of convulsive and inflammatory disorders, including *epilepsy, tetanus, diphtheria,* and *tonsillitis.*

The tincture affords the most eligible mode of administration; in asthmatic cases it may be given in doses of fifteen minims (0.9 mil) every hour until an effect is produced. The fluidextract and the tincture are official. The process for the vinegar, which was dropped by the U. S. Pharmacopœia of 1890, will be found in the U. S. Dispensatory, 19th edition, p. 749. Nunes (*T. G.*, 1889) asserts that he has used lobeline in a number of cases of *asthma* with most excellent results in doses of from three-fourths of a grain to six grains a day; but it can scarcely be doubted that he had a very impure alkaloid, and that such doses of a pure sample would be highly dangerous.

Dose, antispasmodic, two to eight grains (0.12–0.5 Gm.).

Off. Prep.—Fluidextractum Lobeliæ, *U. S.;* Tinctura Lobeliæ, *U. S.;* Tinctura Lobeliæ Ætherea, *Br.*

LOTIO HYDRARGYRI FLAVA. Br.

YELLOW MERCURIAL LOTION

(lō'tĭ-ō hȳ-drär'gy-rī flā'va)

Lotio Flava, *N. F.;* Aqua Phagedænica Flava; Yellow Wash, Yellow Lotion; Eau phagédénique, *Fr. Cod.;* Eau divine de Fernel, Phagédénique, *Fr.;* Phagedänisches Wasser, Altschadenwasser, *G.*

"Mercuric Chloride, 4.6 *grammes;* Solution of Lime, 1000.0 *millilitres.* Mix." *Br.*

This lotion is about 11 per cent. stronger than that official in the Br. Ph., 1885. This preparation is official in the N. F. IV. (See Part III.)

The reaction between the mercuric chloride and the calcium hydroxide in this preparation results in the precipitation of the yellow mercuric oxide in a very finely divided condition. It is used as a soothing and antiseptic application in *scrofulous* or *syphilitic ulcers;* it has been especially recommended in scrofulous *conjunctivitis.*

LOTIO HYDRARGYRI NIGRA. Br.

BLACK MERCURIAL LOTION

(lō'tĭ-ō hȳ-drär'gy-rī nī'gra)

Lotio Nigra, *N. F.;* Aqua Phagedænica Nigra; Aqua Nigra, Aqua Mercurialis Nigra; Black Wash, Black Lotion; Eau Phagédénique noire, *Fr.;* Schwarzes Wasser, *G.*

"Mercurous Chloride, 6.85 *grammes;* Glycerin, 50.00 *millilitres;* Solution of Lime, sufficient to produce 1000.00 *millilitres.* Triturate the Mercurous Chloride with the Glycerin and gradually add sufficient Solution of Lime to produce the required volume." *Br.*

The addition of glycerin improves this lotion by aiding in the suspension of the insoluble powder. By the reaction between the calomel and calcium is formed the black mercurous oxide. This lotion has medical properties very similar to those of the yellow wash. It has also been recommended by Shoemaker in *ivy poisoning.* This preparation is official in the N. F. IV. (See Part III.)

LOTIONES

LOTIONS

(lō-tĭ-ō'nēṣ)

Washes; Lotions, *Fr.;* Waschungen, *G.*

This class has been introduced into the British Pharmacopœia in order to give official recognition to two preparations, the *black wash* or *lotio nigra,* and the *yellow wash,* or *lotio flava,* which have long been in use, and which will be found above.

LYCOPODIUM. U. S.

LYCOPODIUM Lycopod.

(lĭ-cŏ-pō'dĭ-ŭm)

"The spores of *Lycopodium clavatum* Linné (Fam. *Lycopodiaceæ*), without the presence or admixture of more than 2 per cent. of impurities." *U. S.*

Club Moss, Stag's horn, Semen Lycopodii, Pulvis Lycopodii, Sulphur Vegetabile; Vegetable Sulphur; Lycopede, *Fr. Cod.;* Soufre végétal, *Fr.;* Lycopodium, *P. G.;* Bärlappsamen, Streupulver, Hexenmehl, Blitzpulver, *G.;* Licopodio, *It., Sp.*

Lycopodium clavatum, commonly called *club moss,* has a trailing, branching stem, several feet long, and thickly beset with linear-awl-shaped, flat, ribless, smooth leaves, tipped with a fine bristle, curved upward, and of a light green color. The fructification is in terminal spikes, single or in pairs, with crowded ovate, entire, pointed scales, bearing in the axil a transversely oval sporangia which splits nearly to the base and contains the narrow reticulate spores. The plant is a native of Europe, Asia, and America, being especially common in the dry woods northward.

The spores are collected in Switzerland and Germany. Lycopodium is "a light yellow, very mobile powder, nearly inodorous and tasteless. It is not wetted by water but floats upon it; when boiled with water it sinks; when thrown into a flame it burns with a quick flash. Under the microscope, the spores of Lycopodium are spherical tetrahedrons, from 0.025 to 0.04 mm. in diameter; in section they vary from plano-convex to triangular, the outer wall or exosporium being extended in the form of slight irregular projections, giving the surface of the spore a reticulate appearance, the reticulations being polygonal and formed of straight sides; when viewed so that the rounded surface of the spores is on the under side, the upper surface is characterized by a distinct, triangular marking, being the edges of the three straight surfaces, extending from the center of the spores to near the outer edge. Lycopodium shows very few, if any, pollen grains of species of Pine, the latter being from 0.04 to 0.07 mm. in diameter, and consisting of three parts, in which a central, convex, generative cell separates the two spherical cells or wings which are blackish, due to the inclusion of air. Lycopodium yields not more than 3 per cent. of ash." *U. S.*

Flückiger by thoroughly comminuting the spores of lycopodium with sand, obtained 47 per cent. of a bland oil of bright yellow color and sp. gr. 0.925, which does not congeal even at –15° C. (5° F.). A. Barkowski obtained from the spores of Lycopodium 48.5 per cent. of a neutral non-drying oil, very similar to almond oil. This oil contains 2 per cent. of a fatty acid called *lycopodic acid* ($C_{18}H_{36}O_4$), 80 per cent. of oleic acid, a minute quantity of a vegetable cholesterin similar to that obtained by Hesse from Calabar beans, 8.2 per cent. of glycerin and 3 per cent. of arachidic, palmitic and stearic acids. The lycopodic acid crystallizes in silky needles, it is doubly refracting like quartz, and appears to be isomeric with dioxystearic acid. (*D. C.,* 1891, 155; see also *A. Pharm.,* 1908, 246.) Stenhouse found volatile bases to be present in very small amount. The ash amounts to 4 per cent. It contains alumina and 1 per cent. of phosphoric acid, and is not alkaline. (*Pharmacographia,* 2d ed., 732.) Lycopodium is sometimes admixed with pine pollen which is probably to be looked upon as an accidental contamination. In the same way, it may contain small quantities of talcum and starch. It is sometimes adulterated with a resinous compound made from rosin, ferruginous earths, shellac, sulphur, turmeric, talcum, dextrin or the cereal starches.

In Nashville, Tenn., a specimen came into the possession of Benj. Lillard which was found to contain one-half of its bulk of dextrin. (*Ch. Ph.,* Sept., 1873.) Folleto recommends two reactions to detect pollen: one by adding to a syrupy solution of zinc chloride, potassium iodide and iodine to saturation; the pollen is colored yellow by this reagent, lycopodium is not colored; the other reagent is methyl-green, which colors pollen green, but does not color lycopodium. (*Ph. Centralh.,* 1896, 527.)

Uses.—Lycopodium is used as an absorbent application to *excoriated surfaces,* especially those which occur in the folds of the skin in infants. In pharmacy it answers the purpose of facilitating the rolling of the pilular mass, and of preventing the adhesion of the pills when formed. The moss itself has been esteemed diuretic and antispasmodic; its decoction has been employed in *rheumatism, diseases of the lungs and kidneys,* and in the removal of *plica Polonica,* but it has fallen into complete desuetude. One of the ingenious uses for lycopodium in microscopy is to mix a little of it with an unknown powder or on a slide on which a mount is made. The spores are easily recognizable and

distinguishable from other elements and give an excellent idea of the approximate size of the elements which are being observed, as the spores are almost uniformly 40 microns in size.

MAGMA BISMUTHI. U.S.

BISMUTH MAGMA Magma Bism. [Milk of Bismuth]

(măg'mą bĭz-mū'thī)

"Bismuth Magma yields not less than 5.6 per cent. nor more than 6.2 per cent. of Bi_2O_3.

* "Bismuth Subnitrate, *eighty grammes* [or 2 ounces av., 360 grains]; Nitric Acid, *one hundred and twenty mils* [or 4 fluidounces, 28 minims]; Ammonium Carbonate, *ten grammes* [or 154 grains]; Ammonia Water, Distilled Water, each, *a sufficient quantity* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the bismuth subnitrate with *sixty mils* [or 2 fluidounces, 14 minims] of distilled water and *sixty mils* [or 2 fluidounces, 14 minims] of nitric acid in a flask and agitate, warming gently until solution is effected. Pour this solution, with constant stirring, into *five thousand mils* [or 169 fluidounces, 33 minims] of distilled water containing *sixty mils* [or 2 fluidounces, 14 minims] of nitric acid. Dilute *four hundred and eighty mils* [or 16 fluidounces, 111 minims] of ammonia water with *four thousand mils* [or 135 fluidounces, 122 minims] of distilled water in a glazed or glass vessel of at least *twelve thousand mils* [or 405 fluidounces, 367 minims] capacity. Dissolve the ammonium carbonate in this solution and then quickly pour the bismuth solution into it with constant stirring. If the mixture is not distinctly alkaline, add sufficient ammonia water to make it so and allow it to stand until the precipitate has subsided, then pour or siphon off the supernatant liquid and wash the precipitate twice with distilled water, by decantation. Afterwards transfer the magma to a strainer of close texture, arranged in a percolator so as to provide continuous washing with distilled water, the outlet tube being elevated to prevent the surface of the magma from becoming dry, and allow the operation to proceed until the washings cease to react with phenolphthalein T.S. Then drain the moist magma, transfer it to a graduated vessel and add sufficient distilled water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly, transfer to bottles and stopper tightly." *U. S.*

It is officially described as "a thick, white, opaque liquid containing bismuth hydroxide and bismuth subcarbonate in suspension in water. It is neutral to litmus and phenolphthalein. One mil of hydrochloric acid added to 1 mil of Bismuth Magma produces a clear solution. Pour the clear solution into 10 volumes of distilled water; a white precipitate is produced.

"**Assay.**—Evaporate to dryness about 10 Gm. of Bismuth Magma, accurately weighed, and ignite the residue to constant weight; the residue corresponds to not less than 5.6 per cent. nor more than 6.2 per cent. of the weight of Bismuth Magma taken." *U. S.*

This preparation was introduced into the U. S. P. IX with a view of affording a liquid preparation which may be used in some cases to replace the powdered form of bismuth salt.

A modified formula has been suggested by S. Bertha Müller (*A. J. P.*, 1914, ii), in which 50 grammes of bismuth subnitrate are dissolved in 50 grammes of nitric acid which has previously been diluted with an equal volume of water; the solution is then made up to a volume of 300 mils by adding water, and it is then filtered through cotton. Eighty grammes of ammonium carbonate are dissolved in 3000 mils of distilled water containing 3 grammes of sodium chloride. The acid solution of bismuth nitrate is then poured into the alkaline solution with constant stirring, the resulting precipitate is washed thoroughly by decantation, using a 1-1000 sodium chloride solution. Finally it is allowed to settle to 1000 mils.

Uses.—This new preparation of bismuth affords a convenient form for exhibiting this metal, especially to infants. Hulse (*J. A. M. A.*, 1910, lxv, p. 236) finds, however, that this type of preparation does not produce as satisfactory therapeutic results in children as the powdered bismuth subnitrate. It is used in various forms of *diarrhea*, especially in the so-called *summer complaint*.

The *dose* for an adult is one to four fluidrachms (3.9–15.0 mils), equivalent to, approximately, four to sixteen grains (0.25–1.0 Gm.) of bismuth subcarbonate.

MAGMA MAGNESIÆ. U. S.

MAGNESIA MAGMA Magma Mag. [Milk of Magnesia]

(măg'mą măg-nē'shĭ-æ)

"Magnesia Magma yields not less than 6.5 per cent. nor more than 7.5 per cent. of $Mg(OH)_2$ (58.34)." *U. S.*

* "Magnesium Carbonate, in fine powder, *one hundred and twenty-five grammes* [or 4 ounces av., 179 grains]; Sodium Hydroxide, *eighty grammes* [or 2 ounces av., 360 grains]; Distilled Water, *a sufficient quantity* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the magnesium carbonate with enough distilled water (about *five hundred mils* [or 16 fluidounces, 435 minims]) and make a smooth mixture. Dissolve the sodium hydroxide in *four hundred mils* [or 13 fluidounces, 252 minims] of distilled water, add the solution to the magnesia mixture with constant stirring, and agitate it frequently during fifteen minutes. Wash the resulting magma by decantation, using *two thousand mils* [or 67 fluidounces, 301 minims] of distilled water each time, until the red color produced in 50 mils of the washings by 3 drops of phenolphthalein T.S. is discharged by the addition of 1 drop of diluted sulphuric acid. Then allow the precipitate to subside until it measures *one thousand mils* [or 33 fluidounces, 6½ fluidrachms], decant the

supernatant liquid, transfer the product to wide-mouthed bottles, and tightly stopper with corks which have been dipped in melted paraffin. NOTE.—The distilled water in this preparation may be replaced by water which has been heated to boiling with powdered magnesium carbonate (5 Gm. in each 1000 mils) and then filtered. One-half mil of oil of peppermint, or a sufficient quantity of oil of anise or other suitable flavoring may be added if desired." *U. S.*

This preparation was introduced into the U. S. P. IX for the first time. The N. F. III magma was made by the interaction of magnesium sulphate and sodium hydroxide in water.

It is officially described as "a thick, white liquid containing magnesium hydroxide in suspension in water. It is alkaline to litmus and phenolphthalein. The addition of 2 mils of diluted hydrochloric acid to 1 mil of Magnesia Magma causes the evolution of not more than a few isolated bubbles and the resulting solution is not more than slightly turbid. Add 0.5 Gm. of ammonium chloride to the solution, filter, and render the filtrate alkaline with ammonia water; no precipitate is produced, but upon the addition of sodium phosphate T.S. to this alkaline solution, a white precipitate appears. Dilute 10 mils of Magnesia Magma with distilled water to make 100 mils, and allow it to stand until the precipitate has settled. Then remove 50 mils of the clear liquid and evaporate it to dryness on a water bath. The residue, when dried to constant weight, does not exceed 0.005 Gm., and, when dissolved in a few mils of distilled water and a drop of methyl orange T.S. added, yields a red color upon the addition of 5 drops of tenth-normal sulphuric acid V.S.

"**Assay.**—Transfer about 5 Gm. of Magnesia Magma to a tared flask, stopper and weigh accurately, add 25 mils of normal sulphuric acid V.S., and, after solution is complete, titrate the excess of acid with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows an amount of magnesium hydroxide corresponding to not less than 6.5 per cent. nor more than 7.5 per cent. of the weight of Magnesium Magma taken.

"Each mil of normal sulphuric acid V.S. used corresponds to 0.02917 Gm. of $Mg(OH)_2$. Each gramme of Magnesia Magma corresponds to not less than 2.23 mils nor more than 2.57 mils of normal potassium hydroxide V.S." *U. S.*

The official process which is that of McNeary (*J. A. P. A.*, 1916, p. 611) works very well, and is a great improvement over the process of the N. F. III and other processes based upon the double decomposition of soluble magnesium salts and alkaline carbonates in aqueous solutions. Of the double decomposition processes the best is that of Beringer. (*Proc. N. J. P. A.*, 1913, p. 46.) Another formula was suggested by Hensel, *J. A. P. A.*, 1914, p. 1118. A report on the assay of commercial samples was made by LaWall, *J. A. P. A.*, 1914, p. 1002. Another method of making milk of magnesia is to take a freshly calcined magnesium oxide made especially for the purpose, and hydrating it under carefully specified conditions with distilled water. This method has the advantage that no washing whatever is necessary. It does not give uniform results, however, in the hands of different persons.

Magma magnesia, popularly known as *milk of magnesia,* is an excellent and convenient alkali, useful as an antacid and mild laxative in *hyperacidity of the stomach,* whether due to *hypochlorhydria* or *fermentative dyspepsia,* and is useful for the other purposes for which magnesium oxide is used. One drachm is equivalent to approximately four grains of magnesium oxide. Milk of magnesia is also widely employed as a dentifrice, and especially for the correction of acid conditions of the mouth. For this purpose the addition of a trace of some aromatic oil, such as peppermint or anise, is a great advantage.

Dose, one to four fluidrachms (3.75–15 mils).

MAGNESII CARBONAS. U. S. (Br.)

MAGNESIUM CARBONATE Mag. Carb.

(măg-nē'şĭ-ī cär'bo-năs)

"A mixture of hydrated magnesium carbonate and magnesium hydroxide, corresponding to not less than 39.2 per cent. of MgO (40.32) and containing not more than 0.8 per cent. of CaO." *U. S.*

Magnesii Carbonas Levis, Light Magnesium Carbonate, *Br.;* **Magnesii Carbonas Ponderosus,** Heavy Magnesium Carbonate, *Br.;* Magnesia Hydrico-carbonica, Carbonas Magnesicus, Magnesia Alba, Magnesiæ Carbonas, Carbonate of Magnesia; Carbonate de Magnésie officinal, *Fr. Cod.;* Magnésie blanche, *Fr.;* Magnesium carbonicum, *P. G.;* Magnesiumcarbonat, Kohlensaure Magnesia, Weisse Magnesia, *G.;* Idrocarbonato di Magnesio Carbonato, Carbonato di Magnesia, *It.;* Carbonato Magnesico, Magnesia blanca, *Sp.*

In the U. S. P. IX magnesium carbonate is official under one name "Magnesii Carbonas;" this corresponds nearly with "Magnesii Carbonas Levis" of the British Pharmacopœia. A Heavy Magnesium Carbonate is also official in the British Pharmacopœia.

Magnesium carbonate sometimes occurs as a native mineral known as *magnesite,* the best deposits of which are those of the Grecian Archipelago, though a common variety is found in Chester Co., Pa. That which is sold in commerce is prepared on a large scale by the manufacturer. In the British Pharmacopœia directions are given for preparing it in two forms: that of *Magnesii Carbonas Levis,* or Light Magnesium Carbonate; and that of *Magnesii Carbonas Ponderosus,* or Heavy Magnesium Carbonate. The following are the directions:

1. MAGNESII CARBONAS LEVIS. *Light Magnesium Carbonate,* Br.—"Light Magnesium Carbonate is a hydrated magnesium oxycarbonate obtained by the following process:—Magnesium Sulphate, 125 *grammes;* Sodium Carbonate, 150 *grammes;* Distilled Water, *a sufficient quantity.* Dissolve the Magnesium Sul-

phate and the Sodium Carbonate separately, each in one thousand *millilitres* of cold Distilled Water; mix the solutions; boil the mixture for fifteen minutes; transfer the precipitate to a calico filter; wash it with boiling Distilled Water until the washings are free from sulphates, and dry at a temperature not exceeding 100° C. (212° F.)." *Br.*

The resulting carbonate is characterized in the British Pharmacopœia as "a very light, white powder, which, when examined under the microscope, is found to consist of amorphous particles with numerous slender prisms intermixed. It otherwise possesses the general characters and responds to the tests described under 'Magnesii Carbonas Ponderosus.'" *Br.*

2. MAGNESII CARBONAS PONDEROSUS. *Heavy Magnesium Carbonate,* Br.—"Heavy Magnesium Carbonate is a hydrated magnesium oxycarbonate obtained by the following process:—Magnesium Sulphate, 125 *grammes;* Sodium Carbonate, 150 *grammes;* Distilled Water, boiling, *a sufficient quantity.* Dissolve the Magnesium Sulphate and the Sodium Carbonate separately, each in two hundred and fifty *millilitres* of the Distilled Water; mix the solutions, and evaporate to dryness; digest the residue for half an hour with five hundred *millilitres* of the Distilled Water; collect the insoluble matter on a calico filter, wash with the Distilled Water until the washings are free from sulphates, and dry at a temperature not exceeding 100° C. (212° F.)." *Br.*

This is essentially the old process of the Dublin College, and yields a product which is characterized in the British Pharmacopœia as "a white granular powder. Readily soluble with effervescence, in the diluted mineral acids, the solutions yielding the *reactions* characteristic of magnesium. Loses from 56 to 58 per cent. of its weight when heated to redness. Yields no characteristic *reactions* for aluminium, copper, or calcium, and not more than the slightest *reactions* for iron, chlorides, or sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million." *Br.*

The following method is said to be pursued by some of the best manufacturers. To a saturated solution of 100 parts of magnesium sulphate, a solution of 125 parts of crystallized sodium carbonate is gradually added, the solutions being constantly stirred. The mixture is heated to ebullition, to complete the precipitation of the magnesia, which is then washed with tepid and finally with cold water, until the washings no longer give a precipitate with barium salts. When sufficiently washed, the carbonate is allowed to drain for one or two days on large linen filters, and is then placed in wooden moulds with a porous bottom of brick or gypsum, and subjected to pressure in order to give it a square and compact form. According to Otto and Gabler, very pure magnesium carbonate is made at Nauheim, Germany. Pattinson's process is used. It depends upon the fact that, on treating calcined dolomite, in the presence of water, with carbon dioxide under pressure, the magnesia dissolves as bicarbonate before any of the accompanying lime enters in solution. The calcined and finely powdered mineral is introduced, together with water, into a cylinder with a horizontal axis, and, while it is being kept in constant motion by a stirring apparatus, carbon dioxide, under a pressure of five to six atmospheres, is forced into it. The resulting solution of magnesium bicarbonate, which is perfectly free from lime, if the process has been properly managed, is then transferred to a vertical cylinder, where it is heated with steam, whereby magnesium carbonate is separated, which is collected, formed into prismatic pieces, and dried. The carbon dioxide required issues from the earth immediately outside of the factory, and the dolomite is furnished by the quarries of May and Urban, near Dietz and Steelen on the Lahn. (*A. Pharm.*, Aug., 1880; *N. R.*, Sept., 1881.) J. G. Ferrier criticized the processes for making the carbonates by the British Pharmacopœia; he stated that there was a conspicuous want of uniformity in the results obtained. (*P. J.*, 1904, 586.)

The density of magnesium carbonate is said to depend upon the strength of the solutions from which it is first precipitated, and its fineness and softness to the touch upon the use of sodium carbonate in its preparation. Much of the magnesium carbonate formerly used in this country was imported from England and Ireland, but that now consumed in the United States is chiefly a home product. The Keasbey & Mattison Company, who are the largest manufacturers of carbonate at the present time, use the process of decomposing calcined dolomite by forcing carbon dioxide into its aqueous mixture, and heating this to precipitate the carbonate. When made from bittern, magnesium carbonate is contaminated with calcium carbonate, salts of lime being contained in sea water, and when it is prepared from magnesite, or from magnesian schist, iron is almost always present. The only way in which these impurities can be avoided is to prepare pure magnesium sulphate by repeated crystallization, and to use a pure sodium carbonate. It is also necessary that the water with which the precipitate is washed should be free from earthy salts, which would be decomposed and contaminate the magnesia. Kippenberger prepares crystallized magnesium carbonate by shaking *freshly* precipitated magnesium carbonate with a solution of potassium bicarbonate at the ordinary temperature; much of the magnesium carbonate dissolves and crystallizes out of the filtered solution upon standing for a day. Sodium bicarbonate may be used instead of the potassium salt, but the crystals are smaller. (*Zeit. Anorg. Chem.*, 1894, 177.)

Properties.—Magnesium carbonate is inodorous, nearly insipid, perfectly white, smooth to the touch, and nearly insoluble in water, requiring 2493 parts of cold and 9000 parts of hot water for solution. It is decomposed by

strong heat, by all the acids, by potassium sodium, calcium, barium and strontium hydroxides, and by acidulous and metallic salts. It is officially described as in "light, white, friable masses, or as a bulky, white powder, without odor, and having a slight, earthy taste; permanent in the air. Magnesium Carbonate is practically insoluble in water, to which, however, it imparts a slightly alkaline reaction; insoluble in alcohol; dissolved by dilute acids with effervescence. When strongly heated, it loses water and carbon dioxide, and is converted into magnesium oxide. A solution of Magnesium Carbonate in diluted hydrochloric acid, when mixed with ammonium chloride T.S. and an excess of ammonia water, yields with sodium phosphate T.S. a white crystalline precipitate. Heat to boiling, 1 Gm. of Magnesium Carbonate with 50 mils of distilled water, and, after cooling, filter and evaporate the filtrate to dryness on a water bath; not more than 0.01 Gm. of residue remains (*soluble salts*). Dissolve 2.5 Gm. of Magnesium Carbonate in 50 mils of diluted hydrochloric acid and 200 mils of distilled water. The solution is colorless, and a 20 mil portion does not give an immediate blue coloration upon the addition of 5 drops of potassium ferrocyanide T. S. (*iron*). Dissolve 0.5 Gm. of Magnesium Carbonate in a slight excess of diluted hydrochloric acid (about 5 mils) and dilute with distilled water to 25 mils. Ten mils of this solution does not respond to the Test for heavy metals (see Part III, Test No. 3). Dissolve 4 Gm. of Magnesium Carbonate in 50 mils of diluted hydrochloric acid, in a beaker of about 800 mils capacity. Dilute this solution to about 400 mils with distilled water, add 5 Gm. of ammonium chloride, heat to boiling, then add 50 mils of ammonium oxalate T.S., followed by 5 drops of methyl orange T.S., and afterward by ammonia water (previously diluted with two volumes of distilled water), added slowly in small portions, stirring constantly, until the liquid has assumed a yellow color. This operation should require about twenty minutes. Allow the liquid to stand for four hours or over night, collect the precipitate on a filter, wash it with hot distilled water, containing 1 per cent. of ammonium oxalate T.S., until the washings, after strongly acidifying with nitric acid, cease to react with silver nitrate T.S. Dissolve the precipitate by pouring 50 mils of warm diluted hydrochloric acid in small portions over the filter, wash the filter with about 100 mils of distilled water, collect the solution of the precipitate and washings in the same beaker, then dilute to 400 mils with distilled water, precipitate, allow to stand, and wash as before, omitting, however, the addition of 5 Gm. of ammonium chloride. Dry the precipitate and filter obtained in the second precipitation and cautiously ignite in a platinum crucible, heating gently at first, gradually increasing the temperature, and finally heating it over a blast lamp for fifteen minutes or longer, if necessary, until of constant weight. Cool the crucible and contents in a desiccator before weighing. The weight of CaO so obtained does not exceed 0.032 Gm., corresponding to not more than 0.8 per cent. (*calcium oxide*).

"**Assay.**—Dissolve 1 Gm. of Magnesium Carbonate in 30 mils of normal sulphuric acid V.S. and determine the residual acid by titrating with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. The amount of normal sulphuric acid V.S. consumed, exclusive of the normal sulphuric acid V.S. corresponding to the calcium oxide found, is not less than 19.44 mils, indicating the presence of not less than 39.2 per cent. of MgO.

"Each mil of normal sulphuric acid V.S. corresponds to 0.02016 Gm. of MgO or to 0.028035 Gm. of CaO." *U. S.*

Pereira states that the *light carbonate*, when examined with the microscope, is seen to consist of an amorphous powder, more or less intermingled with slender prismatic crystals, which appear as if they were eroded or efflorescent; the *heavy carbonate* consists of granules of various sizes, without any traces of the prismatic crystals observed in the former variety.

A solution in carbonic acid water, prepared by passing carbon dioxide into a reservoir containing magnesium carbonate suspended in water, has been introduced into use as a cathartic and antacid. *Dinneford's Magnesia* is a solution of this nature and contains the dissolved magnesia in the form of bicarbonate into which the carbonate is converted by the carbon dioxide under pressure. According to Christison, it contains only nine grains of carbonate in the fluidounce, though alleged to contain twice that quantity. Its taste is more disagreeable than that of the undissolved carbonate. A formula for this preparation has been introduced into the British Pharmacopœia, with the name of *Liquor Magnesii Bicarbonatis* (see page 647).

Magnesium carbonate may contain an alkaline carbonate or sulphate, or both, from insufficient washing; also sodium chloride, alumina, and calcium carbonate. If water boiled with it changes turmeric, an alkaline carbonate is indicated. If barium chloride produces a precipitate in the water, the presence of a sulphate or carbonate is shown, and if silver nitrate produces precipitation, a chloride is indicated. When dissolved in an excess of hydrochloric acid, an excess of ammonia will throw down alumina, which is almost always present in minute quantity, and ammonium oxalate, afterwards added to the filtered chloride solution, will throw down calcium oxalate if lime be present. When the same solution, nearly neutralized, is rendered blue by potassium ferrocyanide, iron is indicated.

Composition.—According to Berzelius, magnesium carbonate of commerce (*magnesia alba*) was a combination of three molecules of magnesium carbonate with one of magnesium hydroxide. According to Phillips, whose analysis agrees with a subsequent one by Fownes, four molecules of the carbonate are combined with

one of the hydroxide and four of water. (*P. J.*, iii, 480.) The formula given by the British Pharmacopœia of 1898 is $3MgCO_3 + Mg(OH)_2 + 4H_2O$; in other words, a combination of three molecules of magnesium carbonate, one of magnesium hydroxide, and four of water. While the U. S. Pharmacopœia IX gives no formula in the text it is written in the molecular weight tables as follows: "Basic (approximately) $(MgCO_3)_4Mg(OH)_2 + 5H_2O$." The composition of this salt varies with the mode of preparation.

Uses.—Magnesium carbonate is antacid, and, by combining with acid in the stomach, becomes generally cathartic. When it undergoes no change in the alimentary canal it produces no purgative effect. Under these circumstances it may usually be made to operate by following it with draughts of lemonade. It is useful in all cases which require a laxative antacid, and, though prone to produce flatulence in consequence of the liberation of its carbon dioxide in the stomach and bowels, and therefore, inferior to calcined magnesia, it sometimes operates favorably, in consequence of this very property, in *sick stomach* attended with acidity. As an antacid, it has the advantages over sodium carbonate of being less irritating and of neutralizing a larger proportion of acid. It is best administered in water or milk. In order that it may be uniformly diffused through water, it should be previously rubbed up with syrup or ginger syrup. Magnesium carbonate is a useful agent for diffusing camphor and the volatile oils through water, in preparing unofficial medicated waters, and is also used with a similar purpose as a diffusing agent in preparing syrups or elixirs.

Dose, as an antacid, five to twenty grains (0.32–1.3 Gm.); as a laxative, one-half to two drachms (2–7.7 Gm.).

Off. Prep.—Trochiscus Bismuthi Compositus, *Br.;* Mistura Carminativa, *N. F.*

MAGNESII OXIDUM. U. S. (Br.)

MAGNESIUM OXIDE, MAGNESIA Mag. Oxid. [Magnesia, U. S. 1890, Calcined Magnesia, Light Magnesia]

(măg-nē'shĭ-ī ŏx'ĭ-dŭm)

"It contains, after ignition, not less than 96 per cent. of MgO (40.32) and not more than 2 per cent. of CaO. It contains not more than 10 per cent. of water. Preserve it in well-closed containers." *U. S.* "Light Magnesia, MgO, is prepared by exposing Light Magnesium Carbonate to a dull red heat." *Br.*

Magnesia Levis, *Br.;* Calcined Magnesia; Magnesia Calcinata; Magnésie calcinée, *Fr. Cod.;* Magnésie, *Fr.;* Magnesia Usta, *P. G.;* Gebrannte Magnesia, *G.;* Ossido di magnesio, *It.;* Oxido magnesico, *Sp.*

In the British Pharmacopœia, 1885, directions were given for preparing two forms of magnesia, one called *Magnesia Levis,* or *Light Magnesia,* from the *Light Carbonate,* and the other *Magnesia Ponderosa,* from the *Heavy Carbonate.* It is the former which corresponds with our ordinary magnesia. Neither Pharmacopœia gives a detailed process. "Take of Light Carbonate of Magnesium, *four ounces.* Put it into a Cornish or Hessian crucible closed loosely by a lid, and expose it to a low red heat until a small quantity, taken from the centre of the crucible, cooled, moistened with water, and dropped into warm diluted sulphuric acid, causes no effervescence." *Br.,* 1885.

By exposure to a red heat, the water and carbon dioxide of the magnesium carbonate are expelled, and the earth is obtained pure. According to Black, the carbonate loses seven-twelfths of its weight by calcination. Brande says that the loss varies from 50 to 60 per cent., of which from 15 to 20 per cent. is water:

$$(MgCO_3)_4 + Mg(OH)_2 + 5H_2O = 5MgO + 6H_2O + 4CO_2$$

About the close of the process the earth exhibits a luminous or phosphorescent appearance, which is said to be a good criterion of its freedom from carbon dioxide. (Duncan.) A more certain indication, however, is the absence of effervescence when hydrochloric acid is added to a little of the magnesia, previously mixed with water. It is an error to suppose that a very intense heat is requisite in the calcination. The temperature of ignition is sufficient for the expulsion of the water and carbon dioxide, and any increase serves only to render the magnesia harder, denser, less readily soluble in acids, and consequently less useful as a medicine. In order to insure a pure product, care should be taken that the carbonate employed be free from lime. It should be rubbed to powder before being introduced into the pot or crucible, and, as in consequence of its lightness it occupies a very large space, the plan has been proposed of moistening and compressing it in order to reduce its bulk; but the French pharmaceutical writers direct that the vessels employed should be sufficiently large to contain a considerable quantity of the carbonate, without the necessity of resorting to compression. The official direction, to keep the magnesia, after it has been prepared, in well closed vessels, is founded on the fact that it absorbs carbon dioxide and water from the air, but, as the absorption of the gas goes on very slowly, and that of water does not injure the preparation, the caution is often neglected. (See *P. J.*, 1898, 389.) The great bulk of the oxide renders its introduction into small bottles inconvenient. A four ounce bottle holds only about an ounce of the purest and finest magnesia. But its specific gravity is greatly increased by trituration, and four times the quantity may be thus pressed into the same space. The density of *Henry's Magnesia,* which is at least four times that of the oxide prepared in the ordinary way, has been ascribed to this method of preparation. It has also been attributed to the influence of intense heat employed in the calcination. The conjecture has even been advanced, that this magnesia, which

has enjoyed so great a popularity in England and this country, is prepared by precipitating a solution of magnesium sulphate by potassium hydroxide, as the product afforded by this plan is comparatively dense. It is asserted that the magnesia prepared from the carbonate procured by precipitating magnesium sulphate with potassium carbonate is softer to the touch and bears a closer resemblance to Henry's than that prepared from the ordinary carbonate. The fact is explained by the presence in such magnesia of a little potassium sulphate, from which it is difficult entirely to free it in consequence of the sparing solubility of this salt, and of a portion of silica, which originally existed in the potassium carbonate employed to decompose the magnesium sulphate, and of which sodium carbonate is destitute. According to Richard Phillips, Jr., if equivalent quantities of crystallized magnesium sulphate and crystallized sodium carbonate be boiled together in water, the mixture evaporated to dryness, the residual salts calcined, and the sodium sulphate dissolved out by water, the magnesia obtained will be dense. (See *A. J. P.*, xvi, 118.) By packing the carbonate closely in the crucible, or by moistening and then compressing it strongly in a cloth, before calcination, a heavy magnesia is obtained. The advantages of Henry's magnesia, independently of the convenience of its less bulk, are its greater softness and more ready miscibility with water. A preparation similar to Henry's was originated by T. J. Husband, of Philadelphia. In reference to the preparation of heavy magnesia, T. H. Barr, after trying various methods, obtained the best results either by precipitating a hot concentrated solution of magnesium sulphate with a like solution of sodium carbonate, or by decomposing magnesium chloride by heat. (*A. J. P.*, xxvi, 193.) P. E. Alessandri proposes the following method, which is both simple and rapid, for preparing heavy magnesia. Take ordinary calcined magnesia, free from carbonate, moisten it, in a mortar, with pure absolute alcohol, and triturate it, at first gently, afterwards with some force, but not rapidly. During the agitation, the magnesia is to be moistened three or four times with fresh portions of the alcohol, and the operation is suspended when the bulk of the magnesia appears to remain stationary. Then remove the mass, dry it, rub it to powder, and pass it through a sieve. The product occupies only about one-fifteenth of the original bulk; but it is too expensive for practical uses. (*N. R.*, March, 1882.)

Properties.—Magnesium oxide or magnesia is a very light, white, inodorous powder, of a feeble alkaline taste. Its sp. gr. is commonly stated at 2.3. It was deemed infusible until melted by means of the oxyhydrogen blowpipe of Hare. When sufficiently heated, it conducts electricity and shines with an intense light, which fact is utilized in the Nernst lamp. Water sprinkled upon it is absorbed to the extent of about 18 per cent., but with scarcely any increase of temperature, producing thereby the hydroxide $Mg(OH)_2$. It is almost insoluble, requiring, according to Fyfe, 5142 parts of water at 15.5° C. (60° F.), and 36,000 parts of boiling water, for solution. Water thus impregnated has no effect on vegetable colors, but magnesia itself produces a brown stain by contact with moistened turmeric paper. Magnesia is a metallic oxide, consisting of one atom of magnesium and one of oxygen. It is officially described as "a white, very bulky, and very fine powder, without odor, and having an earthy, but not a saline taste. On exposure to the air, it slowly absorbs moisture and carbon dioxide. Magnesium Oxide is almost insoluble in water; insoluble in alcohol; dissolved by dilute acids. A solution of Magnesium Oxide in diluted hydrochloric acid, mixed with ammonium chloride T.S. and an excess of ammonia water, yields with sodium phosphate T.S. a white crystalline precipitate. Heat to boiling 1 Gm. of Magnesium Oxide with 50 mils of distilled water, and, after cooling, filter; the filtrate is not more than faintly alkaline to litmus, and when evaporated to dryness leaves not more than 0.02 Gm. of residue (*soluble salts*). Heat to boiling, a mixture of 0.1 Gm. of Magnesium Oxide with 5 mils of distilled water, and, after cooling, pour it into 5 mils of acetic acid. Solution takes place without the evolution of more than a few isolated gas bubbles (*carbonate*). Dissolve 1 Gm. of Magnesium Oxide in 50 mils of diluted hydrochloric acid and 200 mils of distilled water. The solution is colorless, and a 20 mil portion does not give an immediate blue coloration upon the addition of several drops of potassium ferrocyanide T.S. (*iron*). Dissolve 0.5 Gm. of Magnesium Oxide in a slight excess of diluted hydrochloric acid and dilute with distilled water to 25 mils. Ten mils of this solution does not respond to the Test for heavy metals (see Part III, Test No. 3). Transfer to a porcelain crucible about 1 Gm. of Magnesium Oxide, weigh accurately, and expose it to a low red heat; it loses not more than 10 per cent. of its weight (*water*). To test for calcium proceed as directed under *Magnesii Carbonas*, using about 1.5 Gm. of recently ignited Magnesium Oxide, accurately weighed. It shows not more than 2 per cent. of CaO." *U. S.*

"A white powder differing only from 'Magnesia Ponderosa' in its bulk, the volumes corresponding to the same weight having the ratio of three and a half to one." *Br.*

"**Assay.**—Dissolve about 0.5 Gm. of Magnesium Oxide, which has been recently ignited to constant weight and accurately weighed, in 30 mils of normal sulphuric acid V.S. and determine the residual acid by titrating with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. The amount of normal sulphuric acid V.S. consumed, exclusive of the normal sulphuric acid V.S. corresponding to the calcium oxide found, when calculated to 1 Gm. of the ignited Magnesium Oxide, is not

less than 47.62 mils, indicating the presence of not less than 96 per cent. of MgO.

"Each mil of normal sulphuric acid V.S. used corresponds to 0.02016 Gm. of MgO or to 0.028035 Gm. of CaO." *U. S.*

Magnesium is a white, very brilliant metal, of sp. gr. 1.75, resembling silver, malleable, fusible at a low temperature, and convertible into magnesia by the combined action of air and moisture. It burns with great facility, and yields by its combustion a light which is intensely white and very rich in actinic, or chemically active, rays, so that it finds wide application in signal lights and for photography. Many of the so-called "flash powders" contain metallic magnesium in a finely divided state as their basis. There is a magnesium hydroxide, possessing the formula $Mg(OH)_2$, which is the basis of the Magma Magnesiæ. With nitric and hydrochloric acids magnesium forms salts which are soluble in alcohol and very deliquescent. It is precipitated from its saline solutions by the pure alkalies in the state of a hydroxide, and by potassium and sodium carbonates as a carbonate, but it is not precipitated by the alkaline bicarbonates, nor by common ammonium carbonate.

Magnesia is liable to contain, as impurities, magnesium carbonate, lime, alumina, silica, and small quantities of the soluble salts employed or produced in the preparation of the carbonate from which it is procured. Lime, which is a very frequent impurity, and imparts to the magnesia a more strongly alkaline and more disagreeable taste, is detected by ammonium oxalate or potassium bicarbonate. Neither of these salts disturbs a neutral solution of pure magnesium salts, but if lime is present, both produce a precipitate, the former of calcium oxalate, the latter of calcium carbonate. According to Wittstein, calcium oxalate is soluble in the neutral salts of magnesium, requiring 50 parts of magnesium chloride, and 90 of magnesium sulphate, and consequently there might be no precipitate, or one redissolved by the liquid, should the proportion of lime be very small. (*J. P. C.*, 4e sér., iii, 216.) On this account a special method of determining small amounts of calcium salts has been introduced into the texts of magnesium oxide and magnesium carbonate of the U. S. P. IX.

Uses.—Magnesium oxide is used in medicine chiefly for its antacid properties. In cases of *gastric hyperacidity*, whether due to overactivity of the acid-secreting glands of the stomach or to fermentative changes in the foodstuff, it is one of the best correctives that we have. It has the advantages over bicarbonate of soda that it is less irritating to the mucous membrane, that it does not evolve any gas, and that the dose required is smaller. One grain of magnesium oxide has about the same neutralizing power as four grains of sodium bicarbonate. When given in large enough dose it exercises a laxative effect. This aperient action is due to the union of the magnesium with the acids of the primæ viæ. When it meets with no acid, it is apt to linger in the stomach or bowels, and should in that case be followed by lemonade. It may be administered in water or milk, and thoroughly triturated so as to render the mixture uniform. If mixed with less than 14 or 15 times its weight of water, and allowed to stand for a day or two, magnesia is apt to form a more or less concrete mass, owing to the production of a hydroxide. This change does not take place, or at least takes place much less readily, when magnesia already saturated with moisture is employed instead of that freshly calcined. In this connection Duncan recommends boiling the magnesia for a few moments with half the quantity of water prescribed to prevent subsequent caking. It has been conjectured that anhydrous magnesia might prove injurious to the stomach by solidifying its liquid contents, and the oxide which has become saturated with moisture by exposure to a damp air is preferably recommended. Freshly precipitated magnesium hydroxide will serve as an antidote to arsenic trioxide, though less efficient than ferric hydroxide. The experiments of Carles have shown that the soluble *magnesium saccharate* is not superior as an antidote for arsenic to simple magnesia. Ohleyer (*L. L.*, July, 1873) employs magnesia as a dressing in *ulcers* and *abrasions*, while Vergley recommends for *burns* calcined magnesia triturated with milk so as to form a paste, which should be applied thickly several times a day.

Dose, as an antacid, five to twenty grains (0.32–1.3 Gm.); as a laxative, one-half to one drachm (2–3.9 Gm.).

Off. Prep.—Ferri Hydroxidum cum Magnesii Oxido, *U. S.*; Pulvis Rhei Compositus, *Br.*

MAGNESII OXIDUM PONDEROSUM. U. S. (Br.)

HEAVY MAGNESIUM OXIDE Mag. Oxid. Pond.
[Heavy Magnesia Magnesia Ponderosa, Pharm. 1890]

(măg-nē′shĭ-ĭ ŏx′ĭ-dŭm pŏn-dẹ-rō′sŭm)

"It contains, after ignition, not less than 96 per cent. of MgO (40.32) and not more than 2 per cent. of CaO. It contains not more than 10 per cent. of water. Preserve it in well-closed containers." *U. S.* "Heavy Magnesia, MgO, is prepared by exposing Heavy Magnesium Carbonate to a dull red heat." *Br.*

Magnesia Ponderosa, *Br.*, Heavy Calcined Magnesia; Oxide of Magnesium; Magnésie Calcinée pesante, *Fr.*; Schwere gebrannte Magnesia, *G.*

This was directed, in the British Pharmacopœia, 1885, to be prepared precisely in the same manner as light magnesia, using, however, the heavy carbonate (Heavy Magnesium Carbonate, *Br.*). "Heavy Magnesium Oxide is a white, dense, and very fine powder, which conforms to the reactions and tests under *Magnesii Oxidum.*" *U. S.* It is described by the Br. Ph., as "a white powder, insoluble in *water*, but readily dissolved by acids, the solution yield-

ing the *reactions* characteristic of magnesium. Yields no characteristic *reactions* for aluminium and copper, and not more than the slightest *reactions* for iron, calcium, carbonates, and sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million. Loses not more than 1 per cent. of its weight when heated to dull redness." *Br.*

The two varieties of light and heavy magnesia differ only in their weight in the same bulk, the volumes corresponding to the same weight being to each other in the ratio of three and one-half to one. (See *Magnesii Oxidum*, page 674.)

Dose, five to sixty grains (0.32–3.9 Gm.).

Off. Prep.—Pulvis Rhei et Magnesiæ Anisatus, *N. F.*

MAGNESII SULPHAS. U. S., Br.

MAGNESIUM SULPHATE Mag. Sulph. [Epsom Salt]

(măg-nē'shĭ-ī sŭl'phăs)

"It contains not less than 48.59 per cent. nor more than 53.45 per cent. of anhydrous magnesium sulphate, corresponding to not less than 99.5 per cent. of the crystallized salt [$MgSO_4 + 7H_2O = 246.50$]. Preserve it in well-closed containers." *U. S.* "Magnesium Sulphate may be obtained by the interaction of the native magnesium carbonates and diluted sulphuric acid; or by purifying the native sulphate. It contains not less than 97.4 per cent. of pure magnesium sulphate, $MgSO_4,7H_2O$." *Br.*

Sal Amarum, Sal Epsomense, Sal Anglicum, Sal Sedlicense, Sulfas Magnesicus; Sulphate of Magnesia; Sulfate de Magnésie, *Fr. Cod.*; Sel d'Epsom, Sel de Sedlitz, Sel amer, *Fr.*; Magnesium Sulfuricum, *P. G.*; Magnesiumsulfat, Schwefelsaures Magnesia, Bittersalz, *G.*; Solfato di magnesio, Sulfato magnesico, *Sp.*

Magnesium Sulphate is a constituent of sea water, and of some saline springs. It also occurs native, either crystallized in slender, prismatic, adhering crystals, or as an efflorescence on certain rocks and soils which contain magnesia and a sulphate or sulphide. In the United States it is found in the great caves so numerous to the west of the Allegheny Mountains. In one of these caves, near Corydon in Indiana, it formed a stratum on the bottom several inches deep, or appeared in masses sometimes weighing ten pounds, or disseminated in the earth of the cavern, one bushel of which yielded from four to twenty-five pounds of the sulphate. It also appeared on the walls of the cavern, and, if it was removed, acicular crystals again appeared in a few weeks. (Cleveland.)

Under the name of *kieserite*, a mineral is obtained from the saline deposits at Stassfurt, in Germany, which consists chiefly of impure magnesium sulphate. It is used as a source for preparing magnesium sulphate, and is exported from Germany; for a historical paper on Epsom salt by M. I. Wilbert, see *Proc. A. Ph. A.*, 1904, 351.

Magnesium sulphate was originally procured by evaporating the waters of saline springs at Epsom, in England. Grew prepared it in this manner in 1675. It was afterwards discovered that the brine remaining after the crystallization of common salt from sea water furnished by careful evaporation precisely the same salt, and, as this was a much cheaper product, it superseded the former. The residual brine, or bittern, consists of magnesium sulphate and magnesium and calcium chlorides. As the magnesium sulphate crystallizes first, it may with proper care be obtained nearly pure, although most frequently the salt prepared in this way is deliquescent from the presence of magnesium chloride. It may be freed from this impurity by washing the crystals with their own saturated solution. It was from this source that the greater part of the Epsom salt of commerce was long obtained in Europe. The salt works of New England supplied our own market with an impure and deliquescent sulphate. With the improvements of chemistry, other and better processes have been adopted. In the neighborhood of Genoa and Nice, magnesium sulphate is prepared in large quantities from a schistose rock containing magnesia and iron sulphide. The mineral is roasted, and exposed in heaps for some months to the action of air and water. It is then lixiviated, the ferrous sulphate decomposed by lime water, and the salt obtained pure by repeated solution and crystallization.

William Henry, of Manchester, whose calcined magnesia became famous throughout the world, took out a patent for a mode of preparing magnesia and its salts from the double magnesium and calcium carbonate—the *dolomite* of mineralogists. His process was to drive off the carbon dioxide by heat, and to convert the residue into hydroxide. He treated this with a sufficient quantity of hydrochloric acid to dissolve out the calcium hydroxide, and then converted the magnesia which remained into a sulphate either by sulphuric acid or by ferrous sulphate.

The salt was extensively manufactured in Baltimore and Philadelphia from a silicious magnesium hydroxide. This mineral occurs in veins in the serpentine and other magnesian rocks which abound in the neighborhood of Baltimore and in the southern counties of Pennsylvania. The advantage which it possesses over the dolomite, in the preparation of this salt, is the almost entire absence of lime, owing to which there is little or no waste of acid, and the operation is much simplified. The mineral is reduced to a fine powder and saturated with sulphuric acid. The mass is then dried and calcined at a red heat, in order to convert any ferrous sulphate which may be present into ferric oxide. It is then dissolved in water, and calcium sulphide added to separate any remaining portion of iron. The salt is crystallized and dissolved a third time, in order to purify it. The sulphate prepared by this process is generally very pure and clean, although it sometimes contains a trace of ferrous sulphate. A very pure magnesium sulphate free from chlo-

ride is obtained as a by-product in the manufacture of carbon dioxide from magnesite when sulphuric acid is used to decompose the carbonate. This industry at one time assumed large proportions because of the demand for liquefied carbon dioxide in the manufacture of aerated and effervescing mineral waters. In the modern method of making carbon dioxide, however, acid is not used, the CO_2 being evolved by simply heating the magnesite (magnesium carbonate) to a little over 300° C. (572° F.). Magnesium sulphate is also obtained from *kieserite* from the Stassfurt mines, Germany.

Properties.—Magnesium sulphate is in "small, colorless, prismatic needles or rhombic prisms, without odor, and having a cooling, saline, and bitter taste; slowly efflorescent in the air. One Gm. of Magnesium Sulphate dissolves in 1 mil of water at 25° C. (77° F.); also in about 0.2 mil of boiling water; almost insoluble in alcohol at 25° C. (77° F.). An aqueous solution of the salt (1 in 20) is neutral to litmus. When exposed to warm air, the salt loses some of its water of crystallization and is converted into a white powder. Further heating removes more water, and at a temperature somewhat above 200° C. (392° F.) it is rendered anhydrous. An aqueous solution of the salt (1 in 20), when mixed with ammonium chloride T.S. and ammonia water, yields with sodium phosphate T.S. a white, crystalline precipitate. An aqueous solution (1 in 20) yields with barium chloride T.S. a white precipitate insoluble in hydrochloric acid. Add a few drops of silver nitrate T.S. to 10 mils of an aqueous solution of the salt (1 in 20), previously mixed with a few drops of nitric acid; not more than an opalescence is produced (*chloride*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of the salt meets the requirements of the Test for arsenic (see Part III, Test No. 1)." *U. S.*

"In small, colorless, transparent, rhombic prisms. Taste bitter. Soluble in 1 part of *water.* Yields the *reactions* characteristic of magnesium and of sulphates. When 0.5 gramme is dissolved in 50 millilitres of *water,* and to the solution 20 millilitres of *solution of ammonium chloride,* 20 millilitres of *strong solution of ammonia,* and excess of *solution of sodium phosphate* are added in succession, the mixture, after well stirring and setting aside for twelve hours, yields a precipitate which, when collected, washed with *strong solution of ammonia* diluted with three times its volume of *water,* dried and heated to redness, weighs not less than 0.220 and not more than 0.226 gramme. Yields no characteristic *reactions* for zinc, and not more than the slightest *reactions* for chlorides. *Lead limit* 5 parts per million. *Arsenic limit* 5 parts per million. 10 grammes dissolved in 20 millilitres of *water,* and heated on a water-bath for one hour in a closed flask, yield a clear, colorless solution (absence of insoluble impurities and of more than traces of iron)." *Br.*

"**Assay.**—Dissolve about 1 Gm. of Magnesium Sulphate, accurately weighed, in 100 mils of distilled water, gradually add to the solution, with constant stirring, an excess of sodium phosphate T.S. (about 20 mils), allow to stand for ten minutes, then add 30 mils of ammonia water and allow to stand for four hours. Collect the precipitate on a filter, wash it with dilute ammonia water (1 volume of ammonia water to 3 volumes of distilled water) until 10 mils of the washings, when acidulated with hydrochloric acid, yields no turbidity on the addition of a few drops of barium chloride T.S. Dry and ignite to constant weight. The weight of the magnesium pyrophosphate so obtained corresponds to not less than 48.59 per cent. nor more than 53.45 per cent. of $MgSO_4$.

"Each gramme of Magnesium Sulphate corresponds to not less than 0.4495 Gm. nor more than 0.4944 Gm. of magnesium pyrophosphate ($Mg_2P_2O_7$)." *U. S.*

It usually occurs in small acicular crystals, which are produced by agitating the solution while crystallizing. It slowly effloresces in the air. Exsiccated magnesium sulphate is employed in some localities under the title *Magnesium Sulphuricum Siccum.* It is a fine white powder of which about 65 parts represents 100 parts of the crystallized salt.

Magnesium sulphate is completely decomposed by potassium and sodium hydroxides and their carbonates, by lime, barium and strontium oxides, and their soluble salts. Ammonia partially decomposes it, and forms with the remainder a double sulphate. Potassium and sodium bicarbonates do not decompose it, except by the aid of heat. An economic use which has been recommended of magnesium sulphate is the addition of a strong solution to ordinary white-wash, whereby a beautiful whiteness may be given to walls and ceilings. A little of it, moreover, added to starch considerably increases its stiffening properties, and at the same time in some degree resists the action of fire. (*Chem. News,* April, 1867.)

Uses.—Magnesium sulphate is an active cathartic operating with but little pain or nausea, and producing watery stools. Its cathartic action is due in part to its attraction for water, but it seems also to exercise a direct stimulant effect upon the glands of the intestinal tract. It has but little direct effect upon peristalsis, the increased movements of the intestinal muscles being due chiefly to the over distention with the fluid. It may be used whenever it is desired to clean out the alimentary canal, especially when a prompt action is desired, as in cases of *poisoning* or certain types of *acute enteritis.* It is a valuable remedy when it is desired to encourage the elimination of metabolic poisons through the bowel, as in *gout* or *uremia.* It is also highly esteemed for the evacuation of *dropsical effusions.* As an habitual laxative, although widely used, it is generally inferior to the vegetable cathartics.

When injected into the circulation magnesium

sulphate acts as a violent poison, lessening respiration and depressing the circulation by a direct action upon the heart. It also paralyzes the peripheral ends of the motor nerves and, according to Meltzer and Auer (*A.J.Phys.*, 1905, xiv, p. 366, and xvii, p. 313), also the sensory nerves. Guthrie and Ryan (*A. J. Phys.*, 1910, xxiv, p. 329) dispute the conclusions of Meltzer and Auer that it has a true anesthetic action, believing that the apparent anesthesia is due to the motor paralysis, but the experiments of Wiki (*A. I. P. T.*, 1911, xxi, p. 415) seem to demonstrate that when applied locally it is a paralyzant to the sensory nerves. As an internal remedy it has been employed by intraspinal injection as an anesthetic and in the treatment of *tetanus*. Its action in tetanus appears to be solely that of an anticonvulsant, not a true curative, and whether it has any superiority over other methods of controlling the convulsions is at present uncertain. As an antitetanic fifteen to thirty grains (1–2 Gm.) may be injected daily into the subarachnoid space in 10 per cent. solution. For intraspinal anesthesia, although it has been used with apparent success in a few cases, it appears to have no advantage over the cocaine series and has shown itself distinctly irritant to the kidney.

As Christison reported the case of a boy ten years old who was said to have been killed by two ounces of the salt without the induction of purgation, it is possible that, under some circumstances, when very large amounts of magnesium sulphate are given by the mouth, sufficient may be absorbed to produce poisonous effects.

It is also used locally in saturated solution for its anesthetic effect in *sprains* and *bruises*, and appears to be possessed of some sort of antiphlogistic action. Tucker (*T. G.*, 1907) has used it with favorable results as a topical application in *erysipelas, cellulitis, epididymitis*, and other localized inflammatory conditions.

Dose, one to eight drachms (3.9–31 Gm.).

Off. Prep.—Infusum Sennæ Compositum, *U. S.;* Magnesii Sulphas Effervescens, *Br.;* Mistura Sennæ Composita, *Br.;* Liquor Magnesii Sulphatis Effervescens, *N. F.;* Sal Kissingense Factitium, *N. F.;* Sal Kissingense Effervescens, *N. F.;* Sal Vichyanum Factitium, *N. F.;* Sal Vichyanum Factitium Effervescens, *N. F.;* Sal Vichyanum Factitium Effervescens cum Lithio, *N. F.*

MAGNESII SULPHAS EFFERVESCENS. Br.

EFFERVESCENT MAGNESIUM SULPHATE

(măg-nē'şĭ-ī sŭl'phăs ĕf-fẹr-vĕs'cẹnş)

Magnesium Sulphuricum Effervescens; Magnesiæ Sulphas Effervescens; Effervescent Sulphate of Magnesia; Effervescent Epsom Salt; Brausendes Magnesiumsulfat, *G.;* Sulfato magnesico effervescente, *Sp.*

This preparation was dropped from the U. S. P. IX. The process of U. S. P. VIII is appended.

* "Magnesium Sulphate, uneffloresced crystals, *five hundred grammes* [or 17 ounces av., 279 grains]; Sodium Bicarbonate, dried and powdered, *four hundred and three grammes* [or 14 ounces av., 94 grains]; Tartaric Acid, dried and powdered, *two hundred and eleven grammes* [or 7 ounces av., 193 grains]; Citric Acid, uneffloresced crystals, *one hundred and thirty-six grammes* [or 4 ounces av., 349 grains]; to make *one thousand grammes* [or 35 ounces av., 120 grains]. Dry the magnesium sulphate on a water-bath, until it ceases to lose weight, then, after powdering the dry salt, mix it intimately with the citric acid, which has previously been powdered, and the tartaric acid, and thoroughly incorporate the sodium bicarbonate. Place the mixed powders on a plate of glass or in a suitable dish, in an oven heated to between 93° and 104° C. (199.4° and 219.2° F.). When the mixture has acquired a moist consistence by the aid of careful manipulation with a wooden spatula, rub it through a No. 6 tinned-iron sieve, and dry the granules at a temperature not exceeding 54° C. (129.2° F.). Keep the product in well-stoppered bottles."

"Magnesium Sulphate, in crystals, 500 *grammes;* Sodium Bicarbonate, in powder, 360 *grammes;* Tartaric Acid, in powder, 190 *grammes;* Citric Acid, in powder, 125 *grammes;* Refined Sugar, in powder, 105 *grammes*. Dry the Magnesium Sulphate at about 55° C. (131° F.) until it has lost twenty-three per cent. of its weight; powder the dried product; mix it with the Refined Sugar and then with the other ingredients. Place the mixture in a dish or pan of suitable form heated to between 90° and 105° C. (194° and 221° F.). When the mixture, by the aid of careful manipulation, has assumed a granular character, separate it into granules of uniform and convenient size by means of suitable sieves. Dry the granules at a temperature not exceeding 55° C. (131° F.). The product weighs about one thousand *grammes*." *Br.*

This effervescent salt is intended to furnish a less disagreeable form of administering Epsom salt. Although it represents only 50 per cent. of magnesium sulphate, it is almost equally active, both the sodium tartrate and citrate which are formed being laxative.

Dose, from two drachms to one ounce (7.7–31 Gm.).

MALTUM. U. S.

MALT

(măl'tŭm)

"The grain of one or more varieties of *Hordeum sativum* Jessen (Fam. *Gramineæ*), partially germinated artificially, and then dried at a temperature not exceeding 55° C. (131° F.). It is capable of converting not less than 5 times its weight of starch into sugars. Protect it from heat and moisture." *U. S.*

Maltum Hordei; Barley Malt; Malt d'Orge, *Fr.;* Gerstenmalz, Malz, *G.*

Preparation.—Malt is prepared on an enormous scale for brewing purposes in all parts of the world where the climate is suited to the

growth of barley. The object of the process for making malt, commonly known as malting, is to allow germination of grain to go just far enough to develop the maximum amount of *diastase,* the ferment by which the starch is converted into sugar, which may afterwards undergo the alcoholic fermentation during the process of brewing. In order to achieve this, the barley is first *steeped—i.e.,* allowed to remain one or two days in cold water, of which it absorbs from 10 to 50 per cent.; second, *couched—i.e.,* thrown into heaps upon a floor and allowed to develop heat and germinate; third, when the *acrospire* or shoot is one-third the length of the grain, the latter is *floored—i.e.,* spread upon wide floors to dry; fourth, *kiln-dried—i.e.,* exposed to such a temperature as thoroughly to dry it and kill the young plant. If the temperature be raised high enough to scorch the grain, it becomes *Amber Malt,* or *Black Malt,* according to the extent of the caramelizing; only the light colored varieties of malt are suitable for pharmaceutical purposes, the black varieties being practically devoid of diastatic value and being used for coloring mainly. Besides the diastase, a second soluble ferment is formed during the malting process, the so-called *peptase,* which in the after-mash process changes the proteids of the malt into peptones and parapeptones which give nutritive value to the beer. Malt contains an alkaloid *hordenine* ($C_{10}H_{15}ON$); for a description of the physiological properties, see Part II.

Malt is now frequently germinated by what is called the pneumatic system in which the operation is carried out in large perforated iron drums which are caused to revolve very slowly, and in which the temperature is carefully regulated by ventilating fans. Another mechanical system of malting which is extensively used in some countries, especially in France, is based upon the principle of the ordinary conveyor, a separate section being used for each day that the germination lasts.

The commercial value of a sample of malt is determined by its diastatic power and also by its content of aqueous extract estimated under specified conditions. Between one-half and three-fourths of malt is soluble in cold water.

Properties.—It is composed of germinated grains with the radicles and acrospires adhering, and is officially described as follows: "Yellowish or amber-colored grains; crisp when fractured, the interior surface nearly white. It has an agreeable, characteristic odor, and a sweet taste due to the conversion of the starch in the seed into maltose, through the action of diastase. Malt floats in cold water. For the subsequent tests, prepare an infusion as follows: Mix 10 Gm. of Malt in No. 12 powder, with 100 mils of distilled water and maintain the mixture at a temperature of from 50° to 55° C. (122°–131° F.) for one hour with occasional stirring. Place it upon a filter and when the liquid has passed through, wash the contents of the filter with distilled water, in small portions, until the combined infusion and washings measure 200 mils. The weight of the solid soluble constituents of Malt, obtained by evaporating to dryness on a water bath an aliquot portion of the freshly prepared, aqueous infusion, and subsequently drying it for one hour at 100° C. (212° F.) in an air bath, corresponds to not less than 70 per cent. of the Malt taken. The acidity of Malt (calculated as lactic acid) does not exceed 0.3 per cent. as determined by titrating an aliquot portion of the freshly prepared infusion with tenth-normal potassium hydroxide V.S., phenolphthalein T.S. being used as indicator. Each mil of tenth-normal potassium hydroxide V.S. used corresponds to 0.009 Gm. of lactic acid.

"**Assay.**—To determine the starch converting power of Malt, proceed as directed under *Diastasum,* page 403, using 20 mils of the fresh infusion of malt, prepared as directed above, in place of the quantity of solution of diastase there directed." *U. S.*

Uses.—Malt is not itself used directly in medicine, but is official as the basis of Malt Extract. From it are also prepared the so-called *Malt Liquors* by making an infusion (*wort*) of the bruised malt, adding hops and various other substances, and fermenting. *Ale, brown stout,* and *porter* are made by rapid fermentation at a comparatively high temperature 23.8° C. (75° F.), while *lager beer* is prepared by a very slow, prolonged fermentation at a low temperature.

Off. Prep.—Extractum Malti, *U. S.*

MANGANI DIOXIDUM PRÆCIPITATUM. U. S.

PRECIPITATED MANGANESE DIOXIDE Mangan. Diox. Præc. [To Replace Mangani Dioxidum, U. S. 1890]

(măn'gą-nī dī-ŏx'ĭ-dŭm præ-cĭp-ĭ-tā'tŭm)

"It consists chiefly of manganese dioxide [$MnO_2 = 86.93$] with small amounts of other oxides of manganese, corresponding to not less than 80 per cent. of MnO_2." *U. S.*

Manganese Peroxide, *Br., Appendix;* Manganum Hyperoxydatum; Oxydum Manganicum; Peroxide of Manganese; Deutoxide of Manganese, Black Oxide of Manganese, Pyrolusite; Oxyde (Bi-) de Manganèse, *Fr. Cod.;* Oxyde noir de Manganèse, *Fr.;* Braunstein, *G.;* Biossido di manganese, *It.;* Manganesa, Pyrolusita, *Sp.*

The U. S. P. IX omitted a process for its manufacture, but the U. S. P. VIII process was as follows:

* "Manganese Sulphate, *fifty grammes* [or 1 ounce av., 334 grains]; Ammonia Water, *two hundred and fifty mils* [or 8 fluidounces, 218 minims]; Solution of Hydrogen Dioxide, *two hundred and fifty mils* [or 8 fluidounces, 218 minims]; Distilled Water, *a sufficient quantity.* Dissolve the manganese sulphate in *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of distilled water. Dilute the ammonia water with an equal volume of distilled water, and mix it with the solution of hydrogen dioxide, which has

also been diluted with an equal volume of distilled water. Pour the mixed solutions, slowly, with constant stirring, into the solution of manganese sulphate. Allow the mixture to stand for one hour, stirring frequently. Then decant the supernatant clear liquid from the precipitate, and wash the latter repeatedly by affusion and decantation with hot distilled water, using *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] each time. Collect the precipitate on a plain filter, and continue the washings with hot distilled water until the washings no longer have an alkaline reaction upon red litmus paper, and produce no turbidity when mixed with barium chloride test solution. Allow the precipitate to drain, then dry it at 150° C. (302° F.)." *U. S. VIII.*

The official precipitated manganese dioxide of the U. S. P. (8th Rev.) is prepared from manganous sulphate by the simultaneous action of ammonium hydroxide (which precipitates manganese hydroxide), and of hydrogen dioxide, which oxidizes this at once into the hydrated manganese dioxide. This precipitate, after thorough washing, is dried at 150° C. (302° F.), so that there remains MnO_2 as the final product.

A change was made in the U. S. P. VIII, and a process for preparing manganese dioxide was introduced; this was due to the fact that it has become very difficult to obtain native manganese dioxide of good quality; the precipitated manganese dioxide is, of course, more expensive than the native oxide, but much to be preferred in making pharmaceutical preparations. There is no method officially directed in the U. S. P. IX.

Metallic manganese was discovered by Scheele and Gahn in 1774, and is obtained from the native black oxide by intense ignition with charcoal. As obtained by C. Brunner, manganese is brittle, grayish-white, and very hard, being capable of cutting glass and scratching the best tempered steel. It is susceptible of the most perfect polish, and in the form of a fine powder decomposes water at a boiling temperature. Its sp. gr. is about 7.9.

Deville obtained the metal by heating the black oxide with charcoal in excess in a lime crucible. The metal thus obtained is more refractory than iron, while that procured by Brunner fused at the same heat as white cast iron. Greene and Wahl have lately succeeded in getting the metal in large masses by the reduction of the ores with the aid of silicon, which they add in the form of an iron silicide. The atomic weight of manganese is 54.93. With oxygen it forms five and possibly seven compounds: MnO, Mn_2O_3, Mn_3O_4, MnO_2, and Mn_2O_7. The *monoxide* is of a light green color, and is the oxide present in, or corresponding to, manganous salts. The *sesquioxide* is black or dark brown, when in the hydrated state; the *magnetic oxide*, Mn_3O_4, is red; the dioxide is black; and the permanganic oxide, Mn_2O_7, is, when in the free state, a very unstable dark reddish-brown liquid. The monoxide is a stable base, the sesquioxide is feebly basic, and the dioxide when acted upon by acids yields manganous salts, while oxygen is evolved. The highest oxide is acid-forming yielding permanganic acid, $HMnO_4$, the salts of which are known as permanganates. (See *Potassii Permanganas.*) There exists also an acid, H_2MnO_4 (*manganic*), of which the salts formed are called manganates. The oxide corresponding is not known, however. Metallic manganese is an occasional constituent of organic matter. It has been detected in minute quantity in bone, hair, brain, epidermis, gastric juice, bile, urine, and pus, and has been found by Millon and others in the blood. Glénard of Lyons, denies that it is a normal constituent of the blood, although sometimes present, but the evidence of numerous experimenters shows that it generally exists in that fluid, and when not detected it may be because the quantity present is too minute to be easily discovered. According to E. Davy, potassium hydroxide, dissolved in an equal weight of water, forms a delicate test for manganese, not obscured by the presence of other metals. The smallest portion of matter suspected to contain the metal, being finely pulverized or in solution, is placed upon a slip of silver foil, and a drop of the test added. Upon evaporation to dryness with a spirit lamp, and raising the heat, the characteristic green potassium manganate will appear on the foil. (*Chem. Gaz.*, March 15, 1854.) Manganese is a constituent of all arable land, and is found in the ashes of most of the vegetables which form the food of man and the inferior animals. In the mineral kingdom it occurs sometimes as silicate (*rhodonite*) or carbonate (*diallogite* and *rhodocrosite*), and very abundantly as the black oxide, or dioxide, called *pyrolusite* or other oxides (*hausmannite* and *braunite*). The latter mineral was formerly the British official oxide. It is now in the Appendix of the British Pharmacopœia and is defined as follows: "Manganese Peroxide, MnO_2, the powdered native pyrolusite."

But few mines of manganese dioxide exist, though the metal itself is very generally diffused throughout the mineral kingdom. It occurs most abundantly in the Russian Caucasus, which furnishes nearly half of the annual production of the world, in Chili, Cuba, Great Britain, Turkey, and Australia. In the United States it occurs in largest amount at Crimora, Va., Cartersville, Ga., and Batesville, Ark.; other isolated localities exist in California, Utah, Alabama, and Tennessee. The amount of manganese ore mined in the United States is at present very small, being only 3146 tons in 1904, although large quantities of manganiferous iron ores, manganiferous silver ores and manganiferous zinc residues are obtained, which go into the manufacture of spiegeleisen and ferro-manganese. On the other hand, very pure manganese ore is imported chiefly from the Caucasus, the amount in 1905 having been 257,033 tons. It comes packed in casks or barrels, gen-

erally in lumps and coarse powder, just as it is dug out of mines, though occasionally it is received from England in a pulverized condition. It is a good rule to buy it unpowdered, as its quality can be better judged in that state. A dark shining crystalline appearance is an indication of good quality, although an assay will alone determine its quality with certainty.

Properties.—Manganese dioxide, as it occurs in nature, is very diversified in its appearance. Its sp. gr. varies from 4.7 to 4.9. It is found sometimes in brilliant needle-shaped crystals, often in compact masses having the metallic luster, but far more frequently in the form of a dull earthy-looking substance of a black or brown color. It is purest when crystallized. As it occurs in commerce, it is usually in the form of a black powder, insoluble in water, and containing more or less oxidized iron, calcium carbonate, barium sulphate, and earthy matter. Iron, which is rarely absent, is detected by the production of a green or blue tint on the addition of potassium ferrocyanide to its hydrochloric acid solution. When exposed to a red heat it yields a portion of its oxygen, and is reduced to manganoso-manganic oxide. Hence its use in obtaining that gas. Good samples, after being dried, lose, when heated to whiteness, 12 per cent. of oxygen. It is distinguished from antimony sulphide which it physically resembles by its infusibility, and by causing the evolution of chlorine on being heated with hydrochloric acid. When of a brown color, it is not of good quality.

The U. S. Pharmacopœia describes the precipitated manganese dioxide as "a heavy, very fine, black powder, without odor or taste; permanent in the air. It is insoluble in water or alcohol. When heated with hydrochloric acid, it is converted into manganous chloride and chlorine is evolved. At a red heat Precipitated Manganese Dioxide gives off oxygen and is converted into reddish-brown manganous-manganic oxide (Mn_3O_4). Add 2 drops of hydrochloric acid to about 0.1 Gm. of Precipitated Manganese Dioxide contained in a test tube, boil the mixture for one minute with 0.5 Gm. of lead peroxide and 5 mils of nitric acid and then add 5 mils of distilled water; the liquid assumes a reddish-violet color. Add 20 mils of distilled water to 1 Gm. of Manganese Dioxide and 2 Gm. of oxalic acid, follow this by 3 mils of sulphuric acid, and digest the mixture for several hours on a water bath; not more than 0.2 per cent. of residue remains (*insoluble substances*).

"**Assay.**—Dissolve about 0.2 Gm. of Precipitated Manganese Dioxide, accurately weighed, in a mixture of 50 mils of tenth-normal oxalic acid V.S. and 3 mils of sulphuric acid, heat to 80° C. (176° F.) on a water bath, and titrate the residual oxalic acid with tenth-normal potassium permanganate V.S. It shows not less than 80 per cent. of MnO_2.

"Each mil of tenth-normal oxalic acid V.S. used corresponds to 0.0043465 Gm. of MnO_2. Each gramme of Precipitated Manganese Dioxide corresponds to not less than 184 mils of tenth-normal oxalic acid V.S." *U. S.*

Uses.—Because manganese has been found to be a normal constituent of hemoglobin it was conjectured that it might have a similar effect to iron in restoring impoverished blood, and it was at one time used to a considerable extent in the treatment of various forms of *anemia,* but experience has proven it to be a drug of little or no value in this condition. It appears to possess some stimulant action upon the uterine mucosa and is still used in the treatment of *amenorrhea.* Its ancient employment in *syphilis, scurvy,* and various *skin diseases,* does not appear to be founded on any rational basis. Leared (*Glasgow Med. Journ.,* Jan., 1865) has suggested the use of manganese dioxide for its antacid effects in gastric conditions, such as *pyrosis.*

The native oxide is used in the arts for obtaining chlorine in the manufacture of bleaching powder, for giving a black glazing to pottery, and for freeing glass from the color which it derives from iron. In the laboratory it is employed to obtain oxygen and chlorine, and to form the salts of manganese. It is also used for liberating chlorine from hydrochloric acid and from sodium chloride, and iodine from sodium iodide contained in kelp.

Dose, three to ten grains (0.2–0.65 Gm.).

MANNA. U. S.

MANNA

(măn'nạ)

"The dried saccharine exudation of *Fraxinus Ornus* Linné (Fam. *Oleaceæ*)." *U. S.*

Manne, *Fr. Cod.;* Manna, *P. G., It.;* Mana, *Sp.*

Manna is said to be obtained from several other trees besides *Fraxinus Ornus,* among which *F. rotundifolia, F. excelsior,* and *F. parviflora* have been particularly designated. Many saccharine substances, generally exudations from plants, have, from their resemblance to this substance, obtained the name of manna, and attracted more or less attention from writers. The term "manna" has been applied to certain substances which have no relation to true manna, notably to the lichen *Lecanora esculenta,* which at times has suddenly fallen like rain over immense tracts of country, from Persia to the African Sahara. It occurs in the form of small roundish lumps, from the size of a pin's head to that of a pea, yellowish or grayish externally and whitish within, hard, inodorous, and insipid. It has been affirmed that this lichen does not contain starch, but it is really used as an article of food, and good bread is said to have been made out of it. (*Nature,* Jan., 1891.) It is probable that it is the manna of Scripture.

The proper false mannas, exudations from various trees, are best considered under the headings of the countries which yield them:

European False Manna, or *Briançon Manna,* an exudation from the common European larch

(*Larix europæa,* or *Pinus Larix*), differs chemically from ordinary manna in containing no mannite. Berthelot found in it a peculiar sugar, which he named *melezitose.* (See *A. J. P.,* 1859, p. 61.) To this the formula $C_{18}H_{32}O_{16} + 2H_2O$ is given showing that it belongs to the class of the saccharides.

American False Manna.—A substance resembling manna, of a sweet, slightly bitter and terebinthinate taste, and actively purgative, exudes from incisions in *Pinus lambertiana,* of Oregon, and was used by the natives. Berthelot has extracted from this product a peculiar saccharine principle, which he calls *pinite.* It is very sweet, but does not undergo the vinous fermentation. (See *A. J. P.,* xxviii, 157.) Pinite was for a long time classed among the sugars, but the latest researches seem to show that it is a hexahydric phenol derived from hexahydrobenzene. The formula is $C_{17}H_{14}O_6$, and it is a methyl derivative of inosite.

California Manna, or *Father Picolo's Manna.*—Proust (*Ann. d. Chim.,* 1806, 145) alludes to a manna mentioned by Father Picolo as being deposited on a species of grass in California. J. U. Lloyd (*A. J. P.,* 1897, 337) believes Picolo's manna to be a saccharine deposit, caused by aphides on *Phragmites communis.* It is apparently still collected by the Indians.

African False Mannas.—Turkish Manna is a sweet product obtained from *Echinops persica* Fisch., and is obtained by treating the cocoons of a coleopterous insect (*Larinus maculatus*) with hot water, filtering and crystallizing the sugar. From it Berthelot obtained a new variety of sugar, *trehalose,* $C_{12}H_{22}O_{11} + 2H_2O$. (*Gaz. Méd. de Paris,* 1857.) *Pinus Cedrus,* of Mount Lebanon, yields a similar product, which has some repute in Syria as a remedy in *phthisis.* (*P. J.,* xiii, 411.) In the neighborhood of Diarbekir, in Asiatic Turkey, a saccharine substance, known as *Diarbekir manna,* is found on the leaves of dwarf oaks, from which it appears to be exuded. (*P. J.,* Nov., 1862, p. 546.) The manna of the oak of Kurdistan, spoken of by Flückiger, is probably the same as that of Diarbekir, which may be its entrepôt. According to Flückiger, this consists chiefly (90 per cent.) of a crystallizable sugar. It deviates to the right the plane of polarized light, and reduces in the cold the solution of copper oxide in soda and glycerin. This manna contains a mucilage, but no cane sugar or dextrin. (*J. P. C.,* April, 1873, p. 335.) *Quercus Vallonea* Kotschy, and *Q. persica* Jaub. et Spach, yield "*oak manna,*" through insect agency, while certain species of *Echinops* (probably *E. persica* Fisch.) yield the singular manna-like substance that is known as *Trehala* in Syria and as *Shukkar Tigal* in India. *Pyrus glabra* yields a manna which is collected by the people of Luristan, in Persia. It has long been known that *Salix fragilis* and probably other species of willow yield to the Persians a manna-like exudation. According to Raby (*L'Union Pharm.,* May, 1889), there are two varieties, *chirkhest* and *bidenguébin,* which contain respectively, according to the analysis of Ludwig, *chirkhestite* ($C_6H_{14}O_6$), allied to sorbite, and *bidenguebinose* ($C_{12}H_{22}O_{11}$), allied to melezitose. Whether these mannas are really distinct from those sold in the Indian bazaars as coming from Afghanistan and Persia seems uncertain. Of these bazaar mannas the most important is the *Shirkoit* or *Oriental* manna. By Haussknecht it is referred to *Atraphaxis spinosa;* but J. E. T. Atchison states that it is yielded by the *Cotoneaster nummularia* Fisch. et Mey., a tall, stout shrub, whose smaller branches in July become covered with an exudation, which is eaten as a sweetmeat, and exported in quantity to Russia and India. The second variety, *Taranjabin,* is yielded by the camelthorn, *Alhagi Camelorum* Fisch., in Persia and Afghanistan, and probably by *Alhagi Maurorum* of De Candolle, a leguminous thorny shrub abundant in India—if indeed the two species be distinct. According to A. Villiers, it is nearly pure melezitose. (*P. J.,* 1876, 3d ser., vii, 917.) Another kind of manna is *Gazangabin,* or *Gazanjabin,* yielded by *Tamarix gallica* Linn., var. *mannifera;* a fourth kind is obtained from the *Salsola fœtida* DC. (*P. J.,* Dec. 11, 1886, 467.) The *tamarisk* of Northern Africa (*Tamarix gallica* Ehr.), which produces the small *tamarisk galls* of Mogador, containing 40 per cent. of tannic acid (*A. J. P.,* 1878, p. 27; also *N. R.,* 1877, p. 41), according to Burckhardt also gives origin to a species of manna that is used by the Bedouin Arabs near Mount Sinai with their food. This substance, however, according to Mitscherlich, contains no mannite, but consists wholly of mucilaginous sugar. Berthelot found a manna from Sinai to consist of 55 per cent. of cane sugar, 25 of levulose and glucose, and 20 of dextrin and analogous substances. (*Ann. Ch. Phys.,* lxvii.)

Persian Manna, or *Gez,* has been identified (*C. D.,* 1894, 790) as being derived from *Astragalus anisacanthus,* and is found in the districts of Khonsar, Feridan and Chahar Mahal, and Ispahan. In the form of sweetmeat, having the appearance of flour, it is sent all over Persia and much esteemed.

Australian Mannas.—A manna-like exudation on the *Eucalyptus viminalis* Labill., growing in New South Wales, contains a saccharine matter called *melitose,* different in properties from mannite and from all the varieties of sugar, though isomeric with glucose. It is susceptible of the vinous fermentation. (See *A. J. P.,* xxviii, 157.) *Lerp* is produced upon the leaves of *Eucalyptus dumosa,* when very small, and sometimes appears spread over large extents of country like a kind of snow. The natives use it for food. It is a complex body, containing an unfermentable sugar, *eucalin,* gum, starch, inulin, and lignin. (*J. P. C.,* xvi, 240.) It is said to be a secretion from an insect, formed into minute cells, each of which is the abode of one of the insects. (See *A. J. P.,* 1862, p. 547.) *Myoporum platycarpum* R. Br., the *sandalwood-* or *dogwood-tree* of Australia, exudes

an exceedingly sweet and pleasant manna, which is much used as an article of food. The product is identical with the official manna, containing nearly 90 per cent. of mannite. F. W. Passmore obtained from *Eucalyptus Gunnii* Hook., a sugar termed *melitriose.* (*P. J.*, 1891, 718.)

New South Wales Manna.—According to R. T. Baker (*Journ. and Proc. Roy. Soc. New South Wales*, xxx, 1897), this manna is produced in the form of nodules at the nodes of the stems of the blue grass *Andropogon annulatus.* It contains numerous crystals of mannite, amounting, according to the analysis of H. G. Smith, to 50 per cent.

Fraxinus Ornus, or the *European flowering ash* is a tree of moderate height, usually from twenty to twenty-five feet, very branching, with opposite, petiolate, pinnate leaves, composed of three or four pairs of leaflets, and an odd one at the end. The leaflets are oval, acuminate, obtusely serrate, about an inch and a half in length, smooth, of a bright green color, and supported on short footstalks. The flowers are white, and usually expand with the leaves. They grow in close panicles at the extremities of the young branches, and have a very short calyx with four teeth, and four linear-lanceolate petals.

Fraxinus Ornus is native of Sicily, Calabria, and Apulia, and is cultivated in Sicily. It yields manna after the eighth year, and continues to yield it for ten or twelve years, when it is usually cut down and young sprouts are allowed to grow up from the root. (Stettner, *A. Pharm.*, liii, 194.) During the hot months the juice exudes spontaneously from the bark, and concretes upon its surface, but, as the exudation is slow, it is customary to facilitate the process by making deep longitudinal incisions on one side of the trunk. In the following season these are repeated on the other side, and thus alternately for the whole period during which the tree yields manna, extending sometimes, it is said, to thirty or even forty years. Straw or chips are frequently placed so as to receive the juice, which concretes upon them. The manna varies in its character according to the mode of collection, the nature of the season, and the period of the year at which the exudation takes place. That procured in Sicily is said to be the best. Daniel Hanbury travelled through the old manna region, and satisfied himself that the collection of manna for commercial purposes is confined almost exclusively to Sicily. (*P. J.*, Nov., 1872, 421.) For information on manna collection in Sicily, see notes by J. S. Ward. (*P. J.*, 1893, 381.) For an interesting description of California mannas by J. U. Lloyd, particularly *Picolo's manna*, see *A. J. P.*, 1897, 329.

In commerce three varieties are distinguishable:

1. Flake Manna, or *manna canulata* (*cannellata*), is the purest variety, and is chiefly obtained from Palmero. It exudes spontaneously, or from incisions, during the hottest and dryest weather in July and August. According to Stettner, it is furnished by the upper incisions upon the trunk, while the lower incisions yield the inferior varieties. It is in irregular, unequal pieces, often several inches long, resembling stalactites, rough, light, porous, brittle, whitish or yellowish-white, and frequently concave on the surface by which they were attached to the trunk, and which is often soiled by impurities, sometimes by adherent fragments of the bark. When broken, these pieces exhibit a crystalline or granular structure. This variety is sometimes in small fragments, generally less than an inch in length.

2. Common Manna—*manna communis*, or the *manne en sorte* of French pharmacy—is next in quality, and is collected in Sicily in September and the beginning of October, when the heat of the weather has begun to moderate. The juice does not now concrete so readily, and a portion, falling on the ground at the root of the tree, becomes more or less mixed with impurities, and forms imperfectly solid masses, which require to be further dried in the sun. Common manna consists of whitish or yellowish fragments, similar to the pieces of flake manna, but much smaller, mixed with a soft, viscid, uncrystallized brownish matter, identical with fat manna.

3. Fat Manna, or *Manna* (*pinguis*) *sordida*, is collected in the latter part of October and November, when the weather is cooler and rains are more common. The juice is now still less disposed to concrete, and flowing down the trunk is received in a small excavation at its base. As found in commerce, it is in the form of a soft, viscous mass, containing few crystalline fragments, of a brown or yellowish-brown color, and full of impurities. The U. S. Pharmacopœia directs that such manna should be rejected.

Fictitious Manna.—Attempts have been made to counterfeit manna, but the facility of detection renders such frauds unprofitable, and they are not often practised. R. P. Thomas described (*A. J. P.*, xxiv) a sophisticated manna which differed from the genuine drug both in sensible and in chemical properties, not even containing mannite. Baumé describes a method in which common manna is purified so as to resemble flake manna. It consists in dissolving common manna in a little water, allowing the liquid to settle, decanting it in order to separate the impurities, then inspissating it so that it will congeal on cooling, and immersing threads in the inspissated liquid, several times successively, in the manner practised by candle makers. It may be still further purified by the use of animal charcoal. Thus prepared, it contains less mannite than flake manna, and less of the nauseous principle, but is said not to operate less effectively as a laxative. A fictitious manna is described by Edmond Histed (*P. J.*, April, 1870) as having been taken from Paris to London, which bears a close resemblance to

flake manna, for which it might be mistaken upon a hasty notice. The resemblance was, moreover, increased by the fact that it contains mannite, of which Histed obtained 40 per cent., while fine natural flake manna yielded him 70 per cent. Closely examined, it is found to differ essentially from genuine flake manna, showing no crystals of mannite when broken, not having the taste and smell characteristic of good manna, and, besides, being cleaner, lighter-colored, more solid, and making a clearer solution in water. (See *A. J. P.*, 1870.) This may have been a specimen of artificial flake manna, prepared from the inferior or common manna.

Properties.—Manna is officially described as "in irregular, more or less elongated, flattened, 3-sided pieces; externally yellowish-white; friable, somewhat waxy; internally nearly white, porous and crystalline in appearance; odor slight, but characteristic; taste sweet, slightly bitter and faintly acrid. Manna also occurs in irregular masses, consisting in part of brittle or soft, resin-like fragments; from yellowish-white to yellowish-gray in color. The quantity of the yellowish-white fragments must not be less than 40 per cent. of the whole. Add 5 Gm. of Manna to 100 mils of alcohol, heat to boiling and filter; on cooling, the filtrate rapidly deposits crystals of mannite." *U. S.*

Manna has a slight, peculiar odor, and a sweet taste, which in the impure kinds is also very nauseous, but in the finest flake manna scarcely so much so as to be disagreeable. Its sp. gr. is 0.834. It melts with heat, and takes fire, burning with a blue flame. When pure it is soluble in three parts of cold and in its own weight of boiling water. From a boiling saturated aqueous solution it separates in partially crystalline masses on cooling. Alcohol also dissolves it. Boiling alcohol will dissolve 15 parts of manna, and upon cooling deposit beautiful crystals of mannite.

Ebert (*Zeit. Oest. Apoth. Ver.*, xlvi, p. 427) has contributed a very able paper, containing citations of all the literature up to 1908, regarding the origin and pharmacognosy of the different varieties of manna. Probably the most comprehensive monograph on the ash manna is that of Tschirch in his large work entitled "*Handbuch der Pharmakognosie.*" Band II, p. 103.

Fourcroy and Vauquelin found manna to consist of (1) a peculiar sweet principle, *mannite*, which constitutes 75 per cent.; (2) a variety of sugar; (3) a yellow nauseous matter, upon which the purgative property is thought chiefly to depend; and (4) a little mucilage. Leuchtweiss obtained from 105 parts of manna, 11.6 of water, 0.4 of insoluble matter, 9.1 of sugar, 42.6 of mannite, 40.0 of a mixture of mucilaginous matter containing mannite, resin, organic acid, and a nitrogenous substance, and 1.3 of ashes. In *manna canellata in fragmentis* he found 37.6 per cent. of mannite, and in *manna Calabrina* 32 per cent. (*Pflanzenstoffe*, 2d ed., p. 180.) Buignet discovered in manna a considerable proportion of dextrin. He appears to have been led to this discovery by observing a very energetic dextrogyrate power in flake manna, which could not be owing to the saccharine matter it contained, because the same power continued after all the sugar had been destroyed by fermentation. Dextrin forms about one-fifth part of flake manna, and a much larger part of the inferior kinds. Tanret (*Bul. Soc. Ch.*, 1902, p. 947) finds manna to contain several new carbohydrates and reports the composition as follows: mannitol, 40 to 55 per cent.; levulose, 2.5 to 3.4 per cent.; dextrose, 2.2 to 3.0 per cent.; manneotetrose ($C_{24}H_{42}O_{21} + 4H_2O$), 12 to 16 per cent.; manneotriose ($C_{18}H_{32}O_{16}$), 6 to 16 per cent., with small amounts of resin and ash.

Flückiger found in all samples of mannite examined a small amount of a dextrogyrate mucilage, which is precipitated by neutral lead acetate, and yields mucic acid when boiled with strong nitric acid. The greenish color of certain pieces of manna is produced by *fraxin*, $C_{16}H_{18}O_{10}$, a glucoside closely resembling *æsculin*. Fraxin crystallizes in colorless prisms, easily soluble in hot water and in alcohol, and has a faintly astringent and bitter taste. By diluted acids it is resolved into *fraxetin*, $C_{10}H_8O_5$, and *glucose*, $C_6H_{12}O_6$. Even its diluted solutions are fluorescent. (*Pharmacographia*, 2d ed.)

Mannite (*mannitol*) is white, inodorous, crystallizable in semi-transparent needles, of a sweetish taste, soluble in five parts of cold water, scarcely soluble in cold alcohol, but readily dissolved by that liquid when hot, and deposited when it cools. Its composition is $C_6H_{14}O_6$, and it is considered as belonging to the class of *hexatomic alcohols*. If mixed with chalk and cream-cheese and kept for some weeks at the temperature of 40° C. (104° F.), it yields alcohol largely, with the disengagement of carbonic acid and hydrogen and the production of lactic acid. No fungus is produced, as in the ordinary fermentation of sugar. (Berthelot, *J. P. C.*, xxx.) With lime, barium and strontium oxides, it forms definite compounds, soluble in water, and precipitable from their aqueous solutions by alcohol. (*Ibid.*, Jan., 1860.) It does not reduce an alkaline solution of copper oxide; and a test of its purity is thus presented. (*A. J. P.*, Jan., 1861, p. 26.) It is optically inactive except after the addition of borax. It is then found to be dextrorotatory. Emil Fischer has shown that there are three mannites obtainable; the ordinary mannite is the dextrorotatory variety, and is always obtained in the reduction of *a*-mannose with sodium amalgam; a lævorotatory variety is obtained by the reduction of *l*-mannose; and an inactive mannite is obtained from the inactive mannose. These three physical isomers differ slightly in their fusing points and crystalline form. The native variety may be obtained by boiling manna in alcohol, allowing the solution to cool, and redissolving the crystalline precipitate; pure mannite is now deposited. An-

other method is to dissolve flake manna in water, precipitate by solution of lead subacetate, filter, throw down the excess of lead by sulphuric acid, evaporate the solution, and mix with alcohol. On cooling, the mannite is deposited. (Bonsall, *A. Pharm.*, cxxxiv, 70.) This principle has been found in numerous vegetables. It is said to be gently laxative in the dose of from one to two ounces (31–62 Gm.).

Manna, when long kept, acquires a deeper color, softens, and ultimately deliquesces into a liquid, which on the addition of yeast, undergoes the vinous fermentation. This is probably owing to its conversion into sugar by the absorption of enough oxygen to cause it to pass over into some variety of glucose or fermentable sugar. That which is driest resists this change the longest. It is said that manna recently gathered is less purgative than it afterwards becomes.

Uses.—Manna is a gentle laxative, usually operating mildly, but in some cases producing flatulence and pain. It is usually prescribed with other purgatives, particularly senna, rhubarb, magnesia, and the neutral salts, the taste of which it conceals, while it adds to the purgative effect. It is usually given dissolved in water or some aromatic infusion; but the best flake manna may be administered in substance. Manna forms a combination with iron, which it preserves against oxidation. (See *P. J.*, March, 1873.) Under the name of *dulcinol* a mixture of mannite and common salt has been recommended by Sternberg (*D. M. W.*, 1906, p. 1707) as a sweetening agent in *diabetes*.

Dose, half to one ounce (15.5–31 Gm.).

Off. Prep.—Infusum Sennæ Compositum, *U. S.*; Syrupus Mannæ, *N. F.*

MASSA FERRI CARBONATIS. U. S.

MASS OF FERROUS CARBONATE Mass. Ferr. Carb.
[Vallet's Mass]

(măs'sa fĕr'rī cär-bo-nā'tĭs)

"It contains not less than 35 per cent. of $FeCO_3$ (115.84)." *U. S.*

Pilula Ferri Carbonatis, *Br.* 1885, also *U. S.* 1870; Pilulæ Ferri Carbonici, Pilulæ Ferratæ Valleti; Pill of Carbonate of Iron, Vallet's Ferruginous Pills, Vallet's Pill Mass; Pilules de Carbonate ferreux, *Fr. Cod.*; Pilules ferrugineuses, Masse Pilulaire de Vallet, *Fr.*; Valletsche Pillen, *G.*; Pillole di Vallet, *It.*

* "Ferrous Sulphate, *one hundred grammes* [or 3 ounces av., 231 grains]; Monohydrated Sodium Carbonate, *forty-six grammes* [or 1 ounce av., 272 grains]; Clarified Honey, *thirty-eight grammes* [or 1 ounce av., 150 grains]; Sugar, in coarse powder, *twenty-five grammes* [or 386 grains]; Syrup, Distilled Water, each, *a sufficient quantity*, to make *one hundred grammes* [or 3 ounces av., 231 grains]. Dissolve the ferrous sulphate and the monohydrated sodium carbonate, each separately, in *two hundred mils* [or 6 fluidounces, 366 minims] of boiling distilled water, and, having added *twenty mils* [or 325 minims] of syrup to the solution of the iron salt, filter both solutions, and allow them to become cold. Place the solution of monohydrated sodium carbonate in a bottle having a capacity of about *five hundred mils* [or 16 fluidounces, 435 minims], and gradually add the solution of the iron salt, rotating the bottle frequently, until carbonic acid gas no longer escapes. Add sufficient distilled water to fill the bottle; then cork it and set it aside, so that the ferrous carbonate may subside. Pour off the supernatant liquid, and, having mixed syrup and distilled water in the proportion of *one volume* of syrup to *nineteen volumes* of distilled water, wash the precipitate with the mixture by decantation until the washings no longer have a saline taste. Drain the precipitate on a muslin strainer, and express as much of the water as possible. Lastly, mix the precipitate at once with the clarified honey and sugar, and, by means of a water-bath, evaporate the mixture in a tared dish, with constant stirring, until it is reduced to *one hundred grammes* [or 3 ounces av., 231 grains]." *U. S.*

"**Assay.**—Dissolve about 1 Gm. of Mass of Ferrous Carbonate, accurately weighed, in 15 mils of diluted sulphuric acid, dilute the solution with distilled water to about 100 mils and immediately titrate with tenth-normal potassium dichromate V.S., potassium ferricyanide T.S. being used as indicator. It shows not less than 35 per cent. of $FeCO_3$.

"Each mil of tenth-normal potassium dichromate V.S. used corresponds to 0.011584 Gm. of $FeCO_3$. Each gramme of Mass of Ferrous Carbonate corresponds to not less than 30.2 mils of tenth-normal potassium dichromate V.S." *U. S.*

The effect of saccharine matter in protecting iron from oxidation has been explained under the heads of *Ferri Carbonas Saccharatus* and *Syrupus Ferri Iodidi*. The U. S. mass of ferrous carbonate is another example of a ferruginous preparation in which the iron is protected from further oxidation by the same means. The process of the U. S. P. IX is nearly the same as that of the U. S. P., 1890, excepting that the monohydrated sodium carbonate has replaced the crystallized variety, and the quantity of the alkaline salt has been somewhat increased. The salts employed are the same as those used for obtaining the formerly official ferric subcarbonate which was misnamed, as in forming that preparation the carbonate which is at first precipitated absorbs oxygen, and loses nearly all its carbon dioxide in the processes of washing and drying. When, however, as in the U. S. formula above given, the reacting salts are dissolved in weak syrup instead of water, and the washing is performed with weak syrup also, the absorption of oxygen and loss of carbon dioxide during the separation of the precipitate are almost completely prevented. It only remains, therefore, to preserve it unaltered, and to bring it to the pilular consistence, and this is effected by admixture with honey and sugar, and evaporation by means of a water bath. It is essential to the success

of this process that the ferrous sulphate should be pure, otherwise some ferric oxide will be present in the product. The process is that of Vallet, of Paris, after whom the preparation is popularly called.

The British Pharmacopœia, 1898, omitted Vallet's mass. (See *Ferri Carbonas Saccharatus.*) Gonnermann prepares *powdered Vallet's mass* by mixing intimately ten parts of milk sugar and five parts of powdered licorice root with sufficient freshly precipitated ferrous carbonate to make, when dried, thirty-five parts, and adding enough powdered licorice root to make the whole weigh forty parts. (*Ph. Post,* 1893, 238.)

Properties.—The U. S. preparation is in the form of a soft pilular mass, of a dark greenish-gray color, becoming black on exposure, and with a strong ferruginous taste. When carefully prepared, it is wholly and readily soluble in acids. It contains nearly half its weight of ferrous carbonate. The corresponding pill, obtained from the saccharine carbonate, may be supposed to contain one-third of ferruginous matter.

Uses.—The U. S. mass of ferrous carbonate, or Vallet's ferruginous mass, is an excellent preparation for use in simple *anemia* and *chlorosis.* Its chief merits are its unchangeableness, its freedom from astringency, and its ready solubility in acids.

Dose, in pills, from three to five grains (0.20–0.32 Gm.), after meals.

MASSA HYDRARGYRI. U. S. (Br.)

MASS OF MERCURY Mass. Hydrarg. [Blue Mass Blue Pill]

(măs'sa hȳ-drär'gȳ-rī)

"It contains not less than 32 per cent. nor more than 34 per cent. of Hg. Preserve the product in well-closed containers." *U. S.*

Pilula Hydrargyri, *Br.,* Mercury Pill; Pilulæ Hydrargyri, *U. S.* 1870; Pilulæ Cœruleæ, Massa Cœrulea; Pills of Mercury; Mercurial Pill; Pilules mercurielles simples, *Fr. Cod.;* Pilule de Mercure, Pilules bleues, *Fr.;* Mercurialpillenmasse, *G.*

* "Mercury, *thirty-three grammes* [or 1 ounce av., 72 grains]; Oleate of Mercury, *one gramme* [or 15 grains]; Glycyrrhiza, in No. 60 powder, *ten grammes* [or 154 grains]; Althæa, in No. 60 powder, *fifteen grammes* [or 231 grains]; Glycerin, *nine grammes* [or 139 grains]; Honey of Rose, *thirty-two grammes* [or 1 ounce av., 56 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Triturate the oleate of mercury in a warm mortar, gradually add the mercury, then introduce a small amount of honey of rose and triturate the mixture until globules of mercury are no longer visible under a lens magnifying ten diameters. Now incorporate the remainder of the honey of rose and the glycerin, then gradually add the glycyrrhiza and althæa and continue the trituration until the mass is homogeneous." *U. S.*

"Mercury, 40 *grammes;* Confection of Roses, 60 *grammes;* Liquorice Root, in powder, 20 *grammes.* Triturate the Mercury with the Confection of Roses until metallic globules are no longer visible; add the Liquorice Root; mix to form a mass." *Br.*

"**Assay.**—Place about 0.5 Gm. of Mass of Mercury, accurately weighed, in a porcelain dish, add 10 mils of sulphuric acid, heat on a water bath for ten minutes, then add 10 mils of nitric acid and heat the mixture on a sand bath, adding small portions of nitric acid, if necessary, until a colorless or nearly colorless solution results. Now add potassium permanganate T.S. to the hot solution until the red color persists, then discharge the color by the addition of just sufficient oxalic acid T.S. Wash the solution into a flask with distilled water, dissolve any insoluble residue by the addition of nitric acid, dilute the solution to about 150 mils, add 2 mils of ferric ammonium sulphate T.S. and titrate the solution with tenth-normal potassium sulphocyanate V.S. to the production of a pink tint. It shows not less than 32 per cent. nor more than 34 per cent. of Hg.

"Each mil of tenth-normal potassium sulphocyanate V.S. used corresponds to 0.01003 Gm. of Hg. Each gramme of Mass of Mercury corresponds to not less than 31.9 nor more than 33.9 mils of tenth-normal potassium sulphocyanate V.S." *U. S.*

The mercury constitutes one-third of the mass. The U. S. process is well suited for the needs of the pharmacist, as the mass can be made with ordinary apparatus extemporaneously. The proportion of glycerin, in the formula which was increased in the U. S. VIII overcomes the tendency to harden slowly and become unfitted for use which was characteristic of the U. S., 1890, preparation.

The precise condition of the mercury in this preparation is somewhat uncertain. By far the greater proportion is in a state of minute mechanical division, and not chemically altered. Some maintain that the whole of the metal is in this state, others, that a small portion is converted during the trituration into mercurous oxide, and that this is the ingredient upon which the activity of the pill depends. The supposed oxidation is attributed partly to the influence of the air upon the surface of the metal, greatly extended by the separation of its particles, partly to the action of the substance used in the trituration. If the mercury is not oxidized during the trituration, there can be little doubt that it becomes so, to a slight extent, by subsequent exposure. The obvious changes which the mass undergoes by time can be explained in no other way, and mercurous oxide is asserted to have been actually extracted from old mercurial pill. Harold Senier analyzed a number of samples of blue mass, with the view of determining the amount of metallic mercury and of mercurous and mercuric oxides. The results showed that the latter gradually increased in quantity with the age of the blue mass, which, 18 hours after preparation, con-

tained but a trace of mercurous oxide; after three months, 0.24 per cent. of mercuric and 0.62 per cent. of mercurous oxides were obtained, and in another sample, 0.44 and 1.60 per cent., respectively. After two years, 1.80 per cent. of mercuric and 4.22 per cent. of mercurous oxides were present. (*P. J.*, 1876.) Nevertheless, it scarcely admits of dispute that the metal, independently of oxidation out of the body, is capable of producing the peculiar mercurial effects when introduced into the stomach, probably undergoing chemical changes there. The U. S. VIII provided a test which limited the quantity of mercurous oxide and proved the absence of mercuric oxide; it will be difficult for the ordinary "blue mass" of commerce to withstand these requirements: "If a portion of the Mass be triturated in a mortar, with warm acetic acid, the filtrate should not become more than slightly opalescent on the addition of a few drops of hydrochloric acid (limit of *mercurous oxide*). If another portion of the Mass be digested with warm, diluted hydrochloric acid and a little purified animal charcoal, the filtrate should not be affected by hydrogen sulphide T.S., or by stannous chloride T.S. (absence of *mercuric oxide*)." *U. S. VIII.* All agree that the efficacy of the preparation is proportionate to the extinguishment of the mercury; in other words, to the degree in which the metallic globules disappear. This may be effected by trituration with various substances, and manna, syrup, honey, licorice, mucilage, soap, guaiac, and extract of taraxacum have been recommended, among others, for this purpose; but the oleate of mercury has been adopted by the U. S. P. IX as less open to objection than any other. The mercury is known to be completely extinguished when, upon rubbing a portion of the mass with the end of the finger upon a piece of paper, no globules appear, or the extinguishment may be more accurately judged by the official microscopic test. Powdered licorice root and powdered marshmallow root are added in order to give due consistence to the mass. It is possible for the apothecary to make moderate quantities extemporaneously with no other appliances than the mortar and pestle. As the trituration requires to be long continued, which renders the process very laborious when conducted on the large scale, it is customary to prepare the mass by machinery. A machine which has been employed consisted of "a circular iron trough for the reception of the materials, in which revolve four wooden cylinders, having also a motion on their axes." A machine for preparing blue mass, capable of being worked by hand or steam power, was invented by J. W. W. Gordon, of Baltimore, and, having been found to answer well, was at one time in extensive use. (*A. J. P.*, xxi, 6.) We have referred, under *Hydrargyrum cum Creta* (page 569) to another ingenious apparatus, invented by Squibb, by which the extinguishment of mercury is very satisfactorily effected. Formerly much of the blue mass used in this country was imported, but at present the market is chiefly supplied by our own manufacturers. The preparation slowly changes color upon being kept, assuming an olive and sometimes even a reddish tint, in consequence, probably, of the further oxidation of the mercury.

In consideration of the incomplete extinguishment of the mercury in many specimens of the blue pill, arising from the tedious process employed, F. B. Benger proposed to obtain the metal in a state of minute division by reduction of mercuric chloride solution by means of stannous chloride. An obvious objection to the process is the possibility, with carelessness of manipulation, of having in the preparation a minute proportion of corrosive sublimate or stannous chloride.

The blue pill is sometimes wanted in the state of powder, but, from its peculiar constitution, it is not eligible for reduction to this form, as the mercury is disposed to aggregate during pulverization, and, from the honey it contains, it is likely, when pulverized, to attract moisture from the air. Chas. Bullock recommended the following method of preparing a powder which, as nearly as possible, represents the blue pill, in reference to its therapeutic effects:

Powdered Blue Mass.—Take of finely powdered Elm bark, finely powdered Sugar, and Mercury, equal parts, and of Alcohol a sufficiency. Rub the mercury with the powdered bark, adding from time to time enough alcohol to maintain a pasty consistence, until the mercury is completely extinguished; then spread the mass on paper to dry. When dry, powder it, add the sugar, and rub the mixture thoroughly until the powder will pass through a sieve of fine bolting cloth. (*A. J. P.*, 1859, p. 271.)

Uses.—Blue mass has the therapeutic properties of the mercurials (see *Hydrargyrum*), but is to-day chiefly employed for its cathartic action. It seems to be somewhat less irritant than calomel and the purgation caused is less frequently accompanied with griping. When used as a cathartic it is sometimes necessary to follow it after some hours with a saline.

Dose, as an alterative, one to three grains (0.065–0.2 Gm.), as a laxative, from five to fifteen grains (0.32–1.0 Gm.).

Off. Prep.—Pilulæ ad Prandium (Cole's), *N. F.;* Pilulæ Aloes, Hydrargyri et Podophylli, *N. F.;* Pilulæ Aloes, Hydrargyri et Scammonii, Compositæ, *N. F.;* Pilulæ Antidyspepticæ, *N. F.;* Pilulæ Digitalis, Scillæ et Hydrargyri, *N. F.*

MATRICARIA. U. S.

MATRICARIA Matricar. [German Chamomile Wild Chamomile]

(măt-rĭ-cā'rĭ-ă)

"The dried flower-heads of *Matricaria Chamomilla* Linné (Fam. *Compositæ*), without the presence or admixture of more than 5 per

cent. of stems or foreign matter. Preserve it in tightly-closed containers and guard against attack by insects." *U. S.*

Flores Chamomillæ Vulgaris; Horse Gowan, Dog's Camovyne; Camomille commune (d'Allemagne), *Fr. Cod.*; Flores Chamomillæ, *P. G.*; Kamillen, Kamillenblumen, *G.*; Camomilla comune, *It.*; Manzanilla (Flor de), *Sp.*

Matricaria Chamomilla is an annual plant, with a branching stem a foot or two in height, bearing alternate leaves, the lower being tripinnate, the upper bipinnate or simply pinnate, and all of them very green, and nearly or quite smooth. The leaflets are linear and very small. The flower-heads appear singly at the ends of the stem and branches. The bracts of the involucre are obtuse, green in the middle, and whitish, membranous, and translucent at the margin. The ray-florets are pistillate white, at first spreading, and ultimately reflected. The disk is of a deep yellow color, at first flat, but in the end convex, and in some cases somewhat conical. The plant is a native of Europe and western Asia, and is occasionally cultivated in our gardens. It is also naturalized in North America and Australia. Mitlacher gives the results of methods of cultivating matricaria in *Zeit. Oest. Apoth. Ver.*, l, p. 410. Meyer has suggested (*Pharm. Zeit.*, lviii, p. 790) the practicability of scientifically collecting matricaria from the wild grown plants. All parts of it are active, but the flowers only are official. These are gathered from May to August, shrink in drying, so that they are scarcely half as large as in their recent state. Those found in commerce are imported from Germany.

Properties.—Matricaria is officially described as follows: "Flower-heads composed of a few white ray-florets and numerous yellow disk-florets on conical, more or less hollow receptacles, the latter being from 3 to 10 mm. in breadth; disk-flowers tubular, perfect, and without a pappus; ray-flowers from 10 to 20, pistillate, corolla white, 3-toothed and 4-veined, usually reflexed; involucre hemispherical, composed of from 20 to 30 imbricated, oblanceolate, and pubescent scales; peduncles light green to brownish-green, longitudinally furrowed, more or less twisted and attaining a length of 2.5 cm.; achenes somewhat obovoid and faintly 3- to 5-ribbed; pappus none, or only a slight membranous crown; odor pleasant, aromatic; taste aromatic and bitter. Matricaria yields not more than 13 per cent. of ash." *U. S.*

"The similar flower-heads of *Anthemis arvensis* L., and *Maruta Cotula* De Candolle (Fam. *Compositæ*), have conical, solid, and chaffy receptacles." *U. S. VIII.*

In addition to the above it is sometimes admixed with the flower-heads of other European species of *Anthemis*. Sometimes the flower-heads of the common daisy (*Chrysanthemum Leucanthemum* L.) as well as other species of *Chrysanthemum* are present in the drug of commerce.

The dried flowers of matricaria are considerably smaller than those of common chamomile, and exhibit a larger proportion of the disk-florets compared with those of the ray. They have a strong, peculiar, rather unpleasant odor, and a disagreeable, bitter taste. Their active constituents are volatile oil and bitter extractive, which are readily taken up by water and alcohol. The oil, which is obtained by distillation with water, is thick, somewhat tenacious, and of a fine deep blue color becoming green and brown by age, and almost opaque in mass. Though supposed by Gerhardt to be identical with the oil of chamomile (*Anthemis nobilis*), it has been shown to be distinct. (*P. J.*, Feb., 1862, p. 429.) It congeals at −20° C. (−4° F.), has the sp. gr. 0.93, and contains a terpene, $C_{10}H_{16}$, and a colorless oil, $C_{10}H_{16}O$. *Schimmel & Co.'s Report* for April, 1897, states that the German chamomile oil contains a paraffin hydrocarbon, which was obtained as a snowy white solid melting at 53° to 54° C. (127.4°–129.2° F.). The blue color is due to a volatile principle called *azulene* by Piesse, and *cærulein* by Gladstone and others; also found in oil of absinthe, yarrow and some other blue volatile oils. This, when distilled with potassium, yields a terpene, $(C_{10}H_{16})_3$, and with phosphoric oxide a hydrocarbon, $C_{10}H_{14}$. (Kachler, *Ber. d. Chem. Ges.*, iv, 36.)

Uses.—Matricaria is a mild tonic, very similar to chamomile in medicinal properties, and, like it, in very large doses an emetic. It is considered also in Europe to be antispasmodic and anthelmintic. It is much employed in Germany, but in this country scarcely at all, unless by German practitioners. It may be given for the same purposes and in the same manner as chamomile.

Dose, half an ounce (15.5 Gm.).

Off. Prep.—Species Emollientes, *N. F.*

MEL. U. S.

HONEY

(mĕl)

"A saccharine secretion deposited in the honey-comb by the bee, *Apis mellifera* Linné (Fam. *Apidæ*)." *U. S.*

Miel, *Fr. Cod.*; Mel, *P. G.*; Honig, *G.*; Miele, *It.*; Miel, *Sp.*

From the nectaries of various flowers the bee and other insects extract a thin, aqueous fluid, nearly without flavor and insipidly sweet, usually known as *nectar*. As honey is made out of this substance it is very much affected by the character of the nectar, so that the nature of the plants which predominate in the vicinity of the hive is a matter of great importance to the bee culturist, not only in regard to the flavor of the honey which is yielded, but even to its freedom from poisonous qualities, cases having been reported from time to time of poisoning produced by the eating of honey which had not been tampered with after extraction from the hive. In the United States honey made by the

bee from the flowers of the Mountain Laurel (*Kalmia*) is especially poisonous. See *N. J. M. R.*, 1852, 46; "*Poisonous Honey*," by L. F. Kebler, *Proc. A. Ph. A.*, 1896, 167; H. Bley, *Ph. Ztg.*, Nov., 1885. The latter states that *Datura Stramonium* and *Gelsemium* are for honey making especially dangerous plants. The nectar when taken in by the bee is chemically changed by secretions from glands in the head and thorax, levulose, dextrose, and rarely sucrose being formed. The finest honey is that which is allowed to drain from the comb. If obtained from hives that have never swarmed, it is called *virgin honey*. An inferior kind is procured by submitting the comb to pressure, and if heat be employed previous to expression, the product is still more impure. The honey which is most highly esteemed is that made from the nectar of the white clover blossom. Equally valuable is the honey derived from raspberry blossoms and bass-wood flowers. The honey made late in the summer from the flowers of the buckwheat is darker in color. The largest producer of honey in the United States is California. The United States is said to be the greatest honey producing region on the globe, the annual production being between 60,000,000 and 75,000,000 pounds annually. Nearly 2,000,000 pounds of wax are also produced in this country.

Propolis is a resinous substance, deposited by bees at the base of the hive, and in other parts which require protection from the outer air, of a nature entirely different from that of wax or honey, and supposed to be intended for the protection of the comb from injurious agencies. H. O. Hitchcock (*Chicago Med. Journ.*, 1867) considers it one of the best remedies in *diarrhea* and *dysentery*. It is of a dark reddish or yellowish-brown color, of a shining fracture, an aromatic taste and odor, quite insoluble in water, nearly so in ether, but readily dissolved by alcohol and solution of potassium hydroxide. Hitchcock used a tincture (two drachms of propolis and four fluidounces of alcohol) in doses of from thirty minims to a fluidrachm (1.8–3.75 mils).

Bee bread is the name given to a material found in some of the cells of the comb, consisting mainly of the pollen of plants. (*Chicago Med. Examiner*, Sept., 1865.) Jas. S. Whitmire found that in the dose of a drachm (3.9 Gm.) three times a day it caused great increase of the urinary secretion. No disagreeable affects followed its use, except a slight flatulency and looseness of the bowels. It is entirely palatable and inoffensive to the stomach. (*A. J. P.*, 1866.)

Eucalyptus Honey, or *Black Honey*.—This honey, a detailed description of which may be found in *U. S. D.*, 16th ed., appears to have been not a natural but a sophisticated article.

In the recent state honey is fluid, but on being kept it is apt to form a crystalline deposit, and to be ultimately converted into a soft granular mass. In commerce it is found of every consistence, from that of a viscid liquid, like thin syrup or oil, to that of lard or soft suet. Its color is sometimes white, but usually yellowish, and occasionally of a brownish or reddish tinge. It has a peculiar agreeable odor, varying somewhat with the flowers from which it was collected, and a very sweet, feebly aromatic taste, which is followed by a slight prickling or sense of acridity in the fauces. Cold water dissolves it readily, alcohol with less facility. "Honey is a thick, syrupy liquid of a light yellowish or yellowish-brown color, translucent when fresh, but gradually becoming opaque and crystalline; having a characteristic odor, and a sweet, faintly acrid taste. It is slightly acid to litmus and is lævorotatory. Dilute Honey with twice its weight of water; the resulting liquid is only moderately turbid, not stringy, and has a specific gravity of not less than 1.099 at 25° C. (77° F.) (corresponding to a specific gravity of not less than 1.370 for the original Honey). Incinerate about 1 Gm. of Honey, accurately weighed, in a platinum crucible, in small portions at a time; not more than 0.3 per cent. of ash remains. Separate portions of 5 mils each of a filtered aqueous solution of Honey (1 in 5) acidified with nitric acid, are not rendered more than slightly opalescent by the addition of a few drops of silver nitrate T.S. (*chlorides*), nor more than slightly cloudy by a few drops of barium chloride T.S. (*sulphates*). Boil about 2 Gm. of Honey with 10 mils of distilled water; the resulting solution, when cold, is not rendered blue, green or reddish on the addition of iodine T.S. (*starch or dextrins*). The color of an aqueous solution of Honey (1 in 2) is not changed at once when mixed with an equal volume of ammonia water (*foreign coloring matter*); 5 mils of an aqueous solution of Honey (1 in 2) does not at once acquire a red or rose color on the addition of a few drops of hydrochloric acid (*azo dyes*). A solution of 10 Gm. of Honey in 50 mils of distilled water requires not more than 0.5 mil of normal potassium hydroxide V.S. for neutralization, phenolphthalein T.S. being used as indicator. Triturate about 1 Gm. of Honey with 20 mils of ether in a mortar, filter it into a porcelain dish or crucible, allow the filtrate to evaporate and add to the residue one drop of resorcinol T.S. At most only a pink color may be produced, which disappears in half a minute, but not an orange, cherry, or brown-red color (*artificial or added invert sugar*)." *U. S.*

It is essentially a strong aqueous solution of mixed dextrose and levulose, amounting generally to from 70 to 80 per cent. According to Wm. A. Selser, who separated wax from honey on a large scale, the proportion of wax in the honey comb averages 1 per cent.; from 1500 pounds he obtained 14¼ pounds of wax by actual experiment. (*A. J. P.*, 1904, 267.)

A large number of samples of genuine honey analyzed in 1897 for the Department of Inland Revenue, Canada (Bull. 47), showed the following variations:

Direct polarization, −2.4 to −19.
Invert polarization, −10.2 to −28.
Sucrose (by Clerget), 0.5 to 7.64 per cent.
Invert sugar, 60.37 to 78.8 per cent.
Water, 12 to 33 per cent.
Ash, 0.03 to 0.50 per cent.

Neufeld in *Der Nahrungsmittelchemiker als Sachsverständiger*, Berlin, 1907, p. 275, gives the following limits for pure honey of European origin:

Water	8.30	to 33.59	per cent.
Protein	0.03	to 2.67	per cent.
Invert sugar	49.59	to 93.96	per cent.
Sucrose	0.10	to 10.12	per cent.
Dextrin	0.99	to 9.70	per cent.
Formic acid	0.03	to 0.21	per cent.
Ash	0.02	to 0.68	per cent.

Browne has published a comprehensive article on American honey (*U. S. Dept. Agric., Bur. of Chem., Bull.* 110, 1908) of which the tabular analyses are given in Leach, *Food Inspection and Analysis*, 3d ed., p. 635.

The *honey sugar* may be obtained by treating granular honey with a small quantity of alcohol, which, when expressed, takes along with it the other ingredients, leaving the crystals nearly untouched. The same object may be attained by melting the honey, saturating its acid with calcium carbonate, filtering the liquid, then setting it aside to crystallize, and washing the crystals with alcohol. Inferior honey usually contains a large proportion of uncrystallizable sugar and vegetable acid. Diluted with water, honey undergoes the vinous fermentation. In warm weather, honey, itself, if not very pure, sometimes ferments, acquiring a pungent taste and deeper color. The presence of dextrin in pure honey seems to be established. G. L. Spencer (*A. J. P.*, 1895, 27) has found as much as 4 per cent. of dextrin, and Haenle (*Zeit. An. Chem.*, xciv, 99) has found that honey from *Coniferæ* always contains dextrin. Künnmann and Hilger (*A. J. P.*, 1896, 570) state that dextrin is present in all honey, whether dextrorotatory or lævo-rotatory, and claim to have identified it as achroo-dextrin. Müllenhoff believes that the honey is preserved in the sealed cells of the comb by the secretion with it of a minute quantity of formic acid, and has found by experiment that the addition of one part of 25 per cent. formic acid is sufficient to keep permanently 250 parts of honey, but in this connection it should be remembered that the absence of contact with the air would account for the preservation of honey in the comb. Starch is said to be occasionally added to the inferior kinds to give them a white appearance. The adulteration may be detected by adding water, which dissolves the honey and leaves the starch at the bottom of the vessel. Dilution with water may be suspected from the greater thinness of the honey and its want of disposition to crystallize.

Honey is sometimes adulterated with artificial glucose. This cannot be detected by the official tests with certainty, but the safest method is to employ the polariscope. (See Leach, "*Food Adulteration and Analysis.*")

According to Oscar Haenle, glucose can also be detected by first dialyzing thoroughly and then polarizing, under which circumstance, if glucose be present, rotation to the right occurs; if the honey be pure the light is not affected. Undialyzed honey ordinarily polarizes to the left, but unadulterated conifer honeys are dextrogyrate. (*P. J.*, xxi.)

Honey has been frequently adulterated with artificial invert sugar. This is best detected by the official method given above.

Uses.—Honey possesses the same medicinal properties as sugar, but is more disposed to affect the bowels. Though largely consumed as an article of food, it is seldom employed medicinally, except as a vehicle. Its taste and demulcent qualities render it a useful addition to gargles, and it is sometimes employed as an application to *foul ulcers*.

Off. Prep.—Mel Depuratum, *U. S., Br.*

MEL BORACIS. Br.

BORAX HONEY

(mĕl bo-rā′cĭs)

Mel Sodii Boratis, *U. S.* 1870; Honey of Borax, Honey of Borate of Sodium; Miel boraté, Mellite de Borax, *Fr.*; Boraxhonig, *G.*

"Purified Borax, in powder, 10 *grammes;* Glycerin, 5 *grammes;* Purified Honey, 85 *grammes.* Mix." *Br.*

This preparation was very properly dropped from the U. S. Pharmacopœia at the 1880 revision, but is recognized by the N. F. IV, the formula being identical with the British process given above. Borax honey is used in the *thrush* of infants and in *aphthous ulcerations* of the mouth.

MEL DEPURATUM. U. S., Br.

CLARIFIED HONEY Mel Depurat. [Mel Despumatum, U. S. 1890]

(mĕl dĕp-ū-rā′tŭm)

"Purified Honey is honey of commerce melted and strained, the specific gravity, if necessary, being adjusted to 1.36 by the addition of Distilled Water." *Br.*

Purified Honey; Mellite simple, *Fr. Cod.*; Miel déspumé, *Fr.*; Mel depuratum, *P. G.*; Gereinigter Honig, *G.*; Miele depurato, *It.*; Miel depurada, *Sp.*

* "Honey, *a convenient quantity,* Distilled Water, Glycerin, each, *a sufficient quantity.* Weigh the honey in a tared dish, mix it intimately with *two per cent.* of paper pulp, which has been previously reduced to shreds, thoroughly washed and soaked in water, and then strongly expressed and again shredded. Then heat on a water bath at a temperature not exceeding 70° C. (158° F.), and carefully remove the scum which rises to the surface. Add

enough distilled water to make up the loss incurred by evaporation, strain, and mix the strained liquid with *five per cent.* of its weight of glycerin." *U. S.*

The U. S. method of clarifying honey was new as far as the Pharmacopœia was concerned in 1890. Paper-pulp is very effective as a clarifying agent, and the glycerin offers some protection to the honey against change. Honey may be made brilliant by hot filtration through paper. (See Remington's *Practice of Pharmacy*, "Hot Filtration."

Honey, by the heat of the water bath, becomes so fluid that the wax and other lighter impurities which it contains rise to the surface and may be skimmed off, while the heavier substances which may have been accidentally or fraudulently added, such as sand or other earth, sink to the bottom. It is officially required that "Clarified Honey, diluted with twice its weight of water, has a specific gravity of not less than 1.095 at 25° C. (77° F.); in other respects it conforms to the tests for purity under *Mel.*" *U. S.*

A neat method of separating is described in *N. R.*, Feb., 1880. It is as follows: "Pour the honey into a perfectly clean cylindrical vessel, with straight sides, rather narrow, and having a small lip at the open margin, and heat the vessel on a water-bath. When the water is hot, pour enough honey into the vessel to fill it to within about 1 inch of the edge, and allow it to remain at rest in the water-bath, at a moderate heat, for about one hour. During this time, most of the impurities will rise to the top, while some others may sink to the bottom. Now remove the vessel very carefully from the water-bath, and pour on top of the hot honey, very gently, a sufficient amount of cold water to fill the vessel completely. This will cause all the impurities floating on the honey to rise at once to the top of the cold water, where they will often solidify to a tough skin or cake, which may be taken off without difficulty. Then pour off the water through the lip, remove the last remnants, if necessary, by means of blotting paper, and filter the honey through a piece of well-washed, wetted, and dense white flannel. The resulting product—if the honey be pure—will be very brilliant." The French Codex directs one part of honey to be diluted with one part of distilled water. The specific gravity of this solution should be not less than 1.300.

(For other processes of purifying honey, see 14th edition of this work, p. 1321, also 19th ed., p. 775, and *A. J. P.*, 1877, p. 19; also 1879, pp. 193, 598; and 1880, p. 132.) Heugel's method is to mix two pounds each of honey and water with a half-ounce of magnesium carbonate, frequently agitate for two or three hours, filter through doubled white filtering paper, boil slowly, remove the scum carefully, and evaporate upon a steam bath to a syrupy consistence. Dieterich recommends the following process: Mix the honey with sufficient water (the amount depending on the consistence), heat for about seven hours on a water bath, and clarify it with 5 per cent. of its weight of powdered talc, neutralize, if necessary, with magnesium carbonate; allow to deposit, filter, add a few drops of acetic acid, and evaporate to the proper specific gravity. (*Ph. Ztg.*, 93, 712.)

The British Pharm. describes it as "a syrupy, translucent, pale yellowish liquid. Aromatic odor; taste at first sweet, afterwards faintly acrid. Specific gravity 1.36. *Optical rotation* at 15.5° C. (60° F.) of a solution in *water*, containing 25 grammes in 100 millilitres, decolorised by filtration with *animal charcoal*, in a tube 200 millimetres long, between 0° and –5° C. (32° and 23° F.); 5 millilitres of the same solution when mixed with 15 millilitres of *absolute alcohol* do not become more than faintly opalescent (absence of starch sugar). When 2 grammes are dissolved in 20 millilitres of boiling *water* and cooled, the solution does not become blue on the addition of one drop of *N/10 solution of iodine* (absence of starch). Ash not more than 0.25 per cent.; solution of the ash in *water* is not alkaline to *litmus*, and when acidified with *nitric acid* yields not more than a very faint opalescence with *solution of barium chloride*, or with *solution of silver nitrate* (limit of sulphates and of chlorides)." *Br.*

Honey clarified with calcium carbonate and animal charcoal, or as in the first process described, is as clear and colorless as syrup made with sugar, but still retains a peculiar flavor. It is less disposed to ferment than crude honey, and is said not to be so liable to produce griping pain when swallowed.

Dose, one to four fluidrachms (3.75–15 mils).

Off. Prep.—Confectio Piperis, *Br.;* Mel Boracis, *Br.;* Mel Rosæ, *U. S.;* Oxymel, *Br.;* Confectio Rosæ, *N. F.;* Mel Sodii Boratis, *N. F.*

MEL ROSÆ. U. S.

HONEY OF ROSE

(mĕl rō'şæ)

Mellitum Rosatum; Mellite de Rose rouge, *Fr. Cod.;* Miel Rosat, *Fr.;* Mel Rosatum, *P. G.;* Rosenhonig, *G.;* Miele rosato, *It.;* Miel de rosas, *Sp.*

* "Fluidextract of Rose, *one hundred and twenty mils* [or 4 fluidounces, 28 minims]; Clarified Honey, *a sufficient quantity* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Mix the fluidextract of rose in a tared vessel with enough clarified honey to make the product weigh *one thousand grammes* [or 35 ounces av., 120 grains]." *U. S.*

Though one of the official preparations in the London and Edinburgh Pharmacopœias, the Honey of Rose has been dropped in the British. The U. S. formula is based on that of Grahame. (See *A. J. P.*, 1859, p. 443.) As is well known, honey of rose deposits honey sugar upon standing even but a short time. Touflet (*Ph. Centralh.*, xxxvi, 307) obviates this precipitation in the following manner: Take of Powdered Rose Leaves, 25 parts; Alcohol, sp. gr. 0.875, 75 parts; Honey, 80 parts; Sugar, 34 parts. Per-

colate the rose leaves with the alcohol, filter and distil off the filtrate to 40 parts. To this add the honey and sugar, and bring to the boiling point. Honey of rose forms a pleasant addition to the gargles employed in *inflammation* and *ulceration* of the *mouth* and *throat*.

Dose, one fluidrachm (3.75 mils).

Off. Prep.—Mel Rosæ et Sodii Boratis, *N. F.*

MENTHA PIPERITA. U. S.

PEPPERMINT Menth. Pip.

(mĕn'thą pĭp-ę-rī'tą)

"The dried leaves and flowering tops of *Mentha piperita* Linné (Fam. *Labiatæ*)." *U. S.*

Brandy Mint; Menthe poivrée, *Fr. Cod.*; Folia Menthæ Piperitæ, *P. G.*; Pfefferminzblätter, Pfeffermünze, *G.*; Menta piperita, *It.*, *Sp.*

The genus *Mentha* comprises at least fifteen species, of which there are also a great many varieties. Some of the mints have been in use for culinary and medicinal purposes since antiquity, but no well defined distinction is made as to just what plants were employed. It is stated that *M. piperita* L. (1753), also Smith (1800)—the most important member of this genus, was long ago cultivated by the Egyptians. It is mentioned in the Icelandic Pharmacopœia of the thirteenth century. Peppermint is now grown in considerable amounts in Europe, North America, and Eastern Asia. It is also found growing wild in other parts of the world, as South America and Australia. The oldest existing peppermint district is in the neighborhood of Mitcham (Surrey), England. In some parts of the United States, especially in Michigan, the western part of New York, Ohio and Indiana, it is largely cultivated. On the continent of Europe other species of *Mentha* (particularly *M. arvensis*) grow with *M. piperita*, deteriorating the product. In America other plants (as *Erigeron canadensis* and *Erechthites hieracifolia*) cause the same trouble. Besides *M. piperita* other species are cultivated, as some Asiatic varieties of *M. arvensis*, *M. spicata*, *M. longifolia* (var. *undulata*), *M. gentilis*, *M. dalmatica*, and *M. Pulegium*. Miss Henkel reviews the situation regarding the cultivation of peppermint in the United States and describes the three kinds of mint grown for the production of peppermint oil: *Mentha piperita* L.; *Mentha piperita vulgaris* Sole, and *Mentha piperita officinalis* Sole. (*Bul. Bur. Plant Ind., U. S. Dept. Agric.*, No. 90, 1906.) A comprehensive article on the cultivation of peppermint in Japan is that by Inouyé in *Schim. Rep.*, November, 1908, p. 199. Peppermint has recently been successfully grown in Wisconsin. (*Paint, Oil and Drug Rev.*, xliv, p. 18.) The cultivation of peppermint is a growing industry on the reclaimed lands of Louisiana. (*Spatula*, xvii, p. 18.) Great interest recently has been taken in the cultivation of peppermint in Germany. (See Thoms in *B. P. G.*, xx, p. 244; *Arb. Pharm. Inst. Univ. Berl.*, viii, p. 93.) Mitlacher reports on the cultivation of peppermint in Austria and outlines methods for its culture on a large scale. (*Ph. Post*, xliv, p. 215; *Zeit. Oest. Apoth. Ver.*, 1, p. 422.) It has been repeatedly pointed out that the essential oil-bearing plants of the *Labiatæ* are very capricious and constantly changing character with change of soil and climate. For an account of the cultivation of peppermint in Russia, see *Proc. A. Ph. A.*, 1902, 831.

Peppermint is a perennial herbaceous plant, producing creeping stolons. The stems are quadrangular, channelled, purplish, somewhat hairy and branching towards the top. The leaves are opposite, petiolate, ovate, sharply serrate, pointed, smoother on the upper than on the under surface, and of a dark green color, which is paler beneath. The flowers are small, purple, and in terminal obtuse spikes, interrupted below, and cymosely arranged. Late in the season, the growth of the lateral lower branches often gives to the inflorescence the appearance of a corymb. The calyx is tubular, often purplish, furrowed, glabrous below, and five-toothed, the teeth being hirsute. The corolla is purplish, tubular, with its border divided into four segments, of which the uppermost is broadest, and notched at its summit. The four short stamens are concealed within the tube of the corolla; the style projects beyond it, and terminates in a bifid stigma. The plant should be cut for medicinal use in dry weather, in August, about the period of the expansion of the flowers. John C. Umney points out differences between white and black peppermint in *P. J.*, 1896, 123. For a paper on the histology of powdered peppermint by Smith Ely Jelliffe, see *D. C.*, 1899, 252.

Properties.—It is officially described as follows: "Leaves more or less crumpled and frequently detached from the stems; stems quadrangular, from 1 to 2 mm. in diameter, glabrous except for a few scattered deflexed hairs; leaves when entire ovate-oblong to oblong-lanceolate, petioles from 4 to 15 mm. in length, slightly pubescent, laminæ from 1 to 9 cm. in length, acute and sharply serrate, light green to purplish-brown, upper surfaces nearly glabrous, lower surfaces glandular hairy, especially on the veins; flower-whorls in oblong or oval spikes which are usually compact, or somewhat interrupted at the base, from 1 to 1.5 cm. in breadth, rounded at the summit, and in fruit attaining a length of from 3 to 7 cm.; bracts oblong-lanceolate, very acuminate, 7 mm. in length; calyx tubular, equally 5-toothed, pubescent and glandular-punctate, often dark purple in color; corolla tubular-campanulate, 4-cleft, about 3 mm. in length and often light purple; stamens 4, short and equal; nutlets ellipsoidal, about 0.5 mm. in diameter, blackish-brown; odor aromatic, characteristic; taste aromatic, pungent, followed by a cooling sensation in the mouth." *U. S.*

The morphology of *Mentha piperita* and other species of *Mentha* are discussed by Eriksson in *B. P. G.*, xviii, p. 244. The herb, both in

the recent and in the dried state, has a peculiar, penetrating, grateful odor. Peppermint is quite frequently contaminated with spearmint and in one instance the leaves of belladonna were found. The latter, while no doubt accidental, shows the necessity for the examination of crude drugs generally. (*Pharm. Prax.*, iv, p. 38.) There is sometimes difficulty in distinguishing between the leaves of *M. piperita* and those of *M. spicata*. According to Joseph Schrenk, crystals can always be found in the glandular hairs of the peppermint, but are absent in those of the spearmint. The crystals are doubly refractive, and so transparent that sometimes a polariscope is necessary for their easy detection. These crystals have been thought to be menthol, but they seem not to dissolve in alcohol, and are probably hesperidin.

The medicinal properties depend on a volatile oil, of which from 1 to 1.25 per cent. can be obtained from the herb. The leaves are said to contain a little tannic acid. The virtues of the herb are imparted to water, and more readily to alcohol.

Uses.—Peppermint is an aromatic stimulant, much used to allay *nausea*, relieve *spasmodic pains of the stomach and bowels*, expel *flatus*, or cover the taste or qualify the nauseating or griping effects of other medicines. The medicine is rarely used in infusion. (See *Oleum Menthæ Piperitæ*.)

Dose, one drachm (3.9 Gm.).

Off. Prep.—Spiritus Menthæ Piperitæ, *U. S.*

MENTHA VIRIDIS. U. S.

SPEARMINT Menth. Vir.

(mĕn'thą vĭr'ĭ-dĭs)

"The dried leaves and flowering tops of *Mentha spicata* Linné (*Mentha viridis* Linné) (Fam. *Labiatæ*)." *U. S.*

Herba Menthæ Acutæ (vel Romanæ); Brown, Lamb, Garden, or Mackerel Mint; Menthe verte, *Fr. Cod.;* Menthe romaine, Baume vert, Menthe à épi, *Fr.;* Grüne Münze, Römische Minze, *G.*

Spearmint, sometimes called simply *mint*, differs from *M. piperita* chiefly in having sessile, or nearly sessile, oblong or ovate-lanceolate, unequally serrate leaves; elongated, interrupted, panicled spikes; setaceous bracts; and stamens longer than the tube of the corolla. It is a native of Europe and Asia, and naturalized in waste places from Nova Scotia and Ontario to Minnesota and Kansas in the West and Florida in the South United States. It is also cultivated for domestic use and for the sake of its oil. Its flowering season is August. Spearmint is officially described as "leaves more or less crumpled and mixed with a large proportion of the light brown or purplish-colored stems, occasionally with their characteristic opposite branches; stems distinctly quadrangular, from 1 to 3 mm. in width, nearly glabrous; leaves when entire ovate-lanceolate, unequally serrate, nearly sessile or with a petiole less than 5 mm. in length, of a bright green color and somewhat glandular-hairy on the under surface; flowers arranged in opposite clusters and in more or less interrupted or crowded lanceolate, nearly acute spikes; bracts linear-lanceolate, subulate, from 7 to 10 mm. in length, subtending the flower clusters; calyx tubular, 5-toothed, glandular punctate and somewhat pubescent near the teeth; corolla nearly white or light brown; stamens extending beyond the corolla tube; odor slightly pungent, characteristic; taste aromatic, characteristic but not followed by a cooling sensation in the mouth." *U. S.*

Spearmint was cultivated in the Convent gardens of the ninth century. It is largely used as a domestic and popular flavor in foods, chewing gum, and confectionery. The plant is widely cultivated, and Schimmel and Co. present a review of its cultivation in Michigan, Indiana and New York in their *Schim. Rep.*, October, 1910, p. 131. Recently experiments have been conducted in Louisiana, and Phenis states the resulting oil to be of the highest grade. (*Paint, Oil, and Drug Review*, xlvi, p. 27.) Successful experiments have also been conducted in Wisconsin. (*Ibid.*, xliv, p. 18.) Mitlacher has reported that *Mentha crispa* can be successfully grown in Austria. (*Ph. Post*, xliv, p. 215.)

Spearmint is sometimes admixed with peppermint. This is probably due to carelessness. The taste and odor of spearmint are retained for some time by the dried plant. They depend on a volatile oil. (See *Oleum Menthæ Viridis*.)

Dose, one drachm (3.9 Gm.).

Off. Prep.—Spiritus Menthæ Viridis, *U. S.*

MENTHOL. U. S., Br.

MENTHOL

(mĕn'thŏl)

"A secondary alcohol [$C_{10}H_{19}OH = 156.16$] obtained from oil of peppermint or other mint oils. Preserve it in well-closed containers, in a cool place." *U. S.* "Menthol, $C_{10}H_{20}O$, is a crystalline substance obtained by cooling the oil distilled from the fresh herb of Mentha arvensis, *DC., vars.* piperascens et glabrata, *Holmes;* and probably other species of Mentha." *Br.*

Pipmenthol, Peppermint Camphor; Menthol, *Fr. Cod.;* Camphre de Menthe, Mentholum, *Fr.;* Mentholum, *P. G.;* Menthol, Pfefferminzkampher, Mentha-Kampher, Pipmenthol, *G.;* Mentolo, *It.;* Mentol, *Sp.*

Menthol, or *peppermint camphor*, may be obtained from either American or *Japanese oil of peppermint* (*Mentha arvensis*), by cooling the oil to a very low temperature, when the menthol crystallizes out, often in a dense mass; the adhering oil may be separated by expression. Menthol may also be obtained by fractional distillation, and there is reason to believe that the oil of peppermint of commerce is often contaminated with the dementholized oil. A larger yield of menthol is obtained from Japanese or Chinese oils, and for this reason Japanese menthol is largely found in commerce. It is practically identical with American menthol,

differing, however, in the character of its crystals, which occur in small prisms instead of in long needles.

Properties.—The U. S. P. describes it as in "colorless, acicular or prismatic crystals, having a strong odor and taste of peppermint; when tasted it produces a sensation of warmth followed by cold when air is drawn into the mouth. Menthol is slightly soluble in water; very soluble in alcohol, chloroform, ether or in petroleum benzin; freely soluble in liquid petrolatum or fixed volatile oils. Its alcoholic solution is neutral to litmus, and is lævorotatory. It melts between 42° and 44° C. (107.6° and 111.2° F.). When Menthol is triturated with about an equal weight of camphor, thymol, or hydrated chloral, the mixture becomes liquid. Heat about 2 Gm. of Menthol in an open dish, on a water bath; it gradually volatilizes without leaving more than 0.05 per cent. of residue (*wax, paraffin, or inorganic substances*). Dissolve a few crystals of Menthol in 1 mil of glacial acetic acid and then add 3 drops of sulphuric acid and 1 drop of nitric acid; no green color is produced (*thymol*)." *U. S.*

"Colorless acicular crystals or crystalline masses. Melting point 42° to 43° C. (107.6°–109.4° F.). Odor and taste recalling peppermint; produces a sensation of warmth on the tongue and, if air is inhaled, a sensation of cold. Entirely volatilised by the heat of a water-bath. Very slightly soluble in *water;* but readily soluble in *alcohol* (90 per cent.), the solutions being neutral to *litmus.* Boiled with *sulphuric acid* diluted with half its volume of *water,* Menthol acquires an indigo-blue or ultramarine color, the acid becoming brown." *Br.*

Menthol is a stearopten and belongs to the class of camphors. Its formula may be written $C_{10}H_{19}OH$ (for structural formula see under *Olea Volatilia,* p. 732), as it is recognized as being a saturated secondary alcohol. Chromium trioxide oxidizes menthol to *dextro-* and *lævo-menthone,* $C_{10}H_{18}O$, which is the ketone corresponding. The *menthones* are liquids, with an odor resembling that of peppermint. They boil at 207° C. (404.6° F.). Distillation with zinc chloride or phosphoric anhydride changes menthol into liquid *menthene,* $C_{10}H_{18}$, boiling at 167° C. (332.6° F.). (See papers by Kremers, Urban, and Richtmann on the menthol group, *Proc. A. Ph. A.,* 1893, 185; also 1896, 200.) Menthol has been grossly adulterated with spermaceti, paraffin, etc., and, after being compressed into pencils or cones, sold as a local panacea for headache and neuralgia.

Uses.—According to Schwenkenbecher (*M. M. W.,* 1908, lv, p. 1495), menthol in large doses is a narcotic, paralyzing eventually both the sensory and motor systems. It cannot, however, be regarded as highly toxic, for he himself, took 8 Gm. within a period of two hours without suffering serious symptoms. When locally applied it stimulates the nerves for the perception of cold, but depresses those for pain. It is actively antibacterial; according to McDonald, it is about twice as powerful as phenol. Menthol is used for its local anesthetic influence in various *skin diseases,* accompanied with *itching,* such as *urticaria.* Probably by virtue of the same property it is also frequently of service in *nausea* and *gastrodynia.* In *headache* and other forms of *neuralgia* the external application of menthol will frequently produce considerable degree of relief; the action in these cases is probably that of a counter-irritant rather than anesthetic. A solution containing one or two per cent. of menthol in liquid petrolatum is very widely employed for its antiseptic and anesthetic influence in inflammations of the upper respiratory tract, such as *acute coryza, pharyngitis,* or *laryngitis.* It is also occasionally employed as a gastro-intestinal antiseptic. According to S. A. Russel an ethereal solution of from 10 to 50 per cent. applied 2 or 3 times a day has a remarkable power of controlling superficial inflammations, such as *boils* or *carbuncles.* Berliner (*B. K. W.,* 1910, p. 967) and others have injected, hypodermically, its oily solution with asserted benefit in various forms of *tuberculosis.* A number of cases of dangerous asphyxiation, at least one of which ended fatally, have followed the local application of menthol in infants for the relief of *coryza.* (See Lublinski, *B. K. W.,* 1912, xlix.)

Dose, one to two grains (0.065–0.13 Gm.).

Off. Prep.—Emplastrum Menthol, *Br.;* Inunctum Mentholis, *N. F.;* Inunctum Mentholis Compositum, *N. F.;* Liquor Antisepticus, *N. F.;* Liquor Pepsini Antisepticus, *N. F.;* Menthol Camphoratum, *N. F.;* Nebula Aromatica, *N. F.;* Nebula Mentholis, *N. F.;* Nebula Mentholis Composita, *N. F.;* Petroxolinum Mentholis, *N. F.;* Pulvis Antisepticus, *N. F.*

METHYLIS SALICYLAS. U. S. (Br.)

METHYL SALICYLATE Methyl. Salicyl. [Oleum Gaultheriæ, U. S. VIII, Oil of Wintergreen, Oleum Betulæ, U. S. VIII, Oil of Sweet Birch, Oil of Teaberry, Methyl Salicylas, U. S., 1890, Synthetic Oil of Gaultheria, Synthetic Oil of Wintergreen]

(mĕth'ĭl-ĭs săl-ĭ-cĭ'lăs)

"It contains not less than 98 per cent. of $CH_3C_7H_5O_3$ (152.06). It is produced synthetically or is obtained by distillation from *Gaultheria procumbens* Linné (Fam. *Ericaceæ*) or from *Betula lenta* Linné (Fam. *Betulaceæ*). The label must indicate whether the methyl salicylate has been made synthetically or distilled from either of the above mentioned plants. Preserve it in well-stoppered amber-colored bottles, in a cool place, protected from light." *U. S.* "Methyl Salicylate is the methyl ester of salicylic acid. It may be obtained by the interaction of methyl alcohol and salicylic acid. It contains not less than 98 per cent. of pure methyl salicylate, $CH_3C_7H_5O_3$." *Br.*

Methyl Salicylas, *Br.;* Salicylate de Méthyle, *Fr.;* Methylsalicylat, Künstliches Wintergrünöl, *G.*

Methyl salicylate, or *artificial oil of wintergreen,* was introduced into the U. S. P., 1890,

largely because of its extensive use and on account of its being a valuable synthetic; it is asserted that it can be produced of more uniform quality and is more definite and certain in its action than either the oil from gaultheria or the oil from birch, which are natural oils. (See *A. J. P.*, 1889, p. 398; *Ph. Rund.*, 1889, 283; see also 1892, p. 7, 9.) Many investigators have attempted to devise tests for differentiating the oils of wintergreen and birch and methyl salicylate, but as soon as a reaction is proposed and described, its unreliability is quickly proved by other investigators. A method is said to have been discovered in the Bureau of Chemistry, U. S. Dept. of Agriculture, which has not yet been made public, but which has been used with success unofficially. Vanillin and alcohol, heliotropin and sulphuric acid, chloral hydrate and sulphuric acid, are among the reagents which have been proposed, none of which seem to be infallible with mixtures, although they do show decided differences with the pure oils. References to some of the articles on this subject are as follows: *Schim. Rep.*, 1914, Apr., p. 99; *J. A. Ph. A.*, 1914, p. 1658; *J. A. Ph. A.*, 1914, p. 1284. Methyl salicylate may be made by distilling salicylic acid or a salicylate, with methyl alcohol and strong sulphuric acid. The reaction is as follows:

$$C_6H_4OHCOOH + CH_3OH = C_6H_4OHCOOCH_3 + H_2O.$$

The sulphuric acid plays no part in the reaction except to serve as a dehydrating agent. The following process was devised by G. M. Beringer (*A. J. P.*, 1887, p. 8). Dissolve half an ounce of salicylic acid in two fluidounces of absolute methyl alcohol, then gradually add one fluidounce of sulphuric acid; warm gently for twenty-four hours, then distil from a retort into which a current of steam is introduced. The distillate is to be well washed, and separated by decantation. The odor improves with age. Methyl salicylate has been found in a great number of plants. (See *A. J. P.*, 1898, 412; *Ph. Rev.*, 1898, 130; *Schim. Rep.*, 1898, 45; 1899, 46.)

Properties.—Methyl salicylate is officially described as "a colorless, yellowish or reddish liquid, having the characteristic odor and taste of gaultheria. It is sparingly soluble in water; miscible with alcohol and glacial acetic acid. It is soluble in 6 volumes of 70 per cent. alcohol at 25° C. (77° F.) with not more than a slight cloudiness. The alcoholic solution is neutral or slightly acid to moistened litmus paper. Specific gravity at 25° C. (77° F.): synthetic, 1.180 to 1.185; when from sweet birch or gaultheria, 1.172 to 1.182. It boils between 218° and 221° C. (424.4° and 429.8° F.). Synthetic Methyl Salicylate, or that from sweet birch, is optically inactive; when obtained from gaultheria, it is slightly lævorotatory, not exceeding –1.5° in a 100 mm. tube at 25° C. (77° F.). A deep violet color is produced by shaking a drop of Methyl Salicylate with about 5 mils of distilled water and adding a drop of ferric chloride T.S. Add 10 mils of potassium hydroxide T.S. to 1 mil of Methyl Salicylate, contained in a capacious test tube, and agitate the mixture. A clear, or slightly cloudy, colorless or faintly yellowish solution results without the separation of any oily drops either on the surface or at the bottom of the liquid (*other volatile oils or petroleum products*). It does not respond to the Test for heavy metals in volatile oils (see Part III, Test No. 3)." *U. S.*

"A colorless liquid. Characteristic, aromatic odor; taste sweetish, warm, aromatic. Slightly soluble in *water;* readily soluble in *alcohol* (90 per cent.), in *glacial acetic acid,* and in *carbon disulphide.* Specific gravity 1.185 to 1.192. Boiling point from 219° to 221° C. (426.2°–429.8° F.). Optically inactive. The solution in *alcohol* (90 per cent.) is neutral or faintly acid to *litmus.* The aqueous solution is colored violet by the addition of a drop of *T. Sol. of ferric chloride.* Contains not less than 98 per cent. of the *ester* methyl salicylate, $CH_3C_7H_5O_3$." *Br.*

"**Assay.**—Introduce about 2 mils of Methyl Salicylate into a tared flask, note the exact weight, add 50 mils of half-normal alcoholic potassium hydroxide V.S., connect the flask with a reflux condenser and heat the mixture on a water bath during two hours. Then add a few drops of phenolphthalein T.S. and titrate the excess of alkali with half-normal hydrochloric acid V.S. It shows not less than 98 per cent. of $CH_3C_7H_5O_3$.

"Each mil of half-normal alcoholic potassium hydroxide V.S. consumed corresponds to 0.07603 Gm. of $CH_3C_7H_5O_3$. Each gramme of Methyl Salicylate corresponds to not less than 12.9 mils of half-normal alcoholic potassium hydroxide V.S." *U. S.*

Uses.—Methyl salicylate is used chiefly in the treatment of various forms of *rheumatism* in which other preparations of salicylic acid are of service. It has the advantage over the inorganic salicylates of being less unpleasant to the taste, but in our experience is somewhat more prone to cause digestive disturbances. Because of its volatility it is capable of being absorbed through the skin and is frequently applied externally for its systemic effect. For this purpose it may be mixed with equal parts of lard and a drachm of the mixture spread over a surface as big as the palm of the hand and covered with an impermeable dressing to prevent evaporation. It is also employed for its counter-irritant action in various liniments. As a flavoring agent two minims may be used for each fluidounce.

Internally it is best administered in emulsion, although sometimes taken by dropping into a teaspoonful of sugar. The custom of giving it in capsules is to be deprecated as it is much more likely to irritate the stomach under these circumstances.

Dose, from five to twenty minims (0.3–1.2 mils).

Off. Prep.—Inunctum Mentholis Compositum, *N. F.;* Liquor Antisepticus, *N. F.;* Liquor Antisepticus Alkalinus, *N. F.;* Liquor Ferri Salicylatis, *N. F.;* Liquor Pepsini Antisepticus, *N. F.;* Nebula Aromatica, *N. F.;* Nebula Mentholis Composita, *N. F.;* Petroxolinum Methylis Salicylatis, *N. F.*

METHYLTHIONINÆ CHLORIDUM. U. S.

METHYLTHIONINE CHLORIDE Methylthionin. Chlor. [Methylene Blue Methylthioninæ Hydrochloridum, U. S. VIII]

(mĕth-ȳl-thī-o-nī'næ ȼhlō'rı̤-dŭm)

"Tetramethylthionine chloride [$C_{16}H_{18}N_3ClS + 3H_2O = 373.75$]." *U. S.*

Chlorhydrate de Tetraméthylthionine, *Fr.;* Tetramethylthioninchlorid, Methylen Blau, *G.*

This synthetic dye color belongs to the class of *thiazines* or dyestuffs in which two benzene nuclei are united by a nitrogen atom and a sulphur atom. *Methylene blue* was discovered by Caro in 1876, and was made by the oxidation of *p*-amido-dimethyl aniline with ferric chloride in the presence of hydrogen sulphide. Both the hydrochloride of the base and the zinc chloride double salt of the same are known by the name of methylene blue. It is only the former that is used in medicine and constitutes the official salt. Methylene Blue must not be confounded with *methyl blue,* a dark blue powder which is used as an antiseptic; the latter is sodium triphenyl-pararosaniline-sulphonate.

Properties.—Methylene blue is officially described in the United States Pharmacopœia as "a dark green, crystalline powder, or in prismatic crystals having a lustre resembling bronze. Methylthionine Chloride is freely soluble in water and alcohol; soluble in chloroform; the solutions have a deep blue color. The addition of hydrochloric acid to its aqueous solution changes the color to a lighter shade of blue. The addition of sodium hydroxide T.S. to its aqueous solution changes the color to a purplish shade, and, if added in excess, produces on standing a precipitate having a dull violet color. A solution of Methylthionine Chloride in diluted sulphuric acid is gradually decolorized upon the addition of zinc dust. Incinerate about 0.5 Gm. of Methylthionine Chloride; not more than 1 per cent. of ash remains. Intimately mix 0.2 Gm. of Methylthionine Chloride with about 0.5 Gm. each of potassium nitrate and anhydrous sodium carbonate and heat the powdered mixture in a crucible until the organic matter is completely oxidized. Then dissolve the cooled residue in 15 mils of diluted sulphuric acid and evaporate the solution over a flame until vapors of sulphuric acid begin to evolve. The residue so obtained meets the requirements of the Test for arsenic (see Part III, Test No. 1). Heat about 0.5 Gm. of Methylthionine Chloride at a temperature below a red heat until it is completely carbonized, boil the powdered residue with 10 mils of diluted hydrochloric acid for five minutes, filter the liquid and wash the residue with 10 mils of distilled water. The combined liquids, when boiled with 1 mil of nitric acid, and supersaturated with ammonia water and filtered, if necessary, remain clear upon the addition of an equal volume of hydrogen sulphide T.S. (*zinc*). Dissolve 1 Gm. of Methylthionine Chloride in 50 mils of boiling alcohol, filter through counter-balanced filters, wash the residue on the filter with boiling alcohol until the washings cease to be colored blue, and dry it at 100° C. (212° F.). The weight corresponds to not more than 1 per cent. (*dextrin*)." *U. S.*

Uses.—When taken internally methylene blue is absorbed and eliminated chiefly from the kidneys, coloring the urine blue or greenish. In therapeutic doses it produces no symptoms except occasionally some irritation of the bladder, and we know of no serious cases of poisoning with the pure article. It is a feeble antiseptic and has been used to a considerable extent in *gonorrhea, cystitis* and *pyelitis,* but its value is certainly not great. As an analgesic, it has been employed in *neuralgia, locomotor ataxia,* etc., but is inferior to other aniline derivatives. In 1891, Ehrlich and Guttmann (*B. K. W.,* xxviii), led by its power as a staining agent over the plasmodium malariæ, suggested its practical use as an antiperiodic, and its value as such is well established. In 425 cases collected by H. C. Wood, Jr. (*Trans. Phila. County Med. Soc.,* 1904), there were 85 per cent. of cures. It does not produce disturbances of the special senses or of the gastro-intestinal tract, and therefore may be preferable to quinine in aural or gastro-intestinal affections. Further, on account of its lack of action upon the kidney, it is especially valuable in those forms of *malaria* accompanied with *hematuria,* the so-called "*black water fever.*" If the statement of Iwanoff, that it especially acts upon the adult forms of plasmodium be correct, it should be especially valuable in *chronic malaria,* and experience may prove that the best treatment of this condition is the administration of full doses of quinine at intervals of seven days, with the continuous use of the methylene blue. Slack (*Atlanta Journal and Record of Medicine,* 1907) recommends the internal use of methylthionine in *carcinoma;* it seems not only to relieve the pain but also to delay the growth of the tumor.

Methylene blue is preferably administered in capsule. In malaria from ten to twenty grains (0.65–1.3 Gm.) may be given in the course of a day for ten days, and after this six to ten grains (0.4–0.65 Gm.) a day for two weeks. In obstinate cases a full dose of quinine may be exhibited every seventh day, the methylene blue being omitted. The staining action of methylene blue upon any portion of the body or clothing with which it may come in contact, and its color effect upon the urine, should always be explained to the patient.

Dose, two to five grains (0.13–0.32 Gm.).

MEZEREUM. U. S.

MEZEREUM [Mezereon]

(mẹ-zē′rē-ŭm)

"The dried bark of *Daphne Mezereum* Linné, *Daphne Gnidium* Linné, or of *Daphne Laureola* Linné (Fam. *Thymeleaceæ*)." *U. S.*

Mezerei Cortex, *Br.* 1898; Mezereon Bark; Cortex Mezerei, Cortex Thymeleæ (vel Coccognidii); Dwarf Bay, Wild Pepper, Spurge-flax, Spurge-olive, Magell; Mézéréon ou Bois gentil, *Fr. Cod.*; Lauréole, Thymelée, *Fr.*; Kellerhals, Seidelbastrinde, Kellerhalsrinde, *G.*; Mezereo, *It.*; Mecereon, *Sp.*

All the species of *Daphne* are possessed of active properties, but three only are official—*D. Mezereum, D. Laureola,* and *D. Gnidium,* all of which are recognized in the United States Pharm., and the last in the former French Codex, 1884.

1. *Daphne Mezereum* is a very hardy, low shrub, with a branching stem, and a smooth, dark gray bark, very easily separable from the wood. The leaves spring from the ends of the branches, are deciduous, sessile, obovate-lanceolate, entire, smooth, and of a pale green color, somewhat glaucous beneath. They are preceded by the flowers, which appear very early in the spring, and sometimes bloom even amidst the snow. These are of a purple-rose color, rarely white, highly fragrant, and disposed in clusters, each consisting of two or three flowers, forming together a kind of spike at the upper part of the stem and branches. At the base of each cluster are deciduous floral leaves. The fruit is oval, shining, fleshy, of a bright red color, and contains a single round seed. Another variety produces white flowers and yellow fruit. This species of *Daphne* occurs throughout the forests of Europe, and extends in Western Asia from the Caucasus to the Altai. It is cultivated in Europe, and is occasionally found in our own gardens. *D. Mezereum* is locally naturalized from New York and Massachusetts to western Quebec and Ontario.

2. *Daphne Gnidium.*—In this species, called *garou* or *sain-bois* by the French, the leaves are linear-lanceolate, acute, entire, smooth, and irregularly but closely set upon the branches. The flowers are white, downy, odoriferous, and disposed in terminal panicled racemes. The fruit is globular, dry, at first green, but ultimately black. *D. Gnidium* grows in dry uncultivated places in the south of Europe, and flowers in June. Its bark, which in France is used indiscriminately with that of the former species, is of a deep purplish-brown color, and hairy in the younger portions. It appears to be equally as active, medicinally, as the other official species.

Besides the species above described, *Daphne Laureola,* or *spurge laurel,* is said to furnish a portion of mezereum of commerce, and is recognized by the U. S. Pharmacopœia, but its product is inferior in acrimony, and consequently in medicinal activity.

Properties.—The bark of the root was formerly directed, but the mezereum with which our markets are supplied is evidently the bark of the stem, and the Pharmacopœias at present very properly direct the bark, without designating the part from which it must be taken. The official description is as follows: "In flexible, tough quilled pieces or somewhat flattened strips, attaining a length of 90 cm.; from 0.3 to 1 mm. in thickness; outer surface yellowish- or olive-brown (*D. Mezereum*) or purplish-brown (*D. Gnidium*) or purplish-gray (*D. Laureola*), smooth, numerous lenticels giving a transversely striated appearance and occasionally with numerous, circular, brownish-black apothecia; outer corky layer easily separable from the middle bark which varies from light green to olive-brown and with more or less detached bast-fibers; inner surface yellowish-white, satiny lustrous, finely striate; fracture tough, fibrous, the inner bark lamellated; odor very slight; taste at first slight, becoming gradually and increasingly pungent and acrid. Under the microscope, transverse sections of Mezereum show a rather thick cork composed of from 20 to 30 rows of cells, the outer being compressed and with yellowish-brown walls, and the inner more or less tabular with nearly colorless walls; a hypodermis of 3 to 5 rows of collenchymatous cells containing chloroplastids or a yellowish-green resinous substance; an inner bark consisting mostly of nearly colorless non-lignified bast-fibers occurring in loosely united groups, and a few starch-bearing medullary rays one cell in width. The powder is light grayish-brown; bast-fibers numerous, from 0.4 to 3 mm. in length and about 0.015 mm. in width, frequently more or less uneven or irregularly bent and considerably attenuated at the ends, the walls being from 0.001 to 0.005 mm. in thickness, colorless, non-lignified and free from pores; fragments of yellowish-brown cork cells and starch-bearing medullary rays; starch grains relatively few, mostly spherical or elliptical, occasionally 2- to 4-compound, the individual grains from 0.003 to 0.015 mm. in diameter." *U. S.*

British writers state that the bark of the root is the most active. The berries and leaves of the plant are also active, and the former have sometimes proved fatal to children who have eaten them. Pallas states that they are used as a purgative by the Russian peasants, and that thirty berries are required to act. French authors observe that fifteen are sufficient to kill. A tincture of them is used in Germany as a local application in *neuralgia.*

Vauquelin discovered a peculiar principle in the bark of *Daphne alpina.* This has subsequently been found in other species, and has received the name of *daphnin.* Gmelin and Bär found it in the bark of *D. Mezereum,* associated with wax, an acrid resin (*mezerein*), a yellow coloring matter, a reddish-brown extractive, and uncrystallizable and fermentable sugar, a gummy matter containing nitrogen, ligneous fiber, malic acid, and several malates. By J. B. Eng it has been discovered, together with a vola-

tile oil, in the flowers of *D. Mezereum.* (*Wittstein's Viertelj.*, viii, 23.) *Daphnin* is in prismatic crystals, grouped together, colorless, transparent, brilliant, slightly soluble in cold water, very soluble in boiling water and alcohol, without odor, and of a bitter, somewhat harsh taste. According to Zwenger (*Ann. Ch. Ph.*, 1860, cxv, 1) it is a glucosidal acid, being resolvable by sulphuric or hydrochloric acid into sugar, and a peculiar crystallizable principle called *daphnetin*, $C_9H_6O_4 + H_2O$. He gives for daphnin the formula $C_{15}H_{16}O_9 + 2H_2O$, the same as that of *æsculin*, of which it is, therefore, an isomer. W. Will and O. Jung (*A. J. P.*, 1885) have investigated daphnetin, which was shown in 1879 by Stünkel to be *dioxycoumarin*,

$$C_6H_2(OH)_2\begin{cases} O & -CO \\ & | \\ CH & =CH \end{cases}$$

; they obtained but about one ounce of daphnetin from fifty pounds of extract of mezereum, and they proved that it has the same relation to pyrogallic acid that coumarin has to phenol, or umbelliferone to resorcinol. (For a method of preparing the glucoside daphnin, see *U. S. D.*, nineteenth edition, p. 781.) *Coccognin*, isolated in 1870 by Casselmann from the fruits of *D. Mezereum*, appears to be closely allied to, if not identical with, daphnin. By the dry distillation of an alcoholic extract of mezereum bark, Zwenger obtained *umbelliferone*, $C_9H_6O_3$.

Uses.—The recent bark applied to the skin produces inflammation followed by vesication, and has been popularly used as an epispastic, from time immemorial, in some of the southern countries of Europe. The dried bark, though less active, is possessed of a similar property, and is occasionally employed in France by regular practitioners for the purpose of forming issues. A small square piece, moistened with vinegar, is applied to the skin, and renewed twice a day until a blister is formed, and occasionally afterwards to keep up the discharge. It is slow in its operation, generally requiring from twenty-four to forty-eight hours to vesicate. The ointment was formerly used for maintaining the discharge from blistered surfaces, and may be applied advantageously to obstinate, ill-conditioned indolent *ulcers*. It was recognized by the U. S. 1880. (See *U. S. D.*, 19th ed., p. 781, for formula.)

An alcoholic extract has also been employed to communicate irritant properties to issue-peas. Internally administered, mezereum is a stimulant capable of being directed to the skin or kidneys, and in large doses likely to excite purging, nausea, and vomiting. In overdoses it produces the fatal effects of the acrid poisons, and a case of apparently severe narcotic effects has been recorded. (*Am. J. M. S.*, xxi.) It had at one time much reputation as an alterative in *syphilis, chronic rheumatism*, etc., but is of no value as an internal remedy and is almost never administered save as an ingredient of the compound fluidextract of sarsaparilla.

Dose, ten grains (0.65 Gm.).

Off. Prep.—Fluidextractum Sarsaparillæ Compositum, *U. S.*; Decoctum Sarsaparillæ Compositum, *N. F.*; Fluidextractum Mezerei, *N. F.*; Linimentum Sinapis Compositum (from Fluidextract), *N. F.*

MISTURA AMMONIACI. Br.

AMMONIACUM MIXTURE

(mĭs-tū'rą ăm-mo-nī'ą-cī)

Emulsum Ammoniaci, U. S. 1890, Emulsion of Ammoniac; Ammoniac Mixture; Emulsio Ammoniaci, Lac Ammoniaci; Milk of Ammoniac; Mixture de Gomme ammoniaque, *Lat;* d'ammoniaque, *Fr.;* Ammoniak-Emulsion, *G.*

"Ammoniacum, in coarse powder, 30 *grammes;* Syrup of Tolu, 60 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Triturate the Ammoniacum thoroughly with a little of the Distilled Water so as to form a thin paste; gradually add the remainder of the Distilled Water and the Syrup of Tolu, triturating until the mixture assumes a uniform milky appearance; strain through muslin." *Br.*

In this emulsion the resinous and oily constituents are suspended by means of the gum of the ammoniac, imparting a milky appearance to the preparation, which from this circumstance was formerly called *lac ammoniaci*, or *milk of ammoniac.* The greater portion of the resin subsides upon standing. This emulsion is no longer official in the U. S. P. IX, the process of the U. S. P., 1890, is as follows:

Emulsum Ammoniaci, U. S. 1890. *Emulsion of Ammoniac.*—"Ammoniac, *forty grammes* [or 1 ounce av., 180 grains]; Water, *a sufficient quantity*, to make *one thousand cubic centimeters* [or 33 fluidounces, 6½ fluidrachms]. Rub the Ammoniac, in a warmed mortar, with *nine hundred cubic centimeters* [or 30 fluidounces, 208 minims] of Water, at first very gradually added, until a uniform emulsion results. Then strain the mixture into a graduated vessel, and wash the mortar and strainer with enough Water to make the product measure *one thousand cubic centimeters* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*, 1890.

The British Pharmacopœia (1898) process directs the addition of a small quantity of syrup of Tolu, doubtless as a flavoring agent. The mixture is slightly curdled by acids.

Dose, one-half to a fluidounce (15–30 mils).

MISTURA CRETÆ. U. S., Br.

CHALK MIXTURE Mist. Cret.

(mĭs-tū'rą crē'tæ)

Mixture avec la Craie, *Fr.;* Kreidemixtur, *G.*

* "Compound Chalk Powder, *twenty grammes* [or 309 grains]; Cinnamon Water, *forty mils* [or 1 fluidounce, 169 minims]; Water, *a sufficient quantity*, to make *one hundred mils* [or 3 fluidounces, 183 minims]. Gradually add the cinnamon water and about *twenty mils* [or

325 minims] of water to the compound chalk powder in a mortar, triturating until the mixture is uniform; transfer this to a graduated vessel, rinse the mortar with enough water to make the product measure *one hundred mils* [or 3 fluidounces, 183 minims], and mix the whole thoroughly. This preparation must not be dispensed unless it has been recently prepared." *U. S.*

"Prepared Chalk, 30 *grammes;* Tragacanth, in powder, 5 *grammes;* Refined Sugar, 60 *grammes;* Cinnamon Water sufficient to produce 1000 *millilitres.* Triturate the Prepared Chalk with the Tragacanth and Refined Sugar, and gradually add, with constant trituration, sufficient Cinnamon Water to produce the required volume." *Br.*

The direction that this mixture be prepared extemporaneously is a decided improvement. Unsuccessful attempts have been repeatedly made to devise a formula which would yield a permanent product, and much injury has been done through the dispensing of chalk mixture in an incipient fermentative condition. The trifling amount of glycerin present in the chalk mixture official in 1870 was totally inadequate to preserve it during the warm summer months, when it is in greatest vogue. Compound Chalk Powder is official (see *Pulvis Cretæ Compositus*); it will keep indefinitely, and, besides being itself a valuable addition to the materia medica, is quickly made into chalk mixture by rubbing it with the water and cinnamon water, so that there can be no excuse for not dispensing a fresh mixture. This mixture is a convenient form for administering chalk, and is much employed in *looseness of the bowels* accompanied with acidity. Laudanum and kino or catechu are very often added to increase its astringency.

Dose, four fluidrachms (15 mils), frequently repeated.

MISTURA FERRI COMPOSITA. Br.

COMPOUND IRON MIXTURE [Griffith's Mixture]

(mĭs-tū'rą fĕr'rī cŏm-pŏz'ĭ-tą)

Mixture ferrugineuse de Griffith, *Fr.;* Griffithsche Eisenmixtur, *G.*

This mixture was dropped from the U. S. P. IX; but is included in the N. F. IV. (See Part III.)

"Ferrous Sulphate, in powder, 6 *grammes;* Potassium Carbonate, 8 *grammes;* Myrrh, 15 *grammes;* Gum Acacia, in powder, 15 *grammes;* Glucose, 15 *grammes;* Spirit of Nutmeg, 10 *millilitres;* Rose Water, sufficient to produce 1000 *millilitres.* Powder the Myrrh; add the Potassium Carbonate, Glucose, and Gum Acacia; triturate the mixture with a small quantity of the Rose Water so as to form a thin paste; gradually add more Rose Water and the Spirit of Nutmeg; continue the trituration and further addition of Rose Water until one thousand *millitres* of liquid are produced; add the Ferrous Sulphate and shake until dissolved." *Br.*

This is very nearly the same as the celebrated tonic or anti-hectic myrrh mixture of Griffith. The ferrous sulphate is decomposed by the potassium carbonate, with the production of potassium sulphate and ferrous carbonate, while the excess of the alkaline carbonate forms a saponaceous compound with the myrrh. The mixture is at first of a greenish color, which it loses upon exposure to the air, in consequence of the conversion of the ferrous carbonate into the ferric compound. The official solution may, however, be kept for some time without change, if the vessel in which it is contained be well closed, but the best plant is to prepare it extemporaneously. The sugar contained in it helps somewhat to retard the further oxidation of the ferrous salt, and if considerably increased in amount would act still more efficiently. The finest pieces of myrrh in lump should be selected, and rubbed down with a little of the rose water, as the powdered myrrh of commerce is often impure, and otherwise does not make a good mixture, owing mainly to its loss of volatile oil.

This mixture is used in *anemia,* especially when attended with derangement of the menstrual function. It has been also employed in the hectic fever of *phthisis.* It is contra-indicated by the existence of inflammation of the gastric mucous membrane.

Dose, from one-half to two fluidounces (15–60 mils) two or three times a day.

MISTURA GLYCYRRHIZÆ COMPOSITA. U. S.

COMPOUND MIXTURE OF GLYCYRRHIZA Mist. Glycyrrh. Co. [Brown Mixture]

(mĭs-tū'rą glĭç-ĭr-rhī'zæ cŏm-pŏz 'ĭ-tą)

Mistura Fusca; Mixture de Réglisse, *Fr.;* Zusammengesetzte Lakritzenmixtur, *G.*

*"Pure Extract of Glycyrrhiza, *thirty grammes* [or 1 ounce av., 25 grains]; Syrup, *fifty mils* [or 1 fluidounce, 331 minims]; Acacia, granulated, *thirty grammes* [or 1 ounce av., 25 grains]; Antimony and Potassium Tartrate, *two hundred and forty milligrammes* [or 3½ grains]; Camphorated Tincture of Opium, *one hundred and twenty mils* [or 4 fluidounces, 28 minims]; Spirit of Nitrous Ether, *thirty mils* [or 1 fluidounce, 7 minims]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Rub the pure extract of glycyrrhiza and acacia in a mortar with *five hundred mils* [or 16 fluidounces, 435 minims] of warm water, until they are dissolved. Allow the solution to cool, transfer it to a graduated vessel, add the antimony and potassium tartrate, dissolved in *twelve mils* [or 195 minims] of hot water, then the other ingredients and rinse the mortar with enough water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the whole thoroughly." *U. S.*

This is an exceedingly popular cough mixture, and has been official for many years. In the

U. S. P. IX a change was made by using a definite quantity of antimony and potassium tartrate instead of wine of antimony, because all wines were deleted. This is an improvement because wine of antimony as found in commerce was sometimes variable in quality.

The spirit of nitrous ether is probably useful by somewhat retarding decomposition. It has been suggested many times that this preparation be filtered and dispensed clear but the revisers of the Pharmacopœia have not considered it of sufficient importance to change the well-known appearance of the mixture and there are no advantages in making a *mixture* transparent. Commercial powdered extract, however, should not be used as it contains about 40 per cent. of insoluble matter and produces a very heavy precipitate. If pure extract is used as officially directed the mixture is but slightly cloudy (see *A. J. P.*, 1892, 563; *M. R.*, 1910, 253).

Uses.—The compound mixture of glycyrrhiza is used very frequently as a vehicle, especially in conjunction with the ammonium salts in the early stages of acute bronchitis. Its use in such manner, however, is not to be encouraged because of the presence of the antimony and opium. While the dose of the latter ingredients is so small that in a teaspoonful there will scarcely be sufficient to exercise any perceptible effect in the adult, yet their exhibition in unsuitable cases is certainly unwise. In large dose it acts as a nauseating expectorant and is sometimes given, especially in children, for its active effects in *bronchitis*. In our opinion, however, the combination is not a very happy one for this purpose.

Dose, from one-half to one fluidounce (15–30 mils) for an adult; one fluidrachm (3.75 mils) for a child two years old. It should be well shaken when administered.

MISTURA GUAIACI. Br.

GUAIACUM MIXTURE

(mĭs-tū'rą guā'ĭą-cī)

Emulsio Resinæ Guaiaci; Mixture de Résine de Gayac, Lait de Gayac, *Fr.*; Guajak-Emulsion, Guajakharzmixtur, *G.*

"Guaiacum Resin, 25 *grammes;* Refined Sugar, 25 *grammes;* Tragacanth, in powder, 5 *grammes;* Cinnamon Water, sufficient to produce 1000 *millilitres*. Triturate the Guaiacum Resin with the Refined Sugar and the Tragacanth; add gradually, with constant trituration, sufficient Cinnamon Water to produce the required volume." *Br.*

For the changes of color which the Guaiac in this mixture undergoes, and which it produces in other substances, see *Guaiaci Resina*, p. 539. Tragacanth was substituted for acacia in the Br. Ph., 1898, process. A similar preparation under this title is official in the N. F. IV. (See Part III.)

Dose, one-half to two fluidounces (15–60 mils), repeated two or three times a day, or more frequently.

MISTURA OLEI RICINI. Br.

CASTOR OIL MIXTURE

(mĭs-tū'rą ō'lę-ī rĭç'ĭ-nī)

Emulsion of Castor Oil; Emulsion d'Huile de Ricin, *Fr.*; Ricinusoelmixtur, *G.*

"Castor Oil, 375 *millilitres;* Gum Acacia, in powder, 100 *grammes;* Orange-flower water of commerce, undiluted, 150 *millilitres;* Cinnamon Water, sufficient to produce 1000 *millilitres*. Triturate the Castor Oil with the Gum Acacia in a dry mortar; add, in one portion, two hundred *millilitres* of Cinnamon Water, and continue the trituration until the oil is completely emulsified; then, with constant trituration, add the orange-flower water and sufficient Cinnamon Water to produce the required volume." *Br.*

Under the title *Emulsum Olei Ricini* a similar preparation is official in the N. F. IV. (See Part III.)

Dose, from one-half to two fluidounces (15–60 mils).

MISTURA SENNÆ COMPOSITA. Br.

COMPOUND MIXTURE OF SENNA

(mĭs-tū'rą sĕn'næ cŏm-pŏs'ĭ-tą)

Black Draught; Mixture de Séné composée, *Fr.*; Zusammengesetzte Senna-Aufguss, Zusammengesetzte Sennamixtur, *G.*

"Magnesium Sulphate, 250 *grammes;* Liquid Extract of Liquorice, 50 *millilitres;* Compound Tincture of Cardamoms, 100 *millilitres;* Aromatic Spirit of Ammonia, 50 *millilitres;* Infusion of Senna, sufficient to produce 1000 *millilitres*. Dissolve the Magnesium Sulphate in five hundred *millilitres* of the Infusion of Senna; add the mixed Liquid Extract of Liquorice, Compound Tincture of Cardamoms, and Aromatic Spirit of Ammonia, and sufficient Infusion of Senna to produce the required volume." *Br.*

This is a form of Compound Infusion of Senna, called commonly *black draught*, which term should never be used, as death has occurred through misreading prescriptions and dispensing *"black drop"* or vinegar of opium. We prefer the form given under *Infusum Sennæ Compositum*, as being more easily prepared and quite as efficient.

Dose (Br. Pharm.), from one to two fluidounces (30–60 mils).

MISTURÆ

MIXTURES

(mĭs-tū'ræ)

Mixtures, *Fr.*; Mixturen, *G.*; Mixtura, *Sp.*

This term should be restricted, in the language of pharmacy, to those preparations in which insoluble substances, whether solid or liquid, are suspended in aqueous fluids, by the intervention of gum arabic, sugar, yolk of egg, or other viscid matter. When the suspended substance is of an oleaginous nature, the mixture is properly called an *emulsion*, and the

U. S. Pharmacopœia has recognized them by creating a special class for these. (See *Emulsa*, p. 419.) The object of these preparations is usually to facilitate the administration, to conceal the taste, or to obviate the nauseating effects of unpleasant medicines, and their perfection depends upon the intimacy with which the ingredients are blended. Some skill and care are requisite for the production of uniform and perfect mixtures. As a rule, the body to be suspended should be thoroughly mixed by trituration with the substance intended to act as the inter-medium, before the aqueous vehicle is added. In Great Britain, and to some extent in this country, the term mixture is used indiscriminately for aqueous medicinal liquids having more than one ingredient, and for aqueous liquids which cannot be easily classified. Many of such liquids are perfectly transparent and should be in the class of Solutions.

A study of the principles of colloid chemistry has been brought to bear upon the subject of pharmaceutical mixtures and their preparation, with great advantage (see *Emulsa*).

MORPHINA. U. S.

MORPHINE

(mör-phī'nȧ)

"An alkaloid [$C_{17}H_{19}O_3N + H_2O = 303.18$] obtained from opium. Preserve it in well-closed containers, protected from light." *U. S.*

Morphia, *U. S.* 1870; Morphinum, Morphium; Morphine, *Fr. Cod.*; Morphin, *G.*; Morfina, *It., Sp.*

The U. S. Pharmacopœia no longer contains a process for the extraction of morphine; that of 1870, which has been known as Staples's process, is given in the *U. S. Dispensatory*, 19th edition, p. 785.

Various processes for preparing morphine have been employed. In most of them the morphine is extracted from opium by maceration with water (either pure or acidulated), then precipitated by ammonia, and the crystals afterwards purified by the agency of alcohol, or by repeated solution in a diluted acid and precipitation. Sertürner, the discoverer of morphine, made an infusion of opium in distilled water, precipitated the morphine by ammonia in excess, dissolved the precipitate in diluted sulphuric acid, precipitated anew by ammonia, and purified by solution in boiling alcohol, and crystallization. In evaporating aqueous solutions containing morphine a temperature of 40° C. (104° F.) should not be exceeded.

Properties.—Morphine crystallizes from alcohol in the form of small, colorless, shining crystals. It is officially described as follows: "Colorless or white, shining, rhombic prisms, in fine needles, or as a crystalline powder; odorless; permanent in the air. One Gm. of Morphine dissolves in 3340 mils of water, 210 mils of alcohol, 1220 mils of chloroform, 6250 mils of ether, and in 100 mils of lime water, at 25° C. (77° F.); also in 1075 mils of boiling water and 98 mils of boiling alcohol; insoluble in benzene. A saturated aqueous solution of Morphine is alkaline to litmus. One mil of sulphuric acid added to about 0.05 Gm. of Morphine produces either no color or at most only a red or yellow tint; on heating, a brown color is developed. Sulphuric acid containing 0.005 Gm. of selenous acid in each mil gives with Morphine a blue color, changing to green and then to brown. (Codeine yields a green color, changing to blue, and afterwards to grass-green; narcotine gives a green color, changing to brown and then to cherry-red.) Nitric acid produces with Morphine an orange-red color fading to yellow. Sulphuric acid containing 0.005 Gm. of molybdic acid in each mil gives a purple color, changing to blue. Sulphuric acid containing in each mil one drop of solution of formaldehyde yields an intense, purple color. Add a few drops of ferric chloride T.S. to a neutral solution of Morphine (1 in 100), made by the careful addition of diluted sulphuric acid; a blue color is produced which is destroyed by acids, alcohol, or by heating. Morphine solutions, when mixed with an aqueous solution of potassium ferricyanide containing a drop of ferric chloride T.S., yield deep blue solutions from which, after standing, a blue precipitate separates (difference from *codeine*). Morphine loses not more than 6.5 per cent. of its weight when dried to constant weight at 100° C. (212° F.) (*moisture*). No weighable ash remains on incinerating 0.5 Gm. of Morphine. Dissolve about 0.1 Gm. of Morphine in 10 mils of diluted hydrochloric acid; no red coloration is produced by the addition of a few drops of ferric chloride T.S. (*meconic acid or meconates*). Warm about 0.2 Gm. of Morphine with 4 mils of potassium hydroxide T.S.; the odor of ammonia is not noticeable (*ammonium salts*). Dissolve 1 Gm. of Morphine in 10 mils of sodium hydroxide T.S., shake out the solution with three successive portions of 15, 10, and 10 mils of chloroform, passing the chloroform solutions through a small filter previously moistened with chloroform. Evaporate carefully the combined chloroform solutions to dryness on a water bath, dissolve the residue in 10 mils of fiftieth-normal sulphuric acid V.S., add a few drops of methyl red T.S. and titrate the excess of acid with fiftieth-normal potassium hydroxide V.S. Not less than 7.5 mils of the latter is required (*foreign alkaloids*)." *U. S.*

Von Gerichten and Schrötter (*Ber. d. Chem. Ges.*, 1882, pp. 1484 and 2179) showed that morphine and codeine were derivatives of phenanthrene, as when distilled with zinc dust they yielded phenanthrene, pyridine, and quinoline. Knorr (*Ber. d. Chem. Ges.*, 22, p. 2081) has shown that it is probable that morphine contains, combined with the phenanthrene nucleus, the *morpholine* group. Morpholine (tetra-hydro-oxazine), $NH<\begin{matrix}CH_2.CH_2\\CH_2.CH_2\end{matrix}>O$, is formed when dioxyethylamine is heated to 160° C. (320° F.) with hydrochloric acid, or is boiled

with alkali. As seen from the formula, it bears a structural relation to both pyrrol and pyridine. For later views on the structure of the morphine molecule by Knorr and Vis, see *Proc. A. Ph. A.*, 1894, 1122. For a chemical bibliography of morphine, by H. E. Brown, see *Ph. Rev.*, 1897, and *Ph. Archiv.*, 1898.

Heated in the open air, morphine burns with a bright flame, and at a red heat is wholly dissipated. In the products resulting from the combustion of opium or morphine this alkaloid may be detected, proving that it is partly volatilized when burned. Morphine in solution is to a considerable extent absorbed by animal charcoal, which, though it will part with most of the alkaloid to alcohol, cannot be wholly deprived of it by repeated washings with that liquid, either cold or hot. It is also absorbed when filtered through kaolin or fuller's earth. (Lefort, *J. P. C.*, Août, 1861, 98.) Its solution restores the blue color of litmus paper reddened by acids, and turns the yellow of turmeric to brown. Hager (*Ph. Ztg.*, 93, 250, also *Proc. A. Ph. A.*, 1893, 680) states that on heating solutions containing morphine, oxygen is absorbed gradually and oxymorphine is formed; at a boiling temperature this change proceeds rapidly. The oxymorphine is much less active as a narcotic than is morphine. This absorption of oxygen takes place most rapidly in alkaline solutions and is also affected by the aid of potassium permanganate, potassium ferricyanide, and ammoniacal copper solution. The reaction is:

$$2C_{17}H_{19}NO_3 + O = (C_{17}H_{18}NO_3)_2O + H_2O$$

This product is known as *oxydimorphine* (or *pseudomorphine*). Morphine is, therefore, a powerful reducing agent, acting upon silver nitrate and gold chloride even in cold solutions. With the acids morphine forms salts, which are generally soluble, and are decomposed by the alkalies. It is dissolved also by the fixed and volatile oils. The solutions of potassium and sodium hydroxides also dissolve morphine, which is precipitated slowly from them on exposure to the air, in consequence of the absorption of carbon dioxide. Solution of ammonia has to a certain extent the same solvent power, and hence the necessity, in precipitating morphine by this alkali, not to employ it in great excess. Solution of iodine with potassium iodide precipitates the salts of morphine in aqueous solution. With chlorine water morphine and its salts assume an orange color, and the same effect is produced on them by solution of chlorinated soda. (Fairthorne *A. J. P.*, xxviii, 9.) By the contact of nitric acid they assume a blood red color, which ultimately changes to yellow, and this is one of the tests of morphine; but, as the same change of color is produced with brucine, it cannot be relied on in the absence of other evidence. Nitric acid also produces a red color with oil of cloves, but in this case the red does not change to yellow. When added to a solution of iodic acid, or an acidulous iodate, morphine and its salts redden the liquid and set iodine free. (Sérullas.) This is a very delicate test, but is not conclusive, as various other organic substances act in a similar manner. J. Lefort, however, has found that the color produced by these substances is removed by ammonia, while the redness produced with morphine is greatly intensified by addition of that alkali. This test, thus modified by the addition of ammonia, is so delicate that, according to Lefort, it will detect one part of morphine in 10,000 parts of a liquid holding it in solution. (*J. P. C.*, Août, 1861, 113.) Husemann's test consists in leaving morphine or its salt in contact with concentrated sulphuric acid for 12 or 15 hours, or in heating for half an hour with the acid to 100° C. (212° F.), and then adding either a little nitric acid, a nitrate or chlorate or chlorine water, or chlorinated soda, when a beautiful bluish or reddish-violet color, passing into deep blood-red and gradually paling, is developed. The presence of small quantities of coloring matter does not prevent this reaction, if chlorinated reagents are selected. A. Husemann asserts that this test will recognize the hundredth part of a milligramme of the alkaloid. (*A. J. P.*, xlvii, 210.) According to R. Schneider, a very delicate test is afforded by putting a drop of the suspected liquid on a plate, saturating with sugar, and putting alongside of it a drop of sulphuric acid; if morphine be present, a very intense purple will be developed at the point of contact, passing after half an hour into violet, then bluish green, and finally dirty yellow. (*J. P. C.*, 4e sér., xviii, 221.) According to H. Weppen, the delicacy of this test is much increased by the addition of a minute quantity of bromine water to the solution. Codeine and aconitine are stated, however, to give the same reaction. (*Ibid.*, 4e sér., xix, 246.)

Fröhde's reagent (a fresh solution of 0.005 Gm. sodium molybdate in 1 mil of pure concentrated sulphuric acid) strikes with morphine and its salts a beautiful blue-violet color, passing into blue then green, finally back to bluish violet. This reaction is stated to be delicate but not characteristic. A. B. Prescott gave a thorough résumé of the views of investigators on this test in *A. J. P.*, 1876, 59. Bruylants combines Fröhde's test with that of Husemann. A trace of Fröhde's reagent added to a solution of morphine in sulphuric acid produces the well-known lilac tint; if the sulphuric acid solution be warmed and treated in the same way, a green tint will be noted. On dropping a particle of potassium nitrate into this green liquid, the color changes to red and finally yellowish. The other opium alkaloids give different tints. (*Proc. A. Ph. A.*, 1895, 1016.) In the presence of sulphuric acid morphine exhibits surprising powers as a reducing agent. Among the most notable instances of deoxidation may be mentioned those of silver oxide, hydrated bismuth oxide, the acids of tin, tungsten, vanadium, titanium, and molybdenum. A solution of titanic acid in con-

centrated sulphuric acid is one of the most delicate reagents for morphine. An intense brown-red to violet color is produced if titanic acid is added to concentrated sulphuric acid containing a trace of morphine in solution. (Flückiger, *N. R.*, Feb., 1880. See also *N. R.*, 1881, p. 237.) M. H. Kahlbrunner states that the most sensitive test is made with a solution (No. 1) of crystallized ferric chloride (thirty grains to four fluidrachms of distilled water) and a fresh solution (No. 2) of potassium ferricyanide (two grains in four drachms). To the suspected liquor five or six drops of No. 1 are added, and afterwards three or four drops of No. 2. If morphine be present, a color varying from deep blue to pale blue and bluish-green, according to the proportion of the alkaloid, is developed. Neither gum, sugar, alcohol, glycerin, atropine, quinine, nor strychnine interferes with this test. An excess of alkali does so by decomposing the ferric chloride. This test depends upon the fact that the potassium ferricyanide solution is reduced by morphine to the ferrocyanide. It is affirmed that even 1-60,000th of one per cent. of morphine can be detected. (See also *Proc. A. Ph. A.*, 1897, 701.) G. Vulpius (*A. Pharm.*, 1887, 25) states that if about 0.00025 Gm. of a morphine salt be dissolved in a porcelain dish in about six drops of concentrated sulphuric acid, a few centigrammes of sodium phosphate added, and the mixture carefully heated, white fumes will be evolved and a violet color appear. On adding water drop by drop, a brilliant red appears, which, on further addition, changes to a dirty green. If the solution be then shaken with the same volume of chloroform, the latter will be colored blue. Isobutylic alcohol has been used by Nagelvoort for the detection of morphine and codeine. (See *Proc. A. Ph. A.*, 1894, 273.)

A delicate reaction for morphine has been reported by T. H. Oliver, which is sensitive to 0.00002 Gm. morphine. It is as follows: To the solution of the suspected substance, add a few mils of hydrogen dioxide solution and a few drops of strong ammonia water. Then stir the solution with a piece of copper wire, whereupon the previously colorless solution becomes of a deep port wine color in the presence of morphine. Codeine and dionine do not give the reaction. (*J. A. M. A.*, 1914, 63, p. 513.)

Siebold heats gently the suspected substance with some drops of concentrated sulphuric acid and a small quantity of chemically pure potassium perchlorate; a deep brown color will be produced if morphine is present. (*P. J.*, Oct., 1873.) According to H. S. Wellcome, one part of morphine in ten thousand parts of water can be recognized by chlorine water, if care be exercised not to decolorize by an excess of the reagent; the color varies from light orange-red to deep red according to the proportion of morphine present. Brucine is the only other alkaloid giving the same reaction, but, while the color produced by morphine is discharged by excess of chlorine, that caused by brucine is not affected. (*A. J. P.*, 1874, p. 305.) Morphine and its salts assume a fine blue color with ferric chloride; at least this is true of the alkaloid, its sulphate, acetate, and oxalate, and the same effect will be produced by the other salts, if previously decomposed by an alkali, but that this test should be satisfactory it is necessary to operate on morphine either in powder or in concentrated solution. (Lefort.) A solution of morphine acetate or sulphate containing only one part of the salt in 100 precipitates silver from a solution of the nitrate of that metal. (Horsley.) Morphine is precipitated from its solutions by potassium or sodium hydroxide, and redissolved by an excess of the alkali. Infusion of galls and other vegetable substances containing tannic acid precipitate morphine in the state of tannate, which is soluble in acetic acid, but according to Dublanc, the alkaloid is not precipitated by pure gallic acid. If ammonia be added to a mixture of the solutions of chlorine and morphine, there will be produced a dark brown color, which will be destroyed by a further addition of chlorine. Sulphuric acid containing a trace of formaldehyde produces a bright purple color with even small traces of morphine. For methods of separating narcotine, see *U. S. D.*, 17th ed., 879.

Formaldehyde reacts with both morphine and codeine to form medicinally active condensation products by the union of two molecules of the base with one molecule of the formaldehyde, with elimination of water; a methylene group, CH_2, uniting with two alkaloidal residues each of which loses an H atom. That formed from morphine is an amorphous base, difficultly soluble in water, but easily soluble in alkaline solution and in alcohol. It melts at 270° C. (518° F.), and forms a hydrochloride soluble in water. (*Proc. A. Ph. A.*, 1897, 702.)

Uses.—There can be no doubt that morphine is the chief narcotic principle of opium, from which, however, it differs somewhat in its mode of action. The effects of morphine are so protean that they can best be considered by taking the different functions of the body seriatim.

Nervous System.—Morphine is a cerebral depressant but a spinal stimulant. The relative predominance of one or the other of these actions depends upon the relative degree of development of the brain or spinal cord; thus in the frog it produces violent convulsions of the strychnic type, but in man the spinal symptoms are usually imperceptible and for medical purposes we may regard it as a general depressant as far as the nervous system is concerned. The primary action upon the cerebrum seems to be a diminution in the powers of perception, especially of pain, although there is often an evident lowering in the acuity of the special senses. With somewhat larger doses intellection becomes depressed and a tendency to drowsiness is manifest, and after toxic doses a deep comatose sleep may follow. The theory that small doses of morphine exercise a primary stimulant influence on intellection we believe is untenable.

When locally applied in sufficient concentration morphine lowers the functional activity of the peripheral nerve endings both motor and sensory. In this way it may, under certain conditions as shown by Wiki (*J. de P. P.*, 1913, xv, p. 848), exercise a local anesthetic action. It is, however, less active in this regard than some of the other allied alkaloids, notably ethyl-morphine or methyl-morphine (codeine). Among the other actions of morphine which are to be attributed to its influence on nerve centers is the contraction of the pupil, due to stimulation of the oculo-motor center, slowing of the pulse from stimulation of the cardio-inhibitory center, slowing of the respiration from depression of the respiratory center, and overcoming the action of nauseants from its action on the emetic center. Cushny and Lieb (*J. P. Ex. T.*, 1915, vi, p. 450) have found that in the period of respiratory depression produced by morphine there is not the same sort of insensibility to carbon dioxide that is caused by some other respiratory depressants, an observation which is of considerable importance in connection with the clinical use of this remedy in dyspneic states.

Circulation.—The action of morphine upon the circulation is quite subsidiary to its effects upon the nervous system. In therapeutic doses the only manifestation of its effects on the part of the circulatory apparatus is slowing of the pulse, due, as mentioned above, to stimulation of the inhibitory center, and flushing of the skin which appears to be the result of a special action on the cutaneous blood vessels. After large doses the blood pressure is generally somewhat lowered, probably from the combined weakening of the heart and vasomotor system.

Nutrition.—Morphine affects the nutrition both through its action upon the digestive processes and through a direct influence on the bodily chemistry. It appears to lessen all the digestive secretions including salivary, gastric, and enteric, also to diminish the peristaltic movements. The direct influence of morphine upon metabolism is not clearly understood, but there is reason to believe that it has some such action.

Elimination.—A large part of the morphine is detoxicated in the body passing out as a dioxymorphine. Some of it, however, is eliminated unchanged, more through the intestinal glands than the kidneys.

Clinical Uses.—Morphine may be used in medicine to fulfil any of seven indications: (1) In its power to relieve *pain* morphine is without rival. Because, however, of its unpleasant action upon the digestive organs and the ever present danger of formation of the habit, it should be reserved for the more severe degrees of suffering, such as in *gall-stone* or *renal colic*, or when other analgesics have failed. In this connection it should be noted that the analgesic action of morphine is greatly enhanced by combining it with even relatively feeble synergists, such as the coal tar series or scopolamine, and by recourse to this principle of combination the physician is often able to assuage the suffering with comparatively small doses of the alkaloid. (2) As a hypnotic morphine is useful, especially when the *insomnia* is due to suffering. In the purely nervous types of sleeplessness it is less valuable than the aliphatic narcotics, but is often of service as an adjuvant. (3) As a sedative to the respiratory center it is a remedy of much value in *asthma* and certain types of *cough*, such as *whooping cough*. In true *bronchitis*, however, it must be used with circumspection. In the acute stage or where the mucous membranes are dry, it often does great harm by a further checking of the bronchial secretions; on the other hand, when the secretions are very profuse it may so benumb the respiratory center as to stop their expectoration and thereby lead to a dangerous retention of fluid in the chest. (4) In intestinal conditions it is used for its influence both on secretion and peristalsis. For the latter action it is of much service in serous *diarrheas*, but when the diarrhea is due to irritation of the intestinal tract it is generally to be avoided, as it defeats nature's purpose to get rid of the irritant. For its influence upon the muscular movements of the bowel it is useful in various forms of intestinal spasm, such as *lead colic*, and also to keep the bowels at rest in certain types of *peritonitis* and other inflammatory conditions. Whole opium is usually preferred to morphine when an action upon the intestines is desired. (5) For the purpose of aiding in the production of diaphoresis it is used, especially in the form of Dover's powder, in the early stages of *colds*, in *rheumatism*, *influenza*, etc. (6) To allay *vomiting*, especially of reflex origin. (7) By its calmative effect it protects the system against exhaustion in debilitated conditions, as certain forms of *typhoid fever*. For the same purpose it is also a very valuable drug in the treatment of *internal hemorrhage*.

In cases where it is desired to make a profound impression upon the general system, morphine should be given hypodermically. The dose varies enormously, according to the susceptibility of the patient and the purpose for which it is used. In a general way the dose of the morphine salts, by mouth, may be given as from one-eighth to one-half grain (0.008-0.032 Gm.), and one-twelfth to one-fourth grain (0.005–0.016 Gm.) hypodermically.

In consequence of its insolubility in water, morphine in its pure state is less convenient than its salts, which are therefore always preferred. The acetate, sulphate, and hydrochloride, which have been employed, act precisely alike therapeutically, and differ from opium chiefly in being less disposed to constipate the bowels. They are also somewhat less likely to cause disagreeable after-effects than is opium, but the deodorized tincture is certainly preferable to them for many purposes. They are further adapted for hypodermic use. Oleic acid has also been proposed as a vehicle for morphine externally used, as it dissolves both the

alkaloid and its salts perfectly in considerable proportion. A liniment of oleate of morphine has been proposed, consisting of 300 parts of oleic acid and 1 part of morphine scented with a little oil of bergamot.

As the proportion of acid necessary to neutralize morphine is very small, the dose of the alkaloid is practically the same as that of its salts.

Dose, one-fifth of a grain (0.012 Gm.), equivalent to a grain of powdered opium.

MORPHINÆ ACETAS. Br.

MORPHINE ACETATE

(mŏr-phĭ'næ ą-cē'tăs)

"Morphine Acetate, $C_{17}H_{19}NO_3,C_2H_4O_2,3H_2O$, is the acetate of an alkaloid, morphine, obtained from opium." *Br.*

Morphiæ Acetas, *Br.* 1867, *U. S.* 1870; Acetate of Morphia; Morphinum Aceticum; Acetas Morphicus; Acétate de Morphine, *Fr.*; Essigsaures Morphium, Morphinacetat, *G.*

A process for this salt is no longer official; that of the U. S. P., 1870, is as follows: "Take of Morphia, in fine powder, *a troyounce;* Distilled Water, *half a pint;* Acetic Acid, *a sufficient quantity.* Mix the Morphia with the Distilled Water; then carefully drop Acetic Acid into the mixture, stirring it constantly until the Morphia is neutralized and dissolved. Evaporate the solution, by means of a water-bath, to the consistence of syrup, and set aside until it concretes. Lastly, dry the salt with a gentle heat, and rub it into powder." *U. S.*, 1870.

In the U. S. process of 1870, morphine is saturated with acetic acid. A small excess of acid is attended with no inconvenience, as it is subsequently driven off by the heat. Care is required not to employ too much heat in the evaporation, as the acetate is easily decomposed, a portion of the acetic acid escaping, and leaving an equivalent portion of uncombined morphine. With attention to arrest the evaporation at a certain point, the acetate may be obtained in the state of crystals, but the crystallization is attended with some difficulty, and evaporation to dryness is almost universally preferred. Some recommend to dissolve the morphine in boiling alcohol, instead of suspending it in water, previously to the addition of the acetic acid. Less heat is thus required in the evaporation, and impurities in the morphine may often be detected, as they are likely to be insoluble in alcohol. To ascertain, in this case, whether the morphine is saturated, it is necessary to employ litmus paper, the blue color of which should not be restored if previously reddened by an acid. If the morphine used in preparing the acetate contain narcotine, it will be best to employ diluted acetic acid as the solvent, and to favor its solvent power by heat. Under these circumstances it dissolves only the morphine, leaving the narcotine nearly or quite untouched. (Hodgson, *A. J. P.*, v.) The British process (1885) differs from that of the U. S. Pharmacopœia of 1870 only in obtaining uncombined morphine, as the first step, by precipitating it from a solution of the hydrochloride, morphine itself not being official. As this salt is prone to decompose it is well to prepare it with a slight excess of acetic acid in order to promote its stability.

Properties.—It is officially described in the British Pharmacopœia as "a white, crystalline or amorphous powder. Taste bitter. Almost entirely soluble in 2.5 parts of *water.* Loses acetic acid when exposed to the air. Yields the reactions for morphine described under 'Morphinæ Hydrochloridum,' and the *reactions* characteristic of acetates. 2 grammes form with 5 millilitres of warm *morphinated water* a slightly turbid solution which is rendered clear by the addition of 0.1 millilitre of *acetic acid,* and this solution, when mixed with a slight excess of *solution of ammonia,* yields a white precipitate which, after washing and drying as described under 'Morphinæ Hydrochloridum,' weighs from 1.41 to 1.44 grammes. No appreciable ash." *Br.*

Uses.—This and the other official salts of morphine are of identical medicinal value. The solutions for hypodermic use should be freshly prepared, as morphine salts, especially the acetate, are very prone to undergo decomposition, through the growth of a fungus.

Dose, one-twelfth to one-half grain (0.005–0.032 Gm.).

Off. Prep.—Liquor Morphinæ Acetatis, *Br.*

MORPHINÆ HYDROCHLORIDUM. U. S., Br.

MORPHINE HYDROCHLORIDE Morph. Hydrochl. [Morphinæ Hydrochloras, U. S. 1890, Morphine Hydrochlorate Morphine Chloride]

(mŏr-phĭ'næ hȳ-drǫ-ȼhlō'rī'dŭm)

"The hydrochloride [$C_{17}H_{19}O_3N.HCl + 3H_2O = 375.68$] of the alkaloid morphine. Preserve it in well-closed containers protected from light." *U. S.* "Morphine Hydrochloride, $C_{17}H_{19}NO_3,HCl,3H_2O$, is the hydrochloride of an alkaloid, morphine, obtained from opium." *Br.*

Morphiæ Murias, *Br.* 1867, *U. S.* 1870; Murias (Hydrochloras) Morphicus; Morphiæ Hydrochloras; Muriate of Morphia; Chlorhydrate de Morphine, *Fr. Cod.*; Morphinum Hydrochloricum, *P. G.*; Morphinhydrochlorid, Salzsaures Morphin, *G.*

A process for this salt is no longer official. The British process (1885) will be found in *U. S. D.*, 17th ed., 882. See also *U. S. D.*, 19th ed., 790.

Properties.—This salt crystallizes in "white, silky, glistening needles or cubical masses, or as a white, crystalline powder; odorless; permanent in the air. One Gm. of Morphine Hydrochloride dissolves in 17.5 mils of water and 52 mils of alcohol at 25° C. (77° F.); also in 0.5 mil of boiling water and 46 mils of alcohol at 60° C. (140° F.); soluble in glycerin; insoluble in chloroform or ether. Its aqueous solution (1 in 20) is neutral or slightly acid to litmus. Silver nitrate T.S., when added to an aqueous solution of the salt, produces a white precipitate

insoluble in nitric acid. Add potassium carbonate T.S. to 5 mils of an aqueous solution of the salt (1 in 30), a white precipitate is produced, which does not become green on exposure to air nor yield a color to chloroform when shaken with it (*apomorphine*). Morphine Hydrochloride loses not more than 15 per cent. of its weight when dried to constant weight at 100° C. (212° F.) (*moisture*). In all other respects the salt responds to the tests for identity and purity under *Morphina.*" *U. S.*

"Acicular crystals, or a white microcrystalline powder. Taste bitter. Soluble in 25 parts of *water*. 1 drop of *solution of ammonia* added to 5 millilitres of an aqueous solution (1 in 30) produces a white crystalline precipitate easily soluble in *solution of sodium hydroxide,* but soluble with difficulty in excess of *solution of ammonia;* this precipitate yields mere traces to *benzene* (absence of certain other alkaloids). Yields, when moistened with *nitric acid,* an orange-red color; with *T. Sol. of ferric chloride,* a dull greenish-blue. A trace added to 5 millilitres of a very dilute solution of *potassium ferricyanide* to which 1 drop of *T. Sol. of ferric chloride* has been added produces a deep blue color. 0.1 gramme dissolves in 2 millilitres of *sulphuric acid* without coloration, or with the production of not more than a faint pink color; if a portion of this solution is heated on a water-bath for fifteen minutes, cooled, and treated with a few drops of *diluted nitric acid,* a violet coloration, rapidly changing to blood-red, is produced; the addition of *sodium arsenate* to another portion of the original solution produces a bluish-green color. 1 drop of *solution of potassium carbonate* added to 5 millilitres of an aqueous solution (1 in 30) yields a pure white precipitate which does not become colored on exposure to the air, and does not color *chloroform* when shaken with it (distinction from and absence of apomorphine). When 0.5 millilitre of an aqueous solution (1 in 100) is mixed on a white porcelain tile with 0.5 millilitre of *mucilage of starch* in which 0.005 gramme of *iodic acid* has been dissolved, a blue coloration is immediately produced (distinction from morphine esters). Yields the reactions characteristic of chlorides. 2 grammes dissolved in 50 millilitres of warm *morphinated water* give, on the addition of a slight excess of *solution of ammonia,* a white, crystalline precipitate which, when washed with a little cold *morphinated water* and dried, first at 55° to 60° C. (131°–140° F.), and finally for fifteen minutes at 115° C. (239° F.), weighs from 1.50 to 1.52 grammes. Loses about 14 per cent. of its weight when dried at 100° C. (212° F.). No appreciable ash." *Br.*

A saturated solution in boiling water forms a solid crystalline mass on cooling. The solution of morphine hydrochloride, when kept several months, has been known to produce vomiting, through the formation of traces of apomorphine. (*Ph. Centralh.*, 1885, 93.) Potassium hydroxide throws down from its solution a precipitate which is redissolved by an excess of the alkali. The salt is affected by heat, nitric acid, iodic acid, ferric chloride, and chlorine followed by ammonia, in the same manner as morphine. Sugar is said to have been used largely in the adulteration of this salt. It may be detected most readily by the deep red color produced when the adulterated salt is dissolved in strong sulphuric acid. (See *Saccharum.*)

This preparation of morphine is much used in Great Britain, but in this country less than the sulphate. For medicinal properties, see *Morphina.*

Dose, one-twelfth to one-half grain (0.005–0.032 Gm.).

Off. Prep.—Liquor Morphinæ Hydrochloridi, *Br.;* Suppositoria Morphinæ, *Br.;* Tinctura Chloroformi et Morphinæ Composita, *Br.;* Trochiscus Morphinæ, *Br.;* Syrupus Morphinæ et Acaciæ, *N. F.;* Trochiscus Morphinæ et Ipecacuanhæ, *Br.*

MORPHINÆ SULPHAS. U. S.

MORPHINE SULPHATE Morph. Sulph.

(mör-phī'nē sŭl'phās)

"The sulphate $[(C_{17}H_{19}O_3N)_2.H_2SO_4 + 5H_2O = 758.49]$ of the alkaloid morphine. Preserve it in well-closed containers, protected from light." *U. S.*

Morphiæ Sulphas, *Br.* 1867, *U. S.* 1870; Morphinum Sulphuricum, Sulphas Morphicus; Sulphate of Morphia; Sulfate de Morphine neutre, *Fr. Cod.;* Schwefelsaures Morphium, Morphinsulfat, *G.;* Sulfato morifico, *Sp.*

No process is given in the present U. S. P.; for that of the U. S. P., 1870, see *U. S. Dispensatory,* 19th ed., p. 791. Morphine sulphate is no longer official in the British Pharmacopœia, 1898, the hydrochloride being used in Great Britain, as in Germany, almost exclusively.

In the process of 1870 the morphine is known to be saturated when it is wholly dissolved by the water. To ascertain whether the acid is added in excess, litmus paper may be resorted to. If the morphine employed contain narcotine, this will remain in the mother liquor, and will not contaminate the product. The mother liquor remaining after the first crystallization may be evaporated so as to afford a fresh supply of the sulphate, but, if the morphine was not originally quite pure, the second product will contain the impurities, and should not be used till it has undergone further purification. When impure morphine is employed, the mother liquor should be mixed with alcohol, or boiled with purified animal charcoal and filtered, and then decomposed by ammonia, which will precipitate the morphine; or the mother liquor may be mixed with a little milk of lime, filtered, and precipitated with solution of ammonium chloride, when the morphine will be nearly pure. This may be converted into the sulphate in the manner directed by the U. S. P., 1870.

Another mode of obtaining morphine sulphate is to dissolve the alkaloid in boiling alcohol of 36° Baumé (sp. gr. 0.8428), saturate it

while hot with sulphuric acid, add purified animal charcoal, boil for a few minutes, and filter the solution at the boiling temperature. Upon cooling, it deposits most of the sulphate, and the remainder may be obtained by evaporating the mother liquor. According to J. Calvert (*Pac. Drug.*, June, 1893), morphine sulphate is made as follows: Opium in any quantity is exhausted with water; the resulting liquid is precipitated with an alkaline base and crude morphine is the result. The crude morphine is dissolved in diluted sulphuric acid, solution filtered through animal charcoal and evaporated to a density of 4½° to 5° B. The crystallizing apparatus is a leaden tank, about six inches in depth, of any size to correspond with the amount of morphine sulphate. It is hinged on a frame and has an outlet, with a plug or faucet at the lower end for drainage. The solution being ready and the apparatus adjusted, the hot solution is run into the crystallizer; the solution is stirred gently every few minutes until crystals commence to form on the surface, and then, by carefully stirring, when the solution has come to the right temperature, the morphine sulphate crystallizes suddenly into a solid mass. The mass of crystals is allowed to repose for 48 hours, the plug at the lower end of the tank is removed and the mother liquor is allowed to run off, at first slowly, and afterwards by elevating the tank the last of the liquor is removed; the drainage requires several days. The crystals in the apparatus are then cut up into pieces of the shape of bricks (commencing at the upper end), which are placed on an absorbent, and removed to a drying-room. In ordinary crystallization a certain part of the coloring matter is retained in the crystals. In this case, when the morphine is crystallized as described, and dried in bricks, nearly all the retained coloring matter comes to the surface, so that when the bricks come out of the drying-room the surfaces are brown and in some cases almost black, showing that the coloring matter is eliminated. The next part of the process is to remove the colored part. This is effected by slicing off the dark portions, leaving the morphine sulphate perfectly white. The masses of crystals of morphine sulphate (which have been heretofore described as bricks) are in a condition to be made into a merchantable article. A very sharp knife and delicate handling is used. The bricks are placed on a table and cut into slices each measuring about ¼ inch. These slices are very gently crumbled in the hands or they are preferably cut into cubes or small pieces to distinguish them from other white crystals of a less poisonous nature.

In the evaporation of the solution of this salt, care should be taken not to carry the heat too far, for when pushed to incipient decomposition with an excess of acid, a new substance is formed containing no morphine. This salt is sometimes adulterated. D. B. Dott met with a sample in the English market which contained 34.63 per cent. of anhydrous sodium sulphate. Such an adulteration, however, would be readily detected by the ignition test of the U. S. P. IX. (*P. J.*, August 4, 1877.)

Properties.—It is officially described as in "white, feathery, acicular, silky crystals, or in cubical masses; odorless, permanent in the air. One Gm. of Morphine Sulphate dissolves in 15.5 mils of water and 565 mils of alcohol at 25° C. (77° F.); also in 0.7 mil of water at 80° C. (176° F.), and 240 mils of alcohol at 60° C. (140° F.); insoluble in chloroform or ether. Its aqueous solution (1 in 20) is neutral or slightly acid to litmus. Barium chloride T.S. produces a white precipitate insoluble in hydrochloric acid when added to an aqueous solution of the salt. Morphine Sulphate loses not more than 7.5 per cent. of its weight when dried for four hours at 100° C. (212° F.) (*moisture*). In all other respects the salt responds to the tests for identity and purity under *Morphina*." *U. S.*

By exposure to a heat of 120° C. (248° F.) it loses 9.66 parts of the water, but cannot be deprived of the remainder without decomposition. (Liebig.) The official tests for it are those for sulphuric acid and for morphine. Considerable discussion has taken place in the pharmaceutical journals about the solubility in water of morphine sulphate. Owing to the ease with which the salt parts with its water of crystallization, even at ordinary temperatures, it is not difficult to account for some of the discrepancies that exist in the text-books on this subject. Yet there can be no doubt that the heretofore commonly quoted solubility, "twice its weight of cold water," is an oft-repeated error. J. U. Lloyd (*N. R.*, May, 1882) found it soluble in 21.60 parts of cold water. F. B. Power, after a determination by precipitation with barium chloride, found a commercial specimen of undoubted purity to require very nearly 24 parts of cold water, and the U. S. P., 1880, adopted his results. (*A. J. P.*, 1882, p. 97.) Virgil Coblentz subsequently examined five commercial samples and practically confirmed Power's results, finding the specimens soluble respectively in 21.38, 23.90, 23.18, 17.69, and 18.97 parts of water. D. B. Dott criticizes the methods employed by J. U. Lloyd, and to some extent those of Power, but fails to establish a very different result. (*P. J.*, 1882, p. 252.) The temperature used in obtaining these figures was 15.6° C. (60° F.). The solubility according to the U. S. P. (8th Rev.) is 15.3 parts of water at 25° C. (77° F.).

The *solution of morphine sulphate* formerly official was made by dissolving 1 grain of morphine sulphate in 1 fluidounce of distilled water, and, although the solution is more stable than that of any other of the morphine salts in common use, it will in time become weakened through the presence of microscopic plants belonging to the Confervoideæ, and hence it is not desirable to keep it on hand. According to Hamberg, of Stockholm, the sulphate should be dissolved in boiling distilled water which is free from ammonia, phosphoric, nitric, and nitrous acids; the solution should be filtered through paper not

previously moistened and is best preserved in small well-filled vials closed with a glass stopper. (*Ph. Ztg.*, No. 49; *A. J. P.*, 1881.)

In the United States this salt of morphine is used almost to the exclusion of all others. For medicinal properties, see *Morphina.*

Dose, from one-twelfth to one-half grain (0.005–0.032 Gm.).

Off. Prep.—Mistura Chloroformi et Morphinæ Composita, *N. F.;* Syrupus Pini Strobi Compositus cum Morphina, *N. F.*

MORPHINÆ TARTRAS. Br.

MORPHINE TARTRATE

(mör-phī'næ tăr'trăs)

"Morphine Tartrate, $(C_{17}H_{19}NO_3)_2,C_4H_6O_6, 3H_2O$, is the tartrate of an alkaloid, morphine, obtained from opium." *Br.*

Morphinum Tartaricum; Tartrate de Morphine, *Fr.;* Morphintartrat, Weinsaures Morphium, *G.*

This salt of morphine was brought into notice by Erskine Stuart (1880), and recommended for hypodermic injection because of its greater solubility in water over the other salts of morphine. (See *Injectio Morphinæ Hypodermica,* p. 585, and *Liquor Morphinæ Tartratis,* p. 649.) It is officially described as "minute acicular crystals, efflorescent at 20° C. (68° F.). Taste bitter. Soluble in 11 parts of *water,* forming a clear solution neutral to *litmus.* Yields the reactions for morphine described under 'Morphinæ Hydrochloridum,' and the *reactions* characteristic of tartrates. 2 grammes dissolved in 20 millilitres of warm *morphinated water* give, on the addition of a slight excess of *solution of ammonia,* a precipitate which, after washing and drying as described under 'Morphinæ Hydrochloridum,' weighs from 1.46 to 1.49 grammes. No appreciable ash." *Br.*

A. E. Tanner (*P. J.*, 1903, 134) found morphine tartrate in the English market of low solubility; he investigated the subject and stated that an acid tartrate of morphine was sparingly soluble, that this was found in commerce and that it required 100 parts of cold water for its solution.

Dose, one-twelfth to one-half grain (0.005–0.032 Gm.).

Off. Prep.—Injectio Morphinæ Hypodermica, *Br.;* Liquor Morphinæ Tartratis, *Br.*

MOSCHUS. U. S.

MUSK Mosch. [Tonquin Musk, Deer Musk]

(mŏs'ḉhŭs)

"The dried secretion from the preputial follicles of *Moschus moschiferus* Linné (Fam. *Moschidæ*). Preserve it carefully in glass-stoppered bottles." *U. S.*

Moschus Orientalis, M. Chinensis, M. Tibetanus; Chinese Thibet or Tonquin Musk; Musc, *Fr. Cod.;* Bisam, Moschus, *G.;* Muschio, *It.;* Almizcle, *Sp.*

Musk was deleted from the British Pharmacopœia, 1914.

The *muskdeer* differs from other deer in not having antlers in either sex, and having only one lachrymal orifice, and in the possession of a gall-bladder. The male animal contains in addition the musk-bearing gland to which the animal owes its name. The animal is usually not over 20 inches high with haunches considerably more elevated than the shoulders. From its upper jaw two tusks project downward out of the mouth, each about two inches long, curved backward, and serving to extract the roots which are used as food by the animal. The ears are long and narrow, and the tail very short. The fleece, consisting of strong, elastic, undulated hairs, varies in color with the season, the age of the animal, and perhaps the place which it inhabits. The general color is a deep iron-gray. The musk is contained in an oval, hairy, projecting sac, found only in the male, situated between the umbilicus and the prepuce, from two or three inches long, and from one to two broad, opening by a small hairy orifice at its anterior part, and marked posteriorly by a groove or furrow which corresponds with the opening of the prepuce. It is lined internally by a smooth membrane, thrown into a number of irregular folds, forming incomplete partitions. In the vigorous adult animal, the sac sometimes contains six drachms of musk; but in the old, seldom more than two drachms, and none in the young. According to Frederick Markham, the musk of the younger animals is not so strong as that of the old, but is much pleasanter. (*P. J.*, xv, 472.) The musk is secreted by the lining membrane, and in the living animal forms a consistent mass, which on the outside is compact, and marked with the folds of the membrane, but is less firm towards the center, where there is sometimes a vacant space. As first secreted it is probably liquid, and a portion is occasionally forced out by the animal, to which it communicates its odor. The musk-deer inhabits the mountainous regions of Central Asia, extending from India to Siberia, and from the country of the Turcomans to China. It is an active and timid animal, springing from rock to rock with surprising agility, and frequenting the snowy recesses and most inaccessible crags of the mountains. Concealing itself during the day, it chooses the night for roaming in search of food, and is taken with difficulty. It is hunted for its hide, as well as for the musk. The natives often take it by snaring. As soon as the animal is killed, the sac is cut off, dried, and sent into the market.

Attention has been drawn by E. Bertherand to the excrement of the *Algerian gazelle, Antilope dorcus* L., which possesses a powerful musk-like odor. It is said to contain about 7 per cent. of an acid resin having a musky odor. (*Proc. A. Ph. A.*, xxvi, 332.)

American Musk.—Owing to the costliness of true musk, the sacs derived from *Fiber zibethicus,* the common *musk-rat,* have been used as a substitute. This product possesses many of the

properties of musk, and, although the odor is not identical, it can often replace it in perfumery if used judiciously. If the fatty matter present has become rancid, it should be washed out by agitating the bruised sacs with a little ether and pouring off the ethereal solution, then allowing the musk to become dry by exposure to the air, and carefully preserving the product in sealed packages.

Musk varies in quality with the country inhabited by the animal. That procured from the mountains on the southern borders of Siberia, and brought into the market through Russia, is comparatively feeble. Chinese musk has been said to come from Tonquin, but appears really to be chiefly obtained in Yun-Nan, a province in the extreme south of China, whence it is sent 1400 miles to Shanghai, the export center. A variety intermediate between these is procured in the Himalaya Mountains and Thibet and sent to Calcutta. This is sometimes enclosed in the membranous lining of the sac, without the hairy envelope, and in this condition is said to be quite equal if not superior to that surrounded by the skin, as in the former condition it dries readily in the sun, while in the latter the aid of artificial heat is deemed necessary, by which the musk may sometimes be injured. (F. Peake, *P. J.*, Feb., 1861.) A musk, which is also said to pass from Thibet into China, is known as *Cabardine* musk. (See *C. D.*, 1890.)

Two varieties are known in commerce, the *Chinese, Thibet* or *Tonquin* musk, and *Russian* or *Siberian* musk. Both come in sacs, convex and hairy on one side, flat and destitute of hair on the other. The hairs are brownish-yellow, grayish, or whitish, stiff and short, and arranged concentrically around the orifice of the sac. The Chinese, which is the more highly valued, is in bags of a rounder shape, covered with brownish-yellow or reddish-brown hairs, and containing at most a drachm and a half of large grained, dark, strong scented musk, of an ammoniacal odor. The Russian is in longer and larger bags, small-grained, of a light yellowish-brown color, and of a weaker and more fetid odor, with less odor of ammonia. The annual exportation of musk from Shanghai to New York is about 300 catties, which consists of boxes about 19 cm. in length, 12 cm. wide, and 9 cm. high.

Properties.—Musk is in grains or lumps concreted together, soft and unctuous to the touch, and of a reddish-brown or ferruginous color resembling that of dried blood. Some hairs of the pod are generally mixed with it. It is officially described as "usually in small irregular granules, not more than 2 mm. in thickness, blackish with a few brown fragments and becoming somewhat grayish on aging; glistening and somewhat oily; odor peculiar, penetrating, powerful and persistent; taste somewhat bitter. Add a few granules of Musk to 2 mils of water in a watch crystal and stir with a glass rod; a light brown solution is obtained. The undissolved portion consists of irregular fragments containing a finely granular substance, numerous rod-like bacteria and occasionally the hyphæ of a fungus. Add a drop of iodine T.S. to a few granules of Musk on a slide and examine it under the microscope; the particles are not colored blue or bluish-black (*starch*). Add a few granules of Musk to 2 mils of alcohol contained in a watch crystal; the grains sink to the bottom, and upon stirring with a glass rod, a pale brown, slightly cloudy solution is obtained, leaving a somewhat oily stain upon the upper portion of the watch crystal as the alcohol evaporates; the undissolved portion or residue resembles that obtained with the aqueous mixture, except that the particles are less disintegrated. Add a few granules of Musk to 2 mils of chloroform in a watch crystal; the grains float on the surface and upon stirring with a glass rod, the solution remains nearly colorless, and as it evaporates there separates around the particles a small quantity of a whitish, oily or fatty substance. Not less than 50 per cent. of Musk is soluble in water, the solution having a strong, distinctly characteristic odor, and a slightly acid reaction. Not less than 10 per cent. of Musk is soluble in alcohol, the solution being of a light, yellowish-brown color and becoming slightly turbid upon the addition of water. Musk loses not more than 15 per cent. of moisture when dried to constant weight in a desiccator over sulphuric acid. Musk yields not more than 8 per cent. of ash." *U. S.*

The odor is strong, penetrating and so diffusive that one part of musk communicates its odor to more than 3000 parts of inodorous powder. (Fée.) In some delicate individuals it produces headache and other disagreeable symptoms, and it has even caused convulsions. The color of the powder is reddish-brown. Musk is inflammable, burning with a white flame, and leaving a light spongy charcoal. Reduced to ashes, it leaves less than 8 per cent. of residue, containing potassium, calcium, magnesia, iron, carbonic, phosphoric, and sulphuric acids, chlorine, and traces of potassium ferrocyanide and ammonium sulphide. (W. Bernatzik.) It yields, upon analysis, a great number of proximate principles. Guibourt and Blondeau obtained water, ammonia, stearin, olein, cholesterin, an oily acid combined with ammonia, volatile oil, ammonium chloride, potassium and calcium chlorides, and unidentified acid combined with ammonia, potassium, and calcium, gelatin, albumin, fibrin, a highly carbonaceous matter soluble in water, a soluble calcareous salt and a combustible acid, calcium carbonate, and phosphate, with hair and sand. (*Ann. Ch. Phys.*, ix, 327.) Besides these constituents, Geiger and Reinman found a peculiar bitter resin, a peculiar substance in part combined with ammonia, and lactic acid both free and in combination. According to Guibourt and Blondeau, it contains 47 per cent. of volatile matter, thought by

some to be chiefly ammonia, by others to be a compound of ammonia and volatile oil. Theimann obtained only from 10 to 15 per cent. But the quantity of volatile as well as of soluble matter varies exceedingly in different specimens. Thus, Theimann found from 80 to 90 per cent. of matter soluble in water, Buchner only 54.5 per cent., and other chemists intermediate proportions. The proportion soluble in alcohol, as ascertained by different experimenters, varies from 25 to 62 per cent. Ether is a good solvent. The aqueous infusion has a yellowish-brown color, a bitterish taste, a strong odor, and an acid reaction. The alcoholic tincture is transparent, and of a reddish-brown color, with the peculiar odor of musk. The action of potassium hydroxide upon musk is accompanied with the extrication of ammonia and an increase of its peculiar odor. By the influence of heat and moisture long continued, ammonia is developed, which acts upon the fatty matter, producing a substance resembling adipocere, but, according to Guibourt, without diminishing the medicinal activity. The correctness of this opinion, however, is perhaps questionable, and it is advisable to preserve the musk as much as possible unaltered. When kept in glass bottles, in a situation neither moist nor very dry, it remains for a great length of time without material change. The odor of musk is very much diminished by mixing it with emulsion or syrup of bitter almond, or with cherry-laurel water. From the experiments of Wimmer, it appears that musk loses its odor when rubbed with golden sulphide of antimony, and reacquires it on the addition of a little solution of ammonia. Camphor rubbed up with musk is also said to destroy its odor. (See *Artificial Musk*, Part II.)

Adulterations.—The price of this medicine is so high, and its sources are so limited, as to offer strong temptations to adulteration, and little genuine unmixed musk is to be found in the market. The sophistication commences in China, and is completed in Europe and this country. A common practice in the East is to open the sac and to supply the place of the musk with an adulterated mixture. Sometimes the scrotum of the animal is filled with this mixture, and not infrequently the sacs are made out of the skin. Dried blood, from its resemblance to musk, is one of the most common adulterations; but, besides this, sand, lead, iron filings, hair, animal membrane, tobacco, the dung of birds, wax, benzoin, storax, asphaltum, artificial musk, and other substances are introduced. These are mixed with a portion of musk, the powerful odor of which is diffused through the mass and renders the discovery of the fraud sometimes difficult. It is said that the Chinese sometimes mix the musk of Tonquin with that of Siberia. The bags containing the drug should have the characters before described as belonging to the natural sac, and should present no evidence of having been opened. The slit is sometimes carefully sewed up, sometimes glued together. The former condition may be discovered by close inspection, the latter by immersion in hot water. When the bag is made from any other portion of the skin, the difference may be detected, according to Neligan, by the microscope. The genuine hairs exhibit innumerable cells, which are wanting in the spurious. (*Chem. Gaz.*, Feb., 1846, p. 79.) Musk which burns with difficulty, has a feeble odor and a color either pale or entirely black, feels gritty to the finger, is very moist so as to lose much weight in drying, or contains obvious impurities, should be rejected. Russian musk is said never to be adulterated before leaving Russia.

For an account of the effects of numerous re, agents on musk, and other modes of identification, as well as of detecting adulterations, see a paper by W. Bernatzik, in *A. J. P.*, 1861, p. 427. There is a discrepancy between Bernatzik's statement of the solubilities of musk and that quoted in the text above. According to the latter, ether is a good solvent; according to the former, ether and chloroform possess scarcely any solvent power. Solubility, however, cannot be relied upon as a test.

Uses.—Musk is stimulant and antispasmodic, in some way stimulating very decidedly the nervous centers when exhausted, without producing either in health or in disease very pronounced symptoms. It is a very valuable remedy in the treatment of nervous exhaustion coming on at or about the crisis of acute disease. When, in low cases of *typhus affections, subsultus tendinum, tremors, singultus,* and similar symptoms indicate the failure of nerve power, its exhibition is often of great advantage. We have seen it apparently save life in the acme of *typhoid fever,* when the vital powers seemed to have almost succumbed, and when violent alterations of temperature or symptoms resembling those of coma vigil had manifested themselves. It was many years ago especially commended by Trousseau in the treatment of *adynamic pneumonia* of drunkards with severe cerebral symptoms. Under these circumstances it certainly appears to do great good. In very obstinate *hiccough* it is one of the most efficient of all of our remedies, and, according to G. B. Wood, it is very effective in those alarming *convulsions of infants* originating in spasm of the intestines. In the *laryngismus stridulus* Bouchut relied mainly on musk, having found it more efficacious than any of the narcotics. (*N. Y. M. J.*, Sept., 1868, p. 545.) According to our experience, musk rapidly loses its power of influencing the nerve centers, and for this reason, and on account of its costliness, its employment should always be delayed until severe nervous exhaustion becomes alarming. It may be given in pill, but is commonly given in emulsion or administered as an enema.

Dose, from five to fifteen grains (0.32–1.0 Gm.).

Off. Prep.—Tinctura Moschi, *U. S.*

MUCILAGINES

MUCILAGES

(mū-cĭ-lăg'ĭ-nēs)

Mucilages, *Fr.;* Schleime, *G.;* Mucilagines, *It.*

Mucilage, in the ordinary acceptation of the term, and in the sense in which it is employed in the U. S. Pharmacopœia, is an aqueous solution of gum, or of substances closely allied to it. In the British Pharmacopœia (1885) the term is applied also to the semi-liquid, jelly-like substance resulting from the cooling of a hot solution of starch.

MUCILAGO ACACIÆ. U. S., Br.

MUCILAGE OF ACACIA Mucil. Acac.

(mū-cĭ-lā'gō ą-cā'cĭ-æ)

Mucilage of Gum Arabic; Mucilage of Gum Acacia; Mucilage de Gomme, *Fr. Cod.;* Mucilage arabique, *Fr.;* Mucilago Gummi Arabici, *P. G.;* Gummischleim, *G.;* Mucilagine di gomma arabica, *It.;* Mucilago de goma arabica, *Sp.*

℞ "Acacia, in small fragments, *three hundred and fifty grammes* [or 12 ounces av., 151 grains]; Distilled Water, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Place the acacia in a tared bottle or flask having a capacity not exceeding *one thousand mils* [or 33 fluidounces, 6½ fluidrachms], wash the drug with cold water, allow it to drain, and then add enough warm distilled water to make the mixture weigh *one thousand grammes* [or 35 ounces av., 120 grains]. Securely stopper the container, and agitate it from time to time until the acacia is dissolved. Strain the Mucilage and preserve it in small, well-filled bottles in a refrigerator or in a cool place. Mucilage of Acacia should be frequently made and must not be dispensed if it has become sour or moldy." *U. S.*

"Gum Acacia, 100 *grammes;* Distilled Water, 150 *millilitres.* Rapidly rinse the Gum Acacia with a little *water;* then dissolve it in the Distilled Water in a closed vessel and strain. The Mucilage should be recently prepared. In India and the Eastern Divisions of the Empire, Mucilage of Indian Gum may be employed in making the official preparations for which Mucilage of Gum Acacia is directed to be used (see 'Gummi Indicum')." *Br.*

The gum used for this purpose should be in small fragments or coarse powder, as it is more readily dissolved in this state than when finely pulverized. Straining is necessary to separate the foreign substances which are often mixed with gum arabic. This mucilage is semi-transparent, almost colorless, if prepared from good gum, viscid, tenacious, of a feeble, peculiar odor, and nearly tasteless. By straining a solution of gum through a layer of freshly precipitated alumina it can be almost entirely decolorized, particularly if the operation be repeated several times. By keeping, the mucilage becomes sour, and this happens even though it be enclosed in well-stoppered bottles; but, according to Guérin, the solution of pure gum undergoes no change *in vacuo.* Heat in its preparation is said to favor the production of acid, and hence cold has been substituted for boiling water in the present formulas. The U. S. P. VIII directed the addition of lime water in making this mucilage; this addition has proved advantageous by neutralizing the acidity generally found in acacia and it promotes stability, but the U. S. P. IX process deleted the lime water. According to R. Rother (*A. J. P.,* xliv, 113), if glycerin be employed in the proportion of one to eight of the mass, and the mixture of water and glycerin be added to the gum in a bottle and solution secured by agitation at intervals over several hours, the resulting mucilage does not spoil; the presence of glycerin is objectionable, however, for many of the uses of mucilage of acacia. E. D. Oesch (*West. Drug.,* 1892, 38) adds about 6 per cent. of alcohol as a preservative. Keller preserves the mucilage by the addition of acetanilid (two grains in the fluidounce). (*C. D.,* 1896, 378.) Archer & Co. have found (*A. J. P.,* xlvi, 469) that if "Tolu water" be substituted for water the mucilage will keep for months. The Tolu water is made by rubbing two drachms of the tincture with magnesium carbonate and two pints of water, and filtering. Mucilage is employed chiefly in the making of pills, and in suspending insoluble substances in water. In prescribing it for mixtures, it should be recollected that it is a solution of definite strength, containing, according to the U. S. formula, half an ounce of the gum to each fluidounce of mucilage. The British mucilage is a little stronger. The adhesiveness of the mucilage is stated to be very much increased by the addition of one part of aluminum sulphate to one hundred and twenty-five parts of the mucilage, but this would not be permissible for a mucilage intended for medicinal purposes.

MUCILAGO GUMMI INDICI. Br.

MUCILAGE OF INDIAN GUM

(mū-cĭ-lā'gō gŭm'mī ĭn'dĭ-cī)

"Indian Gum, 50 *grammes;* Distilled Water, 150 *millilitres.* Rapidly rinse the Indian Gum with a little *water;* then dissolve it in the Distilled Water in a closed vessel and strain. The Mucilage should be recently prepared. In India and the Eastern Divisions of the Empire, Mucilago of Indian Gum may be employed in making the official preparations for which Mucilage of Gum Acacia is directed to be used (see 'Gummi Indicum')." *Br.*

This mucilage was made official in the British Pharmacopœia (1914); it is not as adhesive as the mucilage of acacia.

MUCILAGO TRAGACANTHÆ. U. S., Br.

MUCILAGE OF TRAGACANTH Mucil. Trag.

(mū-cĭ-lā'gō trăg-ą-căn'thæ)

Mucilage de Gomme Adragante, *Fr. Cod.,* Mucilag adragant, *Fr.;* Traganthschleim, *G.;* Mucilagine di gomma adragante, *It.*

℞ "Tragacanth, *six grammes* [or 93 grains]; Glycerin, *eighteen grammes* [or 278 grains];

Water, *a sufficient quantity,* to make *one hundred grammes* [or 3 ounces av., 231 grains]. Mix the glycerin with *seventy-five mils* [or 2 fluidounces, 257 minims] of water in a tared vessel, heat the mixture to boiling, remove the heat, add the tragacanth, and macerate during twenty-four hours, stirring occasionally. Then add enough water to make the mixture weigh *one hundred grammes* [or 3 ounces av., 231 grains], beat it until of a uniform consistence, and strain it forcibly through muslin." *U. S.*

"Tragacanth, in powder, 1.25 *grammes;* Alcohol (90 per cent.), 2.50 *millilitres;* Distilled Water, sufficient to produce 100.00 *millilitres.* Mix the Tragacanth with the Alcohol; add the Distilled Water as quickly as possible, and shake vigorously." *Br.*

A part only of *tragacanth* is soluble in water. The remainder swells up and forms a soft tenacious mass, which may be mechanically mixed with water, but does not form a proper solution. Hence trituration is necessary to complete the incorporation of the ingredients. This mucilage is thick and very viscid, but not permanent, as the water separates from the insoluble portion of the tragacanth on standing. It is chiefly used in making pills and troches. The addition of glycerin renders it more serviceable as an excipient. From its great tenacity, it may be advantageously employed for the suspension of heavy insoluble substances, such as the metallic oxides, in water. When kept long, it is apt to undergo decomposition, and to become offensive, but it will keep well if phenol be added. (*A. J. P.,* 1864.) Lyon (*P. J.,* 1901, 600) recommends the use of chloroform water as a preservative in making this mucilage; this is preferred in all cases if the mucilage is not to be used internally. The alcohol in the British process facilitates the quick production of the mucilage, and in addition acts as a preservative.

MYRISTICA. U. S., Br.

MYRISTICA Myrist. [Nutmeg]

(mȳ-rĭs'tĭ-cą)

"The ripe seeds of *Myristica fragrans* Houttuyn (Fam. *Myristicaceæ*), deprived of the arilli and seed-coats. Preserve the kernels in tightly-closed containers, adding a few drops of carbon tetrachloride or chloroform from time to time to prevent attack by insects. Reject broken or wormy kernels." *U. S.* "Nutmeg is the dried kernel of the seed of Myristica fragrans, *Houtt.*" *Br.*

Muscade, *Fr. Cod.;* Nux Moschata, Noix muscade, *Fr.;* Semen Myristicæ, *P. G.;* Muskatnuss, *G.;* Noce moscata, *It.;* Nuez moscada, *Sp.*

The nutmeg tree is about thirty feet high, with numerous branches, and an aspect somewhat resembling that of the orange tree. The leaves are alternate, petiolate, oblong-oval, pointed, entire, bright green and somewhat glossy on their upper surface, whitish beneath, and of an aromatic taste. The staminate and pistillate flowers are upon different trees. The former are disposed in axillary, peduncled, solitary clusters; the latter are single, solitary, and axillary; both are minute and of a pale yellowish color. The fruit, which appears on the tree mingled with the flowers, is round or oval, of the size of a small peach, smooth, at first pale green, but yellow when ripe, and marked with a longitudinal furrow. The external covering, which is at first thick and fleshy and abounds in an austere, astringent juice, afterwards becomes dry and coriaceous, and, separating into two valves from the summit, discloses a scarlet reticulated membrane or arillus, commonly called *mace,* closely investing a thin, brown, shining shell, which contains the kernel or *nutmeg.* The nutmeg tree is a native of the Moluccas and other neighboring islands, and abounds especially in that small cluster distinguished by the name of Banda, whence the chief supplies of nutmegs were long derived. But numerous varieties of the plant are now cultivated in Sumatra, Java, Singapore, Penang, Ceylon, and other parts of the East Indies, and have been introduced into the Isles of France and Bourbon, Cayenne, and several of the West India islands. Various species of the genus *Myristica,* other than those which are official, yield commercial seeds or products:

The larger part of the nutmegs of commerce is said still to come from the Dutch Banda Islands. The Penang nutmegs are distinguished by not being limed. The tree is produced from the seed. It does not flower until the eighth or ninth year, after which it bears flowers and fruit together, without intermission, and is said to continue bearing for seventy or eighty years. Little trouble is requisite in its cultivation. A branch of the staminate tree is grafted into all the young pistillate plants when about two years old, so as to insure their early fruitfulness. J. H. Hart presented an interesting report (*Bull. Bot. Dept.,* Trinidad, 1907, p. 202) showing that 16-year-old nutmeg trees growing in Trinidad bear both staminate and pistillate flowers. Indeed, he found both kinds of flowers on the same branch of the tree, and he therefore suggests that an attempt should be made to perpetuate this variety by grafting.

In the Moluccas the tree yields three crops annually. The fruit is gathered by hand, and the outside covering rejected. The arillode, constituting the mace of commerce, is then carefully separated, so as to break it as little as possible. It is flattened, dried in the sun, and afterwards sprinkled with salt water, with the view of contributing to its preservation. The nuts are dried in the sun or by ovens, and exposed to smoke until the kernel rattles in the shell. They are then broken open, and the kernels, having been removed and steeped for a short time in a mixture of lime and water, in order to preserve them from the attacks of worms, are next cleaned, and packed in casks or chests for exportation. Lumsdaine has found them to keep better if rubbed over with dry lime than when prepared in the moist

way. (See *Am. J. Sci.*, Nov., 1851.) Tschirch confirms the value of liming as a preservative against the attacks of insects. (*Ph. Rev.*, 1898, 196.) This is, however, not sufficient protection, as the commercial nutmegs are sometimes "wormy." Nutmegs are brought to this country either directly from the East Indies or indirectly from England and Holland. They are also occasionally imported in small quantities from the West Indies.

The amount of unground nutmegs imported into the United States averages about two million pounds a year.

Properties.—Myristica is officially described as "ovoid or ellipsoidal, from 20 to 30 mm. in length and about 20 mm. in thickness; externally light brown to dark brown, reticulately furrowed, the broad end with a large, circular upraised scar from which arises a furrow extending to the chalaza; easily cut, the surface having a waxy luster and mottled by reason of the light brown perisperm penetrating into the yellowish-brown endosperm; a longitudinal section through the endosperm above the large scar shows a small irregular cavity with the more or less shrunken remains of the embryo, and usually containing a growth of mold; odor and taste agreeably aromatic. The powder is dark reddish-brown; consisting of irregular, yellowish-brown or brownish-black fragments; fragments of perisperm yellowish-brown with large, circular or elliptical oil reservoirs containing a volatile oil, small, thin-walled parenchyma cells, and occasional spiral tracheæ; parenchyma cells of endosperm more or less polygonal and filled with starch grains and aleurone grains; starch grains single or compound, the individual grains being spherical, plano-convex or polygonal, from 0.003 to 0.02 mm. in diameter and colored blue with iodine T.S. (distinction from starch grains in mace, which are colored yellowish-red); mounts in hydrated chloral T.S. show numerous globules of a fixed oil which later may separate in the form of rod-like crystals; mounts in fixed oil show the separation of spheroidal aggregates of crystals which polarize light strongly. The powder made from 'limed' nutmegs show under the microscope, upon the addition of water containing 25 per cent. of sulphuric acid, the immediate separation of crystals of calcium sulphate in the form of small needles or short rods which do not polarize light. Myristica yields not more than 5 per cent. of ash." *U. S.*

"Broadly oval or rounded, rarely more than twenty-five millimetres long; greyish-brown externally, marked with reticulated furrows, and minute black points and lines; internally greyish-red with darker brownish-red veins. Transverse section marbled. Strong aromatic odor; taste aromatic, warm and somewhat bitter." *Br.*

The microscopical structure of nutmeg and mace have been well illustrated by Winton and Moeller in the "*Microscopy of Vegetable Foods.*" Spaeth has recently made an interesting contribution to the pharmacognosy of nutmeg and the detection of the prevalent adulterations in *Ph. Zentralh.*, xlix, p. 627. It has been stated that much of the ground nutmeg of commerce has been made from small, stunted and worthless nutmegs, so-called "grinding nutmegs." The powdered drug is sometimes adulterated with corn meal, powdered beans, curcuma and various nut-shells.

Under the names of *long, female,* or *wild nutmeg, Macassar nutmeg, Papua nutmeg, New Guinea nutmeg, horse nutmeg,* certain seeds have long been known in European commerce; they have finally become an important article of trade, nearly 77,000 kilos of them having been sold in Holland in the year 1894. These seeds have been variously ascribed to *M. fatua* Houtt. (*M. tomentosa* Thumb., *M. macrophylla* Roxb.), and other species of the genus *Myristica,* but by Bassermann and Warburg have in all their varieties been traced to the *M. argentea* Warburg, of New Guinea, from which country they are often taken to Macassar to finally enter commerce as Macassar nutmegs. (*P. J.*, 1898, 97.) The numerous varieties of these false nutmegs are readily reducible to two, which differ chiefly in size, the larger being commonly known as the Papua nuts, the smaller as the Macassar nuts. They are distinguished from the nutmeg by their greater length, their elliptical shape, their comparatively feeble odor and disagreeable taste, and by the absence of the dark brown veins. (Holmes, *P. J.*, lxxxii, p. 459.) Heckel has described two new so-called wild nutmegs from Madagascar. (*Rep. d. Pharm.*, 1909, p. 49.)

Clifford Richardson (*Bulletin U. S. Dept. Agriculture,* No. 13, 1887) gives as the average of three analyses of imported nutmegs: water, 5.56 per cent.; ash, 2.88; volatile oil, 3.23; fixed oil or fat, 34.22; starch, etc., 39.62; crude fiber, 9.21; albuminoids, 5.28; total, 100.00. The volatile oil is obtained by distillation with water. (See *Oleum Myristicæ.*) The virtues of nutmeg are extracted by alcohol and ether.

Nutmegs have been punctured and boiled in order to extract their essential oil, and the orifice afterwards closed so carefully as not to be discoverable unless by breaking the kernel. The fraud may be detected by their lightness. They are also apt to be injured by worms, which, however, attack preferably the parts least impregnated with the volatile oil. The Dutch were formerly said to heat them in a stove in order to deprive them of the power of germinating and thus prevent the propagation of the tree. The largest nutmegs now command the highest prices. They should be rejected when very light in weight, with a feeble taste and odor, worm eaten, musty, or marked with black veins.

The *concrete* or *expressed oil of nutmeg* (*Oleum Myristicæ Expressum,* Br., 1885), often called *oil of mace,* or *nutmeg butter,* is obtained by bruising nutmegs, exposing them in a bag

to steam, and then compressing them strongly between heated plates. A liquid oil flows out, which becomes solid when it cools. Nutmegs are said to yield from 10 to 12 per cent. of this oil, but Flückiger and Hanbury obtained as much as 28 per cent. (See analyses of Richardson, quoted previously.) A process for obtaining it by means of carbon disulphide has been proposed by Lepage, of Gisors, in France, and has received the sanction of the Society of Pharmacy of Paris. It consists in treating the nutmeg, thoroughly comminuted, with three times its weight of the well-rectified liquid referred to, agitating the mixture frequently for 24 hours, expressing, repeating the process with two parts only of the menstruum, mixing the products of the two macerations, filtering in a covered vessel, and then distilling off the disulphide until the residue is entirely deprived of the solvent. (*J. P. C.*, 3e sér., xxxi, 28.) It would seem difficult to prevent the retention of a little of the solvent. The best nutmeg butter is imported from the East Indies in stone jars, or in rectangular blocks 10 inches long by 2½ inches wide, wrapped in palm leaves. It is solid, soft, unctuous to the touch, of a yellowish or orange-yellow color, more or less mottled, with the odor and taste of nutmeg. It is composed, according to Schrader, of 52.09 per cent. of a soft oily substance, yellowish or brownish, soluble in cold alcohol and ether; 43.75 of a white, pulverulent, inodorous substance, insoluble in these liquids; and 4.16 of volatile oil. The pulverulent constituent, which received from Playfair the name of *myristin*, has a silky luster, melts at 31° C. (88° F.), and yields on saponification glycerin and *myristic acid*, $C_{14}H_{28}O_2$. Myristin, $C_3H_5(OC_{14}H_{27}O)_3$, is a true fat, or *glyceryl myristate*. It is also found in spermaceti, in cocoanuts, and in the fixed oil of linseed and poppy oil. It may be obtained directly from nutmeg by exhausting it by means of benzene, filtering the liquid, and allowing it to crystallize by spontaneous evaporation. To purify the product, it may be dissolved in a mixture of two parts of absolute alcohol and three of benzene with the aid of heat, then filtering the liquid while hot, and setting it aside. On cooling, it deposits the pure myristin in crystals. (*J. P. C.*, June, 1859, p. 471.) Analyzed by Koller, the expressed oil was found to contain, in 100 parts, 6 of a volatile oil analogous to the oil of mace, 70 of myristin, 20 of olein, 3 of resin, and 1 of salts, etc. (*A. Pharm.*, clxxiii, 280.) Wallach found in the volatile oil *pinene* and *dipentene* of the class of terpenes and Semmler found *myristicol*, $C_{10}H_{18}O$, which is liquid, and *myristicin*, a solid ester of the composition $C_{12}H_{14}O_3$. An inferior kind of the oil is prepared in Holland, and sometimes found in commerce. It is in hard, shining, square cakes, lighter-colored than that from the East Indies, and with less odor and taste. It is supposed to be derived from nutmegs previously deprived of most of their volatile oil by distillation. An artificial preparation is sometimes sold for the genuine oil. It is made by mixing various fatty matters, such as suet, palm oil, spermaceti, wax, etc., adding some coloring substance, and giving flavor to the mixture by the volatile oil.

Ucuhula nut is a round or oval seed of *Myristica surinamensis*. It is one-half to two-thirds of an inch in diameter, light brown, but usually covered by a blackish, thin, friable testa. Internally it resembles the nutmeg, but is distinguished by the presence of extraordinarily large and handsome albuminous crystalloids. These seeds are said to contain over 70 per cent. of a solid yellow fat, melting at 36° C. (96.8° F.). (See *A. J. P.*, 1886; also *A. Pharm.*, July, 1888.) The kernel of the fruit of the Brazilian *Myristica officinalis* Mart. (*M. Bicuhyba* Schott), resembles the nutmeg in form and structure, but is covered with a black shell marked with broad furrows. It contains crystals like those above spoken of, but less splendid and regular, and apt to be in three forms. It yields a fat (*bicuhyba fat*, or *bicuhyba balsam*) very much like that of the ordinary nutmeg, but having a rather sour, sharp taste, melting at 47° C. (116.6° F.). It contains a peculiar fatty acid, *bicuhybastearic* acid. The *otoba fat* is the product of the fruit of *Myristica Otoba*. It is almost colorless, when fresh has a nutmeg-like odor, melts at 38° C. (100.4° F.), and contains *myristin*, *olein*, and *otobite*. The latter principle crystallizes in shiny, colorless crystals, melting at 133° C. (271.4° F.). The fruit of *Virola sebifera* Aubl. (*s. Myristica sebifera* Lam.), also yields a fatty substance which is known as *ocuba wax*. The so-called *California nutmeg* is not a nutmeg at all, but the seed of a coniferous tree, *Torreya californica*. It is oblong, with a smooth, brownish, thin testa, and affords a marbled cross-section. Its odor and taste are terebinthinate. Neither are the *Jamaica* or *calabash nutmeg*, from *Monodora Myristica*, the *New Holland* or *plume nutmeg*, from *Atherosperma moschata*, and the *clove nutmeg*, from *Agathophyllum aromaticum*, true nutmegs.

Uses.—Nutmeg owes its medicinal and toxic properties solely to the volatile oil which it contains. For the consideration of the effects and uses of this, see page 777. Powdered nutmeg is rarely used in medicine alone, although it enters into the composition of a number of galenicals. The expressed oil is occasionally used as a gentle external stimulant and was an ingredient in the *Emplastrum Picis* of the 1885 British Pharmacopœia. *Mace* possesses properties essentially the same as those of nutmeg.

Dose, five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Fluidextractum Aromaticum (from Aromatic Powder), *U. S.*; Pulvis Aromaticus, *U. S.*; Tinctura Lavandulæ Composita, *U. S., Br.*; Trochisci Sodii Bicarbonatis, *U. S.*; Pulvis Catechu Compositus, *Br.*; Pulvis Cretæ Aromaticus, *Br.*; Spiritus Armoraciæ Compositus, *Br*; Acetum Opii, *N. F.*; Cordiale Rubi Fructus, *N. F.*; Pulvis Cretæ Compositus, *N. F.*

MYROBALANUM. Br.

MYROBALANS

(mȳ-rō-bă-lā'nŭm)

"Myrobalans are the dried immature fruits of Terminalia Chebula, *Retz.*, usually distinguished in commerce as Chebulic myrobalans." *Br.*

Five varieties of these East India fruits are distinguished by authors. The most important are as follows: (1) *Myrobalani Chebulæ.* This is the only variety which is official. It is produced by the *Terminalia Chebula* Retz (*Buceras Chebula*). This by some is believed to be identical with the *T. Bellerica* noted below. The fruit is roundish or ovate, varying in size from that of a hazel nut to that of a walnut. It consists of an exterior firm fleshy portion and an interior kernel which is light brown, inodorous and with a bitterish, astringent taste.

(2) *Myrobalani Bellericæ.* This is obtained from the *T. Bellerica* Roxb. It closely resembles the previous variety but is of a more grayish brown color and is sometimes supplied with a short thick foot stalk which is lacking in the official form.

(3) *Myrobalani citrinæ* vel *flava.* These are from a variety of the same tree which affords the chebula myrobalans, from which they differ only in being somewhat smaller, of a light brown or yellowish color, and of a taste rather more bitter. They were formerly sometimes sold in the shops of Philadelphia, under the name of *white galls,* to which, however, they bear no other resemblance than in taste.

(4) *Myrobalani indicæ* vel *nigræ.* These are thought to be the unripe fruit of *T. Buceras* (*Bucida Buceras*). They are ovate-oblong, from four to eight lines long and from two to three lines thick, of a blackish color, wrinkled longitudinally, and presenting, when broken, a thick brown mass, without kernel, but with a small cavity in the center. They are sourish and very astringent.

(5) *Myrobalani emblicæ.* This variety is wholly different from the preceding, and derived from a plant having no affinity to the Terminaliæ, of the fam. *Combretaceæ*—namely, the *Phyllanthus Emblica* L. (fam. *Euphorbiaceæ*).

Myrobalans are officially described in the Br. Pharm., 1914, as "irregularly ovoid or fusiform, from ten to thirty millimetres or more long and from five to fifteen millimetres wide; strongly shrivelled longitudinally, dark brown or nearly black; in transverse section dark, with a small central cavity; hard. No odor; taste very astringent." *Br.*

When the fruit is entire, it is blackish, spherical depressed, of the size of a cherry, presenting six obtuse ribs with as many deep furrows, and separating into six valves, and has a strongly astringent and acidulous taste. It is often in segments, as found in commerce. These fruits contain about 40 per cent. of tannin which is identical with gallotannic acid. They have occasionally been used for the commercial manufacture of tannin. The resulting product is less pure, however, than that from nut galls.

Uses.—Myrobalans were in high repute with the Arabians, and were long employed by European practitioners, as primarily laxative and secondarily astringent, in various complaints, particularly *diarrhea* and *dysentery.* Pierre Apery states that when roasted they are still used in Turkey with excellent results in *intestinal* catarrhs. (*R. T.,* Dec., 1887.) Although the myrobalans are of various origin, they all probably depend for their physiological activity upon the presence of gallotannic acid. Procter states that they contain from 30 to 35 per cent. of gallotannic and ellagitannic acids.

The ointment is used as a local astringent.

The internal *dose* of myrobalans is one-half to one drachm (2.0–3.9 Gm.), given in the form of a powder.

Off. Prep.—Unguentum Myrobalani, *Br.;* Unguentum Myrobalani cum Opio, *Br.*

MYRRHA. U. S., Br.

MYRRH Myrrh. [Gum Myrrh]

(mȳr'rhą)

"A gum-resin obtained from one or more species of *Commiphora* (Fam. *Burseraceæ*)." *U. S.* "Myrrh is an oleo-gum-resin obtained from the stem of Commiphora Myrrha, *Holmes,* and probably other species." *Br.*

Arabian or Somali Myrrh, Herabol Myrrh; Gummi Resina Myrrha; Myrrhe, *Fr. Cod.;* Myrrha, *P. G.;* Myrrhe, *G.;* Mirra, *It., Sp.;* Murr, *Ar.;* Bowl, *Hindost.*

Though *myrrh* has been employed from the earliest times, it is still uncertain by what plant it is yielded. The *Amyris Kataf* of Forskhal, seen by that traveller in Arabia, was supposed by him to be the myrrh tree, but without sufficient proof. Afterwards Ehrenberg met on the frontiers of Arabia Felix with a plant from the bark of which he collected a gum-resin precisely similar to the myrrh of commerce. From the specimens of the plant taken by Ehrenberg to Germany, Nees von Esenbeck referred it to the genus *Balsamodendron* of Kunth, and named it *Balsamodendron Myrrha.* It was not thought by De Candolle sufficiently distinct, but is now generally recognized under the name of *Commiphora,* first given it by Jacquin in 1797, and therefore preceding the name of Kunth by some 27 years. Berg found another species in Ehrenberg's collection, to which was attached a label by the discoverer, stating that he had collected myrrh from it, and proposed to call it *Balsamodendron ehrenbergianum.* (*A. J. P.,* 1873, 314.) Both Oliver and Trimen agree that this plant is not specifically distinct from *B. Opobalsamum.* It is probable that there are gum resins from several species of the *Commiphora* which furnish commercial myrrh. Hildebrand (*P. J.,* 1878, ix, p. 893) collected the *C. Myrrha* on the north Somali

coast in 1873, and presents evidence to show that it yields myrrh. Although this view has been disputed, E. M. Holmes (*Y. P. B.,* 1913, p. 453) supports it and this species is recognized by the British Pharmacopœia. Defiers and Schweinfurth (*Ber. d. Pharm Ges. zu Berlin,* 1893), however, believe that genuine myrrh is yielded by *Commiphora abyssinica* (Berg.) Engl., which is found in Southern Arabia, Erithrea, and Northern Abyssinia. *C. Schimperi* (Berg.) Engl., occurring in the Yemen, Abyssinia, and from Kern to Tigré, is likely also to yield some of the commercial Arabian myrrh. It appears to be established that *C. Myrrha* produces *myrrh,* but it is probable that it is also yielded by other trees belonging to the genus *Commiphora,* which genus includes more than 60 species, natives of Arabia and Africa.

Commiphora Myrrha (Nees) Engler (Syn. *C. Myrrha* Holmes) is a small tree, with a stunted trunk, covered with a whitish-gray bark, and furnished with rough abortive branches terminating in spines. The leaves are ternate, consisting of obovate, blunt, smooth, obtusely denticulate leaflets, of which the two latter are much smaller than the one at the end. The fruit is oval-lanceolate, pointed, longitudinally furrowed, of a brown color, and surrounded at its base by the persistent calyx. The tree grows in Arabia Felix, in the neighborhood of Gison, in dwarfish thickets, interspersed among the *Acaciæ* and *Euphorbiæ.* The juice concretes spontaneously upon the bark.

Formerly the best myrrh was brought from the shores of the Red Sea by way of Egypt and the Levant, and hence received the name of *Turkey myrrh,* while the inferior qualities were imported from the East Indies, and were commonly called *India myrrh.* These titles have ceased to be applicable, as myrrh of all qualities is now brought from the East Indies, whither it is carried from Arabia and the northeastern coast of Africa. Aden in the former region, and Berbera in the latter, would appear, from the statements of James Vaughan, to be the chief entrepôts of the trade. (*P. J.,* xii, 226.) It is usually imported in chests containing between one and two hundred-weight. Sometimes the different qualities are brought separate, but oftener more or less mingled. Only the best kind should be selected for medicinal use.

There are several varieties of myrrh recognized in commerce. The official description corresponds to that of that known as the Arabian myrrh or Somalian myrrh.

Another variety of myrrh coming from Arabia known as the *Fahdi myrrh* is described in the *Pharmacographia* as "occurring in irregular masses, seldom exceeding 1½ inches long, and having a somewhat gummy-looking exterior. The larger lumps seem formed by the cohesion of small, rounded, translucent, externally shining drops or tears. The fracture is like that of common myrrh, but less unctuous, and has not the whitish markings. The odor and taste are those of the ordinary drug." This myrrh is said to be collected on the hills about Shugraeea and Sureeae, east of Aden. "*Meetiya,*" or *Arabian Myrrh of Dymock,* is said to be sold in India as true myrrh. It has a dull surface, a dark reddish-brown color, a more unctuous and waxy fracture, and has white marks like Somali myrrh, which it resembles in taste, but its odor is rather less fragrant. *Yemen Myrrh,* which is said by Hanbury to contain a resin which differs from that of Somali myrrh and the Arabian myrrh or Fahdi in that its solution in petroleum spirit does not give a violet color on the addition of bromine. This myrrh is said to enter commerce chiefly from Makulla via Aden and Bombay. It occurs in large pieces 1 to 3 inches long, irregularly rounded and characterized by a dark reddish-brown color with a similarly colored fracture free from whites streaks. Odor and taste similar to Somali myrrh, but stronger and more rank.

Mecca balsam, according to G. Schweinfurth, is yielded by *Commiphora Opobalsamum,* from which it is collected in the valleys near Mecca. It is said to be the myrrh of the Bible, the error of translation having been made on account of the similarity of the old Hebrew word "mar" with the modern Arabic word "morr," the name of the true myrrh.

Properties.—Myrrh is "in rounded or irregular tears or masses, brownish-yellow or reddish-brown, and covered with a brownish-yellow dust; fracture waxy, somewhat splintery, translucent on the edges, sometimes marked with nearly white lines; odor balsamic; taste aromatic; bitter and acrid. The powder is yellowish-brown; 0.001 Gm. of the powder, when added to a drop of fixed oil on a slide and examined under the microscope, shows numerous angular fragments varying in color from pale yellow to yellowish-brown; when mounted in hydrated chloral T.S. the color of the yellowish fragments is intensified; the addition of iodine T.S. to the powder, previously mounted in hydrated chloral T.S., may show the presence of a few starch grains varying in shape from spherical, polygonal, and narrowly ellipsoidal to somewhat pear-shaped, from 0.01 to 0.035 mm. in diameter; when mounted in phloroglucinol T.S. and hydrochloric acid the powder may show a few fragments of lignified tissues consisting of either sclerenchymatous fibers, or of small groups of stone cells, the individual cells of the latter with very thick, porous walls and from 0.015 to 0.05 mm. in length. Not less than 35 per cent. of Myrrh is soluble in alcohol. Myrrh yields not more than 8.5 per cent. of ash." *U. S.*

"In rounded or irregular tears, or masses of agglutinated tears, varying much in size; reddish-brown or reddish-yellow externally, dry, and more or less covered by a fine powder; brittle, the fractured surface irregular, somewhat translucent, of a rich brown color, oily, and frequently exhibiting whitish marks. Aromatic odor; taste aromatic, bitter and acrid. Not more than 70 per cent. insoluble in *alcohol* (90

per cent.). The solution obtained by boiling 0.1 gramme of coarsely powdered Myrrh with 2 millilitres of *alcohol* (90 per cent.), evaporated in a porcelain dish so as to leave a thin film, yields a residue which assumes a violet color in contact with *nitric acid* diluted with an equal volume of *water*. Ash not more than 5 per cent." *Br.*

Under the teeth it is at first friable, but soon softens and becomes adhesive. It is inflammable, but does not burn vigorously, and is not fusible by heat. Its sp. gr. is stated as 1.36. The inferior kind is in pieces much darker, more opaque, less odorous, and often abounding with impurities. We have seen pieces of India myrrh enclosing large crystals of sodium chloride, as if the juice had fallen from the tree and concreted upon the ground where this mineral abounds. Pieces of *bdellium*, and other gummy or resinous substances of unknown origin, are often mixed with it. Among these is a product which may be called *false myrrh*. It is in irregular pieces, of a dirty reddish-brown color, a vitreous brownish-yellow fracture, semi-transparent, of a faint odor of myrrh, and a bitter balsamic taste. Myrrh is best purchased in mass, as in powder it is liable to adulterations not easily detected. It is sometimes admixed with small stones which are added when the myrrh is in a moist state. Much of the commercial article is contaminated with the so-called Somali myrrh which does not meet the Pharmacopœia requirements. It is also adulterated with senegal gum and chestnuts.

George F. Merson (*P. J.*, Jan., 1900, 42) proposes as a test of the quality of myrrh that it should yield not more than 5 per cent. of ash, which should be almost entirely soluble in diluted hydrochloric acid, and that when exhausted with 90 per cent. alcohol and dried at 100° C. (212° F.) one gramme should not afford more than 0.6 Gm. of residue.

Myrrh is partially soluble in water, alcohol, and ether. Triturated with water it forms an opaque yellowish or whitish emulsion, which deposits the larger portion upon standing. Its alcoholic tincture is rendered opaque by the addition of water, but throws down no precipitate. According to Neumann, alcohol and water severally extract the whole of its odor and taste. By distillation a volatile oil rises, having the peculiar flavor of myrrh, and leaving the residue in the retort simply bitter. The gum-resin is soluble in solutions of the alkalies, and, when triturated with them in a crystalline state, forms a tenacious liquid. Hence potassium carbonate may be used to facilitate its suspension in water. Hirschsohn recommends as a reagent for myrrh, trichlor-acetal-chloroform, which is obtained by conducting chlorine into seventy-five per cent. alcohol until turbidity ensues and two layers are formed; the lower of these is shaken with an equal volume of water and then with calcined magnesia and filtered. In one part by weight of the trichloracetal thus obtained, four parts by weight of hydrated chloral are dissolved by heating. The syrupy reagent thus made, which fumes slightly in the air, gives a violet color with the smallest quantity of pure Herabol myrrh. Hirschsohn failed to get a similar reaction with any other resin, not even with Bisabol myrrh. (*Ph. Centralh.*, 1903, 809.) An analysis by Ruickoldt gave 2.183 per cent. of volatile oil, 44.760 of resin, 40.818 of gum or arabin, 1.475 of water, and 3.650 of calcium and magnesium carbonate, with some gypsum and ferric oxide. The volatile oil has been called *myrrhol* or *myrrhenol*, and, according to Ruickoldt, has the formula $C_{10}H_{14}O$. Koehler (*A. J. P.*, 1890, p. 346) confirms this formula, and states that this body, while isomeric with thymol and carvol, is distinct from them. He found 7 or 8 per cent. of essential oil, instead of 2.18 as previously given. Gladstone (*J. Chem. S.* [2], 2, 1) found that the oil had a sp. gr. of 1.0189 at 7.5° C. (45.5° F.), a boiling point of 266° C. (510.8° F.), and was lævorotatory. The resin, which he calls *myrrhin*, $C_{45}H_{32}O_{10}$, is neutral, but becomes acid when kept for a short time in fusion. In the latter state Ruickoldt proposes to call it *myrrhic acid*. (*A. Pharm.*, lxi, 1.) Koehler has found in the portion soluble in alcohol an indifferent soft resin, to which he gave the formula $C_{26}H_{34}O_5$, containing three replaceable OH groups, and two dibasic resin acids, of the formulas $C_{26}H_{32}O_{16}$ and $C_{26}H_{32}O_9$. An investigation of the essential oil of Bisabol myrrh from the interior of the Somali country was made by W. Tucholka. (*Schim. Rep.*, Oct., 1897, 36.) He obtained by distillation 7.8 per cent. of an oil of 0.8836 sp. gr., boiling at from 220° to 270° C. 428°–518° F.). From this was separated, by means of the crystalline hydrochloride, a terpene boiling at from 259° to 260.2° C. (498.2°–500.36° F.), which the author calls *bisabolene*, and an oxygenated portion to which he gives the rather strange formula $C_{56}H_{96}O$. According to Bley and Diesel, myrrh containing a little volatile oil always has an acid reaction, which they ascribe to the oxidation of the oil. They also found formic acid in the specimen examined by them. The same investigators propose as a test of myrrh the production of a transparent dirty-yellow liquid with nitric acid, while false myrrh affords a bright-yellow solution in the same fluid, and bdellium is not dissolved, but becomes whitish and opaque. (*A. J. P.*, xviii, 228.) According to Righini, if powdered myrrh, rubbed for fifteen minutes with an equal weight of ammonium chloride, and fifteen times its weight of water gradually added dissolves quickly and entirely, it may be considered pure. Chas. E. Escott (*A. J. P.*, 1887) extracted a sample of myrrh with petroleum benzin, and on spontaneous evaporation of the solvent obtained 18.75 per cent. of oily residue. The gum left after treatment with alcohol had a barely perceptible odor of myrrh and a slightly mucilaginous taste, was neutral to test paper, and, though of a pale color, gave with water a dark-brown solution. The insoluble portion amounted

to 15 per cent., or 8.4 per cent. of the weight of the myrrh. The diluted solution acquired a purple color by ferric chloride, changed to reddish-yellow by ammonia. Stronger solutions were precipitated by alcohol, not gelatinized by borax, and the precipitate with lead subacetate was not redissolved. The gum makes a good mucilage, and, when making tincture of myrrh, the residue insoluble in the alcoholic menstruum should be saved for that purpose.

Uses.—Myrrh is a stimulant tonic, with some tendency to the lungs, and perhaps to the uterus. It is also employed as a tonic in *dyspepsia,* and as an expectorant and emmenagogue in *debilitated states* of the system, in the absence of febrile excitement or acute inflammation. The diseases in which it is usually administered are *chronic catarrh, phthisis pulmonalis,* other *pectoral affections* in which the secretion of mucus is abundant but not easily expectorated, *chlorosis, amenorrhea,* and the various affections connected with this state of the uterine function. It is generally given combined with chalybeates or other tonics, and in *amenorrhea* very frequently with aloes. It is used also as an application to *spongy gums,* the *aphthous sore mouth* of children, and various kinds of *unhealthy ulcers.*

A *plaster of myrrh* is made by rubbing together powdered myrrh, camphor, and balsam of Peru, of each an ounce and a half, then adding the mixture to 32 ounces of lead plaster previously melted, and stirring well until the plaster thickens on cooling. It is then to be formed into rolls. This plaster may be employed in all cases where a gentle and long-continued rubefacient effect is desired.

Myrrh may be given in the form of powder or pill, or suspended in water, as in the famous antihectic mixture of Griffith. (*Mistura Ferri Composita.*) The infusion is also sometimes given, and an aqueous extract has been recommended as milder than myrrh in substance. The tincture is used chiefly as a local application.

Dose, ten to thirty grains (0.65–2 Gm.).

Off. Prep.—Decoctum Aloes Compositum, *Br.;* Mistura Ferri Composita, *Br.;* Pilulæ Aloes et Myrrhæ, *N. F.* (*Br.*); Pilulæ Rhei Compositæ, *U. S.* (*Br.*); Tinctura Myrrhæ, *U. S., Br.;* Pilulæ Aloes, Hydrargyri et Scammonii Compositæ (from Tincture of Aloes and Myrrh), *N. F.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodicæ sine Aloe, *N. F.;* Tinctura Aloes et Myrrhæ, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.;* Tinctura Capsici et Myrrhæ, *N. F.*

NITROGENII MONOXIDUM. U. S.

NITROGEN MONOXIDE Nitrogen. Monox. [Nitrous Oxide]

(nī-trō-gĕn'ī-ī mō-nŏx'ĭ-dŭm)

"Nitrogen Monoxide gas [$N_2O = 44.02$]." *U. S.*

Laughing gas; Oxyde nitreux, Potoxide d'Azote, *Fr.;* Stickstoffoxydul, Lachgas, *G.*

These names were originally given to a gaseous substance, discovered by Priestley in 1776, but first brought into general notice in 1800 by Humphry Davy, who discovered and made known the remarkable exhilarating properties which earned for it the name of laughing gas.

Preparation.—In its preparation, pure fused ammonium nitrate is submitted in a glass retort to a heat sufficient to decompose it, not exceeding 204.4° C. (400° F.), and the resulting gas and vapor are collected in a glass receiver over warm water or a saturated aqueous solution of common salt. Warm water is preferred because cold water absorbs much of the gas, and would consequently occasion loss, and even warm water, though it takes up much less, is not entirely unobjectionable on this score; the saline solution is therefore probably, on the whole, best adapted to the purpose. When ammonium nitrate is heated to the point of decomposition, it is wholly resolved into aqueous vapor and nitrogen monoxide, according to the reaction:

$$NH_4.NO_3 = 2H_2O + N_2O$$

But it is necessary not to let the heat employed in the process be too high, as otherwise, besides nitrous oxide, there will come over portions of nitric oxide, uncombined ammonia, and probably even nitric acid, which contaminate the product, and render it unfit for use. This may be avoided by arresting the process as soon as any white fumes appear in the retort. Peculiar care also must be taken that the ammonium nitrate should be pure, and especially free from ammonium chloride, which might cause an admixture of chlorine in the product. To insure against impurities of this kind, it is best in any case in the least doubtful, and perhaps it might be best in all cases, to cause the nitrous oxide, before it is used by inhalation, to pass successively through two solutions: one, of ferrous sulphate, to remove any nitric oxide that might be present; the second, of potassium or sodium hydroxide, to neutralize acid impurities and chlorine. At times nitrogen gas is also found in the nitrogen monoxide, probably resulting from a trace of nitrite present or some reducing action upon the nitrate in the moment of its decomposition. When the monoxide is liquefied under pressure this free nitrogen remains as unliquefied gas.

Among the impurities sometimes found in commercial specimens of NO are free ammonia or free nitric acid, which, under ordinary circumstances should recombine to form ammonium nitrate. If, however, the apparatus is metallic, the nitric acid may combine with the metal to form a nitrate and the corresponding amount of ammonia cannot recombine with acid and is thus left free as a dangerous impurity.

Nitrogen monoxide gas is colorless, inodorous, slightly sweetish to the taste, and of the sp. gr. 1.527 compared with air. Cold water will absorb about three-fourths of its bulk of the gas,

and, under pressure, much more, and, thus impregnated, has a slight, not unpleasant odor, and a sweetish taste. By the joint influence of cold and pressure the gas may be condensed into a liquid, which is colorless, very mobile, and capable, under the ordinary atmospheric pressure, of remaining liquid at –12.7° C. (9° F.). The liquefaction was effected by Bianchi at 0° C. (32° F.), under a pressure of thirty atmospheres. (*A. J. P.*, 1865, 275.) Inflammable bodies will generally burn with increased vigor in nitrous oxide, but it is entirely incapable of giving oxygen to the blood.

It is officially described as "a colorless gas possessing a slight characteristic odor and a somewhat sweet taste. It supports the combustion of many substances. For convenience in handling and use, it is compressed in metal cylinders. It is quite soluble in water at low temperatures; 1 volume of water dissolves about 1.3 volumes of nitrous oxide at 25° C. (77° F.). Pass 2000 mils of the gas, measured under normal atmospheric pressure at about 25° C. (77° F.), through 100 mils of barium hydroxide T.S. at a rate not exceeding 4000 mils per hour; not more than a slight turbidity is produced (*carbon dioxide*). No opalescence is produced in a mixture of 100 mils of distilled water and 1 mil of silver nitrate T.S. by 2000 mils of the gas under the conditions described above (*halogens*). No change in color is produced in 100 mils of distilled water to which 5 drops of litmus T.S. have been added, by the passage of 1000 mils of the gas through the liquid under the conditions described above (*acids or bases*). No alteration in color is produced in a solution of 0.2 mil of tenth-normal potassium permanganate V.S. in 100 mils of distilled water, by the passage of 1000 mils of the gas through the liquid under the conditions described above (*reducing substances*)." *U. S.*

Uses.—Although Sir Humphry Davy as far back as 1800 suggested the use of nitrous oxide for the production of anesthesia, the first practical employment of it was in 1844 by Horace Wells, of Connecticut. Nitrous oxide is remarkable among anesthetics in being almost physiologically inert, save in its effect on the cerebrum. While as it is ordinarily administered there are marked alterations in the circulation owing to partial asphyxia, by carefully combining pure oxygen with the gas it is possible to induce with nitrous oxide a state of complete anesthesia without any considerable change in either the rapidity of the pulse, the blood pressure, or the respiration. It differs also from the liquid anesthetics in that it is not depressant to the spinal cord. For operations of short duration, such as extraction of teeth, opening of abscesses, and the like, it should always be the anesthetic of preference if available. The mortality in this group of operations is almost nil; it has been estimated variously as from one death in a hundred thousand to one in a million. The two great drawbacks to its more frequent employment are its cumbersomeness of transportation and the shortness of the narcosis. By administering it in conjunction with pure oxygen the inhalation may be continued for long periods of time, so that it can be employed in major operations. There is, however, great difference of opinion as to the advisability of its use for this purpose; Crile (*J. A. M. A.*, 1910, liv), who has had a large experience with it, believes that with a skilful anesthetist it is safer than ether, but that in the hands of the inexperienced is more dangerous.

NUX VOMICA. U. S., Br.

NUX VOMICA Nux Vom. [Strychni semen, P. I.]

(nŭx vŏm'ĭ-cą)

"The dried, ripe seeds of *Strychnos Nux-vomica* Linné (Fam. *Loganiaceæ*), yielding not less than 2.5 per cent. of the alkaloids of Nux Vomica." *U. S.* "Nux Vomica consists of the dried ripe seeds of Strychnos Nux-vomica, *Linn.*" *Br.*

Semen Nucis Vomicæ; Poison Nut, Quaker Buttons, Dog Buttons; Noix vomique, *Fr. Cod.*; Semen Strychni, *P. G.*; Krähenaugen, Brechnuss, *G.*; Noce vomica, *It.*; Nuez vomica, *Sp.*

Strychnos Nux-vomica is a tree of a moderate size, with numerous strong branches, covered with a smooth, dark gray bark. The young branches are long, flexuous, smooth, and dark green, with opposite, roundish-oval, petiolate, entire, smooth, and shining leaves. The flowers are small, white, funnel-shaped and in terminal corymbs. The fruit is a round berry, about as large as an orange, with a smooth, yellow or orange-colored, hard, fragile rind, and many seeds in a juicy pulp. It has frequently been asserted that the pulp is innocuous, but Flückiger and Hanbury, and also Dunstan and Short (*P. J.*, 3d series, xv, 1) have demonstrated that it contains strychnine. Dunstan and Short have also proved that of the commercial varieties of nux vomica Bombay seed stands first in percentage of contained strychnine, then Cochin, and lastly Madras. (*P. J.*, 1883, xiv, 1053.)

The tree is a native of the East Indies, growing in Bengal, Malabar, on the Coromandel Coast, in Ceylon, in many islands of the Indian Archipelago, in Cochin China, and in Northern Australia. The drug is largely shipped from Madras, where it is estimated that in 1912 nearly 400,000 pounds were marketed. Much of the nux vomica shipped to the United States is exported from Bombay, and in 1910–1911 some 45,000 pounds of nux vomica were exported to the United States from the Bombay district. The chief markets for nux vomica are China, and America, small quantities are shipped to London, and the importations to Hamburg are very irregular. Joblin states that during the fiscal year 1909 there were imported into the United States 1,666,957 pounds of nux vomica; in 1910, 2,738,662 pounds. (*Cons. & Tr. Rep.*, 1911, p. 350.)

The wood and root are very bitter, and are employed in the East Indies for the cure of

intermittents. The *radices colubrinæ* and *lignum colubrinum* of the older writers, long known in Europe as narcotic poisons, have been ascribed to this species of *Strychnos,* under the impression that they were identical with *Strychnos colubrina,* to which Linnæus refers them. They were ascertained by Pelletier and Caventou's researches to contain a large quantity of strychnine. The bark has been mistaken for cusparia, and hence is sometimes referred to as *false angustura.* Gehe & Co. (*Handelsbericht,* 1914, p. 119) state that a new variety of nux vomica, the origin of which is unknown, is being exported from Burma. The seeds are externally light gray, internally yellow and are devoid of strychnine.

Properties.—Nux vomica is officially described as "orbicular, nearly flat, occasionally irregularly bent, from 10 to 30 mm. in diameter and from 4 to 5 mm. in thickness, very hard when dry; externally grayish or greenish-gray, covered with appressed hairs giving it a silky luster, hilum indicated by a circular scar at the center of one of the flattened sides and connected with the micropyle at the edge by a ridge; internally showing a thin, hairy seed-coat and a large grayish-white endosperm at one end of which is embedded a small embryo with two broadly ovate, 5- to 7-nerved cotyledons; inodorous; taste intensely and persistently bitter. The powder is light gray; consisting chiefly of thick-walled endosperm cells containing globules of a fixed oil and a few small aleurone grains, and fragments of strongly lignified, non-glandular hairs, the walls of the latter possessing large, circular, or long, slit-like pores. In the tissues of the adhering pulp occur a few small, nearly spherical starch grains. Nux Vomica yields not more than 3.5 per cent. of ash." *U. S.*

"Seeds disc-shaped, nearly flat, but sometimes irregularly bent; rounded or somewhat acute at the margin, from a small prominence on which a raised line passes to the central hilum. Ash-grey or greenish-grey. From two to two and a half centimetres in diameter, and about six millimetres thick. Surface densely covered with short, satiny, radiately arranged and closely appressed hairs. Endosperm large and horny; cotyledon small and leafy. Powdered Nux Vomica exhibits fragments of the endosperm, the cell-walls of which are very thick but not lignified, also slender rod-like fragments of the hairs and their thickened, pitted, lignified basal portions. No odor; taste extremely bitter. Yields not less than 1.25 per cent. of strychnine when tested by the following process." *Br.*

The seeds are destitute of odor, but have an acrid, very bitter taste, which is much stronger in the kernel than in the investing membrane. They impart their virtues to water, but more readily to diluted alcohol. For a method of distinguishing powdered nux vomica from powdered ignatia and other powders, see *Proc. A. Ph. A.,* 1897, 503.

Herder has proposed a detection of the alkaloids in nux vomica by various microchemical means and shows how they may be localized in the seeds and growing plants. (*A. Pharm.,* 1906, p. 129.) Tunmann (*A. Pharm.,* 1910, 644) has studied the distribution of the alkaloids in the germinating seeds of *Strychnos Nux vomica,* and concludes that the embryo of the seed contained only brucine and that strychnine, which was contained in the endosperm only in the cell plasma of the cell content, appears to act as a protection for the growing plant. Grutterink has also published an illustrated article on the microchemical examination of the several alkaloids of nux vomica. (*Zeit. An. Chem.,* li, p. 187.) Rusby has reported the shipment of nux vomica which consisted of small inferior seeds which had been rolled in some mixture of clay. (*Proc. A. Ph. A.,* 1908, lvi, p. 794.) Powdered nux vomica has been adulterated with ground olive stones and the raspings of vegetable ivory. (See *Rep. d. Pharm.,* 1909, p. 241; *Ann. d. chim. Analyt.,* 1909, p. 261.)

The chemists Pelletier and Caventou discovered in nux vomica two alkaline principles, *strychnine* and *brucine,* united with a peculiar acid which they named *igasuric.* Its other constituents are a yellow coloring matter, a fixed oil, gum, starch, a small quantity of wax, and several earthy phosphates. Charles Bullock, in preparing the alcoholic extract of nux vomica with a moderate continuous heat, so as to dry it sufficiently to be pulverized, separated from 150 pounds of the seeds 5 pints of a liquid oil. This oil has a saponification number of 124, and an iodine number of 64 to 67. The unsaponifiable portion of the oil was identified as a mixture of phytosterin. (*A. Pharm.,* 1912, p. 398.) F. Meyer (*In. Dis.,* St. Petersburg, 1875) investigated the fatty oil from nux vomica, and found it to consist of the glycerides of capric, caprylic, caproic, butyric, and palmitic acids. (*A. J. P.,* 1874, 405.) Shenstone (*J. Chem. S.,* xxxix, 453) has shown that the *igasurine* of Desnoix is a mixture of strychnine and brucine. A glucoside, *loganin,* has also been found in the nux vomica seeds, but it exists more largely in the surrounding pulp. Dunstan and Short, its discoverers (*P. J.* 1883, xiv, 1025), gave to it the formula $C_{25}H_{34}O_{14}$. Boorsma stated that he had discovered a new alkaloid in the leaves of *S. Nux vomica* (*Bull. de l'Inst. Bot. de Buitenzorg*) and he named it *strychnicine;* it is only slightly poisonous. (See also *P. J.,* 1902, 65.)

Hugo H. Schafer (*J. A. P. A.,* 1914, p. 1077) announces a new alkaloid in nux vomica which he has named *struxine.* This alkaloid is stated to have the chemical formula $C_{21}H_{30}O_4N_2$. It is present only in the drug coming from Cochin China, and was found in an amount of 0.1 per cent.

Igasurine was said to be found in the mother waters from which strychnine and brucine have been precipitated by lime. Jörgensen believed that it was identical with brucine (see *A. J. P.,* June, 1872, p. 257), and W. A. Shenstone confirmed this view. (*A. J. P.,* Dec., 1881.)

Loganin is present in the pulp to the amount of 4 or 5 per cent., and is contained in small quantity also in the seeds. It was obtained by exhausting the pulp with a mixture of chloroform and alcohol (100 : 25). The exhaustion was effected in an apparatus for hot repercolation. The percolate, on cooling, deposited crystals, which when recrystallized a number of times from alcohol, and finally from absolute alcohol, were obtained pure. Loganin is easily soluble in water and alcohol, less soluble in ether, chloroform, and benzene. Its aqueous solution is not precipitated by any of the alkaloidal reagents. Its most characteristic reaction is found in its behavior with concentrated sulphuric acid. A very small quantity of loganin, when gently warmed with a few drops of concentrated sulphuric acid, yields a fine red color, which, on standing, develops into a deep purple. By boiling with dilute sulphuric acid, loganin is resolved into glucose (reducing Fehling's solution) and a body for which the name *loganetin* is proposed. This substance, like loganin, gives the characteristic reaction with sulphuric acid, but the purple color does not develop so rapidly. Loganetin is soluble in water and alcohol, less soluble in ether, carbon disulphide and chloroform. (*P. J.*, 1884, p. 1025.)

Strychnine ($C_{21}H_{22}O_2N_2$) was discovered by Pelletier and Caventou in 1818, in both the nux vomica and the bean of St. Ignatius, and received its name from the generic title of the plants (*Strychnos*) to which these two products belong. According to these chemists, it exists much more abundantly in the bean of St. Ignatius than in the nux vomica, the former yielding 1.2 per cent., the latter only 0.4 per cent., of strychnine, but Dragendorff obtained from nux vomica from 1.9 to 2.1 per cent. of mixed alkaloids, about half of which was strychnine. (*Jahresbericht*, 1874, 103.) For valuable practical information about the yield of the alkaloids, extracts, etc., by E. L. Patch, see *Proc. A. Ph. A.*, 1891, 91; also *P. J.*, 1889, 341; *Proc. Michigan Pharm. Assoc.*, 1889; *Proc. Ohio Pharm. Assoc.*, 1889; *P. J.*, 1890, 493.

Other species of *Strychnos* contain the poisonous alkaloids, and may some time become a commercial source of them. *Bidara laut* of the Indian bazaars, believed to be obtained from *S. ligustrina*, has been analyzed by Russow, who found the wood to contain 2.26 per cent. and the bark 7.38 per cent. of brucine without strychnine. Henry G. Greenish found in the wood and bark respectively of *S. colubrina* 0.96 per cent. and 5.54 per cent. of mixed alkaloids; the same analyst obtained from false Angustura bark (*S. Nux vomica*), young bark 3.10 per cent., old bark 1.68. (*P. J.*, 3d ser., ix, 1014.) According to Bernelot-Moens, the dry seeds of the *S. tieute* contain 1.469 per cent. of strychnine, with a trace of brucine. (*A. J. P.*, 1866, p. 506.) From the seeds of *Strychnos Rheedii*, W. R. Dunstan obtained a yield of 0.06 per cent. of brucine and no strychnine. (*Imp. Inst. Rep.*, 1901–1902.) The Congo poison known as *Cupua Apus*, according to Vinci (*A. I. P. T.*, xx), is produced from the *Strychnos kipapa*. The bark of the root contains 6 per cent. of strychnine and the wood 0.1 per cent.

Brucine ($C_{23}H_{26}O_4N_2$) was discovered by Pelletier and Caventou, first in the bark called *false Angustura*, in combination with gallic acid, and subsequently, associated with strychnine in the form of igasurates, in the nux vomica and the bean of St. Ignatius. It is crystallizable from alcohol, the crystals then containing $4H_2O$. It is without odor, but of a permanent, harsh, very bitter taste; is soluble in 850 parts of cold and in 500 of boiling water; very soluble in alcohol, whether hot or cold; it dissolves in 4 parts of chloroform, 440 parts of ether, 60 parts of benzene, and 120 parts of petroleum benzin. It is permanent in the air, but melts at a temperature a little above that of boiling water, and on cooling congeals into a mass resembling wax. The hydrated crystals melt at 115° C. (239° F.), and sublime at 204° C. (399.2° F.), while the anhydrous base melts at 178° C. (352.4° F.), changing color, and depositing carbon. (*P. J.*, 1868, 375.) It forms crystallizable salts with acids. Concentrated nitric acid produces with brucine or its salts an intense crimson color, which changes to yellow by heat, and upon the addition of stannous chloride becomes violet. A test for brucine, given by Stanislas Cotton, consists in adding to a warm solution of brucine (from 40° to 50° C. (104°–122° F.)) in nitric acid, a concentrated solution of sodium thiosulphate. The mixture first becomes violet, and then passes to green when the alkaline salt is in excess. (*J. P. C.*, Juillet, 1869, 18.) These effects serve to distinguish brucine from strychnine, and, if produced with the latter alkaloid, evince the presence of the former. According to Larocque and Thibierge, auric chloride produces, with solutions of the salts of brucine, precipitates at first milky, then coffee-colored, and finally chocolate-brown. (*Journ. de Chim. Méd.*, Oct., 1842.) Chlorine water produces with solution of brucine a rose color, due to the formation of *dichlor-brucine*. This is a reddish-brown, hygroscopic powder. (*A. Pharm.*, 1886, 934.) A *dinitro-brucine*, $C_{23}H_{24}(NO_2)_2N_2O_4$, has also been obtained by the action of nitrogen trioxide upon the brucine in alcoholic solution. Brucine appears to bear a definite relation to strychnine in chemical constitution, being a *dimethoxy-strychnine*. According to the analyses of Shenstone and Dragendorff, the bark of the nux vomica contains brucine, with a trace of strychnine, while in the leaves Hooper found only brucine. (*P. J.*, 1890, xxi.)

Brucine may be procured from false Angustura bark, in a manner essentially the same as that in which strychnine is procured from nux vomica, with this difference, that the alcoholic extract obtained from the precipitate produced by lime or magnesia should be treated with oxalic acid, and subsequently with a mix-

ture of rectified alcohol and ether, which takes up the coloring matter, leaving brucine oxalate. This is decomposed by magnesia, and the brucine is separated by alcohol, which by spontaneous evaporation yields it in the state of crystals. Prescott (*Organic Analysis,* 1887, p. 458) gives two methods for the separation of strychnine from brucine; first, by the use of alcohol of 0.97 sp. gr., which easily dissolves brucine, but has very slight solvent power upon strychnine; second, by Dunstan and Short's method with potassium ferrocyanide. This method has been reported upon by Holst and Beckurts (*Ph. Centralh.,* N. F., 1887, p. 119), who find that if the hydrochloric acid solution containing mixed alkaloids is not too dilute, on the addition of potassium ferrocyanide the whole of the strychnine will be precipitated as ferrocyanide, while the brucine salt will remain in solution.

The separation of brucine from strychnine is most conveniently effected by exposing the mixed alkaloids to the action of diluted nitric acid, which destroys brucine very rapidly while having no appreciable action on strychnine; this method is used in the former official assay process.

Igasuric acid has been regarded as erroneously named, and investigators have stated that it was malic acid and tannic acid, while G. Sander (*A. Pharm.,* 1897, 133) believes that the acid found in nux vomica, heretofore known as igasuric acid, is *caffeo-tannic acid.*

The official process for determining the amount of alkaloids present in nux vomica is as follows:

Assay.—"Introduce 15 Gm. of Nux Vomica, in No. 40 powder, into a 250 mil flask and add 150 mils of a mixture of chloroform, 1 volume, and ether, 2 volumes. Stopper the flask, shake it well and allow it to stand ten minutes, then add 10 mils of ammonia water, and, after shaking the flask vigorously every ten minutes during two hours, allow it to stand ten hours. Now add 25 mils of distilled water, again shake the flask well, and, when the drug has settled, decant 100 mils of the solution, representing 10 Gm. of Nux Vomica, and proceed as directed under *Belladonnæ Radix,* page 222, beginning with the word 'filter,' line 12 of the Assay. For the titration, dissolve the alkaloids from the residue with 10 mils of tenth-normal sulphuric acid V.S. instead of 5 mils. Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 36.4 milligrammes of the total alkaloids of Nux Vomica." *U. S.*

"Shake 7.5 grammes of Nux Vomica in No. 60 powder frequently during half an hour with a mixture of 25 millilitres of *chloroform,* 50 millilitres of *ether,* and 5 millilitres of *solution of ammonia.* Transfer 50 millilitres of the clear ethereal liquid to a separator, and extract the alkaloids by shaking with three successive portions, each of 10 millilitres, of *N/1 solution of sulphuric acid,* transferring the acid solutions to a second separator. Make the acid solutions alkaline with *solution of ammonia,* and again extract the alkaloids by shaking successively with 10, 5, and 5 millilitres of *chloroform,* drawing off the chloroformic solutions into a small flask. Recover the chloroform by distillation, dissolve the residue in a mixture of 5 millilitres of *diluted sulphuric acid* and 10 millilitres of water, heat the solution to 50° C. (122° F.), add 3 millilitres of a mixture of equal volumes of *nitric acid* and *water,* and set aside for ten minutes. Transfer the solution to a separator, rinsing the flask with a little *water,* make alkaline with *solution of sodium hydroxide,* and extract the alkaloid by shaking successively with 10, 5, and 5 millilitres of *chloroform.* Wash the mixed chloroformic solutions in a separator with 5 millilitres of *water,* transfer to a tared dish and allow the chloroform to evaporate, adding towards the end 5 millilitres of *alcohol* (90 per cent.). Evaporate to dryness, dry the residue at 100° C. (212° F.), and weigh. This weight, multiplied by 20, is the weight of strychnine in 100 grammes of the powdered Nux Vomica. Powdered Nux Vomica, when used for official purposes other than the production of standardised preparations, must be adjusted, if necessary, by the addition of powdered Milk Sugar to contain in 100 grammes 1.25 grammes of strychnine when tested by the foregoing process. *Limit of error* 0.05 gramme in excess or defect." *Br.*

As a test for nux vomica, Vielgruth proposes to treat a few grains of the suspected powder with proof spirit, evaporate the tincture to dryness at a heat not exceeding 35.5° C. (96° F.), then add a drop or two of diluted sulphuric acid, and again raise to the heat mentioned. If nux vomica be present, a beautiful carmine-red color will be produced, which will disappear in ten or fifteen minutes after cooling, and reappear, but less brightly, on the reapplication of the heat. Schweissinger recommended the direct determination of the alkaloids in nux vomica by titration with hydrochloric acid as the best way of ascertaining the strength of pharmaceutical preparations. (*A. Pharm.,* 1885, 579.) Keller's method of estimating the alkaloids in nux vomica (see *Proc. A. Ph. A.,* 1895, 1024) is commended by Sander. (*A. Pharm.,* 1897, 133; see also *A. J. P.,* 1896, 189.) A new method of assay for nux vomica and its preparations has been proposed by M. Azadain (*P. J.,* xciii, 371) which involves the precipitation of the alkaloids by silico-tungstic acid.

Uses.—The medicinal and toxic properties of nux vomica are those of its alkaloid. (See *Strychnina.*) The belief held by some physicians that it acts more favorably as a bitter upon the stomach has only this much of justification—namely, that it is more slowly absorbed, and therefore acts locally somewhat more persistently.

BRUCINE.—On account of the difficulty of separating strychnine from brucine, it has been found by physiologists difficult to determine the exact action upon the human organism of the pure alkaloid. It was formerly taught that

brucine closely resembled strychnine in its physiological action, except that it was less poisonous and that it was depressant to the peripheral sensory nerves. Dickson and Harvey (*P. J.*, 1908, lxxxi, p. 367), however, experimenting with a chemically pure brucine, reach the conclusion that its dominant action is a paralysis of the peripheral motor nerves, and that the convulsive action which is the characteristic effect of strychnine is almost entirely absent in the case of brucine. According to the observation of Mays, brucine is an active paralyzant to the sensory nerves and a 5 or 10 per cent. solution applied to the mouth causes local anesthesia. He has used it for the relief of *pruritus*. Burnett also asserts that a 5 per cent. solution is a valuable local anodyne in inflammations of the external ear.

Dose, of nux vomica, one to four grains (0.065–0.26 Gm.).

Off. Prep.—Extractum Nucis Vomicæ (from Liquid Extract), *U. S., Br.;* Fluidextractum Nucis Vomicæ, *U. S.* (*Br.*); Tinctura Nucis Vomicæ (from Extract), *U. S.* (from Liquid Extract), *Br.;* Elixir Phosphori et Nucis Vomicæ (from Tinctura), *N. F.;* Pilulæ Aloes et Podophylli Compositæ (from Extract), *N. F.;* Pilulæ Ferri, Quininæ, Aloes et Nucis Vomicæ (from Extract), *N. F.;* Pilulæ Laxativæ Post Partum (from Extract), *N. F.*

OLEA.

OILS

(ō'lę-a)

These are liquid or solid substances, unctuous to the touch and characterized by inflammability. They are divided into two classes, the *fixed* and the *volatile,* because distinguished, as their names imply, most readily by their different behavior on the application of heat.

OLEA FIXA. *Fixed Oils.*

Fats, Fatty Oils; Huiles Graisses, Huiles fixés, *Fr.;* Fette, Fette Oele, *G.;* Olios, *It.;* Aceites, *Sp.*

These are sometimes termed *fatty oils,* because they constitute in part the vegetable and animal fats. The distinction between liquid and solid fats is for the most part a physical one only, as they contain the same chemical compounds, although in relatively different proportions. The fatty oils, though existing in greater or less proportion in various parts of plants, are furnished for use exclusively by the fruit, and, as a rule, are most abundant in the dicotyledonous seeds. They are obtained either by submitting the bruised seeds to pressure in hempen bags, or by boiling them in water, and skimming off the oil as it rises to the surface. When pressure is employed, it is customary to prepare the seeds for the press by exposing them to a moderate heat, so as to render the oil more liquid and thus enable it to flow out more readily. Another mode of extracting certain oils is by means of liquids having the power of dissolving them, and this method is now largely used in practice, carbon disulphide, carbon tetrachloride, and petroleum benzin being used. For the details of the process, see *A. J. P.,* Nov., 1868, 549. Fixed oils may be clarified and decolorized by subsidence, filtration through animal charcoal, clays or earths, or porous solids, precipitation with tannin, lead acetate, plaster of Paris, albumin, gelatin, or other agents; cellulose and asbestos filters are often used, and on the large scale, for separating mechanical impurities, centrifugal machines like those employed for milk. Some oils are given a preliminary treatment with sulphuric acid which is later removed by treatment with alkali. Fixed oils containing stearin or palmitin are likely to deposit these fats in cold weather, leaving the olein in a liquid condition. The olein may be separated by filtration in the cold.

Hydrogenated Fats and Oils.—A class of solid fats has appeared upon the market which are produced by a process known as hydrogenation, which is carried out in practice by bringing liquid fats into intimate contact with metallic catalyzers (finely divided nickel is usually employed), at elevated temperatures (160°–200° C. or 320°–392° F.). Under these conditions the unsaturated members of the fatty acid series which are usually liquid and are represented by oleic acid, become converted into the solid members of the series, which are saturated as stearic acid. The best known commercial product made in this way is the proprietary fat known as *Crisco,* largely used for culinary purposes.

Classification.

The following scheme of classification of the fixed oils, both liquid and solid (Allen, *Com. Org. Anal.,* 3d ed., vol. ii, Part I, pp. 88–102), gives a general view of their essential characters, points of difference, etc.

I. Olive Oil Group. *Vegetable Non-drying Oils.*—The oils of this group solidify on treatment with nitrous acid or mercuric nitrate, but do not lose their power of producing a greasy stain on paper, however long they may be exposed to the air. Their density varies from 0.914 to about 0.920, and hence is less than that of Groups III, IV, and V. Their viscosity is notably greater than that of the drying oils.

This group includes almond oil (from *Amygdalus communis*), peach oil (from kernels of *Prunus Persica*), apricot oil (from kernels of *Prunus armeniaca*), oil of ben (from *Moringa oleifera*), earth nut oil (from *Arachis hypogæa*), and olive oil (from *Olea europæa*).

II. Rape Oil Group.—The oils of this group are all derived from seeds of the family *Cruciferæ.* They are non-drying but less distinctly so than the oils of Group I. They show higher saponification values, higher iodine absorption and less solid elaidins than Group I.

This group includes Colza oil and rape seed oil (from *Brassica campestris, B. napus* and other species); oil of black mustard (from seeds of *Brassica nigra*); oil of white mustard (from seeds of *Sinapis alba*).

III. Cotton Seed Oil Group.—The oils of this group occupy a position intermediate between the vegetable non-drying and the true drying oils (Groups I and IV). In density they somewhat exceed the oils of Group I, but are lighter than those of Groups IV and V. They form more or less elaidin on treatment with nitrous acid or mercuric nitrate, but do not become wholly solidified. On the other hand, they undergo more or less drying on exposure to the air, but not so markedly as the oils of Group IV.

This group includes beech nut oil (from *Fagus sylvatica*), cotton seed oil (from *Gossypium* species), hazel nut oil (from *Corylus avellana*, see *Proc. A. Ph. A.*, 1893), sesame or teel oil (from *Sesamum orientale*), and sunflower oil (from *Helianthus annuus; H. perennis*), camelina oil (from *Myagrum sativum*), cress seed oil (from *Lepidium sativum*), and maize oil (*Corn Oil*).

IV. Linseed Oil Group. *Vegetable Drying Oils.*—These oils are not solidified by treatment with nitrous acid or mercuric nitrate, but become gradually converted into solid masses or varnishes, by exposure to the air. In density the oils of this group vary from about 0.923 to 0.937, and hence are distinctly heavier than the non-drying oils and than most of the oils of Group III. On the other hand, they are lighter than the oils of Group V. The fluidity of the drying oils is also much higher than that of the non-drying oils.

This group includes niger seed oil (from *Guizotia oleifera*), hemp seed oil (from *Cannabis sativa*), linseed oil (from *Linum usitatissimum; L. perenne*), poppy seed oil (from *Papaver somniferum*), Scotch fir seed oil (from *Pinus sylvestris*), tobacco seed oil (from *Nicotiana Tabacum*), walnut oil (from *Juglans regia*), weld seed oil (from *Reseda Luteola*), and soya bean oil (from *Soja hispidus*).

V. Castor Oil Group.—The oils of this group are distinguished from those of Groups I, II, III, and IV, by their very high density and viscosity. They are also remarkable for their ready solubility in alcohol, and their marked purgative properties. In their drying characters and behavior with the elaidin test they resemble the oils of the cotton seed oil group. Both castor and croton oil are miscible in all proportions with glacial acetic acid.

This group includes castor oil (from *Ricinus communis*), croton oil (from *Croton Tiglium*), Japanese or Chinese wood oil (from seeds of *Aleurites cordata* or *Elæococca vernicia*), boiled linseed oil, blown oils (made by oxidation of rape seed, cotton seed, linseed, lard, and other oils).

VI. Palm Oil Group. *Solid Vegetable Fats.*—This group includes solid fats not containing notable quantities of glycerides of lower fatty acids. The densities for the melted fats at 98° and 99° C. (208.4°–210.2° F.) are compared with the density of water at 15.5° C. (60° F.) taken as 1.000, and vary from 0.920 to 0.995.

This group includes palm oil (from fruit of *Elæis guineensis*), cacao butter (from nuts of *Theobroma Cacao*), nutmeg butter (from nuts of *Myristica fragrans*), and shea butter (from seeds of *Bassia Parkii*).

VII. Cocoanut Oil Group. *Solid Vegetable Fats.*—This group includes solid fats containing notable quantities of glycerides of lower fatty acids—that is, of acids distilling with more or less facility in a current of steam at 100° C. (212° F.). The group includes cocoanut oil (from the nuts of *Cocos nucifera*), palm oil (from the kernels of the nuts from *Elæis guineensis*), laurel oil (from fruit of *Laurus nobilis*), Japan wax (berries of *Rhus succedanea*), myrtle wax (berries of *Myrica cerifera*). For a description with constants of some of the rarer fixed oils belonging to the vegetable group, see papers by J. A. Wijs, *Ph. Ztg.*, 1903, 563; by Pancoast and Graham, *A. J. P.*, 1904, 70; and by Lewkowitsch, *P. J.*, 1904, 492.

VIII. Lard Oil Group. *Animal Oleins.*—This group includes those oils fluid at ordinary temperatures which are obtained from terrestrial animals. They resemble the whale or fish oils in their reaction with chlorine, but are not turned red or brown by boiling with caustic soda. On exposure to air and on treatment with nitrous acid or mercuric nitrate, they behave like the non-drying vegetable oils (Group I). This group includes bone oil, lard oil, tallow oil, and neat's-foot oil. For a paper by P. L. Simmonds on various animal oils, see *Bull. Pharm.*, 1893, 297, 344.

IX. Tallow Oil Group. *Solid Animal Fats.*—This group comprises oils that are solid or semisolid at ordinary temperatures. Their melting points vary somewhat, and are capable of permanent alteration. The group includes bone fat, butter fat, hog's lard, horse fat, beef tallow and mutton tallow.

X. Whale Oil Group. *Marine Animal Oils.*—This group comprises the various fluid oils obtained from fish and cetaceous mammals. They are distinguished as a class by their offensive fishy odor, by the brown color they assume when subjected to the action of chlorine, and by the reddish color which is produced on boiling them with a solution of caustic alkali. With sulphuric acid they give colorations varying from light red to purple or brown. The fish oils do not dry on exposure to air, and mostly yield but little elaidin on treatment with nitrous acid. The term "*train oil*" includes whale, seal, shark, cod, and all similar oils. Cod oil (from *Gadus morrhua* and allied species), cod liver oil (from the same), menhaden oil (from *Alosa menhaden*), porpoise oil (from *Delphinus phocæna* and allied species), seal oil (from *Phoca* of various species), shark oil (from *Squalus maximus* and allied species), and whale oil (from *Balaena mistecetus* and allied species) are all members of this group.

XI. Sperm Oil Group. *Liquid Waxes.*—The members of this group differ from all the fatty

oils of previous classes in not being glycerides, consisting essentially of esters of monatomic alcohols of the ethylic series, in which respect they resemble the true waxes, but are fluid at ordinary temperatures. They are less dense than glycerides, they do not dry or thicken notably on exposure to air, but they yield solid elaidins on treatment with nitrous acid. The group includes sperm oil (from cranial cavities of *Physeter macrocephalus*), doegling or bottle-nose oil, and dolphin oil.

XII. Spermaceti Group. *Waxes Proper.*—Spermaceti and the various waxes differ from the true fixed oils and fats in not forming glycerin when saponified, yielding instead certain of the higher monatomic alcohols, the identity of which varies with the nature of the wax. These alcohols are insoluble in water, and dissolve to but a limited extent in alcohol, but they are soluble in ether, chloroform, carbon disulphide, benzene, and petroleum benzin, and are apt to be mistaken for added paraffin wax when the substance is saponified and the soap extracted with a solvent.

This group includes beeswax (from honeycomb of various species of bees), Carnauba or Brazil wax (from the leaf-coverings of *Copernicus cerifera*), Chinese wax or Pela wax (produced by a species of *Coccus* which punctures the branches of certain trees), myrtle wax (from berries of *Myrica cerifera*), Ocuba wax (from *Myrica Ocuba*), palm wax (from bark of *Ceroxylon andicola*, of the Cordilleras), and spermaceti (deposit from the oil found in the cranial cavities of the sperm whale, *Physeter macrocephalus*). Wool fat, which consists largely of *cholesterol* (an alcohol), belongs to this group.

When oils are decomposed by heat they emit vapors of *acrolein allyl aldehyde*, CH_2CHCHO, a highly volatile liquid resulting from the decomposition of glycerin, upon which the fumes of oils mainly depend for their irritating effects on the eyes and nostrils. Exposed to a red heat, in closed vessels, they yield, among other products of the destructive distillation, a large quantity of combustible and illuminating gases, among which ethylene and acetylene are readily recognized. Heated in the open air, they take fire, burning with a bright flame, and producing water and carbon dioxide. When kept in air-tight vessels, they remain unchanged for a great length of time, but exposed to the atmosphere they attract oxygen and undergo change.

Effervescent Oils.—K. Dieterich recommends oils and fats which have been supersaturated with carbon dioxide and introduced by him under the name of "effervescent oils." (See *Proc. A. Ph. A.*, 1900, 494.) Under the influence of carbon dioxide, compounds which are easily split with the fatty acids are produced, which, particularly in the case of cod liver oil, permit the more complete absorption of the oil than is the case with oil not treated with carbon dioxide. The latter, moreover, acts as a preservative of the oils and renders them more palatable, destroying the unpleasant taste of cod liver oil, and to a certain extent also that of added medicaments, very materially. The absorbability of carbon dioxide is, however, not the same in all oils. Cod liver oil is capable of absorbing the largest quantity, castor oil the smallest, while olive oil stands intermediate. (*Ph. Centralh.*, 1901, 485.)

Some fixed oils, in drying, lose their unctuous character, and are converted into a transparent, yellowish, flexible solid. These are called *drying oils.* Others, especially such as contain mucilaginous impurities, become rancid, acquiring a sharp taste and an unpleasant odor. This change is owing to the development or liberation of free fatty acids, from which the oil may be freed by boiling it for a short time with magnesium hydroxide and water.

Cloes has made investigations in relation to the influence of light in promoting oxidation, and obtained some curious results. The general influence of light is very great, as oils undergo comparatively little change in the dark for a long time; though in relation to some of them the change is at length as great as under the light. Thus, while the oil of poppies had in 30 days increased about 5 per cent. in weight under white light, and had gained only a 5000th in the dark, yet at the end of 150 days the weight in the former condition was rather lessened than augmented, and in the latter, or in the dark, had increased 6.4 per cent. The effect of the different colored rays is also very different. The change is at first most rapid under the white light, less so under the blue, and much less under the red, yellow, and green, being least of all with the green; but with the advance of time the blue overtakes and even passes the white and at the end of three or four months all are about equal in effect. Heat also accelerates the concretion of the oils, by favoring their oxidation; and the same effect is produced by introducing into the unchanged oil a little which has already been altered by exposure to the air. The oxidation of an oil may be very greatly hastened in this way without the aid of heat.

The fixed oils are insoluble in water, but are miscible with that fluid by means of mucilage, forming mixtures which are called emulsions. They are in general very sparingly soluble in alcohol, but readily dissolved by ether, which serves to separate them from other vegetable proximate principles. By the aid of heat they are enabled to dissolve sulphur and phosphorus. The stronger acids decompose them, giving rise, among other products, to oleic, palmitic, and stearic acids. Boiled with diluted nitric acid, some of them give rise to malic and oxalic acids, besides other substances usually resulting from the action of this acid upon vegetable matter. Several acids are dissolved by them without producing any sensible change. They are sa-

ponified by various alkalies. The compounds which these acids form with potassium and sodium hydroxide are the common detergent soaps, although strictly speaking, a soap is the combination of a fatty acid with any metal or base. (See *Sapo* and *Emplastrum Plumbi.*) By the addition of one part of potassium or sodium carbonate, 160 parts of oil may be brought with distilled water into the form of an emulsion. The potassium and sodium soaps and the alkaline sulphides have a similar effect, but not the bicarbonates. The fixed oils also serve as good vehicles for various metallic bases and subsalts, which form soaps to a certain extent soluble in the oil, and thus become less irritant to the tissues. Oils thus impregnated may, like the pure oils, be brought to the state of emulsion with water, for convenient administration, by the addition of a small proportion of potassium carbonate. The fixed oils dissolve many of the alkaloids, the volatile oils, resin, and other proximate principles of plants. The alkaloids are more readily dissolved in them by being first combined with oleic acid, the oleates being more soluble than the alkaloids themselves. According to Buignet, they are, with very few exceptions, indifferent to polarized light; of all those used in medicine, the only exceptions are the liver oils of the ray and dog fish, which have a very feeble lævorotatory power, and castor oil, which is decidedly dextrogyrate.

It is very likely that, with the exception of castor oil, whose rotatory power is due to the asymmetric carbon atom of the ricinoleic acid, the rotatory power is not due to the glycerides themselves but to small proportions of optically active substances such as cholesterol. (Lewkowitsch, *Chem. Analysis of Oils Fats and Waxes,* p. 121.)

The fixed oils, whether animal or vegetable, in their natural state consist in most cases of at least two or three distinct constituents, one liquid at ordinary temperatures, and the other two solid or semisolid. The liquid is a distinct proximate principle, called *olein;* the more solid principles consist of *stearin* and *palmitin,* the former being found most largely in animal and the latter in vegetable oils or fats, and the two in most cases existing together in the same oil. The substance formerly known as *Margarin* is now generally recognized to be a mixture of palmatin and stearin. As the most frequent of these proximate constituents of the fixed oils, and existing in many different oleaginous substances, olein, palmitin, and stearin merit a special notice. Preliminarily to their individual consideration, it will be proper to refer to their nature and composition generally.

These three substances, *olein, palmitin,* and *stearin,* together with *butyrin, caprin,* and other minor fat principles, are *glycerides;* that is, esters or salts of the triatomic alcohol glycerol, $C_3H_5(OH)_3$, and of the several fatty acids, oleic, palmitic, stearic, etc., all of which are monobasic acids. The three mentioned glycerides have the following composition:

$$\text{Olein (triolein)},\ C_3H_5\begin{cases}OC_{18}H_{33}O\\OC_{18}H_{33}O\\OC_{18}H_{33}O\end{cases}$$

$$\text{Palmitin (tripalmitin)},\ C_3H_5\begin{cases}OC_{16}H_{31}O\\OC_{16}H_{31}O\\OC_{16}H_{31}O\end{cases}$$

$$\text{Stearin (tristearin)},\ C_3H_5\begin{cases}OC_{18}H_{35}O\\OC_{18}H_{35}O\\OC_{18}H_{35}O\end{cases}$$

There are also mixed glycerides exemplified by the following formula:

$$\text{(oleopalmitostearin)}\quad C_3H_5\begin{cases}OC_{18}H_{33}O\\OC_{16}H_{31}O\\OC_{18}H_{35}O\end{cases}$$

When these substances, or oils composed principally of them, are treated with alkali with the aid of heat, decomposition takes place, which may be illustrated as follows:

$$C_3H_5\begin{cases}OC_{18}H_{33}O\\OC_{18}H_{33}O\\OC_{18}H_{33}O\end{cases}+3NaOH=$$

$$C_3H_5\begin{cases}OH\\OH\\OH\end{cases}+3Na.OC_{18}H_{33}O$$

that is, olein is decomposed by sodium hydroxide into *glyceryl hydroxide,* or *glycerin,* and *sodium oleate,* or a sodium soap.

The waxes differ from the fats proper in being esters of the higher monatomic alcohols like *cetyl alcohol,* $C_{16}C_{33}.OH$, and *myricyl alcohol,* $C_{30}H_{61}.OH$, instead of being glycerides. The fatty acids present are partly palmitic and stearic, but more largely still higher ones, like *cerotic acid,* $C_{27}H_{54}O_2$.

Other fatty acids represented in fixed oils are: butyric acid, $C_4H_8O_2$; valeric acid, $C_5H_{10}O_2$; caproic acid, $C_6H_{12}O_2$; caprylic acid, $C_8H_{16}O_2$; capric acid, $C_{10}H_{20}O_2$; lauric acid, $C_{12}H_{24}O_2$; myristic acid, $C_{14}H_{28}O_2$; arachidic acid, $C_{20}H_{40}O_2$; erucic acid, $C_{22}H_{42}O_2$; hypogæic acid, $C_{18}H_{30}O_2$. The first few members of the above list are known as the volatile fatty acids, which serve as the basis for the determination of what is known as the Reichert-Meissl number.

Olein. Elain. Liquid Principle of Oils.—It is extremely difficult to obtain olein pure. Being in most oils associated with the solids stearin and palmitin, it must be separated by pressure and other mechanical means, which separation is not always perfectly effected. As ordinarily procured, therefore, olein contains more or less

of palmitin or stearin, or both. In this somewhat impure state it is obtained either by the agency of alcohol or by expression. When one of the oils, olive oil, for example, is dissolved in boiling alcohol, the solution, on cooling, deposits the concrete principles, still retaining the olein, which it yields upon evaporation. The other method consists in compressing one of the solid fats, or one of the liquid oils rendered concrete by cold, between folds of bibulous paper, which absorb the olein, and give it up afterwards by compression under water. Olein is a liquid of oily consistence, congealing at –6° C. (21.2° F.), colorless when pure, with little odor and a sweetish taste, insoluble in water, soluble in boiling alcohol and ether. Its formula, as already stated, is $C_3H_5(OC_{18}H_{33}O)_3$, being an oleate of the triad radical *glyceryl*, C_3H_5. By reaction with nitric acid, or, more exactly stated, under the influence of nitrous acid fumes, olein is converted into a deep yellow, butyraceous mass. If this be treated with hot alcohol, a deep orange-red oil is dissolved, and a peculiar fatty matter remains, called *elaidin*. This is white, crystalline, fusible at 34° C. (93.2° F.), insoluble in water, readily soluble in ether, and appears to be isomeric with olein. It is resolved by saponification with the alkalies into *elaidic acid* and glycerin.

Palmitin.—Palmitic acid occurs in the more liquid fats, such as palm oil and cocoa-nut oil, as well as in butter and human fat, as glyceride, while in spermaceti and some forms of wax it is combined with monatomic alcohol radicals. Palmitin is the *palmitic acid glyceride*, or *glyceryl tripalmitate*. It is best obtained from palm oil.

Stearin.—This exists abundantly in tallow and other animal fats. It may be obtained by treating the concrete matter of lard, free from olein, by cold ether so long as anything is dissolved. The palmitin is thus taken up, and stearin remains. A better method is to dissolve suet in heated oil of turpentine, allow the solution to cool, submit the solid matter to expression in unsized paper, repeat the treatment several times, and finally dissolve in hot ether, which deposits the stearin on cooling. This is concrete, white, opaque in mass, but of a pearly appearance as crystallized from ether, pulverizable, fusible at 66.5° C. (151.7° F.), soluble in boiling alcohol and ether, but nearly insoluble in those liquids cold, and quite insoluble in water. It consists of glyceryl and stearic acid in combination as a glyceride, $C_3H_5(OC_{18}H_{35}O)_3$, and has been formed synthetically by heating a mixture of these two materials to 280° to 300° C. (536°–572° F.).

Commercially the fixed oils are frequently sold under the names *summer pressed* and *winter pressed*. These were once really seasonal designations, as an oil pressed during the warmer months would contain more dissolved stearin and would consequently congeal or cause a deposit when chilled, while an oil pressed during cold weather would remain transparent at low temperatures, and thus *winter pressed* oils were safer for lubricating purposes and commanded a higher price. Artificial refrigeration now makes it possible to make either grade of oil at any season of the year, although the former seasonal names are still used.

The fixed oils are liable to certain spontaneous changes, which have been investigated by Pelouze and Boudet. It appears from their researches that the oils are accompanied, in the seeds which contain them, with principles which act as a ferment and cause the oils to resolve themselves spontaneously into the several fatty acids which they afford on saponification, and into glycerin. This change takes place in the seeds as soon as the cells containing the oils are broken, so as to permit the contact of the fermenting principle existing in the grain. The decomposition of fats by the action of enzymes has been made a working method capable of technical application, by Connstein, Hoyer and Wartenburg. The enzyme contained in the castor oil bean has been found best adapted for this. An emulsion of fats, water, 10 per cent. of ground castor oil beans and a small amount of free acid are used, when the decomposition proceeds rapidly. As rancidity in fats renders them altogether useless in pharmacy, and as it is not always readily discoverable by the senses in its earlier stages, it becomes desirable to possess a test by which it may be detected. Such a test is to be found, according to Thos. B. Groves, in potassium iodide, which is rapidly decomposed by the new principles developed, and the orange-brown discoloration produced by the liberation of the iodine indicates the existence of rancidity, and the degree of that discoloration, approximately, the extent of the change. The alteration of color is said by Groves to be plainly perceptible when only one-twentieth of rancid fat is present. The presence of water in a fatty oil favors the production of rancidity.

It is also extremely important to be able to protect fats against this change. The complete exclusion of air, light, and moisture—and, when in relation to air this may not be entirely practicable, the destruction by heat of the ferment-germs contained in the air, by which the decomposition is often originated—will go far to effect this object; but it would often be very inconvenient, if not impossible, to carry these measures into complete effect, and hence the discovery of substances which may have the effect of retarding, if not wholly preventing, these fermenting processes, whether by the destruction of the ferment-germs or otherwise, is extremely desirable; this preservative effect has been known and practically used many years, and since the principle upon which they are supposed to act has been discovered the number has been extended. Thus, benzoin rubbed up with fats is well known to preserve them long against rancidity, and *benzoinated lard*, made by extracting ten per cent. of benzoin with melted lard, is one of the official

preparations, and the buds of the poplar (*Populus nigra*) are perhaps still more effectual, as, according to Deschamps, lard impregnated with their virtues will keep good indefinitely. In the French Codex the poplar buds are employed in the *Pommade de Bourgeon de Peuplier,* in which 8 parts of the dried buds are used to 40 parts of the ointment, consisting of lard impregnated with the virtues of several narcotic substances, the fresh narcotic plants being boiled with lard until all their water is evaporated, and the buds afterwards digested in the strained liquid for twenty-four hours. Groves made experiments with many volatile oils and other analogous substances to test their preservative power. (See *A. J. P.,* 1865, 54, 61.) Hirzel says that animal fats may be kept in a good condition for a year by the following plan. Mix 14 pounds of the recently melted fat with 5 drachms of common salt and 15 grains of alum, in fine powder, heat till a scum is formed on the surface, separate the scum, and, when the clear liquid has cooled, wash it many times with water with malaxation, so as to remove all the salt, then evaporate the water at a heat insufficient to injure the fat. (*A. J. P.,* 1868, 334.)

The adulteration of the fixed oils may be effected in several ways—by admixture with the fatty oil of substances distinctly foreign to the fats, and by adding a cheaper or inferior oil to one of greater value. In the former case we may have the addition of paraffin wax, ceresine, mineral oils, neutral tar oils, resin oils, resin, and waxes. Of these, the first three are entirely unsaponifiable, resin oils contain but small quantities of saponifiable substances, waxes are partly saponifiable, and resin almost completely saponifiable. The determination of unsaponifiable matter is therefore of great importance. The common method for this is to saponify the suspected sample with alcoholic potassium hydroxide and then to shake out the unsaponifiable matter with ether or petroleum ether. From this solution, on evaporation, will be obtained the mineral, resin, or tar oils that may have been present. For these there are appropriate tests elsewhere noted. In case a cheaper oil or fat has been added for the purpose of adulterating a more valuable one, we must be guided by the determination of certain constants, such as those mentioned below by Cowley, or by the indication of certain qualitative color tests. The constants referred to are much more to be depended upon in such a case.

R. C. Cowley (*P. J.,* 1897, 331) regards the following as the most important determinations in examining fats and fixed oils. 1. Specific gravity. 2. Melting and solidifying points. 3. Melting and solidifying points of fatty acids. 4. Behavior with solvents. 5. The Hehner value. 6. The Reichert-Meissl value. 7. The saponification value. 8. The iodine value. To these have been added during recent years: 9. The refractive index. 10. The acetyl number. 11. The temperature rise with sulphuric acid (Maumené number).

It is sometimes desirable to deprive the fixed oils of color. The following process for this purpose is recommended by Brunner. The oil is first brought to the state of emulsion by strongly agitating it with water rendered mucilaginous by gum or starch; the emulsion is treated for each part of oil with two parts of wood charcoal, previously well heated and coarsely powdered, the finer particles being sifted out; the pasty mass is then completely dried at a heat not exceeding 100° C. (212° F.), and exhausted by cold ether in a percolator; finally, the ethereal solution, having been allowed to stand, in order that any charcoal present in it may subside, is submitted to distillation, so as to separate the ether, and the oil remains colorless in the retort. (*J. P. C.,* Sept., 1858.) Berlandt recommends the following method: Shake strongly for some minutes 900 parts of the fixed oil with 120 parts of water holding in solution 3 parts of potassium permanganate, allow the mixture to stand for some hours in a warm place, and then filter. The oil becomes colorless. (*J. P. C.,* Oct., 1867.)

The modern method of decolorizing vegetable oils is to filter them through kaolin or Fuller's earth. Preliminary treatment with acids and alkalies is sometimes advisable.

OLEA VOLATILIA. [*Olea Destillata.*]

Volatile Oils.

Olea Ætherea, Ætherolea; Ethereal Oils, Essential Oils, Distilled Oils; Huiles Volatiles, Huiles Essentielles, Huiles Distillées, Essences, *Fr.;* Flüchtige Oele, Aetherische Oele, *G.;* Essenze, *It.;* Esencias, *Sp.*

These are sometimes called *distilled oils,* from the mode in which they are usually procured; sometimes *essential oils,* from the circumstance that they possess, in a concentrated state, the organoleptic properties of taste and odor of the plants from which they are derived. The word *essence* is used in some countries to designate the volatile oils themselves, but in America this word has unfortunately been largely applied to the alcoholic solutions of the volatile oils, usually called the *spirits,* and the word *soluble essence* has been used to describe hydroalcoholic solutions of volatile oils which possess the property of mixing clear with water.

The term *Ætherolea* is used in some countries to distinguish the volatile oils in general from those which are produced by destructive distillation, like oil of amber, oil of cade, oil of tar, etc., which are given the collective name *pyrolea* (pyroligneous oils).

They exist in all odoriferous vegetable tissues, sometimes pervading the plant, sometimes confined to a single part; in some instances contained in distinct cells, and partially retained after desiccation, in others formed upon the surface, as in many flowers, and exhaled as soon as formed. Occasionally two or more are found in different parts of the same plant. Thus, the orange tree produces one oil in its leaves, another in its flowers, and a third in the rind of

its fruit. In a few instances, when existing in distinct cells, they may be obtained by pressure, as from the rind of the lemon and orange; but they are generally procured by steam distillation. (See page 738.) Some volatile oils, as those of bitter almond and mustard, are formed in the presence of moisture out of substances of a different nature pre-existing in the plant, and may be subsequently distilled.

The volatile oils are usually colorless when freshly distilled, or at most yellowish, but some are brown, red, green, or blue. There is reason, however, to believe that in all instances the color depends on foreign matter dissolved in the oils. Septimus Piesse succeeded, by the fractional distillation of certain volatile oils, in separating a blue liquid, which, by repeated rectification, he has obtained quite pure. In this state it has the sp. gr. 0.910, and a fixed boiling point of 302.3° C. (576° F.), and yields a dense blue vapor having peculiar optical properties. He named this principle *azulene,* and believed that upon it depends the blueness of volatile oils wherever existing. The yellowness of the oils he ascribed to the resin resulting from their oxidation, the green and brown colors to a mixture of azulene and resin in various proportions. The formula of azulene he gave as $C_{15}H_{26}O$. (*Chem. News,* Nov. 21, 1863, p. 245.) Gladstone named this blue coloring constituent *cærulein,* and stated that it contains nitrogen and is colored green by acids and alkalies. The volatile oils differ from the fixed oils in not yielding glycerol when treated with alkalies.

The volatile oils have a strong odor, resembling that of the plants from which they were procured, though generally less agreeable. Their taste is hot and pungent, and, when they are diluted, is often gratefully aromatic. The greater number are lighter than water, though some are heavier; their sp. gr. varies from 0.847 to 1.17. They vaporize at ordinary temperatures, diffusing their peculiar odor, and are completely volatilized by heat. When distilled alone, they nearly always undergo partial decomposition. Heated in the open air, they take fire and burn with a bright flame attended with much smoke. Almost all of them are optically active, and advantage may sometimes be taken of this property to detect adulterations of one of these oils with another. The refractive index is another physical constant that is being studied in connection with volatile oils, but the accumulation of data is not yet sufficiently large to give the factor much value as yet. Exposed at ordinary temperatures, some of them absorb oxygen, assume a deeper color, become thicker and less odorous, and are ultimately converted into resin. This change takes place most rapidly under the influence of light. Before the alteration is complete, the remaining portion of oil may be recovered by distillation.

The volatile oils are sometimes hydrocarbons, although with these are frequently associated alcohol- or ketone-like bodies called *camphors,* and products of oxidation known under the general name of resins, and undoubtedly formed from the hydrocarbons. Phenols, aldehydes, esters, ethers, and sulphides are also represented. The hydrocarbons are generally known as *terpenes,* from oil of turpentine, which is taken as a type. *Olea ætherea sine terpeno* is the name proposed by Schweissinger for concentrated volatile oils made so by the removal of the non-fragrant hydrocarbon, and representing from two to thirty volumes of the ordinary essential oils. Thus, one volume of the concentrated oil represents two volumes of the oils of anise, cassia, fennel, gingergrass, mentha crispa, mentha piperita, cloves, sassafras, and star anise; two and one-half volumes of the oils of bergamot, caraway, and lavender; four volumes of cumin and rosemary; five volumes of thyme; six volumes of coriander; eight volumes of calamus; ten volumes of absinthe; twenty volumes of juniper; thirty volumes of angelica, lemon and orange. It is asserted that these concentrated oils are more permanent, more soluble in alcohol and in water, have a finer odor, and are of constant composition, thus enabling the specific gravity and boiling point to be used as tests of purity. They should be kept in the dark. (*Ph. Centralh.,* 1888, No. 25.) Under the name of "*terpeneless volatile oils,*" similar products can now be found in the market; they are undoubtedly superior to the ordinary volatile oils both in odor and strength.

Wallach, to whom much of our knowledge on volatile oils is due, divides the hydrocarbons into classes, as follows:

1.—*True terpenes,* of the formula $C_{10}H_{16}$, of which there are two main groups: (*a*) the *terpane* group, uniting with two molecules of haloid acid or four atoms of bromine; this group includes limonene, dipentene, sylvestrene, terpinolene, terpinene, thujene, and phellandrene, and its members boil between 175° and 185° C. (347° and 365° F.); (*b*) the *camphane* group, uniting with one molecule of haloid acid or two atoms of bromine; this group includes pinene, bornylene, camphene, and fenchene, and its members boil between 151° and 161° C. (303.8° and 321.8° F.).

2.—*Hemiterpenes,* of the formula C_5H_8, such as isoprene.

3.—*Polyterpenes,* such as cedrene, cubebene, etc., of the formula $C_{15}H_{24}$ (sesquiterpenes); colophene, of the formula $C_{20}H_{32}$; and caoutchouc, of the formula $(C_{10}H_{16})_x$.

Hydrocarbons other than those of the terpene class or derivable from them, occur very sparingly in the natural oils. Thus there is of the paraffin series of saturated hydrocarbons, *heptane,* C_7H_{16}, occurring in the oil from the *Pinus sabiniana,* or California *digger pine,* and solid hydrocarbons of the same series in oil of rose, and probably in oils of wintergreen and sweet birch. Of the benzene series there is a single representative in *cymene,* $C_{10}H_{14}$, found in the oils of the *Thymus* and *Monarda* species.

In addition to these naturally occurring hydrocarbons, there is a class of artificially pre-

pared hydrocarbons known as *hydroterpenes*, such as dihydrodipentene from dipentene, menthene and carvomenthene from menthol and carvone.

The terpenes in general are practically insoluble in water, but soluble in alcohol, ether, chloroform, benzene, petroleum benzin, and the fixed and volatile oils.

Many of the essential oils, however, owe their essential character and their value to other constituents than hydrocarbons. We shall briefly notice the most important of these, either describing them or referring to other places in the text where they are already described, and shall then give a classification of the commonly known essential oils based upon the character of the most important compounds present in them.

I. Alcohols.

Geraniol, Linalool, Citronellol, Terpineol, Menthol, Borneol, Nerol, Sabinol, Santalol.

II. Aldehydes.

Citral, Citronellal, Salicyl Aldehyde, Cumic Aldehyde, Benzaldehyde, Cinnamic Aldehyde, Anisic Aldehyde, Piperonal, Santalal.

III. Ketones.

Methyl-amyl-ketone, Ionone, Methyl-nonyl-ketone, Methyl-heptenone, Carvone, Pulegone, Menthone, Camphor, Fenchone, Thujone, Irone.

IV. Esters.

Methyl Salicylate, Methyl Anthranilate, Benzyl Acetate, Linalyl Acetate, Geranyl Acetate, Bornyl Acetate, Menthyl Acetate, Bornyl Valerate, Geranyl Tiglate.

V. Phenols and Phenol Ethers.

Chavicol, Methyl-chavicol, Anethol, Thymol, Carvacrol, Eugenol, Methyl-eugenol, Iso-eugenol, Chavibetol, Safrol, Iso-safrol, Thymohydroquinone dimethyl ether, Asarol, Apiol, Diosphenol.

VI. Neutral Bodies, Oxides, etc.

Cineol (*Eucalyptol*).

VII. Sulphides and Sulphur Compounds.

Diallyl Disulphide, Allyl Isothiocyanate, Dimethyl Sulphide, Butyl Isothiocyanate, Vinyl Sulphide, Acrinyl Isothiocyanate, Phenyl Ethyl Isothiocyanate.

The classification of the volatile oils in any rational and practical manner is a difficult task.

Any system that is devised is either exceedingly complex and cumbersome or, if conciseness is attempted, there are too many inconsistencies and discrepancies. For instance, one of the favored methods of classification is to divide them into four groups, *i.e.*, the terpenes, oxygenated oils, nitrogenated oils, and sulphurated oils. If this be critically studied it is seen that oil of lemon, which is usually given as a typical example of the terpene class, owes its real identity and value to citral, an aldehyde present in only a very small proportion (less than 5 per cent.), and that oil of bitter almond, which is given as the example of the nitrogenated class, owes its classification in this respect only to the incidental presence of hydrocyanic acid, which is frequently removed from the oil, especially when it is used for flavoring purposes. This leaves the sulphurated class, which contains only one important member and the oxygenated class, which is the repository of over 90 per cent. of oils of diversified character.

It is therefore more suitable to follow the foregoing outline adding such explanatory matter and examples as will serve to make it intelligible and valuable for either study or reference purposes.

NOTE.—Although the alcohols only were mentioned in the first group given above it will be found convenient to refer to the more important esters of these alcohols as they are taken up for discussion.

I. Alcohols and Their Esters.—This is an interesting group of open chain, unsaturated alcohols, which, with their esters and aldehydes, play a very important part in the composition of many essential oils. It is the geraniol, linalool and citronellol group.

1.—*Geraniol*, $C_{10}H_{17}OH$, or $\begin{matrix}CH_3\\CH_3\end{matrix}\!>\!C=CH.CH_2.CH_2.C\!<\!\begin{matrix}CH_3\\CH.CH_2OH\end{matrix}$, is a colorless liquid of a pleasant rose geranium odor, boiling at 229° to 230° C. (444.2°–446° F.), under ordinary pressure, and at 129° C. (264.2° F.) under a pressure of 16 mm. Its specific gravity is about 0.881 and its refractive index 1.478. It is optically inactive. By careful oxidation with chromic trioxide it yields its aldehyde, citral, and by heating it in an autoclave with water to 200° C. (392° F.), it is partly converted into its isomer, linalool. It is a monatomic, primary, open chain alcohol, and is the principal constituent of true geranium (pelargonium) oil, as well as of the so-called "*Turkish geranium oil*," or *oil of palmarosa*. It is a constituent of rose oil, of citronella oil and in very small proportions of a number of other oils. Of the esters of geraniol the most important is the *geranyl acetate*. This is a fragrant oil of specific gravity 0.917, boiling at from 128° to 129° C. (262.4°–264.2° F.), under a pressure of 16 mm. It occurs naturally in several essential oils, and can be made artificially by the action of acetic anhydride upon geraniol. Commercial geraniol is also known as *rhodinol*.

2.—*Linalool*, $C_{10}H_{17}OH$, or $\begin{matrix}CH_3\\CH_3\end{matrix}\!>\!C=CH.CH_2.CH_2.C\!<\!\begin{matrix}CH_3\\OH\end{matrix}\!-\!CH=CH_2$, is known in both of the optically active forms as well as

in the inactive. It is a liquid having a pleasant odor, and boils under normal pressure at about 198° C. (388.4° F.), and at from 86° to 87° C. (186.8°–188.6° F.) at 14 mm. pressure. Its specific gravity ranges from 0.868 to 0.877, and its refractive index is 1.463. It is a monatomic, tertiary, open chain alcohol, and is an essential constituent of oil of linaloe, and is found in the free state or as an acetic ester in oils of bergamot, coriander, lavender, neroli, etc. The most important of its esters is *linalyl acetate,* which occurs in many essential oils, as in oil of bergamot. It is an odoriferous liquid of the specific gravity 0.912, and boiling at from 105° to 108° C. (221°–226.4° F.) at 11 mm. pressure. It is so prepared artificially, and the artificial ester is an important commercial article.

3.—*Citronellol,* $C_{10}H_{19}OH$, or $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C\!-\!CH_2.CH_2.CH_2.CH\!<\!\begin{matrix}CH_3\\CH_2.CH_2OH\end{matrix}$, is found in oil of rose and in Spanish geranium oil. It is an odoriferous oil, boiling at from 117° to 118° C. (242.6°–244.4° F.), under a pressure of 17 mm.; specific gravity, 0.8565 at 17.5° C. (63.5° F.); refractive index, 1.457. It is an open chain alcohol closely related to geraniol and is found in oil of rose, oil of geranium, etc. When obtained from oil of rose it is lævogyrate, while when obtained by reducing the aldehyde it is dextrogyrate; in most geranium oils both varieties exist.

A second group comprises the mono-cyclic alcohols, terpineol, which is unsaturated, and menthol, a saturated compound.

4.—*Terpineol,* $C_{10}H_{17}OH$, $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH\!-\!COH.CH_2.CH_2.CH_2.CH.C\!-\!CH_3$, occurs in liquid and solid modifications, inactive, as well as in the two optically active, varieties. Besides occurring naturally it is made artificially by the dehydration of terpin hydrate, and is largely used in the perfume industry because of its lilac odor. It has a sp. gr. of 0.940 at 15° C. (59.2° F.). Its most important ester is the acetate, which occurs in cajuput and cardamom oils.

5.—*Menthol, menthyl alcohol,* $C_{10}H_{19}OH$, $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!CH\!-\!CH.CH_2.CHOH.CH_2.CH_2CH\!-\!CH_3$, is now official, and will be found described on page 695. Two of its esters are recognized as occurring with it in peppermint oil, menthyl acetate and menthyl iso-valerate. Of these the former is the more important. It is an oil having a penetrating odor, boiling at 224° C. (435.2° F.).

To a third group of compounds known as dicyclic, belongs:

6.—*Borneol,* $C_{10}H_{17}OH$, or $CH.CH_2.CH_2.CH_2.CH_3.C.CH_3.CH_2.CHOH.C\!-\!CH_3$.—This compound occurs naturally in both optically active modifications. It also occurs optically inactive. It forms crystalline masses, which, when quite pure, melt at 203° C. (397.4° F.). Borneol can be prepared artificially by reducing its ketone (camphor) with metallic sodium. In this case, however, there results a mixture of borneol and iso-borneol. Borneol forms a number of esters, of which *bornyl acetate* is the most important. This compound melts at 29° C. (84.2° F.), and has a specific gravity of 0.991 at 15° C. (59° F.). It is the characteristic constituent of the pine needle oils.

Nerol is an alcohol discovered in oil of neroli. It is a stereo-isomer of geraniol. Santalol, so called, is found as an alcoholic constituent of oil of sandalwood. It has been given the formula $C_{15}H_{25}OH$, but is probably a mixture of several isomeric or closely related alcohols. Sabinol, $C_{10}H_{15}OH$, is a constituent of oil of savin.

Fenchyl alcohol, thujyl alcohol, and pulegol, all having the same empiric formula as geraniol, $C_{10}H_{17}OH$, do not occur naturally, but are produced from the respective ketones.

II. Aldehydes.—Of the alcohols just enumerated, only the first group are primary alcohols, and will yield aldehydes. Thus, from geraniol, there is obtained by oxidation, citral, the corresponding aldehyde, and from its isomer, linalool, the same.

1.—*Citral,* $C_9H_{15}COH$, or $(CH_3)_2C.CH.CH_2.CH_2.C(CH_3)CH.COH$.—Although at one time called *geranial,* this compound is now universally known as citral, which indicates its importance in the oils of the *citrus* family. It is obtained most abundantly from lemon grass oil by the aid of the bisulphite process. It is an oily liquid, boiling at from 228° to 230° C. (442.4°–446° F.), under ordinary pressure, and at 110° C. (230° F.), under 12 mm. Its specific gravity is about 0.89 and its refractive index 1.49. It is optically inactive. Under the influence of alkalies, citral condenses with acetone with the elimination of water to form pseudo-ionone, $C_{13}H_{20}O$, which is converted into its isomer ionone by means of acids. Reduction with sodium produces the alcohol geraniol.

2.—*Citronellal,* $C_9H_{17}OH$, or $C(CH_3)_2CH.CH_2CH_2CH(CH_3)CH_2COH$, the aldehyde of citronellol, occurs in several essential oils, as in citronella oil. It is an oily liquid of characteristic odor; specific gravity 0.8768, refractive index 1.4481. It is dextrogyrate.

Of the class of aromatic aldehydes, there are found in essential oils, salicyl aldehyde, cumic aldehyde, benzaldehyde, and cinnamic aldehyde.

3.—*Salicyl Aldehyde,* $C_6H_4(OH)COH$.—This body is an oily liquid of aromatic odor, boiling at 196° C. (384.8° F.), and having a specific gravity of 1.172. It occurs in the oils of the several varieties of *Spiræa.* It can also be formed by the oxidation of its alcohol saligenin, or by the action of chloroform and potassium hydroxide on phenol.

4.—*Cumic Aldehyde,* $C_6H_4(C_3H_7)COH$.—This is p-isopropyl-benzaldehyde, and is found in several essential oils, as in cumin oil. It is an aromatic oil, having a specific gravity of 0.973, and boiling at 235° C. (455° F.).

5.—*Benzaldehyde,* $C_6H_5.COH$.—This is now official. (See page 223.)

6.—*Cinnamic Aldehyde,* $C_6H_5.CH:CH.COH$. —This was official in the U. S. P. VIII.

Anisic Aldehyde, $C_6H_4(OCH_3)COH$ (oxymethyl-benzaldehyde), is a synthetic product used in artificial hawthorn perfume.

Piperonal or *Heliotropin,* $C_6H_3O_2CH_2COH$, is a synthetic product used in heliotrope perfume.

Santalal, $C_{14}H_{23}COH$, is found in sandalwood oil.

III. Ketones.—This class of chemical compounds is largely represented in essential oils. Of aliphatic saturated ketones there is only one fairly important representative.

1.—*Methyl-nonyl-ketone,* $CH_3.CO.C_9H_{19}$, which is found in oil of rue, is a liquid of strong odor, boiling at 225° C. (437° F.), and specific gravity 0.8295 at 17° C. (62.6° F.). It solidifies when cooled, and melts at 13° C. (55.4° F.).

Of aliphatic unsaturated ketones there is also one occurring naturally.

2.—*Methyl-heptenone,* $CH_3.CO.C_6H_{11}$, is found in lemon grass oil and other oils, and results from the oxidation of citral or the distillation of cineolic anhydride. It has a specific gravity of 0.853 at 20° C. (68° F.) and boils at 174° C. (345.2° F.).

A *methyl-amyl-ketone,* $C_5H_{11}COCH_3$, boiling at 151° C. (303.8° F.) and having a specific gravity of 0.837 at 50° C. (122° F.), is found as a minor constituent in oil of cloves.

The most commonly occurring ketones, however, belong to the cyclic compounds:

3.—*Carvone,* $C_{10}H_{14}O$, $CH_3C\begin{matrix}\diagup\!\!\diagup CH—CH_2\\ CO—CH_2\end{matrix}\rangle CH—C\begin{matrix}\diagup CH_3\\ \diagdown CH_2\end{matrix}$. —This compound, found in oils of caraway fennel and dill, is a colorless oil boiling at 225° C. (437° F.) and having a sp. gr. of 0.960 at 18° C. (64.4° F.). It is optically active, occurring in both forms. Its most interesting addition compound is that with hydrogen sulphide; this is obtained in crystals, decomposing with alcoholic potassium hydroxide and liberating pure carvone. When heated with glacial phosphoric acid, it is changed into the isomeric carvacrol, a phenol compound.

4.—*Pulegone,* $C_{10}H_{16}O$, $CH_3CH\begin{matrix}\diagup CH_2—CO\\ \diagdown CH_2—CH_2\end{matrix}\rangle C{=}C\begin{matrix}\diagup CH_3\\ \diagdown CH_3\end{matrix}$.—This characteristic ketone of pennyroyal oil is a liquid boiling at 221° C. (429.8° F.), and having a specific gravity of 0.9323 at 20° C. (68° F.). An isomeric body, iso-pulegone, has been obtained artificially.

5.—*Menthone,* $C_{10}H_{18}O$, $CHCH\begin{matrix}\diagup CH_2—CH_2\\ \diagdown CH_2—CO\end{matrix}\rangle CHCH(CH_3)_2$.—This occurs along with the corresponding secondary alcohol menthol, in oil of peppermint. It is an oily liquid boiling at 206° C. (402.8° F.), with a specific gravity of 0.897 at 15° C. (59° F.). By the action of oxidizing agents it can be converted into thymol, $C_{10}H_{14}O$.

To the class of dicyclic ketones belong the following isomeric bodies:

6.—*Camphor,* $C_{10}H_{16}O$, $C_8H_{14}\begin{matrix}\diagup CH_2\\ \diagdown CO\end{matrix}$.—This most important compound of the ketone class is official, and is described on page 270.

7.—*Fenchone,* $C_{10}H_{16}O$, $\begin{matrix}CH_2—CH_2—\!\!-CCH_3\\ \quad\quad\quad\quad\quad\quad\diagup\\ \quad\quad\quad C(CH_3)_2\\ \quad\quad\quad\quad\quad\quad|\\ CH_2—CH—\!\!-CO\end{matrix}$.— This ketone occurs as dextro-fenchone in oil of fennel, and as lævo-fenchone in oil of thuja. When purified, it forms an oil of camphoraceous odor, boiling at 193° C. (379.4° F.), and having a specific gravity of 0.9465 at 19° C. (66.2° F.).

8.—*Thujone,* $C_{10}H_{16}O$, $CH_3—CH\begin{matrix}\diagup CO—CH_2\rangle\\ \diagdown CH—CH_2\end{matrix}C—CH\begin{matrix}\diagup CH_3\\ \diagdown CH_3\end{matrix}$.—This ketone is found in oils of thuja, tansy, wormwood and sage, and is identical with the bodies formerly known as *tanacetone* and *salvone.* It is an optically active liquid, boiling at from 200° to 203° C. (392°–397.4° F.) and having a specific gravity of 0.9126 at 20° C. (68° F.).

A more complex ketone yet to be noted is:

9.—*Irone,* $C_{13}H_{20}O$, $(CH_3)_2C\begin{matrix}\diagup CH(CH:CH.\\ \diagdown CH:CH—\end{matrix}CO.CH_3)CH.CH_3\rangle CH_2$.—The characteristic constituent of orris oil, to which also the violet odor is due, is irone. It is an oil almost insoluble in water, but readily soluble in alcohol, boiling at 144° C. (291.2° F.) at 16 mm., and having a specific gravity of 0.939 at 20° C. (68° F.). In the attempt to effect the synthesis of irone, Tiemann and Krüger obtained an isomeric body, *ionone,* from citral, which is now used as the artificial violet odor.

IV. Acids and Their Esters.—While esters of several of the fatty acids, both saturated and unsaturated, are found in the essential oils, the compounds are not so distinctive or characteristic, that they require mention here. Some of the esters have been already described under the appropriate alcohols, see geraniol, linalool, etc. Of esters of aromatic acids there are several of importance, however, comprising the most valuable constituents of the oil in which they occur.

1.—*Methyl Salicylate* is the chief constituent of the oils of wintergreen and sweet birch. As it is now official as a pure compound, it is described on page 696.

2.—*Methyl Anthranilate* (*o-amidobenzoate*), $C_6H_4(NH_2)COOCH_3$.—This is the odoriferous constituent of neroli oil. It is an oil solidifying at low temperatures in crystals melting at 24.5° C. (76.1° F.), and boiling at 127° C. (260.6° F.) at 11 mm. Its specific gravity is 1.163 at 26° C. (78.8° F.). It is strongly fluorescent and has a powerful neroli odor.

V. Phenols and Phenol Ethers.—This is an important class, largely represented in the volatile oils. Of monatomic phenols there are:

1.—*Chavicol* (para allyl-phenol), $C_6H_4(OH)C_3H_5$.—This occurs in the *oil of Chavica Betle*, and is a colorless liquid having a strong odor and a specific gravity of 1.035 at 20° C. (68° F.), boiling at 237° C. (458.6° F.). Still more abundantly formed in nature is its methyl ether, which is:

2.—*Methyl-chavicol*, $C_6H_4(OCH_3)C_3H_5$.—This occurs in the oils of anise, star anise, sweet-basil, bay, etc. It is a colorless liquid of an anise-like odor, boiling at from 215° to 216° C. (419°–420.8° F.), and having a specific gravity of 0.979 at 12° C. (53.6° F.).

3.—*Anethol*, $C_6H_4(OCH_3)C_3H_5$, is the methyl ether of p-propenyl-phenol, and is therefore isomeric with methyl-chavicol. It can be formed from the latter by heating it with alcoholic potassium hydroxide. It is the most abundant constituent of the oils of anise, star anise and fennel. It forms white scales having a specific gravity of 0.986 at 25° C. (77° F.), melting at 21° C. (69.8° F.), and boiling at 232° C. (449.6° F.).

4.—*Thymol* (methyl-propyl-phenol), $C_6H_3.CH_3(OH)C_3H_7$ 1 : 3 : 4.—This is one of the best known of the phenols occurring in volatile oils. As it is official its description will be found under *Thymol*.

5.—*Carvacrol* (methyl-propyl-phenol), $C_6H_3.CH_3(OH)C_3H_7$ 1 : 2 : 4.—This important phenol, occurring in oils of marjoram and savory, is isomeric with thymol. It is a thick oil, solidifying at 0° C. (32° F.) and boiling at 236° C. (456.8° F.). It can be prepared artificially by heating carvone, an isomeric ketone, with phosphoric acid or by heating camphor with iodine.

Of diatomic phenols and their ethers, there are the following:

6.—*Eugenol*, $C_6H_3.OH.OCH_3.C_3H_5$ 4 : 3 : 1, is the methyl ether of allyl-dioxybenzene. It occurs in the oils of cloves, allspice, bay, Ceylon cinnamon and cinnamon leaves. As it is now official, its description will be found on page 432.

7.—*Methyl-eugenol*, $C_6H_3.(OCH_3)_2.C_3H_5$, is found together with eugenol in oil of bay. It has a specific gravity of 1.041 at 11° C. (51.8° F.) and boils at 248° C. (478.4° F.).

8.—*Iso-eugenol* is the methyl ether of propenyl-dioxybenzene, and is produced from eugenol when the latter is heated with alcoholic potassium hydroxide. It is used in the manufacture of artificial vanillin.

9.—*Chavibetol*, $C_6H_3(OCH_3)OH$, is another isomer of eugenol, and occurs with chavicol in oil of betel leaves.

10.—*Safrol*, $C_6H_3\begin{matrix}O\\O\end{matrix}\!\!>CH_2.C_3H_5$, is the methylene ether of allyl-dioxybenzene. It is found quite largely in the oils of sassafras, camphor, etc. It was official in the U. S. P. VIII.

11.—*Iso-safrol* is the methylene ether of propenyl-dioxybenzene, and is produced from safrol by heating the latter with alcoholic potassium hydroxide. It is used in the manufacture of *piperonal* (artificial heliotropin).

12.—*Thymohydroquinone dimethyl-ether*, $C_6H_2.(OCH_3)_2.CH_3.C_3H_7$, constitutes the bulk of the oil of arnica root. It is a liquid distilling at from 248° to 250° C. (478.4°–482° F.).

Of triatomic phenols and their ethers, the representative is:

13.—*Asarol*, $C_6H_2(C_3H_5)(OCH_3)_3$.—This is the trimethyl ether of propenyl-trioxybenzene. It forms the solid constituent of the oil of *Asarum europæum*, and occurs in prisms melting at 61° C. (141.8° F.), and boiling at from 295° to 296° C. (563°–564.8° F.). It has also been made synthetically.

Of tetratomic phenols and their ethers, there is also a representative, as follows:

14.—*Apiol*, $C_{12}H_{14}O_4$, $C_6H_6(OCH_3)_2O_2.CH_2$, is the dimethyl-methylene ether of allyl-tetroxybenzene. It occurs in two isomers—the apiol from oil of parsley and dill apiol from some varieties of oil of dill. Of these, the former is a crystalline solid melting at 30° C. (86° F.) and boiling at 294° C. (561.2° F.) and the latter is an oily liquid boiling at 288° C. (550.4° F.).

VI. Neutral Bodies, Oxides, etc.—One important compound of frequent occurrence in volatile oils has not been classified under any of the preceding groups, for the reason that it is relatively inert in a chemical way and is considered as an oxide of neither distinct acid or basic character.

1.—*Cineol* (*Eucalyptol*), $C_{10}H_{18}O$.—This is found in nature in large amounts in eucalyptus oil (hence the name "eucalyptol" sometimes given to it), in cajuput oil (hence the name of "cajuputol"), in lavender, wormseed, and other oils. As it is now official under the name of *eucalyptol*, its description will be found on page 429.

VII. Sulphides and Sulphur Compounds.

1.—*Di-allyl-disulphide*, $C_6H_{10}S_2$, is a constituent of oil of garlic and occurs in many oils belonging to the *Cruciferæ*. It is a liquid of very unpleasant odor, boiling at 140° C. (284° F.)

2.—*Allyl-isothiocyanate*, $C_3H_5.NCS$, is the principal constituent of the volatile oil of mustard. It is, however, a decomposition product of the glucoside potassium myronate, which breaks up under the influence of the ferment myrosin. The allyl thiocyanate can also be obtained artificially by distilling allyl iodide or bromide with alcoholic potassium thiocyanate. This artificial product is largely sold in place of the natural oil. It is a liquid having a very unpleasant odor, boiling at 151° C. (303.8° F.), and having a specific gravity of 1.017 at 10° C. (50° F.).

Vinyl sulphide, $(C_2H_3)_2S$, is found in a variety of garlic.

Butyl isothiocyanate, $CH(CH_3)C_3H_5NCS$, is found in oil of horseradish, *acrynyl isothiocyanate*, C_7H_7ONCS, is found in white mustard

and *phenylethyl isothiocyanate,* $C_2H_4(C_6H_5)NCS$, is found in oil of mignonette.

CLASSIFICATION.

Classification of the more commonly occurring volatile oils.—In considering the question of classifying the volatile oils, two methods of arrangement naturally suggest themselves, viz.: a classification according to the botanical natural orders to which they belong, and a chemical classification based on the most important chemical constituents of the oils themselves. While the first of these is the more readily made, it suffers from the disadvantage of being cumbrous and less readily understood except by the botanist. On the other hand, the second plan shows at a glance the sources of the valuable odoriferous and medicinally and technically important constituents for which the volatile oils are largely used. That it has not been generally adopted is no doubt due to the fact that many of the oils contain several different constituents of value, and it is therefore difficult to make an assignment of some of them to individual chemical groups. Nevertheless, it is believed that the chemical classification adopted here will be found to have practical value for reference.

Group I.—*Oils containing mainly Terpenes and Sesquiterpenes.*

Oil of Cedarwood; cedrene and cedrol (an oxygenated constituent).
Copaiba Balsam; caryophyllene.
Cubeb; cadinene and cubeb camphor (an oxygenated constituent).
Dog Fennel; phellandrene.
Fleabane; d-limonene.
Galbanum; pinene and cadinene.
Ginger; sesquiterpene and phellandrene.
Hemp; cannibene and other terpenes.
Hops; humulene and tetrahydrocymene.
Myristica; terpenes and myristicol (an oxygenated constituent).
Orange; limonene with small amount of citral and citronellal (both oxygenated constituents).
Turpentine; pinene and sylvestrene.

Group II.—*Oils containing mainly Alcohols and their esters.*

a. Aliphatic saturated alcohols:
Oil of Heracleum; octyl alcohol and octyl ester.

b. Aliphatic unsaturated alcohols:
Oil of Bergamot; linalool and linalyl acetate.
Coriander; linalool and d-pinene.
Geranium; geraniol and geranyl esters.
Lavender; linalyl acetate and geraniol.

Group II.—(*Continued.*)

Lime; linalyl acetate and limonene.
Linaloes; linalool and geraniol.
Petit Grain; linalool and linalyl acetate.
Rose; geraniol and citronellol with esters.

c. Monocyclic and dicyclic alcohols.
Oil of Angostura; galipol, galipene, and cadinene.
Fir Cones; bornyl acetate and terpenes.
Golden Rod; borneol and bornyl esters.
Juniper Berries; juniper camphor and cadinene.
Ledum; ledum camphor.
Lovage; terpineol.
Mace; myristicol.
Patchouli; patchouli camphor and cadinene.
Peppermint; menthol and menthone.
Pine Needles; bornyl acetate and terpenes.
Rosemary; borneol and bornyl acetate.
Sandalwood; santalol and esters.
Savin; sabinol and sabinyl acetate.
Valerian; borneol and bornyl esters.

d. Aromatic Alcohols and Esters:
Oil of Jasmine; benzyl acetate and benzyl alcohol.

Group III.—*Oils containing Aldehydes as characteristic constituents.*

a. Aliphatic unsaturated aldehydes:
Oil of Citron peel; citral and limonene.
Citronella; citronellal and geraniol.
Lemon; Citral and citronellal (this oil might also properly be classed in Group I, as the terpenes constitute over 90 per cent. of the oils).
Lemon grass; citral, citronellal, and methyl-heptenone.
Verbena; citral.

b. Aromatic aldehydes:
Oil of Bitter Almond; benzaldehyde.
Cassia; cinnamic aldehyde.
Cinnamon; cinnamic aldehyde and eugenol.
Cumin; cumic aldehyde.
Meadow Sweet; salicyl aldehyde.

Group IV.—*Oils containing Ketones as characteristic constituents.*

a. Aliphatic saturated aldehydes:
Oil of Rue; methyl-nonyl-ketone.

b. Aliphatic unsaturated aldehydes:
Oil of Lemon grass; methyl-heptenone.

Group IV.—(*Continued.*)

c. Monocyclic and dicyclic ketones:

Oil of Artemisia; thujone.
Camphor; camphor.
Caraway; carvone and limonene.
Dill; carvone and limonene.
Orris; irone.
Pennyroyal; pulegone.
Peppermint; menthone and menthol.
Sage; thujone with borneol and cineol.
Spearmint; carvone.
Tansy; thujone with borneol.
Thuja; thujone and fenchone.
Wormwood; thujone and thujyl alcohol.

Group V.—*Oils containing Esters.*

a. Aliphatic Acids:

Oil of Angelica; methyl-ethyl-acetic esters.
Calamus; heptylic and palmitic acid and esters.
Cardamom; acetic esters and cineol.
German Chamomile; caproic acid esters.
Roman Chamomile; butyric, angelic and tiglic esters.

b. Aromatic acid esters:

Oil of Neroli; o-amido-benzoic-methyl ester.
Sweet Birch; methyl salicylate.
Gaultheria; methyl salicylate.

c. Undetermined acids:

Oil of Celery; sedanolide and lactone.
Elecampane; alantic acid and lactone.

Group VI.—*Oils containing Phenols and Phenol Ethers.*

a. Monatomic phenols and their ethers:

Oil of Ajowan; thymol and cymene.
Anise; anethol and methyl-chavicol.
Betel; chavicol and methoxy-chavicol.
Fennel; anethol and fenchone.
Marjoram; carvacrol and linalool.
Savory; carvacrol, pinene, and cymene.
Star Anise; anethol, methyl-chavicol and safrol.
Sweet Basil; Methyl-chavicol and d-linalool.

b. Diatomic phenols and their ethers:

Oil of Arnica Root; thymohydroquinone dimethyl-ether.
Bay; eugenol, methyl-eugenol and methyl-chavicol.
Camphor; safrol, eugenol and camphor.
Cascarilla Bark; eugenol and terpenes.

Group VI.—(*Continued.*)

Cinnamon Leaf; eugenol and cinnamic aldehyde.
Cloves; eugenol and sesquiterpene.
Pimenta; eugenol and sesquiterpene.
Sassafras; safrol and camphor.

c. Triatomic phenols and their ethers:

Oil of Asarum; asarol and methyl-eugenol.
Matico; asarol.

d. Tetratomic phenols and their ethers:

Oil of Parsley; apiol.

Group VII.—*Oils containing Neutral Bodies.*

Oil of Cajuput; cineol, terpineol and terpenyl acetate.
Eucalyptus; cineol, pinene, and aldehydes.
Laurel Leaves; cineol and pinene.
Myrtle; cineol, d-pinene and dipentene.
Wormseed; cineol and dipentene.

Group VIII.—*Oils containing Sulphur.*

Oil of Asafœtida; sulphides and pinene.
Garlic; diallyl-disulphide and allylpropyl sulphide.
Mustard; allyl-thiocyanate, allyl-cyanide and carbon disulphide.
Onion; allyl-propyl sulphide.

Properties.—Volatile oils are slightly soluble in water. Agitated with this fluid they render it milky, but the major portion separates upon standing, leaving the water impregnated with their odor and taste. This impregnation is more complete when water is distilled with the oils, or from the plants containing them. Trituration with insoluble powders, as tale, magnesium carbonate, kieselguhr, etc., renders them much more soluble, probably in consequence of their minute division. The intervention of sugar also greatly increases their solubility, and affords a convenient method of preparing them for internal use. The hydrocarbon oils are scarcely soluble in diluted alcohol, and, according to De Saussure, the solubility of volatile oils generally in this liquid is proportionate to the oxygen which they contain. The volatile oils dissolve sulphur and phosphorus with the aid of heat, and deposit them on cooling. By long boiling with sulphur they form brown, unctuous, fetid substances, formerly called *balsams of sulphur.* They absorb chlorine, which converts them into resinous oxidation products and then combines with these. Iodine produces a similar effect. They are decomposed by the strong mineral acids, and unite with some organic acids. When treated with a caustic alkali, some of them are saponified or otherwise decomposed. Several of the metallic oxides, and various salts which easily part with oxygen, convert them into resinous oxidation products. The volatile oils dissolve many of the proximate

principles of plant and animal tissues, such as the fixed oils and fats, resins, camphor, and many of the alkaloids when in the free state. Exposed to air and light, many of them absorb oxygen and become what are termed ozonized oils which possess oxidizing properties.

Adulterations.—The volatile oils are often sophisticated. Among the greater adulterations are fixed oils, resinous substances, chloroform, hydrocarbon oils, and alcohol, but the most dangerous are those made by mixing the pure oil with the cheaper volatile oils and terpenes and fractions from other oils like limonene. The presence of the fixed oils may be known by the permanent greasy stain which they leave on paper, while that occasioned by a pure volatile oil disappears entirely when exposed to heat. They may also in general be detected by their comparative insolubility in alcohol. Both the fixed oils and resins are left behind when the adulterated oil is distilled with water. If alcohol be present, the oil will become milky when agitated with water in a graduated tube, and after the separation of the liquids the water will occupy more space and the oil less than before. The following method of detecting alcohol was proposed by Beral. Put twelve drops of the suspected oil in a perfectly dry watch-glass, and add a piece of potassium about as large as the head of a pin. If the potassium remains for twelve or fifteen minutes in the midst of the liquid, there is either no alcohol present, or less than 4 per cent. If it disappears in five minutes, the oil contains more than 4 per cent. of alcohol; if in less than a minute, 25 per cent. or more. Borsarelli employs calcium chloride for the same purpose. This he introduces in small pieces, well dried and perfectly free from powder, into a small cylindrical tube, closed at one end, and about two-thirds filled with the oil to be examined, and heats the tube to 100° C. (212° F.), occasionally shaking it. If there is considerable proportion of alcohol, the chloride will be entirely dissolved, forming a solution which sinks to the bottom of the tube; if only a very small quantity, the pieces will lose their form, and collect at the bottom in a white adhering mass; if none at all, they will remain unchanged. (*J. P. C.*, xxvi, 429.) J. J. Bernoulli proposes as a test dry potassium acetate, which remains unaffected in a pure oil, but will be dissolved if alcohol be present, and form a distinct liquid. (See *A. J. P.*, xxv, 82.) Distillation, catching the first portion, and testing for alcohol by the iodoform reaction, will detect very small additions of alcohol. The most dangerous adulterant of volatile oils is a liquid sold under some "fancy name," found in the markets of London and other large cities, and recommended for "reducing" essential oils; one specimen examined by John Barclay (*P. J.*, 1896, 463) had a delicate odor, and could be mixed with oils of lemon and bergamot without being detected by odor or taste. It was believed to be a *lævo-pinene*. There are good reasons for believing that similar liquids are used to an enormous extent.

Sometimes volatile oils of little value are mixed with the more costly. The taste and odor afford in this case the best means of detecting the fraud. The specific gravity of the oils may also serve as a test of purity. When two oils, of which one is lighter and the other heavier than water, are mixed, they may be separated by long agitation with this fluid, and will take a place corresponding to their respective specific gravities, but it sometimes happens that an unadulterated oil may thus be separated into two portions. The difference of apparent effect produced by iodine with the several oils has been proposed as a test, and bromine was employed for the same purpose by John M. Maisch, who used both these tests preferably in the state of ethereal solution, which, as it is liable to spontaneous change by keeping, should be prepared when wanted for use. According to Liebig, when iodine is made to act on a volatile oil, a portion of it combines with the hydrogen of the oil, forming hydriodic acid, while another portion takes the place of the lost hydrogen. Oil of turpentine may be detected by remaining in part undissolved when the suspected oil is treated with three or four times its volume of alcohol of the sp. gr. 0.84; or, according to Mero, by causing the suspected oil, when agitated with an equal measure of poppy oil, to remain transparent, instead of becoming milky, as it would do if pure. The latter test will not apply to the oil of rosemary. (*J. P. C.*, 3e sér., vii, 303.) G. S. Heppe suggests a very delicate test of oil of turpentine and most other non-oxygenated oils, when used to adulterate one of the oils containing oxygen. A piece of copper nitroprusside, of the size of a pin's head, is put into a little of the suspected oil in a test-tube, and heated until the liquid begins to boil. The boiling must be continued only a few seconds. If the oil be pure and oxygenated, the copper nitroprusside will become black, brown, or gray; if oil of turpentine or other non-oxygenated oil be present, the deposit will be green or bluish-green, and the supernatant liquid colorless or yellowish.

The different relations of the volatile oils to polarized light may, to a certain extent, be made available for the detection of adulterations, especially where the action of the adulterating oil is in an opposite direction to that of the oil adulterated. Thus, the oils of juniper, lavender, and rosemary, rotate the plane of polarization to the left, while American oil of turpentine rotates it to the right; and if this should be added to one of the other oils it might in some degree neutralize their action, and thus offer one means for its detection. Unfortunately, the French oil of turpentine, from the juice of the *Pinus maritima*, acts strongly in the opposite direction. But the very strength of its left-rotatory power might lead to its detection by the abnormal increase

of this power which it would impart to the oils in question. Synthetic or artificial volatile oils are now largely manufactured. They vary greatly at times in their resemblance to the natural products. They will be considered under their respective titles elsewhere, a number having received official recognition.

Volatile oils may be preserved without change in small, well-stoppered amber-colored bottles, entirely filled with the oil, and secluded from the light.

They may also be preserved by mixing with them about 5 per cent. of a bland fixed oil which will remain undissolved when the volatile oil is added to alcohol and for which allowance must be made, of course, in the volume of the oil used in formulas, etc. (LaWall, *Proc. A. Ph. A.*, 1910, 1121.)

Manufacture.—Most of the volatile oils may be prepared by the general formula of the U. S. P. 1870: "Put the substance from which the Oil is to be extracted into a retort or other vessel suited for distillation, and add enough water to cover it; then distil by a regulated heat into a large refrigeratory. Separate the Distilled Oil from the water which comes over with it."

A large proportion of the volatile oils of European commerce is produced in Grasse, a town of France, twenty-five miles west of Nice. For an elaborate article on this industry and methods of preparation, see *A. Pharm.*, xxii, 473, abstracted in the *P. J.*, vol. xv, 468. Schimmel & Co., Miltitz, Germany, are large producers of volatile oils.

Under the general observations on the *Aquæ*, or *Waters*, will be found remarks upon the use of steam in preparing the Distilled Waters, which are to a considerable extent applicable also to the volatile oils.

The substances from which the volatile oils are extracted may be employed in either the recent or the dried state. Certain flowers, however, such as orange flowers and roses, must be used fresh, or preserved with salt or by means of glycerin, as they afford little or no oil after desiccation. Most of the aromatic herbs, also, as peppermint, spearmint, pennyroyal, and marjoram, are usually distilled while fresh, although it is thought by some that when moderately dried they yield a larger and more grateful product. Dried substances, before being submitted to distillation, require to be macerated in water until they are thoroughly penetrated by this fluid, and to facilitate the action of the water it is necessary that, when of a hard or tough consistence, they should be properly comminuted by slicing, shaving, rasping, bruising or other similar mechanical operation.

The water which is introduced into the still with the substance answers the double purpose of preventing the decomposition of the vegetable matter by regulating the temperature, and of facilitating the volatilization of the oil, which, although in most instances readily rising with the vapor of boiling water, requires, when distilled alone, a considerably higher temperature, and is at the same time liable to be partially decomposed. Some oils, however, will not ascend readily with steam at 100° C. (212° F.), and in the distillation of these it is customary to use water saturated with common salt, which does not boil under 110° C. (230° F.). Recourse may also be had to a bath of strong solution of calcium chloride, or to an oil bath. Other oils, again, may be volatilized with water at a temperature below the boiling point, and, as heat exercises an injurious influence over the oils, it is desirable that the distillation should be effected at as low a temperature as possible. To prevent injury from heat, it has been recommended to suspend the substance containing the oil in a wire basket, or to place it upon a perforated shelf, in the upper part of the still, so that it may be penetrated by the steam, without being in direct contact with the water. Another mode of effecting the same object is to distil it *in vacuo*. Duncan stated that the most elegant volatile oils he had even seen were prepared in this manner by Barry, the inventor of the process. The employment of steam heat also prevents injury, and the best volatile oils are now prepared by manufacturers in this way. Steam can be very conveniently applied to this purpose by causing it to pass through a coil of tube, of an inch or three-quarters of an inch bore, placed in the bottom of a common still. The end at which the steam is admitted enters the still at the upper part, and the other end, at which the steam and condensed water escape, passes out laterally below, being furnished with a stop-cock, by which the pressure of the steam may be regulated and the water drawn off when necessary. In some instances it is desirable to conduct the steam immediately into the still near the bottom, by which the contents are kept in a state of brisk ebullition. This method is used in the preparation of the oil of bitter almond. The same method is applicable to the preparation of distilled waters.

The quantity of water added is not a matter of indifference. An excess above what is necessary acts injuriously by holding the oil in solution when the mixed vapors are condensed, and if the proportion be very large, it is possible that no oil whatever may be obtained separate. On the contrary, if the quantity be too small, the whole of the oil will not be distilled, and there will be danger of the substance in the still adhering to the sides of the vessel and thus become burnt. (See page 180.) Enough water should always be added to cover the solid material and prevent the latter accident. Dried plants require more water than the fresh and succulent. The whole amount of material in the still should not exceed three-fourths of its capacity, as otherwise there would be danger of the liquid boiling over. The form of the still has an influence over the quantity of water distilled, which de-

pends more upon the extent of surface than upon the amount of liquid submitted to evaporation. By employing a high and rather narrow vessel one may obviate the disadvantage of an excessive quantity of water. Sometimes the proportion of oil in the substance employed is so small that it is wholly dissolved in the water distilled, even though the proportion of the liquid in the still is not greater than is absolutely essential. In this case it is necessary to redistil the same water several times from fresh portions of the plant, until the quantity of oil exceeds the solvent power of the water. This process is called *cohobation.*

The more volatile of the oils pass with facility along with the steam into the neck of the common still, but some which are less volatile are apt to condense in the head and thus return into the still. For the distillation of the latter, a copper still should be employed having a very low head. As, after the distillation of any one oil, it is necessary that the apparatus should be thoroughly cleansed before being used for the preparation of another, it is better that the condensing tubes should be straight, rather than spiral as in the ordinary still. It should be recollected, moreover, that certain oils, such as those of anise and fennel, are rendered solid by a comparatively slight reduction of temperature, and that in the distillation of these the water employed for refrigeration should not be below 5.5° C. (42° F.).

The mixed vapors are condensed into a milky liquid, which is collected in a receiver, and, after standing for some time, separates into the oil and a clear solution of it, the former floating on the surface, or sinking to the bottom, according as it is lighter or heavier than water. The distillation should be continued so long as the liquid coming over has a milky appearance.

The last step in the process is to separate the oil from the water. For this purpose the *Florentine receiver* may be used. For illustrations of this, and other forms of receivers, for collecting and separating immiscible liquids, see Remington's *Practice of Pharmacy,* 6th edition, p. 250. This is a conical glass vessel, broad at the bottom and narrow towards the top, and very near its base furnished with a tubulure or opening, to which is adapted, by means of a pierced cork, a bent tube so shaped as to rise perpendicularly to seven-eighths of the height of the receiver, then to pass off from it at right angles, and near the end to bend downward. The condensed liquid being admitted through the opening at the top of the receiver, the oil separates, and, rising to the top, occupies the upper narrow part of the vessel, while the water remains at the bottom, and enters the tube affixed to the receiver. When the surface of the liquid attains in the receiver a higher level than the top of the tube, the water will necessarily begin to flow out through the latter, and may be received in bottles. The oil thus accumulates as long as the process continues, but it is evident that the plan is applicable only to the oils lighter than water. For the heavier oils, cylindrical vessels may be employed, to be renewed as fast as they are filled; but, as all the water cannot be removed by these plans, it is necessary to resort to some other method of effecting a complete separation. An instrument called a *separator* is usually employed for this purpose. It consists of a glass funnel, or a globular vessel, furnished with a stopper, and prolonged at the bottom into a very narrow tube. The lower opening being closed, the mixed liquids are introduced and allowed to stand until they separate. The orifice at the bottom is then opened, and, the stopper at the top being a little loosened, so as to admit the air, the heavier liquid slowly flows out, and may be separated to the last drop from the lighter, which floats above it. If the oil is heavier than the water, it passes out of the separator; if lighter, it remains within. According to George Leuchs, all oils obtained by distillation with water, even when perfectly clear, contain some water.

The water saturated with oil should be preserved for use in future distillations, as it can dissolve no more of the oil. One or more volatile acids are frequently found in the distilled water, as acetic, butyric, or valerianic, and Wunder has detected all three of these acids in the water distilled from chamomile flowers. (*J. Pr. Chem.,* lxiv, 499.) For an illustration of a cheap apparatus for distilling volatile oils by steam under slight pressure, see *Proc. A. Ph. A.,* 1894, 680.

According to Overbeck, all the volatile oils may be decolorized by distilling them from an equal weight of poppy seed oil and a saturated solution of common salt. (*A. Pharm.,* lxxxiv, 149.)

When first procured, some volatile oils have a disagreeable somewhat empyreumatic odor, from which they may be freed by allowing them to stand for some days in vessels loosely covered with paper. They should then be filtered and introduced into small opaque bottles, which should be well stoppered so as to exclude the air. When altered by exposure to air, they may sometimes be restored to their original appearance and quality by agitation with a little recently heated animal charcoal, and the same method may be employed for freeing them from adhering water.

They may be administered upon a lump of sugar; or triturated with at least ten times their weight of sugar, forming *oleosaccharates,* which are then dissolved in water; or made into emulsions with water, sugar, and gum arabic. In making emulsions with volatile oils, it has been recommended first to dissolve them in one of the fixed oils, the oil of almond for example, and then to emulsionize the oleaginous solution with syrup and gum arabic. For 100 parts of water, 15 of the almond oil in which the volatile oil is to be dissolved, 10 of powdered gum arabic,

and 25 of syrup may be taken. The volatile oils are often kept dissolved in alcohol under the name of essences.

Enfleurage.—This term is applied by the French to the impregnation of fixed oils and fatty matters with the odors of certain sweet scented plants, such as jasmine, tuberose, and mignonette, the oils of which are so delicate and fugitive that they cannot well be separated by distillation. The process consists in exposing the fatty matter, placed in layers, in suitable frames, to the exhalations from the flowers, which are absorbed, and give their characteristic odor to the fat. Another plan is to expose alternate layers of the flowers, and of cotton impregnated with bland fixed oil, to the sun, and afterwards to express the oil from the cotton. (*A. J. P.*, xxix, 551.) The French sometimes give to the spirituous solutions made by extracting the odors from fats and oils with alcohol the name of *Essences*.

The following suggestions on preparing emulsions of the volatile oils may be useful. Oil of turpentine and other volatile oils, to be emulsionized in quantity, are most successfully treated by rubbing them with one-half their weight of powdered gum arabic, and, when intimately mixed, adding at once, with rapid trituration, water in the proportion of one and a half times the weight of the gum used. Such an emulsion is more permanent when a little fixed oil is used.

Uses.—While substances differing so widely in their source and in their chemical composition must manifestly exercise dissimilar effects upon the body, but there are certain properties common to so many of the volatile oils that a word concerning the therapeutic effects of this group of principles may be in place. Practically all of the official volatile oils are more or less irritant; some of them only feebly so and some very actively so. By virtue of this action when taken into the intestinal tract they excite peristalsis and are therefore used for the expulsion of flatus in *colic* as well as to enhance the effect of cathartic drugs. It is probably also to this local irritant effect that their uses as expectorants, diaphoretics, and diuretics is to be attributed. A large number of them are powerful germicides and nearly all of them more or less antiseptic. The antibacterial property of the volatile oils has been investigated especially by Martindale (*Perfume and Essential Oil Record*, 1910, i, p. 266) by Gilmore (*P. J.*, 1910, p. 844) and by Peck (*J. A. M. A.*, 1899, xxxii, p. 6). According to Martindale the oil of origanum is twenty-five times as actively germicidal as phenol and the oil of cloves about 9 times; while Peck finds that the oil of cloves prevents the multiplication of bacteria when present in about 1 part to 1100. The following volatile oils are powerfully germicidal: origanum, thyme, cinnamon, cassia, cloves, bay, and sassafras. Of considerable disinfectant power but weaker than the preceding are: peppermint, eucalyptus, cajuput, bitter almond, sandal wood, spearmint and lavender. The following are feeble in their antibacterial properties: anise, bergamot, juniper, cade, and turpentine. Concerning most of the other oils figures are lacking. While the cost of the volatile oils precludes their use for many disinfectant purposes yet for others they are very valuable agents, especially are they employed for their antibacterial properties in the mouth and nose.

Some of the essential oils possess marked local anesthetic powers, among which may be mentioned especially cloves, peppermint, thyme, and cajuput. For this influence they are used in *toothache* and *pruritus*.

OLEATA.

OLEATES

(ō-lę-ā'tą)

Oléates, *Fr.*; Oleate, *G.*

The *oleates* are a class of preparations which were introduced to the medical profession by John Marshall, F.R.S., in 1872. They are usually solutions of certain bases in oleic acid, and are made by triturating the solid substance with the oleic acid until it is dissolved. Whenever it is possible, the application of heat should be avoided, and it has been observed that the freshly precipitated oxides of the metals dissolve more readily than those which are old. The title oleate is probably the best that could be devised, although it must be understood that, as found in the Pharmacopœias, they are not pure chemical compounds, but merely compounds of the oxides or the alkaloids, as the case may be, with oleic acid dissolved in a great excess of the latter.

Oleates may be made either by direct combination of the ingredients or by double decomposition. When made by the latter method, a good quality of oleic acid should be treated with the proper quantity of solution of sodium hydroxide, to saponify it, any excess of the alkali being neutralized with a little tartaric acid. This soap solution is preferably used diluted.

J. M. Good, in making the oleates of the alkaloids, proposes the use of sufficient oleic acid to dissolve the alkaloid and then diluting the solution with a bland fixed oil, such as almond oil. (*Proc. Missouri Pharm. Association*, 1891, p. 65.)

The *medicinal properties* of the oleates are, of course, dependent upon the base, so that these preparations may be considered the equivalents of the corresponding ointments, over which, however, they have certain advantages. They are much cleaner and more elegantin appearance. They seem to be more irritating than the ointments, and, unless diluted with an equal bulk of cottonseed, olive, or other bland oil, are, when applied with friction, likely to provoke a cutaneous eruption or even pustulation. Marshall recommends that they be applied with a brush, or gently spread over the part with the finger.

OLEATUM HYDRARGYRI. U. S. (Br.)

OLEATE OF MERCURY Oleat. Hydrarg.

(ō-lē-ā'tŭm hȳ-drär'gy-rī)

Hydrargyrum Oleatum, *Br.;* Mercuric Oleate; Hydrargyrum Oleicum; Oléate de Mercure, *Fr.;* Oelsaures Quecksilber, Quecksilberoleat, Mercurioleat, *G.*

* "Yellow Mercuric Oxide, in very fine powder, *twenty-five grammes* [or 386 grains]; Alcohol, *twenty mils* [or 325 minims]; Oleic Acid, *a sufficient quantity,* to make *one hundred grammes* [or 3 ounces av., 231 grains]. Mix the yellow mercuric oxide with the alcohol in a tared dish, add *seventy-five grammes* [or 2 ounces av., 282 grains] of oleic acid, warm the mixture to a temperature not exceeding 50° C. (122° F.), stir constantly for five minutes and then continue the heat, stirring frequently, until the alcohol is expelled and the mercuric oxide is dissolved. Now add sufficient oleic acid to make the product weigh *one hundred grammes* [or 3 ounces av., 231 grains] and mix thoroughly. Preserve Oleate of Mercury in tightly-closed containers protected from strong light and do not dispense it if globules of mercury are visible at the bottom of the container. In the preparation of this Oleate avoid all contact with metallic utensils." *U. S.*

"Yellow Mercuric Oxide, 20 *grammes;* Liquid Paraffin, 5 *grammes;* Oleic Acid, 75 *grammes.* Triturate the Mercuric Oxide with the Liquid Paraffin until it is thoroughly subdivided; add the Oleic Acid with vigorous stirring. Heat the mixture to 50° C. (122° F.) triturating occasionally until combination is effected, and, when cool, a yellowish unctuous preparation is obtained." *Br.*

This oleate is now made with 25 per cent. of mercuric oxide; that of the British Pharm. (1914) contains 20 per cent. Water was used in this oleate in order to facilitate combination in the U. S. P. VIII, but it was replaced by alcohol in the U. S. P. IX.

This preparation was introduced by Marshall in 1872. If made from oleic acid which has been purified from the usual contaminations (palmitic and stearic acids), it is a clear yellowish liquid of a thick consistence and having the peculiar odor of oleic acid. As usually seen, however, it is of the consistence and appearance of petrolatum, due to the presence of small quantities of mercuric palmitate and stearate. (See *Acidum Oleicum,* p. 52.) The formula of a normal oleate of mercury would be $(C_{18}H_{33}O_2)_2Hg$. For its formation we should reckon for every 25 parts of mercuric oxide from 65 to 66 parts of oleic acid. Free oleic acid is intentionally present in this U. S. preparation, which is known frequently as "25 per cent. oleate of mercury." In making this preparation, care must be exercised in the selection of the oleic acid, and to avoid exceeding the degree of heat directed in the official process; indeed, our experience has been that it keeps better if made by the cold process—*i.e.,* by simply mixing the freshly precipitated yellow oxide with the oleic acid, and allowing them to stand at ordinary temperatures until the precipitate has dissolved. The British preparation (1898) was modelled after Shoemaker's process, but in the Br. Pharm., 1914, the mercuric oxide is triturated with liquid paraffin. The precipitated mercuric oleate is difficult to free from water, and is prone to change. In time, even with the best oleic acid that can be procured, some decomposition will take place, and metallic mercury will be found at the bottom of the containing bottle. The rapidity of the change will be in proportion to the impurities in the oleic acid and the degree of heat employed. Beringer's process, by the double decomposition of potassium oleate and mercuric nitrate, is commended by Edel. (See *West. Drug.,* 1894, 85.)

Uses.—This preparation may often be substituted with advantage for mercurial ointment, which it closely resembles in its medicinal properties, except that it is more readily absorbed, and therefore more effective. It has been especially commended by Marshall in cases of *chronically inflamed joints,* and in *hordeolum, indurations after abscesses,* and various other forms of superficial local inflammations of a slow type; also in *sycosis, tinea, psoriasis, eczema,* and as a constitutional alterative in *hereditary syphilis.*

Dose, one-half to two drachms (2–8 Gm.) applied externally.

Off. Prep.—Massa Hydrargyri, *U. S.;* Unguentum Hydrargyri, *U. S.;* Unguentum Hydrargyri Oleati, *Br.*

OLEORESINA ASPIDII. U. S. (Br.)

OLEORESIN OF ASPIDIUM Oleores. Aspid. [Oleoresin of Male Fern]

(ō-lē-ō-rĕs'ĭ-nă ăs-pĭd'ĭ-ī)

"Liquid Extract of Male Fern contains in 100 grammes not less than 20 grammes of filicin." *Br.*

Extractum Filicis Liquidum, *Br.;* Oleoresina Filicis, *Pharm.* 1870; Liquid Extract of Male Fern, Oil of Fern; Oleum Filicis Maris; Extrait de Fougère Mâle, *Fr. Cod.;* Extractum Filicis, *P. G.;* Farnextrakt, Wurmfarnextrakt, Wurmfarnöl, *G.;* Estratto de felce maschio etero, *It.;* Extracto etereo de helecho macho, *Sp.*

* "Aspidium, recently reduced to No. 40 powder, *five hundred grammes* [or 17 ounces av., 279 grains]; Ether, *a sufficient quantity.* Place the aspidium in a cylindrical glass percolator, provided with a stop-cock, and arranged with a cover and a receptacle suitable for volatile liquids. Pack the powder firmly, and percolate slowly with ether, added in successive portions, until the drug is exhausted. Recover the greater part of the ether from the percolate by distillation on a water bath, and, having transferred the residue to a dish, allow the remaining ether to evaporate spontaneously in a warm place. Keep the Oleoresin in a well-stoppered

bottle. Note: Oleoresin of Aspidium, on standing, usually deposits a granular, crystalline substance. This should be thoroughly mixed with the liquid portion before use." *U. S.*

"Male Fern, in No. 20 powder, 1000 *grammes;* Ether, *a sufficient quantity.* Exhaust the Male Fern by percolation with the Ether; from the clear percolate recover the ether by distillation and finally evaporate on a water-bath until an oily extract remains. Specific gravity not less than 1.000. *Refractive index* at 40° C. (104° F.) not less than 1.490. Contains in 100 grammes not less than 20 grammes of filicin as determined by the following process:—Dissolve 5 grammes of the Liquid Extract in 40 millilitres of *ether,* transfer to a separator, add 100 grammes of *solution of barium hydroxide* and shake vigorously and continuously for five minutes. Allow the liquids to separate and filter off 86 grammes of the aqueous liquid. Acidify this with *hydrochloric acid* and extract with three successive portions of 30, 20, and 15 millilitres of *ether.* Filter the mixed ethereal solutions, wash the filter paper with *ether,* evaporate, dry the residue at 100° C. (212° F.) and weigh. It weighs not less than 0.8 gramme, equivalent to not less than 20 grammes of filicin in 100 grammes of the Liquid Extract. This Liquid Extract contains not less than 20 per cent. of filicin." *Br.*

This is the only preparation of male fern which should be used; in its making aspidium which is green in color and recently collected should be employed. It is a thick, dark green liquid, usually containing a granular deposit of crystalline *filicic anhydride,* often erroneously called *filicin* or *filicic acid,* which is regarded as the active ingredient and should not be separated. For a method of determining the percentage of filicic acid by Daccomo and Scoccianti, see *Ph. Centralh.,* 1896, 208. Wm. G. Greenawalt found both the liquid and the sediment effective tenicides, the sediment somewhat the more active. It has the odor of fern, and a nauseous, bitterish, somewhat acrid taste. According to Hayes, when an absolutely dry root and an anhydrous ether (containing but little alcohol) of a specific gravity below 0.728 are used, the oleoresin remains clear. Kramer states that a very active extract of male fern may be prepared by exhausting with ether the fresh juicy rhizomes collected in May or October freed from scales and cut into small pieces. The ethereal tincture should be kept in a cool place until wanted, when the necessary quantity should be converted into extract. One dose, two to four drachms, of such an extract is said to have always produced satisfactory results. (*Ph. Cb.,* xxv, 578.) Oleoresin of male fern is sometimes found in the market containing noticeable proportions of copper, and in many cases it is colored green artificially.

For therapeutic properties of this oleoresin, see *Aspidium.*

Dose, from one-half to one fluidrachm (1.8–3.75 mils), administered in emulsion.

OLEORESINA CAPSICI. U. S.

OLEORESIN OF CAPSICUM Oleores. Capsic.

(ō-lę-ō-rĕs'ĭ-nȧ kăp'sĭ-cī)

Oléorésine (Extrait éthéré) de Capsique, *Fr.;* Spanisch-pfeffer-Oelharz, Aetherisches Spanischpfeffer-extrakt, *G.*

* "Capsicum, in No. 40 powder, *five hundred grammes* [or 17 ounces av., 279 grains]; Ether, *a sufficient quantity.* Place the capsicum in a cylindrical glass percolator, provided with a stop-cock, and arranged with a cover and a receptacle suitable for volatile liquids. Pack the powder firmly, and percolate slowly with ether, added in successive portions, until the percolate measures *eight hundred mils* [or 27 fluidounces, 24 minims]. Recover the greater part of the ether from the percolate by distillation on a water bath, and, having transferred the residue to a dish, allow the remaining ether to evaporate spontaneously in a warm place. Then pour off the liquid portion, transfer the remainder to a glass funnel provided with a pledget of cotton, and, when the separated fatty matter (which is to be rejected) has been completely drained, mix the liquid portions together. Keep the Oleoresin in a well-stoppered bottle." *U. S.*

One of the active principles of capsicum, called *capsaicin,* $C_9H_{14}O_2$, is very soluble in ether, and is wholly extracted in the process. Its precise nature has not been determined. Another principle, even still more pungent than *capsaicin,* is *capsacutin* which is also extracted by the official solvent in making this oleoresin. (See *Capsicum.*) After the concentration of the acetone solution, a solid fatty matter separates on standing, but a portion of fixed oil probably still remains. The preparation is a very thick liquid, capable, however, of being dropped, of a dark reddish-brown color, and, though opaque in mass, yet transparent in thin layers. It has not very decidedly the odor of capsicum, but to the taste is intensely pungent. W. C. Alpers found a capsicum which yielded 16 per cent. of oleoresin; the statement has been frequently made that 5 per cent. is the usual yield. (*M. R.,* 1896, 593.) It may be usefully employed to give locally stimulant properties to substances administered internally in a pilular form, in cases of *gastric insensibility* and excessive *flatulence.* One drop given three times a day has produced cystic irritation and strangury. It may be used also as a powerful rubefacient, in strengths of from one to two per cent., diluted with olive oil or soap liniment.

Dose, from one-fourth to one grain (0.015–0.065 Gm.).

Off. Prep.—Emplastrum Capsici, *U. S.*

OLEORESINA CUBEBÆ. U. S.

OLEORESIN OF CUBEB Oleores. Cubeb.

(ō-lę-ō-rĕs'ĭ-nȧ cū-bē'bæ)

Extractum Cubebæ Æthereum; Oléorésine de Cubèbe, *Fr.;* Extractum Cubebarum, *P. G.;* Aetherisches Kubebenextrakt, Kubebenextrakt, *G.*

* "Cubeb, in No. 30 powder, *five hundred grammes* [or 17 ounces av., 279 grains]; Alco-

hol, *a sufficient quantity.* Place the Cubeb in a cylindrical glass percolator, pack the powder firmly, and percolate slowly with alcohol, added in successive portions, until the drug is exhausted. Recover the greater part of the alcohol from the percolate by distillation on a water-bath, and, having transferred the residue to a dish, allow the remaining alcohol to evaporate in a warm place, stirring frequently. Keep the Oleoresin in a well-stoppered bottle.

"NOTE: Oleoresin of Cubeb, after standing for some time, deposits a waxy and crystalline precipitate, which should be rejected, the liquid portion only being used." *U. S.*

A change was made in the menstruum for this oleoresin in the U. S. P. (8th Rev.) alcohol now being used instead of ether or acetone. The use of alcohol was suggested by E. R. Squibb. This oleoresin consists mainly of the volatile oil and resin, with a portion of the cubebin and waxy matter of the cubeb. The consistence differs according to the character of the cubeb employed, its degree of fluidity being proportionate to the amount of volatile oil contained in the medicine. The color is usually blackish brown, with more or less of a greenish hue, according to the quantity of chlorophyll present, which varies with the character of the cubeb and with that of the menstruum, pure ether extracting more of the green coloring matter, while alcohol extracts the brown; unripe fruit or berries yield more chlorophyll than do the ripe fruit. Cubeb yields from one-eighth to one-fifth of its weight of the oleoresin. The preparation deposits waxy matter and crystals of cubebin on standing, which should be separated and discarded; its efficacy is not impaired on this account. It was first introduced into use by Procter. (*A. J. P.*, xviii, 168.)

From carefully conducted experiments by F. V. Heydenreich, it would appear that, of the various constituents of cubeb contained in the official oleoresin, the cubebin has no perceptible effect in the dose of the medicine ordinarily given, that the volatile oil is simply stimulant and carminative, and, finally, that the soft resin has all the diuretic properties of the cubeb. Of the last-mentioned ingredient, twenty grains (1.3 Gm.) given every two hours until five doses were taken considerably increased the secretion of urine, producing at the same time a slight burning sensation in the passage, which ceased with the diuretic action. Pushed beyond this amount, it occasioned severe irritation of the urinary passages, with some fever.

This oleoresin, as it occurs in the market, often has a thin consistence. In one specimen three-eighths of its weight were lost in a short time by the spontaneous evaporation of the ether improperly left in the product.

Dose, from five to ten minims (0.3–0.6 mil), given suspended in water, or mixed with powdered sugar.

Off. Prep.—Trochisci Cubebæ, *U. S.*

OLEORESINA PETROSELINI. U. S.

OLEORESIN OF PARSLEY FRUIT Oleores. Petrosel. [Liquid Apiol]

(ō-lē-ō-rĕs'ĭ-nă pĕ-trŏ-sĕ-lī'nī)

Apiol, Oil of Parsley Seed.

* "Parsley Fruit, in No. 60 powder, *five hundred grammes* [or 17 ounces av., 279 grains]; Ether, *a sufficient quantity.* Place the parsley fruit in a cylindrical glass percolator provided with a stop-cock and arranged with a cover and a receptacle suitable for volatile liquids. Pack the powder firmly and percolate slowly with ether, added in successive portions until the drug is exhausted. Recover the greater portion of the ether by distillation on a water bath, and, having transferred the residue to a dish, remove the remaining ether by spontaneous evaporation in a warm place, stirring frequently. Allow the Oleoresin to stand without agitation for four or five days, decant the clear liquid portion from any solid residue, and preserve it in well-stoppered bottles." *U. S.*

This oleoresin is commonly called "liquid apiol." The official process should be strictly followed as cases are on record where commercial gasoline or benzin has been used as the menstruum and the percolate evaporated spontaneously, whereupon a yield of as much as 50 per cent. of a non-volatile, oily liquid was obtained which consisted chiefly of the non-volatile portions from the gasoline. Such a procedure cannot be too severely condemned.

According to L. Wolff (*A. J. P.*, 1877, 2), commercial *apiol* is merely the oleoresin; he proposes a very simple process for true apiol. Powdered parsley seed is exhausted with petroleum benzin, and the liquid is spontaneously evaporated; the residue is a mixture of fixed oil, wax, and apiol; the apiol alone being soluble in alcohol can easily be separated by repeated washings with strong alcohol; the washings evaporated over a water bath at a gentle heat leave as a residue "true apiol." L. Ough (*C. D.*, 1894, 17) obtains apiol by percolating freshly powdered parsley seeds with alcohol, recovering the alcohol from the percolate by distillation, and separating the oily residue from the deposited waxy solid.

Ciamician and Silber (*Ph. Post,* 1888, 391) have investigated apiol, and state that the pure substance occurs in white crystals having the composition $C_{12}H_{14}O_4$, melting at 30° C. (86° F.), and boiling at 294° C. (561° F.). *Isapiol, apiolic acid, apiolaldehyde,* and *apion* are decomposition products. They state that isapiol has physiological properties resembling those of pure apiol.

H. C. Whitney (*N. R.*, January, 1880) proposed to change the name of commercial apiol, and call it *oil of parsley seed.* He believed that the volatile oil of parsley seed is the active and emmenagogue principle, and obtained it by distilling the freshly powdered seed with salt water. The yield is 4.27 per cent. of an oil which corresponded closely with Joret and Homolle's apiol.

Von Gerichten (*Ber. d. Chem. Ges.*, 16, 17) obtained besides the peculiar terpene, *parsley camphor*, which he thinks is alone entitled to the name of apiol. He gives its melting point as 30° C. (86° F.), boiling point 300° C. (572° F.), and sp. gr. 1.015.

Parsley camphor has been given the formula CH_2: $CH.CH_2.C_6H(OCH_3)_2$: O_2: $CH_2.CH$.—It may be prepared by extracting the oleoresin of parsley seed with ether and subsequent purification. It crystallizes in long needles of a slight parsley odor—insoluble in water, but readily soluble in alcohol. With strong sulphuric acid it gives a blood-red color.

Uses.—The oleoresin of parsley contains a number of bodies of considerable physiological power. The most important of these are crystalline apiol, white apioline, and myristicin. According to the experiments of Lutz (*Bull. Sci. Pharm.*, 1910, xvii, p. 1) the actions of these substances are similar in kind. They produce marked slowing of the pulse with fall of the blood pressure, tremors, and weakness of the extremities, followed by paralysis with epileptiform convulsions and gasping respirations. After death there was found marked congestion in the lungs and in the pelvic organs. Rimini and Dilitala (*Archiv. di. Farmacologia e. Terap.*, 1908, xiv) have shown that apiol produces in the cat fatty degeneration of the liver of the same type as is caused by myristicin (see page 777). They also noted that it had a direct weakening action on the voluntary muscles.

Oleoresin of parsley and other principles derived from this plant have been used in various uterine disorders, especially in *dysmenorrhea*. Our knowledge of its physiological action, however, furnishes no ground for attributing to it valuable properties in this or any other disease. The congestion in the pelvic organs found after death from this drug, may easily be attributed to the asphyxial nature of the poisoning. There is no evidence that in quantities approaching those used in medicine it has any influence of any kind upon the uterus. Glatard (*Journ. de Med. et Chir. Prat.*, 1910, p. 674) reports a case of apiol poisoning in a pregnant woman who took six grammes in a period of forty-eight hours. There was vertigo, nausea and vomiting, urticaria, liver swollen and painful, mild icterus, urine scanty and high colored, but free from albumen; pregnancy was not interrupted. Sardou (*A. G. M.*, 1906) recommends apiolin as an antispasmodic in *intestinal colic*.

Dose, five to fifteen minims (0.3–0.9 mil).

OLEORESINA PIPERIS. U. S.

OLEORESIN OF PEPPER Oleores. Piper.

(ō-lē-ō-rĕs'ĭ-nȧ pĭp'ẹ-rĭs)

Extractum Piperis Fluidum, *U. S.* 1850; Fluid Extract of Black Pepper; Oléorésine de Poivre noir, *Fr.*; Aetherisches Pfefferextrakt, *G.*

* "Pepper, in No. 40 powder, *five hundred grammes* [or 17 ounces av., 279 grains]; Ether, *a sufficient quantity*. Place the pepper in a cylindrical glass percolator, provided with a stop-cock, and arranged with a cover and a receptacle for volatile liquids. Pack the powder firmly, and percolate slowly with ether, added in successive portions, until the drug is exhausted. Recover the greater part of the ether from the percolate by distillation on a water bath, and, having transferred the residue to a dish, set this aside in a warm place until the remaining ether has evaporated, and the deposition of piperine has ceased. Lastly, separate the Oleoresin from the piperine by straining through purified cotton. Keep the Oleoresin in a well-stoppered bottle." *U. S.*

A substance has long been in use under the name of *oil of black pepper*, consisting mainly of the volatile oil, fixed oil, and resin of the pepper, and belonging, therefore, to the oleoresins. As usually found, it is almost black and of a thick consistence, and is a residue of the process for preparing piperine. The official oleoresin made with ether has the same general character, but is more fluid and of more uniform strength, and should, therefore, be preferred. It contains almost all the volatile oil and acrid resin of black pepper, with little of the piperine, and, as the last-mentioned principle, when quite pure, is of doubtful efficacy, the oleoresin may be considered as representing the virtues of the fruit. The color is greener than that of the common oil of black pepper, and not so dark, owing to the fact that the solvent dissolves the green more readily than the brown coloring matter. A pound of black pepper yields about six drachms of the oleoresin.

Dose, from one-fourth to one minim (0.015–0.06 mil), in emulsion or pill.

OLEORESINA ZINGIBERIS. U. S.

OLEORESIN OF GINGER Oleores. Zingib.

(ō-lẹ-ō-rĕs'ĭ-nȧ zĭn-gĭb'ẹ-rĭs)

Extractum Zingiberis Æthereum; Oléorésine (Piperoide) de Gingembre, *Fr.*; Zingiberin, Aetherisches Ingwerextrakt, *G.*

* "Ginger, in No. 60 powder, *five hundred grammes* [or 17 ounces av., 279 grains]; Ether, *a sufficient quantity*. Place the ginger in a cylindrical glass percolator, provided with a stop-cock, and arranged with a cover and a receptacle suitable for volatile liquids. Pack the powder firmly, and percolate slowly with ether, added in successive portions, until the drug is exhausted. Recover the greater part of the ether from the percolate by distillation on a water bath, and, having transferred the residue to a dish, allow the remaining ether to evaporate spontaneously in a warm place. Keep the Oleoresin in a well-stoppered bottle." *U. S.*

In the U. S. formula of 1870 for this preparation alcohol was used in connection with ether, on the score of economy: it was added in order to displace the ether and thus save an unnecessary expenditure of the more costly fluid. A little of the alcohol mixed with the ether at their surface of contact. In the present

process both ether and alcohol have been replaced by the solvent, ether. The whole of the virtues of the root are extracted in this preparation, as the residuary ginger is nearly or quite tasteless. The oleoresin constitutes about 5 per cent. of the dried root. It is the *piperoid of ginger* of Beral. (Soubeiran's *Traité de Pharm.*, i, 371.) It is a clear, dark-brown liquid, of a thick consistence (though capable of being dropped), with the flavor of ginger, and very pungent.

The oleoresin of ginger is a useful stimulant in *alcoholic gastritis, chronic serous diarrheas* and other atonic conditions of the alimentary canal.

Dose, one-half to one minim (0.03–0.06 mil), well diluted.

OLEORESINÆ

OLEORESINS

(ō-lę-ō-rĕs'ĭ-næ)

Oléo-résines, Extraits éthérés, *Fr.*; Oelharze, Aetherische Extrakte, *G.*

The oleoresins, as a class of preparations, were introduced into the U. S. Pharmacopœia at the revision of 1860, having been previously classed with the Fluidextracts. Their peculiarity is that they consist of principles which, when extracted by means of ether, alcohol, or acetone, retain a liquid or semi-liquid state upon the evaporation of the menstruum, and at the same time have the property of self-preservation, differing from the fluidextracts in not having a definite relation of strength to the drug. They consist chiefly, as their name implies, of oil, either fixed or volatile, holding resin and sometimes other active matter in solution. Their preparation is very simple, consisting in the exhaustion of the drug with acetone, alcohol or ether by means of percolation, and the subsequent evaporation of the menstruum. In consequence of the great volatility of the solvent, it may in great measure be recovered by distillation, thus very materially diminishing the costliness of the process. It is proper not to continue the heat necessary for the recovery of the solvent by distillation until the whole of the solvent is driven over, lest, towards the close, a portion of the volatile matters also should pass, and the strength of the oleoresin be impaired. Hence in every instance the last portions of the menstruum are allowed to separate by spontaneous evaporation. Petroleum benzin has been proposed as a substitute for other solvents in these preparations, but should not be permitted to supersede them until officially sanctioned. It is difficult, if not impossible, to remove the last traces of this solvent without loss of volatile oil. Acetone replaced ether in most of the formulas of the U. S. P. VIII on account of economy, but as ether is again the cheaper solvent because of the use of denatured alcohol in its manufacture, it is again officially directed in the U. S. P. IX. Oleoresin of cubeb is made with alcohol.

OLEUM ABIETIS. Br.

OIL OF SIBERIAN FIR [Oil of Pine]

(ō'lę-ŭm ă-bī-ē'tĭs)

"Oil of Siberian Fir is the oil distilled from the fresh leaves of Abies sibirica, *Ledeb.*" *Br.*

"Colorless or nearly so. Aromatic odor; taste pungent. Specific gravity 0.900 to 0.920; *optical rotation* —32° to —42°; *refractive index* at 25° C. (77° F.) about 1.474. Contains from 30 to 40 per cent. of *esters*, calculated as bornyl acetate, $C_{10}H_{17}C_2H_3O_2$." *Br.*

This is practically the same in its properties and uses as pine needle oil. (See *Oleum Pini Pumilionis.*)

OLEUM AJOWAN. Br.

AJOWAN OIL [Ptychotis Oil]

(ō'lę-ŭm ă'jō-wän)

"Ajowan Oil is the oil distilled from the fruit of Carum Copticum, *Benth. and Hook. f.*" *Br.*

Under the name of *ajowan, ajwain, ajwan,* and other vernacular appellations, the fruit of the *Carum Ajowan* Bentley (*C. Copticum* Benth. and Hook. f.) are largely used in India as an aromatic. They resemble in size the fruits of the ordinary parsley and are of a grayish-brown color and have a tubercular surface with five prominent ridges to each mericarp. The odor and taste resemble that of thyme. These fruits yield from 4 to 6 per cent. of an agreeably aromatic volatile oil. Ajowan oil is "colorless, with an odor and taste resembling thyme. Specific gravity 0.910 to 0.930. *Optical rotation* +1° to +2°. When 10 millilitres with 100 millilitres of *solution of sodium hydroxide* in a flask with a narrow graduated neck are heated on a water-bath, well shaken, and allowed to stand, the uncombined oil, cooled to 15.5° C. (60° F.), measures not more than 6 millilitres (presence of not less than 40 per cent. of thymol)." *Br.*

This oil, besides containing thymol, contains a terpene and also the cyclic hydrocarbon cymene.

The oil of ajowan is one of the most important commercial sources of thymol. Its medicinal virtues are due entirely to this ingredient.

Dose, one-half to five minims (0.03–0.3 mil).

OLEUM AMYGDALÆ AMARÆ. U. S.

OIL OF BITTER ALMOND Ol. Amygd. Amar. [Bitter Almond Oil]

(ō'lę-ŭm ą-mŭg'dą-læ ą-mă'ræ)

"A volatile oil obtained by maceration and distillation from the ripe kernels of *Prunus Amygdalus amara* DeCandolle (Fam. *Rosaceæ*), and from other kernels containing amygdalin. It yields not less than 85 per cent. of benzaldehyde [C_7H_6O] and not less than 2 per cent. nor more than 4 per cent. of hydrocyanic acid [HCN]. The botanical source from which it is derived must be stated on the label. Preserve it in small, well-stoppered, completely filled, amber-colored bottles protected from light and

air. Oil showing crystals of benzoic acid must not be dispensed.

"NOTE: This Oil is intended for medicinal use; it must not be used for flavoring foods." *U. S.*

Oleum Amygdalarum (Amararum) Æthereum; Oleum Amygdalæ Volatile; Volatile Oil of Almond; Huile volatile d'Amande amère, *Fr. Cod.*; Essence d'Amandes amères, *Fr.*; Bittermandelöl, *G.*; Esencia de almendras amargas, *Sp.*

When bitter almonds are expressed, they yield a bland fixed oil, and the residuary cake, reduced to powder by grinding, and submitted to distillation with water, yields *oil of bitter almond.* This does not pre-exist in the almond, but is produced by the action of water upon the amygdalin contained in it, through the intervention of an enzyme called *emulsin* (see *Amygdala Amara*), according to the reaction:

$$C_{20}H_{27}NO_{11} + 2H_2O = C_7H_6O + 2C_6H_{12}O_6 + HCN$$

It is obtained also by the distillation of the leaves of the cherry-laurel, by the bark of the wild cherry, and of various products of the genera *Amygdalus, Cerasus, Prunus,* etc. Whipple obtained, upon an average, from the ground bitter almond cake, 1.35 per cent. of the oil. (*P. J.*, x, 297.) Pettenkofer has ascertained that the yield is greater if the cake be macerated in water for forty-eight hours before being submitted to distillation. (*J. P. C.*, May, 1862, p. 432.) It is sometimes produced from peach kernels. Schimmel's Report for April, 1914, refers to the fact that the sole source of the oil at that time was apricot kernels.

Oil of bitter almond has a yellowish color, a bitter, acrid, burning taste, and the odor of the kernels in a high degree. It is heavier than water, soluble in alcohol and ether, according to Flückiger soluble in 300 parts of hot or cold water, and deposits, upon standing, a white crystalline substance consisting chiefly of benzoic acid. It is officially described as "a clear, colorless or yellow, strongly refractive liquid, having the characteristic odor and taste of benzaldehyde. It is slightly soluble in water and soluble in all proportions in alcohol or ether. It dissolves, forming a clear solution, in 2 volumes of 70 per cent. alcohol. Specific gravity: 1.038 to 1.060 at 25° C. (77° F.). Refractive index: 1.5428 to 1.5439 at 20° C. (68° F.) (see Part III, Test No. 22). It is optically inactive or dextrorotatory, not exceeding +0° 10′ in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21). When first prepared, the Oil is neutral to litmus paper, but afterwards develops an acid reaction due to the formation of benzoic acid. It does not respond to the Test for heavy metals in volatile oils (see Part III, Test No. 3). Hold the looped end of a piece of clean copper wire in a non-luminous flame until it glows without coloring the flame green, cool the wire, dip the loop into Oil of Bitter Almond, ignite the latter and hold it so that the liquid burns outside of the non-luminous flame. On slowly bringing the flame from the burning Oil of Bitter Almond on the loop in contact with the lower outer edge of the non-luminous flame, no green tinge is discernible (*chlorinated products*). Add 10 drops of the Oil to a little alcohol, then add a small amount of zinc dust and 2 mils of acetic acid and boil the mixture for a short time; no odor of phenylisocyanide develops after rendering it strongly alkaline with potassium hydroxide T.S., adding a few drops of chloroform and heating (*nitrobenzene*)." *U. S.*

Besides the peculiar volatile oil, it contains also hydrocyanic acid, with usually a small proportion of benzoic acid produced by oxidation of the aldehyde. It may be obtained pure by agitating it strongly with calcium hydroxide and a solution of ferrous chloride, submitting the mixture to distillation, and drying the oil which comes over by digestion with calcium chloride. George Whipple states that if crude oil be redistilled into a solution of silver nitrate, and again distilled from a fresh solution of the same salt, it is obtained entirely free from hydrocyanic acid, which reacts with the silver and remains behind as silver cyanide. (See *A. J. P.*, xxvi, 348.) Thus purified, it is colorless, but still retains its peculiar odor, with a burning, aromatic taste, and is destitute of those poisonous properties of the crude oil which are dependent on hydrocyanic acid. The odor of the oil of bitter almond has been erroneously ascribed to that acid, which, on examination, will be found to have a different and more feeble odor. Like most other volatile oils, this may produce deleterious effects if taken very largely. Hippuric acid is found in the urine of animals to which the oil has been given freely. The sp. gr. of the crude oil varies from 1.05[illegible] to 1.082, and is said to be greater when the oil is distilled from salt water than when distilled by the ordinary mode. That of the purified oil is 1.060, and its boiling point 180° C. (356° F.). It is *benzoic aldehyde,* $C_6H_5.COH$, which may also be produced by the action of oxidizing agents upon benzyl alcohol, $C_6H_5.CH_2OH$, and yields itself, when oxidized, benzoic acid, $C_6H_5.COOH$. The benzoic acid which the oil of bitter almond deposits on standing does not pre-exist in it, but results from the absorption of oxygen, as just stated. The U. S. P. IX provides for an assay for benzaldehyde and also one for hydrocyanic acid, see page 747.

Schimmel & Co. (*Semi-Annual Report,* April, 1893) state that an oil of high specific gravity should be carefully examined for benzo-nitrile, C_6H_5CN, which may form by condensation from benzaldehyde and hydrocyanic acid, and when distilled even *in vacuo* will decompose into the same components.

Benzoic aldehyde is now made synthetically from toluene, C_7H_8. (See *Benzaldehydum.*) By the action of chlorine upon the hot hydrocarbon, benzyl chloride, $C_6H_5CH_2Cl$, results, and this yields benzoic aldehyde on distillation with lead nitrate and water in an atmosphere of carbon dioxide gas. More generally, however, *benzal chloride,* $C_6H_5CHCl_2$, is taken, as this, when heated under pressure with water or sulphuric

acid, readily yields the benzaldehyde. The product is purified by conversion into the acid sulphite compound. Lippmann and Hawliczek have made exhaustive researches on the identity of the artificial with the natural oil of bitter almond, and have found the two oils absolutely identical, physically as well as chemically. At the present time benzaldehyde, or synthetic oil of bitter almond, is very largely used, its chief advantages being uniformity of composition and absence of hydrocyanic acid. To prevent the formation of benzoic acid in oil of bitter almond, Schimmel & Co. recommend the addition of 10 per cent. of alcohol to the oil.

If sulphuric acid produce with the oil a bright-red instead of a brownish-red color, the oil has probably been distilled with salt water, in which case it is prone, according to Ferris, to deposit a blood-red substance, occasionally complained of by druggists.

Wm. A. Tilden has found that the introduction of a little fused calcium chloride into purified oil of bitter almond contributes to its preservation, probably by the absorption of the last traces of water contained in it. Of two specimens of the oil, which had been set aside for two years, one without addition, the other containing a fragment of the fused chloride, the former was found filled with crystals of benzoic acid, and the latter was perfectly free from crystalline deposit and quite fluid. (*P. J.*, 2d ser., 1866, viii, 325.)

Nitrobenzene was at one time a frequent adulterant of oil of bitter almond. It may best be detected by the U. S. P. IX test given above, for additional tests see U.S.D., 19th ed., p. 830–831.

Hager's test may be used quantitatively for the estimation of the amount of nitrobenzene present. Oil of bitter almond requires for solution sixteen to seventeen times its volume of 45 per cent. alcohol. Two mils of the oil are agitated with 34 mils of the 45 per cent. alcohol, and the mixture set aside. After the lapse of a day, the nitrobenzene (all but a trace which remains in solution) will be found collected at the bottom. An important indication of the presence of a sophistication is the cloudiness produced at the first moment. (*N. R.*, Oct., 1880.)

Assay for Benzaldehyde.—"Dissolve about 3 mils of freshly redistilled phenyl hydrazine in 60 mils of alcohol and titrate 25 mils of this solution, which must always be freshly prepared, with half-normal hydrochloric acid V.S., using methyl orange T.S. as indicator. To about 1 Gm. of the Oil of Bitter Almond, accurately weighed, add 25 mils of the phenylhydrazine solution just prepared and allow it to stand for thirty minutes. Add a drop of methyl orange T.S., and acidify the mixture by adding a measured excess of half-normal hydrochloric acid V.S. Filter the mixture and wash the precipitate with small portions of distilled water until the washings cease to redden blue litmus paper. Then titrate the excess of hydrochloric acid in the filtrate with half-normal potassium hydroxide V.S. and subtract the number of mils of the half-normal hydrochloric acid V.S. consumed from the number of mils of the half-normal hydrochloric acid V.S. used in titrating the 25 mils of phenylhydrazine solution; the difference multiplied by 0.053 gives the weight of benzaldehyde." *U. S.*

Assay for Hydrocyanic Acid.—"Dissolve 15 Gm. of crystallized magnesium sulphate in enough distilled water to measure 100 mils, add 5 mils of this solution to 40 mils of distilled water, then add 5 mils of half-normal sodium hydroxide V.S. and two drops of potassium chromate T.S., and titrate the solution with tenth-normal silver nitrate V.S. to the production of a permanent reddish tint. Pour this mixture into a 100 mil flask containing about 1 Gm. of Oil of Bitter Almond, accurately weighed, mix well and titrate again with tenth-normal silver nitrate V.S. until a red tint, which does not disappear on shaking, is reproduced. Conduct this titration as rapidly as possible. One mil of tenth-normal silver nitrate V.S. corresponds to 0.0027 Gm. of hydrocyanic acid. One gramme of the Oil corresponds to not less than 7.4 mils nor more than 14.8 mils of tenth-normal silver nitrate V.S." *U. S.*

Uses.—The unpurified volatile oil of bitter almond, which is the product directed by the Pharmacopœia, acts physiologically like hydrocyanic acid. Death is said to have occurred in a man ten minutes after taking two fluidrachms (7.5 mils) of the oil. It might be substituted with advantage for medicinal hydrocyanic acid, if it always contained a uniform percentage of the acid, as the acid contained in the oil is much less liable to decomposition, remaining for several years unaltered, provided the oil be preserved in well-stoppered bottles. According to Schrader, 100 parts of the oil contain sufficient acid for the production of 22.5 parts of Prussian blue, but the proportion is not constant, varying, according to Groves, from 8 to 12.5 per cent., the U. S. official standard is, however, not less than 2 per cent. and not more than 4 per cent. It has been employed externally, dissolved in water in the proportion of one minim (0.06 mil) to a fluidounce (30 mils), in *prurigo senilis* and other cases of troublesome *itching*. To facilitate the solution in water, the oil may be previously dissolved in spirit. Oil of bitter almond is sometimes used to conceal the taste of cod liver oil and of castor oil.

Dose, one-fourth to one minim (0.015–0.06 mil).

Off. Prep.—Aqua Amygdalæ Amaræ, *U. S.;* Spiritus Amygdalæ Amaræ, *U. S.;* Elixir Amygdalæ Compositum, *N. F.;* Elixir Anisi (from Spirit), *N. F.*

OLEUM AMYGDALÆ EXPRESSUM. U. S. (Br.)

EXPRESSED OIL OF ALMOND Ol. Amygd. Exp. [Oil of Sweet Almond]

(ō'lē-ŭm ą-mŷg'dą-læ ęx-prĕs'sŭm)

"A fixed oil obtained from the kernels of varieties of *Prunus Amygdalus* Stokes (Fam. *Rosaceæ*). Preserve it in well-closed containers,

in a cool place." *U. S.* "Almond Oil is the oil expressed from the Bitter or Sweet Almond." *Br.*

Oleum Amygdalæ *Br.*; Almond Oil; Oleum Amygdalæ Dulcis, *U. S.* 1860; Oil of Sweet Almond; Huile d'Amande douce, *Fr. Cod.*; Huile d'Amandes, *Fr.*; Oleum Amygdalarum, *P. G.*; Mandelöl, *G.*; Olio di mandorle dolci, *It.*; Aceite de almendras dulces, *Sp.*

This oil is obtained equally pure from sweet and from bitter almonds. In its preparation, the almonds, having been deprived of a reddish-brown powder adhering to their surface, by being rubbed together in a piece of coarse linen, are ground in a mill resembling a coffee-mill, or bruised in a stone mortar, and then pressed in canvas sacks between plates of iron slightly heated. The oil, which is at first turbid, is clarified by rest and filtration. Sometimes the almonds are steeped in very hot water, deprived of their cuticle, and dried in a stove, previous to expression. The oil is thus obtained free from color, but in no other respect better, while it is more likely to become rancid on keeping. Bitter almonds treated in this way impart an odor of hydrocyanic acid to the oil. Boullay obtained 54 per cent. of oil from sweet almonds. Munch gives 55.4 per cent. as the yield of the former, and 52 per cent. as that of the latter. (*J. P. C.*, 4e sér., iii, 400.) These figures are not realized, however, in the ordinary expression methods. Schaedler (*Technologie der Fette und Oele*, 2te Auf., 532) gives 45 per cent. as the average obtained from the sweet almonds, and 38 per cent. from bitter almonds. Though sometimes expressed in this country from imported almonds, the oil is generally brought from Europe.

Properties.—It is "a clear, pale straw-colored or colorless, oily liquid, almost odorless, and having a bland taste. It is slightly soluble in alcohol, miscible with ether, chloroform, benzene, or petroleum benzin. Specific gravity: 0.910 to 0.915 at 25° C. (77° F.). The oil remains clear at –10° C. (14° F.), and does not congeal until cooled to nearly –20° C. (–4° F.) (*olive or lard oil*). Shake vigorously 2 mils of the Oil with a mixture of 1 mil of fuming nitric acid and 1 mil of water; a whitish mixture is formed, which, after standing for several hours at about 10° C. (50° F.), separates into a solid white or nearly white mass and a slightly colored liquid (*oil of peach or apricot kernels*, yielding a red color, and *sesame or cottonseed oil*, yielding a brown color). Heat 10 mils of the Oil with 15 mils of an aqueous solution of sodium hydroxide (1 in 6) and 30 mils of alcohol on a water bath in a flask having a small funnel inserted in the neck, occasionally agitating the mixture until it becomes clear, then transfer the solution to a shallow dish and evaporate the alcohol on a water bath. The residue, when mixed with 100 mils of distilled water, produces a clear solution (*paraffin oil*). Add an excess of hydrochloric acid to this solution; a layer of oleic acid rises to the surface, which, when separated, washed with warm water and clarified by heating on a water bath, remains clear if cooled to 15° C. (59° F.) (*various foreign oils*). One volume of the oleic acid obtained in the last test, when mixed with 1 volume of alcohol, yields a clear solution, which at 15° C. (59° F.) does not deposit any fatty acids, nor become turbid upon the further addition of 1 volume of alcohol (distinction from *olive, arachis, cottonseed, sesame, or other fixed oils*). Saponification value: not less than 191 nor more than 200 (see Part III, Test No. 9). Iodine value: not less than 93 nor more than 100 (see Part III, Test No. 8)." *U. S.*

"Pale yellow. Nearly inodorous; taste bland and nutty. Specific gravity 0.915 to 0.920. *Saponification value* 188 to 196; *iodine value* 93 to 100; *acid value* not more than 6.0; *refractive index* at 40° C. (104° F.) 1.4624 to 1.4640. Remains clear after exposure for three hours to a temperature of –10° C. (14° F.), and does not congeal till the temperature has been reduced to about –18° C. (–0.4° F.). When 1 millilitre of a freshly prepared mixture of equal parts by weight of *sulphuric acid, fuming nitric acid*, and *water*, kept cool while cautiously mixed, is vigorously shaken with 5 millilitres of the Oil for one minute, a whitish mixture with not more than the very slightest tinge of red or brown is produced; after some hours a white solid, sometimes tinged with green, separates, the lower acid layer remaining colorless (absence of peach oil and apricot oil)." *Br.*

From the statement of Braconnot, it appears to contain 76 per cent. of olein and 24 per cent. of a mixture of palmitin and stearin.

According to H. Hager, the oils expressed from the large sweet and the smaller bitter almonds differ considerably, as shown by the elaidin test,—the former oil congealing rapidly, and almost completely, the latter about twelve hours later, and the smaller the bitter almond has been the more imperfectly the oil congeals. Only about one-third of the bulk congeals when the oil is from the small Oporto almonds.

Oil of almond is said to be sometimes adulterated with poppy seed oil, or other drying oils of less value. This sophistication may be detected, as suggested by Wimmec, by taking advantage of the property, belonging to the olein of the non-drying but not to that of the drying oils, of being converted into solid elaidic acid by the action of nitrous acid. By treating iron filings with nitric acid in a flask, nitrous acid is produced, which is to be conducted into water upon which the suspected oil is placed. If the almond oil contains even a small quantity of poppy seed oil, or other drying oil, this will remain in the form of drops on the surface, while the genuine oil will be converted entirely into crystallized elaidin. (*J. P. C.*, Dec., 1862, p. 500.) Colza oil, another not uncommon adulteration, may be detected, according to Schneider, by the action of silver nitrate. Dissolve the oil in twice its volume of ether, add about 30 drops of concentrated alcoholic solution of the nitrate, shake the mixture, and allow it to stand in the dark. If there be much

colza oil, the lower part of the liquid will become first brown and then black; if but little, the brown color will not appear for twelve hours, but the discoloration will always be obvious on the evaporation of the ether. (*P. J.*, March, 1862.)

J. D. Bieber communicates the following test. Equal weights of pure concentrated sulphuric acid, red fuming nitric acid, and water are mixed, and the mixture allowed to cool. On mixing five parts of the oil with one part of this acid liquid, pure almond oil gives a yellowish-white liquid; oil of peach kernels assumes the red color of peach blossoms, turning to dark orange; benne oil turns pale yellowish red, then dirty orange-red; poppy and walnut oils yield a somewhat whiter liquid than almond oil. This test permits the detection of 5 per cent. of peach kernel and benne oil. Mixed with pure nitric acid, sp. gr. 1.40, almond oil yields a pale-yellowish liquid, peach kernel oil a red, benne oil a yellowish green, afterwards reddish, and poppy and walnut oils a white mixture. It was found that the oil expressed, cold or warm, from either fresh almonds or from such as had been kept up to ten years, gave the same reaction. Most of the commercial oil was found to be adulterated with the oil of either peach kernels or benne seed. (*A. J. P.*, Dec., 1877.)

Oil of almond may be used for the same purposes as is olive oil, and, when suspended in water by means of mucilage or the yolk of egg and loaf sugar, forms a pleasant emulsion, useful in pulmonary affections attended with *cough*.

Dose, one fluidrachm to one fluidounce (3.75–30 mils).

OLEUM ANETHI. Br.

OIL OF DILL

(ō'lē-ŭm ą-nē'thī)

"Oil of Dill is the oil distilled from Dill Fruit." *Br.*

Huile volatile d'Aneth, Essence d'Aneth, *Fr.*; Dill, Dillöl, *G.*

Oil of dill is of a pale yellow color, with the odor of the fruit, and a hot, sweetish, acrid taste. Its sp. gr. varies between 0.895 and 0.915. The fruit yields about 3.5 per cent. of it. The oil is a mixture of a paraffin hydrocarbon, and 40 to 60 per cent. of *d*-carvone, $C_{10}H_{14}O$, with *d*-limonene, $C_{10}H_{16}$. (See *Oleum Cari.*) Phellandrene is present in the English and Spanish oils, but not to any appreciable extent in the German oil. "Colorless or pale yellow, darkening on keeping. Odor that of Dill Fruit; taste at first sweet and aromatic, but subsequently pungent. Specific gravity 0.900 to 0.915; *optical rotation* +70° to +80°; *refractive index* at 25° C. (77° F.) 1.483 to 1.488. Soluble in 3 parts of *alcohol* (90 per cent.)." *Br.* R. Nietski obtained from dill, the fruit of *Anethum graveolens*, a volatile oil, which commenced to boil at 155° C. (311° F.), the boiling point rising gradually to 260° C. (500° F.). About 10 per cent. of the oil consists of a hydrocarbon, $C_{10}O_{16}$, having the boiling point from 155° to 160° C. (311°–320° F., 60 per cent. boiling at from 170° to 175° C. (338°–347° F.), of the same composition, and 30 per cent. with the boiling point from 225° to 230° C. (437°–446° F.), composition $C_{10}H_{14}O$, and identical with carvol. The odor of the first portion of hydrocarbon is similar to that of turpentine; that of the second portion resembles oil of mace, but when mixed with a little carvol the characteristic dill odor is at once produced. (*A. J. P.*, 1874.) The oil is sometimes used for the preparation of dill water.

***Dose*, from one to three minims** (0.065–0.2 mil).

OLEUM ANISI. U. S., Br.

OIL OF ANISE Ol. Anisi [Anise Oil]

(ō'lē-ŭm ą-nī'sī)

"A volatile oil distilled from the ripe fruit of *Pimpinella Anisum* Linné (Fam. *Umbelliferæ*) or from the ripe fruit of *Illicium verum* Hooker filius (Fam. *Magnoliaceæ*). The botanical source from which it is derived must be stated on the label. If solid material has separated, carefully warm the Oil until liquefied, and thoroughly mix it before dispensing. Preserve it in well-stoppered, amber-colored bottles, protected from light." *U. S.* "Oil of Anise is the oil distilled from Anise Fruit; or from the fruit of the star-anise, Illicium verum, *Hook. f.*" *Br.*

Huile volatile d'Anis vert (Badaine), *Fr. Cod.*; Essence d'Anis, *Fr.*; Oleum Anisi, *P. G.*; Anethol, Anisöl, *G.*; Essenza di anice, *It.*; Esencia de anis, *Sp.*

The product of oil from anise is variously stated at from 1.56 to 3.12 per cent. The oil employed in this country is imported. It is colorless or yellowish, with the peculiar odor and taste of the seed. At 10° C. (50° F.) it crystallizes in flat tables, and it does not melt under 16.6° C. (62° F.). Its sp. gr. increases with age, and is variously given at from 0.9768 to 0.9903. It is soluble in all proportions in alcohol of 0.806; but alcohol of 0.840 dissolves at 25° C. (77° F.) only 42 per cent. Ether dissolves oil of anise in all proportions.

Properties.—"Oil of Anise is a colorless or pale yellow, strongly refractive liquid, having the characteristic odor and taste of anise. It is soluble with not more than a slight cloudiness in 3 volumes of 90 per cent. alcohol. Specific gravity: 0.978 to 0.988 at 25° C. (77° F.). Refractive index: 1.544 to 1.560 at 20° C. (68° F.) (see Part III, Test No. 22). The optical rotation varies from +1° to −2° in a 100 mm. tube at 25° C. (77° F.) (*oil of fennel*) (see Part III, Test No. 21). An alcoholic solution prepared as above is neutral to litmus and develops no blue or brownish color upon the addition of a drop of ferric chloride T.S. (*phenols*). It does not respond to the Test for heavy metals in volatile oils (see Part III, Test

No. 3). When tested by the following method, the congealing point of the Oil does not fall below 15° C. (59° F.). Transfer about 10 mils of the Oil to a test tube, place it in a water bath cooled with ice, insert a thermometer at once into the Oil and allow it to remain undisturbed until the temperature has fallen to about 12° C. (53.6° F.). Then induce crystallization either by rubbing the inner wall of the test tube with the thermometer or by the addition of a particle of solid anethol, remove the test tube from the bath and stir during the solidification of the Oil. The highest temperature reached during the crystallization is regarded as the congealing point." *U. S.*

"Colorless or pale yellow. Odor that of Anise Fruit; taste sweet and aromatic. Specific gravity at 20° C. (68° F.) (compared with *water* at 15.5° C. (60° F.)) 0.975 to 0.990; *optical rotation* –2° to + 1°; *refractive index* at 25° C. (77° F.) 1.552 to 1.558. Congeals, when stirred, at about 15.5° C. (60° F.), and does not again liquefy below 17° C. (62.6 ° F.). Not less than 80 per cent. distils between 225° and 235° C. (437° and 455° F.). Soluble in 3 parts of *alcohol* (90 per cent.)." *Br.*

It consists of a small quantity of terpene, $C_{10}H_{16}$, but mainly of *anethol,* parapropenylanisol, $C_6H_4C_3H_5OCH_3$ (about 85 per cent.), which is present, however, in two isomeric modifications, one solid at ordinary temperatures and heavier than water (*solid anethol*), the other liquid and more volatile (*estragol* or *methyl chavicol*). *Anethol,* both in the liquid and in the solid form, is present, and is the chief constituent of the oils of anise, star ansie, and fennel. The solidification test of the U. S. P. IX is based upon the anethol content. By oxidation, by means of nitric acid, or chromic anhydride, the different forms of anethol yield *anisic acid,* $C_8H_8O_3$. Oil of anise, by exposure to air, is oxidized with the formation of anisic aldehyde, acetic aldehyde and anisic acid, and becomes less disposed to congeal.

Star anise oil contains besides anethol, pinene and phellandrene and some samples have been reported as containing safrol which is present to an appreciable extent in the so-called Japanese star anise oil which is from the leaves instead of the fruit. This latter oil contains eugenol as well as much less anethol than the oil from the fruit.

In consequence of its high price, it is frequently adulterated with spermaceti, wax, or camphor. The first two may be detected by their insolubility in cold alcohol, the last by its odor. In one instance as much as 35 per cent. of spermaceti was found. Schimmel & Co. have found fennel stearoptene in commercial oil of anise. (*Ph. Rev.*, 1897, 94.) Procter met with a parcel, of which not less than five-sixths was alcohol. (*A. J. P.*, xxvii, 513.) Its comparative mildness adapts it to infantile cases. Most of the oil of anise of commerce is the *oil of star aniseed* (*Oleum Badiani*, or *Oleum Illicii*). Oil of anise has also been distilled from the sweet cicely, *Osmorrhiza longistylis,* of the United States and Canada. (*Ph. Rund.*, July, 1887.) For description and analysis of Russian oil of anise, see *P. J.*, 1896, 164, also 243. Anisic acid is said to be antiseptic, resembling salicylic acid in its action.

Anethol which was official in the U. S. P. VIII is now recognized by the N. F. The description and tests are as follows: "The methyl ether of para-propenyl phenol [$C_6H_4.C_3H_5.OCH_3 = 148.1$]. It is the main constituent in the oils of anise, star anise, and fennel, and is usually obtained from these by fractioning, chilling and crystallizing. Preserve it in well-stoppered, amber-colored bottles protected from light and air. Anethol is a colorless or faintly yellow, highly refractive liquid at a temperature of 23° C. (73.4° F.) or above, having a sweet taste and the aromatic odor of anise. At from 20° to 21° C. (68°–69.8° F.) it solidifies to a white, glistening, crystalline mass which remelts at from 22° to 23° C. (71.6°–73.4° F.). Anethol is almost insoluble in water, readily soluble in ether or chloroform, and forms a clear solution with two volumes of alcohol. Specific gravity: 0.984 to 0.986 at 25° C. (77° F.). Boiling point: 232° to 234° C. (449.6°–453.2° F.). Refractive index: 1.5 at 20° C. (68° F.). It is optically inactive or shows a deviation of not more than 0.08° in a 100 mm. tube at 25° C. (77° F.), due to slight traces of the oil from which the Anethol has been prepared (if prepared from oil of anise, this deviation will be lævorotatory, if from oil of fennel, dextrorotatory). Shake 10 mils of Anethol with 50 mils of a saturated aqueous solution of sodium bisulphite in a graduated cylinder and allow the mixture to stand for six hours. No appreciable diminution in the volume of Anethol will be observed nor does a crystalline deposit separate (*aldehydes*)." *N. F.*

Uses.—As a flavoring agent the oil of anise rivals any of the aromatic oils in the extent of its applicability. It is especially enjoyed by young children. Therapeutically it is useful to stimulate peristalsis in *colic* and, according to Kobert, also as an *expectorant.* It has also been recommended as a means of destroying body vermin.

Dose, from three to five minims (0.2–0.3 mil).

Off. Prep.—Aqua Anisi, *U. S.;* Elixir Aromaticum (from Spirit), *U. S.;* Spiritus Anisi, *U. S., Br.;* Spiritus Aurantii Compositus, *U. S.*

OLEUM ANTHEMIDIS. Br.

OIL OF CHAMOMILE

(ō'lē-ŭm an-thĕm'ĭ-dīs)

"Oil of Chamomile is the oil distilled from Chamomile Flowers." *Br.*

Oleum Chamomillæ Romanæ; Essence de Camomille romaine, *Fr.;* Römisch-Kamillenöl, *G.*

This oil was introduced into the British Pharmacopœia 1885 with the direction that it should be distilled in Britain. No such restriction is found in the Pharmacopœia of 1898 or 1914. It is seldom prepared in this country. Baumé obtained thirteen drachms of the oil from

eighty-two pounds of the flowers; according to Brande, the average product of 100 pounds is two pounds twelve ounces. It has the peculiar odor of chamomile, with a pungent somewhat aromatic taste.

It is "blue when freshly distilled, but gradually becoming greenish or brownish-yellow under the influence of air and light. Odor that of Chamomile Flowers; taste aromatic, characteristic. Specific gravity 0.905 to 0.915. *Optical rotation* —1° to +3°; *refractive index* at 25° C. (77° F.) about 1.445. Soluble in less than 1 part of *alcohol* (90 per cent.)." *Br.*

The oil was thoroughly investigated in Fittig's laboratory during the years 1878–1879. It was found to consist of a mixture of angelic, butyric, methacrylic, and tiglinic esters of isobutyl, isoamyl, hexyl, and probably a higher alcohol. *Angelic acid* and *tiglinic acid* are isomeric, and have the formula $C_5H_8O_2$. The relative proportions of these two acids varied in different oils. An ester of a lower homologue of angelic acid having the formula $C_4H_6O_2$ was also obtained. Naudin obtained a small amount of a solid paraffin, $C_{18}H_{36}$, melting at 63° C. to 64° C. (145.4°–147.2° F.), to which the name of *"anthemen"* was given. (Gildemeister and Hoffmann, *Aetherische Oele,* p. 881.) An isomer of camphor has also been reported. It has sometimes been employed in spasm of the stomach, and as an adjunct to purgative medicines. Its chief use, however, appears to be as an ingredient of the extract of chamomile of the British Pharmacopœia, to which it is added in order to supply the place of the oil driven off by the heat used in its preparation. This oil must not be confounded with that of *Matricaria Chamomilla,* employed on the continent of Europe under the name of oil of chamomile. (See *Matricaria.*)

Dose, one to three minims (0.06–0.2 mil).

OLEUM ARACHIS. Br.

ARACHIS OIL

(ō'lę-ŭm ą-rā'ȼhĭs)

Arachis Oil is the oil expressed from the seeds of Arachis hypogæa, *Linn.*

Earth-nut Oil, Ground-nut Oil, Pea-nut Oil.

For description of the pea-nut plant (*Arachis hypogæa*) see Part II. The oil consists of the glycerides of four different fatty acids. The chief of these is oleic acid, $C_{18}H_{34}O_2$, with which are associated *linoleic acid,* $C_{18}H_{32}O_2$, *hypogæic acid,* $C_{16}H_{30}O_2$, *arachidic acid,* $C_{20}H_{40}O_2$, and *lignoceric acid,* $C_{24}H_{48}O_2$. It should be obtained by expression without heat. It is usually of a pale yellowish or green color with a faint odor, and a more distinct taste of the nuts, although on rectification a nearly colorless and tasteless oil may be obtained. Upon exposure to the air the oil slowly thickens and becomes rancid. It is soluble in all proportions in ether, chloroform, and petroleum benzin, but insoluble in alcohol.

"Pale yellow or greenish-yellow. Faint, nut-like odor; taste bland, nutty. Specific gravity 0.916 to 0.921; *saponification value* 190 to 196; *iodine value* 83 to 101; *acid value* not more than 6; *refractive index* at 40° C. (104° F.) 1.4628 to 1.4645. When 1 millilitre of the Oil and 15 millilitres of *N/1 alcoholic solution of potassium hydroxide* are boiled for twenty minutes in a flask provided with a reflux condenser, set aside for twenty-four hours at a temperature not exceeding 15.5° C. (60° F.), and afterwards heated on a water-bath for three minutes, the solution deposits crystals on standing. When a mixture of 2 millilitres of the Oil and 1 millilitre of *hydrochloric acid* containing 1 per cent. of *refined sugar* is shaken for half a minute, and allowed to stand for five minutes, the acid layer does not become pink (absence of sesame oil). When 2 millilitres of the Oil are mixed with 1 millilitre of *amylic alcohol* and 1 millilitre of a solution (1 in 100) of *precipitated sulphur* in *carbon disulphide,* and the mixture heated in a test-tube immersed in boiling *water,* no red color is developed within fifteen minutes (absence of cotton seed oil)." *Br.*

At 3.3° C. (38° F.) it thickens, solidifies at about –5° C. (23°F.), and at 326.6° C. (620° F.) is decomposed, giving out spontaneously inflammable vapors. Winter made experiments to ascertain how far it might be employed with advantage in pharmacy, and found that it answered well in the preparation of cerates and ointments, but would not serve as a substitute for olive oil in the preparation of lead plaster. (See *Proc. A. Ph. A.,* 1897, 179.) Its use is permitted, by the British Pharmacopœia, in India, and in the Eastern, African, and Australasian Divisions of the Empire, for making the official Liniments, Ointments, Plasters, and Soaps for which Olive Oil is directed to be used. It is a non-drying oil, and therefore will not answer for painting; but it is enormously used for adulteration (particularly of French olive oils) and for various purposes in the arts, as for lubricating machinery, and in the manufacture of woollen cloths; in lamps it burns with a bright light. It saponifies slowly, but yields an excellent firm, white, and odorless soap.

OLEUM AURANTII. U. S.

OIL OF ORANGE Ol. Aurant. [Oleum Aurantii Corticis, U. S. VIII Orange Oil, Oil of Sweet Orange]

(ō'lę-ŭm âu-răn'tĭ-ī)

"A volatile oil obtained by expression from the fresh peel of sweet orange, *Citrus Aurantium sinensis* Gallesio (Fam. *Rutaceæ*), and its varieties. Preserve it in small, well-stoppered, amber-colored bottles, in a cool place, protected from light. Oil of Orange having a terebinthinate odor is not to be dispensed." *U. S.*

Oleum Aurantiorum; Essential Oil of Orange Peel, Essence of Orange; Huile volatile d'Orange, *Fr. Cod.;* Apfelsinenchar-enöl, Pomeranzenschalenöl, *G.;* Essenza di arancio amara, Essenza della corteccia, *It.*

This oil is used only for flavoring purposes, and has been introduced principally because of its employment in elixirs and in *Spiritus Aurantii Compositus.*

Oil of orange is prepared in Calabria and Sicily in three ways: 1, by scraping off the exterior part of the rind and submitting it to expression; 2, by putting the scrapings into hot water, depressing the pulp beneath, and skimming off the oil as it rises; 3, by distillation. The best Sicily orange oil is procured by dexterous compression, within a cask, of the fresh rind by the hand, the oil being driven out in jets. It is sometimes absorbed by a sponge. (*A. J. P.*, 1868.) It is largely made at Messina, and in the south of France. It is also extracted by the écuelle process, and partly from the Bigarade and partly from the sweet or Portugal orange, the scarcely ripe fruit being in either case employed. The oil made from the former is much more valuable than that obtained from the latter, and the two are distinguished in price-currents as *Essence de Bigarade* and *Essence de Portugal.*

Under the name of *Oleum Aurantii Amari* (Oil of Bitter Orange), the National Formulary IV has introduced the oil of bitter orange, which it defines as "a volatile oil obtained by expression from the fresh peel of the bitter orange, *Citrus Aurantium amara* Linné (Fam. *Rutaceæ*). Preserve it in small, well-stoppered, amber-colored bottles, in a cool place, protected from light. "Oil of Bitter Orange having a terebinthinate odor is not to be dispensed." *N. F. IV.*

The description is as follows: "Oil of Bitter Orange is a pale yellow liquid, having the characteristic, aromatic odor of the Seville orange, and an aromatic somewhat bitter taste. Soluble in 4 volumes of alcohol, the solution being neutral to litmus paper. Also soluble in all proportions in dehydrated alcohol and in an equal volume of glacial acetic acid. Specific gravity: 0.842 to 0.848 at 25° C. (77° F.). It is dextrorotatory, the angle of rotation varying from +92° to +98°, in a 100 mm. tube, at 25° C. (77° F.). Introduce 50 mils of Oil of Bitter Orange into a 200 mil, three-bulb, fractionating flask. Distil the Oil at the rate of 2 mils per minute until a distillate measuring 5 mils has been collected. The angle of rotation of this distillate is equal to, or only slightly lower than, that of the original Oil." *N. F. IV.*

This oil is supposed to have a more delicate odor than the oil from the sweet orange.

Properties.—Oil of orange peel consists, as has been shown by Wallach, of *d-limonene* to the extent of at least 90 per cent.; of the remainder, about 5 per cent. are the odorous constituents, among which are citral, traces of citronellal, and the methyl ester of *anthranilic acid.* The inner thick part of the rind contains also a bitter principle, called *hesperidin,* discovered by Lebreton in 1828, but more fully studied by Hoffmann (*Ber. d. Chem. Ges.*, 1876, pp. 26, 685). It is best prepared from the unripe bitter orange. Its formula is $C_{22}H_{28}O_{12}$, and it is a glucoside, as is shown by the reaction with diluted sulphuric acid, whereby it is decomposed into *hesperetin,* $C_{16}H_{14}O_6$, and glucose, $C_6H_{12}O_6$.

The U. S. Pharmacopœia describes the oil as "a yellow liquid having the characteristic odor and taste of orange peel. Specific gravity: 0.842 to 0.846 at 25° C. (77° F.). Refractive index: 1.4723 to 1.4737 at 20° C. (68° F.) (see Part III, Test No. 22). Its optical rotation is not less than +94° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21). Introduce 50 mils of Oil of Orange into a 200 mil, three-bulb Ladenburg flask of approximately the following dimensions: The lower or main bulb 6 cm. in diameter with the smaller condensing bulbs 3.5 cm., 3.0 cm. and 2.5 cm. in diameter, respectively; with the distance from the bottom of the flask to the side arm 20 cm. Then distil the Oil at the rate of one drop per second until 5 mils has been obtained. The angle of rotation of the distillate thus obtained is equal to or only slightly greater than that of the original Oil, and the refractive index of this portion, at 20° C. (68° F.), is not less than 0.0008 nor more than 0.0015 lower than that of the original Oil at 20° C. (68° F.)." *U. S.*

A waxy non-volatile substance is present in oil of orange, which interferes with the transparency of solution made with 90 per cent. alcohol. This oil is one of the most difficult to preserve. A method for its preservation, which we have used for years, is to shake the oil briskly with one-eighth of its volume of distilled water, and allow it to separate, then remove the essential oil, filter rapidly if necessary, and mix the filtered oil with 95 per cent. alcohol in the proportion of one volume of the oil to seven volumes of alcohol.

It may be preserved indefinitely by adding 10 per cent. of its volume of olive oil.

The oil of orange is used chiefly as a flavoring agent but Zickgraf (*M. M. W.*, 1910, lvii, p. 1070) speaks very highly of its effect in *chronic bronchitis* for the same class of cases in which oil of turpentine is used. It has the advantages over the latter of being much more pleasant to take and non-irritant to the kidneys.

Dose, three to five minims (0.2–0.3 mil).

Off. Prep.—Elixir Aromaticum (from Spirit), *U. S.;* Spiritus Aurantii Compositus, *U. S.;* Elixir Cardamomi Compositum (from Compound Spirit), *U. S.;* Elixir Vanillini Compositum (from Compound Spirit), *N. F.;* Spiritus Cardamomi Compositus, *N. F.;* Spiritus Myreiæ Compositus, *N. F.;* Spiritus Vanillini Compositus, *N. F.*

OLEUM CADINUM. U. S., Br.

OIL OF CADE Ol. Cadin. [Cade Oil Oil of Juniper Tar, Oleum Juniperi Empyreumaticum]

(ō'lę-ŭm cą-dī'nŭm)

"An empyreumatic oil obtained by the dry distillation of the wood of *Juniperus Oxycedrus* Linné (Fam. *Pinaceæ*)." *U. S.* "Oil of Cade is an empyreumatic oily liquid obtained by the destructive distillation of the woody portions of Juniperus Oxycedrus, *Linn.*" *Br.*

Juniper Tar Oil; Huile de Cade, *Fr.;* Kadeöl, Kadiöl, *G.*

The *Juniperus Oxycedrus,* Linné, *prickly*

cedar, or *large brown-fruited juniper,* is a common tree in the waste places and stony hill-sides of the Mediterranean districts of Northern Africa, Spain, Portugal, and France, reaching up in its distribution as high as 3000 feet in the Apennines. It commonly attains a height of from ten to twelve feet, sometimes much more, with long spreading branches and slender drooping branchlets, covered with light-green scattered and spreading leaves of medium size, lanceolate or awl-shaped, sharply pointed, having two furrows on their upper edge. The fruits are numerous, large (half an inch in diameter), globular, shining, reddish or chestnut-brown, and marked on the apex with two white scars indicating the separation of the carpels.

From the heart-wood of this tree the oil of cade is prepared by a process of distillation in ovens *per descensum,* similar to that practised in the making of ordinary tar. It is a brownish or dark brown liquid, much more mobile and less thick than tar, having a tar-like but distinct odor, and a smoky, acrid, bitterish, disagreeable taste. In mass it is dark and opaque, but in very thin layers clear; the oil contains phenols and a sesquiterpene termed *cadinene,* $C_{15}H_{24}$, the latter boiling at from 274° to 275° C. (525.2°–527° F.), and having a sp. gr. of 0.918 at 20° C. (68° F.).

"Oil of Cade is a dark brown, clear, thick liquid, having a tarry, empyreumatic odor and a warm, faintly aromatic, and bitter taste. It is almost insoluble in water, but imparts to it an acid reaction. It is only partially soluble in alcohol or petroleum benzin, completely soluble in 3 volumes of ether, soluble in amyl alcohol, chloroform, glacial acetic acid, or oil of turpentine. Specific gravity: 0.980 to 1.055 at 25° C. (77° F.). Shake 1 part of Oil of Cade with 20 parts of warm distilled water and filter; separate portions of this filtrate give a red coloration with a few drops of ferric chloride solution (1 in 1000) and reduce silver ammonium nitrate T.S. in the cold and alkaline cupric tartrate T.S. on heating. Agitate 1 mil of Oil of Cade with 15 mils of purified petroleum benzin, filter the benzin solution, add an equal volume of copper acetate solution (1 in 100), shake the mixture and then allow it to separate. On adding an equal volume of ether to the separated benzin solution, it produces no intensely green coloration and does not become colored more than light yellow to brown (*rosin and rosin oil*)." *U. S.*

"A dark reddish-brown or nearly black, oily liquid. Empyreumatic odor; taste aromatic, bitter and acrid. Specific gravity about 0.990. Soluble in *ether,* and in *chloroform;* partially soluble in cold, almost wholly soluble in hot *alcohol* (90 per cent.); very slightly soluble in *water,* the filtered aqueous solution being almost colorless and acid to *litmus.* Yields no reaction for pine tar when tested as follows: Shake 1 millilitre of the Oil vigorously with 15 millilitres of *petroleum spirit,* and filter; to 10 millilitres of the filtrate add 10 millilitres of *solution of copper acetate,* shake vigorously, and set aside until separation into two layers is complete; 5 millilitres of the upper layer, when mixed with 10 millilitres of *ether,* become pale brownish-yellow, but not green (absence of pine tar)." *Br.*

Yaucher recommends acetone for disguising the odor of oil of cade, and proposes an *oil of cade collodion* in which acetone is used to dissolve the pyroxylin instead of the usual solvents. (*C. D.,* 1897, 16.)

Uses.—Oil of cade has been used locally, by the peasantry, in the treatment of the cutaneous diseases of domestic animals almost from time immemorial. More recently it has been largely employed in the treatment of *chronic eczema, psoriasis,* and other skin diseases of man, and has also been found to be an efficient parasiticide in *psora* and *favus.* It is applied, sometimes of full strength, sometimes diluted with a bland oil, well rubbed into the affected parts with the fingers, or with a cloth, and is also made into ointments, and especially into soaps. A glycerite is also prepared. It is very rarely, if ever, used internally, but probably resembles oil of tar in its physiological action.

Dose, one to three minims (0.06–0.2 mil).

Off. Prep.—Linimentum Saponis Mollis Compositum, *N. F.;* Petroxolinum Cadini, *N. F.;* Petroxolinum Sulphuratum Compositum, *N. F.;* Unguentum Sulphuris Compositum, *N. F.*

OLEUM CAJUPUTI. U. S., Br.

OIL OF CAJUPUT Ol. Cajup. [Cajuput Oil Oil of Cajeput]

(ō'lę-ŭm căj-ų-pū'tī)

"A volatile oil distilled from the fresh leaves and twigs of several varieties of *Melaleuca Leucadendron* Linné, especially the var. *Cajeputi* Roxburgh and the var. *minor* Smith (Fam. *Myrtaceæ*). Preserve it in well-stoppered, amber-colored bottles, in a cool place." *U. S.* "Oil of Cajuput is the oil distilled from the leaves of Melaleuca Leucadendron, *Linn.,* and other species of Melaleuca." *Br.*

Oleum Cajeputi; Essence de Cajeput, Huile volatile de Cajeput, *Fr.;* Cajeputöl, *G.;* Essenza di Cajeput, *It.;* Esencia de Cayeput, *Sp.;* Kayuputieh, *Mal.*

It was long supposed that the *oil of cajuput* was derived only from *Melaleuca Leucadendron,* but it is now well established that it is derived chiefly from one or more varieties of this species. They are trees indigenous to upper India, the Islands of the Indian Ocean, Northern Australia, Queensland and New South Wales. (See *The Volatile Oils,* Gildemeister and Hoffmann.) It is possible, however, that the oil may also be obtained from different species of *Melaleuca,* as Stickel of Jena, succeeded in procuring from the leaves of *M. hypericifolia,* cultivated in the botanical garden of that place, a specimen of oil not distinguishable from the cajuput oil of commerce, except by a pale-green color. (*Ann. Pharm.,* xix, 224.) *M. viridifolia* and *M. latifolia,* large trees growing abundantly in the Island of New Caledonia, yield a volatile oil very analogous to the oil of cajuput.

Melaleuca Leucadendron Linné (*M. Cajuputi*

Rumphius) grows with an erect but crooked stem, and scattered branches, the slender twigs of which droop like those of the weeping willow. The bark is of a whitish ash color, very thick, soft, spongy, and lamellated, throwing off its exterior layer from time to time in flakes. The leaves have short footstalks, are alternate, lanceolate, when young sericeous, when full-grown smooth, deep green, three- and five-nerved, slightly falcate, entire, from three to five inches long, from one-half to three-quarters of an inch broad, and when bruised exhale a strong aromatic odor. The flowers are small, white, inodorous, sessile, and disposed in terminal and axillary downy spikes, with solitary, lanceolate, three-flowered bracts. The filaments are three or four times longer than the petals, and both are inserted in the rim of the calyx. The oil is obtained from the leaves by distillation. It is prepared chiefly in Amboyna and Bouro, and is exported from the East Indies in glass bottles. The small proportion yielded by the leaves and the extensive use made of it in India render it somewhat costly.

Properties.—Cajuput oil is very fluid, transparent, of a fine green color, a lively and penetrating odor analogous to that of camphor and cardamom, and a warm, pungent taste. Upon rectification the green color disappears. It is very volatile and inflammable, burning without any residue. The sp. gr. varies from 0.914 to 0.9274. Its chief constituent has the formula $C_{10}H_{18}O$, and by repeated distillation over phosphoric oxide the hydrocarbon, $C_{10}H_{16}$, called *cajuputene,* can be obtained. The oil is, therefore, said to contain *cajuputene hydrate,* or *cajuputol.* The identity of cajuputol with *cineol* and *eucalyptol* from *Eucalyptus Globulus* in both chemical and physical properties was established by Wallach in 1884 and by C. Jahns (*A. J. P.,* 1885, 237.) It boils at 175° C. (347° F.). A second constituent of the formula $C_{10}H_{18}O$ is the solid *terpineol,* which is present both in the free state and as acetic ester. A small amount of l-pinene and traces of aldehydes have been found, including valeraldehyde and benzaldehyde. (*Schimmel & Co.'s Report,* April, 1897.) Oil of cajuput is "a colorless or yellowish liquid having a peculiar, agreeable, distinctly camphoraceous odor, and an aromatic, slightly bitter taste. It is soluble in 1 volume of 80 per cent. alcohol. Specific gravity: 0.912 to 0.925 at 25° C. (77° F.). Its optical rotation does not exceed –4° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21). It does not respond to the Test for heavy metals in volatile oils (see Part III, Test No. 3)." *U. S.*

"Green or bluish-green. Agreeable, camphoraceous odor; taste aromatic, bitter and camphoraceous. Specific gravity 0.919 to 0.930; *optical rotation* not more than –4°; *refractive index* at 25° C. (77° F.) 1.460 to 1.467. When 10 millilitres of the Oil are mixed with 4 to 5 millilitres of *syrupy phosphoric acid* in a vessel surrounded by a freezing mixture, and then pressed strongly in a piece of fine calico between folds of blotting-paper, the pressed cake, decomposed by warm *water* in a graduated vessel, yields an oily layer, which, on cooling to 15.5° C. (60° F.), measures not less than 4.5 millilitres (presence of not less than 45 per cent. of cineol)." *Br.*

The U. S. requires the oil to be colorless or yellow, but according to the Br. it has a greenish tint. When it is distilled, a light, colorless liquid first comes over, and afterwards a green and denser one. The green color has been ascribed to a salt of copper derived from the vessels in which the distillation is performed, and Guibourt obtained two grains and a half of copper oxide from a pound of the commercial oil. But neither Brande nor Goertner could detect copper in specimens examined by them, and Lesson, who witnessed the process for preparing the oil at Bouro, attributes its color to chlorophyll or some analogous principle, and states that it is rendered colorless by rectification. Guibourt, moreover, obtained a green oil by distilling the leaves of a *Melaleuca* cultivated at Paris. A fair inference is that the oil of cajuput is naturally green, but that as found in commerce it sometimes contains copper, either accidentally present or added with a view of imitating or maintaining the fine color of the oil. The proportion of copper, however, is not so great as to forbid the internal use of the oil, and the metal may be separated by distillation with water, or by agitation with a solution of potassium ferrocyanide. This statement as to the frequent occurrence of copper in the cajuput oil of commerce, though at the same time its presence is not desirable, has been confirmed by experiments by Edward Histed, who found copper in all of six specimens of the commercial oil, obtained from different sources. When redistilled, the oil became perfectly colorless, but after a few days' exposure to copper filings reassumed its green color. (*P. J.,* 1872, p. 804.)

Oil of cajuput is said to be often adulterated with oils derived from other than the official species of *Melaleuca.* Oil of rosemary, and oil of turpentine, impregnated with camphor and colored with the resin of milfoil, are also said to be employed as adulterants. The best test, according to Zeller, is iodine, which, after a moderately energetic reaction, with little increase of temperature and but a slight development of orange vapors, occasions immediate inspissation into a loose coagulum, which soon becomes dry, greenish-brown, brittle mass.

Uses.—This oil is highly stimulant, producing when swallowed, a sense of heat, with an increased fulness and frequency of pulse, and exciting in some instances profuse perspiration. It is much esteemed by the Malays and other people of the East, who consider it a panacea. Formerly the oil of cajuput was used internally in *chronic rheumatism, low fevers,* and various other complaints, but is rarely employed at present for its alterative effects. It is useful internally as a stimulating expectorant in *chronic laryngitis* and *bronchitis,* as a urinary antiseptic in *cystitis,* and as an anthelmintic

especially against the *round worm.* Its most frequent uses, however, are externally in the treatment of various skin diseases. For this latter group of affections it is used for its antiparasitic effect in such diseases as *scabies, tinea versicolor,* etc., and for its stimulating action in *acne rosaceæ, psoriasis,* and other chronic conditions. It is also used externally as a counter-irritant in *chronic rheumatism* and other painful conditions. Like many other essential oils it *relieves toothache* if introduced into the hollow carious tooth.

Dose, from three to ten minims (0.2–0.6 mil).

Off. Prep.—Linimentum Crotonis, *Br.;* Spiritus Cajuputi, *Br.;* Linimentum Tiglii, *N. F.*

OLEUM CARI. U. S. (Br.)

OIL OF CARAWAY Ol. Cari [Caraway Oil]

(ō'lę-ŭm cā'rī)

"A volatile oil distilled from the fruit of *Carum Carvi* Linné (Fam. *Umbelliferæ*), and yielding not less than 50 per cent., by volume, of carvone [$C_{10}H_{14}O = 150.11$]. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.* "Oil of Caraway is the oil distilled from Caraway Fruit, and rectified." *Br.*

Oleum Carui, *Br.;* Huile volatile de Carvi, *Fr. Cod.;* Essence de Carvi, *Fr.;* Oleum Carvi, *P. G.;* Kümmelöl, Carvon, *G.*

This oil is prepared to a considerable extent by our distillers. The fresh fruit as cultivated in Holland yields nearly 6 per cent. of oil, while the German fruit yields about 4 per cent. The oil of caraway is somewhat viscid, of a pale yellow color, becoming brownish by age, with the odor of the fruit, and an aromatic acrid taste. Its sp. gr. is differently given at 0.946 (Baumé), 0.931 (Brande), 0.916 (Buignet), and 0.900 to 0.910 at 25° C. (77° F.). (*U. S. P.*) It is dextrogyrate in its relation to polarized light. (Buignet, *J. P. C.,* Oct., 1861, p. 261.) It consists of two liquid oils, of different boiling points, and separable by distillation:—one a hydrocarbon called *carvene,* $C_{10}H_{16}$, of the specific gravity 0.849 and boiling point 176° C. (349° F.), now recognized as identical with d-limonene, the other, the valuable constituent, *d-carvone,* $C_{10}H_{14}O$, of the sp. gr. 0.9638 and boiling point 224° C. (435° F.). This latter constituent is often extracted from the oil and prepared in a pure state by taking advantage of the formation of a crystalline compound of carvone and hydrogen sulphide, which can then be decomposed by treatment with alcoholic potassium hydroxide.

Sulphides are found in the aqueous distillate which comes over with the oil, as are also several constituents which are ordinarily considered only to accompany destructive distillation products as methyl alcohol, acetaldehyde, etc.

Properties.—It is officially described as "a colorless or pale yellow liquid, having the characteristic odor and taste of caraway. It is soluble in 8 volumes of 80 per cent. alcohol. Specific gravity: 0.900 to 0.910 at 25° C. (77° F.). Its optical rotation varies between +70° and +80° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21)." *U. S.*

"Colorless or pale yellow. Odor and taste those of Caraway Fruit. Specific gravity 0.910 to 0.920; *optical rotation* +75° to +82°; *refractive index* at 25° C. (77° F.) 1.485 to 1.497. Soluble in 1 part of *alcohol* (90 per cent.), and in 10 parts of a mixture of equal volumes of *alcohol* (90 per cent.) and *alcohol* (70 per cent.). When fractionally distilled from a distillation flask at the rate of one drop per second, not less than 50 per cent. distils at a temperature above 200° C. (392° F.)." *Br.*

"**Assay.**—Introduce 10 mils of the Oil into a 200 mil flask with a long graduated neck (cassia flask) by means of a pipette, add 50 mils of a saturated solution of sodium sulphite, which has been carefully rendered neutral to phenolphthalein T.S. by means of acetic acid, heat the mixture in a bath containing boiling water and shake the flask repeatedly, neutralizing the mixture from time to time by the addition of a few drops of diluted acetic acid. When no coloration appears, upon the addition of a few more drops of phenolphthalein T.S. and heating for fifteen minutes, cool, and, when the liquids have separated completely, add sufficient of the sodium sulphite solution to raise the lower limit of the oily layer within the graduated portion of the neck and note the volume of the residual liquid. This measures not more than 5 mils, indicating the presence of not less than 50 per cent., by volume, of carvone." *U. S.*

For additional tests, see *Schim. Rep.,* 1893, 10; also *Bull. Pharm.,* 1894, 257. Kremers and Schreiner (*Ph. Rev.,* xiv, 76) recommend a method of determining the value of oil of caraway based on the conversion of carvone into its oxime, and the separation of the carvoxime from the terpenes by steam distillation; it is as follows: "To a solution of 10 Gm. of oil, dissolved in 25 mils of alcohol, 5 Gm. of hydroxylamine hydrochloride and 6.5 Gm. of sodium bicarbonate are added. This mixture is boiled on a water bath for half an hour in a flask connected with a reflux condenser, 25 mils of water are then added, and the alcohol is distilled off on the water bath. Steam is then passed through the liquid until traces of carvoxime come over. The last portions of the distillate are collected separately in test tubes, and when traces of crystals of carvoxime appear on the surface, the operation is interrupted. The tube of the condenser is washed with a little hot water, and this, as well as the last collected distillate, containing some carvoxime, is returned to the flask. The contents of the flask are allowed to cool, and after the carvoxime has completely solidified, it is removed from the sides of the flask by means of a loop of stiff wire, thrown upon a force filter, washed, and dried by suction. The air-dried carvoxime is transferred to a tared glass dish and heated for 1 hour on a water bath, and when cool, weighed. To the weight thus obtained 0.100 Gm. is added, as this is about the quantity lost during heating. From the

weight of the carvoxime that of the carvone may be readily calculated, 164.67 parts of the former corresponding to 149.66 parts of the latter, or the weight of carvoxime obtained, expressed in Gm., when multiplied by 0.9088, gives he weight of the equivalent amount of carvone."

When oil of caraway is distilled over glacial phosphoric acid or powdered sodium hydroxide, the distilled liquor being poured back into the retort until it ceases to have the odor of caraway, it yields carvacrol. (See Part II.)

Oil of caraway is used to impart flavor to medicines, and to correct their nauseating and griping effects.

Gmeiner (*B. Thier. W.*, 1909, p. 695) recommends the use of oil of caraway in the treatment of *scabies*. He employs a solution in castor oil containing five parts of alcohol and oil of caraway in seventy-five parts of castor oil.

Dose, from one to five minims (0.06–0.3 mil).

Off. Prep.—Pilula Aloes, *Br.;* Spiritus Juniperi Compositus, *U. S.;* Elixir Cardamomi Compositum (from Compound Spirit), *N. F.;* Mistura Carminativa, *N. F.;* Spiritus Cardamomi Compositus, *N. F.*

OLEUM CARYOPHYLLI. U. S., Br.

OIL OF CLOVE Ol. Caryoph. [Clove Oil Oil of Cloves]

(ō'lę-ŭm căr-ŷ-o-phŷl'lī)

"A volatile oil distilled from the flower-buds of *Eugenia Aromatica* (Linné) O. Kuntze [*Jambosa Caryophyllus* (Sprengel) Niedenzu] (Fam. *Myrtaceæ*), and yielding not less than 82 per cent., by volume, of eugenol [$C_{10}H_{12}O_2$ = 164.10]. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.* "Oil of Cloves is the oil distilled from Cloves." *Br.*

Huile volatile de Girofle, *Fr. Cod.;* Oleum Caryophyllorum, *P. G.;* Nelkenöl, Eugenol, *G.;* Essenza di garofani, *It.;* Esencia de clavo, *Sp.*

This oil is obtained by distilling cloves with water, to which it is customary to add common salt, in order to raise the temperature of ebullition, and the water should be repeatedly distilled from the same cloves, in order completely to exhaust them. Scharling has found advantage from the application of superheated steam to the distillation of this oil. (*P. J.*, xi, 469.) It is essential also to use the same water over and over again, in order to avoid loss by the solution of the oil in the water. The product of good cloves is said to be about one-fifth or one-sixth of their weight. The oil was formerly brought from Holland or the East Indies, but since the introduction of the Cayenne cloves into our markets the reduced price and superior freshness of the drug have rendered the distillation of oil of clove profitable in this country, and the best now sold is of domestic extraction. The exportation of clove from Zanzibar in 1909 was over 20,000,000 pounds. We have been informed that from seven to nine pounds of clove yield to our distillers about one pound of the oil.

Properties.—Oil of cloves, when recently distilled, is very fluid, clear, and colorless (but becomes yellowish by exposure, and ultimately reddish-brown). It has the odor of cloves, a hot, acrid, aromatic taste, and a slightly acid reaction. Its sp. gr. is variously stated at from 1.034 to 1.061, the latter being given by Bonastre as the sp. gr. of the rectified oil.

"Oil of Clove is a colorless or pale yellow liquid, becoming darker and thicker by age and exposure to the air, having the characteristic odor and taste of clove. It is soluble in 2 volumes of 70 per cent. alcohol. Specific gravity: 1.038 to 1.060 at 25° C. (77° F.). Its optical rotation does not exceed –1° 10′ in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21). Shake 1 mil of the Oil with 20 mils of hot distilled water; the water shows not more than a scarcely perceptible acid reaction with litmus. After cooling, pass the aqueous layer through a wetted filter; the clear filtrate, with a drop of ferric chloride T.S., yields only a transient, grayish-green color, but not a blue or violet color (*phenol*).

"**Assay.**—Introduce 10 mils of the Oil into a flask with a long graduated neck (cassia flask), add 50 mils of potassium hydroxide T.S., shake the mixture for five minutes and then heat it on a water bath during ten minutes, cool and when the liquids have separated completely, add sufficient potassium hydroxide T.S. to raise the lower limit of the oily layer within the graduated portion of the neck and note the volume of the residual liquid. This measures not more than 1.8 mils, indicating the presence of not less than 82 per cent., by volume, of eugenol." *U. S.*

"Colorless or pale yellow when fresh, darkening with age and on exposure to air. Odor and taste those of Cloves. Specific gravity 1.047 to 1.065; *refractive index* at 25° C. (77° F.) 1.528 to 1.540. Soluble in 3 parts of *alcohol* (70 per cent.), the solution yielding a blue color with *T. Sol. of ferric chloride.* When 10 millilitres of the Oil are well shaken with 100 millilitres of *solution of sodium hydroxide*, heated on a water-bath in a flask with a narrow graduated neck, and then allowed to stand, the uncombined oil, cooled to 15.5° C. (60° F.), measures not more than 1.5 millilitres (presence of not less than 85 per cent. of eugenol)." *Br.*

Oil of clove is one of the least volatile of the essential oils and requires for congelation a temperature from –17.8° to –20° C. (0° to –4° F.). It is completely soluble in alcohol, ether, and strong acetic acid. Nitric acid changes its color to a deep red, and converts it by the aid of heat into oxalic acid. The same change to red is produced by nitric acid on morphine, but in this case the red is followed by yellow, which does not happen with the oil of clove. Besides, if to a solution of morphine with nitric acid a solution of chlorinated lime be added, and the mixture be exposed for some hours to the light, the solution of morphine will retain a straw color, while if oil of clove be treated in the same manner the color disappears. (Haselden, *B. F. M. R.*, July, 1867, 265.) It is frequent adulterated with fixed oils, and sometimes with oil of pimenta and with copaiba.

When pure, it sinks in distilled water. According to E. Scherer, these adulterations may sometimes be detected by attention to the specific gravity and the boiling point, pure oil of clove varying in specific gravity from 1.03 to 1.06, and boiling at from 240° C. (464° F.) to 255° C. (491° F.). According to Zeller, its character of congealing entirely into a crystalline mass with the alcoholic solution of potassium hydroxide, losing at the same time its peculiar odor, affords a sufficient criterion of its purity. This, however, while included among the official tests, is not sufficient, the percentage of eugenol as determined by the official assay being now a requirement.

Oil of clove contains small amounts of vanillin, methyl alcohol and furfurol, but is mainly composed of an unsaturated phenol termed eugenol which is now an official product (see *Eugenol*) and its acetic derivative and a sesquiterpene *caryophyllene*. Eugenol acetyl salicylate has also been reported. The U. S. Pharm. IX introduced an assay process for the eugenol content.

Eugenol, $C_{10}H_{12}O_2$ (see p. 432), has been shown to be the methyl ether of allyl-dioxybenzene, $C_6H_3\begin{cases}C_3H_5\\OCH_3\\OH\end{cases}$. One of its most important reactions is its conversion into *vanillin*. For this purpose it is boiled with acetic anhydride, whereby *aceteugenol* is formed, which, oxidized in weak acid solution by potassium permanganate, yields *acetvanillic acid*, and this with weak potassium hydroxide solution is changed into vanillin, which is then extracted by acidifying and shaking up with ether. (See also *Ph. Era*, 1887, 444.) For the estimation of eugenol in the form of its crystalline benzoyl compound, see *A. J. P.*, 1892, 26 and 508; also *Schim. Rep.*, April, 1892, 28. The characteristic aromatic odor of oil of clove is due to *methylamylketone*, $CH_3.CO.C_5H_{11}$, which has been isolated by the chemists of Schimmel & Co., and found to be present only in minute quantity. (*Ph. Rev.*, 1897, 115.)

Uses.—By virtue of its local irritant effect oil of clove stimulates peristalsis and is frequently a useful remedy in the treatment of *flatulent colic*. It is also an active local anesthetic and is a favorite remedy for *toothache;* for this purpose a small pledget of cotton is saturated with oil and inserted into the carious cavity. It is a powerful germicide, far exceeding phenol in activity, but is not frequently used for this purpose. Eugenol has been used internally in doses of forty-five grains (3 Gm.) *per diem* as an antiseptic antipyretic. Little, however, is known of its physiological action. According to Leubuscher (*W. M. Bl.*, 1889) it is a feeble local anesthetic. Landis (*T. G.*, 1909, xxxiii, 386) has used oil of clove as a stimulant expectorant in *tuberculosis* and *bronchiectasis* with good results.

Dose, from two to six minims (0.12–0.4 mil).

Off. Prep.—Elixir Cardamomi Compositum (from Compound Spirit), *N. F.;* Elixir Glycyrrhizæ Aromaticum, *N. F.;* Nebula Aromatica, *N. F.;* Spiritus Cardamomi Compositus, *N. F.*

OLEUM CASSIÆ. U. S. (Br.)

OIL OF CINNAMON Ol. Cass. [Oleum Cinnamomi U. S. VIII Cassia Oil]

(ō'lę-ŭm căs'si-æ)

"A volatile oil distilled from *Cinnamomum Cassia* (Nees) Blume (Fam. *Lauraceæ*), rectified by steam distillation and yielding not less than 80 per cent., by volume, of cinnamic aldehyde [C_9H_8O = 132.06]. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.* "Oil of Cinnamon is the oil distilled from Cinnamon Bark." *Br.*

Oleum Cinnamomi, *Br.;* Oleum Cinnamomi Cassiæ; Oil of Chinese Cinnamon, Essence de Cannelle de Chine, Huile volatile de Cannelle, *Fr.;* Oleum Cinnamomi, *P. G.;* Zimmtöl, Zimmtkassienöl, *G.;* Essenza di Cannella, *It.*

There are two oils of cinnamon in commerce, one procured from the Ceylon cinnamon, the other from the Chinese cinnamon, and often distinguished by the name of *oil of cassia*. There is no essential difference in the two oils, and that of the Chinese cinnamon, as much the cheaper and more abundant of the two, will probably continue to be generally employed, notwithstanding that the Ceylon product has the finer flavor. The U. S. P. IX and the German Pharmacopœia recognize as oil of cinnamon only that obtained from cassia. The British Pharmacopœia and French Codex make Oil of Ceylon Cinnamon official.

Preparation.—Oil of cinnamon of Ceylon is distilled from inferior kinds of cinnamon, of insufficient value to pay the export duty. The following account of the method of extraction is given by Marshall. The bark, having been coarsely powdered, is macerated for two days in sea water, and then submitted to distillation. A light and a heavy oil come over with the water, the former of which separates in a few hours and floats upon the surface, the latter falls to the bottom of the receiver, and continues to be deposited for ten or twelve days. In future distillations, the saturated cinnamon water is employed with sea water to macerate the cinnamon. Eighty pounds of the freshly prepared bark yield about 2.5 ounces of the lighter oil, and 5.5 of the heavier. From the same quantity kept for several years in store, about half an ounce less of each oil is obtained. The two kinds are probably united in the oil of commerce. The oil is also distilled in Ceylon from the leaves, but the product is said to be too small to yield a fair profit. (*C. D.*, 1888.) The exportation of cinnamon chips from Ceylon has assumed large proportions, amounting in 1904 to 2,135,220 pounds. (*Schim. Rep.*, May, 1905.)

Properties.—Oil of Ceylon cinnamon is of a light-yellow color, becoming deeper by age, and ultimately red. Pereira stated that the London druggists redistilled the red oil, and thus obtained two pale-yellow oils, one lighter and the

other heavier than water, with a loss of about 10 per cent. in the process. The oil has the flavor of cinnamon, and when undiluted is excessively hot and pungent. It is said sometimes to have a peppery taste, ascribable to an admixture of the leaves with the bark in the preparation of the oil. *Oil of Ceylon cinnamon* has "a slightly acid reaction. Sp. gr. about 1.040. It is readily soluble in alcohol. When cooled to –10° C. (14° F.), it remains clear, but at a lower temperature a solid portion separates from it." *U. S.* 1880. To ascertain whether, in the distillation of oil of cinnamon from the bark, some of the oil is oxidized to cinnamic aldehyde in part and thus the yield lowered, H. A. Phillips (*Tr. Br. Ph. Conf.*, 1914, 371) made a thorough investigation of the subject and concludes that under the ordinary conditions of steam distillation, cinnamic aldehyde is not appreciably oxidized. The British Pharmacopœia 1914 recognizes oil of Ceylon cinnamon only, and gives the following description and tests: "Yellow when freshly distilled, gradually becoming reddish. Odor and taste those of Cinnamon Bark. Specific gravity 1.000 to 1.030; *optical rotation* –0.5° to –1°; *refractive index* at 25° C. (77° F.) 1.565 to 1.580. Soluble in from 3 to 4 parts of *alcohol* (70 per cent.). 1 drop dissolved in 5 millilitres of *alcohol* (90 per cent.) assumes a pale green, but not a blue or brown coloration, on the addition of 1 drop of *T. Sol. of ferric chloride* (absence of cinnamon leaf oil and cassia oil). Contains from 55 to 65 per cent. of cinnamic aldehyde as determined by the following test: To 10 millilitres of the Oil add 70 millilitres of an aqueous solution (1 in 5) of *sodium sulphite* and sufficient *solution of phenolphthalein* to give a well marked pink coloration. Heat the mixture on a water-bath, shake well, and neutralise with *acetic acid* diluted with twice its volume of *water;* repeat the heating and neutralisation until no further pink coloration is developed, the time occupied being from thirty to forty-five minutes. The oily layer which separates on standing, cooled to 15.5° C. (60° F.), measures not more than 4.5 or less than 3.5 millilitres (presence of 55 to 65 per cent. of cinnamic aldehyde)." *Br.*

Chinese oil of cinnamon is imported from Canton and Singapore. It is pale yellow, becoming red with age. Its flavor is similar to that of the Ceylon oil, though inferior, and it commands a much lower price. It is officially described as follows: "Oil of Cinnamon (Cassia) is a yellowish or brownish liquid, becoming darker and thicker by age and exposure to the air and having the characteristic odor and taste of cinnamon. Specific gravity: 1.045 to 1.063 at 25° C. (77° F.). The optical rotation varies from +1° to –1° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21). It does not respond to the Test for heavy metals in volatile oils (see Part III, Test No. 3). Shake 2 mils of the Oil in a test tube with from 5 to 10 mils of purified petroleum benzin, and decant the latter; this liquid is colorless and does not assume a green color upon shaking it with an equal volume of (1 in 1000) copper acetate solution (*rosin*).

"**Assay.**—Proceed as directed under *Oleum Cari,* using 10 mils of Oil of Cinnamon. It shows not less than 80 per cent., by volume, of cinnamic aldehyde." *U. S.*

The researches of Schimmel & Co. seem to show that the Chinese cassia oil of commerce is distilled from the leaves, leaf-stalks, and young twigs of the cassia plant—probably with broken bark and various refuse products from the tree; also that much of the oil is adulterated with rosin and petroleum. (See official tests above.) The value of cassia oil depends upon the percentage of cinnamic aldehyde which it contains. Cinnamyl acetate and cinnamic acid are also present as well as small amounts of phenylpropyl acetate and orthocumaric aldehyde. In the oil of Ceylon cinnamon, cinnamic aldehyde is the chief constituent, but eugenol is present to the extent of over 5 per cent., and phellandrene has also been reported. Cinnamon leaf oil contains much eugenol and very little cinnamic aldehyde, safrol and benzaldehyde being present as minor constituents. (See *Cinnaldehydum* and the official assay of oil of cinnamon for the percentage of cinnamic aldehyde.) In a series of analyses made by Schimmel & Co. of oils having a specific gravity of 1.064 to 1.065, the proportion of aldehyde varied from 73.5 to 88 per cent. In the distillation by Schimmel & Co. the various portions of the cassia plant obtained from China yielded the following results. 1. Cassia bark, *Cassia lignea* of commerce: yield of essential oil 1.5 per cent.; aldehyde in oil 92 per cent.; sp. gr. 1.035. 2. Cassia buds, *Flores Cassiæ* of commerce: yield of essential oil 1.550 per cent.; aldehyde in oil 80.4 per cent.; sp. gr. 1.026. 3. Cassia budsticks: yield of essential oil 1.64 per cent.; aldehyde in oil 92 per cent.; sp. gr. 1.046. 4. Cassia leaves, leaf-stalks, and young twigs mixed: yield of essential oil 0.77 per cent.; aldehyde in oil 93 per cent.; sp. gr. 1.055. Zeller states that oil of cassia is heavier, less liquid, and sooner rendered turbid by cold, and that in the Ceylon oil, iodine dissolves rapidly, with a considerable increase of heat, and the production of a tough residue, like an extract, while in oil of cassia the reaction is slow, quiet, and with little heat, and the residue is soft or liquid.

The *cinnamon leaf oil,* as formerly imported into Great Britain, was of two kinds, one containing a considerable quantity of a fatty fixed oil, perhaps cinnamon-suet from the fruit, the other a pure volatile oil. The oil was said to be obtained by distilling the leaves after maceration in sea water. It resembled the oil of clove and pimento in sensible properties, having a brownish color, a penetrating, fragrant odor, and a very pungent taste. According to Stenhouse, it was of the sp. gr. 1.053, had an acid reaction, and consisted of eugenol, a neutral substance with the formula $C_{10}H_{16}$, and a minute proportion of benzoic acid. (*P. J.*, xiv, 319.) Schimmel & Co. found it to have a sp. gr. 1.056

to 1.060, and contained 87 per cent. of eugenol, and about 0.1 per cent. of cinnamic aldehyde.

When exposed to the air, the oil absorbs oxygen, and is slowly converted into cinnamic acid, two distinct resins, and water. Of the two resins, one is soluble both in hot and in cold alcohol; the other readily in the former, but sparingly in the latter. *Cinnamic acid,* $C_9H_8O_2$, is colorless, crystalline, sourish, volatilizable, slightly soluble in water, readily dissolved by alcohol, and convertible by nitric acid with heat into benzoic acid. It is sometimes seen in crystals in oil of cinnamon which has been long kept. Like benzoic acid, it is said when swallowed to cause the elimination of hippuric acid by the urine. (*J. P. C.,* 3e sér., iii, 64.) It may be obtained by distilling the balsam of Tolu. Oil of cinnamon is almost wholly converted by nitric acid, slowly added, into a crystalline mass, producing a compound of the oil and the acid. These several facts are explained when it is found that oil of cinnamon contains from 75 to 90 per cent. of *cinnamic aldehyde,* C_9H_8O (see *Cinnaldehydum,* U. S. P. VIII), which by moderate oxidation yields the corresponding cinnamic acid, $C_9H_8O_2$, but by more energetic oxidation yields benzoic acid, $C_7H_6O_2$. The oil has been produced artificially by Strecker from styrone, a derivative from styrax (see *Styrax*), and more recently from benzaldehyde and acetaldehyde, a mixture of which is saturated with hydrochloric acid gas, when a condensation takes place, as follows:

$$C_6H_5COH + CH_3COH = C_6H_5.CH:CH.CHO + H_2O$$

Ordinary sodium hydroxide will also bring about the reaction between the two aldehydes, and is to be preferred to hydrochloric acid for this purpose.

Oil of cinnamon is said to be frequently adulterated with oil of cloves, which, according to Ulex, cannot be detected by the odor or taste. Thus sophisticated, it is stated, on the same authority, to evolve a very acrid vapor when a drop is heated on a watch glass, to swell up and evolve red vapors if treated with fuming nitric acid, to remain liquid with concentrated potassium hydroxide, and to assume an indigo-blue color when ferrous chloride is added to its alcoholic solution, none of which reactions occur with pure oil.

Uses.—Although a very powerful germicide the oil of cinnamon, because of its irritant properties, is rarely used in medicine as an antibacterial. It has the cordial and carminative properties of cinnamon, without its astringency, and is much employed as an adjuvant to other medicines, the taste of which it corrects or conceals, while it conciliates the stomach. As a powerful local stimulant, it is sometimes prescribed in *gastrodynia, flatulent colic,* and *gastric debility.* Mitscherlich found six drachms to kill a moderate-sized dog in five hours, and two drachms one in forty hours. Inflammation and corrosion of the gastro-intestinal mucous membrane were observed after death.

Dose, one to three minims (0.06–0.2 mil).

Off. Prep.—Aqua Cinnamomi, *U. S.;* Spiritus Cinnamomi, *U. S., Br.;* Infusum Digitalis (from Water), *U. S.;* Mistura Cretæ (from Water), *U.S.;* Elixir Cardamomi Compositum (from Compound Spirit), *N. F.;* Elixir Glycyrrhizæ Aromaticum, *N. F.;* Elixir Vanillini Compositum (from Compound Spirit), *N. F.;* Mistura Oleo-Balsamica, *N. F.;* Nebula Aromatica, *N. F.;* Nebula Mentholis Composita, *N. F.;* Spiritus Cardamomi Compositus, *N. F.;* Spiritus Vanillini Compositus, *N. F.*

OLEUM CHAULMOOGRÆ. Br.

CHAULMOOGRA OIL

(ō'lę-ŭm ċhâul-moog'rą)

"Chaulmoogra Oil is the fatty oil expressed from the seeds of Taraktogenos Kurzii, *King.*" *Br.*

Oleum Gynocardiæ, Gynocardia oil, Chaulmugra oil.

Under the name of chaulmoogra oil there has long been used in Southeastern portions of Asia a semi-solid fat. This was at one time believed to be derived from the *Gynocardia odorata* and has therefore been erroneously called gynocardia oil, but the investigations of Power (*A. J. P.,* 1915, p. 493) have shown that the oil from the gynocardia seed is very different both in chemical composition and physical properties. The true chaulmoogra oil is derived from the *Taraktogenos Kurzii* King (Fam. *Bixaceæ*). It is possible that some of the commercial oil may also be derived from the species of the allied genus *Hydnocarpus.* The chaulmoogra seeds are from one to one and a quarter inches long, more or less angular or flattened, and yield upon expression, from 25 to 30 per cent., to ether, about 50 per cent. of oil. The commercial oil is obtained by expression, or sometimes by boiling the crushed seeds with water. It is "a brownish-yellow oil or soft fat. Characteristic odor; taste somewhat acrid. Melting point about 22° to 30° C. (71.6°–86° F.). Specific gravity at 45° C. (113° F.) about 0.940; *saponification value* 198 to 213; *iodine value* 96 to 104; *acid value* 21 to 27. Soluble in *ether,* in *chloroform,* and in *carbon disulphide;* partially soluble in cold *alcohol* (90 per cent.); almost entirely soluble in hot *alcohol* (90 per cent.)." *Br.*

The genuine chaulmoogra oil is dextrorotatory, having a specific rotation of about +52°. It consists of the glycerides of cyclic organic acids of which the most important is *chaulmoogric acid,* $C_{18}H_{32}O_2$, melting at 68° C. (154.4° F.), while a homologue, *hydnocarpic acid,* $C_{16}H_{28}O_2$, melts at 60° C. (140° F.). Palmitic acid and a phytosterol are also present.

The so-called chaulmoogra oil, from gynocardia, is optically inactive and contains none of the acids peculiar to the genuine chaulmoogra oil. It consists of glycerides of linolic, palmitic, linolenic, isolinolenic and oleic acids and a phytosterol, as well as a glucoside, *gynocardin,* $C_{13}H_{19}O_9N$, which resembles amygdalin and which

is associated in the seeds with an enzyme, gynocardase.

Uses.—Chaulmoogra oil was originally employed in its native countries both internally and externally in the treatment of *scrofula, skin diseases,* and *rheumatism.* In England it is very widely used as a counter-irritant application in *bruises, sprains,* and similar local inflammations both of man and beast as well as in *open sores* and *wounds.* Its most important use, however, is in the treatment of *leprosy.* There seems to be little doubt that it is the most useful remedy known for this intractable infection, indeed many authorities have claimed that it will often produce complete and permanent cures. For review of the literature see Engel (*Monatsh. f. prakt. Dermat.,* 1909, xlix, p. 290.) It should be used freely both internally and externally. Donato (*Leprosy in the Philippines and Its Treatment,* Manila, 1915) believes that its action is due to the stimulation of leucocytosis. He recommends the following solution for intramuscular injection: Camphorated oil (10 per cent. camphor), chaulmoogra oil (sterilized), of each, 60 mils; resorcinol, 4 Gm.; ether, 2.5 Gm. Of this solution 1 mil (15 minims) is injected intramuscularly every alternate day, gradually increasing the dose up to 8 or 10 mils or until reaction becomes severe.

Unna has proposed, for oral administration, the use of a soap made from the oil as affecting the stomach and intestines less unpleasantly than the oil itself. (See *P. J.,* lxiv, 615.)

Dose, five to ten minims (0.3–0.6 mil) gradually increased to one fluidrachm (3.75 mils).

Off. Prep.—Unguentum Chaulmoogræ, *Br.*

OLEUM CHENOPODII. U. S.

OIL OF CHENOPODIUM Ol. Chenopod. [Oil of American Wormseed]

(ō'lę-ŭm ȩhĕn-ǫ-pō'dĭ-ī)

"A volatile oil distilled from *Chenopodium ambrosioides anthelminticum* Linné (Fam. *Chenopodiaceæ*). Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

Huile volatile d'Ansérine vermifuge, *Fr. Cod.;* Essence de Chénopode anthelmintique, *Fr.;* Amerikanisches Wurmsamenöl, Chenopodiumöl, *G.*

For description of the plant from which this oil is derived see *Chenopodium,* Part II. The oil is largely distilled in Maryland. It is of a light-yellow color when recently distilled, but becomes deeper yellow and even brownish by age. Its reaction is neutral. It has in a high degree the peculiar odor of the plant. It is officially described in the United States Pharmacopœia as "a colorless or pale yellowish liquid, having a characteristic, disagreeable odor and taste. It is soluble in 8 volumes of 70 per cent. alcohol. Specific gravity: 0.955 to 0.980 at 25° C. (77° F.). Its optical rotation varies between –4° and –10° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21)." *U. S.*

When freshly prepared, it has the sp. gr. 0.908, which, according to S. S. Garrigues, is increased by time to 0.960. A portion examined by him, which was of a brownish-yellow color, had the sp. gr. 0.959 at 16.1° C. (61° F.), boiled at 190° C. (374° F.), and was freely soluble in alcohol and ether. He found it to be composed of two distinct oils, separable by distillation; one of these has the formula $C_{10}H_{16}$, and is probably limonene; the other is heavier, and possesses the formula $C_{10}H_{18}O_2$. This constitutes over 50 per cent. of the commercial oil and has been given the name *ascaridol,* which is an unstable organic dioxide, decomposing with explosive violence with inorganic acids. (*A. J. P.,* xxvi, 405.)

Uses.—The oil of chenopodium is used in medicine almost exclusively as an anthelmintic. Although it has been official in the Pharmacopœia for many years, it owes its modern popularity to the investigations of Brunning. (*Z. E. P. T.,* 1905, i, and 1906, iii, p. 564.) This author showed that one part in five thousand paralyzed although it did not kill the round worm of dogs, and that one part in two hundred had a distinct antiseptic action. In mammals, if given in sufficient dose, it depresses the spinal cord and finally kills by arrest of respiration. According to Salant and Livingston (*A. J. Phys.,* 1915, xxxviii) the oil of chenopodium in doses of 0.02 mil per kilo, or more, produces a lowering of the blood pressure through a cardiac action and diminution in the amplitude and rate of respiration. Because of its efficiency, ease of administration, and low toxicity, it is perhaps the most valuable of all the vermifuge remedies. Although originally recommended against the *ascarides* it has been shown to be also of great service against both the *tapeworm* and the *hookworm.* In the comparative studies of Schuffner and Verwoort (*M. M. W.,* 1913, lx, p. 129) it gave better results in uncinariasis than either eucalyptus, betanaphthol, or thymol.

Levy (*J. A. M. A.,* 1914, lxiii, p. 1946) has collected from the literature twelve cases of poisoning by oil of chenopodium of which nine ended fatally. The smallest dose in this series was four drops three times a day for two days, which caused death in a baby one year old. In another case a child of two recovered from a dose of two teaspoonfuls given in the course of one afternoon. The symptoms of poisoning by oil of chenopodium—which may not appear for several hours after taking the oil—are nausea, vomiting, headache followed by drowsiness, ringing in the ears, and sometimes deafness. In the fatal cases there develop coma and convulsions. The usual method of administration is to give from ten to fifteen drops either in sugar or as an emulsion twice a day for two days and followed on the second day by an ounce of castor oil. For children between the ages of six and twelve the dose should be one drop for each year of age.

Dose, five to fifteen minims (0.3–0.9 mil).

OLEUM COPAIBÆ. Br.

OIL OF COPAIBA

(ō'lę-ŭm cọ-pā'i-bæ)

Oil of Copaiva; Oleum Balsami Copaivæ; Essence de Copahu, *Fr.;* Copaivaöl, *G.*

Oil of copaiba was not admitted to the U.S.P. IX. The oil constitutes from one-third to one-half or more of the copaiba. From one specimen of recent copaiba as much as 80 per cent. has been obtained. (*A. J. P.,* xxii, 289.) It is prepared largely by the application of steam heat. As it first comes over it is colorless, but the later product is of a fine greenish hue. By redistillation it may be rendered wholly colorless. It has the odor and taste of copaiba, a neutral reaction, boils at 252° to 256° C. (485.6°–492.8° F.), solidifies, partly crystalline, at –26.1° C. (–15° F.) (Gmelin), is soluble in ether and in an equal weight of absolute alcohol. The oil consists chiefly of *caryophyllene,* a sesquiterpene, $C_{15}H_{24}$. It was officially described as "a colorless or pale yellow liquid, having the characteristic odor of copaiba, and an aromatic, slightly bitter, and pungent taste. Specific gravity: 0.895 to 0.905 at 25° C. (77° F.), increasing with age. It is lævogyrate." *U.S. VIII.*

"Colorless or pale yellow. Odor and taste those of Copaiba. Specific gravity 0.896 to 0.910; *optical rotation* –7° to –35°; *refractive index* at 25° C. (77° F.) 1.494 to 1.500. Distils between 250° and 275° C. (482° and 527° F.). A solution of 1 millilitre of the Oil in 5 millilitres of *glacial acetic acid* does not develop more than a faint violet coloration on the addition of 4 drops of *nitric acid* (absence of gurjun oil). When distilled in a vacuum the first 10 per cent. of the distillate has an *optical rotation* lower than that of the original Oil (absence of oil of African copaiba)." *Br.*

From its want of oxygen, it answers even better than naphtha for preserving potassium, a fact first observed by Durand, of Philadelphia. It dissolves sulphur and phosphorus.

Its effects on the system are those of copaiba. From the experiments of C. Mitscherlich, it is one of the least injurious of the volatile oils to the animal system, six drachms of it having been introduced into the stomach of a rabbit without causing death. Externally it produces much less irritation than does oil of turpentine. It may be used for the same purposes as copaiba.

Dose, five to fifteen minims (0.3–0.9 mil).

OLEUM CORIANDRI. U. S., Br.

OIL OF CORIANDER Ol. Coriand. [Coriander Oil]

(ō'lę-ŭm cō-ri-ăn'drī)

"A volatile oil distilled from the ripe fruit of *Coriandrum sativum* Linné (Fam. *Umbelliferæ*). Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.* "Oil of Coriander is the oil distilled from Coriander Fruit." *Br.*

Essence de Coriandre, *Fr.;* Koriander öl, *G.*

This oil may be obtained by distillation with water from the bruised fruit in the manner directed in the U. S. Pharm. 1870, for volatile oils. The average yield of oil from coriander grown in different countries is from 0.2 to 1 per cent. It is pale yellow and colorless, and has the characteristic odor and taste of coriander, and a neutral reaction. Its sp. gr. is from 0.863 to 0.878 at 25° C. (77° F.), *U. S.,* and its boiling point 150° C. (302° F.). It is an oxygenated oil, consisting chiefly of a compound, *coriandrol,* $C_{10}H_{18}O$. According to Semmler (*Ber. d. Chem. Ges.,* 24, 206), coriandrol boils between 194° and 198° C. (381.2° and 388.4° F.), is optically dextrogyrate, and has a sp. gr. of 0.8679 at 20° C. (68° F.). Coriandrol is now known as dextrogyrate *linalool.* Schimmel & Co. (*Schim. Rep.,* April, 1892) have also found in coriander oil about 5 per cent. of dextropinene. The characteristic odorous principle or principles are unknown. It is officially described as "a colorless or pale yellow liquid, having the characteristic odor and taste of coriander. It is soluble in 3 volumes of 70 per cent. alcohol. Specific gravity: 0.863 to 0.875 at 25° C. (77° F.). The optical rotation varies from +8° to +13° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21)." *U. S.*

"Colorless or pale yellow. Odor and taste those of Coriander Fruit. Specific gravity 0.870 to 0.885; *optical rotation* +8° to +14°; *refractive index* at 25° C. (77° F.) 1.463 to 1.467. Soluble in 3 parts of *alcohol* (70 per cent.)." *Br.*

Oil of coriander is extensively adulterated with colorless rectified oil of orange, which can be detected by its insolubility in 90 per cent. alcohol, in which pure coriander oil dissolves in every proportion; equal parts of oil of orange and 90 per cent. alcohol make a turbid mixture. (*A. J. P.,* Sept., 1878.) The oil has the medicinal properties of the fruit, and, like the aromatic oils generally, may be used to cover the taste or correct the nauseating or griping properties of other medicines. It has the great advantage of being more stable and retaining its agreeable odor longer than any other oil of its class.

Dose, one to three minims (0.06–0.2 mil).

Off. Prep.—Spiritus Aurantii Compositus, *U. S.;* Elixir Aromaticum (from Spirit), *U. S.*

OLEUM CUBEBÆ. U. S., Br.

OIL OF CUBEB Ol. Cubeb. [Cubeb Oil]

(ō'lę-ŭm cū-bē'bæ)

"A volatile oil distilled from the unripe fruit of *Piper Cubeba* Linné filius (Fam. *Piper-*

aceæ). Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.* "Oil of Cubebs is the oil distilled from Cubebs." *Br.*

Oleum Cubebarum; Oil of Cubebs; Huile volatile (Essence) de Cubèbe, *Fr.*; Kubebenöl, *G.*

The oil is obtained from cubeb by grinding the berries, and then distilling with water. From ten pounds Schönwald procured eleven ounces of oil, and this result very nearly coincides with the experiments of Christison, who obtained 7 per cent.; but by better methods of distillation 10 to 18 per cent. have been obtained. When recently distilled from the fruit, the oil is somewhat greenish, becoming yellowish by age, but when carefully redistilled it is colorless. It has the odor of cubeb, a warm, aromatic, camphoraceous taste, and a neutral reaction, is of a consistence approaching that of almond oil, is lighter than water, having the sp. gr. 0.920 (0.910 to 0.930, *Br.*), and when exposed to the air is said to thicken without losing its odor. It is soluble in an equal weight of alcohol. It is described in the U. S. P. IX as follows: "Oil of Cubeb is a colorless or a pale green to yellowish-green liquid, having the characteristic odor and taste of cubeb. Specific gravity: 0.905 to 0.925 at 25° C. (77° F.). Its optical rotation varies from –20° to –40° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21). Its alcoholic solution is neutral to litmus." *U. S.*

"Colorless, pale green, or greenish-yellow. Odor and taste those of Cubebs. Specific gravity 0.910 to 0.930; *optical rotation* –25° to –40°; *refractive index* at 25° C. (77° F.) 1.486 to 1.500. Not less than 60 per cent. distils between 250° and 280° C. (482°–536° F.)." *Br.*

The oil consists chiefly of sesquiterpenes which distil over between 250° and 280° C. (482° and 536° F.), one of which is *cadinene*, $C_{15}H_{24}$, with some dipentene, and probably pinene or camphene. Upon standing, it sometimes deposits rhomboidal prismatic crystals of a stearopten. The camphor of cubeb has the formula $C_{15}H_{26}O$, is fusible at from 66° to 68° C. (150.8°–154.4° F.), and volatilizes without change at from 148° to 150° C. (298.4°–302° F.). According to Schmidt, it does not pre-exist in the cubeb, but is formed by the prolonged action of the air and therefore does not occur in oil distilled from new berries. (*J. P. C.*, June, 1875.) The oil has the aromatic properties of cubeb, but it is probably not the sole active ingredient, as it is much less pungent than the fluidextract or the oleoresin. It may, however, often be advantageously substituted for the powder, the dose to be gradually increased until its effects are obtained, or until it proves offensive to the stomach. It may be given suspended in water by means of sugar, in the form of emulsion, or enclosed in capsules of gelatin.

Dose, five to fifteen minims (0.3–0.9 mil).

OLEUM EUCALYPTI. U. S., Br.

OIL OF EUCALYPTUS Ol. Eucalypt. [Eucalyptus Oil]

(ō'lę-um eu-ca-lyp'tī)

"A volatile oil distilled from the fresh leaves of *Eucalyptus Globulus* Labillardière (Fam. *Myrtaceæ*) or from some other species of *Eucalyptus*, and yielding not less than 70 per cent., by volume, of eucalyptol (cineol) [$C_{10}H_{18}O$ = 154.14]. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.* "Oil of Eucalyptus is the oil distilled from the fresh leaves of Eucalyptus Globulus, *Labill.*, Eucalyptus dumosa, *A. Cunn.*, and other species of Eucalyptus, and rectified." *Br.*

Oil of Eucalyptus Globulus; Huile volatile (Essence) de Eucalyptus, *Fr. Cod.*; Eucalyptusöl, *G.*; Esencia de eucalipto, *Sp.*

Various species of the genus *Eucalyptus*, grown in Australia and Algeria, yield volatile oils in sufficient quantity to be commercial products. Probably the most important of these plants is *E. Globulus*, on account of its high cineol (eucalyptol) content. Large quantities of oil are also distilled from other species, viz., *E. odorata, E. oleosa, E. cuenfolia* and *E. dumosa.*

Oil of eucalyptus is officially described as "a colorless or pale yellow liquid, having a characteristic, aromatic, somewhat camphoraceous odor, and a pungent, spicy, and cooling taste. It is soluble in 4 volumes of 70 per cent. alcohol. Specific gravity: 0.905 to 0.925 at 25° C. (77° F.). Mix 2 mils of the Oil with 4 mils of glacial acetic acid and gradually add 3 mils of a saturated solution of sodium nitrite. When gently stirred, the mixture does not form crystals of phellandrene nitrite (*other eucalyptus oils containing large amounts of phellandrene*)." *U. S.*

"Colorless or pale yellow. Aromatic, camphoraceous odor; taste pungent, leaving a sensation of cold. Specific gravity 0.910 to 0.930; *optical rotation* –10° to +10°. Soluble in 5 parts of *alcohol* (70 per cent.). Contains not less than 55 per cent. by volume of cineol as determined by the process described under 'Oleum Cajuputi.' When 1 millilitre is mixed with 2 millilitres of *glacial acetic acid* and 5 millilitres of *petroleum spirit*, 2 millilitres of a saturated aqueous solution of *sodium nitrite* being added, and the mixture gently shaken, no crystalline precipitate forms in the upper layer (absence of oils containing much phellandrene)." *Br.*

Assay.—"Measure 10 mils of the Oil, from a pipette, into a round-bottom glass dish of 50 mils capacity, which is imbedded in finely broken ice. Add 10 mils of arsenic acid T.S. and stir until precipitation is complete. When the mixture ceases to congeal further, allow it to stand for ten minutes in the ice bath. (If at this point a hard mass is formed, add 5 mils of purified petroleum benzin, and mix the mass well before proceeding with the assay.) Then

transfer it immediately to a hardened filter paper, about 18.5 cm. in diameter, by means of a pliable horn spatula; spread it evenly over the surface of the paper and lay a second hardened filter paper over the top. Wrap several thicknesses of absorbent or filter paper around the hardened filters, and place the whole between the plates of a press and bring to bear all the pressure possible for about one minute. Change the outside absorbent papers and press again, repeating the operation, if necessary, until the eucalyptol arsenate is apparently dry, and separates readily when touched with a spatula. The pressing is not complete when a hard mass remains which is broken up with difficulty; and usually two changes of filter paper are required, pressing each time for about two minutes; if left too long in the press the compound may decompose. Now, transfer the compound completely by means of the horn spatula to a glass funnel inserted into a 100 mil cassia flask with a neck graduated to 10 mils into tenths. Wash the last portions of the precipitate into the flask with a stream of hot distilled water from a wash bottle, assisting the disintegration with a glass rod, place the flask in boiling water and rotate it until the compound is thoroughly broken up. Then add enough distilled water to cause the eucalyptol to rise into the neck of the flask, cool it to room temperature and read its volume. This volume, multiplied by 10, shows the percentage of eucalyptol (cineol) in the Oil." *U. S.*

The official method of assay of this oil for cineol content was developed by Jos. L. Turner and R. C. Holmes. (*A. J. P.*, 1915, p. 101.)

Power has modified the test for phellandrene so as to make it more delicate. According to his directions, 1 mil of the oil is mixed with 5 mils of petroleum benzin, 1 or 2 mils of a concentrated solution of sodium nitrite added, and subsequently glacial acetic acid added, a drop or two at a time, with vigorous agitation after each addition. If phellandrene is present in any considerable amount, its crystalline nitrosite, $C_{10}H_{16}(NO)NO_2$, will separate from the benzin solution. The oil from eucalyptus globulus contains *pinene,* $C_{10}H_{16}$, and *eucalyptol* (or *cineol*), $C_{10}H_{18}O$. Schimmel & Co. also state (*Ber. d. Chem. Ges.*, April, 1888) that they have obtained several of the aldehydes of the fatty series, notably valeraldehyde, and probably butyraldehyde and capronaldehyde, in their distillation of the oil from *Eucalyptus Globulus.*

The valuation of eucalyptus oil being based upon its cineol (eucalyptol) content the commercial oils from other species of eucalyptus are regarded with much less favor for medicinal purposes, because of their variable quality in this respect, and the fact that the other oils contain such constituents as phellandrene, cymene, citronellal, citral and other less known constituents. Cineol being optically inactive and high in its specific gravity communicates specific properties to such oils as contain it in large amounts by which their approximate value or their genuineness may be determined irrespective of the assay for cineol, which, of course, must be the ultimate deciding factor. There is much variation in the physical constants found in the literature of the eucalyptus oils as determined by different observers, and much work yet remains to be done upon the subject.

Eudesmol, $C_{10}H_{16}O$ (possibly a ketone), is the name given to a crystalline camphor obtained from the oil from *E. piperita;* H. G. Smith and R. T. Baker isolated this product, and later H. G. Smith read a paper upon it before the Royal Society of New South Wales. It proved to be isomeric with camphor, but chemically it is shown to have its oxygen atom combined in a different way.

Uses.—In the belief that the medicinal properties of oil of eucalyptus depend upon cineol, the Pharmacopœia rejects those oils which contain chiefly phellandrene, but as a matter of fact, we have no definite knowledge concerning the physiological action of phellandrene. Whether or not the medicinal virtues of the official oil are due entirely to its cineol is uncertain, but many prefer to use the pure eucalyptol to the oil itself.

Oil of eucalyptus is an active germicide, although surpassed in power by many of the other volatile oils. Cineol is probably a less efficient antibacterial agent than oil of eucalyptus. When taken in overdose it causes rapidity of the pulse with general excitement and restlessness, nausea, vomiting, frequently dilatation of the pupils, and symptoms of collapse. In the lower animals it reduces the arterial pressure and the bodily temperature, causes muscular weakness, irregular respiration and death from respiratory failure. It is absorbed from the intestinal tract, eliminated partially through the breath to which it imparts its odor, and also, as an oxidation product, through the urine to which it gives an odor resembling that of violets.

The oil of eucalyptus is used locally as an antiseptic, especially in the treatment of infections of the upper respiratory tract and in certain forms of *skin disease.* Internally it is used as a stimulating expectorant in *chronic bronchitis* and *tuberculosis.* In these conditions it is also frequently given by inhalation; a few drops of the oil may be added to boiling water and the mixed vapors and steam inhaled. It has been specially praised in *asthma,* given internally or preferably by inhalation by means of cigarettes, which may be made by rolling up the dried leaves, or the vapor from boiling water containing the oil may be inhaled. It is also used as a remedy against the *hookworm,* but is probably of inferior value. It possesses also some antiperiodic power and may be used in *malarial fever* when for any reason quinine or methylthionine are not available.

Dose, three to ten minims (0.2–0.6 mil), best administered in emulsion.

Off. Prep.—Unguentum Eucalypti, *Br.*

OLEUM FŒNICULI. U. S.

OIL OF FENNEL Ol. Fœnic. [Fennel Oil]

(ō'lę-ŭm fœ-nĭc'ù-lī)

"A volatile oil distilled from the ripe fruit collected from cultivated varieties of *Fœniculum vulgare* Miller (Fam. *Umbelliferæ*). If wholly or partly solidified, carefully warm the Oil until liquefied and thoroughly mix it before dispensing. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

Huile volatile de Fenouil, *Fr. Cod.*; Essence de Fenouil, *Fr.*; Oleum Fœniculi, *P. G.*; Fenchelöl, *G.*

Fennel seeds yield about 2.5 per cent., or, according to Zeller, from 3.4 to 3.8 per cent., of oil. That used in this country is imported. "A colorless or pale yellow liquid, having the characteristic odor and taste of fennel. It is soluble in 8 volumes of 80 per cent. alcohol and in 1 volume of 90 per cent. alcohol, forming a solution neutral to litmus. Specific gravity: 0.953 to 0.973 at 25° C. (77° F.). The optical rotation varies from +12° to +24° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21). When tested by the method under *Oleum Anisi*, with the following modifications, the congealing point of the Oil does not fall below 3° C. (37.4° F.). Cool the test tube containing the 10 mils of Oil of Fennel in a freezing mixture until the temperature has fallen to 0° C. (32° F.), and induce crystallization as directed." *U. S.*

It congeals below 10° C. (50° F.) into a crystalline mass, separable by pressure into a solid and a liquid portion, the former heavier than water, and less volatile than the latter, which rises first when the oil is distilled. It contains *anethol*, $C_{10}H_{12}O$ (a phenol-ether forming a white solid melting at 21° C. (69.8° F.)) (see *Oleum Anisi*), the latter usually in amounts of about 60 per cent., d-pinene, phellandrene, dipentene, *fenchone*, $C_{10}H_{16}O$ (a liquid ketone), chavicol, anisic aldehyde, and anisic acid. Fenchone is the constituent which when present gives the disagreeable bitter taste to many of the commercial oils. *Schimmel's Report* for April, 1897, mentions limonene as also at times present as a constituent. Umney finds that Japanese oil contains about 75 per cent. of anethol and 10 per cent. of fenchone, besides terpenes. (*Proc. A. Ph. A.*, 1897, 516.) There is reason to believe that much of the commercial oil is adulterated with oil from which the anethol or crystalline constituent has been separated; the official solidifying point not below 5° C. (41° F.) should be required. Flückiger states (*Pharm. Chem.*, 2d ed., 1888, 422) that it contains more hydrocarbon than oil of anise, and notably that from Nîmes, in Southern France, contains much less anethol, and hence has a milder and sweeter taste which is also probably due to the absence of the bitter fenshone. As found in commerce, therefore, the oil of fennel is not uniform, and a specimen examined by Montgomery did not congeal at −5.5° C. (22° F.). (See *Oleum Anisi.* It is slightly dextrogyrate.

Dose, three to five minims (0.2–0.3 mil).

Off. Prep.—Aqua Fœniculi, *U. S.*

OLEUM GAULTHERIÆ. Br.

OIL OF GAULTHERIA [Oil of Wintergreen]

(ō'lę-ŭm gâul-thē'rī-æ)

"Oil of Gaultheria is the oil distilled from the leaves of Gaultheria procumbens, *Linn.*, or from the bark of Betula lenta, *Linn.*" *Br.*

Oil of Teaberry, Oil of Partridge-berry; Huile volatile (Essence) de Winter-green, *Fr. Cod.*; Essence de Gaulthérie, *Fr.*; Wintergrünöl, Bergtheeöl, *G.*

Oil of gaultheria is no longer official in the U. S. P. IX. Under *Methylis Salicylas* the Pharmacopœia directs that oil of gaultheria and oil of betula or sweet birch may be used.

The volatile oil of gaultheria is largely obtained in the United States by distillation of the plant. It probably does not exist in the plant, but is formed by a reaction between water and a neutral principle analogous to amygdalin, to which Procter has given the name of *gaultherin*. (*A. J. P.*, xv.) This substance, which was called by Schneegans *bétulase*, probably exists in all the numerous plants which yield methyl salicylate on distillation. The oil occurs in various of our native plants, and has been detected in *Polygala paucifolia, Spiræa Ulmaria, Spiræa lobata*, and *Gaultheria chiogenes*. T. E. de Vrij found it in considerable proportion in the *Gaultheria leucocarpa* and *G. punctata*, plants which are abundant in the volcanic regions of Java (*A. J. P.*, 1879); while Bourquelot (*C. R. S. B.*, iii, 1896) detected it in *Monotropa Hypopitys*, in *Polygala Senega*, and in other species of Polygala. (See also *A. J. P.*, 1898, 412.) Much of the so-called oil of wintergreen is obtained from *Betula lenta*, which yields a product physically indistinguishable and difficult to differentiate chemically from methyl salicylate.

The still in which oil of wintergreen is distilled is generally a wooden box, about eight feet long, four feet wide, four feet high, with a copper bottom and stayed with bolts. The head of the still is copper, and connecting with this is a circular worm of the same material or of tin, placed in a barrel. The still being filled with wintergreen to within about twelve inches of the top, a sufficient quantity of water is added, and this is allowed to macerate from ten to twelve hours. The fire being started, the distillation commences, and continues for about eight hours; but during the first two or three hours ninety per cent. of the oil has passed over. For collecting the distillate, most of the distillers use a wide-mouthed bottle, fitted with a large cork having two holes. A small funnel is put into one of the holes, so that the beak is below the shoulder of the receiving vessel, and connected with the other hole is a suitable pipe

forming an outlet. The oil and the water separate, the oil going to the bottom, and the water passes into a larger receptacle, where it is reserved for a subsequent operation (cohobation).

Occasionally the oil is very highly colored, and the wholesale dealers have three ways of "cleaning" it—redistillation, filtration, and decolorization. In the last method the oil to be decolorized is put into a bottle, crystals of citric acid are added, and the whole is allowed to stand, agitating occasionally, until the oil is colorless, or nearly so.

Oil of gaultheria when freshly redistilled is nearly colorless, but as found in commerce has a brownish-yellow or reddish color. The U. S. P. VIII described it as "a colorless or almost colorless liquid, having a characteristic, strongly aromatic odor, and a sweetish, warm, and aromatic taste. Specific gravity: 1.172 to 1.180 at 25° C. (77° F.). Boiling point: 218° to 221° C. (424.4°–429.8° F.). It is slightly lævogyrate, up to –1° in a 100 Mm. tube, at 25° C. (77° F.). In other respects it has the same properties as, and conforms to the reactions and tests given under, *Methylis Salicylas.*"

"Colorless or nearly colorless. Strong, characteristic odor; taste pungent. Specific gravity 1.180 to 1.187; *optical rotation* at 25° C. (77° F.) 0° to –1°; *refractive index* 1.537 to 1.539. Soluble in 6 parts of *alcohol* (70 per cent.) at 25° C. (77° F.). Contains not less than 99 per cent. of *esters*, calculated as methyl salicylate, $CH_3C_7H_5O_3$." *Br.*

It is stated to have been largely adulterated with chloroform. This and other impurities are to be detected by a comparison of the specific gravities and boiling points, or by fractional distillation. It is readily soluble in alcohol. When heated to about 80° C. (176° F.), the oil should not yield a colorless distillate having the characteristics of chloroform or of alcohol. (*A. J. P.*, 1873, p. 521.) Another distinguishing property is that in aqueous solution it gives a purple color with ferric salts. Oil of sassafras may be detected by the separation of a deep-red resinous mass on treatment with nitric acid in the cold. Japanese oil of camphor and other light volatile oils used as adulterants can be detected by simply dropping the suspected oil in water; if pure, it sinks in a few seconds; if adulterated, some minutes are required. Cahours states that one-tenth of the oil consists of a peculiar hydrocarbon, which he called *gaultherilene*, and the remaining nine-tenths of *methyl salicylate*. (*A. J. P.*, xiv, 211, xv, 241.) Trimble and Schroeter (*A. J. P.*, 1889, 398) found that the amount of the hydrocarbon *gaultherilene* was much less than that stated by Cahours—in fact, only 0.3 per cent. By analysis and vapor density determination they fixed its formula as $C_{15}H_{24}$, but they state that it may consist of a solid and a liquid portion. Power and Kleber (*Fritzsche Bros. Circ.*, No. 7) assert that this hydrocarbon belongs to the paraffin series, and state that it is probably *triacontane*, $C_{30}H_{62}$. They also find in the oil an aldehyde or ketone, with an odor like œnanthic aldehyde, an apparently secondary alcohol, $C_6H_{12}O$, and an ester, $C_{14}H_{24}O_2$. To the alcohol and the ester are attributed the characteristic odor of the oil. True oil of gaultheria contains about 99 per cent. of methyl salicylate. *Synthetic oil of wintergreen* is now extensively manufactured and used instead of the natural oil. For a process by H. T. Thayer, see *A. J. P.*, 1895, 244. (See *Methylis Salicylas*, p. 695.)

Uses.—The therapeutic properties of this oil are precisely the same as those of *Methyl Salicylate.*

Dose, ten to twenty minims (0.6–1.3 mils).

OLEUM GOSSYPII SEMINIS. U .S.

COTTONSEED OIL Ol. Gossyp. Sem. [Cotton Seed Oil]

(ō'lę-ŭm gŏs-sŷp'ĭ-ī sĕm'ĭ-nĭs)

"A fixed oil obtained from seeds of cultivated varieties of *Gossypium herbaceum* Linné, or of other species of *Gossypium* (Fam. *Malvaceæ*). Preserve it in well-closed containers." *U. S.*

Oleum Gossypii; Cotton Oil; Huile de Semences de cotonnier, *Fr.*; Baumwollsamenöl, Bauməl, *G.*

This fixed oil has no other medicinal properties than those of a bland neutral oil, and has been introduced especially on account of its use in official liniments. The amount of cottonseed produced in 1914 was 7,186,000 tons, of which 5,779,665 was worked up into its various products. The oil obtained was 229,260,000 gallons. The oil cake is largely exported to England, where it is used as food for cattle, and the oil to France, Italy, and other olive growing countries of Europe, whence much of it returns to us mixed with olive oil. The exportation of cottonseed oil for 1915 amounted to 318,366,525 lbs., valued at $21,872,948. For a description of the process of extraction, see *A. J. P.*, 1896, 42; also 1898, 497. Among the recent improvements in the purification of cottonseed oil are the processes of Chisholm using silicate of soda for clarifying and of Baskerville using a paper pulp or cellulose fiber.

This oil is obtained by expression from the seeds previously deprived of their shells. In this state they yield two gallons of oil to the bushel. As first obtained, it is thick and turbid, but it deposits a portion of its impurities on standing.

The oil is clarified by first boiling it with water, to separate the mucilage, and then heating it with a weak solution of sodium hydroxide, which combines with the coloring matter and saponifies a part of the oil. The mixture becomes filled with black flocks, which deposit on standing and leave the oil but slightly colored. The loss in refining is usually from 4 to 7½ per cent., but occasionally amounts to 12 or 15.

Besides this crude oil, there are three varieties in commerce, more or less purified, recognized as the *clarified*, the *refined*, and the *winter bleached*. The last mentioned is of a pale straw-color, a mild peculiar odor, and a bland sweetish

taste, not unlike that of almond oil. The oil is used in the preparations of woollen cloth and morocco leather, and for oiling machinery. It has been found to be an excellent substitute for almond and olive oils in most pharmaceutical preparations in which they are employed, but it does not answer so well in the formation of lead plaster. Citrine ointment carefully prepared with it, too great heat being avoided, retains a rich orange color and proper unctuous consistence.

Properties.—It is officially described as "a pale yellow, oily liquid, odorless or nearly odorless, and having a bland taste. It is slightly soluble in alcohol; miscible with ether, chloroform, petroleum benzin, or carbon disulphide. Specific gravity: 0.915 to 0.921 at 25° C. (77° F.). On cooling the Oil to a temperature below 12° C. (53.6° F.) particles of solid fat separate. At about 0° to –5° C. (32°–23° F.) the Oil becomes nearly or quite solid. Add sulphuric acid (specific gravity 1.6 to 1.7) to the Oil, preferably diluted with carbon disulphide; a reddish-brown color is rapidly produced. Mix 2 mils of the Oil in a test tube with 2 mils of a mixture of equal volumes of amyl alcohol and a 1 per cent. solution of sulphur in carbon disulphide, and immerse the test tube to one-third of its depth in a boiling, saturated aqueous solution of sodium chloride; a red color develops in from ten to fifteen minutes. Saponification value: not less than 190 nor more than 198 (see Part III, Test No. 9). Iodine value: not less than 105 nor more than 114 (see Part III, Test No. 8)." *U. S.*

As this oil is much used for adulterating olive oil, tests to distinguish it are very desirable. The test most depended upon is that known as *Halphen's test,* a mixed solution of amyl alcohol and carbon disulphide containing 1 per cent. of dissolved sulphur. This is given in the official test. It is stated that cotton seed oil, which has been heated to 250° C. (482° F.) no longer gives many of the characteristic reactions for detecting the oil.

Dose, two to six fluidrachms (7.5–22.5 mils).

Off. Prep.—Linimentum Camphoræ, *U. S.;* Linimentum Ammoniæ, *U. S.*

OLEUM GRAMINIS CITRATI. Br.

OIL OF LEMON GRASS

(ō'lę-ŭm grā'mĭ-nĭs cĭ-trā'tī)

"Oil of Lemon Grass is the oil distilled from Cymbopogon citratus, *Stapf,* and Cymbopogon flexuosus, *Stapf.*" *Br.*

Lemon-grass Oil.

The *East Indian Lemon Grass Oil* comes from Malabar, Cochin, India and the Malay Peninsula. A product of the *C. citratus* comes from Ceylon, Burma and adjacent countries, as well as from Mexico and the West Indies.

It is officially described in the British Pharmacopœia, 1914, as "Dark yellow. Odor resembling that of verbena. Specific gravity 0.880 to 0.905; *optical rotation* –3° to +3°. Contains not less than 70 per cent. of aldehydes as determined by the process described under 'Oleum Cinnamomi." *Br.*

The chief aldehyde present is citral, of which it contains 70 to 85 per cent. Linalool, geraniol and methyl peptenone are also reported present in small amounts. The principal use of the oil is in perfuming cheap soaps. (See also *Oil of Citronella,* Part II.)

Oil of lemon grass is sometimes used in Eastern countries as a carminative and stimulant in *doses* of one-half to three minims (0.03–0.2 mil). Its chief use is in perfumery.

OLEUM JUNIPERI. U. S., Br.

OIL OF JUNIPER Ol. Junip. [Juniper Oil, Oil of Juniper Berries]

(ō'lę-ŭm jū-nĭp'ę-rī)

"A volatile oil distilled from the ripe fruit of *Juniperus communis,* Linné (Fam. *Pinaceæ*). Preserve it in well-stoppered, amber-colored bottles in a cool place, protected from light." *U. S.* "Oil of Juniper is the oil distilled from the ripe fruit of Juniperus communis, *Linn.,* and rectified." *Br.*

Oleum Fructus (vel Baccæ) Juniperi; Huile volatile (Essence) de Genièvre, *Fr.;* Oleum Juniperi, *P. G.;* Wachholderöl, Wachholderbeeröl, *G.;* Essenza di ginepro, *It.*

The proportion of oil which juniper berries afford is stated very differently by different authors. Trommsdorff obtained 1 per cent. The highest quantity given in the table of Recluz is 2.34, the lowest 0.31 per cent. Zeller gives as the product of the fresh ripe fruit 1.3 per cent., of that a year old 0.86 per cent. The berries are most productive when bruised. The oil of juniper consumed in this country is brought from Europe, and is believed to be procured chiefly from the tops of the plant, being sold for a price which is altogether incompatible with the idea that it is prepared from the fruit alone. "A colorless or faintly green or yellow liquid, having the characteristic odor and taste of juniper fruit. It is soluble in 4 volumes of alcohol with not more than a slight cloudiness. Specific gravity: 0.854 to 0.879 at 25° C. (77° F.). The optical rotation varies from 0° to –15°, in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21)." *U. S.*

"Colorless or pale yellowish-green. Odor that of the fruit; taste warm, aromatic and bitter. Specific gravity 0.862 to 0.890, increasing with age; *optical rotation* –3° to –15°; *refractive index* at 25° C. (77° F.) 1.472 to 1.488. Soluble, when freshly distilled, in 4 parts of a mixture of equal volumes of *alcohol* (90 per cent.) and *absolute alcohol,* becoming less soluble with age." *Br.*

According to Flückiger (*Pharm. Chem.,* 2d ed., 1888, 402), it is composed essentially of two hydrocarbons, the more abundant of which, boiling at 160° C. (320° F.), has been shown

by Wallach to be pinene, $C_{10}H_{16}$. Above 175° C. (347° F.) another oil is obtained, which seems to be cadinene, $C_{15}H_{24}$. It also contains a small amount of an ester to which the peculiar juniper-like odor and taste was supposed to be due, but this cannot be the case, as the odor persists after the complete saponification of the small amount of ester. *Juniper camphor* is also present, its melting point is 165° to 166° C. (329°–330.8° F.). Oil of turpentine is often fraudulently added, but may be detected by the specific gravity of the mixture being less than that of the unadulterated oil of juniper.

Uses.—Oil of juniper is occasionally used as a carminative in *intestinal flatulence,* but is more popularly employed for its diuretic effect. Because of its local irritant action it should never be used when there is an active inflammatory process in the kidney or urinary tract. It is frequently combined with potassium bitartrate. To it gin owes its peculiar flavor as well as its diuretic effects.

Dose, two to ten minims (0.12–0.6 mil).

Off. Prep.—Spiritus Juniperi, *U. S., Br.;* Spiritus Juniperi Compositus, *U. S.;* Acetum Aromaticum, *N. F.*

OLEUM LAVANDULÆ. U. S., Br.

OIL OF LAVENDER Ol. Lavand. [Oleum Lavandulæ Florum, U.S. P. VIII]

(ō'lę-ŭm lą-văn'dŭ-læ)

"A volatile oil distilled from the fresh flowering tops of *Lavandula vera* De Candolle (*Lavandula officinalis* Chaix, *Lavandula spica* Linné) (Fam. *Labiatæ*). Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.* "The oil distilled from the flowers of Lavandula vera, *DC.*" *Br.*

Huile volatile de Lavande officinale, *Fr. Cod.;* Essence de Lavande, *Fr.;* Oleum Lavandulæ, *P. G.;* Lavendelöl, *G.;* Essenza di lavanda, *It.;* Esencia de espliego, *Sp.*

This oil is usually distilled from the flowers and flower stems conjointly, though of finer quality when obtained from the former exclusively. Dried lavender flowers are said to yield from 1 to 1.5 per cent. of oil. According to Zeller, the fresh flowers yield 1.03, the dried 4.3, the whole fresh herb in flower 0.76 per cent. It is stated that the lavender produced by an acre of ground under cultivation will yield from 10 to 12 pounds of the oil. (*P. J.,* 1864, p. 257.) The oil is very fluid, of a lemon-yellow color, with the fragrance of the flowers and an aromatic, burning taste. That met with in commerce has the sp. gr. 0.898 at 20° C. (68° F.), which is reduced to 0.877 by rectification (Berzelius), or 0.886 (Buignet). It is lævogyrate. According to Brande, the sp. gr. of the oil obtained from the whole herb is 0.9206. Alcohol of 0.830 dissolves oil of lavender in all proportions, that of 0.877 only 42 per cent. (Berzelius.) Proust states that when allowed to stand in imperfectly stoppered bottles it lets fall a crystalline deposit, which often amounts to one-fourth of its weight. This has been found by Dumas to have the same point of volatilization and the same composition as true camphor, but to differ in the total want of rotatory power. It is said that the portion of oil first distilled is most fragrant, and is often kept separate, and sold at a higher price. "Oil of Lavender is a colorless or yellow liquid, having the characteristic odor and taste of lavender flowers. It is soluble in 3 volumes of 70 per cent. alcohol. Specific gravity: 0.875 to 0.888 at 25° C. (77° F.). The optical rotation varies from –1° to –10° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21). When shaken in a narrow glass cylinder with an equal volume of distilled water, its volume does not diminish (*alcohol*). Shake 20 mils of the Oil with 40 mils of 5 per cent. alcohol and, when the mixture has cleared, withdraw 30 mils of the alcoholic solution. Neutralize this with half-normal potassium hydroxide V.S., using phenolphthalein T.S. as indicator, then add 5 mils of half-normal potassium hydroxide V.S. and heat the mixture on a water-bath, under a reflux condenser, during one hour. Not less than 4.7 mils of half-normal hydrochloric acid V.S. is required for neutralization (*foreign esters*)." *U. S.*

"Pale yellow or yellowish-green. Odor that of the flowers; taste pungent, slightly bitter. Specific gravity 0.883 to 0.900; *optical rotation* –3° to –10°. Soluble in 4 parts of *alcohol* (70 per cent.). Contains from 7 to 11 per cent. of *esters* (English oil), or not less than 30 per cent. of *esters* (foreign oil), calculated as linalyl acetate, $C_{10}H_{17}C_2H_3O_2$." *Br.*

The principal constituent is an alcohol, $C_{10}H_{18}O$, identical with the linalool. Besides linalool, lavender oil contains linalyl acetate (from 30 to 45 per cent. in the oil from French flowers, and from 7 to 10 per cent. in the oil from English flowers), the butyric ester of the same alcohol, geraniol, a very small amount of cineol (more in the English than in the French oil), and sometimes traces of pinene, limonene, and a sesquiterpene.

Oil of Spike is procured from the broad leaved variety of lavender which grows wild in Europe, the *Lavandula Spica* of De Cavanilles. Its odor is less fragrant than that of common oil of lavender, and is somewhat analogous to that of oil of turpentine, with which it is said to be often adulterated. It is used by artists in the preparation of varnishes. The oil of spike contains about 30 per cent. of cineol and but small quantities of esters. Oil of lavender is used chiefly as a perfume, though possessed of carminative and stimulant properties, and sometimes useful in cases of *nervous languor* and *headache.*

Dose, from one to five minims (0.06–0.3 mil).

Off. Prep.—Spiritus Lavandulæ, *U. S., Br.;* Tinctura Lavandulæ Composita, *U. S., Br.;* Acetum Aromaticum, *N. F.;* Spiritus Odoratus, *N. F.*

OLEUM LIMONIS. U. S., Br.

OIL OF LEMON Ol. Limon. [Lemon Oil]

(ō'lę-ŭm lĭ-mō'nĭs)

"A volatile oil obtained by expression from the fresh peel of the ripe fruit of *Citrus medica Limonum* (Risso) Hooker filius (Fam. *Rutaceæ*), and yielding not less than 4 per cent. of the aldehydes from Oil of Lemon, calculated as citral [$C_{10}H_{16}O = 152.13$]. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light. Oil of Lemon having a terebinthinate odor is not to be dispensed." *U. S.* "Oil of Lemon is the oil obtained from Lemon Peel by various methods of expression." *Br.*

Oleum Limonum; Huile volatile de Citron, *Fr. Cod.*; Essence de Citron, *Fr.*; Oleum Citri, *P. G.*; Citronenöl, *G.*; Olio de limone, *It.*; Esencia de limon, *Sp.*

The exterior rind of the lemon abounds in a volatile oil, which, being contained in distinct cells, may be separated by simple expression. The rind is first grated from the fruit, and then submitted to pressure in a bag of fine cloth. The oil thus obtained is allowed to stand till it becomes clear, when it is decanted, and kept in stoppered bottles. By a similar process, the oil called by the French *huile de cédrat* is procured from the citron. (See *Oil of Bergamot*, Part II, and *Succus Limonis.*) These oils may also be obtained by distillation, but thus procured, though clearer, and, in consequence of the absence of mucilage, less liable to change on keeping, they have less of the peculiar flavor of the fruit, and the mode by expression is generally preferred. A third method of separating the oil, used in Calabria and Sicily, is to put the grated rind into hot water and skim off the oil as it rises to the surface. (*A. J. P.*, 1868, p. 27.) The method employed to obtain the finest oil is, however, that known as the écuelle process. The écuelle is an instrument usually made of tinned copper, bowl-shaped, and armed with concentric rows of short spikes. Attached to the bottom of the bowl is a hollow handle, closed at the bottom. This acts as a reservoir for the oil as the fruit is rubbed by the workmen over the sharp teeth. The oils are brought from Italy, Portugal, or Southern France.

The oils of lemons and oranges, as well as those of the other *Aurantiaceæ*, will keep indefinitely upon admixture with a small proportion of alcohol (one ounce to a pound of the oil). When wanted for use, a quantity of water equal to that of alcohol, added to the mixture, will unite with the alcohol, and subside, leaving the oil free of the alcohol for all practical purposes. (Carl Früh, *A. J. P.*, 1871, 201.) E. J. Parry (*Ch. & Dr.*, 1913, p. 378) discusses at some length the relative advantages of terpeneless and sesquiterpeneless oils and normal oils. The ordinary terpeneless oils contain from 42 to 45 per cent. of citral, while those that are sold as sesquiterpeneless contain from 65 to 72 per cent. citral. He states that the latter products lack the sweetness and softness of odor of those containing less citral, the overpowering odor of the latter constituent destroying the balance of harmony in the odor of the oil. He states that users of these products claim to get the best results from oils containing slightly less than 40 per cent. of citral and from which the whole of the terpenes have not been removed. The characters of the commercial terpeneless oils are as follows: sp. gr. at 15° C. (59° F.), 0.8935 to 0.899; optical rotation, −5° to −8° 30′; refractive index, 1.4810; citral, 42 to 48 per cent. The sesquiterpeneless oils are slightly higher in specific gravity, lower in optical rotation and always run above 65 per cent. of citral.

The great extent of the production and export of Sicilian and Calabrian essential oils (lemon, orange, bergamot, etc.) may be seen from the Italian official statistics, according to which the number of trees producing in 1896 was 17,084,569, yielding 3,337,000,000 fruits. Of these 1,897,000,000 were exported, leaving 1,439,555,000 fruits for home consumption inclusive of those used in the manufacture of essences. (*Schim. Rep.*, Oct., 1897, 23.)

Parry (*Schim. Rep.*, Apr., 1912, p. 78) reports several shipments of lemon oil which upon investigation were found to be adulterated with Greek turpentine oil. They were noted by their low optical rotation, + 50° to + 54°, and their low citral content, 3.3 to 4.1 per cent.

Properties.—Oil of lemon is "a pale yellow or greenish-yellow liquid, having the characteristic odor and taste of lemon. Specific gravity; 0.851 to 0.855 at 25° C. (77° F.). Refractive index: 1.4744 to 1.4755 at 20° C. (68° F.) (see Part III, Test No. 22). The optical rotation varies from + 57° to + 64° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21). The angle of rotation of the first 10 per cent. of the distillate, obtained as directed under *Oleum Aurantii*, is not more than 5 degrees less than that of the original Oil. The refractive index of this first 10 per cent. of distillate is not less than 0.002 nor more than 0.0027 lower than that of the original oil." *U. S.*

"Pale yellow. Volatile; odor that of lemons; taste warm, afterwards slightly bitter. Specific gravity 0.857 to 0.860: *optical rotation* + 58° to + 64°; *refractive index* at 25° C. (77° F.) 1.473 to 1.476. Contains not less than 4 per cent. by weight of aldehydes, calculated as citral, $C_{10}H_{16}O$, as determined by the following process." *Br.*

Assay.—"Introduce about 15 mils of Oil of Lemon into a tared 300 mil flask and note the exact weight; add 10 mils of an alcoholic solution of phenylhydrazine (1 in 10) (not darker in color than pale yellow), and allow it to stand for one-half hour at room temperature. Then add a few drops of methyl orange T.S. and neutralize the liquid exactly by the cautious addition of half-normal hydrochloric acid V.S. If difficulty is experienced in detecting the end point of the reaction, continue the titration until the solution is distinctly acid, transfer it to a

separatory funnel and draw off the alcoholic portion. Now wash the Oil with distilled water, adding the washings to the alcoholic solution, and titrate the latter with half-normal potassium hydroxide V.S. Carry out a blank test identical with the foregoing, except that the Oil of Lemon is omitted, and note the amount of half-normal hydrochloric acid V.S. consumed. Subtract the number of mils of half-normal potassium hydroxide V.S. from the number of mils of half-normal hydrochloric acid V.S. consumed in the original test and this result from the corresponding number of mils required in the blank test; each mil of this difference corresponds to 0.076 Gm. of aldehydes, calculated as citral. It shows, when calculated from the weight of Oil taken, not less than 4 per cent. of aldehydes from Oil of Lemon, calculated as citral." *U. S.*

"To 20 grammes of the Oil contained in a flask add 20 millilitres of *N/2 solution of hydroxylamine hydrochloride,* 8 millilitres of *N/1 alcoholic solution of potassium hydroxide* and 20 millilitres of *alcohol* (90 per cent.). Attach a reflux condenser, boil for thirty minutes, cool, and dilute with 250 millilitres of *water,* rinsing the condensing tube into the flask with part of this quantity. Neutralise the solution thus obtained with *N/1 alcoholic solution of potassium hydroxide, solution of phenolphthalein* being used as indicator, and then titrate with *N/2 solution of sulphuric acid, solution of methyl orange* being used as indicator. Repeat the experiment, omitting the Oil of Lemon. The quantity of *N/2 solution of sulphuric acid* required in the second experiment exceeds that required in the first experiment by not less than 10.5 millilitres (presence of not less than 4 per cent. of aldehydes, calculated as citral, $C_{10}H_{16}O$)." *Br.*

Oil of lemon contains a small amount of pinene, with dextrogyrate limonene, about 7 to 8 per cent. of *citral,* $C_{10}H_{16}O$, an aldehyde yielding geraniol upon reduction, and a small amount of *citronellal,* $C_{10}H_{18}O$, also an aldehyde. Pinene, phellandrene, higher aldehydes, as octyl and nonyl, terpineol and geranyl acetate have also been reported in small amounts. Of these the citral is the constituent to which the oil chiefly owes its aroma and value. Umney and Swinton (*P. J.,* 1898, 196) state that citral, citronellal, and an ester of geraniol are all necessary to form the true odor of oil of lemon. Citral boils under normal atmospheric pressure at from 228° to 229° C. (442.4°–444.2° F.) without decomposition if pure, and, like aldehydes, forms stable compounds with alkaline bisulphites. Schimmel & Co. now prepare the citral in a pure state, and recommend its use for enriching the ordinary oil of lemon.

Oil of lemon is often adulterated by the fixed oils and by alcohol, and sometimes with purified oil of turpentine, which is difficult of detection from its similar composition and specific gravity except with the polariscope. One of the tests for the presence of this oil is the terebinthinate odor produced when the adulterated oil is evaporated from heated paper; the official quantitative test defining the percentage of citral will be of service in detecting these adulterations. The most dangerous adulteration of oil of lemon is the use of *citrene,* the terpene left after the extraction of citral from oil of lemon which has been used in making terpeneless oil. Oil of lemon procured by expression is apt to precipitate and to undergo chemical change. J. S. Cobb has found no method so effectual to obviate this result, and at the same time to retain unimpaired the flavor of the oil, as to shake it with a little boiling water and allow the mixture to stand. A mucilaginous matter separates, and floats on the surface of the water, from which the purified oil may be decanted. (*Ann. Pharm.,* ii, 86.) The best method of preservation is to add 10 per cent. of a bland fixed oil such as olive or cottonseed, which must subsequently be allowed for in measuring the oil for use.

Adulteration of Lemon Oil with Pinene.—In consequence of some seizures of lemon oil alleged to be adulterated with turpentine, in 1906, a number of importers stated their belief that pinene was normally present in appreciable amounts in some lemon oils. In consequence of this the U. S. Dept. of Agriculture undertook a special investigation of the subject, sending a trained observer and analyst to the producing countries, and published the results of the investigation in a special bulletin called "Circular 46, by E. M. Chace." The investigation showed conclusively that lemon oil shows no appreciable amount of pinene.

Spirit of Lemon (Spiritus Limonis, *U. S.* 1890) is no longer official. It was made by dissolving 50 mils of oil of lemon in 900 mils of deodorized alcohol, to which 50 Gm. of freshly grated lemon peel were added, the whole macerated for twenty-four hours, filtered, and enough deodorized alcohol added through the filter to make the whole measure 1000 mils.

Uses.—The oil of lemon is much less active than most of the other official volatile oils, and is used almost exclusively for its flavoring properties.

Dose, two to five minims (0.12–0.3 mil).

Off. Prep.—Elixir Aromaticum (from Spirit), *U. S.;* Spiritus Aurantii Compositus, *U. S.;* Acetum Aromaticum, *N. F.;* Spiritus Odoratus, *N. F.*

OLEUM LINI. U. S., Br.

LINSEED OIL. Ol. Lini. [Oil of Flaxseed Raw Linseed Oil]

(ō'lē-ŭm lī'nī)

"A fixed oil obtained from Linseed. Preserve it in well-stoppered containers. Linseed Oil which has been 'boiled' must not be used nor dispensed." *U. S.* "Linseed Oil is the oil expressed from Linseed." *Br.*

Huile de Semence de Lin, *Fr.;* Oleum Lini, *P. G.;* Leinöl, Leinsamenöl, *G.;* Olio di lino, *It.;* Aceite de linaza, *Sp.*

This oil is obtained by expression from the

seeds of *Linum usitatissimum,* or common flax, which, according to Berjot, contain 34 per cent. (*J. P. C.,* April, 1863, p. 277.) In its preparation on a large scale, the seeds are usually roasted before being pressed, in order to destroy the gummy matter contained in their coating. The oil is thus obtained more free from mucilage, but more highly colored and acrid than when procured by cold expression. For medicinal use, therefore, it should be prepared without heat, and, as it is apt to become rancid quickly on exposure, it should be used as soon after expression as possible. It may, however, be rendered sweet again by agitation with warm water, rest, and decantation. It is said to be obtained purer and in larger proportion by treating the crushed seeds with carbon disulphide than by expression. (*A. J. P.,* xxvi, 265.)

Oil of flaxseed is "a yellowish, oily liquid, having a peculiar odor and a bland taste. When exposed to the air, it gradually thickens, darkens in color, and acquires a strong odor and taste. It is slightly soluble in alcohol, miscible with ether, chloroform, petroleum benzin, carbon disulphide, or oil of turpentine. Specific gravity: 0.925 to 0.935 at 25° C. (77° F.). It is not more than slightly acid to litmus paper which has previously been moistened with alcohol (*free acid*). Linseed Oil when spread in a thin layer on a glass plate and allowed to stand in a warm place is gradually converted into a hard, transparent resin (*non-drying oils*). To 10 mils of the Oil add 3 Gm. of potassium hydroxide, 10 mils of alcohol and 10 mils of distilled water, and heat the mixture on a water bath with frequent agitation, until a clear solution results. The addition of 100 mils of distilled water to this solution yields a clear liquid free from oily drops (*mineral or rosin oils*). Warm 2 mils of the Oil with frequent agitation in a test tube with an equal volume of glacial acetic acid, and, after cooling, add to the mixture 1 drop of sulphuric acid. A greenish color is produced (a violet color under these circumstances indicates the presence of *rosin or rosin oils*). Saponification value: not less than 187 nor more than 195 (see Part III, Test No. 9). Iodine value: not less than 170 (see Part III, Test No. 8)." *U. S.*

"Yellowish-brown. Characteristic odor; taste bland. Specific gravity 0.930 to 0.940; *saponification value* 187 to 195; *iodine value* not less than 170; *acid value* not more than 3.0; *unsaponifiable matter* not more than 1.0 per cent.; *refractive index* at 40° C. (104° F.) 1.4725 to 1.4748. Does not congeal at temperatures higher than –20° C. (–4° F.). Gradually thickens on exposure to the air, forming, when spread in thin layers, a hard transparent varnish. A mixture of 2 millilitres of the Oil with an equal volume of *acetic anhydride,* warmed and shaken, and then cooled to 15.5° C. (60° F.), is not colored violet by the addition of 2 drops of a cooled mixture of 2 parts by weight of *sulphuric acid* and 1 part by weight of *water* (absence of resin and resin oils)." *Br.*

It has the property of drying or becoming solid on exposure to the air, acquiring during the process a strong odor and taste, and increasing as much as 12 per cent. of its weight, owing to the formation of *linoxyn* by atmospheric oxidation. The drying property resides in a constituent which, to distinguish it from the olein of the non-drying oils, is named *linolein,* and is the glyceride of *linoleic acid.* Linseed oil contains about 10 to 15 per cent. of glycerides of solid fatty acids, palmitic, myristic, and stearic, and 85 to 90 per cent. of liquid glycerides. Hazura (*J. Soc. Chem. Ind.,* 1888, 506) states that the liquid fatty acids consist of about 5 per cent. of oleic acid, $C_{18}H_{34}O_2$, 15 per cent. of *linoleic acid,* $C_{18}H_{32}O_2$, 65 per cent. of *isolinolenic acid,* $C_{18}H_{30}O_2$, and 15 per cent. of *linolenic acid,* $C_{18}H_{30}O_2$. Boiled with litharge, red lead, manganese dioxide, and other so-called "driers," it absorbs oxygen still more rapidly, and gains 14 per cent. in weight. Its acridity is owing to the presence of a small proportion of an acrid oleoresin. From its drying property, it is useful in painting and in making printers' ink and in linoleum and oil cloth manufacture. The chief adulteration of linseed oil is with mineral oils and rosin oil. For their detection, see official tests already given.

It is said that crude cod liver oil has been used for the adulteration of the oil of flaxseed, especially where the latter is intended for preparing printers' ink. Aug. Morell detects the adulteration by the following method. Take 10 parts by weight of the suspected oil, mix it in a small cylindrical glass tube with 3 parts of crude nitric acid, agitate the mixture well, and allow it to rest. If cod liver oil be present, the oily layer at top will assume a dark-brown to blackish-brown color, while the acid at bottom will vary from bright orange to orange or dark yellow. So little as 3 per cent. of cod liver oil may thus be detected. If the flaxseed oil be pure, it will become, during the agitation, first sea green, and afterwards dirty greenish-yellow, the acid being bright yellow. The prohibition of the use of boiled linseed oil for medicinal purposes has its origin in the fact that much of the boiled linseed oil of commerce contains a compound of lead or manganese as a drying agent. Instances are on record where lead-containing boiled linseed oils caused the death of cattle to which the oil had been administered.

Uses.—The oil is laxative in the dose of a fluidounce (30 mils), but, on account of its disagreeable taste, is seldom given internally. It has, however, been highly recommended as a cure for *piles,* in the dose of two fluidounces (60 mils) of the fresh oil, morning and evening. It is sometimes added to purgative enemata. Particular care must be observed not to use boiled linseed oil for any medicinal purposes, as the latter frequently contains compounds of lead which give it poisonous properties.

Dose, one to two fluidounces (30–60 mils).

Off. Prep.—Linimentum Calcis, *U. S.;* Ceratum Resinæ Compositum, *N. F.*

OLEUM MENTHÆ PIPERITÆ. U. S., Br.

OIL OF PEPPERMINT **Ol. Menth. Pip.** [Peppermint Oil]

(ō'lę-ŭm mĕn'thæ pīp-ę-rī'tæ)

"A volatile oil distilled from the flowering plant of *Mentha piperita* Linné (Fam. *Labiatæ*), rectified by steam distillation, and yielding not less than 5 per cent. of esters, calculated as menthyl acetate [$C_{10}H_{19}C_2H_3O_2 = 198.18$], and not less than 50 per cent. of total menthol [$C_{10}H_{19}OH = 156.16$], free and as esters. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

"Oil of Peppermint is the oil distilled from fresh flowering peppermint, Mentha piperita, *Sm.*, and rectified, if necessary." *Br.*

Huile volatile de Menthe poivrée, *Fr. Cod.*; Essence de Menthe poivrée, *Fr.*; Oleum Menthæ piperitæ, *P. G.*; Pfeffermünzöl, *G.*; Essenza di menta, *It.*; Esencia de menta piperita, *Sp.*

Peppermint varies exceedingly in the quantity of oil which it affords. Four pounds of the fresh herb yield, according to Baumé, from a drachm and a half to three drachms of the oil. Zeller gives as the product of the fresh herb, from 0.37 to 0.68 per cent., of the dried 1.14 per cent. The yield is generally less than 1 per cent. This oil is largely distilled in the States of Michigan, Indiana, and New York. For a valuable account of its method of production in Michigan, by A. M. Todd, see *A. J. P.*, 1888, 328. The oil is also largely produced in Japan. (See illustrated paper, *C. D.*, 1896, 601.) Gildemeister and Hoffmann (*Aetherische Oele*, p. 836) estimate the world's production of peppermint oil at 175,000 kilos, of which the United States furnishes 90,000 kilos, and Japan 70,000 kilos. It is officially described as "a colorless liquid, having a strong odor of peppermint, and a pungent taste, followed by a sensation of cold when air is drawn into the mouth. It is soluble in 4 volumes of 70 per cent. alcohol, showing not more than slight opalescence and no separation of oil globules. Specific gravity: 0.896 to 0.908 at 25° C. (77° F.). The optical rotation varies between –23° and –33° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21). Distil about 1 mil from 25 mils of the Oil and pour the distillate on 5 mils of mercuric chloride T.S.; a white film does not form at the zone of contact within one minute (*dimethyl sulphide* found in non-rectified oils)." *U. S.*

"Colorless, pale yellow, or greenish-yellow. Odor that of peppermint herb; taste pungent and aromatic, followed by a sensation of cold. Specific gravity 0.900 to 0.920; *optical rotation* –20° to –35°. Soluble in 4 parts of *alcohol* (70 per cent.). Contains not less than 50 per cent. of total *alcohols*, free and combined, calculated as menthol, $C_{10}H_{20}O$, and not less than 5 per cent. of *esters*, calculated as menthyl acetate, $C_{10}H_{19}C_2H_3O_2$." *Br.*

"Assay for Esters.—Introduce 10 mils of Oil of Peppermint into a tared flask and note the exact weight. Add 25 mils of half-normal alcoholic potassium hydroxide V.S., connect the flask with a reflux condenser, and boil the mixture during one hour. After cooling, titrate the residual alkali with half-normal sulphuric acid V.S., using phenolphthalein T.S. as indicator. Subtract the number of mils of half-normal sulphuric acid V.S. required from the 25 mils of half-normal alcoholic potassium hydroxide V.S. taken, multiply the difference by 9.909, and divide the product by the weight of the Oil of Peppermint taken to find the percentage of menthyl acetate.

"Assay for Total Menthol.—Introduce 10 mils of the Oil into a flask provided with a ground-glass tube-condenser (acetylization flask), add 10 mils of acetic anhydride and about 1 Gm. of powdered anhydrous sodium acetate, and boil the mixture gently during one hour. Allow it to cool, wash the acetylized oil with distilled water, and afterwards with sodium carbonate T.S., diluted with an equal volume of distilled water, until the mixture is slightly alkaline to phenolphthalein T.S., and then dry it with the aid of fused calcium chloride, and filter. Transfer 5 mils of the dry acetylized oil to a tared 100 mil flask, note the exact weight, add 50 mils of half-normal alcoholic potassium hydroxide V.S., connect the flask with a reflux condenser, and boil the mixture during one hour. After cooling, titrate the residual alkali with half-normal sulphuric acid V.S., using phenolphthalein T.S. as indicator, and calculate the percentage of menthol present by the following formula:

$$\text{Percentage of menthol} = \frac{A \times 7.808}{B - (A \times 0.021)}$$

In which A is the result obtained by subtracting the number of mils of half-normal sulphuric acid V.S. required in the above titration from the number of mils of half-normal alcoholic potassium hydroxide V.S. originally taken, and B is the weight of acetylized oil taken." *U. S.*

Upon cooling or long standing it deposits a stearopten. Berzelius stated that at –13.3° C. (–8° F.) the oil deposits small capillary crystals. These are called *peppermint camphor* or *menthol*, $C_{10}H_{19}OH$. (See *Menthol*, p. 694.) A complete summary of the composition of American peppermint oil, on the authority of Power and Kleber, given in *Schimmel & Co.'s Report* for April, 1897, shows the following constituents: acetaldehyde, isovaleraldehyde, dimethyl sulphide, amyl alcohol, isovaleric acid, pinene, phellandrene, cineol, limonene, *menthone*, $C_{10}H_{18}O$, menthol, the acetate and isovalerate of menthyl, *a-lactone*, $C_{10}H_{16}O_2$, and cadinene. Menthol, its oxidation product menthone, and the acetic and isovaleric esters of menthyl have been identified as present in English and French peppermint oils, which probably also contain most of the other constituents mentioned above. Menthol and its esters are regarded as the main constituents of oil of peppermint and an official assay for determining

the percentage of menthol will be found above. The dimethyl sulphide and some of the other constituents are objectionable from the flavoring standpoint, and are largely removed by the steam distillation which is required for rectification. The polariscope has been shown to be an uncertain guide in determining the quality of oil of peppermint. (A. B. Stevens, *Proc. A. Ph. A.*, 1888, p. 97.)

Flückiger discovered that from 50 to 70 drops of peppermint oil, shaken with one drop of nitric acid, sp. gr. 1.2, turn faintly yellowish brown, and after an hour or two a most beautiful blue-violet or greenish-blue by transmitted light, or copper color by reflected light. Either a greater amount of acid or heating hastens the reaction. The color is very persistent. The presence of 5 per cent. of turpentine does not interfere with the reaction. (*P. J.*, Feb., 1871.)

Since menthol has been prepared largely from American peppermint oil, much of the latter has been put upon the market deprived of its menthol. To detect this fraud, Fritzsche Brothers recommend that a test tube partially filled with the oil and corked should be placed in a freezing mixture of ice and salt for ten or fifteen minutes. At the end of that time, if the oil has not been tampered with, it will have become cloudy, thick, or of a jelly-like consistence If then four or five small crystals of menthol be added, and the tube be replaced in the freezing mixture, the oil will in a very short time form a solid mass of crystals. For another method of testing dementholized oil, see a paper by E. C. Federer, *Ph. Era*, 1887, 36; also 1887, 97.

Power and Kleber first proposed (*Ph. Rund.*, 1894, 157) to estimate the menthol in oil of peppermint by acetylizing a sample and saponifying an exactly weighed portion of the acetylized oil after washing, drying, and filtering the same. Kleber (*A. J. P.*, 1897, 192) proposed to take instead a weighed quantity of the oil, acetylize it, and then saponify the product after washing and neutralizing it. In *Schimmel & Co.'s Report* for October, 1897, Kleber criticizes Kebler's modification, and claims greater accuracy for the original method. Of course, this determination gives the total menthol; a determination of the combined menthol is had by titrating with alcoholic alkali.

Peppermint oil has been variously mixed and adulterated with the following substances: alcohol, oil of turpentine, oil of copaiba, oil of erigeron (from the erigeron plant growing with the peppermint plant, and being collected with it for distillation), oil of eucalyptus, oil of pennyroyal, and others. Most of these are detectable by the official tests, or when present lower the assay strength, or are readily recognized by the odor or taste, which they communicate to the oil. For further details concerning some of these adulterants and their detection, see *U. S. D.*, 19th ed., p. 854, 855.

Chinese Oil of Peppermint has not found its way to any extent into commerce, yet it has at times attracted much attention. According to John Mackey, some of it has reached London in cylindrical tin canisters, and it is to be obtained in San Francisco. Some specimens resemble the ordinary oil, but become solid in cold weather; others remain liquid and show no tendency to deposit a camphor, while others are solid crystalline masses at all temperatures. It seems probable that the original Chinese oil contains a great excess of menthol, and constitutes the variety first spoken of, and that the solid and liquid oils are prepared by separating it into its two constituents. The solid oil Flückiger states not to differ from American menthol. (See *P. J.*, v, 366, 825.)

Uses.—Oil of peppermint possesses the physiological properties and therapeutic virtues of menthol, and may be used for practically all those conditions in which menthol is of service. It is generally preferred for internal use because of its more pleasant taste. It is an excellent carminative and gastric stimulant, and is widely employed in *flatulence*, *nausea*, and *gastralgia*. It adds to a stimulating effect upon the alimentary canal an antiseptic and local anesthetic influence. As a local application for *coryza* it may be used in strengths of from five to ten minims to an ounce of liquid petrolatum or olive oil. Incorporated into a lozenge it offers a pleasant and efficient antiseptic and anesthetic in *pharyngitis*. Internally it may be given either rubbed up with sugar and then dissolved in water, or more commonly in the form of the spirit. It is extremely popular as a flavoring agent.

Dose, one to five minims (0.06–0.3 mil).

Off. Prep.—Aqua Menthæ Piperitæ, *U. S., Br.;* Spiritus Menthæ Piperitæ, *U. S., Br.*

OLEUM MENTHÆ VIRIDIS. U. S., Br.

OIL OF SPEARMINT Ol. Menth. Vir. [Spearmint Oil]

(ō'lē-ŭm mĕn'thæ vīr'ĭ-dīs)

"A volatile oil distilled from the flowering plant of *Mentha spicata* Linné (*Mentha viridis* Linné) (Fam. *Labiatæ*), and yielding not less than 43 per cent., by volume, of carvone [$C_{10}H_{14}O = 150.11$]. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.* "Oil of Spearmint is the oil distilled from fresh flowering spearmint, Mentha viridis, *Linn.*, or mentha crispa, *Roth.*" *Br.*

Huile volatile (Essence) de Menthe verte, *Fr.;* Römischminzöl, Krauseminzöl, *G.*

According to Lewis, ten pounds of spearmint yield an ounce of oil; by others the product is stated not to exceed one part from five hundred. The oil is largely distilled in this country, the whole plant being used. It is pale yellow or greenish when recently prepared, but becomes red with age, and ultimately almost of a mahogany color. It is officially described as "a colorless yellow or greenish-yellow liquid, having the characteristic odor and taste of spearmint.

It is soluble in 1 volume of 80 per cent. alcohol, forming a clear solution; on further dilution, it usually becomes cloudy. Specific gravity: 0.917 to 0.934 at 25° C. (77° F.). The optical rotation varies between –38° and –55° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21).

"**Assay.**—Proceed as directed under *Oleum Cari*, using 10 mils of Oil of Spearmint." *U. S.*

"Colorless, pale yellow, or greenish-yellow, becoming darker on keeping. Odor and taste those of spearmint herb. Specific gravity 0.925 to 0.940; *optical rotation* –30° to –50°. Soluble in 3 parts of *alcohol* (90 per cent.). Forms a clear solution with 1 part of a mixture of equal volumes of *alcohol* (90 per cent.) and *alcohol* (70 per cent.), the solution becoming turbid on further dilution." *Br.*

Oil of spearmint contains a terpene, l. limonene, $C_{10}H_{16}$, and *l. carvone*, $C_{10}H_{14}O$. Baeyer found the *l. carvone* in both German and American oils to the amount of from 35 to 56 per cent. (*A. Pharm.*, cexii, 283.) Schimmel & Co., in an investigation of Russian oil, found from 5 to 10 per cent. of carvone only, but 50 to 60 per cent. of linalool, together with some cineol and l. limonene. (*Schim. Rep.*, April, 1898.) It is used chiefly for its flavor, especially in chewing gum.

The peculiar odor of spearmint oil has not yet been definitely associated with any of its constituents. It was for a time thought to be due to an acetic derivative of dihydrocuminyl, but this has recently been denied so far as the oil of American origin is concerned.

Dose, one to six minims (0.06–0.4 mil).

Off. Prep.—Aqua Menthæ Viridis, *U. S., Br.;* Spiritus Menthæ Viridis, *U. S.*

OLEUM MORRHUÆ. U. S., Br.

COD LIVER OIL. Ol. Morrh. [Oleum Jecoris Aselli]

(ō'lę-ŭm mör'rhú-æ)

"A fixed oil obtained from the fresh livers of *Gadus morrhua* Linné and of other species of *Gadus* (Fam. *Gadidæ*). Preserve it in a cool place, in well-closed containers, which have been thoroughly dried before filling." *U. S.* "Cod-liver Oil is the oil expressed from the fresh liver of the cod, Gadus morrhua, *Linn.*, at a temperature not exceeding 85° C. (185° F.), and from which solid fat has been separated by filtration at about –5° C. (23° F.)." *Br.*

Oleum Hepatis Morrhuæ; Cod Oil; Huile de Foie de Morue, *Fr. Cod.;* Huile de Morue, *Fr.;* Oleum Jecoris Aselli, *P. G.;* Leberthran, Stockfischleberthran, Dorschleberthran, Kabliauleberthran, *G.;* Olio di fegato di merluzzo, *It.;* Aceite de higado de bacalao, *Sp.*

Gadus morrhua Linn.; *Morrhua vulgaris* Storer.—The *common cod* is between two and three feet long, with brown or yellowish spots on the back. The body is moderately elongated and somewhat compressed, and covered with soft, rather small scales, being quite conspicuous also on the head. Of the fins, which are soft, there are three on the back (dorsal), two anal, and a distinct caudal, and the fin (ventral) under the throat is narrow and pointed. The jaws are furnished with pointed irregular teeth, in several ranks. The gills are large, with seven rays. This species of cod inhabits the cold waters of the Northern Atlantic, and is especially abundant on the Banks of Newfoundland, where it finds food adapted to its wants.

Besides the common cod, several other species of *Gadus*, frequenting the seas of Northern Europe and America, contribute to furnish the cod liver oil of commerce. Among these De Jongh mentions *Gadus callarias*, or *dorsch* (*Morrhua americana* of Storer), *G. molva*, or *ling*, *G. carbonarius*, or *coal fish*, and *G. pollachius*, or *pollack*, as affording the oil on the coast of Norway, where from 17,000,000 to 35,000,000 of codfish are annually taken. For an account of the mode of fishing for cod and of preparing the oil practised in Norway and Denmark, see *P. J.*, April, 1877, p. 810; *N. R.*, March, 1878; *Ph. Ztg.*, 1900, 261; *Ph. Era*, 1904, 111; *C. D.*, 1904, 21.

On the American coast, in addition to the pollack above mentioned, it is obtained also from the *hake* (*G. merluccius*) and the *haddock* (*G. æglefinus*). It is produced on our coast north of Boston. The oil is also largely produced in Newfoundland, Great Britain, Norway, and to some extent in Iceland.

Preparation.—Fishermen were for a long time in the habit of collecting this oil, which was largely consumed in the arts, particularly in the preparation of leather. Upon the coasts of Newfoundland, Nova Scotia, and New England, the boats which fish near the shore, being small, soon obtain a load, and, running in to land, deliver their cargoes to persons whose business it is to cleanse and salt the fish. The oil was formerly prepared in the huts of the fishermen, but is now prepared more largely at establishments to which the livers are conveyed in quantities. These are put into a boiler with water, and heated until they are broken up into a pultaceous mass, which is thrown upon a strainer covering the top of a cask or tub. The liquid portion passes, and upon standing separates into two parts, the oil rising to the surface of the water. The oil is then drawn off, and, having been again strained, is prepared for the market. Another and improved method, which has come into use since the extensive employment of the oil as a medicine, is to heat the livers in a wooden butt by means of low pressure steam. The pultaceous mass resulting is drained as before mentioned—the livers themselves containing, besides oil, a considerable portion of aqueous fluid, which passes off with it in the form of emulsion and separates on standing. In the case of the finest American varieties, the oil, which is made only in the winter months, is drawn off by taps from the bottom of the cooking butt, and then put into a cooling house to freeze. The solid frozen mass is put into canvas bags, and submitted, while at a low temperature, to severe pressure, whereby the pure liquid oil is forced out, leav-

ing a whitish, tallow-like mass, composed of stearin and liver débris. This residue is sold to the soap makers, and the oil bottled without further process. The oil thus variously procured was called *shore oil,* and is the purest kind. The manufacture of refined oil by improved processes is developing rapidly in Newfoundland. (See *West. Drug.,* 1897, 13.)

Formerly the crews of the larger boats, which fish upon banks far from land, cleansed the fish on board, and, throwing the offal into the sea, put the livers into barrels or other receptacles, where they underwent a gradual decomposition, the oil rising to the surface as it escaped from the disintegrating tissue. From this was obtained the so-called "Straits oil" and "banks oil." The method is, however, no longer in vogue and these forms of the oil are unknown in commerce. For further details see *U. S. D.,* 19th edition, p. 857, and *A. J. P.,* xxiii, 97; xxvi, 1. Large quantities of Norwegian cod liver oil are sold in the United States; the method of extraction depending on the action of steam does not differ greatly from that used in America. Another oil is made by the cold process and B. Rauitz, *Ph. Ztg.,* 1900, 261, furnishes the following account: The fresh livers, separated from the gall-bladder, are placed in a wooden tub, 5 feet in height by 7 feet in diameter, until the tub is nearly full, which is then left exposed to the action of the sun, shining day and night in these high latitudes. After about three weeks the extraction is completed, and, owing to the favorable atmospheric conditions and the evident absence of germs in this far polar region, not the slightest evidence of decomposition manifests itself during this process. The oil runs off pure and simply has the odor characteristic of cod liver oil, and while the "steam cod liver oil" requires refining, that obtained by the "cold process" described is ready for the market as run off from the tubs. This explains why in more southerly latitudes it is impossible to prepare a satisfactory cod liver oil; the cold process is not available, while the steam process does not yield a desirable oil.

The oil is sometimes procured by expression. Donovan recommends the following plan, which affords a very fine oil. The livers, perfectly sound and fresh, are to be placed in a clean iron pot over a slow fire, and stirred until they assume the condition of a pulp, care being taken that the mass be not heated beyond 88.9° C. (192° F.). When this temperature is attained, the pot is to be removed from the fire, and its contents introduced into a canvas bag, through which water and oil will flow into a vessel beneath. After twenty-four hours, the oil is to be decanted and filtered through paper. In this state it is pale yellow, with little odor, and a bland not disagreeable taste.

Properties.—Cod liver oil prepared by the putrefactive method had a brown color and a strong offensive odor and flavor. It contained a large proportion of free fatty acids. The color of the modern oil is from the slightest tint of transparent yellow to a fine golden yellow. It is of a rather thin consistence, and has a characteristic odor and taste, by which it may be distinguished from other oils. We regard the sensible properties as the most certain tests of the genuineness of the oil. They are much less distinguishable in the pale than in the dark brown varieties, but we have met with no specimen which did not possess them in some degree. In the purest they are scarcely repulsive, in the dark brown they are very much so. When a decided odor of ordinary fish oil is perceived, the genuineness may always be suspected. It is quite distinct from that peculiar to the cod liver oil. The pale yellow oil is now exclusively used for medicinal purposes. The sp. gr. at 22.4° C. 72° F.), as ascertained by Procter, varied from 0.915 to 0.9195—the first being that of the *hake* oil, the second that of the *haddock,* while the sp. gr. of the purest oil from the common cod was 0.917. De Jongh found the sp. gr. at 17.2° C. (63° F.) of the pale 0.923, of the light brown 0.924, of the dark brown 0.929. The oil from the cod does not congeal at –10° C. (14° F.), though that of *G. carbonarius* and that of the livers of different species of *Raja* let fall at that temperature a solid fatty matter, supposed to be palmitin. Alcohol dissolves from 2.5 to 6 per cent., water from 0.637 to 1.28 per cent., of different varieties, the pale yielding least to these solvents. (*J. P. C.,* Jan., 1854, p. 39.) The official description is as follows: "Cod Liver Oil is a pale yellow, thin, oily liquid, having a peculiar, slightly fishy, but not rancid odor, and a fishy taste. It is slightly soluble in alcohol; soluble in ether, chloroform, carbon disulphide, or ethyl acetate. Specific gravity: 0.918 to 0.922 at 25° C. (77° F.). A solution of 1 drop of the Oil in 1 mil of chloroform when shaken with 1 drop of sulphuric acid acquires a violet-red tint, gradually changing to reddish-brown. Allow 2 or 3 drops of fuming nitric acid (specific gravity about 1.44) to flow alongside of 10 or 15 drops of the Oil contained in a watch glass; a reddish or purplish color is produced at the zone of contact. On stirring the mixture with a glass rod, this color becomes bright rose-red (distinction from *seal oil,* which shows no change in color, and from *other fish oils,* which become blue). Cod Liver Oil is only slightly acid to litmus paper which has been previously moistened with alcohol (*free fatty acids*). Saponification value: not less than 180 nor more than 190 (see Part III, Test No. 9). Iodine value: not less than 140 nor more than 180 (see Part III, Test No. 8)." *U. S.*

"Pale yellow. Slight, fishlike, but not rancid odor; taste bland, fishlike. Specific gravity 0.920 to 0.930; *saponification value* 179 to 192; *iodine value* 155 to 173; *acid value* not more than 2.5; *refractive index* at 40° C. (104° F.) 1.4704 to 1.4745; *unsaponifiable matter* not more than 1.5 per cent. When exposed for three hours to a temperature of 0° C. (32° F.), no solid fat separates." *Br.*

The chemical composition of the glycerides in

cod liver oil is very complicated. Palmitic and stearic acids are present. But the so-called "stearin" separating from cod liver oil on cooling contains some unknown unsaturated compounds, as the cod liver stearin has a very high iodine value (113.4, Heyerdahl; 94, Lewkowitsch). The glycerides of the lower fatty acids, such as acetic, butyric, valeric, and capric acids, stated by various authors to occur in cod liver oil, are according to Salkowski and Steenbuch, secondary products due to the putrefaction of the livers. The researches of Heyerdahl (*Cod Liver Oil and Chemistry*, P. Möller, London, 1895) give as present in the mixed fatty acids about 4 per cent. of palmitic acid, 20 per cent. of *jecoleic acid*, $C_{18}H_{36}O_2$, and 20 per cent. of *therapic acid*, $C_{17}H_{26}O_2$, *morrhuic acid*, $C_9H_{13}O_3N$, and *asellic acid*, $C_{17}H_{32}O_2$, have also been reported. The former is a nitrogenous compound and is supposed to be identical with a basic substance named *gaduine* which had been reported. Heyerdahl states that in the fresh state cod liver oil contains no hydroxy-acids.

A characteristic constituent of cod liver oil is *cholesterol*, which can be isolated by saponifying the oil and exhausting the soap with ether. The quantity of cholesterol, according to Allen and Thomson, is from 0.46 to 1.32 per cent. By reaction with ammonia in distillation the oil yields a volatile alkaloid, *trimethylamine*, C_3H_9N, which has a strong pungent odor, recalling that of herring pickle, of which the same alkaloid is an ingredient. No other official fatty oil yields a similar product. (See *A. J. P.*, xxiv, 343.) Gautier has obtained from cod liver oil the leucomaines *butylamine, iso-amylamine, hexylamine*, and *dihydrolutidine*, and two fixed bases, *aselline*, $C_{25}H_{32}N_4$, and *morrhuine*, $C_{19}H_{27}N_3$. Aselline was found by its discoverer to be relatively feeble physiologically; morrhuine, of which about 2 milligrammes are believed to exist in a tablespoonful of ordinary cod liver oil, is affirmed to have the properties of exciting the appetite and acting as a powerful diuretic and diaphoretic. Besides these bases, an acid containing nitrogen has been found. This acid, *morrhuic acid*, $C_9H_{13}NO_3$, is probably identical with De Jongh's *gaduine*. Some have been disposed to ascribe the virtues of cod liver oil to its iodine and bromine, but these are in too small proportion for any effect, and the oil has produced results which have never been obtained from iodine and bromine themselves. The presence of iodine cannot be detected by the usual tests. It is necessary to convert the oil into a soap, and to carbonize this, before it will give evidence of iodine. The proportion never exceeds 0.05 per cent., or 1 part in 2000, and it is by no means certain that iodine is always, if ever, present in pure oil. The proportion of iodine present has been investigated by E. C. Stanford (*P. J.* [3], xiv, 353), who found it to be extremely minute, ranging from 0.00138 to 0.00433 per cent., with an average of 0.00322 per cent. The oil is capable of dissolving a larger proportion of iodine, and, if any specimen contain more than 0.05 per cent., there is reason to suspect that iodine has been added. Cod liver oil becomes rancid so easily that it contains varying amounts of free fatty acids, frequently showing their presence, even when freshly rendered. Medicinal oils, however, should not show more than from 0.3 to 0.7 per cent. of free acid, calculated as oleic acid.

The so-called active principles of cod liver oil which are found in the market under various names indicative of their origin are usually made by alcoholic extraction of the oil or of the livers themselves. They consist almost entirely of crude fatty acids, no iodine, bromine or phosphorus is detectable, the bases which are sometimes present are in very minute amount, and are probably of the ptomaine type, derived from partly decomposed products. These so-called alcoholic extracts or active principles are themselves scarcely soluble in diluted alcoholic menstrua, such as are used in preparing the so-called "tasteless" preparations of cod liver oil, so that such preparations can possess little or no activity due to cod liver products.

Tests of Purity.—In consequence of the great demand for this oil, it has not infrequently been adulterated with other fixed oils, and occasionally others have been fraudulently substituted for it. The importance, therefore, of ascertaining some mode of testing its purity and genuineness is obvious.

There is reason to believe that all the oils from the livers of the *Gadidæ* have analogous properties. They have been indiscriminately used, and upon the results of their employment is based, in part, the present reputation of the medicine. They may, therefore, be considered as in fact one oil, so far as their medicinal use is concerned. Unfortunately, chemistry has yet discovered no perfectly reliable test. The furthest it has gone is to point out certain reactions, which may be considered as evidences of the presence of biliary principles in the oil, thus indicating its hepatic origin. Among these probably the most characteristic is that of Hager and Salkowski, in which a drop of sulphuric acid, added to fresh cod liver oil, on a porcelain plate, causes a centrifugal movement in the oil, and gives rise to a fine violet color, soon passing into a yellowish or brownish-red. Sometimes, instead of assuming the violet hue, the color immediately becomes a clear red or a dark brownish-red. This is said to be especially the case with those specimens of the oil which have been prepared by boiling the livers with water. Shark liver oil responds in like manner to the test of sulphuric acid, but is said to have the sp. gr. 0.866, which is much lower than that of any variety of the genuine oil. Rauitz (*Ph. Ztg.*, 1900, 261) states that Norwegian oil prepared by the cold process is often adulterated with the oil from a species of shark, *Scymnus vulgaris*. According to Kremel, fuming nitric acid causes instantly, when agitated with cod liver oil, a pinkish or rose-red color, which soon becomes

brown, while no such effect is produced on other animal or vegetable oils. According to Winckler, the oil should afford the odor of herring pickle when heated with potassium hydroxide, lime, and ammonium chloride. But the most reliable tests are the sensible properties of odor and taste. If there be none of the peculiar shoe leather odor and taste, or if a strong lamp oil odor be perceptible, the oil may be suspected. Little of importance can be inferred from the color.

Uses.—Dr. Owen T. Williams (*P. J.*, 1912, p. 806), in discussing the subject of cod liver oil from the pharmacological and biochemic standpoint, states that the idea that the value of cod liver oil is due to the presence of infinitesimal amounts of constituents, such as sulphur, iodine, phosphorus, etc., is not true, but that its peculiar effectiveness in *tuberculosis* is intimately associated with its food value and is due to the fat itself, which being free from phosphates and consisting almost entirely of unsaturated fatty compounds is a different type of fat from those usually administered or found in foods of the oils on the market. He states that those have the greatest value which have been prepared under the most favorable conditions to prevent oxidation.

The questions of the way in which cod liver oil exercises its beneficent influence in morbid conditions, and to which of its numerous ingredients it owes its therapeutic value, are still matters of difference of opinion. Formerly many attributed its actions to the traces of iodine, phosphorus, or organic bases it contained. This view has, however, been generally abandoned; the extracts containing these principles separated from the oil have not yielded the same results. The therapeutic virtues, therefore, apparently reside in some of the constituents of the oil itself. Whether or not it acts simply as a foodstuff or whether it has some direct influence on the bodily metabolism, is open to dispute. It seems pretty well established that not only is cod liver oil absorbed from the intestinal tract better than any other fats, but that it actually increases the utilization of other forms of fatty foods. An interesting observation has been made by Osborne and Mendel that young rats who have been fed on a diet containing no form of fat but lard until their growth has ceased, will immediately recommence growing when cod liver oil is substituted for the lard. Williams (*B. M. J.*, 1912, ii, p. 700) believes that the unsaturated fatty acids have a direct inhibiting effect on the growth of the tubercle bacilli which may in part explain its action in tuberculosis.

Cod liver oil is used in all forms of *malnutrition*, especially, however, in various forms of *tuberculosis*. The old idea that it had a specific influence in this infection is probably incorrect, but in the reaction against its use the pendulum has swung too far and it is ofttimes neglected or even condemned in cases in which it might be well employed. It is often of service in those types of *chronic rheumatism* or *gout* which are associated with malnutrition, and has been highly lauded in *rickets* and other diseases of the bones. It is unique among the oils in that it is absorbable through the skin, at least by young infants, in sufficient quantity to have a perceptible influence upon nutrition.

Various measures have been recommended for overcoming the objectionable taste which is a great obstacle to the wider use of this remedy. None of these, however, are entirely successful. It is most frequently exhibited in the form of one of the numerous emulsions upon the market, of which that with malt extract is one of the best. It is sometimes given in flexible capsules, but these have the objection that they can only hold comparatively small doses. Dufourmantel (*J. P. C.*, June, 1864) prepared a jelly by dissolving half a drachm of ichthyocolla in as little hot water as possible, and then gradually mixing with it a fluidounce of the oil with four drops of the oil of anise, taking care that the temperature should not rise above 24° C. (75.2° F.).

Phosphorized cod liver oil may be made by dissolving one grain of phosphorus in four fluidounces of cod liver oil.

Glyconin Emulsion of Cod Liver Oil.—The formula proposed by Close, and at one time largely used by Andrews, Beard, and others, is as follows: Cod liver oil, 4 fluidounces; glyconin, 9 fluidrachms; aromatic spirit of ammonia, 1 fluidrachm; sherry wine, 2 fluidounces, diluted phosphoric acid, 4 fluidrachms, essence of bitter almond (made by dissolving 1 fluidrachm of the volatile oil in half a pint of alcohol) 2 fluidrachms. The cod liver oil is to be added *very slowly* to the glyconin with brisk stirring, and the other ingredients added in the order named. *Glyconin* or *Glyceritum Vitelli* is made by mixing 45 Gm. of fresh yolk of egg with 55 Gm. of glycerin.

The following is Carlo Pavesi's formula for deodorized cod liver oil. Cod liver oil, 1000 parts; ground roasted coffee, 50 parts; animal charcoal, 25 parts. Place the ingredients in a flask, which is to be well closed, and digest on a water bath during the space of one hour; then set it aside for three days, occasionally shaking the contents, and filter. This preparation has a peculiar coffee flavor, and is quite pleasant to take, the only objection being the liability to cultivate in the patient a distaste for using coffee as a beverage. (*N. R.*, Jan., 1876.)

The *olein* of cod liver oil has been recommended by Arthur Leared, when the oil itself disagrees with the stomach. He has found it to produce the same remedial effects, and to be borne much better. It may be given in the same dose. A *solution of quinine in the oil* may be made by heating the freshly precipitated alkaloid with the oil, in the proportion of two grains to a fluidounce, by means of a water bath, until the mixture becomes quite clear.

Dose, one to four fluidrachms (3.75–15 mils).

Off. Prep.—Emulsum Olei Morrhuæ, *U. S.;* Emulsum Olei Morrhuæ cum Calcii Lactophosphate, *N. F.;* Emulsum Olei Morrhuæ cum Calcii Phosphate, *N. F.;* Emulsum Olei Morrhuæ cum Malto, *N. F.;* Emulsum Olei Morrhuæ cum Hypophosphitibus, *N. F.;* Emulsum Olei Morrhuæ cum Pruno Virginiana, *N. F.;* Emulsum Olei Morrhuæ cum Vitello, *N. F.*

OLEUM MYRISTICÆ. U. S., Br.

OIL OF MYRISTICA Ol. Myrist. [Myristica Oil, Oil of Nutmeg]

(ō'lę-ŭm mȳ-rĭs'tĭ'cæ)

"A volatile oil distilled from the kernel of the ripe seed of *Myristica fragrans* Houttuyn (Fam. *Myristicaceæ*). Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.* "Oil of Nutmeg is the oil distilled from Nutmeg, and rectified." *Br.*

Volatile oil of Nutmeg; Oleum Myristicæ Ætherеum, Oleum Nucis Moschati, Oleum Nucistæ Ætherеum; Huile volatile (Essence) de Muscade, *Fr.;* Oleum Macidis, *P. G.;* Aetherisches Muskatöl, Aetherisches Muskatnussöl, *G.*

This oil is obtained from nutmegs after powdering them by distillation with water. A better method, according to J. Cloez, is to exhaust the powder with carbon disulphide or ether, distil off the solvent by means of a water bath, and expose the butter-like residue to a current of steam, the vapor being conveyed into a refrigerated receiver, where it condenses. (*J. P. C.,* Fév., 1864.) Schimmel & Co. (1899) state that oil of nutmeg is made from the light, worm-eaten nuts, of which large quantities are rejected in sorting the different qualities in Holland. The worm most strangely robs the nutmeg of its fat oil, while the essential oil remains in the nut in full. Oil of myristica is colorless or of a pale straw color, limpid, lighter than water, soluble in an equal volume of glacial acetic acid, in alcohol and ether, with a neutral reaction, a pungent spicy taste, and a strong odor of nutmeg. It is officially described in the United States Pharmacopœia (Ninth Revision) as "a colorless or pale yellow liquid, having the characteristic odor and taste of nutmeg. It is soluble in an equal volume of alcohol; also soluble in 3 volumes of 90 per cent. alcohol. Specific gravity: 0.859 to 0.924 at 25° C. (77° F.). The optical rotation varies from +12° to +30° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21). Evaporate 3 Gm. of the Oil on a water bath; not more than 0.06 Gm. of residue remains." *U. S.*

"Colorless or pale yellow. Odor and taste those of Nutmeg. Specific gravity 0.870 to 0.925; *optical rotation* +13° to +30°; *refractive index* at 25° C. (77° F.) 1.474 to 1.484. Soluble in 3 parts of *alcohol* (90 per cent.). Leaves not more than 5 per cent. of residue when evaporated on a water-bath." *Br.*

The mixture of volatile and fixed oils obtained by powerfully expressing nutmegs between heated plates may be separated by agitation with water. Upon standing, the latter deposits a crystalline solid, which was called by Playfair *myristin.* From its solution in alcohol he obtained it in extremely light crystalline scales, which, after repeated crystallization, had still the odor of nutmeg, were fusible at 31° C. (87.8° F.), soluble in the ordinary menstrua of substances of the same class, and, as just said, insoluble in water. By glacial acetic acid it was first colored red. (*P. J.,* March, 1874, 714.) It was identified as the glyceride of *myristic acid,* $C_{14}H_{28}O_2$, and had, therefore, the formula $C_3H_5(C_{14}H_{27}O_2)_3$. Besides the myristin or solid fat, there is present about an equal amount of a liquid fat containing free acid. The essential oil consists chiefly of pinene with probably some dipentene, also *myristicol,* $C_{10}H_{16}O$, and *myristicin,* $C_{11}H_{12}O_3$, linalool, borneol, terpineol, geraniol, eugenol, and a number of organic acids. Semmler (*Ber. d. Chem. Ges.,* 1890, 1803) examined an oil of myristica of sp. gr. 0.8611 which contained only terpenes; these boiled at about 50° C. (122° F.) under a pressure of 8 mm.

Uses.—The oil of nutmeg unites to the common properties of the aromatics considerable narcotic power. It causes in the lower animals dilatation of the pupils, unsteadiness of the gait followed by sleepiness, with slow respiration, and, if the dose be large enough, loss of reflexes. According to Dale (*Proc. Royal Soc. Med.,* Feb., 1909) doses large enough to produce narcosis in the cats are invariably fatal through fatty degeneration of the liver. A number of fatal cases of nutmeg poisoning have been reported in human beings. The symptoms have been the same as those which are observed in the lower animals. The toxic ingredient is myristicin.

The oil of nutmeg is used to correct the taste of various drugs and as a local stimulant to the gastro-intestinal tract.

Dose, one to five minims (0.06–0.3 mil).

Off. Prep.—Spiritus Myristicæ, *Br.;* Elixir Glycyrrhizæ Aromaticum, *N. F.;* Elixir Pepsini et Rennini Compositum, *N. F.;* Mistura Oleo-Balsamica, *N. F.*

OLEUM OLIVÆ. U. S., Br.

OLIVE OIL Ol. Oliv.

(ō'lę-ŭm ǫ-lī'væ)

"A fixed oil obtained from the ripe fruit of *Olea europæa* Linné (Fam. *Oleaceæ*). Preserve it in well-closed containers, in a cool place." *U. S.* "Olive Oil is the oil expressed from the ripe fruit of Olea europæa, *Linn.,* and refined." *Br.*

Sweet Oil; Huile d'Olive, *Fr. Cod.;* Oleum Olivarum, *P. G.;* Olivenöl, *G.;* Olio di olive, *It.;* Aceite de olivas, *Sp.*

Olea europæa L. is one of the leading fruit trees of the world. It is usually from fifteen to twenty-five feet in height, though sometimes much larger, especially in Greece and the Levant. It has a solid, erect, unequal stem, with numer-

ous straight branches, covered with a grayish bark. The leaves, which stand opposite to each other on short footstalks, are evergreen, firm, lanceolate, entire, two or three inches in length, with the edges somewhat reverted, smooth and of a dark green color on their upper surface, whitish and almost silvery beneath. The flowers are small, yellowish-white, and disposed in opposite axillary clusters, about half as long as the leaves, and accompanied with small, obtuse, hoary bracts. The fruit, or olive, is a smooth, oblong or oval drupe, greenish at first, but of a deep violet color when ripe, with a fleshy pericarp, and a very hard nut of a similar shape. Clusters of not less than thirty flowers yield only two or three ripe olives.

The olive tree, though believed by some to have been originally from the Levant, flourishes at present in all the countries bordering on the Mediterranean, and has been cultivated from time immemorial in Spain, the south of France, and Italy. It begins to bear fruit after the second year, is in full bearing at six years, and continues to flourish for a century. There are forty varieties, distinguished by the form of the leaves and the shape, color, and size of the fruit. The variety *longifolia* of Willdenow is said to be chiefly cultivated in Italy and the south of France, and the *latifolia* in Spain. The latter bears much larger fruit than the former, but the oil is less esteemed. The olive is largely cultivated in the north of Africa, especially in the vicinity of Tunis, and considerable quantities of the oil are exported from that city. (*P. J.*, Sept., 1873, 204.) The tree has been introduced into South Australia, and the oil will probably become of commercial importance there.

Olives are cultivated especially in Spain in the district of Cadiz. Two classes are produced, the one known as the "Queen olive," a large olive, which is mostly exported to the United States; the other the Manzanillo, or small olive, which is chiefly consumed in Spain, South America and Cuba. The Spanish production for 1916 amounted to 1,146,599 metric tons of olives and the oil to 207,115 tons. The olive is largely cultivated in California, where it grows luxuriantly. The production of olive oil in the United States in 1916 was 1,336,674 lbs. produced in 22 establishments. The importation of edible olive oil amounted to 7,382,353 gallons.

There are many varieties of the olive grown in California. J. L. Howland, of Pomona, reports the following percentage of oil yielded by each variety as cultivated in California as the result of two years' test; Pendulina, 21; Rubra, 18.5; Oblonga, 18; Mission, 17.9; Uvaria, 17.5; Nevadillo Blanco, 16.5; Columella, 16.5; Precox, 14; Picholine, 10; Manzanillo, 8.5. For further information concerning the subject the reader is referred to the various Proceedings of the California State Convention of Olive Growers.

Pickled olives, made by soaking green olives first in dilute solution of sodium hydroxide and then in salt water, are largely used as an article of food; the ordinary green olive of commerce has been picked before ripening. The ripe olive, which, in the United States, is chiefly obtained from California, is dark-purple, often almost black, very different in taste from the ordinary unripe pickled fruit, and is said to contain about 50 per cent. of olive oil, so that it affords an excellent method of administering fat.

The leaves and bark of the olive tree have an acrid and bitterish taste, and have been employed as substitutes for cinchona, though with no great success. Attention has been called, in France, to a hydro-alcoholic extract of the leaves, as having considerable febrifuge powers. In the quantity of from ten to twenty grains daily, in divided doses, it has been found useful in preventing the hectic paroxysms. In hot countries, a substance resembling the gum-resins exudes spontaneously from the bark. It was thought by the ancients to possess useful medicinal properties, but is not now employed. Analyzed by Pelletier, it was found to contain resin, a little benzoic acid, and a peculiar principle analogous to gum, which has been named *olivile*. But the fruit is by far the most useful product. In the unripe state it is hard and insupportably acrid, but when macerated in water or an alkaline solution, and afterwards introduced into a solution of common salt it loses these properties, and becomes a pleasant and highly esteemed article of diet. Mannite has been found in all parts of the tree while in vital activity, as in the green leaves and unripe fruit, but cannot be detected in the yellow fallen leaves or in the perfectly ripe fruit. (*A. J. P.*, 1866, p. 179.) The pericarp, or fleshy part of the ripe olive, abounds in a fixed oil, which constitutes its greatest value, and for which the tree is chiefly cultivated in Southern Europe. In the unripe olive a peculiar green substance, together with mannite, has been found by S. de Lutz, both of which disappear as the fruit ripens, being probably converted into oil, which now takes their place. (*J. P. C.*, June and Dec., 1862.) The olives ripen from November to March, and the oil is obtained by first bruising them in a mill and then submitting them to pressure. The product varies much, according to the state of the fruit and the circumstances of the process. The best, called *virgin oil*, is obtained from the fruit picked before perfect maturity, and immediately pressed. It is distinguished by its greenish hue. The common oil used for culinary purposes and in the manufacture of the finest soaps is procured from very ripe olives, or from the pulp of those which have yielded the virgin oil. In the latter case the pulp is thrown into boiling water, and the oil removed as it rises. An inferior kind, employed in the arts, especially in the preparation of the coarser soaps, plasters, unguents, etc., is afforded by fruit which has been thrown into heaps, and allowed to ferment for several days, or by the marc left after the expression of the finer kinds of oil, broken up, allowed to ferment, and again introduced into the press. The

remarks made under the head of *Oleum Myristicæ* in relation to the extraction of the fixed oils by means of solvents are applicable also to olive oil.

Properties.—The pure oil is an unctuous liquid, or "a pale yellow or light greenish-yellow, oily liquid, having a slight, peculiar odor and taste, with a faintly acrid after-taste. It is slightly soluble in alcohol, but miscible with ether, chloroform, or carbon disulphide. Specific gravity: 0.910 to 0.915 at 25° C. (77° F.). When cooled to from 10° to 8° C. (50°–46.4° F.), the Oil becomes somewhat cloudy from the separation of crystalline particles, and at 0° C. (32° F.) it usually forms a whitish, granular mass. Mix 5 mils of the Oil in a test tube with 5 mils of a mixture of equal volumes of amyl alcohol and carbon disulphide, which contains 1 per cent. of sulphur in solution, and immerse the test tube to one-third its depth in boiling, saturated aqueous salt solution; no reddish color develops in fifteen minutes (*cottonseed oil*). Mix 2 mils of the Oil with 1 mil of hydrochloric acid containing 1 per cent. of sugar, shake the mixture for half a minute and allow it to stand for five minutes; on now adding 3 mils of distilled water to the mixture and again shaking it, the acid layer shows no pink color (*sesame oil*). Saponification value: not less than 190 nor more than 195 (see Part III, Test No. 9). Iodine value: not less than 79 nor more than 90 (see Part III, Test No. 8)." *U. S.*

"Pale yellow or greenish yellow. Faint but not rancid odor; taste bland. Frequently assumes a pasty consistence when maintained for some time at a temperature of 10° C. (50° F.), and at a lower temperature may become a soft granular mass. Specific gravity 0.915 to 0.918; *saponification value* 188 to 197; *iodine value* 79 to 87; *acid value* not more than 6.0; *refractive index* at 40° C. (104° F.) 1.4605 to 1.4635. A mixture of 2 millilitres of the Oil with 1 millilitre of *amylic alcohol* and 1 millilitre of a solution (1 in 100) of *precipitated sulphur* in *carbon disulphide*, placed in a test-tube immersed in boiling *water*, does not assume a red color within thirty minutes (absence of cottonseed oil). When a mixture of 2 millilitres of the Oil and 1 millilitre of *hydrochloric acid* containing 1 per cent. of *refined sugar* is shaken for half a minute, and allowed to stand for five minutes, the acid layer does not become pink (absence of sesame oil). When 1 millilitre of the Oil and 15 millilitres of *N/1 alcoholic solution of potassium hydroxide* are boiled for twenty minutes in a flask provided with a reflux condenser, set aside for twenty-four hours at a temperature not exceeding 15.5° C. (60° F.), and afterwards heated on a water-bath for three minutes, the solution does not deposit crystals on standing for twenty-four hours further (absence of arachis oil)." *Br.*

The concrete portion, about 28 per cent. of the oil, which separates at a freezing temperature, consists chiefly of the glyceride of *palmitic acid*, $C_{16}H_{32}O_2$, together with a smaller amount of glyceride of *arachidic acid*, $C_{20}H_{40}O_2$ (stearic acid is stated by Hehner and Mitchell to be absent entirely); the liquid portion is essentially olein, $C_3H_5(O.C_{18}H_{33}O)_3$, with a small amount (seven parts for ninety-three of olein) of the glyceride of the less saturated linolic acid. According to Braconnot, the oil contains 72 per cent. of olein and 28 of palmitin. A small quantity of phytosterin has also been found in the oil. Olive oil is solidified by nitrous acid and mercuric nitrate, and converted into a peculiar fatty substance, called *elaidin*. The olein of all oils which have not the drying property undergoes the same change when acted on by nitrous acid.

The greenish color is owing to the presence of a trace of chlorophyll, and a trace of cholesterin is also extracted by repeated agitation with glacial acetic acid.

For discussion of the spectra of olive oil, see *P. J.*, 3d series, vii, 22, 110.

Olive oil, when exposed to the air, is prone to become rancid, acquiring a disagreeable odor, a sharp taste, and a thicker consistence; it also loses its color, and the change is promoted by heating it.

It is frequently adulterated with the cheaper fixed oils, especially with cottonseed oil, arachis oil, sesame oil and poppy seed oil; the adulteration may sometimes be detected by reducing the temperature to the freezing point. As other oils are less readily congealed than is the olive oil, the degree of its purity will be indicated by the degree of concretion. Another mode has been indicated by Poutet, founded on the property possessed by mercuric nitrate of solidifying the oil of olives, without a similar influence upon other oils. Six parts of mercury are dissolved at a low temperature in seven and a half parts of nitric acid of the sp. gr. 1.35, and this solution is mixed with the suspected oil in the proportion of one part to twelve, the mixture being occasionally shaken. If the oil is pure, it will be converted after some hours into a yellow solid mass; if it contains a minute proportion, even so small as a twentieth, of poppy or cottonseed oil, the resulting mass will be much less firm, and a tenth will prevent a greater degree of consistence than oils usually acquire when they concrete by cold. Lewkowitsch (*Chemical Analysis of Oils, Fats, and Waxes*, 2d ed., 1898, 462) says that the color reactions proposed by various authors are altogether unreliable and yield no definite results, with the exception of the color test (Baudoin's test, see *Oleum Sesami*) for sesame oil and perhaps Bechi's and Milliau's or Halphen's for cottonseed oil. For a method of detecting the *oil of arachis* (*ground nut oil*) in olive oil, see *J. P. C.*, Jan., 1872, 48. Bulletin 77 (1905), of the Bureau of Chemistry, United States Department of Agriculture, showed that most of the spurious and adulterated olive oil in the United States was of domestic origin and that the oil as imported in original packages was mostly genuine. This has been verified by numerous other investigators during recent years. Since the passage of the Food and Drugs

Act in 1906 it is rare to find a labeled container of olive oil adulterated, although much that is sold in bulk is still found to be spurious. In several states it has been judicially decided that the synonyms "sweet oil" and "salad oil" when unqualified mean olive oil. A low grade of olive oil used for soap making and other technical purposes is imported at a less rate duty than is collected on edible olive oil. The frequent use of such low grade oil for table purposes by those who are not particular about quality and flavor led to the requirement on the Part of the U. S. Treasury Department that such "technical oil" must be denatured for admission. There are three alternative and optional methods of denaturing. They consist in adding to the oil a small portion of oleoresin of capsicum, of oil of rosemary or of kerosene. Arachis oil, which is produced in large quantities in Marseilles, has been found in numerous samples of imported olive oil. According to Tambon, the present-day adulterations do not consist in the addition of a single cheaper oil, but of ingeniously prepared mixtures of different oils in such proportions to each other that on analysis it becomes difficult or impossible to distinguish the adulterated from the genuine oil by the chemical and physical constants accepted for the latter. The chief adulterants are benne, peanut and cottonseed oils. Of these, benne is easily recognized; for peanut oil there is as yet no reliable color reaction, and while Bechi's reaction may, under certain conditions, answer well for the detection of cottonseed oil, this, under others, has also proven unreliable. (*Ph. Ztg.*, 1904, 104.) According to Kreis and Grob (*S. W. P.*, 1901, 88) Billier's test is very sensitive. It is carried out by shaking the suspected oil with a solution of resorcinol in benzene and afterwards with nitric acid. Olive oil under these circumstances remains unchanged in color, cottonseed and nut oil become red violet and maw seed oil is turned brown red. Bechi's test for ascertaining the admixture of cottonseed oil with olive oil has received the approval of the Commission of Florence after most exhaustive experiments, and is as follows: One grain (0.065 Gm.) of silver nitrate is dissolved in fifteen minims (0.9 mil) of water, and six and a half fluidounces (195 mils) of alcohol are added. Two fluidounces (or 60 mils) of ether may be added to render the solution more easily miscible with the oil, but it is not absolutely necessary. A solution of eighty-five parts of amyl alcohol and fifteen parts of rape seed oil is prepared. These reagents should not be kept on hand any length of time. To ten mils of the oil to be examined one mil of the solution of silver nitrate is added, and then from eight to ten mils of the amyl alcohol reagent; the mixture is agitated strongly, and heated on a water bath for five or ten minutes. In the case of pure oils the color is unaltered by the addition of the reagents; if cottonseed oil be present, a brownish color or turbidity, varying from a light brown to a deep maroon or black (according to the extent of the adulteration), will be produced. (*A. J. P.*, 1887.) See also the official silver nitrate test. Milliau's test is a modification of the foregoing. If the fatty acids instead of the oil itself are treated with the same reagents, the same reduction of the silver salts occurs and the same brown color as in the Bechi test. Halphen's test with a mixture of amyl alcohol and carbon disulphide containing about 1 per cent. of sulphur in solution is now regarded as the most distinctive for cottonseed oil. For details see the official test.

Uses.—Olive oil is nutritious and mildly laxative and is often used in milder cases of chronic *constipation*, especially when associated with malnutrition. In the form of enema it is often a useful remedy in *fecal impaction*. It has also been recommended as a remedy for *worms*, but is of doubtful value. It was formerly largely used in the treatment of *gall stones* with the idea that it stimulated the secretion of bile. The concretions which were passed by these patients, however, were shown to be masses of hardened soap and it is extremely questionable whether the oil has any real value in this disease. Externally it is useful to soften and relax the skin and to protect it against the action of the air. The most extensive use of olive oil is in pharmacy as a constituent of liniments, ointments, cerates, and plasters.

Dose, as a laxative, from one to two fluidounces (30–60 mils).

Off. Prep.—Linimentum Ammoniæ, *Br.;* Linimentum Calcis, *Br.;* Linimentum Camphoræ, *Br.;* Oleum Phenolatum, *N. F.;* Unguentum Fuscum, *N. F.*

OLEUM PHOSPHORATUM. Br.

PHOSPHORATED OIL

(ō'lę-ŭm phŏs-phọ-rā'tŭm)

"Phosphorated Oil contains 1 per cent. by weight of Phosphorus. It should be freshly prepared." *Br.*

Huile phosphorée, *Fr. Cod.;* Liniment phosphoré, *Fr.;* Phosphorhaltiges Oel, *G.;* Aceite fosforado, *Sp.*

"Phosphorus, 1 *gramme;* Almond Oil, previously heated to 150° C. (302° F.), cooled and filtered, 98 *grammes;* Oil of Lemon, 1 *gramme*. Add the Phosphorus to the Almond Oil contained in a stoppered bottle capable of holding rather more than the required quantity; warm to about 80° C. (176° F.), and shake until the Phosphorus is entirely dissolved; cool, and add the Oil of Lemon. A clear, pale-yellow liquid, phosphorescent in the dark." *Br.*

Phosphorated oil was not retained in the U. S. P. IX, but has been transferred to the N. F. IV (see Part III).

The U. S. 1890 process, which has been retained in the N. F., does not differ essentially from that of the Br. Pharm. Both are one per cent. solutions; the British formerly contained but 0.75 per cent.

The object of heating the oil is to expel air and traces of water, which would oxidize the phosphorus. The ether not only assists in the preservation of the finished preparation, but is

also of use in rendering the oil less disagreeable to the taste. E. R. Squibb passes a current of carbon dioxide through the oil contained in the bottle in which it is to be kept, to expel the air and prevent oxidation. This is a clear and colorless or but slightly colored oil, phosphorescent in the dark, and having the odor and taste of phosphorus quite distinctly. It should be perfectly free from any particles of undissolved phosphorus. It may be administered in the form of an emulsion, like the official almond emulsion, and flavored with oil of bitter almond, or preferably in capsules; each minim contains about 1-115 of a grain of phosphorus.

Dose, one to two minims (0.06–0.13 mil).

OLEUM PICIS LIQUIDÆ RECTIFICATUM. U. S.

RECTIFIED OIL OF TAR Ol. Pic. Liq. Rect. [Oleum Picis Liquidæ, U. S. VIII Rectified Tar Oil]

(ō'lę-ŭm pī'cĭs lĭq'uį-dæ rĕc-tį-fį-cā'tŭm)

"A rectified volatile oil distilled from Tar." *U. S.*

Huile volatile de Goudron, *Fr.;* Theeröl, Pechöl, *G.*

This oil is prepared by distilling wood tar, the residue left in the still being known as pitch. It represents thoroughly the medicinal properties of tar, and is preferable on account of its less offensive taste. (See *Pix Liquida.*) It is officially described as follows: "Rectified Oil of Tar is a thick liquid having a dark reddish-brown color, and a strong, empyreumatic odor and taste. It is soluble in alcohol, the solution being acid to litmus. Specific gravity: 0.960 to 0.990 at 25° C. (77° F.)." *U. S.*

The thick tarry oil of high viscosity and almost black color, found upon the market and frequently supplied for oil of tar, does not comply with the U. S. P. requirements of sp. gr., as it is usually much heavier than water, while the U. S. P. is lighter.

Uses.—The oil of tar is used chiefly in the treatment of *chronic bronchitis.* Its action is practically the same as that of creosote, which is indeed its most important constituent. It may be administered either in emulsion or by dropping it on sugar. It is often added to boiling water for inhalation in the proportions of five to ten minims to a pint. It is also used externally in various *skin diseases.*

Dose, one to five minims (0.06–0.3 mil), administered in capsule or in emulsion.

Off. Prep.—Mistura Olei Picis, *N. F.;* Petroxolinum Picis, *N. F.;* Unguentum Picis Compositum, *N. F.*

OLEUM PIMENTÆ. U. S.

OIL OF PIMENTA Ol. Piment. [Oil of Allspice Pimento Oil]

(ō'lę-ŭm pī-mĕn'tæ)

"A volatile oil distilled from the fruit of *Pimenta officinalis* Lindley (Fam. *Myrtaceæ*), yielding not less than 65 per cent., by volume, of eugenol [$C_{10}H_{12}O_2$ = 164.10]. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

Oleum Amomi; Oil of Pimento; Huile volatile (Essence) de Piment de la Jamaïque, *Fr.;* Nelkenpfefferöl, Pimentöl, *G.*

Oil of pimenta was deleted from the British Pharmacopœia 1914.

The berries yield from 1 to more than 4 per cent. of the volatile oil, which as found in commerce is brownish-red, and has the odor and taste of pimenta, though warmer and more pungent. It has a slightly acid reaction.

"Oil of Pimenta is a colorless, yellow or reddish liquid, becoming darker with age and having the characteristic odor and taste of allspice. It is soluble in an equal volume of 90 per cent. alcohol; also soluble in 2 volumes of 70 per cent. alcohol. Specific gravity: 1.018 to 1.048 at 25° C. (77° F.). The optical rotation varies from 0° to −4° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21).

"**Assay.**—Proceed as directed under *Oleum Caryophylli,* using 10 mils of Oil of Pimenta. The residual liquid measures not more than 3.5 mils, indicating the presence of not less than 65 per cent., by volume, of eugenol." *U. S.*

It consists, like oil of clove, of two distinct portions, one a sesquiterpene, $C_{15}H_{24}$, and the other a phenol, *eugenol,* capable of extraction by shaking out with alkaline hydroxide solution. They may be separated by distilling the oil from potassium hydroxide solution. After the hydrocarbon is distilled off the phenol may be obtained by liberation from its combination with sulphuric acid and distilling. It is readily recognized as eugenol, so that oil of pimenta is analogous in its constitution to oil of clove (see *Oleum Caryophylli*). Nothing is known of the constituents which give oil of pimenta its characteristic odor.

Oil of pimenta is given for the same purposes as are the other stimulant aromatic oils.

Dose, from three to six minims (0.2–0.4 mil).

Off. Prep.—Liquor Pepsini Aromaticus, *N. F.;* Spiritus Myrciæ Compositus, *N. F.*

OLEUM PINI PUMILIONIS. U. S.

OIL OF DWARF PINE NEEDLES Ol. Pin. Pumil. [Dwarf Pine Oil]

(ō'lę-ŭm pī'nī pū-mĭ'lį-ō-nĭs)

"A volatile oil distilled from the fresh leaves of *Pinus montana* Miller (*Pinus Pumilio* Haenke) (Fam. *Pinaceæ*). Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

Oleum Pini, *Br.,* 1898; Oil of Pine; Pine Needle Oil; Latschenkieferöl, Krummholzöl, *G.;* Oleum templinum, Pumiline.

The British Pharmacopœia 1898 replaced fir wood oil by making oil of pine official. This was largely due to the investigations of J. C. Umney (*P. J.,* 1895, 161, 173, 542), who found that the *Pinus Pumilio* (now recognized as *P. montana* Miller) (*Mountain Pine*) furnished an oil of fairly constant character and superior to that from the *Pinus sylvestris* (*Scotch Fir*)

of the British Pharmacopœia 1885. It was not included in the Br. 1914 but is recognized by the U. S. IX. It "is a colorless or faintly yellowish oil having a pleasant, aromatic odor, and a bitter and pungent taste. Specific gravity: 0.853 to 0.869 at 25° C. (77° F.). No portion of the Oil distils below 170° C. (338° F.)." It resinifies on exposure, and in medicinal qualities resembles oil of turpentine, but is milder. Pine oil contains lævo-pinene, lævo-phellandrene, sylvestrene, *bornyl acetate,* and in the last portions of the distillate, cadinene. (Gildemeister and Hoffmann, *Aetherische Oele,* p. 338.) It is supposed that the pine oil owes its odor to the presence of the acetic ester of borneol, which is ordinarily present to the amount of about 3.5 per cent., and Schimmel & Co. (*Schim. Rep.* for Oct., 1897) found in a sample of American fir oil as much as 12.1 per cent.

Uses.—In medicine it may be employed for many of the purposes for which oil of turpentine has been used. As an expectorant in *chronic bronchitis* it may be administered by the mouth but is especially prized as an inhalant because of its pleasant odor. For this purpose a few drops may be placed in boiling water and the vapors inhaled. It has also been employed internally in the treatment of *chronic rheumatism.*

The leaves of the *Pinus sylvestris,* with those of other European firs and pines, by pounding are converted into a fibrous substance, known as *fir wool* (*Fichtenwolle*), which is much used in Germany as a local application in *chronic rheumatism,* the affected part being enveloped in a thick batting of the fir wool, which is also sometimes made into clothing for rheumatic persons. An extract of the leaves is also sold under the name of *fir wool extract,* for use in rheumatism.

Dose of oil of pine needles five to ten minims (0.3–0.6 mil).

OLEUM RICINI. U. S., Br.

CASTOR OIL Ol. Ricin.

(ō'lę-ŭm rĭç'ĭ-nī)

"A fixed oil obtained from the seeds of *Ricinus communis* Linné (Fam. *Euphorbiaceæ*). Preserve it in well-closed containers." *U. S.* "Castor Oil is the oil expressed from the seeds of Ricinus communis, *Linn.*" *Br.*

Huile de Ricin, *Fr. Cod.;* Oleum e semine Ricini, *Fr.;* Oleum Ricini, *P. G.;* Ricinusöl, *G.;* Olio di ricino, *It.;* Aceite de ricino; Oleum Palmæ Christi, *Sp.*

The castor oil plant, or *palma Christi,* is a native of India and is now extensively cultivated in the warmer regions throughout the world. In India there are about seventeen different varieties grown which are grouped into two types. (1) The one consisting of tall shrubs or small trees, being usually planted as a shade for other crops and yielding large seeds which contain an abundance of inferior oil. (2) The second type includes the herbaceous annuals, which, while they produce small yields, yield a much better grade of fixed oil.

The following description applies to the plant as cultivated in cool latitudes. The stem is of vigorous growth, erect, round, hollow, smooth, glaucous, somewhat purplish towards the top, branching, and from three to eight feet or more in height. The leaves are alternate, peltate, palmately six to eleven lobed, the lobes acute or acuminate and serrate, smooth on both sides, and of a bluish-green color. The flowers are monœcious, stand upon jointed peduncles, and form a pyramidal terminal raceme, of which the lower portion is occupied by the male flowers, the upper by the female. Both are destitute of corolla. In the staminate flowers the calyx is divided into five oval, concave, pointed, reflected, purplish segments, and encloses numerous stamens, united into fasciculi at their base. In the pistillate the calyx has three or five narrow lanceolate segments, and the ovary, which is roundish and three-sided, supports three linear, reddish stigmas, forked at their apex. The fruit is a roundish, glaucous capsule, with three projecting sides, covered with tough spines, and divided into three loculi, each containing one seed, which is expelled by the bursting of the capsule. This species of *Ricinus* is a native of the East Indies and Northern Africa, naturalized in the West Indies, and cultivated in various parts of the world, in few countries more largely than in the Middle and Western United States. The flowers appear in July, and the seeds ripen successively in August and September. A decoction or poultice of the leaves is sometimes used as a local galactagogue, and an infusion has been given internally for a similar purpose. (*L. L.,* Dec., 1859.)

1. The Seeds.—These are from 8 to 18 mm. long and 4 to 12 mm. broad, oval, compressed, obtuse at the extremities, very smooth and shining, and of a grayish or ash color, marbled with reddish-brown spots and veins. At one end of the seed is a small yellowish caruncle, from which an obscure longitudinal ridge proceeds to the opposite extremity, known as the raphe. In its general appearance the seed is thought to resemble the insect called the *tick,* the Latin name of which has been adopted as the generic title of the plant. Its variegated color depends upon a very thin pellicle closely investing a hard, brittle, blackish, tasteless, easily separated shell, within which is the kernel, highly oleaginous, of a white color, and of a sweetish taste succeeded by a slight degree of acrimony. The seeds easily become rancid, and are then unfit for the extraction of the oil, which is acrid and irritating. In 100 parts Geiger found, exclusive of moisture, 23.82 parts of envelope, and 69.09 of kernel. These 69.09 parts contained 46.19 of fixed oil, 2.40 of gum, 20.00 of starch and lignin, and 0.50 of albumen. Henry Bower could find no starch, but separated from the seeds an albuminoid principle, which acted with amygdalin and water like emulsin, producing the odor of oil of bitter almond, though in a less degree. (*A. J. P.,* xxvi, 208.) It is highly probable that it is

this principle which, acting as an enzyme on the oily matter of the seeds, gives rise to changes in its nature which render them rancid. (See *Olea Fixa,* p. 810.) G. J. Scattergood found the odor of castor oil to be developed in the beans when bruised with water, and much more powerfully in those long kept than in the fresh. The water distilled from the seeds has a peculiar nauseous odor, quite distinct from that of the oil. (*A. J. P.,* xxvii, 207.)

Taken internally the seeds are powerfully cathartic, and often emetic. Two are sufficient to purge with great violence, and three have produced fatal gastro-enteritis in the adult. After expression of the oil, and treatment with pure alcohol, Calloud found the residue to be powerfully emetic in the quantity of 30 grains, taken in two doses. (*J. P. C.,* 3e sér., xiv, 190.) According to Guibourt, the toxic property pervades the whole kernel, the integuments being inert. The experiments of Scattergood, who found that the water distilled from the seeds is emetic and cathartic, would seem to show that the active principle is volatile, but the researches of Stillmark indicate that it is an enzyme, *ricin,* which is a so-called phytalbumose and has been obtained as a white amorphous powder, and is best dissolved in a 10 per cent. salt solution. The aqueous solution of the pure ricin has a neutral reaction. It is a violent poison. E. L. Boerner (*A. J. P.,* 1876, p. 481) obtained butyric acid by macerating the exhausted marc of the seeds with water until decomposed.

2. The Oil.—This may be extracted from the seeds in three ways: 1, by decoction; 2, by expression; 3, by the agency of alcohol or other solvent.

The process by decoction, which has been practised in the East and West Indies, consists in bruising the seeds, previously deprived of their husk, and then boiling them in water. The oil, rising to the surface, is skimmed or strained off, and afterwards again boiled with a small quantity of water to dissipate the acrid principle. The seeds, it is said, are sometimes roasted, to increase the yield. But by a temperature much above 100° C. (212° F.) the oil is rendered brownish and acrid, and the same result takes place in the second boiling, if care is not taken to suspend the process soon after the water has been evaporated; hence it happens that the West India oil has generally a brownish color, an acrid taste, and irritating properties.

The oil is obtained in this country by expression. The following, we have been informed, are the outlines of the process usually employed by those who prepare it on a large scale. The seeds, having been thoroughly cleansed from the dust and fragments of the capsules with which they are mixed, are conveyed into a shallow iron reservoir, where they are submitted to a gentle heat insufficient to scorch or decompose them, and not greater than can be readily borne by the hand. The object of this step is to render the oil sufficiently liquid for easy expression. The seeds are then introduced into a powerful hydraulic press. A whitish oily liquid is thus obtained, which is transferred to clean iron boilers supplied with a considerable quantity of water. The mixture is boiled for some time, and, the impurities being skimmed off as they rise to the surface, a clear oil is at length left upon the top of the water, the mucilage and starch having been dissolved by this liquid, and the albumen coagulated by the heat. The latter ingredient forms a whitish layer between the oil and the water. The clear oil is now carefully removed, and the process is completed by boiling with a minute proportion of water, and continuing the application of heat until aqueous vapor ceases to rise, and until a small portion of the liquid, taken out in a vial, continues perfectly transparent when it cools. The effect of this last operation is to clarify the oil, and to render it less irritating by driving off the acrid volatile matter. But much care is requisite not to push the heat too far, as the oil then acquires a brownish hue and an acrid peppery taste. After the completion of the process, the oil is put into barrels and sent into the market. See article on the preparation of castor oil. (*A. J. P.,* 1879, p. 481.) There is reason, however, to believe that much of the American oil is prepared by merely allowing it to stand for some time after expression, and then drawing off the supernatant liquid. One bushel of good seeds yields five or six quarts, or about 25 per cent. of the best oil. If not carefully prepared, it is prone to deposit a sediment upon standing, and the apothecary may find it necessary to filter it through coarse paper before dispensing it. Perhaps this may be owing to the plan just alluded to of purifying the oil by rest and decantation. We have been told that the oil in barrels usually deposits in cold weather a copious whitish sediment, which is redissolved when the temperature rises. A large proportion of the oil consumed in the eastern section of the Union has been derived, by the way of New Orleans, from Illinois and the neighboring States, where it has been at times so abundant that it has been used for burning in lamps and for lubricating machinery.

The process for obtaining castor oil by means of alcohol has been practised in France, but the product is said to become rancid more speedily than that procured in the ordinary mode. Such a preparation has been employed in Italy, and is asserted to be less disagreeable to the taste, and more effective, than the common oil obtained by expression. According to Parola, an ethero-alcoholic extract and an ethereal or alcoholic tincture of the seeds operate in much smaller doses than the oil, and with less disposition to irritate the bowels or to cause vomiting. (See *Am. J. M. S.,* N. S., xiii, 143.)

Owing to the presence of ricin, "*castor pomace,*" or the oil cake obtained by the extraction of castor oil, is unfit for animal food.

For the process of removing the poisonous principle see *P. J.*, lxviii, 213.

Italian Castor Oil.—The castor oil plant is cultivated throughout Italy, but especially in the neighborhood of Verona, where the oil is prepared with great care and is remarkably free from the peculiar odor and taste which render this medicine so repulsive to many palates. As it is highly desirable, for certain purposes, that the oil should be as free from these properties as possible, it is a point worthy of investigation, why it is that the Italian oil is superior to most commercial varieties of the oil in these respects. The following facts in relation to the mode of preparing the oil practised at Verona, published by H. Groves, of Florence, acquire on this account a special value. One point of importance is that the seeds are used fresh, as the oil rapidly becomes rancid in them when kept. Another fact is that the seeds are entirely deprived of their coating before being submitted to pressure. This is effected by passing them between two revolving wooden rollers, with a winnowing machine beneath, and, to secure the complete absence of integument, they are afterwards assorted by the hand, all being rejected which are not perfectly decorticated. They are then put into hempen bags, which are arranged in layers with a sheet of iron heated to 32.2° C. (90° F.) between them, so as to enable the oil to flow. Lastly, they are submitted to pressure by hydraulic presses. The oil which now flows is of the finest quality. An inferior kind is obtained by pressing the marc at a somewhat higher heat. An interesting and valuable article on the cultivation of the castor bean in the United States appears in the *Proc. P. Ph. A.*, 1916, p. 209, by Joseph L. Lemberger.

Properties.—Pure castor oil is a thick, viscid, colorless liquid, with little odor, and a mild though somewhat nauseous taste, followed by a slight sense of acrimony. As found in commerce it is often tinged with yellow and has an unpleasant odor, and parcels are sometimes, though rarely, met with of a brownish color and hot acrid taste. It does not readily congeal by cold. When exposed to the air it slowly thickens, without becoming opaque. When exposed to the air in a thin layer, it slowly dries to a varnish-like film. It is heavier than most of the other fixed oils. It differs also from most other fixed oils in being soluble in all proportions in cold absolute alcohol. "Castor Oil is a pale yellowish or almost colorless, transparent, viscid liquid, having a faint, mild odor, and a bland, afterwards slightly acrid and generally nauseating taste. It is miscible with dehydrated alcohol or glacial acetic acid. Specific gravity: 0.945 to 0.965 at 25° C. (77° F.). Castor Oil is only partly soluble in petroleum benzin (distinction from *most other fixed oils*). Castor Oil produces a clear liquid with an equal volume of alcohol (*foreign oils*). Saponification value: not less than 179 nor more than 185 (see Part III, Test No. 9). Iodine value: not less than 83 nor more than 88 (see Part III, Test No. 8)." *U. S.*

"Nearly colorless, or with a yellowish tinge, viscid. Liable to solidify at low temperatures. Slight odor; taste at first bland, but afterwards acrid and unpleasant. Specific gravity 0.958 to 0.970; *saponification value* 177 to 187; *iodine value* 83 to 90; *acid value* not more than 4.0; *refractive index* at 40° C. (104° F.) 1.4695 to 1.4730. Soluble in all proportions of *absolute alcohol*, and in 3.5 parts of *alcohol* (90 per cent.). 10 millilitres shaken with 7 millilitres of *petroleum spirit* in a stoppered glass cylinder form a clear mixture at 15.5° C. (60° F.); on shaking with a further addition of 3 millilitres of *petroleum spirit* a turbid mixture is formed, which becomes clear when maintained for five minutes at 21° C. (69.8° F.), but again becomes turbid when the temperature falls below 18° C. (64.4° F.) (absence of other fixed oils)." *Br.*

Weaker alcohol, of the sp. gr. 0.8425, takes up about three-fifths of its weight. It has been supposed that adulterations with other fixed oils might thus be detected, as the latter are much less soluble in that fluid, but Pereira has shown that castor oil has the property of rendering a portion of other fixed oils soluble in alcohol, so that the test cannot be relied on. (*P. J.*, ix, 498.) Such adulterations, however, are seldom practised in this country. Castor oil is soluble also in ether, and in its weight of glacial acetic acid. Its proximate composition has been repeatedly investigated. The bulk of it is *ricinolein*, $C_3H_5(C_{18}H_{33}O_3)_3$, which is the *ricinoleic acid* ($C_{18}H_{34}O_3$) glyceride. At the same time it also contains a small quantity of tristearin and of the glyceride of dihydroxystearic acid, together with from 0.30 to 0.37 per cent. of unsaponifiable matter. Ricinoleic acid, as obtained from the decomposition of the glyceride, is a viscid oil, which solidifies below 0° C. (32° F.), does not solidify in contact with the air by absorption of oxygen, and is not homologous with oleic or linoleic acid, neither of which is found in castor oil. On warming with 1 part of starch and 5 parts of nitric acid (sp. gr. 1.25) castor oil thickens, owing to the formation of *ricinelaidin*. From this *ricinelaidic acid* may be obtained in brilliant crystals. Ricinoleic acid is converted by potassium hydroxide into caprylic alcohol and sebacic acid, with disengagement of hydrogen, and the same products are obtained by the reaction of potassium hydroxide with the oil itself. (See *J. P. C.*, Août, 1885, 113.) Its purgative property is supposed by Bussy and Lecanu to belong essentially to the oil, and not to any distinct principle which it may hold in solution. According to O. Popp, castor oil differs from most other fixed oils in turning the plane of polarized light to the right. (*A. J. P.*, Aug., 1871, 354; from *A. Pharm.*, 1871.) Various substances containing coloring principles, which they yield to castor oil, produce beautiful fluorescence in that fluid when heated with it, such as logwood, turmeric, camwood, etc. (Charles Horner, *P. J.*, Oct., 1874, p. 282.)

Ricinine is a basic substance, $C_8H_8O_2N_2$,

which is soluble in all of the ordinary solvents and which occurs as colorless crystals optically inactive and neutral in reaction. It is precipitated from aqueous solutions by Mayer's reagent and Wagner's reagent, showing alkaloidal properties thereby. It is not especially toxic.

Buchheim believes the active principle of castor oil to be *ricinoleic acid;* this has been confirmed by the experiments of Hans Meyer (*A. E. P. P.,* xxviii, 1890), who finds that both pure ricinoleic acid and the ricinoleate of glyceryl are active purgatives. Ricinelaidic acid, which Buchheim believed to be inactive, Meyer finds when given in fine emulsion to act as powerfully as does castor oil.

By the action of concentrated sulphuric acid upon castor oil is formed a valuable product known as *"Turkey-red oil,"* much used in dyeing and printing with madder and alizarine. The water-soluble portion of this Turkey-red oil is *ricinoleo-sulphuric acid,* $C_{18}H_{33}O.O.HSO_3$. Turkey-red oil acts as a fixing agent, imparting a superior luster to the fiber dyed with its aid.

Castor oil which is acrid to the taste may sometimes be rendered mild by boiling it with a small proportion of water. If turbid, it should be clarified by filtration through coarse paper. On exposure to the air it is apt to become rancid, and is then unfit for use.

Twombly finds that the best method for removing the odor and taste of castor oil is by washing a cold pressed oil several times with boiling water. After separating, the oil is filtered cold very slowly through a thick layer of powdered animal charcoal. Any effort to quicken the method gives poor results.

Commercially ricin has been employed for the detection of pepsin. For details of the method see Solms. (*Z. K. M.,* 1907.)

Uses.—The cathartic effects of castor oil are due to its ricinoleic acid which is split off in the intestinal tract. This, by gentle irritation of the mucous membrane, excites active peristalsis in the upper bowel and probably also somewhat increases the intestinal secretions, although the main action appears to be due to the increased peristalsis. Because of the thoroughness with which it empties the enteric canal there is on the following day an insufficient accumulation of intestinal contents and hence constipation is liable to follow. Because it cleans out the whole alimentary system and that with relatively small degree of irritation, it is especially valuable in conditions of irritation or inflammation of the bowels, as *colic, enteritis,* or *dysentery;* on account of the tendency to subsequent constipation it is not to be recommended as a habitual laxative. It is habitually resorted to in cases of *pregnant* and *puerperal women,* and is decidedly, as a rule, the best and safest cathartic for children. Infants usually require a larger relative dose than adults.

Externally it is useful for its emollient effects in *seborrhea* and other *skin diseases,* having the advantage over other oils of being soluble in alcohol.

The *dose* for an infant is from one to three or four fluidrachms (3.75–11.25–15 mils). It is difficult of administration, from its peculiarly disagreeable taste and from its clamminess and adhesiveness to the mouth. In a few cases, the disgust which it excites is utterly unconquerable by any effort of resolution. A common method of disguising the taste is to give it floating in mint or cinnamon water, but that which we have found, upon the whole, the least offensive is to give it floating on the froth of sarsaparilla syrup mixed with carbonic acid water. Some take it in wine, or spirituous liquors, or the froth of porter, but these are often contra-indicated by their stimulant property. When the stomach is unusually delicate, the oil may be made into an emulsion with mucilage or the yolk of an egg, loaf sugar, and an aromatic water. Tragacanth has been recommended as producing a better emulsion than gum arabic. Tincture of opium may be added in cases of intestinal irritation. A *castor oil jelly* containing over 90 per cent. of the oil may be made by adding a little stearic acid to the melted oil and then saponifying with a very small amount of an alcoholic solution of sodium hydroxide. This form a jelly-like preparation which may be sweetened with saccharin and flavored with any desired volatile oil. Castor oil may also be beneficially used as an enema, in the quantity of two or three fluidounces (60 or 90 mils), mixed with some mucilaginous liquid. It has been recommended as a local application to the breasts of nursing women, to promote the secretion of milk.

Though prone to become rancid by itself, it loses much of its susceptibility when mixed with lard, and some druggists are said to use it as a substitute for olive oil in ointments and cerates.

Dose, half a fluidounce to two fluidounces (15–60 mils).

Off. Prep.—Mistura Olei Ricini, *Br.;* Emulsum Olei Ricini, *N. F.;* Oleum Ricini Aromaticum, *N. F.;* Pilulæ Antimonii Compositæ, *N. F.*

OLEUM ROSÆ. Br.

OIL OF ROSE

(ō'lę-ŭm rō'şæ)

"Oil of Rose is the oil distilled from the fresh flowers of Rosa damascena, *Linn.*" *Br.*

Oleum Rosarum; Attar or Otto of Rose; Huile volatile de Rose pâle, *Fr. Cod.;* Essence de Rose, *Fr.;* Oleum Rosae, *P. G.;* Rosenöl, *G.;* Essenza de rose, *It.*

Oil of Rose was not admitted to the U. S. P. IX. Fats and oils saturated with the rose perfume have been used since the earliest times. Of the seven thousand or more cultivated varieties of rose only a few are used for the production of oil. The chief of these is *Rosa damascena,* which is supposed to be a hybrid between *R. gallica* and *R. canina.* The volatile oil from this species is commonly called *attar, otto,* or *essence of roses.* It is prepared on a large scale in Turkey in Europe, especially in the Balkan Mountains, in Egypt, Persia, Cashmere, India, and other countries of the East, but European

and American commerce is at present supplied chiefly from the region constituting the southern slope of the Balkans, and to some extent, from flowers cultivated in Germany. Synthetic Oil of Rose has entered commerce. The Bulgarian production of rose oil for 1913 amounted to 3600 kilos. (*Schim. Rep.*, Oct., 1913.) The roses are gathered in May, and are distilled with the green leaves of the calyx. From thirty to sixty pounds are put into a tinned copper boiler, of the capacity of about 150 pounds, nearly filled with water. The heat is applied over an open fire, and a boiling temperature is continued for two hours, when the first part of the distilled fluid is returned to the boiler, and the process is continued to completion. The oil collects on the top of the water in the receiver, when it is removed from time to time as it accumulates. (*P. J.*, June, 1872, p. 1051.) In the south of France a small quantity of oil of rose is prepared by distilling the petals with water and separating the oil which floats to the surface. The annual output of the oil is small, most of it being marketed in the form of rose water of which over 3,600,000 liters are produced annually. (*Schim. Rep.*, Oct., 1907.)

Oil of rose is furnished in very minute proportion, not more than three drachms having been obtained by Polier in Hindostan, from 100 pounds of the petals. It is usually imported in small bottles, and is very costly. Oil of rose was at one time prepared in Macedonia by crushing the petals in mills, expressing the fluid part, filtering it, and then exposing it to the sun in small glass vessels. The oil gradually collects on the surface of the liquid, and is removed. (*Ph. Cb.*, 1847, p. 783.) Landerer states that at Damascus and in other parts of Asia Minor the oil is prepared by dry distillation. The buds, being collected before sunrise, are placed in a glass retort, and the distillation is effected by a salt water bath, care being taken so to regulate the heat as not to scorch the petals. The water of the fresh roses and their oil come over together, and the latter, floating on the top, is readily separated.

For an account by R. Bauer of Constantinople, of oil of rose, its production, properties, adulteration, etc., see *P. J.*, Dec., 1867, 286; also *A. J. P.*, 1881, 367.

The experiments of Schimmel are said to indicate that the oil of rose can be prepared from German-grown flowers with commercial success. It is affirmed that the product is superior to the Turkish oil in fineness and strength of aroma, and also that it differs in having a higher congealing point, German oil solidifying at 32° C. (89.6° F.), Turkish oil at 20° C. (68° F.). For an account of its production, see *P. J.*, Aug., 1886; also *P. J.*, 1893, 262.

Oil of rose is nearly colorless, or presents some shade of green, yellow, or red, but, according to Polier, the color is no criterion of its value. Its odor is very powerful and diffusive. At 32.2° C. (90° F.) its sp. gr. is 0.832. Alcohol dissolves it, though not freely when cold. It was officially described in U. S. P. VIII as "a pale yellowish, transparent liquid, having the strong, fragrant odor of rose, and a mild, slightly sweetish taste. Specific gravity: 0.855 to 0.865 at 25° C. (77° F.). The addition of 70 per cent. alcohol precipitates the paraffin hydrocarbons of the Oil, but forms a clear solution with its other constituents, the solution being slightly acid to litmus T.S. The congealing point, when determined according to the following method, should be between 18° and 22° C. (64.4° and 71.6° F.). Introduce about 10 mils of Oil into a test-tube of about 15 Mm. diameter; insert a thermometer in such a manner that it touches neither the bottom nor the sides of the tube. Raise the temperature of the Oil in the tube from 4° to 5° above the saturation point by grasping it in the hand, and shake the tube gently. Allow the Oil to cool, and when the first crystals appear, note the temperature. This is regarded as the congealing point; a second test should be made for confirmation." *U. S. VIII.*

"A pale yellow or yellowish-green crystalline mass, semi-solid at ordinary temperatures. Strong, fragrant, rose-like odor; taste sweetish. Specific gravity at 30° C. (86° F.) (compared with *water* at 15.5° C. (60° F.)) 0.854 to 0.862; *optical rotation* –2° to –4°; *refractive index* at 25° C. (77° F.) 1.456 to 1.465; melting point 20° to 23° C. (68°–73.4° F.)." *Br.*

Oil of rose consists of two portions, one liquid, the other solid at ordinary temperatures. These may be separated by freezing the oil and compressing it between folds of blotting paper, which absorbs the liquid oil and leaves the concrete stearopten. The liquid portion is oxygenated, while the solid portion, which is odorless when pure, consists of a mixture of several hydrocarbons, one of which melts at from 35.5° to 36.5° C. (96°–97.7° F.), and is a paraffin of the formula $C_{16}H_{34}$. A sample of oil of rose distilled in Leipsic in 1884 yielded 28 per cent. of this stearopten, an inferior oil distilled in London gave 68 per cent., and a very good oil from the Balkans gave 9.20 per cent. The oxygenated portion consists of the two alcohols, $C_{10}H_{18}O$ geraniol, and $C_{10}H_{20}O$ citronellol, the former constituting 75 per cent. of the oil. The rhodinol of Eckart was a mixture of these two alcohols. (*Schim. Rep.*, April, 1898, 40.) While these two alcohols are mainly found in rose oil in the free state, esters of the same are also present in amounts varying from 2.5 to 3.5 per cent. (Gildemeister and Hoffmann, *Aetherische Oele*, p. 565.) Linalool, citral and phenyl ethyl alcohol are also present in small amounts.

The U. S. P. VIII considered the saponification value as of sufficient importance to incorporate it as an official test, as follows:

Assay.—"Place in a weighing-bottle about 2 mils of the Oil of Rose, and weigh it accurately. Transfer it, with the aid of a little alcohol, to a 100 mil flask, and add 20 mils of half-normal alcoholic potassium hydroxide V.S. Connect the flask with a reflux condenser, and boil the mixture during thirty minutes on a water-bath.

When cool, add 50 mils of distilled water and a few drops of phenolphthalein T.S., and titrate with half-normal sulphuric acid V.S. Subtract the number of mils of half-normal sulphuric acid V.S. required, from 20 (the 20 mils of half-normal alcoholic potassium hydroxide V.S. taken), multiply the difference by 27.87, and divide by the weight of the Oil to obtain the saponification value." *U. S. VIII.*

Oil of santal, other volatile oils, fixed oils, spermaceti, etc., are said to be added almost universally as adulterations. The volatile additions may be detected by their not being concrete; the fixed, by the greasy stain they leave on paper when heated. Guibourt has offered certain tests by which he thinks the purity of the oil may be determined. (See *A. J. P.*, xxi, 318.) A. Ganswindt recommends the following tests. Agitate 1 drop of the oil with 45 Gm. of warm water, and sprinkle the solution in a moderately warm room, which will soon be filled with a rose odor, in which foreign odors may be detected without difficulty. An adulteration with a fixed oil produces a permanent grease stain upon paper, and spermaceti is left behind on the evaporation of a few drops of the oil from a watch crystal in a water bath. On mixing a few drops of pure oil of rose with an equal bulk of sulphuric acid, the rose odor is not changed, but oils used for adulteration change their odor, which becomes apparent in the rose odor. Or 5 drops of the oil are mixed in a dry test tube with 20 drops of pure concentrated sulphuric acid; when the mixture is cool it is agitated with 20 Gm. of absolute alcohol, when a nearly clear solution should be obtained, which, heated to boiling, remains clear yellowish-brown on cooling. In the presence of the oil of rose geranium, palmarosa, etc., the alcoholic mixture is turbid, and on standing separates a deposit without becoming clear. (*Seifens. Ztg.*, 1881, p. 32; *A. J. P.*, May, 1881.) The oil of one of the sweet scented *Pelargoniums*, perhaps the *rose geranium*, is much employed in Turkey for the purpose of adulteration. According to Hanbury, who appears to have thoroughly investigated the subject, two substances especially are used in Constantinople for adulterating the oil—one spermaceti, the other a volatile oil produced by certain grasses in the East Indies belonging to the genus *Andropogon*, large quantities of which are exported from Bombay, partly directly to Europe, partly through the Arabian Gulf, whence it reaches Constantinople. The same oil is imported into London under the name of *Turkish essence of geranium*, or *geranium oil*.

Tedermann (*Zeit. An. Chem.*, 1895, 5) reached the conclusion, after much experimenting, that there is no reliable chemical or physical test for the adulteration of oil of rose with geranium oil. The sense of smell, according to Conroy, furnishes the best means of determining the quality; he recommends the dissolving of one drop of oil of rose in twenty drops of alcohol, pouring the solution in one fluidounce of warm water, shaking, and comparing the odor with that of a standard sample treated in the same way. (*P. J.*, 1896, 474; see also *C. D.*, 1897, 53.) O. Helm (*A. Pharm.*, 1885) states that the test with a mixture of five parts of chloroform and twenty parts of alcohol cannot be relied upon, as no separation of crystalline scales took place in four different rose oils which were doubtless genuine. But Flückiger, on the other hand, stated that in an experience of many years it had never failed. According to Bauer, the best tests of the purity of the oil are found in its congealing, in five minutes, at a temperature of 12.5° C. (54.5° F.), and its crystallizing, as a solid mass, in light, shiny plates, present everywhere throughout the liquid. These crystals are truncated semi-sided prisms, the angles of which are unequal, and which must be classed in the rhombic system. This stearoptene melted and allowed to cool, crystallizes in a manner so complete that the microscope can readily reveal the presence of foreign substances, such as spermaceti, fatty bodies, wax, and other analogous amorphous substances.

Oil of rhodium (*Oleum ligni Rhodii, Aspalathum*). This oil was attributed by Lewis to the *Convolvulus Scoparius*, but according to Holmes (*Perfume and Essential Oil Record*, 1911, ii, p. 29) is the product of a species of *Genista*, either *G. canariensis* or *virgata*. It is used to adulterate oil of rose. Guaiac wood oil is also occasionally used for the same purpose. A factitious oil of rhodium is sometimes sold as a lure for rats and other animals. It is made from oil of copaiba flavored with a trace of oil of rose. The synthetic oil of rose has largely replaced that obtained by distillation.

Oil of rose may be added, as a grateful perfume, to various spirituous preparations for internal use, and to cerates and ointments.

Off. Prep.—Unguentum Aquæ Rosæ, *Br.*

OLEUM ROSMARINI. U. S., Br.

OIL OF ROSEMARY Ol. Rosmar. [Rosemary Oil]

(ō'lē-ŭm rŏs-mă-rī'nī)

"A volatile oil distilled from the fresh flowering tops of *Rosmarinus officinalis* Linné (Fam. *Labiatæ*), yielding not less than 2.5 per cent. of ester, calculated as bornyl acetate [$C_{10}H_{17}C_2H_3O_2 = 196.16$], and not less than 10 per cent. of total borneol [$C_{10}H_{17}OH = 154.14$]. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.* "Oil of Rosemary is the oil distilled from the flowering tops of Rosmarinus officinalis, *Linn.*" *Br.*

Oleum Rorismarini, Oleum Anthos; Huile volatile de Romarin, *Fr. Cod.*; Essence de Romarin, *Fr.*; Oleum Rosmarini, *P. G.*; Rosmarinöl, *G.*; Essenza di rosmarino, *It.*; Esencia de romero, *Sp.*

The fresh leaves of rosemary yield, according to Baumé, 0.26 per cent. of volatile oil, but the percentage is rated much higher by others. Schimmel & Co. obtained by distillation

from dry French rosemary flowers 1.4 per cent. of oil.

This oil is colorless, with an odor similar to that of the plant, though less agreeable. Its sp. gr. is said to be 0.911, but reduced to 0.8886 by rectification (0.894 to 0.912, *U. S.*). Buignet gives the sp. gr. of the rectified oil at 0.896, and states that it is moderately dextrogyrate. Its reaction is neutral. It is soluble in all proportions in alcohol of 0.830, but requires for solution at 17.7° C. (64° F.) forty parts of alcohol of 0.887. (Berzelius.) It is officially described as "a colorless or pale yellow liquid, having the characteristic odor of rosemary, and a camphoraceous taste. It is soluble in 10 volumes of 80 per cent. alcohol. Specific gravity: 0.894 to 0.912 at 25° C. (77° F.)." *U. S.*

"Colorless or pale yellow. Odor that of rosemary; taste warm, camphoraceous. Specific gravity 0.895 to 0.920; *optical rotation* −2° to +15°; *refractive index* at 25° C. (77° F.) 1.463 to 1.473. Soluble in 1 part of *alcohol* (90 per cent.), and in 5 to 10 parts of a mixture of equal volumes of *alcohol* (90 per cent.) and *alcohol* (70 per cent.). Contains not less than 10 per cent. of total *alcohols*, calculated as borneol, $C_{10}H_{18}O$, and not less than 1.8 per cent. of *esters*, calculated as bornyl acetate, $C_{10}H_{17}C_2H_3O_2$." *Br.*

Assay for Esters and Total Borneol.—"Proceed as directed for menthyl acetate and for menthol under *Oleum Menthæ Piperitæ*, using 10 mils of Oil of Rosemary for each assay. In place of the factor and formula for menthyl acetate and menthol, respectively, under *Oleum Menthæ Piperitæ* use the factor 9.808 in calculating the percentage of bornyl acetate and the following formula in calculating the percentage of borneol.

$$\text{Percentage of borneol} = \frac{A \times 7.707}{B - (A \times 0.021)}$$

In which *A* is the result obtained by subtracting the number of mils of half-normal sulphuric acid V.S. required in the titration from the number of mils of half-normal alcoholic potassium hydroxide V.S. originally taken, and *B* is the weight of acetylized oil taken." *U. S.*

Kane gives its sp. gr. at 0.897, its boiling point at 185° C. (365° F.). Kept in bottles imperfectly stoppered, it deposits a stearopten, sometimes amounting, according to Proust, to one-tenth of the oil. Both Gladstone and Flückiger find that most of the oil consists of a hydrocarbon of the composition $C_{10}H_{16}$, boiling at 165° C. (329° F.), and Schimmel & Co. (*Schim. Rep.*, Oct., 1889) identified this hydrocarbon as pinene, but there is a smaller fraction boiling at from 200° to 210° C. (392°–410° F.), which at low temperatures deposits a camphor, $C_{10}H_{18}O$, identified as borneol. Weber examined oil of rosemary in Wallach's laboratory (*Ann. Ch. Ph.*, ccxxxviii, 89), and found that the fraction boiling between 176° and 182° C. (348.8°–359.6° F.) contains cineol, $C_{10}H_{18}O$. The oil is therefore recognized at present as containing d-pinene, camphene, cineol, borneol (10–15 per cent.), and camphor. According to Flückiger (*A. J. P.*, 1885, 132), from 20,000 to 25,000 kilogrammes of oil of rosemary were produced in Grasse every year. It is said to be sometimes adulterated with oil of turpentine, which may be detected by mixing the suspected liquid with an equal volume of pure alcohol, the oil of rosemary is dissolved, and that of turpentine left. This oil is stimulant, but is employed chiefly as an ingredient in rubefacient liniments. For a case of fatal poisoning, see *A. J. P.*, xxiii, 286.

Dose, three to six minims (0.2–0.4 mil).

Off. Prep.—Spiritus Rosmarini, *Br.*; Tinctura Lavandulæ Composita, *U. S.*, *Br.*; Spiritus Odoratus, *N. F.*

OLEUM SANTALI. U. S., Br.

OIL OF SANTAL. Ol. Santal. [Oil of Sandalwood Santalwood Oil]

(ō'lē-ŭm săn'tă-lī)

"A volatile oil distilled from the wood of *Santalum album* Linné (Fam. *Santalaceæ*), yielding not less than 90 per cent. of alcohols, calculated as santalol [$C_{15}H_{26}O$ = 222.21]. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.* "Oil of Sandal Wood is the oil distilled from the wood of Santalum album, *Linn.*" *Br.*

Oleum Ligni Santali; Oleum Santali Flavi; Oil of Sandal Wood; Huile volatile (Essence) de Santal, *Fr.*; Oleum Santali, *P. G.*; Ostindisches Sandelholzöl, Santelöl, *G.*; Esencia de sandalo, *Sp.*

Under the name of sandalwood various drugs of diverse origin and character find their way into commerce. Of these, the wood of the *Pterocarpus santalinus* is described in this book under its official name of *Santalum Rubrum*, or *Red Saunders*. *Sandal wood bark*, which is believed by H. Stieren to be obtained from some species of *Myroxylon* or *Myrospermum*, is described as occurring in irregular, more or less smooth or unevenly corrugated pieces, of a light, whitish-cinnamon color, with dark, hard epidermis, and of an agreeable, custard-like odor, and an aromatic, slightly acrid, balsamic, bitterish taste. From it Stieren obtained over fifteen per cent. of a clear substance resembling Peruvian balsam. This bark is used for burning in churches as a substitute for frankincense, and bears no relation to sandalwood proper. (*P. J.*, xv, 680.) A sandal wood is yielded by the *Fusanus spicatus* (*S. Cygnorum*) and *F. acuminatus* (*S. acuminatum*) of Australia, whence it is shipped in large quantities to China. An oil distilled from this wood, now coming into the European market, is said to be less odorous than the official product.

Other varieties of sandal wood are collected in the Hawaiian Islands from *Santalum Freycinetianum* Gaud., and *S. pyrularium* A. Gray; in the Fiji Islands from *S. Yasi* Seem.; in New Caledonia from *S. austrocaledonicum* Vieillb.; and in Queensland from *Eremophila Mitchelli* Benth. (Fam. *Myoporaceæ*). For an

account of the sandal wood oil industry of Western Australia, see *C. D.*, 1898, 708. For elaborate microscopic descriptions of the sandalwoods, method of obtaining the oil, etc., see various papers in the *P. J.*, vol. xvi; also *Bull. Pharm.*, 1895, 55. West Australian sandalwood is derived, according to Parry (*C. D.*, 1898, 11), from four species of Santalum, *S. Cygnorum* Miq. (*Fusanus spicatus* R. Br.), *S. lanceolatum* Schlecht (*F. spicatus* R. Br.), *S. acuminatum* A.DC. (*F. acuminatus* R. Br.), and *S. persicarum* F. Muell. (*F. persicarius* F. Muell.), *Venezuelan sandal wood*, the source of the so-called *West Indian sandal wood* of commerce, is, according to E. M. Holmes (*P. J.*, lxii), obtained from the *Schimmelia oleifera* Holmes, now recognized as *Amyris Balsamifera* L. (Fam. *Rubaceæ*). A tree-like shrub, *Osyris tenuifolia* Engl., belonging to the *Santalaceæ*, and a native of East Africa, is said to yield a wood which is very similar to that of the genuine Indian sandal wood. (*P. J.*, 60.)

The *Santalum album*, which yields the official oil, is a small tree twenty or thirty feet high, a native of the mountainous portions of India and of various islands of the Eastern Archipelago, but cultivated in India for the sake of its oil. J. L. Pigot furnished an interesting account of sandalwood cultivation accompanied by a map. (*Schimmel's Report*, 1900.)

Oil of santal is distilled in the United States, Germany, England, and India, the ordinary method of steam distillation being applied after the wood has been reduced to small particles by chipping or grinding. According to the Indian Pharmacopœia the yield of oil is about 2.5 per cent. Oil of santal is habitually adulterated, castor oil and other fixed oils being added, and on the continent of Europe by the volatile *oil of cedar*, which is obtained by distilling the chips left in the making of lead pencils. Chapoteaut (*Bull. Soc. Chim.*, 37, p. 353) found two constituents, one of which he calls *santalol*, $C_{15}H_{26}O$, boiling at 310° C. (590° F.), and the other *santalal*, $C_{15}H_{24}O$, boiling at 300° C. (572° F.). Both of these are decomposed by distilling over phosphoric anhydride, the one yielding $C_{15}H_{24}$, boiling point 260° C. (500° F.), and the other $C_{15}H_{22}$, boiling point 245° C. (473° F.). Sesquiterpenes are also believed to be present in oil of santal. A specimen of oil of santal from South Australia, examined by Schimmel & Co. (*Schim. Rep.*, Oct., 1891), afforded a white crystalline principle, melting at 104° to 105° C. (219.2°–221° F.), which crystallized out in the oil. Parry (*P. J.*, lv, p. 118) found that a portion of the oil was saponifiable, so he assumed the presence of esters of santalol. The U. S. Pharmacopœia describes the oil of santal as "a pale yellow, somewhat thick liquid, having the characteristic odor and taste of sandalwood. It is soluble in 5 volumes of 70 per cent. alcohol, forming a solution which is slightly acid to litmus. Specific gravity: 0.965 to 0.980 at 25° C. (77° F.). The optical rotation varies from –15° to –20° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21)." *U. S.*

"Pale yellow or nearly colorless, somewhat viscid in consistence. Aromatic odor; taste unpleasant. Specific gravity 0.973 to 0.985; *optical rotation* –13° to –21°; *refractive index* at 25° C. (77° F.) 1.498 to 1.508. Soluble in 6 parts of *alcohol* (70 per cent.) at 20° C. (68° F.). Contains not less than 90 per cent. of total *alcohols*, calculated as santalol, $C_{15}H_{24}O$." *Br.*

Assay.—"Proceed as directed for menthol under *Oleum Menthæ Piperitæ*, using 10 mils of Oil of Santal. Use the following formula in calculating the percentage of santalol in place of that given for menthol under *Oleum Menthæ Piperitæ*.

$$\text{Percentage of santalol} = \frac{A \times 11.11}{B - (A \times 0.021)}$$

In which *A* is the result obtained by subtracting the number of mils of half-normal sulphuric acid V.S. required in the titration from the number of mils of half-normal alcoholic potassium hydroxide V.S. originally taken, and *B* is the weight of acetylized oil taken." *U. S.*

The following equations represent the reactions involved in the official assay:

$$C_{15}H_{25}OH + (C_2H_3O)_2O = C_{15}H_{25}OCOCH_3 + CH_3CO_2H$$

Santalol + Acetic anhydride = Santalol acetate + Acetic acid

$$C_{15}H_{25}O.COCH_3 + KOH = C_{15}H_{25}OH + CH_3CO_2K.$$

Santalol acetate + Potassium hydroxide = Santalol + Potassium acetate.

In a number of specimens examined by Holmes (*P. J.*, xvi, 821) the sp. gr. varied from 0.96 to 0.99. The sp. gr. of the oil of cedar wood, according to Ince, is 0.948. A large percentage of it may be added to the oil of santal without affecting its density sufficiently to be detected. Holmes states that the presence of more than 10 per cent. of the cedar oil can be recognized through the different solubilities of the oils in alcohol. (See *P. J.*, xvi, 820.) R. A. Cripps, after a thorough examination of the oils in the London market (see *P. J.*, 1892, 461), gives this test: "Two drops of the oil added to six drops of nitric acid, sp. gr. 1.5, on a white tile, should give a yellow to bright reddish-brown coloration, without any green, indigo, or violet tint at the edges during five minutes. For complete saponification in alcoholic solution, it requires not more than 1 per cent. of potassium hydrate." (See also *A. J. P.*, 1893, 20; *Schim. Rep.*, Oct., 1893; *P. J.*, 1895, 118; *West. Drug.*, 1897, 262.) West India oil can be distinguished from the genuine oil by its deviating the plane of polarization to the *right* instead of to the *left*. (*Pharmacographia.*) In two specimens of oil of santal, sp. gr. 0.9649 and 0.9573, F. H. Alcock found strong fluorescence. (*P. J.*, 1886, 923.)

Oil of amyris is the name commercially applied to the "so-called" West Indian sandalwood oil. This adulterant and substitute (which

may be added in amounts up to 5 per cent. without fear of detection) has a sp. gr. of 0.955 to 0.965, an optical rotation of + 25° to + 30° and contains from 30 to 40 per cent. of alcohols capable of being estimated and calculated as santalol by the official method of assay. One of its principal characteristics in a state of purity is its insolubility in 70 per cent. alcohol. Vansoden (*Ph. Ztg.*, 1900, 45, 878) reports the presence of a sesquiterpene alcohol named by him *amyrol,* and having the composition $C_{15}H_{26}O$.

Uses.—The oil of sandalwood is used largely as a perfume. In medicine its chief use is in *gonorrheal urethritis,* although it is sometimes employed in *chronic bronchitis* and *cystitis.* Its general antibacterial power is comparatively weak, but it has special relations towards certain micro-organisms; thus in the experiments of Jordan (*B. M. J.*, Sept. 13, 1913) twenty minims of oil of sandal wood three times a day had practically no effect on the growth of *B. coli* in the urine, but markedly retarded the multiplication of staphylococci. It was first recommended in medicine by Thomas B. Henderson who, however, is said to have used the oil of *S. myrtifolium.*

Dose, five to twenty minims (0.6–1.3 mils), in emulsion, or in capsule, three or four times a day.

OLEUM SASSAFRAS. U. S.

OIL OF SASSAFRAS Ol. Sassaf. [Sassafras Oil]

(ō'lę-ŭm săs'są-frăs)

"A volatile oil distilled from the root of *Sassafras variifolium* (Salisbury) O. Kuntze (Fam. *Lauraceæ*). Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

Huile volatile (Essence) de Sassafras, *Fr.;* Sassafrasöl, *G;* Esencia de sasafras, *Sp.*

The proportion of oil yielded by the root of sassafras is variously stated at from less than 1 to somewhat more than 2 per cent. The bark of the root, directed by the U. S. Pharmacopœia, would afford a larger amount. The usual yield is said by Sharp to be one pound from three bushels of the root. From fifteen to twenty thousand pounds were sent annually, before 1861, to the Baltimore market. (*A. J. P.*, Jan., 1863, p. 53.) The root, chopped fine by machinery, has steam forced through it in a closed tub, and the oil is then distilled in the ordinary way. 800 pounds of unrectified oil are said to be obtained from 40,000 pounds of root. (*M. S. Rep.*, Aug. 26, 1871.) The oil is of a yellow color or colorless, becoming reddish by age. It has the fragrant odor of sassafras, with a warm, pungent, aromatic taste, and a neutral reaction. It is among the heaviest of the volatile oils, having the sp. gr. of 1.094, or 1.087 at 15° C. (59° F.) on the authority of Buignet, who states also that it is very slightly dextrogyrate. Oil of sassafras is officially described in the United States Pharmacopœia IX as "a yellow or reddish-yellow liquid, having the characteristic odor and taste of sassafras. It is soluble in 2 volumes of 90 per cent. alcohol, forming a solution neutral to litmus. Specific gravity: 1.065 to 1.077 at 25° C. (77° F.). The optical rotation varies from +3° to +4° in a 100 mm. tube at 25° C. (77° F.) (see Part III, Test No. 21)." *U. S.*

The most complete investigation of sassafras oil is that made by Power and Kleber in 1896. (*Schim. Rep.*, April, 1896.) They find it to have the following composition: safrol, $C_{10}H_{10}O_2$, about 80 per cent.; pinene and phellandrene, $C_{10}H_{16}$, about 10 per cent.; dextrogyrate camphor, $C_{10}H_{16}O$, about 6.8 per cent.; eugenol, $C_{10}H_{12}O_2$, about 0.5 per cent.; a high boiling portion consisting of cadinene and residue, 3 per cent. They say that the hydrocarbon constituent of sassafras oil, to which Grimaux and Ruotte gave the name of *safrene,* is, as just stated, a mixture of pinene and phellandrene. *Safrol* crystallizes well in hard four- or six-sided prisms, with the odor of sassafras. It liquefies at 11° C. (51.8° F.), boils at 232° C. (449.6° F.), has a sp. gr. of 1.106, and is destitute of rotatory power. Variation in the sp. gr. of oil of sassafras may often arise through the congelation and separation of safrol, or through stratification. (LaWall and Pursel, *A. J. P.*, 1898, 340.) Flückiger ascertained that safrol was one of those remarkable bodies which are capable of existing either in a solid or in a fluid condition long after they have passed their freezing or their melting point. Chemically, it has been found to be the *methylene ether of allyl-dioxybenzene.* Safrol appears to be widely distributed in the vegetable kingdom, probably existing in the bark of the *Mespilodaphne Sassafras,* also in the *Puchury* or *Sassafras nuts* (see *Pichurim Beans,* Part II), both of Brazil, as well as in the barks of *Atherosperma moschatum* and of *Beilschmiedia obtusifolia* of Australia, and in the bark of *Doryphora Sassafras* of New Caledonia. The bark described by Dymock as that of *Beilschmiedia fagifolia,* according to the researches of E. S. Hooper, contains saponin and probably is not derived from Beilschmiedia or any other genus of the *Lauraceæ.* (*P. J.*, lxxii.) Safrol is now commercially extracted from oil of camphor, and it probably could be obtained from the oil of various species of the genus *Cinnamomum.* (See *P. J.*, June, 1887.)

Uses.—Oil of sassafras is chiefly used for flavoring purposes, but has physiological properties similar to those of the oil of clove and other allied volatile oils, and may be used for similar purposes. It is a powerful antiseptic and has been highly praised by Peck (*J. A. M. A.*, 1899, xxxii, 6) as a dental disinfectant.

A teaspoonful of it produced in a young man vomiting, collapse, somewhat dilated pupils, and pronounced stupor. (*Cincinnati Lancet-Clinic,* Dec., 1888.) According to the experiments of

A. Heffter (*Atti Dell' XI. Congres. Med. Internaz.*, iii, 1894), safrol is slowly absorbed from the alimentary canal, and escapes through the lungs unaltered and through the kidneys oxidized into *piperonalic acid.* When taken in sufficient dose, it quickly kills by a centric paralysis of respiration, preceded by great depression of the circulation, and when taken in smaller yet toxic amount, it causes death by widespread fatty degeneration of the heart, liver, kidneys, etc. Its isomer, *isosafrol,* is in warm-blooded animals much less active as a poison than is safrol, and is chiefly eliminated as *piperonalic acid.*

Dose, of oil of sassafras, two to six minims (0.12–0.4 mil).

Off. Prep.—Trochisci Cubebæ, *U. S.;* Linimentum Tiglii Compositum, *N. F.;* Mistura Opii et Sassafras, *N. F.*

OLEUM SESAMI. U. S., Br.

SESAME OIL. Ol. Sesam. [Teel Oil, Benne Oil]

(ō'le-ŭm sĕ'sa-mī)

"A fixed oil obtained from the seeds of one or more cultivated varieties of *Sesamum indicum* Linné (Fam. *Pedaliaceæ*). Preserve it in well-closed containers." *U. S.* "Sesame Oil is the oil expressed from the seeds of Sesamum indicum, *Linn.*" *Br.*

Sesame oil, which was official in the U. S. P. 1890, was restored to an official position by the U. S. P. IX. It is reputed by many pharmacists to resist rancidity better than other fixed oils of its class. It is especially recommended by Prof. Otto Raubenheimer, of Brooklyn. It is officially described in the U. S. Pharmacopœia as "a pale yellow, oily liquid, almost odorless, and having a bland taste. It is slightly soluble in alcohol, miscible with ether, chloroform, petroleum benzin, or carbon disulphide. Specific gravity: 0.916 to 0.921 at 25° C. (77° F.). Shake 1 mil of the Oil for half a minute with a solution of 0.1 Gm. of sugar in 10 mils of hydrochloric acid; the acid layer becomes bright red and changes to dark red on standing. Blue litmus paper previously moistened with alcohol is not more than slightly reddened by 2 mils of the Oil (*free acid*). Mix 5 mils of the Oil in a test tube with 5 mils of a mixture of equal volumes of amyl alcohol and a 1 per cent. solution of sulphur in carbon disulphide and immerse the test tube to one-third of its depth in a boiling saturated aqueous solution of sodium chloride; no reddish color develops in fifteen minutes (*cottonseed oil*). Saponification value: not less than 188 nor more than 193 (see Part III, Test No. 9). Iodine value: not less than 103 nor more than 112 (see Part III, Test No. 8)." *U. S.*

"Pale yellow. Faint odor; taste bland. Specific gravity 0.921 to 0.924; *saponification value* 189 to 193; *iodine value* 103 to 114; *acid value* not more than 8; *refractive index* at 40° C. (104° F.) 1.4650 to 1.4675. When a mixture of 2 millilitres of the Oil and 1 millilitre of *hydrochloric acid* containing 1 per cent. of *refined sugar* is shaken for half a minute, and allowed to stand for five minutes, the acid layer becomes pink. When 1 millilitre of the Oil and 15 millilitres of *N/1 alcoholic solution of potassium hydroxide* are boiled for twenty minutes in a flask provided with a reflux condenser, set aside for twenty-four hours at a temperature not exceeding 15.5° C. (60° F.), and afterwards heated on a water-bath for three minutes, the solution does not deposit crystals on standing for a further twenty-four hours (absence of arachis oil). When 2 millilitres of the Oil are mixed with 1 millilitre of *amylic alcohol* and 1 millilitre of a solution (1 in 100) of *precipitated sulphur* in *carbon disulphide,* and the mixture heated in a test-tube immersed in boiling *water,* no red color is developed within fifteen minutes (absence of cotton seed oil). In India, and in the Eastern, African, and North American Divisions of the Empire, Sesame Oil may be employed in making the official Liniments, Ointments, Plasters, and Soaps for which Olive Oil is directed to be used." *Br.*

Benne Oil, or *Teel Oil,* is inodorous, of a bland, sweetish taste and a neutral reaction, and will keep long without becoming rancid. Flückiger found that 76 per cent. of the oil consists of olein, and that the solid portions yield on saponification palmitic, stearic, and myristic acids. Linoleic acid was afterward discovered in the oil. The oil also contains a small quantity of what is probably a resinoid substance, which may be removed by glacial acetic acid or alcohol. It bears some resemblance to olive oil in its properties, and may be used for similar purposes. It is not a drying oil. Villavecchia and Fabris (*Zeit. für Ang. Chem.*, 1893, 505) have investigated sesame oil, and find, in addition to the main constituents before mentioned, a higher alcohol of the formula $C_{25}H_{44}O$, fusing at 137° C. (278.6° F.), a finely crystallizing substance of the formula $C_{11}H_{12}O_3$, fusing at 123° C. (253.4° F.), which substance they name *sesamin,* and a thick uncrystallizable oil, non-nitrogenous, which is the cause of the cherry-red coloration which sesame oil shows with hydrochloric acid and sugar. Tocher (*P. J.*, 1893, 700), after analyzing *sesamin* and determining its molecular weight by Raoult's method in benzene and glacial acetic acid, maintains that its formula should be $C_{18}H_{18}O_5$. Tocher, as quoted by Lewkowitsch (*Chem. Anal. of Oils, Fats, and Waxes,* 2d ed., 389), also believes that the higher alcohol mentioned is cholesterol. "When cooled to –3° C. (26.6° F.) it becomes thick, and at –5° C. (23° F.) it congeals to a yellowish-white mass. Concentrated sulphuric acid converts it into a brownish-red jelly. If 5 mils of the Oil be shaken with an equal volume of concentrated hydrochloric acid, the latter will usually assume a bright emerald-green color, especially if the Oil has been exposed for some time to the action of air and light." Soltzien recommends stannous chloride solution for testing benne oil. (*Proc. A. Ph. A.*, 1897, 195.) According to Schaedler, if one mil of pure benne oil is shaken with one mil of pure hydrochloric acid, sp. gr. 1.125, and one

gramme of cane sugar, a rose-red color is developed in fifteen minutes, changing to violet in twenty-five minutes, and increasing in intensity until, after five hours, the acid has assumed a violet color corresponding in intensity to that of a solution of iodine in carbon disulphide or in chloroform. In the case of all other fixed oils, this color reaction does not begin until after three-quarters of an hour. Olive and almond oils containing as little as one-fourth per cent. of benne oil exhibit the reaction in from twenty to twenty-five minutes. The failure of some experimenters to find the reactions available rests upon the fact that they searched for the color in the oil, and not, as they should have done, in the acid. (*A. Pharm.*, 1887, p. 185.) Benne oil was known to the ancient Persians and Egyptians, and is esteemed by the modern Arabs and other people of the East both as food and as an external application to promote softness of the skin. It is laxative in large doses.

The name sesame oil is also sometimes applied to the oil from the cruciferous seed of *Camelina sativa.*

OLEUM SINAPIS VOLATILE. U. S., Br.

VOLATILE OIL OF MUSTARD Ol. Sinap. Vol. [Mustard Oil]

(ō'lę-ŭm sĭ-nā'pĭs vŏ-lą-tĭ'lē)

"A volatile oil produced synthetically or obtained from the seed of *Brassica nigra* (Linné) Koch (Fam. *Cruciferæ*) (freed from fatty oil) by maceration with water and subsequent distillation. It yields not less than 92 per cent. of allyl isothiocyanate [C_3H_5SCN = 99.12]. The label must indicate whether the Oil has been made synthetically or obtained from black mustard. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.* "Volatile Oil of Mustard is the oil obtained by distillation from black mustard seeds, deprived of most of their fixed oil and macerated in water for several hours." *Br.*

Oleum Sinapis, *Br.* 1885; Oleum Sinapis Æthereum; Oil of Mustard; Huile volatile (Essence) de Moutarde, *Fr.;* Oleum Sinapis, *P. G.;* Senföl, Aetherisches Senföl, *G.;* Essenza di senape, *It.;* Esencia de mostaza negra, *Sp.*

The volatile oil of mustard is usually obtained from seeds which have been deprived of their fixed oil by pressure. It is "a colorless or pale yellow, strongly refractive liquid, having a very pungent and irritating odor and an acrid taste. *Great caution should be exercised in smelling this Oil. It should not be tasted except when highly diluted.* Specific gravity: 1.013 to 1.020 at 25° C. (77° F.). It is optically inactive. The Oil distils completely between 148° and 154° C. (298.4°–309.2° F.), and both the first and last portions of the distillate have nearly the same specific gravity as the original Oil (*alcohol, chloroform, petroleum, or fatty oils*). The addition of a drop of ferric chloride T.S. to the Oil, diluted with several volumes of alcohol, does not produce a blue coloration (*phenols*)." *U. S.*

"Assay.—Dilute about 4 mils of Volatile Oil of Mustard, accurately weighed, with sufficient alcohol to make exactly 100 mils. Transfer 5 mils of this solution to a 100 mil measuring flask, and add 50 mils of tenth-normal silver nitrate V.S. and 5 mils of ammonia water. Stopper the flask, connect it with a reflux condenser and heat it on a water bath during one hour. Allow it to cool, dilute the contents of the flask with distilled water to the 100 mil mark, mix well and filter. Add 4 mils of nitric acid and 2 mils of ferric ammonium sulphate T.S. to 50 mils of the filtrate and titrate the excess of the silver nitrate with tenth-normal potassium sulphocyanate V.S. When calculated from the weight of Oil taken for the assay it shows not less than 92 per cent. of allyl isothiocyanate. Each mil of tenth-normal silver nitrate V.S. consumed corresponds to 0.004956 Gm. of allyl isothiocyanate." *U. S.*

"Colorless or pale yellow. Intensely penetrating odor. Produces almost immediate vesication when applied to the skin. Specific gravity 1.014 to 1.025. Distils between 148° and 156° C. (298.4° and 312.8° F.). Contains in 100 millilitres not less than 92 grammes of allyl isothiocyanate, C_3H_5NCS, as determined by the following process:—

"With *alcohol* (90 per cent.) prepare a solution containing 1 gramme of the Oil in 50 millilitres. To 5 millilitres of this solution in a 100 millilitre flask add 30 millilitres of *N/10 solution of silver nitrate* and 5 millilitres of *solution of ammonia.* Heat on a water-bath to 80° C. (176° F.) for thirty minutes, shaking frequently; cool to 15.5° C. (60° F.), make up to exactly 100 millilitres with *water,* and filter. To 50 millilitres of the filtrate add 4 millilitres of *nitric acid,* a few drops of *solution of ferric sulphate,* and sufficient *N/10 solution of ammonium thiocyanate* to produce a permanent red color. Not more than 5.7 millilitres of the latter reagent are required (presence of not less than 92 grammes of allyl isothiocyanate in 100 millilitres of the Oil)." *Br.*

Will considers volatile oil of mustard to be *allyl isosulphocyanate,* $CSNC_3H_5$ (*allyl isothiocyanate*), it being related to oil of garlic, which is sulphide of allyl. It sometimes contains allyl cyanide and traces of carbon disulphide. (*Chem. Gaz.*, Nos. 62 and 64.) It is the principle upon which black mustard seeds depend for their activity. Volatile oil of mustard was first produced artificially by Berthelot and S. de Luca, by treating allyl iodide, C_3H_5I, with an alcoholic solution of potassium sulphocyanate. It is now extensively manufactured artificially by this method. What first forms is allyl sulphocyanate, which is not identical with, but only an isomer of, mustard oil (allyl isosulphocyanate). But if the sulphocyanate be heated to its boiling point 161° C. (321.8° F.) the thermometer sinks rapidly to 150° C. (302° F.), because of the change into the isosulphocyanate, or mustard oil. This change also takes place spontaneously at summer temperature. A small quantity of

carbon disulphide seems always to be produced at the same time. Allyl iodide is procured by treating glycerin with phosphorus iodide. According to Zeller, the seeds yield from 0.33 to 0.63 per cent. of the oil. Will and Koerner in 1863 explained the occurrence of this allyl isosulphocyanate in mustard oil. It does not occur ready formed in the seeds, but is produced by the decomposition of a compound, *sinigrin* (*potassium myronate*), occurring there. This sinigrin, $C_{10}H_{18}KNS_2O_{10}$, is decomposed under the influence of *myrosin*, an albuminous ferment which is present, and yields as products of decomposition C_3H_5CNS (allyl isosulphocyanate), $HKSO_4$ (acid potassium sulphate), and $C_6H_{12}O_6$ (glucose). "The aqueous solution of myrosin coagulates at 60° C. (140° F.), and then becomes inactive; hence mustard seed which has been heated to 100° C. (212° F.), or has been roasted, yields no volatile oil, nor does it yield any if powdered and introduced at once into boiling water." (*Pharmacographia*, p. 67.) As it is often adulterated with other oils, a test has been proposed consisting of concentrated sulphuric acid, 50 drops of which are to be mixed with 5 drops of the suspected oil in a small glass tube. If the oil be pure, little change of color will be produced, but if any adulterating oil be present, a red or brown color will soon appear. Rectified oil of petroleum is the only exception, as the color of this is not affected by the acid, but it would be recognized by its insolubility in sulphuric acid. (See *A. J. P.*, July, 1865, p. 285.) Adulteration with alcohol is readily detected by its much lower boiling point, which also enables it to be separated by distillation. It has been adulterated with considerable quantities of carbon disulphide, which may be detected by distillation at a temperature not exceeding 80° C. (176° F.) and mixing the distillate with sulphuric acid, when the carbon disulphide rises to the surface. Ammonia converts the mustard oil into *thiosinamin* (see Part II), according to the reaction which separates

$$CSNC_3H_5 + NH_3 = C_4H_8N_2S$$

in colorless rhombic crystals, melting at 70° C. (158° F.), and soluble in water, alcohol, and ether. The reaction is stated by Flückiger (*Pharm. Chem.*, 2d ed., 1888, p. 20) to be quantitative. Oil of mustard naturally contains about 0.56 per cent. of carbon disulphide. (*A. J. P.*, 1881, p. 572.)

White mustard seeds yield different products. When deprived of fatty oil they yield to boiling alcohol colorless crystals of *sinalbin*, an indifferent substance readily soluble in cold water, but sparingly so in cold alcohol. According to Will, it breaks up under the action of myrosin into *acrinyl sulphocyanate*, $C_7H_7O.CNS$, *sinapine sulphate*, $C_{16}H_{25}NSO_9$, and *glucose*, $C_6H_{12}O_6$. This acrinyl sulphocyanate is a nearly colorless, non-volatile oil, and the rubefacient and vesicating principle of white mustard. *Sinapine* has not yet been isolated, but it is an unstable alkaloid.

Uses.—Oil of mustard is a powerful rubefacient, although liable to blister unless used with much caution. Diluted, either with alcohol or lard, it is used as a counter-irritant application in *sprains, rheumatism* and like conditions. It may employed in strengths of from two to four per cent.

The volatile oil of mustard has been employed as a substitute for the mustard plaster. For this purpose one part may be mixed with sixty parts of alcohol, and the mixture sprinkled, not too thickly, on piline or muslin, covered with waxed paper. It acts speedily and efficiently.

The oil is too pungent and irritating to be given internally.

Off. Prep.—Linimentum Sinapis, *Br.;* Linimentum Sinapis Compositum, *N. F.;* Spiritus Sinapis, *N. F.*

OLEUM TEREBINTHINÆ. U. S.

OIL OF TURPENTINE Ol. Tereb. [Turpentine Oil "Spirits of Turpentine"]

(ō'lę-ŭm tĕr-ę-bĭn'thĭ-næ)

"The volatile oil distilled with water from the concrete oleoresin obtained from *Pinus palustris* Miller or from other species of *Pinus* (Fam. *Pinaceæ*). Preserve it in well-closed containers." *U. S.*

Essence de Térébenthine, *Fr. Cod.;* Huile volatile de Térébenthine, *Fr.;* Oleum Terebinthinæ, *P. G.;* Terpentinöl, *G.;* Essenza di trementina, *It.;* Esencia de trementina, Aceite volatil de trementina, *Sp.*

This oil is commonly called *spirits* (or *spirit*) *of turpentine*. It is prepared by distillation from our common turpentine, though equally afforded by other varieties. It may be distilled either with or without water, but in the latter case a much higher temperature is required, and the product is liable to be empyreumatic. To obtain it quite pure it should be redistilled from a solution of potassium hydroxide. The turpentine of *Pinus palustris* is said to yield about 17 per cent. of oil, while that from *Pinus Pinaster* affords 25 per cent., and that from *Pinus sylvestris* 32 per cent. Large quantities are distilled in North Carolina. The exportations of turpentine oil from the United States in 1913 amounted to 21,039,597 gallons, valued at $8,794,656; and in 1914, 18,900,704 gallons, valued at $8,095,958.

Pure oil of turpentine is "a colorless liquid having a characteristic odor and taste, both of which become stronger and less pleasant on aging or exposure to the air. Soluble in 5 volumes of alcohol. Specific gravity: 0.860 to 0.870 at 25° C. (77° F.). Optical rotation variable. Distil 200 mils of the Oil, at the rate of two drops per second, from a 300 mil globe flask, having the side tube 8 cm. above the bulb. Ninety per cent. of the Oil distils between 154° and 170° C. (309.2° and 338° F.), the temperature being read with the mercury column of the thermometer immersed in the vapor. Five mils

of the Oil, shaken with an equal volume of potassium hydroxide T.S., does not become darker than a light straw yellow after standing twenty-four hours. Five mils of the Oil, evaporated in a small dish on a water bath, leaves not more than 0.1 Gm. of residue. Three drops of the Oil, placed on unsized, white paper, and exposed to the air, evaporates entirely without leaving a permanent stain (*fixed oils*). Five mils of the Oil shaken vigorously with an equal volume of hydrochloric acid in a test tube, and allowed to stand for a few minutes, does not produce a brownish or greenish color. Into a flask of from 35 to 50 mils capacity, having a long graduated neck (cassia flask), and containing 25 mils of fuming sulphuric acid, introduce very slowly, *drop by drop,* with constant shaking 5 mils of Oil of Turpentine, keeping the temperature just below 65° C. (149° F.) by immersion in cold water during the addition of the oil, and for five minutes thereafter, in the meantime frequently agitating the mixture cautiously but vigorously. Then cool, and add sulphuric acid until the flask is filled to the upper graduation on the neck. The clear, reddish, viscous layer, which forms after the dark mass has settled for two hours, does not exceed 1 per cent. of the volume of Oil taken. A large layer of colorless liquid with a refractive index of less than 1.5 at 20° C. (68° F.) shows the presence of mineral oil.

"*Caution.*—The addition of the Oil of Turpentine to the fuming sulphuric acid, drop by drop, is necessary because of the violence of the reaction." *U. S.*

As found in commerce, it is always somewhat ozonized, but when perfectly pure it consists exclusively of carbon and hydrogen, and is composed of one or more *terpenes,* among which are pinene, which constitutes the major portion of the oil, and small amounts of camphene and fenchene with derivatives of pinene. (See p. 730.) The English or American oil (prepared from *Pinus australis*) is composed of *dextro-pinene,* while the French oil (prepared from *Pinus Pinaster*) is composed of *lævo-pinene.* On the other hand, the Russian turpentine contains, in addition to *pinene, dipentene* (or *cinene*) and *sylvestrene,* and the Swedish turpentine contains *pinene* and *sylvestrene.* Both the American and the French oil of turpentine boil at about 156° C. (312.8° F.). On heating oil of turpentine to about 300° C. (572° F.) in a sealed tube for several hours it is converted into a polymer called *iso-terebenthene,* $C_{20}H_{32}$, which is so oxidizable that it is converted into a viscid mass on exposure to the air for a few hours. It has, moreover, a marked odor, resembling oil of lemon, and boils at 176° to 177° C. (348.8°–350.6° F.). On treatment with a small portion of sulphuric acid, oil of turpentine yields an optically inactive liquid, which boils at 160° C. (320° F.). This is a mixture resolvable by repeated fractional distillation into *terebene,* $C_{10}H_{16}$, boiling at 150° C. (302° F.); *cymene,* $C_{10}H_{14}$, boiling at 175° C. (347° F.); a small quantity of a camphor-like body, boiling at 200° C. (392° F.); *colophene,* $C_{20}H_{32}$, boiling at 318° C. (604.4° F.), and a mixture of semisolid products of higher boiling point. Oil of turpentine absorbs hydrochloric acid gas, forming with it two compounds, one a red dense liquid, the other a white crystalline substance resembling camphor, and hence called *artificial camphor.* Both are mono-hydrochlorides, $C_{10}H_{16}.HCl$, but the latter is much more stable, and can be purified by crystallization from alcohol or ether. When turpentine oil is left in contact with concentrated hydrochloric acid a dihydrochloride is formed, $C_{10}H_{16}.2HCl$. This forms rhombic plates, insoluble in water, and decomposed by boiling with alcoholic potash, with formation of *terpinol* $(C_{10}H_{16})_2.H_2O$. (Allen, *Com. Org. Anal.,* vol. ii, p. 51.) Nitric acid converts oil of turpentine into resin, and by long boiling into *terebic acid,* $C_7H_{10}O_4$. Mixed with water and chlorinated lime, and then distilled, the oil yields a liquid which Chautard found to be identical with chloroform (*J. P. C.,* 3e sér., xxi, 88). Turpentine oil and other terpenes unite with water to form crystals of *terpin hydrate,* $C_{10}H_{18}(OH)_2.H_2O$, which sublimes often from turpentine oil which has long stood in contact with water and has then been heated to water bath temperature. These crystals are sometimes found in the natural oil also. The presence of alcohol with the water and turpentine oil facilitates their formation. Thus, a mixture of 1 part of nitric acid, 1 part of alcohol, and 4 parts of turpentine oil, spread out in flat dishes, will yield within a few days crystals amounting to 20 per cent. of the oil taken. If these crystals be fused at 116° C. (240.8° F.) they will lose water, and *terpin,* $C_{10}H_{18}(OH)_2$, will remain in crystalline needles, fusing at 104° C. (219.2° F.), and boiling at 258° C. (496.4° F.). If either of the hydrates just mentioned be boiled with sulphuric, phosphoric, or glacial acetic acid, *terpineol,* $C_{10}H_{17}OH$, will be formed along with hydrocarbons of the formula $C_{10}H_{16}$, such as *terpinene, terpinolene,* and *dipentene.* Terpineol is a thick, colorless, optically inactive liquid, with a pleasant hyacinthine odor and a bitter, feebly pungent taste. It is used extensively in perfumery. Baeyer (*Ber. d. Chem. Ges.,* xxvi, p. 826) has also prepared the methyl ether of terpineol. Oil of turpentine may be made to yield cymene identical with that existing in the oil of cumin and with that obtained by dehydrating camphor. (See *Cumin Seed,* in Part II; also see under *Olea Volatilia.*) Exposed to the air the oil absorbs oxygen, becomes thicker and yellowish, and loses much of its activity, owing to the formation of resin. A small proportion of formic acid is said also to be generated. Hence the older pharmacopœias directed the oil to be rectified by distilling it with about four measures of water. But the process is difficult, in consequence of the great inflammability of the vapor, and its rapid formation, which causes the liquid to boil over. In

this country it is scarcely necessary, as the recent oil can be obtained at an expense less than that which would be incurred by redistillation on a small scale. Another mode of purifying the oil is to agitate it with one-eighth of alcohol, which dissolves the resinous portion. About one-fifth of the alcohol is retained by the oil, but is readily separated by agitation with water. (See *Oleum Terebinthinæ Rectificatum.*) For tests, see *Proc. A. Ph. A.*, 1893, 156.

C. T. Kingzett has shown that the atmospheric oxidation of turpentine is accompanied by the formation of a body having the formula $C_{10}H_{14}O_4$, which he regards as *camphoric peroxide*. This substance, by the action of water, is converted into hydrogen peroxide and camphoric acid. The disinfectant known as *"sanitas"* is produced by passing air through Russian oil of turpentine in contact with warm water. Berthelot has shown that oil of turpentine has, under certain conditions, the power, while undergoing oxidation itself, of causing the oxidation of other bodies, to which it imparts a portion of the oxygen absorbed from the air. All that is necessary to give this power to the oil is that soon after distillation it should be exposed to the air, as in a bottle half filled. Sunlight assists, but is not essential to, the change, which goes on even in the dark. The oil retains indefinitely the property thus acquired, but may be deprived of it by exposure to a boiling heat, or by agitation with reducing substances. No other chemical or physical change can be detected in the oil. (*J. P. C.*, May, 1860, 351.)

In this country the oil of turpentine is frequently adulterated with petroleum distillates. The adulteration is best detected by the treatment with sulphuric acid followed by steam distillation of the oil layer remaining above the sludge acid; this treatment with acid and after-distillation to be repeated if necessary. The sulphuric acid will thus completely polymerize the essential oil, leaving the paraffin hydrocarbons unaffected in the residual oily layer. A shorter and more readily executed test with sulphuric acid, though not so complete, is now given in the official test of the U. S. P. IX.

Considerable quantities of a turpentine obtained by steam distillation of the so-called "lightwood," or resin saturated stumps and pieces of pine wood, have been offered in recent years. For an experimental study of this process and an account of the product see an article by Walker, Wiggins and Smith. (*Chemical Engineer*, Dec., 1905, p. 78.)

The several species of pine indigenous to California and the slopes of the Sierra Nevada appear to yield quite different products. Wenzell (*A. J. P.*, March, 1872) described, under the name of *abietene*, an oil distilled from the exudation of the *Pinus sabiniana* (*Nut Pine* or *Digger Pine*). He found it to have a sp. gr. of 0.694, and to boil at 101° C. (213.8° F.). Sadtler (*A. J. P.*, April, 1879, p. 176) examined an oil of turpentine from California said to have been obtained from the *Pinus ponderosa* (*Heavy Pine*), and found it to agree substantially with Wenzell's abietene. It had a sp. gr. at 16.5° C. (62° F.) of 0.6974, boiled at 101° C. (213.8° F.), and was slightly lævogyrate. It gave negative results when treated with hydrochloric acid for the formation of a hydrochloride, did not form a hydrate, and was not acted upon by sulphuric acid or by nitrosyl chloride. These anomalous results were at once explained by the publication of a study of the abietene which had been made by Thorpe, who showed (*A. J. P.*, 1879, p. 293) that this exudation of the California pine is almost pure *heptane*, C_7H_{16}, one of the chief constituents of American petroleum. His results were also confirmed by Schorlemmer, who established the identity of the pine heptane with that from petroleum naphtha.

Uses.—The oil of turpentine is locally irritant and feebly antiseptic. It is absorbed through the mucous membrane of the alimentary canal and apparently also of the respiratory tract, and is eliminated partly with the breath to which it imparts its own odor, and through the urine to which it gives an odor resembling that of violets. After the ingestion of large doses it produces a sense of warmth in the stomach, accelerates the circulation, and causes a feeling of exhilaration associated with more or less vertigo and a sense of fullness in the head. These symptoms are attended frequently with nausea and frequently, although not always, succeeded by brisk catharsis. When given in small doses frequently repeated it at first stimulates the kidneys, augmenting the secretion of urine, but if the administration is continued too long it produces painful irritation of the urinary vessels amounting at times to violent strangury and may cause inflammation of the kidney with scanty, albuminous, or even bloody urine. In some constitutions it produces, even when taken internally, an erythematous eruption of the skin. Apparently enough may be absorbed after the inhalation of its vapor to irritate the urinary organs and it is stated that seamen of vessels loaded with turpentine sometimes develop strangury and hematuria.

Most of the therapeutic uses of the oil of turpentine may be attributed to its local irritant influence; thus during its elimination through the mucous membrane of the lungs it acts as a stimulant expectorant and is a useful remedy in *chronic bronchitis*. In the same way it acts as a stimulant to the kidney and is occasionally used as a diuretic, although this employment has largely passed out of vogue. As a carminative in *flatulent colic* it is one of the most valuable remedies we possess. It is sometimes of service for its local stimulant action for *chronic diarrheas* or *dysentery*. In *typhoid fever* it is useful not merely in tympanitic states for its carminative effects, but appears to have a direct influence upon the disease itself. According to the observations of Omelchenko (*B. G. T.*, 1891), while it is very feeble in its general antibacterial properties it has a special

toxicity for the typhoid bacillus and this organism will not grow in an atmosphere saturated with turpentine vapor.

Oil of turpentine has been used for many years in the treatment of *hemoptysis*. Of its mode of action we have no knowledge, but there is considerable clinical evidence as to its power to check bleeding; Smith (*B. M. J.*, 1908, i, p. 1218) has even recommended it in *purpura hemorrhagica*. Among other conditions in which it has been from time to time recommended with more or less reasonableness, are *helminthiasis, leucorrhea, chronic rheumatism, amenorrhea,* and *puerperal fever*.

For ordinary purposes the dose is from 5 to 10 minims (0.3–0.6 mil) repeated every two to six hours as may be necessary. As a remedy against the *tapeworm* the dose is from one-half to one fluidounce (15–30 mils), followed in half an hour by castor oil; the safety of these large doses is dependent upon the catharsis sweeping out the bowel before the turpentine can be absorbed. It is best administered in the form of an emulsion, although it is frequently given by dropping into a teaspoonful of sugar. The use of gelatin-coated capsules is not to be recommended because as soon as the gelatin dissolves in the stomach the undiluted oil comes in contact with the gastric mucosa and is liable to produce an undue degree of irritation. Lacambre gives the following process for making a pill of the oil. Take of oil of turpentine 8 grammes, white wax 20 grammes, powdered sugar 9 grammes, oil of lemon, 2 drops. Melt the wax in the oil of turpentine, pour into a mortar, allow to cool, then add the sugar and oil of lemon, and form a mass to be divided into pills of 0.2 or 0.25 Gm. (3 or 4 gr.) each. Roll them in powdered starch, and keep in a well-stoppered bottle. (*J. P. C.*, Sept., 1873, p. 223.)

In the form of an enema the oil of turpentine is highly useful in obstinate *constipation, tympanitis,* and *seat-worms*. From one-half to two fluidounces (15–60 mils) may be added to a pint of warm soapsuds.

Externally it is an excellent rubifacient and is widely employed in the form of liniments in various rheumatic affections as *lumbago, arthritis, neuralgias,* and the like. For this purpose it should be diluted with from one to three parts of cottonseed or other bland oil. In the form of turpentine stupe it is advantageously employed as a counter-irritant in various deep-seated inflammations, especially of the abdomen. The turpentine stupe is made as follows: a piece of flannel is wrung out in hot water and then dipped in previously warmed turpentine, quickly wrung out and applied to the part. It was also formerly employed as a local application to *burns* in which it was supposed to allay the pain and promote healing. For this purpose it was usually mixed with the rosin cerate so as to form a liniment capable of being spread upon linen (see *Linimentum Terebinthinæ*).

The following is the formula adopted many years ago by the Philadelphia College of Pharmacy for the rubefacient liniment known as *British Oil*, which is still in use in some parts of the country as a popular remedy. Oil of Turpentine, Linseed Oil, of each, 8 fl. oz., Oil of Amber, Oil of Juniper, of each, 4 fl. oz., Barbados Petroleum 3 fl. oz., Crude American Petroleum 1 fl. oz.

It has likewise been recommended as a local application in parasitic *skin diseases,* especially *pediculus capitis*. The inhalation of its vapors has been employed in *chronic bronchitis* and has been especially recommended by Skoda in *gangrene of the lungs*.

For internal use the rectified oil should be used. (See *Oleum Terebinthinæ Rectificatum.*)

Dose, five to ten minims (0.3–0.6 mil).

Off. Prep.—Linimentum Terebinthinæ, *U. S.;* Oleum Terebinthinæ Rectificatum, *U. S.;* Linimentum Opii Compositum, *N. F.;* Linimentum Terebinthinæ Aceticum, *N. F.;* Linimentum Tiglii Compositum, *N. F.;* Petroxolinum Sulphuratum Compositum, *N. F.*

OLEUM TEREBINTHINÆ RECTIFICATUM. U. S., Br.

RECTIFIED OIL OF TURPENTINE. Ol. Tereb. Rect. [Rectified Turpentine Oil]

(ō'lę-ŭm tĕr-ę-bĭn'thį-næ rĕc-tį-fį-cā'tŭm)

"Rectified Oil of Turpentine is the oil distilled from the oleo-resin (turpentine) obtained from various species of Pinus, and rectified." *Br.*

Essence de Térébenthine purifiée, *Fr.;* Oleum Terebinthinæ Rectificatum, *P. G.;* Gereinigtes Terpentinöl, *G.*

* "Oil of Turpentine, *a convenient quantity;* Solution of Sodium Hydroxide, *a sufficient quantity*. Shake the oil of turpentine thoroughly with an equal volume of solution of sodium hydroxide, and introduce the mixture into a still connected with a well-cooled condenser. Recover about three-fourths of the oil by distillation, separate the clear oil from the water, dry it by shaking with anhydrous calcium chloride, filter and preserve. Keep the product in well-stoppered, amber-colored bottles, in a cool place. Rectified Oil of Turpentine is to be dispensed when oil of turpentine is required for internal use." *U. S.*

When oil of turpentine is distilled in contact with sodium hydroxide solution, the distillate comes over purified and freed from the decomposition products which give the commercial oil the disagreeable odor and taste which are inseparable by ordinary distillation without alkali; hence this rectified oil is much preferable for internal administration. In the U. S. P. VIII and IX solution of sodium hydroxide was preferred to lime water, which was used in the U. S. P. 1890 to furnish an alkali to combine with resinous substances in commercial oil of turpentine. It has in other respects the same properties as Oleum Terebinthinæ. "Rectified Oil of Turpentine is a colorless liquid which conforms to the properties and tests under *Oleum Terebinthinæ,* specific gravity excepted.

Specific gravity: 0.856 to 0.865 at 25° C. (77° F.). Evaporate 5 mils of the Oil rapidly in a tared dish on a water bath; not more than 0.015 Gm. of residue remains. *U. S.*

"A colorless, limpid liquid. Characteristic odor; taste pungent, somewhat bitter. Specific gravity 0.860 to 0.870; *refractive index* at 25° C. (77° F.) 1.465 to 1.480. Distils almost entirely between 156° and 180° C. (312.8 and 356° F.), leaving no appreciable residue." *Br.*

For uses see p. 795.

Dose, five to ten minims (0.3–0.6 mil).

Off. Prep.—Emulsum Olei Terebinthinæ, *U. S.;* Linimentum Terebinthinæ, *Br.;* Linimentum Terebinthinæ Aceticum, *Br.*

OLEUM THEOBROMATIS. U. S., Br.

OIL OF THEOBROMA Ol. Theobrom.
[Butter of Cacao, Cacao Butter]

(ō'lę-ŭm thē-ǫ-brō'mą-tĭs)

"A concrete fixed oil obtained from the roasted seeds of *Theobroma Cacao* Linné (Fam. *Sterculiaceæ*)." *U. S.* "Oil of Theobroma is a solid fat expressed from the seeds of Theobroma Cacao, *Linn.*" *Br.*

Oleum Theobromæ, *U. S.* 1880; Cocoa butter (improperly); Beurre de Cacao, *Fr. Cod.;* Oleum concretum e semine Theobromæ Cacao, *Fr.;* Oleum Cacao, *P. G.;* Kakaobutter, *G.;* Manteca de coco, Aceite de coco, *Sp.*

Theobroma Cacao Linn. is a handsome tree, from twelve to twenty feet in height, growing in Mexico, the West Indies, and South America. It is largely cultivated in all tropical countries, particularly in Guayaquil, Venezuela, Mexico, Trinidad, and the Philippines. The fruit is an oblong-ovate capsule or berry, six or eight inches in length, with a thick, coriaceous, somewhat ligneous rind, enclosing a whitish pulp, in which numerous seeds are embedded. These are ovate, somewhat compressed, about as large as an almond, and consist of an exterior thin shell and a brown oily kernel. Separated from the matter in which they are enveloped, they constitute the *cacao,* or *chocolate nuts,* of commerce. The cacao tree is usually cultivated in large estates, where it is grown in the shade of the banana or other large plant, and develops its pods from the stem continually, so that the harvest goes on all the time, although the product is greater in the spring and in the autumn. The pods are cut off, opened, and the beans contained in the glutinous sweet acid pulp are allowed to ferment, during which process the outer integument comes off easily. The beans are finally carefully dried, commonly in the sun, sometimes by means of a steam drying shed. If the sweating process is carried too far, or the beans during drying are wetted by rain, they blacken and are much lowered in value. These blackened beans are sometimes artificially whitened. Cacao beans have a slightly aromatic, bitterish, oily taste, and, when bruised or heated, an agreeable odor. (See *Am. Drug.,* 1897, 311; also *Ph. Ztg.,* 1900, 756.)

The average of a number of analyses of raw nuts gave H. Weigmann (*König's Nahrungs- und Genussmittel,* 3d ed., vol. i, 1019) water, 7.93 per cent.; nitrogenous matter, 14.19 per cent.; theobromine, 1.49 per cent.; fatty matter (cacao butter), 45.57 per cent.; starch and other carbohydrates, 22.92 per cent.; crude fiber, 4.78 per cent.; pure ash, 3.99 per cent.; sand, 0.62 per cent. The coloring matter is probably the result of chemical change, as the fresh seeds are white. Theobromine has been found also in the shells in the proportion of about 1 per cent. (*A. J. P.,* 1862, 509.) The latter impart to boiling water a taste analogous to that of chocolate, but weaker, and are used for making a table beverage.

Theobromine was discovered by Woskresensky, who obtained it by the following method. The kernels are exhausted with water by means of the water bath; the solution is strained through linen, precipitated by lead acetate, and filtered; the filtered liquor is freed from lead by hydrogen sulphide, and evaporated; the brown residue is treated with boiling alcohol, and the liquor filtered while hot. Upon cooling, the theobromine is deposited in the form of a reddish-white powder, which is rendered colorless by repeated crystallization. Keller obtained it still purer by heating the powder between two watch glasses, by which a brilliant white sublimate was obtained. According to O. Donker and C. Treumann, theobromine is contained not only in the cotyledons but also in the shells of the cacao seeds. Four kilos of the latter yielded 13.5 Gm. of pure theobromine. Theobromine is now official. (See *Theobrominæ Sodio-Salicylas.*)

For Emminger's method of determining theobromine in cacao, see *P. J.,* 1896, 289.

Cocoa or *Prepared Cacao* is also official in the N. F. IV under the title *Cacao Præparata.* The description and tests are as follows:

"A powder prepared from the roasted, cured kernels of the ripe seeds of *Theobroma Cacao* Linné and of other species of *Theobroma* (Fam. *Sterculiaceæ*), deprived of a portion of its fat. A brownish powder having a chocolate-like odor and taste, free from sweetness. Extracted with cold water Cocoa yields not less than 14 per cent. nor more than 22 per cent. of soluble matter. Extracted with ether, Cocoa yields not less than 18 per cent. of fat, and the fatty residue does not have a spicy odor or taste. The residue, insoluble in ether, when examined under the microscope, shows not more than 3 per cent. of Cocoa shells, and no foreign starch granules or other foreign substances. Cocoa contains not more than 6 per cent. of crude fiber and not more than 12 per cent. of starch. Cocoa yields not less than 3.5 per cent. nor more than 8 per cent. of ash, which has a distinctly reddish color." *N. F.*

Cacao, usually but erroneously known as cocoa, is often sold in powder which is sometimes adulterated with various other ingredients such as ground rice, barley flour, sugar, etc. Mixed with hot milk or water it is much employed as a drink. It has the advantages over

tea and coffee that it is less stimulating to the nervous system and contains some nutriment. Chocolate is the solid substance expressed from the cacao bean after roasting. In Great Britain and the United States it is usually made, when pure, exclusively of the kernel of the cacao or chocolate nuts, which are first roasted, then deprived of their shells, and lastly reduced, by grinding between heated stones, to a paste, which is moulded into oblong cakes. Sometimes rice flour or other farinaceous substance, with foreign fats, is added, but these must be considered as adulterations. In the compounded form known as sweet chocolate, sugar is generally incorporated with the paste, and spices, especially cinnamon, are often added; vanilla is a favorite addition in America, France, and Spain. The well-known confection known as *"milk chocolate"* contains either whole or skim milk powder in addition to the foregoing ingredients. The U. S. Department of Agriculture standards for cocoa products are as follows:

"1. *Cocoa beans* are the seeds of the cacao tree, *Theobroma cacao,* L. 2. *Cocoa nibs, cracked cocoa,* is the roasted, broken cocoa bean freed from its shell or husk. 3. *Chocolate, plain chocolate, bitter chocolate, chocolate liquor, bitter chocolate coatings,* is the solid or plastic mass obtained by grinding cocoa nibs without the removal of fat or other constituents except the germ, and contains not more than three (3) per cent. of ash insoluble in water, three and fifty hundredths (3.50) per cent. of crude fiber, and nine (9) per cent. of starch, and not less than forty-five (45) per cent. of cocoa fat. 4. *Sweet chocolate, sweet chocolate coatings,* is chocolate mixed with sugar (sucrose), with or without the addition of cocoa butter, spices, or other flavorng materials, and contains in the sugar- and fat-free residue no higher percentage of either ash, fiber, or starch than is found in the sugar- and fat-free residue of chocolate. 5. *Cocoa, powdered cocoa,* is cocoa nibs, with or without the germ, deprived of a portion of its fat and finely pulverized, and contains percentages of ash, crude fiber, and starch corresponding to those in chocolate after correction for fat removed. 6. *Sweet cocoa, sweetened cocoa,* is cocoa mixed with sugar (sucrose), and contains not more than sixty (60) per cent. of sugar (sucrose), and in the sugar- and fat-free residue no higher percentage of either ash, crude fiber, or starch than is found in the sugar- and fat-free residue of chocolate."

Hagenbuch examined several commercial brands of chocolate, and found that the amount of fat or cacao butter present varied from 12 to 45.8 per cent. (*A. J. P.,* 1885, p. 276.) From this it would seem that manufacturers do not uniformly extract the fat from commercial chocolate.

Oil of Theobroma. Cacao Butter.—This is the fixed oil of the chocolate nut. It is extracted either by expression, decoction, or the action of a solvent. Soubeiran recommends that the seeds, previously ground, be mixed with one-tenth of their weight of water and then pressed between hot plates of tinned iron. It is advisable that the heat should not exceed that of boiling water, and even a lower heat will answer. When the method of decoction is used, the cacao should be slightly roasted before boiling. As a solvent, carbon disulphide has been found to answer well, as recommended in the preparation of the expressed oil of nutmeg. (See *Oleum Myristicæ.*) Upon the whole, the method of expression is perhaps preferable. The presence of water in the ground seeds is said greatly to facilitate the process. The expressed oil, now made largely in Philadelphia as a by-product in the manufacture of cocoa, occurs in the shape of oblong cakes, like those of chocolate, weighing about half a pound each. It is "a yellowish-white solid, having a faint, agreeable odor, and a bland, chocolate-like taste. It is usually brittle at temperatures below 25° C. (77° F.). It is slightly soluble in alcohol, soluble in boiling dehydrated alcohol, and freely soluble in ether, chloroform or benzene. Specific gravity: about 0.973 at 25° C. (77° F.). It melts between 30° and 35° C. (86° and 95° F.). Dissolve 1 Gm. of Oil of Theobroma in 3 mils of ether in a test tube at a temperature of 17° C. (62.6° F.), and immerse the tube into water having the temperature of melting ice. The liquid does not become turbid nor deposit white flakes in less than three minutes; and if the mixture after congealing is again brought to 15° C. (59° F.), it gradually forms a perfectly clear liquid (*wax, stearin, or tallow*). Saponification value: not less than 188 nor more than 195 (see Part III, Test No. 9). Iodine value: not less than 33 nor more than 38 (see Part III, Test No. 8)." *U. S.*

"A yellowish-white solid, breaking with a smooth fracture. Odor resembling that of cocoa; taste bland, agreeable. Somewhat brittle at ordinary temperatures, but softening at 25° C. (77° F.). Specific gavity 0.990 to 0.998; melting point 30° to 33° C. (86°–91.4° F.); *saponification value* 188 to 195; *iodine value* 35.5 to 37.5; *acid value* not more than 2.0; *refractive index* at 40° C. (104° F.) 1.4565 to 1.4575. In ascertaining the melting point and specific gravity, seventy-two hours should be allowed to elapse between the time of melting and the time of determining the constants. When 1 gramme is dissolved at 17° C. (62.6° F.) in 3 millilitres of *ether* in a test-tube, and the tube placed in *water* at 0° C. (32° F.), the solution neither becomes turbid nor deposits a granular or flaky mass in less than three minutes; and if, after congealing, it is exposed to a temperature of 15.5° C. (60° F.), a clear solution is gradually formed (absence of certain other fats)." *Br.*

Cacao butter consists chiefly of the glycerides of stearic, palmitic, and lauric acids, and, further, of small quantities of the glycerides of arachidic, linolic, formic, acetic, and butyric acids. The percentage of stearic acid obtainable is from 39.9 to 40.6. Kingzett believes it to contain in addition a peculiar acid which he

calls *theobromic,* and to which he gives the formula $C_{64}H_{128}O_2$, but his results have not been confirmed by subsequent investigators. From its large proportion of stearin, it is one of the best fats for the preparation of stearic acid. It is said to be frequently adulterated with animal fats, which, according to E. Lamhofer, may be detected by attention to the fact that pure cacao butter dissolves entirely in ether or petroleum benzin, separating out in minute granular crystals when immersed in water of 0° C. (32° F.), the liquid portion remaining transparent for 30 or 40 minutes, when the whole solidifies. After solidification, if the oil be kept at a temperature of about 14.4° C. (58° F.), it will redissolve without turbidity. (*A. J. P.,* 1877, p. 238.) G. Ramsperger concludes, as the result of much experimentation, that ether affords the best test of purity (see the official tests).

Uses.—Butter of cacao is used as an ingredient in cosmetic ointments, and in pharmacy for coating pills and preparing suppositories. For the last purpose it is well adapted by its blandness, and the fact that although liquefying at a temperature below that of the body, it is of firm consistence at 21.1° C. (70° F.). It is also valuable for the reason that easily decomposable substances like silver nitrate, potassium permanganate, etc., may be incorporated in it without material change and it is therefore valuable as an excipient. It was chiefly on this account that it was introduced into the U. S. Pharmacopœia of 1860. It has the emollient properties of the fats and is used to soften and protect *chapped hands* or *lips.* F. Bringhurst prepared a *lip salve* by melting together 28 ounces of cacao butter, 4 ounces of yellow wax, and a drachm, each, of balsam of Peru and benzoic acid, straining, adding perfuming oils, as those of rose, bergamot, and bitter almond, in sufficient quantity, and finally, when nearly cool, an ounce of glycerin. (*A. J. P.,* July, 1867, p. 348.)

OLEUM THYMI. U. S.

OIL OF THYME Ol. Thymi [Thyme Oil]

(ō'lę-ŭm thī'mī)

"A volatile oil distilled from the flowering plant of *Thymus vulgaris* Linné (Fam. *Labiatæ*), and containing not less than 20 per cent., by volume, of phenols. Preserve it in well-stoppered, amber-colored bottles, in a cool place, protected from light." *U. S.*

Huile volatile de Thym, *Fr. Cod.;* Essence de Thym, *Fr.;* Oleum Thymi, *P. G.;* Thymianöl, *G.;* Esencia de tomillo, *Sp.*

In the south of France thyme grows wild in great abundance, and is largely collected for distillation. The oil is taken from France to England, and thence reaches this country under the name of *oil of origanum,* having, probably from its greater cheapness, been substituted for the latter. (See Part II.)

Thymus vulgaris is a very common plant, indigenous to Southern Europe, and cultivated in our gardens. It possesses a subcampanulate two-lipped calyx, villous in the throat; corolla limb two-lipped, the upper erect and emarginate, the lower spreading, three-cleft. It is a low under-shrub, procumbent at the base, with ovate-linear, revolute leaves, the flowers occurring in a whorled spike. The herbaceous portion, which should be gathered when the plant is in flower, has a peculiar, strong, aromatic, agreeable odor, not lost by drying, and a pungent, aromatic, camphoraceous taste. Its active constituent is the volatile oil, which is obtained separate by distillation with water.

The oil, as prepared in Southern France, is, after one distillation, of a reddish-brown color, and called the *red oil,* but when again distilled is colorless, and in this condition is distinguished as the *white oil.* Oil of thyme is officially described as "a colorless or red liquid, having a characteristic odor and taste. It is soluble in 2 volumes of 80 per cent. alcohol. Specific gravity: 0.894 to 0.930 at 25° C. (77° F.). It is slightly lævorotatory. Shake 1 mil of the Oil with 10 mils of hot distilled water, and, after cooling, pass the aqueous layer through a wetted filter; the filtrate does not assume a blue or violet color upon the addition of a drop of ferric chloride T.S."

The U. S. Pharmacopœia introduced an assay based on the phenols content as follows:

"**Assay.**—Introduce 75 mils of sodium hydroxide T.S. into a flask with a long graduated neck (cassia flask), add 10 mils of the Oil to be assayed, stopper the flask tightly, shake the mixture thoroughly and set it aside for from twelve to twenty-four hours. Then add sufficient sodium hydroxide T.S. to raise the lower limit of the oily layer within the graduated portion of the neck of the flask, and, after the alkaline solution has become clear, adjust it to the temperature at which it was measured, and note the volume of the residual liquid. This measures not more than 8 mils, indicating the presence of not less than 20 per cent., by volume, of phenols." *U. S.*

According to Zeller, one pound of the fresh herb yields 45.7 grains of the oil, of the dried herb 38 grains. The oil, as found in commerce, is of a reddish-brown color, and of an odor recalling that of thyme, but less agreeable. Its specific gravity is stated at 0.905, but probably varies, as the oil is a complex body. The more volatile portion, that coming over below 180° C. (356° F.) in distillation, is a mixture of cymene, $C_{10}H_{14}$, boiling at 175° C. (347° F.), and pinene, $C_{10}H_{16}$, boiling at 161° C. (321.8° F.). The less volatile and most valuable portion is chiefly *thymol,* $C_{10}H_{14}O$, a white crystalline solid, melting at 50° C. (122° F.), and possessing a pungent taste. (See *Thymol.*) *Carvacrol* is also present, at times replacing part or all of the thymol, and in addition linalool and bornyl acetate have been found in small amount. (See *Proc. A. Ph. A.,* 1897, 637.)

The true oil of thyme, according to Bennett (*P. J.,* 1908, lxxx, p. 803), differs from the various oils known commercially under this

name, as well as the oils of origanum, in that it contains thymol, while the other oils of thyme contain the isomeric carvacrol. While it is probable that carvacrol has similar therapeutic properties to thymol, it has not been employed in medicine to any considerable extent and is far less well known.

The oil is commonly adulterated with the oil of turpentine, the *white oils* being especially impure. The presence of oil of turpentine, according to Duyk (*J. P. A.*, 1899, 41), is due to the fact that the French peasants place in the body of the still as a foundation for the herbs a layer of pine and fir branches.

The annual production of oil of thyme at Grasse, according to Flückiger (*A. J. P.*, 1885, 132), amounted to 40,000 kilogrammes.

Oil of thyme has been largely replaced in medicine by thymol. According to Camperdon, in doses of from three to fifteen grains (0.2–1.0 Gm.), oil of thyme causes mental excitement, and is a valuable diffusible stimulant in *collapse*. It is powerfully germicidal. (See *Thymol.*)

Dose, three to five minims (0.2–0.3 mil).

Off. Prep.—Liquor Antisepticus, *N. F.*; Liquor Zinci et Alumini Compositus, *N. F.*; Liquor Zinci et Ferri Compositus, *N. F.*; Mistura Oleo-Balsamica, *N. F.*; Oleum Hyoscyami Compositum, *N. F.*

OLEUM TIGLII. U. S. (Br.)

CROTON OIL Ol. Tiglii

(ō'lę-ŭm tĭg'lĭ-ī)

"A fixed oil expressed from the seeds of *Croton Tiglium* Linné (Fam. *Euphorbiaceæ*). Preserve it in small, well-stoppered bottles, protected from light." *U. S.* "Croton Oil is the oil expressed from the seeds of Croton Tiglium, *Linn.*" *Br.*

Oleum Crotonis, *Br.*; Huile de Croton Tiglium, *Fr. Cod.*; Huile de Graines de Tilly, *Fr.*; Oleum Crotonis, *P. G.*; Krotonöl, *G.*; Olio di crotontiglio, *It.*; Aceite de croton tiglio, Aceite de grano tiglio, *Sp.*

Croton Tiglium Willd. is a small tree or shrub, with a few spreading branches, bearing alternate petiolate leaves, which are ovate, acuminate, serrate, smooth, of a dark-green color on the upper surface, paler beneath, and furnished with two glands at the base. The flowers are in erect terminal racemes, scarcely as long as the leaf—the lower being female, the upper male—with straw-colored petals. The fruit is a smooth capsule, about the size of a filbert, with three cells, each containing a single seed.

The tree is a native of Hindostan, Ceylon, the Moluccas, and other parts of India. It is pervaded by an acrid purgative principle, probably analogous to that found in other plants belonging to the family of *Euphorbiaceæ*. Rumphius says that the root is employed in Amboyna, in the dose of a few grains, as a drastic purge in dropsy, and, according to the same author, the leaves are so acrid that when chewed and swallowed they excite inflammation in the lips, mouth, and throat, and along the whole course of the alimentary canal. The wood is said in small doses to be diaphoretic, in larger, purgative and emetic. But the seeds are the most active part. These have been long used in India as a powerful purgative, and were employed so early as 1630 in Europe, under the names of *grana Molucca* and *grana tiglia*. But in consequence of their violent effects they fell into neglect, and had ceased to be ranked among medicines, when, at a comparatively recent period, attention was again called to them by the writings of some English physicians in India. They are now imported for their oil, which is the only official product of the plant. It is probable that most if not all of the *Crotons* are purgatives. The oil of the Mexican *Croton morifolius* is said to be mildly purgative in doses of two or three minims (0.12–0.2 mil). In India, under the name of *Kowli seeds* (*Kuli seeds*), are used certain beans, which have been referred by authorities to the *Croton oblongifolius* Roxb., and also to the *C. persimilis* Müll.-Arg. (See *Ph. Rev.*, Oct., 1896.) Kowli seeds reach a length of 2.1 cm., a breadth of 1.2 cm., a thickness of 0.8 cm., ovate, having pointed ends with a marked caruncle. The outer side shows the grayish-brown crusty seed coat with irregular rough longitudinal stripes; the cross-section shows a large endosperm, in the middle the embryo of considerable size with flat cotyledons. Besides the fatty oil and protoplasm, the cells of the endosperm show longitudinally very large aleurone grains, which contain a considerable number of small globoids and badly formed crystalloids.

The seeds of the *C. Tiglium* resemble castor beans in size and general structure. They are oblong, rounded at the extremities, with two faces, the dorsal considerably more convex than the ventral, separated from each other by longitudinal ridges, and each divided by a similar longitudinal ridge, so that the whole seed presents an irregular quadrangular figure. Sometimes their ventral surface is flat, with a longitudinal groove, owing to the presence of only two seeds in the capsule, the groove being produced by the central column or axis. The shell is covered with a soft, yellowish-brown epidermis, beneath which the surface is black and smooth, and, as the epidermis is often partially removed by friction during their carriage, the seeds as they come to us are frequently mottled, and sometimes nearly black. The kernel or endosperm is yellowish-brown, and abounds in oil. In India the seeds are prepared for use by submitting them to slight torrefaction, by which the shell is rendered more easily separable. In the dose of one or two grains (0.065 or 0.13 Gm.) the kernel purges severely.

The oil is obtained by expression from the seeds, previously deprived of the shell. It may also be separated by decoction in water, or by the action of ether, or carbon disulphide, which dissolves the oil and leaves it behind when evaporated. Guibourt recommends, after the first expression, to digest the residue with alco-

hol at a temperature of 48.8° to 60° C. (120°–140° F.), and then submit it to a new expression. The alcohol is to be separated by distillation from the oil, which is then to be mixed with the first product. Great care must be used, during this distillation, to prevent blistering the unprotected skin of the operator.

Extraction by Ether.—Having washed and dried the seeds, grind them in a coffee mill, and form a soft paste with ether. Introduce this into a narrow percolation tube, and gradually pour ether upon it until it is exhausted. Evaporate the ether by means of a water bath, and filter the remaining oil.

Extraction with Carbon Disulphide.—The seeds, well bruised, are introduced into a bottle with three times their weight of carbon disulphide, well rectified; the mixture is allowed to stand, with frequent agitation, for 24 hours; the whole is then poured upon a cloth and rapidly expressed. The residue is similarly treated with twice its weight of the disulphide, and expressed, after standing as before. The products of the two macerations are mixed, then filtered in a covered funnel, and finally submitted to distillation, by means of a water bath, in a glass retort, at the temperature of 71.1° or 76.6° C. (160° or 170° F.). The disulphide should be recovered by condensing its vapor in a refrigerated receiver. The oil is to be poured into a dish, to show that it contains none of the disulphide, and then introduced into a bottle and closely stoppered.

Properties.—The seeds consist of 64 per cent. of kernel and 36 of envelope. From the seeds imported into England, about 22 per cent. of oil is obtained by simple expression. Guibourt, by his process, obtained 52 per cent. from the kernels, equivalent to about 35 per cent. from the seeds. Croton oil consists chiefly of the glycerides of stearic, palmitic, myristic, lauric, and oleic acids. There are also present, in the form of glycerin ethers, the more volatile acids, as formic, acetic, isobutyric, and isovalerianic acids. The volatile part of the acid yielded by croton oil contains, moreover, an acid of the oleic series, named by Geuther and Frölich *tiglic* or *tiglinic acid,* $C_5H_8O_2$. It is isomeric with angelic acid, but the melting points (angelic acid 45° C. (113° F.), tiglic acid 64° C. (147.2° F.)) and the boiling points (angelic acid 185° C. (365° F.), tiglic acid 198.5° C. (389.3° F.)) differ. *Crotonic acid,* $C_4H_6O_2$, was thought by Schlippe to be present, but later investigation does not confirm the statement. *Crotonol,* announced by Schlippe as the vesicating principle of the oil, has likewise been found only by the discoverer.

In 1823 John Nimmo, of Glasgow, found that about 45 per cent. of croton oil is soluble in alcohol, the insoluble 55 per cent. being inert. Recent researches have shown that the percentage of soluble portion varies greatly. (See also below.) In this soluble portion Buchheim found an acid, *crotonolic acid* or *crotonoleic acid,* which he believed to be the active principle. It is an oily substance, readily decomposable, having the character of a weak acid, and forming various salts. It is freely soluble in alcohol, and is extremely irritant to the skin and the mucous membrane. As pointed out in 1889 by Stillmark and Kobert, croton seeds contain one or more toxic albuminoids, which have been especially studied under the name of *crotin* by Elfstrand. Dunstan and Boole (*Proc. Roy. Soc. London,* lxiii, 1895) found that crotonoleic acid, prepared by the method of Kobert and Hirscheydt, is a mixture of inactive oily acids and a resinous substance having extraordinary power as a vesicant, for which they have proposed the name of *croton resin,* assigning to it the empirical formula $C_{13}H_{18}O_4$, and the molecular formula $(C_{13}H_{18}O_4)_2$, or $C_{36}H_{36}O_8$. It is described as a hard, pale yellow resin, nearly insoluble in water, and benzene, but readily dissolved by alcohol, ether, and chloroform. It is neither a glyceride, a ketone, nor an aldehyde.

Crotonoleic acid may be readily prepared by treating the portion of croton oil soluble in alcohol with a hot saturated solution of baryta in a water bath, washing the stiff white paste that forms with cold distilled water to remove excess of baryta and barium compounds with acetic, butyric, and tiglic acids, repeatedly treating with water, and lastly agitating with ether, which takes up only the barium oleate and crotonoleate. The crotonoleate is separated by dissolving it out in alcohol, decomposing it carefully with sulphuric acid, and the solution containing the free acids carefully evaporated. (See also *Kobert's Arbeiten,* 1890, p. 30.)

Crotin is described as a yellowish powder, yielding about 21 per cent. of ash, soluble in water, and possessed of such active poisonous properties that the subcutaneous lethal dose for the rabbit is from 0.05 to 0.08 Gm. per kilo. It attacks the blood corpuscles as well as the centric nervous system, and, indeed, probably affects all protoplasm. (*On Some Toxic Albumins,* Upsala, 1897.)

Croton oil, as found in commerce, varies greatly in color, from a pale yellow to a dark reddish-brown. That imported from India is usually pale, that expressed in Europe dark, like the deepest-colored sherry. Its consistence is rather viscid, and is increased by time. Its odor is faint, but peculiar, its taste hot and acrid, leaving in the mouth a disagreeable sensation which continues for many hours. It is officially described as "a pale yellow or brownish-yellow, somewhat viscid and slightly fluorescent liquid, having a slight, characteristic odor. *Great caution is necessary in tasting it,* and it must be handled carefully as it causes a pustular eruption, when applied to the skin. It is slightly soluble in alcohol, the solubility increasing with age; freely soluble in ether, chloroform, or in fixed or volatile oils. It is acid to litmus paper previously moistened with alcohol. Specific gravity: 0.935 to 0.950 at 25° C. (77° F.). When gently heated with twice its volume of dehydrated alcohol, it forms a

clear solution from which the Croton Oil separates, either partially or completely on cooling. Add 1 mil each of fuming nitric acid and of distilled water to 2 mils of the Oil, and shake the mixture vigorously for a few minutes; it does not solidify either completely or partially after standing for twenty-four hours. Saponification value: not less than 200 nor more than 215 (see Part III, Test No. 9). Iodine value: not less than 104 nor more than 110 (see Part III, Test No. 8)." *U. S.*

"Brownish-yellow to dark reddish-brown; viscid, slightly fluorescent. Disagreeable odor; when cautiously tasted, acrid. Blisters the skin and mucous membrane. Specific gravity 0.940 to 0.960; *saponification value* 210 to 215; *iodine value* 102 to 106. Freely soluble in *ether* and in *chloroform*. Miscible with half its volume of *absolute alcohol*. Thickens slightly but does not solidify, either completely or partially, when vigorously shaken with half its volume of *fuming nitric acid* and the same proportion of *water* (absence of other non-drying oils)." *Br.*

The oil is wholly soluble in ether and oil of turpentine. Its relations to pure alcohol differ somewhat with the variety of the oil. That obtained by expression in England was formerly wholly and readily soluble, but, according to Harold Senier, the croton oil now produced acts towards alcohol as do foreign oils (*P. J.*, 3d ser., xiv, 704), forming a solution which is permanent at ordinary temperatures, while the India or pale oil forms an opaque mixture, which becomes clear and uniform upon being heated, but separates on standing into two portions, one consisting of alcohol somewhat diminished in bulk, the other of the oil correspondingly increased in bulk by retaining a portion of the alcohol. It is probable that the difference in color, and in their relations to alcohol, between the India and English oils may be owing to a change in the kernels from being kept, and to the age of the oil. According to Senier, confirmed by Binz, Kobert, and others, it increases with the age, freshly expressed oil containing only 20 per cent., oil over four years old 60 per cent. It is known that croton oil is often adulterated with other fixed oils, which having a different saponification and iodine number can usually be detected by those tests.

Croton oil may be detected when present in admixture with other oils by the following reaction: The sample of oil is shaken with twice its volume of dehydrated alcohol; the clear solution is superimposed upon a highly concentrated solution of potassium hydroxide in a test tube, which is then carefully warmed for thirty minutes on a water bath and then examined. If croton oil is present, an intense reddish-brown or reddish-violet ring forms at the junction of the two liquids. (*J. P. C.*, 1916, xiv, 38.)

For tests for croton oil, including iodine and acid numbers, see *Ph. Rev.*, 1897, 113.

According to M. Burrough, who was for some time in India, much of the oil there prepared is derived from the seeds of *Jatropha Curcas*, or *Curcas purgans*, the so-called *Barbados nuts*. This oil, though weaker than the genuine, was said by Burrough to be an efficient cathartic in the dose of three or four drops (0.15 or 0.2 mil). Hamilton states that croton seeds are afforded by *Croton pavana*, growing in Ava and Bengal, and probably a portion of the croton oil of commerce is obtained from these seeds. These facts may explain some of the discrepancies which have been observed in the effects of the oil.

Cash and Dilling (*J. P. Ex. T.*, 1914, v, p. 235) have also found a purgative oil in the seeds of the *Croton elliotianus* which grows in British East Africa.

Uses.—Croton oil is a powerful drastic purgative, in large doses apt to excite vomiting and severe griping pains, and capable, if immoderately taken, of producing fatal effects. It acts with great rapidity, frequently evacuating the bowels in less than an hour, and generally exciting a rumbling sensation in half that period. It possesses also great advantage in the minuteness of the dose, on account of which it may frequently be given when we should fail with more bulky medicines, as in *mania, coma,* and the cases of children. A drop placed on the tongue of a comatose patient will generally operate. Though long used in India, and known for two centuries to the Dutch physicians, it did not attract general notice till about 1820, when it was introduced into England by Conwell. It is chiefly employed in cases of *obstinate constipation,* in which it often produces the happiest effects after the failure of other medicines, but it may also be advantageously used in almost all cases in which powerful and speedy purging is demanded, especially where an irritation of the gastric mucous membrane and a derivative action are desired. The seeds are said to have been used successfully in India, in *amenorrhea.* Applied externally, the oil produces inflammation of the skin, attended with pustular eruption, and has been used as a counter-irritant in *rheumatism, gout, neuralgia, bronchitis* and other inflammations. It should be diluted with three parts of olive oil, soap liniment, oil of turpentine, or other convenient vehicle, and applied as a liniment twice or oftener in twenty-four hours. Sometimes the insusceptibility of the skin is such as to require its application undiluted. The oil may also be applied externally, in the form of a plaster, made by incorporating one part of it with four parts of lead plaster, melted by a very gentle heat. Sometimes it appears to produce inflammation in parts distant from those to which it was directly applied. It has been said that four drops, used externally by friction around the umbilicus, will produce a purgative effect, but this is denied by Barlai of Tuscany, who states that it is only when the oil is applied to the skin divested of the cuticle that it will operate upon the bowels.

Croton Oil Crayons.—In order to prevent the spreading of croton oil beyond the limits intended, Limousin prepared crayons by melting

1 part each of cacao butter and white wax in a small glass flask, and then adding 2 parts of croton oil, taking care to close the orifice of the flask at once with a cork. When the mixture begins to get thick, it is poured into cylindrical moulds, where it speedily solidifies. These crayons may be made of a thickness of about 8 or 9 millimeters (⅓ inch), and may be covered with tin foil to protect them from change. (*N. R.*, May, 1877.)

The oil is most conveniently administered in the form of pill. A safe and convenient plan is to make two drops into four pills with crumb of bread, and to give one every hour until they operate. The oil may also be given in emulsion.

Crotonoleic acid has been shown by Kobert to be a very active irritant poison, much more harsh and severe in its influence than croton oil itself. Hirscheydt has found that its salts injected into the blood are extremely powerful depressants to the circulation. It has appeared in commerce, but after trial has been found by Hirscheydt to act badly as a practical remedy. It probably also varies greatly in purity. Ten milligrammes were found by Hirscheydt to be very uncertain in their purgative effect, while large doses commonly produced excessive gastro-intestinal irritation. The superiority of croton oil over the acid probably depends upon the fact that the acid exists in it chiefly in combination with glycerin, and that this crotonoleic glyceride acts with comparative kindness because of the slow decomposition and setting free of the acid which occur in the intestines. This being the case, it follows as a corollary that old, acid croton oil must be more irritant than the fresher and nearly neutral oil. Kobert has confirmed this conclusion by actual trial, and asserts that the neutral oil should always be preferred in practice, and that the acid oil should be rejected.

Dose, one-half to two minims (0.03–0.12 mil).

Off. Prep.—Linimentum Crotonis, *Br.;* Collodium Tiglii, *N. F.;* Linimentum Tiglii, *N. F.;* Linimentum Tiglii Compositum, *N. F.;* Pilulæ Aloes, Hydrargyri et Scammonii Compositæ, *N. F.*

OLIVERI CORTEX. Br.

OLIVER'S BARK [Black Sassafras]

(ŏ-lĭ'vẹ-rī cŏr'tĕx)

"Oliver's Bark is the dried bark of Cinnamomum Oliveri, *Bailey*." *Br.*

The genus *Cinnamomum* comprises some fifty-four species which are mostly tropical or subtropical evergreen shrubs or trees. They are mostly aromatic and comprise two principal groups: The one yielding camphor, and the other aromatic barks like cinnamon. Oliver's bark was official in the Ind. and Col. Add. for the Australian Colonies and is now official in the British Pharmacopœia. The tree which furnishes this bark is *Cinnamomum Oliveri* Bailey (Fam. *Lauraceæ*). It is indigenous to New South Wales and Queensland. It is much of the same habit as the trees yielding cinnamon and the bark is used as a substitute for this spice in the Australian Colonies.

"In flat pieces usually about twenty centimetres long, four centimetres wide and one centimetre thick. Cork greyish-brown, very warty. Inner surface umber-brown, satiny. Fracture short, slightly fibrous. In transverse section, umber-brown, a pale line separating the cork from the inner tissues. Aromatic odor; taste aromatic, bitter, camphoraceous." *Br.*

Off. Prep.—Tinctura Oliveri Corticis, *Br.*

OPII PULVIS. U. S.

POWDERED OPIUM Opii Pulv. [Opii pulvis, P. I.]

(ō'pĭ-ī pŭl'vĭs)

"Opium dried at a temperature not exceeding 70° C. (158° F.), reduced to a very fine powder, and yielding not less than 10 per cent. nor more than 10.5 per cent. of anhydrous morphine. Powdered Opium of a higher morphine percentage may be brought within the required limits by admixture with powdered opium of a lower percentage, or with some inert diluent. Preserve it in well-closed containers." *U. S.*

Poudre d'Opium, *Fr. Cod.;* Opiumpulver, *G.;* Polvo de opio, *Sp.*

"Powdered Opium is light brown; consisting chiefly of yellowish-brown to brownish-red, more or less irregular and granular fragments, varying from 0.015 to 0.15 mm. in diameter; a few fragments of strongly lignified, thick-walled, 4- to 5-sided or narrowly elongated, epidermal cells of the poppy capsule; and very few fragments of tissues of poppy leaves, poppy capsules, and rumex fruits.

"Assay.—Proceed as directed under *Opium*." *U. S.*

The strength of powdered opium has been altered in the last revision. The U. S. P. VIII required that it should yield not less than 12 per cent. nor more than 12.5 per cent. of *crystallized* morphine, but it will be observed that the figures have been lowered, and the assay process based upon an anhydrous instead of a crystallized morphine. The preparation is thus made to conform to the International Protocol standard. For assay and preparations see pp. 817 and 822, respectively.

The German Pharmacopœia requires that the strength be adjusted to 10 per cent. of morphine by the use of rice starch. Ground cacao shells and powdered sugar of milk are commonly used as diluents for adjusting the strength of powdered opium.

Dose, one-half to one grain (0.032–0.065 Gm.).

OPIUM. U. S., Br.

OPIUM

(ō'pĭ-ŭm)

"The air-dried, milky exudation obtained by incising the unripe capsules of *Papaver somniferum* Linné and its variety *album* De Candolle (Fam. *Papaveraceæ*), and yielding, in its

normal, moist condition, not less than 9.5 per cent. of anhydrous morphine." *U. S.* "Opium is the juice obtained by incision from the unripe capsules of Papaver somniferum, *Linn.*, inspissated by spontaneous evaporation. Any suitable variety of opium may be employed as a source of Tincture of Opium and Extract of Opium, provided that when dry it contains not less than 7.5 per cent. of anhydrous morphine; but, when used for official purposes other than the preparation of the alkaloids or their salts, opium must be of such a strength that when dried, and powdered, the resulting powder dried at 60° C. (140° F.) yields not less than 9.5 per cent., and not more than 10.5 per cent., of anhydrous morphine. Opium yielding when dried more than 10 per cent. of anhydrous morphine must be diluted to that percentage either with powdered Milk Sugar or with any opium containing when dried between 7.5 and 10 per cent. of anhydrous morphine." *Br.*

Lachryma Papaveris, Meconium, Succus Thebaicus, Thebaica; Opium, *Fr. Ged.*; Opium, *P. G.*; Mohnsaft, *G.*; Oppio, *It.*; Opio, *Sp.*; Affioni, *Turk.*; Ufyoon, *Arab.*; Sheerikhaskash, *Pers.*; Ufeem, *Hindost.*

Opium is generally believed to be derived exclusively from *Papaver somniferum,* though every species of poppy is capable of yielding it to a greater or less extent, and some authors assert that *Papaver orientale* is its real source. The United States, British, and French Pharmacopœias recognize only the first-mentioned species and its varieties.

Papaver somniferum, or *Opium Poppy.*—There are several varieties of this species, of which the two most prominent are distinguished by the titles of the white and the black poppy, derived from the color of their seeds. It is the former (var. *P. album* DC.) which is usually described as the proper opium plant. The *white poppy* is annual, with a roundish, smooth, erect, glaucous, often branching stem, usually rising two or three feet in height, but sometimes five or even six feet in favorable situations. The leaves are large, variously lobed and toothed, and alternately disposed on the stem, which they closely embrace. The flowers are terminal, very large, and of a white or silver-gray color. In India they appear in February, in Europe and the United States not earlier than June, July, or August. The calyx is smooth and composed of two leaves, which fall when the petals expand. These are usually four in number, but there is a variety in which the flower is double. The ovary is smooth and globular, supports a radiated stigma, and is surrounded by numerous short and slender filaments, with erect, oblong, compressed anthers. The capsule is smooth and glaucous, rounded, from two to four inches in diameter, somewhat flattened at the top and bottom, and crowned with the persistent stigmas, the diverging segments of which are arranged in a circle upon the summit. It contains numerous minute white seeds, which when perfectly ripe escape through small openings beneath the stigma. In the *black poppy,* the flower, though sometimes white, is usually violet-colored or red, the capsule somewhat smaller and more globular, and the seeds of a brown or blackish color.

There is a third variety, *Papaver somniferum setigerum* DC., which, however, is not cultivated as a source of opium.

All parts of the poppy contain a white, opaque, narcotic juice, but the leaves, analyzed by Blondeau, yielded none of the active principles by which opium is characterized. (*J. P. C.*, vii, 214.) It is in the capsule that the juice most abounds and the virtues of the plant chiefly reside, hence this part is sometimes employed medicinally and was official in the British Pharmacopœia of 1898 (*Papaveris Capsulæ*). The dried poppy capsules vary in size from 5 to 7.5 cm. in diameter, and in shape from ovoid to globular, according to the variety of the poppy from which they are procured. Those commonly found in commerce are spheroidal, flattened below, and surrounded by a crown-like expansion—the persistent stigma—which is marked by numerous diverging rays that rise somewhat above the surface and appear to be prolongations of partial septa or partitions, proceeding along the interior circumference of the capsule from the top to the bottom. They are of a dirty white or purplish brown color, of a consistency somewhat like that of paper, inodorous and with little taste unless long chewed when they are decidedly bitter. They contain the same principles as opium but in much smaller amounts. The seeds are destitute of narcotic properties, and are even used as food. The Romans employed them in the preparation of various dainties. They are commercially known as *maw seed* (probably a corruption of the German *mohnsamen*) and frequently used for culinary purposes, they abound with a bland oil, called commercially *poppy seed oil,* or maw oil, which may be extracted by expression. The latter is of a straw-yellow color, without odor, and of a pleasant almond taste. It is without narcotic properties, and much resembles olive oil, as a substitute for which and an adulterant of which it is very largely used on the continent of Europe. It has a low congealing point, thickening only at –15° C. (5° F.) and solidifying at –20° C. (–4° F.). The black variety is specially used for the expression of oil, as its culture is easier, and the oil percentage in both varieties is practically the same, ranging between 50 and 60 per cent. As the oil cake generally retains about 8 per cent. of the oil, the yield by expression is from 42 to 50 per cent. Poppy oil contains the glycerides of stearic and palmitic acids, together with those of linolic, linolenic, and oleic acids. Of the liquid fatty acids, linolic constitutes about 65 per cent., oleic 30 per cent., and linolenic 5 per cent. Myristic and lauric acid seem to be absent. The oil is an article of much importance on the continent of Europe, particularly in France and Germany, where it is employed for culinary and pharmaceutical purposes, in painting and the manufacture of soap, and in other ways, as a substitute for olive oil. The poppy does

not appear to elaborate the milky fluid in which its narcotic properties reside before a certain period of its growth, for we are told that, in Persia, the young plants which are pulled up to prevent too thick a crop, are used as potherbs, and the μήκων of the Greeks, which is believed to be identical with the *Papaver somniferum*, is said by Hippocrates to have been nutritive.

Though generally believed to be a native of Asia Minor, this species of poppy grows wild in the south of Europe, and even in England, whither its seeds are supposed to have been brought at a very early period. It was cultivated by the ancient Greeks, and is mentioned by Homer as a garden plant. It is at present cultivated very extensively in India, Persia, Egypt, China, Japan and Asiatic Turkey, for opium, and in certain parts of Europe chiefly for its seeds. Attempts have been made both in Europe and the United States to produce opium from the poppy, but although it is possible to obtain the product, commercial success has not been and probably never will be achieved in America because of the cost of labor. A very good quality of opium is said to have been produced in Australia. (See *Australian Journal of Pharmacy*, Nov., 1887.)

The British Parliament has condemned the opium traffic and the Chinese Government has provided for the suppression of the use of opium. While there is no doubt that the people of China even more than the Government recognize in opium a deadly national evil and have resolved upon its extirpation, yet the statistics do not show any great reduction of the cultivation of opium in China.

Various attempts have been made in England to cultivate the poppy, all of which have resulted in commercial failure. (For particulars, see Seventeenth edition, *U. S. D.;* also *Edinb. Phil. Journ.*, i, 258.) The same may be said of the attempts to cultivate opium in France, which have apparently ceased since the death of Aubergier, who devoted much time and money to the subject. (For particulars, see 15th ed., *U. S. D.;* also *P. J.*, xv, 693.)

In 1865, Robertson, of Campbell Co., Virginia, produced opium which yielded to the analysis of I. J. Grahame 4 per cent. of morphine, besides narcotine. (*A. J. P.*, 1867, p. 50.) H. Black, of Bolivar, Tennessee, produced an opium from which E. S. Wayne obtained 10.2 per cent. of morphine. (*Ibid.*, Jan., 1868.) Very fine opium has been produced by J. H. Flint, of California (*A. J. P.*, 1874, p. 105); also in Minnesota, by E. Weschke (*Contributions Dep. Pharm. University of Wisconsin*, 1886), but in the opinion both of Flint and of Weschke, the high price of labor forbids the profitable production of opium in the United States. For an account of North Carolina opium, see *Proc. A. Ph. A.*, 1894, 286; also *A. J. P.*, 1896, 435; also *Proc. A. Ph. A.*, 1904, 438. True reports on some experiments in the cultivation of opium poppy in the United States and states that it yields a good crop in Vermont, and a bumper crop in the dry climate of the state of Washington. (*Proc. N. W. D. A.*, 1911, p. 17.) He also outlines a plan for converting the waste product of the poppy seed industry, the capsule, into a valuable source of opium alkaloids. (*Oil, Paint, and Drug Rep.*, 1906, lxx, p. 37.)

Considerable interest is being manifested in the cultivation of opium throughout the world. Thoms reports on the cultivation of opium poppy and the production of opium at Dahlen, near Berlin. His article not only includes his own experiments, but contains an excellent summary of the work done elsewhere. (*Ber. d. Pharm. Ges.*, xvii, p. 24.) Mitlacher gives the results of his experiments in the cultivation of *Papaver somniferum* and *P. Rhoeas* in *Zeit. Oest. Apoth.*, l, p. 431. (See also *Sudd. Apoth. Zeit.*, liv, p. 239; and *Ph. Zentralh.*, lv, p. 110.) The following articles are of interest in this connection: Stahl "On Persian Opium" (*Chem. Zeit.*, xxxii, p. 804); van Itallie and Kerbosch "On Opium in Northern China" (*Arch. Pharm.*, 1910, p. 614); "Opium Cultivation in Turkey" (*C. D.*, lxxxiii, p. 134); "On the Cultivation of Opium at Dorpat" (Muszynski in *Apoth. Zeit.*, xxvi, p. 431).

The opinion that a hot climate is not necessary for the production of the narcotic principles has the support of Guibourt (*J. P. C.*, Sept., 1867, p. 222), and would seem to be established by the facts that the opium of Anatolia is richer in morphine than that of the much hotter regions of Bengal and Upper Egypt, and that good quality of opium is produced in the northern United States as well as in France and Germany.

Opium is obtained from the capsule of the poppy in a manner almost the same as that described by Dioscorides eighteen hundred years ago. A few days after the petals have fallen from the flower, when the capsule is approaching maturity, horizontal incisions into the capsule are made, usually with a several-bladed knife, care being taken not to penetrate the cavity. The white juice which exudes is allowed to harden for twenty-four hours, when it is scraped off by means of a large, blunt knife, a portion of the epidermis of the capsule being removed and constituting about six to ten per cent. of the product. In some places the poppy-head yields opium but once, but in Persia and probably other very hot countries the operation is repeated two or three times after periods of rest. The quality of the product depends largely upon the weather; if this is very hot and dry, the juice will be scanty and very thick, but if the weather is moist the product will be larger but more aqueous. After gathering, the poppy juice is worked up into opium in a manner which differs in different producing countries. An opium-like substance has been in past times, and perhaps even is at present in some districts, produced by making an aqueous extract from the nearly ripe capsule of the poppy. Accord-

ing to the writings of Dioscorides the ancient Greeks were acquainted with both processes of producing the drug from the poppy capsule. The term *ὀπίον*, derived from *ὀπος, juice,* they applied to the substance procured by incisions, which answers precisely to the modern opium. The inspissated expressed juice they called *μηκωνιον*, from *μήκων*, the name of the plant.

Commercial History.—Commerce is supplied with opium chiefly from Asia Minor, China, India, Persia and Egypt. The Smyrna or Asiatic opium constitute the principal commercial article, the total annual output being nearly 1,000,000 pounds. Of this it has been variously estimated that from one-third to two-thirds is shipped to the United States, the latter country being the greatest consumer of opium of any country in the world. (*C. D.,* lxxix, p. 384; *Oil, Paint, and Drug Rep.,* lxxx, p. 7.) The importations in 1914 were 441,621 pounds of crude and 32,105 pounds of powdered opium; in 1915, 353,006 pounds of crude and 38,977 pounds of powdered opium.

The commercial opiums may be classified into the following varieties: (1) Levant or Turkey opium, including Asia Minor or Smyrna opium; (2) Persian opium; (3) Egyptian opium; (4) East Indian and China opium; (5) Grecian opium; (6) Bulgarian and Macedonian opium; (7) German opium; (8) French opium; and (9) Australian opium.

Turkey Opium.—This title belongs to the opium produced in the Turkish province of Anatolia, and exported from Smyrna and Constantinople. According to some authorities, there is no essential difference between the parcels of the drug brought from these two ports. Others maintain that they are distinct varieties, differing in their interior structure, and probably also in the precise place of their production and the mode of their collection. The truth probably is that most of the opium shipped at Constantinople is produced in the more northern parts of the opium districts of Anatolia, while that from Smyrna is collected in the provinces more convenient to the latter city, and, although it is possible that an identical drug may often be brought from the two ports, yet there are grounds for arranging it under different varieties, as derived from these different sources. There can be little doubt also that a portion of opium which is taken to Constantinople is produced in Macedonia in Europe, which must, therefore, be added to the opium producing regions.

Smyrna Opium.—This is the variety which is, beyond all comparison, most abundant in our markets, and it is from this that the ordinary descriptions of opium are drawn up. It comes to us in masses of various size, usually from half a pound or somewhat less, to a pound in weight, sometimes, though rarely, as much as two or even three pounds; originally, perhaps, of a globular form, but variously indented, and rendered quite irregular in shape by the pressure to which they have been subjected, while yet soft, in the cases which contain them. Sometimes they are even pressed out into flat cakes. As brought into market, the lumps are usually hard on the outside, but still soft within. They are covered externally with the remains of leaves, and with the reddish fruits of a species of *Rumex,* which have no doubt been applied in order to prevent the surfaces from adhering. Notwithstanding, however, this coating, the masses sometimes stick together, and two or more become consolidated into one. In this way the fact may be accounted for, that the seeds of the *Rumex* are occasionally found in the interior of the masses. In the finer parcels of Smyrna opium the color internally is light brown; in the inferior it is darker. A peculiar character of this variety is that, when a lump of it is cut into and then carefully torn, numerous minute shining tears are observable, particularly under a microscope, bearing some resemblance to small seeds, but readily distinguishable by pressure between the fingers. They are undoubtedly formed from the drops of juice which escape from the incisions in the capsules, and which, according to Bélon, are allowed to concrete before they are removed. From the account of the same author it appears that after the juice has been collected it is not subjected to the process of kneading or beating, as in the case of other varieties of the opium; so that the tears preserve their original shape in the mass. It is probably owing to the peculiar mode of collecting Smyrna opium, that minute pieces of the epidermis of the poppy capsules are found intermingled in the mass, these being separated in the process of removing the adhering tears. In the best specimens of Smyrna opium, these fragments of the capsules are the only impurities. This variety of the drug is of very different qualities, the finest kinds yielding, according to Merck, as much as 13 per cent. of pure morphine, while from some very bad parcels he could not procure more than 3 or 4 per cent. In these inferior specimens the color is darker, the odor is often musty, and there is very generally more or less mouldiness both upon the surface and in the interior of the masses, indicating perhaps too much moisture in the opium originally, or its subsequent exposure to an injurious degree of dampness. Good Smyrna opium ought to yield 10 to 11 per cent. of morphine. Christison, however, states that he has not been able to procure more than 9 per cent. from the finest Smyrna opium. According to Landerer, little of the opium is produced in the immediate neighborhood of Smyrna, the greater portion being brought, on the backs of camels, from a distance of from ten to eighteen days' journey. (*J. P. C.,* 3e sér., xxiii, 33.) The same writer states that the opium is chiefly prepared at Kara-Hissar, near Magnesia. The incisions are generally made before sunrise. The juice is partly caught in mussel-shells, and dried in the sun. This is considered the best. Every evening the juice which has dried upon the capsules is scraped off, with a portion of the epidermis. The poppy plant is then cut down,

and stripped of its leaves, which are boiled in water, and the liquor is evaporated to the consistence of an extract. With this the inspissated juice is incorporated, and the mixture is then formed into cakes, wrapped in poppy leaves, and placed on shelves to dry. (See *A. J. P.*, xxiii, 251.) It is very evident, from the interior structure of the *best Smyrna opium*, that it has not been prepared in the way described by Landerer, though his account is probably true in reference to inferior varieties.

Constantinople Opium.—Most of the Constantinople opium is in flattened lumps from half a pound to two and a half pounds in weight, and scarcely distinguishable in exterior appearance from those of the former variety, being equally irregular in shape, and in like manner covered with the fruits of the *Rumex*. According to Merck, however, it often differs strikingly from the Smyrna opium in its interior constitution, being wholly destitute of the tears which characterize that variety. This would indicate some difference in the mode of collecting and preparing the juice. In the case of the Constantinople opium it is probably removed from the capsules before concretion. Merck says that he has not discovered in this variety those minute portions of the poppy capsules which are usually present in Smyrna opium. The average quality of the Constantinople opium, as above described, is about equal to that of the drug from Smyrna, but it appears to be occasionally purer, as Merck obtained from one specimen as much as 15 per cent. of pure morphine. R. Bauer, of Constantinople, in 1867 denied that any of the varieties produced near Smyrna contain tears, except the single one from Magnesia. (*N. R. Pharm.*, xvi, 751.)

In an account, by Bourlier, of the culture of the poppy and collection of opium in Bithynia, a province of Asia Minor, near Constantinople, it is stated that the lumps, when formed out of the concrete juice, are enveloped in poppy leaves, and no mention is made of the use of the Rumex fruits to prevent adhesion. It is the opium here collected which, according to Bourlier, is known throughout the Levant and in Europe as Constantinople opium. The same authority states that the yolk of egg is sometimes largely used for adulterating opium—a fraud which may be detected by the large proportion of fatty matter which the adulterated drug yields to ether, and by the impossibility of drying it so as to fit it for pulverization. (*Ann. Thér.*, 1859, p. 4.) See also Guibourt (*Ann. Pharm.*, xxiv, p. 65; and *U. S. D.*, 19th ed.).

Egyptian Opium.—Much opium was formerly produced in Upper Egypt, especially in the district of ancient Thebes, which was supposed to yield it in greatest perfection, hence the term *Opium Thebaicum*, and the old name of laudanum, *Tinctura Thebaica*. This variety occurred in flat roundish cakes, of various dimensions, sometimes as much as six inches in diameter and a pound in weight, usually, however, much smaller, and sometimes not weighing more than half an ounce. These cakes were either wrapped in a poppy leaf, so placed that the mid-rib divided the surface into two equal parts, or exhibited vestiges of such a covering. Occasionally the brown color of the opium was seen through the leaf, and the surface appeared as if uncovered, while the leaf was still present. The fracture was conchoidal and of a waxy luster and small fragments of it were translucent. Its color was usually redder than that of Smyrna opium, though sometimes dark. Some of the pieces, on exposure to the air, became damp and sticky on the surface, indicating the fraudulent addition of a deliquescent substance. The odor was similar to that of Smyrna opium, but weaker. It was an inferior variety, as the best of it, examined by Merck, yielded only 6 or 7 per cent. of morphine, and a specimen of it was found by J. Evans, of Philadelphia, to contain not more than 3.55 per cent.

India Opium.—The opium of Hindostan is distributed extensively through continental and insular India, where it is habitually employed as a narcotic-stimulant. Great quantities were also sent to China, into which it found an easy entrance, notwithstanding prohibitory laws. Much was formerly imported by the East India Company into England, through which a small proportion reached our own country. For various reasons India opium no longer enters Western commerce to any extent. It is not suitable for medicinal purposes.

There appear to be two chief varieties of it—one produced in Bahar and Benares, in the Bengal Presidency, and called *Bengal opium*, the other in the interior provinces, and designated by the name of *Malwa opium*. For minute description of Indian opium, see *P. J.*, xi, xii, abstracted *A. J. P.*, xxiv, 118; also *Pharmacographia*.

Bengal Opium, Benares Opium, Patna Opium.—This is produced in Hindostan chiefly under government supervision. The drug as first obtained is semiliquid, owing to the excessive dews, but is allowed to drain and dry by spontaneous evaporation until only 30 per cent. of moisture is left, when it is taken to the government factories. Great care is exercised to prevent adulteration. In the factories it is worked up with the drainings (known as *passewā*), poppy petals, and ground poppy plant into balls of standard strength. These are called "*cakes*," are about six inches in diameter, and are prevented from adhering by being rolled in the ground poppy plant. It is in round balls, weighing three pounds and a half, invested by a coating half an inch thick, composed of agglutinated leaves and poppy petals. The interior of the mass is of a brownish-black color, of the consistence of a stiff paste, and possessed in a high degree of the characteristic odor and taste of opium. The analyses of India opium vary decidedly in their results; Eatwell, 2.17 to 3.67 per cent. of morphine, 3.85 to 5.70 per cent. of narcotine; Procter (Patna opium), morphine, 5 per cent.; Flückiger and Hanbury (Khandesh opium), morphine, 6.07 per cent. (Patna

opium), morphine, 8.6 per cent., narcotine, 4 per cent.; Solly (Khandesh opium), morphine, 7 per cent.; Watson (a number of varieties), 3.5 to 6.1 per cent. of morphine. (*P. J.*, xi, 362; *A. J. P.*, xxi, 194; *Pharmacographia*, 2d ed., p. 61.) India opium is, therefore, much inferior to the best Smyrna opium in its yield of morphine, while it is richer in narcotine. Its inferior character is possibly, in some degree, owing to the circumstance that the juice, after collection, is kept for some time before it is made up, and consequently undergoes fermentation. (See *P. J.*, 1895, 208; *Ph. Centralh.*, 1895, 589; also *C. D.*, 1896, 134.)

Malwa Opium.—Malwa opium is a variety not made in Hindostan proper nor under government supervision. Its quality varies greatly. It sometimes occurs in flat, roundish cakes, five or six inches in diameter, and from four to eight ounces in weight. In other instances it is in rectangular masses called bricks, or even in roundish balls. It seems never to be encased in poppy remnants. The masses are commonly quite hard, dry, and brittle, of a light-brown color, a shining fracture, a compact homogeneous texture, and free from mechanical impurities. A specimen of Malwa Opium described by Carson (*A. J. P.*, xxi, 195) broke with a rough fracture, which was of a blackish-brown color, here and there showing irregular oily spots. Procter obtained from it 9¼ per cent. of morphine. For other varieties of Indian opium, see *U. S. D.*, 19th ed., p. 892.

Persian Opium.—This variety of opium is distinguished from the Turkey gum in having a uniform non-granular consistence. It has been produced in Persia for a great many years, but about 1870 a great stimulus seems to have been given to the cultivation of the poppy and to the improvement of the product. At that time it was described as follows: Sometimes it is in cylindrical pieces, about three and a half inches long and half an inch thick, wrapped in glossy paper, tied with a cotton thread, and each weighing about half an ounce; more frequently it is in short rounded cones weighing from 6 to 10 ounces; it also occurs in flat circular cakes. It has the liver-brown color of Egyptian opium, a virose musty odor, and a very bitter taste, and, like Egyptian opium, softens in a moist atmosphere. The character of the opium has undoubtedly changed of late years. The most important local varieties of Persian opium appear to be the so-called *Mesched opium*, which occurs in grayish-brown shining sticks, wrapped in paper, and *Ispahan opium*, of similar appearance, but of a purer brown color. According to the investigations of Schindelmeiser (*Ap. Ztg.*, 1904, 19) the Mesched opium, when freed from moisture, yields from 5.9 to 8.7 per cent. of morphine; while Ispahan opium has in it from 11.9 to 19 per cent. of the alkaloid. *Tschakida* of the Persians is a dark brown, blackish impure opium occurring in cakes prepared for smoking, and according to Schindelmeiser contains not more than 0.4 per cent. of morphine. Schindelmeiser states that Caucasian opium is largely adulterated with inspissated fruit juices, and frequently contains less than 2 per cent. of morphine.

According to Seidler, in 1903 the making of opium in Persia was flourishing, amounting to 3000 chests, each containing 60 kilogrammes, a year, but the drug is chiefly consumed in Persia by the opium smokers, and of that which was exported in 1903, 90 per cent. is said to have gone to Hong Kong and 10 per cent. to London and Egypt; so that very little of the Persian opium finds its way into the European market, and the last of its importation into the United States of which we have knowledge was in 1902. According to Seidler, Persian opium now occurs in two forms, one in irregular masses with rugous irregularly fissured surface; the other in elongated squarish rods or masses, 0.7 to 1 centimeter in thickness, with a smooth surface and fracture. W. D. Howard examined a sample of the Persian opium sent to England as "perfectly pure," which yielded to him on analysis, without previous drying—morphine, 10.40 per cent.; codeine, anhydrous, 0.29 per cent.; narcotine, 2.50 per cent.; thebaine, 0.57 per cent.; cryptopine, 0.09 per cent.; papaverine, a trace. He is unable to say whether it contained any narceine. Rosengarten and Sons (now Powers-Weightman-Rosengarten Company), of Philadelphia, formerly used large quantities of the Persian opium in the production of morphine, obtaining from it an average of 10 per cent. of that alkaloid. In their more recent analyses the drug has yielded from 10 to 12.8 per cent. of actual morphine, the codeine in percentage varying very greatly apparently with the crop of the year; in some years the opium contained no codeine, in others 0.6 per cent.; commonly the percentage varies from 0.3 to 0.4 per cent.

Between 1910 and 1915 there were occasional importations into the United States of a high assaying granulated form of opium, which ranged in morphine content from 20 to 23 per cent., an amount greater than is present even in official extract of opium. It required special modification of the ordinary methods of assay to allow for the abnormal amount of active principle present.

"Boston opium," so called, was a sophisticated article.

The table below exhibits the results obtained by Guibourt in the analysis of various opiums. (*J. P. C.*, Jan., Feb. and March, 1862.)

Table showing percentage of morphine in varieties of opium (Guibourt).

Opium.		Soft.	Hard.	Dried.
Anatolia (Smyrna)	lowest	9.60	10.82	11.70
" "	highest	18.24	19.77	21.46
" "	mean	12.40	13.57	14.78
Constantinople	lowest	10.90	13.32	14.40
"	highest	14.00	15.72	17.00
Egyptian	lowest		5.19	5.81
"	highest		11.45	12.21
Persian			10.52	11.37
Indian (Patna)	lowest		5.09	5.27
" "	highest		6.93	7.72
French	lowest		14.21	14.83
"	highest		21.10	22.88
"	mean		16.77	17.69

Adulterations.—The adulteration of opium has given rise to much complaint on the part of pharmacists, and various plans of customs legislation have been suggested by which it has been thought that these adulterations could be prevented. It is, however, obviously impossible to pronouncedly affect the action of the semi-barbarians who are engaged in the cultivation of opium, by any American legislation. Usually the substances which are used to adulterate the drug are inert, and therefore do no harm except by weakening its activity. The U. S. Custom House requires that opium, in order to enter the United States as opium, shall conform to the U. S. P. standard and contain not less than 9.5 per cent. of anhydrous morphine.

It is asserted by some French writers that extensive frauds are practised at Marseilles. The opium taken thither from the Levant is first softened, and then adulterated with various matters which are incorporated in its substance. To use a strong expression of Guibourt, they make the opium over again at Marseilles. According to A. T. Thomson, one-fourth part of Turkey opium generally consists of impurities. Sand, ashes, the seeds of different plants, extracts of the poppy, *Lactuca virosa*, *Glycyrrhiza glabra*, and *Chelidonium glaucum*, gum arabic, tragacanth, salep, aloes, even small stones and minute pieces of lead and iron, are mentioned among the substances employed in the sophistication of the drug. Tschirch (*A. J. P.*, 1898, 488) proposes the use of the Roentgen ray in detecting such adulterations.

Masson described a product which was sold under the name of "Smyrna" or "manipulated," and which consisted of a mixture of the natural juice with substances more or less inert. The samples varied very widely in composition, and in some cases were so altered that the active ingredients could not be readily dissolved. (*J. P. C.*, 1905, p. 529.) Stahl found in some samples of Turkish opium the possible admixture of fruit pulp or fruit extracts. (*Ph. Zentralh.*, xlix, p. 958.)

Landerer, of Athens, was informed by a person who had been engaged in the extraction of opium, that grapes, freed from their seeds and crushed, were almost universally mixed with the poppy juice, and that another adulteration consisted of the epidermis of the capsules and stem of the plant, pounded in a mortar with the white of an egg. (*A. J. P.*, xv, 238.) According to Wilkins, who witnessed the collection of opium, the inspissated juice of the grape, thickened with flour, is often used for the same purpose. (*P. J.*, xiv, 400.)

Opium is regarded as inferior when it has a blackish color, a weak or empyreumatic odor, a sweet or slightly nauseous and bitter taste, a soft, viscid, or greasy consistence, a dull fracture, or an irregular, heterogeneous texture, from the intermixture of foreign substances. It should not impart a deep-brown color to the saliva, nor leave a dark uniform trace when drawn over paper, nor form with water a thick viscid solution.

Properties.—Good opium has a strong, peculiar odor, and a bitter, somewhat acrid taste. It is officially described as "in more or less rounded, mostly somewhat flattened masses of variable size, but usually about 8 to 15 cm. in diameter; externally grayish-brown, covered with fragments of poppy leaves and at times with some fruits of a species of rumex adhering from the packing; more or less plastic when fresh, becoming hard and brittle on keeping; internally dark brown, interspersed with lighter areas, somewhat lustrous; odor characteristic, narcotic; taste bitter, characteristic. For a description of the powder, see *Opii Pulvis*." *U. S.*

"Usually in rounded, irregularly formed, or flattened masses, varying in weight, but commonly weighing from about 250 to 1000 grammes. When fresh, plastic, and internally somewhat moist, coarsely granular, or nearly smooth, and reddish or chestnut-brown; but becoming harder on keeping, and darkening to blackish-brown. Strong and characteristic odor; taste bitter." *Br.*

When long chewed it excites much irritation in the lips and tongue, and may even blister the mouths of those unaccustomed to its use. Its color is reddish-brown or deep fawn; its texture compact; its sp. gr. 1.336. When drawn over paper it usually leaves an interrupted trace of a light-brown color. It is often soft in the interior of the mass, and in this state is tenacious; but when exposed to the air it gradually hardens, and ultimately becomes brittle, breaking with a shining fracture, and affording, when pulverized, a yellowish-brown powder, which becomes adhesive upon a slight elevation of temperature. It readily inflames upon the application of a lighted taper. On heating opium on a watch crystal and collecting the sublimate on a slide, Rosenthaler found the sublimate to give the characteristic red color reaction for narcotine. (*Ph. Zentralh.*, liv, p. 1250; *Apoth. Zeit.*, xxviii, p. 991.)

Opium yields its virtues to water, alcohol, and diluted acids, but not to ether, benzine and some of the other immiscible solvents. To all these menstrua it imparts a deep-brown color. Alcohol dissolves about four-fifths of it. Pelletier stated that the proportion taken up by water varies in the specimens. He never found the quantity of extract prepared with cold water to exceed 12 parts out of 16.

Chemical Constituents.—Much attention has been devoted to the chemical constitution of opium. It was through the researches into the nature of this substance that chemists were led to the discovery of the alkaloids. To Sertürner, an apothecary at Eimbeck, in Germany, belongs the credit of having opened the important field of alkaloidal research. The development of the alkaloids in opium has been the object of the studies of A. Müller. (*Ph. Ztg.*, lix, p. 600.) He found the seeds to be alkaloid free, but that the sprouts, after two weeks, show the presence

of alkaloids. The alkaloidal content of the plant slowly increases until the flowers appear, when there is a sharp increase lasting until the floral leaves fall. After the ripening of the capsule, the alkaloidal nitrogen content of the entire plant was found to be 0.0094 per cent.; of the stem and leaves alone, 0.0085 per cent.; and of the capsule walls only 0.0168 per cent. The alkaloidal content was found to vary from day to day, being less on cloudy than on sunny days. His conclusions were that the alkaloids of the poppy plant are not excretion material intended to protect the plant from animal enemies, as has been suggested, but that they are present to afford a source of nitrogen for the synthesis of reserve protein. A comprehensive study of the market conditions of the more important opium alkaloids was contributed by L. E. Warren, *A. J. P.*, 1915, p. 439.

In the year 1803 Derosne made known the existence of a crystallizable substance which he had discovered in opium, and which he erroneously believed to be the active principle. In the following year Seguin discovered another crystallizable body, which experience has proved to be the true narcotic principle of opium, but he did not fully investigate its nature, and no immediate practical advantage accrued from his excellent analysis. About the same time, Sertürner was engaged in a similar investigation, the results of which, very analogous to those obtained by Seguin, were published in a German journal, without, however, attracting general attention. In this state the subject remained until 1817, when Sertürner announced the existence of a saline compound in opium, consisting of a peculiar alkaline principle united with a peculiar acid, and clearly demonstrated the precise nature of a substance which, though discovered both by Seguin and himself, had been hitherto but vaguely known. To the alkaloid, in which he correctly conceived the narcotic powers of opium to reside, he gave the name of *morphium*, which has been since changed to *morphine*, in order to render it conformable with the titles of the other alkaloids. The acid he called *meconic*, a term derived from the Greek name of the poppy. The correctness of the statements of Sertürner was confirmed by Robiquet, who also satisfactorily demonstrated that the substance obtained by Derosne and called by him the *salt of opium* was a principle altogether distinct from morphine, though supposed to possess considerable influence over the system. In the belief in its narcotic powers, Robiquet denominated it *narcotine*, a title which it still retains. A number of other alkaloids have since been discovered in opium, although most of these are in very limited amount, and the existence of some is not quite definitely established. According to the views of its constitution at present accepted, it contains: (1) *Morphine*, $C_{17}H_{19}O_3N$; (2) *Codeine*, $C_{18}H_{21}O_3N$; (3) *Thebaine*, $C_{19}H_{21}O_3N$; (4) *Papaverine*, $C_{20}H_{21}O_4N$; (5) *Meconidine*, $C_{21}H_{23}O_4N$; (6) *Codamine*, $C_{20}H_{25}O_4N$; (7) *Laudanidine*, $C_{20}H_{25}O_4N$; (8) *Laudanine*, $C_{20}H_{25}O_4N$; (9) *Laudanosine*, $C_{21}H_{27}O_4N$; (10) *Lanthopine*, $C_{23}H_{25}O_4N$; (11) *Protopine*, $C_{20}H_{19}O_5N$; (12) *Cryptopine*, $C_{21}H_{23}O_5N$; (13) *Rhœadine*, $C_{21}H_{21}O_6N$; (14) *Narcotine*, $C_{22}H_{23}O_7N$; (15) *Oxynarcotine*, $C_{22}H_{23}O_8N$; (16) *Narceine*, $C_{23}H_{29}O_9N$; (17) *Pseudomorphine*, $C_{34}H_{36}O_6N_2$; (18) *Gnoscopine*, $C_{22}H_{23}O_7N$; (19) *Xanthaline*, $C_{37}H_{36}O_9N_2$; (20) *Tritopine*, $C_{42}H_{54}O_7N_2$; (21) *Hydrocotarnine*, $C_{12}H_{15}O_3N$. In addition to the above list, *Deuteropine*, *Opianine*, *Papaverosine*, and *Porphyroxine* are possible alkaloids that have been announced, but not sufficiently established as yet. Still others, like *Apomorphine* (see p. 157), can be produced from those existing in the opium. At least two acids occur in opium combined with these bases —*meconic acid*, $C_7H_4O_7$, and *lactic acid*, $C_3H_6O_3$. This latter, supposed by T. and H. Smith to be a peculiar variety of lactic acid, and named by them *thebolactic acid*, was ascertained by Stenhouse to be the ordinary variety. Sulphuric acid is found in the ash along with the bases calcium, magnesium, and potassium. Opium also contains mucilage, pectic matter, and a glucose sugar. The wax gathered from the refuse of opium yielded Hesse cerotyl palmitate and cerotate. Three neutral pirinciples have, moreover, been extracted from opium—*meconin* (*opianyl*), $C_{10}H_{10}O_4$, *meconoisin*, $C_8H_{10}O_2$, and *opionin*, which, according to Hesse, is contained in small quantities in Smyrna opium. The first of these forms prisms which fuse under water at 77° C. (170.6° F.), or *per se* at 110° C. (230° F.), and boil at 155° C. (311° F.); the second melts at 88° C. (190.4° F.), and the third at 227° C. (440.6° F.). None of these neutral principles contain nitrogen. All the organic bases of opium polarize to the left. (Bouchardat and Boudet, *J. P. C.*, 3e sér., xxiii, 294.)

Of the principles above mentioned, *morphine* is by far the most important. It is generally admitted to exist in opium united with meconic acid in the state of meconate, and to a certain extent also as a sulphate, although A. R. L. Dohme (*A. J. P.*, 1891, p. 168) believes that the results of a dialysis of opium show that the morphine is combined with sulphuric acid alone. Smith, of Edinburgh, obtained from 100 parts of fine opium, 10 parts of morphine, 6 of narcotine, 0.15 of thebaine, 1 of papaverine, 0.3 of codeine, 0.02 of narceine, 0.01 of meconin, 4 of meconic acid, and 1.25 of theobolactic acid. (*P. J.*, Oct., 1865, p. 183.)

Codamine.—*Codamina*, $C_{20}H_{25}O_4N$, is isomeric with laudanine, but is readily distinguished from it by the effect of ferric chloride and nitric acid, both of which color it deep green. According to Allen, codamine also gives a dark green coloration with sulphuric acid and, in the presence of a minute quantity of ferric chloride, a greenish-blue. It is in anhydrous crystals. It can be purified by taking advantage of the feeble solubility of its iodide. Hav-

ing decomposed this salt by ammonia, dissolve the precipitate in ether, wash the ethereal solution with solution of sodium bicarbonate, then filter through animal charcoal. By evaporation the liquid deposits the alkaloid in beautiful colorless crystals. Codamine crystallizes also from petroleum benzin; but thus obtained it melts at 126° C. (258.8° F.), while that procured through ether melts at about 120° C. (248° F.). The acid iodide, tartrate, and oxalate are crystallizable.

CODEINE.—*Codeina,* $C_{18}H_{21}O_3N$ (or $C_{17}H_{17}NO(OH).OCH_3$), was discovered in 1832 by Robiquet in morphine hydrochloride prepared according to the process of Gregory, and was prepared synthetically by Grimaux by the action of methyl iodide and sodium hydroxide upon morphine, thus proving its chemical character as a morphine methyl-ether (Allen). It exists in opium combined like morphine with meconic acid, and is extracted along with that alkaloid in the preparation of the hydrochloride. (See *Morphina.*) When the solution of the mixed morphine and codeine hydrochlorides is treated with ammonia, the former alkaloid is precipitated, and the codeine, remaining in solution, may be obtained by evaporation and crystallization. It may be purified by treating the crystals with hot ether, which dissolves them, and yields the codeine in colorless crystals by spontaneous evaporation. This alkaloid and its phosphate and sulphate are now official. (See *Codeina.*) For a paper on the determination of codeine in opium, by Chas. E. Caspari, see *Proc. A. Ph. A.,* 1904, 386. Dobbie and Lauder (*J. Chem. S.,* 1911, xcix), describe a new alkaloid, *neopine,* which they believe to be a *hydroxycodeine.*

CRYPTOPINE. *Cryptopina,* $C_{21}H_{23}NO_5$.—This alkaloid was discovered by T. and H. Smith, of Edinburgh. (*P. J.,* 1867, p. 595.) They obtained it from the weak alcoholic washings of crude morphine after precipitation, by precipitating with milk of lime, and separating from the thebaine by fractional crystallization. (For details of their method, see *U. S. D.,* 19th ed., p. 895.) To obtain the pure alkaloid, it is precipitated from solution of the hydrochloride by ammonia, washed, dried, and finally washed with ether or alcohol, which readily dissolves thebaine, but has little effect on cryptopine. It may be obtained in a crystallized state by boiling it with a large quantity of alcohol, which, on cooling, will slowly deposit the alkaloid in crystals. The quantity in opium is extremely small.

Cryptopine is without color or odor, and its salts, though at first bitter to the taste, afterward cause a sense of coolness in the mouth, like that produced by peppermint. It melts at 217° C. (422.6° F.), and, on cooling, crystallizes in radiated forms at 171° C. (339.8° F.), and, heated to redness, is decomposed, blackening and giving forth aqueous vapors, but without properly subliming. It is insoluble in water and in ether, very sparingly soluble in alcohol, requiring 1265 parts of that liquid when cold to dissolve it. Chloroform dissolves it almost as freely as narcotine. Oil of turpentine and benzene do not appear to dissolve it. It has very strong alkaline powers, and forms crystallizable salts with the acids, which are distinguishable from all the other salts of the opium alkaloids by a strong tendency to gelatinize. If the hydrochloride is dissolved in about 30 parts of hot water, and set aside, instead of crystallizing, it forms a jelly closely resembling that of pure gelatin. From all the constituents of opium, except the alkaloids, morphine, codeine, and thebaine, it is distinguished by its strong alkaline properties. From morphine it is distinguished by its very sparing solubility in alcohol, and from codeine and thebaine by its total insolubility in ether. It differs also in the effect of strong sulphuric acid, which produces a blue color with the minutest quantity of cryptopine, a blood red with thebaine, and none with morphine or codeine.

DEUTEROPINE, $C_{20}H_{21}O_3N$, according to Allen, is an alleged homologue of protopine and cryptopine. It requires further examination.

GNOSCOPINE, $C_{22}H_{23}O_7N$, was found by T. and H. Smith in 1878. They first gave to it the formula $C_{34}H_{36}O_{11}N_2$, but in a later communication (*P. J.,* 1893, 1794) gave it the simpler formula which makes it an isomer of narcotine. It is crystallizable, melts at 233° C. (451.4° F.), with partial decomposition, is soluble in chloroform and carbon disulphide, slightly so in benzene, not in ether. The salts have an acid reaction.

HYDROCOTARNINE.—*Hydrocotarnina,* $C_{12}H_{15}O_3N$, is obtained from the mother waters of thebaine, after the removal of cryptopine and protopine with warm petroleum benzin, by precipitation with ammonia; laudanosine, which is also precipitated, is removed by treatment of the benzin solution with sodium bicarbonate. The hydrocotarnine is retained in solution by the benzin, from which the laudanosine has been deposited on cooling. Hydrochloric acid gas being made to pass through this solution, hydrocotarnine hydrochloride crystallizes out. This alkaloid, as the name indicates, can be formed from cotarnine, by the action of zinc and hydrochloric acid. It also seems to result from the decomposition of narcotine. (See *Narcotine.*) If the latter be made to boil some time with baryta water, a portion of it will be decomposed, giving rise to a crystallizable substance soluble in ether, which appears to be identical with hydrocotarnine. This alkaloid is very soluble in alcohol, acetone, chloroform, benzin, and ether. It melts at 50° C. (122° F.), and loses at 57° C. (134.6° F.) the half molecule of water with which it crystallizes. Sulphuric acid dissolves it, coloring it yellow in the cold, and crimson red if heated. Nitric acid colors it yellow; ferric chloride does not affect its color. It has been physiologically studied by

Stockman and Dott (*B. M. J.*, Jan., 1891), who find that it produces in the lower animals symptoms similar to those caused by narcotine.

LANTHOPINE.—*Lanthopina,* $C_{23}H_{25}O_4N$, differs from pseudomorphine in not becoming blue with ferric chloride, and in giving, when entirely pure, with sulphuric and nitric acids, colorless solutions. It forms colorless microscopic prisms, which fuse at about 200° C. (392° F.). Its acid oxalate and tartrate are crystallizable. The alkaloid is crystallizable, does not have an alkaline reaction, is sparingly soluble in hot or cold alcohol, ether, or benzene, but readily soluble in chloroform. (See *U. S. Dispensatory,* 19th ed., p. 896.) According to Allen, it is obtained from the mother liquor, left from the preparation of morphine by the Robertson-Gregory process. It is a weak base, and is colored orange-red by nitric acid, and pale violet by sulphuric acid, the latter color changing to a dark brown on heating.

LAUDANIDINE, $C_{20}H_{25}O_4N$, was discovered by Hesse in 1894. It closely resembles laudanine.

LAUDANINE.—*Laudanina,* $C_{20}H_{25}O_4N$, as first prepared, is mixed with cryptopine, from which it is separated by dissolving it in acetic acid, and adding a slight excess of diluted solution of sodium hydroxide, by which the cryptopine is entirely precipitated. The liquid being filtered, and treated with ammonium chloride, lets fall the laudanine, which soon assumes the crystalline form. The acetate, with the addition of potassium iodide, gives rise to laudanine hydriodide, from which ammonia separates the base perfectly pure. It crystallizes from its solution in boiling alcohol in transparent granules or hexagonal prisms melting at 166° C. (330.8° F.). It is lævorotatory, tasteless, and poisonous, the hydrochloride resembling strychnine in its effects. It is dissolved at 18° C. (64.4° F.) by 647 parts of ether. Sulphuric acid gives with it characteristic reactions. When pure, at common temperatures it assumes a pale rose color, and at 150° C. (302° F.) a reddish-violet. When ferric oxide is added, it exhibits the same changes, but with much greater intensity. Laudanine is an energetic base, and with potassium hydroxide forms a crystallizable compound. Its salts, except the neutral sulphate, oxalate, and tartrate, are crystallizable.

LAUDANOSINE.—*Laudanosina,* $C_{21}H_{27}O_4N$, exists in the mother waters of thebaine, with cryptopine and protopine. The thebaine having been precipitated by tartaric acid, the mother water is neutralized by ammonia, and sodium bicarbonate is added. After eight days' rest, a blackish mass separates. The limpid liquid with an excess of ammonia yields a copious precipitate, which, agitated with heated petroleum benzin, gives to that liquid a mixture of several alkaloids. The benzin solution upon cooling to 40° C. (104° F.), deposits the cryptopine and protopine. On agitation anew with heated sodium bicarbonate and subsequent complete refrigeration, the laudanosine crystallizes. It is entirely purified by ether, which dissolves it abundantly, and its hydriodide is but slightly soluble in water. It is itself insoluble in water and the alkalies, but it is soluble in alcohol, acetone, and chloroform. It melts at 89° C. (192.2° F.), and is decomposed at 110° C. (230° F.). Ferric chloride does not color it. Sulphuric acid gives it a rose color in the cold, and violet when heated. Nitric acid transforms it into a nitro-base. The crystals are anhydrous. It forms crystallizable salts, which are soluble and bitter.

MECONIDINE, $C_{21}H_{23}O_4N$, was discovered by Hesse in 1870. It is brownish-yellow, amorphous, alkaline, melts at 58° C. (136.4° F.), and is not stable, the salts also being easily altered. It is easily soluble in alcohol, ether, benzene, chloroform, and acetone. It is dissolved by sulphuric acid with an olive-green color, and by nitric acid with an orange-red.

MORPHINE, $C_{17}H_{19}O_3N + H_2O$, and its preparations are treated under another head. (See *Morphina.*)

NARCEINE, *Narceina,* $C_{23}H_{29}O_9N$, discovered by Pelletier in 1832, is in white, silky crystals, inodorous, of bitter taste, the fusing point of which was given at 145.2° C. (293.3° F.) according to Hesse, and as 92° C. (197.6° F.) according to Pelletier. E. Merck has shown, however (*Chem. Ztg.,* 1889, p. 525), that the ordinary commercial alkaloid of English manufacture melts between 150° and 160° C. (302°–320° F.) and the pure base at 170° to 171° C. (338°–339.8° F.). Out of water at 60° C. (140° F.) it crystallizes with 2 molecules of water, which it loses at 100° C. (212° F.) and at 140° C. (284° F.) another molecule of water escapes, leaving in the fused residue a mixture of bases. Soluble in 375 parts of cold and 220 of boiling water, soluble also in alcohol, and insoluble in ether. It forms a bluish compound with iodine, the color of which is destroyed by heat and the alkalies. Besides, according to Stein, the blue color is not produced when there is too much of the iodine present, which then causes a brown color with narceine, the blue color appearing under such circumstances, only when the excess of iodine is saturated by ammonia. (*J. P. C.,* Jan. 1872, p. 59.) It is rendered blue by the action of mineral acids so far diluted as not to decompose it, but it does not, like morphine, become blue by the action of ferric salts, nor red by that of nitric acid. According to P. C. Plugge, if a trace of narceine be covered in a porcelain dish with *diluted* sulphuric acid, no change will be observable; but if the dish be heated on the water bath, a blue color will be developed as soon as the acid has become sufficiently concentrated; this by prolonged heating will pass to cherry-red. If to this red liquid, after cooling, a trace of nitric acid or potassium nitrite be added, blue-violet streaks will be produced. (*A. Pharm.,* 1887, p. 425.) It is dissolved by the acids, but was thought not to neutralize them, and, though at first considered alkaline by

Pelletier, was afterwards ranked with indifferent bodies. At present, however, its alkaloidal character is admitted; it unites with sulphuric acid to form a crystallizable sulphate. (*J. P. C.*, April, 1864, p. 367.) Dragendorff announced that solution of narceine gives a crystalline precipitate with the double zinc and potassium iodide. This reaction may be employed with iodine as a test of narceine. If a solution of this salt, with a little iodized water, be added to solutions of narceine, and the mixture then agitated with ether to remove the iodine in excess, a solution containing a very small quantity of narceine will distinctly assume a blue color. The other alkaloids of opium are destitute of this property. (*J. P. C.*, April, 1870, p. 346.) Pelletier obtained it in the course of his analysis of opium. Having formed an aqueous extract of opium, he treated it with distilled water, precipitated the morphine by ammonia, concentrated the solution, filtered it, threw down the meconic acid by baryta water, separated the excess of baryta by ammonium carbonate, drove off the excess of the ammoniacal salt by heat, evaporated the liquor to the consistence of syrup, set it aside till a pulpy matter formed containing crystals, separated and expressed this pulpy matter, then treated it with alcohol, and concentrated the alcoholic solution. This, on cooling, deposited crystals of narceine, which were easily purified by repeated solution and crystallization. Meconin, which often crystallizes with it, may be separated by the agency of ether. The discordancy of the statements of physiologists and clinicians concerning the action of narceine can only be explained by the presence of impurities in the specimens used. The pure alkaloid would seem to be very feeble in its influence, Mitchell having taken five grains without any other effect than causing some headache. The narceine of commerce has been used in doses of one-third to three-fourths of a grain (0.021–0.048 Gm.) as a mild narcotic, probably acting through contaminating morphine.

NARCOTINE. *Narcotina*, $C_{22}H_{23}O_7N$.—It exists in opium, chiefly, at least, in the free state, and is left behind in considerable quantity when the drug is macerated with water. It is white, tasteless, and inodorous, and crystallizes in silky flexible needles, usually larger than the crystals of morphine, fusible at 176° C. (349° F.), and decomposes at higher temperature with evolution of ammonia. Heated to 220° C. (428° F.), the residue which remains is *hemipinic acid*, $C_{10}H_{10}O_6$, insoluble in cold water, soluble in 400 parts of boiling water, in 100 parts of cold and 24 of boiling alcohol, which deposits it upon cooling, and very soluble in ether. The fixed and volatile oils, and the diluted acids, also dissolve it; and it has been found to be soluble in the volatile oil of turpentine, which, aided by heat, will extract it from opium, and yield it in crystals by evaporation. (*J. P. C.*, 4e sér., ii, 156.) As it exerts no alkaline reaction upon vegetable colors, and does not prevent the acids from reddening litmus paper, there would appear to be some reason for denying it the rank of an alkaloid. But it unites with some of the acids, forming definite compounds, which may be procured in a separate state; and Robiquet obtained narcotine sulphate and hydrochloride well crystallized. (*J. P. C.*, xvii, 639, and xix, 59.) Hence it is now generally considered as a weak base, and perhaps this view of it is the most convenient. It must be admitted, however, to have a very feeble neutralizing power. With acetic acid it does not appear to form a permanent combination, for, though dissolved by cold acetic acid, it is separated by heating the solution. It is decomposed by long boiling, or by heating with nitric acid, into *cotarnine*, $C_{12}H_{13}O_3N$ (see p. 384) and *meconin*, $C_{10}H_{10}O_4$, and by heating with water to 100° C. (212° F.) in sealed tubes, into *hydrocotarnine*, $C_{12}H_{15}NO_3$, and *opianic acid*, $C_{10}H_{10}O_5$, while, on the other hand, the action of nascent hydrogen (from zinc and hydrochloric acid) converts it into *hydrocotarnine* and *meconin*, and that of oxidizing agents into *cotarnine* and *opianic acid*. It may be distinguished from morphine by its insipidity, by its solubility in ether and insolubility in alkaline solutions, by not affecting vegetable colors, by assuming a yellowish instead of a blood-red color under the action of strong nitric acid, by not decomposing iodic acid, and by not producing a blue color with ferric salts. It is, however, reddened by a mixture of nitric and sulphuric acids. Hence, if to a mixture of it with strong sulphuric acid a small piece of potassium nitrate is added, a deep blood-red color is produced; while morphine, under the same circumstances, yields a brownish or olive green color. It gives a greasy stain to paper when heated upon it over a candle. Distilled with potassium hydroxide, or simply by heating to 250° C. (482° F.), it yields *trimethylamine*, $N(CH_3)_3$. Heated with strong hydrochloric acid, it loses two groups, CH_2, and with concentrated hydriodic acid a third, CH_2, so that the existence of three methyl groups (CH_3) in narcotine have been established. Water extracts narcotine partially from opium, in consequence of the acid which the latter contains, either free or combined with the narcotine. It is usually obtained mixed with morphine in the processes for procuring that principle, and may be separated by the action of ether, which dissolves it without affecting the morphine, and yields it upon evaporation. It may also be obtained by digesting opium in ether, and slowly evaporating the ethereal solution, which deposits crystals of narcotine. It is said that the same result may be obtained by using the oil of turpentine as the menstruum, first heating it with opium, and then evaporating the solution. Another mode of procuring it is to treat opium, exhausted by previous maceration in water, with diluted acetic acid, filter the solu-

tion, precipitate by an alkali, wash the precipitate with water, and purify it by solution in boiling alcohol, from which it crystallizes as the liquid cools. Should it still be impure, the solution in alcohol and crystallization may be repeated. The proportion of narcotine in opium varies extremely in the different varieties, and in different specimens of the same variety. Thus, in Smyrna opium it has been found by different observers, in quantities varying from 1.30 to nearly 11 per cent. Though narcotine itself is tasteless, its salts are very bitter, even more so than those of morphine. (Berzelius.) Their solution reddens litmus, and yields precipitates with the alkalies and infusion of galls. For physiological study of the methylamide derivatives of narcotine (*narcotine methylamide*), see *V. A. P. A.*, 142, 1895.

ANARCOTINE has been described as an alkaloid especially abundant in the India opium. According to Wm. Roberts (*B. M. J.*, 1895, ii), while Smyrna opium containing 8 per cent. of morphine has in it 2 per cent. of anarcotine, Bengal opium contains 4 per cent. of morphine with 6 per cent. of anarcotine. Anarcotine appears, however, to be simply pure narcotine. (*Merck's Jahresber.*, 1896, 101.) It is said to be nearly destitute of active physiological properties. In the experiments of Surveyor (*B. M. J.*, 1896), one drachm of it given subcutaneously to an anesthetized dog produced no sensible effect. The continuous use of it in large doses seemed, however, to affect the nutrition of the dog. It was at one time largely used in India as an antiperiodic on account of its being cheaper than quinine, but has fallen into desuetude because of the present low price of the cinchona alkaloids.

It has been asserted that narcotine is identical with *aconella*, an alkaloid said to have been extracted by the Messrs. Smith, of Edinburgh, from aconite, but Groves failed to find aconella. (See page 79, *U. S. D.*, 14th edition.) Many years ago O'Shaughnessy, of Calcutta, recommended narcotine as an antiperiodic, in doses of three grains (0.2 Gm.) three times a day, but it has failed to acquire reputation. See an elaborate paper on the pharmacology of narcotine by A. C. Crawford and A. R. L. Dohme, *Proc. A. Ph. A.*, 1902, 472.

OPIANINE, which has been claimed to have the formula $C_{21}H_{21}O_7N$, is now supposed to be impure narcotine.

OXYNARCOTINE. *Oxynarcotina*, $C_{22}H_{23}O_8N$.—This alkaloid accompanies narceine, from which it can be separated by treating the mixture with dilute sulphuric acid. On neutralizing the solution with the theoretical amount of sodium hydroxide and heating to boiling, a part dissolves. The undissolved residue is the oxynarcotine. It can also be obtained from the mother liquors of narcotine. According to Beckett and Wright, it crystallizes out of alcohol in very fine needles, which are difficultly soluble in boiling water and boiling alcohol, insoluble in other neutral solvents. Heated to 140° or 150° C. (284° or 302° F.) it is carbonized. It is oxidized by ferric chloride to *hemipinic acid* and *cotarnine*. It is a monacid base, and forms crystallizable salts.

PAPAVERINE. *Papaverina*, $C_{20}H_{21}O_4N$.—The discovery of this alkaloid was announced by G. Merck. It is crystallizable in needles, fusing at 147° C. (296.6° F.), insoluble in water, very sparingly soluble in cold alcohol or ether, more soluble in these liquids boiling hot, and deposited by them on cooling. With acids it forms salts, most of which are very sparingly dissolved by water. The hydrochloride crystallizes with extraordinary facility. The alkaloid is readily dissolved by moderately concentrated hydrochloric acid, from which, on the addition of more acid, the hydrochloride separates, assuming the form of an oily layer at the bottom of the vessel, which is readily converted on standing into a mass of acicular crystals. These crystals are very sparingly soluble in cold water. The hydrochloride yields with platinic chloride a yellow precipitate which is insoluble in boiling water or alcohol. By the action of hydrochloric acid at 130° C. (266° F.), however, it is decomposed into methyl chloride and homopyrocatechol. By the action of concentrated nitric acid there is formed, on heating, the nitrate of nitropapaverine, $C_{20}H_{20}(NO)_2O_4.NHNO_3$, which separates in crystals. The nitro-base can be separated in clear yellow flocks by the addition of ammonia. By the action of tin and hydrochloric acid there is formed a tetrahydropapaverine, $C_{20}H_{25}O_4N$. Cold concentrated sulphuric acid does not color it, but on warming a violet color is obtained; an impure papaverine is colored violet, however, with sulphuric acid even in the cold. Papaverine is prepared by precipitating the aqueous infusion of opium with soda, exhausting the precipitate with alcohol, evaporating the tincture to dryness, treating the residue with a dilute acid, filtering, precipitating by ammonia, dissolving the precipitate in hydrochloric acid, mixing sodium acetate with the solution, and treating the resulting precipitate with boiling ether. The ethereal solution deposits the papaverine on cooling. Leubuscher (*D. M. W.*, 1892) asserts that it acts as a sedative to intestinal peristalsis without producing other effects, and is valuable in the *diarrhea* of children.

Dose, for a two-year-old child, two-fifths of a grain (0.024 Gm.), repeated three or four times a day.

PORPHYROXINE, according to K. L. Dey (*P. J.* [3], xii, p. 397), is a definite basic substance, always present in Indian opium, but absent from Turkey or Smyrna opium.

PROTOPINE.—*Protopina*, $C_{20}H_{19}O_5N$, is an alkaloid which Hesse separated from cryptopine. Both are precipitated as insoluble hydrochlorides by hydrochloric acid in excess; but if the precipitate be dissolved by an excess of oxalic acid, the acid cryptopine oxalate will crystallize, and protopine remain in the mother waters. The liquid is separated, precipitated

by ammonia, and agitated with ether, and the ethereal solution is taken up by hydrochloric acid. Protopine hydrochloride being dense and granular, while cryptopine hydrochloride is very light, the two are separated by levigation —eighty grammes of crude cryptopine furnishing one and a half of protopine. Separated from the hydrochloride by ammonia, protopine constitutes a crystalline powder, insoluble in water, soluble in alcohol and in hot petroleum benzin and acetone, more soluble in chloroform, insoluble in the alkalies generally, but slightly soluble in ammonia. It melts at 202° C. (395.6° F.), undergoing decomposition, and is in anhydrous crystals. Ferric chloride does not color it; nitric acid colors it yellow; sulphuric acid dissolves it, coloring it first yellow, then red, and lastly violet. The alcoholic solution has an alkaline reaction. The salts are neutral and crystallizable.

E. Schmidt (*A. Pharm.*, 231 (1893), 136) states that protopine is identical with *maclayine*, an alkaloid, which has been found by Eykman in *Maclaya cordata*, and that it is also found in *Sanguinaria canadensis*, *Stylophorum diphyllum*, *Eschscholtzia californica*, and other plants.

PSEUDOMORPHINE.—*Pseudomorphina*, $C_{34}H_{36}O_6N_2$, was discovered by Pelletier in 1835, and is said by Hesse to be identical with Polstorff's *oxydimorphine;* but, as it exists in small quantities, and was thought to be only an occasional ingredient in opium, little attention has been paid to it. An interesting fact, however, in relation to it, and one of some toxicological importance, is that it possesses two properties considered characteristic of morphine, those, namely, of being reddened by nitric acid and of striking a blue color with ferric salts, and yet it is without any poisonous influence upon the animal economy. (*J. P. C.*, xxi, 575.) Hesse has investigated the subject, with the following results. He found that it accompanies morphine procured by Gregory's method, and may be separated from that alkaloid by adding ammonia in excess to an alcoholic solution containing both. The morphine is precipitated, and pseudomorphine, remaining in solution, may be obtained by evaporating the mother liquid. It is probably produced from morphine by the following reaction:

$$2C_{17}H_{19}O_3N - H_2 = C_{34}H_{36}O_6N_2.$$

It is tasteless, insoluble in water, alcohol, ether, chloroform, and diluted sulphuric acid, but easily soluble in solution of potassium and sodium hydroxide, and lime, and in alcoholic solution of ammonia, though sparingly in an aqueous solution of ammonia. It does not neutralize hydrochloric acid, dissolves in concentrated sulphuric acid with the production of an olive-green color, in concentrated nitric acid with an intense orange-red, and in solution of ferric chloride with a blue color. At 120° C. (248° F.) it loses two molecules of water of crystallization, and at higher temperatures is decomposed without melting. It forms sparingly soluble salts with sulphuric, nitric, oxalic, and tartaric acids, and a crystalline deposit, very slightly soluble in hydrochloric acid, with solution of corrosive sublimate. (*Chem. News*, 1867, p. 188.) Hesse is of the opinion that pseudomorphine is identical with the oxymorphine prepared by the action of oxidizing agents upon morphine by Schutzenberger.

RHŒADINE, $C_{21}H_{21}O_6N$, discovered by Hesse in 1865, is crystallizable, but not distinctly alkaline. It fuses at 232° C. (449.6° F.), and can be sublimed at higher temperatures. It is nearly insoluble in ether, alcohol, benzene, chloroform, water, and ammonia. Its solutions in dilute acids acquire an intense purple color on addition of strong hydrochloric or sulphuric acid, due to the formation of a coloring matter. This is destroyed by alkalies and restored by acids, and is so intense that 1 part of rhœadine will color 10,000 parts of water purple-red, 200,000 deep rose-red, and 800,000 distinctly red, although only a portion of the base is converted into coloring matter. The solution then filtered through bone-black shows the presence of a base, *rhœagenine*, isomeric with rhœadine, but fusing at 223° C. (433.4° F.), and forming a different series of salts. This alkaloid occurs also in *Papaver Rhœas*.

THEBAINE (*Paramorphina*).—*Paramorphine*, $C_{19}H_{21}O_3N$ (or $C_{17}H_{15}ON(OCH_3)_2$), was discovered by Pelletier in the precipitate thrown down from an infusion of opium treated with milk of lime. The precipitate being washed with water until the liquid came away colorless, and then treated with alcohol, instead of affording morphine to this solvent, as was anticipated, yielded a new alkaloid, which was obtained separate by evaporating the alcohol, acting on the residue with ether, allowing the ethereal solution to evaporate spontaneously, and then purifying the resulting crystalline mass by dissolving it in an acid, precipitating by ammonia, and recrystallizing by means of alcohol or ether. Pelletier named it paramorphine, from its close analogy in composition with morphine, from which, however, it is quite distinct in properties. The name of *thebaine* was proposed for it by Couërbe, who was disposed to give the credit of its discovery to Thiboumery, the director of Pelletier's laboratory. It is white, crystallizable, and of an acrid and styptic rather than bitter taste, fusing at 193.4° C. (380° F.), and, according to Hesse, confirmed by D. B. Dott, is not sublimable. Other observers state that it sublimes at 135° C. (275° F.) without fusing, and is deposited in minute crystals resembling caffeine. It is scarcely soluble in water, very soluble in alcohol and ether when cold, and still more so when heated, and capable of combining with the acids, with which it forms salts not crystallizable from their aqueous solution. Alkalies precipitate it from its acid solutions, and unless in very concentrated solution, do not dissolve it when added in excess. It is not like morphine, reddened

by nitric acid, nor does it become blue with solutions of ferric salts. From codeine it differs in never being in large crystals, in not forming crystallizable salts, in being always precipitated from its acid solutions by ammonia, and in not melting in oily drops. From narcotine, which it most resembles, it may be distinguished by its shorter crystals, which lack the pearly appearance of those of narcotine, by its different taste, by its much greater solubility in cold alcohol, of which 10 parts will dissolve 1 of this principle, while narcotine requires 100 parts, and by the action of nitric acid, which converts it into a resin-like matter before dissolving it, while the same acid instantly dissolves narcotine. Diluted sulphuric or hydrochloric acid in excess changes thebaine, according to Hesse, into two isomeric bases, *thebenine* and *thebaicine*. When heated to 90° C. (194° F.) under pressure with fuming hydrochloric acid, thebaine yields a base having the probable formula $C_{17}H_{15}NO(OH)_2$, and called by its discoverer, W. C. Howard (*Ber. d. Chem. Ges.*, xvii, 527, xix, 1596), *morphothebaine*, to indicate its origin and relation to morphine.

Thebaine salicylate is practically insoluble in water; hence in the assay of opium the German Pharmacopœia directs the addition of sodium salicylate to the aqueous solution, thus removing the thebaine before precipitating the morphine.

Tritopine, $C_{42}H_{54}O_7N_2$, was discovered in 1890 by Klauder. (*A. Pharm.*, 228, p. 419.) It resembles morphine and laudanine in being soluble in sodium hydroxide solution, but is precipitated in the form of an oil by a large excess of the reagent. Tritopine crystallizes in characteristic, anhydrous, transparent, needle-like plates, melting at 182° C. (359.6° F.), easily soluble in chloroform, but only slightly so in ether. With sulphuric acid it behaves like laudanine. It appears to be a divalent base.

Xanthaline, $C_{37}H_{38}O_9N_2$, is a base obtained by T. and H. Smith (*P. J.*, 1893, 772) from the acid mother liquors resulting from the crystallization of morphine or codeine hydrochloride, and purification of the product.

Meconic Acid, $C_7H_4O_7 + 3H_2O$, is in white crystalline scales, of a sour taste followed by bitterness, fusible and volatilizable by heat, soluble in four parts of boiling water, soluble also in cold water and alcohol, with the property of reddening vegetable blues and forming salts. Its compounds with the earths and heavy metallic oxides are generally insoluble in water. Its characteristic properties are that it produces a blood-red color with ferric salts, which is not destroyed by mercuric chloride as is the similar reaction produced by sulphocyanates, a green precipitate with a weak solution of ammoniated copper sulphate, and white precipitates, soluble in nitric acid, with lead acetate, silver nitrate, and barium chloride. It is obtained by macerating opium in water, filtering the infusion, and adding a solution of calcium chloride. Calcium meconate and sulphate are precipitated. The precipitate, having been washed with hot water and with alcohol, is treated with diluted hydrochloric acid at 82.2° C. (180° F.). The calcium meconate is taken up, and, upon the cooling of the liquid, calcium bimeconate is deposited. This is dissolved in warm concentrated hydrochloric acid, which deposits pure meconic acid when it cools. It may be freed from coloring matter by neutralizing it with potassium hydroxide, decomposing the meconate thus obtained by hydrochloric acid, and again crystallizing. When heated, it loses first its water of crystallization, and then at 120° C. (248° F.) a molecule of CO_2, and yields *comenic acid*, $C_6H_4O_5$; this at 260° C. (500° F.) or over, loses another molecule of CO_2, and yields *pyromeconic acid*, $C_5H_4O_2$. By the action of nascent hydrogen (from sodium amalgam) it yields *hydromeconic acid*, $C_7H_{10}O_7$. Meconic acid has little or no action on the system, and is not used separately in medicine; but its natural relation to morphine requires that it should be understood. The three related compounds, meconic acid, comenic acid, and pyrocomenic acid, are now considered to be derivatives of the fundamental compound *pyrone*, $CO<\begin{matrix}CH=CH\\CH=CH\end{matrix}>O$. Thus, from pyrone, $C_5H_4O_2$, are obtained *oxypyrone* (pyromeconic acid), $C_5H_3O_2(OH)$, and *oxypyrone-carboxylic* (comenic) *acid*, $C_5H_2O_2(OH)COOH$, and *oxypyrone dicarboxylic* (meconic) *acid*, $C_5HO_2(OH)(COOH)_2$. Pyrone itself is formed when comenic and chelidonic acids are heated to 250° C. (482° F.). Most of the pyrone derivatives are converted by the action of ammonia into pyridone and pyridine compounds.

Meconic acid was formerly recognized by the British Pharmacopœia, but was dropped at the 1898 revision. It appears to be nearly free from active physiological properties. Sertürner took 4.5 grains of sodium meconate, and Grape and Loewer 12 grains of the pure acid, without the production of any symptoms, while, according to Mulder, Pereira, Lange, and others, 20 grains of the acid cause no sensible effect in the dog.

Meconin, $C_{10}H_{10}O_4$, a neutral principle before referred to, the existence of which was announced in 1832, by Couërbe, is identical with a substance discovered several years previously by Dublanc, Jr., but of which no account was published. It is perfectly white, in the form of acicular crystals, soluble in about 265 parts of cold and 18 of boiling water, very soluble in alcohol, chloroform, and the essential oils, but only sparingly in ether; fusible under water at 77° C. (170.6° F.), *per se* at 110° C. (230° F.), sublimable on careful heating, and possessed of a degree of acrimony which favors the supposition that it may not be without action upon the system. It is neither acid nor alkaline, and contains no nitrogen. Meconin is obtained by precipitating the aqueous infusion of opium with ammonia, washing the pre-

cipitate with water until the latter nearly ceases to acquire color, mixing the aqueous fluids, evaporating them to the consistence of molasses, setting them aside for two or three weeks, during which a mass of granular crystals is formed, then decanting the liquid, expressing the mass, and drying it with a gentle heat. The meconin may be separated from the mass by treating it with boiling alcohol of 36° Baumé, evaporating so as to obtain crystals, dissolving these in boiling water with animal charcoal, filtering the liquid, while hot, and subjecting the crystals formed upon the cooling of the solution to the action of ether, which dissolves the meconin, and yields it in a state of purity by spontaneous evaporation. It may be produced from narcotine by oxidation with nitric acid.

MECONOISIN, $C_8H_{10}O_2$.—This principle was discovered by T. and H. Smith, in 1878, who obtained it from the oil-like liquid containing meconin, which, upon being left to itself for some days, sets into a mass of crystals. These crystals, upon being drained and cautiously washed with cold weak spirit, are to be boiled in a large quantity of water. The filtered liquid gives a crystallization of meconin, and the mother liquor, when concentrated, and upon being set aside for a time, yields beautiful leaf-like crystalline masses of meconoisin, fusing at 88° C. (190.4° F.). This principle is neutral, and it may be distinguished from meconin by the following test of T. and H. Smith. "When heated with slightly diluted sulphuric acid, and when the evaporation has reached a certain point, meconin produces a beautiful green color. With meconoisin, under the same circumstances, the coloration is deep red, becoming purple." This substance has been found by Stockman and Dott (*B. M. J.*, Jan., 1891) to be a tetanizant.

OPIONIN, as before stated, was found by Hesse in small quantities in Smyrna opium. It forms white needles, which melt at 227° C. (440.6° F.). These are insoluble in water, but dissolve in alkalies, alcohol, and ether.

LACTIC ACID, which was discovered by T. and H. Smith, of Edinburgh, and at first named by them thebolactic acid under the supposition that it differed from ordinary lactic acid, appears to be a constant ingredient in opium. These chemists were led to search for it by the consideration that the quantity of meconic acid present is insufficient to saturate the whole of the morphine and other bases, which must, therefore, be neutralized by some other acid. They obtained it from the impure mother liquid of morphine, after all the alkaloids had been thrown down by the addition of an alkali, by concentrating the liquors to a thick consistence, adding alcohol largely, filtering, precipitating any basic matter by sulphuric acid, filtering again, carefully neutralizing by milk of lime, distilling to recover the alcohol, and finally evaporating the residuary contents of the still to a syrupy consistence. After standing for about a week, the syrupy liquid will be seen to have set into a crystalline mass of calcium thebolactate. This, being purified by repeated solution and crystallization, and by animal charcoal, is decomposed by adding the equivalent quantity of sulphuric acid, and separating the liberated thebolactic acid by means of alcohol. Stenhouse showed that the new acid had the composition of lactic acid and was identical with the common variety, and his results were confirmed by J. Y. Buchanan. (*Ber. d. Chem. Ges.*, 1870, p. 182.) The ready crystallization of its salts with lime is a characteristic property.

Morphiometric Assays of Opium.—The proportion of morphine which any particular specimen of opium will furnish may be considered the best test of its value, except that of actual trial upon the system. The U. S. Pharmacopœia directs that opium, in its normal, moist condition should contain not less than 9.5 per cent. of anhydrous morphine, and powdered or granulated opium, dried at a heat not exceeding 85° C. (185° F.), should contain not less than 10 nor more than 10.5 per cent. of anhydrous morphine when assayed by the official process, which is as follows:

Assay of Opium. U. S. P. IX.—"Introduce 8 Gm. of Opium, which if fresh should be in very small pieces, and if dry in fine powder, into an Erlenmeyer flask having a capacity of about 250 mils, add 80 mils of distilled water, stopper the flask, and agitate it every ten minutes (or continuously in a mechanical shaker) during three hours. Then pour the contents as evenly as possible upon a wetted filter having a diameter of not over 12 cm., and, when the liquid has drained off, wash the residue with distilled water, carefully dropped upon the edges of the filter and its contents, until 120 mils of filtrate have been obtained. Carefully transfer the moist Opium to a mortar by means of a spatula, and rub to a smooth paste, then rinse into the original flask with 50 mils of distilled water, agitate it thoroughly and return the whole to the filter. When the liquid has drained off, wash the residue with 75 mils of distilled water. Evaporate the mixed filtrates and washings on a water bath to about 40 Gm. Transfer the extract to a 50 mil graduated flask and wash the evaporating dish with sufficient distilled water to make the entire volume measure exactly 50 mils when cooled to room temperature. Place in a small mortar 4 Gm. of freshly slaked lime (see Reagents, Part III), add about 10 mils of the opium extract and rub to a smooth paste, then add the remainder of the extract and rinse the flask with exactly 10 mils of distilled water, adding the rinsings to the mortar, and stir frequently during fifteen minutes, avoiding unnecessary loss by evaporation. Filter through a dry filter, about 10 cm. in diameter, and transfer exactly 30 mils of the filtrate, representing *four grammes* of Opium, to an Erlenmeyer flask of suitable capacity. To this add 2 mils of alcohol and 15 mils of ether, and, after shaking the mixture, add 1 Gm. of ammonium chloride, stopper the flask and shake

it frequently during half an hour, then set it aside in a cool place for twelve hours or over night. Remove the stopper and brush any adhering crystals back into the flask. Decant the ethereal layer into a small funnel, the neck of which has been previously closed with a pledget of purified cotton. Rinse the flask and contents with 15 mils of ether, and, when the ether has passed through, wash the funnel and cotton with a small quantity of ether, and then pour the aqueous liquid into the funnel without trying to remove the crystals. Wash the crystals in the flask and the contents of the funnel with distilled water, previously saturated with morphine, until the washings are colorless. Then add a few drops of distilled water to replace the morphinated water. Incline the edge of the funnel over the mouth of the flask and by means of a glass rod carefully transfer the cotton with adhering crystals to the flask. Insert the funnel into the neck of the flask and wash the funnel with 20 mils of tenth-normal sulphuric acid V.S., followed by 10 mils of distilled water, applied drop by drop around the edge of the funnel. Remove the funnel, replace the cork, warm gently, and agitate until the crystals are dissolved. Rinse the cork with distilled water and titrate the excess of acid with fiftieth-normal potassium hydroxide V.S., cochineal T.S. being used as indicator. Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 0.028516 Gm. of anhydrous morphine." *U. S. P. IX.*

Assay of Opium, Br.—"Opium, in No. 50 powder, dried at 60° C. (140° F.), 8 *grammes;* Calcium Hydroxide, freshly prepared, 2 *grammes;* Ammonium Chloride, 2 *grammes;* Alcohol (90 per cent.), Ether, Distilled Water, of each, *a sufficient quantity.* Triturate together the Opium, *calcium hydroxide,* and 20 millilitres of *water,* in a mortar until a uniform mixture results; add 60 millilitres of *water* and stir occasionally during half an hour. To 51 millilitres of the filtered liquid (representing 5 grammes of Opium) in a convenient vessel add 5 millilitres of *alcohol* (90 per cent.), and 25 millilitres of *ether;* shake the mixture; add the *ammonium chloride,* shake well and frequently during half an hour; set aside for twelve hours for the morphine to separate. Counterbalance two small filters; place one within the other in a small funnel in such a way that the triple fold of the inner filter shall be superposed upon the single fold of the outer filter; wet them with *ether;* remove the ethereal layer of the liquid in the vessel as completely as possible by means of a small pipette, transferring the liquid to the filter; rinse the vessel with 10 millilitres of *ether,* again transferring the ethereal layer, by means of the pipette, to the filter; wash the filter with a total of 5 millilitres of *ether,* added slowly and in portions. Let the filter dry in the air, and pour upon it the contents of the vessel in portions, in such a way as to transfer the granular crystalline morphine as completely as possible to the filter. When all the liquid has passed through, wash the remainder of the morphine from the vessel with *morphinated water,* until the whole has been removed. Wash the crystals with *morphinated water* until the washings are free from color; allow the filter to drain, and dry it, first at 60° C. (140° F.) and finally, for two hours, at 115° C. (239° F.). Weigh the crystals in the inner filter, counterbalancing by the outer filter. Dissolve 0.2 gramme of the crystals in 10 millilitres of *N/10 solution of sulphuric acid,* and titrate back with *N/10 solution of sodium hydroxide, solution of methyl orange* being used as indicator. Each millilitre of the acid neutralised by the alkaloid corresponds to 0.0285 gramme of pure anhydrous morphine. The weight of pure anhydrous morphine obtained, as indicated by the titration, plus 0.051 gramme, the average loss of morphine during the process, together amount to 0.5 gramme, representing in 100 grammes of the dry powdered Opium 10 grammes of morphine, calculated as anhydrous. *Limit of error* 0.5 gramme in excess or defect." *Br.*

Morphinated Water.—"Prepared by digesting pure morphine in chloroform water for seven days at a temperature of 15.5° C. (60° F.), with shaking occasionally, so as to obtain a saturated solution of the alkaloid, and filtering from the undissolved morphine." *Br.*

The U. S. and Br. methods of assay are practically identical in principle, belonging to the class of assays known as "lime processes." Experience has proved that the "lime processes" have some objectionable features, depending as they do upon the principle that opium in the presence of lime is treated with a definite quantity of water until the latter has extracted as much as possible of the soluble portions, after which a certain portion of the solution, which is *assumed to represent* a corresponding fraction of the weight of the opium, is weighed or measured off, the morphine determined in it, and the percentage calculated from the quantity found in this fraction or aliquot part. The "lime processes," in the hands of ordinary operators, "register too low," the assay being applied to a proportion of the opium which may or may not be an aliquot part of the whole, but is generally less than it is assumed to be, because no allowance is made for the increase in volume due to the solution of the solid constituents of the opium. The British Pharmacopœia overcomes this objection by requiring 104 mils of liquid to be taken instead of 100 mils. A. B. Stevens has improved the lime method and it is conceded by many that the crystallized morphine by this process is freer from impurities than that obtained by Squibb's method, and that it takes less time to perform the assay than that required for the U. S. P. (8th Rev.) method. The U. S. P. assay of 1890 was based on the method of E. R. Squibb, which requires the complete exhaustion of the sample of opium of its soluble matter, the concentration of this solution, and the determination of the morphine in it. The morphine is separated in a crystal-

line form from its combination with its natural acids in the opium solution, by the addition of the ammonia water; the alcohol present serves to hold up the coloring matter, while the ether facilitates the precipitation of the alkaloidal morphine in crystals, pure morphine requiring 4000 parts of ether for its solution. The U. S. P. VIII assay was also based upon Squibb's method, with the modification of the introduction of a correction factor, *i.e.*, the washing of the morphine crystals with lime water and deducting the weight of the impurities. Want of space prevents our giving a critical review of the other methods of assay in use. (See *U. S. Dispensatory,* 19th ed., p. 905.) Teschemacher and Smith (*Chem. News,* 1888, pp. 93, 103) criticise severely several well known methods of assay, and recommend their own, which does not vary greatly from others in use; indeed, it is difficult to resist the conclusion that the differences in the results arrived at by various operators are largely chargeable to personal error and unfamiliarity with other processes than their own. (See *Ephem.,* June, 1888, 1113; *A. J. P.,* 1887, 74; Prescott's *Organic Analysis,* 1887, 375; Lyon's *Handbook on Assaying Drugs,* 1899, 201; Allen's *Com. Org. Anal.,* vol. iii, Part II, p. 342.)

For other methods of assay, and comments, see *U. S. Dispensatory,* 14th edition, 675, and 15th edition, 1072; *A. J. P.,* 1876, 358; 1878, 184; 1879, 369; 1894, 445; 1897, 244; *N. R.,* Feb., 1880, Dec., 1880, 1881, 174; *West. Drug.,* 1885, 231, also 1886, 442; *Am. Drug.,* 1885, 221, also 1886, 203; Dieterich's method modified by Schlickum, *Ph. Era,* 1887, 325, also 1888, 9; assay adopted by U. S. Laboratory in New York, *Ph. Era,* 1887, 151; *B. C. D.,* 1894, 372; *P. J.,* 1897, 542; *J. I. and E. C.,* 1912, p. 514; *Gehes. Rep.,* 1912; *Year Book of Pharm.,* 1913, 443.

Moerk recommended the treatment of the crystallized morphine with lime water; see U. S. P. VIII assay. (*Proc. Penn. Pharm. Assoc.,* 1897, 65.) Gordin and Prescott propose a volumetric assay based on the estimation of morphine as periodide, after separation by treatment with benzene, acetone, and lime water. (*M. R.,* 1898, 526.) See also *C. D.,* 1898, 20; *D. C.,* 1902, 161; *Ph. Archiv.* 1898, 121; 1901; 1902, 81, 87; *Proc. A. Ph. A.,* 1899, 263; 1902, 425; 1904, 369; *P. J.,* 1903, 909; 1904, 719; *Chem. News,* 1903, 286.

Tests for Opium.—It is sometimes highly important to be able to ascertain the presence or absence of opium in any suspected mixture. As meconic acid and morphine have been found only in the products of the poppy, if either or both of them be shown to exist in any substance, very strong evidence will be afforded of the presence of opium. The test should, therefore, be applied in reference to the detection of these two principles. If an aqueous infusion of the substances examined yields a red color with the tincture of ferric chloride, there is presumptive evidence of the presence of meconic acid. Greater certainty may be obtained by the following process. Add in excess to the filtered liquor a solution of lead acetate. If opium be present, there will be a precipitate of lead meconate, and the morphine and lead acetates will remain in solution. The precipitate is then to be suspended in water, and decomposed, either by adding a little diluted sulphuric acid, which forms lead sulphate and leaves the meconic acid in solution, or by passing through it a stream of hydrogen sulphide, removing by filtration the precipitated lead sulphide, and heating the clear liquor, so as to drive off the hydrogen sulphide. With the clear liquor thus obtained, if it contain meconic acid, the tincture of ferric chloride will produce a striking red color, ammoniated copper sulphate a green precipitate, and lead acetate, silver nitrate, and barium chloride, white precipitates soluble in nitric acid. Potassium sulphocyanate, which, according to Wright, is an invariable constituent of saliva (*Simon's Chemistry,* ii, 6), produces a red color with ferric salts, resembling that produced by meconic acid, but, according to Everitt, this color is entirely and at once destroyed by a solution of corrosive sublimate, which has no effect on the red color of iron meconate. (*A. J. P.,* xii, 88.) On the contrary, gold chloride reddens a solution of sulphocyanic acid or a sulphocyanate, but not of meconic acid. Pereira says the acetates also redden ferric salts, but do not afford the results just mentioned with lead acetate and barium chloride. To test for the presence of morphine, the liquid from which the lead meconate has been precipitated, and which may be supposed to contain the morphine and lead acetates, must be freed from the lead by a stream of hydrogen sulphide, and then from the hydrogen sulphide by heat, after which the following reagents may be applied—viz., (1) nitric acid, which colors the morphine red; (2) iodic acid, which is decomposed by the morphine with the extrication of iodine, which colors the liquid reddish-brown, and, if starch is present, unites with it to form a blue compound; (3) solution of ammonia, which, if carefully added, so as not to be in excess, throws down a precipitate of morphine soluble in a great excess of that alkali or of potassium hydroxide; and (4) tannic acid, which precipitates morphine tannate. If the precipitate thrown down by ammonia affords a deep-red color becoming yellow with nitric acid, and a blue color with ferric chloride, the proofs may be considered complete. Merck has proposed a test of opium, founded on the property, which characterizes porphyroxine, of assuming a red color when heated in diluted hydrochloric acid. The suspected liquid is first carefully evaporated, a few drops of solution of potassium hydroxide are added, and the mixture agitated with ether. The ethereal solution being filtered off, a slip of unsized paper is to be dipped into it and dried, and the moistening and drying should be repeated several times. The paper thus prepared is to be moistened with diluted hydrochloric acid, and then exposed to the vapor

of boiling water. If it become reddened, opium may be inferred to exist in the liquid tested. Heusler states that this test is not applicable to the aqueous solution or extract of opium, because porphyroxine is insoluble in water, but Robertson, of Rotterdam, has found it to succeed with the aqueous extract, and infers that the porphyroxine is so combined in opium as to render it in some measure soluble. (*J. P. C.*, 3e sér., xxii.)

Though opium is little injured by time if well kept, yet it does undergo spontaneous change, and Guibourt found less morphine in a specimen which had been in his possession nearly twenty years than it had yielded in its recent state. There was also more coloring matter, due to the darkening by age. (*Ann. Thér.*, 1863, p. 5.)

Among the adulterations of opium, starch has been detected in a specimen examined by J. T. King. The drug was unduly brittle, and evidences of starch were afforded both by the microscope and by iodine. From the size and form of the granules, King inferred that the starch was that of the bean. (*A. J. P.*, Jan., 1869, p. 1.) The probability is that powdered beans were the substance used.

Incompatibles.—The substances which produce precipitates with opium do not all necessarily affect its medicinal virtues, but the *alkalies*, and all vegetable infusions containing *tannic* and *gallic acids*, are incompatible, the former separating and precipitating the free alkaloids, the latter forming with it an insoluble compound.

Uses.—The use of opium as a medicine can be clearly traced back to Diagoras, who was nearly contemporary with Hippocrates, and it was probably employed before his time.

Opium owes its activity chiefly to the alkaloid morphine and the physiological actions and therapeutic uses of the whole drug are very similar to those of its dominant alkaloid. Sufficient has been said on this subject under *Morphina* (see page 704). Certain of the other alkaloids present in opium differ somewhat in their action from that of morphine, and to a certain extent modify the effects of opium, and we shall therefore consider here the medical properties of some of these secondary alkaloids, and point out the conditions in which opium is preferred to morphine.

The most abundant of the alkaloids after morphine is *narcotine;* indeed, in some varieties of opium it is said to be present in larger quantities than morphine. This alkaloid appears to be almost, if not entirely, free of the characteristic narcotic properties of morphine. In large doses it is a spinal stimulant and produces in the lower animals convulsions. According to Macht (*J. P. Ex. T.*, 1915, xii, p. 339), narcotine differs essentially from morphine in its action upon the respiratory center, acting as a stimulant rather than a depressant. He finds also that because of this antagonistic action upon respiration very much larger doses of morphine can be given if combined with narcotine, without dangerous respiratory depression. It was at one time recommended as an antiperiodic, but is probably of no value; the *dose* employed was from two to three grains (0.13–0.2 Gm.).

Papaverine is the only other alkaloid which occurs naturally in opium in large enough quantity to perceptibly modify the effect of the crude drug. Although much less potent than morphine it possesses distinct narcotic powers. According to Pal (*D. M. W.*, 1914, xl, p. 164) papaverine is an active local anesthetic and is especially valuable because of its power in allaying spasm of the involuntary muscles. Macht (*loc. cit.*) finds that papaverine, like narcotine, antagonizes morphine in its effect upon the respiratory center. Papaverine has been recommended in clinical medicine in *diarrhea*, various forms of *gastric* or *intestinal spasms, asthma*, *biliary colic*, and other conditions of excitability of the involuntary muscles. It, as well as its hydrochloride and sulphate, are recognized by the *N. N. R.*, 1916. The *dose* recommended is usually from one-half to one and one-half grains (0.032–0.096 Gm.), although it is stated that much larger quantities may be given without any evil effects.

Thebaine.—This is chiefly of interest because of its action on the spinal cord. In the lower animals it produces convulsions closely simulating those caused by strychnine. In large quantities it seems to be paralyzant to the peripheral motor nerves. It does not appear to possess narcotic properties.

Codeine being official is considered elsewhere (see page 367). The other alkaloids occur in such small quantities and are mostly of such feeble powers that it is improbable that they play any part in the effects of opium. For further information on the minor alkaloids of opium, see Crawford and Dohme (*Proc. A. Ph. A.*, 1902, p. 472); Leubuscher (*D. M. W.*, 1892); Macht (*J. P. Ex. T.*, 1915, vii, and 1916, viii); and Pal (*D. M. W.*, 1913, xxxix, and 1914, xl).

In a general way it may be said that opium is more constipating and more nauseating in proportion to its narcotic power than is morphine. According to the experiments of Macht, which have received clinical confirmation from the observations of Sahli and others, it would appear that it is also less dangerous because not so depressing to the respiratory center. Why opium should act more powerfully upon the intestinal tract than does morphine is at present not clear; Vamossy (*D. M. W.*, 1897, xxiii) investigated the action of a number of the alkaloids upon the intestines and found that none of them equalled morphine in power. Nevertheless, clinical experience abundantly sustains the statement made above. Although capable of fulfilling all the indications for which morphine is employed, when used as an analgesic or somnifacient, the alkaloid is usually preferred because of its lesser liability to disturb digestion. On the other hand in *diarrhea* and

spasmodic colic the whole drug is superior to the alkaloid. Opium is frequently a valuable remedy in *diabetes mellitus*. How it acts is uncertain, but the whole drug is to be preferred to any of its alkaloids. Because of its peculiar power in dilating the vessels of the skin opium tends to increase the sweat and is therefore useful in minor infections, such as *colds, grippe, muscular rheumatism,* and the like. As a sudorific it is generally combined with ipecac in the form of Dover's Powder.

Opium is largely used locally in the form of its tincture either in combination with a solution of lead subacetate or by itself. While it possesses feeble counterirritant and anesthetic powers the freedom with which it is used as a local application verges on the superstitious.

Poisoning.—In moderately large doses opium produces, generally, a pleasurable feeling of languor followed by drowsiness. In toxic dose the most prominent symptom is sleep, from which, in the moderate degrees of poisoning, the patient can easily be awakened by loud noises, shaking, etc. At this stage of the poisoning the respirations are generally slower than normal but of good depth, the pulse is slow and full, the skin warm and flushed and moist, the pupil contracted. As the intoxication deepens the respirations become slower and shallower and often irregular, and the skin is frequently more or less cyanotic from imperfect aeration of the blood; the pupils grow smaller and are eventually reduced in size to almost complete invisibility; the patient can be aroused only with difficulty and when left to himself immediately sinks back into a comatose sleep. The reflexes are generally not greatly affected. When the dose has been very large there may develop, late in the poisoning, failure of the circulation with rapid, feeble pulse and cold, clammy, cyanotic skin. The quantity required to take life varies enormously according to the individual susceptibility of the patient. On the one hand, several fatalities have been reported from less than one-half a grain of morphine and from four or five grains of opium. On the other hand, we have seen an opium habitué take 8 grains of morphine at a dose with no serious effect, and Fell has reported recovery following 33 grains of morphine.

Treatment of Opium Poisoning.—For the evacuation of the stomach, unless the drug has been taken in solid form, the stomach tube is preferable to emetics, the latter often failing to act because of the effect of the drug upon the vomiting center. In the absence of a stomach tube, however, twenty or thirty grains of zinc sulphate may be given as an emetic. The best chemical antidote is potassium permanganate, which oxidizes the active principle of the drug to a harmless compound; four or five grains of the permanganate may be given at a dose. Where the stomach tube is employed it is well to wash out the stomach with a 1 to 500 solution of potassium permanganate leaving 3 or 4 ounces of this solution in the stomach to neutralize any alkaloid which may be later excreted. If this antidote be not at hand tannic acid may be used as a partial but less satisfactory antidote; it is well to follow this with a saline cathartic as the tannate of morphine is slowly absorbable. Fantus has obtained favorable results in experimental morphine poisoning with the use of Fuller's earth (see *Terra Silicea Purificata*). Aside from the prevention of absorption, the most important measures are those directed towards maintaining respiratory function. As this is always in abeyance during sleep the patient should, if possible, be kept awake. Many of the measures, however, which have been employed for preventing sleep have done as much harm in exhausting the patient's strength as the wakefulness has done good. By far the best means for this purpose is the faradic battery, using either a brush electrode or a bare metal upon the skin; with this apparatus an exquisite pain can be caused without any injury to the body. Slapping the skin with the fringe of a wet towel is also useful, but care must be exercised not to bruise. Alternate dashes of hot 40.5° C. (105° F.) and cold water 10° C. (50° F.) upon the bare chest may also be of service. Occasionally by repeated shouting the patient may be kept from going to sleep. We do not believe that the advice, so often given, to keep the patient constantly walking is sound. Among the respiratory stimulants the most useful is probably cocaine or strychnine; caffeine and atropine are also of much service. There was at one time a wide-spread belief that atropine was a complete physiological antagonist to morphine. This, however, is erroneous; while the drug may be useful for its stimulating effects upon the respiratory center, it must be remembered that large doses of atropine are depressant, and if used too freely may injure rather than benefit. If, despite these measures, respiration remains dangerously insufficient, recourse should be had to artificial respiration either by the Sylvester or Schaefer method, or preferably with one of the apparatuses for forced artificial respiration, such as the pulmotor. By means of a simple bellows apparatus Fell (*Medical Examiner,* June, 1899) succeeded in maintaining life for seventy-three hours with the eventual recovery of the patient. The intravenous injection of salt solution has also been recommended with the idea of diluting the poison in the blood. Cardiac stimulants, as ammonia, may occasionally be required in severe cases.

Opium Smoking.—By the various nations of the Orient opium is employed as an intoxicant by smoking in two ways. In Turkey and its neighboring countries it is placed upon tobacco, in a small pipe. In the East it is usually made into a very thick, almost plastic, liquid, and a drop of it is held over the flame of a small oil-lamp, and the resulting fumes inhaled through pipes of various forms. In China, opium is prepared for smoking by mixing it with various ingredients to give form and flavor. It occurs

as a soft blackish paste and contains less than 9 per cent. of morphine. The importation of smoking opium is forbidden in the United States. For an elaborate study of the chemistry of the opiums used for smoking in various countries, see *Ap. Ztg.*, 1903.

Moissan has found in opium smoke, morphine, pyrrol, pyridine with various homologues, acetone, and various hydropyridine bases, all of which are physiologically active. This analysis has been confirmed by Hartwich and Simon, who believe that the activity of the opium smoke depends not so much upon the morphine as upon the other products of the destructive distillation.

Dose, from one to two grains (0.065–0.13 Gm.).

Off. Prep.—*From opium.*—Extractum Opii Liquidum (from Dry Extract), *Br.;* Extractum Opii Siccum, *Br.;* Linimentum Opii (from Tincture), *Br.;* Opii Pulvis, *U. S.;* Opium Granulatum, *U. S.;* Tinctura Camphoræ Composita (from Tincture), *Br.;* Tinctura Opii, *Br.;* Tinctura Opii Ammoniata (from Tincture), *Br.;* Linimentum Opii Compositum, *N. F.;* Lotio Plumbi et Opii, *N. F.;* Mistura Camphora Acida, *N. F.;* Mistura Carminativa, *N. F.;* Mistura Magnesiæ, Asafœtidæ et Opii, *N. F.;* Mistura Opii et Chloroformi Composita, *N. F.;* Mistura Opii et Rhei Composita, *N. F.;* Mistura Opii et Sassafras, *N. F.;* Mistura Pectoralis, Stokes, *N. F.;* Syrupus Ipecacuanhæ et Opii (from Tincture), *N. F.;* Tinctura Ipecacuanhæ et Opii (from Tincture of Deodorized Opium), *N. F.;* Tinctura Kino et Opii Composita (from Tincture), *N. F.;* Tinctura Pectoralis (from Tincture), *N. F.*

From powdered opium.—Acetum Opii, *N. F.;* Extractum Opii, *U. S.;* Opium Deodoratum, *U. S.;* Pilula Plumbi cum Opio, *Br.;* Pilula Saponis Composita, *Br.;* Pulvis Cretæ Aromaticus cum Opio, *Br.;* Pulvis Ipecacuanhæ et Opii, *U. S.* (*Br.*); Pulvis Kino Compositus, *Br.;* Pulvis Opii Compositus, *Br.;* Suppositoria Plumbi Composita, *Br.;* Tinctura Opii Camphorata, *U. S.;* Unguentum Myrobalani cum Opio, *Br.;* Unguentum Gallæ cum Opio, *Br.;* Pilulæ Opii et Camphoræ, *N. F.;* Pilulæ Opii et Plumbi, *N. F.;* Pulvis Cretæ et Opii Aromaticus, *N. F.;* Pulvis Kino et Opii Compositus, *N. F.*

From granulated opium.—Tinctura Opii, *U. S.;* Tinctura Opii Deodorati, *U. S.;* Acetum Opii, *N. F.;* Tinctura Opii Crocata, *N. F.*

OPIUM DEODORATUM. U. S.

DEODORIZED OPIUM Opium Deod.

(ō′pĭ-ŭm dē-ō-dō-rā′tŭm)

"Deodorized Opium yields not less than 10 per cent. nor more than 10.5 per cent. of anhydrous morphine. Deodorized Opium of a higher morphine percentage may be brought within the required limits by admixture with deodorized opium of a lower percentage or with some inert diluent. Preserve it in well-closed containers." *U. S.*

Opium Denarcotisatum, *U. S.* 1880; Denarcotized Opium.

* "Powdered Opium, *five hundred grammes* [or 17 ounces av., 279 grains]; Purified Petroleum Benzin, *a sufficient quantity.* Macerate the powdered opium for twenty-four hours in a wide-mouthed, well-closed bottle with sufficient purified petroleum benzin to cover it completely, shaking the mixture occasionally. Then decant the clear benzin layer as closely as possible and repeat the maceration for twenty-four hours with another portion of purified petroleum benzin. Again decant the clear benzin layer and transfer the remaining contents of the bottle to a plain filter. Closely cover the funnel, allow the mixture to drain and then slowly percolate the residue with purified petroleum benzin until the latter passes through without color. Remove the filter containing the Opium from the funnel, expose the powder to the open air, so that it may dry thoroughly, and add sufficient sugar of milk to restore the original weight. Care should be used to guard against the danger due to the inflammability of the benzin. Granulated opium may also be deodorized in the manner directed above.

"**Assay.**—Proceed as directed under *Opium.*" *U. S.*

The use of purified petroleum benzin (in place of ether) in the U. S. P. VIII and IX process is an improvement. The use of benzin has often been proposed by Ebert and others, but the objection has always been that it was difficult to obtain it of sufficient purity.

This preparation represents the medicinal properties of opium without the presence of the odorous principles, which are believed by many physicians to play an important part in the nausea and depression produced in some people by opium.

Dose, one to two grains (0.065–0.13 Gm.).

OPIUM GRANULATUM. U. S.

GRANULATED OPIUM Opium Gran.

(ō′pĭ-ŭm grăn-ū-lā′tŭm)

"Opium dried at a temperature not exceeding 70° C. (158° F.) reduced to a coarse (No. 8 to No. 20) powder and yielding not less than 10 per cent. nor more than 10.5 per cent. of anhydrous morphine. Granulated Opium of a higher morphine percentage may be brought within the required limits of strength by admixture with granulated opium of a lower percentage, or with some inert diluent. Preserve it in well-closed containers.

"**Assay.**—Proceed as directed under *Opium.*" *U. S.*

This form of opium was introduced into the U. S. P. because, on account of its being in coarse powder, it is better fitted for use in making the liquid preparations of opium. (See *Opium.*)

Dose, one to two grains (0.065–0.13 Gm.).

OXYGENIUM. U. S.

OXYGEN Oxygen.

(ǫx-ў-ǧēn'ị-ŭm)

"It contains not less than 95 per cent. by volume of O(16). For convenience it is usually compressed in metal cylinders." *U. S.*

Oxygen was discovered about 1774 almost simultaneously by Priestley and Scheele. Both evolved it from metallic oxides or calces as they were called. Priestley called it *dephlogisticated air,* and Scheele called it *fire air,* it not then being recognized as a gaseous element, but was thought to be a kind of air. It is the most abundant of the elemental substances constituting, according to the calculations of some authorities, one-half of the weight of the earth and its atmosphere.

For experimental and laboratory purposes it is usually prepared by heating a mixture of potassium chlorate and manganese dioxide, the latter substance acting as a catalyst and remaining unchanged at the end of the operation, possessing the property of allowing the reaction $KClO_3 = KCl + O_3$ to take place at lower temperatures and without danger. Industrially it is usually prepared by the continuous process known as Brin's, in which BaO is heated in porcelain tubes to 500° C. (932° F.) in a current of carbon dioxide free air. This produces BaO_2, which upon further heating to 800° C. (1472° F.) again evolves the oxygen ($BaO_2 = BaO + O$). Upon lowering the temperature to 500° C. (932° F.) the absorption of oxygen again occurs and the alternate absorption and liberation may be repeated indefinitely, or until as is found in practice, the barium oxide loses its activity. Oxygen is also produced commercially from liquid air, taking advantage of the facts that the nitrogen is more volatile, and that the oxygen has a tendency to liquefy first.

G. Kassner has described a method for producing oxygen from the air by the use of a mixture of *sodium metaplumbate,* Na_2PbO_3, and *sodium manganate,* Na_2MnO_4. This combination, which is emerald-green in color, he calls *plumboxan.* The mixture is placed in a combustion tube and heated to between 430° C. and 450° C. (806° and 842° F.). Air freed from CO_2 is then passed through it and the oxygen is absorbed by the plumboxan while pure nitrogen passes through unchanged. Steam is then passed into the mass, which liberates the oxygen in an exceedingly pure condition. By alternately injecting air and steam, nitrogen and oxygen can be evolved in the order given indefinitely. The reaction, as given by the author, to account for the changes, are very complex. (*A. Pharm.,* ccli, 251, p. 596.)

Oxygen has also been produced commercially by heating sodium permanganate or by liberating it from sodium peroxide by the action of water. Oxygen comes into commerce for laboratory or medicinal purposes compressed into steel cylinders.

"Oxygen is a colorless, odorless, and tasteless gas. It supports combustion more readily than air; a glowing splinter of wood held in the gas bursts into flame. One volume of Oxygen dissolves in about 34 volumes of water and in about 3.6 volumes of alcohol at 25° C. (77° F.). Pass 2000 mils of Oxygen, measured under normal atmospheric pressure at about 25° C. (77° F.), at a rate not exceeding 4000 mils per hour, through 100 mils of barium hydroxide T.S.; not more than an opalescent turbidity is produced (*carbon dioxide*). Pass 2000 mils of Oxygen, under the conditions described above, through a mixture of distilled water and 1 mil of silver nitrate T.S.; no opalescence is produced (*halogens*). Pass 2000 mils of Oxygen through 100 mils of distilled water, colored with a few drops of litmus T.S., under the conditions described above; the color of the liquid is not changed (*acids or bases*).

"**Assay.**—Mix about 50 mils of Oxygen, accurately measured in a calibrated tube, with 10 mils of alkaline pyrogallol T.S.; not less than 95 per cent. by volume is absorbed, corresponding to not less than 95 per cent. by volume of O." *U. S.*

Uses.—Pure oxygen is so irritant locally that it is difficult to respire it; the statements sometimes made, however, that it is impossible to live in an atmosphere of pure oxygen do not seem to be well supported, at least as far as human beings are concerned. In normal health it is doubtful whether the respiring of pure oxygen has any marked effect upon the bodily processes except that which is due to the irritation of the mucous membrane. It must be remembered that the oxygen-carrying power of the blood is due to the chemical change of hemoglobin in the corpuscles, and enough oxygen is, ordinarily, absorbed by the lungs from the atmosphere to fully oxidize the hemoglobin, so that the blood leaving the lungs contains almost entirely oxyhemoglobin. The only increase in the amount of oxygen the blood will carry is in the relatively small proportion which is dissolved in the blood plasma. While this quantity may be notably increased by inhaling oxygen, in conditions of health its proportion to the oxygen in oxyhemoglobin is so small that it does not greatly affect oxidative processes in the body. On the other hand when the oxygen-carrying power of the blood is reduced—as, for instance, in *carbon monoxide poisoning* or *nitrite poisoning*—through chemical change in the hemoglobin the amount of oxygen which may be dissolved by the plasma becomes a matter of practical importance and Haldane has experimentally shown (*J. P.,* 1897, xxi, p. 160) that animals will survive a supra-fatal dose of nitrites in an atmosphere of pure oxygen. Again in cyanotic conditions due to insufficiency of the circulation, as in cases of *heart failure,* the small increase in the oxygen of the blood may be sufficient to supply the needs of the body and clinical improvement is often seen from the use of oxygen in such instances. In cases

where the passage of air in and out of the lungs is obstructed, as in *asthma* or *pneumonia*, the use of oxygen is still more rational because of the small amount of air which comes in contact with the blood. Therefore in practically all cases in which cyanosis indicates a deficient amount of oxygen being carried by the blood, the inhalation of this gas is a reasonable procedure and clinically has in many cases given great relief. It must be remembered, however, that the oxygen does not act by stimulating any vital function, in the sense that strychnine or ammonium might, but it merely supplies a deficient necessity of life. The custom of having a patient inhale oxygen for ten or fifteen minutes at a time three or four times a day, is foolish; the inhalation of the gas must be kept up more or less continuously as long as the symptoms indicate the need of it.

OXYMEL. Br.

OXYMEL

(ŏx'y-mĕl)

"Acetic Acid, 100 *millilitres;* Distilled Water, 100 *millilitres;* Purified Honey, 500 *millilitres.* Mix." *Br.*

Oxymel Simplex; Mel Acetatum, Mellite de Vinaigre, *Fr. Cod.;* Oxymelite simple, Acétomel, *Fr.;* Sauerhonig, *G.;* Oximiel simple, *Sp.*

"Specific gravity 1.27. 25 grammes require for neutralisation not less than 32 millilitres of *N/2 solution of sodium hydroxide.* The liquid obtained by mixing 25 grammes of Oxymel with 1 millilitre of *solution of lead subacetate,* diluting to 100 millilitres with *water,* adding 1 gramme of *animal charcoal,* and filtering until bright, has an *optical rotation* at 15.5° C. (60° F.) of not more than –3.9° in a tube 200 millimetres long." *Br.*

This mixture of honey and vinegar forms a pleasant addition to gargles, and is sometimes used as a vehicle of expectorant medicines and to impart flavor to drinks in febrile diseases.

Dose, from one to two fluidrachms (3.75–7.5 mils).

OXYMEL SCILLÆ. Br.

OXYMEL OF SQUILL

(ŏx'y-mĕl sçĭl'læ)

"Vinegar of Squill, 200 *millilitres;* Purified Honey, 500 *millilitres.* Mix." *Br.*

Mellite de Vinaigre Scillitique, Oxymel Scillitique, *Fr. Cod.;* Oxymel Scillæ, *P. G.;* Meerzwiebelhonig, *G.;* Ossimiele scillitico, *It.;* Oximiel escilítico, *Sp.*

"Specific gravity 1.29. 25 grammes require for neutralisation not less than 11.9 millilitres of *N/2 solution of sodium hydroxide.* The liquid obtained by mixing 25 grammes of Oxymel of Squill with 1 millilitre of *solution of lead subacetate,* diluting to 100 millilitres with *water,* adding 1 gramme of *animal charcoal,* and filtering until bright, has an *optical rotation* at 15.5° C. (60° F.) of not more than –3.9° in a tube 200 millimetres long." *Br.*

After a long vogue, this preparation fell into such neglect that it was abandoned by the Pharmacopœias. Its reintroduction, however, into the Br. Pharmacopœia indicates that it is still prescribed; it has also been introduced into the N. F. IV (see Part III). It has the virtues of syrup of squill, but no advantages. It is chiefly used as an expectorant in those states of the pulmonary organs in which the bronchial tubes are loaded with a viscid mucus of difficult expectoration.

Dose, from one-half to one fluidrachm (1.8–3.75 mils). In large doses it is emetic, and as such is sometimes used in *infantile croup.*

OXYMEL URGINEÆ. Br.

OXYMEL OF URGINEA [Oxymel of Indian Squill]

(ŏx'y-mĕl ŭr-gĭ'nē-æ)

"Vinegar of Urginea, 200 *millilitres;* Purified Honey, 500 *millilitres.* Mix." *Br.*

"Specific gravity 1.29. 25 grammes require for neutralisation not less than 11.9 millilitres of *N/2 solution of sodium hydroxide.* The liquid obtained by mixing 25 grammes of Oxymel of Urginea with 1 millilitre of *solution of lead subacetate,* diluting to 100 millilitres with *water,* adding 1 gramme of *animal charcoal,* and filtering until bright, has an *optical rotation* at 15.5° C. (60° F.) of not more than –3.9° in a tube 200 millilitres long." *Br.*

This is a new preparation of the British Pharmacopœia, 1914. It is used for the same purposes as the *oxymel scillæ.*

Dose, from one-half to one fluidrachm (1.8–3.75 mils).

PANCREATINUM. U. S.

PANCREATIN Pancreat.

(păn-crē-ą-tĭ'nŭm)

"It contains enzymes, consisting principally of amylopsin, trypsin, and steapsin, found in the pancreas of warm-blooded animals, and obtained from the fresh pancreas of the hog (*Sus scrofa* var. *domesticus* Gray) (Fam. *Suidæ*), or of the ox (*Bos taurus* Linné) (Fam. *Bovidæ*). It converts not less than 25 times its own weight of starch into soluble carbohydrates when assayed as directed on page 826. Pancreatin of a higher digestive power may be brought to this standard by admixture with sugar of milk. Preserve it in well-closed containers." *U. S.*

Pancréatine médicinale, Pancreatina, *Fr. Cod.;* Pancreatina, *Sp.*

The term "pancreatin" has been variously used for many different preparations from the pancreatic gland, and has long been popularly employed for the purpose of distinguishing preparations more or less of the nature of extracts made from the gland. The *pancreatic juice* is an albuminous, transparent liquid, odorless, alkaline, and containing about eight per cent. of organic matter. It is now generally

recognized that there are present in the pancreatin secretion three distinct enzymes: *trypsin*, whose function it is to convert albuminous matters into peptone, and probably also peptones into their aminoacids; *amylopsin* or *amylase*, a ferment closely allied if not identical with the ptyalin of the saliva, which hydralizes starch into maltose and dextrin; and *steapsin* (*lipase*), which has the power of splitting up fats into glycerin and fatty acids. Besides these ferments there is apparently present also another substance which has the property of curdling milk. Because of its fat splitting properties the pancreatic juice has a strong emulsifying effect, the viscous agent being the soap formed through the splitting of the fat. The activity of the lipase is greatly increased by the presence of bile. This emulsifying action takes place very rapidly; according to Rachford (*J. Chem. S.*, 1891, 948) a spontaneous emulsion may be formed in two minutes at room temperature.

All of the pancreatic ferments are active in neutral or mildly alkaline media, but the most favorable reaction is not the same for all of them, thus trypsin is best with an alkalinity corresponding to about 1 per cent. of sodium carbonate, but amylopsin acts most rapidly in the presence of 0.01 per cent. of hydrochloric acid, and the action of the fat splitting ferment is also accelerated by a faintly acid reaction.

The pancreatin of the U. S. Pharmacopœia is composed of all these ferments, with more or less extraneous matter. It is officially described as "a cream-colored, amorphous powder, having a faint, characteristic, but not offensive odor. It is slowly and incompletely soluble in water; insoluble in alcohol. Pancreatin changes proteins into proteoses and derived substances, and converts starch into dextrins and sugars. Its peculiar activities are best exhibited in neutral or faintly alkaline media; more than traces of mineral acids or large amounts of alkali hydroxides render it inert. An excess of alkali carbonates also inhibits its action. Introduce 2 Gm. of Pancreatin into a flask of about 50 mils capacity, add 20 mils of ether, stopper and set it aside for several hours, shaking by rotating at frequent intervals. Decant the supernatant ether, by means of a guiding rod, into a plain filter of about 7 cm. diameter, previously moistened with ether, and collect the filtrate in a tared beaker. To the residue remaining in the flask add a further portion of 10 mils of ether, proceeding as directed before, then a third portion of 10 mils of ether and transfer the ether and the remainder of the pancreatin to the filter. Allow the filter and contents to drain, then allow the ether to evaporate spontaneously and dry the beaker and residue to constant weight at 100° C. (212° F.). The residue weighs not more than 0.06 Gm. (*fat*). Add 0.28 Gm. of Pancreatin and 1.5 Gm. of sodium bicarbonate to 100 mils of tepid distilled water contained in a flask, then add 400 mils of fresh milk which has previously been heated to 40° C. (104° F.), and maintain the temperature of the mixture at this point for thirty minutes. At the end of this time the milk is so completely peptonized that on diluting 3 mils with 9 mils of distilled water and then mixing with 3 mils of acetic acid no coagulation occurs." *U. S.*

R. H. Jones found commercial pancreatin unable to withstand the U. S. P. 1890 tests, which he stated were too stringent; he suggested the addition of a starch digestion test. (*P. J.*, 1896, 194.) (See official assay of pancreatin.)

Various methods of manufacturing pancreatic extracts are employed. Water readily dissolves all the ferments and the French Codex directs that pancreas gland purified by separating foreign matter is to be cut into small pieces, macerated in chloroform water, then expressed, the liquid filtered and rapidly evaporated at a temperature not exceeding 45° C. (113° F.). Choay (*P. J.*, 1898, 505) criticizes the temperature for evaporation and recommends evaporation *in vacuo* at 38° C. (100.4° F.). Biernacki (*A. J. P.*, 1892) previously stated that digestive ferments require for their efficient action a temperature little over that of the human body, 39° C. (102.2° F.). The process described by R. V. Mattison, based on the method of Scheffer for obtaining pepsin, is as follows: Macerate the cut-up pancreas in water acidulated with hydrochloric acid for forty-eight hours; filter until clear. Add a saturated solution of sodium chloride, and allow to stand until pancreatin rises to the top; skim this, drain on a muslin filter, wash with a less concentrated solution of salt, and press until nearly dry; then rub up with sugar of milk, dry thoroughly, without heat, and dilute with sugar of milk until ten grains just emulsify two drachms of cod liver oil. The mixed pancreatic enzymes may be extracted from the gland by means of glycerin, and such an extract may be preserved indefinitely. A useful and permanent extract may also be obtained by exhausting the finely divided pancreas with water containing about 2 per cent. of boric acid and 1 per cent. of borax. (Allen, *Com. Org. Anal.*, 2d ed., vol. iv, 354.) The mixed pancreatic enzymes may also be extracted by means of glycerin which gives an active extract which may be preserved indefinitely, but one which cannot be reduced to the dry state. For this purpose the gland is finely minced, rubbed up with some clean sand, shaken with from 10 to 20 parts of glycerin and allowed to stand for about two weeks, then filtered. Another method of extracting its activity is by macerating the minced gland with four times its weight of 25 per cent. alcohol for four or five days. If the pancreas be allowed to stand for two or three days before extracting the resulting pancreatin will be richer in the trypsin and amylopsin, but will have very little fat splitting powers. Where it is desirable to make a pancreatin containing active lipase it should be made from the fresh gland.

As the amount of digestive ferment secreted by the pancreas varies greatly according to the time since feeding, it is manifest that pancreatic extract will contain more or less of the enzymes according to the time of the animal's death, and that the commercial pancreatin must consequently vary greatly in strength. As the power of pancreatin cannot be judged accurately by its physical appearance it is very important to have some test which will rigidly decide as to its value. If pancreatin be added to fresh milk without an alkali, in the course of a few minutes the liquid acquires the property of curdling abundantly upon boiling, and Wm. Roberts (*Digestive Ferments*, London, 1881) estimates the value of a pancreatin by the number of mils of milk which are transformed by one mil of the sample at a temperature of 40° C. (104° F.) to the curdling point in five minutes. (See *Liquor Pancreatis*, p. 650.)

A method of determining the value of pancreatin has been made official and is as follows:

Assay of Pancreatin. U. S. P. IX.—"Shake 10 Gm. or more of powdered potato starch (see Part II) with about 10 times its weight of cold distilled water, and, after draining the mixture on a filter, wash it with the same quantity of distilled water. Place the washed starch at once in an air bath and maintain a temperature of about 50° C. (122° F.) until the starch is sensibly dry. Reduce it to a fine powder and place it in a well-stoppered bottle. Determine the percentage of water still remaining in the starch by drying about 0.5 Gm. of it in an air bath, gradually raising the temperature to 120° C. (248° F.), and maintaining it at that temperature for four hours. Of the washed and partially dried starch, mix a quantity equivalent to 7.5 Gm. of dry starch in a 400 mil beaker with 10 mils of cold distilled water, add 190 mils of boiling distilled water and boil the mixture gently (for approximately five minutes) with constant stirring until a translucent uniform paste is obtained. Replace the water lost by evaporation and cool the paste to 40° C. (104° F.) in a water bath previously adjusted to this temperature and add a solution of 0.3 Gm. of Pancreatin in 10 mils of distilled water, just previously made at 40° C. (104° F.). Mix well and maintain the same temperature for exactly five minutes, when a thin, nearly clear liquid is produced. At once add 0.1 mil of this liquid to a previously made mixture of 0.2 mil of tenth-normal iodine V.S. and 60 mils of distilled water; no blue, red, or violet color is produced." *U. S.*

Uses.—Pancreatin was first used in medicine on account of its emulsifying properties. Horace Dobell, noticing that consumptives are very likely to have a dislike for fat, conceived the idea that this was due to lack of pancreatic digestion, and administered an emulsion made with the fat of beef stirred in milk with the pancreatic juice of the pig. A little later, pancreatic preparations of cod liver oil were prepared, and still have much vogue. Besides this employment, pancreatin has two distinct uses; first, as a ferment to be administered in dyspepsia; second, as a valuable means for the predigestion of food. As pancreatin acts in an alkaline solution and pepsin in an acid one, it would seem *a priori* not probable that pancreatin given by the stomach would be of avail in cases of feeble digestion. Nevertheless, as the experiments of Schweitzer, which have been confirmed by Gross, seem to show, some hours' digestion is necessary for the pancreatin to be destroyed by acid solutions. It is therefore probable that when given internally pancreatin may escape from the stomach into the intestines and the combination of pepsin and pancreatin in *dyspepsia* is not unphilosophical. In the predigestion of food by pancreatin, five grains of commercial pancreatin of good quality, with twenty grains of sodium bicarbonate, in an ounce of warm water, may be added to a pint of milk, and kept at the temperature of 43.3° C. (110° F.) for from twenty minutes to an hour. As the thoroughly peptonized or pre-digested food is very bitter, when the milk is to be given by the mouth it is better to arrest the peptonizing process by boiling the milk after digestion has continued for twenty to thirty minutes, unless the milk can be used at once. For receipts for preparing various peptonized foods, see H. C. Wood's *Therapeutics*. Nutritive enema should be thoroughly pancreatized.

Trypsin has been used in medicine in a variety of conditions. Beer (*Lancet*, 1905) has recommended it as a local treatment for *inoperable cancers*, Schiller (*K. T. W.*, 1910) in the treatment of *tuberculous abscesses*, and Lamballe (*N. Y. M. R.*, 1913) asserts that the intramuscular injection of solutions of trypsin have curative value in *malaria*.

Dose, of pancreatin, eight to fifteen grains (0.5–1.0 Gm.).

Off. Prep.—Liquor Pancreatis, *Br.;* Liquor Pancreatini, *N. F.;* Pulvis Pancreatini Compositus, *N. F.*

PARAFFINUM. U. S. (Br.)

PARAFFIN Paraff.

(păr-ăf-fī'nŭm)

"A purified mixture of solid hydrocarbons, usually obtained from petroleum." *U. S.* "Hard Paraffin is a mixture of solid hydrocarbons." *Br.*

Paraffinum Durum, *Br.*, Hard Paraffin; Paraffin Wax; Solid Paraffin; Paraffine, *Fr. Cod.;* Paraffinum solidum, *P. G.;* Festes Paraffin, Gereinigtes Erdwachs, *G.;* Parafina, *Sp.*

The name *paraffin*, often spelled *paraffine*, was originally bestowed by Baron von Reichenbach upon a waxy substance obtained through the destructive distillation of wood. He derived it from *parum affinis*, and thus intended to indicate its very neutral character. The name is now popularly applied to a solid white diaphanous substance, resembling white wax, which is procured from petroleum or bituminous shales by distillation, or from ozokerite by puri-

fication. (See *Ozokerite, Ceresin,* in Part II.) In the manufacture from petroleum, as carried out in the United States, the residuum from the distillation of crude petroleum for illuminating oil is taken. This is redistilled from what are called "tar stills," in which the distillation is pushed until only coke remains. The paraffin oil distillate obtained in this way is treated with from 4 to 5 per cent. of sulphuric acid, washed, and treated with caustic soda, the mixture being kept liquid by the aid of steam coils. After settling, the paraffin oil goes to the "chill-rooms," where, by the aid of the ammonia refrigerating machines and the circulation of cooled brine, the whole mass is brought to a semisolid condition. This is subjected to powerful pressure, and the refined heavy oil which drains off is collected as lubricating oil. Its specific gravity should be about 32° B. The press cake may be broken up, melted, and allowed to solidify, and then submitted to still greater pressure at a higher temperature 21.1° C. (70° F.) than before, when the product is known as "refined wax." To convert it into block paraffin it must be washed with petroleum benzin, pressed, melted, and filtered through bone black or other medium, when it solidifies in a hard, translucent, colorless condition.

Properties.—Paraffin, in its pure condition, is a white, waxy, inodorous, tasteless substance, harder than tallow, softer than wax, with a specific gravity of 0.900. Its melting point is variable, depending somewhat upon its origin. It ranges between 43° and 65° C. (109.4° and 149° F.). An ultimate analysis yields, on the average, carbon 85 per cent. and hydrogen 15 per cent. It is insoluble in water, is indifferent to the most powerful acids, alkalies, and chlorine, and can be distilled unchanged with strong oil of vitriol. Warm alcohol, ether, oil of turpentine, olive oil, benzene, chloroform, and carbon disulphide dissolve it readily. It can be mixed in all proportions with wax, stearin, palmitin, and resin. As stearin is less soluble in benzene than paraffin, Vogel proposes this reaction as a method for detecting the adulteration of paraffin with stearin. (Joy.) It is officially described as "a colorless, or white, more or less translucent mass, crystalline when separating from solution, without odor or taste, and slightly greasy to the touch. It is insoluble in water or alcohol; slightly soluble in dehydrated alcohol, freely soluble in ether, petroleum benzin, benzene, carbon disulphide, volatile oils, or in most warm fixed oils. Specific gravity: about 0.900 at 25° C. (77° F.). It melts between 50° and 57° C. (122° and 134.6° F.). When strongly heated, it ignites, burns with a luminous flame, and deposits carbon. Heat about 0.5 Gm. of Paraffin in a dry test tube with an equal weight of sulphur; the mixture becomes black from separated carbon, and hydrogen sulphide gas is evolved. Paraffin is not acted upon or colored by concentrated sulphuric acid or nitric acid in the cold. Shake melted Paraffin with an equal volume of hot alcohol; the separated alcohol does not redden moistened blue litmus paper (*acids*)." *U. S.*

The Br. Pharm. describes it as "colorless, crystalline, more or less translucent; wax-like, slightly greasy to the touch. No odor or taste. Melting point 50° to 60° C. (122°–140° F.). 5 millilitres of *alcohol* (90 per cent.) shaken with 5 grammes of the melted Paraffin are not acid to *litmus*. 5 grammes, when heated, burn with a luminous flame, leaving no appreciable ash." *Br.*

The fact that solid paraffin wax is essentially made up of a mixture of hydrocarbons of the series C_nH_{2n+2} was established by Gill and Meusel, who studied the action of bromine upon it. The fact that when paraffin wax is oxidized by concentrated nitric acid or by chromium trioxide mixture we obtain *paraffinic acid,* $C_{24}H_{48}O_2$, and *cerotic acid,* $C_{27}H_{54}O_2$, shows that it is essentially made up of hydrocarbons between $C_{24}H_{50}$ and $C_{27}H_{56}$. For *Soft Paraffin,* or *Paraffinum Molle,* see *Petrolatum,* p. 922.

It would be beyond the scope of this work to give all the uses of this very valuable substance. In the arts paraffin is used for many purposes, especially in the manufacture of candles, and sealing various vessels to exclude air. Lemons and eggs coated with paraffin may be kept for long periods of time without decomposition. It is also valuable to saturate paper, rendering it impervious to moisture. In pharmacy it is used chiefly to give stiffness to ointments. It was at one time employed in cosmetic surgery by injecting melted paraffin for filling out undesirable hollows. The treatment resulted in a number of cases, however, in extensive sloughing and has been largely abandoned.

PARAFORMALDEHYDUM. U. S.

PARAFORMALDEHYDE Paraform. [Paraform, Trioxymethylene, Triformal]

(păr-ă-fôr-măl-dē-hȳ′dŭm)

"It contains not less than 95 per cent. of $(HCHO)_3$ (90.05), a polymeric form of formaldehyde. Preserve it in well-closed containers in a cool place, protected from light." *U. S.*

Paraformaldehyde is always produced to a greater or lesser extent when solutions of formaldehyde are allowed to evaporate. The change from the ordinary into the polymeric form also takes place at low temperatures, especially when the solution is free from methyl alcohol. This is the way in which it is now produced commercially.

"Paraformaldehyde occurs in white, friable masses, or as a powder, having a slight odor of formaldehyde. On heating it is partly converted into formaldehyde and partly sublimed unchanged. It is slowly soluble in cold water, more readily soluble in hot water with the formation of formaldehyde; insoluble in alcohol or ether; soluble in fixed alkali solutions. A mixture of about 0.01 Gm. each of Paraformalde-

hyde and morphine sulphate and 10 drops of sulphuric acid assumes a violet-red color, changing to blue. Incinerate about 2 Gm. Paraformaldehyde; not more than 0.1 per cent. of ash remains. Shake about 0.5 Gm. of Paraformaldehyde, finely powdered, with 10 mils of distilled water; the latter remains neutral to litmus.

"**Assay.**—Mix about 1 Gm. of Paraformaldehyde, finely powdered and accurately weighed, with 50 mils of normal potassium hydroxide V.S. in a 250 mil flask, and add immediately, but slowly, through a small funnel, 50 mils of solution of hydrogen dioxide which has been previously rendered neutral to litmus with sodium hydroxide. When the reaction has ceased and the foam subsided, rinse the funnel and the sides of the flask with distilled water, allow the liquid to stand for half an hour and then determine the excess of alkali with normal sulphuric acid V.S., using litmus T.S. as indicator. It shows not less than 95 per cent. of $(HCHO)_3$.

"Each mil of normal potassium hydroxide V.S. corresponds to 0.03002 Gm. of $(HCHO)_3$. Each gramme of Paraformaldehyde corresponds to not less than 31.6 mils of normal potassium hydroxide V.S." *U. S.*

Uses.—Although trioxymethylene appears to possess some antibacterial properties *per se*, it is used chiefly as a source for the generation of formaldehyde. The especial utility of the substance for this purpose lies in the fact that by simply heating it is converted into the active gas. Special lamps are upon the market in which a small alcohol flame serves to at once depolymerize the paraform while the moisture from the combustion of the alcohol increases the activity of the formaldehyde. Rideal (*Disinfection and the Preservation of Food*, 1903, p. 309) finds that 10 Gm. of paraformaldehyde per thousand cubic feet of air space in a properly sealed room, is sufficient to destroy the vitality of most pathogenic organisms, but will not certainly kill those enclosed in bedding or similarly protected. The room should be left closed for twenty-four hours. Because of the comparative cost, however, this method is not to be recommended for disinfection of large spaces, but is very convenient for the sterilization of various surgical materials which might be injured by boiling. For this purpose small air-tight chambers are employed in which from 1 to 2 Gm. (15–30 grains) for each cubic yard of air space is evaporated.

Paraformaldehyde is also occasionally used internally as a gastro-intestinal disinfectant. Pauchet and Sourdat (*B. A. M.*, 1914) highly laud gauze impregnated with paraform for the treatment of gunshot and other *wounds*. For the preparation of this the gauze is placed in a tin box with a few tablets of trioxymethylene and the box closed, and then put in a warm place, about 50° C. (122° F.) for an hour. It is also used externally as a caustic, for the destruction of warts, in 10 per cent. solution.

***Dose*, five to fifteen grains (0.3–1.0 Gm.)**

PARALDEHYDUM. U. S., Br.

PARALDEHYDE Paraldehyd.

(pa-răl-dē-hī'dŭm)

"A polymer $[(CH_3CHO)_3 = 132.10]$ of acetaldehyde. Preserve it in well-closed containers, in a cool place, protected from light." *U. S.*

"Paraldehyde, $C_6H_{12}O_3$, is a product of the polymerisation of acetaldehyde." *Br.*

Paraldéhyde, Elaldéhyde, *Fr. Cod.*; Paraldehydum, *P. G.*; Paraldehyd, *G.*; Paraldehido, *Sp.*

Small quantities of acids like hydrochloric and sulphuric, and of certain salts like zinc chloride, $ZnCl_2$, convert aldehyde at ordinary temperatures into its polymer *paraldehyde*. Commercially it is prepared by the action of hydrochloric upon aldehyde until the resulting product is no longer soluble in its own volume of water, and then purifying by redistillation and freezing and expressing. Its properties are thus described officially: "Paraldehyde is a colorless, transparent liquid, having a strong, characteristic, but not unpleasant or pungent odor, producing first a burning and then a cooling sensation in the mouth. One mil of Paraldehyde dissolves in 8 mils of water at 25° C. (77° F.); also in 17 mils of boiling water; miscible with alcohol, chloroform, ether, or volatile oils. It is neutral or only slightly acid to moistened litmus paper. Specific gravity: about 0.990 at 25° C. (77° F.). It boils between 120° and 125° C. (248° and 257° F.). Congealing point: not below 6° C. (42.8° F.). When heated with a small portion of sulphuric acid, Paraldehyde is converted into acetaldehyde, recognizable by its odor. Heat 5 mils of Paraldehyde on a water bath; no disagreeable odor is noticeable as the last portions evaporate (*impurities derived from fusel oil*) and not more than 0.0025 Gm. of residue remains. One mil of Paraldehyde forms a clear solution free from oily drops with 10 mils of distilled water (*amyl alcohol*), and 5 mil portions of this solution, tested separately, when acidulated with nitric acid, yield no turbidity on the addition of a few drops of barium chloride T.S. (*sulphuric acid*) nor an opalescence with a few drops of silver nitrate T.S. (*hydrochloric acid*). A mixture of 8 mils of Paraldehyde and 8 mils of alcohol with 1 drop of phenolphthalein T.S. acquires a pink color upon the addition of 0.5 mil of normal potassium hydroxide V.S. (*free acid*). Shake 5 mils of Paraldehyde with 5 mils of potassium hydroxide T.S.; the aqueous layer is not colored yellow or brown within one hour (*acetaldehyde*)." *U. S.*

The British Pharmacopœia gives the following properties and tests: "A clear, colorless liquid. Characteristic, ethereal odor; taste acrid, afterwards cool. Soluble in 9 parts of *water;* less soluble in hot *water*. Miscible in all proportions with *alcohol* (90 per cent.), and with *ether*. Aqueous solution neutral or only slightly acid to *litmus*. Specific gravity 0.998 to

1.000. Solidifies at a low temperature; melting point not under 10° C. (50° F.). Not more than 5 per cent. distils under 123° C. (253.4° F.), and the remainder distils between 123° and 125° C. (253.4° and 257° F.). When 5 millilitres are shaken with 5 millilitres of *solution of sodium hydroxide* and allowed to separate, the aqueous layer does not exhibit more than a faint yellow coloration within one hour (limit of acetaldehyde). An aqueous solution (1 in 10) yields no characteristic *reactions* for chlorides or for sulphates." *Br.*

Uses.—In moderate doses paraldehyde causes, both in man and the lower animals, sleep which is indistinguishable from natural sleep and is unaccompanied with any marked change in the circulation, respiration, or sensibility. After large quantities the sleep becomes of a more comatose character, there is diminution of reflex activity and considerable slowing of the respiration, the circulation, however, being scarcely affected. It is asserted by Quinquaud that after fatal doses methemoglobin appears in the blood. Death is alleged to have been produced by four ounces in man, but Probst reports a case in which five ounces were taken within a period of sixty hours, causing a profound coma, lividity, and slight fall of bodily temperature, but with no pronounced circulatory disturbances and recovery on the seventh day. It is eliminated partly through the urine and partly with the breath in each of which it may be detected by its odor.

Paraldehyde is a promptly acting somnifacient of moderate power, useful in those types of *sleeplessness* which are not dependent upon pain. Its effects are generally manifest within fifteen to thirty minutes and last two or three hours. Its chief disadvantages are its occasional tendency to cause gastric disturbance and the unpleasant odor which it imparts to the breath. It has also been recommended for the relief of *asthma.*

Dose, one-half to one and one-half fluidrachms (1.8–5.5 mils).

PELLETIERINÆ TANNAS. U. S., Br.

PELLETIERINE TANNATE Pellet. Tann.

(pĕl-lę-tĭ-ę-rĭ'næ tăn'năs)

"A mixture in varying proportions of the tannates of four alkaloids (punicine, isopunicine, methyl-punicine, and pseudo-punicine), obtained from pomegranate. Preserve it in small, well-closed containers, protected from light." *U. S.* "Pelletierine Tannate is a mixture of the tannates of the alkaloids obtained from the bark of the root and stem of Punica Granatum, *Linn.*" *Br.*

Pelletierinum Tannicum, Punicinum Tannicum; Punicine Tannate; Tannate de Pelletiérine, *Fr. Cod.*; Gerbsaures Pelletierin, Punicin, *G.*

Preparation.—The bark of *Punica Granatum* is ground, and mixed with milk of lime; the mixture is percolated with water, the percolate shaken with chloroform, and the separated chloroformic liquid which contains in solution the mixed alkaloids, is treated with a weak solution of sulphuric acid; upon the addition of a solution of tannic acid to the neutralized acid solution of the alkaloids, tannates are precipitated; these are washed and dried.

Properties.—The alkaloidal mixture known as Pelletierine Tannate is officially characterized as follows: "A light yellow, odorless, amorphous powder, having an astringent taste, and a weak acid reaction. One Gm. of Pelletierine Tannate dissolves in 240 mils of water, 16 mils of alcohol, and in 420 mils of ether at 25° C. (77° F.); dissolved by warm dilute acids; insoluble in chloroform. Ferric chloride T.S. colors aqueous solutions of the salt blue-black. No weighable ash remains on incinerating 0.2 Gm. of Pelletierine Tannate. Platinic chloride T.S. produces no precipitate in a cold solution of about 0.1 Gm. of Pelletierine Tannate in a mixture of 4 mils of distilled water and 1 mil of diluted hydrochloric acid (*foreign alkaloids*). Dissolve about 0.5 Gm. of Pelletierine Tannate, accurately weighed, in 5 mils of potassium hydroxide T.S. and shake the solution in a separator with 10 mils of chloroform and then with two or more successive portions of 5 mils each of chloroform. Acidulate the combined chloroform solutions with 0.1 mil of hydrochloric acid, evaporate it to apparent dryness, dissolve the residue in 5 mils of alcohol, again evaporate, and dry for one hour at 60° C. (140° F.). The weight of residue so obtained corresponds to not less than 20 per cent. of the weight taken. The residue obtained in the preceding test responds to the following tests for identity and purity. Stir about 0.001 Gm. of the residue on a white porcelain surface with 2 drops of sulphuric acid containing 0.005 Gm. of selenous acid in each mil. and warm the mixture; a light bluish-green color is produced which gradually changes to dark green. Stir about 0.001 Gm. of the residue on a white porcelain surface with 2 drops of sulphuric acid or nitric acid; no color other than a light yellow is produced." *U. S.*

"A light yellow, amorphous powder. Slightly soluble in *water,* more soluble in *alcohol* (90 per cent.). An aqueous solution gives with *T. Sol. of ferric chloride* a bluish-black color; with *solution of silver nitrate* a brown color rapidly deepening, with separation of metallic silver; and with *solution of auric chloride* a deep purple color, with separation of metallic gold. When heated, Pelletierine Tannate turns brown at about 150° C. (302° F.), softens at about 165° C. (329° F.); and at a higher temperature decomposes without melting. No appreciable ash." *Br.*

Uses.—Pelletierine tannate represents the tenicidal properties of Granatum, see page 533.

Dose, three to five grains (0.2–0.3 Gm.).

PEPO. U. S. (Br.)

PEPO [Pumpkin Seed]

(pē'pō)

"The dried ripe seeds of cultivated varieties of *Cucurbita Pepo* Linné (Fam. *Cucurbitaceæ*), without the presence or admixture of more than 5 per cent. of other substances." *U. S.* "Melon Pumpkin Seeds are the prepared fresh ripe seeds of cultivated plants of Cucurbita maxima, *Duch.* Melon Pumpkin Seeds must not be more than one month old, and when required for use about 100 grammes are bruised with a little water or milk to a creamy consistence and administered as a single dose." *Br.*

Cucurbitæ Semina Præparata, *Br.;* Melon Pumpkin Seeds; Semen Peponis, Semina Cucurbitæ; Semences de Potirons ou de Courge, *Fr.;* Kürbissamen, Kürbiskörner, Graumontsamen, *G.;* Calabaza (Semilla), *Sp.*

The *Cucurbita Pepo,* or *common pumpkin,* is a plant almost too well known to need description. The seeds are the part used. These are officially described as follows: "Broadly elliptical or ovate, from 15 to 23 mm. in length and from 2 to 3 mm. in thickness; externally yellowish-white, very smooth, occasionally with thin, transparent fragments of adhering pulp and with a shallow groove parallel to and within 1 mm. of the margin; fracture short, seed-coat consisting of a white coriaceous outer layer and a membranous inner layer occasionally of a dark green color; embryo whitish, straight, with a small conical hypocotyl and two plano-convex cotyledons; slightly odorous when contused; taste bland and oily. Under the microscope, sections of Pepo show an outer epidermal layer consisting of palisade-like cells, the radial walls attaining a length of 1 mm., the outer walls being usually torn off so that it appears as though the seeds were covered with very long hairs; a sub-epidermal layer consisting of from 5 to 12 rows of cells with slightly thickened, lignified and porous walls; a layer of strongly lignified stone cells, elliptical in outline and about 0.075 mm. in length; a single layer of small cells resembling those of the sub-epidermal layer; several rows of parenchyma cells with characteristic reticulate markings and separated from each other by large intercellular spaces; several layers of parenchyma cells, the inner layer being more or less collapsed and bounded on the inside by a single epidermal layer, the cells having rather thick walls; the perisperm cells are usually more or less collapsed and the endosperm consists of a single layer of cells filled with small aleurone grains; the cotyledons consist of thin-walled, isodiametric, elongated or palisade-like cells containing a fixed oil and numerous small aleurone grains." *U. S.*

The British Pharmacopœia recognizes the melon pumpkin seeds, under the title of *Cucurbitæ Semina Præparata.* These are derived from a closely related species, *Cucurbita maxima* Duch., which closely resembles *C. Pepo* and differs in that the margins of the leaves possess rounded teeth, whereas in *C. Pepo* they are acute. The British definition and description are as follows: "Flat, ovate, white, and exalbuminous, consisting of two fleshy, easily separable cotyledons, freshly deprived of the yellowish outer, and brownish inner integument. Faint odor; taste very slight. Before preparation, the seeds measure from eight to twenty millimetres in length, and from nine to twelve millimetres in breadth." *Br.*

They contain a fixed oil, consisting of the glycerides of palmitic, myristic, and oleic acids, with some free fatty acid, an aromatic principle, chlorophyll, sugar, starch, and, according to Dorner and Wolkowich, an alkaloid, *cucurbitine.* Deprived of their coating, and exhausted by ether, they yield 30 per cent. of fixed oil. (*Ann. Thér.,* 1862, p. 176.) The researches of Dorner and Wolkowich have not received confirmation, and their alkaloid probably has no existence. Pumpkin seed oil has a sp. gr. at 15° C. (59° F.) of 0.923, and solidifies at –15° C. (5° F.). The cold drawn oil is used for culinary purposes and the lower qualities for burning. The oil dries very slowly. (Lewkowitsch, *Chem. Analysis of Oils,* etc., 2d ed., 1898, 372.) Sieker obtained 30 per cent. of the oil from the seeds; it was reddish-yellow in color, soluble in ether, benzene, and carbon disulphide, but insoluble in alcohol. (*Proc. A. Ph., A.,* 1897, 545.) Willard Graham endeavored to prepare *Oil of Pumpkin Seed* by expression, but failed to obtain appreciable quantities even under a pressure of 3000 pounds. By extraction with acetone the ground seed yielded 25 per cent. of oil, clear reddish, limpid, and of agreeable odor and taste. Its sp. gr. at 15° C. (59° F.) was 0.9208; saponification number, 192.5; acid number, 18.9; ether number, 173.6; soluble in all proportions of carbon disulphide, ether, chloroform, and in twenty parts of absolute alcohol, and drying on standing to a tough, yellowish, transparent mass. These properties and constants agree well with a commercial specimen, evidently also obtained by extraction. The latter, however, had a lower acid number, 3.5, while the ether number was somewhat higher, 191.7. (*A. J. P.,* 1901, 352.) J. C. Lyons used an ounce of the oil with success in a case of tapeworm (*A. J. P.,* 1865, 253), but Wolff has found it inert when pure and free from resin, which he prepares by extracting the oil from the powdered seeds by means of petroleum benzin, then treating the remaining powder with ether, chloroform, and alcohol, which yields on evaporation a soft greenish-brown resinous liquid resembling the oleoresin of male fern. Heckel was the first to assert that the active principle is a resin, and in this he has been corroborated by L. Wolff (pamphlet, Phila., 1882), who found the resin to be efficient in doses of fifteen grains (1 Gm.), given in pill followed in two or three hours by castor oil, and who recommends an alcoholic fluidextract as the best preparation of the drug after the resin.

Power and Salway (*J. Am. C. S.*, 1910, p. 346) found the resin as well as the oil which they separated from the seed, destitute of anthelmintic powers.

W. E. Miller (*A. J. P.*, 1891, 585) analyzed both the shells and the kernels of pumpkin seed. He also found a resin soluble in alcohol, and a dark reddish fixed oil.

Uses.—It is said that in Italy the seeds of the *Cucurbita maxima,* and in the West Indies those of *C. occidentalis,* have been long used in doses of an ounce and a half as tenifuges. In the *Dictionary of Materia Medica* by Mérat and De Lens (ii, 493) it is stated that Hoarau had reported that in the Isle of France the seeds of a small variety of pumpkin were used against the *tapeworm,* and with never-failing success. In the year 1820, Mongeney, a physician of Cuba, published the results of his experience with the flesh of the pumpkin in the same disease. He had discovered the remedy by accident, and found it uniformly successful. He gave to the patient, in the morning, fasting, about three ounces of the fresh pumpkin in the form of a paste, and followed it at the end of an hour by about two ounces of honey, which latter was twice repeated at intervals of an hour. So far as we know, attention was first directed to it in this country by Richard Soule. (*B. M. S. J.*, Oct., 1851.) Since this time the drug has steadily grown in favor, and, properly used, is one of our most efficient and harmless tenifuges. The patient should be allowed only a light supper of bread and milk, in the morning early should take an ounce and a half of the seeds, a cup of tea or coffee an hour later, but no food, at 10 A.M. a brisk cathartic, and two hours later a substantial meal. We have obtained excellent results from the exhibition of the beaten seeds in the form of an electuary strongly flavored with oil of cinnamon or of gaultheria.

Dose, one to two ounces (31–62 Gm.).

PEPSINUM. U. S., Br.

PEPSIN Pepsin.

(pĕp-sĭ'nŭm)

"A mixture containing a proteolytic ferment or enzyme, obtained from the glandular layer of the fresh stomach of the hog (*Sus scrofa,* var. *domesticus* Gray) (Fam. *Suidæ*). It digests not less than 3000 times its own weight of freshly coagulated and disintegrated egg albumen. Pepsin of a higher digestive power may be brought to this standard by admixture with pepsin of a lower digestive strength or with sugar of milk. Preserve it in well-closed containers." *U. S.* "Pepsin is an enzyme obtained from the fresh and healthy stomach of the pig, sheep, or calf." *Br.*

Pepsine, *Fr. Cod;* Pepsinum, *P. G.;* Pepsin, *G.;* Pepsina, *It.;* Pepsina medicinal, *Sp.*

The U. S. P. 1890 recognized two pepsins, one under the name "Pepsinum," the other "Pepsinum Saccharatum": the first, or strong pepsin, should digest at least 3000 times its own weight of freshly coagulated albumin; the other is the first product diluted with enough sugar of milk to make it contain 10 per cent. of the strong pepsin. The U. S. P. (8th Rev.) retained the standard of strength of the previous Pharmacopœia for the strong pepsin, but modified the assay process, and dropped Saccharated Pepsin, but the latter is included in the N. F. IV. (See Part III.) The U. S. P. IX pepsin is practically the same as that of the previous edition.

It is now clearly recognized that pepsin owes its digestive action to the presence of a ferment or enzyme, and, although many researches have been made to obtain the pure principle, the nearest approaches have resulted only in producing pepsin of increased digestive power. Pepsins having much greater digestive capacity than that chosen for the U. S. official standard have been manufactured, but for all practical purposes the official pepsin is sufficiently concentrated, and indeed it is usually diluted for internal administration.

Various attempts have been made to concentrate and bring to a convenient form for administration the peptic principle of the gastric juice. It must not be supposed that the substances prepared with this object and sold under the name of pepsin have any claim to be considered as a pure definite principle. The one which for a long time was the best in the market was prepared by Boudault by a process which was afterwards essentially adopted in a former French Codex.

The U. S. Pharmacopœia recognized pepsin for the first time in the revision of 1880, but it had then been for some years largely used by the American profession. Much of the pepsin thus employed was obtained from Europe, and was of very various quality, most of it being heavily loaded with starch, and some of it containing little or no pepsin. Several American brands were early put upon the market which were superior to Boudault's pepsin. For the process for *Boudault's pepsin,* see *U. S. D.,* 17th ed., 1014. Various processes also have been recommended for obtaining pepsin. The most elaborate and valuable investigation of the subject as yet made is that of E. Scheffer (*A. J. P.,* 1872). He found that various salts, such as sodium and magnesium sulphates and sodium chloride, precipitate pepsin, and, acting upon this discovery, he devised the following processes: Mucous membrane of the pig's stomach, dissected off and finely chopped, is macerated in water acidulated with hydrochloric acid for several days, with frequent stirring. The strained liquid, if not clear, is clarified by allowing it to stand for twenty-four hours and decanting. Sodium chloride is then thoroughly mixed with it. After several hours the floating pepsin is skimmed from the surface and put on a cotton cloth to drain, and finally submitted to strong pressure

to get rid of saline solution." This pepsin, when air dried, is very tough, parchment-like or leathery, varying in color from a dim straw-yellow to a brownish-yellow. To make his *saccharated pepsin,* Scheffer added sugar of milk until a powder was obtained of which 10 grains dissolved 120 grains of coagulated albumin. After framing his original process, he increased the strength of saccharated pepsin. *Purified pepsin* he made by redissolving the pepsin in acidulated water and precipitating as before, immersing the product when perfectly dry in pure water for a short time. A half-grain of this dissolved 1500 grains of albumin.

The chemical relations of pepsin are so delicate and wide spread that it ought to be given by itself, or in combination only with an insoluble substance, or suspended in inert liquids. For an interesting paper by B. T. Fairchild on Animal Digestive Ferments, reader is referred to *A. J. P.,* Feb. and Mar., 1902.

Since Scheffer's researches were made known, pepsin has been manufactured in the United States in immense quantities, the tendency having been towards strengthening and purifying the product. For Jenkin's process for making pepsin on a large scale, see *U. S. Dispensatory,* p. 920, 19th ed. Many other substances than sugar of milk have been used to mix with pepsin, as egg and blood albumin, fibrin, and substances which are easily converted into peptones. The process for making most commercial pepsins may be briefly stated as follows. The inner membranous linings of hogs' stomachs are washed, passed through a mincing machine, and the resulting mass digested with diluted hydrochloric acid; the solution is strained or filtered and evaporated *in vacuo* or placed on shallow trays, so that a syrupy liquid which has not been subjected to a higher temperature than 44.5° C. (112° F.) is produced; this is spread upon glass plates to dry, and the scales which are formed scraped off. The thickness of the scales may be varied by using more or less concentrated solutions, and the proportion of peptone is increased by extending the length of time in the digestion process and raising the temperature to the utmost safe limit. Numerous pepsins of value are upon the market, and they are so readily tested that the practitioner need not be at a loss. (See *Proc. A. Ph. A.,* 1884, 1886, and 1890; *Ph. Rec.,* 1893, 104; *West. Drug.,* 1887, 69; *Am. Drug.,* 1885, 103.)

Properties.—Pepsin is in "lustrous, white, pale yellow or yellowish, transparent or translucent scales, grains or spongy masses, or as a fine, white or cream-colored, amorphous powder, free from any offensive odor, and having a slightly acid or saline taste. It is not more than slightly hygroscopic. One Gm. of Pepsin dissolves in about 50 parts of water, the solution being more or less opalescent; nearly insoluble in alcohol, chloroform or ether. An aqueous solution of Pepsin (1 in 50) is acid to litmus. When in solution, Pepsin is incompatible with alkalies, alkali earths, or alkali carbonates. The presence of hydrochloric acid of greater strength than 0.5 per cent. in Pepsin solutions inhibits its proteolytic activity. A precipitate is produced in its solution by the salts of many heavy metals, and by tannic acid or gallic acid. A saturated solution of Pepsin in acidulated water when heated to 100° C. (212° F.) becomes milky, or yields a light, flocculent precipitate, and loses all proteolytic power. In a dry state it is not injured if subjected to the above temperature. The activity of Pepsin in solution is destroyed by temperatures exceeding 70° C. (158° F.).

"**Assay.**—Mix 25 mils of normal hydrochloric acid V.S. with 275 mils of distilled water and dissolve 0.1 Gm. of Pepsin in 150 mils of this liquid. Immerse a hen's egg, which is not less than five nor more than twelve days old and has been kept in a cool place, in boiling water during fifteen minutes. As soon as the egg has sufficiently cooled to handle it, remove the pellicle and all of the yolk; at once rub the albumen through a clean, dry, hair or brass, No. 40 sieve, reject the first portion that passes through the sieve, and place 10 Gm. of the succeeding portion in a wide-mouthed bottle of 100 mils capacity. Immediately add 2 mils of the acid liquid and, with the aid of a rubber-tipped glass rod, moisten the albumen uniformly. Again add 2 mils of the acid liquid, repeat the manipulation with the glass rod, and with gradually increasing portions of the acid liquid, until the total amount added measures 20 mils. Thoroughly separate the particles of albumen from each other, rinse the rod with 15 mils more of the acid liquid, and, after warming the mixture to 52° C. (125.6° F.), add exactly 5 mils of the solution of Pepsin. At once cork the bottle securely, invert it three times, and place it in a water bath that has previously been regulated to maintain a temperature of 52° C. (125.6° F.). Keep it at this temperature for two and one-half hours, agitating the contents every ten minutes by inverting the bottle once. Then remove it from the water bath, pour the contents into a conical measure having a diameter not exceeding 1 cm. at the bottom, and transfer the undigested egg albumen which adheres to the sides of the bottle to the measure with the aid of small portions (about 15 mils at a time) of distilled water, until the total amount used measures 50 mils. Stir the mixture well and let it stand for half an hour; the deposit of undissolved albumen does not then measure more than 1 mil. The relative proteolytic power of Pepsin, stronger or weaker than that just described, may be determined by ascertaining through repeated trials the quantity of the Pepsin solution, made as directed in the assay, required to digest, under the prescribed conditions, 10 Gm. of boiled and disintegrated egg albumen. Divide 15,000 by this quantity expressed in mils to ascertain how many parts of egg albumen one part of Pepsin will digest." *U. S.*

"A light yellowish-brown powder, or pale

yellowish, translucent scales, having a faint odor. Tested as follows it dissolves 2500 times its weight of coagulated white of egg in six hours, the resulting solution being faintly opalescent:—Prepare some coagulated white of egg by boiling fresh eggs in water for fifteen minutes, immersing them in cold water until cool, separating the whites, at once rubbing these through a hair-sieve having 12 meshes to a centimetre, and using the product before it has lost moisture by evaporation. Prepare also a Pepsin solution by triturating 0.25 gramme of the Pepsin with 1 gramme of *sodium chloride* in a small mortar until thoroughly mixed, adding by degrees acidified water (prepared by diluting 6.5 millilitres of *hydrochloric acid* to 1000 millilitres with *water*), continuing the trituration, transferring to a litre flask, washing the mortar with acidified water, and adding the washings to the contents of the flask until 1000 millilitres are produced, then shaking frequently during six hours, and again immediately before use. Introduce 20 millilitres of the Pepsin solution so prepared into a 250 millilitre flask. Triturate 12.5 grammes of the freshly prepared coagulated white of egg in a small mortar with 50 millilitres of acidified water until reduced to uniform granules. Transfer to the flask, rinsing the mortar with a further 50 millilitres of acidified water, adding the rinsing to the contents of the flask. Immerse the flask in a water-bath so that its contents are on a lower level than the water in the bath, and digest at a temperature between 40° and 41° C. (104° and 105.8° F.) for six hours, shaking at intervals of fifteen minutes." *Br.*

In estimating the proteolytic power of pepsin by any method it is very important to adhere strictly to each requirement, otherwise great variations may be expected. (*Proc. A. Ph. A.*, 1893, 411, 722; 1894, 221; 1895, 244, 338; 1896, 260, 263; 1897, 745; *Am. Drug.*, 1894, 212; 1895, 101; *D. C.*, 1896, 52; *P. J.*, 1897, 561; *Proc. A. Ph. A.*, 1899, 307; *Ap. Ztg.*, 1900, 485, 512; *D. C.*, March, 1902.)

Three distinct types of pepsin are found in commerce: (1) Pepsins insoluble in water without the addition of traces of acids; (2) Pepsins soluble in water forming transparent solutions; (3) Pepsins not entirely soluble in water or in diluted hydrochloric acid. The objection to the insoluble pepsins is, of course, the inconvenience resulting from their insolubility in water, but, on the other hand, they are not hygroscopic, do not deteriorate so rapidly, and are active in contact with the gastric juice. The objection to the soluble pepsins is that they are hygroscopic, but they are, when good, well suited for making solutions, wines, etc. Most of the pepsin used at the present time is what is known as scale pepsin and contains from 8 to 12 per cent. of hydrochloric acid.

The inner coat of the gizzard of the South American ostrich is said, in the state of powder, to be used in Buenos Ayres as a remedy in *dyspepsia* (E. S. Wayne, *A. J. P.*, March, 1868, p. 123), and the dried crops and gizzards of chickens and turkeys have long been used in some portions of this country as a domestic remedy. For an account of *Rennet*, see Part II.

Carl T. Hackenberg (*Ph. Ztg.*, 1913, p. 592) condemns the practice of pharmacists of keeping on hand stock solutions of pepsin and alleges that in the concentration of hydrochloric acid necessary to preserve them the deterioration in proteolytic power is rapid. The peptic ferment is an extremely unstable body being destroyed by tannins, alcohol, the salts of the heavy metals and strong acids. Tocher, as the result of an experimental study, concludes that: Solutions of sodium bicarbonate, sodium, potassium, and ammonium hydrates when added to solutions of pepsin in the cold have an immediate inhibitory or destructive effect on pepsin, according to the concentration; dilute solutions of caustic alkali immediately destroy the activity of dilute solutions of pepsin; carbonate of bismuth precipitates pepsin from aqueous solutions; sub-nitrate does not; compound mixtures containing solution of bismuth, morphine, carmine, etc., should contain no pepsin, since the activity of the enzyme is much retarded by the morphine and is destroyed proportionately to the amount of alkali present in solution. (*Year Book of Pharmacy*, 1906, pp. 307–313.)

Uses.—Gastric juice was used by Dr. P. S. Physick, the celebrated physician of Philadelphia, nearly a century ago as a local application in *cancers* and *sloughing ulcers*, with a view of removing the dead flesh and correcting the offensive odor and affording a healthy stimulus to the diseased surface. The first to have suggested pepsin as a remedy in disturbances of the stomach seems to have been Corvisart. (*J. P. C.*, xxx, p. 169.) It is now very largely used with the idea of improving the digestive powers of the stomach by supplying the essential ferment. Its value in *dyspepsia*, however, is greatly over-estimated. *Pepsinogen*—from which the active peptic enzyme is derived by the action of the hydrochloric acid—is rarely lacking save in cases of cancer and other very severe diseases of the stomach. When gastric digestion fails it is generally because of the absence of hydrochloric acid in sufficient quantity to activate the pepsinogen. Therefore in our opinion pepsin is not indicated in the ordinary types of *indigestion* or *gastritis*. It appears, however, to have some sedative influence upon the mucous membrane of the stomach, not due to its digestive powers, and is often of service for the relief of certain forms of *nausea* and to lessen the ill effects of such drugs as the iodides and salicylates upon the stomach. Locally it is still used occasionally for the purpose of dissolving the false membrane in *diphtheria* and hastening the sloughing off of dead tissue in *foul ulcers*.

It would seem trite to say that when pepsin

is used as a digestive ferment it must be given in an active form and in sufficient dose to have some influence, were it not for the fact that this truism is so often forgotten. The enzymic activity of pepsin is so easily destroyed by heat and chemical agents, that it should be administered always either alone as a powder or in solution with minute quantities of hydrochloric acid only. The dose of four or five grains of pepsin so often recommended is quite inadequate to seriously influence gastric digestion; if the physician is employing the pepsin with any idea of hastening digestion he should give at least from fifteen to thirty grains (1–2 Gm.) at a dose.

Pepsin should preferably be administered in its original form. It is well to combine it with hydrochloric acid, and the powder is often advantageously exhibited in *infantile diarrhea* along with bismuth subnitrate. With these exceptions, it is usually preferable to give it by itself.

Dose, of official pepsin, may be set down as from ten to sixty grains (0.65–3.9 Gm.).

Off. Prep.—Glyceritum Pepsini, *Br.;* Elixir Pepsini (from Glycerite), *N. F.;* Elixir Pepsini, Bismuthi et Strychninæ, *N. F.;* Elixir Pepsini et Bismuthi, *N. F.;* Elixir Pepsini et Ferri, *N. F.;* Elixir Pepsini et Rennini Compositum, *N. F.;* Glyceritum Pepsini, *N. F.;* Liquor Pepsini (from Glycerite), *N. F.;* Liquor Pepsini Antisepticus, *N. F.;* Liquor Pepsini Aromaticus, *N. F.;* Pepsinum Saccharatum, *N. F.;* Succus Citri et Pepsini (from Glycerite), *N. F.;* Vinum Pepsini (from Glycerite), *N. F.*

PETROLATUM. U. S. (Br.)

PETROLATUM Petrolat. [Petroleum Ointment, Petroleum Jelly, Petrolatum Molle, Petrolatum Spissum, U. S., 1890]

(pĕt-rō-lā′tŭm)

"A purified mixture of semi-solid hydrocarbons, obtained from petroleum." *U. S.* "Soft Paraffin is a mixture of semi-solid hydrocarbons." *Br.*

Paraffinum Molle, Soft Paraffin, *Br.;* Adeps Petrolei, Unguentum Paraffinum; Soft Petrolatum, Cosmoline, Vaseline, Paraffin Jelly, Soft Petroleum Ointment, Hard Petroleum Ointment, Hard Petrolatum; Pétroléine, *Fr. Cod.;* Graisse minérale, Pétréoline, *Fr.;* Weiches Paraffin, Paraffinsalbe, *G.;* Vaselina, *It., Sp.*

Petrolatum in its various forms has of late years acquired considerable importance, under various trade names, as a bland neutral body well fitted to take the place of animal and vegetable fats as a base for ointments and for other purposes. It is prepared from the residue left in the stills after a distillation of petroleum *in vacuo,* or from the residue or sediment deposited in tanks containing crude petroleum, of which large quantities collect in the storage tanks in the oil districts of Western Pennsylvania. The substances known commercially as *cosmoline* (*Unguentum Petrolei*) and *vaseline* are now made on a large scale from residues, but more largely from what are termed "reduced oils," that is, crude oils from which the lighter fractions (those included under the heads of petroleum benzin, naphtha, illuminating and paraffin oils) have been removed by distillation. This process of reducing would leave an increasing amount of black pyrogenous products in the residue, were it not that the reducing is carried out under diminished pressure, by what is termed the "vacuum process," in which, moreover, the heat is not applied directly to the still bottoms, but by means of coils of pipe, through which superheated steam is made to pass. These reduced oils can be brought to 337.7° C. (640° F.) fire-test without acquiring the slightest pyrogenous odor. They are then filtered through well-dried bone black, in chambers kept at a temperature of from 43.3° to 54.4° C. (110°–130° F.), or in some cases higher. The first portions of the filtrate are colorless, and then pass from a light straw or amber color to a color red by transmitted light and light green by reflected light. The latter product is known as "cylinder stock," and is highly prized as a lubricating oil. The clearer portion of the filtrate is then brought to the proper melting point, if necessary, by the addition of pure block paraffin, which dissolves perfectly in the warm liquid oil. The crude oil tank residues are purified in a similar manner. The "B. S. Oil," or "rod wax," as it is technically termed, is placed in a still, heat applied, and after the lighter products have distilled over, and indications of congelation are noticed when a portion of the distillate is allowed to cool, the heat is withdrawn, and the contents of the still, after having cooled, are transferred gradually to a percolator which contains recently heated animal charcoal. In place of bone black, clay has in recent years been quite largely used for clarifying purposes, the same being revivified by heat. A somewhat different process is used in Germany; the crude product is derived from crude *ozokerite,* obtained from Alsace and Galicia, or American residue is sometimes used. (1) The oil is heated by steam to about 30° C. (86° F.), mixed, at this temperature, with 10 per cent. of its weight of sulphuric acid of 60° B., stirred for half an hour, and then allowed to stand at rest, so that the carbonized portions may separate. (2) When clear, the oil is washed with an aqueous solution of potassium dichromate, whereby any remaining excess of sulphuric acid is at the same time removed. (3) The residue from the acid treatment is mixed with lime, neutralized, and disposed of to fertilizer factories. (4) The clear oil from the second step of the process, after being washed, is heated by steam to 80° C. (176° F.), mixed with 10 per cent. of its weight of granular animal charcoal, and then allowed to stand at rest, to permit the animal charcoal to settle. (5) After the latter is separated, the liquid portion is filtered through filters heated by steam. (6) The residuary magma of animal charcoal is subjected to hydraulic pressure, the expressed

oil filtered, and the solid residue again used in the next operation, a sufficient quantity of fresh animal charcoal being added to make up for any loss or waste.

The commercial varieties of petrolatum may be classed under two heads: (1) Those which, like the American vaseline, are obtained as a ready formed mixture of hydrocarbons of gelatinous consistence; (2) those made by directly mixing solid paraffin of low melting point with heavy lubricating oil, such as are known in Germany as "artificial vaseline." The latter varieties are less homogeneous, and are liable to deposit granules of paraffin on keeping, and hence are not so suited for the preparation of ointments as true American petrolatum.

In warm ether, American petrolatum dissolves freely to a clear solution exhibiting a strong blue fluorescence, and the liquid remains clear, or at most becomes only slightly turbid, on cooling. German petrolatum, on the contrary, is said to form a thick solution with warm ether, and to give a considerable deposit on cooling. Russian petrolatum is stated to dissolve completely in warm ether and give a clear solution which becomes turbid on cooling. (Allen, *Com. Org. Anal.*, 2d ed., 1887, ii, p. 408.) In the U. S. P. (8th Rev.) there are three forms of petrolatum as follows: Petrolatum, Petrolatum Album, and Petrolatum Liquidum. In the British Pharmacopœia there are three as follows: Paraffinum Liquidum, Paraffinum Molle, and Unguentum Paraffini. The Petrolatum of the U. S. P. (8th Rev.) corresponds with the Petrolatum Spissum of the U. S. Pharm. 1890. The Paraffinum Molle of the British Pharmacopœia resembles the Petrolatum Molle of the U. S. P. 1890, but is somewhat softer in consistence.

Chemical Constitution.—Petrolatum, as made from American petroleum, consists mainly of the higher members of the paraffin series, but undoubtedly contains also the higher olefines. These may possibly alter in time, and give rise to rancidity, although this is not certainly established. The paraffins, which make up the bulk of it, are not capable of direct oxidation, and are therefore not affected by atmospheric influences. Petrolatum contains hydrocarbons of the paraffin series, like $C_{16}H_{34}$, $C_{17}H_{36}$, $C_{18}H_{38}$, etc., up probably to $C_{32}H_{66}$, together with hydrocarbons of the olefine series, $C_{16}H_{32}$, $C_{17}H_{34}$, etc. These latter are less concrete than the corresponding paraffin hydrocarbons, and give petrolatum its oleaginous characters. Puckner (*A. J. P.*, July, 1914) states that American petrolatum is made up of hydrocarbons of the methane series while the Russian oil contains naphthenes.

Properties.—The U. S. Pharmacopœia describes petrolatum as follows: "An unctuous mass, varying in color from yellowish to light amber, having not more than a slight fluorescence, even after being melted; it is transparent in thin layers; completely amorphous; free or nearly free from odor or taste. Petrolatum is insoluble in water; almost insoluble in cold or hot alcohol, or in cold dehydrated alcohol; freely soluble in ether, chloroform, carbon disulphide, oil of turpentine, petroleum benzin, benzene, or in most fixed or volatile oils. Specific gravity: 0.820 to 0.865 at 60° C. (140° F.). It melts between 38° and 54° C. (100.4° and 129.2° F.). Heat about 2 Gm. of Petrolatum in an open porcelain or platinum dish, over a Bunsen flame; it volatilizes without emitting an acrid odor, and on incineration not more than 0.05 per cent. of ash remains. Shake melted Petrolatum with an equal volume of hot distilled water; the latter remains neutral to litmus (*acids or alkalies*). Digest 10 Gm. of Petrolatum at 100° C. (212° F.) for half an hour with 10 Gm. of sodium hydroxide and 50 mils of distilled water, then separate the aqueous layer and supersaturate it with sulphuric acid; no oily or solid substance separates (*fixed oils, fats,* or *rosin*)." *U. S.*

"White or yellow, translucent, soft, unctuous to the touch, not allowing any liquid to separate on keeping. No odor. Melting point 42° to 46° C. (107.6°–114.8° F.). On heating to 80° C. (176° F.) no unpleasant odor is evolved. 10 millilitres of *alcohol* (90 per cent.) boiled with 5 grammes of Soft Paraffin are not acid to *litmus*. When 10 grammes are boiled with 20 millilitres of *solution of sodium hydroxide* for ten minutes and allowed to separate, the aqueous layer yields no precipitate or oily matter when acidified with *sulphuric acid* (absence of fixed oils, fats, and resin). 5 grammes when heated burn with a luminous flame, leaving no appreciable ash." *Br.*

As it is found in the market, petrolatum varies in color, odor, and melting point. The statement frequently made by the manufacturers that it is unalterable in the air is incorrect, as we have frequently noticed that exposure to light and air causes it to assume a disagreeable odor resembling that of crude petroleum. It has been observed to have at times irritating properties. These may be due to imperfect removal of the sulphuric acid or similar agents used, but are more probably caused by rancidity or decomposition. The test of the U. S. P., 1890, which directed that only a brown color should result when sulphuric acid be added to melted petrolatum was dropped in the U. S. P. IX because it was found that a black color always results, with petrolatum now produced.

Uses.—Petrolatum is used almost exclusively as a bland, neutral, protective dressing and as a substitute for the true fats in ointments. For local applications it has the advantage over the fats that it does not become rancid. It is not suited, however, for the preparation of ointments when absorption is desired, for it is not capable of penetrating the skin. Although it was at one time suggested as a substitute for butter and animal fats for culinary purposes it has absolutely no food value. Randolph (*T. G.*, 1885, ix, p. 732) appears to have been the

first to demonstrate its non-absorbability from the intestinal tract, and Robinson (*M. News*, 1900, lxxvii, p. 56) recovered the entire amount of liquid petrolatum from the feces which was administered by mouth. Randolph also showed that when taken internally, in doses of from one to four drachms (3.9–15.5 Gm.), it acts as a feeble laxative and soothes irritation, so as to be advantageous in inflammations of the gastro-intestinal mucous membrane. (See *Petrolatum Liquidum.*)

Off. Prep.—Unguentum Paraffini, *Br.;* Emulsum Petrolati, *N. F.*

PETROLATUM ALBUM. U. S.

WHITE PETROLATUM Petrolat. Alb. [White Petroleum Jelly]

(pĕt-rŏ-lā'tŭm ăl'bŭm)

"Petrolatum wholly or nearly decolorized." *U. S.*

Preparation.—*White petrolatum* was introduced for the first time into the U. S. P. (8th Rev.) under its present official title; there are reasons for believing that much that is in the market is not the natural product deprived of its color by treatment with animal charcoal, but an artificial compound made by melting together paraffin wax and liquid petrolatum, and stirring until cold. This manufactured product is opalescent and usually granular in appearance and is excluded by the official description.

This artificial product, under the name of *Snow white mineral jelly,* is extensively used in preparing petrolatum cold creams, but usually separates some of the liquid portion when the attempt is made to incorporate other ingredients by rubbing.

Properties.—It is officially described as "White Petrolatum is a white or faintly yellowish unctuous mass, transparent in thin layers even after cooling to 0° C. (32° F.); completely amorphous. In other respects White Petrolatum has the characteristics of and responds to the tests for identity and purity under *Petrolatum.*" *U. S.*

Uses.—See *Petrolatum.*

PETROLATUM LIQUIDUM. U. S. (Br.)

LIQUID PETROLATUM Petrolat. Liq. [Mineral Oil]

(pĕt-rŏ-lā'tŭm lĭq'ŭ-dŭm)

"A mixture of liquid hydrocarbons obtained from petroleum. Preserve it in well-closed containers, protected from light." *U. S.* "Liquid Paraffin is a mixture of liquid hydrocarbons." *Br.*

Paraffinum Liquidum, *Br.,* Liquid Paraffin; Paraffine liquide, Huile de Paraffine, *Fr.;* Flüssiges Paraffin, Paraffinöl, *G.;* Aceite de paraffina, *Sp.*

Preparation.—*Liquid petrolatum* is made by distilling the residuary liquid boiling between 330° and 390° C. (626° and 734° F.), obtained after removing the lighter hydrocarbons from petroleum. It is purified and decolorized by first treating it with sulphuric acid and then with caustic soda and passing it while hot, through animal charcoal. By cooling, some solid paraffins will separate; the liquid is then redistilled, and the portion boiling below 360° C. (680° F.), rejected. It has been sold under various proprietary names as *albolene, glycoline,* etc., and since its introduction into the U. S. P., 1890, has been largely used in medicine and for pharmaceutical purposes.

Properties.—It is described officially as follows:

"**Heavy Liquid Petrolatum.**—Heavy Liquid Petrolatum has a viscosity of *not less* than 3.1 when determined by the test given below.

"**Light Liquid Petrolatum.**—Light Liquid Petrolatum has a viscosity of *not more* than 3 when determined by the test given below and vaporizes freely. *Each variety conforms to the following description and tests:* Specific gravity for Liquid Petrolatum 0.828 to 0.905 at 25° C. (77° F.). A colorless, transparent, oily liquid, free, or nearly free, from fluorescence, odorless and tasteless when cold, and possessing not more than a faint petroleum odor when heated. When cooled to 10° C. (50° F.), Liquid Petrolatum does not become more than opalescent (*solid paraffins*). Insoluble in water or alcohol; soluble in ether, chloroform, petroleum benzin, or in fixed or volatile oils. Camphor, menthol, thymol, and many similar substances are dissolved by Liquid Petrolatum. Boil 10 mils of Liquid Petrolatum with an equal volume of alcohol; the alcoholic liquid is not acid to litmus (*acids*). Introduce into a glass-stoppered cylinder, which has been previously rinsed with sulphuric acid, 5 mils of Liquid Petrolatum and 5 mils of colorless sulphuric acid, heat in a water bath during ten minutes, shaking well at intervals of thirty seconds; the oil remains unchanged in color and the acid does not become darker than pale amber (*carbonizable impurities*). Prepare a clear, colorless saturated solution of lead oxide in an aqueous solution of sodium hydroxide (1 in 5), and mix 2 drops of this solution with 4 mils of Liquid Petrolatum and 2 mils of dehydrated alcohol; the mixture does not darken after heating for ten minutes at 70° C. (158° F.) and cooling (*sulphur compounds*).

"**Viscosity.**—Make a permanent mark about 2 cm. below the bulb of a 50 mil pipette of the usual type and note the time, in seconds, required at 25° C. (77° F.) for the level of distilled water to fall from the upper to the lower mark as the liquid flows from the pipette. The time should not be less than twenty-five seconds nor more than thirty seconds for the pipette selected. Draw the Liquid Petrolatum to be tested into this pipette, which should be clean and dry, and note the time, in seconds, required at 25° C. (77° F.) for its level to fall from the same upper to the lower mark as used for the water. Divide the number of seconds thus noted by the number of seconds required for water to fall from the upper to the lower mark, as above determined. The quotient indi-

cates the viscosity. Distilled water at 25° C. (77° F.) is taken as 1." *U. S.*

In the U. S. P. IX two kinds of Liquid Petrolatum were introduced, one being called "heavy," the other "light." The proportion of viscosity is the determining factor, "heavy" requiring not less than 3.1, "light" not more than 3, as determined by the official test. For atomizing purposes light liquid Petrolatum is used and for constipation treatment heavy liquid petrolatum is preferred.

The British Pharmacopœia describes it as "transparent, colorless, not fluorescent. No odor or taste. Specific gravity 0.860 to 0.890. A mixture of 4 millilitres of Liquid Paraffin, 2 millilitres of *absolute alcohol,* and 2 drops of a clear saturated solution of *lead oxide* in *solution of sodium hydroxide,* remains colorless when kept at 70° C. (158° F.) for ten minutes (absence of sulphur compounds). When 3 millilitres are heated with an equal volume of *sulphuric acid* in a test-tube placed in boiling *water* for ten minutes, and frequently shaken, the acid layer, after separation, is not darker than pale-brown. 10 millilitres of *alcohol* (90 per cent.) boiled with 5 millilitres of Liquid Paraffin are not acid to *litmus*." *Br.*

Uses.—Liquid petrolatum is used chiefly for its demulcent effect upon the mucous membrane of the upper respiratory tract in acute *coryza, pharyngitis,* and *laryngitis.* It is usually applied by atomization but is sometimes dropped directly into the nostril. It has also been recommended as a dressing for *wounds* and *ulcers.* Chrysopathes (*Cb. Chir.,* 1913, p. 1739) believes that it has an antiseptic effect, but it is more probable that its beneficial action is due to the exclusion of air. Although vaseline as recommended many years ago by Randolph for its laxative effect, it was not used to any large extent until in 1913 Lane (*B. M. J.,* 1913, ii, p. 1126) introduced the use of the heavy Russian liquid petrolatum in the treatment of *chronic constipation.* Since this time it has become a favorite remedy for this purpose. Its action is purely mechanical rendering the feces soft and perhaps lubricating the bowel. There is a wide spread belief among the medical profession that where used as a laxative the more viscid petrolatums are preferable. In a comparative study, however, of both the Russian and American oils ranging in specific gravity from 0.857 to 0.885, carried out by eight of the most prominent clinicians in the United States under the auspices of the Council on Pharmacy and Chemistry of the American Medical Association (*J. A. M. A.,* 1915, lxiv, p. 808), the conclusion was reached that as far as the therapeutic results, either as regards the quantity required or the liability to leakage around the anus or other disagreeable effects, there is no difference in the effects of the heavy or light oils. The ordinary quantity required varied from one-half to three ounces, and the effects were the same whether taken in one or three doses.

The number of fancy names which have been applied to proprietary brands of liquid petrolatum has become a crying evil. The following are some of the common names and special brands of liquid petrolatum:

Adepsine oil	Nujol
American oil	Olo
Amilee	Paraffin oil
Atoleine	Paroline
Atolin	Petralol
Bakurol	Petro
Blandine	Petrolax
Crysmalin	Petrolia
Deeline	Petronol
Glyco	Petrosio
Glycoline	Rock oil
Glymol	Russian liquid petrolatum
Heavy petroleum oil	Russian mineral oil
Interol	Russian paraffin oil
Lilyolene	Russol
Liquid albolene	Seneprolin
Liquid cosmoline	Saxol
Liquid fossiline	Stanolax
Liquid geoline	Stanolind
Liquid paraffin	Terraline
Liquid petrolatum	Terralbolia
Liquid saxoline	Usoline
Liquid vaseline	Water-white mineral oil
Mineral glycerin	White liquid vaseline
Mineral oil	White paraffin oil
Minol	Whiteruss.
Muthol	
Neutralol	

A formula for an emulsion of liquid petrolatum was contributed by Miles Shimer (*Proc. P. Ph. A.,* 1916, p. 298), as follows: Soft petrolatum, 40 Gm.; white mineral oil, 200 Gm.; powdered acacia, 60 Gm.; syrup, 50 mils; rum (Jamaica), 50 mils; water, q. s. ad., 500 mils.

PETROSELINUM. U. S.

PARSLEY FRUIT Petrosel. [Parsley Seed]

(pē-trō-sę-lī'nŭm)

"The dried ripe fruit of *Petroselinum sativum* Hoffman (Fam. *Umbelliferæ*), without the presence or admixture of more than 5 per cent. of foreign seeds or other matter. Preserve Parsley Fruit carefully in tightly-closed containers, protected from light." *U. S.*

Ache, Persil, *Fr.;* Petersilie, *G.;* Prezzemolo, *It.*

Petroselinum sativum Hoffman (*Apium petroselinum* L.).—The *common parsley,* which is used extensively as a culinary herb, is a hardy biennial bearing pinnately-compound leaves, which in the cultivated varieties are greatly divided. During its early stages the leaves are arranged in rosettes and the plant is six inches or less above the ground; the flowering and fruiting plant, however, is from 2 to 3 feet in height. It is a native of Sardinia and was introduced into England in 1548, and is

naturalized in salt marshes on the coast of California. It has been cultivated as a sweet herb since earliest times and was used by the ancient Greeks and Romans as a part of their festive garlands on account of retaining its color so long.

Parsley-root is recognized by the N. F. (see Part II); it is spindle-shaped, about 1 cm. in thickness, externally white and marked with close annular wrinkles, internally fleshy and white with a yellowish central portion. It has a pleasant odor and sweetish slightly aromatic taste, but loses this property by long boiling and by time. It was formerly used as a diuretic in dropsical affections, but has been shown by Cow (*A. E. P. P.*, 1912, lxx, p. 393) to possess very feeble powers.

The fruit, which has been admitted into the U. S. P. IX consists of two dry, seed-like, mericarps, which are in the fresh state joined along the central commissure. It is officially described as follows: "Mericarps usually separated, ovoid-crescent shaped, from 2 to 3 mm. in length and about 1 mm. in diameter; externally grayish-brown, becoming grayish or brownish on aging, having 5 yellowish, filiform, prominent ribs, alternating with the coarsely roughened furrows; in transverse section nearly hemispherical, the commissural surface with 2 vittæ or oil-tubes, the dorsal surface usually with a single vitta, occasionally 2 vittæ in the groves between the primary ribs; endosperm large, oily, enclosing a small embryo; odor and taste characteristic and aromatic, especially when bruised. Under the microscope, sections of Parsley Fruit show an epidermal layer with thick cuticularized walls having numerous small centrifugal projections; several layers of small, thin-walled parenchyma cells, being usually considerably collapsed and occasionally containing a rosette aggregate of calcium oxalate; a single, large, brown, elliptical vitta or oil-tube between each of the primary ribs and surrounded by a layer of comparatively large yellowish-brown, tangentially elongated cells; a single fibrovascular bundle more or less surrounded by a few or occasionally numerous sclerenchymatous fibers; inner epidermis of narrow, thin-walled elongated cells closely cohering with the brownish tabular cells of the seed-coat; commissural surface usually with 2 large vittæ, a very few stone cells and showing a slight separation of pericarp and seed-coat; endosperm of polygonal, thick-walled parenchyma cells containing fixed oil and numerous, small aleurone grains usually containing a small rosette aggregate of calcium oxalate. The vittæ usually contain yellowish oil globules or a resin-like mass adhering to the walls, and occasionally are divided by a radial wall. The powder is grayish-brown; mostly of large, irregular fragments; cells of endosperm with aleurone grains, each usually containing a rosette aggregate of calcium oxalate, from 0.003 to 0.007 mm. in diameter; fragments with light yellow vittæ and the yellowish-brown cells of the pericarp: fragments with narrow tracheæ and more or less lignified sclerenchymatous fibers." *U. S.*

All parts of the plant contain a volatile oil, to which it owes its odor and mainly its taste, as well as its use in seasoning. This oil consists of a hydrocarbon, $C_{10}H_{16}$, probably pinene, and apiol. Braconnot obtained from the herb a peculiar substance, resembling pectic acid in appearance, which he named *apiin*. It is procured by boiling the herb in water, straining the liquor, and allowing it to cool. The apiin then forms a gelatinous mass, which requires only to be washed with cold water. (*Ber. d. Chem. Ges.*, 1876, 1121) found that by repeated dissolving of this gelatinous mass in alcohol and precipitation by water it could be purified and then obtained from concentrated alcoholic solution in silky needles of the formula $C_{27}H_{32}O_{16}$. Joret and Homolle found the seeds to contain a volatile oil, a crystallizable fatty matter, pectin, what they believe to be the apiin of Braconnot, chlorophyll, tannin, a coloring matter, extractive, lignin, various salts, and, in addition to these, a peculiar substance to which they gave the name of *apiol*. This, however, is a mixture only partly consisting of true apiol which is the di-methoxymethylene ether of allyl-tetraoxybenzene, $C_{12}H_{14}O_4$. (See *Oleoresina Petroselini.*)

Off. Prep.—Oleoresina Petroselini, *U. S.*

PHENOL. U. S. (Br.)

PHENOL [Carbolic Acid, Acidum Carbolicum, Pharm. 1890]

(phē′nŏl)

"Hydroxybenzene obtained from coal-tar or made synthetically. It contains not less than 97 per cent. of C_6H_5OH (94.05). Preserve it in well-closed containers, protected from light." *U. S.* "Phenol, C_6H_6O, commonly termed carbolic acid, may be obtained from coal-tar oil." *Br.*

Acidum Carbolicum, *Br.*, also *U. S.* 1890; Acidum Phenicum s. Phenylicum Crystallisatum; Phenic Acid, Phenylic Acid, Phenylic Alcohol, Phenic Alcohol, Benzophenol; Phénol, Acide carbolique, Acide Phénique, *Fr. Cod.*; Hydrate de Phényle, *Fr.*; Acidum carbolicum, *P. G.*; Karbolsaure, Phenylsaure, Phenylalkohol, *G.*; Fenolo cristallizzato, Acido carbolico, *It.*; Acido fenico, *Sp.*

This important medicine was discovered in 1834, in the tar of coal, by Runge, who gave it the name of carbolic acid. When on the subject of its composition, we shall have occasion to show that, although more closely related chemically with the alcohols than the acids, it belongs to a peculiar class known in common as *phenols*. The U. S. P. (8th Rev.) dropped the names of Acidum Carbolicum and carbolic acid and adopted the correct title of Phenol for this substance. The British Pharmacopœia recognizes the name Acidum Carbolicum, but uses "phenol" as the English name for this substance.

Preparation.—For the commercial preparation of phenol the light oil fraction is collected until a sample of the oil that runs from the still

sinks in water. This fraction, with a sp. gr. of from 0.94 to 0.99, boils between 90° and 250° C. (194° and 482° F.) and contains from 4 to 10 per cent. of acids, and therefore nearly all the true phenol which boils at 182° C. (359.6° F.). The oil from which the phenol is to be extracted is agitated with a weak solution of sodium hydroxide, 10 per cent. strength being strong enough. If a stronger solution is used many impurities, like naphthalene, are dissolved and contaminate the finished product. After agitation, the mixture, on standing, separates into two layers, the upper consisting of the extracted oil and the lower the solution of sodium phenolate. To this solution, after separation from the oily layer, an amount of hydrochloric or diluted sulphuric acid calculated from a special test with a small portion, as just sufficient, is then added in order to set the phenol free. It separates as an oily layer upon the surface, and, after being washed with a saturated solution of sodium chloride, is dried over calcium chloride and again distilled. The product thus obtained crystallizes out largely on a cooled surface, and, after removing the crystals from adhering liquid, and drying them by pressure, they are again submitted to the same process of distillation. Only by such a detailed procedure can phenol be separated from its homologues, like cresol (cresylic acid), $C_6H_4(CH_3)OH$, which accompany it, smell much like it, and boil between 185° C. (365° F.) and 200° C. (392° F.).

Church (*Chem. News*, Oct. 13, 1871) proposed to prepare *pure* phenol by agitating the best commercial product with 20 parts of water, siphoning off the clear solution from the undissolved portion which retains the impurities, and adding to the solution pure sodium chloride to saturation, when the purified phenol rises to the top, and may afterwards be dehydrated by distillation with lime.

Within recent years manufacturers have put upon the market "*synthetical phenol*," for which is claimed a greater purity than that extracted from coal tar. It may be made synthetically in one of two ways—either from benzene, which is converted into *benzene-sulphonic acid*, the sodium salt of which is then fused with an excess of sodium hydroxide, producing sodium phenolate and sodium sulphite, from which, on the addition of sulphuric or hydrochloric acid, the phenol separates and may be distilled off; or a pure aniline oil is taken, neutralized with sulphuric acid, and to the acid solution sodium nitrite is added. The nitrous acid liberated forms at first *diazobenzene sulphate*, but this at once decomposes into phenol, sulphuric acid, and nitrogen, the reactions being as follows:

$$(C_6H_5NH_2)_2H_2SO_4 + 2HNO_2 = (C_6H_5N=N)_2SO_4 + 4H_2O$$

$$(C_6H_5N=N)_2SO_4 + 2H_2O = 2C_6H_5OH + H_2SO_4 + 4N$$

The synthetic phenol melts at 41° to 42° C. 105.8°–107.6° F.), and boils at 178° C. (352.4° F.). The practicability of manufacture of synthetic phenol by the above process was made possible by the great increase in price soon after the beginning of the European war. It is made in America by a number of manufacturing firms.

Commercial Forms.—In one of his publications in reference to phenol, F. Grace Calvert, to whom probably more than to any other person is due the introduction of this substance into use in Great Britain and the United States, informed us that the phenol obtained by Laurent, melting at 34° C. (93° F.), and boiling at 186° C. (367° F.), was not quite pure. By successive steps of improvement in the process employed by the manufacturing house of Manchester with which he was connected, they had at length succeeded in preparing the pure crystallized acid, without color or sulphurous odor.

Impure liquors were formerly sold sometimes under the improper name of *coal tar creosote*. They were recognized in the U. S. Pharmacopœia, 1890 (*Acidum Carbolicum Crudum*), which was officially described as "a nearly colorless, or reddish, or brownish-red liquid, of a strongly empyreumatic and creosote-like odor; having a benumbing, blanching, and caustic effect upon the skin or mucous membrane; and gradually turning darker on exposure to air and light. The aqueous solution of Crude Carbolic Acid has a slightly acid reaction on litmus paper. In an aqueous solution of the Acid, bromine water produces a white precipitate. Crude Carbolic Acid should not be soluble in less than 15 parts of water at 15° C. (59° F.), and the aqueous solution should not have an alkaline reaction (absence of *alkalies*). If 50 volumes of the Acid be thoroughly agitated with 950 volumes of water, in a capacious vessel, on allowing the mixture to separate, the undissolved portion should not exceed 5 volumes, or 10 per cent. by volume of the acid (limit of other *less soluble constituents of coal-tar*)." *U. S.*, 1890. It is superior in germicidal power to pure phenol. (See *Cresol.*)

Properties.—Phenol, in its pure state, is a solid at ordinary temperatures, crystallizing in minute plates or long rhomboidal needles, white or colorless, of a peculiar odor recalling that of creosote, and an acrid burning taste. Its sp. gr. is 1.065. (Lemaire.) It is likely to become colored pinkish or brown under the influence of light and air. This reddening has been ascribed to various causes, such as ammonia and ammonium nitrite in the air, rust spots in tinned iron vessels, alkali in glass vessels, organic matter, etc. It is said to be due to oxidation; stannous chloride solution acquires a green color when shaken with the red colored phenol. Demant recommends the removal of the red color by adding to 89 parts of the melted substance 11 parts of alcohol, subjecting the mixture to freezing, and then draining off the portion remaining liquid. Perfectly white crystals can be thus obtained. A slight discoloration does not

interfere with any of the medicinal uses of phenol. Phenol deliquesces on exposure, and becomes liquid, and the presence of water in the smallest proportion causes it to liquefy. It is customary to add 10 per cent. of water or glycerin to phenol for dispensing, as it is more convenient to use in a liquid form. Such a form is now official (see *Phenol Liquefactum*). Its solution in glycerin is very useful, as the glycerite mixes with water very readily. (See *Glyceritum Phenolis.*) When diluted it has a sweetish taste with a slightly nauseating after-taste, and a faintly acid reaction. When quite pure it melts at 41° C. (106° F.), forming an oily looking, colorless liquid, and boils at 182° C. (359.6° F.) (Calvert); but, as often met with, its point of fusion is lower, and that of volatilization higher, than those named. The official tests and requirements are as follows: "Colorless, interlaced, or separate needle-shaped crystals, or as a white, crystalline mass, sometimes acquiring a red tint; having a characteristic, somewhat aromatic odor. When undiluted it cauterizes and whitens the skin and mucous membrane. One Gm. of Phenol dissolves in about 15 mils of water at 25° C. (77° F.); very soluble in alcohol, glycerin, chloroform, ether, carbon disulphide, or in fixed or volatile oils. An aqueous solution of Phenol (1 in 15) is clear and neutral or at most only faintly acid to litmus. When gently heated Phenol melts, forming a highly refractive liquid. It is also liquefied by the addition of about 8 per cent. of water. Congealing point: not below 38° C. (100.4° F.). Its aqueous solution yields with bromine water a white precipitate of tribromphenol, which at first redissolves, but becomes permanent as more of the reagent is added, and appears crystalline when viewed under the microscope. Add 1 drop of ferric chloride T.S. to 10 mils of an aqueous solution of Phenol (1 in 100); the liquid acquires a violet-red color. Heat about 10 Gm. of Phenol on a water bath; it is volatilized without leaving more than 0.05 per cent of residue. The vapor is inflammable." *U. S.*

"Small, colorless, deliquescent crystals; odor peculiar but not fetid or tarry; taste sweetish, pungent. Has a caustic action on skin and mucous membrane. Freely soluble in *alcohol* (90 per cent.), in *ether, chloroform, glycerin,* in the fixed and volatile oils, and in solutions of alkalies. Exposed to moist air it may acquire a pinkish tinge. At 15.5° C. (60° F.), 100 parts of Phenol are liquefied by the addition of 10 parts of *water,* form a clear liquid with 30 to 40 parts of *water,* and are completely dissolved by 1200 parts of *water.* The aqueous solution is clear and colorless. Melting point from 39° to 40° C. (102.2°–104° F.); boiling point not higher than 183° C. (361.4° F.). Specific gravity at the melting point 1.060 to 1.066. Phenol does not immediately redden *blue litmus paper.* Optically inactive. Coagulates *collodion* and *solution of albumen.* An aqueous solution of Phenol becomes deep purple with *T. Sol. of ferric chloride;* yields a white precipitate with excess of *solution of bromine;* and when mixed with one-fourth of its volume of *solution of ammonia,* and then with a few drops of *solution of chlorinated soda,* becomes blue after a time, or immediately on gently heating. One volume of Phenol liquefied by the addition of 10 per cent. of *water,* forms with 1 volume of *glycerin* a clear liquid which is not rendered turbid by the addition of 3 volumes of *water* (absence of cresol). Evaporated on a water-bath it leaves not more than 0.1 per cent. of residue." *Br.*

Its solubility in water increases on heating the water; at 84° C. (183.2° F.) both liquids are miscible in all proportions. Its solution is, if pure, colorless, and remains so, but, if impure, is colored brownish by exposure. It is but slightly soluble in cold petroleum benzin, but dissolves largely on heating. *Sodium sulphoricinate* has been used to increase the solubility of phenol, the advantage being that it will retain 40 per cent. of phenol in solution without destroying its antiseptic power, making a solution without causticity.

"**Assay.**—Dissolve about 1.5 Gm. of the Phenol to be assayed, accurately weighed, in sufficient distilled water to make 1000 mils. Transfer an aliquot portion of this solution, containing not less than 0.038 Gm. nor more than 0.041 Gm. of Phenol, to a 500 mil glass-stoppered flask having a long, narrow neck, add 30 mils of tenth-normal bromine V.S., then 5 mils of hydrochloric acid and immediately insert the stopper. Shake the flask repeatedly during half an hour, allow it to stand for fifteen minutes, remove the stopper just sufficiently to introduce quickly 5 mils of an aqueous solution of potassium iodide (1 in 5), being careful that no bromine vapor escapes, and at once stopper the flask. Shake the latter thoroughly, remove the stopper and rinse it and the neck of the flask with a little distilled water, so that the washings may flow into the flask, then add 1 mil of chloroform, shake the mixture well and titrate with tenth-normal sodium thiosulphate V.S., using starch T.S. as indicator. It shows not less than 97 per cent. of C_6H_5OH.

"Each mil of tenth-normal bromine V.S. corresponds to 0.001568 Gm. of C_6H_5OH. Each gramme of Phenol corresponds to not less than 618.6 mils of tenth-normal bromine V.S." *U. S.*

For methods of assaying Phenol, see *Y. B. P.*, 1891, 190; *Chem News*, 1891, 74; *J. P. C.*, 1894, 105; *A. J. P.*, 1892, 164; *Ph. Centralh.*, 1892, 479; *D. C.*, 1896, 158; *A. J. P.*, 1898, 369.

Though nearly neutral to test paper, it combines feebly with some bases, its salts being decomposed by carbon dioxide, and those with the alkalies having an alkaline reaction. The potassium phenolate is said to be decomposed even by water. Nitric acid converts it into picric acid, for the manufacture of which it is largely used. It reduces many metallic salts, especially those of silver and copper, and co-

agulates collodion. Bromine water, added in excess of a weak solution, produces a flocculent white precipitate. This precipitate, which consists of tribromophenol, $C_6H_2Br_3.OH$, with some tribrom-phenol-bromide, $C_6H_2Br_3.OBr$, is so insoluble that it separates even in the most dilute solutions, and affords an extremely delicate test. In twenty-four hours a solution containing but 1-60,000th of phenol gives the reaction. (Allen, *Com. Org. Anal.*, 2d ed., vol. ii, p. 540.) If an aqueous solution of phenol be gently warmed with ammonia and solution of sodium hypochlorite (avoiding excess), a deep blue color is obtained, which is lasting, but turns to red on the addition of acids. Solutions containing 1 part of phenol in 5000 parts of water react well when 20 mils are employed. Much smaller quantities give the reaction after a time. (*Ibid.*, p. 539.) Ferric chloride (avoiding excess) gives a fine violet color, by which 1 part of phenol in 3000 parts of water can be detected. The presence even of neutral salts often interferes with this reaction.

The substances with which phenol is most likely to be confounded are cresol or cresylic acid and creosote, the former, like it, extracted from coal tar, the latter from wood tar exclusively. As cresol is incapable of crystallizing at ordinary temperatures, the two cannot be confounded in the solid state, and, as before observed, its presence in the liquid state is of little consequence, as its virtues are of the same kind, and at least equal. Its boiling point, however, is considerably higher than that of phenol, being about 204° C. (400° F.), and it may, therefore, be supposed to be present in any suspected liquid which will not crystallize at any common temperature, or boil under 202° C. (395° F.) to 204° C. (400° F.). It is also distinguished by being less soluble in water, ammonia water, glycerin, and solution of sodium hydroxide than is the case with phenol, but it is more soluble in petroleum benzin. (Allen.) (*A. J. P.*, Jan., 1879.) Creosote is distinguished by its lower density, its liquid form, and its higher boiling point; by its insolubility in strong ammonia water, or in 6 per cent. sodium hydroxide solution, as well as its insolubility in pure glycerin (see *Creosotum*); by not coagulating collodion and albumin; and by the different effects on it of strong nitric acid, which with phenol produces pure picric or trinitrophenic acid, and with creosote, oxalic acid, resinous matter, and but a small portion of picric acid. (Calvert, *L. L.*, 1863, p. 523.) Phenol differs also in having no effect on polarized light.

The commercial phenol powders and liquids all contain not only cresol, but also nearly inactive and valueless neutral tar oils, and it is important to be able to determine the percentage of the *tar acids* and that of simple *tar oils* in a commercial sample. John Muter (*A. J. P.*, Nov., 1887, p. 581) has worked out a simple method for this, based upon the following four observed facts: (1) Phenol, cresol, and their homologues are completely soluble when shaken up with a 5 per cent. solution of sodium hydroxide; (2) Liquefied phenol and the corresponding cresol are insoluble in a saturated solution of chloride; (3) In the presence of a sufficient excess of alkali even a largely diluted solution may be boiled down without the slightest appreciable loss of phenol or cresol; (4) Tar oils and naphthalene are only very slightly dissolved by alkali, and may be perfectly removed from the solution by agitating it with benzene.

E. W. Davy proposes, as a test for phenol, sulpho-molybdic acid, made by dissolving 1 part of molybdic acid in 10 or even 100 parts of pure concentrated sulphuric acid; 3 or 4 drops of this solution are added to the phenol placed on white porcelain; a beautiful blue coloration will be produced upon standing, particularly if the liquid be gently heated; if this reagent is applied to wood creosote in aqueous solution, a brownish-red color is produced. Phenol in creosote may be detected by distilling an aqueous solution of the mixture; the first portion of the distillate will give the reaction for creosote, the last portion that for phenol. (*P. J.*, June 22, 1878.)

Composition.—The view of the composition of phenol now universally accepted is that it is the hydroxyl (OH) derivative of benzene, C_6H_6, and its formula is $C_6H_5.OH$. This would ally it to the alcohols, and it may be compared, in fact, to what are known as *tertiary* alcohols. The *primary* alcohols, like ethyl alcohol, C_2H_5 OH, yield corresponding aldehydes and acids on oxidation. The counterpart of these in the aromatic series are the aromatic alcohols, like $C_6H_5.CH_2OH$, which yield benzoic acid, C_6H_5 COOH, on oxidation. The name *phenols* has therefore been given to these derivatives in which H of the benzene group is replaced by OH. Phenol is commonly called *carbolic acid*, but its claims to be considered as an acid are very feeble, as, though it combines with salifiable bases, it is incapable of neutralizing the alkalies, does not affect the color of litmus, and may be separated from its combinations with great facility, sometimes, it is asserted, even by water. Shaken in the liquid form with one-fourth of water, and cooled at 4.5° C. (40° F.), it crystallizes in the form of a hydrate, $C_6H_5.OH + H_2O$, which fuses at 17° C. (62.6° F.).

Uses.—Pure phenol is locally irritant, anesthetic and mildly caustic. When applied undiluted to the skin or mucous membrane it causes a sharp pain, followed by numbness, and accompanied by a whiteness and corrugation of the surface due to coagulation of albumen. In dilute solution, up to 3 or 4 per cent., it is only mildly irritant but is actively anesthetic and germicidal. In appropriate strengths phenol is a rapid and certain destroyer of the vegetative forms of bacteria, but against the more resistant spores it is comparatively useless. A 1 per cent. solution will destroy non-sporulating

micro-organisms after sufficiently prolonged exposure, and a 2 per cent. solution promptly. On the other hand, the anthrax spores are not killed with certainty even after twenty-four hours' exposure to a 5 per cent. solution. It is antiseptic—that is, inhibits the multiplication of bacteria—when present in the proportion of about 1 to 800. Its peculiar value as a germicide is due largely to the fact that its activity is but slightly diminished by the presence of albuminous material. Although in sufficient concentration phenol precipitates albumen, it does not do so by forming chemical union with it, as does bichloride of mercury, but by changing the character of the solvent; the precipitation is analogous to that which takes place when water is added to an alcoholic solution of resin. Partly because of the widespread familiarity with phenol and partly for certain technical reasons it has been adopted by the United States Government as a standard for comparison of disinfectant power. The *phenol coefficient* of the United States Government (*Hygienic Lab. Bulletin* No. 82, April, 1912) represents the amount of phenol required to exercise the same degree of germicidal action against the typhoid bacillus, under certain standard conditions of testing, as one part of the disinfectant to be tested; for instance, if disinfectant X has a phenol coefficient of 2 that means that it would require 2 parts of phenol to equal one of X, or in popular parlance that X is twice as strong as phenol; a phenol coefficient of 0.5 means that the disinfectant is only one-half as active as phenol.

Phenol is widely used as a disinfectant not only for sanitary but for surgical and medical purposes. For the disinfection of the surgeon's hands its local anesthetic action is a great disadvantage and its uncertain effect upon sporulating organisms almost excludes its use for the disinfecting of surgical instruments. As a dressing for *wounds* it is, however very widely employed. In *burns* and other painful *ulcerations* its local anesthetic action often makes it peculiarly valuable. When applied continuously for several days it in some way interferes with the nutrition of the part, and a number of cases of local gangrene have followed the use of phenol dressings. Chlunsky (*Cb. I. M.*, 1912, p. 226) asserts that the addition of camphor lessens the caustic action of phenol and has employed a mixture containing 30 parts of phenol, 60 of camphor, and 10 of alcohol, as a local application in the treatment of *erysipelas*. This *phenol-camphor* (which is also known under the name of *kamphenol* and *erypol*), has also been used by a number of surgeons as a local application to infected *wounds, furuncles,* and as an injection into *cold abscesses,* with asserted excellent results. According to Horowitz (*D. M. W.*, 1913) the diminution of the corrosive action of the phenol is due to the action of the alcohol rather than to the camphor. Phenol is also used to a large extent in the form of oily or watery solutions in the treatment of *coryza, stomatitis,* and other infected conditions of the mucous membranes.

For ordinary surgical purposes it may be used in strengths of from 3 to 5 per cent. The liquid phenol is often applied undiluted as a germicide and caustic in badly infected wounds. Various fabrics are impregnated with phenol for surgical use.

Lister's gauze may be made by soaking a loose cotton cloth with a mixture of 5 parts rosin, 7 parts paraffin, and 1 part phenol. Bruns improves upon this, making a more flexible dressing, by dissolving 400 grammes of powdered rosin in 2 liters of alcohol, adding 40 grammes of castor oil and 100 grammes of phenol; this will impregnate 2 pounds of the gauze, which is to be dried by spreading it out in the air. (See also Lund's process, *A. J. P.*, Feb., 1874.) *Carbolized jute* may be made by Rosenwasser's process by soaking in a percolator 1 pound of jute with a solution of crystallized phenol 700 grains, paraffin 700 grains, rosin 2800 grains, petroleum benzin 3 pints. (*A. J. M. S.*, 1879, p. 458. See also *N. R.*, April 1879, and April, 1880.) For burns and scalds 1 part of phenol in 6 parts of olive oil may be applied on lint. For the dressing of *cancerous* and other foul *ulcers,* a cerate (ten grains to the ounce) may be used. There is an official ointment.

Phenol is frequently employed as an antiseptic in various forms of gastro-intestinal affections. Because of the rapidity of its absorption as well as the relatively large dose which would be required, it is doubtful whether it exercises any efficient action in the intestines, but in fermentative *gastritis* it is often a useful remedy. It is also of service in *nervous vomiting,* and in *gastrodynia* for its local anesthetic action upon the mucous membrane of the stomach. Externally it is of much service as a local anesthetic in *urticaria, sunburn,* and other conditions attended with *itching* or burning of the skin.

The hypodermic injection of phenol has been highly lauded by Baccelli in the treatment of *tetanus* and his recommendations have had many followers. The method consists in injecting hypodermically two or three mils (30–45 minims) of a 2 per cent. solution every two or three hours, a total dose of 0.5 to 1.5 Gm. (eight to twenty-three grains) of phenol being given in the twenty-four hours. Baccelli has collected from his own experience and the literature, over three hundred cases treated by this method with a mortality of about 10 per cent.

Phenol Poisoning.—Because of the ease with which it is obtained and the rapidity and certainty of its effects, phenol is a very frequently used poison for suicidal purposes, and cases of accidental poisoning are also quite common. The symptoms usually develop very rapidly; indeed death has occurred in 2 or 3 minutes, the patient dying in immediate coma and col-

lapse. After small amounts the symptoms are nausea and vomiting, collapse with pallor and cold sweats, feeble pulse, stupor deepening into complete insensibility and disturbances of the breathing, the respirations are usually hurried and shallow, often irregular and sometimes paroxysmally arrested. There is usually paralysis of both sensation and motion, but in some cases violent epileptiform convulsions have occurred. The urine is generally scanty and albuminous and of a greenish or blackish color. The diagnosis is usually not difficult, being made upon the odor, the smoky urine, and the presence of white corrugated spots in the mucous membrane of the mouth or throat. The ordinarily fatal dose of phenol is about half an ounce, but De Vries (*Th. M.*, 1890, iv, p. 644), has reported death in a woman from 22 grains. On the other hand, recovery has followed after the ingestion of an ounce. In the fatal cases death usually occurs in less than 2 hours from respiratory failure, although in some instances weakness of the heart has been the cause of the lethal termination. In the treatment of carbolic acid poisoning the stomach should be immediately emptied, preferably by means of the stomach pump. There is no known efficient chemical antidote. Because of the fact that phenol unites in the body with sulphuric acid, being eliminated as a phenol-sulphonate, the sodium sulphate was at one time routinely employed in carbolic acid poisoning, but the latest investigations throw grave doubt upon its efficacy. Alcohol has also been recommended on the grounds that it lessens the caustic action of the poison, but the effects of alcohol are due simply to the fact that phenol is rapidly soluble in this fluid and is therefore immediately diluted; while alcohol is useful to prevent external burns by phenol and may be of service for the purpose of washing out the stomach, it has no real antidotal properties. The best method of treating phenol poisoning is to wash the stomach out with diluted whiskey or 25 per cent. alcohol, and afterwards with water, and the administration of strychnine and other stimulants to combat the depressant action on the vital centers. Magnesium sulphate may be administered for the purpose of emptying the intestinal tract as well as in the hope, rather than the expectation, that it may exercise some antidotal influence.

Dose, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Glyceritum Phenolis (from Liquefied Phenol), *U. S.* (*Br.*); Phenol Liquefactum, *U. S.* (*Br.*); Unguentum Phenolis (from Liquefied Phenol), *U. S.* (*Br.*); Suppositoria Acidi Carbolici, *Br.;* Trochiscus Acidi Carbolici, *Br.;* Aqua Phenolata (from Liquefied Phenol), *N. F.;* Liquor Iodi Phenolatus (from Liquefied Phenol), *N. F.;* Liquor Sodii Boratis Compositus (from Liquefied Phenol), *N. F.;* Nebula Aromatica, *N. F.;* Oleum Phenolatum, *N. F.;* Petroxolinum Phenolis, *N. F.;* Petroxolinum Phenolis Camphoratum, *N. F.;* Phenolum Iodatum, *N. F.;* Pulvis Antisepticus, *N. F.*

PHENOL LIQUEFACTUM. U. S. (Br.)

LIQUEFIED PHENOL Phenol Liq.

(phē'nŏl lĭq-uę-făc'tŭm)

"A liquid containing not less than 87 per cent. of C_6H_5OH (94.05)." *U. S.*

Acidum Carbolicum Liquefactum, *Br.;* Liquefied Carbolic Acid; Acidum carbolicum liquefactum, *P. G.;* Verflüssigte Karbolsäure, *G.;* Fenolo liquido, *It.;* Acido Fenico liquido, *Sp.*

* "Phenol, *a convenient quantity;* Distilled Water, *a sufficient quantity.* Liquefy the phenol by placing the unstoppered container in a water bath, and applying heat gradually until the crystals have melted; transfer the liquid to a tared vessel and weigh it; then add for each *nine grammes* [or 139 grains] of phenol *one gramme* [or 15 grains] of distilled water and mix thoroughly. Preserve it in well-closed containers, protected from light." *U. S.* "Phenol, 100 *grammes;* Distilled Water, sufficient to produce 115 *grammes.* Mix." *Br.*

It is officially described as "a colorless liquid, which may develop a red tint upon keeping. It has a characteristic, somewhat aromatic odor. When undiluted it cauterizes and whitens the skin and mucous membrane. Liquefied Phenol is miscible with alcohol, ether, or glycerin. When it is diluted with an equal volume of glycerin, the mixture is miscible with water. Specific gravity: about 1.065 at 25° C. (77° F.). When subjected to distillation, the boiling point does not rise above 182° C. (359.6° F.). In other respects Liquefied Phenol responds to the tests for identity and purity under *Phenol* (omitting the congealing point).

"**Assay.**—Proceed as directed under *Phenol.*

"Each gramme of Liquefied Phenol corresponds to not less than 554.8 mils of tenth-normal bromine V.S." *U. S.*

"A liquid, at first colorless, but usually acquiring a pinkish hue. Forms a clear solution on the addition of 12 to 20 per cent. by weight of *water* at 15.5° C. (60° F.). Specific gravity 1.067 to 1.069. Boiling point gradually rising to a temperature not higher than 183° C. (361.4° F.)." *Br.*

Peter Boa prefers to re lace a portion of the water used for liquefying the phenol with alcohol, and he found the following mixture to remain fluid even at a temperature of 4.5° C. (40° F.); 100 parts of phenol, 7½ parts of water, and 2½ parts of alcohol.

Dose, one to three minims (0.06–0.2 mil).

Off. Prep.—Glyceritum Phenolis, *U. S.;* Unguentum Phenolis, *U. S.;* Aqua Phenolata, *N. F.;* Liquor Iodi Phenolatus, *N. F.;* Liquor Sodii Boratis Compositus, *N. F.*

PHENOLPHTHALEINUM. U. S., Br.

PHENOLPHTHALEIN Phenolphthal.

(phē-nŏl-phthă-lę-ĭ'nŭm)

"A dibasic phenol derivative (dihydroxyphthalophenone) [$C_{20}H_{14}O_4$ or $(C_6H_4OH)_2CO.C_6H_4CO = 318.11$]." *U. S.* "Phenolphthalein,

or dihydroxy-diphenyl-phthalide, $C_{20}H_{14}O_4$, may be obtained by heating phenol with phthalic anhydride and sulphuric acid, and purifying the product." *Br.*

Phenolphthalein is made by heating phenol, 10 parts, phthalic anhydride, 5 parts, and sulphuric acid, 4 parts, for a number of hours to 120° C. (248° F.). The sulphuric acid acts merely as a dehydrating agent and is subsequently removed by washing with water. The crude phenolphthalein is subsequently purified by dissolving in an alkali, precipitating with an acid and then dissolving in alcohol and decolorizing with animal charcoal. It may be recovered from the alcohol by evaporation or precipitated by diluting the solution with water. The reaction for its formation is as follows:

$$2C_6H_5OH + C_6H_4(CO)_2O = (C_6H_4OH)COC_6H_4CO + H_2O$$

It is officially described as follows: "Phenolphthalein occurs as a white or faintly yellowish-white, crystalline powder, odorless and tasteless; permanent in the air. One Gm. of Phenolphthalein dissolves in 13 mils of alcohol, and in about 70 mils of ether at 25° C. (77° F.); almost insoluble in water. Melting point: not below 253° C. (487.4° F.). It is dissolved by solutions of the alkali hydroxides and carbonates with a red color. The solutions are decolorized by the addition of acids in excess or by heating with zinc dust. Incinerate about 2 Gm. of Phenolphthalein; not more than 0.05 per cent. of ash remains. A solution of 0.5 Gm. of Phenolphthalein in 30 mils of alcohol is colorless. One-half Gm. of Phenolphthalein dissolves completely in a mixture of 4 mils of sodium hydroxide T.S. and 50 mils of distilled water (*fluorane*). A mixture of 250 mils of cold, recently boiled, distilled water and 0.5 mil of a solution of Phenolphthalein (1 in 100) in diluted alcohol requires not more than 0.5 mil of hundredth-normal potassium hydroxide V.S. to produce a pink coloration. Heat about 0.5 Gm. of Phenolphthalein on a water bath for five minutes with 10 mils of diluted hydrochloric acid, filter the liquid and evaporate the filtrate to dryness; the residue, when dissolved in 25 mils of distilled water, slightly acidulated with hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3). Heat a crucible to redness and introduce, in small portions, an intimate mixture of 0.2 Gm. of Phenolphthalein, about 0.5 Gm. of potassium nitrate, and about 0.3 Gm. of anhydrous sodium carbonate. Maintain a red heat until the reaction ceases, then boil the cooled residue for five minutes with 10 mils of diluted sulphuric acid, filter, and wash the undissolved residue with 10 mils of distilled water. Evaporate the filtrate and washings until sulphuric acid vapors begin to evolve. The residue, dissolved in 5 mils of distilled water, meets the requirements of the Test for arsenic (see Part III, Test No. 1)." *U. S.*

"A white, or yellowish-white, crystalline or amorphous powder. No odor or taste. Soluble in *alcohol* (90 per cent.), the solution being colorless. Almost insoluble in *water*, but soluble in *solution of sodium hydroxide*, forming an intensely red liquid. Melting point 250° to 253° C. (482°–487.4° F.). Not more than 0.1 millilitre of *N/10 solution of sodium hydroxide* is required to produce a red coloration in 250 millilitres of recently boiled and cooled *water* to which has been added 0.5 millilitre of a solution (1 in 100) of Phenolphthalein in *alcohol* (60 per cent.). No appreciable ash." *Br.*

A derivative of phenolphthalein known as *phenolsulphonephthalein*, is used in the form of a monosodium derivative as a test of renal function. It consists of a bright red, crystalline powder, slightly soluble in water, with the formation of a yellow solution which is turned red or purple by alkalies. It is marketed in ampuls, each one of which holds an amount sufficient for a test. It is administered hypodermically and the urine is collected for one hour thereafter and tested quantitatively by adding an alkali and matching the shade of the solution colorimetrically with standards. The normal kidneys excrete from 40 to 60 per cent. of the ingested amount within one hour, irrespective of the amount of urine voided.

Uses.—The discovery that phenolphthalein possessed cathartic properties was made accidentally; it was used in Hungary as a means for the ready identification of artificial wines, and the observation that these wines were laxative led to an investigation of its properties. H. C. Wood, Jr. (*J. A. M. A.*, 1911, liv, p. 348) has found that it increases intestinal secretions, and that, when given intravenously to dogs in doses equivalent to 60 grains for a man, it produced no change in circulation or respiration. According to Berthomeau and Daguin (*Press Med.*, 1908, xvi, p. 378), the cathartic effects are due to combined stimulation of secretion and peristalsis. Although it seems to be slightly irritant to the kidneys, when introduced into the blood stream there is little danger of this action because its slight absorbability by the bowel.

Hydrick (*J. Bi. Chem.*, 1914, xvii) found albuminuria in every one of twenty experiments after the administration of 1 to 2 grain doses of phenolphthalein, but the results are so contrary to common experience that one is tempted to doubt the accuracy of his observations. Orland (*Med. Klin.*, 1913, p. 257) reported a case of a child aged three years who took 1.8 Gm. (27 grains) in the form of tablets with no more serious effect than violent purgation. The urine for four days showed the presence of phenolphthalein, but showed neither albumin nor sugar.

Phenolphthalein is a mildly acting cathartic, usually requiring from 4 to 8 hours for catharsis, and producing large, soft discharges without much gripeing. Although when used continuously the alimentary canal seems to become accustomed to it, it is nevertheless useful

as a variant from the vegetable laxatives in chronic as well as in the more occasional types of *constipation.*

Dose, one-half to three grains (0.032–0.2 Gm.).

Off. Prep.—Trochisci Phenolphthaleini, *N. F.*

PHENYLIS SALICYLAS. U. S. (Br.)

PHENYL SALICYLATE Phenyl. Salicyl. [Salol, Pharm. 1890]

(phē'nȳl-ĭs săl-ĭ-cȳ'lăs)

"The phenyl ester [$C_{13}H_{10}O_3$ or $C_6H_4(OH)COOC_6H_5$ 1:2 = 214.08] of salicylic acid. Preserve it in well-closed containers in a cool place." *U. S.* "Salol, or phenyl salicylate, $C_{13}H_{10}O_3$, may be obtained by the interaction of salicylic acid and phenol." *Br.*

Salol, *Br., U. S.* 1890; Salicylate de Phénol, Salicylate de Phényle, *Fr. Cod.;* Phenylum salicylicum, *P. G.;* Phenylsalicylat, Salicylsaurephenylester, *G.;* Salol, *It.;* Salicilato de fenol, *Sp.*

Preparation.—*Phenyl salicylate* was first produced by Nencki, of Basel, and introduced to the medical profession by Sahli, of the same place. It is prepared by heating salicylic acid with phenol in the presence of phosphorus pentachloride or phosphorus oxychloride; the action dehydrates and withdraws the elements of water, and unites the phenyl group with the salicylic acid radical. According to Ernert, nearly the theoretical yield of phenyl salicylate may be obtained by heating salicylic acid to a temperature between 160° and 240° C. (320° and 464° F.), and preventing the access of air while water is being disengaged; it is probable that salicylic anhydride is formed, and the phenyl resulting from its decomposition combines with unaltered salicylic acid to produce phenyl salicylate according to the following reaction:

$$2C_6H_4OHCOOH = (C_6H_4OHCO)_2O + H_2O$$

Then

$$(C_6H_4OHCO)_2O = C_{13}H_{10}O_3 + CO_2$$

Properties.—It is described as "a white, crystalline powder, having an aromatic odor and a characteristic taste. One Gm. of Phenyl Salicylate dissolves in 6670 mils of water and in 6 mils of alcohol at 25° C. (77° F.); very soluble in chloroform, ether, benzene, or in fixed or volatile oils. It melts between 41° and 43° C. (105.8° and 109.4° F.). The addition of diluted ferric chloride T.S. to an alcoholic solution of the salt (1 in 20) produces a violet color. Dissolve from 0.2 to 0.3 Gm. of Phenyl Salicylate in 2 mils of hot sodium hydroxide T.S., and acidify the solution with hydrochloric acid; salicylic acid separates and the odor of phenol is recognizable. Incinerate about 2 Gm. of Phenyl Salicylate; not more than 0.05 per cent. of ash remains. Phenyl Salicylate does not redden moistened blue litmus paper (*free acids*). Shake about 1 Gm. of Phenyl Salicylate with 50 mils of distilled water and filter the liquid; the addition of 1 drop of ferric chloride T.S. to 10 mils of the filtrate produces no violet color (*uncombined phenol or salicylic acid*). Ten mil portions of the same filtrate tested separately with barium nitrate T.S. and silver nitrate T.S. show no turbidity (*sulphate or chloride*)." *U. S.*

"Colorless crystals, or crystalline powder. Aromatic odor; taste slight. Almost insoluble in *water;* soluble in 15 parts of *alcohol* (90 per cent.), in 0.3 part of *ether* or of *chloroform,* and in fixed and volatile oils. Melting point from 42° to 43° C. (107.6°–109.4° F.). Alcoholic solution neutral to *litmus;* yields a white precipitate with *solution of bromine,* and a violet coloration with dilute *T. Sol. of ferric chloride.* When 0.2 gramme is boiled with 5 millilitres of *solution of sodium hydroxide,* and the cooled solution acidified with *hydrochloric acid,* the odor of phenol is developed and a crystalline precipitate is formed. *Water* which has been shaken with Salol is not affected by *T. Sol. of ferric chloride* (absence of free salicylic acid and of readily soluble salicylates), and yields no characteristic *reactions* for sulphates or chlorides. No appreciable ash." *Br.*

Uses.—In the small intestine phenyl salicylate is broken up by the pancreatic juice, and yields about thirty-six per cent. of phenol and sixty-four per cent. of salicylic acid. The completeness and rapidity of this action depend upon the amount of phenyl salicylate ingested and the alkalinity of the juice in the intestines. The change is, however, sufficient, when phenyl salicylate is freely given, for the production of salicylic acid intoxication, and for the blackening of the urine with educts from phenol. Because this change occurs in the intestines somewhat slowly, the remedy has been used as an internal antiseptic in the treatment of *enteritis* and *intestinal fermentation,* but its value is questionable. It has been largely used in *rheumatism* as a substitute for salicylic acid, but it is much less prompt and certain in its action than is that remedy. Moreover, on account of the large proportion of phenol which it contains, it is much more dangerous than the corresponding dose of salicylic acid. Hesselbach has shown that it is prone to affect the secreting structure of the kidneys, and two fatal cases of poisoning by it have been reported. (*L. L.,* May, 1891.) It is especially dangerous when the kidneys are diseased. Phenyl salicylate is used as a test of gastric motility, the time required for the appearance of salicylic acid in the urine depending largely upon the rapidity with which it passes out of the stomach. It has also been employed as a surgical dusting powder on the basis that it will be slowly decomposed by the wound secretions, liberating its antiseptic constituents.

Dose, from five to fifteen grains (0.32–1.0 Gm.).

PHOSPHORUS. U. S., Br.

PHOSPHORUS Phosphor.

(phŏs'phọ-rŭs)

"Phosphorus [P = 31.04] must be carefully preserved under water, in strong, well-closed containers, in a secure and moderately cool place, protected from light." *U. S.* "Phosphorus is a solid non-metallic element. It may be obtained from calcium phosphate." *Br.*

Phosphore, *Fr. Cod.*; Phosphorus, *P. G.*; Phosphor, *G.*; Fosforo, *It., Sp.*

This non-metallic element was discovered in 1669 by Brandt, an alchemist of Hamburg, who obtained it from evaporated urine by a process which remained a secret until 1737. As thus procured, it was exceedingly scarce and costly. In 1769 the Swedish chemist Gahn discovered it in bones, and shortly afterwards published a process by which it might be extracted.

Preparation.—Powdered calcined bones (calcium bone phosphate) are digested for twenty-four hours with two-thirds of their weight of sulphuric acid previously diluted with twelve times its weight of water. The sulphuric acid separates the greater part of the lime from the phosphoric acid, and precipitates as calcium sulphate, while an acid calcium phosphate, $Ca H_4(PO_4)_2$, remains in solution. The liquid is then strained through a linen cloth to separate the calcium sulphate, and afterwards submitted to evaporation, which causes a fresh precipitation of sulphate, to be separated by a new straining. The strained solution is evaporated to a syrupy consistence, and then thoroughly mixed with half its weight of powdered charcoal, so as to form a mass, which is dried by being heated to dull redness. At this temperature the acid phosphate is changed into metaphosphate, $Ca(PO_3)_2$, by the loss of two molecules of water. The mass when cool is quickly transferred to a coated earthenware retort, furnished with an adapter of copper, bent downward at right angles, so as to enter a bottle with a large neck containing water, which should rise about two lines above the orifice of the adapter. The bottle is closed round the adapter with a cork, which is traversed by a small glass tube, to give exit to the gaseous products. The retort is heated in a furnace, furnished with a dome, in the most gradual manner, so as to occupy about four hours in bringing it to a red heat. Afterwards the heat is pushed vigorously, so long as any phosphorus drops into the water, and this takes place generally for from twenty-four to thirty hours. During this part of the process the metaphosphate is decomposed, its oxygen combining with the charcoal, and the liberated phosphorus distilling over. The calcined bones of the sheep are preferred, as they contain the largest proportion of calcium phosphate and are most readily acted on by the acid. In the process as described, only two-thirds of the phosphorus is set free, the remainder being still combined. If, however, silica is added to the mixture before the distillation, all the phosphorus is liberated.

The manufacture of phosphorus by the use of the electric furnace, first brought out by Readman and Parker some years ago, has now practically displaced the older methods for the production of phosphorus. Albright and Wilson, who formerly manufactured phosphorus by the distillation method at Oldbury, England, have built works at Niagara Falls, and practically control the production by the electric furnace method in the United States and England.

A mixture of calcium phosphate, carbon, and sand or kaolin is submitted to the temperature of the electric arc while packed in a covered plumbago crucible. The phosphorus is then distilled off in a current of an inert gas. It is very pure, and it is claimed that 86 per cent. is recovered. The native Redonda phosphate, an aluminum phosphate, is also taken for this process instead of the calcium phosphate, and phosphorus obtained from it without any previous purification. The great bulk of the phosphorus is consumed in the manufacture of matches, a smaller amount in the production of phosphor bronze, and another portion in making the chemical compounds of the element. The present annual production (1906) is about 3000 tons, produced in three factories: Oldbury in England, Lyons in France, and Niagara Falls in the United States.

Properties.—Phosphorus is a semi-transparent solid, without taste, but possessing an alliaceous odor. When perfectly pure it is colorless, but as usually prepared it is yellowish or reddish yellow. It is flexible, and when cut exhibits a waxy luster. It was said by Boettger to be easily pulverizable by agitation with a solution of urea. (*J. P. C.*, June, 1863, p. 488.)

"Phosphorus is a translucent, nearly colorless solid, of a waxy luster, having at ordinary temperatures about the consistence of beeswax. By long keeping the surface becomes white or red, and occasionally black. It has a distinctive and disagreeable odor and taste, *but should not be tasted, except in very dilute solution.* When exposed to the air, it emits white fumes, which are luminous in the dark, and have an odor somewhat resembling that of garlic; on longer exposure to the air, it often takes fire spontaneously. Specific gravity: about 1.830 at 10° C. (50° F.). It melts at about 44° C. (111.2° F.). One Gm. of Phosphorus dissolves in about 400 mils of dehydrated alcohol, about 17 mils of chloroform, 102 mils of absolute ether, 31.5 mils of benzene, and in 0.9 mil of carbon disulphide at 25° C. (77° F.), sparingly soluble in fixed oils. It is almost insoluble in water, to which it imparts its characteristic disagreeable odor and taste. Add 1 Gm. of Phosphorus to 10 mils of nitric acid, diluted with 10 mils of distilled water, in a flask having a capacity of 50 mils, and digest the mixture at a gentle heat on a water bath until the

Phosphorus is dissolved, passing a current of carbon dioxide into the flask over the surface of the liquid during the heating. Transfer this solution to a dish, evaporate it until nitrous vapors are no longer given off, and then dilute the solution to 250 mils with distilled water. One mil of this solution meets the requirement of the Test for arsenic (see Part III, Test No. 1). Add barium chloride T.S. to another portion of the latter solution; not more than a slight opalescence is produced (*sulphur*)." *U. S.*

"A semi-transparent, wax-like solid, which emits white vapors and is luminous in the dark when exposed to the air. Insoluble in *water;* soluble in 350 parts of *absolute alcohol,* in 80 parts of *olive oil,* in 80 parts of *ether,* in 25 parts of *chloroform,* and in 0.5 part of *carbon disulphide.* Soft and flexible at ordinary temperatures. Melting point 44° C. (111.2° F.). Ignites in the air at a temperature a little above its melting point, burns with a luminous flame and produces dense white fumes. 1 gramme is slowly attacked and finally dissolved without residue when boiled with 10 millilitres of *nitric acid* diluted with an equal volume of *water,* and the resulting solution yields not more than the slightest *reaction* for sulphates." *Br.*

Its pulverization may be readily effected by melting it in hot water, and agitating until it is thoroughly cooled, and the powder is obtained finer in saline solutions than in pure water.

According to Flückiger, carbon disulphide is capable of dissolving twenty times its weight of phosphorus without losing its fluidity.

Phosphorus boils at 287.7° C. (550° F.), air being excluded. During its combustion it combines with the oxygen of the air, and forms phosphoric oxide. On account of its great inflammability, it must be kept under water. When exposed to the air it undergoes a slow combustion, emitting white vapors, which are luminous in the dark. It sometimes contains arsenic, and therefore, when used in forming medicinal preparations, should be tested for that metal. C. J. Rademaker obtained out of 100 parts of phosphorus about one part of arsenic. (*A. J. P.,* Nov., 1870.) It occasionally contains antimony or sulphur, the latter rendering it brittle.

When phosphorus is kept in ordinary water it becomes covered with a whitish layer, of the nature of which there are different opinions, it being looked upon by some as a phosphorus hydrate, by others as an allotropic condition of that element, and by others again as a partial crystallization, but all these opinions have apparently been disproved by Ernest Baudrimont, who seems to have demonstrated that *white phosphorus* is entirely identical with this whitish layer in its ordinary state, and results from a kind of erosion of the surface, owing to partial oxidation by the free oxygen held in solution by the water. The change never takes place in water entirely deprived of air, and the water when it has taken place holds phosphorous acid in solution. (*J. P. C.,* 4e sér., iii, 17, 1866.)

Schroetter, of Vienna, discovered an allotropic form of phosphorus, which he called *red* or *amorphous phosphorus.* It is formed when ordinary phosphorus is kept long at a temperature between 215° C. (419° F.) and 250° C. (482° F.), in atmospheres which have no action on it, or in closed glass tubes. Red phosphorus is much more indifferent than the ordinary substance, and is denser, its sp. gr. being 2.11. It is much less easily acted on by the air than ordinary phosphorus, and is insoluble in carbon disulphide, alcohol, and ether, in all of which ordinary phosphorus is soluble. Solidified from the fused state, it is brittle, and breaks with a conchoidal fracture. Its hardness is considerable. Obtained by distillation in a non-acting gas, it is mixed with ordinary phosphorus, from which it may be freed by carbon disulphide, which dissolves the ordinary variety and leaves the allotropic as a deep red amorphous powder. It may also be purified by shaking it with a solution of calcium chloride of a density intermediate between that of red and that of ordinary phosphorus, and with a little carbon disulphide. The red variety will sink to the bottom, and the ordinary float on top of the solution, dissolved in the disulphide. (E. Nicklés.) Red phosphorus when pure is not poisonous. This has been proved beyond a doubt by the experiments of Reynal and Lassaigne and of L. Orfila and Rigaut. It is applicable to the manufacture of lucifer matches, and forms a much safer material than ordinary phosphorus. It does not take fire by friction at common temperatures, and therefore may be transported with the greatest safety. It has been said to be unchangeable in the air but this is not exactly true, as proved by an observation of T. B. Groves, who, having set aside some red phosphorus in a bottle that was not air tight observed for a year or more no visible change, but found at length that oxidation had taken place, with the result of forming a large quantity of phosphoric and phosphorous acids, in the proportion of 5 molecules of the former to 2 of the latter. (*P. J.,* June, 1865, p. 621.) Besides the white and red forms of phosphorus, there is another, called the *black,* first noticed by Thènard and investigated by Blondlot, who found that it is pure phosphorus, and that its production is owing to some modification in the mode of cooling, when it has been in the liquid state. (*J. P. C.,* 1865, 4e sér., i, 407.) Flückiger doubted the existence of black phosphorus, however, and, after an investigation, states that the black color is due to arsenical contamination. (*Chem. Ztg.,* 1892, 181.)

Still another modification of phosphorus has been made known by Hittorf, who obtained it by heating red phosphorus and lead together in a closed vessel. The lead on melting dissolved the phosphorus, and on cooling deposited it in the state of black crystals resembling the crys-

tals of arsenic. In this form, phosphorus is a conductor of electricity, and its sp. gr. at 16.6° C. (62° F.) is 2.34. Hittorf distinguishes it by the name of *metallic phosphorus,* and ranks it in the same category with red phosphorus, the latter differing simply in being amorphous. (*Chem. News,* March 23, 1866, p. 133.) Blondlot has succeeded in crystallizing common phosphorus by means of sublimation, operating in an atmosphere of nitrogen. (*J. P. C.,* 4e sér., iv, 321.)

Phosphorus forms with oxygen two oxides, *phosphoric,* P_2O_5, and *phosphorous,* P_2O_3. Corresponding to the first of these are three acids, known as *orthophosphoric* (tribasic phosphoric), H_3PO_4, *pyrophosphoric,* $H_4P_2O_7$, and *metaphosphoric,* HPO_3. The first of these is formed by dissolving P_2O_5 in boiling water, or by the action of nitric acid upon phosphorus itself; the second by the heating of the tribasic phosphoric acid to 213° C. (415.4° F.); and the third by the ignition of the tribasic variety, or by dissolving P_2O_5 in cold water. To the second oxide corresponds *phosphorous acid,* H_3PO_3, although it cannot be formed directly from the oxide. This is a dibasic acid, containing one hydrogen atom not replaceable by metal. To the hypothetical *hypophosphorous oxide,* P_2O, corresponds *hypophosphorous acid,* H_3PO_2. It is monobasic, containing two hydrogen atoms which are not replaceable by metal.

Phosphorus is frequently used as an ingredient in rat pastes. A method for the determination of the free phosphorus in such preparations as well as in the phosphoretted resin, tablets, pills, etc., has been described by E'we and Vanderkleed (*J. A. P. A.,* 1914, p. 1684), in which the phosphorus is distilled in an atmosphere of CO_2, and the distillate collected in a silver nitrate solution and the resulting silver compound decomposed and the phosphorus estimated in the ordinary manner.

Uses.—The continued use of small doses of phosphorus stimulates the blood-making organs, but especially the growth of bone. When administered to growing animals the spongy tissue of the bone becomes thickened and the compact tissue more dense. There is some evidence also that it has a tonic effect upon the nervous system. Phosphorus is used in medicine in the treatment of diseases of the osseous tissues, such as *rickets, ununited fracture,* and *osteomalacia.* It is also widely employed in corections of nervous exhaustion, such as *neurasthenia* and some types of *neuralgia.* It is even believed by some to be of service in degenerative conditions of the nervous system, and has been used in *brain softening,* but with less positive results. Leubuschur (*M. M. W.,* 1913, xxx, p. 494), lauds it in the management of *epilepsy.* It has also been asserted to be of benefit in certain *skin diseases,* notably *acne, psoriasis,* and *chronic eczema.*

Phosphorus Poisoning.—Phosphorus is a very virulent poison, as little as one-eighth of a grain having proven fatal, and an infant was killed by eating the heads of two friction-matches. The symptoms usually do not manifest themselves until some hours after the ingestion of the phosphorus. General malaise then becomes very pronounced, and is soon accompanied by nausea, abdominal pain, and vomiting of food, mucus, and bile. On the second and third day the vomiting is likely to cease, but the abdominal tenderness remains, and there is some fever. Later the patient becomes jaundiced and severe vomiting of a coffee-ground liquid, free from bile and similar to the black vomit of yellow fever, may set in; the urine is scanty and albuminous, often with tyrosine and leucine in it, or it may finally be suppressed. Frequently there is wild delirium. The temperature falls markedly, and the patient sinks into a coma which ends in death. After death a peculiar fatty degeneration is found affecting almost all the soft tissues. The parts which suffer first are the liver, the gastro-intestinal mucous membrane, and the kidneys. Both in its symptoms and in its lesions phosphorus poisoning so closely resembles acute atrophy of the liver that only by detecting the phosphorus in the matters vomited, in the excretions, or in the tissues of the body, can a positive diagnosis be made. As the phosphates are normally abundant in the urine it is necessary to find the phosphorus in the elemental state.

For methods of detecting phosphorus in cases of suspected poisoning, see *U. S. D.,* 19th ed., p. 935.

E. Mitscherlich gave the following as a delicate test for phosphorus. The suspected substance is distilled with sulphuric acid and water from a flask, by means of a tube bent twice at right angles, into a vertical cooling-tube, passing through the bottom of a wide glass cylinder filled with water, which is constantly kept cold by passing cold water in at the bottom, while the warm water escapes at the top. Under the cooling-tube is placed a vessel to receive the distillate. If phosphorus is present, its vapor, mixed with steam, distils over, and gives rise to a distinct luminous appearance, visible in the dark, at the point where it enters the cold part of the cooling-tube.

This test while very sensitive is interfered with by a variety of substances notably iodine, calomel, corrosive sublimate, alcohol, and oil of turpentine. It acts well in the presence of fatty matters, as has been shown by de Vrij, but Roussin finds that the presence of free butyric acid prevents the luminous appearance of the phosphorus. After neutralizing with potassium carbonate, however, it can be seen. (Sonnenschein, *Gerichtl. Chem.,* 1881, p. 27.) L. Hofmann gives the following method of detecting phosphorus in the viscera in cases of poisoning. The viscera, mixed with water and a little sulphuric acid, are distilled until two drachms of liquid are obtained; to this a few drops of ammonium sulphide (ammonium sulphydrate) are

to be added, and the liquid is to be evaporated to dryness in a porcelain dish. If phosphorus be present in the minutest quantity, a drop of solution of ferric chloride will produce a deep violet and brownish, though evanescent, color. (*Chem. News,* Feb. 3, 1865, p. 53.) In addition to Mitscherlich's test, Dusart's is also used. This consists in passing pure hydrogen gas, evolved in a separate vessel, through the solution supposed to contain phosphorus, which solution has been previously warmed to about 50° C. (122° F.). The gas then is allowed to issue from a fine jet and is lighted. If phosphorus be present, the flame will show a green color in the center.

It is evident from the widespread lesions caused by phosphorus that after its absorption no treatment can be of service. It is therefore of the utmost importance that chemical antidotes and emetics be used promptly. Probably the best chemical antidote is potassium permanganate, which acts by oxidizing the poison, but copper sulphate is of great value as it not only forms a non-toxic phosphide of copper but also acts as an emetic. The oil of turpentine has been stated to possess antidotal properties, but this is not true of the American oil. If the stomach tube be at hand probably the best treatment is washing out the stomach with a one-half per cent. solution of potassium permanganate repeatedly and leaving about half a pint of the solution in the stomach. In the absence of the stomach pump, three grains of copper sulphate may be given every five minutes until free emesis, and after the stomach has been thoroughly emptied a dose of four grains of potassium permanganate should be given. Formerly workers in match factories were frequently attacked with a peculiar form of chronic phosphorus poisoning of which the most characteristic symptom was a necrosis of the jaw, whence the popular name of "phossy jaw." Since the introduction, however, of the harmless sesquisulphide this condition has become much less common. The safety matches do not contain ordinary or yellow phosphorus, an igniting composition containing red phosphorus, which when pure is harmless, being painted on the box. The use of the poisonous forms of phosphorus in matches is now prohibited by law in this and most civilized countries.

Phosphorus should never be exhibited in substance, but the official pill is an eligible preparation. The phosphorated oil (*Br.* and *U. S. P.,* 1890) is also a useful means of administering the drug.

The allotropic red phosphorus sometimes called *amorphous phosphorus,* is non-toxic. It has been suggested for therapeutic purposes but appears to be quite inert.

The *elixir* (*Elixir Phosphori,* N. F. IV) is probably the most eligible of the liquid preparations, but the *oil* (*Oleum Phosphoratum,* N. F. IV) is very efficient, as is also the official pill (*Pilulæ Phosphori*). Great caution is necessary in the exhibition of phosphorus, and its effects should be closely watched. It ought never to be given in substance.

Dose, of phosphorus, from 1-100th to 1-80th of a grain (0.0006–0.0008 Gm.). Much larger doses than these have been given, but have in various cases produced unpleasant symptoms.

Off. Prep.—Oleum Phosphoratum, *Br., N. F.;* Pilulæ Phosphori, *U. S.* (*Br.*); Elixir Phosphori, *N. F.;* Liquor Phosphori, *N. F.*

PHYSOSTIGMA. U. S.

PHYSOSTIGMA Physostig. [Calabar Bean, Ordeal Bean]

(phȳ-sọ-stīg'mą)

"The dried ripe seeds of *Physostigma venenosum* Balfour (Fam. *Leguminosæ*), yielding not less than 0.15 per cent. of the alkaloids of Physostigma." *U. S.*

Physostigmatis Semina, *Br.* 1898; Chopnut; Ordeal Bean of Calabar; Faba Calabarica; Fève du Calabar, *Fr. Cod.;* Kalabarbohne, *G.;* Haba del calabar, Eseve, *Sp.*

Physostigma venenosum is a climbing plant, with a ligneous stem, and frequenting especially the banks of streams, into which it often drops its fruit when ripe, and it is said that the people of Calabar derive their supply principally from the borders of the streams down which the fruits are carried. The rhizome is spreading, with numerous rootlets, often having attached to them small succulent tubers. The flowers are in axillary, multiflorous, pendulous racemes. The corolla is papilionaceous, of a pale pink color, with a purplish tinge. The legume when ripe is about seven inches long, and contains two or three seeds. It ripens at all seasons, but is most abundant during the rainy season from June to September. The seeds are the part used. The plant, which is indigenous to Western Africa, has been introduced into India and Brazil, and is said to flourish in the latter country. The market supplies are obtained from the regions surrounding the mouth of the Niger and the lower portion of the Calabar River, the chief port of export being Lagos (*Ap. Ztg.,* xxvi, p. 568; xxvii, p. 137). Only one other species (*P. mesoponticum* Taub.), also of tropical Africa, is known. For a paper on the botanical description, history, etc., of *Physostigma venenosum* by J. U. Lloyd, see *West. Drug.,* 1897, 249.

This bean was brought to the notice of the scientific public by Daniell, in 1846. Considerable attention was attached to the subject, and specimens of the bean were obtained by Christison from the Gold Coast. These were planted in the Botanical Garden at Edinburgh, and produced a perennial creeper. In the year 1859, specimens of the plant were sent from Calabar, which came under the observation of Balfour, of Edinburgh, who was thus enabled to ascertain its botanical character.

Properties.—The seeds are officially described as follows: "Oblong or ellipsoidal, somewhat compressed reniform, from 15 to 30 mm. in length and from 10 to 15 mm. in thickness;

externally reddish or chocolate brown, smooth, somewhat wrinkled near the brownish-black groove, the latter being about 2 mm. in width and extending almost the entire length of the convex edge and in which are found frequently the remains of the white membranous funiculus, the margins of the seed-coat on both sides of the groove somewhat elevated, of a yellowish-red or brownish-red color and somewhat thickened; embryos large, white, with short hypocotyl and two concavo-convex cotyledons; taste at first starchy, afterwards acrid. The powder is grayish-white, starch grains numerous, from 0.005 to 0.15 mm. in diameter, ellipsoidal or somewhat reniform, and usually with a distinct cleft and frequently with radiating or irregular fissures; fragments of seed-coat with very thick, reddish-brown cells, being either palisade-like or very irregular and resembling stone cells, but the walls are not lignified; an occasional fragment with tracheæ showing reticulate thickenings. Physostigma yields not more than 3 per cent. of ash." *U. S.*

Physostigmine was official in the Br. Pharm., 1885, and was thus described: "In colorless or pinkish crystals, slightly soluble in water, but readily soluble in alcohol and in diluted acids. The aqueous solution has an alkaline reaction, when warmed with or when shaken with dilute solution of potash becomes red, and when evaporated to dryness over a water bath leaves a bluish residue, the acidified solution of which is beautifully dichroic, being blue and red." *Br.*, 1885.

Assay.—"Introduce 15 Gm. of Physostigma in No. 60 powder, into a flask of about 250 mils capacity, and add 150 mils of ether. Stopper the flask, shake it well and allow it to stand ten minutes, then add 10 mils of an aqueous solution of sodium bicarbonate (1 in 20) and shake the mixture vigorously at intervals during four hours. Now add 15 mils of distilled water, again shake the flask well, and, when the drug has settled, decant 100 mils of the ether solution, representing 10 Gm. of Physostigma. Filter the solution through a pledget of purified cotton into a beaker and rinse the graduate and cotton with ether. Add 20 mils of tenth-normal sulphuric acid V.S. and evaporate off the ether, stirring during the evaporation with a rubber-tipped glass rod. After the resinous and fatty matter has agglutinated, pour off the acid solution through a wetted filter into a separator. Redissolve the residue in the beaker in about 15 mils of ether, add 2 mils of tenth-normal sulphuric acid V.S., evaporate off the ether with continued stirring as before and pour the acid solution on the filter. Repeat this operation until all the alkaloid is extracted and then wash the filter with distilled water until it is free from alkaloids. Collect the solution and washings in a separator, add sufficient sodium bicarbonate to make the solution decidedly alkaline to litmus and completely extract the alkaloids by shaking it out repeatedly with ether. Wash the combined ether solutions with 10 mils of distilled water, separate the water completely, and filter the ether solution, washing the container and filter with ether. Evaporate the ether solution to dryness, dissolve the alkaloids from the residue in exactly 5 mils of tenth-normal sulphuric acid V.S. and titrate the excess of acid with fiftieth-normal potassium hydroxide V.S., using cochineal T.S. as indicator.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 27.52 milligrammes of the alkaloids of Physostigma (see Part III, Proximate Assays, No. 15)." *U. S.*

Calabar beans are occasionally substituted by a number of more or less similar seeds of African plants. Hartwich (*S. W. P.*, 1905, p. 441) calls attention to a false physostigma found in the Hamburg drug market which is derived from *Pentaclethra macrophylla* Benth., a leguminous tree indigenous to tropical Africa. The seeds are dark reddish-brown, from 5 to 7 cm. long, about 5 cm. broad and about 1 cm. thick. They are flattened-oval or roundish-triangular.

Physostigma yields its virtues to alcohol, and imperfectly to water. The shell constitutes, according to Edwards, 30 per cent., the kernel 70 per cent., of the bean. Jobst and Hesse (*J. P. C.*, March, 1864, p. 277) first isolated an active principle, which they found exclusively in the cotyledons. They obtained it by exhausting an alcoholic extract of the seeds with water, adding magnesia to neutralization, which is indicated by the liquid becoming brown, then concentrating, and treating with ether. The ethereal solution was shaken with a little weak sulphuric acid. The liquid separated into two layers—the upper, ethereal, containing no alkaloid, and the lower, a solution of the sulphate in water. The latter was separated, treated with magnesia, and afterwards with ether, which yielded the alkaloid on evaporation. The substance thus obtained they proposed to name *physostigmine*. In 1865 Vée and Leven (*C. R. A. S.*, 60, 1194) obtained, by treating the seeds in nearly the same manner, an alkaloid to which they gave the name *eserine*, which formed colorless tabular crystals of a bitter taste, readily soluble in ether, alcohol, or chloroform, but sparingly in water. The crystals contain 1 molecule of water, which they lose at 100° C. (212° F.), and the anhydrous alkaloid then fuses at from 102° to 103° C. (215.6°–217.4° F.). Eserine is now generally accepted as identical with physostigmine. In 1867, Hesse (*Ann. Ch. Ph.*, 141, 82) obtained the same alkaloid in a still purer state, perfectly colorless and tasteless, fusing at 45° C. (113° F.), and decomposing at 100° C. (212° F.) with red coloration. He gives it the formula $C_{15}H_{21}O_2N_3$.

A peculiarity of the alkaloid is that an aqueous solution of it, or of one of its salts, exposed to the air in the presence of potassium or sodium hydroxides, or lime, becomes red, owing to the absorption of oxygen. The coloring

matter is taken up by chloroform. The color is not permanent, but gradually changes to yellow, green, or blue. This test will detect less than the hundred-thousandth part of the alkaloid. The same property is possessed by the alcoholic extract of the bean. This is the cause of the color changes taking place in solutions dispensed in ordinary glass bottles. The change may be retarded by previously rinsing out the bottle with diluted hydrochloric acid, and subsequently with distilled water, or it may be entirely prevented by coating the inner surface of the dispensing vial with paraffin.

Harnack and Witkowski (*A. E. P. P.*, v; also x) in 1876 obtained still another alkaloid, which they named *calabarine*. It is soluble in alcohol and water, nearly insoluble in ether, melts at 132° C. (269.6° F.), and differs in physiological character from physostigmine. It is now generally known under the name of *eseridine*. The formula $C_{15}H_{23}O_3N_3$ has been given to it by Eber (*Ph. Ztg.*, 1888, p. 611), which differs from that of physostigmine, it will be seen, by H_2O only, and it is stated that the one can be changed into the other by the action of dilute acids. It has properties like eserine but in a milder degree. *Eseramine*, $C_{16}H_{25}O_3N_4$, is another alkaloid of feeble activity which is present. It was announced by Ehrenberg in 1893 (*Verhand. d. Gesellsch. Deutsche Natur. u. Aertzte.*, 1893, ii, p. 102). There is much reason for believing that calabarine is a decomposition product derived from physostigmine. (Husemann, *A. E. P. P.*, 1878, 14; Harnack, *A. E. P. P.*, x.)

Still another alkaloid announced by Salway is *physorenine*, $C_{14}H_{18}O_3N_2$. It is a powerful myotic like eserine. It is believed to be an intermediate product in the decomposition of eserine by alkalies, which results in the formation of a new base called *eseroline*, $C_{13}H_{18}ON_2$. Another decomposition product of eserine is produced by an excess of ammonia and is called *eserine blue*, $C_{17}H_{23}O_2N_3$.

Hesse obtained also a neutral fatty body, *physosterin*, by exhausting the cotyledons with petroleum benzin. It is closely allied to cholesterin, but its chloroform solution is devoid of rotatory power. Its formula is $C_{26}H_{44}O + H_2O$, and its melting point is 133° C. (271.4° F.).

Uses.—The action of physostigma is practically that of its dominant alkaloid physostigmine, but the effects are more or less modified by the other alkaloids; thus calabarine is a stimulant to the spinal cord and in this regard antagonistic to physostigmine, while isophysostigmine possesses the physiological properties of the dominant alkaloid upon the unstriped muscle, but apparently not upon the other structures of the body. For this reason whenever the systemic action is desired the alkaloid should be given the preference over preparations of the whole drug. On the other hand, as a stimulant to the unstriped muscle of the intestines, as in *constipation*, the whole drug may properly be used.

Poisoning.—Calabar bean has been used from time immemorial by the natives of Africa as an ordeal, and, when given by their head men, usually proves fatal to the accused, unless free vomiting occurs. A draught containing 19 seeds pounded and infused in water is said to have killed a man in an hour. In the experiments of Fraser, it was found that the integuments of the seeds, as well as the shell, are distinctly purgative. It is probable that in the fresh bean they are also emetic, and that the priests or chiefs who administer the ordeal take advantage of this in regulating the effects of the poison to suit their own purposes; sometimes, however, even the pure alkaloid causes vomiting. (Gubler.) Of seventy children poisoned in Liverpool by eating Calabar beans which had been thrown upon a waste heap, vomiting occurred, or was produced by emetics, in all except one, in whom four kernels caused death. The nausea and vomiting came on in about half an hour, the nervous symptoms in less than an hour.

There are generally diminution of reflexes, coarse muscular tremors which may be sufficiently violent to suggest convulsions, contraction of the pupil, and progressive diminution of motor power. In the fatal cases death is generally due to paralytic asphyxia.

In the treatment of physostigma poisoning the stomach should be thoroughly washed out either with an emetic or the stomach pump, and tannic acid or compound solution of iodine given as a chemical antidote. Atropine, which is a partial physiological antagonist, should be given in doses of about one-fiftieth of a grain (0.0013 Gm.), and strychnine and other stimulants employed as indicated.

Dose, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Extractum Physostigmatis, *U. S.*; Tinctura Physostigmatis, *U. S.*

PHYSOSTIGMINÆ SALICYLAS. U. S.

PHYSOSTIGMINE SALICYLATE Physostig. Salicyl. [Eserine Salicylate]

(phȳ-sǫ-stĭg-mĭ'næ săl-ĭ-cȳ'lăs)

"The salicylate [$C_{15}H_{21}O_2N_3.C_7H_6O_3 = 413.25$] of an alkaloid obtained from physostigma. Preserve it in small, well-closed containers, protected from light." *U. S.*

Salicylate d'Esérine, *Fr. Cod.*; Physostigminum salicylicum, *P. G.*; Physostigminsalicylat, Eserinsalicylat, *G.*

Preparation.—This salt is preferred to the sulphate of the alkaloid (see page 852) on account of its greater stability. Its advantage is that it is not deliquescent. Birkenwald (*Ph. Z. R.*, 1891, 657) gives the following process: 100 parts of physostigmine sulphate are dissolved in a suitable quantity of water, and an excess of a solution of sodium bicarbonate added and agitated with several portions of absolute ether; the ethereal solutions

are filtered into a beaker containing 35.5 parts of salicylic acid dissolved in ether, thoroughly mixed, and the physostigmine salicylate collected upon a filter, washed with absolute ether and dried, protected from sunlight and air. Any excess of salicylic acid that may have been present is removed by the washing with ether. The success of this method depends upon rapid manipulation and preventing exposure to sunlight, otherwise the salt obtained will be of a red color due to the decomposition of physostigmine and formation of *rubeserine;* washing the crystals with alcohol will remove any red color, but with loss of physostigmine salicylate.

Properties.—It is officially described as "colorless or faintly yellowish, shining, acicular, or short columnar crystals; odorless. It acquires a red tint when long exposed to light and air. *Great caution must be used in tasting it.* One Gm. of Physostigmine Salicylate dissolves in 75 mils of water, 16 mils of alcohol, 6 mils of chloroform, and in 250 mils of ether at 25° C. (77° F.); also in 16 mils of water at 80° C. (176° F.) and in 5 mils of boiling alcohol. Its cold, saturated aqueous solution is neutral or at most only faintly acid to litmus. Upon standing twenty-four hours, this solution usually acquires a pink color. This color is produced rapidly by the addition of a few drops of sodium hydroxide T.S. Ferric chloride T.S. produces a deep violet color in an aqueous solution of Physostigmine Salicylate; a solution of chlorinated lime added to an aqueous solution of the salt produces a red color. Evaporate about 0.005 Gm. of the salt to dryness with a few drops of ammonia water; a blue residue is produced, which is soluble in alcohol, and, when so dissolved, yields a red fluorescent solution upon the addition of acetic acid in excess. No weighable ash remains on incinerating 0.1 Gm. of Physostigmine Salicylate. Precipitate the salicylic acid from 10 mils of a cold, saturated aqueous solution of the salt with a slight excess of hydrochloric acid and filter the mixture; the filtrate is not rendered turbid at once by the addition of a few drops of barium chloride T.S. (*sulphate*). A solution of about 0.1 Gm. of Physostigmine Salicylate in 2 mils of sulphuric acid does not become darker than yellow within five minutes (*readily carbonizable impurities*)." *U. S.*

Uses.—The physiological actions of physostigmine divide themselves into three groups: depression of the central nervous system, increased irritability of the autonomic nerves, and stimulation of unstriped muscles. The depression of the central nervous system is most noticeably manifested in the diminution of reflex activities from depression of the spinal cord. After toxic doses the drug also depresses the respiratory center. Its effects upon the autonomic nerves are antagonistic to those of atropine (see p. 206). Among the most important of these actions are the slowing of the pulse by stimulation of the vagus, and the contraction of the pupil by stimulation of the oculomotor nerve. In large doses it also increases secretion, although it is not employed practically for this purpose. Although in sufficient dose physostigmine causes a rise in blood pressure by its stimulating action upon the cardiac and vascular muscles, the only therapeutically important action upon muscle tissue is the intestinal tract. According to the studies of Magnus (*A. G. P.,* 1905, cviii, p. 1), it increases both the tone and the extent of contraction of the intestinal muscles.

Physostigmine is used in medicine chiefly to meet one of three indications. To contract the pupil in *glaucoma* and other diseases of the eye, it may be directly instilled into the diseased organ in strengths of from one-foruth to one-half of one per cent. As a stimulant to peristalsis it is useful in *chronic constipation, phantom tumor,* post-operative *intestinal atony, flatulent colic,* and other conditions of deficient activity of the alimentary muscles. As a sedative to the spinal cord it has been used in *tetanus* and *strychnine poisoning,* but clinical experience has shown that it is of much less value than chloral or the bromides. Recently it has been recommended by Kaufmann in the treatment of *tachycardia.* (*W. K. W.,* 1912, p. 1080.)

Dose, one-sixtieth to one twenty-fourth of a grain (0.0011–0.0025 Gm.).

PHYSOSTIGMINÆ SULPHAS. Br.

PHYSOSTIGMINE SULPHATE [Eserine Sulphate]

(phȳ-sǫ-stĭg-mĭ'næ sŭl'phās)

"Physostigmine Sulphate, $(C_{15}H_{21}N_3O_2)_2$, H_2SO_4, is the sulphate of an alkaloid, physostigmine, obtained from the seeds of Physostigma venenosum, *Balfour.*" *Br.*

Sulfate d'Eséŕine, *Fr. Cod.;* Physostigminum sulfuricum, *P. G.;* Physostigminsulfat, *G.;* Sulfatu de eserina, *Sp.*

This salt was not admitted to the U. S. P. IX, but is retained in the Br.; it is preferable to the salicylate on account of its greater solubility, but on exposure to the air it soon assumes an extractive consistence which renders it difficult to dispense; the salicylate is free from this objection.

Preparation.—*Physostigmine* or *eserine sulphate* is obtained by M. A. Petit in the following manner: A hydro-alcoholic extract of the bean is dissolved in four parts of distilled water, and the solution filtered. To the solution is added one gramme of potassium bicarbonate for every 20 grammes of extract, and the mixture is shaken with ether in excess. The ether, which takes up nearly all the alkaloid, is separated after standing for a few minutes. A little distilled water is then added, and afterwards sulphuric acid drop by drop, the liquid being shaken after each drop, and tested with litmus paper until exactly neutral. After standing, the aqueous solution is separated from the ether, which now contains none of the alkaloid. This ether is then employed as before, and the

operation repeated three or four times, so as completely to exhaust the original solution, and the liquid obtained each time is added to the last aqueous solution. This contains the physostigmine sulphate nearly pure. To purify this, it should be passed through the same process as the original solution of the extract. The resulting solution may be evaporated to crystallization if desired; but usually the evaporation is carried only so far as to get rid of all the ether present. If enough water be added to the solution to make as many grammes as there were drops of sulphuric acid (H_2SO_4) employed, each gramme will represent approximately one centigramme of the alkaloid.

Petit and Polonovski conducted experiments with the view of discovering salts of eserine which would be stable and non-hygroscopic; they made *eserine benzoate, eserine meta-cresotate, eserine citrate,* and *eserine tartrate.* Processes will be found in *J. P. C.,* 1894, 55.

Properties.—It is officially described as "minute white crystals, becoming yellowish on exposure to air and light; very deliquescent. Readily soluble in *water,* soluble in *alcohol* (90 per cent.). Aqueous solution neutral to *litmus;* yields the *reaction* characteristic of sulphates; yields with dilute *solution of sodium hydroxide* a white precipitate turning pink and forming a red solution with excess of the reagent; when mixed with *solution of ammonia* and evaporated to dryness on a water-bath it leaves a bluish residue, the solution of which in very dilute acids is dichroic, being red by reflected and blue by transmitted light. A minute fragment dissolved in a few drops of *fuming nitric acid* forms a yellow liquid, which, on warming on a water-bath, turns orange, then blood-red, and on evaporation to dryness leaves a green residue; this residue turns violet-blue on exposure to the fumes of *nitric acid,* and when moistened with the acid gives gradually a blood-red color, which changes to greenish-yellow on the addition of *water.* A dilute aqueous solution applied to the eye causes contraction of the pupil. No appreciable ash." *Br.*

Physostigmine sulphite has been patented and it is stated that it is more stable than either the salicylate or sulphate.

The medicinal properties, uses, and dose of physostigmine sulphate are the same as those of *Physostigminæ Salicylas.*

Dose, from one-sixtieth to one twenty-fourth of a grain (0.0011–0.0025 Gm.).

Off. Prep.—Lamellæ Physostigminæ, *Br.*

PICRORHIZA. Br.

PICRORHIZA

(pĭc-rō-rhī'zą)

"Picrorhiza is the dried rhizome of Picrorhiza Kurroa, *Royle.*" *Br.*

Kutki, Katki, Kuru, Kuruwa, Kaur, Karru, Kutaki, Kali-kutki, or Black Kutki, Katukurogani.

Picrorhiza Kurroa Royle (*P. Kurrooa* Benth.), more properly known as *P. Lindleyana* (Wall. Wettst.), is a low, hairy perennial herb (Fam. *Scrophulariaceæ*), indigenous to the Alpine Himalayas. The rootstalk or the rhizome has long been used in India and has been frequently spoken of by European and Mahometan writers as *black hellebore,* but is essentially different.

Properties.—*Picrorhiza* occurs "in cylindrical pieces two to five centimetres long, and four to eight millimetres thick, sometimes terminating in a stem or scaly leaf-bud; brittle. Cork greyish-brown, wrinkled, with transverse leaf scars and small buds. Fracture short. In transverse section internally dark and porous, with a thin, greyish cork and narrow ring of tangentially elongated wood-bundles. No odor; taste very bitter." *Br.*

Picrorhiza resembles externally the rhizome of *Gentiana Kurroo* Royle (Fam. *Gentianaceæ*), the latter, however, is uniformly brown internally, whereas the rhizome of Picrorhiza is darker or black, whence its name kali or black kutki. It is the dried rhizome of an Alpine-Himalayan plant, *Kurroa.* From this rhizome H. Warden has separated a glucoside, *picrorhizin,* which is freely soluble in water and alcohol and appears to be the bitter principle of the drug; also a red-brown, resinous, tasteless body, *picrorhizetin,* and, perhaps, cathartic acid (*Pharmacog. Indica,* vol. 3).

Uses.—The natives of India attribute active antiperiodic power to picrorhiza, which appears to be a powerful bitter tonic with slight laxative action. It is given in *doses* of from one to twenty grains (0.065–1.3 Gm.) as a tonic and from forty to fifty grains (2.6–3.2 Gm.) as an antiperiodic, usually in combination with aromatic.

Off. Prep.—Extractum Picrorhizæ Liquidum, *Br.;* Tinctura Picrorhizæ, *Br.*

PILOCARPINÆ HYDROCHLORIDUM. U. S.

PILOCARPINE HYDROCHLORIDE Pilocarpin. Hydrochl. [Pilocarpine Chloride, Pilocarpine Hydrochlorate, Pilocarpinæ Hydrochloras, U. S. 1890]

(pī-lo-căr-pī'næ hȳ-dro-ȼhlōr'ī-dŭm)

"The hydrochloride ($C_{11}H_{16}O_2N_2.HCl = 244.62$) of an alkaloid obtained from pilocarpus. Preserve it in well-closed containers, protected from light." *U. S.*

This alkaloidal salt is usually obtained by the process given under *Pilocarpus* for the alkaloid (see page 857).

Properties.—Pilocarpine hydrochloride is officially described as in "colorless, translucent crystals, odorless and having a faintly bitter taste; hygroscopic on exposure to the air. One Gm. of Pilocarpine Hydrochloride dissolves in 0.3 mil of water, 3 mils of alcohol, and in 366 mils of chloroform at 25° C. (77° F.); also in 1.5 mils of alcohol at 60° C. (140° F.); insoluble in ether. Its aqueous solution (1 in

20) is neutral or at most only slightly acid to litmus. When dried to constant weight at 100° C. (212° F.) it melts between 195° and 198° C. (383°–388.4° F.). Silver nitrate T.S. produces in an aqueous solution of the salt a white precipitate, insoluble in nitric acid. Dissolve 0.01 to 0.02 Gm. of Pilocarpine Hydrochloride in 2 mils of distilled water in a test tube, add 2 mils of a slightly acid solution of hydrogen dioxide, and then cover the mixture with a small layer of benzene. Now add 3 or 4 drops of a solution of potassium dichromate (1 in 300) and shake the mixture gently; the benzene layer acquires a violet color, while the aqueous layer remains yellow (distinction from *other alkaloids*). (If more than 0.02 Gm. of the salt is used, the benzene turns blue, and the reaction is no longer characteristic.) No weighable ash remains on incinerating 0.1 Gm. of Pilocarpine Hydrochloride. A solution of about 0.1 Gm. of the salt in 2 mils of sulphuric acid is colorless or at most only faintly yellow (*readily carbonizable impurities*). The addition of ammonia water or potassium dichromate T.S. to 10 mils of an aqueous solution of the salt (1 in 100) produces no turbidity (*various foreign alkaloids*)." *U. S.*

Uses.—Pilocarpine is the physiological antagonist of atropine, exciting those nerve endings which are paralyzed by that alkaloid. Thus it causes contraction of the pupil by stimulating the peripheral ends of the oculomotor nerve, increased flow of saliva by acting on the chorda tympani, slowing of the pulse through vagal stimulation (for some unknown reason the pulse rate is often increased in human beings), free sweating, and increased peristalsis of the intestines. The effects upon secretion are especially pronounced, the quantity of sweat brought out by a single dose of the alkaloid has been estimated at from 9 to 15 ounces. Ewing has shown that in the case of the salivary glands at least (*J. P. Ex. T.*, 1911, iii, p. 1) the increase is not merely in the watery constituents, but represents a true excitation of glandular activity because the solid matters and specific ferment of the secretion are also augmented. Usually there is more or less compensatory corollation between the degree of action on the various glandular structures, that is, if the sweat is greatly increased the effects upon the salivary glands, for instance, will be comparatively slight. There has been considerable difference of opinion among clinicians as to whether pilocarpine has any effect upon the kidney, and if so, what is the nature of this action, but the studies of Baco and Plumier (*J. de P. P.*, 1908, x, p. 32) have shown that the changes in the urinary output are secondary to the effects on the circulation; thus if the drug causes a fall of blood pressure the quantity of urine is diminished, but if there is no change in the circulation the kidney activity is unaffected. It is probable that in human beings the loss of water through the skin will also affect the quantity of urine.

Pilocarpine is used in medicine chiefly as a sudorific, either for the purpose of evacuating *dropsies* or aiding in the elimination of toxic substances, as in *uremia, gout, chronic rheumatism* and similar complaints. It should always, if possible, be used in conjunction with some form of external heat so as to determine the blood towards the skin. If used incautiously it may give rise to a very dangerous pulmonary edema. The mechanism of this is three-fold, an increase in the bronchial secretions, a reduction of the force of the circulation, and a spasm of the bronchial muscles. If the action of the drug has been directed towards the skin by other diaphoretic measures and the dose has not been unduly large, the likelihood of this accident is extremely remote. Its occurrence is the signal for the immediate exhibition of atropine. We believe that the doses sometimes employed are much larger than necessary. If properly used more than one-eighth of a grain hypodermically is very rarely needed. Pilocarpine has also been recommended by Reid (*J. A. M. A.*, 1911, lvi, p. 1739) in the treatment of *pruritus*. It is believed by some to have an effect upon the growth of the hair and is used both internally and topically in the treatment of *baldness*. Robinson (*J. A. M. A.*, 1914, lxiii, p. 63) reports favorable results in the treatment of *hypertension*. It is also asserted to be of value in *catarrhal jaundice*. As a local remedy it is employed by ophthalmologists as a myotic in strengths of one-half to one per cent.

Dose, one-twentieth to one-fourth of a grain (0.003–0.016 Gm.).

PILOCARPINÆ NITRAS. U. S., Br.

PILOCARPINE NITRATE Pilocarpin. Nit.

(pī-lo-cär-pī'næ nī'trăs)

"The nitrate [$C_{11}H_{16}O_2N_2.HNO_3 = 271.17$] of an alkaloid obtained from pilocarpus. Preserve it in well-closed containers, protected from light." *U. S.* "Pilocarpine Nitrate, $C_{11}H_{16}N_2O_2.HNO_3$, is the nitrate of an alkaloid, pilocarpine, obtained from the leaves of Pilocarpus microphyllus, *Stapf*, and other species of Pilocarpus." *Br.*

Preparation.—This salt may be made by adding pure pilocarpine to diluted nitric acid, carefully evaporating the solution, and purifying the crystals by solution in alcohol and recrystallizing.

Properties.—The official description is as follows: "Pilocarpine Nitrate occurs in shining crystals; odorless; permanent in the air. One Gm. of Pilocarpine Nitrate dissolves in 4 mils of water and in 75 mils of alcohol at 25° C. (77° F.); also in 21 mils of alcohol at 60° C. (140° F.); insoluble in chloroform or ether. It melts between 170° and 173° C. (338° and 343.4° F.). Carefully pour an aqueous solution of the salt, mixed with an equal volume of ferrous sulphate T.S., over sulphuric

acid without shaking; a brown ring appears at the juncture of the two layers. The addition of a few drops of silver nitrate T.S. to 5 mils of an aqueous solution of the salt (1 in 20), acidulated with nitric acid, produces not more than an opalescence (*chloride*). In other respects the salt responds to the tests for identity and purity under *Pilocarpinæ Hydrochloridum.*" *U. S.*

"A white crystalline powder. Soluble in 8 parts of *water.* Melting point about 176° C. (348.8° F.). Yields with *sulphuric acid* a colorless solution slowly becoming green on the addition of *potassium bichromate.* When a solution of 0.01 gramme in 5 millilitres of *water* is mixed with 2 drops of *diluted sulphuric acid* and then with 1 millilitre of *solution of hydrogen peroxide,* 1 millilitre of *benzene,* and 1 drop of *solution of potassium chromate,* and the mixture well shaken and allowed to separate, the benzene is colored bluish-violet. No appreciable ash." *Br.*

The medicinal properties and dose are the same as those of *Pilocarpinæ Hydrochloridum.*

Dose, from one-twentieth to one-fourth of a grain (0.003–0.016 Gm.).

PILOCARPUS. U. S.

PILOCARPUS Pilocarp. [Jaborandi]

(pī-lō-cär'pŭs)

"The dried leaflets of *Pilocarpus Jaborandi* Holmes, known in commerce as Pernambuco Jaborandi, or of *Pilocarpus microphyllus* Stapf, known in commerce as Maranham Jaborandi (Fam. *Rutaceæ*), without the presence or admixture of more than 5 per cent. of the stalks bearing the leaflets and stems of the same plant, or other matter, and yielding not less than 0.6 per cent. of the alkaloids of Pilocarpus." *U. S.*

Jaborandi Folia, *Br.* 1898; Jaborandi leaves, Pilocarpi Foliola; Jaborandi, *Fr. Cod.*; Folia Jaborandi, *P. G.*; Jaborandiblätter, *G.*; Jaborandi, *It.*; Jaborandi (Hoja de), *Sp.*

It is unfortunate in our opinion that this drug was omitted from the Br. Pharm., 1914; it was official in the Br. Pharm., 1898, under the title "Jaborandi Folia."

Pilocarpus was first introduced to the notice of the European profession by Coutinho (*J. P. C.,* 4e sér., xx, 51) under the name of Jaborandi, a name which has adhered to the drug, although the terms Jaborandi, Iaborandi and Jamborandi are used in South America to designate various pungent, sudorific plants, most of which belong to the genus Piper, but some of which have no botanical relation at all with the peppers. Although the leaves of the *Piper Jaborandi* have been sent into commerce as Jaborandi, none of the true jaborandis of South America have any physiological relations with the official drug, which in South America is known as *Arruda do Mato* or as *Arruda brava* or, rarely, as *Jamguarandi* or *Jaurandi.*

The genus Pilocarpus consists of woody shrubs belonging to the Rutaceæ and inhabits tropical and subtropical America, including Cuba, Guadeloupe, Martinique, and probably other islands. For elaborate botanical and histological studies of the commercial species of Pilocarpus, see the articles by A. Duvall, *B. Sc. Pharm.,* iii, pp. 41 and 98; Geiger, *Ber. d. D. Phar. Ges.,* 1897, p. 356; Hartwich, *Apoth. Zeit.,* 1900; Holmes *P. J.,* 1903, p. 713; and 1904, p. 54; Schneider, *Jour. of Pharmacology* (N. Y. C. P.), 1897, No. 6; Tunman, *S. W. P.,* xlvii, p. 177. The following species of the genus have been used in medicine:

P. Jaborandi Holmes (*P. officinalis* Poehl).—This plant inhabits the northern and northeastern part of Brazil whence its leaves find their way through Sergipe, Allogoa, Sobral and Ceará, etc., to Liverpool and Hamburg, the chief centers of European commerce in the drug. Like those of *P. selloanus* its leaves are two or three jugate and are especially separated from those of the *P. pennatifolius* by the fact that all of the leaflets except the terminal one have their bases cordate, while the bases of all the leaflets of *P. pennatifolius* are attenuate. This species is practically no longer obtainable in commerce, only occasional lots being imported.

P. pennatifolius Lemaire (*P. simplex* Baillon) inhabits the southern portion of Brazil and Paraguay, whence its leaves were formerly largely exported through Buenos Ayres and Rio Janeiro; at present they seem to have almost disappeared from commerce. The leaves are grayish-green in color, oval, elliptical, obtuse, attenuate at the summit, which is feebly emarginate, and also attenuate at their base but not petiolated. The species is recognized in the Belgian Pharmacopœia.

In the original specimens of jaborandi seen by Coutinho, and also in other specimens received from the doctor's family by F. V. Greene, U. S. N., some of the leaves are hairy, although most of them are smooth, and it seems probable that the species does contribute somewhat to the jaborandi of commerce.

P. selloanus Engler, formerly official in the U. S. P., appears to be a variety of *P. pennatifolius* Lemaire, from which it differs almost solely in the length of its flower stalk, which is six times as long as the flower bud, while that of *P. pennatifolius,* is but three to four times as long as the bud. *P. selloanus* seems to be the more southern plant of the two, and is especially abundant in Paraguay.

P. trachylophus Holmes.—The leaves of this species are smaller than those of the *P. Jaborandi,* and are oblong, elliptical, obtuse, and emarginate at the summit with cordate bases, symmetrically and shortly petiolate. The plant grows in Northeastern Brazil, especially in the provinces of Ceará and Maranhoa, and the leaves, although they contain so little of the alkaloid (about 0.2 per cent.) as to be of small value, have been sent into commerce in considerable quantities. Their color upon the surface is vivid green, below yellowish-green. The under surface is covered with short hairs.

P. microphyllus Stapf grows in the northeastern part of Brazil, whence the leaves, much mixed with the debris of the petioles, of the twigs and of the fruit, are sent to Liverpool and Hamburg. These leaves are alternate, imparipinnate having from one to five pairs of leaflets, or are often apparently simple owing to the failure of the lateral leaflets to develop. The leaflets are opposite, slightly pubescent, their petioles being marked by a deep longitudinal furrow. They vary very much in form, the base usually being attenuate and feebly cordate or unequal.

P. spicatus A. Saint-Hilaire (*P. parviflorus* Martius et Nees), inhabits the southern and northern portions of Brazil and can be recognized at once by its having simple leaves which are from 3 to 11 cm. long and from 1 to 4 cm. broad, and are tender or coriaceous and more or less pubescent and dotted. They are brownish-green above, paler beneath, and attached by a short twisted petiole. They appeared in commerce in 1895 under the name of *Arocati jaborandi. P. subcoriaceus* Engler is probably a variety of this species. *P. racemosus* Vahl, a native of Martinique, Cuba, Guadeloupe and probably other of the West Indian Islands, appeared first in commerce in 1903 as a new variety of jaborandi under the name of *Guadeloupe jaborandi.* The leaves are proportionately broader than those of *Pernambuco jaborandi,* more obovate in outline, of a purer green color, and are trifoliate or apparently simple. Considerable diversity of result has been obtained by chemists in the examination of the Guadeloupe jaborandi. Rocher (*A. J. P.,* 1900) obtained 1 per cent. of total alkaloids of which 0.6 per cent. was believed to be pilocarpine, the remainder jaborine. In the laboratory of Wright, Layman and Umney, only 0.34 per cent. of total alkaloids were reported as existing, while in an assay by A. J. Cownley (*P. J.,* 1903, lxxii) 0.6 per cent. of total alkaloids was obtained, about 50 per cent. of which was believed to be isopilocarpine. The commercial cultivation of jaborandi may some day be successful, as the *P. pennatifolius* has been found to grow freely in Sicily and produce a leaf containing a fair proportion of alkaloid. Pilocarpus is usually bought by assay. The variation in the percentage of alkaloid, according to the observations of A. Duval, depends not merely on the original contents of the drug but upon the fact that the alkaloid disappears when the pilocarpus is kept for some length of time in a moist atmosphere. Pilocarpus was at one time adulterated with spurious jaborandis, other foreign leaves, stems, dirt and mouldy leaves. At the present time the commercial article is of good quality. There are, however, reports of the leaves of other plants being substituted. Weigel states that under the name of *"Feuilles de Bois d'inde,"* the leaves of the logwood plant were substituted for Paraguay jaborandi. The most common adulterant appears to be in lots of *P. microphyllus,* which often contain leaves of the leguminous plant, *Tunatea decipiens* (Holmes), O. Kze. (*Swartzia decipiens* Holmes). In general appearance the two leaves resemble one another, both being imparipinnate and having the leaflets about the same size and shape, but in *P. microphyllus* the leaflets are opposite and the petioles are only slightly pubescent, while in the *Tunatea* the leaflets are alternate, and the petioles very pubescent. Then again, the absence of secreting hairs, the deep green of the upper and lighter green of the lower surface of the leguminous leaf serve easily to distinguish it from the true drug.

The following description of the drug is adapted from that of F. V. Greene, U. S. N., who had unquestionable specimens of the original jaborandi of Coutinho. The package contained several stems branched at an angle of about 20°, these branches being furnished with alternate leaves, which are imparipinnate, with from two to five opposite leaflets (Planchon has met with leaves having as many as seven or nine, and, more rarely, eleven leaflets) articulated to the rachis by short petiolules, thickened at the base. The leaflets, which are coriaceous in texture, vary considerably in size and outline. As a rule, they may be considered as oblong-lanceolate, and are entire, emarginate, with an unequal base. The midrib rises very little above the upper surface of the leaflet, but is very prominent and sharp on the lower. The veins, which are rather more prominent on the lower surface, leave the midrib at an angle of about 60°, pursue a parallel course across the leaflet, and finally turn up and anastomose within about a quarter of an inch of the margin. The leaflets are pellucidly punctate; the dots are the receptacles of secretion, are numerously and irregularly distributed over the whole surface, and are plainly visible when the leaflet is held up to the light. According to Conroy, the leaflets yield 0.76 per cent., the leafstalks only 0.37 per cent. of alkaloid. The fruit consists of five carpels, of which not more than two or three are usually developed to maturity; when ripe, the carpels dehisce into two valves, and then remind one strongly of miniature cockle shells with the valves open exposing the animals. The black, shining, reniform seeds (one for each carpel) have a lancet-shaped hilum, a sharp ridge on the back near the apex, and a smooth, pale yellow endocarp surrounding it.

Paraguay jaborandi from *P. pennatifolius* and *P. selloanus* is an inferior variety of the drug, which reaches European commerce from Buenos Ayres and from Rio Janeiro, and is believed to be collected in Paraguay. The leaves are thinner than those of the Pernambuco jaborandi, and have only two or three, never four, pairs of leaflets. It is also noticeable in the Paraguay variety that the lateral veins are not prominent, that the base is so tapered that the widest portion is above the middle, and that the upper surface is grayish-green.

Properties.—The Pernambuco and Maranham jaborandis are official, being described as follows:

"**Pernambuco Jaborandi.**—Leaflets when entire, oval, oblong, or elliptical, from 4 to 10.5 cm. in length and from 2 to 4 cm. in breadth and with short, stout petiolules; summits more or less rounded or acute and emarginate; bases rounded or acute and mostly unequal; margins entire and narrowly revolute; very smooth, shiny, coriaceous and glandular-punctate; upper surfaces grayish to brownish-green, midribs mostly depressed, under surfaces yellowish- or greenish-brown and slightly pubescent on the prominent midvein; peculiarly aromatic when crushed; taste bitterish, becoming somewhat pungent and having a sialogogue effect.

"**Maranham Jaborandi.**—Leaflets rhomboidally oval to obovate or elliptical from 1.5 to 5 cm. in length and from 1 to 3 cm. in breadth, the lateral ones nearly sessile, the terminal ones on margined petiolules, from 0.5 to 1.5 cm. in length; of a nearly uniform grayish or yellowish-green color, rather thin but otherwise resembling Pernambuco Jaborandi.

"Under the microscope, transverse sections of Pilocarpus show the upper epidermal cells with a yellowish layer of cutin from 0.005 to 0.01 mm. in thickness; palisade cells, 1 to 3 rows deep, being filled with chloroplastids; among the palisade cells occur large, nearly circular, oil-secretion reservoirs from 0.08 to 0.15 mm. in diameter; the dorsal pneumatic layer, from 10 to 20 rows in depth, the cells occasionally containing rosette aggregates of calcium oxalate from 0.01 to 0.025 mm. in diameter; distributed in the center of the leaf are the collateral fibro-vascular bundles each surrounded by a more or less interrupted circle of several rows of thick-walled, slightly lignified bast-fibers, tracheæ associated with strongly lignified wood-fibers; among the cells of the lower epidermis occur numerous stomata. On surface view the stomata are broadly elliptical, from 0.025 to 0.04 mm. in length, being uniformly smaller in Maranham Jaborandi. Upon both surfaces of Pernambuco Jaborandi occur a number of non-glandular, one-celled hairs, more or less bent or curved, from 0.08 to 0.5 mm. in length, thick-walled and with numerous, slight, centrifugal projections.

The powder is dark green or greenish-brown; epidermal cells on surface view 5- or 6-sided; stomata broadly elliptical, from 0.02 to 0.04 mm. in length, usually with four neighboring cells; fragments of fibro-vascular bundles showing tracheæ with simple or bordered pores or spiral thickenings, associated with thick-walled and strongly lignified wood-fibers; bast-fibers few, walls thick and only slightly lignified; calcium oxalate in rosette aggregates, from 0.01 to 0.025 mm. in diameter; fragments of laminæ showing large, oil-secretion reservoirs and usually containing one or more globules of oil; non-glandular hairs having thick walls, usually more or less broken, are occasionally found. Pilocarpus yields not more than 7 per cent. of ash." *U. S.*

An alkaloid was isolated in 1875 from jaborandi almost simultaneously by A. W. Gerrard and M. Hardy. To this the name of *pilocarpine* was given. Gerrard at the same time stated that there were at least two alkaloids in the leaves, and this view seemed to be confirmed when *jaborine* was discovered. He also obtained a volatile oil, tannic acid, a peculiar volatile acid, and potassium chloride. *Pilocarpine* may be prepared as follows. The leaves are exhausted with 80 per cent. alcohol containing 8 grammes of hydrochloric acid in a liter, the tincture is distilled and evaporated to the consistence of a liquid extract, and this is mixed with a small quantity of water, and filtered. The filtrate is treated with a slight excess of ammonia, and then with a large quantity of chloroform. The chloroform solution is agitated with water, to which hydrochloric acid is added, drop by drop, in sufficient quantity to neutralize the alkaloid, the hydrochloride of which is obtained in long needles on evaporating the aqueous solution, while foreign principles remain dissolved in the chloroform. By dissolving the crystals in water, treating the solution with ammonia and chloroform, and evaporating the latter solution, pilocarpine is obtained as a soft viscous mass, which is only slightly soluble in water, but is freely soluble in alcohol, ether, and chloroform.

Kingzett originally assigned pilocarpine the formula $C_{23}H_{34}O_4N_4 + 4H_2O$. Harnack and Meyer, on the other hand, give it as $C_{11}H_{16}O_2N_2$. The latter has been accepted, and is recognized by the U. S. Pharmacopœia. It was later definitely established as correct by the synthesis of pilocarpine afterwards effected by Hardy and Calmels. (*C. R. A. S.*, cv, pp. 68 to 71; also *A. J. P.*, 1887, p. 632.) By the action of hydrochloric acid or of barium hydroxide, pilocarpine, $C_{11}H_{16}O_2N_2$, is changed into *pilocarpidine*, $C_{10}H_{14}O_2N_2$, by the loss of a methyl group. Now Hardy and Calmels have converted β-pyridine-α-lactic acid, into *pilocarpidine*, the methyliodide of which by oxidation is converted into pilocarpine. The synthetical pilocarpidine and pilocarpine yield gummy derivatives similar to those obtained by Harnack and Meyer from the natural products. The physiological action of synthetical pilocarpine is identical with that af the natural alkaloid. Knudsen, E. Merck, and Petit and Polonovski all dispute the conclusions of Hardy and Calmels, and state that they failed to get pilocarpine by the synthetic method of these investigators. (*Proc. A. Ph. A.*, 1897, 716.) Petit and Polonovski (*J. P. C.* (6), v, 481) obtained *pilocarpic* and *pilocarpidic acids* from pilocarpine and pilocarpidine. Harnack and Meyer first stated that *jaborine* is easily formed from pilocarpine, and may be produced by simply heating the latter alkaloid. They also showed

that *pilocarpine* has physiological effects analogous to those of *nicotine*, while *jaborine* resembles *atropine* in its effects. Hardy and Calmels (*J. Chem. S.*, Sept., 1886, 815) state that pure, dry pilocarpine does not yield *jaborine* when heated at 100° C. (212° F.) for six hours, neither can this substance be obtained by the action of alcoholic iodide upon argentopilocarpidine. If, however, carefully dried pilocarpine be heated rapidly to 175° C. (347° F.), kept at this temperature for about half an hour, and the product extracted with water, made alkaline with baryta and shaken with ether, the ether will contain jaborine, the aqueous solution will contain pilocarpidine, $C_{10}H_{14}O_2N_2$, and *jaboric acid*. *Jaborine* separates from alcohol or ether in a brown mass, which changes to a brittle resinous solid. Its composition is considered to be $C_{22}H_{32}O_4N_4$; it has exactly twice the molecular formula of pilocarpine. It is insoluble in water, but dissolves readily in ether, and is soluble in jaboric acid. *Jaboric acid*, $C_{19}H_{25}N_3O_5$, is separated from pilocarpidine by precipitating with excess of silver nitrate, which forms a curdy precipitate of the composition $C_{19}H_{24}N_3O_5,AgNO_3$. Jaboric acid resembles jaborine in appearance, but is very soluble in water, and is not removed from its aqueous solution by ether. Pilocarpine contains besides the alkaloids, some resin, tannin, and a small amount of a terpene containing volatile oil. Pilocarpine combines with acids, and a number of the salts are to be had in commerce. The action of heat or alkalies decomposes pilocarpine into *isopilocarpine*, which upon oxidation yields pilocarpic acid, $C_{11}H_{16}N_2O_5$. The nitrate has probably been used most frequently, and it and the hydrochloride are now official. Gerrard tested the solubilities of several of the salts as follows. The nitrate is soluble in water, sparingly in cold but freely in boiling alcohol; it is insoluble in chloroform, benzene, carbon disulphide, and ether. The *phosphate* is soluble in water, sparingly in cold, more freely in boiling alcohol, from which on cooling it crystallizes in lustrous tables; it is insoluble in ether, chloroform, benzene, and carbon disulphide. The *hydrochloride* is freely soluble in water, alcohol and chloroform; insoluble in ether, benzene, and carbon disulphide. The *acetate* is soluble in water, alcohol, chloroform, benzene, and ether; insoluble in carbon disulphide. The *hydrobromide* is soluble in water, alcohol, and chloroform; insoluble in ether and carbon disulphide.

According to the researches of E. Harnack, *pilocarpidine* acts upon the animal organism in the same way as pilocarpine, but is somewhat less powerful.

An essential oil of sp. gr. 0.875, and boiling between 180° and 290° C. (356° and 554° F.), has been obtained by Schimmel & Co., in Leipsic. (*Ber. d. Chem. Ges.*, April, 1888.) The portions going over above 260° C. (500° F.) solidified on cooling, and yielded a solid hydrocarbon, which fuses at 27° to 28° C. (80.6°–82.4° F.). As it decolorizes notable amounts of bromine when in solution in petroleum benzin, it probably belongs to the olefine series. The yield of oil in pilocarpus is about 0.4 per cent. In a later report (Oct., 1893) they give as a probable constituent of the lower boiling portions of the oil, *dipentene*, $C_{10}H_{16}$. The total amount of essential oil varies, according to the freshness of the plant, from 0.2 to 1.1 per cent.

Assay.—"Introduce 15 Gm. of Pilocarpus in No. 60 powder into a 250 mil flask, add 150 mils of chloroform and proceed as directed under *Belladonnæ Radix*, page 222, fifth line of the assay, beginning with the word "Stopper," and decreasing the amount of water to be added after maceration to 5 mils. The 100 mils of chloroform solution must be drawn off from the bottom of the flask, and dissolve the alkaloids from the residue in 8 mils of tenth-normal sulphuric acid V.S.

"Each mil of tenth-normal sulphuric acid V.S. corresponds to 20.8 milligrammes of the alkaloids of Pilocarpus." *U. S.*

Uses.—The therapeutic virtues of jaborandi appear to be due entirely to the alkaloid pilocarpine and the crude drug is very rarely employed. For the consideration of its physiological and therapeutic properties, see page 854.

When an overdose of jaborandi, or its principle alkaloid, has been taken, the symptoms begin with flushing of the face and neck, soon followed by free sweating and salivation, both of which may be extremely profuse. Frequently there is nausea and sometimes vomiting, the pulse is usually somewhat more rapid than normal, the pupils contracted, and often there is *diarrhea*. In patients with circulatory disturbances, pulmonary edema may occur, and prove rapidly fatal. The antagonism between pilocarpine and atropine is about as complete as between any two drugs, and the most certain treatment for cases of poisoning by jaborandi, after evacuating the stomach, is the prompt administration of a full dose of atropine, or some substance containing it.

Dose, of jaborandi, from twenty to forty grains (1.3–2.6 Gm.).

Off. Prep.—Fluidextractum Pilocarpi, *U. S.*

PILULÆ.

PILLS

(pĭl'ù-læ)

Pilules, *Fr.*; Pillen, *G.*; Pillole, *It.*; Píldoras, *Sp.*

These are globular masses of a size convenient for swallowing. They are well adapted for the administration of medicines which are unpleasant to the taste or smell, or insoluble in water, and which do not require to be given in large doses. Deliquescent substances should not be made into pills, and those which are efflorescent should be previously deprived of their water by crystallization. Care should be taken not to combine materials the mutual re-

action of which may result in a change of physical conditions.

Some substances have a consistence which enables them to be made immediately into pills. Such are the softer extracts and certain gum-resins, and the addition of a little water to the former, and of a few drops of alcohol to the latter, will give them the requisite softness and plasticity, if previously wanting. Substances which are very soft, or in the liquid state, are formed into the pilular mass by incorporation with dry and inert powders, such as wheat flour, starch, and powdered gum arabic, or with crumb of bread. Powders must be mixed with soft, solid bodies, as extracts, confections, soap, etc., or with tenacious liquids, as syrup, molasses, honey, mucilage or glycerin and the last-mentioned substance has been especially recommended in connection with a little alcohol. Heavy metallic powders are most conveniently made into pills with the former; light vegetable powders with the latter. Mucilage is very often used, but pills made with it are apt when kept to become hard and of difficult solubility in the liquids of the stomach, and if metallic substances are mixed with it the mass does not work well. A mixture of syrup and powdered gum arabic is not subject to the same inconveniences, and is an excellent material for the formation of pills. Honey evaporated to about half its bulk has been highly recommended. Confection of rose and glucose are among the best excipients, when the pills are to be kept long. For the same purpose of keeping the pills soft, the addition of a small portion of some fixed oil or deliquescent salt has been recommended, but glycerin is still better. Glycerin incorporated with one-twenty-fifth of its weight of powdered tragacanth is said to cause pills to remain soluble for almost any length of time. The official mucilage of tragacanth is an excellent excipient. Martindale prepares a mass by heating together with constant stirring to 115.5° C. (240° F.) five parts by weight of glycerin and one of flour, or, when a very firm mass is required, equal parts of flour and glycerin. It has been objected that pills made with glycerin could not be handsomely gilded or silvered, the luster of the metal disappearing. This is true, however, only of very recent pills, or of those in which an excess of glycerin has been used. Many powders require only water. Such are all those which contain ingredients capable of forming an adhesive or viscid solution with the liquid. Care should always be taken that the substance added is not incompatible with the main constituents of the pill.

The materials should be accurately mixed together, and beaten in a mortar until formed into a perfectly uniform and plastic mass. This should be of such a consistence that the pills may preserve their form, without being so hard as to resist the solvent power of the gastric fluids. As pills frequently become very hard by time, it is often convenient to keep the mass in a state fit to be divided when wanted for use. This may be done by wrapping it in waxed paper, putting it in covered pots, and occasionally moistening it as it becomes dry, or, more effectually, by keeping it in glass or well glazed jars, accurately closed with rubber cloth. The mass is made into pills by rolling it with a spatula, or with a flat, smooth piece of hard wood, into a cylinder of precisely the same thickness throughout, and of a length corresponding to the number of pills required. It is then divided as equally as possible by the hand, or, more accurately, by a machine. (See Remington's *Practice of Pharmacy,* 5th edition, p. 1217.) The pills receive a spherical form by being rolled between the fingers or by the use of one of the pill rolling machines. Mialhe describes a little instrument for rolling pills, composed of two circular plates, one about 12 inches, the other 6, in diameter, the former having a ledge at the border one-third of an inch high, the latter with a similar ledge, varying, according to the size of the pills, from less than a line to nearly two lines, and with a strap on the back by which it can be fitted to the hand. This is to be moved in a rotary manner upon the larger plate, holding the divided portions of the pill mass. Similar pill rollers made of wood are now in use. In order to prevent the adhesion of pills to one another, or to the sides of the vessel in which they may be placed, it is customary to agitate them with some dry powder, which gives them an external coating, that serves also to conceal their taste. For this purpose magnesium carbonate, rice flour, or starch may be used. Magnesium carbonate is sometimes incompatible with one of the ingredients of the pills, and licorice root is then preferable, though it occasionally becomes mouldy with very damp pills. The powder of lycopodium, which has been long in use in Europe, is now considerably employed in this country, and is perhaps one of the best substances for the purpose. It is the custom in some sections of the United States, particularly on the Pacific coast, to give the pill a coating of gold or silver leaf. This is done by agitating the pills, prepared without dusting powder, and with their surface still damp, or coated with a very small quantity of mucilage, with gold or silver leaf, in a hollow spherical wooden box made by turning two hemispheres out of hard wood, fitting each other, and provided with a short handle.

It was proposed by Garot to cover pills with gelatin, which answers the purpose of concealing their taste and odor and counteracting deliquescence or chemical change from exposure to the air, but it sometimes interferes with their solubility in the stomach. This method of coating is largely used at the present time. One of the best machines that have been devised for gelatin coating pills extemporaneously on the small scale is that of H. Maynard, of Chicago. This consists of a circular plate in which are affixed twenty fine

needles; the pills are rolled into depressions, and are easily impaled on the points of the needles; they are then dipped into a solution of gelatin, gently rotated, and allowed to cool. Another plan, less effectual, but more convenient, is to introduce the pills into a spherical box, to drop on them enough syrup simply to moisten their surface, then to give a rotary movement to the box until the pills are uniformly covered, and finally to add by degrees either powdered French chalk, elm bark, or some similar substance, shaking the box with each addition, and continuing the process until nothing more will adhere to the pills. The investing material may be rendered agreeable to the taste and smell by aromatic additions, if deemed advisable. Calloud found that a good powder for coating pills, because little disposed to attract moisture, is made by boiling one part of flaxseed and three parts of white sugar with sufficient water until a thick mucilage is formed, evaporating this carefully to dryness, and then pulverizing. The same writer has since suggested, as still more effective, a powder made by forming a mucilage with one part of tragacanth and two parts of water, pressing this through linen, mixing it with twenty parts of sugar of milk, spreading the paste thus made in thin layers to dry, and then powdering. The pills may be simply moistened with water and then shaken in the powder. L'Hermite proposed first to agitate the pills in a mortar with a little concentrated solution of gum, and afterwards to put them into a box containing dry and very finely powdered sugar, to which a rotary motion is given. If the coating be not sufficiently thick, the process may be repeated. (*J. P. C.*, xxv, 460.) For a list of excipients for pills by J. Cohn, see *Proc. A. Ph. A.*, 1900, 469 from *Ph. Ztg.*, 1900, 221; also G. Grugge, *A. Ph. A. Year Book*, 1914, p. 81.

Gelatin coating on the larger scale is accomplished by the use of the vacuum apparatus of J. B. Russell (see Remington's *Practice of Pharmacy*), or by simply rotating the pills in contact with a solution of gelatin in large spherical vessels, such as are used for sugar coating.

The sugar coating of pills is now conducted upon a large scale by manufacturers, who send immense quantities both of popular and of official pills into the market thus protected. The process employed is similar to that of the confectioners in coating almonds. After having been thoroughly dried, the pills are put into a hemispherical tinned copper basin, which is suspended from the ceiling and moved quickly backward and forward with an eccentric motion, so as to cause a constant attrition among the pills. First a little very thick syrup, or syrup of gum, is introduced in order to give a thin coating to their surface, and afterwards very finely powdered and very dry white sugar is sifted or thrown over them, the motion being constantly maintained. The sugar is fixed by the moist surface of the pills, and the coating made compact and smooth by the attrition. The process is aided by a gentle heat, but the heat must be guarded, lest the pills be much softened, and thus lose their shape and even discolor the coating. Dexterous manipulation is necessary in order that the process may succeed thoroughly. For practical remarks on the sugar coating of pills, see an essay by H. C. Archibald in *A. J. P.*, 1867, p. 199, and by Wm. R. Warner, Jr., and T. S. Wiegand in *A. J. P.*, 1902, 32. On a larger scale a pill coater of copper of peculiar construction, heated by steam pipes, is now used.

Still another method of coating pills, proposed by E. K. Durden, is to cover the pills with collodion, which completely conceals the taste. The solution employed by Durden had the sp. gr. 0.810, and two dippings gave a sufficient coating. (*A. J. P.*, xxi, 183.) It is, however, yet to be determined whether a coating of collodion would yield readily to the solvent powers of the gastric juice. Blanchard covers pills with a solution of Tolu balsam in ether, but H. C. Baildon objects to this, that it takes too long to dry, and suggests as a substitute a solution of a drachm of the balsam in three drachms of chloroform, which dries sufficiently in twenty minutes. If old and solid Tolu balsam be selected, it will be less liable to the objection of drying slowly. This balsam is officially employed in coating the U. S. pills of ferrous iodide. A solution of mastic in ether has also been used for coating pills, and the white of egg has been recommended for the same purpose.

Pills are sometimes coated with substances which do not dissolve in the stomach, with the object of permitting the passage of the undissolved pill into the intestines; for this purpose keratin coating has been largely used. (See *Keratin*, Part II, and Remington's *Practice of Pharmacy*, sixth edition.) *Salol* has also been employed, by melting it in an enamelled pan at a temperature of about 50° C. (122° F.) and dropping in the pills, rotating until covered, and then transferring to a dry pan, still rotating (to prevent adhesion) until cold. For further details, see *Pilulæ*, N. F. IV (Part III); *D. C.*, 1894, 123; *Ph. Ztg.*, xxxviii, 527.

An improved method of salol coating for pills intended for enteric use has been contributed by J. C. and B. L. DeG. Peacock (*Proc. P. Ph. A.*, 1915, p. 258). The particular points to be observed are the amount of salol to be used and the shape and size of the vessel used in melting the salol.

W. G. Toplis (*Proc. P. Ph. A.*, 1915, p. 262) proposes stearic acid as an enteric coating for pills and gives details of the method to be followed in producing a satisfactory article.

Pills which are to be kept long should be well dried, and put into bottles with loosely fitting stoppers to prevent mouldiness. Though the U. S. Pharmacopœia, in almost every instance, orders the mass to be divided into pills,

yet it should be understood rather as indicating the number of pills to be made from a certain quantity of the mass, when particular directions are not given by the physician, than as requiring the division to be made immediately after the materials have been mixed. It will be found convenient by the apothecary to retain a portion of the mass undivided, especially when it is desirable to keep the pills soft. The British Pharmacopœia furnishes formulas for pill masses, using the title of "Pilula" instead of "Massa," the title of the class adopted by the U. S. Pharmacopœia; there is, in our opinion, a decided advantage in selecting a name for the class which is not likely to be confused with that used for the divided pills.

Pills containing silver nitrate, potassium permanganate or other easily oxidizable substances, should be made by diluting with kaolin or talc and massing with petrolatum or mixtures of petrolatum and paraffin. All organic matter should be excluded.

Compressed pills are made directly from the medicinal substance without the aid of an excipient. The drug, if not already in granular powder, is made so, and then forced into pill shape by means of a powerful press. For certain substances which are crystalline in structure, such as quinine bisulphate, potassium bromide, and potassium iodide, and which have some cohesiveness and yet are of easy solubility, the process is a good one. An apparatus was contrived by J. P. Remington for compressing pills (see 16th ed., *U. S. D.*, and *Practice of Pharmacy*, 5th ed., page 1233). It is made of cast steel; the base has two countersunk depressions with a short post in the center of each, and a lenticular depression is made in the upper surface of each post. A steel cylinder having a central aperture of the diameter of the post is placed in the depression, the proper quantity of powder is introduced, and the plunger, which has a corresponding lenticular depression on its lower surface, is placed on the powder and is struck a quick blow with a mallet; the powder is compressed, and the pill adheres to the cylinder; by removing the cylinder and holding it over a box and tapping the plunger again lightly, the pill is forced out and falls into a box.

Compressed tablets are now used to an enormous extent, being made by various manufacturers with machinery of ingenious construction; the fact of their requiring no excipient, the ease with which they can be tested, and their permanent character (in most cases being just as valuable years after they were made as when fresh) have caused their extensive employment. Care should be taken, however, not to use them in those few cases where very prompt action is required, as the powerful compression to which they are subjected renders them less quickly effective than the same drug administered in the form of a loose powder.

For a description of some of the more important forms of pill compressing machines with illustrations, see Remington's *Practice of Pharmacy*, sixth edition.

PILULÆ ALOES. U. S. (Br.)

PILLS OF ALOES Pil. Aloes

(pĭl'ŭ-læ ăl'ō-ēs)

Pilula Aloes, *Br.*; Aloes Pill; Pill of Barbados Aloes, Pill of Socotrine Aloes; Pilules d'Aloés et de Savon, *Fr. Cod.*; Pilules Aloétiques Savoneuses, *Fr.*; Aloepillen, *G.*

* "Aloes, in fine powder, *thirteen grammes* [or 201 grains]; Soap, in fine powder, *thirteen grammes* [or 201 grains]; Water, *a sufficient quantity*, to make *one hundred pills*. Mix the powders intimately, then incorporate sufficient water to form a mass, and divide it into *one hundred pills*." *U. S.*

"Aloes, in powder, 58 *grammes;* Hard Soap, in powder, 29 *grammes;* Oil of Caraway, 3 *millilitres;* Syrup of Glucose, 10 *grammes* or *a sufficient quantity*. Mix to form a mass." *Br.*

In the Br. Pharm., 1898, confection of rose was used as the excipient. It is now replaced by syrup of glucose.

The former British process for *Pill of Socotrine Aloes* was the same except that Socotrine was substituted for Barbados Aloes, and the volatile Oil of Nutmeg for Oil of Caraway.

The soap, in this formula, not only serves to impart a proper consistence to the aloes, but is thought to qualify its operation and diminish its liability to irritate the rectum. Five of the U. S. pills, containing ten grains (0.65 Gm.) of aloes, may be given with a view to their purgative effect, but the preparation is usually employed as a laxative in *habitual costiveness*.

Dose, one, two or three pills at bedtime. The British pill mass is of very nearly the same strength as that of the U. S. Pharmacopœia.

PILULA ALOES ET ASAFETIDÆ. Br.

PILL OF ALOES AND ASAFETIDA

(pĭl'ŭ-lą ăl'ō-ēş ĕt ăs-ą-fĕt'ĭ-dæ)

Pilulæ Aloes et Asafœtidæ, *N. F.*; Pilules d'Aloés et d'Asefétide, *Fr.*; Aloe und Asfœtida-Pillen, *G.*

A process for these pills was not retained in the U. S. P. IX, but are recognized by the N. F. IV (see Part III); the British process is as follows:

"Aloes, in powder, 30 *grammes;* Asafetida, 30 *grammes;* Hard Soap, in powder, 30 *grammes;* Syrup of Glucose, 10 *grammes*, or *a sufficient quantity*. Mix to form a mass." *Br.*

In the Br. Pharm., 1898, confection of rose was used as the excipient. It is now replaced by syrup of glucose.

Pills made from this mass are peculiarly adapted, by the stimulant and carminative properties of the asafetida, to cases of *costiveness* attended with flatulence and debility of the digestive organs.

Dose, about four grains (0.26 Gm.) of the mass.

PILULA ALOES ET FERRI. Br.

PILL OF ALOES AND IRON

(pĭl'ŭ-lą ăl'o-ēş ĕt fĕr'rī)

Pilulæ Aloes et Ferri, *N. F.;* Pilulæ Italicæ Nigræ; Pilules d'Aloés et de Fer, *Fr.;* Pilulæ Aloeticæ ferratæ, *P. G.;* Eisenhaltige Aloepillen, Aloe und Eisenpillen, Italienische Pillen, *G.*

"Exsiccated Ferrous Sulphate, 10 *grammes;* Aloes, in powder, 20 *grammes;* Compound Powder of Cinnamon, 35 *grammes;* Syrup of Glucose, 35 *grammes,* or *a sufficient quantity.* Mix to form a mass." *Br.*

These pills were deleted from the U. S. P. IX, but were introduced without change into the N. F. IV (see Part III).

This pill differs from the preparation of the same name in the British Pharmacopœia in the substitution of aromatic powder for the compound powder of cinnamon. It is essentially an old preparation of the Edinburgh Pharmacopœia, was omitted in the original British, and re-introduced and continued in the present edition. The Br. Pharm., 1898, improved this mass by substituting exsiccated ferrous sulphate for the crystallized salt formerly employed, and by the use of syrup of glucose instead of confection of rose. It is said that the laxative power of aloes is increased, and its tendency to irritate the rectum diminished, by combination with ferrous sulphate. This pill is especially adapted to *amenorrhea* with debility of the stomach and constipation.

Dose, of the Br. mass, from three to eight grains (0.2–0.5 Gm.); of the N. F. pills, from one to three pills.

PILULA ALOES ET MYRRHÆ. Br.

PILL OF ALOES AND MYRRH

(pĭl'ŭ-lą ăl'o-ēş ĕt mŷr'rhæ)

Pilulæ Aloes et Myrrhæ, *N. F.;* Rufus's Pills; Pilule d'Aloés et de Myrrhe, Pilules de Rufus, *Fr.;* Rufussche Pillen, *G.*

"Aloes, in powder, 44 *grammes;* Myrrh, in powder, 22 *grammes;* Syrup of Glucose, 34 *grammes,* or *a sufficient quantity.* Mix to form a mass." *Br.*

These pills were deleted from the U. S. P. IX, but were introduced without change into the N. F. IV (see Part III).

This composition has been long in use, under the name of *Rufus's Pills.* It is employed, as a warm stimulant cathartic, in *general debility* attended with *constipation,* and in *retention* or *suppression of the menses.*

Dose, of the Br. mass, from four to eight grains (0.26–0.5 Gm.); of the N. F. pills, three to six pills.

PILULÆ ASAFŒTIDÆ. U. S.

PILLS OF ASAFETIDA Pil. Asafœt.

(pīl'ŭ-læ ăs-ą-fœt'ĭ-dæ)

Pilules d'Asefétide, *Fr.;* Asafœtida-Pillen, *G.*

* "Asafetida, *twenty grammes* [or 309 grains]; Soap, in fine powder, *six grammes* [or 93 grains]; Water, *a sufficient quantity,* to make *one hundred pills.* Beat the solids together with water, so as to form a mass, and divide it into *one hundred pills.*" *U. S.*

Each of these pills contains three grains (0.20 Gm.) of asafetida. They are a convenient form for administering asafetida, the unpleasant odor and taste of which render it very offensive in the liquid state.

Dose, one to three pills.

PILULÆ CATHARTICÆ COMPOSITÆ. U. S.

COMPOUND CATHARTIC PILLS Pil. Cathart. Co.

(pīl'ŭ-læ cą-thär'tĭ-cæ cŏm-pŏş'ĭ-tæ)

Antibilious Pills; Pilules cathartiques composées, *Fr.;* Abführpillen, *G.*

* "Compound Extract of Colocynth, *eighty grammes* [or 2 ounces av., 360 grains]; Mild Mercurous Chloride, *sixty grammes* [or 2 ounces av., 51 grains]; Resin of Jalap, in fine powder, *twenty grammes* [or 309 grains]; Gamboge, in fine powder, *fifteen grammes* [or 231 grains]; Diluted Alcohol, *a sufficient quantity,* to make *one thousand pills.* Mix the powders intimately, then incorporate a sufficient quantity of diluted alcohol to form a mass, and divide it into *one thousand pills.*" *U. S.*

This cathartic compound was first made official in the second edition of the U. S. Pharmacopœia. It was intended to combine smallness of bulk with efficiency and comparative mildness of purgative action and a peculiar tendency to the biliary organs. Such an official preparation was much wanted in this country, in which bilious fevers, and other complaints attended with congestion of the liver and portal circle generally, so much abound. The object of smallness of bulk is accomplished by employing extracts and the more energetic cathartics; that of a peculiar tendency to the liver, by the use of calomel, and that of efficiency with mildness of operation, by the union of several powerful purgatives. It is a fact, abundantly proved by experience, that drastic cathartics become milder by combination, without losing any of their purgative power. It is highly important that these pills be prepared in exact compliance with the directions, and that the *compound extract of colocynth* and the *resin of jalap* used be of good quality. When they fail, the result is generally ascribable to the substitution of jalap for the resin, or to the use of a compound extract of colocynth made with nearly inert scam-

mony, inferior aloes, and insufficient colocynth, and altogether badly prepared.

Each pill weighs about 3 grains (0.194 Gm.), and contains 2.70 grains (0.175 Gm.) of active ingredients. A single pill will generally be found to operate as a mild laxative. In a full dose, the preparation acts vigorously on the bowels, producing bilious stools, generally without much pain or disorder of the stomach. It may be employed in most instances where a brisk cathartic is required, but is particularly applicable to the early stages of *bilious fevers*, to *hepatitis*, *jaundice*, and all those derangements which depend on congestion of the portal circle. It should not be used in habitual constipation.

Dose, one to three pills.

PILULA COLOCYNTHIDIS COMPOSITA. Br.

COMPOUND PILL OF COLOCYNTH

(pĭl'ŭ-lą cŏl-o-cўn'thį-dĭs cọm-pŏș'į-tą)

Pilulæ Colocynthidis Compositæ, *N. F.*; Cochia Pills; Pilules de Coloquinte composées, *Fr. Cod.*; Pilules cochées mineures, *Fr.*; Zusammengesetzte Koloquinten-Pillen, *G.*

"Colocynth Pulp, in powder, 20 *grammes;* Aloes, in powder, 35 *grammes;* Scammony Resin, in powder, 35 *grammes;* Potassium Sulphate, in powder, 5 *grammes;* Oil of Cloves, 5 *millilitres;* Distilled Water, *a sufficient quantity*. Triturate the Oil of Cloves with the Potassium Sulphate; add the Colocynth Pulp; mix; add the Aloes and Scammony Resin; mix; add Distilled Water, and mix to form a mass." *Br.*

This is not, like the old London pills of the same name, merely another form of the compound extract of colocynth, though containing essentially the same materials—one great difference being that colocynth and aloes are used in substance in the pill, instead of in the state of extract. Potassium sulphate is used to promote the more complete division of the aloes and scammony. The preparation is actively cathartic. This pill is also official in the N. F. IV (see Part III).

Dose, from five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Pilula Colocynthidis et Hyoscyami, *Br.*

PILULA COLOCYNTHIDIS ET HYOSCYAMI. Br.

PILL OF COLOCYNTH AND HYOSCYAMUS

(pĭl'ŭ-lą cŏl-o-cўn'thį-dĭs ĕt hў-ọs-cў'ą-mī)

Pilulæ Colocynthidis et Hyoscyami, *N. F.*; Pilules de Coloquinte et d'Extrait de Jusquiame, *Fr.*; Koloquinten-Bilsenkrautpillenmasse, *G.*

"Compound Pill of Colocynth, 50 *grammes;* Extract of Hyoscyamus, 25 *grammes;* Distilled Water, *a sufficient quantity*. Mix to form a mass." *Br.*

This was an official pill of the Edinburgh College. It is asserted that the compound pill and compound extract of colocynth are almost entirely deprived of their griping tendency by combination, as above, with extract of hyoscyamus, without losing any of their purgative power.

Dose, from five to twenty grains (0.32–1.3 Gm.).

This pill is also official in the N. F. IV (see Part III).

PILULÆ FERRI CARBONATIS. U. S. (Br.)

PILLS OF FERROUS CARBONATE Pil. Ferr. Carb. [Ferruginous Pills, Chalybeate Pills, Blaud's Pills]

(pĭl'ŭ-læ fĕr'rī cär-bọ-nā'tĭs)

"Each Pill contains not less than 0.06 Gm. of $FeCO_3$." *U. S.*

Pilula Ferri, *Br.*; Iron Pill; Pilules Ferrugineuses de Blaud, *Fr. Cod.*; Pilules Chalybées de Blaud, *Fr.*; Pilulæ Ferri carbonici Blaudii, *P. G.*; Blaudsche Pillen, *G.*; Pillole di carbonato ferroso, *It.*; Pildoras de Blaud, *Sp.*

* "Granulated Ferrous Sulphate, *sixteen grammes* [or 247 grains]; Potassium Carbonate, *eight grammes* [or 123.5 grains]; Sugar, *four grammes* [or 62 grains]; Tragacanth, in fine powder, *one gramme* [or 15.5 grains]; Althæa, in fine powder, *one gramme* [or 15.5 grains]; Glycerin, Water, each, *a sufficient quantity*, to make *one hundred pills*. Rub the potassium carbonate, in a mortar, with a sufficient quantity (about *five drops* each) of glycerin and water, then add the ferrous sulphate and sugar, previously triturated together to a uniform, fine, powder, and rub the mass thoroughly, until it assumes a greenish color. When the reaction is complete, incorporate the tragacanth and althæa, and, if necessary, add a little more water, so as to obtain a mass of pilular consistence. Divide this into *one hundred pills*.

"Note.—In this process the 8 Gm. of potassium carbonate may be replaced by 7.2 Gm. of monohydrated sodium carbonate." *U. S.*

"Exsiccated Ferrous Sulphate, in powder, 33 *grammes;* Exsiccated Sodium Carbonate, in powder, 21 *grammes;* Tragacanth, in powder, 2 *grammes;* Gum Acacia, in powder, 8 *grammes;* Glucose, 31 *grammes;* Distilled Water, 2 *millilitres*. Mix the Glucose, Distilled Water, and Exsiccated Ferrous Sulphate; add the Exsiccated Sodium Carbonate; mix and set aside for ten minutes, or until the reaction is complete; add the Tragacanth and Gum Acacia, and mix to form a mass. This Pill contains about 22.5 per cent. of ferrous carbonate." *Br.*

Assay.—"Dissolve three Pills in 15 mils of diluted sulphuric acid and dilute the solution with distilled water to about 100 mils. The immediate titration with tenth-normal potassium dichromate V.S., potassium ferricyanide T.S. being used as indicator, shows not less than 0.06 Gm. of $FeCO_3$ in each pill.

"Each mil of tenth-normal potassium dichromate V.S. used corresponds to 0.011584 Gm. of $FeCO_3$. Each Pill of Ferrous Carbonate corresponds to 5.2 mils of tenth-normal potassium dichromate V.S." *U. S.*

In the U. S. P., 1890, the name of this pill was changed to *Pilulæ Ferri Carbonatis* and the *Pilulæ Ferri Compositæ* of the U. S. P., 1880, was dropped, which sometimes led to a complication; the U. S. P., 1890, has since been retained, as it would lead to confusion to change the name again. It should be remembered, however, that "pills of ferrous carbonate" no longer means pills made from Vallet's Mass but Blaud's pills.

These pills afford one of the best forms of exhibiting iron, in the treatment of *anemia,* being nearly free from astringency. As their peculiar advantages depend upon the presence of ferrous carbonate, which speedily changes into the ferric salt on exposure, it is proper that only so much of the mass should be prepared as may be wanted for immediate use. They are sometimes called *Griffith's pills.* They closely resemble *Blaud's ferruginous pills,* made originally in 1831, and celebrated in France as a remedy in *chlorosis,* prepared from equal weights of ferrous sulphate and potassium carbonate, made into a pilular mass. (See *P. J.,* 1894, 131.) The pills contain, as the result of double decomposition, ferrous carbonate and potassium sulphate. Van de Velde and Van Melckebeke prefer the sodium bicarbonate to the potassium salt. For a brief historical account of these pills, see a paper by John Humphrey in *P. J.,* 1903, 643.

Blaud's pills may become very hard upon standing, but if properly made, they undergo very little alteration. For an assay of a very old specimen, see *N. J. Ph. A.,* 1912, p. 73.

Dose, from two to six pills, to be taken three times a day; of the Br. mass, five to twenty grains (0.32–1.3 Gm.).

PILULÆ FERRI IODIDI. U. S.

PILLS OF FERROUS IODIDE Pil. Ferr. Iod.

(pĭl'ŭ-læ fĕr'rī ī-ŏd'ĭ-dī)

Pilules d'Iodure ferreux, *Fr. Cod.;* Pilules de Blancard, *Fr.;* Eisenjodürpillen, *G.;* Pillole di protojoduro di ferro, *It.;* Píldoras de yoduro ferroso, *Sp.*

* "Reduced Iron, *four grammes* [or 62 grains]; Iodine, *five grammes* [or 77 grains]; Glycyrrhiza, in fine powder, *four grammes* [or 62 grains]; Sugar, in fine powder, *four grammes* [or 62 grains]; Extract of Glycyrrhiza, in fine powder, *one gramme* [or 15.5 grains]; Acacia, in fine powder, *one gramme* [or 15.5 grains]; Water, Balsam of Tolu, Ether, each, *a sufficient quantity,* to make *one hundred pills.* Add *six mils* [or 97 minims] of water to the reduced iron, contained in a small mortar, and then, gradually add the iodine, stirring constantly until the liquid ceases to have a reddish tint. Then add the remaining powders, previously well triturated together, and mix the whole thoroughly. Transfer the mass to a porcelain dish, evaporate the excess of moisture on a water bath, with constant stirring, and when the mass has acquired a pilular consistence divide it into *one hundred pills.* Dissolve *ten grammes* [or 154 grains] of balsam of tolu in *fifteen mils* [or 243 minims] of ether, shake the pills with a sufficient quantity of this solution until they are uniformly coated, and put them on a plate to dry, occasionally rolling them about until the drying is completed. Keep the pills in a well-stoppered bottle. Pills of Ferrous Iodide are free from the odor of iodine. Triturate a few of the pills with water, and filter the liquid; the filtrate does not assume more than a light blue tint upon the addition of starch T.S. (absence of more than traces of *free iodine*)." *U. S.*

This process does not differ essentially from that formerly official.

The pills of ferrous iodide were introduced into the U. S. Pharmacopœia at the revision of 1850. The present official pills are formed on the plan proposed by Procter, in imitation of *Blancard's pills* (*A. J. P.,* May, 1860), and are much superior to those made by the U. S. process of 1850, or by that of the British Pharm., 1885. Magnes-Lahens especially recommended the following formula: "Take of pure Iodine, 4.10 grammes; Powdered Iron, 1.90 grammes; Powdered Sugar, 2.50 grammes; Powdered Gum Arabic, 2.50 grammes; Distilled Water, 2.50 grammes. Put in an iron dish the Water and the powdered Iron, add the Iodine gradually, and facilitate the reaction by stirring with a spatula of iron and by warming a little; when the reaction is complete, add the Gum and the Sugar, then heat to about 50° C. (122° F.), stirring until the mass ceases to drop when a little is taken up on the spatula. If necessary, five grammes of powdered licorice root may be incorporated into the mass, which is then to be rolled into one hundred pills." (*A. J. P.,* 1873, p. 498.) The iodine and iron unite directly to form ferrous iodide in solution, which is protected against the oxidizing influence of the air by the sugar and excess of reduced iron, while the licorice and gum serve to give due consistence and plasticity to the pilular mass. The pills are still further protected from the air by the impervious coating of balsam of Tolu, which readily yields to the softening and solvent properties of the gastric liquids. The great disadvantage of the pill of ferrous iodide, as ordinarily prepared, is that it will not keep—crumbling by time and exposure, and evolving iodine in consequence of the oxidation of the iron. The preparation, made according to the U. S. formula has stood the test of time, and we have seen pills which, four years after their preparation, exhibited no signs of change. Each pill contains about a grain (0.065 Gm.) of ferrous iodide and two-fifths of a grain (0.024 Gm.) of reduced iron. The therapeutic uses of this preparation are the same as those of ferrous iodide. (See *Ferri Iodidum.*)

Dose, one to three pills.

PILULA HYDRARGYRI SUBCHLORIDI COMPOSITA. Br.

COMPOUND PILL OF MERCUROUS CHLORIDE [Compound Calomel Pill, Plummer's Pill]

(pĭl'ū-lą hȳ-drär'gy̨-rī sub-ċhlō'rį-dī cǫm-pŏs'į-tą)

Pilulæ Antimonii Compositæ, *N. F.;* Compound Pills of Antimony; Pilula Calomelanos Composita, *Br.* 1864; Compound Pill of Mercurous Chloride; Pilules alterantes composées, Pilules antidartreuses, Pilules de Plummer, *Fr.;* Plummersche Pillen, Zusammengesetzte Calomelpillen, *G.*

"Mercurous Chloride, 20 *grammes;* Sulphurated Antimony, 20 *grammes;* Guaiacum Resin, in powder, 40 *grammes;* Gum Acacia, in powder, 1 *gramme;* Tragacanth, in powder, 1 *gramme;* Syrup of Glucose, 10 *grammes,* or *a sufficient quantity.* Mix to form a mass." *Br.*

Compound pills of antimony were dropped in the U. S. P. VIII, but the National Formulary IV has introduced the compound pill of antimony of the U. S. P., 1890, without alteration (see Part III). This pill is official in the British Pharmacopœia, 1914, castor oil, which was used as an excipient, being replaced by syrup of glucose.

We prefer the title "Compound Calomel Pill" of the former British Pharmacopœia, as not liable to any mistake, and as most expressive of the quality of the medicine. The antimonial employed, though under a different name, is identical with the old U. S. precipitated sulphide. According to Vogel a reaction takes place between the calomel and the sulphurated antimony, resulting in the production of antimony chloride and mercury sulphide. The preparation was originally introduced to the notice of the profession by Dr. Plummer, who found it useful as an alterative, and upon whose authority it was at one time much employed under the name of *Plummer's Pills.* The combination is well adapted to the treatment of *chronic rheumatism* and of scaly and other *eruptive diseases of the skin,* especially when accompanied with a syphilitic taint.

Dose, four to eight grains (0.26–0.5 Gm.) or more, morning and evening.

PILULA IPECACUANHÆ CUM SCILLA. Br.

PILL OF IPECACUANHA WITH SQUILL

(pĭl'ū-lą ĭp-ę-căc-ū-ăn'hæ cŭm sçĭl'lą)

Pilules d'Ipécacuanha et de Scille, *Fr.;* Brechwurzel-Meerzwiebelpillen, *G.*

"Compound Powder of Ipecacuanha, 30 *grammes;* Squill, in powder, 10 *grammes;* Ammoniacum, in powder, 10 *grammes;* Syrup of Glucose, *a sufficient quantity.* Mix to form a mass. This Pill contains about 5 per cent. of Opium." *Br.*

This is an old-fashioned combination of expectorants, intended for *chronic bronchitis,* but scarcely in keeping with modern practice.

Dose, from five to ten grains (0.32-0.65 Gm.).

PILULA IPECACUANHÆ CUM URGINEA. Br.

PILL OF IPECACUANHA WITH URGINEA

(pĭl'ū-lą ĭp-ę-căc-ū-ăn'hæ cŭm ŭr-gĭn'ē-ą)

"Compound Powder of Ipecacuanha, 30 *grammes;* Urginea, in powder, 10 *grammes;* Ammoniacum, in powder, 10 *grammes;* Syrup of Glucose, *a sufficient quantity.* Mix to form a mass. This Pill contains about 5 per cent. of Opium." *Br.*

This is the same as Pill of Ipecacuanhæ with Squill, except that Indian Squill or Urginea is used in place of the Mediterranean variety.

PILULÆ PHOSPHORI. U. S. (Br.)

PILLS OF PHOSPHORUS Pil. Phosphor.

(pĭl'ū-læ phŏs'phǫ-rī)

Pilula Phosphori, *Br.;* Phosphorus Pill; Pilules au Phosphore, Pilules Phosphorées, *Fr.;* Phosphorpillen, *G.*

* "Phosphorus, *six-hundredths of a gramme* [or 0.93 grains]; Althæa, in No. 60 powder, *six grammes* [or 93 grains]; Acacia, in fine powder, *three grammes* [or 46 grains]; Chloroform, Glycerin, Water, Balsam of Tolu, Ether, each *a sufficient quantity,* to make *one hundred pills.* Dissolve the phosphorus, in a test-tube, in *five mils* [or 81 minims] of chloroform, with the aid of a very gentle heat, replacing from time to time any of the chloroform which may be lost by evaporation. Mix the althæa and acacia in a mortar, next add the solution of phosphorus, then immediately afterwards a sufficient quantity (about *four mils* [or 65 minims]) of a mixture of *two volumes* of glycerin and *one volume* of water, and quickly form a mass; divide it into *one hundred pills.* Dissolve *ten grammes* [or 154 grains] of balsam of tolu in *fifteen mils* [or 243 minims] of ether, shake the pills with a sufficient quantity of this solution until they are uniformly coated, and put them on a plate to dry, occasionally rolling them about until the drying is completed. Keep the pills in a well-stoppered bottle." *U. S.*

"Phosphorus, 1 *gramme;* Oil of Theobroma, 40 *grammes;* Wool Fat, 11 *grammes;* Kaolin, 16 *grammes;* Sodium Sulphate, dried at 100° C. (212° F.), 32 *grammes;* Carbon Disulphide, 20 *millilitres.* Dissolve the Phosphorus and 20 *grammes* of the Oil of Theobroma in the Carbon Disulphide. Allow the solution to evaporate in a mortar until a pasty mass is obtained. To this add the remainder of the Oil of Theobroma together with the other ingredients, and mix to form a mass. This Pill contains 1 per cent. of Phosphorus. It is of one-half the strength of the corresponding preparation of the British Pharmacopœia, 1898. It should be freshly prepared." *Br.*

The increasing use of phosphorus in the free state made the introduction of phosphorus pills a necessity. The problem of preventing the oxidation of the phosphorus is believed to be

solved by dissolving it in an excess of warm chloroform; this is accomplished in a stoppered test-tube, for it has been shown that no oxidation takes place in the presence of chloroform vapor. It is necessary to form the mass quickly, so that the chloroform may not all evaporate and leave the phosphorus exposed to the action of the air. Chloroform is preferable to carbon disulphide, as recommended in the Br., for, although the latter is a better solvent, it is difficult to rid the mass of the disgusting odor. (See *A. J. P.*, 1875, 253, 501; 1878, 584; and *N. R.*, 1876, 189, 332; 1877, 32; *D. C.*, 1883, 180; *P. J.*, 1883, 923.)

The formula for this pill in the British Pharmacopœia, 1914, has been improved and simplified by replacing white wax and lard with oil of theobroma and wool fat, and its strength has been reduced to one-half of that of the Br., 1898.

Each official U. S. pill contains about 1-100th of a grain (0.0006 Gm.) of phosphorus.

Dose, of the U. S. pills, one pill three times a day; of the Br. mass, one grain (0.065 Gm.).

PILULA PLUMBI CUM OPIO. Br.

PILL OF LEAD WITH OPIUM

(pĭl'ū-lą plŭm'bī cŭm ō'pĭ-ō)

Pilulæ Opii et Plumbi, *N. F.;* Pilules d'Acétate de Polmb et d'Opium, *Fr.;* Bleiacetat-Opiumpillenmasse, *G.*

"Lead Acetate, in powder, 80 *grammes;* Opium, in powder, 12 *grammes;* Syrup of Glucose, 8 *grammes,* or *a sufficient quantity.* Mix to form a mass. This Pill contains about 12 per cent. of Opium." *Br.*

This pill would be better left to extemporaneous prescription, the requisite proportion of opium to the acetate varying in different cases. It is also official in the N. F. IV (see Part III).

Dose, two or three grains (0.13–0.20 Gm.) to begin with.

PILULA QUININÆ SULPHATIS. Br.

PILL OF QUININE SULPHATE

(pĭl'ū-lą quĭ-nī'næ sŭl-phā'tĭs)

Pilule de Quinine Sulfate, *Fr.;* Chininpillenmasse, *G.;* Píldoras de sulfato quinico, *Sp.*

"Quinine Sulphate, 82 *grammes;* Tartaric Acid, in powder, 3 *grammes;* Glycerin, 12 *grammes;* Tragacanth in powder 3 *grammes.* Triturate the Quinine Sulphate with the Tartaric Acid; add the product to the previously mixed Glycerin and Tragacanth; mix to form a mass." *Br.*

The reason for introducing a quinine pill mass in the British Pharm. is doubtless to serve the convenience of dispensers and to save time; tartaric acid aids in solubility and in making the pills smaller, while glycerin keeps the mass from undue hardening.

Dose, two to eight grains (0.13–0.5 Gm.).

PILULÆ RHEI COMPOSITÆ. U. S. (Br.)

COMPOUND PILLS OF RHUBARB Pil. Rhei Co.

(pĭl'ū-læ rhē-ī cŏm-pŏs'ĭ-tæ)

Pilula Rhei Composita, *Br.;* Pilules de Rhubarbe composées, *Fr.;* Rhabarber und Aloepillen, *G.*

* "Rhubarb, in No. 80 powder, *thirteen grammes* [or 201 grains]; Aloes, in fine powder, *ten grammes* [or 154 grains]; Myrrh, in fine powder, *six grammes* [or 93 grains]; Oil of Peppermint, *five-tenths of a mil* [or 8 minims]; Water, *a sufficient quantity,* to make *one hundred pills.* Mix the oil of peppermint intimately with the powders, then incorporate sufficient water to form a mass; divide it into *one hundred pills.*" *U. S.*

"Rhubarb, in powder, 25 *grammes;* Aloes, in powder, 20 *grammes;* Myrrh, in powder, 14 *grammes;* Hard Soap, in powder, 14 *grammes;* Oil of Peppermint, 2 *millilitres;* Syrup of Glucose, 25 *grammes,* or *a sufficient quantity.* Mix to form a mass." *Br.*

This is a tonic laxative, useful in *costiveness.* If made in quantity the pills should be kept in loosely stoppered bottles. The use of glycerin favors the formation of mouldiness through the attraction of moisture, and it was replaced in the formula of the Br. Ph., 1898, by syrup of glucose.

Dose, of the compound rhubarb pills, two to four pills, or from five to fifteen grains (0.32–1.0 Gm.) of the mass, twice a day.

PILULA SAPONIS COMPOSITA. Br.

COMPOUND PILL OF SOAP

(pĭl'ū-lą są-pō'nĭs cŏm-pŏs'ĭ-tą)

Pilulæ Opii, *U. S. VIII,* Pill of Opium; Pilules de Savon composées, *Fr.;* Seifenpillenmasse, *G.*

"Opium, in powder, 20 *grammes;* Hard Soap, in powder, 60 *grammes;* Syrup of Glucose, 20 *grammes,* or *a sufficient quantity.* Mix to form a mass. This Pill contains about 20 per cent. of Opium." *Br.*

This pill is practically identical with the opium pill of the U. S. VIII. There is no evident need of such a pill; it might much more wisely be left to extemporaneous prescription. The name was probably intended to conceal the nature of the preparation, but, in our opinion, it is a mistake to omit the only important ingredient from the title. One grain (0.065 Gm.) of opium is contained in five grains (0.32 Gm.) of the mass.

Dose, from two to five grains (0.13–0.32 Gm.).

PILULA SCILLÆ COMPOSITA. Br.

COMPOUND SQUILL PILL

(pĭl'ū-lą sçĭl'læ cŏm-pŏs'ĭ-tą)

Pilules de Scille composées, *Fr.;* Meerzwiebelpillenmasse, *G.*

"Squill, in powder, 25 *grammes;* Ginger, in powder, 20 *grammes;* Ammoniacum in powder, 20 *grammes;* Hard Soap, in powder, 15 *grammes;* Syrup of Glucose, 20 *grammes,* or

a sufficient quantity. Mix to form a mass." *Br.*

This preparation was dropped at the 1880 revision of the U. S. Pharmacopœia.

This is a stimulating expectorant compound, depending for its virtues chiefly on the squill, and applicable to the treatment of *chronic bronchitis.* The mass should be freshly made when wanted, as the squill which it contains is liable to be injured by keeping.

Dose, from five to ten grains (0.32–0.65 Gm.).

PILULA URGINEÆ COMPOSITA. Br.

COMPOUND URGINEA PILL

(pĭl'ŭ-lą ŭr-gĭn'ē-æ cǫm-pŏs'ĭ-tą)

"Urginea, in powder, 25 *grammes;* Ginger, in powder, 20 *grammes;* Ammoniacum, in powder, 20 *grammes;* Hard Soap, in powder, 15 grammes; Syrup of Glucose, 20 *grammes,* or *a sufficient quantity.* Mix to form a mass." *Br.*

This pill is the same as the Compound Squill pill, except that the Indian Squill, Urginea, replaces the ordinary variety.

Dose, from five to ten grains (0.32–0.65 Gm.).

PIPER. U. S.

PEPPER [Black Pepper]

(pī'pẹr)

"The dried, unripe fruit of *Piper nigrum* Linné (Fam. *Piperaceæ*), without the presence or admixture of more than 2 per cent. of stems or other foreign matter." *U. S.*

Piper Nigrum, *Br.* 1898; Common Pepper; Poivre noir, *Fr. Cod.;* Poivre, *Fr.;* Schwarzer Pfeffer, *G.;* Pepenero, *It.;* Pimienti negra, *Sp.;* Fifil uswud, *Arab.;* Lada, *Malay;* Maricha, *Jav.;* Sahan, *Palembang.*

The pepper vine (*Piper nigrum*) is a perennial plant, with a round, smooth, woody, articulated stem, swelling near the joints, branched, and from eight to twelve feet or more in length. The leaves are entire, broad-ovate, acuminate, seven-nerved, coriaceous, very smooth, of a dark green color, and attached by strong sheath-like footstalks to the joints of the branches. The flowers are small, whitish, sessile, covering thickly a cylindrical spadix, and succeeded by globular berries, which are red when ripe.

The plant grows wild in Cochin-China and various parts of India. It is cultivated on the coast of Malabar, in the peninsula of Malacca, in Siam, Sumatra, Java, Borneo, the Philippines, Japan, and many other places in the East; also to some extent in the West Indies. The best pepper is affirmed to be produced in Malabar, but Europe and America derive their chief supplies from Sumatra and Java. The plant is propagated by cuttings, and is supported by props, or trees planted for the purpose, upon which it is trained. In three or four years from the period of planting, it begins to bear fruit. The plant sometimes begins to bear as early as the first year after planting, increases in its yield to the fifth or sixth year, when it produces eight or ten pounds, and begins to lose its productiveness about the fifteenth year. The berries are gathered as soon as one is seen to turn red—*i.e.,* before they are all perfectly ripe—and upon being dried, become black and wrinkled. The greatest production is in Sumatra, and the ports of export are principally Singapore and Penang, the Malabar pepper coming from Tellicherry. In England, at least, it is customary to mix peppers of different origin in grinding, taking Malabar for weight, Penang for strength, and Sumatra for color. (*Bulletin U. S. Dept. of Agric.,* No. 13, 1887.) The importations from the Strait Settlements to the United States of unground black and white pepper is on an average about 20,000,000 pounds annually. Owing to the widespread cultivation of pepper a large number of varieties exist; these receive their names from the place of their production or their ports of shipment, as Singapore, Acheen, Penang, Siam, Tellicherry, Trang, Lampong, etc. For a description of the most important of these varieties with the percentage of active constituents contained in each, see J. W. Gladhill, *A. J. P.,* Feb., 1904; Kraemer and Sindall, *A. J. P.,* 1908, p. 1; also Blyth, *Foods: Their Composition and Analysis.*

White pepper is the ripe berry, deprived of a part of its pericarp by maceration in water and subsequent friction, and afterwards dried in the sun. It occurs as yellowish more or less broken grains with a smooth shiny surface from which the epicarp or outer layer of the fruit has been removed. It is sold in the market either as a whole white pepper or as broken white pepper; the whole peppers are very likely to have some of the epicarp or hull remaining. The removed hull is sold separately under the name of "pepper hulls;" it forms a light to dark brown powder, with a very pungent odor and taste and contains large amounts of the oleoresin of pepper, but according to Gladhill, no piperine. The hulls are sometimes sold mixed with broken white pepper. This mixture contains more oleoresin and less piperine than does the pure pepper; the percentage of the two active constituents varying according to the percentage of drugs in the mixture. White pepper is much less pungent but more aromatic than black pepper.

Long Pepper is obtained from *Piper officinarum* DC., and *P. longum* L., the former species yielding the principal commercial supplies and being grown in Java, India, and the Philippines. The plants are distinguished in having their flowers in dense, short, terminal, and nearly cylindrical spikes and their fruits, consisting of very small one-seeded berries or drupes, embedded in a pulpy matter. The fruit is green when immature, and becomes red as it ripens. It is gathered in the former state, as it is then hotter than when perfectly ripe. The whole spike is taken from the plant, and dried

in the sun. The fruit of the *P. officinarum* is cylindrical, 2 to 6 cm. long and 4 to 7 mm. in diameter, indented on its surafce, of a dark-gray color, a weak aromatic odor, and a pungent fiery taste. The fruits of *P. longum* are shorter and thicker. Dulong found its chemical composition to be closely analogous to that of black pepper. Like that, it contains *piperine,* a concrete oil or soft resin upon which its burning acridity depends, and a volatile oil to which it probably owes its odor. Its medicinal virtues are essentially the same as those of black pepper, but it is inferior to that spice, and is seldom used except as an adulterant. *West African* or *Ashantee Pepper* is the fruit of *P. Clussii,* C. DC., which grows abundantly in tropical Africa. It does not come into Western commerce, although much used in Africa. The berry is described as resembling cubeb, but less rugose, and with a more slender pedicel, and having the odor and taste of black pepper. Stenhouse found piperine in this variety of pepper.

Kissi Pepper is a fruit yielded by the *Piper Famechoni,* Heckel, of Upper Guinea. The berries, which grow in cylindrical clusters, are small, blackish-brown, ovoidal, with a cubeb-like pedicel at their base. Their powder is very aromatic, with an especially pleasant taste. They have been found by A. Barille to contain 4.5 per cent. of volatile oil and 3.7 per cent. of piperine. (*J. P. C.,* 1903, 106.)

Properties.—The dried berries are "nearly globular, from 3.5 to 6 mm. in diameter, epicarp very thin, easily separable from the sarcocarp; externally blackish-brown or grayish-black, coarsely reticulate; unilocular, 1-seeded; seed nearly white, hollow, adhering to the pericarp; odor aromatic, slightly empyreumatic; taste aromatic and very pungent. The powder is a mixture of blackish-brown fragments of the pericarp and nearly white fragments of the endosperm and embryo; starch grains spherical or somewhat angular, from 0.001 to 0.003 mm. in diameter, mostly in the polygonal cells of the endosperm; stone cells of the epicarp varying from nearly isodiametric or palisade-like to long tapering or somewhat irregular in shape, with thick porous walls and large lumina frequently containing a reddish-brown pigment; stone cells of the endocarp unevenly thickened, the outer walls being usually rather thin, and the lumina usually filled with a reddish-brown substance; oil cells with suberized walls and containing a yellowish oil, from which monoclinic prisms of piperine occasionally separate. Pepper yields not less than 6 per cent. of non-volatile extract, soluble in ether (see Part III, Test No. 13). It contains not less than 25 per cent. of starch. Pepper yields not more than 7 per cent. of ash. The amount of ash in Pepper, insoluble in diluted hydrochloric acid, does not exceed 2 per cent. of the weight of Pepper taken." *U. S.*

For information on the pharmacognosy of pepper, see Winton and Moeller in the "*Microscopy of Vegetable Foods;*" Winton and Bailey, *Ztchr. f. Unters. d. Nahr. u. Genussm.,* 1905, ix, p. 227; Spaeth, *Ibid.,* 1908, xv, p. 472; Kraemer and Sindall, *A. J. P.,* 1908, lxxx, p. 1; Collin in *Ann. des. Falsifications,* 1910, iii, p. 272.

They yield their virtues partially to water, entirely to alcohol and ether. Pelletier found them to contain a peculiar principle called *piperine* (see Part II), an acrid concrete oil or soft resin of a green color, a balsamic volatile oil, isomeric with oil of turpentine, a colored gummy substance, an extractive matter, like that found in leguminous plants capable of being precipitated by infusion of galls, starch, a portion of bassorin, tartaric and malic acids, lignin, and various salts. William Johnston (König's *Nahrungs- und Genussmittel,* 3d ed., Bd. i, 1046) finds that *piperidine,* $C_5H_{11}N$, is an invariable constituent of pepper in amounts varying from 0.21 to 0.77 per cent.

Piperidine is of great chemical interest as being a simple derivative of pyridine, which seems to underly the molecular structure of so many alkaloids. Piperidine is a hexalhydropyridine and can easily be obtained from pyridine by the action of tin and hydrochloric acid. Conversely piperidine can be changed into pyridine when sulphuric acid at 300° C. (572° F.) or gentle oxidizing agents act upon it. Coniine, it will be remembered, is a normal propylpyridine. Moore and Row (*J. P.,* 1898) have shown that piperidine resembles coniine in its physiological effects.

Heliotropin. (*Piperonal.*)—This interesting substance, although used almost exclusively in perfumery, has been recommended by Fraggani (*Ph. Centralh.,* xxviii, 253) as an antiseptic and antipyretic. It may be obtained by the oxidation of piperic acid. This piperonal is the aldehyde of piperonylic acid, $C_6H_3(CO\,OH)\begin{matrix}O\\O\end{matrix}>CH_2$, which, as the formula indicates, is the methylene ester of protocatechuic acid, $C_6H_3COOH(OH)_2$. See also *Schim. Rep.,* 1903, 133.

The taste and medicinal activity of pepper depend mainly on the concrete oil or resin, and on the volatile oil. The concrete oil is of a deep green color, very acrid, and soluble in alcohol and ether. The volatile oil is limpid, colorless, becoming yellow by age, of a strong odor, and of a taste less acrid than that of pepper itself. It consists of terpenes including dipentene, phellandrene, etc., and it forms a liquid but not a solid compound with hydrochloric acid. According to Weigle (*Ap. Ztg.,* 1893, 626), pepper contains, besides cellulose, starch, and coloring matter, (1) Volatile oil, smelling strongly of pepper, but without pungency; (2) a thick oil, tasteless and nearly odorless; (3) odorless piperine whose solutions possess the pungency of pepper. Weigle believes that in the fresh fruit the volatile oil acts as a solvent for the piperine and he thus accounts for their pungency.

For a paper on commercial peppers, by J. W. Gladhill, see *A. J. P.*, 1904, 71.

Adulterations.—On account of its extensive use as a condiment, pepper has been largely adulterated, especially when sold in the form of a powder. Chief of the adulterants are pepper-hulls, ground olive pits, wheat middlings, and roasted cereals. Among the other substances sometimes used have been ground beans or peas, corn starch, flaxseed, mustard hulls, and coffee hulls. The adulterated articles are usually fortified with the addition of Cayenne pepper. At the present time, by virtue of the National and state Food Laws, black pepper is seldom adulterated. Adulterations can be detected by the microscope with more or less ease (see *P. J.*, lxxi, 269; *P. J.*, June, 1890; *Bull. U. S. Dept. of Agriculture*, No. 13, Part II, pp. 183, 1887; *A. J. P.*, 1887, 146); but when pepper has been adulterated to the amount of 10 per cent. the discovery of the fraud is best made by determining the proportion of ash, of ether extract and of piperine present. The ash should never be above 6.5 per cent. for black and 3 per cent. for white pepper; the ether extract should be between 7.5 and 10 per cent. for black and 6 to 9 per cent. for white pepper, the U. S. standard being not less than 6 per cent. in which not less than 3.25 per cent. nitrogen shall be present. Piperine should be present in from 5.5 to 9 per cent. in good black pepper. The amount of oleoresin in any pepper can readily be determined by subtracting the weight of piperine from that of the mixture. Penang pepper is sometimes made to resemble the higher priced white peppers by coating the grains with an earthy matter (lime or clay). According to A. Mennechet, the fruits of *Myrsine africana* and of *Embelia Ribes* may sometimes be detected in the powder of pepper by extracting with ether and adding a little water, followed by a few drops of ammonia, when after shaking, a deep lilac-red color will appear in the aqueous layer. (*J. P. C.*, xiv, 587.)

Uses.—Black pepper is a warm carminative stimulant, capable of producing general arterial excitement, but acting with greater proportional energy on the part to which it is applied. From the time of Hippocrates it has been used as a condiment and in medicine. Its chief medicinal application is to excite the languid stomach and correct *flatulence*. It was for years occasionally administered for the cure of *intermittents*, but its employment for this purpose had passed from the profession to the laity, till a few years since revived by an Italian physician, to be again consigned to forgetfulness. Piperine has also been employed in the same disease, and has even been thought superior to quinine sulphate, but experience has not confirmed this favorable opinion. That, in its impure state, when mixed with a portion of the acrid principle, it will occasionally cure intermittents, there can be no doubt, but it is not comparable to the preparations of cinchona, and is certaintly less active than the official oleoresin of pepper. In intermittent fever, pepper may be found a useful adjuvant to the more powerful febrifuge. It may be given whole or in powder, but is more energetic in the latter state.

Dose, of pepper, five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Confectio Piperis, *Br.;* Oleoresina Piperis, *U. S.;* Pulvis Opii Compositus, *Br.;* Tinctura Antiperiodica, *N. F.;* Tincture Antiperiodica sine Aloe, *N. F.*

PIX CARBONIS PRÆPARATA. Br.

PREPARED COAL TAR

(pĭx cär'bŏ-nĭs præ-pą-rā'tą)

"Prepared Coal Tar is obtained by maintaining commercial coal tar at a temperature of 50° C. (122° F.) in a shallow vessel for one hour, stirring frequently." *Br.* "The tar obtained as a by-product in the destructive distillation of coal in the manufacture of illuminating gas." *N. F.*

Pix Lithanthracis, *N. F.;* Coal Tar.

When bituminous coal is subjected to dry distillation, besides the incondensible gases which serve for lighting, and the charcoal left behind as coke, which is a valuable fuel, there are formed numerous other pyrogenic products, necessarily more or less varying in character and amount, not only according to the kind of coal used, but also with the varying circumstances of the decomposing process. Most of these newly formed bodies, all of which are volatile, are condensed into a dark thick liquid or semi-liquid substance called *coal tar*. Formerly this was considered as refuse matter, but from it are now prepared substances of great value in the arts and in medicine. We can give here only a brief review of the more important of these substances.

The composition of coal tar varies considerably with the temperature at which the distillation of the coal is effected, the yield of solid bodies and of gases being larger when the temperature is higher, while at a lower temperature the liquid portion of the tar is in increased amount. When coal tar is submitted to distillation and rectification, it yields the following products, solids, liquids, and gases, in variable proportion:

1. *Solids.*—Naphthalene, $C_{10}H_8$, methyl-naphthalene, $C_{11}H_{10}$, naphtha-ethylene and diphenyl, $C_{12}H_{10}$, fluorene, $C_{13}H_{10}$, anthracene and phenanthrene, $C_{14}H_{10}$, fluoranthene, $C_{15}H_{10}$, methyl-anthracene, $C_{15}H_{12}$, retene, $C_{18}H_{12}$, chrysene, $C_{18}H_{12}$, pyrene, $C_{16}H_{10}$, picene, $C_{22}H_{14}$, and carbazol, $C_{16}H_{11}N$.

2. *Liquids.*—These may be neutral hydrocarbons, acids, and ethers of the same, or bases. The *neutral hydrocarbons* are benzene, C_6H_6, toluene, C_7H_8, methyl-toluene, and iso-xylene, C_8H_{10}, pseudocumene, and mesitylene, C_9H_{12}, cymene, $C_{10}H_{14}$. The *acid constituents* are phenol, C_6H_6O, orthocresol, paracresol, and meta-

cresol, C_7H_8O, phlorol, $C_8H_{10}O$, rosolic acid, $C_{20}H_{16}O_3$, pyrocatechin, $C_6H_6O_2$, and creosote, consisting of the methyl ethers of pyrocatechin and its homologues, $C_7H_8O_2$, $C_8H_{10}O_2$, and $C_9H_{12}O_2$. There are also present, probably in combination with the ammonia of the ammoniacal liquor, acetic, butyric, carbonic, hydrocyanic, sulphocyanic, and hydrosulphuric acids. The *bases* are ammonia, NH_3, methylamine, $CH_3.NH_2$, ethylamine, $C_2H_5NH_2$, phenylamine, $C_6H_5.NH_2$, pyridine, C_5H_5N, picoline, C_6H_7N, lutidine, C_7H_9N, collidine, $C_8H_{11}N$, leucoline, C_9H_7N, iridoline, $C_{10}H_9N$, cryptidine, $C_{11}H_{11}N$, acridine, $C_{12}H_9N$, coridine, $C_{10}H_{15}N$, rubidine, $C_{11}H_{17}N$, and viridine, $C_{12}H_{19}N$.

3. *Gases.* (1) *Illuminating gases.*—Acetylene, C_2H_2, ethylene, C_2H_4, propylene, C_3H_6, butylene, C_4H_8, allylene, C_3H_4, crotonylene, C_4H_6, terene, C_5H_8, and vapors of benzene, C_6H_6, styrolene, C_8H_8, naphthalene, $C_{10}H_8$, methylnaphthalene, hexane, C_6H_{14}, heptane, C_7H_{16}, and octane, C_8H_{18}.

(2) *Heating and diluting gases.*—Hydrogen, H_2, marsh-gas (methane), CH_4, carbon monoxide, CO.

(3) *Impurities.—Carbon dioxide,* CO_2, ammonia, NH_3, cyanogen, $(CN)_2$, methyl cyanide, $CH_3.CN$, sulphocyanic acid, CN,SH, hydrogen sulphide, H_2S, carbon disulphide, CS_2, carbon oxysulphide, COS, and nitrogen, N_2.

For description of coal-tar colors and derivatives, see Part II.

Properties.—Prepared coal tar is "a nearly black, viscous liquid, brown in very thin layers; heavier than *water.* Strongly empyreumatic characteristic odor. Almost entirely soluble in *benzene* and in *chloroform;* partially soluble in *alcohol* (90 per cent.), and in *ether;* very slightly soluble in *water.*" *Br.*

"A nearly black, thick liquid or semi-solid, heavier than water and possessing a characteristic, naphthalene-like odor and a sharp burning taste. It is only slightly soluble in water, to which it imparts its characteristic odor and taste and a faintly alkaline reaction. It is but partially dissolved by alcohol, acetone, methyl alcohol, or purified petroleum benzin; almost entirely dissolved by ether; entirely dissolved by benzene, carbon disulphide, or chloroform. On ignition it burns with a reddish, luminous and very sooty flame and upon strong heating is almost entirely consumed, leaving not more than 2 per cent. of ash." *N. F.*

Uses.—Coal-tar is occasionally used as a substitute for wood-tar in external applications, and according to Dind (*An. de Derm. et de Syph.,* 1909), has advantages over wood-tar that it is less irritant and less likely to produce nephritis or other toxic conditions after absorption. It is employed locally to relieve *itching* and to combat inflammation in such diseases as *lichen ruber, prurigo, eczema,* etc. It should not be used where the skin is infected with pyogenic cocci. It is most frequently applied in solution combined with saponin. (See *Liquor Picis Carbonis.*)

Off. Prep.—Liquor Picis Carbonis *Br.*

PIX LIQUIDA. U. S., Br.

TAR Pix Liq. [Pine Tar]

(pĭx lĭq'uĭ-dȧ)

"A product obtained by the destructive distillation of the wood of *Pinus palustris* Miller, or of other species of *Pinus* (Fam. *Pinaceæ*)." *U. S.* "Tar is a bituminous liquid, obtained by destructive distillation from the wood of Pinus sylvestris, *Linn.,* and other species of Pinus. Known in commerce as Stockholm tar." *Br.*

Resina Empyreumatica Liquida; Goudron végétal, *Fr. Cod.;* Goudron, *Fr.;* Theer, *G.;* Pece liquida, *It.;* Brea de pino, Alquitran vegetal, *Sp.*

The tar used in this country is prepared from the wood of various species of pine, particularly *Pinus palustris,* or the long-leaved, yellow or Georgia pine, of the Southern States. (See *Terebinthina.*) The dead wood is usually selected, because, when vegetation ceases, the resinous matter becomes concreted in the interior layers. The wood is cut into billets of a convenient size, which are placed together so as to form a large stack or pile and then covered with earth as in the process for making charcoal. The stack is built upon a small circular mound of earth previously prepared, the summit of which gradually declines from the circumference to the center, where a cavity is formed, communicating by a conduit with a shallow ditch surrounding the mound. Fire is applied through an opening in the top of the pile, and a slow combustion is maintained, so that the resinous matter may be melted by the heat. This runs into a cavity in the center of the mound, and passes thence by the conduit into the ditch, whence it is transferred into barrels. Immense quantities of tar are thus prepared in North Carolina and the southeastern parts of Virginia, sufficient, after supplying our own consumption to afford a large surplus for exportation. Considerable quantities of tar have been prepared also in the lower parts of New Jersey, in some portions of New England, and in Pennsylvania west of the Allegheny Mountains, from the *Pinus rigida,* or pitch pine, and perhaps from some other species.

Properties.—Tar has an acid reaction, a peculiar empyreumatic odor, a bitterish, resinous, somewhat acrid taste, a color almost black, and a tenacious consistence intermediate between that of a liquid and that of a solid; by age it becomes granular and opaque. It consists of resinous matter, united with acetic acid, oil of turpentine, and various volatile empyreumatic products, and colored with charcoal. By distillation it yields an acid liquor called *pyroligneous acid* (see *Acidum Aceticum*), and an empyreumatic oil called *oil of tar;* what is left behind is *pitch.* It is officially described in the United States Pharmacopœia as "semi-liquid, viscid, blackish-brown, non-crystalline, translucent in thin layers, becoming granular and opaque with age; odor empyreumatic, terebinthinate, taste sharp and empyreumatic. Tar is miscible with alcohol, ether, chloroform, glacial acetic acid, or fixed or volatile oils; it is heavier

than water and is slightly soluble in it, the solution being of a pale yellowish to yellowish-brown color and acid to litmus. The addition of a drop of ferric chloride T.S. to 10 mils of an aqueous solution of tar produces a greenish-brown color." *U. S.*

"Dark brown or nearly black; semi-liquid; empyreumatic characteristic odor; heavier than *water*. *Water* shaken with it acquires a pale-brown color, sharp empyreumatic taste, and acid reaction; very dilute *T. Sol. of ferric chloride* colors the solution red. Tar is completely soluble in ten times its volume of *alcohol* (90 per cent.)." *Br.*

The first examination of the empyreumatic oil was made by Reichenbach, of Moravia, who found a variety of substances, to which he gave the names of *paraffin, eupion, creosote, picamar, capnomor,* and *pittacal.* It has been found by more careful study of wood tar that it contains a great variety of compounds, including the hydrocarbons *toluene,* C_7H_8, *xylene,* C_8H_{10}, *mesitylene* and *pseudocumene,* C_9H_{12}; phenols like common *phenol,* C_6H_6O, *cresol,* C_7H_8O, *guaiacol,* $C_7H_8O_2$, *creosol,* $C_8H_{10}O_2$, *phlorol,* $C_8H_{10}O$, and *methylcreosol,* $C_9H_{12}O_2$, the last four constituting the mixture known as creosote; and, lastly, *paraffin* in variable quantity, depending upon the temperature of distillation, *naphthalene,* $C_{10}H_8$, *pyrene,* $C_{16}H_{10}$, *chrysene,* $C_{18}H_{12}$, and *retene,* $C_{18}H_{18}$. *Pyrocatechol,* $C_6H_4(OH)_2$, is also obtained, either in the pyroligneous acid, as it is soluble in water, or in the tarry mixture. It crystallizes readily, fuses at 104° C. (219.2° F.), and sublimes at a temperature slightly above this. Tar yields a small proportion of its constituents to water, which is thus rendered medicinal, and is employed under the name of *tar water* (see below). Tar is dissolved by alcohol, ether, chloroform, and the volatile and fixed oils, and by a solution of potassium or sodium hydroxides. On spreading tar in a thin layer on a pane of glass it should present a homogeneous appearance. Those specimens which contain granular transparent masses should be rejected. These masses, which polarize brilliantly, are said to be *pyrocatechol.* Tar should have a specific gravity of 1.03 to 1.07; it should boil at from 250° to 400° C. (482°–752° F.). Its reaction should be acid. "*Steam refined tar*" is tar which has been simply heated in steam caldrons and strained to remove foreign impurities.

Hirschsohn has suggested the following plan for the identification of different varieties of tar. (1) *Completely soluble in 95 per cent. acetic acid. Pine Tar.*—French turpentine dissolves it completely. The petroleum ether extract of the tar is colored greenish when shaken with a dilute solution of cupric acetate (1 : 1000). Chloroform and absolute ether dissolve it completely. *Beech Tar.*—Turpentine oil dissolves it only partially. The petroleum ether extract is not colored by copper acetate solution. Chloroform and absolute ether do not entirely dissolve it. (2) *Not completely soluble in 95 per cent. acetic acid. Juniper Tar.*—Turpentine oil dissolves it completely. Aniline dissolves it completely. The aqueous extract (1 : 20) yields a red coloration with dilute solution of ferric chloride (1 : 1000). *Birch Tar.*—Turpentine oil dissolves it completely. Aniline does not dissolve it completely. The aqueous extract is colored greenish by ferric chloride. *Aspen Tar.*—Benzene, chloroform, absolute ether, and olive oil dissolve it only partially. (*Ph. Ztg.,* 97, 396; *Ph. Z. R.,* 97.)

The pitch left after the evaporation of tar was formerly official with the British Colleges, under the names of *Pix nigra, Pix arida,* or simply *Pix.* It has a shining fracture, softens and becomes adhesive with a moderate heat, melts in boiling water, and consists of the unaltered resin of the pine and of various empyreumatic resinous products which have received the name of *pyretin.* (Berzelius, *Traité de Chimie,* vi, 641, 680.) It has been used internally in *ichthyosis* and other cutaneous diseases, and in *piles.* The dose is from ten grains to a drachm (0.65–3.9 Gm.), given in pill. Pitch is also used externally in the form of ointment.

Uses.—Tar owes its medicinal virtues chiefly to the phenol-like bodies which it contains; its effects resemble closely those of creosote, but it is less active and less liable to irritate the digestion. It is occasionally employed as a urinary antiseptic, but its most important internal use is as a stimulating expectorant in subacute or chronic bronchitis. Externally it is widely employed as a stimulating and antiseptic application in various *skin diseases.* (See *Unguentum Picis Liquidæ.*)

In reference to the administration of tar, it has always been considered desirable to have it in a soluble state, so that it might be brought with facility into a liquid form if required. Besides, tar in the stomach will probably be found efficacious in proportion to its solubility. This desired end was attained when it was discovered that tar was capable of forming a definite, solid compound with sugar which was very soluble in water. Saccaharated tar contains 4 per cent. of pure tar, resembles sugar in appearance, having a sweet taste and the odor of tar, and may be given in substance or solution as deemed desirable. (*P. J.,* Sept., 1871.) (See *Syrupus Picis Liquidæ.*) But glycerin is a more convenient vehicle, and glycerite of tar was an official preparation in 1870. Its vapor, inhaled into the lungs, may be serviceable in *chronic bronchitis* and *phthisis.* Its effects are most conveniently obtained by placing tar or oil of tar in a tin dish containing hot water, and heating this; the fumes may be inhaled by inverting a funnel to which a rubber tube is attached, over the dish. Tar was formerly used to a considerable extent in the form of *tar water, Infusum Picis Liquidæ,* U. S., 1870. This was made by macerating one part of tar in four parts of water with frequent agitation and decanting the clear fluid. Tar water is "a pale yellowish-brown color and acid reaction, and yields with ferric chloride test solution a transient green color, and is colored brownish-red by

an equal volume of calcium hydrate test solution." Two or three fluidounces (59–89 mils) of this infusion may be given several times a day. Tar may also be administered mixed with sugar in the form of an electuary.

Pulverulent tar is prepared by Magnes-Lahens, by mixing, in an earthenware vessel, two parts of finely divided charcoal and one part of liquid tar. The resulting mixture resembles small grains of gunpowder, does not soil the vessel or the fingers, and yields readily to water the tar which it contains—the most favorable temperature for solution being about 20° C. (68° F.). Magnes-Lahens recommends a syrup prepared from the powder as follows. Take of pulverulent tar, 50 Gm., water, 180 Gm., granulated sugar, 320 Gm. Mix the tar and sugar in a mortar, then add the water, and heat the mixture by a water bath at 60° C. (140° F.). Then remove from the bath, shake until the sugar is all dissolved, and strain when hot, and afterwards again when cold. A tablespoonful of the syrup, added to a tumbler of water, yields a tar water resembling that of the French Codex. The pulverulent tar may also be used for pills. (*P. J.*, April, 1872, 850.)

Dose, five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Syrupus Picis Liquidæ, *U. S.;* Unguentum Picis Liquidæ, *U. S., Br.;* Glyceritum Picis Liquidæ, *N. F.;* Liquor Picis Alkalinus, *N. F.;* Vinum Picis, *N. F.*

PLUMBI ACETAS. U. S., Br.

LEAD ACETATE Plumb. Acet. [Sugar of Lead]

(plŭm'bī ă'cę-tăs)

"It contains not less than 85.31 per cent. nor more than 89.57 per cent. of anhydrous lead acetate, corresponding to not less than 99.5 per cent. of the crystallized salt [$Pb(C_2H_3O_2)_2 + 3H_2O = 379.20$]. Preserve it in well-closed containers." *U. S.* "Lead acetate may be obtained by dissolving lead oxide or lead carbonate in acetic acid. It contains not less than 99.5 per cent. of pure lead acetate, $Pb(C_2H_3O_2)_2,3H_2O$." *Br.*

Acetas Plumbicus, Saccharum Saturni, Cerussa Acetata; Acétate neutre de Plomb, Sucre de Plomb, Sel de Saturne, *Fr. Cod.;* Plumbum Aceticum, *P. G.;* Bleiacetat, Essigsaures Bleioxyd, Bleizucker, *G.;* Acetato neutro di plombo, Zucchero di Saturno, *It.;* Acetato plumbico neutro, Azucar de Saturno, *Sp.*

Preparation.—Lead acetate is obtained by two methods. By one method, thin plates of lead are placed in shallow vessels filled with distilled vinegar, in such a manner as to have a part of each plate rising above the vinegar, and these are turned from time to time, so as to bring different portions of the metallic surface in contact with the air. The metal, in the presence of the oxygen of the air, dissolves in the vinegar to saturation, and the solution is evaporated to the point of crystallization. This process is a slow one, but furnishes a salt which is perfectly neutral. The other method consists in dissolving, by the assistance of heat, litharge, in 60 per cent. acetic acid, in large wooden vats provided with mechanical stirrers. The acetic acid is heated to 60° C. (140° F.) and the litharge added by means of a distributing device. The oxide is quickly dissolved, and, when the acid has become saturated, the solution is permitted to clarify by subsidence in vessels provided with strips of lead which coming into contact with the solution remove small amounts of copper which may be present, and it is then transferred to other vessels to cool and crystallize. The crystals having formed, the mother waters are decanted, and, by evaporation, made to yield a new crop. These are generally yellow, but may be rendered white by repeated solutions and crystallizations.

Lead acetate is extensively manufactured in Germany, Holland, France and England, as well as in the United States. It is principally consumed in the arts of dyeing and calico printing, in which it is employed with alum, to form aluminum acetate, which acts as a mordant.

Properties.—"Lead Acetate occurs as colorless, shining, transparent, monoclinic prisms or plates, or as heavy, white, crystalline masses, or granular crystals, having a faintly acetous odor, and a sweetish, astringent, afterwards metallic taste; efflorescent, and absorbing carbon dioxide on exposure to the air. One Gm. of Lead Acetate dissolves in 1.4 mils of water, and in 38 mils of alcohol at 25° C. (77° F.); also in about 0.5 mil of boiling water; freely soluble in glycerin. When heated to 40° C. (104° F.) the salt loses its water of crystallization. When heated rapidly to 75° C. (167° F.) it fuses in its water of crystallization, and at a temperature above 280° C. (536° F.) it finally decomposes, leaving a residue of finely divided metallic lead mixed with lead oxide. An aqueous solution of Lead Acetate (1 in 10) is slightly alkaline to litmus and separate portions yield a black precipitate with hydrogen sulphide T.S., a yellow precipitate with potassium iodide T.S., and a white precipitate with diluted sulphuric acid. Add 0.1 Gm. of the salt to a mixture of 1 mil of sulphuric acid and 1 mil of alcohol and warm the mixture; ethyl acetate is formed, recognizable by its odor. A solution of the salt (1 in 10), prepared with distilled water which has been recently boiled, is clear, or only slightly opalescent (*carbonate*) and yields with potassium ferrocyanide T.S. a precipitate which is not perceptibly blue or red (*iron or copper*).

"**Assay.**—Dissolve about 5 Gm. of Lead Acetate, accurately weighed, in sufficient recently boiled distilled water to make exactly 100 mils of solution. Mix 10 mils of this solution with 50 mils of tenth-normal oxalic acid V.S. in a 200 mil measuring flask, agitate the mixture thoroughly for five minutes, then fill the flask to the mark with distilled water; filter, and titrate 100 mils of the filtrate (representing one-twentieth of the amount of Lead Acetate originally taken) with tenth-normal potassium permanganate V.S., the filtrate being previously acidulated with 10 mils of sulphuric acid and warmed to 80° C. (176° F.). It shows not less

than 85.31 per cent. nor more than 89.57 per cent. of $Pb(C_2H_3O_2)_2$.

"Each mil of tenth-normal oxalic acid V.S. used corresponds to 0.016257 Gm. of $Pb(C_2H_3O_2)_2$. Each gramme of Lead Acetate corresponds to not less than 52.5 mils nor more than 55.1 mils of tenth-normal oxalic acid V.S." *U. S.*

"Small, white, monoclinic prisms, or crystalline masses, slightly efflorescent. Acetous odor; taste sweet, astringent. Soluble in 2.5 parts of *water,* and in 30 parts of *alcohol* (90 per cent.). Aqueous solution slightly acid to *litmus,* clear, or with only a slight turbidity which disappears on the addition of *acetic acid.* Yields the *reactions* characteristic of lead and of acetates. Yields no characteristic *reactions* for silver, copper, arsenic, iron, zinc, calcium, chlorides, or nitrates. When 0.5 gramme is dissolved in *water* acidified with *acetic acid,* excess of *N/1 solution of oxalic acid* added, the precipitate collected, washed, transferred to a flask and decomposed with excess of *diluted sulphuric acid,* the mixture thus obtained, heated to 60° C. (140° F.), decolorises not less than 26.2 millilitres of *N/10 solution of potassium permanganate* (presence of not less than 99.5 per cent. of pure lead acetate, $Pb(C_2H_3O_2)_2,3H_2O$)." *Br.*

Exposed to the air, it effloresces slowly. In pure distilled water, free from carbon dioxide, it ought to dissolve entirely and form a clear solution. Commercial acetate is sometimes impure from the presence of lead sulphate and carbonate. In purchasing it large crystalline masses should be selected. Sulphuric acid, when added to a solution of lead acetate, produces instantly a precipitate of lead sulphate, and the disengaged acetic acid gives rise to vapors having the odor of vinegar. An important property of lead acetate is its power of dissolving a large quantity of lead monoxide. (See *Liquor Plumbi Subacetatis.*) It consists of one atom of lead, which has replaced the two hydrogen atoms furnished by two molecules of acetic acid, $C_2H_3O_2.H$, so that its formula becomes $Pb(C_2H_3O_2)_2$, and this in crystallizing takes $3H_2O$. Its molecular weight is therefore 376.15.

Incompatibles and Tests.—Lead acetate is decomposed by all acids, and by those soluble salts the acids of which produce with lead monoxide insoluble or sparingly soluble compounds. Acids of this character are sulphuric, hydrochloric, phosphoric, tannic, citric, and tartaric. It is also decomposed by lime water, and by ammonia, potassium and sodium hydroxides; the last two, if added in excess, dissolving the precipitate at first formed. It is decomposed by hard water, in consequence of the calcium sulphate, carbonates and sodium chloride which such water usually contains.

Uses.—Lead acetate, in medicinal doses, is a powerful astringent and sedative; in overdoses, an irritant poison, which has in a number of cases caused death. Burning epigastric pain, vomiting of a white curdy matter (lead chloride), and diarrhea or constipation with black stools (lead sulphide), and finally collapse, are the characteristic symptoms. Its antidote is any soluble sulphate, common salt, soap, or an alkali.

In medicinal doses lead acetate is a powerful sedative astringent. It is especially useful in the treatment of *diarrheas,* and even of *dysentery,* when the discharges are excessive. At one time it was very much used for the relief of *gastric* or *intestinal hemorrhages,* but is rarely employed for this purpose to-day. In many cases of *chronic diarrhea* or in *diarrheas* occurring in exhaustive, uncontrollable disease, such as *phthisis,* lead acetate, combined with opium, may be a valuable palliative in checking discharges. Externally it has been applied in weeping *eczema,* in *pruritus vulvæ,* and similar conditions of irritation, but is less frequently employed than formerly. The prolonged medicinal use of acetate of lead may give rise to subacute or chronic lead poisoning.

Internally, lead acetate should always be given in the form of pill, and is often combined with opium. The solution for external use may be made by dissolving from two to three drachms in a pint of water, and, if it be wanted clear, a fluidrachm of vinegar or of diluted acetic acid may be added, which immediately dissolves the lead carbonate, to which its turbidity is owing. When the skin is denuded of the cuticle, the solution should be weaker. The usual strength of the solution as a collyrium is from one to two grains (0.065–0.13 Gm.) to the fluidounce (30 mils) of *distilled* water. In this case, acetic acid should not be used to clear up the solution, which should simply be filtered.

Dose, one to three grains (0.065–0.20 Gm.).

Off. Prep.—Glycerinum Plumbi Subacetatis, *Br.;* Liquor Plumbi Subacetatis, *U. S.* (*Br.*); Pilula Plumbi cum Opio, *Br.;* Suppositoria Plumbi Composita, *Br.;* Unguentum Plumbi Subacetatis, *Br.;* Lotio Plumbi et Opii, *N. F.;* Pilulæ Opii et Plumbi, *N. F.*

PLUMBI IODIDUM. Br.

LEAD IODIDE

(plŭm'bī ī-ŏd'ĭ-dŭm)

"Lead Iodide, PbI_2, may be obtained by the interaction of aqueous solutions of lead nitrate or acetate and potassium iodide." *Br.* "It contains not less than 99 per cent. of PbI_2 (460.94). Preserve it in well-closed containers, protected from light." *N. F.*

Plumbum Iodatum, Ioduretum Plumbicum, Iodure de Plomb, *Fr. Cod.;* Jodblei, *G.;* Yoduro plumbico, *Sp.*

"Take of Nitrate of Lead, Iodide of Potassium, each *four ounces* [avoirdupois]; Distilled Water *a sufficiency.* Dissolve the Nitrate of Lead, by the aid of heat, in a pint and a half, and the Iodide of Potassium in half a pint of the Water, and mix the solutions. Collect the precipitate on a filter, wash it with Distilled Water, and dry it in a warm place." *Br.,* 1885.

No process was given in the U. S. P. VIII nor Br. Ph., 1914, for lead iodide. The process of the U. S. P., 1870, was identical with that of the British Pharm., 1885, given above.

The lead nitrate gives up its metal to the iodine, receiving the potassium, the operation taking place between one molecule of the lead nitrate and two molecules of the potassium iodide. The potassium nitrate thus formed remains in solution, while the lead iodide is precipitated,

$$Pb(NO_3)_2 + 2KI = 2KNO_3 + PbI_2$$

The theoretical quantities of lead nitrate and potassium iodide are 331.12 of the former and 332.04 of the latter, or almost precisely equal quantities. The proportions should be as nearly as possible those of exact saturation. An excess of the potassium iodide, independently of the waste, has the disadvantage of holding a portion of the lead iodide in solution, while, according to Christison, an excess of lead over the iodine disposes to the formation of the lemon-yellow insoluble lead oxyiodide. By the use of equal quantities of the two salts these disadvantages are avoided. As lead iodide is slightly soluble in cold water, it is desirable to use as little of the solvent as will answer, and hence the comparatively small proportion of water employed.

In the former London process lead acetate was employed instead of the nitrate, but Depaire, of Brussels, ascertained that in this process a considerable amount of iodide remains in solution after the precipitation of the lead iodide. Boudet (*J. P. C.*, 3e sér., xi, 274) ascribes this result to the formation of a portion of soluble potassium and lead iodide, whenever lead iodide and potassium acetate are in contact. T. Huraut has found that of the two lead salts employed, the nitrate was to be preferred, and of the various iodides, though potassium iodide yielded a very handsome product, yet calcium iodide afforded one not inferior in quality, and somewhat greater in quantity. Upon a small scale, as the process is performed by the apothecary, the difference would be of little consequence, but it might be important to the manufacturer. (See *A. J. P.*, xxi.)

Properties.—As officially described, it is in the form of "a heavy, bright-yellow powder. Soluble in about 2000 parts of cold *water*, and in about 200 parts of boiling *water*, from which it is deposited in golden-yellow crystalline scales as the solution cools; entirely soluble in *solution of ammonium chloride*. Yields the *reactions* characteristic of lead and of iodides. Yields no characteristic *reactions* for nitrates or acetates." *Br.*

"Lead Iodide occurs as a heavy, bright yellow powder, without odor or taste; permanent in the air. One gramme dissolves in about 1300 mils of water at 25° C. (77° F.) and in about 200 mils of boiling water, separating from the latter solution on cooling in brilliant, golden-yellow crystalline laminæ; very slightly soluble in alcohol; soluble, without color, in solutions of the fixed alkalies, in concentrated solutions of the alkali acetates, of potassium iodide, and of sodium thiosulphate, and in a hot solution of ammonium chloride. When moderately heated, the salt fuses to a thick, reddish-brown liquid, which congeals, on cooling, to a yellow, crystalline mass. At a higher temperature it is decomposed, with the evolution of violet vapors of iodine, leaving a lemon-yellow residue of lead oxyiodide. Triturate 1 Gm. of the salt with 2 Gm. of ammonium chloride and 2 mils of distilled water; a nearly white mixture results. Transfer this to a test tube, and heat in a water bath for a few minutes; a clear, almost colorless solution is formed (*chromate and other insoluble foreign salts*). On cooling this solution, a solid mass of nearly colorless, fine, silky crystals is produced, and on adding water or diluted sulphuric acid to this mass, yellow Lead Iodide separates. Add 0.1 Gm. of the salt to 5 mils of distilled water, and heat the mixture until it boils; cool the liquid and filter it into a test tube of about 40 mils capacity, then add 5 mils of sodium hydroxide T.S. and about 0.2 Gm. of aluminum wire; insert in the upper portion of the test tube a pledget of purified cotton, and over the mouth place a piece of moistened red litmus paper and then heat the tube on a water bath during fifteen minutes; no blue coloration of the paper will be discernible (*nitrate*). Boil 1.5 Gm. of Lead Iodide for a few minutes with 15 mils of distilled water, cool and filter. To 5 mils of the filtrate add a slight excess of silver nitrate T.S., then a slight excess of hydrochloric acid and filter. Neutralize the filtrate with ammonia water and add a drop of ferric chloride T.S. No red color is produced (*acetate*). To another 5 mil portion of the filtrate add an excess of hydrogen sulphide T.S., filter, evaporate to dryness and ignite; not more than 0.002 Gm. of residue remains." *N. F.*

It is freely soluble in a concentrated solution of sodium acetate. (Donato Tommasi, *P. J.*, 3d series ii, 805). It should be kept excluded from the light. It is stated by Engelhardt that iodine is separated from lead iodide by ferric and cupric chlorides, while the other metallic chlorides have no such effect, producing compounds of iodides of the metal employed with lead chlorides.

Uses.—This compound is supposed to have the resolvent properties of iodine, combined with those which are peculiar to lead, and is said to have been usefully employed in the discussion of *scrofulous tumors* and other indolent swellings, and in the cure of obstinate *ulcers*, both internally and locally. According to Cogswell, if given for some time in small doses, it produces the effects of lead, but not those of iodine, upon the system. It is more dangerous than useful. The plaster of lead iodide was dropped from the British Pharm., 1914, but the ointment was retained.

Dose, half a grain to four grains (0.032–0.26 Gm.).

Off. Prep.—Unguentum Plumbi Iodidi, *Br.*

PLUMBI OXIDUM. U. S., Br.

LEAD OXIDE Plumb. Oxid. [Litharge]

(plŭm'bī ŏx'ĭ-dŭm)

"It contains, when freshly ignited, not less than 96 per cent. of PbO (223.10). Preserve it in well-closed containers." *U. S.* "Lead Oxide, PbO, may be obtained by the action of air on melted lead." *Br.*

Oxide of Lead; Lithargyrum, Plumbum Oxydatum, Plumbi Oxidum Semivitreum; Oxide (proto) de Plomb fondu, Litharge, *Fr. Cod.*; Protoxide de Plomb, *Fr.*; Bleiglätte, Bleioxyd, *G.*; Litargirio, *It.*, *Sp.*

When lead oxide is rendered semi-crystalline by incomplete fusion it becomes the *semi-vitrified oxide*, or litharge. Almost all the litharge of commerce is obtained, as a secondary product, in the process for extracting silver from argentiferous galenas. After extracting the argentiferous lead from the ore, the alloy is placed upon an oval slightly concave dish, about three feet long and twenty inches wide, called a *test*, made by beating pulverized bone ash, formed into a paste with water, into a mould, the sides of which consist of an elliptical band of iron, and the bottom of strips of sheet iron, placed at short distances apart. The test is of such a size as exactly to fit an opening in the floor of a reverberatory furnace, where it is placed and adjusted to the level of the floor. On one side of the test the fireplace is situated, and exactly opposite, the chimney, while at one extremity of it the pipe of a strong bellows is placed, and at the other a vertical hole is made, communicating with a gutter leading from the test. The furnace is now lighted, and shortly afterwards the bellows are put in motion. The lead fuses and combines with oxygen, and the resulting oxide, melting also, forms a stratum which floats on the surface, and which is driven by the blast of the bellows along the gutter and through the vertical hole into a receiver below, where, upon solidifying, it crystallizes in small scales, which form the litharge. In proportion as the lead is oxidized and blown off the test, fresh portions are added so as to keep it always sufficiently full. The process is continued for eight or ten days, after which no more lead is added. The operation is now confined to the metal remaining on the test, and, the oxidation proceeding, a period at last arrives when the whole of the lead has been blown off as litharge, and the silver, known to be pure by it brilliant appearance in the fused state, alone remains. This is then removed, and the process repeated on a fresh portion of argentiferous lead. The yellow amorphous lead oxide as a paint color is known as *massicot*, and is prepared by careful heating of lead carbonate or nitrate to a point short of the fusion of the resulting oxide.

Properties.—It is officially described as "a heavy, yellowish or reddish-yellow powder, or in minute scales, without odor or taste. On exposure to the air it slowly absorbs moisture and carbon dioxide. Lead Oxide is almost insoluble in water, to which, however, it imparts a faintly alkaline reaction; insoluble in alcohol; dissolved by acetic or diluted nitric acid, and by warm solutions of the fixed alkali hydroxides. When heated, the Oxide becomes darker in color, but assumes its original color on cooling; it fuses at a red heat. When heated in contact with charcoal, it is reduced to metallic lead. A solution of the Oxide in diluted nitric acid (1 in 10) is colorless, and, when nearly neutralized by ammonia water, separate portions yield with hydrogen sulphide T.S. a black precipitate, with potassium iodide T.S. a yellow precipitate, and with diluted sulphuric acid a white precipitate. Shake 5 Gm. of the Oxide in a small flask with 5 mils of distilled water, and add 20 mils of acetic acid. Boil the mixture for a few minutes, filter it, wash the insoluble residue well with diluted acetic acid, and dry it at 110° C. (230° F.); it weighs not more than 0.15 Gm. When strongly heated in a porcelain crucible, the Oxide loses not more than 4 per cent. of its weight (*carbonate and moisture*)." *U. S.*

"Heavy scales, or powder, of a pale yellowish-red color. Soluble in *diluted nitric acid* and in *acetic acid* with but slight effervescence, leaving not more than traces of insoluble residue. Yields the reactions characteristic of lead. Yields no characteristic *reactions* for copper, and not more than the slightest *reactions* for iron." *Br.*

It slowly attracts carbon dioxide from the air, and contains more of this acid the longer it has been exposed. It is on this account that it commonly effervesces slightly with the diluted acids. It has the property of decolorizing wines, when agitated with them. When heated with the fats and oils, in connection with water it saponifies them. (See *Emplastrum Plumbi.*) Heated with charcoal, it is reduced to the metallic state. In diluted nitric acid it should be almost entirely soluble; and the solution is affected by potassium hydroxide in the same manner as that of the carbonate. (See *Plumbi Carbonas.*) As it occurs in commerce, it usually contains iron, copper, and a little silver and silica. It may be purified from iron and copper by digestion in diluted sulphuric acid. The English litharge is most esteemed, that from Germany being generally contaminated with iron and copper. In choosing litharge, samples should be selected which are free from copper and from fragments of vegetable matter. Copper is detected if upon adding potassium ferrocyanide to a nitric acid solution of the litharge a brown instead of a white precipitate is produced. Two varieties of litharge are distinguished in commerce, named from their color, and dependent on differences in the process employed. Sometimes it has a pale yellow color and silvery appearance, and is then denominated *argyritis, silver litharge* or *yellow litharge*; at other times it is of a red color, and is known under the names of *crystitis, gold litharge* or *red litharge*. The latter was supposed to owe its color to the presence of a portion of red lead, but Leblanc has shown that the two varieties of litharge differ in color, structure, and density only, and not in chemical composition. In this respect litharge

is essentially identical with lead oxide. (See *Plumbum.*) The carbon dioxide which it contains is variable, but its average amount is about 4 per cent. Lead peroxide and red lead in litharge may be detected by heating it in a test tube with sodium chloride and potassium bisulphate and introducing a slip of paper colored blue by indigo. If either of these oxides be present, the paper will be bleached by the chlorine evolved.

"**Assay.**—Dissolve about 0.4 Gm. of freshly ignited Lead Oxide, accurately weighed, in 4 mils of acetic acid and 25 mils of recently boiled distilled water, in a 200 mil graduated flask, and mix the solution with 50 mils of tenth-normal oxalic acid V.S. Fill the flask to the mark with distilled water, mix well, filter through a dry filter into a dry flask, rejecting the first 20 mils of filtrate, and titrate 100 mils of the filtrate (representing one-half of the amount of Lead Oxide originally taken) with tenth-normal potassium permanganate V.S., the filtrate being previously acidulated with 20 mils of diluted sulphuric acid and warmed to 80° C. (176° F.). It shows not less than 96 per cent. of PbO.

"Each mil of tenth-normal oxalic acid V.S. corresponds to 0.011155 Gm. of PbO. Each gramme of Lead Oxide, after ignition, corresponds to not less than 86.1 mils of tenth-normal oxalic acid V.S." *U. S.*

Uses.—Litharge is never used internally, but is employed in several pharmaceutical operations, and forms an ingredient in various external applications, used for abating inflammation, and for other purposes. In the arts it is employed in the glazing of pottery, in painting to increase the drying property of oils, and as an ingredient in flint glass.

Off. Prep.—Emplastrum Plumbi, *U. S., Br.;* Glycerinum Plumbi Subacetatis, *Br.;* Liquor Plumbi Subacetatis, *U. S.* (*Br.*).

PLUMBUM

LEAD

(plŭm'bŭm)

Plomb, *Fr.;* Blei, *G.;* Lood, *Dutch;* Piombo, *It.;* Plomo, *Sp.*

Lead is not official in its metallic state, but enters into a number of important medicinal preparations. It occurs in nature as an oxide, as a sulphide called *galena,* and in saline combinations, forming the native lead sulphate, phosphate, carbonate, chromate, molybdate, tungstate, and arsenate. The oxide is rare, but galena is exceedingly abundant, and is the ore from which nearly all the lead of commerce is extracted. The extraction is effected either by melting the ore in contact with charcoal, or, in the case of pure galenas, by what is termed the *air reduction* process. In this case the galena is first roasted, when it is in part changed into oxide, PbO, and sulphate, $PbSO_4$. The doors of the furnace are then closed, and the unchanged sulphide reacts with both the oxide and the sulphate as follows:

$$2PbO + PbS = 3Pb + SO_2$$
$$PbSO_4 + PbS = 2Pb + 2SO_2$$

whereby all the lead is obtained in the metallic state. Lead is also successfully obtained by electrolysis directly from the galena. This is reduced at the cathode of an electrolytic cell, while hydrogen sulphide is formed at the same time and may be collected or burned to form sulphur dioxide, which is then utilized. The process is now in operation at Niagara Falls. The richest and most extensive mines of galena are found in this country. The non-argentiferous lead region of the United States extends in length from Wisconsin in the north to the Red River of Arkansas in the south, and in breadth about one hundred and fifty miles, being chiefly in the State of Missouri, while Utah, Idaho, Montana, and Colorado furnish argentiferous galena. The total production of lead in the United States in 1915 was 615,253 tons, made up of 565,356 tons from domestic ores (317,463 from silver bearing lead ore and 247,893 from non-silver bearing), and 49,897 tons from imported ores.

Properties.—Lead is a soft, bluish-gray, and very malleable metal, presenting a bright surface when newly melted or cut. It has a perceptible taste, and a peculiar odor when rubbed. It undergoes but little change in the air, but is acted on by the combined influence of air and rain water, which gives rise to a hydrate, which is afterwards changed, in part, into carbonate, by absorbing carbon dioxide from the atmosphere, and if in water, the carbonate is imparted to it in the state of bicarbonate, which dissolves and renders the liquid poisonous. This chemical effect on the metal is greater in proportion as the water is purer. Aqueous vapor passed through leaden pipes has a similar corroding effect, which is greater as the lead is purer. Spring and river water act on lead differently, the lead becoming slowly oxidized, and covering itself with a black coating of suboxide, which adheres strongly to the metal, and thus in some measure protects the water. Hard water forms a protective coating of lead carbonate or lead sulphate on the inner surface of pipes through which it flows, but it is stated that this protective condition disappears in waters which have been treated with chlorine or hypochlorites for the purpose of purification. (Langlois, *J. P. C.*, 4e sér., ii, 29.) Stalmann has satisfied himself, by experiment, that an extremely minute quantity of ammonia or of nitric acid will very much promote the action of water upon lead—a millionth of ammonia being sufficient for the purpose. (*J. P. C.*, iv, 467.) Metallic lead seems to be liable to the attacks of certain insects, which bore into and sometimes through it, not using it as food, but apparently in search of secure places of retreat for future development. A knowl-

edge of this fact may sometimes be important. (*A. J. P.*, Jan., 1865, p. 72.) Its sp. gr. is 11.4, melting point 334° C. (633.2° F.), and atomic weight 207.10. Exposed to a stream of oxygen on ignited charcoal, it burns with a blue flame throwing off dense yellow fumes. The best solvent of lead is nitric acid, but the presence of sulphuric acid destroys, and that of hydrochloric acid lessens, its solvent power, on account of the insolubility of the lead sulphate and chloride. Lead forms a suboxide, Pb_2O, a monoxide, PbO, a sesquioxide, Pb_2O_3, a dioxide, PbO_2, and a compound of the monoxide and the dioxide, which has a varying composition, but is usually Pb_3O_4. The *monoxide* is called in commerce *massicot*, or *litharge*.

On a large scale it is made by exposing melted lead to the action of the air. Its surface becomes encrusted with a gray pellicle, which, being scraped off, is quickly succeeded by another; and the whole of the metal, being in this way successively presented to the air, becomes converted into a greenish-gray powder, consisting of monoxide and metallic lead. This, on exposure to a moderate heat, absorbs more oxygen, and is converted wholly into monoxide. This oxide has a yellowish color, and is the only oxide capable of forming salts with the acids. It consists of one atom of lead and one of oxygen. *Litharge,* PbO, is very much used in pharmacy, and is official in all the Pharmacopœias. (See *Plumbi Oxidum.*) The *sesquioxide,* discovered by Winckelblech, is unimportant. The *dioxide,* PbO_2, called also *puce* oxide, from its flea-brown color, may be obtained by treating red lead with nitric acid. The acid takes up the monoxide and leaves the dioxide, which may be purified by washing with boiling water. A more productive process is to precipitate four parts of lead acetate by three of sodium carbonate, and then to pass into the thin pasty mass of lead carbonate a stream of chlorine, which converts the monoxide of the carbonate into the brown dioxide. (F. Wöhler.) Solution of chlorinated soda may be conveniently employed to furnish the necessary chlorine. Lead forms two classes of compounds in one of which it acts as a base (as illustrated by the official salts of lead), and in the other of which it is contained in the acid group forming a class of compounds known as *plumbates* and *plumbites;* Na_2PbO_2 and Na_2PbO_3, are examples of the sodium salts of this composition. Lead dioxide is a tasteless powder, of a dark brown color. When heated to redness it loses half its oxygen and becomes monoxide. It consists of one atom of lead and two atoms of oxygen. The *red oxide,* Pb_3O_4, called in commerce *minium,* or *red lead,* is described under another head. (See *Lead Oxide, Red,* Part II.) Lead combines with iodine, forming the official lead iodide. The acetate is also official.

The best tests for lead are hydrogen sulphide or a solution of potassium iodide. The former produces a black precipitate of lead sulphide, the latter a yellow one of lead iodide.

Poisoning.—In concentrated form and sufficient amount the soluble preparations of lead are violent irritant poisons. (See *Plumbi Acetas,* p. 873.) The insoluble preparations of lead are incapable of acting as acute irritant poisons, but are the common causes of a chronic poisoning. The most common form of the poisoning, the so-called *colica pictonum,* is very common among painters, makers of white lead, and other artisans who work in the metal. It is, however, also frequently seen in other persons, into whom the lead finds entrance in almost innumerable ways, especially with drinking water and food. Colica pictonum usually begins with dyspeptic symptoms and obstinate constipation, associated with violent pain of a twisting character, which seems to center round the umbilicus; the abdominal walls are spasmodically retracted.

Accompanying these symptoms there is loss of appetite, pallor, lassitude, and failure of the general health. The stools are whitish and usually constipated, although occasionally there is diarrhea. A characteristic symptom is a blue line situated upon the margin of the gums where they join the teeth, due to the deposit of the lead sulphide. This blue line, if present, is pathognomonic, but may be absent even in the most severe cases. Basophilic degeneration of the red blood cells can be found in the majority of cases, and if present is a very suggestive symptom. The pulse is usually slow and hard.

Various symptoms of disorder of the nervous system or of nutrition may occur later. Occasionally these nervous disturbances are the sole evidence of the intoxication, although more frequently they are either accompanied with, or preceded by, the typical lead colic. The most characteristic of the nervous phenomena is the double wrist drop due to paralysis of the extensors of the fore arm, and associated with wasting and degenerative changes in the muscles involved. Rarer manifestations are: paraplegia simulating anterior poliomyelitis; cerebritis with wild delirium and sometimes convulsions; occasionally arthritis very much like that of typical gout may be seen. Chronic lead poisoning in rare cases may take on many other forms; indeed, it has been said that lead poisoning may simulate any known nervous disease. For further information on chronic lead poisoning, see Hamilton (*J. A. M. A.*, 1911, lvi, p. 1240).

The diagnosis of chronic lead poisoning is of the utmost importance, but sometimes of great difficulty. The blue line upon the gums, if present, is practically pathognomonic, but its absence is of no negative value. Extensive degeneration of the blood corpuscles is also a symptom of great diagnostic importance, but may be absent in even severe cases. In doubtful cases a chemical examination of the urine for the presence of lead should be made. It must be remembered, however, that the presence of the metal does not prove that the case is one of lead poisoning; lead has been found in the urine of many persons in apparently normal health. As the elimination of lead through the kidneys is hastened by the administration of potassium iodide it is generally advisable to give

this salt two or three days before the collection of the sample for examination.

The treatment of chronic lead poisoning resolves itself into three divisions: to stop the ingestion of the poison, to hasten its elimination, and to relieve symptoms. The most important step in the first of these is to find the source. While in the majority of instances the disease is an occupational one, yet in some cases much ingenuity is required to trace its origin. It has been attributed in obscure cases to the use of various cosmetics containing lead, to lead-foil around chewing tobacco or confectionery, to biting of silk thread which has been weighted with lead, to the use of improperly glazed earthenware vessels, etc., but outside of workers in the metal it most commonly obtains entrance into the body with the drinking water. The daily use of magnesium sulphate serves the double purpose of keeping the bowels open and of precipitating any lead which may be eliminated into the intestinal tract. For the purpose of aiding in the excretion of the metal the most important single measure is the administration of potassium iodide which forms a soluble compound with the metal. The use of sweat baths containing sulphur has also been recommended.

Warm *sulphuretted baths* may be provided by dissolving four ounces of potassium sulphide in thirty gallons of water, in a wooden tub. These baths cause discoloration of the skin, from the formation of lead sulphide, and should be repeated every few days, until this effect ceases to be produced. After each bath the patient should be well washed with soap and water with the aid of a flesh brush, in order to remove the discoloration. By proceeding in this way, the lead on the skin, or in its pores, is rendered insoluble and inert, and at the same time removed.

The manifestations are so protean that it is impossible to consider here all the measures for relief of symptoms. For the colic the most generally useful drug is belladonna in full dose. If the pain is very severe morphine may be given which acts not only by its direct analgesic effect, but by relaxing the intestinal spasm.

We have seen life apparently saved in a violent attack of lead cerebritis by free venesection and the injection of physiological salt solution.

PODOPHYLLI INDICI RESINA. Br.

INDIAN PODOPHYLLUM RESIN [Podophyllum Emodi Resin]

(pŏd-o-phy'lī ĭn'dĭ-çī rĕ-sī'nă)

"Indian Podophyllum Resin is a powdered resin prepared by the same process as that described under 'Podophylli Resina,' employing Indian Podophyllum Rhizome in place of Podophyllum Rhizome. It possesses the characters and responds to the tests described under 'Podophylli Resina.'" *Br.*

(See *Podophylli Indici Rhizoma.*)

The rhizome of the Indian podophyllum has become a commercial article and appears to have been largely used in the making of podophyllin. The question as to the relative yield of the Indian and American plants is a matter of great importance to the manufacturer, it usually being stated that the Indian rhizome is twice as active. Some years since Dymock and Hooper obtained 12 per cent. of resin from *P. Emodi;* Umney, working with large quantities (*P. J.*, Sept., 1902), got out 11.4 per cent.; since then John Barclay (*P. J.*, 1903, lxx) was not able to obtain a greater yield than 6.69 per cent. Umney, commenting on this, believes that of late years the Indian plant gives a much smaller product than formerly, probably on account of the time of year in which it is now dug. In regard to the therapeutic interchangeability of the two resins it has been demonstrated by the researches of Dunstan and Henry and J. C. Umney that the active substances in true podophyllin are all present in the Indian resin, but it is not assured that the proportion of these active principles is the same in the two resins. At one time it was claimed that the resin from the Indian species was more active than that obtained from the American plant, but this appears not to be correct. In the present state of our knowledge, the manufacturer is certainly not justified in putting upon the market a resin made from the Indian plant unless it is plainly marked as the Indian podophyllin. Distinguishing between the two resins has become a question of importance. The presence of a yellowish-green color does not, as has been affirmed, prove that a podophyllin is impure or of Indian origin. The test of solubility is also uncertain. The Indian podophyllin, properly prepared, is freely soluble in alcohol. It is commonly stated that the true podophyllin will dissolve in ammonia (1 to 100). The Indian species is seemingly much less soluble in ammonia than this, but a properly prepared official resin does not always come up to this standard. E. J. Millard (*P. J.*, lx) states that the Indian resin strikes with strong sulphuric acid an orange to red color, the official resin yellow coloration, tending to brown, but especially commends the following test:

To six grains (0.4 Gm.) of the resin in a test tube add one fluidrachm (3.75 mils) of diluted alcohol sp. gr. 0.920, and eight or ten drops (0.4–0.5 mil) of solution potash, B. P.; shake gently by rotating the test tube. In case of the Indian resin, the mixture becomes in a few seconds a semi-solid gelatinous mass, so that the test tube can be safely inverted. If this does not occur quickly, the mixture should be heated until it just begins to boil, and when cold it will be found to have gelatinized. The official resin similarly treated gives a dark fluid that shows no signs of gelatinizing even after standing for days. The Indian Podophyllum Resin is used for the same purposes as the American. (See *Resina Podophylli.*)

Dose, one-fourth to one grain (0.016 to 0.065 mil); of the *tincture* (*Tinctura Podophylli Indici*), five to fifteen minims (0.3–0.9 mil).

PODOPHYLLI INDICI RHIZOMA. Br.

INDIAN PODOPHYLLUM RHIZOME [Podophyllum Emodi Rhizome]

(pŏd-o-phy̆l'lī ĭn'dĭ-çī rhī-zō'mą)

"Indian Podophyllum Rhizome is the dried rhizome and roots of Podophyllum Emodi, *Wall.*" *Br.*

Podophyllum Emodi (Fam. *Berberidaceæ*) is a perennial herb which is indigenous to Thibet and Afghanistan. It somewhat resembles our American Podophyllum. The stem rises to a height of six or twelve inches before the leaves, which attain a diameter of six to ten inches when fully expanded. The latter are curiously reflexed, droop umbrella-like and are often spotted. The plant produces in May a large sub-sessile pinkish-white flower which arises from the axil of one of the leaves, maturing before the latter are fully expanded. The fruit is about the size of a small lemon, of a bright orange color, being fully ripe in about August or September.

The contorted rhizome of *Podophyllum Emodi* is from six to eight mm. in thickness, crowded above with numerous buds or short branches, marked by depressed oval or circular scars, and giving off numerous simple rootlets from the whole of the under surface. The terminal bud is enclosed in whitish papery sheaths. The color is earthy-brown. The fracture is white, short, and mealy, or yellow and horny, exhibiting a circular arrangement of yellow vascular bundles, and bounded on the outside by a thin brown cortical layer.

"Rhizome cylindrical or flattened, contorted, earthy-brown; usually about ten millimetres thick; below with numerous root-scars, or with stout roots, and crowned with the short remains of aerial stems, bearing cup-shaped scars. In transverse section, pale-brown and starchy or horny, with a ring of radially elongated wood-bundles. Slight odor; taste bitter and acrid." *Br.*

It is used for the same purposes as podophyllum.

Off. Prep.—Podophylli Indici Resina, *Br.;* Tinctura Podophylli Indici (from Resin), *Br.*

PODOPHYLLUM. U. S. (Br.)

PODOPHYLLUM Podoph. [Mandrake, May Apple Rhizome]

(pŏd-o-phy̆l'lŭm)

"The dried rhizome and roots of *Podophyllum peltatum* Linné (Fam. *Berberidaceæ*), yielding not less than 3 per cent. of resin." *U. S.*
"Podophyllum Rhizome is the dried rhizome and roots of Podophyllum peltatum, *Linn.*" *Br.*

Podophylli Rhizoma, *Br.;* Podophyllum Root, Wild Mandrake, Devil's Apple, Umbrella Plant, Vegetable Calomel, *Mandrake,* American Mandrake, Wild Lemon, Ground Lemon, Hog Apple, Indian Apple, Raccoon Berry, Duck's Foot, Rhizome de Podophyllum, *Fr. Cod.;* Fussblattwurzel, *G.;* Podofillo, *It.;* Podofilo (Rizoma de), *Sp.*

Podophyllum peltatum (May-apple) is an indigenous herbaceous plant. The rhizome is perennial, creeping, usually several feet in length, about one-quarter of an inch thick, brown externally, smooth, jointed, and furnished with roots at the joints. The stem is about a foot high, erect, round, smooth. The basal leaves are centrally peltate, with six or seven wedge-shaped lobes, irregularly incised at their summits, yellowish-green on their upper surface, paler and slightly pubescent beneath. The flower-bearing stems bear from one to three similar leaves. The flower is nodding, and appears between two leaves at the apex of the stem or at the base of the upper leaf when three leaves are present. The calyx is composed of three oval, obtuse, concave, deciduous sepals. The corolla has from six to nine white, fragrant petals, which are obovate, obtuse, concave, with delicate transparent veins. The stamens are from thirteen to twenty, shorter than the petals, with oblong, yellow anthers, of twice the length of the filaments. The stigma is sessile, and rendered irregular on its surface by numerous folds or convolutions. The fruit is a large oval berry, crowned with the persistent stigma, and containing a sweetish fleshy pulp, in which about twelve ovate seeds are embedded. It is, when ripe, of a lemon-yellow color, diversified by round brownish spots. Two species of the genus Podophyllum are known as growing in China while *Podophyllum Emodi,* which inhabits the interior ranges of the Himalayas and is very abundant in Cashmere, is recognized in the Br.

The plant has been found on Mount Togakushi, in Japan, and is extensively diffused through the Eastern United States, growing luxuriantly in moist shady woods and in low marshy grounds from Canada to Minnesota and southward to Florida and Texas. It is propagated by its creeping rhizome, and is often found in large patches. The flowers appear about the end of May and the beginning of June, and the fruit ripens in the latter part of September. The leaves are said to be poisonous. The fruit has a subacid, sweetish, peculiar taste, agreeable to some palates, and may be eaten freely with impunity. From its color and shape, it is sometimes called *wild lemon.* The rhizome is the official portion, and is said to be most efficient when collected after the falling of the leaves. It shrinks considerably in drying.

Properties.—The dried rhizome is much wrinkled lengthwise, is yellowish or reddish-brown externally, and furnished with roots of a similar but somewhat paler color. It was determined, by an experiment of Wm. Saunders, that these roots contain as much active matter as the rhizome itself. It is officially described as follows: "Rhizome horizontal, nearly cylindrical, jointed, compressed on the upper and lower surfaces, sometimes branched; in pieces from 3 to 20 cm. in length, the internodes from 2 to 9 mm. in diameter; externally dark brown, longitudinally wrinkled or nearly smooth with irregular, somewhat V-shaped scars of scale leaves,

nodes annulate, upper portion marked with large, circular, depressed stem-scars and sometimes with buds or stem-bases; at or near the nodes on the lower portion occur numerous root-scars or roots from 2 to 7 cm. in length and about 2 mm. in thickness; fracture short; internally, bark light brown, wood with small yellowish, vascular bundles, pith large and white; odor slight; taste sweetish, disagreeably bitter and acrid. Under the microscope, a transverse section of the rhizome of Podophyllum shows an outer layer of one or two rows of reddish-brown cells; parenchyma of cortex and pith with numerous single, spherical, polygonal, or 2- to 6-compound starch grains, or rosette aggregates of calcium oxalate; vascular bundles from 24 to 34, arranged in a circle between cortex and pith. The powder is light brown, with a pronounced and characteristic odor; starch grains numerous, spherical, polygonal or 2- to 6-compound, the individual grains from 0.003 to 0.015 mm. in diameter; calcium oxalate crystals few, in rosette aggregates from 0.05 to 0.08 mm. in diameter and occasionally in raphides from 0.03 to 0.09 mm. in length; tracheæ with simple pores or reticulate thickenings; fragments of starch-bearing parenchyma and reddish-brown cork cells. Podophyllum yields not more than 3 per cent. of ash.

"**Assay.**—Proceed as directed for the preparation of *Resina Podophylli* (see page 944), using 10 Gm. of Podophyllum in No. 60 powder. It shows not less than 3 per cent. of resin." *U. S.*

"Rhizome nearly cylindrical, of very variable length, usually about five millimetres thick; dark reddish-brown, smooth or only slightly wrinkled; enlarged at intervals of about five centimetres, the upper surface of each enlargement being marked by a depressed circular scar, below which, on the under surface, are rather stout, brittle, brown roots, or the scars corresponding to them. In transverse section, either nearly white and starchy, or pale yellowish-brown and horny. Characteristic odor; taste slightly bitter and acrid." *Br.*

The root in its aggregate state is nearly inodorous, but in powder has a sweetish not unpleasant odor. The taste is at first sweetish, afterwards bitter, nauseous, and slightly acrid. Both the decoction and the tincture are bitter, but alcohol is said to be the best solvent of the active matter. V. Podwyssotzki (*Ph. Z. R.*, Bd. xx, 777) announced the active principle to be solely a neutral crystalline principle, *picropodophyllin*. This principle is associated with an inactive resin-acid, *picropodophyllic acid*, and the combination of the two he named *podophyllotoxin*. Picropodophyllin is in colorless, silky, extremely delicate needles, very soluble in chloroform, readily soluble in 95 per cent. alcohol, but very slighty in 75 per cent. alcohol. It is soluble in ether, and crystallizes from a warm saturated solution on cooling. It is insoluble in water, turpentine, or benzin. Podophyllotoxin is a bitter, white, resinous powder, soluble in weak alcohol and hot water. It may be precipitated from its alcoholic solution by water in large quantity. (*P. J.*, 1882, 1011.) Podwyssotzki also obtained *podophylloquercetin*, the coloring principle, which is closely allied to quercetin and is the cause of the varying color of resin of podophyllum. His results have since been corrected and supplemented by R. Kürsten (*A. J. P.*, 1891, 485), who has obtained the several principles in a purer state. The results of Kürsten's investigation are as follows: The podophyllotoxin prepared by Podwyssotzki's method was not constant in composition, and its melting point varied from 100° to 125° C. (212°–257° F.); further, the podophyllic acid of that author is composed mainly of a crystallizable, active, but very impure substance.

Podophyllotoxin, $C_{22}H_{24}O_8$, is obtained by extracting the coarsely powdered rhizome with cold, light petroleum, until freed from fat; after drying in the air, the extraction is continued with chloroform, until the liquid comes away almost free from yellow color. As it is not possible to work with alcohol-free chloroform, too prolonged extraction with chloroform would yield a more impure extract. The chloroform extract is distilled and the residue is dried over a not too warm water bath, partially dissolved in benzene, filtered, and the filtrate allowed to remain from three to eight days, when a brownish-yellow mass of well-formed, thick, strongly refractive prisms is produced. This is purified by washing with a 50 per cent. alcohol, then with ether, recrystallizing first from boiling benzene, and finally from solution in hot 45 per cent. alcohol; the compound is thus obtained in long, well-formed prisms which melt at 94° C. (201.2° F.).

Podophyllotoxin, when oxidized in an alkaline solution in the cold by means of potassium permanganate, yielded, besides a little carbonic anhydride and a brown amorphous substance, principally two compounds, the more considerable of which was *podophyllic acid*, obtained as well-formed, colorless crystals from solution in a mixture of benzene and alcohol. The compound is without action on animals. It melts at from 158° to 160° C. (316.4°–320° F.). Its aqueous solution, neutralized with aqueous potassium hydroxide, gives no precipitate with gold, calcium, or barium chlorides; silver nitrate gives a white precipitate, soluble in much water; copper acetate gives a blue precipitate. The copper salt was prepared as beautiful light green prisms and analyzed.

Picropodophyllin results from the action of alkalies on podophyllotoxin; thus, on heating the latter with aqueous ammonia, a well-crystallized product is obtained, which at first was recrystallized from strong alcohol; but this was found to be unnecessary, as the melting point, 227° C. (440.6° F.), was not affected by it. Picropodophyllin has the same composition as podophyllotoxin, but they differ in melting point and in their action on polarized light,—the former inactive, the latter lævo-rotatory; the

former is less soluble in all liquids than the latter; the latter gives Millon's reaction, the former does not. By oxidation and reduction the two compounds yield the same products.

Dunstan and Henry (*Proc. Chem. Soc.*, March, 1898) find that the constituents of the Indian podophyllum (*Podophyllum Emodi*) and of the American podophyllum (*Podophyllum peltatum*) are identical. The chief constituent is the *podophyllotoxin* of Podwyssotzki and Kürsten. It is strongly lævorotatory, and acts as a powerful purgative and intestinal irritant. They found that when heated with alkalies, it is converted by hydration into the salt of an unstable gelatinous acid, *podophyllic acid*, $C_{15}H_{16}O_7$, of which several salts were obtained and analyzed. This acid very readily loses water, and furnishes the crystalline *picropodophyllin* of Podwyssotzki and Kürsten, which is isomeric with podophyllotoxin. It passes again into podophyllic acid when warmed with aqueous alkalies. Podophyllotoxin and picropodophyllin furnish identical decomposition products; when oxidized with nitric acid, oxalic acid is the principal product; when fused with alkalies, *orcinol* and acetic acid are produced. Both substances contain three methyl groups and no hydroxyl. It is likely that picropodophyllin is the lactone of podophyllic acid. Picropodophyllin is therapeutically inactive. The yellow coloring matter of podophyllum, called by Podwyssotzki *podophylloquercetin*, was proved by the authors to be identical with quercetin, the yellow coloring matter of quercitron bark. An uncrystallizable resin, *podophylloresin*, was also isolated and found to exert a purgative action. A fatty oil has been separated from the rhizome of podophyllum by Dohme and Engelhardt. (See *Proc. A. Ph. A.*, 1904, 340.) Gordin and Merrell (*Proc. A. Ph. A.*, 1902, 343) proposes to judge of the quality of resin of podophyllum by an assay based on the percentage of crude picropodophyllin and the following requirements: 1. Pure podophyllin must be completely soluble in about twice its weight of cold alcohol. 2. It should contain about 64 per cent. ether-soluble and about 74 per cent. chloroform-soluble matter. 3. It should yield about 22 per cent. crude picropodophyllin when assayed by the method described by them.

Manlius Smith recommended that the resin should be prepared by forming an alcoholic tincture of the root, evaporating the tincture until most of the alcohol is driven off, and throwing the residue into water, by which the resin is precipitated. The concentration should not be carried too far, as otherwise the resin separates in clots, which cannot be easily washed. According to Smith, the resin, when pure, is white, and purges actively. It has been called *podophyllin* for many years. (*A. J. P.*, xxiv. 306. See *Resina Podophylli.*) The proportion of resin contained in the root of the *P. peltatum* appears to vary very much, the variation possibly depending upon the season of the year at which the drug has been gathered. John Barclay (*P. J.*, 1903, Feb., 164) obtained a percentage of 1.6 to 3.86 per cent., stating that these figures were confirmed by the results of the manufacturers of podophyllin on a large scale, but J. C. Umney states that in five years' experience working with batches of 1000 pounds, the rhizome averaged a yield of 6.6 per cent. Both observers noticed that the Indian rhizome (*P. Emodi*) contains a much larger proportion of resin, the average according to Umney being 11.4 per cent. How far the proportion of podophyllotoxin varies in the different rhizomes does not seem to have been determined. (See B. D. Dott, *P. J.*, 1903, Mar. 460.) (*P. J.*, 1911, lxxxvii, p. 156.)

From the *leaves* of *P. peltatum* Thos. J. Husband, Jr., obtained berberine and a resin which was free from purgative properties, 8 grains producing no other effect than slight headache. (*A. J. P.*, 1869.)

B. F. Carter (*A. J. P.*, 1886, p. 449) also examined the leaves. He found tannin, uncrystallized sugar, coloring matter, and 6 per cent. of resin. This latter seems to be of twofold character, ether dissolving the soft resin, while the hard resin remains behind. The resin has a bitter taste and a much milder action than that of the rhizome. Fused with potassium hydroxide a small amount of protocatechuic acid seems to be formed.

A method of assay for Podophyllum has been proposed by W. M. Jenkins (*J. I. and E. C.*, 1914, p. 671) which is based upon a shaking out method using a mixture of chloroform and alcohol.

Uses.—Podophyllum is a slow but active and certain cathartic producing copious liquid discharges often with much griping. It has been attributed with cholagogic properties and is used in various forms of *hepatic torpor* but its virtues in this direction are probably no greater than that of other active purgatives. In small doses it is frequently used in *chronic constipation*, especially in conjunction with aloes or cascara.

In overdoses podophyllum acts as an irritant poison; an amount estimated at five grains of the resin caused death in a woman sixty years old (*N. Y. M. R.*, April, 1890); the symptoms were vomiting and purging, followed some hours after their cessation by coma, full soft pulse, slight elevation of temperature, and hæmoglobinuria.

Dose, five to ten grains (0.32–0.65 Gm.), but it is rarely exhibited in the crude form.

Off. Prep.—Fluidextractum Podophylli, *U. S.*; Resina Podophylli, *U. S.* (*Br.*); Tinctura Podophylli (from Resin), *Br.*; Extractum Podophylli, *N. F.*; Pilulæ Aloes et Podophylli Compositæ (from Resin), *N. F.*; Pilulæ Aloes, Hydrargyri et Podophylli (from Resin), *N. F.*; Pilulæ Aloini Compositæ (from Resin), *N. F.*; Pilulæ Catharticæ Vegetabiles (from Resin), *N. F.*; Pilulæ Colocynthidis et Podophylli (from Resin), *N. F.*; Pilulæ Laxativæ Post Partum (from Resin), *N. F.*

POTASSA SULPHURATA. U. S., Br.

SULPHURATED POTASSA Pot. Sulphurat.
[Liver of Sulphur]

(pŏ-tăs'są sŭl-phū-rā'tą)

"A mixture composed chiefly of potassium polysulphides and potassium thiosulphate and containing an amount of sulphides corresponding to not less than 12.8 per cent. of sulphur (S). Preserve it in well-closed containers." *U. S.* "Sulphurated Potash is a mixture of salts of potassium, chiefly sulphides." *Br.*

Sulphurated Potash, *Br.*, Hepar Sulphuris; Potassii Sulphuretum, *U. S.* 1870; Sulphuret of Potassium, Sulphurated Potash; Sulfure (tri) de Potassium solide, *Fr. Cod.*; Sulfure de Potasse, Foie de Soufre, *Fr.*; Kalium Sulfuratum, *P. G.*; Schwefelleber, Kalischwefelleber, *G.*; Sulfuro (tri) potasico hiposulfitado, *Sp.*

"Potassiuum Carbonate, in powder, 100 *grammes;* Sublimed Sulphur, 50 *grammes.* Mix the Potassium Carbonate, previously dried, with the Sulphur; heat in a covered crucible, at first gently, afterwards to dull redness, until effervescence ceases and the mass fuses; pour it on to a clean stone slab, and, after solidification, break it into fragments and transfer to a stoppered bottle." *Br.*

The U. S. P. IX gives no process; that of the U. S. P., 1890, is as follows: "Sublimed Sulphur, *one hundred grammes* [or 3 ounces av., 231 grains]; Potassium Carbonate, dried, *two hundred grammes* [or 7 ounces av., 24 grains]. Mix the powdered and dried Potassium Carbonate thoroughly with the Sublimed Sulphur, and gradually heat the mixture, in a covered crucible, which should be only about half filled with it, until the mass ceases to foam and is in a state of perfect fusion. Then pour the fused mass on a cold marble slab, and, after it has cooled, break it into pieces, and keep it in a well-stoppered bottle."

These processes are essentially the same, except that a greater heat is used in the British process, which somewhat modifies the result. When potassium carbonate is melted with half its weight of sulphur, as in the U. S. P. 1890 process, the carbon dioxide is expelled. The composition varies with the heat employed. If the heat does not exceed 185° C. (365° F.), the resulting preparation will contain potassium thiosulphate; if above 300° C. (572° F.), potassium sulphate. (Fordos and Gélis.) The reaction for the preparation at the lower temperature is

$$3K_2CO_3 + 4S_2 = 2K_2S_3 + K_2S_2O_3 + 3CO_2$$

which at the higher temperature is changed as follows:

$$4K_2S_2O_3 = 3K_2SO_4 + K_2S_5$$

The potassium pentasulphide formed is decomposed at this high temperature into sulphur, which burns off, and K_2S_3. The U. S. preparation, therefore, which is made at the temperature of fusion, probably contains potassium thiosulphate, and may be represented by the formula $2K_2S_3 + K_2S_2O_3$, three molecules of CO_2 escaping, while the British, being prepared at a red heat, contains potassium sulphate, the reaction probably being

$$4K_2CO_3 + 5S_2 = K_2SO_4 + 3K_2S_3 + 4CO_2$$

Potassium carbonate from pearlash is usually employed by the manufacturer, but in the process of Henry, which is stated to be the best yet devised, the pure potassium carbonate is employed. His formula is as follows: Mix two parts of pure potassium carbonate with one of sulphur reduced to powder, and put the mixture into flat-bottomed flasks, which should be only two-thirds filled. These are placed on a sand bath, and the fire is applied so as, at first, to produce only a gentle heat, which is afterwards increased. Care must be taken that the necks of the flasks do not become obstructed. The heat is continued until the matter is brought to a state of tranquil fusion, when it is allowed to cool. The mass obtained, which is compact, smooth, and of a fine yellow color, is broken into pieces, and preserved in well-stoppered bottles. W. Elborne (*Y. B. P.*, 1896, 331) states that when commercial potassium carbonate is used in making sulphurated potassa, a product is obtained which more closely approaches the official compound (Br. Pharm. 1885) than does one made from a pure potassium carbonate. He recommends that dried commercial carbonate containing not less than 90 per cent. K_2CO_3 be employed.

Properties.—Sulphurated potassa, when properly prepared, is a hard, brittle substance, having a nauseous, alkaline, and bitter taste. Its color is liver-brown, and hence its name of *hepar sulphuris,* or *liver of sulphur.* The color of the surface of a fresh fracture is brownish-yellow. It is inodorous when dry, but emits a slightly fetid odor when moist, owing to the extrication of a little hydrogen sulphide gas. It is soluble in water, forming an orange-yellow liquid, and exhaling the odor of hydrogen sulphide. It is described in the U. S. P. IX as follows: "Sulphurated Potassa is in the form of irregular pieces, liver-brown when freshly made, changing to greenish-yellow and finally to gray through absorption of moisture, oxygen, and carbon dioxide from the air. It has a strong odor of hydrogen sulphide and a bitter, acrid, and alkaline taste. Sulphurated Potassa is very soluble in water, usually leaving a slight residue. Alcohol dissolves only the sulphides. An aqueous solution of Sulphurated Potassa (1 in 10) is light brown in color and is strongly alkaline to litmus. The addition of an excess of acetic acid to this solution causes a brisk evolution of hydrogen sulphide and a precipitation of sulphur. In the liquid thus treated, after filtration, an excess of sodium bitartrate T.S. produces an abundant, white crystalline precipitate on standing.

"Assay.—Add a solution of 1 Gm. of crystallized copper sulphate in 15 mils of distilled water to a solution of 1 Gm. of Sulphurated

Potassa in 10 mils of distilled water, shake the mixture in a stoppered vessel for a few minutes and filter. The filtrate, acidulated with acetic acid and filtered if necessary, produces no black precipitate with an equal volume of hydrogen sulphide T.S., corresponding to not less than 12.8 per cent. of sulphur combined as sulphides." *U. S.*

"Solid fragments, externally greenish-yellow, internally pale liver-brown, rapidly changing to greenish-yellow on exposure to the air. Odor that of hydrogen sulphide; taste alkaline and acrid. Readily soluble in *water*. Aqueous solution yellowish, opalescent; deposits only a trace of sediment on standing; evolves hydrogen sulphide freely on the addition of excess of *hydrochloric acid*, sulphur being deposited; this acid liquid, boiled and filtered, gives a yellow precipitate with *solution of platinic chloride*. Sulphurated Potash contains not less than 42 and not more than 45 per cent. of sulphur as determined by the following process:—Dissolve 0.2 gramme in 10 millilitres of *water* in a small flask, add 5 millilitres of *solution of sodium hydroxide*, heat the liquid to boiling, and add slowly, the flask being constantly rotated, *solution of bromine As T.* until a clear solution is obtained and bromine is present in excess. Acidify with *hydrochloric acid*, boil until the excess of bromine is driven off, add excess of *solution of barium chloride*, collect the precipitate formed, wash, dry, ignite, and weigh. It weighs not less than 0.611 or more than 0.655 gramme." *Br.*

By exposure to the air it attracts oxygen, and the potassium sulphide is gradually changed into potassium sulphate, when the preparation becomes inodorous, and white on the surface. The solution is decomposed by the mineral acids, which liberate hydrogen sulphide and precipitate the excess of sulphur. It is also incompatible with solutions of most of the metals, which are precipitated as sulphides. When boiled with an excess of hydrochloric acid and filtered, it gives a yellow precipitate with platinic chloride, and a white one with barium chloride. The preparation of the Br. Pharmacopœia yields about one-half of its weight to alcohol (90 per cent.)—the portion dissolved being potassium sulphide, and the undissolved portion potassium sulphate.

This compound has been used as an ingredient in the preparation known as *Lotio Alba* (*Lotio Sulphurata*) of which the following is the correct formula, according to Otto Raubenheimer (*J. A. Ph. A.*, 1914, 692): Zinc sulphate, 5 Gm.; sulphurated potassa, 5 Gm.; distilled water, q.s. to make 125 mils. Dissolve each chemical in 60 mils of distilled water; filter the solutions separately and mix by slowly pouring the potassa solution into the zinc solution, then add sufficient distilled water to make 125 mils. Rose water may be used in place of distilled water. It is essential that the sulphurated potassa be fresh and free from iron compounds, as has been pointed out by J. C. and B. L. DeG. Peacock, *Proc. P. P. A.*, 1914, 256.

Uses.—Internally sulphurated potassa was formerly employed in *chronic rheumatism, skin diseases, asthma*, etc., but is to-day rarely used as an internal remedy. While if given in sufficient dose it may exercise the same effects upon the system as sulphur it is much more irritant to the stomach and has no advantages. It is, however, a valuable external agent in the treatment of various skin diseases. The alkaline sulphides exercise a solvent action upon the horny element of the skin and therefore sulphurated potassa is useful in *psoriasis* and other conditions in which there is excessive formation of scales. Because of the anti-parasitic action of the hydrogen sulphide which it liberates on contact with the skin, it is one of our most valuable remedies in the treatment of *scabies, ring-worm, tinea versicolor*, and other parasitic diseases. In *acne rosaceæ* and other skin diseases with sluggish circulation its local stimulating action tends to restore tone to the dilated blood vessel. It may be used either as a lotion, an ointment, or bath. As a lotion it is usually used in strengths of about 5 per cent. but in sluggish conditions may be employed up to 10 per cent. For an ointment one-half a drachm of sulphurated potassa (2 Gm.) may be rubbed up with one-half an ounce (15 Gm.) of lard. For a bath about one-half a drachm is employed for each gallon of water. The odor of sulphurated potassa is favorably modified whether in solution or ointment, by incorporating with it a little oil of anise.

Dose, from two to ten grains (0.13–0.65 Gm.).

POTASSII ACETAS. U. S., Br.

POTASSIUM ACETATE Pot. Acet

(pŏ-tăs'sĭ-ī ă'cē-tăs)

"It contains, when dried to constant weight at 150° C. (302° F.), not less than 99 per cent. of $KC_2H_3O_2$ (98.12). Preserve it in air-tight containers." *U. S.* "Potassium Acetate may be obtained by fusing the product of the interaction of acetic acid and potassium carbonate. It contains not less than 90 per cent. of pure potassium acetate, $KC_2H_3O_2$." *Br.*

Kali Aceticum, Sal Diureticum, Acetas Potassicus, s. Kalicus, Terra Foliata Tartari; Acetate of Potassium; Acetate of Potash (Potassa), Diuretic Salt; Acétate de Potasse sec, *Fr. Cod.*; Essigsaures Kali, *G.*; Acetato di potassio, *It.*; Acetato potasico, *Sp.*

As this salt is practically never prepared on a small scale, no process is given in either of the Pharmacopœias; that of the U. S. P., 1870, is as follows: "Take of Acetic Acid *a pint;* Bicarbonate of Potassium *a sufficient quantity*. Add the Bicarbonate gradually to the Acid until it is neutralized; then filter the solution, and evaporate cautiously, by means of a sand-bath, until a dry salt remains."

For drying the potassium acetate, Christison considers the temperature of a vapor bath too low, and that of a sand bath likely to become too high. He therefore recommends the use of a bath of calcium chloride when operating on a small scale. In conducting the evaporation, it

is best to have the solution always slightly acid, for if the alkali predominate, it will react upon the acetic acid when the solution is concentrated, and give rise to discoloration. On account of the liability of discoloration, great care must be observed to avoid the contamination of iron. Some manufacturers use silver dishes.

Potassium acetate may also be obtained by double decomposition between lead acetate and potassium sulphate. When thus procured, it is very white and pure, but liable to the objection, for medicinal use, that it may possibly contain a little lead. Another method by double decomposition is between calcium acetate and potassium sulphate.

Properties.—It is officially described as "a white powder, or in crystalline masses of a satin-like luster; odorless, or with a faint, acetous odor, and having a warming, saline taste. It is very deliquescent on exposure to the air. One Gm. of Potassium Acetate dissolves in 0.5 mil of water and in 2.9 mils of alcohol at 25° C. (77° F.); also in about 0.2 mil of boiling water. An aqueous solution of the salt (1 in 20) is alkaline to litmus, but does not affect phenolphthalein T.S. When slightly heated, the salt fuses. On strong ignition it is decomposed with the evolution of inflammable empyreumatic vapors and leaves a black residue of potassium carbonate and carbon. This residue imparts to a non-luminous flame a violet color, is alkaline to litmus, and effervesces with acids. The addition of 5 mils of sodium bitartrate T.S. to 5 mils of an aqueous solution of the salt (1 in 5) causes a white, crystalline precipitate. Add 0.1 Gm. of the salt to 1 mil of sulphuric acid and 1 mil of alcohol and gently warm the mixture; ethyl acetate is formed, recognizable by its odor. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of the salt meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"**Assay.**—Dry the salt to constant weight at 150° C. (302° F.) and proceed as directed under the Assay for alkali salts of organic acids (see Part III, Test No. 6). It shows, in the dried salt, not less than 99 per cent. of $KC_2H_3O_2$. Each mil of half-normal sulphuric acid V.S. used corresponds to 0.04906 Gm. of $KC_2H_3O_2$. Each gramme of Potassium Acetate, previously dried, corresponds to not less than 20.2 mils of half-normal sulphuric acid V.S." *U. S.*

"White foliaceous satiny masses, or in granules. Taste sharp, saline. Very deliquescent. Soluble in 0.5 part of *water*, and in 2 parts of *alcohol* (90 per cent.). Aqueous solution alkaline to *litmus*. Yields the *reactions* characteristic of potassium and of acetates. Yields no characteristic *reactions* for copper, iron, aluminum, calcium, magnesium, carbonates, or sulphides, and not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million. Loses not more than 10 per cent. of its weight when dried at 100° C. (212° F.). 1 gramme, heated to redness until gases cease to be evolved, leaves an alkaline residue which, when treated with *water*, filtered, and well washed, yields a clear solution requiring for neutralisation not less than 18.3 millilitres of *N/2 solution of sulphuric acid.*" *Br.*

Since the introduction of the cheap method of obtaining pure acetic acid from wood, this salt has scarcely been subjected to adulteration. Potassium acetate is incompatible with the mineral acids, which expel the acetic acid; with sodium and magnesium sulphates; with corrosive sublimate and silver nitrate, and with several other earthy and metallic salts. This salt exists in the juices of many plants, and especially in the sap of trees, and is the principal source of the potassium carbonate existing in the ashes of wood.

Uses.—The effects of potassium acetate upon the system are very similar to those of the citrate (see page 897), except that it is less likely to act upon the bowels. Like the citrate it is oxidized in the system and appears in the urine as a carbonate and therefore tends to render this secretion alkaline. It is usually less acceptable to the palate than the citrate. It is especially employed in the treatment of *rheumatic fever* and the *uric acid diatheses*. It is also sometimes used for its diuretic effect in *dropsies* and *nephritis*. J. A. Easton, of Glasgow, has found it useful in several skin diseases, such as *psoriasis* and *eczema*.

Dose, fifteen to sixty grains (1–3.9 Gm.).

Off. Prep.—Elixir Buchu et Potassii Acetatis, *N. F.*; Elixir Potassii Acetatis, *N. F.*; Elixir Potassii Acetatis et Juniperi, *N. F.*

POTASSII BICARBONAS. U. S., Br.

POTASSIUM BICARBONATE Pot. Bicarb.

(pŏ-tăs'sĭ-ĭ bī-căr'bŏ-năs)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99 per cent. of $KHCO_3$ (100.11). Preserve it in well-closed containers." *U. S.* "Potassium Bicarbonate may be obtained by saturating a strong aqueous solution of potassium carbonate with carbon dioxide. It contains not less than 99 per cent. of pure potassium bicarbonate, $KHCO_3$." *Br.*

Bicarbonas Potassicus, s. Kalicus; Potassium Hydrogen Carbonate; Acid Carbonate of Potassium; Bicarbonate of Potash; Carbonate (bi) de Potasse, *Fr. Cod.*; Bicarbonate de Potasse, *Fr.*; Kalium Bicarbonicum, *P. G.*; Kaliumbicarbonat, Doppelt-Kohlensaures Kali, *G.*; Bicarbonato di potassio, *It.*; Bicarbonato potasico, *Sp.*

The process of the U. S. P. 1870, and also that of the British Pharmacopœia, for this salt were abandoned at former revisions.

The reaction by which it is produced from potassium carbonate by the action of carbon dioxide is as follows:

$$K_2CO_3 + H_2O + CO_2 = 2KHCO_3$$

Brande gives the following proportions for the preparation of potassium bicarbonate: "100 lbs. of purified potassium carbonate are dissolved in 17 gallons of water [Imperial meas-

ure], which, when saturated with carbonic acid, yield from 35 to 40 lbs. of crystallized bicarbonate; 50 lbs. of potassium carbonate are then added to the mother-liquor, with a sufficient quantity of water to make up 17 gallons, and the operation repeated." Wöhler states that charcoal, when mixed with the carbonate, facilitates by its porosity, in a remarkable degree, the formation of the bicarbonate. Thus, he found that, when crude tartar was charred in a covered crucible, and the carbonaceous mass, after having been slightly moistened with water, was subjected to a stream of carbon dioxide, the gas was absorbed with great rapidity, and heated the mass so considerably as to render it necessary to surround the vessel with cold water, to prevent the decomposition of the bicarbonate formed. When the temperature diminished, the saturation was known to be completed. The mass was lixiviated in the smallest quantity of water at the temperature of from 29.4° to 37.7° C. (85°–100° F.), and the solution, after filtration and cooling, deposited the greater part of the bicarbonate in fine crystals. (See *A. J. P.*, x, 82.)

Behrens has proposed to obtain potassium bicarbonate by partially saturating the carbonate, dissolved in an equal weight of water, with acetic acid gradually added. Up to a certain point, no carbon dioxide is extricated, and a precipitate takes place of pure potassium bicarbonate, equal to half the weight of the carbonate employed. After the bicarbonate is separated, the saturation may be completed, and potassium acetate obtained. (*J. P. C.*, 3e sér., iv, 464.) L. Pesci dissolves purified potassium hydroxide in 80 per cent. alcohol, and passes a stream of carbon dioxide through the solution until it is saturated. The white precipitate is collected and washed with alcohol; it is free from chlorides and nitrates. (*Ber. d. Chem. Ges.*, 1876.)

According to Berzelius, the cheapest method of obtaining potassium bicarbonate is to suspend a concentrated solution of the purified carbonate, contained in a stoneware dish, within a cask, over a liquid undergoing the vinous fermentation. The alkali is thus surrounded by an atmosphere of carbon dioxide, and, by absorbing it, crystallizes into bicarbonate in the course of five or six weeks. Distillers and brewers may prepare this salt with great facility by suspending the alkaline solution in the fermenting tun. The salt in powder called *potash sal aëratus*, made principally in New England, is prepared in this way. In composition it is between a carbonate and a bicarbonate and it is sometimes called a sesquicarbonate.

Properties.—Potassium bicarbonate is officially described as in "colorless, transparent, monoclinic prisms or as a white, granular powder, odorless, and having a saline and slightly alkaline taste. It is permanent in the air. One Gm. of Potassium Bicarbonate dissolves in 2.8 mils of water at 25° C. (77° F.); also in 2 mils of water at 50° C. (122° F.); almost insoluble in alcohol. An aqueous solution of Potassium Bicarbonate (1 in 10) is slightly alkaline to litmus but is neutral or slightly alkaline to phenolphthalein T.S., and effervesces with acids. When heated above 50° C. (122° F.) an aqueous solution of the salt rapidly loses carbon dioxide and water, and, at boiling heat, the salt is entirely converted into normal carbonate. The dry salt begins to lose carbon dioxide and water at 100° C. (212° F.) and this loss increases at a higher temperature, until at a red heat a residue of carbonate remains which imparts a violet color to a non-luminous flame. An aqueous solution of Potassium Bicarbonate (1 in 10) yields a white, crystalline precipitate of potassium bitartrate with excess of tartaric acid T.S. Add 2 mils of tenth-normal hydrochloric acid V.S. and 2 drops of phenolphthalein T.S. to 1 Gm. of the salt, dissolved without agitation in 20 mils of distilled water at a temperature not above 15° C. (59° F.); a red tint does not appear immediately (*carbonate*). An aqueous solution of the salt (1 in 50), mixed with a slight excess of hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Dissolve about 4 Gm. of Potassium Bicarbonate, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed, in 25 mils of distilled water and titrate with normal sulphuric acid V.S., methyl orange T.S. being used as indicator. It shows, in the dried salt not less than 99 per cent. of $KHCO_3$.

"Each mil of normal sulphuric acid V.S. used corresponds to 0.10011 Gm. of $KHCO_3$. Each gramme of Potassium Bicarbonate, previously dried, corresponds to not less than 9.9 mils of normal sulphuric acid V.S." *U. S.*

"Colorless, monoclinic, non-deliquescent prisms. Taste saline, feebly alkaline. Soluble in 4 parts of *water*, almost insoluble in *alcohol* (90 per cent.). Yields the *reactions* characteristic of potassium and of bicarbonates. 1 gramme exposed to a low red heat leaves not less than 0.683 or more than 0.690 gramme of a white residue, which requires for neutralisation not less than 19.8 or more than 20 millilitres of *N/2 solution of sulphuric acid.* Yields no characteristic *reactions* for copper, sulphates, or sodium, and not more than the slightest *reactions* for iron or chlorides. *Lead limit* 5 parts per million. *Arsenic limit* 5 parts per million. 20 grammes of Potassium Bicarbonate are neutralised by 14 grammes of Citric Acid, and by 15 grammes of Tartaric Acid." *Br.*

When heated to redness it loses carbon dioxide and returns to the state of carbonate, which, when thus obtained, is free from silica, and otherwise very pure. This method was adopted in the U. S. Pharmacopœia of 1870 for obtaining the pure carbonate. When a perfect bicarbonate, its solution, unless heated, does not precipitate a solution of magnesium sulphate. This negative indication, however, cannot be depended upon as showing the absence of carbonate; for, according to Christison, no precipitate will be occasioned even when 50 per cent. of this impurity is present. Potassium bicar-

bonate does not decompose calomel. When dissolved in 40 parts of water, it produces a white haze merely with a solution of corrosive sublimate; but if it contain so much as a hundredth part of carbonate, a brick-red precipitate is immediately produced. (Christison.) Another way of detecting the presence of carbonate is to add pure glucose to a heated solution of the suspected bicarbonate. If any carbonate be present, the mixture will turn yellow or brown. (Chevallier.) The official test (Hirsch's) given above is, however, more reliable, and admits but traces of carbonate. Potassium bicarbonate consists of one atom of potassium and one of hydrogen, in combination with one carbonic acid group, CO_3.

Uses.—The medicinal properties of this salt are similar to those of the carbonate, to which it is preferable from its milder taste and its greater acceptability to the stomach. It is, however, much more disagreeable than the salts of potassium made from the fruit acids which are now universally used when a decided effect upon the system is desired, the bicarbonate and the carbonate being employed almost exclusively as gastric antacids.

Dose, ten grains to a drachm (0.65–3.9 Gm.).

POTASSII BICHROMAS. Br.

POTASSIUM BICHROMATE [Potassii Dichromas, U. S. 1890, Potassium Dichromate]

(pŏ-tăs'sĭ-ī bī-ĉhrō'măs)

"Potassium Bichromate may be obtained by roasting chrome ironstone with lime in the presence of air, and treating the resulting chromate with a potassium salt, and subsequently with an acid. It contains not less than 99 per cent. of pure potassium bichromate, $K_2Cr_2O_7$." *Br.*

Red Chromate of Potash (Potassa), Bichromate of Potash; Kali Bichromicum, Kali Chromicum Rubrum; Chromate (Bi) de Potasse, *Fr. Cod.;* Bichromate de Potasse, *Fr.;* Kalium dichromicum, *P. G.;* Kaliumdichromat, Zweifach Chromsaures Kali, Doppeltchromsaures Kali, *G.;* Bicromato di potassio, *It.;* Bicromato potasico, *Sp.*

Potassium dichromate was deleted from the U. S. P. IX list, but will be found among the reagents under *Potassium Dichromate, Purified.* (See Part III.)

This salt is most conveniently prepared from the neutral or yellow *potassium chromate,* by acidulating its solution with sulphuric acid and setting it aside for a day or two. In the action which follows we may suppose two reactions take place:

$$2K_2CrO_4 + H_2SO_4 = K_2SO_4 + 2KHCrO_4$$
$$2KHCrO_4 = K_2Cr_2O_7 + H_2O$$

Here the sulphuric acid, taking half the base from the two molecules of neutral chromate, changes them into two molecules of an acid chromate. This, however, is unstable, and the two molecules condense to form one of the dichromate with the elimination of one molecule of water. The yellow chromate is obtained by igniting four parts of powdered chrome-iron ore with one part of potassium nitrate, and lixiviating the resulting mass with water, or it may be produced by heating the chrome iron ore in a reverberatory furnace with access of air in the presence of potassium carbonate and lime. This reaction is as follows:

$$2FeOCr_2O_3 + 4K_2CO_3 + 4CaO + 7O = Fe_2O_3 + 4CaCO_3 + 4K_2CrO_4$$

The solution, by evaporation, yields the yellow salt in crystals. In this process, the nitric acid of the potassium nitrate furnishes oxygen to convert the chromium sesquioxide into chromium trioxide, which then unites with the potassium of the same salt. The iron, in the mean time, is sesquioxidized and rendered insoluble. Sometimes impure potassium carbonate (pearlash) is substituted for part of the potassium nitrate in the calcination. Omitting the potassium nitrate entirely, Stromeyer, of Norway, in performing the ignition, has used lime along with the pearlash, with economical results. When lime is employed, calcium chromate is formed, which is extracted by lixiviation and decomposed by a soluble potassium salt, such as sulphate or carbonate, either of which will carry the lime out of solution. When desired, the dichromate may be obtained directly from the solution of potassium chromate, derived from the treatment of the ore by acidulating it with sulphuric acid, without first crystallizing it. The production of chrome ore in the United States has practically ceased, as the California deposits are no longer worked. The manufacture of potassium and sodium dichromates is therefore carried on with imported ore brought chiefly from Asia Minor and New Caledonia.

Properties.—Potassium dichromate, according to the U. S. P. VIII, is in "large, orange-red, transparent, triclinic prisms, or four-sided tabular crystals, odorless, and having an acidulous, metallic taste. Permanent in the air. Soluble in about 9 parts of water at 25° C. (77° F.), and in 1.5 parts of boiling water; insoluble in alcohol. The salt fuses below a red heat, without loss of weight, forming a dark brown liquid. At a white heat it evolves oxygen and leaves a residue of neutral potassium chromate and green chromic oxide. The aqueous solution of Potassium Dichromate (1 in 20) has an acid reaction upon blue litmus paper. On mixing 4 Cc. of an aqueous solution (1 in 20) with 0.5 Cc. of alcohol, and then adding 1 Cc. of sulphuric acid, the liquid should assume a green color and emit the odor of aldehyde. Sodium cobaltic nitrite T.S. produces in an aqueous solution a copious yellow precipitate."

"In orange-red crystals. Soluble in 10 parts of *water.* Aqueous solution acid to *litmus;* gives a yellowish-white precipitate with *solution of barium chloride;* acquires an emerald-green color when warmed with *sulphuric acid* and *alcohol* (90 per cent.). When 0.1 gramme is dissolved in 20 millilitres of *water* acidified with 5 millilitres of *diluted sulphuric acid,* and then 2 grammes of *potassium iodide* added, the solu-

tion thus obtained, diluted with *water*, requires for decolorisation not less than 20.1 millilitres of *N/10 solution of sodium thiosulphate* (presence of not less than 99 per cent. of pure potassium bichromate, $K_2Cr_2O_7$)." *Br.*

The oxidizing action of potassium dichromate which is so especially marked in the presence of free sulphuric acid may be understood by the following reaction in which it will be seen that each molecule of the bichromate yields 3 atoms of nascent oxygen and a molecule of chrome alum.

$$K_2Cr_2O_7 + 4H_2SO_4 = 4H_2O + Cr_2(SO_4)_3.K_2SO_4 + 3O$$

Uses.—Potassium dichromate is an irritant caustic acting much like chromium trioxide *q. v.* It was used by Robin, in 1850, in the treatment of *syphilis*, but was entirely abandoned. Its use, has, however, been recently revived in this disease by Helbig. (*Aerzt. Runds.*, 1910, p. 157.) He administers one-sixth of a grain (0.01 Gm.) well diluted three times a day. Fenwick (*B. M. J.*, 1909) recommends in *cancer* the injection of eight to fifteen minims (0.5–0.9 mil) of a 10 per cent. solution into the tumor, and Gemmil (*B. M. J.*, 1909) has had good results from its local application in *rodent ulcer*.

In overdoses it operates as a violent irritative and corrosive poison, producing severe vomiting, frequent dark hemorrhagic dejections, violent abdominal pains, pronounced disturbances of the circulation, coma, heart failure, collapse, etc. Less than an ounce has caused unconsciousness in five minutes, with death thirty-five minutes later. (*B. M. J.*, ii, 1888.) Soap, an alkaline carbonate, or magnesia, is the antidote. Potassium dichromate is used largely in calico printing and for other technical purposes. The workmen engaged in making it are liable to painful ulcerations of the hands, and, in consequence of the acrid vapors evolved, violent irritation of the nostrils is apt to be experienced, with severe pricking sensations and excessive sneezing, followed in time by destruction of the mucous membrane and even of the septum itself. It is asserted that this result may be avoided by breathing through the mouth exclusively, the profuse secretion of saliva produced carrying off the poisonous particles. (*B. F. M. R.*, Oct., 1863.)

Mueller's Fluid is used for preserving anatomical specimens. It consists of from 2 to 2.5 parts of potassium dichromate, 1 part of sodium sulphate, and 100 parts of water.

Dose, one-fifth of a grain (0.012 Gm.).

POTASSII BITARTRAS. U. S. (Br.)

POTASSIUM BITARTRATE Pot. Bitart.
[Cream of Tartar]

(pŏ-tăs'sĭ-ī bī-tär'trăs)

"It contains, when dried to constant weight at 100° C. (212° F.), not less than 99.5 per cent. of $KHC_4H_4O_6$ (188.14). Preserve it in well-closed containers." *U. S.* "Acid Potassium Tartrate may be obtained from the crude cream of tartar deposited during the fermentation of grape juice. It contains not less than 99 per cent. of pure potassium hydrogen tartrate, $KHC_4H_4O_6$." *Br.*

Potassii Tartras Acidus, *Br.*, Acid Potassium Tartrate, Crystals of Tartar; Purified Cream of Tartar; Tartrate de Potasse acide, Bitartrate de Potasse, Crème de Tartre, *Fr. Cod.*; Pierre de Vin, *Fr.*; Tartras depuratus, *P. G.*; Weinstein, Kali Bitartaricum, Bitartras Potassicus, s. Kalicus, Cremor Tartari, *G.*; Tartrato acido di potassio, Cremor di tartaro, *It.*; Tartrato (bi)potasico, Cremor de tartaro, *Sp.*

During the fermentation of wines, especially those that are tart, a peculiar matter is deposited in the casks, forming a crystalline crust, called *crude tartar*, or *argol*. That deposited from red wines is of a reddish color, and called *red tartar*, while that derived from white wines is of a dirty-white color, and denominated *white tartar*. Both kinds consist of potassium, united with an excess of tartaric acid, forming acid potassium tartrate, rendered impure by calcium tartrate, more or less coloring matter, and other substances which are deposited during the clarification of the wine. The deposition of the tartar is thus explained. The acid tartrate exists naturally in the juice of the grape, held in solution by saccharine matter. When the juice is submitted to fermentation in the process for converting it into wine, the sugar disappears, and is gradually replaced by alcohol, in which the salt is insoluble. It is from argol that acid potassium tartrate is obtained by a process of purification. The importation of crude tartar, or argol, for the year 1914 was 29,793,011 lbs., valued at $3,228,674, and for 1915, 28,624,554 lbs., valued at $3,094,380. Although the amount of crude tartar produced in the United States is small, compared with the quantity imported from Europe, yet the amount from American wines is rapidly increasing. The process for purifying crude tartar is founded upon the greater solubility of acid potassium tartrate in hot than in cold water. The tartar, previously pulverized, is boiled with water in copper boilers. The solution, when saturated, is transferred to earthen pans, where it deposits on cooling a crystalline layer, nearly free from color. This is redissolved in boiling water, and the solution, having been mixed with 4 or 5 per cent. of pipe clay, or egg albumin and animal charcoal, is evaporated until a pellicle forms. The clay precipitates with the coloring matter, and the clear solution, as it cools, deposits white crystals in crusts, which, upon being exposed to the air on linen for several days, acquire an increased degree of whiteness. These constitute the *crystals of tartar* of pharmacy. The salt, as met with in commerce, is generally, for greater convenience, in the form of powder, to which the name *cream of tartar* properly belongs. (See *Bull. Pharm.*, 1898, 405.) A more recent process is that of roasting the crude argols at a temperature (150° C. (302° F.)) which will decompose albumin and organic coloring matter, but not affect the cream of tartar. The roasted product is divided and treated with a small amount of hydrochloric

acid, which attacks the calcium tartrate and as cream of tartar is almost insoluble in the KCl formed a relatively pure potassium bitartrate separates out.

Properties.—Potassium bitartrate occurs in commerce in white crystalline crusts or masses of aggregated crystals, which are usually powdered before being sold to pharmacists. It is officially described as in "colorless or slightly opaque, rhombic crystals, or as a white, somewhat gritty powder; odorless, and having a pleasant, acidulous taste. It is permanent in the air. One Gm. of Potassium Bitartrate dissolves in 155 mils of water and in 8820 mils of alcohol at 25° C. (77° F.); also in 16 mils of boiling water. A saturated aqueous solution of the salt is acid to litmus. When the salt is heated it chars and emits inflammable vapors having the odor of burning sugar. At a higher temperature, with free access of air, the carbon of the black residue is consumed, and a white, fused mass of potassium carbonate remains, which has an alkaline reaction and effervesces strongly with acids. With sodium cobaltic nitrite T.S. a saturated aqueous solution of the salt yields a yellow precipitate. Neutralize a saturated aqueous solution of the salt with potassium hydroxide T.S., add silver nitrate T.S., then just sufficient ammonia water to dissolve the white precipitate and boil the solution; silver is deposited on the sides of the test tube, forming a mirror. When 0.5 Gm. of the salt is dissolved in 3 mils of ammonia water, no insoluble residue remains (*starch, kaolin, calcium phosphate, or other insoluble matter*). Ten mils of an aqueous solution of the salt (1 in 50), made with the aid of just sufficient hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3). Ammonia is not evolved on heating the salt with a slight excess of potassium hydroxide T.S. Mix 1 Gm. of Potassium Bitartrate, in a platinum crucible, with 0.5 mil of sulphuric acid and 1 mil of nitric acid, and heat the mixture until fumes of sulphur trioxide begin to be liberated. Cool the resulting mass and treat it with 10 mils of distilled water and filter. The filtrate, upon being made slightly alkaline with potassium hydroxide T.S., does not yield a gelatinous precipitate soluble in excess of the reagent (alum). Heat 10 Gm. of Potassium Bitartrate with 15 mils of distilled water and add hydrochloric acid until the salt is dissolved, then add 2 mils of sulphurous acid and boil the mixture until the odor of sulphur dioxide is barely perceptible. Cool the solution, mix it with 1 mil of sodium cyanide T.S., and follow this immediately with stronger ammonia water until the precipitate first formed is redissolved and the solution has a slight odor of ammonia. When it is cold, transfer the solution to a glass-stoppered cylinder graduated to 50 mils, dilute it with sufficient distilled water to measure 50 mils, and add 3 drops of sodium sulphide T.S. After mixing well, the color produced in the solution, if any, when viewed downward against a white surface, is not greater than the color of a control solution prepared as follows: Dissolve 2 Gm. of ammonium chloride (see Reagents, Part III) in 20 mils of distilled water, add 4 mils of a solution containing 0.08 Gm. of lead nitrate in 1000 mils of distilled water, and then 1 mil of diluted hydrochloric acid. Treat this solution with the same quantity of hydrochloric acid, sulphurous acid, sodium cyanide T.S., and stronger ammonia water, as used above, transfer it to another 50 mil glass-stoppered cylinder, and then dilute it with sufficient distilled water to make 50 mils and add 3 drops of sodium sulphide T.S. (before adding the sodium sulphide T.S., the liquid must possess a distinct odor of ammonia and the two cylinders used must be matched, be of practically colorless glass and have the same internal diameter) (*lead*).

"**Assay.**—Dissolve about 6 Gm. of Potassium Bitartrate, previously dried to constant weight at 100° C. (212° F.) and accurately weighed, in 100 mils of boiling distilled water, and titrate with normal potassium hydroxide V.S., using phenolphthalein T.S. as indicator. It shows, in the dried salt, not less than 99.5 per cent. of $KHC_4H_4O_6$. Each mil of normal potassium hydroxide V.S. used corresponds to 0.18814 Gm. of $KHC_4H_4O_6$. Each gramme of Potassium Bitartrate, previously dried, corresponds to not less than 5.29 mils of normal potassium hydroxide V.S." *U. S.*

"A gritty white powder, or fragments of crystalline cakes. Taste acid. Soluble in 220 parts of *water;* insoluble in *alcohol* (90 per cent.). Yields the *reactions* characteristic of potassium and of tartrates. 1 gramme requires for neutralisation not less than 10.5 millilitres of *N/2 solution of sodium hydroxide.* Yields no characteristic *reactions* for copper, or iron, and not more than the slightest *reactions* for calcium, magnesium, sodium, chlorides, or sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 2 parts per million." *Br.*

With salifiable bases which form soluble tartrates, it gives rise to double salts, consisting of neutral potassium tartrate, and the tartrate of the base added. Several of these are important medicines. Cream of tartar, though sparingly soluble in water, becomes abundantly so by the addition of borax or boric acid. *Soluble Tartar* (*Tartarus boraxatus, Kali tartaricum boraxatum, Cremor tartari solubilis.*) Borax, 2 parts; distilled water, 20 parts. Dissolve, and add 5 parts purified cream of tartar. Agitate to dissolve, filter, evaporate to dryness, and powder.

The cream of tartar of commerce is now nearly pure potassium bitartrate. It has been, however, found purposely mixed with various substances, such as sand, clay, gypsum, flour, chalk, alum, and potassium sulphate. Sand, clay, and gypsum may be detected by their insolubility in a hot solution of potassium hydroxide; flour, by its striking a blue color with iodine; chalk, by its effervescing with dilute acids; alum (an unlikely sophistication), by its astringency, and any soluble sulphate, by its

causing a precipitate with barium chloride, not entirely soluble in nitric acid. The action of the last-mentioned test is explained by the fact that the barium tartrate is soluble and the sulphate insoluble in nitric acid. The best security against fraud is to purchase the crystals and have them powdered. Geo. F. Payne examined commercial cream of tartar; of ten samples obtained from grocery stores, five contained no cream of tartar whatever. Some of the spurious samples were mainly composed of a mixture of dried alum and acid calcium phosphate. (*Proc. A. Ph. A.*, 1897, 695.) These adulterations have for the most part long since disappeared from the market product. The U. S. Pharmacopœia admits a slight impurity. It should contain 99 per cent. of pure potassium bitartrate, and there is no difficulty in obtaining it in commerce of this quality. Coupland gives in *P. J.*, 1901, 282, the results of an examination of commercial cream of tartar as follows: While in 1884 the assays of cream of tartar revealed from 8 to 14 per cent. of calcium tartrate, the quality has continuously improved and it contained in 1901, 4.6 per cent. But cream of tartar of greater purity is by no means an exceptional article, potassium bitartrate of a quality of 98 and 99 per cent. being common, the latter coming from America. The competition among makers of "baking powders," into which it enters, explains in part the improvement in the quality of cream of tartar.

Composition.—Cream of tartar consists of one molecule of tartaric acid, $C_4H_4O_6.H_2$, in which one of the two hydrogen atoms has been replaced by an atom of potassium, forming the acid tartrate, $KHC_4H_4O_6$.

Uses.—Potassium bitartrate is a very mild saline cathartic, and an active diuretic. In small doses it acts as a cooling aperient and in large ones as a hydragogue cathartic, producing copious watery stools. It is much used in *dropsy*. It is frequently prescribed in combination with senna, sulphur, or jalap. (See *Confectio Sulphuris* and *Pulvis Jalapæ Compositus*.) Its solution in boiling water, sweetened with sugar and allowed to cool, forms an acid, not unpleasant, refrigerant drink, advantageously used in some *febrile affections*, and frequently employed as a domestic remedy. The beverage called *imperial* (*potus imperialis*) is a drink of this kind, made by dissolving half an ounce of the salt in three pints of boiling water, and adding to the solution four ounces of white sugar and half an ounce of fresh lemon peel. *Cream of tartar whey* is prepared by adding about two drachms of the bitartrate to a pint of milk. It may be given in dropsical diseases.

As a diuretic, cream of tartar may be administered in the dose of a drachm and a half or two drachms (5.8–7.7 Gm.) several times a day. It is believed to escape from the system unchanged, and hence is not available when an alkaline influence upon the blood or renal secretion is desired. In pharmacy, cream of tartar is employed to obtain the neutral potassium tartrate (soluble tartar), potassium and sodium tartrate (Rochelle salt), antimony and potassium tartrate (tartar emetic), and iron and potassium tartrate (tartarized iron). Deflagrated with potassium nitrate, or incinerated alone, it is converted into a pure form of potassium carbonate, called salt of tartar. In the laboratory it is used to procure potassium hydroxide in a pure state, and for making black and white flux. *Black flux* is prepared by deflagrating cream of tartar with half its weight of potassium nitrate, and *white flux*, by deflagrating it with twice its weight of the same salt.

Dose, aperient, one to two drachms (3.9–7.7 Gm.); cathartic, half an ounce to one ounce (15.5–31 Gm.).

Off. Prep.—Confectio Sulphuris, *Br.;* Pulvis Jalapæ Compositus, *U. S., Br.;* Trochiscus Sulphuris, *Br.;* Ferri et Potassii Tartras, *Br.;* Pulvis Kaladanæ Compositus, *Br.;* Liquor Cocci, *N. F.;* Species Laxativæ, *N. F.;* Trochisci Sulphuris et Potassii Bitartratis, *N. F.*

POTASSII BROMIDUM. U. S., Br.

POTASSIUM BROMIDE Pot. Brom.

(pŏ-tăs'sĭ-ī brō'mĭ-dŭm)

"It contains, when dried to constant weight at 100° C. (212° F.), not less than 98.5 per cent. of KBr (119.02). Preserve it in well-closed containers." *U. S.* "Potassium Bromide may be obtained by the interaction of ferrous bromide with potassium carbonate. When dried at 100° it contains not less than 98 per cent. of pure potassium bromide, KBr." *Br.*

Bromide of Potassium; Bromuretum Potassicum, s. Kalicum; Bromure de Potassium, *Fr. Cod.;* Kalium bromatum, *P. G.;* Bromkalium, Kaliumbromid, *G.;* Bromuro di potassio, *It.;* Bromuro potasico, *Sp.*

No process is given in recent Pharmacopœias but in the 1870 U. S. P. a solution of ferrous bromide was formed, and this, by the addition of the solution of potassium carbonate, was decomposed so as to produce ferrous carbonate, which precipitated, while *potassium bromide* remained in solution. By straining, the precipitated carbonate was separated, and from the strained liquor potassium bromide was obtained by due evaporation. The reactions are as follows:

$$Fe + Br_2 = FeBr_2$$

$$FeBr_2 + K_2CO_3 = FeCO_3 + 2KBr$$

By boiling the mixture produced by the last reaction the bulky $FeCO_3$ is converted into the denser Fe_2O_3, and the separation of the potassium bromide solution is facilitated. In the Br. Pharm. 1885, by reaction between potassium hydroxide and bromine, the potassium bromide and bromate are produced in solution, and, having been obtained dry by evaporation, are exposed with the powder of charcoal to a red heat, whereby the potassium bromate is converted into potassium bromide by the separa-

tion of its oxygen. The remainder of the process consists in obtaining the bromide in crystals by solution in boiling water, which deposits it on cooling.

The reactions for this method are as follows:

$$6KOH + 6Br = 5KBr + KBrO_3 + 3H_2O$$

$$KBrO_3 + 3C = KBr + 3CO$$

Properties.—Potassium bromide is in "colorless, or white, cubical crystals, or as a granular powder; odorless, and having a strongly saline taste. It is permanent in the air. One Gm. of Potassium Bromide dissolves in 1.5 mils of water, about 250 mils of alcohol, and in 4.6 mils of glycerin at 25° C. (77° F.); also in 1 mil of boiling water and in about 21 mils of boiling alcohol. Its aqueous solution (1 in 20) is neutral or faintly alkaline to litmus. When the salt is heated upon platinum foil it decrepitates; upon further heating it fuses without decomposition and at a bright red heat volatilizes, communicating a violet color to a non-luminous flame. The addition of 5 mils of sodium bitartrate T.S. to 5 mils of an aqueous solution of the salt (1 in 5) produces a white, crystalline precipitate. Silver nitrate T.S. added to an aqueous solution of the salt (1 in 10) produces a yellowish-white precipitate, insoluble in nitric acid or in a moderate excess of ammonia water. Dissolve 1 Gm. of Potassium Bromide in 10 mils of distilled water and add 0.1 mil of tenth-normal sulphuric acid V.S.; no color is produced by the subsequent addition of a drop of phenolphthalein T.S., even after heating (*alkali*). Add a few drops of ferric chloride T.S. to 10 mils of an aqueous solution of the salt (1 in 20), shake the mixture, and add 1 mil of chloroform; the latter does not acquire a violet tint (*iodide*). Drop 1 mil of diluted sulphuric acid upon about 1 Gm. of the powdered salt; no yellow color appears at once (*bromate*). Separate portions of 10 mils each of an aqueous solution of the salt (1 in 20), when acidulated with hydrochloric acid, are not immediately rendered turbid by the addition of 1 mil of potassium sulphate T.S. (*barium*), nor by 1 mil of barium chloride T.S. (*sulphate*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Dry the salt to constant weight at 100° C. (212° F.) and proceed as directed under the Assay for bromides (see Part III, Test No. 5). It shows, in the dried salt, not less than 98.5 per cent. of KBr. Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.011902 Gm. of KBr. Each gramme of Potassium Bromide, previously dried, corresponds to not less than 82.8 mils nor more than 84.8 mils of tenth-normal silver nitrate V.S." *U. S.*

"Colorless, cubical crystals. No odor; taste pungent and saline. Soluble in 2 parts of *water*, and in 200 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of potassium and of bromides. Loses not more than 1 per cent. of its weight when dried at 100° C. (212° F.); 0.5 gramme of this dried salt requires for complete precipitation not less than 41.2 or more than 42.5 millilitres of *N/10 solution of silver nitrate.* Yields no characteristic *reactions* for copper, iron, barium, calcium, magnesium, carbonates, bromates, or iodates, and not more than the slightest *reactions* for iodides or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

According to Chas. D. Chase, the commercial salt often is decidedly alkaline, and will precipitate the alkaloids from the solution of their salts; a serious mishap from such cause is very conceivable.

Tests.—To determine the percentage of chloride in an impure bromide the process of Baudrimont, as improved by Falières, may be used. It is founded upon the fact that chlorides precipitate more silver than the bromides, because of the lower atomic weight of chlorine as compared with bromine; for an explanation see *P. J.*, 1872, p. 542. Prepare a titrated solution of 0.852 gramme of silver nitrate in 100 cubic centimeters of distilled water. It is necessary, by means of ferric chloride, salts of barium, and strong sulphuric acid in excess, to insure that there are present no other salts, such as potassium iodide, carbonate, or sulphate, or sodium nitrate, which would interfere with the results. Then dissolve one gramme of the bromide in thirty or forty grammes of water in a stoppered bottle, and add 1.427 grammes of silver nitrate in solution. When the precipitate has subsided, add, drop by drop, from a Gay-Lussac burette the titrated solution. If the bromide be pure, no precipitate forms; otherwise the number of cubic centimeters required to completely precipitate it equals the percentage of the chloride. An iodide of alkaline metal may be detected by adding to the solution of the bromide, palladium chloride, which will precipitate all the iodine in the form of palladium iodide, while the bromide of that metal will remain in solution. According to Bobieure and Herbelin, potassium bromide containing iodide may be purified by boiling with bromine water and evaporating, the liberated iodine and the excess of bromine being driven off during the evaporation. (*J. P. C.*, 4e sér., x, 166.)

Uses.—The effects of potassium bromide on the system are due chiefly to the bromine ion, although under certain conditions they may be more or less modified by the potassium. The bromides in sufficient concentration are depressants apparently to all forms of nervous tissue but show a marked selective action for certain centers. In the frog the most susceptible part is the sensory side of the spinal cord and it is possible in these animals to produce a condition of almost complete anesthesia and loss of reflex activity, with the voluntary motion well preserved. In man, however, the first effect seems to be upon the motor area of the brain and while these centers are not com-

pletely paralyzed there is a great reduction in the irritability of the psychomotor tract from doses insufficient to cause any marked diminution of the reflexes or distinct loss of sensation. With sufficient doses, however, both of these evidences of depression of the sensory cells of the cord may be apparent even in human beings. While after toxic quantities or in certain specially susceptible individuals there may be marked disturbances of intellection, this psychical depression is usually a late phenomenon. As far as the circulatory apparatus and other vital functions are concerned the bromides are practically inert. The old belief that the bromides were depressant to the heart was based upon experiments made with the potassium salt and it has been shown by Greene and Kruse (*J. A. M. A.*, 1913, lxi, p. 271), that the depressant action of this salt is due to its potassium rather than to its bromine. When used continuously over long periods of time the bromides exert a profound influence upon the nutritive processes which, however, is not clearly understood. Schultz (*Z. B.*, 1883, xix, p. 301), has found an increase in the quantity of nitrogen eliminated but a diminution in the output of phosphorus.

As the drug is eliminated very slowly, when used continuously it tends to accumulate in the system and in sufficient dose may give rise to the phenomena known as *bromism*. The symptoms are muscular weakness, general mental and bodily sluggishness, loss of memory, often marked sleepiness, depression of spirits deepening into complete apathy, lowering of temperature, and finally a universal depression of function, the patient lying in bed scarcely more than a feeble automaton. Fetor of breath is usually well marked, and an eruption of acne may be the first indication of the constitutional action of the drug. In some cases the effects of the drug upon the skin are most marked, and the pustules, under its continuous exhibition, become furuncular or go on to ulceration. A remarkable thing about bromism is the rapidity and completeness with which the symptoms clear up on ceasing the use of the drug even without any treatment. Despite the fact that it leaves the system through practically all the excretory organs, having been found in the sweat, saliva, urine, and intestinal mucus, it is eliminated very slowly and has been found in the urine as much as a month after the last dose.

The bromides are used in medicine to check *convulsions*, alleviate *pain*, to promote sleep, and to allay general nervous excitation. In *epilepsy* the bromides are the most potent remedial agents that we possess. Their influence, however, is that of a suppressant and rarely, if ever, do they produce a true cure; while under their use the patient may remain free from seizures for months and even years, their withdrawal is generally followed by a return of symptoms. In *tetanus* the fact that they can be given in almost unlimited quantity without serious depression of the circulation renders them of peculiar value for the control of the convulsions. In *strychnine poisoning*, although theoretically important, their action is generally too slow to be of much practical utility. As analgesics the bromides when given by themselves are of only secondary power, but they greatly enhance the anodyne effects of other drugs such as morphine or acetanilid. In *insomnia* they have been greatly abused. They differ sharply from the true somnifacients, such as chloral, in the fact that in ordinary quantity they have almost no depressant action upon the intellectual centers. Their value in promoting sleep is due rather to the obtunding of the general sensibilities so that those distractions, such as noise and bodily discomforts, which may act as contributing causes to the wakefulness, are less potent. They have been used very freely in all forms of functional disorders of the nervous system for some of which they are very useful, but for others entirely unsuited. In *hysteria* they are almost habitually prescribed, but it is extremely doubtful whether they have any effect which cannot be ascribed to the mere effect of taking medicine, at least as far as the immediate relief of symptoms. In *neurasthenia* their analgesic properties often make them useful and there is reason to believe that at times they may exercise a favorable influence upon the metabolism of the nerve centers. In *vomiting* of reflex origin, as that of pregnancy, at times they are of service. Among other conditions in which they are frequently employed may be mentioned *alcoholism, delirium tremens, various* forms of *sexual excitement*, as *nymphomania, urethral fever*, etc.

The dose of potassium bromide varies much according to the purpose for which it is administered and the length of time over which it is employed. In conditions like epilepsy in which the use of the drug is continued, once the system has come under its influence relatively small doses are required to maintain the beneficial impression. Thus, while in the beginning of the treatment 1 or 2 drachms (3.9–7.7 Gm.) a day may be required, after the action of the bromide has once been well established their influence may often be continued by 8 or 10 grains (0.5–0.65 Gm.) three times a day. In tetanus it is essential that large quantities be exhibited; as much as from one-half to one ounce (15.5–31 Gm.) should be administered in the twenty-four hours. When only one dose is given very large quantities may be safely administered, thus for the relief of pain a drachm is generally required and in severe strychnine poisoning one-half ounce (15.5 Gm.), properly diluted, may be exhibited at once.

Dose, ten to forty-five grains (0.65–3.0 Gm.).

Off. Prep.—Elixir Potassii Bromidi, *N. F.;* Elixir Trium Bromidorum, *N. F.;* Liquor Bromi, Mistura Chloralis et Potassii Bromidi Composita, *N. F.;* Sal Potassii Bromidi Effervescens, *N. F.;* Sal Potassii Bromidi Effervescens Compositus, *N. F.;* Syrupus Bromidorum, *N. F.*

POTASSII CARBONAS. U. S., Br.

POTASSIUM CARBONATE Pot. Carb. [Salt of Tartar]

(pŏ-tăs'sĭ-ī căr'bŏ-năs)

"It contains, when dried to constant weight at 180° C. (356° F.), not less than 99 per cent. of K_2CO_3 (138.20). It contains not more than 15 per cent. of moisture. Preserve it in air-tight containers." *U. S.* "Potassium Carbonate may be obtained by the interaction of potassium sulphate and calcium carbonate. It contains not less than 81.5 per cent. of pure potassium carbonate, K_2CO_3." *Br.*

Carbonate of Potassa from Pearlash; Potassii Carbonas Purus, Sal Tartari; Kali Carbonicum, Carbonas Potassicus, s. Kalicus; Carbonate de Potasse pur, Sel de Tartre, *Fr. Cod.*; Kalium Carbonicum, *P. G.*; Kohlensaures kali, Kaliumcarbonat, *G.*; Carbonato di potassio, *It.*; Carbonato potasico, *Sp.*

The present U. S. Pharmacopœia does not give a process for this salt.

The object of the process (formerly official) is to purify the impure *potassium carbonate*, or pearlash. This generally contains certain insoluble impurities, as well as small portions of potassium sulphate, silicate, and chloride, as explained under another head. (See *Potassii Carbonas Impura.*) By dissolving it in a due proportion of water, and filtering the solution, the insoluble impurities are disposed of, as well as the greater part of the foreign salts, which, being much less soluble than the potassium carbonate, are excluded by the superior affinity of this salt for the water. The proper way of conducting the purification is to mix the impure carbonate with an equal weight of *cold water*, and to allow the mixture to stand for a day or two, stirring it frequently to promote the action of the water. The clear liquor obtained by decantation or filtration is then evaporated to dryness. The former official process was conducted very much in this way, cold water being employed, and about equal weights of alkali and water being used. The prolonged contact of the water with the salt, and the occasional stirring of the mixture, formerly ordered by the Dublin College, were useful directions. In no case should the undissolved residue be washed with a fresh portion of water, as by such a proceeding the foreign salts, which it is the object of the process to separate, would be dissolved. Iron vessels are directed, because this metal is not acted on by the alkali, while glass is attacked by it. In granulating the salt by stirring, it is better, when the solution is brought nearly to dryness, to keep it on the fire at a reduced heat until the process is finished, than to remove it the moment it thickens. According to Berzelius, a more productive process for purifying pearlash, though the resulting salt is not so pure as when obtained in the way just described, is to dissolve the pearlash in more than its weight of water, to evaporate the solution until it has the sp. gr. 1.52, and then to put it in a cool place, that the foreign salts, principally potassium sulphate and chloride, may crystallize. The solution is then decanted, and evaporated to dryness. To get rid of the silica, Rieckher proposes to evaporate the solution, exempt from sulphate, to dryness, to moisten the residue with solution of ammonium carbonate, and again evaporate. The silica separates, and passes into the insoluble state at the temperature necessary for evaporation. By again dissolving and evaporating, the carbonate is obtained free from this impurity. (*Chem. Cb.*, 1863, p. 158.)

"Take of Impure Carbonate of Potassium [pearlash] *thirty-six troyounces;* Water *two pints and a half.* Dissolve the Impure Carbonate in the Water, and filter the solution; then pour it into an iron vessel, and evaporate over a gentle fire until it thickens. Lastly, remove it from the fire, and stir constantly with an iron spatula so as to form a granular salt." *U. S.* 1870.

Impure Potassium Carbonate was official in 1870. It is commonly known as *Pearlash, Pearlashes, Impure Potassa; Potasse du Commerce,* Fr.; *Rohe Pottasche,* G. The alkali called potassa is the hydroxide of the metal potassium. (See *Potassium.*) It exists in various states of purity admixed with carbonate. In its most impure state, it is the common potash or *potashes* of commerce. This, subjected to calcination, is rendered purer, and is then called *pearlash,* the form of the alkali which was formerly recognized as *Potassii Carbonas Impura.*

Natural State and Preparation.—Potash and pearlash of commerce were formerly procured largely from the ashes of wood by lixiviation, and the subsequent evaporation of the solution obtained. The alkali exists in the wood in combination with various organic acids, and is left behind after the incineration, principally in the form of carbonate according to the following reaction, taking the acetate as an example:

$$2KC_2H_3O_2 + O_4 = K_2CO_3 + CO_2 + 3H_2O$$

The wood is burned on the ground, in a place sheltered from the wind. The ashes consist of a soluble and an insoluble portion. The soluble part is made up of potassium carbonate, together with potassium sulphate, phosphate, and silicate, and potassium and sodium chlorides; the insoluble portion, of calcium, and aluminum salts, oxidized iron and manganese carbonate and phosphate, and a little carbonaceous matter that has escaped combustion. The ashes are lixiviated in barrels with the addition of a portion of lime, and the soluble substances above mentioned are taken up. The lixivium is then evaporated in large iron kettles, which for several days are kept constantly full. The evaporation is continued until the mass has become of a black color and of the consistence of brown sugar. It is now subjected to as powerful a heat as can be produced by the best wood fire for a number of hours, by which it is fused. During the fusion the combustible impurities are for the most part burnt out, and a gaseous matter is emitted, which agitates the more fluid part. When the fusion is complete, the liquid becomes quiescent, and looks like

melted iron. It is now transferred, by means of large iron ladles, to iron pots, where it congeals in cakes. These are broken up and packed in tight barrels, and constitute the *potash* of commerce. If it is intended to make *pearlash*, the process is varied. In this case the black matter of the consistence of brown sugar, called *black salts* by our manufacturers, instead of being fused, is transferred from the kettles to a large oven-shaped furnace so constructed that the flame may play over the alkaline mass, which in the meantime is stirred by means of an iron rod. The ignition is in this way continued until the combustible impurities are burnt out, and the mass, from being black, becomes of a bluish-white color. The extraction from wood ashes is no longer practised in the United States, but is still carried out, to some extent in Canada and the northern countries of Europe, especially Russia.

Within recent years the residues of beet root molasses, after fermentation of the sugar and distillation of the spirit, have served as a source of potash. The molasses contains 40 to 50 per cent. of sugar and 3 to 4 per cent. of potassium salts. The *suint* of sheep's wool constitutes another source of potashes. The potassium in this case being combined with fatty substances. Potassium sulphate, either the crude salt from Stassfurt deposits or that obtained from the crude potassiuum chloride of the same locality, is also converted into carbonate by a process analogous to Leblanc's soda process. The principle of the ammonia soda process can also be applied to the crude potassium chloride of Stassfurt, with this difference in the practical operation, that, because of the ready solubility of the acid potassium carbonate, trimethylamine is used instead of ammonia, as the chloride of this base is much more soluble than is ammonium chloride.

A review of the recent effort to develop a potash industry in the United States will be found in the article by F. M. de Beers in *Metallurgical and Chem. Engineering*, November 1, 1916. (See also under *Potassii Nitras*, p. 906.)

Crude potash is now prepared in large amount from the "abraum" salts of the German rock salt deposits, in a manner analogous to the preparation of sodium carbonate from sodium chloride. The mixture of magnesium and potassium chlorides found so abundantly in these deposits may also be saturated with carbon dioxide, when an insoluble double salt separates out.

$$3MgCO_3 + 2KCl + CO_2 + 9H_2O = 2(MgCO_3.KHCO_3.4H_2O) + MgCl_2$$

By heating this with water under pressure it decomposes into insoluble magnesium carbonate and soluble potassium carbonate, which remains in solution and is obtained therefrom by evaporation.

$$2MgCO_3.KHCO_3.4H_2O = K_2CO_3 + 2MgCO_3 + 5H_2O + CO_2$$

Other minerals have also become the source of potassium salts, especially a deposit of mixed potassium and magnesium chlorides, overlying a bed of common salt, at Stassfurt, near Madgeburg, in Prussia.

Potassium carbonate may be produced from crude potassium sulphate by the following reaction:

$$K_2SO_4 + CaCO_3 + K_2CO_3 + CaSO_4$$

Feldspar, marl and other minerals, rich in potassium compounds, are now being utilized for the production of potassium carbonate and other salts of the element.

In round figures the importations into the United States of Stassfurt minerals in recent years are: potassium chloride (80 per cent.), 250,000 tons; potassium sulphate (90 per cent.), 50,000 tons; manure salts (20–38 per cent.), 200,000 tons; kainite (12–15 per cent.), 500,000 tons.

Properties.—Potash is in the form of fused masses, of a stony appearance and hardness, and a caustic burning taste. Its color is variegated, but reddish and dark brown are the predominant hues. When exposed to the air, it absorbs moisture and deliquesces, and, if sufficiently long exposed, finally becomes liquid. Pearlash is of a white color, with usually a tinge of blue. As it occurs in commerce, it is in tight casks, containing about three hundred and fifty pounds, in which it forms one entire, hard, concrete mass. In commerce it is found in coarse powder, intermingled with lumps as dug out of the casks, presenting an opaque granular appearance, like table salt or common sugar. It is deliquescent, and has a burning alkaline taste. It is soluble in water, with the exception of impurities. It differs from potash principally in containing fewer combustible impurities and in being less caustic and deliquescent. The coloring matter of both these forms of alkali is derived from carbonaceous impurities and small portions of iron and manganese.

Composition.—The basis of both potash and pearlash is potassium carbonate, but this is associated with certain salts and with insoluble impurities. Several varieties of potash found in commerce were analyzed by Vauquelin, whose principal results are contained in the table below. The quantity examined of each kind was 1152 parts.

These results, calculated for 100 parts, show that the American potash contains 74 per cent. of pure alkali hydroxide and the Russian 67 per cent. Pearlash, it is seen, is more rich in carbonic acid than potash, and this result of analysis corresponds with the qualities of the two substances as prepared in the United States—potash being known to be far more caustic than pearlash. Besides the impurities shown by the table, potassium phosphate and silicate and sodium chloride are present. J. U. Lloyd, in the *Proc. A. Ph. A.*, 1892, p. 190, gives the results of an examination of American commercial potashes; he found that what was sold

in the market as "first sorts" was largely adulterated with common salt, this addition made to the melted potash in the kettle tending to whiten the crude potash and give it increased value in the eyes of those consumers who judge merely by appearance and do not take the trouble to assay it. According to Stevenson Macadam, the potashes of commerce contain iodine and a trace of bromine, which shows that the forest trees from which the alkali is obtained must contain a very minute proportion of these non-metallic elements.

As the potash of commerce is valuable in the arts in proportion to the quantity of real alkali which it contains, it is important to possess an easy method of ascertaining its quality in that respect. (See *Potassii Hydroxidum.*)

Pearlash, from its impurity, is never used as a medicine. Purified to a certain extent, it takes the name of potassium carbonate.

Inasmuch as potassium carbonate is now largely made electrolytically from the chloride, the presence of potassium chlorate as an impurity has been reported in the commercial carbonate.

Properties.—It is officially described as "a white, granular powder; odorless, and having a strongly alkaline taste; very deliquescent. One Gm. of Potassium Carbonate dissolves in 0.9 mil of water at 25° C. (77° F.); also in 0.7 mil of boiling water; insoluble in alcohol. An aqueous solution of Potassium Carbonate (1 in 20) is strongly alkaline to litmus and phenolphthalein T.S., and effervesces with acids. When heated to 180° C. (356° F.), the salt loses all the water which it may have retained or absorbed; at a bright red heat it melts, and at a white heat it volatilizes, communicating to a non-luminous flame a violet color with not more than a transient yellow tinge. An aqueous solution of the salt (1 in 10) yields with an excess of tartaric acid T.S. a white crystalline precipitate of potassium bitartrate. No residue is left on dissolving 1 Gm. of the salt in 20 mils of distilled water (*earthy impurities*). An aqueous solution of Potassium Carbonate (1 in 50), mixed with a slight excess of hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3). Take about 3 Gm. of Potassium Carbonate, weigh accurately, and dry to constant weight in an air bath at 180° C. (356° F.); it loses not more than 15 per cent. in weight.

"Assay.—Dissolve about 3 Gm. of Potassium Carbonate, previously dried to constant weight at 180° C. (356° F.), and accurately weighed in a stoppered weighing-bottle, in 25 mils of distilled water and titrate with normal sulphuric acid V.S., methyl orange T.S. being used as indicator. It shows, in the dried salt, not less than 99 per cent. of K_2CO_3. Each mil of normal sulphuric acid V.S. used corresponds to 0.06910 Gm. of K_2CO_3. Each gramme of Potassium Carbonate, previously dried, corresponds to not less than 14.33 mils of normal sulphuric acid V.S." *U. S.*

"A white crystalline powder, very deliquescent. Taste alkaline and caustic. Soluble in 1 part of *water;* insoluble in *alcohol* (90 per cent.). Yields the *reactions* characteristic of potassium and of carbonates. 1 gramme requires for neutralisation not less than 11.8 millilitres of *H/1 solution of sulphuric acid.* Loses not more than 18.5 per cent. of its weight when exposed to a red heat. Yields no characteristic *reactions* for copper, aluminum, calcium, magnesium, sodium, cyanides, nitrates, sulphates, sulphides, or thiosulphates, not more than the slightest *reactions* for iron, and no strongly marked *reactions* for chlorides. *Lead limit* 5 parts per million. *Arsenic limit* 2 parts per million." *Br.*

The official test permits the presence of 1 per cent. of impurities. It is incompatible with acids and acidulous salts, ammonium chloride and acetate, lime water, calcium chloride, magnesium sulphate, alum, tartar emetic, silver nitrate, ammoniated copper and ammoniated iron, ferrous sulphate, tincture of ferric chloride, calomel and corrosive sublimate, lead acetate and subacetate, and zinc sulphate. It is not decomposed by iron and potassium tartrate.

A solution of the salt, on exposure to the air, or on addition of an acid, deposits flocculi consisting of hydrated silica, resulting from the decomposition of potassium silicate, which is always present as an impurity. The spontaneous deposition of silica is owing to the absorption of carbon dioxide.

Composition.—Potassium carbonate, after exposure to a red heat, is anhydrous. Obtained by the usual processes, it contains two molecules of potassium carbonate and three of water. When exposed to the air, potassium carbonate absorbs sufficient water, before losing its solid form, to give it three molecules; with more it begins to deliquesce. *Potassium percarbonate,* $K_2C_2O_6$, was made by Constans and von Hansen by electrolyzing a saturated solution of potassium carbonate, and gradually lowering the temperature. It is a bluish amorphous powder, hygroscopic and decomposing water at ordinary temperatures, bicarbonate being formed. (*Chem. News,* 1897, 170; 1898, 65.)

Uses.—Potassium carbonate is occasionally used as an antacid in *dyspepsia,* a diuretic in *dropsy,* and an antilithic in *uric acid gravel,* but the purpose to which it was most commonly applied in former years was the formation of the *neutral mixture* and the *effervescing draught.* It should always be administered in dilute solution. In large quantities it acts as a corrosive poison, and is capable of producing death in a few hours; three ounces in very concentrated solution have been recovered from by an adult female. (Espagne, *A. G. M.,* Fèv. 1867.) The antidotes are the fixed oils and the vegetable acids. As a local remedy in *cutaneous affections,* potassium carbonate is used in the form of bath, lotion, and ointment. From eight to sixteen ounces may be used for a single bath, the quantity being gradually in-

creased. Lotions may be made by dissolving two or three drachms in a pint of water; and ointments, by rubbing from ten grains to a drachm with an ounce of lard.

Dose, five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Mistura Carminativa, *N. F.;* Unguentum Sulphuris Alkalinum, *N. F.*

POTASSII CHLORAS. U. S., Br.

POTASSIUM CHLORATE Pot. Chloras

(pŏ-tăs'sĭ-ī ĉhlō'răs)

"It contains not less than 99 per cent. of $KClO_3$ (122.56). Preserve it in well-closed containers. *Great caution should be observed in handling* it, as dangerous explosions are liable to occur when it is heated or subjected to concussion or trituration with organic substances (cork, tannic acid, dust, sugar, etc.), or with sulphur, sulphides, hypophosphites, or other easily oxidizable substances." *U. S.* "Potassium Chlorate, $KClO_3$, may be obtained by passing chlorine into water holding lime or magnesia in suspension, treating the clarified liquid with potassium chloride, and subsequently crystallising out the potassium chlorate." *Br.*

Chlorate of Potash; Kali Oxymuriaticum, Kali Muriaticum Oxygenatum, Chloras Potassicus, s. Kalicus; Hyperoxymuriate of Potassa; Chlorate de Potasse, *Fr. Cod.;* Kalium Chloricum, *P. G.;* Kaliumchlorat, Chlorsaures Kali, *G.;* Clorato di potassio, *It.*

In the U. S. and Br. Pharmacopœias no processes are given for potassium chlorate.

Preparation.—The salt may be obtained by the process of Graham, which consists in mixing potassium carbonate with an equivalent quantity of calcium hydroxide before submitting it to the action of chlorine. The gas is absorbed with avidity, and the mass becomes hot, while water is given off. The lime converts the carbonate into potassium hydroxide, and the reaction then takes place between six molecules of potassium hydroxide and six atoms of chlorine, with the result of forming five molecules of potassium chloride and one of potassium chlorate, while three molecules of water are eliminated, the reaction being analogous to the first one given under the milk of lime method (see below).

The products are, therefore, calcium carbonate, potassium chloride, and potassium chlorate. The chloride and chlorate are separated from the carbonate by solution in hot water, and the chlorate from the chloride by priority of crystallization; a large proportion of the potassium hydroxide is lost by being converted into potassium chloride. In the process which has been generally employed for the commercial manufacture of potassium chlorate this is obviated, as follows. Chlorine is passed into a solution of milk of lime having a specific gravity of 1.04 until the liquid is nearly saturated. The clear solution is evaporated until it has a specific gravity of 1.18, and then potassium chloride added, and the mixture boiled down until a specific gravity of 1.28 is attained. On cooling, crystals of potassium chlorate separate out. The reactions here are

$$6Ca(OH)_2 + 6Cl_2 = 5CaCl_2 + Ca(ClO_3)_2 + 6H_2O$$
$$Ca(ClO_3)_2 + 2KCl = CaCl_2 + 2KClO_3$$

Pechiney's improvement on this process is to separate the greater part of the calcium *chloride* from the calcium *chlorate* before adding the potassium chloride. For details, see *N. R.,* Feb., 1882.

The potassium chlorate of commerce is also prepared by the reaction of solutions of potassium chloride and calcium hypochlorite, with the assistance of heat. The potassium chlorate crystallizes during the refrigeration of the liquor, and calcium chloride remains in solution:

$$2KCl + 3Ca(OCl)_2.CaCl_2 = 2KClO_2 + 6CaCl_2$$

This process has been further improved in Muspratt and Eschellmann's English patents (*J. Soc. Chem. Ind.,* iii, pp. 349 and 445) by substituting magnesia for lime, as potassium chlorate is much less soluble in magnesium chloride solutions than in those of calcium chloride, and consequently much less chlorate is left in solution. The process is said to increase the production of chlorate by from 15 to 20 per cent. It may also be produced by the simple heating of solution of potassium hypochlorite:

$$3KClO = KClO_3 + 2KCl$$

Potassium chlorate is now made commercially, in increasing amounts by the electrolysis of potassium chloride solution at Niagara Falls, and elsewhere, in this country and in various places in Europe. The potassium chloride, on electrolysis in a cell without diaphragm, yields first potassium hypochlorite, but as the temperature of the bath is kept above 50° C. (122° F.), it is changed to a mixture of chlorate and chloride, from which, on cooling, the former crystallizes out.

Properties.—Potassium chlorate is in "colorless, lustrous, monoclinic prisms or plates, or as a white granular powder; odorless, and having a saline taste. It is permanent in the air. One Gm. of Potassium Chlorate dissolves in 11.5 mils of water at 25° C. (77° F.); also in 1.8 mils of boiling water; almost insoluble in alcohol; soluble in glycerin. An aqueous solution of the salt (1 in 20) is neutral to litmus. When heated the salt melts, gives off oxygen, and finally leaves a residue of potassium chloride, readily soluble in water and yielding with silver nitrate T.S. a white precipitate, insoluble in nitric acid, but readily soluble in ammonia water. To a non-luminous flame it imparts a violet color. With an excess of tartaric acid T.S. a solution of the salt (1 in 20) slowly yields a scant, white, crystalline precipitate; with platinic chloride T.S., a similar solution yields a yellow

crystalline precipitate. Add about 0.2 Gm. of the salt to 1 mil of hydrochloric acid; the liquid assumes a deep greenish-yellow color, and chlorine and oxides of chlorine are evolved. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3)." *U. S.*

"Colorless monoclinic crystals. Taste cool, saline. Soluble in 16 parts of *water.* Moistened with *hydrochloric acid* it evolves a yellow gas with an odor of chlorine. Yields no characteristic *reactions* for iron, calcium, magnesium, sodium, ammonium, or nitrates, and not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Assay.—"Transfer to a 250 mil flask about 0.1 Gm. of Potassium Chlorate, accurately weighed, and dissolve it in 10 mils of distilled water, then add 25 mils of acidulated ferrous sulphate T.S. to the solution. Prepare a valve stopper by taking a piece of rubber tubing of convenient diameter and about 5 cm. in length, placing a piece of glass rod in one end and slipping the other end over a glass tube which passes through a perforated stopper of a size convenient to fit the flask used. Cut a longitudinal slit about 15 mm. long in one side of the rubber tube about half way up. Insert this stopper in the flask and boil the mixture for ten minutes. Now cool the mixture, add 10 mils of manganous sulphate T.S. and titrate the excess of ferrous sulphate with tenth-normal potassium permanganate V.S. At the same time conduct a parallel experiment with another portion of 25 mils of acidulated ferrous sulphate T.S. and subtract the result of the former titration from that of the latter. It shows not less than 99 per cent. of $KClO_3$. Each mil of tenth-normal potassium permanganate V.S. used corresponds to 0.0020427 Gm. of $KClO_3$. Each gramme of Potassium Chlorate corresponds to not less than 484.7 mils of tenth-normal potassium permanganate V.S." *U. S.*

Frank X. Moerk (*J. A. P. A.*, 1913, p. 155), reviews various methods for the determination of chlorates and recommends the following: Place 0.1 Gm. of the salt in a glass-stoppered bottle and add 10 mils of distilled water and 15 mils 10 per cent. potassium bromide solution, and 20 mils HCl (sp. gr. 1.20) and allow to stand 40 minutes tightly stoppered. Cool by immersing in water, add 20 mils potassium iodide solution (10 per cent.), carefully rinsing the stopper and neck of the bottle, and titrate with tenth-normal sodium thiosulphate V.S. A blank test should be made with the reagents to prove that no iodine is liberated by them alone.

Potassium chlorate is characterized also by becoming first yellow and then red by admixture with a little sulphuric acid, and by the action of that acid evolving chlorine tetroxide (Cl_2O_4), known by its yellow color, and its explosive property when heated; by its bleaching power when mixed with hydrochloric acid and then with water, and by its property of exploding violently when triturated with a small portion of sulphur or phosphorus or kermes mineral. Potassium chlorate consists of one atom of potassium in combination with the chloric acid group. This salt is an excellent test of manganese existing in organic matter. If a small portion of such matter, containing even a trace of manganese, be thrown on the surface of the *pure* melted salt in a test-glass, after the combustion has ceased the cooled saline mass will be found to have a rose or pinkish tint, caused by the formation of potassium permanganate. (*Neues Repert.*, vi, 247.) A similar discoloration of the salt, produced by the use of pure charcoal in the same manner, will evince the presence of manganese in the chlorate as an impurity.

Uses.—In the belief that potassium chlorate yielded oxygen in the system, it was formerly used in the treatment of various infectious diseases as well as a local disinfectant, but as decomposition of the salt takes place only in highly acid media this liberation in the body cannot occur. As a local antiseptic it is extremely feeble. According to the experiments of Sternberg a 4 per cent. solution—which is almost saturation at ordinary temperatures—is without germicidal power. It is used at present solely as a local remedy in *stomatitis, pharyngitis, vaginitis,* and other forms of *catarrh* as well as in *hemorrhoids* and *indolent ulcers.* Its beneficial influence in these conditions is due to its stimulant saline properties combined with a mild astringent effect. On the theory that it would be eliminated through the salivary glands and keep the mouth constantly bathed with a solution, it has been recommended to administer the drug internally in mercurial *ptyalism* and other inflammatory conditions of the buccal cavity, but as the larger portion of the drug is excreted through the kidneys this use does not commend itself to the thinking physician.

In overdose potassium chlorate is an active poison, four drachms of it having caused death in the adult. The symptoms produced are violent vomiting, profuse diarrhea, excessive dyspnea, great failure of the heart's action, and marked cyanosis. The urine is lessened in quantity, albuminous, often of a dark reddish-brown or blackish color, and containing tube casts and the débris of blood corpuscles. In some cases there have been marked nervous symptoms, such as cramps, delirium, coma, etc. The lesions found after death are those of gastro-enteritis and acute nephritis, with alteration in the character of the blood due to the development in it of methæmoglobin. On account of their irritant action on the kidneys, large doses are especially dangerous in *diphtheria.*

Dose, from five to fifteen grains (0.32–1.0 Gm.).

Off. Prep.—Trochisci Potassii Chloratis, *U. S.* (*Br.*); Gargarisma Guaiaci Compositum, *N. F.*

POTASSII CITRAS. U. S., Br.

POTASSIUM CITRATE Pot. Cit.

(pŏ-tăs'sĭ-ī cī'trăs)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99 per cent. of $K_3C_6H_5O_7 + H_2O$ (324.36). Preserve it in well-closed containers." *U. S.*
"Potassium Citrate may be obtained by the interaction of citric acid and potassium carbonate. It contains not less than 99 per cent. of pure potassium citrate, $K_3C_6H_5O_7,H_2O$." *Br.*

Kalium Citricum, Citras Potassicus, s. Kalicus; Citrate of Potash; Citrate de Potasse, *Fr.*; Kaliumcitrat, Citronsaures Kali, *G.*

Potassium citrate was known formerly by the name of *salt of Riverius.* In the U. S. formula of 1870, mutually saturating proportions of the acid and bicarbonate were intended to be employed, the latter ingredient being preferred to the carbonate on account of its greater purity. The potassium of the bicarbonate unites with the citric acid to form the potassium citrate, and the carbon dioxide escapes, producing effervescence.

$$3KHCO_3 + H_3C_6H_5O_7 = K_3C_6H_5O_7 + 3CO_2 + 3H_2O$$

The resulting solution is directed to be evaporated to dryness, as affording the most convenient form for use. The granulation ordered has a tendency to retard the deliquescence of the citrate. The British 1885 process differed only in the use of the carbonate instead of the bicarbonate, and in providing more carefully for an exact neutralization.

Properties.—Potassium citrate is crystallizable, but, as usually seen, is in the form of a granular powder. The U. S. P. recognizes both forms, and describes it "as transparent, prismatic crystals, or as a white, granular powder; odorless, and having a cooling, saline taste. It is deliquescent when exposed to moist air. One Gm. of Potassium Citrate dissolves in 0.6 mil of water at 25° C. (77° F.); almost insoluble in alcohol; freely soluble in glycerin. An aqueous solution of the salt (1 in 20) is alkaline to litmus but is not reddened by one drop of phenolphthalein T.S. When heated above 100° C. (212° F.), the salt begins to lose water and at about 200° C. (392° F.) the water of crystallization is completely lost. At a higher temperature the salt begins to decompose, turns brown, and upon further heating carbonizes and emits inflammable gases which have a very pungent, acrid odor. At a red heat a residue remains, which has an alkaline reaction and strongly effervesces with acids. An aqueous solution of Potassium Citrate (1 in 10) yields a white, crystalline precipitate with sodium bitartrate T.S. Mix 10 mils of an aqueous solution of the salt (1 in 20) with 10 mils of calcium chloride T.S.; the liquid remains clear until it is boiled, when a white, granular precipitate is produced. A solution of 1 Gm. of Potassium Citrate in 1 mil of distilled water does not deposit any precipitate on the addition of 1 mil of acetic acid (*tartrate*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of the salt meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"**Assay.**—Dry the salt to constant weight in a desiccator over sulphuric acid, and proceed as directed under the Assay for alkali salts of organic acids (see Part III, Test No. 6). It shows, in the dried salt, not less than 99 per cent. of $K_3C_6H_5O_7 + H_2O$. Each mil of half-normal sulphuric acid V.S. used corresponds to 0.05406 Gm. of $K_3C_6H_5O_7 + H_2O$. Each gramme of Potassium Citrate, previously dried, corresponds to 18.3 mils of half-normal sulphuric acid V.S." *U. S.*

The British Pharmacopœia gives the following tests of its character:

"A white, granular, or crystalline powder. Taste saline, feebly acid. Soluble in 1 part of *water.* Yields the *reactions* characteristic of potassium and of citrates. 1 gramme, heated to redness till gases cease to be evolved, leaves an alkaline residue which, when treated with *water,* filtered, and well washed, yields a clear solution requiring for neutralisation not less than 13.3 millilitres of *N/2 solution of sulphuric acid.* Yields no characteristic *reactions* for iron, calcium, magnesium, sodium, carbonates, or tartrates, and not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million." *Br.*

As citric acid is tribasic, this salt consists of three atoms of potassium combined with the citric acid radical $C_6H_5O_7$, and with this one molecule of water, its formula being $K_3C_6H_5O_7 + H_2O$.

Uses.—Potassium citrate is a type of those drugs which increase various secretions by what is known as their salt action. This group of drugs, which includes most of the non-toxic crystalloids, act by increasing the saline concentration of the blood, disturbing the osmotic balance between this fluid and the surrounding tissues thereby attracting water into the vessels and tending towards the production of a hydremic state. This tendency towards an increase in the volume of the blood is counteracted by greater activity on the part of the glandular structures. Not only is the secretion of urine greater, but there is also an increase in the bronchial, sweat, and other glands. The therapeutic uses of potassium citrate, however, are not due alone to this action. The citrates being oxidized in the body into carbonates, the salt tends to correct any systemic hyperacidity; and the potassium apparently increases the completeness of bodily combustion. This combination of actions makes the drug of peculiar value in those forms of metabolic disturbances accompanied with the over-production of uric acid, such as *acute* or *chronic rheumatism* and *gout.* It is, however, a valuable drug in a large variety of other condi-

tions, thus in certain types of *nephritis*, especially when there is diminution in the elimination of solid matters, it is of much service as a diuretic; it is valuable in cases of *cystitis* with hyperacidity of the urine. In *fevers* it is often useful, either for its diuretic or diaphoretic effect, and is especially grateful in forms of the *neutral mixture* or *effervescing draught*. In the early stages of *acute bronchitis* or *tracheitis* by increasing the secretion of the mucous glands it indirectly exercises a sedative action on the inflammatory mucous membrane. It may be most pleasantly exhibited in conjunction with lemon juice which in no way lessens the alkalizing effect.

Dose, of the citrate, from twenty to forty grains (1.3–2.6 Gm.). When a decided effect upon the system is desired, as much as an ounce (31 Gm.) of it may be given in twenty-four hours.

Off. Prep.—Potassii Citras Effervescens, *U. S.*

POTASSII CITRAS EFFERVESCENS. U. S.

EFFERVESCENT POTASSIUM CITRATE Pot. Cit. Eff.

(pŏ-tăs'sĭ-ī cī'trăs ĕf-fẹr-vĕs'cĕnṣ)

"Potassium Citrate, *two hundred grammes* [or 7 ounces av., 24 grains]; Sodium Bicarbonate, dried and powdered, *four hundred and seventy-seven grammes* [or 16 ounces av., 361 grains]; Tartaric Acid, dried and powdered, *two hundred and fifty-two grammes* [or 8 ounces av., 389 grains]; Citric Acid, unefflorescd crystals, *one hundred and sixty-two grammes* [or 5 ounces av., 313 grains], to make about *one thousand grammes* [or 35 ounces av., 120 grains]. Dry the potassium citrate on a water bath until it ceases to lose weight; after powdering the dried salt, mix it intimately with the powdered citric acid and tartaric acid, then thoroughly incorporate the sodium bicarbonate. Place the mixed powders on a plate of glass or in a suitable dish, in an oven heated between 93° and 104° C. (199.4° and 219.2° F.). Manipulate the mixture carefully with a wooden spatula, and, when it has become moist, rub it through a No. 6 tinned-iron sieve, and dry the granules at a temperature not exceeding 54° C. (129.2° F.). Immediately transfer the salt to suitable containers and seal them tightly. Care must be taken to prevent the salt from coming in contact with air containing moisture." *U. S.*

The process of the U. S. P. IX is identical with that of the U. S. P. VIII, but differs from that formerly official, mainly in the absence of sugar which has a tendency to discolor and the use of potassium citrate instead of potassium bicarbonate and citric acid.

This official effervescent salt affords an agreeable mode of administering potassium citrate. It is more prone to exert a laxative effect because of the sodium tartrate formed.

Dose, from one to two drachms (3.9–7.7 Gm.).

POTASSII ET SODII TARTRAS. U. S. (Br.)

POTASSIUM AND SODIUM TARTRATE Pot. et Sod. Tart. [Rochelle Salt]

(pọ-tăs'sĭ-ī ĕt sō'dĭ-ī tär'trăs)

"It contains not less than 73.72 per cent. nor more than 77.39 per cent. of anhydrous potassium and sodium tartrate, corresponding to not less than 99 per cent. of the crystallized salt [$KNaC_4H_4O_6 + 4H_2O = 282.20$]. Preserve it in well-closed containers." *U. S.* "Sodium Potassium Tartrate may be obtained by neutralising Acid Potassium Tartrate with Sodium Carbonate. It contains not less than 98 per cent. of pure sodium potassium tartrate, $NaKC_4H_4O_6,4H_2O$." *Br.*

Sodii et Potassii Tartras, *Br.;* Sodium Potassium Tartrate; Tartrate of Potassium and Sodium; Soda Tartarata; Sodæ et Potassæ Tartras, *Br.* 1864, *U. S.* 1850; Sodæ Potassiotartras, Natro-kali Tartaricum; Tartarated Soda; Sal Polychrestum Seignetti, Tartras Potassico sodicus; Tartrate de Potasse et de Soude, *Fr. Cod.;* Sel de Seignette, Soude Tartarisée, *Fr.;* Tartarus Natronatus, *P. G.;* Seignettesalz, Kaliumnatriumtartrat, *G.;* Tartrate sodico-potassico, *It.;* Tartrato sodico-potasico, *Sp.*

This salt cannot be made profitably on the small scale (for U. S. process, 1870, see the *U. S. Dispensatory*, 19th edition, page 1000); it is a double salt, consisting of a molecule of tartaric acid, $C_4H_4O_6.H_2$, in which one of the basic hydrogen atoms is replaced by potassium and the other by sodium. The theory of its formation is very simple, being merely the replacement of the hydrogen in the potassium bitartrate by the sodium of the sodium carbonate, the carbon dioxide of which escapes with effervescence. The quantities of the materials for mutual saturation are 1224.02 parts of monohydrated carbonate and 376.28 of bitartrate, or one molecule of monohydrated sodium carbonate to two molecules of the acid tartrate.

$$2KHC_4H_4O_6 + Na_2CO_3H_2O = 2KNaC_4H_4O_6 + CO_2 + 2H_2O$$

Properties.—Potassium and sodium tartrate is in the form of "colorless, transparent, rhombic prisms, or as a white powder; odorless, and having a cooling, saline taste. The crystals slightly effloresce in dry air. One Gm. of Potassium and Sodium Tartrate dissolves in 0.9 ml of water at 25° C. (77° F.); almost insoluble in alcohol. An aqueous solution of the salt (1 in 20) is alkaline to litmus, but is not reddened by a drop of phenolphthalein T.S. When heated to about 74° C. (165.2° F.), the salt fuses to a colorless liquid, which at a higher temperature froths, becomes brown, and gradually carbonizes, while inflammable vapors are emitted, having the odor of burning sugar. Finally, a black residue is left, consisting of potassium and sodium carbonates with carbon. To a non-luminous flame this residue imparts an intensely yellow color. An aqueous solution of the salt (1 in 10) yields a white, crystalline precipitate with an equal volume of acetic acid. An aqueous solution of the salt (1 in 10) yields with silver nitrate T.S. a white precipitate which

becomes black on boiling. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). Five mils of an aqueous solution of the salt (1 in 10), when heated with potassium hydroxide T.S., does not evolve *ammonia*. Dissolve 10 Gm. of Potassium and Sodium Tartrate in 20 mils of distilled water, add 2 mils of sulphurous acid and boil the mixture until the odor of sulphur dioxide is barely perceptible. Cool the solution, mix it with 1 mil of sodium cyanide T.S. and follow this immediately with stronger ammonia water until the precipitate formed is redissolved and the solution has a slight odor of ammonia. When cold, transfer the solution to a glass-stoppered cylinder, graduated to 50 mils, dilute it with sufficient distilled water to measure 50 mils and add 3 drops of sodium sulphide T.S. After mixing well, the color produced in the solution, if any, when viewed downward against a white surface, is not greater than the color of a control solution prepared as follows: Dissolve 2 Gm. of ammonium chloride (see Reagents, Part III) in 20 mils of distilled water, add 4 mils of a solution containing 0.08 Gm. of lead nitrate in 1000 mils of distilled water, and then 1 mil of diluted hydrochloric acid. Treat this solution with the same quantity of hydrochloric acid, sulphurous acid, sodium cyanide T.S. and stronger ammonia water, as used above, transfer it to another 50 mil glass-stoppered cylinder, and then dilute it with sufficient distilled water to make 50 mils and add 3 drops of sodium sulphide T.S. (before adding the sodium sulphide T.S., the liquid must possess a distinct odor of ammonia, and the two cylinders used must be matched, be of practically colorless glass, and have the same internal diameter) (*lead*).

"**Assay.**—Proceed as directed under the Assay for alkali salts of organic acids (see Part III, Test No. 6). It shows not less than 73.72 per cent. nor more than 77.39 per cent. of $KNaC_4H_4O_6$.

"Each mil of half-normal sulphuric acid V.S. used corresponds to 0.05253 Gm. of $KNaC_4H_4O_6$. Each gramme of Potassium and Sodium Tartrate corresponds to not less than 14.03 mils nor more than 14.73 mils of half-normal sulphuric acid V.S." *U. S.*

"Trimetric prisms with hemihedral facets. Taste saline, cooling. Soluble in 1.5 parts of *water;* aqueous solution neutral to *litmus*. Yields the reactions characteristic of potassium, of sodium, and of tartrates. 1 gramme, heated to redness till gases cease to be evolved, leaves an alkaline residue which, when treated with *water,* filtered, and well washed, yields a clear solution requiring for neutralisation not less than 13.9 millilitres of *N/2 solution of sulphuric acid.* Yields no characteristic *reactions* for copper, iron, calcium, ammonium, chlorides, or sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 2 parts per million." *Br.*

When the salt is exposed to a very strong heat, it becomes blackened, and gives out inflammable gases with the odor of burnt sugar, the tartaric acid being destroyed, and a mixture of potassium and sodium carbonates left. It sometimes contains calcium tartrate, which may be removed by solution and crystallization, but when the crystals are large and well defined, it may be assumed to be pure. It is incompatible with most acids, and with nearly all acid salts except potassium bitartrate. It is also decomposed by lead acetate and subacetate, silver nitrate, and by the soluble calcium and barium salts unless the solution of the tartrate be considerably diluted.

The way in which the acids act in decomposing potassium and sodium tartrate is by combining with the sodium, and throwing down potassium bitartrate as a crystalline precipitate. This double salt was discovered by Seignette, an apothecary of Rochelle, and hence is frequently called *Seignette's salts* or *Rochelle salt.*

Uses.—This salt is a mild, cooling purgative, well suited to delicate and irritable stomachs, being among the mildest and least unpalatable of the neutral salts. As it is not incompatible with tartar emetic, it may be associated with that salt in solution. It is an ingredient in the effervescing aperient called Seidlitz powders. (See *Pulvis Effervescens Compositus.*) When given in small and repeated doses it usually does not act as a purgative, but is absorbed and renders the urine alkaline. (Millon and Laveran, *J. P. C.,* 3e sér., vii, 222.)

Potassium and magnesium tartrate, formed by saturating cream of tartar with magnesium carbonate, has been proposed by Maillier for use as a safe, pleasant purgative.

Dose, as a purge, from half an ounce to an ounce (15.5–31 Gm.).

Off. Prep.—Pulvis Effervescens Compositus, *U. S.* (*Br.*).

POTASSII HYDROXIDUM. U. S. (Br.)

POTASSIUM HYDROXIDE Pot. Hydrox. [Potassium Hydrate, Caustic Potash, Potassa, U. S. 1890]

(pŏ-tăs'sĭ-ī hȳ-drŏx'ĭ-dŭm)

"It contains not less than 85 per cent. of KOH (56.11). Preserve it in well-closed containers. If bottles are used they must be made of hard glass." *U. S.* "Potassium Hydroxide may be obtained by the interaction of potassium carbonate and calcium hydroxide. It contains not less than 85 per cent. of pure potassium hydroxide, KOH." *Br.*

Potassa Caustica, *Br.;* Kali Purum; Caustic Potassa, Hydrate of Potassa, Potassæ (Potassii) Hydras, Kali Hydricum Fusum, Lapis Causticus Chirurgorum; Potasse caustique *Fr. Cod.;* Potassee Fondue, Pierre à cautère, *Fr.;* Kali Causticum Fusum, *P. G.;* Kaliumhydroxyd, Kalium-Hydrat, Kaustisches Kali, Ætzkali, *G.;* Potassa caustica, *It.;* Hidrato potasico, *Sp.*

"Take of Solution of Potash, *two pints* [Imperial measure]. Boil down the Solution of Potash rapidly in a [clean] silver vessel, until there remains a [clear] fluid of oily consistence, a drop of which when removed on a warm glass rod solidifies on cooling. Pour this into proper moulds, and when it has solidified, and while it is still warm, put it into stoppered bottles." *Br.,*

1885. A process for potassium hydroxide is no longer in the U. S. Pharmacopœia; that of 1870 is identical with the British (1885).

The solid alkali obtained from these processes is potassium hydroxide, sufficiently pure for medicinal purposes. The solution of the alkali freed from carbonic acid having been obtained by another formula (see *Liquor Potassii Hydroxidi*), the formation of the present salt requires merely the evaporation of this solution until nearly the whole of its uncombined water is driven off. The evaporation must be performed in metallic vessels, as those of glass or earthenware are acted on by the alkali, and it should be completed as quickly as possible, in order to abridge the period during which the solution would be liable to absorb carbon dioxide from the atmosphere. When poured out on a metallic plate or dish, the cake, just as it solidifies, may be marked with a knife in the direction in which it is to be divided, and when cold it readily breaks in those directions. A better plan, however, is to run the fused alkali into suitable moulds, as directed in the former U. S. and British formulas. These should be made of silver or iron and have a cylindrical shape, which is the most convenient form of the alkali for surgical use. Green glass bottles with rubber stoppers are best adapted for preserving this preparation, as white flint glass is attacked by the alkali. Potassium hydroxide is now prepared at Niagara Falls, N. Y., by the electrolysis of strong potassium chloride solution. The metal at the cathode acts with water to form potassium hydroxide and free hydrogen, while chlorine is liberated at the anode, and is used in making bleaching powder which is thus prepared simultaneously.

Properties.—It is officially described as in "dry, white, or nearly white, fused masses, or sticks, hard and brittle, showing a crystalline fracture; odorless. *Great caution is necessary in handling it,* as it rapidly destroys organic tissues. When exposed to the air, it readily absorbs carbon dioxide and moisture, and deliquesces. One Gm. of Potassium Hydroxide dissolves in 0.9 mil of water, about 3 mils of alcohol, and in 2.5 mils of glycerin at 25° C. (77° F.); also in 0.6 mil of boiling water; very soluble in boiling alcohol. An aqueous solution of Potassium Hydroxide even when greatly diluted is strongly alkaline to litmus. When introduced into a non-luminous flame, it imparts to it a violet color. An aqueous solution of Potassium Hydroxide (1 in 20) is clear and colorless (*organic matter or insoluble impurities*). An aqueous solution of Potassium Hydroxide (1 in 10), when added to an excess of tartaric acid T.S., produces a white, crystalline precipitate, which redissolves when the Potassium Hydroxide is added in excess. An aqueous solution of Potassium Hydroxide (1 in 50), slightly acidulated with hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Dissolve in a 500 mil graduated flask about 10 Gm. of Potassium Hydroxide, accurately weighed in a glass-stoppered weighing-bottle, in 250 mils of distilled water, which has previously been boiled and cooled, and add 30 mils of barium chloride T.S. Now fill the flask to the mark with distilled water, which has previously been boiled and cooled, and thoroughly agitate the liquid. Then filter the liquid in the flask through a dry filter into a dry flask, rejecting the first 20 mils, and titrate 200 mils of the clear filtrate with normal hydrochloric acid V.S., using phenolphthalein T.S. as indicator. It shows not less than 85 per cent. of KOH when calculated to the amount originally taken.

"Each mil of normal hydrochloric acid V.S. used corresponds to 0.05611 Gm. of KOH. Each gramme of Potassium Hydroxide corresponds to not less than 15.15 mils of normal hydrochloric acid V.S." *U. S.*

"In hard white pencils or cakes, very deliquescent, very alkaline and corrosive. Soluble in 0.5 part of *water,* and in 3 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of potassium. 1 gramme dissolved in *water* or in *alcohol* (90 per cent.) leaves only a slight sediment; the solution requires for neutralisation not less than 15.1 millilitres of *N/1 solution of sulphuric acid.* Yields no characteristic *reactions* for lead, copper, or arsenic." *Br.*

It is important that the requirements of the Pharmacopœia be complied with, and that it should contain not less than 85 per cent. of pure potassium hydroxide.

The *white stick caustic potassa* as found in commerce usually contains from 15 to 28 per cent. of water, which seems to be a necessary impurity, for if a certain quantity of water is not present it is impossible to mould the stick. By heating this so as to drive off the water a purified hydroxide in cakes may be obtained. On account of its deliquescent property, and its strong attraction for carbon dioxide, potassium hydroxide requires to be kept in very accurately stoppered bottles. Official potassium hydroxide may be rendered nearly pure by digestion in alcohol, which takes up only the alkaline hydroxide, evaporating the solution to dryness, and fusing the dry mass obtained. *Potassium hydroxide,* when thus procured, is called *potash by alcohol.* It is generally in flat white pieces, which are dry, hard, brittle, and extremely caustic. Its other properties are similar to those of the impure hydroxide above described. According to H. Wurtz, of New York, commercial potash by alcohol usually contains a trace of potassium silicate, which appears to be taken up by the alcohol. The source of this is the potassium carbonate employed, which may be freed from this impurity by evaporating its aqueous solution, in a sheet iron dish, to dryness, and adding, from time to time, lumps of ammonium carbonate. The silicate is thus converted into the carbonate, and on dissolving the residue the silica appears in flakes, which may be separated by filtration. Potassium hydroxide may be distinguished from the other fixed alkalies (soda and lithia) by its affording, when in solution, a crystalline precipitate (cream of tartar) with an excess of tartaric

acid, and a yellow one with platinic chloride. Potassium hydroxide imparts to the flame of burning alcohol in which it is dissolved a lilac tint; sodium hydroxide colors it yellow even in the presence of potassium hydroxide; and thus a method is afforded of detecting an admixture of the latter with the former alkali. According to Bunsen, when the flame is viewed through a glass having a cobalt-blue color, only the color imparted by potassium is seen, the yellow color of the sodium flame being absorbed by the blue glass. (*J. P. C.*, Oct., 1860, p. 319.) Potassium hydroxide, KOH, is composed of one atom of potassium, united with one hydroxyl group, OH.

Uses.—Probably because of its powerful effect in dissolving the bodily tissues potassium hydroxide is a very potent escharotic. It is the old *causticum commune acerrimum* or *strongest common caustic.* (For description of potassa with lime which was formerly official, see *U. S. Dispensatory,* 19th edition, page 1004.) Its action is not only very thorough, but it penetrates more deeply than either silver nitrate or nitric acid. It is also powerfully germicidal; although Sternberg found that it required a ten per cent. solution to destroy pus cocci in two hours, most authorities agree that one per cent. is sufficient to kill all vegetating bacteria. Because of difficulty of controlling its action it is not commonly employed for the destruction of benign growths as *warts,* but in *poisoned bites,* especially by *rabid animals,* the thoroughness of its action is an advantage.

The most convenient mode of employing the caustic for the formation of an issue is to apply to the skin a piece of linen spread with adhesive plaster, having a circular opening in its center corresponding with the intended size of the issue, and then to rub upon the skin, within the opening, a piece of the caustic previously moistened at one end. The application is to be continued until the life of the part is destroyed, when the caustic should be carefully washed off with a wet sponge, or wet towl, or neutralized by vinegar. In forming from it solutions of potassium hydroxide of definite strength, whether for medicinal or for pharmaceutical use, an allowance should be made for the percentage of water it always contains. (See *Liquor Potassii Hydroxidi.*)

Off. Prep.—Liquor Potassii Hydroxidi, *U. S.* (*Br.*); Liquor Picis Alkalinus, *N. F.*; Potassa cum Calce, *N. F.*

POTASSII HYPOPHOSPHIS. U. S.

POTASSIUM HYPOPHOSPHITE Pot. Hypophos.

(pŏ-tā'sĭ-ī hī-pŏ-phŏs'phĭs)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 98 per cent. of KPH_2O_2 (104.16). Preserve it in well-closed containers in a dry place. Caution should be observed in dispensing Potassium Hypophosphite, as an explosion is liable to occur when it is triturated or heated with nitrates, chlorates, or other oxidizing agents." *U. S.*

Kali Hypophosphorosum, Hypophosphis Potassicus, s. Kalicus; Hypophosphite de Potasse, *Fr.*; Unterphosphorigsaures Kali, *G.*

This salt is prepared by mixing solutions of calcium hypophosphite and granulated potassium carbonate, in the proportion of 6 ounces of the former dissolved in four pints of water to 5.75 ounces of the latter in half a pint. As a result of double decomposition between the two salts, calcium carbonate and *potassium hypophosphite* are formed, the former being precipitated, and the latter held in solution.

$$Ca(H_2PO_2)_2 + K_2CO_3 = CaCO_3 + 2KH_2PO_2$$

The calcium carbonate is removed by filtration, and the clear solution is evaporated until a pellicle forms, after which it is constantly stirred, with continuance of the heat, until the salt granulates. The heat employed in the evaporation should be kept considerably below 100° C. (212° F.), for fear of explosion. If the salt be required pure, it should be dissolved in the granulated state, in official alcohol, and the solution evaporated to a syrupy consistence and then set aside to crystallize. The calcium hypophosphite may be prepared by a formula given under the head of *Calcii Hypophosphis.*

Properties.—"Potassium Hypophosphite occurs as white, opaque, hexagonal plates, or crystalline masses, or as a granular powder; odorless, and having a pungent, saline taste; very deliquescent. One Gm. of Potassium Hypophosphite dissolves in 0.6 mil of water and in 9 mils of alcohol at 25° C. (77° F.); also in 0.4 mil of boiling water and in 5 mils of boiling alcohol. An aqueous solution of the salt (1 in 20) is neutral or slightly alkaline to litmus and yields with sodium bitartrate T.S. a white, crystalline precipitate. When heated in a dry test tube spontaneously inflammable hydrogen phosphide is evolved which burns with a bright yellow flame. When an aqueous solution of the salt (1 in 20), acidulated with hydrochloric acid, is added drop by drop with agitation to an excess of mercuric chloride T.S., a white precipitate of mercurous chloride is formed. Upon the further addition of the solution of Potassium Hypophosphite, the precipitate becomes gray from reduction to metallic mercury. A solution of 1 Gm. of the salt in about 10 mils of distilled water requires not more than 1.5 mils of tenth-normal hydrochloric acid V.S. for neutralization, methyl orange T.S. being used as indicator. Heat 5 mils of an aqueous solution of the salt (1 in 5) with 0.5 mil of diluted hydrochloric acid in a test tube on a water bath for thirty minutes; no offensive odor is developed. Measure 5 mils of an aqueous solution of Potassium Hypophosphite (1 in 25) into a beaker containing 3 mils of nitric acid diluted with about 10 mils of distilled water, and evaporate the mixture to dryness on a water bath; the residue meets the requirements

of the Test for arsenic (see Part III, Test No. 1). Add magnesia mixture T.S. to 10 mils of an aqueous solution of the salt (1 in 20) made alkaline with ammonia water; it is not affected within one minute (*phosphates*).

"**Assay.**—Dissolve about 1 Gm. of Potassium Hypophosphite, dried to constant weight in a desiccator over sulphuric acid and accurately weighed, in 10 mils of distilled water, add 10 mils of nitric acid and evaporate it to dryness on a water bath. Then add 5 mils of nitric acid and again evaporate it to dryness on a water bath. Dissolve the residue in 20 mils of distilled water, add a drop of phenolphthalein T.S. and sufficient special potassium hydroxide T.S. (see page 545) to produce a pink color, and then dilute it to exactly 100 mils with distilled water. Transfer 10 mils of this solution to a 100 mil graduated flask, add 50 mils of tenth-normal silver nitrate V.S. and proceed from this point as directed in the assay under *Sodii Phosphas* (see page 1036). When calculated to the amount originally taken, it shows, in the dried salt, not less than 98 per cent. of KPH_2O_2.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.003472 Gm. of KPH_2O_2. Each gramme of Potassium Hypophosphite, previously dried, corresponds to not less than 282.3 mils of tenth-normal silver nitrate V.S." *U. S.*

Uses.—This salt was introduced along with the other hypophosphites because of the claims made by Churchill of their curative value in *phthisis* (see *Acidum hypophosphorosum*), but has no therapeutic virtues justifying its continued recognition by the Pharmacopœia.

Dose, ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Syrupus Hypophosphitum, *U. S.;* Elixir Hypophosphitum, *N. F.;* Elixir Hypophosphitum et Ferri, *N. F.;* Emulsum Olei Morrhuæ cum Hypophosphitibus, *N. F.;* Liquor Hypophosphitum, *N. F.;* Liquor Hypophosphitum Compositus, *N. F.;* Syrupus Hypophosphitum Compositus, *N. F.*

POTASSII IODIDUM. U. S., Br.

POTASSIUM IODIDE Pot. Iod.

(pŏ-tăs'sĭ-ī ī-ŏd'ĭ-dŭm)

"It contains, when dried to constant weight at 100° C. (212° F.), not less than 99 per cent. of KI (166.02). Preserve it in well-closed containers." *U. S.* "Potassium Iodide may be obtained by adding a slight excess of iodine to a strong solution of potassium hydroxide, evaporating to dryness, fusing with charcoal, and purifying by crystallisation. When dried at 100° C. (212° F.) it contains not less than 99 per cent. of pure potassium iodide, KI." *Br.*

Iodide of Potassium; Potassii Hydriodas; Kali Hydriodicum, Ioduretum Potassicum, s. Kalicum; Iodure de Potassium, *Fr. Cod.;* Kalium Jodatum, *P. G.;* Kaliumjodid, Jodkalium, *G.;* Joduro di potassio, *It.;* Yoduro potasico, *Sp.*

No process is given in the U. S. or Br. Pharmacopœias. That of the U. S. P., 1870, did not differ essentially from the British, 1885. (See *U. S. Dispensatory,* 19th edition, page 1005.)

An aqueous solution of potassium hydroxide is treated with iodine in slight excess. The result of thus saturating potassium hydroxide with iodine is the formation of two salts, *potassium iodide and iodate.* Six atoms of iodine react with six molecules of potassium hydroxide, and there are formed five molecules of potassium iodide and one of potassium iodate,

$$6KOH + 3I_2 = 5KI + KIO_3 + 3H_2O$$

By evaporating the solution to dryness the mixed salts are obtained, and, if the dry mass be exposed to a red heat, the iodate will be converted into iodide, thus removing this impurity from the iodide. In the formula the mixed salts, towards the close of their evaporation to dryness, are directed to be mixed with powdered charcoal, according to the plan of Scanlon, which facilitates the deoxidation of the iodate.

$$KIO_3 + 3C = KI + 3CO$$

This being accomplished by a dull red heat, the potassium iodide is dissolved out of the mass, and the solution is set aside to crystallize.

In the older processes the first step was to form ferrous iodide in solution, precisely as is done in the formula for that compound, and the second to decompose it by potassium carbonate, which gave rise to potassium iodide in solution, and a precipitate of ferrous carbonate. The solution of potassium iodide was separated by filtration and washing from the precipitated carbonate, and evaporated to dryness. The dry salt was then freed from iron and other impurities by solution in boiling water or alcohol, filtration, and crystallization. This method is analogous to that described under potassium bromide, which see. An improvement on this process is to add enough iodine to the ferrous iodide solution first formed to produce ferrous-ferric iodide, $Fe_3I_8(2FeI_3 + FeI_2)$. This solution is now treated with an equivalent quantity of potassium carbonate and boiled when ferrous-ferric oxide precipitates, carbon dioxide escapes, and all the iodine goes into solution as iodide, the reaction being:

$$Fe_3I_8 + 4K_2CO_3 = Fe_3O_4 + 8KI + 4CO_2$$

According to the method of E. Sonstadt, potassium iodide is prepared directly from the mother liquors of kelp by converting the alkaline iodides into iodates by means of chlorine or potassium permanganate, precipitating the iodic acid by a soluble barium salt, heating the precipitate with solution of potassium sulphate, evaporating the resulting potassium iodate solution to dryness, and crystallizing from its solution the potassium iodide thus obtained. (*Chem. News,* xxvi, 182.) Or, these mother liquors are evaporated to dryness, the mass gently roasted to oxidize sulphides, and then extracted with water, evaporated again to dryness and extracted with alcohol, whereby sodium and potassium iodide go into solution. This is treated

with potassium carbonate to change the sodium iodide into potassium iodide, and a stream of CO_2 led through to precipitate the sodium bicarbonate. The remaining solution contains potassium iodide with a little sodium bicarbonate. (Flückiger, *Pharm. Chem.*, 2d ed., 1888, p. 341.) Large quantities are now manufactured from the cuprous iodide coming from the South American sodium nitrate works. The cuprous iodide is suspended in water acidified with hydrochloric acid, and a stream of hydrogen sulphide gas let in, whereby hydrogen iodide enters into solution. This solution is filtered, neutralized with potassium carbonate, and evaporated to crystallization.

$$CuI_2 + H_2S = CuS + 2HI$$
$$2HI + K_2CO_3 = 2KI + H_2O + CO_2$$

Properties.—Potassium iodide, sometimes incorrectly called *hydriodate of potassa*, is in "cubical crystals either transparent and colorless or more or less opaque and white, or as a white, granular powder, having a pungent, saline, afterwards bitter taste. Permanent in dry air, and but slightly deliquescent in moist air. One Gm. of Potassium Iodide dissolves in 0.7 mil of water, 22 mils of alcohol, and in 2 mils of glycerin at 25° C. (77° F.); also in 0.5 mil of boiling water and in 8 mils of boiling alcohol. An aqueous solution of the salt (1 in 20) is neutral or slightly alkaline to litmus. When heated, the salt decrepitates. At a low red heat it fuses, and at a bright red heat it is volatilized without decomposition. Five mils of an aqueous solution of Potassium Iodide (1 in 20) yields a white, crystalline precipitate with 5 mils of sodium bitartrate T.S. Add 1 mil of ferric chloride T.S., diluted with an equal volume of distilled water, to 5 mils of an aqueous solution of the salt (1 in 20), and shake the mixture with 5 mils of chloroform; the latter acquires a violet color. Dissolve 1 Gm. of the salt in 10 mils of distilled water and add 0.1 mil of tenth-normal sulphuric acid V.S.; no color is produced by the subsequent addition of a drop of phenolphthalein T.S. (*alkali*). Add 2 drops of diluted sulphuric acid (free from sulphurous and nitrous acids) to 0.5 Gm. of the salt dissolved in 10 mils of distilled water, which has previously been boiled and cooled; no distinct yellow color appears within half a minute (*iodate*), and no turbidity occurs (*thiosulphate*). Acidulate 10 mils of an aqueous solution of the salt (1 in 20) with hydrochloric acid; it is not rendered turbid by the addition of 1 mil of potassium sulphate T.S. (*barium*); another 10 mil portion of an aqueous solution of the salt (1 in 20), acidulated with hydrochloric acid, is not rendered more than slightly turbid by a few drops of barium chloride T.S. (*sulphate*). Heat gently 5 mils of an aqueous solution of the salt (1 in 10) with one drop of ferrous sulphate T.S. and 0.5 mil of potassium hydroxide T.S.; no blue color appears after acidulating the mixture with hydrochloric acid (*cyanide*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Dry the salt to constant weight and proceed as directed under the Assay for iodides (see Part III, Test No. 5). It shows, in the dried salt, not less than 99 per cent. of KI.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.016602 Gm. of KI. Each gramme of Potassium Iodide, previously dried, corresponds to not less than 59.6 mils nor more than 61.0 mils of tenth-normal silver nitrate V.S." *U. S.*

"Colorless, generally opaque, cubic crystals. Taste saline, slightly bitter. Soluble in less than 1 part of *water*, and in 12 parts of *alcohol* (90 per cent.). Usually slightly alkaline to *litmus*. Yields the *reactions* characteristic of potassium and of iodides. Loses not more than 1 per cent. of its weight when dried at 100° C. (212° F.); 0.5 gramme of this dried salt requires for complete precipitation not less than 29.8 nor more than 30.5 millilitres of *N/10 solution of silver nitrate*. Yields no characteristic *reactions* for copper, iron, aluminium, calcium, magnesium, bromates, cyanides, or nitrates, and not more than the slightest reactions for bromides, iodates, carbonates, or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

According to T. and H. Smith, of Edinburgh, it is not at all deliquescent when perfectly pure. It generally crystallizes in cubes. If solution of potassium iodide be mixed with solution of starch, and a minute quantity of solution of chlorine be added, a blue color will be produced, the chlorine combining with the potassium liberating the iodine, which forms a blue compound with starch.

R. Van Vorst has pointed out (*Ph. Ztg.*, 1914, p. 342) that the red spots seen sometimes upon crystals of potassium iodide are not always due to free iodine, as in a case which he investigated the salt dissolved to a colorless solution leaving an insoluble red precipitate, which upon closer investigation was found to be the cell structure of a microscopic form of mold.

Its solution is quickly decomposed by the addition of a few drops of sulphuric acid, hydriodic acid being generated, which speedily undergoes decomposition, with evolution of iodine, and, if starch be added after the lapse of a few minutes, a blue color will be produced. The starch test will not give the characteristic blue color immediately, if added simultaneously with the acid, unless the potassium iodide contains potassium iodate, which impurity causes an immediate liberation of iodine. The blue color being produced by the starch and acid, if simultaneously added, is, therefore, a sign of impurity. Hydrogen dioxide solution may be used in this test as it causes the liberation of free iodine from soluble iodides. A very delicate test for potassium iodide and other soluble iodides is that of Grange. It consists in pouring a little of the liquid to be examined into a test tube, adding a few drops of solution of starch, and passing through the mixture a few

bubbles of fuming nitrous acid. The liquid immediately assumes a pale rose color, inclining to violet, if containing 1-200,000th of its weight of the iodide, and a bright blue color if 1-100,000th is present. (See page 591.) When tartaric acid is freely added to a strong solution of the iodide, it occasions a white crystalline precipitate, and the supernatant liquid, if mixed with starch, becomes first purple, and finally blue. The aqueous solution is capable of taking up a large quantity of iodine, forming a liquid of a deep brown color.

Payen has noticed a curious effect produced by potassium iodide. In saturated solution, this salt causes in starch added to it an enlargement of its granules to twenty-five or thirty times their original volume, dissolving the interior substance of the granules, and enormously distending the exterior layer. Potassium bromide produces the same effect, but the alkaline chlorides cause neither the enlargement referred to, nor a solution of the amylaceous substance, and if the saturated solution of the iodide be diluted with three and a half volumes of water or more, it is inert in reference to starch in the cold. (*J. P. C.*, 4e sér., ii, 373.) Ferières found that ether added to a solution of potassium iodide decomposes it, but it was stated by the researches of de Vrij and of Magnes-Lahens that this does not happen with pure ether, but is due to the acetic acid which is developed by sunlight in ether. (*J. P. C.*, 4e sér., xvi, 107, 468; xvii, 116.) This change is now known to be due to minute amounts of peroxide which are present in ether which has been exposed to air.

Exposed to a dull red heat, potassium iodide fuses, and on cooling concretes into a crystalline pearly mass, without loss of weight; but at a full red heat it is slowly volatilized without decomposition. The most usual impurities contained in this salt are potassium and sodium chlorides, potassium bromide, and potassium carbonate and iodate. Potassium iodide, to conform to the U. S. P. IX, must contain 99 per cent. of the pure salt.

The low price of potassium bromide, compared with that of the iodide, has caused the former to be used for the adulteration of the latter. When potassium bromide is sold for the iodide, the fraud may be detected by the fact that the addition of sulphuric acid produces copious reddish fumes, instead of the purple ones arising from the iodide. A very delicate test for bromide in iodide is based upon the different actions of iodide and bromide with lead dioxide. This reagent will liberate iodine from iodide on boiling, but will not decompose any bromine by boiling. Therefore, after the suspected sample has been boiled with the lead dioxide until all the iodine is driven off, and then filtered, the filtrate may be treated with fresh dioxide and a little acetic acid, when any bromine present is decomposed, and the free bromine will color carbon disulphide or answer other tests. (Flückiger, *Pharm. Chem.*, 2d ed., 1888, p. 350.)

In order to detect bromine, Personne first precipitated from an aqueous solution of the suspected iodide the whole of the iodine as cuprous iodide, by successively adding, in excess, a solution of copper sulphate and aqueous sulphurous acid, and then treats the filtered liquid with ether and chlorine water, the whole being shaken together and left at rest. If bromine be present, the ether which rises to the surface will be tinged of a reddish-yellow color. Fresenius's test of gold chloride is, according to J. H. Bill, of the U. S. Army, very delicate. The iodine having been separated by palladium, and the excess of palladium by hydrogen sulphide, the solution supposed to contain bromine, if treated first with a drop of hydrochloric acid, and then with a drop of solution of gold chloride, will, if bromine be present, exhibit a decided yellowness, which will appear more obviously if the solution be compared with pure water or a weak solution of a chloride. (See *A. J. P.*, 1868, 272.) Potassium carbonate may be detected by lime water, which causes a milkiness (calcium carbonate), and by tincture of iodine, the color of which is destroyed. The iodate may be detected by adding a solution of tartaric acid to a solution of the suspected iodide. Potassium bitartrate will be precipitated, and, if the iodide be pure, a yellow color will, *after a short time,* be developed by the action of the air on the liberated hydriodic acid; but if any iodate be present the test will give rise to both iodic and hydriodic acids, which, by their mutual action, will *instantly* develop iodine.

According to Payen, a saturated solution of potassium iodide, which will evince signs of decomposition by becoming orange-yellow, in the presence of atmospheric air, on the addition of small quantities of acetic, nitric, oxalic, and probably many other acids, remains unaffected by these additions if atmospheric air be excluded. It was first pointed out by Loew (*A. J. P.*, xlii, 80), and afterwards confirmed by Vidau in an elaborate series of experiments, that iodine is liberated from a solution of potassium iodide by direct sunlight; the more concentrated the solution the more energetic is the action. (*J. P. C.*, 4e sér., xx, 351.)

Potassium iodide is incompatible with a few alkaloids, calomel, mercurous and mercuric oxides, turpeth mineral, white precipitate, blue mass, and metallic mercury. Melsens observed that potassium iodide given in connection with the insoluble preparations of mercury rendered them soluble and much more active. (See *A. J. P.*, xxvi, 222.) With nitrous ether potassium iodide reacts, yielding, among other products, ethyl iodide and a little ordinary ether. (Juncadella, *C. R. A. S.*, Fév., 1859, p. 345.) At ordinary temperatures potassium iodide is slowly decomposed, with evolution of iodine, by ammonium nitrate or boric acid, and at high temperatures, in a glass test tube, with escape of violet vapors, not only by the two substances just named, but also by ammonium sulphate, oxalate, carbonate, and chloride, sodium sulphate, phosphate, nitrate, and borate, potassium and magnesium sulphates, calcium nitrate,

sodium, potassium, and calcium chlorides, and silicic acid. (Ubaldini, *J. P. C.*, Oct., 1859, p. 292.) Melsens has noticed another very important fact in relation to the operation of potassium iodide. When this salt and potassium chlorate are mixed in solution, no change takes place at ordinary temperatures; but if a certain amount of a mineral acid be added to the solution of the mixed salts, a reaction occurs, attended with the escape of iodine, and evidences are presented of the existence of iodic acid in the solution. Now, Melsens has ascertained by experiments on dogs that neither of these salts, if given separately and at different times, produces an evil effect, while if given together, so as to be in the system at the same time, they act as a poison, and may cause death in a few days. Seven grammes (108 grains) of a mixture of potassium iodide and potassium chlorate, in equivalent proportions, given daily to a dog of medium size, uniformly proved fatal in less than a month, and often as early as the fifth day. Melsens ascribed the result to the production of potassium iodate, which he has shown to be a poisonous salt. (*A. J. P.*, Nov., 1866, p. 521; from *Bull. Soc. Chim.*) With certain alkaloids potassium iodide is incompatible, partly on account of the fact that it is permitted to contain a little alkaline carbonate to retard discoloration, and partly because with some alkaloids insoluble iodides are formed, and fatal results have been caused by the strychnine iodide crystallizing out of a prescription, so that the whole of it was taken at a single dose.

Uses.—The general therapeutic properties of potassium iodide are the same as those of iodine. (See page 591.) Like the other salts of this element, potassium iodide is useful especially in *syphilis, chronic fibrinous inflammations,* and certain *metallic poisons.* With corrosive sublimate it forms a soluble potassio-mercuric iodide which is the basis of the so-called *mixed treatment* for *syphilis.* When it is administered in large repeated doses it produces evidences of systemic affection, known as *iodism.* The most usual indication of its constitutional action is a pain over the brow, with coryza; in some cases a mild ptyalism, with fetor of the breath and slight swelling of the gums, is produced. In a number of cases it causes an eruption, sometimes simply of macula, but usually of acne and occasionally bullous or hemorrhagic. In unusual conditions of the system these skin affections may become very severe and ulcerations result. Knowles (*J. A. M. A.*, 1910, lv, p. 100) gives an extensive bibliography of the literature of this subject.

The dose of potassium iodide varies enormously, many persons will show symptoms of iodism from twenty grains (1.3 Gm.) a day, but other cases as much as one or two drachms (3.9–7.7 Gm.) have been given three times a day without toxic symptoms. Many clinicians believe that syphilitics are abnormally tolerant of the drug.

Potassium iodide is eliminated through the urine unchanged and may be detected by acidulating with nitric acid which causes the liberation of the free iodine, and by testing with starch.

Potassium iodide is employed as an external application in the form of ointment, either alone or mixed with iodine. (See *Unguentum Potassii Iodidi* and *Unguentum Iodi.*)

Dose, five to twenty grains (0.32–1.3 Gm.); in special cases much larger doses may be exhibited.

Off Prep.—Linimentum Potassii Iodidi cum Sapone, *Br.;* Liquor Iodi Compositus, *U. S.* (*Br.*); Tinctura Iodi, *U. S., Br.;* Unguentum Iodi, *Br., N. F.;* Unguentum Potassii Iodidi, *U. S., Br.;* Liquor Hydrargyri et Potassii Iodidi, *N. F.;* Tinctura Iodi Fortior, *N. F.*

POTASSII NITRAS. U. S., Br.

POTASSIUM NITRATE Pot. Nit.
[Nitre Saltpetre]

(pŏ-tăs'sĭ-ī nī'trās)

"In contains, when dried to constant weight at 100° C. (212° F.), not less than 99 per cent. of KNO_3 (101.11). Preserve it in well-closed containers." *U. S.* "Potassium Nitrate, KNO_3, may be obtained by the interaction of sodium nitrate and potassium chloride." *Br.*

Potassæ Nitras; Nitrum Depuratum, Sal Petræ, s. Nitri, Nitras Potassicus, s. Kalicus; Nitrate of Potash, Nitre; Nitrate de Potasse, Azotate de Potasse, *Fr. Cod.;* Nitre prismatique, Salpêtre, *Fr.;* Kalium Nitricum, *P. G.;* Kaliumnitrat, Salpetersaures Kali, Salpeter, Kalisalpeter, *G.;* Nitrato di potassio, Nitro, *It.;* Nitrato potasico, *Sp.*

Potassium nitrate or *nitre,* is both a natural and an artificial product. It occurs in many countries, existing in the soil, on which it forms a saline efflorescence, in the fissures of calcareous rocks, and in caves. It has been found in different parts of Europe, in South Africa, in Egypt, and in Chili, Peru and Bolivia, but the country in which it has been most largely produced is India. In the United States it has been found in caverns situated in limestone rock, called saltpetre caves, where it is associated with calcium nitrate. A large proportion of the potassium nitrate consumed in the South, during the Civil War was obtained from such caves in Kentucky. Considerable deposits also occur in San Bernadino County in California, but have not been developed as yet (1916). At present it is chiefly obtained from deposits in India, or by acting on sodium nitrate with potassium chloride. Potassium nitrate exists also in the vegetable kingdom, having been found in tobacco, borage, bugloss, parietaria, hemlock, and the sunflower. The artificial sources are certain mixtures of animal and vegetable substances with wood ashes and calcareous matter, called nitre-beds, and certain materials impregnated with saltpetre, consisting principally of plaster rubbish, derived from the demolition of old buildings. The ashes of tobacco stems, consisting almost exclusively of potassium carbonate and chloride, have been proposed by Commaille as an artificial source of potassium

nitrate by adding them to the ordinary nitre-beds. (*J. P. C.*, Fév., 1856.)

The nitrifying bacteria, usually *B. nitrificans*, so common in nature, acting over a period of one or two years, which is necessary for these artificial nitre beds, form calcium nitrate first, which then reacts with the potassium carbonate of the wood ashes to form potassium nitrate, according to the following reaction:

$$Ca(NO_3)_2 + K_2CO_3 = 2KNO_3 + CaCO_3$$

Preparation from its Natural Sources.—In India the saline earth, which contains about seven parts of potassium nitrate in a thousand, is lixiviated in large mud filters lined with stiff clay, and furnished with false bottoms of bamboo, covered with grass mats, on which wood ashes are laid. The filters being then filled with the saline earth, water is added, and the solution filters through the wood ashes, with the effect of converting the calcium nitrate present, amounting to nearly 1 per cent., into potassium nitrate. The solution obtained is evaporated in earthen pots, filtered, and set aside to crystallize. The impure potassium nitrate thus obtained contains from 45 to 70 per cent. of the pure salt. It is redissolved and crystallized, and thrown into commerce under the name of crude saltpetre. Besides the nitre obtained in India by the filtration of the soil deposited during the overflow of the Ganges, it appears, from the report of J. W. Palmer, that much of the crude salt is procured, in the northwestern provinces of Hindostan, from the saline incrustations formed in and around the mud walls surrounding the dwellings of the natives. The scrapings from these sources are lixiviated, and the impure solution allowed to evaporate in shallow pans exposed to the sun. The impure nitre extracted from the earthy matters crystallizes out, while from 1 to 9 per cent. of sodium chloride remains in the mother liquor, and is recovered by evaporation. (*A. J. P.*, 1868, 436.) *Juar*, a plant used in India as fodder, contains in its stems during dry seasons a large quantity of potassium nitrate (17 per cent.); when in this condition it is poisonous to animals. (*P. J.*, 1896, 380.)

Within recent years potassium nitrate has been most largely manufactured from the native potassium chloride of Stassfurt and the native sodium nitrate of Chili, two cheap and abundant crude materials, which by their reaction yield potassium nitrate. For this purpose equal molecular quantities of the two salts are dissolved in water with the aid of heat until the specific gravity of the liquor reaches 1.5. The resulting sodium chloride, being less soluble in hot water, is precipitated, and the solution on cooling and agitation deposits the saltpetre as a fine powder. This so-called "conversion saltpetre" can be produced 99.9 per cent. pure nitrate.

Artificial Preparation.—Since the importations from Germany have been interrupted in 1914, the search for new sources of supply in the United States has been pushed actively. The chief sources so far developed are: the sea kelp from the Pacific coast, containing as much as 2.45 per cent. of K_2O; *alumite*, a natural hydrated double sulphate of potassium and aluminum found in southern Utah; certain lakes in Nebraska containing salines relatively rich in potassium chloride; flue dust from cement works and from blast furnaces, both of which yield soluble potash salts. *Artificial nitre beds* are formed of animal and vegetable remains, together with ashes and calcareous earth, which are mixed up with a portion of loose soil and placed under sheds, to shelter the mixture from the rain, while the sides are left open, to admit the free access of air. The mixture is disposed in little rangse or heaps, which are frequently turned over with a spade, and sprinkled with urine, as a substance containing a large quantity of nitrogen. At the end of two or three years the nitrogen is converted into nitric acid, and this, by reacting with the potassium compounds existing in the vegetable remains, forms nitre. When the contents of the bed contain about four ounces of the salt for every cubic foot of the materials, they are deemed fit to be lixiviated. The lixiviation is performed with boiling water, which is repeatedly thrown upon fresh portions of the mass, until the solution obtained is sufficiently strong. The lixivium is of a brown color, and contains chiefly potassium nitrate, but at the same time more or less of calcium and magnesium nitrates and of sodium chloride. The earthy nitrates are then decomposed by a solution from wood ashes, the potassium carbonate of which converts them into nitre and precipitates the earths. The solution being further evaporated, the common salt rises to the surface as a scum, and is removed. The solution is then allowed to cool, and the nitrate crystallizes in dirty-white crystals, called crude nitre. Calcium nitrate may be converted into nitre by adding it to a solution of potassium sulphate. Calcium sulphate is precipitated, and potassium nitrate remains in solution.

Theory of Nitrification.—The continuous formation of nitre in nitre earths and in artificial nitre beds result from the oxidation of the nitrogen of ammonia, thus generating nitric acid, the formation of which is facilitated by the presence of alkaline and earthy bases, with which the acid unites, but in reality depends upon the presence of nitrifying micro-organisms (*Bacillus nitrificans*), so that nitrification is not strictly an oxidation process, as was at one time supposed. The ammonia is derived, for the most part, from the organic remains in the nitre earths, and from the animal matter which is an essential ingredient in the artificial mixtures. According to Schoenbein, whose statement has been confirmed by Goppelsröder, the formation of the nitric acid is always preceded by that of nitrous acid.

Purification.—Potassium nitrate, as first obtained, either from natural or from artificial

sources, is called in commerce crude saltpetre, and requires to be purified before it can be used in medicine or in most of the arts. The process, which is founded principally on the fact that nitre is more soluble than common salt in hot water, is conducted in France as follows: Thirty parts of saltpetre are boiled with six parts of water, and the portion which remains undissolved or is deposited, consisting of common salt, is carefully removed. As the ebullition proceeds, a little water is added from time to time, to hold the nitre in solution. When common salt ceases to be separated, the solution is clarified with glue, and more water is added, at intervals, until the whole, including that previously added, amounts to ten parts. The clear solution is now transferred to large, shallow copper coolers, where it is agitated with wooden instruments to hasten the cooling and to cause the nitre to crystallize in small grains. The purification is completed by washing the salt with water, or a saturated solution of nitre, in a kind of wooden hopper with holes in the bottom stopped with pegs. The liquid employed is allowed to remain in contact with the nitre for several hours, after which it is permitted to drain off by taking out the pegs. The salt is now dried, and takes the name of purified nitre.

Properties.—Potassium nitrate occurs "as colorless, transparent, six-sided rhombic prisms, or a white, crystalline powder; odorless, having a saline taste and producing a cooling sensation in the mouth. Slightly hygroscopic in moist air. One Gm. of Potassium Nitrate dissolves in 2.8 mils of water and in 620 mils of alcohol at 25° C. (77° F.); also in 0.5 mil of boiling water; soluble in glycerin. Its aqueous solution (1 in 10) is neutral to litmus. When strongly heated, the salt melts without decomposition. At higher temperatures it evolves oxygen and is partly reduced to nitrite. When Potassium Nitrate is heated with charcoal, the mixture deflagrates. With sodium bitartrate T.S. an aqueous solution of the salt (1 in 20) yields a white crystalline precipitate. Mix an aqueous solution of Potassium Nitrate (1 in 10) in a test tube with a drop of diphenylamine T.S. and slowly add sulphuric acid so as to form a separate layer; a deep blue color appears at the line of contact. An aqueous solution of Potassium Nitrate does not respond to the Test for heavy metals (see Part III, Test No. 3). No yellow color appears when 0.1 Gm. of the dry salt is sprinkled upon 1 mil of concentrated sulphuric acid (*chlorate or perchlorate*).

"**Assay.**—Dissolve about 0.4 Gm. of Potassium Nitrate, previously dried to constant weight at 100° C. (212° F.) and accurately weighed, in 10 mils of hydrochloric acid in a small dish, and evaporate the solution to dryness on a water bath. Dissolve the residue in 10 mils of hydrochloric acid and again evaporate it to dryness on a water bath, continuing the heat until the residue, when redissolved in distilled water, is neutral to litmus. Transfer the residue with the aid of 25 mils of distilled water to a flask and proceed as directed under the Assay for chlorides (see Part III, Test No. 5), deducting from the amount of tenth-normal silver nitrate V.S. consumed, the amount which would be consumed by the chlorides present in an equivalent weight of the salt originally taken, and previously estimated by taking about 1 Gm. of the salt, accurately weighed, and proceeding as directed under the Assay for chlorides (see Part III, Test No. 5). It shows, in the dried salt, not less than 99 per cent. of KNO_3. Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.010111 Gm. of KNO_3. Each gramme of Potassium Nitrate, previously dried, corresponds to not less than 97.9 mils of tenth-normal silver nitrate V.S." *U. S.*

"White crystalline masses, or colorless fragments of six-sided rhombic prisms. Taste cool, saline. Soluble in 4 parts of *water*. Yields the *reactions* characteristic of potassium and of nitrates. Yields no characteristic *reactions* for copper, iron, aluminium, zinc, calcium, magnesium, sodium, ammonium, chlorides, iodides, or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

It is devoid of water of crystallization, but is apt to contain a portion of liquid mechanically lodged within the substance of the crystals. This is particularly the case with the large crystals, and, according to Berzelius, is a source of impurity, as the liquid in question is a portion of the mother water in which they were formed. It is on this account that Berzelius recommends that the solution of the purified salt should be stirred during crystallization, so as to cause it to shoot into small crystals. The fused mass, when cast in moulds, or formed into little circular cakes, constitutes that form of nitre found in commerce under the name of *crystal mineral* or *sal prunelle*. If the heat is increased, the salt is decomposed, evolves pure oxygen, and is reduced to the state of nitrite, which, in powder, emits orange-colored fumes of hyponitric acid, and nitrous oxide on the addition of sulphuric acid. Upon a further continuance of the heat, the nitrous acid itself is decomposed, and a large additional quantity of oxygen is evolved, contaminated, however, with more or less nitrogen. On account of the large proportion of oxygen which it affords, nitre increases the combustion of many substances in a remarkable degree. When thrown on burning coal, it deflagrates with bright scintillations. In the reaction of nitre with charcoal, carbon dioxide is produced, and never carbon monoxide, and the nitric acid is variously decomposed into nitrous oxide, nitrogen dioxide, or nitrogen, according to the proportion of the charcoal and to the heat employed. (A. Vogel, Jr.)

Potassium nitrate may be very readily recognized by its effect in increasing the combustion of live coals when thrown upon them, and by evolving white or reddish vapors on the addition of sulphuric acid. If the residue in this case weighs less than the amount calculated for potassium sulphate, part of it is probably

sodium sulphate, and the nitre tested may be assumed to have contained sodium nitrate. The most usual impurity is sodium chloride, which is seldom entirely absent, and which injures it for the manufacture of gunpowder. The refined or purified saltpetre of commerce is sufficiently pure for medicinal use. Potassium nitrate is composed of one atom of potassium in combination with one nitric acid group, which latter is monobasic.

Uses.—Potassium nitrate, when in sufficient concentration, acts upon a raw surface or a mucous membrane as a violent irritant, and taken internally in concentrated form produces violent burning pain, vomiting, purging, and other evidences of gastro-enteritis, which may end in collapse and death. Inflammation and ulceration of the mucous membrane are commonly found at the autopsies.

Potassium nitrate was formerly used extensively, and still is to a lesser extent, as a diuretic in *dropsy* and chronic *nephritis;* it has, however, no advantage over the vegetable salts and is much more prone to unduly irritate the kidney.

At one time potassium nitrate was used in very large doses in acute *rheumatism*, but the practice has passed out of vogue. An ounce taken in a little water has produced death, while recovery has been known from a dilute solution of several ounces. According to Lauter Brunton potassium nitrate has the same effect on the vascular system as the nitrite except that it is slower in its action. He recommends its use in the early stages of *arterio-capillary fibrosis* and other conditions of high arterial tension.

As a local remedy the nitrate is similar in its action to potassium chlorate, but it is probably less efficient, and certainly has been largely replaced by the chlorate in the treatment of *stomatitis, angina,* and local inflammations. In *asthma,* nitrous fumigation is often useful, performed by inhaling the fumes from burning torch paper, prepared by dipping blotting paper in a saturated solution of nitre and afterwards drying it. Such paper was official in the U. S. P. 1890. (See *Charta Potassii Nitratis,* Part III.) Vohl has examined the vapor resulting from the burning paper thus impregnated, and found it to consist of carbon dioxide and oxide, cyanogen, ammonia, nitrogen, aqueous vapor, and potassium carbonate and nitrite, and he ascribes the beneficial results of its inhalation to the ammonia and potassium nitrite. It is habitually added to stramonium leaves in the preparation of so-called asthmatic powders, but it is used under these circumstances more for its oxidizing effect in encouraging the combustion than for its own therapeutic action.

In pharmacy, potassium nitrate was formerly employed to form crocus of antimony, to procure nitric acid, and sometimes in the preparation of spirit of nitrous ether. In the laboratory it is used to make black and white flux, as an oxidizing agent, and to yield oxygen at a red heat. It was formerly employed in the production of aqua fortis (common nitric acid) and in the manufacture of sulphuric acid, and is yet employed in the fabrication of gunpowder. The Br. Pharmacopœia 1885 used it in the purification of bismuth.

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Charta Potassii Nitratis, *N. F.*

POTASSII PERMANGANAS. U. S., Br.

POTASSIUM PERMANGANATE Pot. Permang.

(pŏ-tăs'sĭ-ī pĕr-măn'gą-năs)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99 per cent. of $KMnO_4$ (158.03). Preserve it in glass-stoppered bottles. Potassium Permanganate when in solution or in the dry condition must not be brought into contact with organic or other readily oxidizable substances." *U. S.*

"Potassium Permanganate may be obtained by the interaction of potassium chlorate, potassium hydroxide, and manganese dioxide. It contains not less than 99 per cent. of pure potassium permanganate, $KMnO_4$." *Br.*

Potassæ Permanganas; Kali Hypermanganicum Crystallisatum; Hypermanganas Potassicus, s. Kalicus; Permanganate of Potash; Permanganate de Potasse, *Fr. Cod.;* Kalium permanganicum, *P. G.;* Kaliumpermanganat, Chamäleon, Uebermangansaures Kali, *G.;* Permanganato di potassio, *It.;* Permanganato potasico, *Sp.*

The British Pharmacopœia 1885 furnished a detailed process for this salt. (See *U. S. D.,* 19th edition, page 1013.)

By the British process potassium chlorate yields oxygen to manganese dioxide, converting it into manganic acid, which unites with the potassium hydroxide to form the manganate, potassium chloride being formed at the same time; the reaction being

$$3MnO_2 + 6KOH + KClO_3 = 3K_2MnO_4 + KCl + 3H_2O$$

When this solution is boiled, the green potassium manganate which is sometimes called *chameleon mineral,* reacts with the water and yields potassium permanganate, according to the reaction

$$3K_2MnO_4 + 3H_2O = K_2Mn_2O_8 + H_2MnO_3 + 4KOH$$

the hydrated peroxide separating out. Hence, when exhausted by water, the solution requires the saturation of the free alkali with carbon dioxide, as stated in the process above. At best, the product is small and uncertain in amount. A cheaper commercial preparation, consisting of a mixture more or less pure of sodium manganate and permanganate, is manufactured on a large scale for disinfecting purposes. It is obtained by mixing the sodium hydroxide obtained from 1500 kilogrammes of soda ash with 350 kilogrammes of finely divided manganese dioxide in a flat vessel, and heating this mixture for forty-eight hours to dull redness. The product is then lixiviated with water, and the solution either boiled down to the requisite

degree of strength or evaporated to dryness. Potassium permanganate has also been made by the electrolysis of the manganate, the products being permanganate, potassium hydroxide, and hydrogen. A still more interesting result of electrolysis is the production of potassium permanganate by the electrolysis of potassium hydroxide, in which the negative electrode is of porous copper oxide and the positive electrode a piece of manganese or ferro-manganese held immersed by a loop of platinum wire. A process for the complete conversion of manganate into permanganate has been patented in Germany. The crude manganate obtained in the usual way by melting manganese dioxide and alkali under access of air, is exhausted with water and a current of *ozonized* air is passed into and through the alkaline solution. The conversion of the manganate into permanganate is complete and rapid, whereas when ordinary oxygen is thus introduced the formation is slow and incomplete. (*Ph. Ztg.*, 1901, 517.)

Properties.—It is officially described as in "slender, monoclinic prisms, of a dark purple color, almost opaque by transmitted light, and of a blue, metallic luster by reflected light; odorless, and having (in solution) a taste at first sweet, but afterwards disagreeable and astringent. Permanent in the air. One Gm. of Potassium Permanganate dissolves in 13.5 mils of water at 25° C. (77° F.); also in 3.5 mils of boiling water; it is decomposed by alcohol. When heated, the salt decrepitates, and at about 240° C. (464° F.) it decomposes, yielding oxygen, potassium manganate, and manganese dioxide. An aqueous solution of the salt is of a deep violet-red color when concentrated, and of a rose color when highly diluted. The color is discharged by hydrogen sulphide, ferrous sulphate, oxalic acid, alcohol, and many other substances, especially if the solution is first rendered acid by sulphuric acid.

"**Assay.**—Dissolve about 0.15 Gm. of Potassium Permanganate, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed, in 25 mils of distilled water, mix the solution with 1 mil of sulphuric acid and 50 mils of tenth-normal oxalic acid V.S. and warm the mixture to about 80° C. (176° F.). The residual titration with tenth-normal potassium permanganate V.S. shows, in the dried salt, not less than 99 per cent. of $KMnO_4$.

"Each mil of tenth-normal oxalic acid V.S. used corresponds to 0.0031606 Gm. of $KMnO_4$. Each gramme of Potassium Permanganate, previously dried, corresponds to not less than 313.2 mils of tenth-normal oxalic acid V.S." *U. S.*

"Dark purple, slender, prismatic, iridescent crystals. Taste sweet, astringent. Soluble in 20 parts of *water*. Aqueous solution neutral to *litmus*. The crystals heated to redness decrepitate, evolve oxygen, and leave a black residue from which *water* extracts potassium hydroxide, the resulting solution yielding the *reactions* characteristic of potassium. Yields no characteristic *reactions* for lead, arsenic, iron, sodium, ammonium, chlorides, nitrates, or sulphates. 1 gramme dissolved in *water*, acidified with 5 millilitres of *diluted sulphuric acid*, and heated to about 60° C. (140° F.), requires for complete decolorisation not less than 31.3 millilitres of *N/1 solution of oxalic acid.*" *Br.*

If the solution be evaporated to dryness, the salt has the form of an intensely black powder. If suddenly heated, the crystals detonate, evolving oxygen, and leaving a black residue, which yields potassium hydroxide to water, recognized by its alkaline reaction, and by giving, when acidulated with hydrochloric acid, a yellow precipitate with platinic chloride.

Moderately heated, the crystals are partially volatilized, giving out violet vapors of a disagreeable metallic odor. The salt, in consequence of the facility with which it parts with oxygen, is one of the most powerful oxidizing agents known. It causes the combustion of certain inflammable bodies, imparts oxygen to almost all organic substances, and in chemistry is employed to bring various compounds to a higher degree of oxidation. The readiness with which it yields oxygen in the nascent state is sufficient to account for its oxidizing power. It may be kept indefinitely if pure, and carefully secured from contact with organic substances, or other decomposing agents. In reference to the metals, mercury is quickly oxidized at the expense of the salt, a mixture of mercurous oxide and manganese oxide being deposited as a brown powder, and potassium hydroxide remaining in solution. Zinc remains unchanged indefinitely in a solution of the permanganate, silver is little affected, and copper not at all, even at 100° C. (212° F.). (Giles, *J. P. C.*, Mai, 1868, p. 397.)

H. B. Condy introduced (*J. Soc. Chem. Ind.*, 1885, p. 567) a permanganate disinfectant, which is commonly called *Condy's Fluid*, which contains also aluminum sulphate, which is said to increase the oxidizing effect of the permanganic acid. He asserts that in this disinfectant solution all the available oxygen of the permanganic acid is utilized, whereas only 60 per cent. of this amount is utilized with the simple alkaline permanganate.

Uses.—Potassium permanganate was brought to the notice of the profession by Condy in 1857, who recommended it as a powerful disinfectant. The findings of bacteriologists concerning the germicidal powers of this substance have varied most extraordinarily. These discrepancies have been due not solely to variations in the susceptibility of different species of bacteria but probably in greater degree, as pointed out by Sternberg, to the difference in conditions of test. In the absence of organic matter it is distinctly superior in power to phenol but it is so readily decomposed that in the presence of any considerable amount of pus or other albuminous matters it is almost inert. It appears to be especially poisonous towards *staphylococcus pyogenes*, Sternberg having shown that one part

in 833 is sufficient to destroy these bacteria in the absence of organic matter. Because of its activity as an oxidizant it is useful as a cleanser of *wounds* and the more so because of its deodorizing properties. One great disadvantage is its strong staining powers of the skin, clothes, etc. The stain may be removed with oxalic acid in places where the use of this substance is permissible. It is used in the treatment of *fetid* and *gangrenous ulcers, hospital gangrene, abscesses, carbuncles,* and *wounds* of all kinds, of fetid discharges from the mucous membrane, as in *ozena, otorrhea, gonorrhea,* and *leucorrhea,* and of *diphtheritic affections;* and it has proved serviceable even in *cancerous ulcers.* As a local stimulant it has also been used in *chronic* and *indolent ulcers.* In all these cases it is applied to the diseased surface in solution of various strengths, according to the effect desired. In concentrated solution it is capable of acting as a caustic and therefore requires caution. With the view to its caustic action, it may be sprinkled on the diseased surface by means of a pepper-box, or applied in saturated solution.

As an external disinfectant it is generally employed in strengths of from 1 to 5 per cent., but for application to mucous surfaces its strength must be greatly reduced and may be employed in strengths of from 1 part in 2000 and upwards.

Probably through its oxidizing influence potassium permanganate destroys many poisons and is a useful chemical antidote in *morphine* and *strychnine poisoning,* but especially in *snake bite.* The use of potassium permanganate as an antidote to snake poison was first suggested by Fayrer in 1869 and confirmed by Lauter Brunton in 1878. Rogers, of the Indian Medical Service (*C. D.,* June 18, 1904, and *Indian Medical Gazette,* December, 1912, xlvii), recommends the use of potassium permanganate crystals and has devised a special lancet. The instrument consists of a small lancet about half an inch long with a hollow wooden handle, in which crystals of permanganate are contained. The way in which it is proposed to apply the permanganate is that any one bitten by a snake should at once tear a strip from a turban, shirt, or any other article of clothing, and tie it as quickly as possible above the bite. A cut should then be made with the lancet over the site of the bite so as to convert the puncture made by the snake's tooth into a small wound. Into this the crystals of permanganate, moistened with saliva if necessary, are to be rubbed. This method of treatment he found to be highly successful in experimental poisoning of lower animals, but Bannerman (*Indian Journal of Medical Research,* 1913) concludes that a dog bitten by a cobra cannot be saved by the local application of powdered potassium permanganate rubbed in after free incision of the bitten place; nor by a similar application of a solution of the powder. It may be saved, however, by the immediate subcutaneous injection of 10 mils of a 5 per cent. solution of potassium permanganate; but this solution is so strong that gangrene of all the tissues of the foot is produced. If this treatment be delayed for even two minutes, a fatal result cannot be averted.

It is evident that like any other chemical antidote potassium permanganate must come in direct contact with the poison and since it is immediately decomposed by the tissues of the body, contrary to the statements occasionally made, it is useless after the absorption of the drug.

It is also recommended as a local hemostatic. Voerner (*M. M. W.,* 1905) recommends a mixture of one part of infusorial earth and two parts of potassium permanganate made up into a paste with one-third their bulk of petrolatum. Internally it was at one time employed in various *infectious diseases,* but its use for this purpose has entirely ceased. It is occasionally administered in *atonic amenorrhea.*

In overdose potassium permanganate may give rise to serious poisoning. Rubin and Dorner (*D. A. K. M.,* 1910, xcviii, p. 267), report a fatal case in which an unknown quantity was taken with suicidal intent. The symptoms were violent vomiting, profuse salivation with brownish masses of mucus, rapid respiration, albuminuria, and death fifty hours later. At autopsy there was found a bronchial pneumonia and punctiform hemorrhages in the pericardium.

Dose, from one to two grains (0.065–0.13 Gm.).

Off. Prep.—Liquor Potassii Permanganatis, *Br.*

POTASSII SULPHAS. Br.

POTASSIUM SULPHATE

(pŏ-tăs'sĭ-ī sŭl'phās)

"Potassium Sulphate may be obtained by the interaction of sulphuric acid and potassium chloride or certain other potassium salts. It contains not less than 99 per cent. of pure potassium sulphate, K_2SO_4." *Br.* "It contains, when dried to constant weight at 100° C. (212° F.), not less than 99 per cent. of K_2SO_4 (174.27)." *N. F.*

Potassæ Sulphas; Sulfas Potassicus, s. Kalicus, Tartarum Vitriolatum, Arcanum Duplicatum, Sal Duobus, Sal Polychrestum Glaseri; Sulphate of Potash, Vitriolated Tartar; Sulfate de Potasse, *Fr. Cod.;* Potasse vitriolée, *Fr.;* Kalium Sulfuricum, *P. G.;* Kaliumsulfat, Schwefelsaures Kali, *G.;* Solfato di Potassio, *It.;* Sulfato potasico, *Sp.*

Potassium sulphate was deleted from the U. S. P. IX, but was introduced into the N. F. IV.

Potassium sulphate is naturally present in sea water, in some mineral waters, and in some other naturally occurring sources.

Several chemical processes give rise to potassium sulphate as a secondary product. Thus, it is produced in the distillation of nitric acid from a mixture of potassium nitrate and sulphuric acid; in the decomposition of magnesium sulphate by potassium carbonate, in one of the processes for preparing magnesium carbonate; in the manufacture of sulphuric acid; in the manufacture of potassium dichromate; and in the decomposition of potassium tartrate by cal-

cium sulphate. When nitric acid is obtained by calcining a mixture of nitre and ferrous sulphate, the residue consists of ferric oxide and potassium sulphate, the latter of which, being alone soluble, is separated by means of water, and crystallized from its solution. The impure potassium sulphate with sulphur, forming the residue of the combustion of sulphur and nitre in making sulphuric acid, is employed in the manufacture of alum. The *kainite* of the Stassfurt salt beds is a native double potassium and magnesium sulphate, combined with magnesium chloride, and the *schœnite,* a double potassium and magnesium sulphate, with 6 molecules of water. To obtain potassium sulphate, the former mineral is exposed to the air; it deliquesces, and as soon as the soluble magnesium chloride has been run off, the remaining salt is partially decomposed by boiling water, so that on cooling the difficultly soluble sulphate separates out.

According to the directions of the former Br. Pharmacopœia, the acid sulphate which remains after the distillation of nitric acid is brought to the neutral state by saturation, in boiling solution, with slaked lime. The solution is then filtered, to separate the calcium sulphate, and potassium carbonate is added at the boiling temperature, to remove lime and calcium sulphate. It is again filtered, then either neutralized or rendered slightly acid with diluted sulphuric acid, and finally, having been evaporated to a pellicle, is set aside for twenty-four hours to crystallize. The manufacturer of tartaric acid who avails himself of calcium sulphate to decompose potassium tartrate forms potassium sulphate as a collateral product. For the manner in which the latter salt may be economically crystallized for use, see *A. J. P.,* xxiii, 343.

Properties.—As officially described, it is in "colorless, hard rhombic prisms terminated by six-sided pyramids. Taste saline, slightly bitter. Decrepitates strongly when heated. Soluble in 10 parts of *water;* insoluble in *alcohol* (90 per cent.). Yields the *reactions* characteristic of potassium and of sulphates. 1 gramme dissolved in water acidified with *hydrochloric acid* gives, with *solution of barium chloride,* a white precipitate, which, when washed and dried, weighs not less than 1.326 grammes. Yields no characteristic *reactions* for copper, iron, calcium, magnesium, sodium, ammonium, or nitrates, and not more than the slightest *reactions* for chlorides. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million. Aqueous solution neutral to *litmus* (absence of acid potassium sulphate)." *Br.*

This salt was introduced into the National Formulary IV. It is an ingredient in *Sal Carolinum Factitium* or *Artificial Carlsbad Salt,* and *Sal Carolinum Factitium Effervescens or Effervescent Artificial Carlsbad Salt.* It is described as follows: "Potassium Sulphate occurs as hard, colorless, translucent, six-sided, rhombic prisms terminated by pyramids, or as a white powder; permanent in the air. Odorless; taste saline, somewhat bitter. One gramme dissolves in 10 mils of water at 25° C. (77° F.), and in 4 mils of boiling water; insoluble in alcohol. When heated the crystals decrepitate. At a bright red heat the salt fuses, and at a white heat partial decomposition occurs. An aqueous solution of the salt (1 in 20) is neutral to litmus. A saturated aqueous solution of the salt yields a white, crystalline precipitate with an excess of sodium bitartrate T.S. An aqueous solution of the salt (1 in 20) yields with barium chloride T.S. a heavy white precipitate, insoluble in hydrochloric acid. An aqueous solution of Potassium Sulphate does not respond to the Test for heavy metals. An aqueous solution of the salt meets the requirement of the Test for arsenic. (See Part III, U. S. P. Test No. 1.)

"**Assay.**—Dissolve about 0.6 Gm. of Potassium Sulphate, previously dried to constant weight at 100° C. (212° F.), and accurately weighed, in 100 mils of distilled water, acidulate the solution with hydrochloric acid and heat it to boiling. Gradually add an excess of barium chloride T.S., and heat for thirty minutes on a water bath; collect the precipitate of barium sulphate on a filter and wash it with distilled water until silver nitrate T.S. fails to produce an opalescence in 2 mils of the filtrate, previously acidulated with nitric acid. Dry the precipitate, ignite and weigh the residue. It corresponds to not less than 99 per cent. of K_2SO_4. Each gramme of Potassium Sulphate corresponds to not less than 1.326 Gm. of $BaSO_4$." *N. F.*

It consists of two atoms of potassium combined with the dyad group, SO_4, characteristic of sulphuric acid.

The *plate-sulphate of potassa,* described by Penny, of Glasgow, is, when pure, the double potassium and sodium sulphate, having the formula $3K_2SO_4 + Na_2SO_4$. It is so called from the circumstance of being crystallized in hard thick cakes, or slabs, consisting of successive crops of crystals. It is a technical product from kelp, and may be formed by allowing successive quantities of concentrated kelp-lye to run into coolers, there to crystallize in successive layers, the mother liquor being drawn off by a siphon after the deposit of each layer. Potassium acid sulphate $KHSO_4$, when subjected to electrolysis, yields potassium persulphate $K_2S_2O_8$, which is a powerful oxidizing agent sometimes used in bleaching. For the mode of preparing and using *Sal Polychrestum, Potassii Sulphas cum Sulphure,* or *Sulphate of Potassa with Sulphur,* see U. S. D., 15th ed., p. 1187.

Uses.—Potassium sulphate is a mild purgative, operating usually without heat, pain, or other symptom of irritation. In small doses, of from twenty grains to half a drachm (1.3–2.0 Gm.), it operates as an aperient; in larger doses, of four or five drachms (15.5–20 Gm.), it acts slowly as a purge, but because of its irritant action is not to be recommended. On the continent of Europe it is frequently given as an aperient after delivery, and for the purpose of drying up the milk. Potassium sulphate is a

powerful irritant in excessive doses, and capable of producing fatal poisoning; an ounce and a half (46.5 Gm.) of it are said to have caused death. It is, like the nitrate and the chlorate, more dangerous when not given in sufficiently dilute solution. (See *Am. J. M. S.*, N. S., vii, 88.)

Dose, twenty grains to two drachms (1.3–7.7 Gm.).

Off. Prep.—Pilula Colocynthidis Composita, *Br.;* Pulvis Ipecacuanhæ Compositus, *Br.;* Sal Carolinum Factitium, *N. F.;* Sal Carolinum Factitium Effervescens, *N. F.*

POTASSII TARTRAS. Br.

POTASSIUM TARTRATE

(pŏ-tăs'sĭ-ī tär'trăs)

"Potassium Tartrate may be obtained by neutralising Acid Potassium Tartrate with potassium carbonate. It contains not less than 99 per cent. of pure potassium tartrate, $(K_2C_4H_4O_6)_2H_2O$." *Br.*

Potassæ Tartras; Tartras Potassicus, s. Kalicus; Tartarus Tartarisatus, Tartarus Solubilis; Tartrate of Potash; Soluble Tartar; Tartrate de Potasse neutre, *Fr. Cod.;* Tartre soluble, Sel végétal, *Fr.;* Kalium Tartaricum, *P. G.;* Kaliumtartrat, *G.;* Tartrato neutro di potassio, *It.;* Tartrato potasico neutro, *Sp.*

This salt was dropped at the 1890 revision of the U. S. Pharmacopœia; it is retained in the 1914 revision of the British authority.

In the U. S. 1870 process the excess of acid in the bitartrate is saturated by the potassium of the carbonate, the carbon dioxide is liberated with effervescence, and the neutral potassium tartrate is formed. On account of the greater solubility of the carbonate than of the bitartrate, the former is first dissolved, and the latter added to the solution to full saturation. As the bitartrate is gradually added, the mutual action of the salts should be promoted by constant stirring, and the addition continued so long as effervescence takes place, which is a better mode of proceeding than to add any specified quantity of the acid tartrate, since, from its variable quality, it is impossible to adjust precisely the proportions applicable to all cases. It is necessary that the solution should be exactly neutral, or a little alkaline, and hence, if inadvertently too much bitartrate has been used, the proper state may be restored by adding a little of the alkaline carbonate. When the saturation has been completed, the solution is filtered, in order to separate calcium tartrate, which appears in white flocks, and which is frequently present in cream of tartar as an impurity. The evaporated liquor should then be placed in *warm* earthenware vessels, to insure a slow refrigeration, and after remaining at rest for several days the crystals begin to form. In order that the crystallization should proceed favorably, it is necessary, according to Baumé, that the solution should be somewhat alkaline. Iron vessels should not be used in the process, as that metal is apt to discolor the salt.

Potassium tartrate is sometimes made in the process for preparing tartaric acid. When thus obtained, the excess of acid of the bitartrate is neutralized by means of calcium carbonate. This generates an insoluble calcium tartrate, and leaves the neutral tartrate in solution, from which it may be obtained by evaporation and crystallization. (See *Acidum Tartaricum.*)

Properties.—Potassium tartrate is officially described in the Br. Ph. 1914 as in "small, colorless, four or six-sided prisms. Taste saline, cooling. Soluble in 1 part of *water.* Yields the *reactions* characteristic of potassium and of tartrates. 1 gramme, heated to redness till gases cease to be evolved, leaves an alkaline residue which, when treated with *water,* filtered, and well washed, yields a clear solution requiring for neutralisation not less than 16.8 millilitres of *N/2 solution of sulphuric acid.* Yields no characteristic *reactions* for copper, or iron, and not more than the slightest *reactions* for calcium, magnesium, sodium, chlorides, or sulphates. *Lead limit* 20 parts per million. *Arsenic limit* 2 parts per million. Aqueous solution neutral to *litmus* (absence of acid potassium tartrate)." *Br.*

Potassium tartrate is composed of two atoms of potassium combined with the dyad group $C_4H_4O_6$ characteristic of tartaric acid.

Uses.—Potassium tartrate is a mild, cooling purgative, operating, like most of the neutral salts, without much pain, and producing watery stools. It is applicable to *febrile diseases,* and is occasionally combined with senna, the griping effects of which it has a tendency to obviate.

Dose, from a drachm to an ounce (3.9–31 Gm.).

POTASSIUM

POTASSIUM

(pŏ-tăs'sĭ-ŭm)

Potassium, *Fr.;* Kalium, Kalimetall, *G.;* Potassio, *It.;* Potasico, *Sp.*

Potassium is a metal forming the radical of potassium hydroxide, and of a number of compounds used in medicine. It was discovered in 1807 by H. Davy, who obtained it by decomposing fused potassium hydroxide by a voltaic current. It was afterwards procured in larger quantity by Gay-Lussac and Thénard, by bringing the fused alkali in contact with white-hot iron, which attracted the oxygen and set free the metal. The process of Brunner, as modified by Wöhler, consists in decomposing potassium carbonate, mixed with charcoal. The mixture of carbonate and charcoal is obtained by heating cream of tartar to redness in a covered crucible. For an account of some improvements in Brunner's process by Mareska and Donny, see *A. J. P.,* xxv, 70. Castner has also prepared it by the process invented by him for the manufacture of metallic sodium. It may also be prepared by distilling a mixture of potassium fluoride or fluosilicate with metallic aluminum. (For commercial sources of potassium salts, see under *Potassii Carbonas.*)

Potassium is solid, softer and more ductile than wax, easily cut with a knife, and of a silver-white color. A newly-cut surface is brilliant, but the metal quickly tarnishes by combining with the oxygen of the air, and assumes the appearance of lead. It possesses a remarkably strong affinity for oxygen, and is capable of taking that element from almost every other substance. On account of this property it must be kept in liquids, such as naphtha, which are devoid of oxygen. On the same account, when exposed with a freshly cut surface to the air, it becomes luminous through a slow combustion, like phosphorus, in the dark. (*Chem. News*, Feb. 28, 1868, p. 108.) Its sp. gr. is 0.865, melting point 62.5° C. (144.5° F.), atomic weight 38.86, and symbol K. It volatilizes at about 720° C. (1328° F.) with the production of greenish vapors. When thrown upon water it floats, takes fire, and burns with a rose-colored flame, combining with oxygen, and generating potassium hydroxide which dissolves in the water. It forms numerous combinations, uniting with most of the non-metallic elements, and with several of the metals. It combines in three proportions with oxygen, forming a suboxide (K_4O) and a monoxide (K_2O) of a gray color, and a tetroxide (K_2O_4) of a yellowish-brown color. It also unites with chlorine, and forms official compounds with iodine, bromine, cyanogen, and ferrocyanogen, under the names of potassium iodide, bromide, cyanide, and ferrocyanide. Its monoxide is a strong salifiable base existing in nature always in combination, and forming with acids a numerous and important class of salts.

Uses.—Although elemental potassium is not used in medicine it enters into so large a number of medicinal salts and so greatly modifies the action of some of them, that the effects of the potassium ion deserve a separate word of consideration. While the presence of a certain amount of potassium in the blood is essential for vital activity, a very slight increase in its percentage has a deleterious influence on many organs. The injection of a potassium salt into the circulation weakens the contractile power of all muscle fiber but affects especially the heart and blood vessels. It also exercises a marked depressant action upon the central nervous system, including the spinal cord, brain, and medulla. Although the depressant action of potassium is strong when it is injected directly into the blood stream, when taken by the mouth it exercises very little influence upon the circulation. This is due to the fact that it is excreted by the kidneys so rapidly that it cannot be absorbed in sufficient amounts through the alimentary tract to cause the accumulation of a poisonous dose in the blood. When the kidneys, however, are diseased it is probable that a poisonous dose of the ion could be absorbed from the intestines, and therefore while the potassium salts can be used with great liberality in healthy persons when there are diseases of the kidneys some caution is necessary in their employment. During the passage of the potassium through the system it appears to exercise a marked effect upon the metabolism. Not only is there an increase in the total solid matters of the urine, but apparently a disproportionate increase in the quantity of urea. This has led to the opinion that the increased elimination is not simply the result of its diuretic action, but betokens a more complete oxidation in the system. Because of this effect the potassium salts are generally preferred in cases of deficient combustion, especially that group of disorders known as *lithemia*.

PRUNUS VIRGINIANA. U. S. (Br.)

WILD CHERRY **Prun. Virg.** **[Wild Black Cherry Bark]**

(prū′nŭs vĭr-ĝĭn-ị-ā′nạ)

"The stem-bark of *Prunus serotina* Ehrhart (*Prunus virginiana* Miller) (Fam. *Rosaceæ*), collected in autumn and carefully dried. Preserve Wild Cherry in tightly-closed containers, protected from light." *U. S.* "Wild Cherry Bark is the bark of Prunus serotina, *Ehrh.*, collected in autumn." *Br.*

Pruni Virginianæ Cortex, *Br.*, Wild Cherry Bark; Virginian Prune Bark; Rum, Whisky, or Cabinet Cherry, Wild Black Cherry; Ecorce de Cerisier de Virginie, *Fr.*; Wildkirschenrinde, Amerikanischer Zierstrauch, *G.*

The genus Prunus now includes the plums, almonds, peaches, apricots, and cherries, and comprises about one hundred and twenty species. They are generally distributed in the temperate regions of the northern hemisphere. In the United States there are about forty indigenous species.

The name *P. virginiana* was applied by Miller (*Dict.*, ed. 8, No. 3), and not Linnæus, to *P. serotina* Ehr. *P. virginiana* L., commonly called *wild cherry* or *choke cherry*, is distinguished from *P. serotina* Ehr., known more properly as *wild black cherry*, by the following characteristics: *P. virginiana* L. has deciduous calyx lobes; oblong-obovate pointed endocarp (or stone); leaves broadly oval to oblong-obovate, and usually abruptly acuminate; inner bark with a rather disagreeable odor. *P. serotina* Ehr. has persistent calyx lobes; the endocarp (or stone) oblong-obovate, usually gradually acuminate; leaves oblong or lanceolate-oblong, usually gradually acuminate; the inner bark and leaves possess an aromatic odor. The British name, "Virginian Prune Bark," for the bark is misleading; Virginian Peach Bark or Virginian Almond Bark would have been no more of a misnomer. The official species is, according to Michaux, one of the largest productions of the American forest. Trees were observed by that botanist on the banks of the Ohio, from eighty to one hundred feet high, with trunks from twelve to fifteen feet in circumference, and undivided to the height of twenty-five or thirty feet. But as usually met with in the Atlantic States the tree is much smaller. In the open fields it is less elevated than in forests, but sends out more numerous branches, which expand into an elegant oval summit. The trunk

is regularly shaped, and covered with a rough blackish bark, which detaches itself semicircularly in thick narrow plates. The leaves are alternate, oval-oblong, or lanceolate-oblong, acuminate, unequally serrate, smooth on both sides, of a beautiful brilliant green; the petioles are furnished with one or more reddish conspicuous glands. The flowers are small, white, and occur in long erect or spreading racemes. They appear in May, and are followed by globular drupes, about the size of a pea, and when ripe of a shining blackish-purple color. For a paper on the structure of species of Prunus, by E. S. Bastin, see *Proc. A. Ph. A.*, 1895, 211.

This tree is distributed from Ontario south to Florida, and westward to Dakota, Nebraska, Kansas, Indian Territory, and Eastern Texas. It extends along the mountain ranges of Western Texas, Mexico, and Pacific regions of Central America, Colombia, and Peru. In the United States it was once common throughout the Appalachian region. In the neighborhood of Philadelphia it affects open situations, growing solitarily in the fields and along fences, and seldom aggregated in woods or groves. It is highly valued by the cabinet-makers for its wood, which is compact, fine-grained, susceptible of polish, and of a light red tint which deepens with age. The leaves have been found by Procter to yield volatile oil and hydrocyanic acid on distillation, and in such proportion that a water distilled from them might with propriety be substituted for the cherry-laurel water. (*Proc. A. Ph. A.*, 1858, 325.) The fruit has a sweetish, astringent, bitter taste, and is much used in some parts of the country to impart flavor to spirituous liquors. The bark is obtained indiscriminately from all parts of the tree, though that of the roots is thought to be most active. The revisers of the Pharmacopœia believe with J. S. Perot that the bark is stronger when collected in autumn than in the spring; from a portion gathered in April Perot obtained 0.0478 per cent. of hydrocyanic acid, and from another in October 0.1436 per cent., or about three times as much. (*A. J. P.*, xxiv, 111.) The bark should be preferred recently dried, as it deteriorates by keeping. A. B. Stevens (*Proc. A. Ph. A.*, 1895, 226; 1896, 215), after testing many specimens, reached the conclusion that bark procured from different parts of the same tree varied in the yield of hydrocyanic acid, the value being in this order: 1, root; 2, twigs; 3, trunk; the bark from young trees yielding more glucoside than that from old trees. Jos. L. Lemberger (*A. J. P.*, 1872, 303) believes that tannic acid is most abundant in the bark in October and November. On the other hand, Grace E. Cooley (*A. J. P.*, August, 1897) concludes that there is more tannic acid in the bark during the active growth of the spring than in the autumn. She further states that in the spring and autumn the bark contains its maximum percentage of starch; so that if the bark, whether powdered or whole, contains much starch in its parenchymatous cells, it has been collected after the time of leaf-fall in the autumn or before the unfolding of the leaves in the spring. Occasionally barks find their way into commerce as Prunus Virginiana which yield no odor of hydrocyanic acid when moistened and are probably obtained from other than the official wild cherry. (See Bastin, *A. J. P.*, 1895, and Finnemore, *P. J.*, 72.)

Moser points out that collectors frequently mistake *P. virginiana* L. or choke cherry for *P. serotina* Ehrh. or black cherry, which is the official source of wild cherry bark. He presents a description of the two trees and of the characteristic features of their barks. (*A. J. P.*, 1909, lxxxi, p. 579.) Farwell reports that the bark of *P. demissa* (Nutt.) Walpers, a tree from west of the Rocky Mountains, has been found in commerce. It is much darker and the lenticels are much more prominent. The preparations made from it resemble the official wild cherry bark in color, odor and taste.

Properties.—Wild cherry bark is officially described as follows: "Usually in transversely curved pieces from 2.5 to 8 cm. in length and from 0.5 to 4 mm. in thickness; outer surfaces light brown or greenish-brown, smooth, except for numerous lenticels from 3 to 4 mm. in length; inner surfaces light brown, longitudinally striate and occasionally fissured; fracture short, granular; odor distinct, bitter almond-like when macerated in water; taste astringent, aromatic, and agreeably bitter. Under the microscope, sections of Wild Cherry show a tendency for the separation in radial segments or bands of the phloem tissues from the rather broad medullary rays; periderm usually of a few layers of cells; outer bark from young twigs with 1 or 2 nearly continuous layers of cells, the latter being of very irregular shape, often branching and with thick lamellated, porous walls; medullary rays extending in more or less scythe-shaped groups from the cambium to the outer bark, from 1 to 10 cells in width, some of the cells occasionally being modified to stone cells; between the medullary rays occur numerous small groups of stone cells, resembling those of the outer bark and occasionally modified to sclerenchymatous fibers; calcium oxalate mostly in crystal fibers consisting of monoclinic prisms, from 0.015 to 0.04 mm. in diameter, also in rosette aggregates from 0.01 to 0.04 mm. in diameter; starch grains numerous, occurring in the medullary rays and parenchyma. The powder is light brown; when examined under the microscope it exhibits bast-fibers and stone cells with thick, strongly lignified walls; crystal fibers with monoclinic prisms and rosette aggregates of calcium oxalate, from 0.01 to 0.04 mm. in diameter; starch grains nearly spherical, from 0.003 to 0.004 mm. in diameter." *U. S.*

"In curved pieces or irregular fragments not more than three millimetres thick. Frequently covered with a smooth, thin, reddish-brown, papery cork, or, if this has been removed, exhibiting a greenish-brown cortex; marked with transversely elongated lenticels. Fracture short, granular; fractured surface reddish-grey. Inner surface reddish-brown, striated or reticulately

fissured. In the bark numerous groups of sclerenchymatous cells of characteristic shape, but no typical bast fibers; in the parenchymatous cells minute starch grains and prismatic crystals of calcium oxalate. Slight odor; taste astringent, aromatic and bitter, recalling that of bitter almonds." *Br.*

In the fresh state, or when treated with water, it emits an odor resembling that of peach leaves. Its taste is agreeably bitter and aromatic, with the peculiar flavor of the bitter almond. It imparts its sensible properties to water, either cold or hot, producing a clear reddish infusion closely resembling Madeira wine in appearance. Its peculiar flavor and its medicinal virtues are injured by boiling, in consequence partly of the volatilization of the principles upon which they depend, partly upon a chemical change effected by the heat. From an analysis by Stephen Procter, it appears to contain starch, resin, tannin, gallic acid, fatty matter, lignin, red coloring matter, salts of calcium, potassium, and iron. He obtained also a volatile oil, associated with hydrocyanic acid, by distilling the same portion of water successively from several different portions of the bark. William Procter proved that, as in the case of bitter almonds, the volatile oil and hydrocyanic acid do not exist ready formed in the bark, but are the result of the reaction of water with amygdalin, which he ascertained to be one of its constituents. In order, however, that this change may take place, he affirmed that the agency of another principle, probably analogous to, if not identical with, *emulsin* or the *synaptase* of Robiquet, was also essential, and, as this principle becomes inoperative at the boiling temperature, one can understand how decoction may interfere with the virtues of the bark. (*A. J. P.*, x, 197.) The bitterness appears to be due to the fluorescent substance described below which confirms Procter, who found the bitterness of an extract of the bark to remain after it had been wholly deprived of amygdalin. Stevens and Judy (*A. J. P.*, 1895, 482, 534) found that the thick bark contains more amygdalin and consequently yields more HCN than the thin bark. The thick bark contains amygdalin, etc., 4.12 per cent., and HCN from 0.32 to 0.35 per cent.; the thin bark, amygdalin, etc., 3.16 per cent., and HCN from 0.24 to 0.27 per cent. F. B. Power and Henry Weimer, on the other hand, state that the bark does not contain crystallizable amygdalin, that the ferment principle is not emulsin, and that it cannot be isolated by an analogous process. The bitter principle, which appears to be the fluorescent substance, has the character of a glucoside, and crystallizes in colorless needles. (*West. Drug.*, 1887, p. 331.)

R. Rother (*A. J. P.*, 1887, p. 286), in searching for the fluorescent principle of wild cherry bark, obtained a reddish crystalline substance, soluble in water, chloroform, ether, and alcohol, the solution of which fluoresced strongly on addition of ammonia. Rother says that it does not agree in crystalline form with mandelic acid, but may be a derivative of it.

Uses.—Wild cherry bark has the stomachic effects of the simple bitters but is comparatively infrequently employed for this purpose. On the theory that hydrocyanic acid is a cough sedative, wild cherry bark has been popularly employed in the treatment of *bronchitis* of various types, but is of doubtful service.

Dose, from thirty to sixty grains (2.0–3.9 Gm.).

Off. Prep.—Syrupus Pruni Virginianæ, *U. S.*, *Br.;* Tinctura Pruni Virginianæ, *Br.;* Elixir Taraxaci Compositum (from Fluidextract), *N. F.;* Emulsum Olei Morrhuæ cum Pruno Virginiana (from Fluidextract), *N. F.;* Fluidextractum Pruni Virginianæ, *N. F.;* Infusum Pruni Virginianæ, *N. F.;* Syrupus Cimicifugæ Compositus, *N. F.;* Syrupus Pini Strobi Compositus, *N. F.;* Syrupus Pini Strobi Compositus cum Morphinæ, *N. F.;* Vinum Pruni Virginianæ, *N. F.;* Vinum Pruni Virginianæ Ferratum (from Wine), *N. F.*

PULVERES

POWDERS

(pŭl'vẹ-rēs)

Poudres, *Fr.;* Pulvern, *G.;* Polveri, *It.;* Polvos, *Sp.*

The form of *powder* is convenient for the exhibition of substances which are not given in very large doses, are not very disagreeable to the taste, have no corrosive property, and do not deliquesce rapidly on exposure.

With regard to keeping powders in well-stoppered bottles, it is asserted by Hérouard, a French pharmacist, that this plan, instead of preserving *some* powders, tends to their more speedy and certain change. Whatever pains may be taken in drying drugs previously to powdering them, most of them during the process attract moisture, so as to put themselves in this respect in equilibrium with the surrounding air; and, if enclosed in this state in air-tight vessels, they are exposed to injurious influence from their own absorbed water, which, vaporized in hot weather, is in the colder seasons condensed on the inner surface of the vessel and determines a movement of fermentation, and even cryptogamic growths appear in some instances. The best method of preservation, the author thinks, is to enclose the powders in strong paper bags of a blue or gray color, so as to exclude the light, while the air has exit or entrance through the porous walls. Whatever may be our theoretical opinions on the point, Hérouard asserts the fact, as the result of observation, that powders keep best in this way, and his statement coincides with our own experience. The powders may be more likely to cake or harden into aggregate masses; but this disadvantage is easily counteracted by a new pulverization when required. (*J. P. C.*, Août, 1862, p. 98.) From these statements the inference may be drawn that, where powders are kept in air-tight bottles, they should be thoroughly dried, after pulveriza-

tion, before being enclosed, and many, such as ergot, rhubarb, etc., should be kept in paper boxes or cartons.

In relation to substances most liable to injury from these causes, the best plan is to powder them in small quantities as wanted for use.

Powders may be divided into the *simple,* consisting of a single substance, and the *compound,* of two or more mixed together. The latter only are embraced under the present head. In the preparation of the compound powders, the ingredients, if of different degrees of cohesion or solidity, should be pulverized separately and then mixed. Deliquescent substances, and those containing fixed oil in large proportion, should not enter into the composition of powders intended to be kept,—the former because they render the preparation damp and liable to spoil, the latter because they are apt to become rancid and impart an unpleasant odor and taste. When deliquescent substances are extemporaneously prescribed, the apothecary should enclose them before delivery in waxed paper or other impervious covering; and the same remark is applicable to volatile powders, as ammonium carbonate and camphor. The lighter powders may in general be administered in water or other thin liquid; the heavier, such as those of metallic substances, require a more consistent vehicle, as syrup, molasses, honey, or one of the confections. Resinous powders, if given in water, require the intervention of mucilage or sugar. For many powders the *cachet de pain* affords the best method of administration.

These very useful articles are wafers made of unleavened bread in such a manner that they offer a concavity, so that when two are placed face to face there is a space in which a powder may be contained. They are of different sizes and capacities, the largest readily holding as much as ten grains of quinine. In filling them, one wafer is placed upon a board, and the requisite amount of medicine is put in it; then a second wafer, whose interior margin has been wetted, is laid upon the first and pressed down upon it. When taken, they should be dipped in water, placed immediately upon a teaspoon containing a little water, and swallowed with a gulp of fluid. For most powders of disagreeable taste, cachets afford the best method of administration.

Gelatin capsules are extensively used for the administration of drugs in powdered form and are admirably adapted for this purpose if the dose is not too large, as they are readily filled and easily taken by the patient.

In the act of powdering, the whole substance in the mortar should not be beaten until completely pulverized, as the portion already powdered interferes with the action of the pestle upon the remainder, while the finer matter is apt to be dissipated, so that there is a loss of time and of material. The proper plan is to sift off the fine powder after a short continuance of the process, then to return the coarser parts to the mortar, and to repeat several times this alternate pulverization and shifting, until the process is completed. Care should be taken to mix thoroughly the several portions of fine powder thus obtained.

PULVIS AMYGDALÆ COMPOSITUS. Br.

COMPOUND POWDER OF ALMONDS

(pŭl'vĭs ą-mŷg'dą-læ cŏm-pŏş'ĭ-tŭs)

Confectio Amygdalæ; Conserva Amygdalarum; Confection of Almond; Conserve d'Amandes, *Fr.;* Mandelconserve, *G.*

"Sweet Almonds, 60 *grammes;* Refined Sugar, in powder, 30 *grammes;* Gum Acacia, in powder, 10 *grammes.* Blanch and dry the Almonds; reduce them to a coarse powder; mix the Gum Acacia and Sugar; add to the powdered Almonds; mix." *Br.*

This is the old *Almond Confection* in powder form. It is intended to afford a speedy method of preparing the almond mixture, which, when made immediately from the almonds, requires much time, and which cannot be kept ready made. But from its liability to be injured by keeping, it was omitted from the U. S. Pharm., which directs the emulsion of almond to be made immediately from the ingredients.

Off. Prep.—Mistura Amygdalæ, *Br.*

PULVIS ANTIMONIALIS. Br.

ANTIMONIAL POWDER [James's Powder]

(pŭl'vĭs ăn-tĭ-mō-nĭ-ā'lĭs)

Pulvis Antimonii Compositus, Pulvis Jacobi; Poudre antimoniale de James, *Fr.;* Jamessches Antimonpulver, *G.*

"Antimonious Oxide, 25 *grammes;* Calcium Phosphate, 50 *grammes.* Mix." *Br.*

This preparation was introduced into the U. S. Pharmacopœia, 1890, as a substitute for the different forms of antimonial powder formerly official with the British Colleges, because of its revived employment at that time, but was not admitted to the U. S. P. VIII or IX, but is included in the N. F. IV (see Part III). The N. F. and the British preparations are identical.

The only essential difference between the official and the Dublin powder is that the ingredients of the former are taken already prepared and mixed in fixed proportion, while those of the latter result simultaneously from one operation. The official powder is, of course, much more easily prepared, and less liable to uncertainty from any error in the process.

Michael Donovan believes that none of the official formulas fairly represent James's powder, and gives an elaborate history of this celebrated proprietary medicine, and a method for its preparation, in *P. J.,* 1869.

Uses.—This preparation is stated to be alterative, diaphoretic, purgative, or emetic, according to the dose in which it is given. Until within a few years it was often prescribed in febrile diseases, with a view to its diaphoretic effect. According to A. T. Thomson, it is advantageously given in *acute rheumatism,* con-

joined with camphor, calomel, and opium, and with calomel and guaiac in several *cutaneous affections.* The estimation in which this preparation is held varies greatly; but it is generally admitted that, as formerly prepared, it was very uncertain in the percentage of antimony trioxide, and consequently in its activity; it was this uncertainty that led to its omission from the U. S. Pharm. of 1830.

The antimonial powder at present official is exempt from the objection of irregularity of composition. Nevertheless, as it depends for its greater or less energy on the presence or absence in the alimentary canal of an acid which may form a salt with the antimonial oxide, it cannot always be relied on for a definite effect, being sometimes mild, and sometimes more active than might be desirable.

Dose, as a diaphoretic, from three to eight grains (0.2–0.5 Gm.) every third or fourth hour, given in the form of pill. In larger doses it is purgative and emetic. Jonathan Osborne has found the trioxide, given separately in three grain (0.2 Gm.) doses, evening and night, to cause in some cases nausea and vomiting, in others mild purgation.

PULVIS AROMATICUS. U. S. (Br.)

AROMATIC POWDER Pulv. Arom.

(pŭl'vĭs ăr-o-măt'ĭ-cŭs)

Pulvis Cinnamomi Compositus, *Br.;* Compound Powder of Cinnamon; Poudre des Épices, P. des Aromates, Poudre aromatique, *Fr.;* Aromatisches Pulver, Gewürzpulver, *G.*

* "Saigon Cinnamon, in No. 60 powder, *thirty-five grammes* [or 1 ounce av., 103 grains]; Jamaica Ginger, in No. 60 powder, *thirty-five grammes* [or 1 ounce av., 103 grains]; Cardamom Seed (deprived of pericarps), *fifteen grammes* [or 231 grains]; Myristica, freshly grated, *fifteen grammes* [or 231 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Triturate the cardamom seed and the myristica with a portion of the saigon cinnamon, until they are reduced to a fine powder; then add the remainder of the cinnamon and the ginger, and rub them together until they are thoroughly mixed." *U. S.*

"Cinnamon Bark, in powder, 25 *grammes;* Cardamom Seeds, in powder, 25 *grammes;* Ginger, in powder, 25 *grammes.* Mix." *Br.*

Properties.—"Light reddish-brown; with a strong, distinctive, aromatic odor; when examined under the microscope it exhibits characteristic starch grains of ginger, being ellipsoidal or ovoid, slightly beaked and from 0.005 to 0.06 mm. in diameter; numerous yellowish-brown, brownish-red and occasional blackish fragments, the cellular structure of which is not distinct; occasional stone cells, the lumina being filled usually with a reddish-brown amorphous substance or containing air; occasional fragments with sclerenchymatous fibers; calcium oxalate crystals, in short raphides, few." *U. S.*

The Aromatic Powder of the U. S. P. IX does not differ essentially from that formerly official. The British and American powders now closely resemble each other. The U. S. process contains nutmeg and the British does not. The cardamom seeds should always be deprived of their pericarps before being weighed, and the powder, when prepared, should be kept in well-stoppered bottles.

Uses.—The aromatic powder is stimulant and carminative, and the U. S. preparation may be given in the dose of from ten to thirty grains (0.65–2.0 Gm.), in cases of *enfeebled digestion with flatulence;* but it is chiefly used as a corrigent and adjuvant of other medicines. A mixture of aromatic powders in the form of a cataplasm is much used as a mild rubefacient, especially in nausea and vomiting, being applied over the epigastrium. Such a mixture is commonly called *spice plaster* and will be found in the N. F. IV (Part III), under the title *Pulvis Aromaticus Rubefaciens.* It contains clove, cinnamon, ginger, and capsicum, and the mixed powder may be distributed in a thin flannel bag, quilted in position, and the whole wet with bathing whisky when applied and covered with oiled silk.

Aromatic Sugar.—Wm. L. Turner proposed a mode of obtaining the effects of the aromatic powder in certain cases where the use of the powder itself would be inconvenient. He prepared an aromatic sugar by submitting eight ounces of the freshly prepared powder to percolation with stronger alcohol to exhaustion, pouring the percolate over eight ounces of sugar, and evaporating at a low heat. The sugar thus prepared may be added to mixtures, solutions, etc., requiring aromatic addition. (*A. J. P.,* 1869, p. 118.)

Dose, ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Fluidextractum Aromaticum, *U.S.*

PULVIS BUTEÆ SEMINUM. Br.

POWDER OF BUTEA SEEDS

(pŭl'vĭs bū-tē'æ sĕm'ĭ-nŭm)

"Soak Butea Seeds in Distilled Water; carefully remove the integuments; dry and powder the kernels." *Br.*

Uses.—(See *Butea Semina.*)

PULVIS CATECHU COMPOSITUS. Br.

COMPOUND POWDER OF CATECHU

(pŭl'vĭs kăt'ę-çhū cŏm-pŏs'ĭ-tŭs)

Pulvis Gambir Compositus, *N.F.;* Poudre de Cashcuttie composée, *Fr.;* Zusammengesetztes Katechupulver, *G.*

"Catechu, in powder, 40 *grammes;* Kino, in powder, 20 *grammes;* Krameria Root, in powder, 20 *grammes;* Cinnamon Bark, in powder, 10 *grammes;* Nutmeg, in powder, 10 *grammes.* Mix." *Br.*

This preparation is also official in the N. F. (see Part III).

The *dose* of this agreeable preparation is from fifteen to thirty grains (1–2 Gm.).

PULVIS CRETÆ AROMATICUS. Br.

AROMATIC POWDER OF CHALK

(pŭl'vĭs crē'tæ ăr-ǫ-măt'ĭ-cŭs)

Confectio Aromatica, *Lond.;* Poudre de Craie aromatique, *Fr.;* Gewürztes Kreidepulver, *G.*

"Cinnamon Bark, in powder, 10 *grammes;* Nutmeg, in powder, 8 *grammes;* Cloves, in powder, 4 *grammes;* Cardamom Seeds, in powder, 3 *grammes;* Refined Sugar, in powder, 50 *grammes;* Prepared Chalk, 25 *grammes.* Mix." *Br.*

This is the former "Aromatic Powder" of the Br. Pharmacopœia, with the addition of chalk and elision of saffron. It is also official in the N. F. IV (see Part III). It is a warm stimulant and astringent, as well as antacid, and is well calculated for *diarrhea* connected with acidity and without inflammation. In such a combination, however, the due proportion and even the choice of the ingredients vary so much with the symptoms that they might well be left to extemporaneous prescription.

Dose, from thirty to sixty grains (2.0–3.9 Gm.), in mucilage or sweetened water, frequently repeated.

Off. Prep.—Pulvis Cretæ Aromaticus cum Opio, *Br.* (*N. F.*).

PULVIS CRETÆ AROMATICUS CUM OPIO. Br.

AROMATIC POWDER OF CHALK WITH OPIUM

(pŭl'vĭs crē'tæ ăr-ǫ-măt'ĭ-cŭs cŭm ō'pĭ-ō)

Pulvis Cretæ et Opii Aromaticus, *N. F.;* Aromatic Powder of Chalk and Opium; Poudre de Craie Opaciée, *Fr.;* Kreidepulver mit Opium, *G.*

"Aromatic Powder of Chalk, 97.5 *grammes;* Opium, in powder, 2.5 grammes. Mix. This Powder contains 2.5 per cent. of Opium." *Br.*

The N. F. powder is identical with the Br. (see Part III).

The addition of the opium greatly increases the efficacy of the compound powder of chalk in *diarrhea,* and its equal diffusion through the powder presents this advantage, that it may be conveniently given in minute doses applicable to infantile cases. Forty grains of the powder contain a grain of opium.

Dose, for adults, ten to twenty grains (0.65–1.3 Gm.).

PULVIS CRETÆ COMPOSITUS. U. S.

COMPOUND CHALK POWDER Pulv. Cret. Co.

(pŭl'vĭs crē'tæ cǫm-pŏs'ĭ-tŭs)

Poudre de Craie composée, *Fr.;* Kreidepulver mit Gummi, *G.*

* "Prepared Chalk, *thirty grammes* [or 1 ounce av., 25 grains]; Acacia, in fine powder, *twenty grammes* [or 309 grains]; Sugar, in fine powder, *fifty grammes* [or 1 ounce av., 334 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Mix the powders intimately by trituration and pass the product through a No. 60 sieve." *U. S.*

This official powder was introduced into the U. S. P., 1890, for the purpose of having on hand, in a convenient form, the dry powders necessary to make chalk mixture. (See *Mistura Cretæ.*)

This powder will be found, however, a very convenient basis for administering chalk in powder, and it will be easy to direct the addition of morphine, kino, pepsin, bismuth subnitrate, or any other suitable agent.

Dose, one-half to two drachms (2.0–7.7 Gm.).

Off. Prep.—Mistura Cretæ, *U. S.*

PULVIS EFFERVESCENS COMPOSITUS. U. S. (Br.)

COMPOUND EFFERVESCING POWDER Pulv. Eff. Co. [Seidlitz Powder]

(pŭl'vĭs ĕf-fẹr-vĕs'cẹns cǫm-pŏs'ĭ-tŭs)

"The weight of the mixture in a blue paper is not less than 9.5 Gm. nor more than 10.5 Gm.; it contains not less than 23 per cent. nor more than 27 per cent. of sodium bicarbonate and not less than 73 per cent. nor more than 78 per cent. of potassium and sodium tartrate." *U. S.*

Pulvis Sodæ Tartaratæ Effervescens, *Br.,* Effervescent Tartarated Soda Powder; Pulveres Effervescentes Aperientes, *U. S.* 1870; Seidlitz Powders; Poudre Gazogène laxative, *Fr. Cod.;* Poudre gazifère purgative, Poudre de Seidlitz, *Fr.;* Pulvis aërophorus laxans, *P. G.;* Pulvis aërophorus Seidlitzensis, Abführendes Brausepulver, Seidlitzpulver, *G.;* Polvo gasifero laxante, *Sp.*

* "Sodium Bicarbonate, dried and in fine powder, *thirty grammes* [or 1 ounce av., 25 grains]; Potassium and Sodium Tartrate, dried and in fine powder, *ninety grammes* [or 3 ounces av., 76 grains]; Tartaric Acid, dried and in fine powder, *twenty-six grammes* [or 401 grains]. Mix the sodium bicarbonate intimately with the potassium and sodium tartrate, divide the mixture into *twelve equal parts,* and wrap each part in a separate blue paper. Then divide the tartaric acid into *twelve equal parts,* and wrap each part in a separate white paper. Keep the powders in well-closed containers, in a dry place.

"To five mils of an aqueous solution of the mixture in a blue paper (1 in 20) add 5 mils of acetic acid, and when effervescence has ceased, shake the solution vigorously; a white crystalline precipitate, soluble in ammonia water, separates." *U. S.*

"No. 1 Sodium Potassium Tartrate, in dry powder, 7.5 *grammes;* Sodium Bicarbonate, in dry powder, 2.5 *grammes.* Mix. No. 2 Tartaric Acid, in dry powder, 2.5 *grammes.* Put No. 1 in blue paper, and put No. 2 in white paper." *Br.*

"**Assay for Sodium Bicarbonate.**—Mix thoroughly the contents of a blue paper, then dissolve 2 Gm. of it in 80 mils of distilled water, add 20 mils of half-normal sulphuric acid V.S., boil the solution until the volume is reduced to about 50 mils, and titrate the excess of acid with half-normal potassium hydroxide V.S., phenolphthalein T.S. being used as indicator.

The number of mils of half-normal sulphuric acid V.S. consumed shows not less than 23 per cent. nor more than 27 per cent. of sodium bicarbonate.

"Each mil of half-normal sulphuric acid V.S. corresponds to 0.04200 Gm. of sodium bicarbonate. Each gramme of the mixture corresponds to not less than 5.48 mils nor more than 6.43 mils of half-normal sulphuric acid V.S.

"Assay for Potassium and Sodium Tartrate.—Proceed as directed under the assay for alkali salts of organic acids (see Part III, Test No. 6), using 2 Gm. of the mixture taken from the blue paper used in the preceding assay. The difference between the number of mils of half-normal sulphuric acid V.S. consumed in this assay and in the assay for sodium bicarbonate, multiplied by 0.07055, represents the potassium and sodium tartrate, and corresponds to not less than 73 per cent. nor more than 78 per cent.

"The sum of the percentages of sodium bicarbonate and of the potassium and sodium tartrate is not less than 99 per cent." *U. S.*

Though named from the saline springs of Seidlitz, in Bohemia, Seidlitz powders do not correspond in composition with those famous waters. Of each pair of powders, one, much the smaller of the two, contains about thirty-five grains (2.25 Gm.) of tartaric acid, the other about forty grains (2.59 Gm.) of sodium bicarbonate mixed with about two drachms (7.7 Gm.) of Rochelle salt. The acid powder is usually put into a white paper, the alkaline into a blue paper, which latter should not be colored by aniline; a number of them are enclosed in a paper or tin box. They should not be kept in a damp place, as the tartaric acid is liable to be dissolved by the moisture and absorbed into the substance of the paper, thus altering the due proportion of the ingredients. We have known the whole of the contents of the white paper thus to disappear in the course of two or three years. The Rochelle salt is the ingredient upon which the aperient property mainly depends. In their administration, each powder is dissolved separately, the smaller in a fluidounce or more of water, the larger in twice or three times the quantity, and the two solutions are mixed gradually. A reaction takes place between the tartaric acid and the sodium bicarbonate, by which sodium tartrate is produced, adding somewhat to the laxative property of the draught, and carbon dioxide escapes, causing a brisk effervescence. The acid is in slight excess, and thus causes an agreeable acidity in the solution.

Uses.—These powders are refrigerant and aperient, and generally very acceptable to the stomach in consequence of the carbon dioxide eliminated. They are especially adapted to *febrile cases* with a somewhat irritable stomach. One pair of them will generally operate slightly, but, if required, two may be given at once, or the dose may be repeated every three or four hours until the desired effect is produced. The flavor may sometimes be advantageously improved by adding syrup of ginger, orange peel, or lemon to one of the solutions before admixture, and most persons prefer to dissolve the salts in very cold water, the saline taste being thereby greatly diminished. A lowering of the temperature always takes place, due to the solution of the salts.

Dose, one set of two powders.

PULVIS GLYCYRRHIZÆ COMPOSITUS. U. S., Br.

COMPOUND POWDER OF GLYCYRRHIZA Pulv. Glycyrrh. Co. [Compound Licorice Powder]

(pŭl'vĭs glĭç-ŷr-rhĭ'zæ cŏm-pŏs'ĭ-tŭs)

Poudre de Réglisse composée, Poudre pectorale, *Fr.;* Pulvis Liquiritiæ Compositus, *P. G.;* Brustpulver, Pulvis Pectoralis Kurellæ, *G.*

* "Senna, in No. 80 powder, *one hundred and eighty grammes* [or 6 ounces av., 153 grains]; Glycyrrhiza, in No. 80 powder, *two hundred and thirty-six grammes* [or 8 ounces av., 142 grains]; Washed Sulphur, *eighty grammes* [or 2 ounces av., 360 grains]; Oil of Fennel, *four grammes* [or 62 grains]; Sugar, in fine powder, *five hundred grammes* [or 17 ounces av., 279 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Mix the oil of fennel thoroughly with about one-half of the sugar, then add the remainder of the sugar and the other ingredients, and mix thoroughly. Finally, pass the powder through a No. 80 sieve, pulverize the residue if any should be left on the sieve, add to the sifted powder, and mix thoroughly. Keep it in well-closed containers." *U. S.*

"Senna Leaves, in powder, 16 *grammes;* Liquorice Root, in powder, 16 *grammes;* Fennel Fruit, in powder, 8 *grammes;* Sublimed Sulphur, 8 *grammes;* Refined Sugar, in powder, 52 *grammes.* Mix." *Br.*

Properties.—"Greenish-yellow to greenish-brown with a fennel-like odor; when mounted in water or hydrated chloral T.S. and examined under the microscope, Compound Powder of Glycyrrhiza shows fragments of glycyrrhiza with their characteristic yellow fibers associated with crystal fibers, large tracheæ with elliptical, bordered pores and cells containing numerous, spherical starch grains varying from 0.002 to 0.02 mm. in diameter; also fragments of senna as shown by their characteristic, more or less bent, unicellular, non-glandular hairs, from 0.1 to 0.35 mm. in length, fragments of epidermis with elliptical stomata and their 2 neighboring cells and fragments with crystal fibers; upon the addition of potassium hydroxide T.S. to aqueous mounts of the powder, some of the fragments are immediately colored a yellowish-red, changing to a reddish-brown. Introduce 0.1 Gm. of Compound Powder of Glycyrrhiza into a test tube, moisten it with 2 mils of alcohol, then add 10 mils of water, boil the mixture, allow it to cool and then filter; the filtrate is of a pale yellowish-brown color, which changes immediately to a yellowish-red on the addition of a drop of potassium hydroxide T.S. Compound Powder of Glycyrrhiza is free from an odor of hydrogen sulphide." *U. S.*

This official preparation, which was introduced

into the U. S. P., 1880, was identical with that of the German Pharmacopœia, and in the 1885 revision of the British Pharmacopœia the preparation was made nearly to correspond, being slightly deficient in senna. The U. S. P., 1890, replaced the powdered fennel with oil of fennel, increasing the proportion of powdered licorice correspondingly which is an improvement, as powdered fennel is variable in quality; great care should be used, however, to employ only fresh oil of fennel. The object of the oil of fennel is patent, but the advantage to be gained by the use of washed sulphur in the proportion of only 8 per cent. must be purely imaginary. In our opinion, an improvement would be the substitution of two grammes each of powdered cinnamon and cloves for four grammes of the sugar, to correct the griping effect which is frequently produced.

Dose, thirty to sixty grains (2.0–3.9 Gm.), used as an agreeable laxative.

PULVIS IPECACUANHÆ ET OPII. U. S. (Br.)

POWDER OF IPECAC AND OPIUM Pulv. Ipecac. et Opii [Compound Powder of Ipecac, Dover's Powder, Opii et Ipecacuanhæ pulvis compositus P. I.]

(pŭl'vĭs ĭp-ẹ-căc-ŭ-ăn'hæ ĕt ō'pĭ-ī)

Pulvis Ipecacuanhæ Compositus, *Br., U. S.* 1870; Compound Powder of Ipecacuanha; Poudre d'Ipécacuanha Opiacée, *Fr. Cod.;* Poudre de Dover, *Fr.;* Pulvis Ipecacuanhæ Opiatus, *P. G.;* Doversches Pulver, *G.;* Polvere di oppio e di ipecacuana, Polvere del Dower, *It.;* Polvo de ipecacuana opiado, Polvo de Dower, *Sp.*

* "Ipecac, in No. 60 powder, *ten grammes* [or 154 grains]; Powdered Opium, *ten grammes* [or 154 grains]; Sugar of Milk, in No. 30 powder, *eighty grammes* [or 2 ounces av., 360 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Triturate these together thoroughly until the mixture is reduced to a very fine, uniform powder." *U. S.*

"Ipecacuanha Root, in powder, 10 *grammes;* Opium, in powder, 10 *grammes;* Potassium Sulphate, in powder, 80 *grammes.* Mix. This Powder contains 10 per cent. of Opium." *Br.*

Properties.—"Grayish-white or very light brown; under the microscope it exhibits coarse, angular, frequently more or less cone-shaped, colorless fragments from 0.03 to 0.4 mm. in length, very slowly soluble in water and hydrated chloral T.S. and strongly polarizing light with a strong display of colors (fragments of *sugar of milk*); numerous starch grains of ipecac, their presence confirmed by the addition of iodine T.S., and varying from 0.003 to 0.017 mm. in diameter; occasional fragments of tracheids of ipecac; and occasional fragments with the more or less tabular, characteristic stone cells of the capsules of the opium poppy, with their light brown, porous and strongly lignified walls." *U. S.*

The substitution of powdered sugar of milk for potassium sulphate in crystals as formerly used cannot be said to have improved this well-known powder, except in making it more agreeable to the taste. The U. S. process should have directed the powder to be sifted, in order to secure a thorough blending of the ingredients; the sifting should on no account be omitted by the operator. The potassium sulphate or the crystalline sugar of milk serves to promote that minute division and consequent thorough intermixture of the opium and ipecacuanha upon which the peculiar virtues of the compound depend, the potassium sulphate being preferable on account of the greater hardness of its particles. They also serve to dilute the active ingredients, and thus allow of their division into minute doses adapted to the complaints of children. This composition, though called Dover's Powder, does not precisely correspond with that originally recommended by Dover, which was prepared as follows: Four ounces of potassium nitrate and the same quantity of potassium sulphate were mixed in a red hot crucible, and afterwards very finely powdered; one ounce of opium, sliced, was then added, and ground to powder with the saline mixture; lastly, an ounce of ipecac and an ounce of licorice root, in powder, were mixed with the other ingredients. This process was adopted in a former French Codex, and has been retained with little change in the present. For a method of valuing Dover's Powder, by A. B. Prescott, see *A. J. P.,* Dec., 1878.

Uses.—This combination is widely employed under the name of Dover's Powder as a diaphoretic and sedative. It is especially prized in the early stages of the milder infections, such as *colds* and *influenza,* in which an effort is to be made to abort the disease by sweating. Because of its combination of sudorific and analgesic action it is also frequently employed in *muscular rheumatism.* Ordinarily as a sudorific about five grains should be administered either stirred up in water or as a bolus and preferably in connection with hot drinks and other measures for encouraging sweating. The dose may be repeated in four to six hours, when it is desirable to maintain a continued sudorific action.

Dose, three to ten grains (0.2–0.65 Gm.).

Off. Prep.—Pilula Ipecacuanhæ cum Scilla, *Br.*

PULVIS JALAPÆ COMPOSITUS. U. S., Br.

COMPOUND POWDER OF JALAP Pulv. Jalap. Co. [Pulvis Purgans]

(pŭl'vĭs jạ-lā'pæ cọm-pŏs'ĭ-tŭs)

Pulvis Purgans, Pulvis Jalapæ Tartratus, Pulvis Cathartic us; Poudre de Jalap composée, *Fr.;* Jalapenpulver mit Weinstein, *G.*

* "Jalap, in No. 60 powder, *thirty-five grammes* [or 1 ounce av., 103 grains]; Potassium Bitartrate, in fine powder, *sixty-five grammes* [or 2 ounces av., 128 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Mix the powders intimately by trituration and pass the product through a No. 60 sieve." *U. S.*

"Jalap, in powder, 30 *grammes;* Acid Potassium Tartrate, in powder, 60 *grammes;* Ginger, in powder, 10 *grammes.* Mix." *Br.*

Properties.—"Very light brown; when examined under a microscope it exhibits numerous, sharp-angular, colorless fragments mostly somewhat rectangular and with straight edges varying from 0.03 to 0.3 mm. in length, slowly soluble in water or hydrated chloral T.S. and polarizing light with a strong display of colors (fragments of crystals of *potassium bitartrate*); numerous starch grains of jalap, readily distinguished without the use of iodine T.S., usually single, occasionally 2- to 3-compound, and varying from 0.003 to 0.035 mm. in diameter; occasional fragments of laticiferous vessels and parenchyma with yellowish-brown walls, or tracheæ with bordered pores, and rosette aggregates of calcium oxalate from 0.01 to 0.035 mm. in diameter, that occur in jalap." *U. S.*

The rubbing of the bitartrate with the jalap is thought to favor its more minute division, while it increases its hydragogue effect. A combination of these two ingredients, though with a larger proportion of cream of tartar (see *Jalapa*), forms a good cathartic in *dropsy*.

Dose, of the powder, from thirty grains to a drachm (2.0–3.9 Gm.).

PULVIS KALADANÆ COMPOSITUS. Br.

COMPOUND POWDER OF KALADANA

(pŭl'vĭs kă-lă-dā'næ cŏm-pŏs'ĭ-tŭs)

"Kaladana, in powder, 30 *grammes;* Acid Potassium Tartrate, in powder, 60 *grammes;* Ginger in powder, 10 *grammes.* Mix." *Br.*

This powder is used as a cathartic.

Dose, from ten to sixty grains (0.65–3.9 Gm.).

PULVIS KINO COMPOSITUS. Br.

COMPOUND POWDER OF KINO

(pŭl'vĭs kī'nō cŏm-pŏs'ĭ-tŭs)

Pulvis Kino et Opii Compositus, *N. F.*, Compound Powder of Kino and Opium; Pulvis Kino cum Opio, *Br.* 1864; Powder of Kino and Opium; Poudre de Kino Opiacée, *Fr.;* Kinopulver mit Opium, *G.*

"Kino, in powder, 75 *grammes;* Opium, in powder, 5 *grammes;* Cinnamon Bark, in powder, 20 *grammes.* Mix. This Powder contains 5 per cent. of Opium." *Br.*

The N. F. powder is practically identical with the Br. (see Part III).

This is an anodyne astringent powder, useful in some forms of *diarrhea*, but of which the composition would be better left to extemporaneous prescription, as the proportion of the ingredients should vary with the circumstances. Twenty grains contain one grain of opium.

Dose, from five to twenty grains (0.32–1.3 Gm.).

PULVIS OPII COMPOSITUS. Br.

COMPOUND POWDER OF OPIUM

(pŭl'vĭs ō'pī-ī cŏm-pŏs'ĭ-tŭs)

Poudre d'Opium composée, *Fr.;* Zusammengesetztes Opiumpulver, *G.*

"Opium, in powder, 10 *grammes;* Black pepper of commerce, in powder, 15 *grammes;* Ginger, in powder, 30 *grammes;* Caraway Fruit, in powder, 42 *grammes;* Tragacanth, in powder, 3 grammes. Mix. This Powder contains 10 per cent. of Opium." *Br.*

This seems to have been introduced in order to have at hand all the dry ingredients of the Confection of Opium. (See *Confectio Opii.*) Ten grains (0.65 Gm.) of the powder contain one grain (0.065 Gm.) of opium.

PULVIS RHEI COMPOSITUS. U. S., Br.

COMPOUND POWDER OF RHUBARB Pulv. Rhei Co.

(pŭl'vĭs rhē'ī cŏm-pŏs'ĭ-tŭs)

Magnesia and Rhubarb, Gregory's Powder; Poudre de Rhubarbe composée, *Fr.;* Pulvis Magnesiæ cum Rheo, *P. G.;* Kinderpulver, Pulvis Infantum, *s. P. Antacidus, G.*

* "Rhubarb, in No. 60 powder, *twenty-five grammes* [or 386 grains]; Magnesium Oxide, *sixty-five grammes* [or 2 ounces av., 128 grains]; Jamaica Ginger, in No. 60 powder, *ten grammes* [or 154 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Rub the rhubarb and ginger together, then gradually add the magnesium oxide and continue the trituration until they are thoroughly mixed, then pass through a No. 60 sieve." *U. S.*

"Rhubarb Root, in powder, 22 *grammes;* Light Magnesia, 66 *grammes;* Ginger, in powder, 12 *grammes.* Mix." *Br.*

Properties.—"A pinkish-white, mobile powder, becoming darker on exposure to moisture; when examined under the microscope it exhibits fine particles of magnesium oxide, numerous starch grains and characteristic fragments of vegetable tissues; starch grains of ginger, more or less elliptical or ovoid, frequently with a prominent beak, from 0.005 to 0.06 mm. in diameter; starch grains of rhubarb, single or compound, either spherical or polygonal, often with a central cleft, from 0.002 to 0.02 mm. in diameter; mounts made with hydrated chloral T.S. give a strong effervescence and show more clearly the fragments of reticulate tracheæ, the reddish-brown parenchyma of rhubarb with numerous small starch grains or rosette aggregates of calcium oxalate, varying from 0.05 to 0.1 mm. in diameter. With solutions of the alkalies many of the fragments of rhubarb become of a deep red color." *U. S.*

This is a good laxative antacid, well adapted to *bowel complaints*, especially in children.

Dose, for an adult, from one-half to one drachm (2.0–3.9 Gm.); for a child two or three years old, from five to ten grains (0.32–0.65 Gm.).

PULVIS SCAMMONIÆ COMPOSITUS. Br.

COMPOUND POWDER OF SCAMMONY

(pŭl'vĭs scam-mō'nĭ-æ cŏm-pŏs'ĭ-tŭs)

"Scammony Resin, in powder, 50 *grammes;* Jalap, in powder, 35 *grammes;* Ginger, in powder, 15 *grammes.* Mix." *Br.*

This does not appear to us a very eligible preparation.

Dose, from ten to twenty grains (0.65–1.3 Gm.).

PULVIS TRAGACANTHÆ COMPOSITUS. Br.

COMPOUND POWDER OF TRAGACANTH

(pŭl'vĭs trăg-ą-căn'thæ cŏm-pŏs'ĭ-tŭs)

"Tragacanth, in powder, 15 *grammes;* Gum Acacia, in powder, 20 *grammes;* Starch, in powder, 20 *grammes;* Refined Sugar, in powder, 45 *grammes.* Mix." *Br.*

This is applicable to the general purposes of the demulcents, but is chiefly employed in Great Britain as a vehicle for heavy insoluble powders.

Dose, one-half to one drachm (2.0–3.9 Gm.).

PYRETHRUM. U. S. (Br.)

PYRETHRUM Pyreth. [Pellitory Root]

(pȳ-rē'thrŭm)

"The dried root of *Anacyclus Pyrethrum* (Linné) De Candolle (Fam. *Compositæ*). Preserve Pyrethrum in tightly-closed containers, adding a few drops of chloroform or carbon tetrachloride, from time to time, to prevent attack by insects." *U. S.* "Pyrethrum Root is the dried root of Anacyclus Pyrethrum *DC.*" *Br.*

Pyrethri Radix, *Br.;* Pyrethrum Root; Radix Pyrethri Romani; Spanish Chamomile, Longwort, Pellitory of Spain; Pyrèthre officinal, *Fr. Cod.;* P. vrai, Salivaire, *Fr.;* Bertramwurzel, Römische Bertramwurzel, *G.;* Pelitre (Raiz de), *Sp.*

Anacyclus Pyrethrum is perennial, and sends up numerous stems, usually trailing at the base, erect in the upper portion, eight or ten inches high, and terminated by one large flower. The leaves are doubly pinnate, with narrow, nearly linear segments of a pale-green color. The florets of the disk are yellow; the rays white on their surface, and reddish or purple beneath and at their edges.

The plant is a native of Northern Africa, the Levant, and the Mediterranean coast of Europe, being also cultivated. The root is the part used under the name of pellitory, or *pellitory of Spain.*

The German Pharmacopœia formerly recognized the root of *Anacyclus officinalis* Hayne (*A. Pyrethrum* Schrader), a plant cultivated in Magdeburg. The roots are smaller and thinner, attaining a length of 25 cm. and a thickness of 5 cm. They are externally grayish-brown; the bark is not radiating and does not contain many stone cells, such as are present in the official pyrethrum. The taste resembles that of the official drug but is even more pungent.

Properties.—Pyrethrum is officially described as "nearly cylindrical, slightly tapering, usually in pieces from 2.5 to 10 cm. in length and from 5 to 20 mm. in diameter; externally dark brown, deeply longitudinally furrowed and somewhat wrinkled, occasionally bearing short, tough, hair-like rootlets, crown more or less annulate, and occasionally tufted with coarse fibers or with long, soft-woolly, nearly straight, 1-celled hairs; fracture short; bark dark brown with 1 or 2 circular rows of resin ducts, closely adhering to the light yellow, radiate, porous wood, in the medullary rays of which occur 1 to 3 rows of resin ducts; odor distinct; taste sweetish, pungent, very acrid, tingling and producing a strong sialogogue effect. The powder is light to dark brown; when examined under the microscope it exhibits numerous spherical or irregular masses of inulin, the nature of which is especially seen with polarized light, and lignified fragments of the woody tissues and stone cells associated with cork; inulin in spherical granules or irregular masses, from 0.01 to 0.1 mm. in diameter, which is not affected by the addition of iodine T.S.; tracheæ with simple pores and reticulate or scalariform thickenings, usually associated with wood parenchyma and with few or no wood fibers; stone cells in groups, the cells more or less tabular in outline and with thick, yellowish porous walls; cork in yellowish-brown or dark brown fragments. Pyrethrum yields not more than 5 per cent. of ash." *U. S.*

"Usually from five to ten centimetres long, and from ten to fifteen millimetres thick; unbranched, nearly cylindrical, or frequently tapering towards both extremities; the crown often bearing a tuft of nearly colorless hairs. Outer surface brown and longitudinally wrinkled. Fracture short. In transverse section, numerous, narrow, yellowish wood-bundles alternating with wider, brownish-grey medullary rays; in the cortex and medullary rays scattered, yellowish-brown oleo-resin ducts; in the parenchymatous tissue inulin, but no starch. Characteristic odor; taste pungent, salivant." *Br.*

Its analysis by Koene gives, in 100 parts, 0.59 of a brown, very acrid substance, of a resinous appearance, and insoluble in potassium hydroxide (this is stated to contain *pelletonin*), 1.06 of a dark brown, very acrid, fixed oil, soluble in potassium hydroxide; 0.35 of a yellow acrid oil, also soluble in potassium hydroxide; traces of tannin; 940 parts of gum; inulin; 7.60 parts of potassium sulphate and carbonate, potassium chloride, calcium phosphate and carbonate, alumina, silica, etc., and 19.80 of lignin, besides loss. (See A. J. P., viii, 175.) Buchheim (*A. E. P. P.,* v, 458) claims to have discovered as the active principle an alkaloid, *pyrethrine,* which, treated with alcoholic potassium hydroxide, splits up like piperine, and yields *pyrethric acid.* Schneegans (*Proc. A. Ph. A.,* 1897, 736) has obtained this pyrethrine in long branched needles united in tufts, melting at 46° C. (114.8° F.), with an extremely burning taste. It is soluble in absolute alcohol, acetone, ether, strong acetic acid, chloroform, and carbon disulphide, yields a yellow solution, which soon changes to red.

A *false pellitory root* has been identified by E. M. Holmes as the product of *Corrigiola telephiifolia.* It is readily distinguished from the true root by its being softer and more flexible, by its having a distinctly sweetish taste, and especially by the transverse section of the root, which is of a yellowish-white color, with from three to five pale opaque concentric rings, each alternating with a narrower translucent horny ring.

Uses.—Pellitory is a powerful irritant, used

almost exclusively as a sialagogue in certain forms of *headache, rheumatic* and *neuralgic affections* of the face, *toothache,* etc., or as a local stimulant, in *palsy of the tongue or throat,* and in relaxation of the uvula. For these purposes it may be chewed, or employed as a gargle in decoction of vinous tincture. The dose as a masticatory is from thirty grains to a drachm (2.0–3.9 Gm.). Its action upon the general system has not been studied to any extent, but 50 minims of a tincture of it very nearly killed a child three and a half years old. The symptoms were those of gastro-enteritis, followed by convulsions. (*London Practitioner,* Aug., 1876.) An alcoholic extract is sometimes employed by dentists as a local anesthetic application to *carious teeth.*

Dose, twenty grains (1.3 Gm.).

Off. Prep.—Tinctura Pyrethri, *U. S., Br.*

PYROGALLOL. U. S.

PYROGALLOL Pyrogall. [Pyrogallic Acid]

(pȳ-rō-găl'lŏl)

"Trihydroxybenzene [$C_6H_3(OH)_3$ 1 : 2 : 3 = 126.05]. Preserve it in well-closed containers, protected from light." *U. S.*

Acidum Pyrogallicum; Trihydroxybenzene; Pyrogallol, *Fr. Cod.;* Acide Pyrogallique, *Fr.;* Pyrogallolum, *P. G.;* Pyrogallol, Pyrogallussäure, *G.;* Pirogallol, *It.*

Of the three triatomic phenols indicated by theory, this is the best known, *phloroglucin* and *oxyhydroquinone* being the other two. It may be prepared synthetically, but is usually obtained as one of the results of the decomposition of gallic acid by heat, and may be obtained by submitting extract of galls to sublimation, the reaction produced by the heat being:

$$C_7H_6O_5 = C_6H_6O_3 + CO_2$$

The vapors of pyrogallol rise, and condense on the upper surface of the paper diaphragm. The chief difficulty in the process is to properly regulate the heat, as at a high temperature this acid passes rapidly into *metagallic acid,* and thus the product is diminished. According to Löwig, it is best prepared by heating gallic acid, previously dried at 100° C. (212° F.), in a glass retort, by means of a zinc chloride bath, to 210° C. (410° F.), when the pure pyrogallol sublimes. It is stated by De Luynes and Espandieu that in the ordinary method of obtaining pyrogallic acid much of the acid is lost. According to Pelouze, the proportion of pyrogallic acid produced ought to be very nearly 75 per cent., but the processes in use yield only 25 per cent., the pyrogallic acid itself undergoing rapid decomposition at an elevated temperature. De Luynes and Espandieu have succeeded in preventing this loss by decomposing gallic acid in water under pressure, instead of by dry sublimation. Gallic acid is introduced into a bronze boiler with twice or three times its weight of water; the temperature is raised to a point ranging from 200° C. (392° F.) to 210° C. (410° F.), and maintained at that point for half an hour, when the liquid is allowed to cool. The boiler now contains a slightly colored solution of pyrogallic acid. This is heated with a little pure animal charcoal, filtered, evaporated sufficiently, and set aside to crystallize. The crystalline mass obtained is somewhat colored. To obtain it entirely white, nothing more is necessary than to distil it in a vacuum. The product is quite 75 per cent. The carbon dioxide escapes through the joinings of the apparatus, while the aqueous vapor is retained. (*A. J. P.,* 1866, p. 22.) Another equally satisfactory procedure is that of Thorpe, for details of which see *A. J. P.,* 1881, p. 53, 236.

Properties.—It is officially described as in "light, white, or nearly white laminæ or fine needles; odorless, and having a bitter taste. It acquires a grayish tint on exposure to air and light. One Gm. of Pyrogallol dissolves in 1.7 mils of water, 1.3 mils of alcohol, and in 1.6 mils of ether at 25° C. (77° F.); very soluble in boiling water or boiling alcohol. It melts between 129° and 133° C. (264.2° and 271.4° F.). An aqueous solution of Pyrogallol (1 in 10) reduces solutions of the salts of silver, gold, and mercury even in the cold. When freshly prepared, 1 mil of an aqueous solution of Pyrogallol (1 in 20) is colored brownish-red by a few drops of ferric chloride T.S. A blue color is produced in an aqueous solution of Pyrogallol (1 in 20) by freshly prepared ferrous sulphate T.S. Incinerate about 1 Gm. of Pyrogallol; not more than 0.1 per cent. of ash remains. A freshly prepared solution of Pyrogallol (1 in 20), in recently boiled distilled water, is colorless or at most slightly yellow, and is neutral or only slightly acid to litmus. The solution gradually acquires a brown color on exposure to the air and an acid reaction due to the absorption of oxygen; the absorption of oxygen and change of color take place very rapidly if the solution contains an alkali hydroxide." *U. S.*

According to Rosing, of Christiana, it is always partially converted, when sublimed, into metagallic acid, to which probably it owes its acid reaction as generally found in commerce; for when quite pure it has no influence on litmus paper. It is a triatomic phenol, $C_6H_3(OH)_3$, and is therefore, properly speaking, not an acid at all; hence the change in the official title to "Pyrogallol." One of its characteristic properties is its strong affinity for oxygen, in consequence of which it instantly undergoes change by contact with chlorine, iodine, bromine, and the acids which readily yield oxygen. Through the same property it rapidly reduces some of the metallic oxides, and its use in photography as a developing agent is based on this effect exercised on the salts of silver. Though unalterable in the air when quite dry, it is rapidly changed in alkaline solution by the absorption of oxygen, so that it may be used for ascertaining the proportion of this gas in a mixture of gases. By the action of phthalic anhydride upon pyrogallol is formed *gallein,* a dye color much used in calico printing. By the action of glacial acetic acid upon pyrogallol in the presence of

zinc chloride is formed *gallacetophenone*, $CH_3—CO—C_6H_2(OH)_3$, which has been used in medicine as a substitute for pyrogallol.

Uses.—Pyrogallol is an active irritant and in concentrated solution even caustic. It is somewhat germicidal, though distinctly inferior to phenol in power; according to Cooper (*B. M. J.*, 1912, i, 1235), its phenol coefficient is 0.8. When taken internally it is actively poisonous, its toxic effect being due in part to its local irritant action upon the alimentary tract, but also partly from a phenol-like action upon the central nervous system and a destructive effect upon the blood corpuscles. It causes a solution of the hemoglobin from the latter and a change of hemoglobin into methemoglobin, which, if death does not occur too soon, is manifested by the appearance of icterus and methemoglobinuria.

The toxic symptoms produced by it are vomiting and purging with collapse, pale or cyanosed lips, the skin often presenting a peculiar greenish hue or sometimes jaundiced; the urine is albuminous and may be brown or black from the presence of hemoglobin or methemoglobin. Fatty degenerations and enlargement of the liver, similar to those produced by phosphorus, have been noted by Personne. (*C. R. A. S.*, Oct., 1869.)

Even its external use is not devoid of danger, two deaths having been reported from its topical application, and Kuseh (*W. K. W.*, 1909) reports abortion in pregnant women from a 10 per cent. ointment.

Pyrogallol is used in medicine solely as an application in various skin diseases, especially *psoriasis*. In this condition it owes its therapeutic action probably to its reducing powers, although its local stimulating effect and antibacterial properties may also play a part in its usefulness. It is occasionally used in *lupus* for its caustic action. For medical purposes it is generally applied in the form of an ointment varying in strengths of from two to ten per cent.

PYROXYLINUM. U. S., Br.

PYROXYLIN Pyroxylin. [Soluble Gun Cotton]

(py-rŏx-y-lĭ'nŭm)

"A product obtained by the action of a mixture of nitric and sulphuric acids on cotton and consisting chiefly of cellulose tetranitrate [$C_{12}H_{16}(ONO_2)_4O_6 = 504.17$]. Preserve it in cartons, packed loosely, and protected from light and moisture." *U. S.*

Pyroxylon, *U. S.* 1870; Colloxylin, Gun Cotton, Collodion Cotton; Fulmicoton soluble. *Fr.*; Kollodiumwolle, *G.*; Piroxilina, *Sp.*

The process of the U. S. P., 1890, for making *pyroxylin* was not introduced into the U. S. P. VIII or IX. It is as follows: "Purified Cotton, *one hundred grammes* [or 3 ounces av., 231 grains]; Nitric Acid, *fourteen hundred cubic centimeters* [or 47 fluidounces, 163 minims]; Sulphuric Acid, *twenty-two hundred cubic centimeters* [or 74 fluidounces, 187 minims]; Alcohol, Ether, Water, each *a sufficient quantity*. Mix the Acids gradually in a glass or porcelain vessel, and, when the temperature of the mixture has fallen to 32° C. (89.6° F.), add the Purified Cotton. By means of a glass rod imbue it thoroughly with the Acids, and allow it to macerate, until a sample of it, taken out, thoroughly washed with a large quantity of Water, and subsequently with Alcohol, and pressed, is found to be soluble in a mixture of *one volume* of Alcohol and *three volumes* of Ether. Then remove the Cotton from the Acids, transfer it to a larger vessel, and wash it, first, with cold Water, until the washings cease to have an acid taste, and then with boiling Water, until they cease to redden blue litmus paper. Finally, drain the Pyroxylin on filtering paper, and dry it in small, detached pellets, by means of a water-bath or steam-bath, at a temperature not exceeding 60° C. (140° F.). Keep the Pyroxylin, loosely packed, in well-closed vessels containing not more than about 25 Gm., in a cool and dry place, remote from lights or fire."

"Cotton, 10 *grammes;* Sulphuric Acid, 50 *millilitres;* Nitric Acid, 50 *millilitres;* Distilled Water, *a sufficient quantity*. Mix the Acids in a porcelain mortar; immerse the Cotton in the mixture, and after it is thoroughly wetted by the Acids stir it for three minutes with a glass rod; transfer it to Distilled Water, wash until free from acid, drain, and dry the Pyroxylin in a warm room." *Br.*

Gun cotton was discovered by Schönbein, of Basel, in Switzerland. The name is applied to several closely related yet distinct products. They are not, as was at first supposed, nitro-derivatives in which the group NO_2 merely replaces hydrogen, atom for atom, but compounds in which the nitric acid residue NO_3 is present, replacing OH groups of the cellulose formula. Thus, taking the doubled formula $C_{12}H_{20}O_{10}$ for cellulose, there is produced by the action of nitric acid under different circumstances $C_{12}H_{14}O_4(NO_3)_6$, and following this, successively, $C_{12}H_{15}O_5(NO_3)_5$, $C_{12}H_{16}O_6(NO_3)_4$, $C_{12}H_{17}O_7(NO_3)_3$, and $C_{12}H_{18}O_8(NO_3)_2$. The first of these, the hexanitrate, is insoluble in alcohol and ether, and constitutes the true explosive gun cotton. The soluble gun cotton used in the preparation of *collodium* is a varying mixture of the four lower nitrates, but is chiefly made up of the tri- and tetra-nitrates. (Tollens, *Handbuch der Kohlenhydrate,* 1888.) The hexanitrate, when very thoroughly washed free from acid, is insoluble in water, alcohol, ether, and all mixtures of alcohol with ether. It constitutes the true explosive gun cotton, which when compressed in cakes and fired by a fulminate explodes with great violence. Other compounds intermediate between some of these have been described by different chemists, but Abel, the chemist of the Woolwich Arsenal in England, has shown that they were imperfectly purified preparations.

Properties.—Gun cotton has the appearance of ordinary cotton, but is harsh to the touch. When intended for solution it is best made by

the joint action of sulphuric and nitric acids, or, as proposed by Ellet of the South Carolina College, of potassium nitrate and sulphuric acid. Experience has thoroughly shown that the use of the acids as practised in the 1890 official formula gives better results than the employment of potassium nitrate and sulphuric acid, which was directed in the U. S. P. 1860. For Flint's process and that of E. Senft, for pyroxylin, see U. S. D., 19th edition, pages 1030 and 1031.

Care should be exercised not to let the mixture attain a temperature much above 32° C. (89.6° F.). It is insoluble in water, and nearly so in alcohol, but dissolves freely in acetic ether and amyl acetate. (*A. J. P.*, 1887, 275.) The following are the official description and tests: "Pyroxylin is a yellowish-white, matted mass of filaments, resembling raw cotton in appearance, harsh to the touch; exceedingly inflammable, burning, when unconfined, very rapidly and with a luminous flame; less explosive than cellulose hexanitrate. When kept in well-closed bottles and exposed to the light, it is decomposed with the evolution of nitrous vapors, leaving a carbonaceous residue. It is slowly but completely soluble in 25 parts of a mixture of 3 volumes of ether and 1 volume of alcohol. Soluble in acetone and in glacial acetic acid and precipitated from these solutions on the addition of water. Saturate 0.5 Gm. of Pyroxylin with alcohol in a dish placed in cold water and then ignite the Pyroxylin at the top. When combustion is completed and the dish heated to redness, not more than 0.3 per cent. of ash remains. Stir 1 Gm. of Pyroxylin with 20 mils of distilled water; the latter does not acquire an acid reaction, and on evaporating 10 mils of the filtered liquid to dryness on a water bath, not more than 0.0015 Gm. of residue remains (*soluble impurities*)." *U. S.*

"Resembles cotton-wool, but is somewhat harsher to the touch. Highly inflammable. Readily soluble in a mixture of equal volumes of *alcohol* (90 per cent.) and *ether* (distinction from gun-cotton)." *Br.*

Guichard proposes the use of chemically pure filtering paper as yielding a superior product to cotton. He takes 1400 parts of sulphuric acid, sp. gr. 1.82; 700 parts of nitric acid, sp. gr. 1.37; 70 parts of the paper; puts the mixed acid in a vessel surrounded by cold water to keep down the temperature, drops the paper in leaf by leaf, allows it to stand three hours, and then washes freely with water. (*J. P. C.*, 4e sér., xii, 290.) When kept for long periods, gun cotton is liable to spontaneous decomposition. The change is shown by the bottle in which the gun cotton is kept becoming full of nitrous acid vapor, and the substance is so far altered that it is no longer explosive or soluble in ether. Bouet states that the decomposition from exposure to light takes place sooner in gun cotton which has been prepared with potassium nitrate and sulphuric acid than where the mixed acids have been used. He says that, with both, the sides and bottom of the bottle are nearly covered with crystals of oxalic acid. (See *A. J. P.*, March, 1862, p. 187.) The official direction to keep pyroxylin "in cartons, protected from the light" is a valuable precaution against decomposition. When kindled, gun cotton flashes off like gunpowder, burning without residue. Yet, according to Bleekrode, when wet with ether, or similar fluid, and touched with a light, the liquid will burn out of it without firing it. (*J. P. C.*, 4e sér., xviii.) Its inflaming point is at 187.7° C. (370° F.). Marx makes it lower. Prepared in various forms after acting upon it with solvents like amyl acetate, etc., to convert it into a plastic mass, the higher nitrates constitute the well known "smokeless powders" now so largely used in warfare. Pyroxylin, or soluble gun cotton, is now extensively used as the basis of transparent varnishes for lacquering metal and wood. The solvent employed is usually a mixture of methyl alcohol or acetone with petroleum benzin, the miscibility of which is affected by the addition of small quantities of compound ethers like amyl acetate. In medicine it is used as a protective covering, especially in the form of collodion.

Off. Prep.—Collodium, *U. S.*, *Br.*

QUASSIA. U. S. (Br.)

QUASSIA Quass. [Bitter Wood]

(quâs'sĭ-ą)

"The wood of *Picrasma excelsa* (Swartz) Planchon, known in commerce as Jamaica Quassia, or of *Quassia amara* Linné, known in commerce as Surinam Quassia (Fam. *Simarubaceæ*)." *U. S.* "Quassia Wood is the wood of the trunk and branches of Picræna excelsa, *Lindl.*" *Br.*

Quassiæ Lignum, *Br.*; Jamaica Quassia, Quassia Wood; Bitter Wood; Bitter Ash; Quassie Amère ou Bois amer de Surinam, *Fr. Cod.*; Bois de Quassie, Quassie de la Jamaïque, *Fr.*; Lignum Quassiæ, *P. G.*; Quassiaholz, Fliegenholz, *G.*; Quassia, Quassia della Giammaica, *It.*

"In logs of varying length, or in chips or raspings; yellowish white, tough and dense, but easily split. In longitudinal section, elongated cells containing single crystals of calcium oxalate; in transverse section, medullary rays mostly two or three cells wide. No odor; taste intensely bitter." *Br.*

The genus *Picrasma* is represented by eight species, which are found in the warmer regions of the Old and New World. They all possess a bitter wood and bark.

Picrasma excelsa (Swartz) Planchon (*Picræna excelsa* Lindley), as its name implies, is a lofty tree, sometimes attaining the height of not less than one hundred feet, with a straight, smooth tapering trunk, which is often three feet in diameter near its base, and is covered with a smooth, gray bark. The leaves are pinnate, the leaflets being petiolate and oblong pointed and arranged in opposite pairs, with a single leaflet at the end. The flowers are small, of a yellowish-green color, and disposed in panicles. They are polygamous and pentandrous. The

fruit is a small black drupe. This species inhabits Jamaica and the Caribbean Islands, where it is called *bitter ash*. Most of the commercial quassia is obtained from this tree.

Quassia amara, or bitter quassia, is a small branching tree or shrub, with alternate leaves, consisting of two pairs of opposite pinnæ, with an odd one at the end. The leaflets are elliptical, pointed, sessile, smooth, of a deep green color on their upper surface, and paler on the under. The common footstalk is articulated and winged. The flowers, which are hermaphrodite and decandrous, are bright red, and terminate the branches in long racemes. The fruit is a two-celled capsule containing globular seeds. *Quassia amara* is a native of Surinam, and is found in Brazil, Guiana, Colombia, Panama, and the West Indies, as also in some tropical countries of the Old World. Its root, bark, and wood were formerly official. They are excessively bitter, as in fact are all parts of the plant. For the botanical description and history of *Quassia amara*, see J. U. Lloyd, *West. Drug.*, 1897, 7; also Gilling (*P. J.*, 1908, lxiii, p. 30).

Properties.—Quassia is at first whitish, but becomes yellow by exposure, and sometimes has blackish spots or markings, due to the presence of the mycelium of a fungus. The two varieties are thus officially described:

"*Jamaica Quassia.*—Usually in chips, raspings or shavings, occasionally in small cubes or billets; yellowish-white or bright yellow, with a few light gray pieces somewhat coarsely grained; fracture tough, fibrous; odor slight; taste bitter. Under the microscope, sections of Jamaica Quassia show large tracheæ either single or in groups of 2 to 5, the walls being marked by numerous, small, bordered pores, and the contents being often of a yellowish color; medullary rays mostly 1 to 5 cells wide and from 10 to 20 rows deep; calcium oxalate, in crystal fibers near the medullary rays, in 4- to 6-sided prisms, from 0.006 to 0.03 mm. in length; wood fibers with thin walls and oblique pores; starch grains few, spherical or ellipsoidal, from 0.01 to 0.015 mm. in diameter.

"*Surinam Quassia.*—The crude drug and microscopic sections closely resemble the Jamaica variety; tracheæ usually single or in pairs, sometimes in groups of 3 or 4; medullary rays in narrower and larger groups than in the Jamaica variety, from 1 to 4 cells wide and from 10 to 30 rows deep; calcium oxalate crystals few or entirely absent, thus distinguishing the variety from Jamaica Quassia." *U. S.*

Quassia imparts its active properties, with its bitterness and yellow color, to water and alcohol. Its virtues depend upon a peculiar bitter crystallizable principle, denominated *quassin*, which was first discovered by Wiggers, who assigned it the formula $C_{10}H_{12}O_3$. Quassin is white, opaque, unalterable in the air, inodorous, and of an intense bitterness, which in the solutions of this principle is almost insupportable. The bitterness is pure, and resembles that of the wood. When heated, quassin melts like a resin. It is but slightly soluble in water, 100 parts, at 54° C. (129.2° F.) dissolving only 0.45 part, and that slowly. By the addition of salts, especially of those with which it is associated in quassia, its solubility is strikingly increased. It is also but slightly soluble in ether, but is very soluble in alcohol, more so in that liquid hot than cold, and the more so the purer it is. Quassin is perfectly neutral, though both alkalies and acids increase its solubility in water. It is precipitated by tannic acid from its aqueous solution, which is not disturbed by iodine, chlorine, corrosive sublimate, the salts of iron, sugar of lead, or even lead subacetate.

Oliveri and Denaro (*A. J. P.*, 1885, p. 29) obtained quassin in a thoroughly pure, crystallized state, and made a complete study of it. They give it the formula $C_{32}H_{44}O_{10}$. It melts at 210° to 211° C. (410°–411.8° F.), and is very soluble in alcohol, chloroform, and acetic acid, but only sparingly so in ether. Its aqueous solution becomes yellow on exposure to the air, is dextro-rotatory, excessively bitter, and reduces Fehling's solution. When quassin is heated to 90° C. (194° F.) for some hours with diluted sulphuric acid (4 per cent.) it yields *quasside*, $C_{32}H_{42}O_9$, a white, amorphous, bitter substance, formed from quassin by removal of H_2O; no glucose could be detected in the mother liquors. Bromine forms a derivative which seems to have the formula $C_{32}H_{41}Br_3O_9$. If quassin is heated with concentrated hydrochloric acid in sealed tubes for four hours at 100° C. (212° F.), methyl chloride is formed and a colorless substance deposited, which the authors call *quassic acid*, $C_{28}H_{38}O_6(COOH)_2$. This is far less soluble in alcohol than quassin, and crystallizes in silky needles, which melt at 245° C. (473° F.), and reduce Fehling's solution and ammoniacal silver nitrate in the cold. The authors consider quassin as the methyl ether of this quassic acid, as follows:

$$C_{28}H_{38}O_6(COOCH_3)_2 = C_{32}H_{44}O_{10}$$

The real nature of quassin is at present somewhat doubtful, it being probably that distinct substances have been confounded by chemists. Dymock and Warden believe that they have obtained quassin from the wood of *Picrasma quassioides* (Ham.) Benn. of India. According to the researches of Massute (*A. J. P.*, 1890, p. 338), *Quassia amara* contains four principles, which are different from those of *Picrasma excelsa*. By shaking an alcoholic extract of quassia wood with chloroform he obtained a mixture of crystals, from which, eventually, four bitter principles, differing in melting point and solubility, were separated. One of these melting at 210° to 211° C. (410°–411.8° F.), and another melting at 239° to 242° C. (462.2°–467.6° F.), were in too small a quantity to be further examined, but the former agreed in melting point and crystalline form with the quassin of Wiggers ($C_{32}H_{40}O_{10}$). Of the other two, one melted at 215° to 217° C. (419°–422.6° F.), and is represented by the formula $C_{35}H_{48}O_{10}$, while the other melted at 221° to 226° C.

(429.8°–438.8° F.), and is represented by $C_{37}H_{50}O_{10}$. From the wood of *Picrasma excelsa* two crystalline compounds were separated by Massute, both having lower melting points than either of the compounds from *Q. amara.* One was in needles, melted at 204° C. (399.2° F.), and had the composition $C_{35}H_{46}O_{10}$, while the other was in prisms, melted at 209° to 212° C. (408.2°–413.6° F.), and had the composition $C_{36}H_{48}O_{10}$. Both of these are homologues of a third crystalline principle, $C_{29}H_{34}O_{10}$, melting point 212° to 216° C. (413.6°–420.8° F.), which occurs with them. When the *picrasmin,* $C_{35}H_{46}O_{10}$, above referred to, melting at 204° C. (399.2° F.), is heated with hydrochloric acid, it is changed like quassin into an acid, which in this case has the formula $C_{33}H_{42}O_{10} + 5H_2O$, and is called *picrasmic acid.* It appears, therefore, that each wood represents a different series of homologous compounds.

Uses.—Quassia was introduced into medicine about the middle of the 18th century by a negro of Surinam, named Quassi, who acquired considerable reputation in the treatment of the malignant fevers of that country by a secret remedy, which we was induced to disclose to Rolander, a Swede, for a valuable consideration. Specimens were taken to Stockholm by this gentleman in the year 1756, and the medicine soon became popular in Europe. The name of the negro has been perpetuated in the generic title of the plant. But the quassia of Surinam is now comparatively little used, it having been superseded by the product of *Picrasma excelsa* from the West Indies.

Quassia is among the most powerful of the simple bitters, useful in *failure of appetite* due to gastric debility, and in overdoses capable of sufficiently irritating the stomach to produce vomiting. Its active principle, *quassin,* has been studied by Comparden, who asserts that in moderate doses it acts as a stimulant to the salivary, hepatic, and renal secretions, and in overdoses causes burning pain in the œsophagus, with headache, nausea, vertigo, vomiting, diarrhea, and muscular cramps. It is also stated that if given in doses of six-tenths of a grain (0.04 Gm.) before meals it increases markedly the alvine discharges, and that it is especially useful in *constipation* from debility of the muscular and intestinal coats. The dose of pure quassin is three-tenths of a grain (0.02 Gm.).

An infusion of quassia, two ounces in a pint of water, affords a valuable and safe injection for *seat-worms.*

Syrupus Quassiæ.—This syrup is used in the preparation of a harmless fly-poison. Macerate, during twenty-four hours, 1000 parts of quassia wood with 5000 parts of water, then boil for half an hour, set aside for twenty-four hours, and press; mix the liquid with 150 parts of molasses, and evaporate to 200 parts. A weaker decoction of quassia does not kill the flies. From this the *Fly Water* or *Fly Plate* is prepared as follows: Mix when needed, and dispense without filtering, 200 parts of syrup of quassia, 50 parts of alcohol, and 750 parts of water. It is used by moistening with the mixture a cloth or filtering paper on a plate.

Quassia is given in infusion, tincture, extract, or fluidextract. Some *dyspeptic* patients who have become habituated to its bitterness, chew the wood occasionally with benefit.

Dose, five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Infusum Quassiæ, *Br.;* Tinctura Quassiæ, *U. S., Br.;* Extractum Quassiæ, *N. F.;* Fluidextractum Quassiæ, *N. F.*

QUILLAIÆ CORTEX. Br.

QUILLAIA BARK

(quĭl-lā'ïæ cŏr'tĕx)

"Quillaia Bark is the dried inner part of the bark of Quillaja Saponaria, *Molina.*" *Br.* "The dried bark of *Quillaja Saponaria* Molina (Fam. *Rosaceæ*), deprived of the periderm." *N. F.*

Quillaja, *N.F.*, **Soap-tree Bark;** Soap Bark; Quillaia, *Pharm.* 1880; Panama Bark; Panama (Bois de), *Fr. Cod.;* Ecorce de Quillaya, *Fr.;* Seifenrinde, *G.*

The name of this genus is said to be derived from the popular name of the tree *Quillay,* which in turn comes from the Chilian word *quillean,* to wash.

Quillaja Saponaria Molina is a tree of moderate size, with alternate oval or oblong leaves having entire or slightly denticulate margins. Staminate and pistillate flowers grow on the same branch, are axillary, pedunculate, and without corolla. The calyx of the pistillate flower persists in fruit, and has its limb deeply divided into five oval acute segments. The bark is thick, the wood very hard. This tree was first described by the famous Abbé Giovanni Ignazio Molina in the *Saggio sulla Storia naturale del Chili,* published at Bologna, in 1782; second edition, 1810. (Translated into German, I. D. Brandis, Leipsic, 1786; into French, Gruvel, Paris, 1789; into English, London, 1809; also Middletown, Conn., 1880.) It is first noticed by systematic writers in the second (Gmelin's) edition of the *Syst. Nat.,* tome ii, p. 767. The tree is a native of Peru and Chili, but is now cultivated in Northern Hindostan, where it is said to resist well the frosts of winter, and to be flourishing.

Properties.—Soap bark is officially described in the Br. as "in flat pieces, from three to eight millimetres thick, but varying considerably in length and width. Outer surface brownish-white, or, where the outer bark has been incompletely removed, reddish or blackish-brown, and longitudinally striated. Inner surface white or yellowish-white and smooth. Fracture splintery and laminated, the tangential surfaces of the laminæ often exhibiting glistening prismatic crystals of calcium oxalate. In transverse section, chequered with delicate radial and tangential lines; medullary rays four cells wide; numerous irregular groups of bast fibres of varying size; scattered starch grains from four to six microns in diameter. Powdered Quillaia Bark is strongly sternutatory; *water* vigorously shaken with it forms copious persistent froth.

Odor not marked; taste astringent and acrid. Ash not more than 15 per cent." *Br.*

It is described in the N. F. IV as "in flat pieces of variable length, from 3 to 8 mm. in thickness, or in small chips; outer surface brownish-white, often with small patches of cork attached, otherwise nearly smooth; inner surface yellowish-white, nearly smooth, with occasional circular depressions, conical projections of transverse channels; fracture uneven and strongly fibrous, the laminæ oblique to each other. Odor slight; taste acrid. The powder is strongly sternutatory, and contains calcium oxalate in monoclinic pyramids and prisms from 0.035 to 0.2 mm. in length. Quillaja yields not more than 10 per cent. of ash." *N. F.*

The fracture exhibits, when slightly magnified, glistening prismatic crystals. Quillaja bark is histologically distinguished and its powder recognizable, by the large and numerous prismatic calcium oxalate crystals, which are from 0.035 to 0.200 mm. long.

When bruised and macerated in water quillaja bark imparts to that liquid the property of frothing like soap when agitated. This has been found by Fleury, Jr., and Boutron-Chalard to be owing to the existence of a *saponin* in the bark. The bark contains neither tannic acid nor any bitter principle. The formula of saponin, given by Rochleder, was $C_{32}H_{54}O_{18}$, and Schiaparelli agreed with him. Stütz, however (*Ann. Ch. Ph.*, 218, 231), gives it as $C_{19}H_{30}O_{10}$, and this is now accepted for the saponin of quillaja bark. Saponin is slowly decomposed by dilute acids into *sapogenin*, $C_{14}H_{22}O_2$, and a glucose. R. Kobert (*Chem. Central.*, 1893, i, 32) gives a list of one hundred and forty plants which contain bodies of the saponin class. He arranges them under several formulas which seem to form an homologous series. Thus, $C_{17}H_{26}O_{10}$ he terms Saponin I (*senegin* or *quillaia sapotoxin*); $C_{18}H_{28}O_{10}$ is Saponin II (Schmiedeberg's *digitonin* or *saprorubrin*); $C_{19}H_{30}O_{10}$ is Saponin III (*quillain* or *quillaiac acid*); $C_{20}H_{32}O_{10}$ is *cyclamin*, Paschki's *digitoxin*, or *sarsaparillsaponin;* $C_{22}H_{36}O_{10}$ is *sarsa-saponin;* $C_{26}H_{44}O_{10}$ is *parillin.*

G. Melliers states that there is present in quillaja bark a carbohydrate which he has identified as *saccharose.* (*P. J.*, Feb., 1901, 161.)

Uses.—In diluted form quillaia saponin is irritant to all tissues, and when concentrated it kills by its local action both muscular and nervous tissue. As was first discovered by H. Köhler, when injected into the leg of the frog in minute quantity it produces not only motor weakness but a rapid loss of sensibility, so that reflex movements can no longer be caused by irritating the foot. The paralysis seems to affect especially the peripheral nerve endings, since irritation of the nerve trunk, although incapable of causing contraction of the muscles supplied by it, elicits pain, cries and other evidences of sensibility. Muscles with which saponin comes in contact become unexcitable and pass into a condition resembling post mortem rigidity. According to Köhler, this occurs without change in the microscopic structure, but Przybyszewski found that in the neighborhood of the injection where the saponin was abundant the muscles underwent structural changes similar to those of myositis. In the frog saponin produces not only local symptoms, but after a time widespread paralysis, with final arrest of the cardiac movements. Given internally to mammals it causes violent gastro-intestinal irritation, progressive loss of power, disturbance of respiration and circulation, and usually clonic and tonic convulsions, which are probably secondary to the perturbations of the cardiac and respiratory functions.

Injected into the circulation in rabbits and dogs, according to the researches of Przybyszewski, it causes fall of the arterial pressure, with great disturbance of the respiration and finally cardiac arrest. According to Köhler, the action of the drug upon the heart is antagonistic to that of digitalin, so that the application of sufficient quantities of saponin to the frog's heart which has been arrested by the local application of digitalin will bring about a return of pulsations, while, on the other hand, digitalin is capable of putting aside cardiac arrest from saponin. As has been shown by Ransom (*D. M. W.*, xxvii), saponin has a powerfully destructive action upon the red blood corpuscles, due to an extraordinary tendency which it has to unite with their cholesterin. The action of saponin upon the respiratory centres is very great, the injection of large doses being followed by immediate arrest of respiration, the heart continuing to beat for some time. As it exists in agrostemma seeds, saponin has several times caused death in the human species. The symptoms have been headache, vertigo, vomiting, hot skin, rapid feeble pulse, progressive muscular weakness, and finally coma. Following out the experiments of Kobert, Ulenburg and Keppler tried saponin as a local anesthetic, but found that it was not practically convenient for use; nor were the essays of Kobert with the glucoside as an antipyretic more encouraging.

According to Kobert (*Gaz. Méd. de Paris*, xiv, 2, 1883), saponin of commerce is composed chiefly of two substances, *quillaic acid* and *sapotoxin.* For method of preparation, see *T. G.*, vol. ii, 540. The quillaic acid is said to be extraordinarily poisonous, three-one-thousandths of a grain for each pound of body weight injected into the veins of a cat being sufficient to cause death, although thirty grains administered by the mouth are safely borne. Lohmann (*P. J.*, 73, 477) affirms that chemically pure saponin is not injurious when taken by the stomach.

Both the active principles, quillaiac acid and sapotoxin, of quillaja bark are violent local irritants. In a case of poisoning by quillaiac acid (*T. G.*, xi) the symptoms were violent vomiting, with epigastric pain, increased diuresis and cystic irritation, accompanied by cold sweats, feeble pulse, threatened syncope, and other evidences of collapse.

Sapotoxin, when in sufficient concentration and amount, is a fatal poison to all forms of protoplasm. Given to the lower animals in very large toxic dose it produces violent convulsions with death from failure of the respiration. When in smaller quantities it causes violent *dysenteric diarrhea*, with ecchymotic hyperæmia, œdema, and necrotic destruction of the intestinal mucous membrane. The smallest lethal doses are said to produce great weakness, death occurring after some days through collapse and general paralysis without intestinal symptoms. In such cases, when the drug is administered hypodermically, a severe hemorrhagic inflammation occurs at the place of injection. Fatty preparations of sapotoxin applied to the sound skin produce redness and burning with, after repeated applications, painful pustulation. Both sapotoxin and quillaiac acid have the power of breaking down the red blood corpuscles, but it is not apparent that such destruction plays an important *rôle* in poisoning by these substances except at the point of injection after hypodermic use.

On account of the active principles of soap bark being the same as those of senega, and to some extent of sarsaparilla, Kobert has proposed the use of quillaja as a cheap substitute for these much used drugs. As a stimulating expectorant he uses a decoction (five parts to two hundred) in doses of a tablespoonful for the adult. As a substitute for syrup of senega Power suggests the *syrup of quillaja*, prepared by adding four parts of the fluidextract (made by the process for fluidextract of arnica root, see p. 524) to sufficient syrup to make twenty-five parts. (*P. J.*, Oct., 1886.)

Quillaja is much used in the arts for washing silk, cloth, and other fabrics, for which soap would not be suitable. It is an emulsifying agent, but unless ordered by the physician should never be used by the pharmacist in the preparation of emulsions, on account of its active medicinal properties.

It has also been largely used in the production of foam on non-alcoholic carbonated beverages. This use has been criticized as harmful and it is now prohibited by law in many jurisdictions.

Off. Prep.—Liquor Picis Carbonis, *Br.*; Tinctura Quillajæ, *N. F.* (*Br.*).

QUININA. U. S.

QUININE Quin.

(quĭ-nĭ'nă)

"An alkaloid [$C_{20}H_{24}O_2N_2 + 3H_2O = 378.26$] obtained from the bark of various species of *Cinchona* (Fam. *Rubiaceæ*). Preserve it in well-closed containers, protected from light." *U. S.*

Chininum; Quinine Hydratée, *Fr. Cod.*; Chinin, *G.*; Chinina, *It.*; Quinina, *Sp.*

This alkaloid is prepared by adding to a solution of quinine sulphate a quantity of ammonia water or solution of sodium hydroxide just a sufficient quantity to cause a precipitation of the alkaloid.

Properties.—Quinine is whitish, rather flocculent, and usually not crystalline; it may with care be crystallized from its alcoholic solution in silky needles, and Liebig obtained it from a somewhat ammoniacal aqueous solution in the same form. It is inodorous and very bitter. The crystals obtained from alcoholic solution have the composition $C_{20}H_{24}O_2N_2 + 3H_2O$, and fuse at 57° C. (134.6° F.). They may be deprived of water by warming or exposure over sulphuric acid, and they then fuse at 171.2° to 172° C. (340°–341.6° F.). By carefully regulated heat, it may be sublimed unchanged, assuming a crystalline form. (Waddington, *P. J.*, March, 1868, p. 413.) According to Hesse, anhydrous crystalline quinine is soluble in 1960 parts of water at 15° C. (59° F.), and the trihydrate in 1670 parts. It is soluble in about 900 parts of boiling water, in about 6 parts of cold and in 2 parts of boiling alcohol, very soluble in ether, chloroform, benzene, petroleum benzin, carbon disulphide, fixed and volatile oils, and in about 200 parts of glycerin. The alcoholic solution is intensely bitter. Quinine is unalterable in the air. It forms salts with the acids which readily crystallize. The tannate, tartrate, and oxalate are said to be insoluble or nearly so, but are dissolved by an excess of acid. The acetate is so slightly soluble that it is precipitated from a solution of the sulphate by magnesium acetate and the other acetates. (*A. J. P.*, xxx, 386.) When recently precipitated quinine, diffused in water, is exposed to the action of a stream of carbon dioxide, the quinine is dissolved, and, if the solution be exposed, acicular crystals of quinine carbonate will be deposited, which effloresce in the air, are soluble in alcohol, but insoluble in ether, have an alkaline reaction, and effervesce with acids. After the deposition of the crystals has ceased, the solution yields quinine on evaporation. (Langlois, *C. R. A. S.*, Nov. 7, 1853, 727.) Freshly precipitated quinine is scarcely soluble to an appreciable extent in an excess of potassium hydroxide, but is more readily dissolved by ammonia. (Wadgymar, *A. J. P.*, Sept., 1866, 451.) Flückiger (1878) noticed that solutions of quinine exposed to sunlight rapidly turned brownish-yellow, and subsequently deposited a flocculent precipitate, which he proved to be neither quinine nor quinicine, but an entirely different substance. It had lost the alkaloidal character, yet possessed the same chemical composition as quinine. He named it *quiniretin*. (*P. J.*, May, 1878.)

Quinine and its salts may be distinguished from all other alkaloids and their salts, except only quinidine and quinicine, by the beautiful emerald-green color (*thalleioquin*) which reults when their solution is treated first with solution of chlorine and then with ammonia, and which changes to a white or violet upon saturation with a dilute acid. The statement which has been frequently made that the chlorine water must be fresh, was disproved by C. F. Zeller, but it has been repeatedly observed that the reaction is inhibited by the presence of even minute

amounts of free inorganic acids and the compound solution of chlorine, made by reacting upon potassium chlorate with hydrochloric acid and then diluting with water, cannot be used to replace chlorine water made by the older process. The reaction with bromine water is much more delicate and satisfactory. (See *A. J. P.*, 1880, p. 385.) The least quantity of quinine may be detected by powdering the substance supposed to contain it, then shaking it with ether, and adding successively the tests just mentioned. Quinine in aqueous solution turns the plane of polarization to the left, to varying degrees, however, according to the concentration, the solvent used, etc. Acids increase the amount of deviation. In relation to the property possessed by quinine of imparting fluorescence to its aqueous solution, which is possessed also, though in less degree, by other cinchona alkaloids, and other properties common to both quinine and its sulphate, there will be occasion to speak under quinine sulphate. A singular discovery was made by Bence Jones of London, of a substance normally present in the animal system having analogous properties, and named by him "*animal quinoidine.*"

Quinine is officially described as "a white, micro-crystalline powder; odorless, having a bitter taste, developing rather slowly, but intense and persistent; efflorescent in dry air. One Gm. of Quinine dissolves in 1560 mils of water, 0.8 mil of alcohol, 1.1 mils of chloroform, 1.9 mils of ether, and in 1890 mils of ammonia water at 25° C. (77° F.); also in 800 mils of boiling water. Its alcoholic solution (1 in 10) is lævorotatory and alkaline to litmus. A solution of Quinine in diluted sulphuric acid shows a vivid blue fluorescence. Add 2 or 3 drops of bromine T.S. to 1 mil of an aqueous solution of Quinine (1 in 100) made with the aid of just sufficient diluted sulphuric acid to effect solution, and then add 1 mil of ammonia water; the liquid acquires an emerald-green color due to the formation of thalleioquin. Quinine loses not more than 15 per cent. of its weight when dried to constant weight at 100° C. (212° F.). Incinerate about 1 Gm. of Quinine; not more than 0.1 per cent. of ash remains. A solution of about 0.1 Gm. of Quinine in 2 mils of sulphuric acid is not darker than light yellow (*organic impurities*). This solution is not colored red on the subsequent addition of a few drops of nitric acid (*morphine*). Heat about 0.2 Gm. of Quinine with 2 mils of potassium hydroxide T.S.; the odor of ammonia is not evolved (*ammonium salts*). Dissolve 1.74 Gm. of Quinine in 20 mils of alcohol, dilute the solution with 50 mils of hot distilled water and neutralize it with normal sulphuric acid V.S., using methyl red T.S. as indicator. Evaporate the liquid to dryness on a water bath, powder the residue, mix it in a test tube with 20 mils of distilled water and complete the test for other cinchona alkaloids as directed under *Quininæ sulphas.*" *U. S.*

Quinicine (*quinicia*).—When quinine and cinchonine, or quinidine and cinchonidine, or their salts, are exposed to heat, they are changed into isomeric alkaloids—quinine and quinidine into *quinicine,* and cinchonine and cinchonidine into *cinchonicine,* each isomeric with its own antecedents. These new alkaloids are, therefore, products rather than educts, and generally result, in greater or less proportion, from the processes employed in extracting the other alkaloids from bark, though it is not impossible that they may pre-exist in bark to a certain extent, being formed by a natural process, from the same original alkaloids, either in the living tree, or in the barks while drying, after separation from the tree. *Quinicine* is almost insoluble in water, but very soluble in alcohol, and differs from quinine in being dextro-rotatory and uncrystallizable. *Cinchonicine* is also insoluble in water and soluble in alcohol. It agrees with cinchonine, from which it is derived, in producing deviation of the plane of polarization to the right, but differs from cinchonidine in this respect, and differs from both in being amorphous or uncrystallizable.

The study of the decomposition products of quinine and associated alkaloids so actively carried on for several years past has thrown considerable light upon its composition. It appears to be a derivative of a partially hydrogenized diquinoline, corresponding to the formula $C_9H_6(OCH_3)N$ — $C_9H_{11}(OH)N.CH_3$. By oxidation with chromic acid it yields *quininic acid,* $C_9H_5(OCH_3)N.COOH$, which is the phenol ester of cinchoninic acid, $C_9H_6N.COOH$; by oxidation with nitric acid it yields *cinchomeronic acid,* $C_5H_3N(COOH)_2$; by the action of potassium hydroxide it yields *methoxyquinoline,* $C_9H_6N(OCH_3)$. For a summary of our knowledge upon the constitution of quinine and cinchonine, see *Guareschi's Einführung in das Studium der Alkaloide,* translated by H. Hermann Kunz-Krause, Berlin, 1896, 524, *et seq.*

The most important salt of quinine is the *sulphate,* the process for procuring which, as well as its properties, will be hereafter described. Besides the salts which are official, the *phosphate, acetate, citrate, lactate, camphorate, ferrocyanide, arsenite, antimonate, urate, hypophosphite, chlorate, citro-thymate, sulphovinate, sulpho-salicylate,* and *meconate,* have also been employed or recommended, but none of them has yet gained admittance into the Pharmacopœias, and none probably is superior to the official salts. The first four may be prepared by saturating a solution of the acids respectively with quinine, and evaporating the solutions. The *camphorate* is recommended as a substitute for the valerate. (*A. J. P.*, July, 1865, p. 254.) The *ferrocyanide* is directed to be made by boiling together four parts of quinine sulphate and one of potassium ferrocyanide, both in concentrated solutions, pouring off the liquor from a greenish-yellow substance of an oily consistence which is precipitated, washing the latter with distilled water, then dissolving it in strong alcohol at 37.7° C. (100° F.), filtering immediately, and afterwards evaporating the solution. Pelouze believes this prep-

aration to be pure quinine, mixed with a little Prussian blue. (*A. G. M.*, 3e sér., xv, 236.)

Quinine arsenite has been recommended by Ringdon, especially in chronic cutaneous affections. Alder prepares it by dissolving arsenic trioxide in water, with enough alkali to make the solution neutral, adding about five times its weight of silver nitrate, washing the precipitated silver arsenite, drying, and mixing with three times its weight of quinine hydrochloride, digesting the mixture for a day with 70 per cent. alcohol, filtering, and allowing the filtrate to evaporate spontaneously. The salt is crystalline, soluble in alcohol, chloroform, and ether, but sparingly so in water. The dose is one-third of a grain (0.021 Gm.), given at first twice a day, and afterwards three or four times a day. *Quinine antimonate* has been recommended by La Camera, of Naples, as a febrifuge, being especially applicable to cases of doubtful periodicity. It unites, he thinks, the evacuant properties of the antimonials with the antiperiodic property of quinine. The dose is two or three grains (0.13 or 0.20 Gm.), four times a day. (*J. P. C.*, 3e sér., xxv, 471.) *Quinine urate* is thought by Pérayre of Bordeaux, to be peculiarly efficacious in obstinate intermittents. It is prepared by boiling 10 parts of crude quinine in water, adding gradually 20 parts of crystallized uric acid, and, after sufficient ebullition, filtering and evaporating. A yellow salt is obtained, sometimes amorphous, more frequently crystalline, soluble in hot and less so in cold water, and, according to the author, capable of curing intermittent fever in smaller doses than the sulphate, with less cerebral disturbance, less bitterness, and easier tolerance by the stomach. (*J. P. C.*, 3e sér., xxxvii, 139.) *Quinine hypophosphite* may be prepared by dissolving 3 parts of calcium hypophosphite in 60 parts of distilled water, and adding the filtered solution to a solution of 13 parts of quinine sulphate in 200 parts of alcohol, allowing the mixture to stand two hours, and filtering, distilling off the alcohol and evaporating the solution and setting aside to crystallize. The salt is soluble in 25 parts of cold water, in 1.5 parts of boiling water, and in 10 parts of alcohol. *Quinine glycerophosphate* exists in two conditions, basic and neutral. The basic salt, which is stable, may be made by dissolving 75.6 Gm. of quinine in 500 mils of ether and mixing with a solution of 17.2 Gm. of glycerophosphoric acid in 60 Gm. of alcohol (95 per cent.), collecting the white precipitate, washing with ether, and drying. (E. Fallières, *P. J.*, 1898, 410.)

Quinine citro-thymate is prepared by Pavesi by heating in a flask on a water bath 4 parts of quinine and 6 parts of oil of thyme, with enough alcohol to dissolve both. After standing 12 hours, 2 parts of powdered citric acid are added, and the whole heated, filtered, evaporated, and allowed to crystallize. For processes for making other quinine salts, see *U. S. D.*, 19th edition, page 1039.

Uses.—In sufficient concentration quinine appears to be poisonous to all forms of protoplasm, as well of the unicellular micro-organisms as of the more highly organized tissue of man. Among the unicellular organisms, in a general way the protozoa are more susceptible than the bacteria, but the drug is peculiarly poisonous to the plasmodia of malaria. In the frog moderate doses of quinine cause a diminution in the reflex activity which is generally attributed to a stimulation of the spinal inhibitory center, commonly known as Setschenow's center. Larger quantities are directly depressant to the motor ganglia. In mammals it frequently gives rise to convulsions, which appear to be due to irritation of the motor area of the brain. Locally applied it is paralyzing to both the motor and sensory nerves, but especially to the latter. In moderate dose it has no demonstrable influence upon the circulation, but large quantities—equivalent to 75 or 80 grains for man—are depressant to the heart. It increases the vigor of the contractions of the voluntary muscles, but apparently lessens resistance to fatigue. According to Cushny, it is a direct stimulant to the uterine muscle, increasing the force of the contractions but not greatly affecting the tonus.

As was shown many years ago by Binz, when added to the blood outside the body in the proportions of about 1 part in 4000, it caused an immediate cessation of the amœboid movements of the white corpuscles. This effect is probably simply one of the manifestations of its general protoplasmic toxicity, and plays little part in its therapeutic action. According to Roth (*J. P. Ex. T.*, 1912, iii, p. 470), it causes a pronounced leukocytosis; at first there is an increase in the number of lymphocytes which he believes is due to contraction of the spleen and lymphatic tissues, but later there is an increase in the number of polymorphonuclear cells. According to De Sandro (*Rif. M.*, 1910), the continued use leads to an increase in the number of both red and white cells in the blood.

Quinine appears to have a powerful influence in lessening the rapidity of catabolism in the body. The evidence in favor of this view is three-fold: first is the well-established fact of diminished excretion of nitrogenous waste products with the urine under its influence; secondly, the observations of Senta (*A. I. P. T.*, xviii, p. 217), who has found a diminution in the absorption of oxygen and gaseous exchange of isolated bits of muscles; and thirdly, its effects upon bodily temperature. Although in normal man ordinary doses do not cause a reduction of temperature, yet they prevent the natural rise of temperature which takes place after violent exercise and in febrile patients often gives rise to distinct lowering.

Quinine is used in medicine for a large variety of purposes. The oldest and most important of these is for the treatment of *malarial fevers*, for which disease it is by far the most reliable remedy that we possess. While the curative value of the drug is universally acknowledged there is some difference of opinion as to its usefulness as a prophylactic against this disease, but despite the contrary results of

Stitt (*J. A. M. A.*, 1908, i, p. 1682), we are inclined to believe in its usefulness.

In various infectious fevers, such as *pneumonia, septicemia,* or *typhoid fever,* it has been widely employed, not merely as an antipyretic, but in the thought that it has a direct influence in lessening the growth of pathogenic bacteria in the body. In *pneumonia* there is reason to believe, although not definitely established, that quinine directly inhibits the growth of the pneumococci in the body. It is probable that the well-known curative action of the drug in *acute coryza* is attributable to some influence upon the causative infection of this common complaint. Moon (*Journ. of Infectious Diseases,* 1913, xiii, p. 165) presented evidence of a curative effect in hydrophobia in dogs, but his results have been called in question by Cumming (*Journ. of Infectious Diseases,* 1914, xv) and by Frothingham and Halliday (*Journ. Med. Research,* 1914, xxx). It appears also to be of use in *whooping-cough.*

Because of its restraining effect upon destructive metabolism as well as its effect as a bitter upon the stomach, quinine is a valuable remedy in the treatment of various form of *malnutrition.* In *Graves's disease* it appears to have an effect not merely in restraining the excessive catabolism which is characteristic of this disorder, but also to have a general sedative influence on the nervous system. Some years ago on the theory that *chorea* was due to a lack of spinal inhibition H. C. Wood suggested the use of quinine in the treatment of this disorder, and in many cases it has proven of marked benefit. Through a similar line of reasoning its use was extended to the treatment of *nocturnal enuresis.* It is also recommended as an internal remedy by a number of authors in the treatment of various forms of skin disease, especially *psoriasis* and *urticaria;* in *lupus erythematosus* it has been used both internally and locally.

Brooke (*J. A. M. A.*, 1914, lxii) experimentally determined that quinine sulphate would kill amœba in solutions of 1 to 20,000, and employed it in the form of enemata in the treatment of amœbic *dysentery* with satisfactory results.

Quinine possesses marked local anesthetic powers and has come into considerable use as a substitute for cocaine. For this purpose the hydrochloride of quinine and urea is generally preferred. (See page 934.)

Because of the insolubility of basic quinine it was formerly believed that the alkaloid was absorbed only from the stomach, but Grosser (*Biochem. Zeit.*, viii, 1907–1908, p. 98) has shown that even the insoluble preparations are completely absorbed. Apparently much of the drug is destroyed in the body as various investigators have succeeded in recovering only from 40 to 60 per cent. of the ingested dose from the excreta. According to Kerner, a portion escapes in an amorphous uncrystallizable form, and a second portion as a substance free from bitter taste, though crystallizable and having the fluorescence of quinine; for this substance he has proposed the name of *dihydroxyl-quinine.*

Elimination seems to be freest between the sixth and twelfth hours, and about two-thirds of that which is recovered from the urine is excreted within twenty-four hours of its ingestion.

The dose of quinine varies greatly according to the purpose for which it is used, as well as the susceptibility of the patient. When used for its tonic effect from three to five grains (0.2–0.32 Gm.) may be given three or four times a day. The antipyretic dose is from fifteen to twenty grains (1.0–1.3 Gm.). S. Solis Cohen has administered, in *pneumonia* with asserted good effects, twenty-five to thirty grains hypodermically (1.7–2.0 Gm.). In the milder forms of *malaria,* such as the ordinary *tertian fever* of temperate climates, from five to ten grains may be given every hour until the patient has taken twenty or thirty grains, and so timed that the last dose comes about an hour before the expected chill. In the tropical varieties of malaria, however, very much larger quantities are required, and in malignant types many authorities recommend to give as high as seventy-five to one hundred grains (5.0–6.5 Gm.) immediately. Such doses cannot be administered by mouth because they are likely to provoke emesis, and moreover, absorption is so slow as to be dangerous in these pernicious fevers. Under such circumstances the quinine may be given hypodermically. The most soluble of the official salts is the dihydrochloride, and by many is the salt of choice for injection, but it is likely to prove irritant because of its acid reaction. The double hydrochloride of quinine and urea is neutral in reaction and is soluble in less than its own weight of water; the 50 per cent. solution may be employed. If injected immediately beneath the skin, solutions of quinine salts are liable to produce local necrosis and ulceration and therefore should always be injected into the muscle substance either in the lumbar or gluteal regions. Extreme care in asepsis is essential in making these injections. A number of cases of *tetanus* have followed the injections of quinine, but McCampbell (*J. A. M. A.*, March 16, 1907) from his experiments concludes that there is no peculiar relation between the quinine and the tetanus germs, except that the spores may be carried in mechanically with the injection and the local necrosis offers a favorable place for their growth.

Toxicology.—Even in the quantities employed for therapeutic purposes quinine frequently produces unpleasant symptoms. The most common of these is ringing in the ears often accompanied with a sensation of fullness in the head, and perhaps some obtunding of the sense of hearing. With the use of larger doses these symptoms are intensified: the deafness is very marked, disturbed vision may exist, and the flushed face, with the sense of distension in the head, may point towards a cerebral congestion, which is in some cases relieved by spontaneous epistaxis. In decided cinchonism, giddiness and staggering in walking are very common. After toxic doses, severe headache, delirium, stupor,

complete deafness and blindness, dilated pupils, embarrassment of respiration, great weakness, convulsions, paralysis, and finally collapse, either comatose or delirious, may result. The deafness produced by large doses of quinine usually passes off rapidly; very rarely is there a permanent impairment of hearing. Amaurosis, with a peculiar ischemia of the retinal vessels, has in a small number of cases been produced by very large therapeutic doses of the alkaloid. Besides its effects on the brain, quinine sulphate sometimes occasions great gastric and intestinal irritation, marked by oppression of stomach, nausea, abdominal pains, vomiting, and purging. In general, these effects of excessive doses gradually pass off, although partial deafness often continues for several days, and sometimes much longer, and permanent deafness has resulted. It is capable of taking life, although enormous amounts of it are requisite for this. Several cases of recovery are recorded after the taking of an ounce by the stomach. Probably only a portion of the drug was absorbed. Five ounces taken in ten days have caused death.

In certain individuals even very small doses may produce toxic symptoms. In these cases the poisoning usually differs very markedly from the ordinary type described above, in most instances being manifest by eruptions on the skin which frequently closely simulate scarlet fever. (See H. C. Wood, Jr., *T. G.*, January, 1902.)

Dose, two to twenty grains (0.13–1.3 Gm.).

Off. Prep.—Elixir Formatum Compositum, *N. F.*; Oleatum Quininæ, *N. F.*; Syrupus Ferri, Quininæ et Strychninæ Phosphatum, *N. F.*; Syrupus Hypophosphitum Compositus, *N. F.*

QUININÆ BISULPHAS. U. S.

QUININE BISULPHATE Quin. Bisulph.

(quĭ-nī′næ bī-sŭl′phăs)

"The acid sulphate [$C_{20}H_{24}O_2N_2.H_2SO_4 + 7H_2O = 548.41$] of the alkaloid quinine. Preserve it in well-closed containers, protected from light." *U. S.*

Chininum Bisulfuricum, Quininæ Sulphas Acidus; Acid Quinine Sulphate; Sulfate de Quinine Neutre, *Fr. Cod.*; Saures Chininsulfat, Chininbisulfat, *G.*; Bisolfato di chinina, *It.*; Sulfato quinico neutro, *Sp.*

This salt is made by suspending 100 Gm. of quinine sulphate in 500 Gm. of warm distilled water, and adding 115 Gm. of diluted sulphuric acid (U. S. P.), filtering and crystallizing. It has been introduced because of the great advantages in solubility that it possesses over the ordinary sulphate. It requires but 8.5 parts of water to dissolve it, while the sulphate requires 720. It is officially described as in "colorless, transparent, or whitish, orthorhombic crystals or small needles; odorless, and having a very bitter taste. It effloresces on exposure to air, and turns yellow on exposure to light. One Gm. of Quinine Bisulphate dissolves in 9 mils of water, 23 mils of alcohol, 15 mils of glycerin, 625 mils of chloroform and in 2500 mils of ether, at 25° C. (77° F.); also in 0.7 mil of boiling water and 0.7 mil of alcohol at 60° C. (140° F.). Its aqueous solution (1 in 20) is strongly acid to litmus and has a blue fluorescence. Add 1 or 2 drops of bromine T.S. to 1 mil of an aqueous solution of Quinine Bisulphate (1 in 100) and then add 1 mil of ammonia water; the liquid acquires an emerald-green color due to the formation of thalleioquin. Barium chloride T.S. added to an aqueous solution of the salt produces a white precipitate, insoluble in hydrochloric acid. Quinine Bisulphate loses not more than 25 per cent. of its weight when dried to constant weight at 100° C. (212° F.). Incinerate about 2 Gm. of Quinine Bisulphate; not more than 0.05 per cent. of ash remains. A solution of about 0.1 Gm. of the salt in 2 mils of sulphuric acid is not darker than light yellow (*organic impurities*). This solution is not colored red by the subsequent addition of a few drops of nitric acid (*morphine*). Dissolve 2.52 Gm. of Quinine Bisulphate in 50 mils of hot distilled water and neutralize the solution with normal sodium hydroxide V.S., using methyl red T.S. as indicator. Evaporate the solution to dryness on a water bath, powder the residue, mix it in a test tube with 20 mils of distilled water and complete the test for other cinchona alkaloids as directed under *Quininæ Sulphas." U. S.*

The acid sulphate of quinine is much more freely soluble than the neutral sulphate and is therefore by many preferred. It has, however, no very real advantage, being inferior for hypodermic injection to the dihydrochloride or the double hydrochloride of quinine and urea because of its lesser solubility, and when given by the mouth the slight increase in solubility over the neutral salt is a matter of small importance. It represents about 80 per cent. of the amount of quinine in the neutral sulphate.

Dose, two to fifteen grains (0.13–1.0 Gm.).

Off. Prep.—Tinctura Antiperiodica, *N. F.*; Tinctura Antiperiodica sine Aloe, *N. F.*

QUININÆ DIHYDROCHLORIDUM. U. S. (Br.)

QUININE DIHYDROCHLORIDE Quin. Dihydrochl.

(quĭ-nī′næ dī-hȳ-drŏ-klō′rīd-dŭm)

"The dihydrochloride [$C_{20}H_{24}O_2N_2.2HCl = 397.15$] of the alkaloid quinine. Preserve it in well-closed containers, protected from light." *U. S.* "Acid Quinine Hydrochloride, $C_{20}H_{24}N_2O_2,2HCl$, is the acid hydrochloride of an alkaloid, quinine, obtained from the bark of various species of Cinchona." *Br.*

Quininæ Hydrochloridum Acidum, *Br.*, Acid Quinine Hydrochloride; Chlorhydrate de Quinine Neutre, *Fr.*; Saures Chininhydrochlorid, Saures Chlorwasserstoffsaures Chinin, *G.*

This was an official quinine salt of the Br. Pharm., 1898. It was introduced into the U. S. P. IX, and retained in the Br., 1914. It has been introduced on account of its remarkable solubility in water—*i.e.*, less than its own weight. It may be made by passing hydrochloric acid gas over dry quinine, but more conveniently by decomposing quinine bisulphate with barium

chloride or by mixing a solution of neutral hydrochloride with one molecular proportion of hydrochloric acid and evaporating the solution at a gentle heat. It is officially described as "a white powder, odorless, and having a very bitter taste. One Gm. of Quinine Dihydrochloride dissolves in about 0.6 mil of water and in 12 mils of alcohol at 25° C. (77° F.); it is slightly soluble in chloroform and very slightly soluble in ether. Its aqueous solution (1 in 20) is strongly acid to litmus. Silver nitrate T.S. added to an aqueous solution of the salt (1 in 20) produces a white precipitate, insoluble in nitric acid. Add 1 or 2 drops of bromine water T.S. to 1 mil of an aqueous solution of the salt (1 in 100) and then add an excess of ammonia water; an emerald-green color is produced due to the formation of thalleioquin. Incinerate about 2 Gm. of Quinine Dihydrochloride; not more than 0.05 per cent. of ash remains. A solution of about 0.1 Gm. of the salt in 2 mils of sulphuric acid is not darker than yellow (*readily carbonizable impurities*). Ten mils of an aqueous solution of the salt (1 in 50) is not rendered more than faintly turbid by the addition of a few drops of barium chloride T.S. (*sulphate*). The addition of a few drops of diluted sulphuric acid to 10 mils of an aqueous solution of the salt (1 in 20) produces no turbidity (*barium*). Dissolve 1.8 Gm. of Quinine Dihydrochloride in 10 mils of distilled water, add a slight excess of ammonia water and extract the precipitate by shaking the mixture with three successive portions of 20, 10 and 10 mils each of chloroform. Evaporate the combined chloroform extracts to dryness on a water bath, dissolve the residue in 25 mils of alcohol, dilute it with 50 mils of hot distilled water and neutralize the liquid with normal sulphuric acid V.S., using methyl red T.S. as indicator. Now evaporate the liquid to dryness on a water bath, powder the residue, mix it with 20 mils of distilled water in a test tube, and complete the test for other cinchona alkaloids as directed under *Quininæ Sulphas.*" *U. S.*

"A white amorphous powder. No odor; taste intensely bitter. Soluble in less than 1 part of *water*. Aqueous solution acid to *litmus*. Yields the *reactions* characteristic of chlorides. Yields not more than the slightest characteristic *reaction* for sulphates. 1 gramme dissolved in 20 millilitres of *water* requires for neutralisation not more than 5.0 millilitres of *N/1 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator. Yields a green coloration when tested as described under 'Quininæ Hydrochloridum.' Loses not more than 3 per cent. of its weight when dried at 100° C. (212° F.). When 2 grammes are dissolved in 15 millilitres of *water*, the solution neutralised with *N/1 solution of sodium hydroxide*, mixed with 1 gramme of powdered non-effloresced *sodium sulphate*, and further treated as described under 'Quininæ Hydrochloridum,' the precipitate produced on the addition of *solution of ammonia* redissolves on rotating the tube (limit of other cinchona alkaloids). No appreciable ash." *Br.*

Uses.—The dihydrochloride is the most freely soluble of the official salts of quinine. For this reason it is frequently preferred for hypodermic injection. Because of its acid reaction, however, it is more likely to produce local irritation than the neutral salts.

Dose, two to ten grains (0.13–0.65 Gm.).

QUININÆ ET UREÆ HYDROCHLORIDUM. U. S.

QUININE AND UREA HYDROCHLORIDE Quin. et Urea. Hydrochl. [Quinine and Urea Chloride]

(quĭ-nī'næ ĕt ū-rē'æ hȳ-drŏ-ȼhlō'rĭ-dŭm)

"A compound of the hydrochlorides of quinine and urea [$C_{20}H_{24}O_2N_2.HCl.CO(NH_2)_2.HCl + 5H_2O = 547.28$] which contains not less than 58 per cent. of anhydrous quinine. Preserve it in well-closed containers, protected from light." *U. S.*

Quinine and Urea Muriate, Chininum Bimuriaticum Carbamidatum.

This salt was discovered by Kutais (1878), is best prepared by Rice's process. Seventy-nine parts of quinine hydrochloride are dissolved in 70 parts of hydrochloric acid (sp. gr. 1.050), the solution filtered, 12 parts of urea added, and the whole warmed until the liquid is clear. It is then set aside, that crystals may form. These are soluble in an equal weight of water, and also in strong alcohol, and are usually purified by recrystallization.

"Quinine and Urea Hydrochloride occurs in colorless, translucent prisms or as a white, granular powder; odorless, and having a very bitter taste; permanent in the air. One Gm. of Quinine and Urea Hydrochloride dissolves in 0.9 mil of water and in 2.4 mils of alcohol at 25° C. (77° F.). An aqueous solution of the salt (1 in 20) is strongly acid to litmus. Silver nitrate T.S. added to an aqueous solution of the salt produces a white precipitate, insoluble in nitric acid. Add 2 mils of colorless nitric acid to a cold solution of about 1 Gm. of the salt in 2 mils of distilled water and cool the mixture at once at the temperature of melting ice. Crystalline leaflets of urea nitrate are formed on standing. Collect the crystals in a funnel upon glass wool, wash them with about 5 mils of a cold mixture of equal volumes of nitric acid and distilled water, and, after draining them, dissolve the crystals in a few mils of distilled water. The addition of a few drops of mercuric nitrate T.S. to the urea nitrate solution, followed by sodium hydroxide T.S., to only a slightly acid reaction, produces a white precipitate. Incinerate about 2 Gm. of Quinine and Urea Hydrochloride; not more than 0.05 per cent. of ash remains. A solution of about 0.1 Gm. of the salt in 2 mils of sulphuric acid is not darker than light yellow (*readily carbonizable matter*). Warm 10 mils of an aqueous solution of the salt (1 in 20) with 5 mils of sodium hydroxide T.S. to 50° C. (122° F.); the odor of ammonia is not evolved at once (*ammonium compounds*). The quinine obtained by precipitating 60 mils

of an aqueous solution of the salt (1 in 20) with sodium hydroxide T.S., washing it on a filter with cold distilled water until the washings give only a faint opalescence with silver nitrate T.S., and then drying it at about 50° C. (122° F.), responds to the test for identity, and 1.5 Gm. of it conforms to the requirement regarding other cinchona alkaloids under *Quinina.*

"**Assay.**—Weigh accurately about 0.5 Gm. of Quinine and Urea Hydrochloride, dissolve it in 5 mils of distilled water in a separator, then add 5 mils of potassium hydroxide T.S., and shake the mixture with successive portions of 10, 5 and 5 mils, respectively, of ether or sufficient to completely extract the quinine. Upon evaporation of the combined ether-extracts and drying to constant weight at 100° C. (212° F.), the residue of anhydrous quinine corresponds to not less than 58 per cent. of the weight of the salt taken." *U. S.*

Uses.—Quinine urea hydrochloride is the most suitable of all the official salts of the alkaloid for hypodermic administration on account of its free solubility and of its neutral reaction. It is, therefore, widely employed in the treatment of the severer types of *malaria,* where the drug must be given subcutaneously, as well as in other conditions where large doses are required. In 1907 Thibault (*Journ. of the Arkansas Medical Soc.,* Sept., 1907), from observing the local effects following the hypodermic administration of this salt, was led to investigate the anesthetic properties of the quinine salts and found that all of the soluble ones produced local anesthesia, if in concentration of greater than 1.5 per cent. Since then quinine and urea hydrochloride as a local anesthetic for all sorts of medical and surgical conditions has been successfully employed by a large number of practitioners. It is somewhat slower than cocaine and in equal solutions distinctly weaker, but because of its lower toxicity is often a remedy of great value. It may be employed in strengths of from 2 to 20 per cent., according to the purpose for which it is used. According to Closson, while inferior to cocaine in its action on nerve endings, it is superior for nerve blocking.

Dose, two to ten grains (0.13–0.65 Gm.).

QUININÆ HYDROBROMIDUM. U. S.

QUININE HYDROBROMIDE Quin. Hydrobr. [Quinine Bromide Quininæ Hydrobromas, U. S., 1890, Quinine Hydrobromate]

(quĭ-nī'næ hȳ-drō-brō'mĭ-dŭm)

"The hydrobromide [$C_{20}H_{24}O_2N_2.HBr + H_2O$ =423.16] of the alkaloid quinine. Preserve it in well-closed containers, protected from light." *U. S.*

Bromhydrate de Quinine Basique, *Fr. Cod.;* Mobobromhydrate de Quinine, *Fr.;* Chininum Hydrobromicum; Chininhydrobromid, Bromwasserstoffsaures Chinin, *G*

This official salt may be made by suspending 10 parts of quinine sulphate in 80 parts of water, boiling, and adding 3.4 parts of barium bromide dissolved in 20 parts of water, filtering, evaporating, and crystallizing. It may also be made by Leger's process, as follows: Quinine sulphate, commercial, crystallized, 40 parts; potassium bromide, dried and powdered, 11 parts; alcohol (80 per cent.), 400 parts; distilled water, 400 parts. Dissolve the sulphate in two hundred parts of alcohol by the aid of heat, add the potassium bromide, dissolved in thirty parts of distilled water, and continue the heat five or six minutes, in order to allow the potassium sulphate, which is formed, to acquire greater compactness, so that it will more readily settle. Filter off from the precipitate, and wash four times with fifty parts of boiling alcohol. Let the alcoholic solution cool, when a further small quantity of potassium sulphate will be deposited. The solution is then again filtered through white filtering paper, and evaporated on a water bath to one hundred parts. Next, four hundred parts of distilled water are poured on, and heat is applied until the hydrobromide is completely dissolved. After allowing the solution to stand in the cold for about twenty-four hours, the dish will be found filled with a compact crystalline mass. The crystals are transferred to a filter, allowed to drain, and dried by exposure to air. Heating would cause them to fuse. The product thus obtained amounts to about thirty parts of perfectly white quinine hydrobromide. By evaporating the mother water to one-third of its volume, about six parts more may be obtained. It is absolutely necessary, as has been already pointed out by Boille, to redissolve the hydrobromide in water as above stated, if the salt is to be obtained in white and bulky crystals. The above quantity of four hundred parts should not be diminished, for, if this were done, the salt would separate at first in the form of an oily liquid, and afterwards would form a crystalline crust. (*Répert. de Pharm.,* 1880, p. 390; *N. R.,* Jan., 1881.)

Properties.—It is in "white, light, silky needles; odorless, and having a very bitter taste. The salt effloresces on exposure to the air. One Gm. of Quinine Hydrobromide dissolves in 40 mils of water, 0.9 mil of alcohol, 7 mils of glycerin, 0.6 mil of chloroform, and in 23 mils of ether at 25° C. (77° F.); also in 3.2 mils of water at 80° C. (176° F.). Its saturated aqueous solution is neutral or not more than slightly alkaline to litmus, and when strongly acidulated with diluted sulphuric acid has a vivid blue fluorescence. Precipitate a saturated aqueous solution of the salt with sodium hydroxide T.S.; filter, supersaturate the filtrate with acetic acid, and then add chloroform and a little chlorine water, and shake the mixture; the chloroform assumes a reddish-brown color. Add 1 or 2 drops of bromine T.S. to 1 mil of an aqueous solution of Quinine Hydrobromide (1 in 100) and then add 1 mil of ammonia water; the liquid acquires an emerald-green color due to the formation of thalleioquin. Quinine Hydrobromide loses not more than 5 per cent. of its weight when dried to constant weight at 100° C. (212°

F.). Incinerate about 2 Gm. of Quinine Hydrobromide; not more than 0.05 per cent. of ash remains. A solution of about 0.1 Gm. of the salt in 2 mils of sulphuric acid is not darker than light yellow (*organic impurities*). On the addition of 0.1 mil of nitric acid to this solution an orange color is produced, due to the liberation of bromine, but no deep color, fading to orange, is noticeable (*morphine*). Ten mils of an aqueous solution of the salt (1 in 50), acidulated with hydrochloric acid, is not rendered more than faintly turbid by a few drops of barium chloride T.S. (*sulphate*). The addition of a few drops of diluted sulphuric acid to 10 mils of a hot aqueous solution of the salt (1 in 20) produces no turbidity (*barium*). Dissolve 2.93 Gm. of Quinine Hydrobromide in 20 mils of distilled water at 65° C. (149° F.), in a test tube of about 80 mils capacity, add a solution of 1.5 Gm. of crystallized sodium sulphate in 10 mils of distilled water warmed to 65° C. (149° F.) and maintain the mixture at this temperature for half an hour, shaking it frequently and thoroughly in the stoppered tube. Then cool it to 15° C. (59° F.) and keep it at this temperature for two hours, shaking it occasionally. Now filter the liquid through a filter paper of 8 to 10 cm. diameter and complete the test for other cinchona alkaloids with 5 mils of the filtrate as directed under *Quininæ Sulphas." U. S.*

Uses.—There is a wide-spread belief that this salt acts somewhat differently from the other preparations of quinine. The proportion of hydrobromic acid is, however, too small to exert any influence upon the system; ten grains of quinine hydrobromide represents less than two grains of hydrobromic acid. The salt has achieved a high reputation in the treatment of *Graves's disease,* and certainly in many cases will cause at least a temporary amelioration of many of the nervous manifestations of this disorder.

Dose, from two to ten grains (0.13–0.65 Gm.).

QUININÆ HYDROCHLORIDUM. U. S., Br.

QUININE HYDROCHLORIDE Quin. Hydroch. [Quinine Chloride, Quininæ Hydrochloras U. S., 1890, Quinine Hydrochlorate]

(quĭ-nī'nē hī-drō-ȼhlō'rĭ-dŭm)

"The hydrochloride [$C_{20}H_{24}O_2N_2.HCl + 2H_2O = 396.71$] of the alkaloid quinine. Preserve it in well-closed containers, protected from light." *U. S.* "Quinine Hydrochloride, $C_{20}H_{24}N_2O_2,HCl,2H_2O$, is the hydrochloride of an alkaloid, quinine, obtained from the bark of various species of Cinchona." *Br.*

Muriate of Quinine; Chlorhydrate de Quinine Basique, *Fr. Cod.;* Chlorhydrate de Quinine, *Fr.;* Chininum hydrochloricum, *P. G.;* Chininhydrochlorid, Salzsaures Chinin, *G.;* Cloridrato di chinina, *It.*

This quinine salt was recommended for admission to the Br. Ph., 1885, by W. Martindale on account of its being more soluble in water and richer in quinine than is the sulphate. It may be readily prepared by treating the alkaloid with diluted hydrochloric acid, or by double decomposition between barium chloride and quinine sulphate. Quinine hydrochloride is in "white, silky, glistening needles; odorless, and having a very bitter taste. The salt effloresces when exposed to warm air. One Gm. of Quinine Hydrochloride dissolves in 18 mils of water, 0.8 mil of alcohol, 7 mils of glycerin, 0.7 mil of chloroform, and in 340 mils of ether at 25° C. (77° F.); also in 0.5 mil of water at 80° C. (176° F.). Its aqueous solution (1 in 20) is neutral or not more than slightly alkaline to litmus, and is not fluorescent, except when highly diluted, or when diluted sulphuric acid is added to it. Silver nitrate T.S. produces in an aqueous solution of the salt a white precipitate, insoluble in nitric acid. Add 1 or 2 drops of bromine T.S. to 1 mil of a solution of Quinine Hydrochloride (1 in 100) and then introduce 1 mil of ammonia water; an emerald-green color is produced due to the formation of thalleioquin. Quinine Hydrochloride loses not more than 10 per cent. of its weight when dried to constant weight at 120° C. (248° F.). Incinerate about 2 Gm. of Quinine Hydrochloride; not more than 0.05 per cent. of ash remains. A solution of about 0.1 Gm. of the salt in 2 mils of sulphuric acid is not darker than light yellow (*organic impurities*); this solution is not colored red by the subsequent addition of a few drops of nitric acid (*morphine*). Ten mils of an aqueous solution of the salt (1 in 50) acidulated with hydrochloric acid is not rendered more than faintly turbid by a few drops of barium chloride T.S. (*sulphate*). The addition of a few drops of diluted sulphuric acid to 10 mils of an aqueous solution of the salt (1 in 20) produces no turbidity (*barium*). Dissolve 2.75 Gm. of Quinine Hydrochloride in 20 mils of distilled water at 65° C. (149° F.) in a test tube of about 80 mils capacity, add a solution of 1.5 Gm. of crystallized sodium sulphate in 10 mils of distilled water warmed to 65° C. (149° F.), and maintain the mixture at this temperature for half an hour, shaking it frequently and thoroughly in the stoppered tube. Cool it to 15° C. (59° F.) and keep it at this temperature for two hours, shaking it occasionally. Now filter the liquid through a filter paper of from 8 to 10 cm. diameter and complete the test for other cinchona alkaloids with 5 mils of the filtrate as directed under *Quininæ Sulphas." U. S.*

"White silky crystals, efflorescent in warm air. No odor; taste very bitter. Soluble in 36 parts of *water,* and in 2 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of chlorides. When to 10 millilitres of an aqueous solution (1 in 1000) 0.5 millilitre of *solution of bromine* and, after well shaking, 1 drop of *strong solution of ammonia* are added, a deep green coloration is produced. When 2 grammes are dissolved in a warm mortar in 20 *millilitres of water* at 60° C. (140° F.), 1 gramme of powdered non-effloresced *sodium sulphate* added, the mixture triturated, cooled, allowed to stand at exactly 15° C. (59° F.) for half an hour with occasional stirring, the crystals of quinine sul-

phate pressed, and the expressed liquid filtered, 5 millilitres of this filtrate, transferred to a dry test-tube and brought to a temperature of 15° C. (59° F.), yield, on the gradual addition of 6 millilitres of *solution of ammonia,* also at a temperature of 15° C. (59° F.), a precipitate which redissolves on rotating the tube (limit of other cinchona alkaloids). Dissolves in *sulphuric acid* and in *nitric acid* without coloration. 1 gramme dissolves in 7 millilitres of a mixture of 2 volumes of *chloroform* and 1 volume of *absolute alcohol.* Loses not more than 9.1 per cent. of its weight when dried at 100° C. (212° F.). Yields no characteristic *reactions* for barium or for sulphates. No appreciable ash." *Br.*

Only the compounds of quinine with the oxy-acids show the fluorescence in acid solution, none of the compounds of the haloid acids showing this reaction.

Quinine hydrochloride has a decided advantage over the sulphate in its greater solubility in water. It is, however, less soluble than the acid quinine hydrochloride.

Dose, two to ten grains (0.13–0.65 Gm.).

Off. Prep.—Tinctura Quininæ, *Br.;* Vinum Quininæ, *Br.;* Elixir Ferri, Quininæ et Strychninæ, *N. F.;* Syrupus Phosphatum cum Quinina et Strychnina, *N. F.*

QUININÆ SALICYLAS. U. S.

QUININE SALICYLATE Quin. Salicyl.

(quĭ-nī'næ săl-ĭ-cĭ'lăs)

"The salicylate [$C_{20}H_{24}O_2N_2.C_7H_6O_3 + H_2O = 480.28$] of the alkaloid quinine. Preserve it in well-closed containers, protected from light." *U. S.*

Salicylate de Quinine Basique, *Fr. Cod.;* Salicylate de Quinine, *Fr.;* Chininsalicylat, Salicylsaures Chinin, *G.;* Salicilato quinico, *Sp.*

Preparation.—Quinine salicylate may be made by adding a solution made by dissolving 3.9 parts of sodium salicylate in 30 parts of water, to a hot solution made by dissolving 10 parts of quinine sulphate in 75 parts of boiling water. The precipitate is collected, washed and dried and recrystallized from its solution in alcohol.

Properties.—It is officially described as in "colorless, odorless needles, having a bitter taste, permanent in the air. It often assumes a pinkish color on keeping. One Gm. of Quinine Salicylate dissolves in 14 mils of alcohol, 13 mils of glycerin, 25 mils of chloroform, and in 160 mils of ether at 25° C. (77° F.); slightly soluble in water. Its saturated aqueous solution is alkaline to litmus and when this solution is treated with a drop of ferric chloride T.S., a violet color develops. Add 1 or 2 drops of bromine T.S. to 10 mils of an aqueous solution of Quinine Salicylate and then introduce an excess of ammonia water; an emerald-green color is produced due to the formation of thalleioquin. Quinine Salicylate loses not more than 5 per cent. of its weight when dried to constant weight at 100° C. (212° F.). Incinerate about 2 Gm. of Quinine Salicylate; not more than 0.05 per cent. of ash remains. Shake about 0.4 Gm. of the salt with 20 mils of distilled water and 1 mil of nitric acid; separate portions of 10 mils each of the filtered solution are not rendered more than slightly turbid by the addition of a few drops of barium chloride T.S. (*sulphate*), nor more than slightly opalescent by a few drops of silver nitrate T.S. (*chloride*). Mix 2.21 Gm. of Quinine Salicylate in a separator with 10 mils of distilled water, add 5 mils of ammonia water, and shake the liquid with three successive portions of 25, 20 and 10 mils, respectively, of ether. Evaporate the combined ether solutions to dryness on a water bath, dissolve the residue in 20 mils of alcohol, dilute it with 50 mils of hot distilled water, and neutralize the liquid with normal sulphuric acid V.S., using methyl red T.S. as indicator. Evaporate it to dryness on a water bath, powder the residue, mix it with 20 mils of distilled water in a test tube, and complete the test for other cinchona alkaloids as directed under *Quininæ Sulphas." U. S.*

Uses.—Quinine salicylate represents approximately 27 per cent. of salicylic acid, and 69 per cent. of anhydrous quinine. It is believed by many practitioners to be a valuable remedy in the advanced stages of an *acute rheumatism,* in *subacute rheumatism,* and in mild *gouty* conditions, but the proportion of salicylic acid seems too small to exercise any pronounced effect on the system.

Dose, from five to ten grains (0.32–0.65 Gm.).

QUININÆ SULPHAS. U. S., Br.

QUININE SULPHATE Quin. Sulph.

(quĭ-nī'næ sŭl'phăs)

"The sulphate [$(C_{20}H_{24}O_2N_2)_2.H_2SO_4 + 7H_2O = 872.62$] of the alkaloid quinine. Preserve it in well-closed containers, protected from light." *U. S.* "Quinine Sulphate, $(C_{20}H_{24}N_2O_2)_2,H_2SO_4,7\frac{1}{2}H_2O$, is the sulphate of an alkaloid, quinine, obtained from the bark of various species of Cinchona." *Br.*

Sulfas Quinicus; Disulphate or Basic Sulphate of Quinia, Sulfate de Quinine Basique, *Fr. Cod.;* Chininum Sulfuricum, *P. G.;* Chininsulfat, Schwefelsaures Chinin, *G.;* Solfato di chinina, *It.;* Sulfato quinico basico, *Sp.*

No process is given in the U. S. Pharm. for preparing quinine sulphate; that of the U. S. P., 1870, will be found in detail in the *U. S. D.,* 17th ed., p. 1141. The process, briefly stated, is to exhaust cinchona bark by boiling with water acidulated with hydrochloric acid and adding milk of lime in excess. The quinine is precipitated with lime, and the dried precipitate digested with boiling alcohol; the alcoholic solution of quinine is evaporated, and the mass dissolved in water acidulated with sulphuric acid. The hot solution is treated with animal charcoal to decolorize it, and then set aside to crystallize.

Pelletier proposed to substitute oil of turpentine for alcohol in the ordinary process for procuring quinine sulphate. The impure quinine, precipitated by lime from the acidulous

decoctions, after being washed, pressed, and dried, is digested with the oil, which dissolves the quinine. The solution thus obtained is agitated with water acidulated with sulphuric acid, by which quinine sulphate is formed. The oil, separating, rises to the top, and is removed for future use, and the aqueous solution of the salt is evaporated, and treated as in the original process. A disadvantage of this method is said to be that the oil does not completely exhaust the precipitate. A similar process has been employed here and in England, either fusel oil or petroleum benzin, or sometimes kerosene being substiuted for oil of turpentine. In this instance, however, the solvent is added to the impure quinine, without separation from the acidulated decoction from which it was precipitated by lime. The mixture being well agitated, the fusel oil or benzene dissolves the alkaloids, and, rising to the surface of the liquid, is drawn off by a siphon. The solution thus drawn off is treated as above with water acidulated with sulphuric acid, and the process is completed in the same manner. (See *P. J.*, xiv, 29, 92, and 139.)

When barks containing the alkaloids *cinchonidine* and *quinidine* are used, as their sulphates are much more soluble than that of quinine, it follows that in the mother waters left after the crystallization of quinine sulphate there will be found a portion of cinchonidine or quinidine sulphate, or of both. In fact, there is generally, under these circumstances, more or less of the sulphates of the four alkaloids, quinine, cinchonine, quinidine, and cinchonidine, all of which are contained in many barks, and, besides these, a portion of amorphous alkaloid, incapable of crystallization, probably resulting, in part at least, from the heat employed in the process. These may in a great degree be separated through their different solubilities in water. Quinine sulphate, being least soluble, will first crystallize, afterwards the cinchonidine or quinidine salt, and finally that of cinchonine, which is the most soluble, while the uncrystallizable salt will remain in solution, and may be obtained in the amorphous state by evaporation to dryness.

Properties.—"Quinine Sulphate occurs in white, silky, light, flexible, glistening crystals, making a very light and easily compressible mass, or as hard, prismatic, monoclinic needles; odorless, and having a persistent, very bitter taste. It effloresces rapidly when exposed to dry air, and then becomes lusterless; when exposed to light, it acquires a brownish tint. One Gm. of Quinine Sulphate dissolves in 725 mils of water, 107 mils of alcohol, and 30 mils of glycerin at 25° C. (77° F.); also in 47 mils of water at 80° C. (176° F.), in about 12 mils of alcohol at 60° C. (140° F.); slightly soluble in chloroform or ether. It is freely soluble in a mixture of 7 volumes of chloroform and 4 volumes of dehydrated alcohol. Its saturated aqueous solution is neutral or not more than slightly alkaline to litmus, and, when acidulated with diluted sulphuric acid, develops a vivid blue fluorescence. When heated to 60° C. (140° F.), or when exposed to dry air, it loses all but two molecules of its water of crystallization. Barium chloride T.S. produces in an aqueous solution of the salt a white precipitate, insoluble in hydrochloric acid. Add 1 or 2 drops of bromine T.S. to 10 mils of an aqueous solution of the salt (about 1 in 1000) and then introduce an excess of ammonia water; the liquid acquires an emerald-green color due to the formation of thalleioquin. Quinine Sulphate loses not more than 16.2 per cent. of its weight when dried to constant weight at 110° C. (230° F.). Incinerate about 2 Gm. of Quinine Sulphate; not more than 0.05 per cent. of ash remains. One Gm. of the salt dissolves completely when heated to 50° C. (122° F.) in 7 mils of a mixture of 2 volumes of chloroform and 1 volume of dehydrated alcohol, and the solution remains clear on cooling (*ammonium sulphate or other inorganic salts*). A solution of about 0.1 Gm. of the salt in 2 mils of sulphuric acid is not darker than light yellow (*organic impurities*); this solution is not colored red by the subsequent addition of a few drops of nitric acid (*morphine*). Dry Quinine Sulphate (which must be neutral or slightly alkaline to litmus) at 50° C. (122° F.) for two hours, and then agitate 1.8 Gm. of the dried salt with 20 mils of distilled water at 65° C. (149° F.) for half an hour. Allow the mixture to cool to 15° C. (59° F.), macerate it at this temperature for two hours with occasional shaking and then filter it through a filter paper of from 8 to 10 cm. in diameter. Transfer 5 mils of this filtrate to a test tube and mix it gently (without shaking) with 7 mils of ammonia water, which must contain not less than 10 per cent. nor more than 10.2 per cent. of NH_3, have a temperature of 15° C. (59° F.), and be added at once. A clear liquid is produced (*other cinchona alkaloids*). If the temperature during the maceration has been 16° C. (60.8° F.), 7.5 mils of ammonia water may be added; if 17° C. (62.6° F.), 8 mils may be added." *U. S.*

"Small, light, white, silky crystals. No odor; taste intensely bitter. Soluble in 800 parts of *water*, and in 65 parts of *alcohol* (90 per cent.). Aqueous solution exhibits a blue fluorescence. Entirely soluble in *water* acidified with a mineral acid. Yields the *reaction* characteristic of sulphates. When to 10 millilitres of an aqueous solution (1 in 1000) 0.5 millilitre of *solution of bromine* and, after well shaking, 1 drop of *strong solution of ammonia* are added, a deep green coloration is produced. Exposed to dry air the crystals effloresce until the water of crystallization is reduced from 7½ molecules to 2 molecules. Aqueous solution yields with *solution of ammonia* a precipitate soluble in *ether*. When 2 grammes, weighed after drying at 50° C. (122° F.), are digested at 60° to 65° C. (140°–149° F.) in a stoppered test-tube with 20 millilitres of *water* for half an hour, repeatedly shaken, then allowed to cool to 15° C. (59° F.), kept at that temperature for half an hour, stirred from time to time, the crystals pressed, and the expressed liquid filtered, then 5 millilitres of this filtrate, transferred to a dry test-tube and

brought to a temperature of 15° C. (59° F.), yield, on the gradual addition of 6 millilitres of *solution of ammonia,* also at a temperature of 15° C. (59° F.), a precipitate which redissolves on rotating the tube (limit of other cinchona alkaloids). 1 gramme dissolves in 7 millilitres of a mixture of 2 volumes of *chloroform* and 1 volume of *absolute alcohol.* No appreciable ash." *Br.*

The acid quinine salts possess fluorescent properties with the exception of those of the haloid acids. It has also been discovered that the presence of acetphenetidin conceals the fluorescence of sulphuric acid solutions of quinine. The diluted acids, and tartaric and oxalic acids in excess, dissolve the sulphate easily. With an additional equivalent of sulphuric acid it forms another sulphate, which is more soluble in water than the official salt, and crystallizes from its solution with much greater difficulty. This is now considered by many as strictly neutral, and therefore entitled to the name of quinine sulphate, while the official salt contains two equivalents of base to one of acid, and is therefore a *quinine subsulphate* or *diquinine sulphate.* The latter name was adopted by the London College, and has been much used by chemical writers. In the U. S., Dublin, and Edinburgh Pharmacopœias, as well as in the French Codex, the name of quinine sulphate, originally given to the official salt, under the impression that it was neutral, was retained; and it has been accepted by the British Pharmacopœia. Hence has arisen a confusion of nomenclature, which must embarrass the student. The following statement may serve to clear up this confusion. There are at least three quinine sulphates that have been obtained, of which two are now official. The first of these,

$$(C_{20}H_{24}N_2O_2)_2H_2SO_4 + 7H_2O$$

is a "*diquinic sulphate,*" but is the official salt known as quinine sulphate, or *Quininæ Sulphas,* U. S.; the second, formed by dissolving this first in dilute sulphuric acid, has the formula

$$C_{20}H_{24}N_2O_2,H_2SO_4 + 7H_2O$$

and is the official quinine bisulphate, or *Quininæ Bisulphas,* U. S.; while the third, a still more acid sulphate,

$$C_{20}H_{24}N_2O_2,2H_2SO_4 + 7H_2O$$

may be obtained from a solution of quinine in excess of diluted sulphuric acid. This salt is not official. Quinine sulphate, owing to the ease with which it parts with its water of crystallization, is apt to mislead those who seek to determine its quality. Forty samples examined by A. J. Cownley showed results varying from 8.1 to 15.95 per cent. of water of crystallization. He recommends for adoption in the Pharmacopœia the air-dried salt, which contains two molecules of water (4.6 per cent.), as being constant in composition. Farr and Wright confirm Cownley's views, and object to "anhydrous" quinine sulphate, which has been proposed by some chemists as the standard, because it has the opposite fault of absorbing moisture. (*P. J.,* 1896, 525; also *P. J.,* 1897, 203.)

The official test (see page 938) is probably the most reliable of all to prove the presence of small quantities of other cinchona alkaloids. It is a modification of Kerner's (see *U. S. D.,* 19th edition, page 1045), and admits the presence of a trace of other alkaloids. This certainly is as pure as the quinine sulphate need be. To separate the remaining trace of alkaloids entirely would require too great an expense, in fact it would more than double the cost of the salt.

Quinine sulphate is decomposed by the alkalies, their carbonates, and the alkaline earths. In solution it affords white precipitates with potassium and sodium hydroxides, and ammonia, which are partly soluble in an excess of alkali. Quinine sulphate is also precipitated by astringent infusions, the tannic acid of which forms a white insoluble compound with quinine. The soluble salts of lead and of barium occasion precipitates; and that produced by the salts of barium is insoluble in the acids. The soluble salts of acetic, oxalic, tartaric, and gallic acids occasion more or less precipitation with solution of quinine sulphate without excess of acid. A solution of chlorine added to a solution of quinine sulphate and followed by the addition of ammonia water occasions an emerald-green color, and, in certain proportions, the deposition of a green precipitate. The green compound has received the name of *thalleioquin.* The drop of ammonia should be put in without agitation. According to Flückiger, 1-5000th part of quinine can thus be found. With bromine instead of chlorine the test is more delicate. Flückiger states that 1-20,000th part of the alkaloid can be detected. (See a paper by C. F. Zeller, *A. J. P.,* 1880, p. 385; *P. J.,* 1872, p. 901.) Some improvements in the thalleioquin test were suggested by LaWall (*A. J. P.,* 1912, p. 484), to obviate the difficulties frequently encountered, which were found to be principally due to oxyacids in the chlorine solution. This solution is frequently not freshly nor properly prepared. A much more delicate reaction is produced by the use of a reagent made by dissolving 0.5 Gm. of potassium bromate and 10 mils of hydrochloric acid in enough water to make 100 mils. With this reagent it was found possible (when using volumes as large as 100 mils of the solution being tested) to detect quinine in dilutions of 1-200,000. The procedure is as follows: Take 100 mils of suspected solution, add 5 to 10 drops of the reagent, agitate well and immediately add 10 drops of stronger ammonia water and mix thoroughly.

F. S. Hyde (*Proc. A. Ph. A.,* 1897, 704) states that a solution of calcium hypochlorite gives more satisfactory results in the thalleioquin test than either chlorine or bromine water, the results being more certain and brilliant. If, previously to the use of ammonia in the chlorine test, a concentrated solution of potassium ferrocy-

anide be added, a dark red color is produced, which persists for several hours, but ultimately passes into green. This does not take place with cinchonine; and, though quinidine sulphate gives the same red color, this does not disappear as with the quinine salt, but is persistent. (Schwartzer, *J. P. C.*, 4e sér., iii, 475.) Quinine sulphate gives a reddish-brown precipitate with iodine dissolved in a solution of potassium iodide. It is possible that under some circumstances the galvanic current may be of service in detecting the alkaloid; a paper on the electrolysis of the salt will be found in the *J. P. C.*, 4e sér., xi, 16. For valuable comments on quinine sulphate tests, see *Proc. A. Ph. A.*, 1897, 705.

Adulterations.—Quinine sulphate has often been adulterated. The effects of adulteration may be produced by the variable quantity of water which quinine sulphate may contain, without any observable alteration in its sensible properties. Millon and Commaille, having exposed quinine sulphate to a very moist atmosphere at the temperature of about 16.6° C. (62° F.), found it always to increase in weight, so that a specimen of the salt, previously deprived of all of its water capable of being separated by heat, had in five days absorbed 28.77 per cent. of water, and another specimen dried after its precipitation simply by draining, and supposed to contain 18 per cent. of water, had in ten days absorbed 14 per cent. more, making its whole percentage of water 32, or about one-third of its weight. This is an important fact, and will explain to some extent the frequent variable effects from apparently the same quantity of the salt. It is easy to detect and to obviate this natural sophistication by exposing a suspected specimen to a heat of 115° C. (239° F.). The loss of weight will indicate the quantity of water not essential to the salt. This is now covered by the official limiting test for the amount of moisture. Calcium sulphate, and other alkaline or earthy salts, gum, sugar, mannite, starch, stearin, caffeine, salicin, phlorizin, and the cinchonine sulphate, and sulphates of other cinchona alkaloids, are among the substances which are said to have been fraudulently added in former times, but such gross adulterants have disappeared from the market product. It is sometimes replaced by or mixed with other cinchona alkaloids. According to W. A. Puckner (*West. Drug.*, 1896, 393), nearly pure crystallized calcium sulphate in fine needle-shaped crystals has been exploited as tasteless quinine sulphate under the name of *flora china*.

By attending to the degree of solubility of the sulphate in different menstrua, and to its chemical relations with other substances already described, there can be little difficulty in detecting these adulterations.

According to Calvert, a saturated solution of quinine sulphate in cold water gives with a solution of chlorinated lime a precipitate soluble in an excess of the latter, while a solution of cinchonine sulphate of the same strength, treated in the same manner, gives a precipitate which is insoluble in a great excess of the reagent. The same effect is produced with lime water, and with solution of ammonia, and solution of calcium chloride, while it furnishes a precipitate with a solution of cinchonine sulphate, yields none with a solution of quinine sulphate. Though commercial quinine sulphate frequently contains a portion of one or more of the other cinchona alkaloids, the salt is only slightly less efficacious on that account, as these alkaloids have been shown to possess similar therapeutic properties with those of quinine, and to be little inferior in strength to them.

Uses.—The fatuous persistence with which the American profession and public continue to prefer this salt is one of the peculiar problems of crowd psychology. It contains less quinine than the hydrochloride, is practically insoluble and has no possible advantages. (See *Quinina*, page 931.)

Dose, two to ten grains (0.13–0.65 Gm.).

Off. Prep.—Ferri et Quininæ Citras, *Br.;* Pilula Quininæ Sulphatis, *Br.;* Syrupus Ferri Phosphatis cum Quinina et Strychnina, *Br.;* Tinctura Quininæ Ammoniata, *Br.;* Elixir Cinchonæ Alkaloidorum and in other Elixirs containing Cinchona alkaloids in combination with Iron, Bismuth, etc., *N. F.;* Elixir Ferri Pyrophosphatis, Quininæ et Strychninæ, *N. F.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Ferri, Quininæ, Aloes et Nucis Vomicæ, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arseni Fortiores, *N. F.;* Pilulæ Ferri, Quiinnæ, Strychninæ et Arseni Mites, *N. F.;* Pilulæ Opii, Digitalis et Quininæ, *N. F.*

QUININÆ TANNAS. U. S.

QUININE TANNATE Quin. Tann.

(quĭ-nī′nē tăn′năs)

"A compound of the alkaloid quinine with tannic acid, of somewhat varying composition and containing not less than 30 per cent. nor more than 35 per cent. of anhydrous quinine ($C_{20}H_{24}O_2N_2$). Preserve it in well-closed containers, protected from light." *U. S.*

"Quinine Tannate is a pale yellow or yellowish-white, amorphous powder; odorless and tasteless, or having not more than a slightly bitter and astringent taste. Quinine Tannate is slightly soluble in water, chloroform, or ether; somewhat more soluble in alcohol. When heated it melts to a purplish, viscous mass. Aqueous and alcoholic solutions of Quinine Tannate are colored blue-black by ferric chloride T.S. Quinine Tannate loses not more than 10 per cent. of its weight when dried to constant weight at 100° C. (212° F.). Incinerate about 0.5 Gm. of Quinine Tannate; not more than 0.3 per cent. of ash remains. Shake about 0.5 Gm. of Quinine Tannate with 50 mils of distilled water and 1 mil of nitric acid and filter the mixture. Ten mils of this filtrate is not colored by 1 mil of hydrogen sulphide T.S.; other portions of the filtrate, 10 mils each, do not become more than slightly turbid on the addition of a few drops of silver nitrate T.S. (*chloride*) or on the addition of a few drops of barium chloride T.S.

(*sulphate*). Shake about 2 Gm. of Quinine Tannate, accurately weighed, with three successive portions of 25 mils each of anhydrous ether, filter the ether solutions, and wash the filter with 10 mils of anhydrous ether. Upon the evaporation of the combined filtrates and washings and drying at 100° C. (212° F.), the residue does not exceed 0.5 per cent. (*uncombined quinine*).

"**Assay.**—Mix about 0.5 Gm. of Quinine Tannate, accurately weighed, in a separator with 10 mils of distilled water and 10 mils of ammonia water, and shake the mixture with 20 mils of ether, then with successive 10 mil portions of ether until the quinine is completely extracted. Upon the evaporation of the combined ethereal liquids and drying the residue to a constant weight at 100° C. (212° F.), the weight of the anhydrous quinine so obtained corresponds to not less than 30 per cent. nor more than 35 per cent. of the weight of the Quinine Tannate taken.

"The alkaloid obtained in the above assay responds to the identity tests under *Quinina.*" *U. S.*

Quinine tannate may be prepared by precipitating one part of quinine sulphate, dissolved in thirty parts of water acidulated with a few drops of sulphuric acid, with a solution of three parts of tannic acid dissolved in thirty parts of cold water, and then washing and drying the precipitate. For other methods of preparing the tannate, see *West. Drug.*, 1893, 352; *Ph. Centralh.*, 1894, 155; *Proc. A. Ph. A.*, 1894, 675. It has the advantage of possessing little taste, but doubts have been repeatedly expressed about its efficiency. At best, it is a feeble preparation, containing as found in commerce, from 22.6 to 34 per cent. of quinine, according to the investigations of the Council on Pharmacy and Chemistry, *J. A. M. A.*, Oct. 14, 1911, p. 1303.

Quinine tannate is one of the least efficacious of all the quinine preparations. It was introduced in the Pharmacopœia because its comparative lack of taste, due to its insolubility, makes it suitable for administration to children in suspension with some thick syrup.

Dose, one to ten grains (0.065–0.65 Gm.).

Off. Prep.—Trochisci Quininæ Tannatis, *N. F.*

RESINA. U. S., Br.

ROSIN Resin. [Resin, Colophony]

(rẹ-sī'nạ)

"The residue left after distilling the volatile oil from the concrete oleoresin obtained from *Pinus palustris* Miller and from other species of *Pinus* (Fam. *Pinaceæ*)." *U. S.* "Resin is the residue left after the distillation of the oil of turpentine from the crude oleo-resin (crude turpentine) of various species of Pinus." *Br.*

Colophone ou Arcanson, *Fr. Cod.;* Résine blanche, Résine jaune, *Fr.;* Colophonium, *P. G.;* Kolophonium, Geigenharz Fichtenharz, *G.;* Colofonia, Pece greca, *It.;* Cologonia, Pez griega, *Sp.*

After the distillation of the volatile oil from the turpentine (see *Terebinthina*), a resinous matter remains, which on the continent of Europe is called *colophony*, but with us is commonly and now officially known by the name of *rosin*. It is the *Resina* of the U. S. and British Pharmacopœias. It is sometimes called *resina flava*, or *yellow rosin*. When this, in a state of fusion, is strongly agitated with water it acquires a distinct appearance, and is denominated *resina alba*, or *white rosin*. The ports from which rosin is shipped are Wilmington, N. C., Charleston, S. C., and Savannah, Ga. The exports of rosin in 1904 amounted to 2,585,108 bbls., valued at $6,621,870; and in 1905 to 2,310,275 bbls., valued at $7,069,084.

Common or *yellow rosin*, in its purest state, is beautifully clear and pellucid, but much less so as usually found in commerce. Its color is yellowish-brown with a tinge of olive, and more or less dark, according to its purity and the degree of heat to which it has been exposed in its preparation. Sometimes it is almost black. It is rather heavier than water. It is completely liquid at 152.5° C. (306° F.), begins to emit bubbles of gas at 157.5° C. (316° F.), and is decomposed at a red heat. The official description is as follows: "Rosin usually occurs in sharp, angular, translucent, amber-colored fragments, frequently covered with a yellow dust, brittle at the ordinary temperature; fracture shiny and shallow-conchoidal; odor and taste slightly terebinthinate. It is freely soluble in alcohol, ether, benzene, glacial acetic acid, or fixed or volatile oils, it is also dissolved by dilute solutions of the fixed alkali hydroxides. Its alcoholic solution is acid to litmus. Specific gravity: 1.07 to 1.09 at 25° C. (77° F.). It is easily fusible and burns with a dense yellowish smoke. Incinerate about 2 Gm. of Rosin; not more than 0.05 per cent. of ash remains. The acid number of Rosin is not less than 150 (see Part III, Test No. 10)." *U. S.*

"Translucent, of a light amber color, compact, brittle, pulverisable; fracture shining; odor and taste faintly terebinthinate. Soluble in *alcohol* (90 per cent.), in *ether, benzene,* and *carbon disulphide.* Readily fusible; burns with a dense yellow flame and much smoke, leaving no appreciable ash." *Br.*

The composition of rosin is expressed by the formula $C_{44}H_{62}O_4$, which is the formula ascribed to *abietic anhydride.* Jean, however (*Chem. News*, xxvi, 207), has separated two other resinoid substances in addition to abietic acid. Lewkowitsch (*Chem. Analysis of Oils*, etc., 2d ed., 236) states that rosin also contains varying quantities of unsaponifiable matter—viz., hydrocarbons due to the partial breaking up of the acid on distilling the pine rosin. This may vary from 5 to 9 per cent. in the American rosin. For a paper on abietic acid by Mead and Kremers, see *Proc. A. Ph. A.*, 1893, 198. By shaking coarsely powdered rosin with dilute alcohol and warming, it is converted into *abietic acid*, $C_{44}H_{64}O_5$, obviously an hydroxide of the first. Rosin may be considered, therefore, as abietic acid anhydride, $C_{44}H_{62}O_4$. Rosin, when it is boiled with alkaline solutions, forms greasy salts of abietic acid, the so-called rosin soaps which

are used in admixture with other soaps. As the acid is dibasic, these salts contain two atoms of alkali metal in combination. Rosin, distilled by itself, yields the so-called "rosin-oil," of which two fractions are taken separately—the first that distilling under 360° C. (680° F.), and the second that over 360° C. (680° F.)—and some 31 per cent. of fixed gases. The lighter fraction is known commercially as *rosin essence*, and is, according to Renard (*J. Chem. S.*, Aug., 1884, p. 843), composed of hydrocarbons, representing almost all series, from the paraffin series to the terpenes, including pentane and hexane, amylene and hexylene, toluene, xylene, and cumene, the tetra- and hexa-hydrides of all three of these, terebenthene and cymene. Several aldehydes and acids of the fatty series, such as isobutyric and valeric, were also recognized. The heavier fraction, or rosin oil in the stricter sense of the word, is composed of polymers of the hydrocarbons C_nH_{2n-2}, which readily resinify by the absorption of oxygen. This accounts for the use of rosin oil as an adulterant of linseed oil in the manufacture of printers' ink. When distilled with superheated steam, rosin yields benzene and toluene. *Sylvic acid*, formerly considered to be a constituent of rosin, is now regarded as a decomposition product of abietic acid. Similarly *pinic* and *pimaric acids*, announced as found in rosin, are impure products, although the latter acid, or one of the same name, is found in galipot resin. Propionic acid has, according to Renard, been obtained in abundance from the tar produced by the destructive distillation of rosin. (*A. Pharm.*, 1886, p. 939.)

A. Tschirch and B. Studer determined the nature of the constituents of American rosin. According to Mohr, the principal plant yielding the turpentine from which the American rosin is obtained is *Pinus palustris* Mill.; to some extent also, *P. heterophylla* Ell.; rarely *P. echinata*, *P. Tæda* and *P. scropida*. The sample under examination (presumably from *P. palustris*) was completely soluble in the ordinary solvents for resin, including petroleum benzin, in which some other varieties of rosin are only partly soluble. Its alcoholic solution is strongly acid in reaction. Its sp. gr. at 15° C. (59° F.) was 1.090. Its composition was proved to be as follows:

1. Acids soluble in ammonium carbonate: *α-abietinic acid*, $C_{19}H_{28}O_2$, forming an insoluble lead salt, 30 per cent. *β-abietinic acid*, $C_{19}H_{28}O_2$, not forming a lead salt, 22 per cent. 2. Acid soluble in sodium carbonate: *γ-abietinic acid*, $C_{19}H_{28}O_2$, insoluble in ammonium carbonate, 31.06 per cent. 3. Volatile oil, 0.4 to 0.7 per cent. 4. Resen, 5 to 6 per cent.

The impurities amounted only to 0.1 per cent., the loss in operation, however, to 10 per cent. Fahrion having proposed a method for the differentiation of different rosins, based upon their relative solubility in petroleum benzin, the authors determined the amount of solvent necessary to dissolve 1 Gm. of rosin, freshly powdered, and old powder; also abietinic acids and the resen in petroleum benzin, with the following results:

Rosin, old powder, 1 Gm. required...	400 mils
Rosin, fresh, 1 Gm. required.....	60 mils
α-Abietinic acid, 1 Gm. required.....	500 mils
β-Abietinic acid, 1 Gm. required.....	100 mils
γ-Abietinic acid, 1 Gm. required.....	100 mils
Resen	50 mils

These results show that all the resin-acids, as well as the rosin, are more or less soluble in petroleum benzin, and that fresh rosin is more readily soluble than the isolated acids, a peculiarity which has also been noticed in the case of other bodies. On the other hand, old rosin is much less soluble in petroleum benzin than is fresh rosin. (*A. Pharm.*, Oct., 1903, 495–522.)

White rosin differs from the preceding only in being opaque and of a whitish color. These properties it owes to the water with which it is incorporated, and which gradually escapes upon exposure, leaving it more or less transparent. A new and very interesting class of derivatives from colophony or rosin has been prepared by Eugen Schaal, of Feuerbach, Germany, and introduced into commerce under the name of *ester gums*. These are the *glyceryl*, *methyl*, and *ethyl esters of abietic acid*, made by heating the resin acid and the alcohol under pressure until saponification takes place. The product is then distilled off under reduced pressure. These "ester gums" are being used to advantage as substitutes for copal, damar, and kauri gums in varnish making.

Uses.—Rosin is important as an ingredient of ointments and plasters, but is rarely used internally. It has been given in *chronic enteritis*, five grains of the powder. According to Olmstead, it has the property of preventing the oxidation of fatty substances, and thus contributes to the preservation of ointments. (*A. J. P.*, xxii, 325.)

Off. Prep.—Ceratum Resinæ, *U. S.* (*Br.*); Emplastrum Calefaciens, *Br.*; Emplastrum Resinæ, *U. S.*, *Br.*; Emplastrum Saponis, *Br.*; Ceratum Resinæ Compositum, *N. F.*; Linimentum Terebinthinæ (from Rosin Cerate), *U. S.*

RESINA JALAPÆ. U. S. (Br.)

RESIN OF JALAP Res. Jalap.

(rẹ-sī'nạ jạ-lā'pæ)

"Jalap Resin is a mixture of resins obtained from Jalap." *Br.*

Jalapæ Resina, *Br.*; Résine de Jalap, *Fr. Cod.*; Jalapenharz, *G.*; Resina di gialappa, *It.*; Resina de jalapa, *Sp.*

* "Jalap, in No. 60 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, Water, each *a sufficient quantity*. Moisten the powder with *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol, and pack it in a cylindrical percolator; then add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having

closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding alcohol, until the percolate ceases to produce more than a slight turbidity when dropped into water. Distil off the alcohol until the percolate is reduced in weight to *two hundred and fifty grammes* [or 8 ounces av., 358 grains], and add the latter slowly, with constant stirring, to *three thousand mils* [or 101 fluidounces, 212 minims] of water. When the precipitate has subsided, decant the supernatant liquid, and wash the precipitate twice, by decantation, with fresh portions of *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] each of hot water. After having drained off all of the liquid, transfer the resin to a porcelain dish and heat it to dryness on a water-bath." *U. S.*

"Exhaust coarsely powdered Jalap with Alcohol (90 per cent.). Recover most of the alcohol by distillation; pour the concentrated solution thus obtained into eight times its volume of Distilled Water; allow the resin that separates to subside, wash with Distilled Water, and dry at a gentle heat." *Br.*

Extract of Jalap was formerly official. It has been dropped from both the U. S. and British Pharmacopœias. Resin of Jalap has taken its place in both authorities. (See *U. S. D.*, 19th edition, page 479.)

Properties.—Resin of jalap is officially described in the U. S. Pharmacopœia as in "yellow to brown colored masses or fragments, breaking with a resinous, glassy fracture and translucent at the edges, or as a yellowish-gray to yellowish-brown powder, having a slight, peculiar odor, and a somewhat acrid taste. It is permanent in the air. Resin of Jalap is soluble in alcohol in all proportions; insoluble in carbon disulphide, benzene, or fixed or volatile oils. Its alcoholic solution is faintly acid to litmus. Add 1 Gm. of the powdered Resin to 10 mils of chloroform in a stoppered flask and shake the mixture occasionally during one hour. Then filter, evaporate the filtrate in a tared dish and dry the residue to constant weight at 100° C. (212° F.); it weighs not more than 0.3 Gm. Add 1 Gm. of the powdered Resin to 10 mils of ether in a stoppered flask and shake the mixture occasionally during one hour. Then filter, evaporate the filtrate in a tared dish and dry the residue to constant weight at 100° C. (212° F.); it weighs not more than 0.12 Gm. (*rosin, orizaba, or other resins*). It is slowly but completely soluble in 5 times its weight of ammonia water, and the solution does not become gelatinous on standing. When this solution is acidified with hydrochloric acid, only a slight turbidity appears (*rosin, guaiac, or other resins*). When Resin of Jalap is heated at 100° C. (212° F.), no material loss in weight is observed (*water*). When Resin of Jalap is triturated with distilled water, the latter does not become colored, none of the Resin dissolves (*soluble impurities*), and the water does not have a bitter taste (*aloin*). Shake 0.02 Gm. of Resin of Jalap with 5 mils of ether, filter and evaporate the ethereal filtrate on a piece of filter paper; no greenish-blue color is produced by the application of a drop of ferric chloride T.S. to the filter paper (*guaiac*). One Gm. of Resin of Jalap when dissolved in 50 mils of alcohol, containing 1 mil of phenolphthalein T.S., requires not more than 0.5 mil of half-normal alcoholic potassium hydroxide V.S. to produce a red color (*acid resins*). Dissolve 0.02 Gm. of Resin of Jalap in 2 mils of glacial acetic acid and add a few drops of sulphuric acid; the mixture does not acquire a pink color (*rosin*)." *U. S.*

"In dark-brown opaque fragments, translucent at the edges; brittle, breaking with a resinous fracture; readily reduced to a pale-brown powder. Characteristic odor; taste acrid. Readily soluble in *alcohol* (90 per cent.). When 1 gramme of the powdered Resin is triturated with 20 millilitres of *water* and filtered, the filtrate is almost colorless. A solution of 0.1 gramme in 10 millilitres of *solution of sodium hydroxide*, boiled for a few moments and cooled, when acidified with *hydrochloric acid* may become opalescent but not immediately turbid (absence of certain other resins). Not more than 15 per cent. of the powdered Resin is soluble in *ether* (absence of scammony resin)." *Br.*

The U. S. resin, although pure enough for practical purposes, is still colored. To obtain it colorless, the powdered jalap should be mixed, before percolation, with an equal quantity of finely powdered animal charcoal, and, previously to the introduction of this mixture into the percolator, half the quantity of animal charcoal, similarly powdered, should be packed in the bottom of the percolator. The coloring matter is thus left behind, and the resulting tincture, treated as directed in the process, yields the resin as white as starch. Resin of jalap consists of two portions, one of which is hard and insoluble in ether, the other is soft and soluble in that menstruum, the former constituting about 90 per cent. It is insoluble in oil of turpentine. (Squire.) For its chemical properties, see *Jalapa*. It was at one time supposed that the purgative properties resided chiefly, if not exclusively, in the hard resin, but experiments by John C. Long appear to prove that the soft resin is equally energetic.

Guaiac, rosin, and other resinous substances are said to be sometimes fraudulently added to the resin of jalap. Guaiac may be detected by the green color it produces when a few drops of solution of sodium or calcium chloride are added to an alcoholic solution of the suspected resin. (*J. P. C.*, 3e sér., x, 357.) When pure jalap resin is dissolved in an alkaline solution, it is not precipitated by the addition of sulphuric or hydrochloric acid, having been converted, through the agency of the alkali, into an acid soluble in water. All the adulterating resins yield precipitates under the same circumstances. The resins of scammony and of fusiform jalap act in this respect like the true jalap resin, but are distinguishable by being

wholly soluble in ether, while jalap resin is not. (*N. R. Pharm.*, No. 1, 1854.)

Power and Rogerson (*P. J.*, 1909, lxxxiii, p. 7) find that the products heretofore obtained from jalap as the active principle possesses the attributes of a homogeneous substance. They found the resin of jalap to be a body of very complex composition, but did not determine any single principle to which its purgative action might be attributed. (See *Jalap* for the chemistry of the resins.)

It is now generally believed that the resin of jalap is the sole purgative principle of jalap, the gummy extractive being either simply diuretic or wholly inert. To obviate the occasional harshness of the resin, it has been advised to triturate it with milk sugar, potassium sulphate, almond emulsion, or other substance calculated to separate its particles. It may be conveniently made into pills with mucilage or alcohol. (Hasselby, *P. J.*, 2d ser., vii, 231.)

Dose, two to five grains (0.13–0.32 Gm.).

Off. Prep.—Pilulæ Catharticæ Compositæ, *U. S.*; Pilulæ Catharticæ Vegetabiles, *N. F.*

RESINA PODOPHYLLI. U. S. (Br.)

RESIN OF PODOPHYLLUM Res. Podoph. [Podophyllin]

(rẹ-sĭ'nạ pŏd-ọ-phĭl'lī)

Podophylli Resina, *Br.;* Podophyllum Resin; Resin of May-Apple; Résine de Podophyllum Peltatum, *Fr. Cod.;* Podophyllinum, *P. G.;* Podophyllin, Podophyllumharz, *G.;* Podofillina, *It.;* Podofilino, *Sp.*

* "Podophyllum, in No. 60 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Hydrochloric Acid, *ten mils* [or 162 minims]; Alcohol, Water, each, *a sufficient quantity.* Moisten the powder with *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol, and pack it in a cylindrical percolator; then add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding alcohol, until the percolate ceases to produce more than a slight turbidity when dropped into water. Distil off the alcohol until the percolate is reduced to the consistence of a thin syrup, and pour this slowly, with constant stirring, into *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of water, mixed with the hydrochloric acid and cooled to a temperature below 10° C. (50° F.). When the precipitate has subsided, decant the supernatant liquid, and wash the precipitate twice, by decantation, with fresh portions of *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of cold water. Spread it in a thin layer upon a strainer and dry the Resin by exposure to the air, in a cool place, protected from the light. Should it coalesce during the drying, or aggregate into lumps having a glossy surface, break it into pieces, and powder it in a mortar. Preserve it in well-closed containers, protected from light." *U. S.*

"Podophyllum Rhizome, in No. 40 powder, 1000 *grammes;* Alcohol (90 per cent.), Distilled Water, Hydrochloric Acid, of each a sufficient quantity. Exhaust the Podophyllum with the Alcohol by percolation; recover the greater part of the alcohol by distillation; pour the resulting liquid into eight times its volume of Distilled Water acidified with one twenty-fourth of its volume of Hydrochloric Acid, constantly stirring; after twenty-four hours collect the deposited resin, wash with Distilled Water, and dry at a temperature not exceeding 40° C. (104° F.)." *Br.*

The British Pharmacopœia (1885) abandoned the use of hydrochloric acid, as it is not necessary if the tincture is evaporated to the consistence of *thick* honey. Hydrochloric acid was directed in the 1898 revision as it seems to aid the precipitation when the tincture is not so concentrated. The color and yield of resin of podophyllum may be made to vary by adding alum, acids, or other substances to the water. It darkens if dried with the aid of heat, and its color is indeed no indication whatever of its quality. The average yield of resin is about 5 per cent.

Resin of podophyllum has usually a light-brown color, an acrid bitter taste, and a slight odor of the rhizome. It consists of two resins, one soluble both in ether and alcohol, the other in alcohol only. The resin extracted by ether constitutes, according to John W. Cadbury, 75 per cent. of the whole (*A. J. P.*, July, 1858, p. 301), according to Harvey Allen, 80 per cent. (*Ibid.*, May, 1859, p. 206.)

For further description of the composition of these resins see *Podophyllum.* Gordon and Merrell (*Proc. A. Ph. A.*, 1902, p. 343) have proposed a method of valuing resin of podophyllum, based upon the content of picro-podophyllin and submit a method of assay.

Properties.—It is officially described as "an amorphous powder varying in color from light brown to greenish-yellow, turning darker when subjected to a temperature exceeding 25° C. (77° F.), or when exposed to light. It has a slight, peculiar odor and a faintly bitter taste. *It is very irritating to the eyes, and to mucous membrane.* It is soluble in alcohol with only a slight opalescence. The alcoholic solution is faintly acid to litmus. Not less than 75 per cent. of Resin of Podophyllum is soluble in ether and not less than 65 per cent. is soluble in chloroform. A hot aqueous solution of Resin of Podophyllum deposits most of its contents on cooling, and if the cooled liquid is filtered, the filtrate has a bitter taste, and turns brown upon the addition of a few drops of ferric chloride T.S. It is soluble in potassium or sodium hydroxide T.S., forming a deep yellow liquid, which gradually becomes darker on standing, and from which the Resin is reprecipitated by acids. Add 0.4 Gm. of Resin of Podophyllum to 3 mils of 60 per cent. alcohol, introduce 0.5 mil of potassium hydroxide T.S., and gently shake the

mixture; it does not gelatinize (*difference from Resin obtained from Podophyllum Emodi*). Resin of Podophyllum yields not more than 1.5 per cent. of ash." *U. S.*

"An amorphous powder, varying in color from pale yellow to deep orange-brown. Taste bitter. Entirely or almost entirely soluble in *alcohol* (90 per cent.) and in *solution of ammonia;* precipitated from the former solution by *water,* from the latter by acids. Partly soluble in *ether.* Ash not more than 1 per cent." *Br.*

The official resin is soluble in alkaline solutions, from which it is precipitated by acids, in this respect differing strikingly from the resins of jalap and scammony. It is insoluble in oil of turpentine. For discussion of the solubilities of the fresh resin, see G. M. Beringer (*A. J. P.,* 1894, 11). The name *podophyllin,* given to it by the eclectic practitioners, who have long been in the habit of using this resin, is inappropriate, and should be abandoned.

Lohmann (*Proc. N. J. Pharm. Assoc.,* 1896, 51) states that the fresh drug does not yield as large a percentage of resin as the same drug would if tested after being stored for several years; his experiments led him to the conclusion that in the order of value of resin of podophyllum obtained by various methods, that made by precipitation with water alone came first, that made by the U. S. P. process second, and that made by precipitation with solution of alum last. Dohme and Kelly (*D. C.,* 1903, 251), replying to statements in a paper by Lohmann (*Proc. A. Ph. A.,* 1903, 317) regarding the yield of resin from podophyllum, state that: 1, the yield from the method of pouring an alcoholic extract into water was 5 per cent.; 2, from pouring an alcoholic extract into acidulated water 5.5 per cent., and 3, from pouring an alcoholic extract into acidulated water containing 5 per cent. of alum, 4.9 per cent. See also *Podophyllum,* page 880. The color by process 1, is grayish-white; 2, light brown; 3, greenish-yellow. The value of resin of podophyllum is accurately estimated by the percentage of podophyllotoxin that it yields. Nearly all of the resin of podohyllum in commerce is made by the alum process, has a deep yellow color and is not wholly soluble in alcohol.

There has been much difference of opinion as to the relative activity of the two resins composing it, some maintaining that both are active, others that the activity resides mainly, if not exclusively, in the resin soluble in ether. It is difficult to resist the evidence of the experiments of Cadbury, who states in the paper above referred to that, while half a grain of the ethereal resin acted energetically, and a cathartic effect was produced by even one-fourth of a grain, the portion insoluble in that menstruum was given in the dose of one grain without any effect whatever. Moreover, this evidence was subsequently confirmed by the experiments of F. B. Power. (*A. J. P.,* xlvi, 227.) It is asserted by Power, and confirmed by Maisch (*Ibid.,* 226), that the purgative principle of podophyllum is soluble in hot water. The researches of Power (*A. J. P.,* l, p. 369), Maisch (*P. J.,* 1880, p. 621), Quereschi (*Ber. d. Chem. Ges.,* xii, p. 683), and Podwyssotzki have established the fact that podophyllum does not contain berberine or any alkaloid, and that its activity is due to principles in the resins. (See *Podophyllum.*)

Uses.—Resin of podophyllum is a mixture of the active and inert principles of the rhizome. Resin of podophyllum is a powerful cathartic, occasionally producing some griping and nausea, but capable of being favorably modified by combination, and of being very usefully employed in connection with other cathartics, to give them increased energy. It was at one time supposed to be especially cholagogue, but this belief has been of late discredited. A small proportion of extract of belladonna or hyoscyamus mitigates its irritant action. Care must be taken in handling it in quantity, as it is a powerful irritant, frequently producing conjunctivitis.

Dose, one-eighth to one-fourth of a grain (0.008–0.016 Gm.).

Off. Prep.—Tinctura Podophylli, *Br.;* Pilulæ Aloes et Podophylli Compositæ, *N. F.;* Pilulæ Aloes, Hydrargyri et Podophylli, *N. F.;* Pilulæ Aloini Compositæ, *N. F.;* Pilulæ Catharticæ Vegetabiles, *N. F.;* Pilulæ Colocynthidis et Podophylli, *N. F.;* Pilulæ Laxativæ Post Partum, *N. F.*

RESINA SCAMMONIÆ. U. S. (Br.)

RESIN OF SCAMMONY Res. Scamm.

(rę-sĭ'nȧ scam-mō'nĭ-æ)

"Scammony Resin is a mixture of resins obtained from Scammony Root or from Orizaba Jalap Root." *Br.*

Scammoniæ Resina, *Br.,* Scammony Resin; Résine de Scammonée, *Fr. Cod.;* Scammoniaharz, *G.;* Resina di scammonea, *It.*

* "Scammony Root in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, Water, each, *a sufficient quantity.* Moisten the scammony root with sufficient alcohol, pack it in a cylindrical percolator, then add enough alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding alcohol, until the percolate ceases to produce more than a slight turbidity when dropped into water. Distil off the alcohol until the percolate is reduced to the consistence of thin syrup, and pour this slowly, with constant stirring, into *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of hot water. When the precipitate has subsided, decant the supernatant liquid, wash

the precipitated Resin twice by decantation with fresh portions of *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] each of hot water and dry the Resin on a water bath." *U. S.*

"Exhaust the coarsely powdered Root with Alcohol (90 per cent.). Recover most of the alcohol by distillation; pour the concentrated solution thus obtained into eight times its volume of Distilled Water; allow the resin that separates to subside, wash it with Distilled Water, and dry at a gentle heat." *Br.*

The U. S. IX and Br. Pharmacopœia 1914 are in accord on the advisability of preparing *Resin of Scammony* from the dried root. This result has been brought about by the practical inability to secure pure resin of scammony from the countries in which the plant grows. Adulteration and sophistication for centuries have at last wrought havoc and the pharmacopœias have been compelled to make scammony resin from scammony root. For an account of the collection of scammony and the sophisticatons and adulterations, see *U. S. D.*, 19th edition, page 1099.

Resin prepared from the root and scammony obtained by evaporating the milky juice of the plant are practically identical. The elaborate researches of H. Spirgatis (*A. J. P.*, xlvi, 421) appear to have established the identity of the two products. A. Hess, however (*A. J. P.*, 1875, p. 210), states that the resin obtained from the root contains tannic acid. The advantage of the preparation is that the resin is obtained free from the inert matters with which it is often associated in the scammony of commerce. When pure virgin scammony can be procured, any preparation is unnecessary. Obtained according to the U. S. process, the resin is of a dirty greenish-brown color, with a feeble odor and taste of scammony, and is very soluble in ether, alcohol, and boiling proof spirit. When purified with animal charcoal it has a pale brownish-yellow color, and is without odor or taste, and retains its purgative property.

"Resin of Scammony consists of brownish, translucent masses or fragments, breaking with a glossy, resinous fracture; odor characteristic and agreeable. It is soluble in alcohol in all proportions, and not less than 95 per cent. is soluble in ether (distinction from *resin of jalap and resin of false scammony*). When triturated with water, it does not form an emulsion. Ammonia water and solutions of the alkali hydroxides dissolve it with the aid of gentle heat, and from these solutions the Resin is not reprecipitated by dilute acids. Its solution in alcohol does not give a blue color with ferric chloride T.S. or with solution of hydrogen dioxide (*guaiac*). Sulphuric acid does not turn red when stirred in a porcelain dish with an equal weight of Resin of Scammony (*rosin*). Resin of Scammony yields not more than 1 per cent. of ash." *U. S.*

"Brownish, translucent, brittle fragments, breaking with a resinous fracture; readily reduced to a pale-brown powder. Characteristic, agreeable odor; taste acrid. Readily soluble in *alcohol* (90 per cent.). When 1 gramme of the powdered Resin is triturated with 20 millilitres of *water* and filtered, the filtrate is almost colorless. A solution of 0.1 gramme in 10 millilitres of *solution of sodium hydroxide*, boiled for a few moments and cooled, when acidified with *hydrochloric acid*, may become opalescent but not immediately turbid (absence of certain other resins). Not less than 75 per cent. soluble in *ether*." *Br.*

The resin of scammony is liable to adulteration. Jalap resin may be detected by its partial insolubility in rectified ether, which dissolves that of scammony in all proportions. Sulphuric acid is the best test for common rosin or colophony, producing instantaneously with this substance an intense red color, while with the resin of scammony it causes no immediate change. For the tests for guaiac, the reader is referred to that article on p. 536. (See also *A. J. P.*, xxiv, 158.) The presence of other resins may be known by the precipitates yielded when sulphuric acid is added to the alkaline solution, the resin of scammony agreeing with that of jalap in not affording a precipitate under such circumstances. Chas. Bullock has found the resins of scammony, of jalap, and of podophyllum to be insoluble in benzene, thus enabling any resin soluble in this liquid, which may be employed in the sophistication, to be readily detected. When rubbed with unskimmed milk, the resin of scammony forms a uniform emulsion, which is not distinguishable from rich milk itself. This is a very excellent mode of administration. The resin should always be given either rubbed up with some mild powder or in emulsion.

L. Lutz (*Pharm. Ztg.*, 1912, xxiii, p. 232) states that the behavior of the resin with iodine when examined microscopically affords a method of distinguishing resin from a number of its substitutes and adulterants.

Uses.—Scammony resin is an energetic cathartic, likely to occasion griping, and sometimes operating with harshness. It was known to the ancient Greek physicians, and was much employed by the Arabians, who used it as a purgative and externally in skin diseases. On account of its occasional violence, it is seldom administered, except in combination with other cathartics, the action of which it promotes, while its own harshness is mitigated. It should be given in emulsion with mucilage, sugar, almonds, licorice, or other demulcent, and its disposition to gripe may be counteracted by the addition of an aromatic.

Dose, from four to eight grains (0.26–0.5 Gm.).

Off. Prep.—Extractum Colocynthidis Compositum, *U. S., Br.;* Pilula Colocynthidis Composita, *Br.;* Pilula Colocynthidis et Hyoscyami, *Br.;* Pilula Scammonii Composita, *Br.;* Pulvis Scammonii Compositus, *Br.;* Pilulæ Aloes, Hydrargyri et Scammonii Compositæ, *N. F.;* Pilulæ Colocynthidis Compositæ, *N. F.;* Pilulæ Colocynthidis et Hyoscyami, *N. F.;* Tinctura Jalapæ Composita, *N. F.*

RESINÆ

RESINS

(rę-sĭ'næ)

The official *Resins,* with a single exception, constitute a peculiar class of preparations, made by exhausting the substances from which they are obtained by alcohol, and then precipitating the resinous matter from the tincture by the addition of water, which abstracts the alcohol by its stronger affinity. It is obvious that the resins thus prepared are different substances from the alcoholic extracts, which contain all the ingredients of the medicine which alcohol is able to take from it. This set of substances has been much employed by the practitioners styling themselves "eclectics," but with great lack of discrimination. They have applied names to these resinous precipitates which, in their proper scientific use, are employed to designate neutral proximate principles of plants, generally representing more or less completely the effects of the plants respectively on the system; as we say *columbin, quassin, santonin,* etc., themselves proper proximate principles, and representing the virtues, in part at least, of calumba, quassia santonica, etc., from which they are obtained, and from which they derive their names. By applying similar names to their precipitated resins, such as podophyllin, iridin, cimicifugin, etc., *i.e.,* to the impure resins obtained by precipitating the tinctures of podophyllum, iris versicolor, cimicifuga, etc., they justify the suspicion either that they ignorantly believe them to be in fact the active principles of these medicines respectively, or that, knowing better themselves, they seek to impose such a conviction upon the ignorant. The fact is that the substances thus obtained, and thus named, are impure resins, which may possibly contain more or less of the active principles mixed with them, but are not entitled to names which imply that they are distinct proximate principles themselves.

Resins are solid, brittle, of a smooth and shining fracture, or in powder and generally of a yellowish-brown color. When perfectly pure, they are probably inodorous and often insipid; but, as usually found, they have a slight odor, and a somewhat acrid or bitterish taste. Their sp. gr. varies from 0.92 to 1.2 They are fusible by a moderate heat, decomposed at a higher temperature, and in the open air take fire, burning with a yellow flame and much smoke. Insoluble in water, they are addition of water. With pure potassium and sodium hydroxides they unite to form soaps, which are soluble in water, and the same result takes place when they are heated with solutions of the alkaline carbonates. Concentrated sulphuric acid dissolves them with mostly soluble in ether and the volatile oils, and in alcohol; and their alcoholic and ethereal solutions afford precipitates upon the mutual decomposition, and nitric acid converts them into artificial tannin. They readily unite by fusion with wax and the fixed oils.

Losch recommends the following process for rendering the resins as white as possible. Boil together 5 parts of the resin, 1 of carbonate of potassium or of sodium, and 20 of water, until a perfectly homogeneous mass is obtained; allow this to cool, and pass into it sulphurous acid, which saturates the alkali, and precipitates the resin in white flakes. Finally, wash the precipitate well with water, and dry it. (*J. P. C.,* June, 1856, p. 465.)

RESORCINOL. U. S. (Br.)

RESORCINOL Resorcin. [Resorcinum, U. S. 1890, Resorcin]

(rę-sör'cĭ-nŏl)

"Metadihydroxybenzene. It contains not less than 99.5 per cent. of $C_6H_4(OH)_2$ 1 : 3(110.05). Preserve it in well-closed containers, protected from light." *U. S.* "Resorcin, or meta-dihydroxy-benzene, $C_6H_6O_2$, may be obtained by the interaction of fused sodium hydroxide and sodium metabenzene-disulphonate." *Br.*

Resorcinum, *Br.;* Metadioxybenzene, Metadihydroxybenzene; Résorcine, *Fr. Cod.;* Resorcinum, *P. G.;* Resorcin, *G.;* Resorcina, *It., Sp.*

Resorcinol is *metadihydroxybenzene,* while pyrocatechin is the *ortho* compound and hydroquinone the *para* compound. Hlasiwetz and Barth first obtained this organic body in 1864 by fusing galbanum resin with potassium hydroxide; it was subsequently obtained from sagapenum, asafetida, ammoniac, and gum acroides. According to Kopp, it is prepared by the destructive distillation of *brazilin,* or from the wash or mother waters obtained in its manufacture from Brazil-wood. It is now generally prepared by fusing sodium benzene-disulphonate with sodium hydroxide. It is important that the benzene which is used as the starting-point in its manufacture, be free from toluene.

Properties.—*Resorcinol* is a diatomic phenol, isomeric with *pyrocatechin* and *hydroquinone.* It crystallizes in prismatic crystals of the rhombic system, distilling at 276.5° C. (529.7° F.), easily soluble in water, alcohol, and ether, insoluble in chloroform and carbon disulphide. A small quantity treated with fuming sulphuric acid is dissolved, with the production of, first, an orange-yellow, then a greenish-blue, and finally a pure blue color. Bromine water precipitates its aqueous solution, *tribromresorcin* separating in minute crystals. Several of the compounds of resorcinol with phthalic anhydride have assumed great technical importance as dye-colors under the names of *fluorescein, eosin,* and *uranine.* Its trinitro derivative is *styphnic acid,* $C_6H(OH)_2(NO_2)_3$, which is also formed from many of the gum-resins by the action of nitric acid. Resorcinol combines with various principles. In this way arise *eucalyptoresorcinol, caffeoresorcinol,* etc. (see *P. J.,* xxi, 997); also a brown powder said to be composed of resorcinol and iodoform which has been commended by Biélaïew (*S. M.,* 1892) as a stimulant application to

foul *ulcers,* in *eczema,* etc. It is very irritant, and usually requires dilution (from 6 to 25 per cent.). It is officially described as in "colorless, or nearly colorless, needle-shaped crystals, or as a powder, having a faint, peculiar odor and a sweetish, followed by a bitter taste. It acquires a pink tint on exposure to light and air. One Gm. of Resorcinol dissolves in 0.9 mil of water and in 0.9 mil of alcohol at 25° C. (77° F.); also in about 0.2 mil of water at 80° C. (176° F.); freely soluble in glycerin or ether; slightly soluble in chloroform. Its aqueous solution (1 in 20) is neutral or only faintly acid to litmus. It melts between 109° and 111° C. (228.2° and 231.8° F.). The addition of a few drops of ferric chloride T.S. to 10 mils of an aqueous solution of Resorcinol (1 in 200) produces a bluish-violet color, changing to brownish-yellow on the addition of ammonia water (distinction from *catechol and quinol*). Dissolve 0.1 Gm. of Resorcinol in 1 mil of potassium hydroxide T.S. and then add a drop of chloroform; the mixture upon being heated assumes an intense, crimson color, and if a slight excess of hydrochloric acid is then added, the color changes to a pale straw-yellow. Incinerate about 2 Gm. of Resorcinol; not more than 0.05 per cent. of ash remains. Lead acetate T.S. produces no precipitate when added to an aqueous solution of Resorcinol (1 in 20) (*catechol*). An aqueous solution of Resorcinol (1 in 20) does not emit the odor of phenol when gently warmed." *U. S.*

"Colorless, shining, acicular or prismatic crystals. Faint odor; taste pungent and sweetish, followed by bitterness. Soluble in less than 1 part of *water,* or of *alcohol* (90 per cent.); very soluble in *ether,* and in *glycerin;* soluble in *olive oil;* slightly soluble in *chloroform.* Melting point 110° to 111° C. (230°–231.8° F.); at a higher temperature sublimes without residue and without evolving an odor of phenol. Alkaline solutions darken in color and exhibit a strong greenish fluorescence. A concentrated aqueous solution is colorless (absence of empyreumatic substances), and neutral or only slightly acid to *litmus;* it is unaffected by the addition of *solution of lead acetate* (absence of catechol). A weak aqueous solution is colored bluish-violet by *T. Sol. of ferric chloride,* the color changing to brownish-yellow on the addition of *solution of ammonia* (distinction from catechol and quinol). When 0.5 gramme is mixed with 2 millilitres of *solution of formaldehyde* and 2 millilitres of *solution of sodium hydroxide,* and the mixture heated to boiling, a deep red coloration is gradually developed." *Br.*

"Assay.—Dissolve about 1.5 Gm. of Resorcinol, accurately weighed, in sufficient distilled water to make 500 mils. Transfer 25 mils of the solution to a 500 mil, glass-stoppered flask having a long and narrow neck, add 50 mils of tenth-normal bromine V.S., and dilute with 50 mils of distilled water. Then add 5 mils of hydrochloric acid and at once stopper the flask. Shake the liquid and allow it to stand for one minute, then dilute it with 20 mils of distilled water, add 5 mils of potassium iodide T.S. and allow it to stand for five minutes. The titration of the liberated iodine with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator, shows not less than 99.5 per cent. of $C_6H_4(OH)_2$.

"Each mil of tenth-normal bromine V.S. corresponds to 0.001834 Gm. of $C_6H_4(OH)_2$. Each gramme of Resorcinol corresponds to not less than 542.5 mils of tenth-normal bromine V.S." *U. S.*

Its official assay is based upon the following reaction:

$$C_6H_4(OH)_2 + 3Br_2 = C_6HBr_3(OH)_2 + 3HBr.$$

The excess of bromine is determined indirectly by titration with sodium thiosulphate V.S.

Dunlop (*P. J.,* 1909, lxxxii, p. 580) investigated the cause of coloration of resorcin. He found that moisture was the most important factor but that it apparently required light and heat to cause the change after it had once begun.

Uses.—Resorcinol appears in its physiological properties to be allied to phenol. It has marked antibacterial properties, and, according to Martin Cohn (*In. Dis.,* Berlin, 1882), a one per cent. solution of it is sufficient to arrest for a long time putrefactive changes; Cooper (*B. M. J.,* 1912, i, 1235) has shown that it is about one-third as actively germicidal as phenol. When given to the lower animals (Dujardin-Beaumetz, *B. G. T.,* ci, 113) it causes tremors, loss of consciousness, and epileptiform convulsions, which, when the dose has been sufficiently large, become more and more violent and associated with marked disturbances of respiration; this function is finally arrested and death ensues. During the spasms the temperature of the animal is distinctly elevated, but when there is quiet narcosis it may fall much below the normal. The urine becomes olive green, deepening into blackish. So far as we know, no case of fatal poisoning in man has been recorded. The largest therapeutic doses produce flushing of the face, with giddiness and buzzing in the ears and some quickening of the breathing and pulse, followed after a time by violent perspiration. Sixty grains caused in man giddiness, violent perspiration with marked anxiety, ending in collapse and unconsciousness. Andeer (*Cb. M. W.,* 1881) took about one hundred and fifty grains of resorcinol dissolved in a pint of water during fifteen minutes. After disturbance of cerebration and of the special senses, he fell into a condition of collapse, with cold extremities, epileptiform convulsions, opisthotonos, loss of consciousness, and marked irregularity of the respiration. Consciousness did not return for five hours.

Resorcinol has been used in medicine as an intestinal antiseptic in *enteritis,* but is probably of no service. In *gastritis* it may exercise some effect but is probably inferior to phenol. Because of its lower toxicity it is frequently employed in gastric lavage or as a wash in *nasal catarrh, chronic colitis, leucorrhea,* and other inflammations of the mucous membranes.

Schaffer (*B. K. W.*, 1910, p. 890) highly recommends as a surgical dressing, especially in *furuncles* and *cellulitis*, the use of 50 per cent. of alcohol with 2 or 3 per cent. of resorcinol added. He states that it has a remarkable effect in preventing suppuration. Elze (*Wochenschrift für Ther. and Hyg. des Auges*, 1909, xii, p. 202) asserts that a 1 or 2 per cent. resorcin ointment is useful in *cataract* and will often clear up opaque parts if not too far developed or too deeply located in the lens. The most important use of resorcin, however, is in the treatment of skin diseases. Many dermatologists attribute it with peculiar alterative properties towards the skin. In dilute solution, 1 or 2 per cent., it is antipruritic as well as antiseptic, and may be used in *acute eczema, urticaria*, and other inflammatory disorders of the epiderm. In stronger solution, 3 to 4 per cent., it is actively stimulating and is employed in the more sluggish conditions as *chronic eczema, seborrhea, psoriasis*, etc. Andeer has used it for its caustic effect in the treatment of *chancres, papilloma*, and *epitheliomata* in the form of a dusting powder.

Dose, three to five grains (0.2–0.32 Gm.).

Off. Prep.—Pasta Resorcinolis Fortior, *N. F.;* Pasta Resorcinolis Mitis, *N. F.;* Unguentum Resorcinolis Compositum, *N. F.*

RHEUM. U. S. (Br.)

RHUBARB

(rhē'ŭm)

"The rhizomes and roots of *Rheum officinale* Baillon, *Rheum palmatum* Linné, and the var. *tanguticum* Maximowicz (Fam. *Polygonaceæ*), and probably other species of *Rheum* grown in China and Thibet, deprived of most of the bark tissues and carefully dried. Preserve Rhubarb in tightly-closed containers, adding a few drops of chloroform or carbon tetrachloride, from time to time, to prevent attack by insects." *U. S.* "Rhubarb is the rhizome of Rheum officinale, *Baill.*, and other species of Rheum, collected in China and Thibet, deprived of most of the cortex, and dried." *Br.*

Rhei Rhizoma, *Br.;* Rhubarb Root; Rhubarbe de Chine, *Fr. Cod.;* Rhubarbe, *Fr.;* Rhabarber, *G.;* Rabarbaro, *It.;* Ruibarbo, *Sp.;* Hainoung, *Chin.;* Schara-modo, *Thibet.*

Notwithstanding the length of time that *rhubarb* has been in use, it has not yet been determined from what precise plant the Asiatic drug is derived, the remoteness of the region where it is collected, and the jealous care with which the monopoly of the trade is guarded, having prevented accurate information.

The terms *rha* and *rheon*, from the former of which were derived the names *rhabarbarum* and *rhubarb*, and from the latter the botanical title *Rheum*, were applied by the ancients to a root which came from beyond the Bosphorus, and which is supposed, though upon somewhat uncertain grounds, to have been the product of *Rheum rhaponticum* L., growing on the banks of the Caspian Sea and the Volga. This species was also at one time believed to be the source of the medicine now in use; but the true rhubarb has long been known to be wholly distinct from the Rhapontic, and derived from a different source. It was not until the year 1732 that any probable information was obtained as to its real origin. At that time plants were received from Russia by Jussieu in France, and Rand in England, which were said to be of the species affording the genuine rhubarb, and were named by Linnæus, under this impression, *Rheum Rhabarbarum*, a title which has since given way to *Rheum undulatum*. Subsequently, Kaau-Boerhaave obtained from a merchant, who dealt in the rhubarb of Tartary, some seeds which he said were those of the plant producing the root sold by him. These, having been planted, yielded two species of Rheum. *R. undulatum*, and another which Linnæus named *R. palmatum*. Seeds transmitted by Mounsey from St. Petersburg to Hope, and planted in the botanic garden at Edinburgh, produced the latter species, and the same was also raised at Upsal from a root received by Linnæus from De Gorter, and was described in 1767 by the younger Linnæus, two years after the appearance of Hope's paper in the Philosophical Transactions. Thus far the evidence appears equally in favor of *R. palmatum* and *R. undulatum*. Colonel Przewalski concluded from personal observation that *R. palmatum* produces rhubarb; but the specimens of the root which he brought to St. Petersburg were stated by Dragendorff to be essentially different from true rhubarb. Claims have also been made from time to time for various other species of Rheum as sources of the drug. Pallas, upon exhibiting the leaves of *R. palmatum* to some Bucharian merchants, was told that the leaves of the rhubarb plant were entirely different in shape, and the description he received of them corresponded more closely with those of *R. compactum* than any other known species. Seeds of this plant were, moreover, sent to Miller from St. Petersburg as those of the true Tartarian rhubarb. Wallich, superintendent of the botanical garden at Calcutta, received seeds that were said to be those of the plant which yielded the Chinese rhubarb, growing on the Himalaya Mountains and the highlands of Tartary. These produced a species not previously described, which Wallich named *R. Emodi*, from the native title of the plant. It is the *R. australe* of Don and of Colebrooke, and has been ascertained to afford a root which, though purgative, is very unlike the official rhubarb. In 1867, French missionaries in Southeastern Thibet forwarded to Soubeiran of Paris, live specimens of a plant which they asserted to yield the true rhubarb, and Baillon subsequently described the flowering plant under the name of *R. officinale*. Its root resembles the true rhubarb, but the most careful cultivation has failed to obtain an identical product, and it cannot yet be considered as settled how far the commercial drug is obtained from it.

Senier found that, as raised in England, the root of *R. officinale* yielded less than half the percentage of extract obtained from the East Indian drug. In ten grain doses the extract was decidedly cathartic.

Tschirch in discussing the origin of Chinese Rhubarb has come to the conclusion that that obtained from Szetschwan, "southern" rhubarb, is derived from *Rheum officinale,* while that obtained from Kukunoor, "northern" rhubarb, is the product of *Rheum palmatum tanguticum* (*A. Pharm.,* 1907, p. 680; and *S. W. P.,* 1910, xlviii, 292).

Hosseus (*P. J.,* 1911, 87, p. 429) as a result of study of material furnished by Tafel, a Tibetan explorer, concludes that the best medicinal rhubarb is derived from *R. palmatum.* He believes that the belief that some of it comes from the *R. officinale* or other species is due to to the fact that Tibetans dig up the root of these other species of rhubarb for the purpose of deceiving Europeans.

All the plants of this genus are perennial and herbaceous, with large branching roots, which send forth vigorous stems from four to eight feet or more in height, surrounded at their base with numerous very large petiolate leaves, and terminating in lengthened branching panicles, composed of small and very numerous nowers, resembling those of the Rumex or dock. There is some difficulty in arranging the species, in consequence of the tendency of the cultivated plants to form hybrids, and it is frequently impossible to ascertain to which of the wild types the several garden varieties are to be referred. Lindley, *Flora Medica,* states that *R. rhaponticum, R. hybridum,* and *R. compactum,* and their hybrids, are the common garden rhubarbs.

R. officinale Baillon is described in the *Pharmacographia* "as a perennial, noble plant, resembling the common garden rhubarb, but of larger size. It differs from the latter in several particulars: the leaves spring from a distinct crown rising some inches above the surface of the ground; they have a subcylindrical petiole, which, as well as the veins of the under side of the lamina, is covered with a pubescence of short erect hairs. The lamina, the outline of which is orbicular, cordate at base, is shortly 5- to 7-lobed, with the lobes coarsely and irregularly dentate; it attains 4 to 4½ feet in length, and rather more in breadth. The first leaves in spring display before expanding the peculiar metallic red hue of copper."

Besides the species already mentioned, *R. leucorrhizum,* growing in the Kirgheeze desert in Tartary, *R. capsicum,* from the Altaï Mountains, *R. webbianum, R. speciforme,* and *R. moorcraftianum,* natives of the Himalaya Mountains and *R. crassinervium* and *R. hybridum,* cultivated in Europe, but of unknown origin, yield roots which have either been employed as purgatives or possess properties more or less analogous to those of official rhubarb, though they have not entered into general commerce. In Java, the root of an indigenous species is used as a purgative. According to the analysis of J. H. Schmidt, it contains more chrysophan and emodin, and less chrysophanic and rheotannic acids, than does the official drug.

According to Aitchison (*Nature,* July 9, 1885), a rhubarb plant has been found in Northern Afghanistan in which there are usually only three enormous root leaves four feet long and five feet broad, lying flat upon the ground. The fruit is large and of a brilliant scarlet. The root is said to possess purgative properties, but the fruit is preferred, and is given in the form of a decoction.

Rhubarb is produced abundantly in the elevated lands of Tartary, about the lake Koko Nor, and is said to be cultivated in the neighboring Chinese province of Shen-see, and in that of Se-chuen. From these sources it is generally supposed that our supplies of Russian and Chinese rhubarb were exclusively derived; but the root is also collected in Bootan and Thibet, on the north of the Himalaya Mountains, and it is probable that the plant pervades the whole of Chinese Tartary. It flourishes best in a light sandy soil. It is stated by Bell, who, on a journey from St. Petersburg to Pekin had an opportunity of observing it in a growing state, that it is not cultivated by the Tartars, but springs up spontaneously, in tufts, wherever the seeds have fallen upon the heaps of loose earth thrown up by the marmots. In other places the thickness of the grass prevents their access to the soil. The root is not considered sufficiently mature for collection until it has attained the age of six years. It is dug up twice a year in Tartary, in the spring and autumn; in China not till the winter. After removal from the ground, it is cleaned, deprived of its cortical portion and the smaller branches, and then divided into pieces of a convenient size. In China these are bored with holes, and strung upon cords to dry—according to Bell, about the tents and on the horns of sheep; according to Sievers, under sheds, by which the rays of the sun are excluded, while the air has free access. The Chinese are said first to place the pieces on a stone slab heated by fire beneath, and afterwards to complete the drying process by exposing them to the sun and air. In Bootan the roots are hung up in a kind of drying room, in which a moderate and regular heat is maintained. Much time and attention are devoted to the preparation of the root, and Sievers states that a year sometimes elapses from the period of its collection before it is ready for exportation. A large proportion of its weight is lost in drying, according to some accounts four-fifths, according to others not less than seven-eighths. It is probably in order to favor the drying that the periderm is removed. Rhubarb which has been dried by artificial heat is known commercially as high dried and often can be recognized by its more or less blackened surface, and its heavy, scarcely fragrant odor. The trade in rhubarb is said to have formerly centred in the Chinese town of Si-nin, where a

Bucharian company or family was established which possessed a monopoly of this trade in consideration of a tribute paid to the government. At present rhubarb is chiefly purchased for the European trade at the town of Hankow, on the upper Yang-tse, the yearly export reaching over 5000 peculs (pecul = 133.33 lbs.). There were formerly two varieties of Asiatic rhubarb, the Russian and the Chinese, but at present little or no rhubarb finds it way overland to Europe. As long back as 1687, the Russian government subjected the export of rhubarb from China into Russia to official surveillance, and finally monopolized the trade entirely. At Kiakhta a very rigorous inspection of the drug was enforced, the selected pieces being finally sewed into linen sacks pitched and coated with hide. All the pieces which did not pass examination were committed to the flames, and the remainder was sent to St. Petersburg. This variety was sometimes called *Turkey rhubarb,* from the circumstance that it was formerly derived from the Turkish ports, whither it is said to have been brought from Tartary by caravans through Persia and Anatolia. Inferior parcels of the root, which could not pass the inspection of the Russian authorities, were said to enter Russia by Tashkend, and to be known to the druggists of that country by the name of *Tashkend rhubarb.* Russian rhubarb no longer occurs in commerce. The description of it is given in the U. S. D., 19th edition, page 1061.

Chinese Rhubarb (*India Rhubarb, Rheum Sinense* vel *Indicum*) is in cylindrical or roundish pieces, sometimes flattened on one or both sides, of a dirty brownish-yellow color externally, appearing as if the cortical portion of the root had been removed by scraping, and the surface rendered smooth and somewhat powdery by attrition. The best pieces have a rather close and compact texture, and, when broken, present a ragged uneven surface, variegated with intermingled shades of dull red, yellowish, and white, which are sometimes diversified or interrupted by darker colors, and especially marked with dark lines so arranged as to form an internal ring of star-like spots. The pieces are generally perforated with small holes, intended for convenience of suspension during the drying process, and portions of the suspending cord are not unfrequently found remaining in the holes. According to Elborne (*P. J.,* xv, 497), Chinese rhubarb is the product of *R. palmatum* and *R. officinale,* the first variety has a red-grained fracture with white latticework veins, while the second variety has a longitudinal ramification of white veins with a black-grained fracture. Chinese rhubarb has a peculiar somewhat aromatic odor, and a bitter, astringent taste, is gritty when chewed, imparts a yellow color to the saliva, and affords a yellowish powder with a reddish-brown tinge. With the pieces of good quality others often come mingled, defective from decay or improper preparation. These are usually lighter, and of a dark or russet color. Like all the other varieties of rhubarb, this is liable to be attacked by insects, and in almost every large parcel pieces may be found which have suffered from this cause. The Shensi variety is preferred, that of Sechuen and Kansuh are less valuable.

Chinese rhubarb is the only kind recognized by the U. S. P., and is officially described as "sub-cylindrical, barrel-shaped, or conical pieces known in commerce as 'rounds,' or in plano-convex pieces known in commerce as 'flats,' or in irregularly formed pieces, frequently with perforations. It is hard and moderately heavy; attaining a length of 17 cm. and a diameter of 10 cm., often cut in pieces of variable form and size; outer surfaces yellowish-brown, mottled, with alternating, longitudinal striæ of grayish-white parenchyma and reddish or brownish medullary rays; small stellate groups of fibro-vascular tissue and occasionally reddish-brown cork patches, smooth and sometimes covered with a bright, brownish-yellow powder; fracture uneven and granular, presenting a characteristic mottled appearance; odor aromatic, characteristic; taste characteristic, slightly bitter and astringent, gritty when chewed and tingeing the saliva yellow. Under the microscope, sections of Rhubarb show numerous thin-walled parenchymatous cells containing either a large number of starch grains or a single large rosette aggregate of calcium oxalate; scattered among the parenchyma are stellate groups of compound fibro-vascular bundles, the latter composed of narrow medullary rays separating the wedges, having large tracheæ in the outer part and separated by a prominent cambium from an internal phloem or sieve; among the grayish-white parenchyma of the inner bark occur narrow, yellowish-brown, irregular medullary rays. Not more than 15 per cent. of the drug should show a hollow or dark central area. The powder is bright orange-yellow to yellowish-brown; becoming red with alkalies; when examined under the microscope it exhibits calcium oxalate in rosette aggregates, mostly from 0.05 to 0.1 mm. in diameter, occasionally attaining a diameter of 0.15 mm.; starch grains numerous, somewhat spherical, single or 2- to 4-compound, each with a single cleft, from 0.002 to 0.02 mm. in diameter; tracheal fragments few, mostly reticulate, occasionally spiral. Boil 0.1 Gm. of powdered Rhubarb with 10 mils of an aqueous solution of potassium hydroxide (1 in 100); allow it to cool, filter, acidulate the filtrate with hydrochloric acid and shake it with 10 mils of ether; on standing the ethereal layer is colored yellow. Shake this ethereal solution with 5 mils of ammonia water; the latter is colored cherry-red (presence of *emodin*) and the ethereal layer remains yellow (presence of *chrysophanic acid*). Rhubarb, when exhausted with diluted alcohol, yields not less than 30 per cent. of dry extract. Rhubarb yields not more than 13 per cent. of ash." *U. S.*

"In compact, firm, cylindrical, barrel-shaped, conical or plano-convex pieces, often perforated, the perforation sometimes containing a fragment of cord. Surface rounded or slightly

angular, but not shrunken, marked with reddish-brown lines embedded in a whitish ground-substance; usually covered with a bright brownish-yellow powder. Fracture granular and uneven, the pinkish-brown fractured surface exhibiting numerous reddish-brown points and lines on a white ground-substance. For a short distance within the cambium the structure is radiate; within this there is a more or less distinct ring of closely approximated vascular bundles with central bast and radiating, reddish-brown medullary rays; in the parenchymatous cells abundant starch grains, an amorphous yellow substance and very large cluster-crystals of calcium oxalate. In powdered Rhubarb large cluster-crystals of calcium oxalate, often more than 100 microns in diameter, simple or compound starch grains, the single grains seldom exceeding 20 microns in diameter, fragments of reticulated vessels and of parenchymatous tissue, and small yellowish masses and globules which assume a reddish-pink color with *solution of ammonia;* it is free from added starch and from sclerenchymatous cells and fibres. Characteristic, somewhat aromatic odor; taste bitter, slightly astringent. Ash not more than 15 per cent." *Br.*

European Rhubarb.—In various parts of Europe, particularly in England, France, Belgium, and Germany, the rhubarb plants have been cultivated for many years, and considerable quantities of the root were at one time brought into the market. At present it appears not to be imported into the United States.

English Rhubarb.—This formerly came in two forms. In one the root was cut and perforated in imitation of the Russian. The pieces were of various shapes and sizes, sometimes cylindrical, but more commonly flat, or somewhat lenticular, and of considerable dimensions. In the other, the so-called *stick rhubarb,* the pieces were somewhat cylindrical, five or six inches long by an inch or less in thickness, and more or less irregular upon the surface, as if they had shrunk unequally in drying. English rhubarb (from *Rheum rhaponticum*) is lighter than the Asiatic, more spongy, and often somewhat pasty under the pestle. It is redder, and when broken exhibits a more compact and regular marbling, the pinkish lines being arranged like rays from the centre towards the circumference. The "star-like spots" are either wanting or very few and scattered. The powder also has a brighter yellow tint. The odor is feeble and less aromatic than that of the Asiatic varieties; the taste is astringent and mucilaginous, with little bitterness, and the root, when chewed, scarcely feels gritty between the teeth, and but slightly colors the saliva. Few crystals of calcium oxalate are discoverable by means of the microscope. Much English rhubarb is obtained from *R. officinale,* and is put on the market in flat, concave, and convex pieces weighing from three to four ounces each. Externally the convex surface has deep longitudinal furrows and a longitudinal ramification of conspicuous veins, giving rise to an appearance of net-vein markings. In the centre of the concave surface is a small hole similar to that formerly seen in Russian rhubarb. On the inner surface the stellate markings resemble very closely those found in the East Indian rhubarb. The fracture of this form is not red, but shows a whitish parenchymatous tissue with blackish veins. When rapidly grown in rich soil, English rhubarb is lighter, more spongy, and less active than when slowly grown without high cultivation. It is probable that the powder is used to adulterate that of true Asiatic rhubarb, but of this we have no positive evidence.

French Rhubarb. Rhapontic Rhubarb. Crimea Rhubarb.—The rhubarb produced in France is, according to Guibourt, chiefly from *R. rhaponticum, R. undulatum,* and *R. compactum,* that of *R. palmatum,* which most closely resembles the Asiatic, having been found to degenerate so much as not to be a profitable object of culture. Most of the French rhubarb is produced in the neighborhood of L'Orient, in the department of Morbihan, and the spot where it grows has, from this circumstance, received the name of *Rheumpole.* Two kinds were described by Guibourt, both under the name of *Rhapontic root*—one proceeding from the *R. rhaponticum,* growing in the gardens in the environs of Paris; the other, from this and the two other species above mentioned, cultivated at Rheumpole.

Rhapontic rhubarb is still found to some extent in European markets. Tschirch has proposed a ready method for detecting the admixture. It depends on the insolubility in ether of the crystalline principle rhaponticin or ponticin. (*A. Pharm.,* 1905, p. 443; and *S. W. P.,* xliii, p. 253.) Hesse has also made an elaborate study on the chemistry of rhapontic root grown in Austria. (*J. f. prakt. Chem.,* 1908, lxxvii, p. 320.)

The *rhapontic root* differs in section from true rhubarb by its distinctly radiated structure, unbroken by the peculiar arrangement (star-like spots) of the vascular tissue which occurs in true rhubarb.

Choice of Rhubarb.—In selecting good rhubarb, without reference to the commercial variety, those pieces should be preferred which are moderately heavy and compact, of a bright color, brittle, presenting when broken a fresh appearance, with reddish and yellowish veins intermingled with white, of an odor decidedly aromatic, of a bitter and astringent not mucilaginous taste, feeling gritty and staining the saliva yellow when chewed, and affording a powder either bright yellow, or yellow with but a slight reddish-brown tinge. When very light, rhubarb is usually rotten or worm-eaten; when very heavy and compact, it is of inferior species, culture, or preparation. Rotten, worm-eaten, or otherwise inferior rhubarb is often powdered, and colored yellow with turmeric, and the shavings left when Chinese rhubarb is trimmed for powdering, or to imitate the Russian, are applied to the same purpose. The stellate markings observed in the cut or

broken surface of the Chinese rhubarb has been believed by various pharmacologists to be of great practical value in determining the true character of the rhizome and especially in enabling a distinction between the Chinese and European rhubarb to be made. There has been a general concurrence with the statements of Tschirch that the star spots are never present in the root, occurring only in the rhizome. In an elaborate re-examination of this subject by Jakabhasy, however, the star spots were found in the root as well as in the root stock and also in the European as well as in the Asiatic rhubarb. Nevertheless, Jakabhasy states that it is possible to distinguish the two rhubarbs by the fact that in the European Rhubarb the star spots occur in greater number on the longitudinal section while in the Chinese rhubarb they are present on the transverse section, where they form a circle. He believes also that the superabundance of starch and the lack of crystals in the star spots are diagnostic of the European drug. When the rhubarb is powdered these characteristics are not available, under which circumstances the percentage of ash seems to be valuable. The Chinese rhubarb, unless of very inferior quality yields from 8 to 25 per cent.; the European 1.3 to 6 per cent. of ash. According to Jakabhasy, Shensi is the best, Shanghai the poorest, and Canton the intermediate variety of Chinese rhubarb. Of the European the English is the most, the French next, and the Austrian the least active.

Chemical Properties.—Rhubarb yields all its activity to water and alcohol. The infusion is of a dark reddish-yellow color, with the taste and odor of rhubarb, and the residue, after sufficient maceration, is whitish, inodorous, and insipid. By long boiling the virtues of the medicine are impaired. The first examination of rhubarb yielding results of value was that of Schlosberger and Döpping. Besides extractive, tannic and gallic acids, sugar, starch, pectin, lignin, calcium oxalate and various inorganic salts, they discovered three coloring principles, holding an intermediate place between resin and extractive matter, being freely soluble in alcohol, and slightly so in water. Two of these were uncrystallizable, and denominated *brown resin* and *red resin*, or *phæoretin* and *erythroretin;* the other, crystallizable in granular crystals, and identical with *chrysophanic acid*, previously discovered by Rochleder and Heldt in the yellow lichen, or *Parmelia parietina* of Sprengel. Chrysophanic acid crystallizes in golden-yellow needles or plates melting at 102° C. (215.6° F.), and is soluble in ether, alcohol, or benzene. Alkalies also dissolve it, forming fine dark red solutions. Its formula is $C_{15}H_{10}O_4$, and it is now recognized as a derivative of anthracene, $C_{14}H_{10}$, and as closely related to alizarine, $C_{14}H_8O_4$. It bears to methyl-anthracene, $C_{14}H_9(CH_3)$, the same relation that alizarine bears to anthracene. Hence, on distilling it with zinc dust, methyl-anthracene is formed from it by reduction. (See *Chrysarobinum.*)

De La Rue and Müller (*J. Chem. S.*, x, 298) extracted from rhubarb *emodin*, which crystallizes in orange-colored prisms. Its formula is $C_{15}H_{10}O_5$, and it is a trioxy-methyl-anthraquinone. The relations of both this compound and chrysophanic acid to alizarine and anthracene will be better shown by writing their molecular formulas, as follows:

$C_{14}H_{10}$	$C_{14}H_6(OH)_2O_2$
Anthracene.	Alizarine.
$C_{14}H_5(CH_3)(OH)_2O_2$	$C_{14}H_4(CH_3)(OH)_3O_2$
Chrysophanic. Acid	Emodin.

Kubli (*Ph. Z. R.*, 6, p. 603) obtained results both confirmatory and explanatory of those already given. He found a glucoside, *chrysophan*, $C_{27}H_{30}O_{14}$, which, under the influence of dilute acids or ferments, splits up into chrysophanic acid and sugar, according to the reaction

$$C_{27}H_{30}O_{14} + 2H_2O = C_{15}H_{10}O_4 + 2C_6H_{12}O_6$$

also a characteristic tannic acid, *rheo-tannic acid*, $C_{26}H_{26}O_{14}$, which is decomposed by dilute acids into *rheumic acid*, $C_{20}H_{18}O_9$, and sugar. Chrysophan is a yellowish powder, abundantly present in rhubarb, soluble in water or alcohol, not in ether; rheo-tannic acid is a reddish brown powder, sparingly soluble in cold water. Kubli found further a colorless neutral compound, sparingly soluble in hot water, of the formula $C_{10}H_{12}O_4$, which he did not name. He stated that chrysophanic acid is not found in rhubarb, but is produced when the root is digested in water through the breaking up of the glucoside *chrysophan*, probably under the action of a ferment. This ferment he believes to be soluble in water, but insoluble in alcohol, and that on this account an alcoholic extract of the root can be evaporated without the formation of chrysophanic acid. On the other hand, it is to the presence of this ferment that he attributes the progressive deposition of chrysophanic acid from an extract of rhubarb prepared with diluted alcohol. (*Ph. Z. R.*, xxiv, 193.) O. Hesse (*Proc. A. Ph. A.*, 1896, 549) found in addition to chrysophanic acid, $C_{15}H_8O_2(OH)_2$, and emodin, $C_{15}H_7O_2(OH)_3$, a third crystalline principle, which he named *rhein*, and ascribes to it the formula $C_{15}H_8O_2(OH)_4$. Hesse calls attention to the relation these formulas bear to one another. Rhein forms microscopic yellowish-brown scales, is insoluble in water, ether, and benzene, but sparingly soluble in alcohol. It dissolves readily in aqueous solutions of the alkalies and alkaline carbonates, forming deep purple-red solutions. Hesse also finds an amorphous resinous substance, upon which, he states, the entire activity of rhubarb depends. Dragendorff states that from 11 to 17 per cent. of arabic acid and pectose are present in rhubarb. Hunkel (*Ph. Archiv.*, Nov., 1900, 201) reviewed the investigations of various chemists and isolated *tanoid* by the process of Löwe and a

phenolic body (unnamed) which had not been previously described.

The most important researches upon the constituents of rhubarb were made by Tschirch and Heuberger (*A. Pharm.*, Nov. 21, 1902, 596, 630, and *Ph. Ztg.*, Aug. 3, 1904, 651). Their conclusions are that rhubarb contains primarily two classes of substances. 1. *Tannoglucosides;* 2. *Anthraglucosides.* These two classes cannot be sharply separated from each other and are therefore associated together in all extractions. Both of these are characterized by their ready decomposition and conversion into secondary products, such conversion resulting even during the treatment of the drug with ordinary solvents. Thus, the ether extraction has been found to contain the products of the hydrolysis of the anthraglucosides, namely, chrysophanic acid, emodin and rhein. It is however not proven (indeed not even probable) that the tannoglucosides combine with the anthraglucosides to form so-called double glucosides. On the contrary, the indications are that these two classes of glucosides occur beside each other; furthermore, the relatively large quantity of tannoglucosides and their hydrolytic products is noteworthy and that, therefore, the activity of rhubarb is not attributable solely to the anthraglucosides; but the activity of the latter must be materially modified by that of the tannoglucosides. To what degree the primary tanno- and anthraglucosides have become hydrolyzed in the drug itself, it is difficult to determine; it is certain, however, that the drug contains a considerable quantity of free oxymethylanthraquinones, while it is probable that the formation of the secondary glucosides results during the extraction and manipulation of the extract.

Tschirch sums up the results of the investigation as follows: Aweng's *Double Glucoside* is in its essentials identical with tannoglucoside, but contains some anthraglucoside. Aweng's *Frangulic Acid* is a secondary product of the decomposition of tannoglucoside, containing variable quantities of anthraglucoside as impurity. Kubli's *Rheumtannic Acid* and Hunkel's *Tanoid* are identical with tannoglucoside, but less pure. Kubli's and Hunkel's *Rheum Acid* is identical with *rheum red,* and therefore a product of the hydrolysis of tannoglucoside. Schlossberger and Dopping's *Aporetin* and *Phaeoretin* are impure, difficultly soluble tannoglucoside. *Erythroretin* is a mixture of chrysophanic acid, emodin and rhein. Garot's *Erythrose* is *chrysamic acid. Rhein,* yielding only a diacetyl derivative, cannot be regarded as being tetraoxymethyl-anthraquinone. It has the composition $C_{15}H_8O_6$ (not $C_{15}H_{10}O_6$, Hesse) which formula corresponds to a methylene ether of a tetraoxyanthraquinone. Dragendorff's, Greenish's and Elborne's *Cathartic Acid* is an impure tannoglucoside, containing anthraglucosides and some albuminoid substances. Gilson's *Chrysophan* belongs to the anthraglucosides. Aweng's Secondary Glucosides are secondary, mostly difficultly soluble hydrolytic products of the primary tanno- and probably also of the anthraglucosides.

Finally, Tschirch determined that rhubarb contains no resins whatever; that the rheotannoglucosides and their products of decomposition and hydrolysis are devoid of purgative activity, and that such activity is due solely to the anthraglucosides and their derivatives. Rhubarb contains no other body besides the latter that has peristaltic effect on the intestinal tract.

As regards the rheo-tannoglucoside, its medicinal activity is confined to the tonic and mildly astringent effect produced on administering the drug. Tschirch (*Ph. Ztg.*, Aug. 3, 1904, 651) recommended a method for assaying rhubarb based on the volumetric estimation of the free oxymethylanthraquinones, dependent on the ease with which the anthraglucosides can be hydrolyzed with sulphuric acid. See also *Proc. A. Ph. A.*, 1905, 627.

There are other interesting principles in rhubarb. Some have been disposed to ascribe its odor to a volatile oil, but this has not been isolated. The calcium oxalate is interesting from its quantity, and from the circumstance that, existing in distinct crystals, it occasions the grittiness of the rhubarb between the teeth. The proportion seems to vary exceedingly in different specimens. According to Scheele and Henry, it constitutes nearly one-third, and Queckett found between 35 and 40 per cent., while Brandes obtained only 11, Schrader only 4.5 parts in the hundred, and Dragendorff, in five samples analyzed, from 1.2 to 5.6 per cent. Little or no difference of composition has been found between the Russian and the Chinese rhubarb. The European contains but a small proportion of calcium oxalate, and is therefore less gritty when chewed. It has, however, more tannin and starch than the Asiatic.

When powdered rhubarb is heated, odorous yellow fumes rise, which are probably in part the vapor of chrysophanic acid. Its infusion is reddened by the alkalies, in consequence of their union with this acid, and their reaction on the other coloring principles. It yields precipitates with gelatin, most of the acids, ferric salts, lead acetate, mercurous nitrate, silver nitrate, stannous chloride, lime water, and solutions of quinine. Nitric acid occasions at first a turbidness, and afterwards the deposition of a yellow precipitate. The substances producing precipitates may be considered as incompatible with the infusion.

For a method of detecting the presence of turmeric in powdered rhubarb by the influence of chloroform on the coloring principles of each of these substances, and of distinguishing through the same agency between the true Chinese rhubarb and that of European origin, the reader is referred to a paper, by W. L. Howie, contained in *A. J. P.* (Jan., 1874, 16), from *P. J.* (Nov. 15, 1873); see also *P. J.*, 1898, 126.

Uses.—Rhubarb contains cathartic principles of the anthraquinone series. It differs from drugs of this group—such as aloes, cascara, etc.

—in that it has a larger percentage of tannic acid. On account of the considerable quantity of tannin its purgative action is often followed by constipation. This sequence of effects has led to its use in the treatment of *diarrheas*, especially of the inflammatory type, on the theory that the catharsis it caused would evacuate the irritant *materies morbi*, and that its subsequent astringency would check the excessive secretion. The logic is plausible, but erroneous. As the action of its cathartic principles is limited to the lower bowel it has very little influence in cleaning out the smaller bowel which is the more frequently involved in acute *diarrheas*. In inflammations of the colon, such as *dysentery*, its use might appear more reasonable, but even here it is greatly inferior to less irritant laxatives because it acts chiefly by virtue of its local irritant influence. Rhubarb is also widely prescribed in atonic *dyspepsia* attended with *constipation*. It is frequently combined with an alkali, either magnesia or soda.

It sometimes occasions griping. Its coloring principle is absorbed, and may be detected in the urine. By its long-continued use the perspiration, especially that of the axilla, is said to become yellow, and the milk of nurses cathartic. It gives a yellow color to the alvine discharges.

By the roasting of rhubarb its cathartic property is diminished, probably by the volatilization of the purgative principle, while its astringency remains unaffected. When so treated it is termed *torrefied rhubarb*. This mode of treatment has been sometimes resorted to in cases of *diarrhea*. By long boiling the same effect is said to be produced.

Powdered rhubarb has been usefully applied to indolent and sloughing *ulcers*. It is said to have proved purgative when sprinkled over a large ulcerated surface, and the same effect is asserted to have been produced by rubbing it, mingled with saliva, over the abdomen.

European rhubarb must be administered in double or treble the dose of true rhubarb to produce an equal effect. Few medicines are used in a greater variety of forms. It is most effectual in substance. It is frequently given in the shape of pill, combined with an equal proportion of soap when its laxative effect is desired. The infusion is much used in cases of delicate stomach, and is peculiarly adapted to children. The syrup, tincture, and fluidextract are also useful preparations. They are all official. The formula for *mixture of rhubarb and soda* which was largely used in New York at one time will be found in the National Formulary IV. The name was changed to *Mistura Rhei Composita*.

Dose, as a purgative, from twenty to thirty grains (1.3–2.0 Gm.); as a laxative and stomachic from five to ten grains (0.32–0.65 Gm.).

Off. Prep.—Fluidextractum Rhei, *U. S.;* Extractum Rhei, *U. S., Br.;* Infusum Rhei, *Br.;* Liquor Rhei Concentratus, *Br.;* Pilulæ Rhei Compositæ, *U. S.* (*Br.*); Pulvis Rhei Compositus, *U. S., Br.;* Syrupus Rhei (from Fluidextract), *U. S., Br.;* Syrupus Rhei Aromaticus (from Aromatic Tincture), *U. S.;* Tinctura Rhei, *U. S.* (*Br.*); Tinctura Rhei Aromatica, *U. S.;* Tinctura Rhei Composita, *Br.;* Elixir Catharticum Compositum (from Fluidextract), *N. F.;* Fluidglyceratum Rhei, *N. F ;* Mistura Opii et Rhei Composita (from Tincture), *N. F.;* Mistura Rhei Alkalina (from Fluidextract), *N. F.;* Mistura Rhei Composita (from Fluidextract), *N. F.;* Pilulæ Antiperiodicæ, *N. F.;* Pilulæ Antiperiodicæ sine Aloe, *N. F.;* Pilulæ Rhei, *N. F.;* Pulvis Rhei et Magnesiæ Anisatus, *N. F.;* Syrupus Sennæ Aromaticus, *N. F.;* Syrupus Sennæ Compositus (from Fluidextract), *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.;* Tinctura Rhei Aquosa, *N. F.;* Tinctura Rhei Dulcis, *N. F.;* Tinctura Rhei et Gentianæ, *N. F.;* Tinctura Zedoariæ Amara, *N. F.;* Vinum Rhei Compositum (from Fluidextract), *N. F.*

RHŒADOS PETALA. Br.

RED POPPY PETALS

(rhœ'ą-dŏs pĕt'ą-lą)

"Red-Poppy Petals are the fresh petals of Papaver Rhœas, *Linn.*" *Br.*

Corn Poppy, Corn Rose; Coquelicot, *Fr. Cod.;* Pavot rouge, *Fr.;* Wilder Mohn, Klapperrose, Llatschrosen, *G.;* Rosolaccio, *It.;* Amapola (Flor de), *Sp.*

The *red* or *corn poppy, Papaver Rhœas*, is distinguished by its hairy stem, which is branched, and rises about a foot in height, by its incised pinnatifid leaves, by its urn-shaped capsule, and by the full, bright, scarlet color of its petals. It is a native of Europe, where it grown wild in great abundance, adorning especially the fields of grain with its brilliant flower. It has been naturalized in this country.

Its capsules contain the same kind of milky juice as that found in *P. somniferum*, and an extract has been prepared from them having the properties of opium; but the quantity is too small to repay the trouble of its preparation. Filhol has shown that the extract contains morphine, but in a proportion exceedingly minute compared with that in which it exists in opium. The petals are the official portion. They have a characteristic odor, and a mucilaginous, slightly bitter taste. By drying, they lose their odor, and assume a violet-red color. "Transversely elliptical, about five centimetres wide, bright scarlet, smooth and lustrous; margin entire. Characteristic, somewhat unpleasant odor; taste slightly bitter." *Br.*

Chevallier believed that he had detected a very minute proportion of morphine in an extract obtained from them; but Attfield seems to have determined satisfactorily the non-existence of morphine in the petals, having sought this alkaloid by three different processes, using a pound of the petals in each experiment, and failed to detect the least evidence of its presence. (*P. J.*, Oct., 1873, p. 291.) Their operation on the system is exceedingly feeble, and they are valued more for their beautiful scarlet color, which they communicate to water, than for

their medicinal virtues According to Leo Meier, the coloring principles of the flowers are two acids, which he denominates *rhœadic* and *papaveric acids.* (See *A. J. P.*, xviii, 211.) A syrup is prepared from them, which was formerly prescribed as an anodyne in catarrhal affections, but is now little esteemed except for its color.

An alkaloid was discovered in this species of poppy by O. Hesse, who proposed to name it *rhœadine.* It seems to pervade all parts of the plant, from which, as the first step in its preparation, an aqueous extract is prepared. This is treated with sodium carbonate, and repeatedly agitated with ether; the ethereal liquid is shaken with a solution of sodium bitartrate, and the mixture is precipitated by ammonia. The precipitate is washed with cold water, dried, and boiled with alcohol, by which coloring matter and another alkaloid in small quantity, probably thebaine, are removed. The residue, consisting mainly of rhœadine, is purified by combining it with acetic acid, treating with animal charcoal, and precipitating with ammonia. The alkaloid is in small white prismatic crystals, tasteless, fusible at 232.2° C. (450° F.), becoming brown at the same temperature and partially subliming. It is almost insoluble in water, alcohol, ether, chloroform, benzene, ammonia, solution of sodium carbonate, and lime water, but is dissolved by dilute acids, which produce colorless solutions. Its composition is represented by the formula $C_{21}H_{21}O_6N$. It does not appear to be poisonous. Hydrochloric and sulphuric acids, moderately concentrated, decompose and dissolve it, with the production of a purple color, which disappears under the action of the alkalies, but is restored by acids. One part of the alkaloid so treated produces a purple color with 10,000 parts of water, rose color with 20,000 parts, and a perceptible redness with 800,000 parts. This change is dependent upon the liberation from the rhœadine of a red coloring matter, while the isomeric *rhœagenine* remains. This forms small white tasteless prisms, which fuse at 223° C. (433.4° F.) and do not sublime, but are decomposed at higher temperatures. This is a very delicate test, by means of which the alkaloid may be detected in all parts of *Papaver Rhœas,* in the ripe capsules of the opium poppy, and in opium itself. It is said also to exist in Merck's prophyroxine. (*A. J. P.*, 1867, p. 122.) According to Hesse, the milky juice also contains *meconic acid.*

Off. Prep.—Syrupus Rhœados, *Br.*

ROSA GALLICA. U. S. (Br.)

RED ROSE Rosa Gall.

(rō'ṣą găl'lĭ-cą)

"The dried petals of *Rosa gallica* Linné (Fam. *Rosaceæ*), collected just before the expansion of the flower. Preserve Red Rose in tightly-closed containers, protected from the light." *U. S.* "Red-Rose Petals are the fresh or dried unexpanded petals of Rosa gallica, *Linn.;* obtained from cultivated plants." *Br.*

Rosæ Gallicæ Petala, *Br.*, Red-rose Petals; Flores Rosarum Rubrarum; Rose rouge ou Rose de Provins, *Fr. Cod.;* Roses rouges, *Fr.;* Sammtrose, Zuckerrose, Französische Rose, Essigrosenblätter, *G.;* Rosa rossa, *It.;* Rosa roja (Flore de), Rosa rubra, *Sp.*

At one time pale rose or *Rosa centifolia* was official in addition to red rose or *Rosa gallica.* There is no uniformity on the subject in the several Pharmacopœias. The Pharmacopœia of the Netherlands and the French Codex still include both species. The German Pharmacopœia, on the other hand, specifies only the petals of *Rosa centifolia.* The British and Austrian Pharmacopœias are in unison with the U. S. Pharmacopœia in restricting the drug to *R. gallica.*

Rosa gallica is smaller than *R. centifolia* L., but resembles it in the character of its foliage. The stem is beset with short bristly prickles. The flowers are very large, with obcordate widely spreading petals, which are of a rich crimson color, and less numerous than in the *R. centifolia.* The stamens on thread-like filaments, and the villose styles bearing papillary stigmas, are numerous. The fruit is oval, shining, and of a firm consistence. The red rose is a native of the south of Europe, and is cultivated in gardens throughout the United States.

The drug is officially described as "petals either separate or imbricated in small cones, broadly ovate, summit rounded and deeply notched, margin entire and somewhat recurved, base obtuse; externally of a purplish-red color except the light-brown claw; texture velvety; when dry, brittle; odor agreeable; taste astringent and slightly bitter. Under the microscope, transverse sections of the petals of Red Rose show the upper epidermal cells modified to conical papillæ and containing a purplish-red cell sap; a loose mesophyll composed of from 2 to 10 rows of cells among which are the fibro-vascular bundles with spiral tracheæ, and a lower epidermis of rectangular cells filled with a purple cell sap. Red Rose yields not more than 3.5 per cent. of ash." *U. S.*

"Usually in little cone-like masses, or sometimes separate and more or less crumpled. Petals velvety, deep purplish-red passing into brownish-yellow towards the base. Fragrant odor; taste slightly astringent." *Br.*

The petals should be gathered before the flower has blown, separated from their claws, dried in a warm sun or by the fire, and kept in a dry place. Their odor, which is less fragrant than that of *R. centifolia,* is improved by drying. They have a velvety appearance, a purplish-red color, and a pleasantly astringent and bitterish taste.

An illustrated article on the structural characteristics of rose petals, whole and powdered, has been published by Hans Kramer in *B. P. G.*, 1907, xvii, p. 354.

Their constituents, according to Cartier, are tannin, gallic acid, coloring matter, a volatile oil, a fixed oil, albumen, soluble salts of potassium, insoluble salts of lime, silica, and ferric oxide.

(*J. P. C.*, vii, 531.) According to Filhol, the astringency of red roses is ascribable less to tannic acid, of which they contain but a trace, than to *quercitrin*, which he obtained in notable proportion, and with which their color is probably connected. Rochleder found that in red roses the gallic acid is accompanied by quercitannic acid. They also contain much uncrystallizable sugar. (*Répert. de Pharm.*, Mai, 1863.) The sensible properties and medicinal virtues of the flowers are extracted by boiling water. Their coloring matter, according to Senier (*Y. B. P.*, 1877, p. 63), is an acid, which appears to form crystallizable salts with potassium and sodium, and amorphous ones with the heavy metals. Senier gives as the formula of the insoluble lead compound $Pb_2C_{21}H_{29}O_{30}$. Their infusion is of a pale reddish color, becoming bright red on the addition of sulphuric acid. As their color is impaired by exposure to light and air, they should be kept in opaque well-closed bottles or canisters.

Uses.—Red rose is slightly astringent and tonic, and it was formerly thought to possess peculiar virtues. It it at present chiefly employed as affording an elegant vehicle for tonic and astringent medicines.

Off. Prep.—Confectio Rosæ Gallicæ, *Br.;* Fluidextractum Rosæ, *U. S.;* Infusum Rosæ Acidum, *Br.* (*N. F.*); Confectio Rosæ, *N. F.;* Syrupus Rosæ (from Fluidextract), *N. F., Br.*

SABAL. U. S.

SABAL [Saw Palmetto Saw Palmetto Berries]

(să'bạl)

"The partially dried, ripe fruit of *Serenoa serrulata* (Michaux) Hooker filius (Fam. *Palmæ*). Preserve Sabal in tightly-closed containers, adding a few drops of chloroform or carbon tetrachloride, from time to time, to prevent attack by insects." *U. S.*

The *Saw palmetto* flourishes on the Atlantic coast from South Carolina to Florida, where it forms the so-called "palmetto scrub." According to Schneider it is also found in southern portions of California. (*Pacific Pharm.*, ii, p. 466.) It was introduced into medicine in 1879. (*Bull. Lloyd Library*, 1911, No. 18, p. 71.) The stem of saw palmetto is from 6 to 10 feet high, has a crown of large leaves, long petioled, with a circular fan-shaped leaf blade split at the edge into from 15 to 30 divisions, which are slightly cleft at their apices. The fruit is a one-sided blackish-brown drupe, from half an inch to one inch long; ovoid-oblong in shape, with a somewhat wrinkled exterior, and a sweetish, not agreeable taste. It occurs in a large panicle which in some cases may weigh as much as nine pounds.

Properties.—Sabal is officially described as follows: "Ellipsoidal or ovoid, occasionally compressed, from 1.5 to 3 cm. in length and from 1 to 1.5 cm. in diameter; externally brownish-black to bluish-black, smooth and somewhat oily, with a few large, more or less angular depressions due to the contraction of the inner layer on drying, summit marked by the scar of the style, and the base either with a short stalk or stem-scar; epicarp and sarcocarp together forming a thin coriaceous shell enclosing a hard but thin endocarp, which is externally reddish-brown and somewhat fibrous as is also the inner layer of the sarcocarp; inner layer of endocarp smooth, enclosing a hard, ellipsoidal or ovoid, somewhat flattened, reddish-brown seed; odor pronounced, aromatic; taste sweetish, aromatic, slightly acrid. The powder is yellowish-brown; when examined under the microscope it exhibits large, irregular fragments; parenchyma cells of sarcocarp containing a yellowish-brown or brownish-red, amorphous substance; whitish fragments of endosperm; the walls being considerably thickened and with large pores; stone cells occasional, nearly colorless, more or less tabular or irregular in shape, about 0.125 mm. in length, walls about 0.015 mm. in thickness, and with numerous simple or branching pores." *U. S.*

Kraemer gives an illustrated article on the pharmacognosy of the saw palmetto in the *Practical Druggist*, 1910, xxviii, p. 97. In it Coblentz (*Proc. New Jersey Pharm. Assoc.*, 1895, 45) believes that he found, besides a volatile oil an alkaloid. In the studies of Sherman and Briggs (*Ph. Archiv.*, vol. 2) no alkaloid could be detected. Sieker (*Ph. Rev.*, 1897, 113) examined the fixed oil: the sp. gr. was 0.9138, and it was soluble in alcohol, ether, and petroleum benzin. By pressure the fruit yields about 1½ per cent. of a brownish-yellow to dark red oil, soluble in alcohol, ether, chloroform and benzene, and partly soluble in dilute solution of potassium hydroxide. It contains, according to Sherman and Briggs (*Ph. Archiv.*, 1899, 101; see also *Ph. Rev.*, 1900, 217), about 63 per cent. of free acids, and 37 per cent. of ethyl esters of these acids. The oil obtained exclusively from the nut was thick and of a greenish color, without fruity odor. It was a glyceride of fatty acids.

Vanderkleed and E'we (*Proc. P. Ph. A.*, 1916, p. 284) contribute formulas for syrup of sabal and elixir of sabal with terpin hydrate. The latter is made as follows:

Dissolve 1.75 Gm. of terpin hydrate in 40 mils of fluidextract of sabal and 10 mils of alcohol. Add 1 mil of tincture of sweet orange peel, 0.2 mil of solution of saccharin, 40 mils of glycerin, and 100 mils of syrup. This preparation will contain 8 grains of terpin hydrate and 184 grains of sabal in each fluidounce.

Uses.—The oil of saw palmetto is probably eliminated through the kidneys unchanged, although we know of no actual experiments to prove this, and appears to exert a stimulant alterative action upon the mucous membrane of the genito-urinary tract, similar to that of other alterative diuretics. Saw palmetto is milder and less stimulant than is cubeb or copaiba, or even the oil of sandal-wood. Like these drugs it also has the power of affecting the respiratory mucous membrane, so that it has been used not only in *chronic* and *sub-acute cystitis*, but also in *chronic bronchitis, laryngitis*, and the catarrhs which accompany *asthma, phthisis*, and other more serious diseases of the lungs. It has been

affirmed that saw palmetto is capable of increasing the nutrition of the testicles and of the mammæ in functional atony of these organs, but this is very doubtful. It has been especially recommended in cases of *enlarged prostate* of old men; it is not probable that it has a direct influence upon the prostatic gland itself but there is much clinical testimony as to its value and it probably acts by reducing the catarrhal irritation and the relaxed condition of the mucous membrane of the bladder and urethra, which are almost universally present in prostatic hypertrophy.

Dose, ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Fluidextractum Sabal, *U. S.*; Tinctura Sabal et Santali, *N. F.*

SACCHARUM. U. S. (Br.)

SUGAR Sacch. [Cane Sugar, Sucrose]

(săc'ȼha-rŭm)

"Sucrose [$C_{12}H_{22}O_{11} = 342.18$] obtained from cultivated varieties of *Saccharum Officinarum* Linné (Fam. *Gramineæ*), and from *Beta vulgaris* Linné, var. *Rappa* Dumort (Fam. *Chenopodiaceæ*) and from other sources." *U. S.* "Refined Sugar is a crystallised sugar, $C_{12}H_{22}O_{11}$, obtained from the juice of the sugar-cane, sugar-beet, and other plants." *Br.*

Saccharum Purificatum, *Br.*; Refined Sugar, Cane Sugar, Sucrose; Sucre de Canne, *Fr. Cod.*; Sucre, Sucre pur, Sucre en Pains, *Fr.*; Saccharum, *P. G.*; Weisser Zucker; Zucker, Rohrzucker, *G.*; Zucchero, *It.*; Azucar, Azucar refinado, *Sp.*

The *sugar cane, Saccharum Officinarum*, is an herbaceous perennial plant, possessing a jointed, succulent rhizome, from which arises several shining, jointed, solid stems, from an inch to two inches in diameter, from six to twelve feet high, and containing a white and juicy pith. The color of the stem is yellow, greenish yellow, purple, or stripped. The joints are about three inches apart, and give origin to the leaves, which embrace the stem at their base, are three or four feet long and about an inch wide, flat, acuminate, longitudinally striated, furnished with a white midrib, glabrous, finely dentate, and of a green color inclining to yellow. The flowers are pinkish, surrounded by a long silky down, and disposed in a large, terminal, nearly pyramidal panicle, composed of subdivided spikes, and two or three feet in length. The plant has a general resemblance to Indian corn. Four varieties are mentioned: 1, the *common*, with a yellow stem; 2, the *purple*, with a purple stem and richer juice; 3, the *gigantic*, with a very large light-colored stem; and 4, the *Otaheitan*, which was introduced into the West Indies from the island of Tahiti (Otaheite) by Bougainville and Bligh, and is distinguished by its greater height, the longer intervals between its joints, and the greater length of the hairs which surround the flowers.

Sugar cane was originally indigenous in all probability to India. It has been cultivated for its saccharine juice since remotest antiquity. At the present time it is cultivated in all tropical and sub-tropical countries.

The sugar cane is cultivated by cuttings, which are planted in rows, and which, by giving rise to successive shoots, furnish five or six crops before the plants require to be removed. At the end of a year or more the plant flowers, but before this takes place the canes are richest in sugar and are cut down. The quantity of sugar which they yield is variable. According to Avequin of New Orleans, the proportion of cane sugar in the recent stalk is about 10 per cent.; of uncrystallizable sugar from 3½ to 4 per cent. Cane juice is said to contain 17 per cent. of crystallizable sugar, though not more than 13 per cent. is extracted in practice.

The *Sugar beet* (*Beta vulgaris* L.) is extensively grown in temperate zones as a source of sugar, or saccharose. It is extensively grown in Europe and the Northern and Western States. The plant is a biennial resembling the ordinary garden beet. The varieties yielding sugar produce rather small tuberous roots, which are either yellowish or whitish internally. They yield 4 to 15 per cent. of cane sugar, depending upon selection and cultivation.

The term "sugars" is applied to a large number of carbohydrates. A classification of these is given below. The sugar of the Pharmacopœia is known by the chemists as *sucrose*.

The name of *glucosides* has been given to certain organic substances which are resolvable, by the presence of acids, or other slight chemical influence, into glucose and some other proximate principle, as in the instance of one variety of tannic acid, which is resolved into glucose and gallic acid. E. Fisher announced (*Ber. d. Chem. Ges.*, 1893, 2400) the discovery of a general method for the formation of glucosides. He finds that, if a glucose be dissolved in an alcohol and gaseous hydrochloric acid be passed into the solution to saturation, the two compounds unite with the elimination of water to form a glucoside or ester of the two. He has found this reaction to extend to methyl ethyl, propyl, isopropyl, amyle, allyl, and benzyl alcohols, to ethyleneglycol, and glycerine, and even to the oxyacids or alcohol acids like lactic acid. He has tested it for mannose, galactose, dextrose fructose, gluco-heptose, arabinose, xylose, and rhamnose. *Fruit sugar or levulose*, is an isomeric form of glucose, found in honey and in the juice of fruits; an uncrystallizable mixture of dextrose and levulose (both varieties of glucose) is generated from cane sugar by solution in water or weak acids, and long boiling. Hence it is present in molasses. An aqueous solution of this sugar, like grape sugar, is susceptible of the vinous fermentation without an intermediate change. In consequence of its effect on polarized light, which is the opposite of that of the cane sugar from which it is prepared, it has been named by the French chemists *invert sugar* (*sucre interverti*). A solution of *cane sugar*, like that of grape sugar, has a rotating power to the right. When it ferments, it is first changed into uncrystalliza-

ble sugar by the invertase of the yeast, according to the reaction :

$$C_{12}H_{22}O_{11} + H_2O = (C_6H_{12}O_6)_2$$

and, as the change proceeds, the rotating power to the right of the cane sugar gradually lessens and disappears, and is replaced by the rotating power to the left of the levulose which remains behind on account of its fermenting more slowly than the dextrose which is simultaneously formed in the process of inversion.

Classification of the Carbohydrates.—The group of the carbohydrates has been studied by Emil Fischer, who has not only made numerous syntheses in this group, but has greatly widened our knowledge of the relations of the several sugars, permitting a more comprehensive classification than formerly. While no sugars are found in nature containing less than six atoms of carbon, synthetic compounds are formed belonging in the first, or monosaccharide, class which contain three, four, and five atoms of carbon, as well as others containing seven, eight, and nine atoms of carbon. The nomenclature of the sugars is based upon the fact that simple sugar molecules are known which are distinguished by the Greek prefixes tri, tetra, etc., indicating the number of carbon atoms in the molecule; thus, glycerose, $C_3H_6O_3$, is a triose, while dextrose, $C_6H_{12}O_6$, is a hexose. These are called monoses. These simple sugar molecules are taken as the basis for a secondary classification based upon the number of monoses or simple sugar molecules represented in the molecular structure of the more complex members of the group. The Greek numerical prefixes are also used to distinguish these; thus, dextrose, $C_6H_{12}O_6$, is a monosaccharid, while sucrose, $C_{12}H_{22}O_{11}$, is a disaccharid produced by the union of two monosaccharid molecules with the elimination of water. Of the simple sugars, members ranging from three to nine carbon atoms are known (trioses to nonoses), while of the broader groupings, monoses, dioses, trioses (monosaccharids, etc.), contain respectively one, two, or three of the simple sugar molecules, while polyoses or polysaccharids contain an indefinite or larger number of monoses. The classification given below, is based on that of Tollens.

I. Monosaccharides.

Trioses.—Glycerose, $C_3H_6O_3$ (prepared from glycerine by oxidation).

Tetroses.—Erythrose, $C_4H_8O_4$ (prepared from erythrite by oxidation).

Pentoses.—Arabinose, $C_5H_{10}O_5$ (prepared by the action of dilute sulphuric acid upon lævorotatory gum arabic ; xylose, $C_5H_{10}O_5$ (prepared by boiling beech wood and jute with dilute acids); rhamnose or isodulcite, $C_5H_8(CH_3)O_5$, methyl pentose (obtained in the decomposition of glucosides like quercitrin).

Hexoses.—Glucose or dextrose, $C_6H_{12}O_6$; fructose or levulose, $C_6H_{12}O_6$; mannose, $C_6H_{12}O_6$ (obtained by the careful oxidation of mannite) ; galactose, $C_6H_{12}O_6$.

Heptoses.—$C_7H_{14}O_7$. Manno-heptose (obtained artificially from the corresponding mannose) ; gluco-heptose (obtained artificially from the corresponding glucose).

Octoses.—$C_8H_{16}O_8$. Manno-octose (prepared from the corresponding manose) ; gluco-octose (prepared from the corresponding glucose).

Nonoses.—$C_9H_{18}O_9$. Manno-nonose (prepared from the corresponding mannose) ; gluco-nonose (prepared from the corresponding glucose).

II. Disaccharides and Trisaccharides.

Tribioses and tetrabioses are as yet unknown.

Pentabioses.—Arabinon, $C_{10}H_{18}O_9$ (has been prepared by the moderated action of dilute sulphuric acid upon arabic acid).

Hexabioses.—Cane Sugar, $C_{12}H_{22}O_{11}$; milk sugar, $C_{12}H_{22}O_{11}$; maltose, $C_{12}H_{22}O_{11}$; isomaltose, $C_{12}H_{22}O_{11}$; trehalose, $C_{12}H_{22}O_{11}$.

Hexatrioses.—Meletriose or raffinose, $C_{18}H_{32}O_{16}$; melezitose, $C_{18}H_{32}O_{16}$.

III. Polysaccharides.

(*a*) *Crystallizable polysaccharides.*—Gentianose, lactosin.

(*b*) *Uncrystallizable polysaccharides.*—Starches, lichnin, inulin, glycogen, dextrin, natural gums, pectin substances, cellulose, lignin, tunicin.

Cane sugar is manufactured extensively on the continent of Europe from the beet, and this industry is now growing in this country, notably in the western states. It is also largely produced in Canada and the northern parts of the United States from the sap of the sugar maple (*Acer saccharium*). This variety is never refined or purified as it owes its value as a confection and flavor to the impurities naturally present in the crude product. Cane sugar may be obtained from cornstalks, and from the *Chinese sugar cane,* or *Sorghum saccharatum,* which latter source for a time assumed some importance in Kansas and the Northwest. In India, sugar is made from the sap of different species of palm. Crude *palm sugar* is called *jaggery.* Next in rank to the sugar beet as a source of cane sugar is the sugar cane, which is extensively cultivated in Africa, the East and West Indies (especially Cuba), Brazil, and some of our Southern States, particularly Louisiana.

Preparation and Purification.—The canes, when ripe, are cut down close to the earth, topped, and stripped of their leaves, and then crushed between a series of horizontally placed iron rollers in a mill, or they are cut in thin transverse slices and the juice extracted by diffusion with warm water. The juice, constituting 90 per cent. of the cane, though much less is actually obtained, is of a pale greenish color, sweet taste, and balsamic odor, and has a sp. gr. varying from 1.033 to 1.106. As it runs out it is received in suitable vessels, and, being quickly removed, is *immediately* mixed with lime,

in the form of milk of lime, in the proportion of about 1 part of the earth to 800 parts of the juice, and heated in a boiler to 60° C. (140° F.). The exact proportion of the lime cannot be determined, as the juice varies in quality in different seasons; but the manufacturer should aim at leaving the juice still slightly acid. The albuminous matter rises to the top, and forms a thick scum, from underneath which the liquid is drawn off by a cock into a copper boiler, where it is concentrated by heat, the scum being carefully skimmed off as it forms. When sufficiently concentrated, the juice is transferred to shallow vessels called coolers, from which, when it assumes a granular aspect, it is drawn off into wooden vessels with perforated bottoms, the holes in which are temporarily plugged. At the end of twenty-four hours the liquid is strongly agitated with wooden stirrers, in order to accelerate the granulation of the sugar, which is completed in six hours. The stoppers are now removed, and the syrup is allowed to drain off from the sugar, which in this state is granular, of a yellowish color, and moist. The syrup, by a new evaporation, furnishes an additional portion of sugar, and the liquid which finally remains, incapable of yielding more sugar with advantage, is called *molasses*. Sugar produced in this way is called "open pan" sugar. It is now almost completely displaced by "vacuum pan" sugar.

In the production of raw sugars by the vacuum pan process, the juice, after "defecation" with lime and removal of excess of lime by carbonic acid gas, is run through large filters of bone black, and then into a vacuum pan for concentration. The vacuum pan is a large evaporating pan, closed above by a dome-like top, which connects with an exhausting steam pump, so that the liquid can be concentrated under very reduced pressure. The heat is supplied by coils of steam pipes which run through the interior of the pan. The saccharine juice is evaporated in this until it begins to crystallize, and even after this fresh portions are added, so that the crystals already formed grow by accretion of fresh material. After the crystallization is complete, the warm mixture of crystals and syrup is run into "centrifugals," to which a rapid motion of revolution is given, and the crystals so drained and dried.

There is no doubt that a large proportion of the sugar is lost in the ordinary process of manufacture. Melsens, of Brussels, proposed a process, which consists in the use of calcium bisulphite. This salt is alleged to act as an antiseptic, preventing the operation of any ferment; as an absorber of oxygen, opposing the action of that gas on the juice; as a clarifier, rendering insoluble at 100° C. (212° F.) all coagulable matters; as a bleacher of pre-existing coloring matters, and a preventive of the formation of a new ones; and, lastly, as a substance furnishing a base to neutralize hurtful acids, which unite with the lime, displacing the weaker sulphurous acid. This process is now largely used, and calcium bisulphite is used in British Guiana and other sugar-producing countries in immense quantities. Émil Pfeiffer proposed another refining process, which consists in the use of acid calcium phosphate, an agent previously recommended by Brande. Reynoso considered alumina the best defecating agent, having succeeded by means of it in throwing down almost all impurities most hurtful. He adds the acid aluminum phosphate to the cane juice, and decomposes this with lime, by which the calcium phosphate is produced and alumina separated, and all these, with some lime in excess, cause the elimination of coloring and nitrogenous matters, so that there remain in the liquid only some of the salts which normally accompany the sugar in the juice. (*J. P. C.*, 4e sér., ii, 232.)

The refining of brown sugar forms a distinct branch of business, and the methods pursued have undergone many improvements. The sugar is first "melted"—that is, dissolved in hot water—and then sometimes clarified by heating it with bullock's blood, although sulphites, phosphates, and other defecating agents may be used. The clarified syrup is then strained through cloth filters, whereby it is rendered limpid. The clear straw colored syrup from the bag filters is then run into the char filters —that is, large filters filled with freshly ignited bone black. The syrup after filtration goes to the vacuum pans. This great step in advance was taken by Philip Taylor and Howard. The former introduced the improvement of heating the syrup with great rapidity by means of steam made to pass through a series of tubes traversing the boiler, and the latter devised the plan of causing the syrup to boil under a diminished pressure, created by a suction pump, set in motion by a steam engine, while it was heated by steam circulating round the boiler. In this way the syrup was made to boil at a lower temperature, and with a diminished contact of the air, and the loss of cane sugar by change in to that which was uncrystallizable was in great measure avoided. Two, three, or even four vacuum pans may be coupled together, so as to economize fuel, and the vapors arising from one made to heat the next, in which a more perfect vacuum exists, allowing of evaporation at still lower temperatures. Such a combination is called a double, triple, or quadruple effect apparatus.

The process of forming *loaf sugar* by claying and displacing colored syrup by white syrup is now almost entirely replaced by the process already described under raw sugars of crystallizing in the vacuum pan and draining with a centrifugal. At one time it was the custom to discontinue the decolorization process before an entirely white sugar was obtained, and then to add a small amount of ultramarine blue to overcome the yellow appearance of the granulated sugar. This process has practically been abandoned within recent years. The syrups of lowest quality are employed in forming in-

ferior white sugar, from which a syrup finally drains containing so little cane sugar as not to repay the expense of extracting it. This constitutes *sugar-house molasses.* Good brown sugar, in the process of refining, yields about 70 per cent. of white sugar. The application of animal charcoal to the refining of sugar is now very extensive. A comprehensive historical article by C. A. Browne, on the development of the sugar industry is found in the *A. J. P.*, 1915, p. 10.

Commercial History.—*Cane sugar* was known to the ancients. It was originally obtained from India, where it was extracted from the sugar cane. About the period of the Crusades, the Venetians brought it to Europe; but at that time it was so scarce and costly as to be used exclusively as a medicine. Upon the discovery of the Cape of Good Hope and the maritime route to the East Indies, the commerce in sugar passed into the hands of the Portuguese. Subsequently the cultivation of the cane extended to Arabia, Egypt, Sicily, Spain, and the Canaries, and finally, upon the discovery of the New World, to America, where it was pursued with the greatest success, and continues to be so. In America it was produced most abundantly in the West Indies, which supplied also a part of the consumption of Europe. The Cuban production has grown rapidly in recent years, having been 2,582,845 tons in 1915, and estimated to have been 3,000,000 tons in 1916. The production in Louisiana, once large, diminished under the competition of the foreign beet sugar production, but in recent years, under the stimulus of a bounty, it has increased, and now amounts to about 300,000 tons per year. However, the American production from the sugar beet has developed rapidly, and in 1915 amounted to 722,054 tons. This production centers in California, Nebraska, Utah, Michigan, Colorado, and Montana, and is now greatly on the increase.

The European production, owing to the war conditions, decreased from 9,000,000 tons to 6,350,000 tons during 1916.

The importations of raw sugars into the United States for 1915 were 2,710,491 tons, valued at $173,992,600.

Properties.—Sugar, in a pure state, is a solid of a peculiar grateful taste, permanent in the air, phosphorescent by friction, and of the sp. gr. 1.6. It forms "white, hard, dry crystals or as a white, crystalline powder, odorless, and having a sweet taste. It is permanent in the air. One Gm. of Sugar dissolves in 0.5 mil of water and in 170 mils of alcohol at 25° C. (77° F.); also in slightly over 0.2 mil of boiling water; insoluble in chloroform or ether. Its aqueous solution (1 in 20) is neutral to litmus and is dextrorotatory. The specific rotation $[\alpha]_D$ of Sugar, determined at 20° C. (68° F.), in a solution in distilled water, containing in 100 mils the equivalent of 26 Gm. of Sugar, previously dried to a constant weight at 105° C. (221° F.), and using a 200 mm. tube, is not less than +65.9° (see Part III, Test No. 21). Its aqueous solution saturated at 25° C. (77° F.) has a specific gravity of about 1.340. Incinerate about 2 Gm. of Sugar; not more than 0.05 per cent. of ash remains. An aqueous solution of Sugar (2 in 1) is colorless when viewed horizontally through a vertical cylinder of colorless glass having an inside diameter of about 25 mm. When kept in large, well-closed, and completely filled bottles, the solution deposits no sediment on prolonged standing (*insoluble salts, ultramarine, Prussian-blue*). Ten mil portions of an aqueous solution of Sugar (1 in 10) tested separately give no precipitate with an equal volume of hydrogen sulphide T.S., and not more than a faint opalescence with a few drops of ammonium oxalate T.S. (*calcium*), barium nitrate T.S. (*sulphate*), and silver nitrate T.S. (*chloride*). Dissolve 20 Gm. of Sugar in enough distilled water to make 100 mils and filter the solution if necessary. To 50 mils of the clear liquid, contained in a 250 mil beaker, add 50 mils of alkaline cupric tartrate V.S., heat the mixture at such a rate that approximately four minutes are required to bring it to the boiling point, and then boil it for exactly two minutes. Add 100 mils of cold, recently boiled distilled water, and collect and weigh the precipitated cuprous oxide in the following manner: Prepare a Gooch crucible with an asbestos layer. Thoroughly wash the asbestos with distilled water, followed successively by 10 mils of alcohol and 10 mils of ether; dry at 100° C. (212° F.) for thirty minutes and then weigh the prepared crucible. Collect the precipitated cuprous oxide on the asbestos, thoroughly wash it with hot distilled water, then with 10 mils of alcohol, and finally with 10 mils of ether and dry it at 100° C. (212° F.). The weight of the cuprous oxide does not exceed 0.155 Gm., corresponding to not more than 0.5 per cent. of invert sugar." *U. S.*

"Colorless and inodorous crystals, or in crystalline masses. Readily and completely soluble in half its weight of *water,* forming a clear, colorless and odorless syrup which does not develop an unpleasant odor when acidified with *hypophosphorous acid* and allowed to stand for twenty-four hours; the syrup, heated to about 82° C. (179.6° F.) with *solution of potassio-cupric tartrate,* does not yield more than a trace of a red or yellow precipitate (absence of glucose). Yields no *reactions* for barium, strontium, calcium, chlorides, or sulphates. Ash not more than 0.05 per cent." *Br.*

Its solution, when thick and strong, is called *syrup,* and when alcohol is mixed with it, the sugar is gradually deposited in crystals. An aqueous solution of sugar, kept in a warm place, has the property of corroding iron, partially immersed in it, just above the line where the surface of the liquid touches the metal, and the solution itself becomes impregnated with ferrous oxide, and of a deep red-brown color. A similar effect is produced on lead, but zinc and copper are but slightly acted on. A solution of sugar possesses the property also of dissolving a large quantity of calcium hydroxide, forming a compound called *calcium*

saccharate. When a concentrated syrup is gently heated, and spirit added to it, the liquid, on cooling, forms white semi-transparent crystals of hydrated sugar, having the shape of oblique four-sided prisms, and called *rock candy.* When heated to 185° C. (365° F.), it melts into a viscid, colorless liquid, which on being suddenly cooled forms a transparent mass, called *barley sugar.* At a higher temperature, between 204.4° and 215.5° C. (400° and 420° F.), it loses two molecules of water, and is converted into a black syrupy liquid called *caramel,* which is now official in the N. F. IV. (See Part II.) At a still higher temperature it yields combustible gases, carbon dioxide, empyreumatic oil, and acetic acid, and there remains about one-fourth of its weight of charcoal, which burns without residue. Sugar renders the fixed and volatile oils to a certain extent miscible with water, which is probably a colloidal suspension; such mixtures are called *oleo-saccharures.* When in solution, it is not precipitated by lead subacetate, a negative property which distinguishes it from most other organic principles.

Sugar is sometimes adulterated with crystallized glucose, and it is a common practice among many sugar refiners to "blue" sugar to conceal the yellowish tint due to insufficient refining; ultramarine was formerly largely used, but the practice has been discontinued. See the official test above. Cane sugar may be distinguished from grape sugar by the fact that it does not reduce alkaline copper tartrate (see official tests), nor basic bismuth nitrate (see *Nylander's Reagent,* Part III). Cane sugar, similarly treated, has no effect on the test. Donaldson's test for sugar in the *animal fluids* is formed of 5 parts of sodium carbonate, 5 of potassium hydroxide, 6 of potassium bitartrate, 4 of copper sulphate, and 32 of distilled water. A few drops of this solution being added to an animal fluid, and the mixture heated over a spirit-lamp, a yellowish-green color is developed, if sugar be present. M. J. Nicklés recommends carbon tetrachloride as a test for distinguishing glucose from cane sugar. This liquid, mixed with cane sugar in a glass tube, kept for some time near 100° C. (212° F.), causes a darkening of the sugar, gradually increasing until it becomes black. Glucose undergoes no such change. (*J. P. C.,* 4e sér., iii, 119.)

Action of Acids and Alkalies.—The mineral acids act differently on cane sugar according as they are concentrated or dilute. Strong nitric acid, with the assistance of heat, converts it into oxalic acid. (See *Oxalic Acid.*) The same acid, when weak, converts it into *saccharic acid,* confounded by Scheele with malic acid. Concentrated sulphuric acid chars it. Diluted hydrochloric acid, when boiled with cane sugar, converts it into a solid, brown, gelatinous mass. Weak sulphuric acid, by a prolonged action at a high temperature, converts cane sugar, first into uncrystallizable invert sugar, afterwards into grape sugar, and finally into *ulmin* and *ulmic acid.* Vegetable acids are supposed to act in a similar way. Maumené found that cane sugar undergoes the change into invert sugar when kept for a long time in aqueous solution, as well as when heated with acids. When the boiling with acids is prolonged for several days in open vessels, oxygen is absorbed, and, besides ulmin and ulmic acid, formic acid is generated. Soubeiran admits the change of the uncrystallizable into grape sugar, but attributes it to a molecular transformation of the sugar, independently of the action of the acid, as, according to his observation, the conversion takes place only after rest. In confirmation of his views, this chemist states that he found the same changes to be produced by boiling sugar with water alone.

Cane sugar unites with the alkalies and some of the alkaline earths, forming definite combinations which render the sugar less liable to change. It also unites with lead monoxide. Boiled for a long time with aqueous solutions of potassium hydroxide, the liquid becomes brown, formic acid is produced, and two new acids are generated,—one brown or black and insoluble in water, called *melassic acid,* the other colorless and very soluble, named *glucic acid.* Alkalies and the alkaline earths are said to lessen the rotatory power of sugar in relation to polarized light, but the sugar recovers its power when the alkali is saturated. (*J. P. C.,* 4e sér., iv, 314.) The action of acids and alkalies on cane sugar explains the way in which lime acts in the manufacture and refining of sugar. The acids naturally existing in the saccharine juice have the effect of converting the cane sugar into invert sugar, by which a loss of the sucrose is sustained. The lime, by neutralizing these acids, prevents this change. An excess of lime, however, must be carefully avoided, as it injures the product of cane sugar in both quantity and quality. The change in sugar which precedes fermentation, namely, the conversion of cane sugar into the uncrystallizable invert sugar, points to the necessity of operating on the juice before that process sets in, and hence the advantage of grinding canes immediately after they are cut, and boiling the juice at once.

Molasses, sometimes Latinized in prescriptions as *Syrupus Fuscus,* is of two kinds, the West India and sugar-house. *West India molasses* is a black thick liquid, of a peculiar odor and sweet empyreumatic taste. When mixed with water and with the skimmings of the vessels used in the manufacture of sugar, it forms a liquor which, when fermented and distilled, yields *rum. Sugar-house molasses, golden drips,* or *grocer's syrup* is thicker than the West India molasses, and has a different flavor; as found in commerce, it is sometimes adulterated with glucose. Its sp. gr. is about 1.4, and it contains about 75 per cent. of solid matter. Both kinds of molasses contain uncrystallizable sugar, more or less cane sugar which has escaped separation in the process of manufacture or refining, and gummy and coloring matter. *New Orleans molasses* was formerly the most largely used variety, but has practically disappeared

from the market, owing to the changed conditions of manufacture.

Uses.—Although sugar is so important a foodstuff to-day, it does not seem to have been widely employed in Europe until the tenth or eleventh century. It was known much earlier to the European writers, such as Dioscorides, who lived in the first century, by whom it seems to have been regarded as a sort of a natural curiosity. Its food value is very high, commercial cane sugar yielding more than 4 calories of energy per gramme. It is not, however, directly utilizable by the body cells, but must first be inverted into dextrose or levulose; this is true also of the other disaccharids such as lactose and maltose. This inversion is accomplished in the system probably in part by the hydrochloric acid of the gastric juice, but chiefly by a specific ferment which is found throughout the whole small intestines. It occurs with great rapidity so that the body can derive energy from ingested cane sugar almost as rapidly as it can be absorbed. So rapidly, indeed, is sugar absorbed from the intestinal tract that eating large quantities of it may overwhelm the inability of the liver to withdraw the sugar from the blood and lead to hyperglycemia and the appearance of glucose in the urine; a condition which is known as alimentary glycosuria. Glucose and levulose are directly assimilable and the body can derive nourishment from them even when injected hypodermically or intravenously.

A large portion of the muscular energy is derived from the oxidation of the blood sugars. There is reason to believe that increasing the amount of sugar in the blood, thereby offering to the working muscle readily-oxidizable, energy-yielding form of carbon, not only increases its immediate efficiency but lessens the call upon the fuel stored up within it. It is to this mechanism and the rapidity of its absorption that sugar owes its power of banishing the sense of fatigue from muscular exertion. Dixon (*J. P.*, 1907, xxxv, p. 346) has shown that a similar effect is produced upon the heart muscle and sugar has been used as a stimulant in the treatment of acute *heart failure*. Denyer (*L. L.*, April 5, 1913) reported a case of severe heart failure in which life was apparently saved by the daily use of 4 ounces of cane sugar by the mouth. Buedingen (*D. A. K. M.*, 1914. cxiv, p. 534) injected intravenously a solution of glucose isotonic with the blood (5.4 per cent.) in the treatment of *heart disease* with asserted good results.

According to S. Meslach, glucose, when given in doses of from six to six and a half ounces per day in the form of the concentrated syrup, acts as a powerful diuretic, and is very useful in the treatment of *cardiac dropsy*. If the kidneys be healthy, the glucose is said not to appear in the urine. The celebrated grape cure of Europe is said to act by virtue of the glucose in the grape.

Schreiber (*Ther. Geg.*, 1913, p. 195) asserts that intravenous injections of glucose increase the coagulability of the blood and are useful in internal *hemorrhages*, but as Kuhn (*D. Z. Chir.*) reached the opposite conclusion and recommends it to prevent *thrombosis*, it seems improbable that it has any marked effect. Magnus (*M. M. W.*, 1913, p. 406) claims that sugar has valuable antiseptic properties and recommends it in the treatment of various forms of *wounds*. *Schuecking's solution* consists of 0.08 p. c. of common salt, 0.033 p. c. of sodium saccharate ($C_{12}H_{21}O_{11}Na$) and in some cases also 0.003 to 0.015 p. c. calcium mono-saccharate. It is used for intravenous injection instead of physiological salt solution in *circulatory failure* and is said to directly stimulate the heart.

The discovery of Minkowski (*T. M.*, 1892), that in dogs, after extirpation of the pancreas, levulose, given in moderate quantities, is consumed in the system, has led to the use of it as a food substitute for true sugar in *diabetes* with some success. As much as two ounces of it a day are sometimes well borne, but levulose frequently appears in the urine when more than one ounce has been given daily and rarely should this amount be exceeded. According to Lepine, levulosuria is likely to occur when there is hepatic disease. Levulose has no direct influence upon the disease but is an addition to the dietary. Under the name of *diabetin* it has been largely advertised as a proprietary preparation. Levulose has been strongly recommended in *phthisis*, in the dose of 4 to 6 tablespoonfuls a day, also as a substitute for sugar of milk for infants when an aperient property is not desired.

Sugar is much used for the purposes of preserving organic substances. It is probable that it acts by producing rapid exosmose of the fluids of the fermentative organisms, its diluted solution being in fact prone itself to undergo fermentative change. All the different kinds of sugar susceptible of the alcoholic fermentation have this power. In pharmacy, sugar is employed to render oils miscible with water, to cover the taste of medicines, to give pharmaceutical preparations consistency, to preserve them from change, and to protect certain ferruginous preparations from oxidation. Accordingly, it enters into the composition of several mixtures, pills, and powders, of syrups and confections, and of all the troches. *Molasses* is used as an excipient for pills, and on account of its hygroscopic properties it prevents hardening.

SACCHARUM LACTIS. U. S., Br.

SUGAR OF MILK Sacch. Lact.
[Milk Sugar, Lactose]

(săc'ȼhą-rŭm lăc'tĭs)

"Lactose [$C_{12}H_{22}O_{11} + H_2O = 360.19$] obtained from the whey of cow's milk. Preserve it in tightly-closed containers." *U. S.* "Milk Sugar is a crystallised sugar, $C_{12}H_{22}O_{11},H_2O$, obtained from the whey of milk." *Br.*

Lactin, Milk Sugar; Lactose; Suere de Lait, *Fr. Cod.*; Saccharum Lactis, *P. G.*; Milchzucker, *G.*; Lattosio, Zucchero di latte, *It.*; Lactosa, Azucar de leche, *Sp.*

Preparation.—Sugar of milk is found only in milk, of which it forms about 5 per cent. (Boussingault). It is manufactured largely in Switzerland and the Bavarian Alps, especially from the whey left over in cheese making. In preparing it, milk is first coagulated by the addition of a little diluted sulphuric acid, and the resulting *whey* boiled down to about one-fifteenth of its original bulk into a brown, viscid, sweetly saline mass, which is put into tubs, where, in from twenty-four to forty-eight hours, the sugar crystallizes in a bright yellow granular mass, constituting the so-called "sugar-sand," which is afterwards decolorized by animal charcoal and repeated crystallizations. (*Am. Drug.*, Sept., 1884.) Within recent years the numerous "creameries" in the United States have produced milk sugar in such large quantities as a by-product that its importation from Switzerland has almost ceased. The American method of manufacturing sugar of milk is radically different from that followed abroad, and it is thus described by LaWall (*Alumni Report Philadelphia Coll. Pharmacy,* April, 1902): The whey left after the first curdling of the milk (by the separator system) is run into vats, and treated with about 1 per cent. of hydrochloric acid to remove remaining proteid matters, the liquid being heated to the boiling point, and exactly neutralized with calcium hydroxide. The whey is then generally filtered through a filter press and evaporated in vacuo to a thick syrup, run into pans, and allowed to stand for two days, when granular crusts form. These are then centrifuged and washed with cold water to remove calcium chloride and soluble impurities, and the washings are reserved for future operations. The crude milk sugar is of a very light yellow color, and has little taste or odor. It is redissolved in water and the solution filtered through bone black in percolators. The colorless syrupy percolate is concentrated in vacuo to a pasty mass, which is placed in a centrifuge and washed with cold water. The mass is then dried on strainers in a drying chamber at 60° C. (140° F.), powdered in a ball mill, and bolted.

The *casein* obtained by acidulation of the skim milk, and subsidence, is washed and heated with water containing a small amount of sulphuric acid, to remove impurities. The moist pulpy mass left after the removal of the water is then shredded by means of cutting knives run by a high-speed engine, the flakes being removed in wire gauze frames and rapidly dried with a current of air at 140° F. (60° C.). It is then powdered with high-speed disintegrators. See a paper on the American Milk Product Industry by J. W. England. (*Proc. A. Ph. A.*, 1902, 354.)

Properties.—"Sugar of Milk occurs in white, hard, crystalline masses, or as a white powder, producing a gritty sensation on the tongue; odorless, and having a faintly sweet taste. It is permanent in the air. It readily absorbs odors. One Gm. of Sugar of Milk dissolves in 4.9 mils of water at 25° C. (77° F.); also in 2.6 mils of boiling water; almost insoluble in alcohol; insoluble in chloroform or ether. An aqueous solution of Sugar of Milk (1 in 20) is neutral to litmus and is dextrorotatory. The specific rotation $[a]_D$ of Sugar of Milk, determined at 25° C. (77° F.), in a solution in distilled water, containing in 100 mils the equivalent of 10 Gm. and using a 200 mm. tube, is from +52.2° to +52.5° (see Part III, Test No. 21). Add an equal volume of sodium hydroxide T.S. to 5 mils of a hot, saturated, aqueous solution of Sugar of Milk and gently warm the mixture; the liquid turns yellow and finally brownish-red. On the subsequent addition of a few drops of cupric sulphate T.S., a precipitate of cuprous oxide appears. Incinerate about 1 Gm. of Sugar of Milk; not more than 0.1 per cent. of ash remains. A solution of 3 Gm. of Sugar of Milk in 10 mils of boiling distilled water is odorless, clear, and colorless or at most faintly yellow. Add 20 mils of alcohol (70 per cent. by volume) to 2 Gm. of Sugar of Milk in a fine powder, shake the mixture frequently during half an hour at 15° C. (59° F.) and then filter it. Ten mils of the filtrate remains clear after admixture with an equal volume of dehydrated alcohol (*dextrin*), and this liquid, upon evaporation on a water bath, leaves not more than 0.03 Gm. of residue (*sucrose or glucose*). An aqueous solution of Sugar of Milk (1 in 20) does not respond to the Test for heavy metals (see Part III, Test No. 3). On boiling about 1 Gm. of powdered Sugar of Milk with 50 mils of distilled water and cooling the solution, no blue color is produced upon the addition of one drop of iodine T.S. (*starch*)." *U. S.*

"A white powder, or in crystalline masses; no odor, taste slightly sweet. Soluble in 7 parts of cold *water* and in about 1 part of boiling *water*. 5 grammes dissolved in *water* require for neutralisation not more than 1.5 millilitres of *N/10 solution of sodium hydroxide* (limit of acidity). When 5 grammes are well shaken with 20 millilitres of *alcohol* (90 per cent.) and filtered, the filtrate leaves no appreciable residue on evaporation (absence of sucrose). Ash not more than 0.25 per cent." *Br.*

In commerce sugar of milk frequently occurs in cylindrical masses, the axis of which is a wooden stick, around which the crystals have been deposited. Experiments have shown that much of the milk sugar of commerce contains micro-organisms which have resulted from the decomposition of animal constituents in milk, and the tests of the Pharmacopœias do not exclude such impurities. (*D. C.*, 1893, 250; *Bull. Pharm.*, 1893, v. 5; *P. J.*, 1894, 853.) Its specific gravity is 1.54. It is not susceptible of the vinous fermentation by the direct influence of yeast; but after the action of dilute acids, which first convert it into a variety of glucose, it is capable of furnishing a spirituous liquor. It is well known that both mares' and cows' milk, after becoming

sour, are capable of forming an intoxicating drink, by fermentation. By the action of nitric acid, sugar of milk is converted into mucic acid. When anhydrous it consists of $C_{12}H_{22}O_{11}$; when crystallized, of $C_{12}H_{22}O_{11} + H_2O$. (Staedeler and Krause.) These formulas make anhydrous sugar of milk isomeric with cane sugar. Sugar of milk, when treated with weak sulphuric acid, is inverted or changed into a mixture of *galactose* and *dextrose*, both of the formula $C_6H_{12}O_6$. The galactose crystallizes in fine needles, fusing at 163° C. (325.4° F.).

Sugar of milk is sometimes adulterated with cane sugar or glucose; Hynson and Dunning (*Proc. A. Ph. A.*, 1901, 207) give the following tests for cane sugar and glucose: The test solution is composed of resorcinol 3 parts, hydrochloric acid 1 part, alcohol 100 parts. Dissolve 0.1 Gm. of the suspected milk sugar in a few drops of water contained in a porcelain dish and add to this solution 5 or 6 drops of the test solution. Evaporate slowly over a spirit lamp and allow the outer edge of the solution to boil a little, then tip the dish to one side. On the surface left moist by the receding liquid continue the heat gently. If a trace of cane sugar be present there will appear flashes of vermilion color over the surface treated. If there be an appreciable amount (5 to 10 per cent.) of cane sugar present a vermilion mirror will be formed which can be more clearly seen upon carefully evaporating the entire solution. The evaporation must take place slowly as the sugars will easily char if exposed to too much heat. A brownish-red color quickly charring and not spreading must not be mistaken for cane sugar. This coloration is caused by the milk sugar but need not be confused with the vermilion coloration of cane sugar.

J. W. England (*Proc. Penna. Pharm. Assn.*, 1915, p. 240) reported upon 17 lots of milk sugar, aggregating one-half million pounds, which showed a minimum purity of 99.73 per cent. by the polariscope with negligible traces of nitrogen, ash, and fat.

Uses.—Sugar of milk differs physically from cane sugar in the fact that it is less sweet. Because of its relative tastelessness it is sometimes preferred as an article of diet, especially in the feeding of infants, especially also, because it does not readily undergo the alcoholic fermentation. Its relation to metabolism is precisely the same as that of cane sugar except that the inversion into galactose takes place after its absorption and is probably accomplished by the epithelial cells of the intestines. Like other crystalloids when ingested in large quantities by modifying the osmotic relations of the blood it acts as a diuretic and has been practically used for this purpose by Germain Sée and others with advantage in the treatment of *cardiac dropsies*. If the kidneys be sound the lactose is said not to appear in the urine. It is used in doses of from 6 drachms to 6 ounces (23.5–186 grammes). It is used as a diluent in various official preparations.

SALICINUM. U. S., Br.

SALICIN Salicin.

(sāl-ĭ-cī′nŭm)

"A glucoside [$C_{13}H_{18}O_7$ = 286.14] obtained from several species of *Salix* and *Populus* (Fam. *Salicaceæ*). Preserve it in well-closed containers." *U. S.* "Salicin, $C_{13}H_{18}O_7$, is a crystalline glucoside, which may be obtained from the bark of various species of Salix, and of Populus." *Br.*

Orthohydroxybenzylglucoside; Salicine, *Fr.*; Salicin, *G.*; Salicina, *It.*

The discovery of salicin is claimed by Buchner of Germany, and Fontana and Rigatelli of Italy; but Leroux of France, deserves the credit of having first accurately investigated its properties. The following is Merck's process for its extraction: A boiling concentrated decoction of the bark is treated with litharge until it becomes nearly colorless. Gum, tannin, and extractive matter, which would impede the crystallization of the salicin, are thus removed from the liquid, while a portion of the oxide is dissolved in combination probably with the salicin. To separate the lead, sulphuric acid is first added, and then barium sulphide, and the liquor is filtered and evaporated. Salicin is deposited, and may be purified by repeated solution and crystallization. Erdmann has given another process. Sixteen ounces of the bark are macerated for twenty-four hours in four quarts of water mixed with two ounces of lime, and the whole is then boiled for half an hour. The process is repeated with the residue. The decoctions having been mixed, and allowed to become clear by subsidence, the liquor is poured off, concentrated to a quart, then digested with eight ounces of ivory black, filtered, and evaporated to dryness. The extract is exhausted by spirit containing 28 per cent. of alcohol, and the tincture evaporated so that the salicin may crystallize. This is purified by again dissolving, treating with ivory black, and crystallizing. Merck obtained 251 grains from 16 ounces of the bark and young twigs of *Salix Helix*, and Erdmann 300 grains from the same quantity of the bark of *Salix pentandra*. It may probably be obtained from any of the willow barks having a bitter taste. T. Fawssett states that the best material for preparing salicin is undoubtedly the willow peelings, obtained as refuse from a basket factory, and known in Belgium as "rood schors." David Brown states that the peelings are produced from *Salix fragilis*, while Crispo considers the source to be *Salix purpurea*. These peelings should be used soon after they are stripped from the twigs, and the method of preparing salicin may be conducted as follows: Macerate willow peelings in water for some hours at a temperature as much below the boiling-point as will exhaust them. Strain and remove all moisture from the marc by hydraulic pressure. Evap-

orate the fluidextract thus formed to a low bulk (*in vacuo*). Precipitate the tannin and extractive by treating the liquid successively with quick lime, lead acetate and lead subacetate, in the order named. Remove an excess of any of these precipitants with oxalic acid. Filter and evaporate the clear solution until crystals appear. This treatment generally sufficed to obtain a satisfactory product, but sometimes a final purification with animal charcoal was necessary. (*P. J.*, June 6, 1903, 784.) For a paper by Jowett on the percentage of salicin obtained from various kinds of willow bark see *Y. B. P.*, 1902, 483, and 1903, 474. Braconnot procured it from various species of *Populus*, particularly *P. tremula*, or European aspen.

Properties.—When pure, salicin is in white, shining, slender crystals, inodorous, but very bitter, with the peculiar flavor of the bark. It is soluble in cold water, much more so in boiling water, soluble in alcohol, and insoluble in ether and oil of turpentine. It neutralizes neither acids nor salifiable bases, and is not precipitated by any reagent. Concentrated sulphuric acid decomposes it, receiving from it an intense and permanent bright-red color, this is called the *rutilin reaction*. It is officially described as in "colorless, silky, shining, crystalline needles or rhombic prisms, or as a white, crystalline powder; odorless, and having a very bitter taste. One Gm. of Salicin dissolves in 23.5 mils of water and in 88.5 mils of alcohol at 25° C. (77° F.); also in 3.3 mils of water at 80° C. (176° F.) and in 30 mils of alcohol at 60° C. (140° F.); insoluble in chloroform or ether. Its aqueous solution (1 in 30) is neutral to litmus and is lævorotatory. It melts between 198° and 202° C. (388.4° and 395.6° F.). Heat a small portion of Salicin in a test tube until it turns brown, then add a few mils of distilled water, and afterwards a drop of ferric chloride T.S.; a violet color is produced. Salicin with sulphuric acid gives a red color which disappears upon the addition of distilled water. Heat gently about 0.1 Gm. of Salicin with about 0.2 Gm. of potassium dichromate and 2 mils of diluted sulphuric acid; the fragrant odor of salicylic aldehyde is developed. Incinerate about 2 Gm. of Salicin; not more than 0.05 per cent. of ash remains. Ten mils of an aqueous solution of Salicin (1 in 50) is not colored violet by a few drops of ferric chloride T.S. (*salicylic acid*). Separate portions of 10 mils each of an aqueous solution of Salicine (1 in 50) yield no precipitate on the addition of 1 mil of tannic acid T.S., picric acid T.S., or mercuric potassium iodide T.S. (*alkaloids*). An aqueous solution of Salicin does not respond to the Test for heavy metals (see Part III, Test No. 3)." *U. S.*

"Colorless, shining, trimetric, tabular crystals, or white, crystalline powder. Taste very bitter. Soluble in 28 parts of *water*, and in 80 parts of *alcohol* (90 per cent.); insoluble in *ether*. Melting point from 200° to 201° C.(392°–393.8° F.). Colored red by *sulphuric acid*. When 0.1 gramme is gently heated with 0.2 gramme of *potassium bichromate* and 2 millilitres of *diluted sulphuric acid* an odor recalling meadow-sweet is developed. No appreciable ash." *Br.*

It belongs to the class of glucosides, being resolved by boiling with diluted hydrochloric and sulphuric acids into grape sugar and *saligenin*, according to the reaction:

$$C_{13}H_{18}O_7 + H_2O = C_6H_{12}O_6 + C_7H_8O_2$$

Saligenin, which is ortho-oxybenzyl alcohol, $C_6H_4(OH)CH_2OH$, is converted by further boiling with dilute acids into a resinous body, *saliretin*, $C_{14}H_{14}O_3$. Nitric acid produces with salicin at first two principles called respectively *helicin*, $C_{13}H_{16}O_7$, and *helicoidin*, $C_{26}H_{32}O_{14}$, and afterwards picric and oxalic acids. (*J. P. C.*, xxx, 43.) Distilled with potassium dichromate and sulphuric acid, salicin yields, among other products, a volatile oleaginous liquid, identical with one of the components of oil of spiræa, and recognized as *salicyl aldehyde*, $C_7H_6O_2$ (incorrectly called *salicylous acid*), while saligenin, $C_7H_8O_2$, is the alcohol, and salicylic acid, $C_7H_6O_3$, the acid corresponding. The synthesis of salicin has been effected by Michael (*A. J. P.*, 1879, 492), who obtained first helicin by the reaction of acetochlorhydrose and salicyl aldehyde, and, by the action of nascent hydrogen upon this, salicin.

Uses.—Salicin acts upon the stomach probably as a simple bitter, and after absorption as a feeble and uncertain form of salicylic acid, since it is rapidly, although not completely, decomposed in the system, the products of its change appearing in the urine fifteen to thirty minutes after the ingestion of a single dose. The elimination is partly as salicin, partly as salicylic acid, partly as a salicyluric acid, and partly as saligenin. It has been highly recommended as a substitute for salicylic acid in *rheumatism* by Maclagan and others, but since it owes its activity to its conversion in the blood into salicylic acid and since this conversion is uncertain, salicin is inferior in power to the salicylates. By some it is believed to be less liable to upset the stomach. Salicin has been used as an antiperiodic. One or two drachms may be given in the intermission.

Dose, from ten to thirty grains (0.65–2.0 Gm.).

SANGUINARIA. U. S.

SANGUINARIA Sanguin. [Bloodroot]

(săn-guĭ-nā'rĭ-ą)

The dried rhizome and roots of *Sanguinaria canadensis* Linné (Fam. *Papaveraceæ*). *U. S.*

Blood-root, Red-root, Puccoon, Red Indian-plant, Puccoon-root, Coon-root, White puccoon, Pauson, Snakebite, Sweet-slumber, Tumeric, Red Puccoon, Tetterwort, Red Indian Paint; Sanguinaire, *Fr.*; Blutwurzel, *G.*

Bloodroot (*Sanguinaria canadensis*), or, as it is sometimes called, *puccoon*, is an herbaceous or perennial plant. The rhizome is horizontal,

abrupt, often contorted, about as thick as the finger, two or three inches long, fleshy, of a reddish-brown color on the outside, and brighter red within. It is furnished with numerous slender roots, and makes offsets from the sides, which succeed the old plant. From the end of the rhizome arise the scape and leaf-stalks, surrounded by the large sheaths of the bud. These spring up together, the folded leaf enveloping the flower-bud, and rolling back as the latter expands. The leaf, which stands upon a long channelled petiole, is reniform, somewhat heart-shaped, deeply lobed, smooth, yellowish green on the upper surface, paler or glaucous on the under, and strongly marked by orange-colored veins. The scape is erect, round, and smooth, rising from a few inches to a foot, and terminating in a single flower. The calyx is two-leaved and deciduous. The petals, varying from seven to fourteen, but usually about eight in number, are spreading, ovate, obtuse, concave, mostly white, but sometimes slightly tinged with rose or purple. The stamens are numerous, with yellow filaments shorter than the corolla, and orange oblong anthers. The ovary is oblong and compressed, with a sessile, persistent stigma. The capsule is oblong, acute at both ends, one-celled, two-valved, and contains numerous oval, reddish-brown seeds. The whole plant is pervaded by an orange-colored sap, which flows from every part when broken, but is of the deepest color in the rhizome. The bloodroot is one of the earliest and most beautiful spring flowers of the Northern United States, growing abundantly in loose, rich soils and shady situations. After the fall of the flower the leaves continue to grow, and by the middle of summer have become so large as to give the plant an entirely different aspect. Except the seeds, all parts of the plant are active.

Properties.—The following is the official description of sanguinaria: "Of horizontal growth, occasionally branching, more or less cylindrical, somewhat flattened, from 2 to 7 cm. in length, and from 5 to 15 mm. in diameter; externally dark brown, slightly annulate, with a few stem-scars on the upper surface and numerous more or less broken filiform roots and root-scars on the lower surface; fracture short and somewhat waxy, brownish-red, occasionally yellowish-white, with numerous, small, circular, yellowish fibro-vascular bundles within about 1 mm. of the epidermis, pith very large; odor slight; taste persistently acrid and bitter. Under the microscope, transverse sections of the rhizome of Sanguinaria show an outer layer of a single row of thin-walled epidermal cells; a cortex of from 10 to 15 rows of thin-walled parenchyma cells containing numerous starch grains, or a small amount of fixed oil; a zone of cambium, most of which is interfascicular; a narrow circular zone of small collateral fibro-vascular bundles, separated from each other by parenchyma; pith large, consisting of starch-bearing parenchyma cells; latex cells containing a red or orange colored secretion, either isolated or connected into irregular chains and distributed among the parenchymatous cells of the middle bark and pith; sections treated with glycerin show in the secretion cells, after twenty-four hours, spheroidal aggregates of crystals which strongly polarize light. The powder is brownish-red, sternutatory; when examined under the microscope it exhibits numerous starch grains, from 0.003 to 0.02 mm. in diameter, being mostly single, seldom 2- to 3-compound, the individual grains nearly spherical or ovoid, sometimes more or less plano-convex, somewhat resembling those of wheat starch in outline but polarizing light more strongly; numerous fragments of short latex cells with reddish-brown resinous masses; tracheal fragments few, having numerous slit-like pores." *U. S.*

For an interesting microscopical description of the rhizome by E. S. Bastin, see *Pharm.*, 1885, p. 201. Sanguinaria has a faint odor, and a bitterish very acrid taste, the pungency of which remains long in the mouth and fauces. Lloyd states that sanguinaria is both a contamination and an adulterant of hydrastis. (*Pharm. Rev.*, 1905, xxiii, p. 332.) It yields its virtues to water and alcohol.

Dana of New York, obtained from it an alkaloid, denominated by him *sanguinarine.* (*Ann. Lyc. of Nat. Hist., New York,* ii, 250.) It may also be conveniently procured by a process similar to that employed by Probst for obtaining chelerythrine from celandine. (*Chem. Gaz.*, i, 145.)

G. König (*A. J. P.*, 1891, p. 457) found *chelerythrine,* which is present in greatest quantity, *sanguinarine,* β- and γ-*homochelidonine,* and *protopine.* Chelerythrine crystallizes with a molecule of alcohol which is not separated at 150° C. (302° F.). Its formula is $C_{21}H_{17}O_4N$, and it is identical with the alkaloid extracted from *Chelidonium majus.* (See Part II.) The salts are lemon-yellow. Sanguinarine has the formula $C_{20}H_{15}O_4N$ (Schmidt, $C_{21}H_{15}O_4N$), and is very similar to chelerythrine in its properties. It crystallizes with one-half molecule of H_2O, and melts at 211° C. (411.8° F.). Its salts are red. The base named γ-homochelidonine is probably identical with that separated by Selle from *Chelidonium majus,* and its formula is $C_{22}H_{21}O_4N$. The fourth alkaloid, protopine, has been prepared from *Chelidonium majus,* from *Sanguinaria canadensis,* and from opium, all three of the specimens being identical. Its formula is $C_{20}H_{17}O_5N$, and it melts at 204° C. (399.2° F.). The virtues of the root are said to be rapidly deteriorated by time. Thos M. Newbold extracted from sanguinaria a non-volatile liquid acid (*sanguinarinic acid*) (*A. J. P.*, 1866, p. 496), which L. C. Hopp has shown to be a solution of impure citric and malic acids. Schlotterbeck (*Ph. Rev.*, 1900, 358) examined sanguinarine nitrate of commerce and found it to consist mainly of chelerythrine, with some sanguinarine and traces of protopine and homochelidonine; he believes that chelerythrine should be called sanguinarine. For methods of assay

of sanguinaria see *A. J. P.*, 1896, 305; *M. R.*, 1900, 451; *Proc. A. Ph. A.*, 1903, 284; *A. J. P.*, 1913, p. 395.

Uses.—Sanguinaria is an active local irritant, in large doses producing nausea and vomiting. When snuffed up the nostrils it excites much irritation and sneezing. According to the investigations of Meyer (*A. E. P. P.*, 1892, xxix, p. 397) sanguinarine is an active stimulant to the spinal cord producing in frogs strychnine-like convulsions followed, after very large doses, by complete paralysis. It also stimulates the respiratory center, increasing both the depth and rate of the breathing. By virtue of a stimulant action upon the vasomotor center it causes a rise in blood pressure which, with toxic doses, is followed by a fall in the blood pressure, due to weakening of the heart action. It also excites the flow of saliva and increases intestinal peristalsis. In toxic doses it acts as a poison to the voluntary muscles. When locally applied it causes at first pain, followed by a local anesthesia. Chelerythrine, although present in larger amounts in sanguinaria, is a much less poisonous alkaloid than sanguinarine and it is probable that it plays a rôle of relatively small importance in the action of the whole drug. It differs widely in its action from sanguinarine, acting chiefly as a paralyzant of the nerve centers, including the spinal cord, the respiratory and the vasomotor centers. It is also a poison to the voluntary muscles. It is locally irritant but has neither anesthetic nor narcotic properties. Beta-homochelidonine, the third most important alkaloid, has a feeble narcotic effect, produces cerebral convulsions, but does not increase reflex activity. It is an active local anesthetic without the irritant effect of sanguinarine.

Sanguinaria is used chiefly as an expectorant, especially in the treatment of subacute or *chronic bronchitis*. Whether it possesses any beneficial action for this purpose except that which may be attributed to its nauseating effect, seems doubtful. It has also been recommended by Graber (*J. A. M. A.*, 1907, xlix, p. 705) as a local application in chronic *eczema*, especially when secondary to *varicose ulcers*.

In toxic quantities sanguinaria produces burning in the epigastrium with vomiting, tormenting thirst, faintness, vertigo, dimness of vision, and alarming prostration. Twenty grains (1.3 Gm.) are said to usually act as a violent emetic. (For fatal cases, see *Am. J. M. S.*, n.s., ii, p. 506.)

The alkaloid sanguinarine has been used in doses of from one-twelfth to one-sixth of a grain (0.005–0.01 Gm.). Sanguinaria is rarely given in substance.

Dose, U. S. P., two grains (0.13 Gm.).

Off. Prep.—Tinctura Sanguinariæ, *U. S.*; Fluidextractum Sanguinariæ, *N. F.*; Syrupus Pini Strobi Compositus, *N. F.*; Syrupus Pini Strobi Compositus cum Morphina, *N. F.*; Syrupus Sanguinariæ, *N. F.*

SANTALUM RUBRUM. U. S. (Br.)

RED SAUNDERS Santal. Rub.

(săn'tą-lŭm rŭ'brŭm)

"The heart-wood of *Pterocarpus santalinus* Linné filius (Fam. *Leguminosæ*)." *U. S.* "Red Sanders Wood is the heart-wood of Pterocarpus santalinus, *Linn. f.*" *Br.*

Pterocarpi Lignum, *Br.*, Red Sanders Wood; Lignum Santalinum Rubrum, Rasura Santalum Ligni; Red Sandal Wood; Red Santal Wood; Ruby Wood; Santal rouge, *Fr. Cod.*; Santelholz, Rothes Santelholz, *G.*; Sandalo rojo (Leno de), *Sp.*

Pterocarpus santalinus is a large tree, with alternate branches, and petiolate ternate leaves, each leaflet being ovate, blunt, somewhat notched at the apex, entire, veined, smooth on the upper surface, and hoary beneath. The flowers are yellow in axillary spikes, and have a papilionaceous corolla, of which the vexillum is obcordate, erect, somewhat reflexed at the sides, toothed and waved, the alæ spreading with their edges apparently toothed, and the carina oblong, short, and somewhat inflated. The tree is a native of India, attaining the highest perfection in mountainous districts, and inhabiting especially the mountains of Coromandel and Ceylon. It is cultivated also in Southern India and in the Philippine Islands. Its wood is the official *red saunders*, though there is reason to believe that the products of other trees are also sold by the same name.

Properties.—The wood comes in heavy, irregular, roundish or angular billets of various size and thickness, externally brown from exposure, internally of a deep blood-red color, on transverse section variegated with zones of a lighter red. The structure is heavy, compact, and fibrous. In the pharmacies red saunders is usually kept in the shape of small chips, or raspings, or coarse powder, of a deep reddish-brown color, slightly astringent in taste, and when rubbed of a faint peculiar odor. It has little odor or taste. Red saunders is officially described as follows: "Usually in the form of a coarse powder, of a brownish-red or dark saffron color and nearly odorless and tasteless. Under the microscope, Red Saunders shows numerous wood-fibers which are mostly irregular in outline, with sharply pointed and occasionally forked ends, the individual fibers from 0.3 to 0.75 mm. in length, the walls being very thick, porous, yellowish, unevenly thickened, and strongly lignified, and the lumina being filled with a fine, granular, protoplasmic content; occasional tracheæ with simple or bordered pores and filled with light lemon-yellow, resinous masses; occasionally fragments showing medullary rays in narrow elliptical groups 1 cell wide and 3 to 6 cells deep; also occasional groups of crystal fibers with calcium oxalate in the form of monoclinic prisms, from 0.01 to 0.02 mm. in diameter. Mounts in hydrated chloral T.S. are of a deep, rich red color. Add 0.5 Gm. of Red Saunders to 10 mils of alcohol; the solution becomes distinctly red. Add 0.5 Gm. of Red Saunders to 10 mils of ether, the solution as-

sumes an orange-yellow color and when held in a bright light shows a distinct, greenish fluorescence. Add 0.005 Gm. of Red Saunders to 10 mils of water; the liquid remains clear and colorless. Red Saunders yields not more than 3 per cent. of ash." *U. S.*

"Imported in irregular logs or billets, freed from the pale sapwood; reddish-brown or blackish-brown externally, deep blood-red internally; hard, but easily split longitudinally. In transverse section, narrow, closely approximated, reddish medullary rays traversing a nearly black wood with scattered, large, isolated vessels. Coloring matter readily soluble in *alcohol* (90 per cent.), but almost insoluble in *water*. Odor of the warmed Wood faintly aromatic; taste very slightly astringent." *Br.*

It imparts a red color to alcohol, ether, and alkaline solutions, but not to water, and a test is thus afforded by which it may be distinguished from some other coloring woods. The alcoholic tincture produces a deep violet precipitate with ferrous sulphate, a scarlet with mercuric chloride, and a violet with the soluble salts of lead. The coloring principle, which was separated by Pelletier and called by him *santalin*, is of a resinous character, scarcely soluble in cold water, more so in boiling water, very soluble in alcohol, ether, acetic acid, and alkaline solutions, but slightly in the fixed and volatile oils, with the exception of those of lavender and rosemary, which readily dissolve it. It is precipitated when acids are added to the infusion of the wood, prepared with an alkaline solution. Weyermann and Haeffely have found it to possess acid properties, and give it the formula $C_{15}H_{14}O_5$. (*Ann. Ch. Ph.*, 74, p. 226.) Weidel (*Wien. Akad. Ber.*, lx, p. 388), by extracting the red saunders with potassium hydroxide, precipitating with hyrochloric acid, and again extracting from the purified precipitate with ether, obtained a colorless crystalline principle, which he calls *santal*, $C_8H_8O_3 + \frac{1}{2}H_2O$.

Cazeneuve and Hugonneng (*C. R. A. S.*, 104, 1722, 1725) have described two crystalline principles which they have extracted from red saunders, *pterocarpin*, $C_{20}H_{18}O_6$, and *homopterocarpin*, $C_{24}H_{24}O_6$, of which the former fuses at 152° C. (305.6° F.) and the latter at from 82° to 86° C. (179.6°–186.8° F.). The wood has no medicinal virtues, and is employed solely for the purpose of imparting color.

Off. Prep.—Tinctura Lavandulæ Composita, *U. S., Br.*

SANTONINUM. U. S., Br.

SANTONIN Santonin.

(săn-tŏ-nĭn'nŭm)

"The inner anhydride or lactone [$C_{15}H_{18}O_3 = 246.14$] of santonic acid obtained from *Artemisia pauciflora* (Ledebour) Weber (Fam. *Compositæ*). Preserve it in well-closed containers, protected from light." *U. S.* "Santonin, $C_{15}H_{18}O_3$, is a crystalline principle which may be obtained from santonica, the dried unexpanded flower-heads of Artemisia maritima, *var.* Stechmanniana, *Besser*." *Br.*

Santonine, Anhydride Santonique, *Fr. Cod.*; Santoninum, *P. G.*; Santonin, *G.*; Santonina, *It., Sp.*

The present U. S. P. and the Br. Ph. 1898 very properly omit processes for the preparation of santonin. (See U. S. D., 17th ed., 1191; also 19th ed., p. 1085.)

It has been intimated to us that the large manufacturers of santonin, abroad, first distil off from the santonica its volatile oil, which has some commercial value in Europe, and that the process for preparing santonin is probably facilitated thereby, the affinity of the oil for the santonin making the latter more difficult of purification.

Santonin was lowered in price after the erection of a factory in Tschimkent, Turkestan, where the Levant wormseed can be furnished cheaply; the process used there is to treat the wormseed with milk of lime; the calcium santoninate formed is next treated with sodium hydroxide and carbon dioxide; the sodium santonate is then decomposed by sulphuric acid. The acid liquid, on refrigeration, deposits the santonin in crystals.

Properties.—Santonin is in "colorless, shining, flattened rhombic prisms, or as a crystalline powder; odorless, and nearly tasteless at first, but afterwards developing a bitter taste; permanent in the air; it becomes yellow on exposure to light. Santonin which has become yellow may be reconverted into colorless crystals by recrystallization from alcohol. One Gm. of Santonin dissolves in 43 mils of alcohol, 1.7 mils of chloroform, and in 110 mils of ether at 25° C. (77° F.); also in 6.5 mils of boiling alcohol; very slightly soluble in water; slightly soluble in boiling water. Its solutions are neutral to litmus and are lævorotatory. It melts between 169° and 171° C. (336.2° and 339.8° F.). Heat about 0.5 Gm. of Santonin with 5 mils of alcoholic potassium hydroxide T.S.; a red color is developed. Shake about 0.01 Gm. of Santonin with a cooled mixture of 1 mil each of sulphuric acid and distilled water, heat the solution to 100° C. (212° F.), and add a minute trace of a very dilute solution of ferric chloride; a violet color results. Incinerate about 1 Gm. of Santonin; not more than 0.1 per cent. of ash remains. Two mils of sulphuric acid added to about 0.1 Gm. of Santonin produces not more than a faint, yellow color (*readily carbonizable organic impurities*). Boil about 2 Gm. of Santonin with 80 mils of distilled water and 5 mils of diluted sulphuric acid, allow the liquid to become cold and then filter it. The addition of mercuric potassium iodide T.S. or of iodine T.S. to 10 mils of the filtrate, mixed with 10 mils of distilled water, produces no cloudiness, even after standing for three hours (*alkaloids*)." *U. S.*

"Colorless, flat, rhombic prisms. Taste slightly bitter. Almost insoluble in *water;* soluble in 2.5 parts of *chloroform*, and in 50 parts of *alcohol* (90 per cent.). Melting point

170° C. (338° F). Sunlight renders it yellow. Added to warm *alcoholic solution of potassium hydroxide* it yields a violet-red color. Insoluble in diluted mineral acids. No appreciable ash." *Br.*

For a test for santonin, see *Ph. Era,* 1898, 210. The air has no effect upon it, but it becomes yellow on exposure to sunlight. According to Sestini, the santonin is changed, through the influence of light, into formic acid, and an uncrystallizable substance, much more soluble in alcohol and ether than santonin itself, which he calls *photosantonic acid,* $C_{15}H_{22}O_5$, and a red resinous substance. If the santonin be in alcoholic solution, after several months of exposure to sunlight it is changed into the ethyl ether of photosantonic acid. In its relations to polarized light it is very strongly lævogyrate, and retains this property with acids, though losing it entirely when combined with salifiable bases. (Buignet, *J. P. C.,* Janv., 1862, p. 26.)

When warmed with alkalies, santonin is changed into monobasic *santoninic acid,* $C_{15}H_{20}O_4$, while concentrated baryta water changes it on prolonged boiling into the isomeric *santonic acid.* Schmidt (*J. P. C.,* 4e sér., iii, 394) disproved the previously accepted statement that santonin was a glucoside; but Hesse (*Ber. d. Chem. Ges.,* vi, 1280) stated santonin to be the anhydride of *santoninic acid,* and prepared this acid by adding an excess of diluted hydrochloric acid to an aqueous solution of the sodium salt, and adding ether, from which the acid may be recovered by evaporation. When santoninic acid is heated to 120° C. (248° F.), it is resolved into santonin and water. It has a strongly acid reaction, and decomposes sodium and calcium carbonate.

Sodium santoninate (*Sodii Santoninas*) was official in the *Pharmacopœia Germanica* of 1872, and was recognized in the U. S. P. 1880. It is a colorless crystalline substance freely soluble in water. It was very properly dropped at the U. S. P. 1890 revision, because it is more easily absorbed than santonin in crystals, and therefore much more dangerous to the patient and much less destructive to *intestinal worms.* For method of preparation and tests of purity, see U. S. D., 19th ed., p. 1243.

For a history with a review of the chemical constituents and decomposition products of santonin see *Y. B. P.,* 1901, 487. Santonin is now considered to be the inner anhydride or lactone of santonic acid.

Cannizzaro and Carnelutti (*Ber. d. Chem. Ges.,* xvi, 2685) have shown that santonic acid breaks up on high heating into *propionic acid,* $C_3H_6O_2$, and *dihydrodimethylnaphthol,* $C_{10}H_7(CH_3)_2.OH$, and distilled over zinc dust it gives a mixture of dimethylnaphthol, $C_{10}H_5(CH_3)_2.OH$, dimethylnaphthalene, $C_{10}H_6(CH_3)_2$, and propylene. *Santonone,* $(C_{15}H_{17}O_2)_2$, a decomposition product of santonin, is made by gradually adding zinc dust to a hot solution of santonin in acetic acid, preferably in the presence of a little platinum tetrachloride. It forms silky white needles, is very soluble in benzene, less so in hot alcohol, ether or diluted acetic acid, and insoluble in water.

Uses.—Santonin is used chiefly as a vermifuge. Against the *round worm* it is generally esteemed as one of the most efficient remedies we possess, its ease of administration as well as its certainty of action making it peculiarly valuable. The coarse crystals should be preferred to the powder as being less readily dissolved, and therefore less likely to be absorbed from the stomach. It may be well administered to children in the form of lozenges made with sugar and tragacanth (for formula, see *A. J. P.,* vi, 124), which if the unbroken crystals are used, can be rendered very pleasant to the taste, so that children will eat them as candy. The dose of santonin for a child two years old is from one-fourth to one-half grain (0.016–0.032 Gm.). To older patients it is best given by enclosing in gelatin capsules. It should always be followed by a cathartic, calomel being perhaps best; although castor oil is sometimes used it should be avoided as likely to increase the absorption. The santoninates or any combination of santonin with alkali carbonates or hydroxides, should be sedulously avoided as vermifuges because of the liability of their being absorbed.

Santonin has been recommended internally in a large variety of conditions, but has failed to establish itself in any of them. It was at one time used as a stimulant to the optic nerve in *amaurosis,* especially due to *nicotinism.* Drake (*S. M.,* 1907, p. 550), reports favorably on its use in *dysentery,* and Negro has used it as an analgesic in *tabes* and various forms of *neuralgia.* The statements of Sejournet that it would diminish the output of sugar in *diabetes* have been contradicted by the observations of Walterhoefer. (*B. K. W.,* 1911).

According to Walter G. Smith, the yellow color imparted to urine by santonin is distinguished from that produced by other substances by becoming purplish-red on the addition of ammonia or other alkali. (*P. J.,* Dec., 1870, p. 528.) For researches upon the character of the urinary coloring matter, consult the same paper.

In overdose santonin produces a poisoning whose symptoms are giddiness, mental apathy or stupor, great paleness and coldness of the surface, vomiting, profuse sweating, trembling, mydriasis, and finally loss of consciousness, with convulsions, often violent and accompanied by opisthotonos and emprosthotonos and failure of respiration. Xanthopsia is an early and characteristic symptom. All objects appear discolored, generally yellow, but frequently green, and sometimes blue. At the same time the urine is tinged of a yellow or a green color. These effects were formerly thought to be due to the staining of the aqueous humor but are more probably to be attributed to a direct action on the retina. In regard to the minimum fatal dose, two grains are said to have killed a feeble child five years old, and one six or seven years old is said to have suffered death from six grains

after development of hæmaturia (*B. G. T.*, lxxiv, 362); four grains produced very serious symptoms in a child four years old. (*P. J.*, ix, 696.) The xanthopsia and discolored urine make the diagnosis of santonin poisoning easy. According to Crouzel the addition of alkalies to the urine will demonstrate the presence of santonin, before the coloration is pronounced, by the development of a characteristic carmine-red tint.

Dose, two to four grains (0.13–0.26 Gm.).

Off. Prep.—Trochiscus Santonini, *Br.*; Trochisci Santonini Compositi, *N. F.*

SAPO. U. S. (Br.)

SOAP [White Castile Soap]

(sā'pō)

"Soap prepared from olive oil and sodium hydroxide. Preserve dried or powdered Soap in well-closed containers." *U. S.* "Hard Soap is soap made from sodium hydroxide and olive oil; it contains not more than 30 per cent. of water." *Br.*

Sapo Durus, *Br.*; Hard Soap, Castile Soap; Savon medicinal, *Fr. Cod.*; Savon amygdalin, Savon blanc, Savon d'Espagne, *Fr.*; Sapo medicatus, *P. G.*; Medizinische Seife, Oel-Sodaseife, Seife, Spanische Seife, *G.*; Sapone medicinale, S. amigdalino, Sapone duro, *It.*; Jabon de aceite de olivas, Jabon, *Sp.*

Soaps embrace all those compounds which result from the reaction of salifiable bases with fats and oils. Fats and oils, as has been explained under the titles *Adeps* and *Olea*, consist generally of three glyceryl esters, two solid, differing in fusibility, called *stearin* and *palmitin*, and one liquid, called *olein*. Stearin is found most abundantly in fats which are firm and solid, as suet and tallow, and palmitin and olein in the oils. When the fats and oils undergo *saponification* by reaction with a salifiable base, these three esters are decomposed into fatty acids peculiar to each, discovered by Chevreul, and called stearic, palmitic, and oleic acids, which unite with the base to form the soap, and into glycerin (glycerol), which is set free. Hence it follows that stearin is a stearate of glyceryl, C_3H_5, the radical of the triatomic alcohol glycerol, $C_3H_5(OH)_3$, palmitin a palmitate, and olein an oleate, and that the fats and oils are mixtures of these three fatty salts. Hence, also, it is obvious that soaps are mixed stearates, palmitates, and oleates of certain bases.

Stearic acid, $C_{18}H_{36}O_2$, is a firm white solid, like wax, fusible at 69.2° C. (157° F.), greasy to the touch, pulverizable, soluble in alcohol, very soluble in ether, but insoluble in water. In the impure state it is used as a substitute for wax in making wax candles. *Palmitic acid*, $C_{16}H_{32}O_2$, forms a white scaly mass, and melts at 62° C. (143.6° F.). *Oleic acid*, $C_{18}H_{34}O_2$, is an oily liquid, insoluble in water, soluble in alcohol and ether, lighter than water, crystallizable in needles, a little below 0° C. (32° F.), and having a slight odor and a pungent taste. (See *Acidum Oleicum.*) *Glycerin* is described under a separate head. (See *Glycerinum.*)

Soaps are divided into the soluble and the insoluble. The soluble soaps are combinations of the fatty acids with sodium, potassium or ammonium hydroxides; the insoluble consist of the same acids united with earths or metallic oxides. It is the soluble soaps only that are detergent, and to which the name *soap* is usually applied. Several of the insoluble soaps are employed in pharmacy, as, for example, the lead monoxide soap, or lead plaster, and the lime soap, or lime liniment. (See *Emplastrum Plumbi* and *Linimentum Calcis.*) The two official soaps are of the soluble kind. One is a soda soap, made with olive oil (Castile soap), the other a potassium soap (soft soap). (See *Sapo Mollis.*) The soap of ammonia is noticed elsewhere. (See *Linimentum Ammoniæ.*)

The consistence of the fixed alkaline soaps depends partly on the nature of the oil or fat, and partly on the alkali present. Soaps are harder the more stearate and palmitate they contain, and softer when the oleate predominates, and, as regards the alkali present, they are harder when formed with sodium hydroxide, and softer when containing potassium hydroxide. Hence it is that of pure soaps, considered as salts, sodium stearate is the hardest and least soluble, and potassium oleate the softest and most soluble.

Liquid soaps are largely coming into use as economical and sanitary substitutes for soap in public lavatories. Several good formulas have been proposed by E. R. Jones (*J. A. Ph. A.*, 1914, 1537) for use with soft, medium and hard waters, respectively.

Preparation.—The following is an outline of the process for making soap. The oil or fat is boiled with a solution of caustic alkali, beginning with a weak solution, and as saponification proceeds using a stronger lye until the whole forms a thick mass, which can be drawn out into long clear threads. After the soap is completely formed, the next step is to separate it from the excess of alkali, the glycerin, and the redundant water. This is effected by adding common salt, or a very strong alkaline lye, in either of which the soap is insoluble. The same end may be attained by boiling down the solution until the excess of the alkali forms a strong alkaline solution, which acts the same part in separating the soap as the addition of a similar solution. As soon as the soap is completely separated, it rises to the surface, and, when it has ceased to froth in boiling, it is ladled out into wooden frames to congeal, after which it is cut into bars by means of a wire. The soap, as first separated, is called *grain soap*. It may be purified by dissolving it in an alkaline lye and separating it by common salt. During this process the impurities subside, and the soap combines with more water, and hence it becomes weaker, although purer and whiter. If the grain soap be not purified, it will form *marbled soap*—the colored streaks arising principally from an insoluble soap of

oxidized iron. Sometimes the marbled appearance is produced by adding to the soap, as soon as it is completely separated, a fresh portion of lye, and immediately afterwards a solution of ferrous sulphate. The greenish-black ferrous hydroxide is precipitated, and gives rise to dark-colored streaks, which, by exposure to the air, become red in consequence of the conversion of the black hydroxide into the ferric hydroxide.

When commercial toilet soap is required, the *grained* soap, or, as it is sometimes called, *boiled* soap, is often remelted, perfumed, and worked over by the process of *milling, plotting,* and *moulding,* whereby the soap is brought into the desired shape for popular use. The *cold process* is also used, and is preferred by many because of its simplicity and economy. The following (from Sadtler's *Industrial Organic Chemistry,* 1906, 64) gives the outlines of the process. The so-called "cold process" requires the use of exact weights of well-refined fats and of caustic soda of a given specific gravity (from 32° to 36° B.), the quantities being such that only just enough soda is present to completely saponify the fat. The materials are allowed to stand together for a short time and then thoroughly mixed in a kettle provided with steam agitating paddles, and kept at a temperature of not over 48.9° C. (120° F.). The reaction proceeds rapidly, and after some fifteen minutes the materials have so far united that they will not separate on standing, although the complete saponification of the charge may require days. They are then run out into the cooling frames. It is obvious that soaps made in this way retain all the glycerin originally combined with the fatty acids disseminated through the particles of soap, and belong to the class of "filled" or "padded" soaps. When cocoanut oil alone is used, the temperature of working in this cold process need not be higher than 23.9° C. (75° F.) in summer and 32.2° C. (90° F.) in winter; if one-half tallow, from 40° to 42.2° C. (104°–108° F.), and if two-thirds tallow, from 45° to 48.9° C. (113°–120° F.) is necessary. A well-refined tallow can be saponified in this way, too, and rosin may be added. For a practical process for making soap in small quantities without boiling, see *U. S. D.,* 19th edition, page 1089.

The official *soap* (*Sapo,* U. S.; *Sapo Durus,* Br.) is an olive oil soda soap, made on the same general plan as that just explained.

Common soap is also a soda soap; but instead of olive oil it contains solid animal fats. This soap corresponds with the white soap of northern European countries and of the United States, and is formed usually from barilla and tallow. In Scotland it was formerly manufactured from kelp and tallow. It was introduced into the U. S. Pharmacopœia of 1860 as the only proper soap for making opodeldoc; but, as this preparation was discarded, this variety of soap was dismissed along with it.

Besides the official soaps of the U. S. and Br. Pharmacopœias, there are many other varieties, more or less used for medicinal or economical purposes. *Starkey's soap* is prepared by uniting, by trituration, equal parts of potassium carbonate, oil of turpentine, and Venice turpentine. *Beef marrow soap* is a fine animal oil soap, also included in the French standard. *Windsor soap* is a scented soda soap, made of one part of olive oil and nine parts of tallow. *Eau de luce* (*aqua luciæ*) is a kind of liquid soap, formed by mixing a tincture of oil of amber and balsam of Gilead with ammonia water. *Transparent soap* is prepared by saponifying kidney fat with soda free from foreign salts, drying the resulting soap, dissolving it in alcohol, filtering and evaporating the solution, and running it into moulds when sufficiently concentrated. The soap is yellow or yellowish-brown, and preserves its transparency after desiccation. Harding (*Proc. Minn. Pharm. Assoc.,* 1896, 116) states that sugar is used in soap to give it transparency and sodium carbonate to give firmness. The German transparent soap always contains a large quantity of cocoanut-oil soap. Modern transparent soaps owe their transparency usually to their having been made into an alcoholic solution and then the alcohol carefully recovered, which leaves the mass transparent. Cheap grades of transparent soaps often owe this property to the presence of sugar which communicates the desired property when present to the extent of 5 or 10 per cent. *Palm soap* is prepared from sodium hydroxide and palm oil, to which tallow is added to increase its firmness. If it be wanted white, the palm oil may be bleached by heat, potassium dichromate with sulphuric acid, chlorine, or exposure to the sun. This soap has a yellowish color, and the agreeable odor of violets derived from the oil. *Soap balls* are prepared by dissolving soap in a little water and then forming it with starch into a mass of the proper consistence. *Common yellow soap* (*rosin soap*) derives its peculiarities from an admixture of rosin and a little palm oil with the tallow employed, the oil being added to improve its color. Sodium silicate has to some extent been substituted for rosin, as more economical. (*A. J. P.,* 1863, p. 466.) Large quantities of lard oil (nearly pure olein) are manufactured into soap.

All the varieties of soap are now manufactured in the United States. Large amounts of olive oil soaps and very fine toilet soaps are, however, imported from France, Italy, and Spain.

Properties.—Soap, whatever may be its variety, has the same general properties. Its aspect and consistence are familiar to every one. Its odor is peculiar, and its taste slightly alkaline. It is usually somewhat heavier than water, and therefore sinks in that liquid. Exposed to heat it quickly fuses, swells up, and is decomposed. It is soluble in water, and more readily in hot than in cold. Potassa soaps and those containing oleic acid are far more soluble than the soda soaps, especially those in which the stearates and palmitates predominate. Acids

added to an aqueous solution of soap combine with the alkali, and set free the oily acids, which, being diffused through the water, give it a milky appearance. Its decomposition is also produced by metallic salts, which invariably give rise to insoluble soaps. Soap is soluble in cold and abundantly in boiling alcohol. This solution constitutes the *tincture of soap,* and forms a very convenient test for discovering lime in natural waters. As the tincture sometimes gelatinizes, it is proposed by Bjorklund to remedy this inconvenience by employing soap in the undried state, that is, containing a large proportion of water. (*J. P. C.*, 4e sér., ii, 179, 1865.) The efficacy of soap as a detergent depends upon its hydrolytic decomposition when in solution, whereby alkali is liberated which saponifies and emulsifies grease and fatty substances rendering them readily removable in the washing processes. The chief adulterations in soap are lime, silica, gypsum, heavy spar, steatite, pipe-clay, and sodium sulphate. When adulterated with these substances, it will not be entirely soluble in alcohol. According to Riegel, glue is an occasional adulteration in Spanish soap, discoverable also by its insolubility in alcohol. The same impurity is sometimes found in other soaps. Soap is officially described as "a white or whitish solid, in the form of bars, hard, yet easily cut when fresh, or as a fine, yellowish-white powder, having a faint, peculiar odor, free from rancidity, and a disagreeable, alkaline taste. It is soluble in water and in alcohol, more readily, however, with the aid of heat. Its aqueous solution is alkaline to litmus. Dissolve about 0.5 Gm. of Soap, accurately weighed, in 10 mils of alcohol, evaporate the mixture to dryness in a tared beaker containing 1 Gm. of clean sand, which has been previously dried at 110° C. (230° F.). Dry the residue at 110° C. (230° F.) to constant weight. The loss does not exceed 36 per cent. for unpowdered Soap or 10 per cent. for powdered Soap (*water*). A solution of a quantity of Soap corresponding to 0.64 Gm. of dried Soap in 25 mils of hot alcohol does not gelatinize on cooling to 20° C. (68° F.) (*soap from animal fats*). Ten mils of an aqueous solution of Soap (1 in 20) remains unchanged in color upon the addition of ammonium sulphide T.S., and upon acidulating another portion of 10 mils of the solution with hydrochloric acid and filtering, the filtrate remains unchanged in color when an equal volume of hydrogen sulphide T.S. is added and the mixture allowed to stand well-stoppered, in a warm place, for half an hour (*metallic impurities*). Dissolve about 10 Gm. of Soap, accurately weighed, in 100 mils of alcohol, with the aid of heat. Transfer the undissolved residue, if any, to a tared filter which has been dried at 100° C. (212° F.), and wash it thoroughly with boiling alcohol. Its weight, after drying at 100° C. (212° F.), does not exceed 1 per cent. of the weight of dry Soap in the original weight taken (*sodium chloride, sodium carbonate, silica*). The weight of this residue, thoroughly washed with distilled water and dried at 100° C. (212° F.) does not exceed 0.15 per cent. of the weight of dry Soap in the original weight taken (*silica and other accidental impurities*). The alcoholic filtrate and washings from the preceding test are not reddened by 3 drops of phenolphthalein T.S. (*sodium hydroxide*). Dissolve about 10 Gm. of Soap in 200 mils of hot distilled water, add 2 drops of methyl orange T.S. and then diluted sulphuric acid with constant stirring until the aqueous layer becomes red. Boil the mixture until the supernatant layer of the fatty acids is clear and free from solid particles. Separate the aqueous layer with the aid of a siphon and wash the fatty acids by decantation with hot distilled water, until 10 mils of the washings, acidulated with a drop of hydrochloric acid, no longer gives a precipitate on the addition of barium chloride T.S. Now place the dish containing the fatty acids on a water bath and heat until the fatty acids are completely liquefied, then filter the warm acids through a dry filter in a hot-water funnel into a flat dish and dry the acids over sulphuric acid. The iodine number of the acids thus obtained is not less than 84 nor more than 90 (see Part III, Test No. 8)." *U. S.*

"Greyish-white, yellowish-white, or greenish-white; becoming horny and pulverisable when dried. Nearly inodorous. Soluble in 20 parts of cold *water,* and in 1.5 parts of hot *water;* soluble in *alcohol* (90 per cent.), more readily when warmed. Responds to the tests for alkaline hydroxides and carbonates and for free fatty acids described under 'Sapo Animalis.' Does not impart a greasy stain to white unglazed paper (absence of free oil). Loses not more than 30 per cent. of its weight when dried at 110° C. (230° F.). Ash not deliquescent (absence of potassium soap). The absence of fatty acids derived from oils other than Olive Oil is determined by the following process:—Dissolve the Soap in hot *water,* add a slight excess of *hydrochloric acid* and heat on a water-bath until the liberated fatty acids form a transparent layer. Separate the fatty acids on a wet filter-paper, and wash with hot *water* until the washings are neutral to *solution of methyl orange.* Filter the oily layer through a dry filter paper in a warm oven. The fatty acids thus separated possess the following characters:—*Iodine value,* 83 to 92; *acid value,* 195 to 205; melting point, 21° to 28° C. (69.8°–82.4° F.); *refractive index* at 40° C. (104° F.), 1.4540 to 1.4580." *Br.*

Olive oil soda soap (Sapo), otherwise called *Castile* or *Spanish soap,* is a hard soap, and is presented under two principal varieties, the white and the marbled. *White Castile soap,* when good, is of a pale yellowish-white color, incapable of giving an oily stain to paper, devoid of rancid odor or strong alkaline qualities, and entirely soluble both in water and in alcohol. It should not feel greasy, nor grow moist, but, on the contrary, should become dry by exposure to the air, without exhibiting any saline efflorescence. This variety of soap contains about 21 per cent. of water. Sometimes it contains a larger proportion of water, with which the soap

is made to combine by the manufacturer, with the fraudulent intention of increasing its weight. Soap thus adulterated is known by its unusual whiteness, and by its suffering a great loss of weight in a dry air. The proportion of water may be ascertained by introducing the soap into a saturated solution of sodium chloride, and boiling, when the soap, nearly free from water, concretes into a solid mass. A more satisfactory method is to evaporate a carefully weighed portion, which has been reduced to fine particles, to a constant weight, upon a water bath. *Marbled Castile soap* is harder, more alkaline, and more constant in its composition than the other variety. It contains about 14 per cent. of water. Having less water than the white Castile, it is a stronger and more economical soap, but at the same time is less pure. The impurity arises from the veins of marbling, consisting of ferruginous matters, as already explained, and from various substances added as make-weights. Soap made with animal fat, with the probable addition of sodium silicate, has been sold for Castile soap. The Italian brands of Castile soap which have been so largely used in past years are rapidly depreciating in quality; they are now chiefly made from cotton seed oil and other substitutes for olive oil. Floating soaps owe their distinctive property in this respect to having been beaten while cooling so as to include innumerable small air bubbles which give the buoyancy to the soap.

Animal oil soda soap (*Sapo Vulgaris*) is a hard soap, of a white color, inclining to yellow. It is made from tallow and sodium hydroxide. This soap possesses the same general properties as the olive oil soda soap.

Composition.—It has been already explained that soap consists of certain fatty acids united with an alkali. As olive oil is a compound of olein with palmitin and small quantities of the esters of other fatty acids, so the official "soap" is a mixed sodium oleate and palmitate. The former official "common soap" is principally a sodium stearate, and "soft soap," as defined in the Br. Pharmacopœia, is a mixed potassium palmitate and oleate.

Incompatibles.—Soap is decomposed by all the acids, earths, and earthy and metallic salts. Acids combine with the alkali, and set free the fatty acids of the soap; the earths unite with the fatty acids, and separate the alkali, while the earthy and metallic salts give rise, by double decomposition, to an insoluble soap of their base and a saline combination between their acid and the alkali of the soap. Hard waters, in consequence of their containing salts of lime, decompose and curdle soap. They may be rendered soft, and fit for washing, by adding alkali carbonates, hydroxides or borates.

Uses.—Soap is laxative and antacid. It acts like an alkaline base and was formerly used to some extent internally, but has been entirely superseded by more elegant alkaline compounds, except in laxative preparations. In *constipation,* particularly when arising from hardened fæces in the rectum, a strong solution of soap, especially of soft soap, forms a useful enema. When the latter is used, two tablespoonfuls may be dissolved in a pint of warm water. Externally soap is used in various *skin diseases,* not merely for its detergent effect, but also to soften the horny layer of the epiderm. In pharmacy, soap is frequently employed for the purpose of giving a proper consistence to pills; but care must be taken not to associate it with a substance which may be decomposed by it. It is an excellent emulsifying agent when the mixture is intended for external use. It is also an ingredient in some liniments and plasters. In toxicology it is used as a chemical antidote for the mineral acids and the caustic salts of iron, and should always be resorted to in poisoning by these agents, without a moment's delay, and its use continued until magnesia, chalk, or sodium or potassium bicarbonate can be obtained. The mode of administration in these cases, is to give a teacupful of a strong solution of soap every three of four minutes, until the patient has taken as much as he can swallow.

Dose, five grains to half a drachm (0.32–2.0 Gm.), given in pill.

Off. Prep.—Emplastrum Saponis, *Br., N. F.;* Linimentum Saponis, *U. S., Br.;* Linimentum Chloroformi (from Soap Liniment), *U. S.*

SAPO ANIMALIS. Br.

CURD SOAP

(sā'pō ăn-ĭ-mā'lĭs)

"Curd Soap is soap made from sodium hydroxide and purified animal fats consisting principally of stearin; it contains not more than 30 per cent. of water." *Br.*

Sapo Sebacinus; Sapo domesticus; Animal Soap, Tallow Soap, Stearin Soap; Savon animal, *Fr. Cod.;* Hausseife, Talgseife, Stearinseife, *G.;* Sapone animale, *It.;* Jabon animal, *Sp.*

The British Pharmacopœia, 1914, has retained curd soap in its list, and thus describes it: "Yellowish-white or greyish-white; nearly inodorous; easily moulded when heated, becoming horny and pulverisable when dried. Sparingly soluble in cold *water;* completely soluble in hot *water;* soluble in *alcohol* (90 per cent.). When 5 grammes of the dried and powdered Soap are dissolved in 50 millilitres of boiling *alcohol* (90 per cent.), and the solution filtered while hot, the filter being thoroughly washed with more of the boiling *alcohol,* the filtrate is neutral to *solution of phenolphthalein* (absence of alkaline hydroxides and free fatty acids), and if the filter is then washed with hot *water,* the washings require for neutralisation not more than 5 millilitres of *N/10 solution of sulphuric acid, solution of methyl orange* being used as indicator (limit of alkaline carbonates). Does not impart a greasy stain to white unglazed paper (absence of free fats). Loses not more than 30 per cent. of its weight when dried at 110° C. (230° F.). Ash not deliquescent (absence of potassium soap)." *Br.*

Soap made from animal oils and fats is very largely used for all domestic purposes; it was long used for making *solid opodeldoc*, but is now replaced by sodium stearate. (See *Linimentum Saponato-Camphoratum*, N. F., Part III.)

Off. Prep.—Linimentum Potassii Iodidi cum Sapone, *Br.*

SAPO MOLLIS. U. S., Br.

SOFT SOAP Sapo Moll. [Green Soap]
(sā'pō mŏl-lĭs)

"Soft Soap is soap made from potassium hydroxide and olive oil." *Br.*

Sapo Viridis, U. S. P. 1880; Savon mou, Savon vert, Savon à Base de Potasse, *Fr.*; Sapo Kalinus, *P. G.*; Kaliseife, Schmierseife, *G.*; Sapone di potassa, *It.*

* "Cottonseed Oil, *four hundred and thirty grammes* [or 15 ounces av., 73 grains]; Potassium Hydroxide, *eighty-six grammes* [or 3 ounces av., 15 grains]; Alcohol, *fifty milliliters* [or 1 fluidounce, 331 minims]; Water, *a sufficient quantity*, to make *one thousand grammes* [or 35 ounces av., 120 grains]. Dissolve *eighty-six grammes* [or 3 ounces av., 15 grains] of potassium hydroxide in *one hundred mils* [or 3 fluidounces, 183 minims] of water in a tared, capacious dish with the aid of heat. Immediately add *four hundred and thirty grammes* [or 15 ounces av., 73 grains] of cottonseed oil to the hot solution and stir the mixture actively for a few moments. Then reapply the heat and, at the first evidence of froth from boiling, pour in the *fifty mils* [or 1 fluidounce, 331 minims] of alcohol, stir it actively until the froth suddenly rises, then withdraw the heat and again stir until the Soap assumes the consistence of a paste. Now determine by the method given below whether the product will contain the required excess of potassium hydroxide when water is added to make *one thousand grammes* [or 35 ounces av., 120 grains]. If the product does not meet the requirements of this test, add more potassium hydroxide or cottonseed oil as may be needed and again heat it until the saponification is complete. Finally add enough water to make the finished product weigh *one thousand grammes* [or 35 ounces av., 120 grains] and warm it gently, stirring carefully, until the water is all absorbed and a clear soap results. The potassium hydroxide used in this process should be of the full strength directed by the Pharmacopœia (85 per cent.). Potassium hydroxide of any other strength, however, may be used, if a proportionally larger or smaller quantity is taken, the proper amount for the above formula being ascertained by dividing 7310 by the percentage of KOH contained therein." *U. S.*

Cottonseed oil is used in the U. S. P. IX in place of linseed oil, which was used in the preparation of soft soap in the U. S. P. VIII. The change is believed to be an improvement. A soft soap process was first introduced into the U. S. P., 1890, with the view of affording a soft soap for medicinal purposes which shall be of uniform strength. Domestic *soft soap* is prepared on the same general principles as hard soap, potassium hydroxide being employed as the alkali, and a fatty matter, rich in olein, as the oil. The French soft soap is made with the seed oils, such as rape seed, hemp seed, etc.; the Scotch and Irish, with fish oil and some tallow, and our own, with refuse fat and grease. A lye of wood ashes is the form of potassium usually employed. In forming this soap it is necessary that it should continue dissolved in the alkaline solution, instead of being separated from it. Hence soft soap is a potassium soap completely dissolved in the solution of its alkali, which is present in excess. As made in this country, it is usually semi-fluid, slippery, capable of being poured from one vessel to another, and of a dirty brownish-yellow color and varying strength.

Properties.—It is officially described as "a soft, unctuous, yellowish-white to brownish-yellow mass, having a slight, characteristic odor and an alkaline taste. An aqueous solution of Soft Soap is alkaline to litmus and phenolphthalein T.S.; a solution in hot distilled water (1 in 20) is nearly clear. Dissolve about 5 Gm. of Soft Soap, accurately weighed, in 100 mils of hot alcohol, collect the residue, if any, on a filter, thoroughly wash it with hot alcohol, and dry it to a constant weight at 100° C. (212° F.). The weight of the residue does not exceed 3 per cent. of the weight of Soap taken. The combined filtrate and washings, on the addition of 0.5 mil of phenolphthalein T.S. and titration with tenth-normal sulphuric acid V.S., shows not less than 0.1 per cent. nor more than 0.25 per cent. of KOH. Each mil of tenth-normal sulphuric acid V.S. used corresponds to 0.00561 Gm. of KOH. Soft soap loses not more than 52 per cent. in weight, when tested for water as directed under *Sapo*." *U. S.*

"Yellowish-white to green; of an unctuous consistence. Nearly inodorous. Readily soluble in *alcohol* (90 per cent.), leaving not more than 3 per cent. of insoluble residue. Responds to the tests for alkaline hydroxides and carbonates and for free fatty acids described under 'Sapo Animalis.' Does not impart a greasy stain to white unglazed paper (absence of free oil). Ash very deliquescent, and yields no characteristic *reactions* for copper. The mixed fatty acids, liberated and treated as described under 'Sapo Durus,' possess the characters there specified." *Br.*

For more than one hundred years, under the name of "*green soap*," there has been used in Europe a soap made by saponifying linseed, rape seed, or other vegetable oils with various refuse oils, usually including fish oils, an excess of potassium hydroxide, and a little sodium hydroxide. The green color of this soap was probably due to the presence of chlorophyll in the impure vegetable oils used. This green soap, or so-called "German soap," was formerly imported into America, but at present has been almost entirely superseded by soft soap made in this country, from which it does

not differ in the nature of its active constituents or in its therapeutic properties.

If a green soap be wanted, it may be made by the process given in the *U. S. D.*, 19th edition, p. 1093. The soft soap of France, formerly the *savon vert* of the French Codex, has a greenish color, and usually the consistence of a soft ointment. It is made of hemp seed oil, or sometimes of the dregs of olive oil, and potassium hydroxide. G. M. Beringer (*Proc. A. Ph. A.*, 1903, 420) prefers to use Malaga olive oil in making green soap, and M. I. Wilbert (*Proc. A. Ph. A.*, 1904, 228) extracts the green coloring matter from hemp seed by macerating 25 parts of ground hemp seed with alcohol and obtains 100 parts of a tincture; by substituting an equal measure of this tincture for the quantity of alcohol used in the official process, a green soap can be made, which will have the color which is regarded by some as a very important characteristic.

Uses.—Soft soap possesses not only the detergent properties of neutral soaps, but because of the excess of alkali has active medical virtues, especially as a topical remedy. In the first place it removes the fat more thoroughly from the skin and is therefore of service in those forms of *skin diseases* accompanied with disturbances of sebaceous secretion, such as *seborrhea* or *comedo*. It has also the property of softening the keratin elements of the epiderm, and is therefore useful in conditions accompanied with crusts and scales, such as *psoriasis* and *chronic eczema*. Because of its local irritating action it may also be used as a stimulant in *acne vulgaris* and *rosaceæ*. It is also asserted to be of adjuvant service in the treatment of various parasitic skin diseases.

Kappesser (*Fort. Med.*, 1912) has reported favorable results from the use of inunctions of one-half to one drachm (2–3.9 Gm.) of soft soap in *scrofulous lymphadenitis*. Kuelbes (*Th. M.*, 1914, xxviii) has found it of occasional benefit also in a large variety of other conditions, especially *cardiac neuroses* and *migraine*. In *chronic bronchitis* and *dyspepsia* he asserts the inunctions often improve the general condition of the patient, but in *asthma* they usually were without influence.

Off. Prep.—Linimentum Saponis Mollis, *U. S.* (*Br.*); Linimentum Saponis Mollis Compositum, *N. F.*; Unguentum Sulphuris Compositum, *N. F.*

SAPPAN. Br.

SAPPAN

(săp′pạn)

"Sappan is the heart-wood of Cæsalpinia Sappan, *Linn.*" *Br.*

Sappan wood, Sampfen wood, Bakam, Tairi, Patang, Teri, Versino, *It.*; False Sandalwood, Indian Redwood, Samfen.

Cæsalpinia Sappan is a small thorny tree indigenous to the Eastern and Western Asiatic Peninsulas, Pegu and Tenasserim, and is also cultivated in Central India. The leaves are large and abruptly bi-pinnate; the flowers being yellow and in axillary racemes; and the pods are oblong, flattened, nearly smooth and dehiscent or indehiscent. The wood yields a valuable red dye which is also prepared from the pods and from the bark. The commercial samples vary considerably. There are two commercial varieties, viz., (1) Singapore or Dhansari, and (2) Ceylon sappan, the former being preferred. According to Dymock, the freshly cut wood is whitish, but becomes red on exposure to the air. He also states that the addition of alkalies increases the yield of coloring matter, turning it a reddish-violet. According to the British Pharmacopœia, it occurs in "hard, heavy pieces of variable size, or in orange-red chips. In transverse section, well-marked concentric rings, numerous narrow medullary rays, and large vessels. No odor; taste slightly astringent. It communicates to *alcohol* (90 per cent.) and to *water* a red color, which becomes carmine-red, but not purple, upon the addition of *solution of sodium hydroxide* (distinction from Logwood)." *Br.*

According to the investigations of Bolley, sappan wood contains *brasilin*, $C_{16}H_{14}O_5$, identical with that of Brazil wood.

Sappan, or samfen, as it is sometimes called, has been an article of commerce for at least five hundred years. It is employed in the arts as a substitute for logwood in dyeing. Medicinally it is used as an astringent in the treatment of *diarrhea*. It may be given in the form of a decoction.

Dose, from fifteen to forty-five grains (1–3 Gm.).

Off. Prep.—Decoctum Sappan, *Br.*

SARSAPARILLA. U. S.

SARSAPARILLA Sarsap.

(sär-sạ-pạ-rĭl′lạ)

"The dried root of *Smilax medica* Chamisso and Schlechtendal, known in commerce as Mexican Sarsaparilla; or *Smilax officinalis* Kunth, or an undetermined species of *Smilax*, known in commerce as Honduras Sarsaparilla; or *Smilax ornata* Hooker filius, known in commerce as Jamaica Sarsaparilla (Fam. *Liliaceæ*)." *U. S.* "The dried root of Smilax ornata, *Hook. f.* Imported from Costa Rica and commonly known as Jamaica sarsaparilla." *Br.* 1898.

Sarsæ Radix, *Br.* 1898; Jamaica Sarsaparilla; Salsepareille, *Fr. Cod.*; Radix Sarsaparillæ, *P. G.*; Sarsaparille, Sarsaparilla, *G.*; Salsapariglia, *It.*; Zarzaparrilla (Raiz de), *Sp.*

The medicinal species of smilax grow in Mexico, Guatemala, and the warm latitudes of South America. The roots are very long and slender, and originate in great numbers from a common head or rhizome, from which the stems of the plant rise. The whole root with the rhizome is usually dug up, and as brought into market exhibits not unfrequently portions of the stems attached, sometimes several inches in length. The commercial sarsaparillas are conveniently divided into the mealy and non-mealy

sarsaparillas. The first class comprises especially the Honduras, Guatemala, and Brazilian varieties; the second the Jamaica, Mexican and Guayaquil sarsaparillas. A very convenient key for distinguishing the commercial sarsaparillas by certain anatomical characters has been devised by Luerssen in his *Handbuch der Medicinpharm. Botanik,* ii, 404.

All the species of Smilax are climbing or trailing plants, with prickly stems—a character expressed in the name of the medicine, which is derived from two Spanish words (*zarza parilla*), signifiying a small thorny vine.

The official species of smilax are as follows:

S. medica has an angular stem, armed with straight prickles at the joints, and a few hooked ones in the intervals. The leaves are smooth, bright green on both sides, shortly acuminate, five-nerved, with the veins prominent beneath. They vary much in form, the lower being cordate, auriculate-hastate, the upper cordate-ovate. In the old leaves the petiole and midrib are armed with straight subulate prickles. The inflorescence is an umbel of from eight to twelve flowers, with a smooth axillary peduncle and pedicels about three lines long.

The *Mexican* or *Vera Cruz sarsaparilla* is derived from this species. Although sometimes in bundles, it commonly comes in large, rather loose bales, weighing about two hundred pounds, bound with cords or leather thongs, and usually containing the roots folded upon themselves, and separately packed. These, as in the Honduras sarsaparilla, consist of a head or caudex with numerous long radicles, which, however, are somewhat smaller than in that variety, and have a thinner bark. They are often also much coiled with earth. It contains but little starch and has quadrangular endodermal cells, with thickened walls, and more or less oval lumen. It was formerly little esteemed; but, from the acrid taste which it possesses, it is probably of equal value to the other kinds.

S. officinalis.—In this species the stem is twining, angular, smooth, and prickly; the young shoots are unarmed; the leaves ovate-oblong, acute, cordiform, five- or seven-nerved, coriaceous, smooth, twelve inches long and four or five broad, with footstalks an inch long, smooth, and furnished with tendrils. The young leaves are lanceolate-oblong, acuminate, and three-nerved. Large quantities of the root are said to be sent down the Magdalena River to Mompox and Carthagena.

It is the source of *Honduras Sarsaparilla.* It is brought from the bay of Honduras and comes in bundles two or three feet long, composed of several roots folded lengthwise, and secured in a compact form by a few circular turns. These are packed in bales imperfectly covered with skins, each bale containing one hundred pounds or more. The roots are usually connected at one extremity in large numbers in a common head, to which portions of the stems are also attached. In some bundles are many small fibers, either lying loose or still adhering to the roots. The roots externally are a dirty grayish or reddish-brown; the cortical portion beneath the epidermis often appears amylaceous when broken.

S. ornata Hook.—This plant was recognized by both Flückiger and Hanbury, and by Bentley and Trimen as *S. officinalis,* and was described by Lemaire with a query to it to express his doubtfulness of its specific distinctness. The species is, however, now generally accepted. The plant has large seven-nerved leaves resembling *S. officinalis.* It is especially distinguished by the young leaves being mottled with white. (See *Botanical Magazine,* 1889, cxv, 7054.)

This species yields *Jamaica* or *red sarsaparilla* of foreign writers, although but little known by the latter name in the United States. It is collected in Central America, especially in Costa Rica, and it owes its name to the fact that it has been largely exported to Europe through the island of Jamaica. As found in commerce it is in rolls from twelve to eighteen inches long by four or five in thickness, composed exclusively of long slender many-radicled roots very loosely held together by a few turns. Sometimes it is pressed into large bales. It is further to be distinguished from Honduras sarsaparilla by its dark color, the greater abundance of coarse rootlets, the less quantity of starch, its relatively thick cortex, and its less sharp taste. Externally it is also redder than is commonly the case with Honduras sarsaparilla. Kobert (*P. J.,* 1912, lxxxviii, p. 779), has found that the *ornata* has only one-eighth of the hemolytic power of the Vera Cruz sarsaparilla, which he takes as a test of its saponin content. He believes the plant is unfit for medical use.

Cultivated Jamaica Sarsaparilla (*Roja Inglesa*) occurs in thick short rolls and is especially characterized by its yellow-brown or orange color. According to W. B. Hemsley, Hooker's I. P. pl. 2589, it is the product of *S. utilis* Hemsley, a species related to *S. ornata,* from which it differs by its long pediculated simple umbels.

An investigation by Power and Salway (*Chem. News,* 1914, p. 56) showed the presence of the following constituents in *Jamaica sarsaparilla:* a glucoside, *sarsaponin,* $C_{44}H_{76}O_{20}7H_2O$, which upon hydrolysis yields *sarsapogenin,* $C_{26}H_{42}O_3$, and dextrose; *sitosterol-d-glucoside,* $C_{33}H_{56}O_6$; *sitosterol,* $C_{27}H_{46}O$; *stigmasterol,* $C_{30}H_{50}O$; *sarsapic acid* (a new dicarboxylic acid), $C_6H_4O_6$, and a mixture of fatty acids, including palmitic, stearic, behenic, oleic and linolic acids. The alcoholic extract contained *acetyl-d-glucoside* and potassium nitrate was also found.

Another variety is the *Carácas sarsaparilla,* brought in large quantities from La Guayra. It is in oblong packages, of about one hundred pounds, surrounded with broad strips of hide, which are connected laterally with thongs of the same material, leaving much of the root exposed. The roots, as in the last variety, are separately packed, but more closely and carefully. The radicles are often very amylaceous internally, in this respect resembling the following variety.

S. papyracea is said to have foliage like *S. officinalis,* with a multiangular stem, with squamiform thorns on the angles, and petioles which are vaginate for one-fourth their length. It is thought to be the source of Para sarsaparilla which is no longer found in commerce.

The *Brazilian,* or, as it is called in Europe, the *Lisbon* or *Pará sarsaparilla,* is not very plentiful in commerce. It comes from the ports of Pará and Maranham, in cylindrical bundles from three to five feet in length by about a foot in thickness, bound about by close circular turns of a very flexible stem, and consisting of unfolded roots, destitute of caudex (rhizome) and stems, and having a few radical fibers. It was also shown in the Brazilian exhibit in the Centennial Exhibition, neatly cut and tied into bundles about a foot long and eight inches in diameter. It is the variety of which Hancock speaks as celebrated throughout South America by the name of *Sarsa of the Rio Negro,* and was considered one of the most valuable varieties of the drug. It is distinguished by the thinness of its cortex, the large amount of starch that it contains and its large, radially elongated endodermal cells. It was said by Martius to be derived from *Smilax syphilitica;* but Hancock considers that portion of it which comes from the Rio Negro, and is shipped at Pará, as the product of an undescribed species, certainly not *S. syphilitica.* As determined by Richard, it is the product of the *S. papyracea* of Poiret.

The variety described by Bentley under the name of *Guatemala sarsaparilla* was collected in the province of Sacatapeques, about ninety miles from the sea. It is in cylindrical bundles about two feet eight inches long by four inches in diameter, composed of separate roots, arranged in parallel order, without rootstalk, and bound together by a few turns of the flexible stem of a monocotyledonous plant. The bundles resemble the Brazilian in arrangement, but are much less compact. It is amylaceous, has considerable acridity, and is probably one of the most efficient varieties. Bentley ascribes it to *S. papyracea.* For a particular description of the root, see *P. J.,* xii, 472.

Guayaquil sarsaparilla, according to Spruce, grows in valleys on the western slopes of the equatorial Andes. It is usually not in bundles, but carelessly packed in bales. "The rhizome and a portion of the stem are often present, the latter being round and prickly. The root is dark, large, and coarse-looking, with a good deal of fiber. The bark is furrowed, rather thick, and not mealy in the slenderer portions of the root, which is near the rootstalk; but, as the root becomes stout, so its bark becomes smoother, thicker, and amylaceous, exhibiting when cut a fawn-colored or pale yellow interior."

The root (rhizome) of *Smilax China,* a native of China and Japan, has been employed under the name of *China Root* for similar purposes with the official sarsaparilla. As it occurs in commerce, it is in pieces from three to eight inches long and an inch or two thick, usually somewhat flattened, more or less knotty, often branched, of a brownish or grayish-brown color externally, whitish or of a light flesh-color internally, without odor, and of a taste flat at first, but afterwards very slightly bitterish and somewhat acrid, like that of sarsaparilla. The root of *Smilax aspera* is said to be employed in the south of Europe as a substitute for sarsaparilla; but it has little reputation. The East India sarsaparilla, which was at one time referred to this species of smilax, is the product of *Hemidesmus indicus.* (See *Hemidesmus.*)

Under the name of *Raiz de china de México,* the Mexican Pharmacopœia recognizes the root of *S. rotundifolia* as diaphoretic and depurative, but, according to Maisch, this reference is incorrect. (See *A. J. P.,* 1879.)

Properties.—The several varieties of sarsaparilla are officially described as follows:

"Mexican Sarsaparilla.—In loose bundles, or pressed into bales, single bundles attaining a length of 60 cm. and composed of from 20 to 35 folded roots attached to a crown with one or more stout stems; roots from 3.5 to 6 mm. in diameter; externally grayish-brown to dark brown, minutely hairy, longitudinally furrowed, the furrows containing more or less of a blackish earth; fracture tough, fibrous; internally light brown with a more or less shrunken, mealy or sometimes horny cortex surrounding the porous central cylinder, pith distinct; nearly inodorous; taste mucilaginous, somewhat sweetish and acrid. Remove the woody, knotty crown with portions of the overground stems.

"Honduras Sarsaparilla.—In more or less compact, cylindrical bundles, attaining a length of 55 cm. and a diameter from 8 to 15 cm., consisting of the long, folded roots bound together by roots of the same plant; roots from 2 to 6 mm. in diameter; externally dark- or reddish-brown, longitudinally furrowed, the furrows usually free from soil; fracture fibrous; internally consisting of a grayish-white or dark brown cortex, a light yellow and porous central cylinder and a whitish pith; taste mucilaginous and slightly acrid.

"Jamaica Sarsaparilla.—In more or less compact and somewhat flattened bundles, from 30 to 45 cm. in length and from 10 to 15 cm. in width, consisting of the folded roots loosely bound with roots of the same plant; roots from 2 to 5 mm. in diameter; externally grayish-brown to reddish-brown, longitudinally wrinkled, more or less furrowed and bearing numerous coarse fibrous rootlets; taste somewhat sweet and slightly bitter.

"Under the microscope, transverse sections of all of the commercial varieties of Sarsaparilla show an epidermal layer with basal portions of root hairs; a hypodermis composed of several layers of strongly lignified cells, the walls being uniformly thickened, except in Mexican Sarsaparilla in which the inner walls are only slightly thickened; a cortex composed of numerous parenchyma cells mostly containing starch, some containing resin or raphides of calcium oxalate; an endodermis of a single layer of strongly lignifed cells, the walls being uni-

formly thickened except in Mexican Sarsaparilla in which the outer walls are only slightly thickened; a central cylinder composed of radial bundles connected with sclerenchymatous fibers, the tracheæ being large and oval and the phloem in small groups at the periphery of the bundle; and a pith composed of starch-bearing parenchyma cells. Powdered Sarsaparilla is light grayish-brown to dark grayish-brown; when examined under the microscope it exhibits numerous starch grains, from 0.003 to 0.023 mm. in diameter, spherical, or biconvex or spherical-tetrahedral, single to 2- to 4-compound, and frequently with a central-elliptical cleft; calcium oxalate in raphides, from 0.006 to 0.035 mm. in diameter, occurring singly or in groups; cells of the hypodermis and endodermis with lemon-yellow or reddish-yellow porous walls and, in the case of Mexican Sarsaparilla, showing an uneven or irregular thickening, the individual cells from 0.08 to 0.5 mm. in length; fragments of tracheæ with simple and bordered pores or scalariform or reticulate thickenings associated with sclerenchymatous fibers having rather thin, very slightly lignified and porous walls. Sarsaparilla yields not more than 10 per cent. of ash." *U. S.*

According to Tunmann (*Apoth. Zeit.*, xxv, p. 475), the consumption of sarsaparilla in Europe has decreased materially, and the chief market for this drug at the present time appears to be the United States. While the U. S. Pharmacopœia recognizes three commercial varieties, most of the drug which is used is the Mexican variety, a relatively small quantity of Honduras sarsaparilla being imported. The *red Jamaica, Orange* or *Native Jamaica* varieties are used chiefly in England. Hartwich has recently pointed out that the varieties of sarsaparilla on the market are more numerous than are generally supposed. He also states that the greatest emphasis should be placed on the structural characteristics in order to distinguish the several varieties, rather than the form of packing and the supposed botanical origin. He is the best authority on this subject and all of his articles, some of which are enumerated, should be consulted (*S. W. P.*, 1897, No. 44 and 45; 1898, No. 37, and 1909, p. 126; *Arch. d. Pharm.*, 1894, p. 37, and 1902, p. 325; *Ber. d. D. Pharm. Ges.*, 1907, p. 250). A recent article on the pharmacognosy of the several commercial sarsaparillas is by Fleury in *Bull. des Sc. Pharmacol.*, xii, p. 190. Rusby reports finding lots of Mexican sarsaparilla which consisted entirely of "butts" or rhizomes. (*Proc. A. Ph. A.*, 1908, lvi, p. 773.) Kraemer reports finding nineteen ounces of dirt in a bundle of Mexican sarsaparilla weighing four and a half pounds. (*Proc. A. Ph. A.*, 1906, liv, p. 345.) Rusby has reported the presence of a thick, blackish, woody and decidedly astringent root in several shipments of Vera Cruz sarsaparilla. (*Jour. A. Ph. A.*, 1913, p. 1104.)

Sarsaparilla is efficient in proportion as it is acrid to the taste, which is said by some authors to be confined to the cortical portion, while the ligneous fiber and medullary matter are insipid and inert. Hancock avers that all parts are equally acrid and efficacious. The truth is probably between the two extremes, and, as in most medicinal roots, it must be admitted that the bark is more powerful than the interior portions, while these are not wholly inactive. The virtues of the root are communicated to water, cold or hot, but are impaired by long boiling. They are extracted also by diluted alcohol. According to Hancock, the whole of the active matter is not extracted by water. In South America it is the custom to prepare sarsaparilla by digestion in wine or spirit, or by infusion in water with additions which may produce the vinous fermentation and thus add alcohol to the menstruum. The same result, as to the superior efficacy of alcohol as a solvent of the acrid principle of sarsaparilla, has been obtained by the French experimentalists. It has been suggested that sarsaparilla, the virtues of which are admitted to be impaired by long boiling, might also be injured by the degree of heat applied in the water or steam bath. But the contrary appears to have been proved by J. F. Judge of Cincinnati. (*Proc. A. Ph. A.*, 1873, p. 595.)

Parillin. (*Smilacin. Pariglin. Salseparin. Parallinic acid.*)—The crystalline principle to which any activity of sarsaparilla is due is now called *parillin*. It was first discovered by Palotta, who described it in 1824 under the name of *pariglin*. Subsequently, Folchi supposed that he had found another principle, which he called *smilacin*. Flückiger recommends the preparation of *parillin* by exhausting the crushed root with warm alcohol and distilling the tincture until the residue weighs one-sixth of the root. It is then gradually mixed with one and a half times its weight of water, and after several days the liquid is decanted from the light yellow precipitate, which is then mixed with about half its volume of alcohol, transferred to a filter, and washed with alcohol of 20 or 30 per cent. because parillin is less soluble in weak alcohol than in strong alcohol. The yield was 0.18 and 0.19 per cent. It is white, inodorous, almost tasteless in the solid state, but bitter, acrid, and nauseous when dissolved in alcohol or water. It is very slightly soluble in cold water, but more readily in boiling water, without crystallizing on cooling. It is very soluble in alcohol, especially at the boiling temperature. Ether and the volatile oils also dissolve it. Its aqueous solution has the property of frothing very much on agitation. According to Flückiger, concentrated sulphuric acid yields a yellow solution, which, on absorbing moisture, gradually turns cherry-red; warm diluted sulphuric acid colors parillin greenish, then red, and finally brown; phosphoric acid has a similar reaction, but the color is more greenish-yellow. The aqueous solution is precipitated by alcoholic solution of lead acetate, by lead subacetate, and by tannin, and when warmed reduces alkaline copper tartrate, but does not react with other tests for sugar until

after it has been boiled with a dilute acid, when the solution acquires a green fluorescence. This is best observed if a trace of parillin is dissolved in warm concentrated sulphuric acid, and disappears on dilution with water or on neutralizing with ammonia. Parillin is not sternutatory; its acrid taste is best observed in alcoholic solution. (See *A. J. P.*, xii, 245.) The solutions of parillin are without acid or alkaline reaction. By treatment with dilute mineral acids, it is resolved into *parigenin* and sugar. Poggiale found parillin both in the cortical and in the medullary part of the root, but most largely in the former. W. von Schulz (*P. J.*, 1892, 6) has shown that Dragendorff's *smilacin, smila-saponin,* or *sarsaparill-saponin,* $C_{20}H_{32}O_{10}$, *sarsa-saponin,* $C_{22}H_{36}O_{10}$, discovered by himself, and Flückiger's *parillin,* $C_{26}H_{44}O_{10}$; are three homologous compounds all belonging to the same series, having the general formula $C_nH_{2n-8}O_{10}$. These three all split up into *sarsasapogenin* (parigenin of Flückiger) and one or more molecules of glucose on boiling with dilute acids. Kobert (*A. J. P.*, 1892, 465) comes to practically the same results, stating the constituents to be *parillin* ($C_{26}H_{44}O_{10} + 2\frac{1}{2}H_2O$), insoluble in water; *saponin* (sarsaparill-saponin), $5(C_{20}H_{32}O_{10} + 2\frac{1}{2}H_2O)$, soluble in water; and *sarsa-saponin,* $12(C_{22}H_{36}O_{10} + 2H_2O)$, easily soluble in water, and the most active of the constituents.

The sarsaparilla of commerce is apt to be nearly if not quite inert, either from age, or from having been obtained from inferior species of Smilax. This inequality of the medicine, with the improper modes of preparing it long in vogue, has probably contributed to its variable reputation. The only criterion of good sarsaparilla to be relied on is the taste. If it leave a decidedly acrid impression in the mouth after having been chewed for a short time, it may be considered efficient; if otherwise, it is probably inert. Various false sarsaparillas have been sent into commerce from South America. For description by C. Hartwich see *A. Pharm.*, July, 1902.

Uses.—The use of sarsaparilla in medicine is an interesting example of the power of superstition to survive the attacks of truth and reason. It was introduced into Europe about the middle of the 16th century as a remedy for *syphilis,* but soon fell into disrepute until revived by Fordyce in 1757. Subsequently it came to be used as an alterative in various other chronic diseases, especially *chronic rheumatism* and *scrofula.* There is, however, no reason to believe that it possesses any virtues except as a mild gastric irritant through its saponin content. Its most popular employment is in the form of its compound syrup which is used as a vehicle especially for mercury and potassium iodide.

Sarsaparilla may be administered in the form of infusion, compound decoction, compound syrup, or fluidextract. A beer made by fermenting an infusion of the drug with molasses is said to be a popular remedy in South America. The smoke of sarsaparilla has been highly recommended in *asthma.* (*J. P. C.*, xviii, 221.)

Dose, thirty to sixty grains (2–3.9 Gm.).

Off. Prep.—Fluidextractum Sarsaparillæ, *U. S.* (*Br.*); Fluidextractum Sarsaparillæ Compositum, *U. S.*; Syrupus Sarsaparillæ Compositus, *U. S.* (from fluidextract); Decoctum Sarsaparillæ Compositum, *N. F.*

SASSAFRAS. U. S.

SASSAFRAS Sassaf.

(săs'sa-frăs)

"The bark of the root of *Sassafras variifolium* (Salisbury) O. Kuntze (Fam. *Lauraceæ*), without the presence or admixture of more than 2 per cent. of adhering wood, collected in the early spring or autumn, deprived of the outer corky layer and dried." *U. S.*

Sassafras Radix, *Br.*; Sassafras Bark, Sassafrax; Sassafras, *Fr. Cod., G.*; Sassafrasso, *It.*; Sasafras (Leño de), *Sp.*

Sassafras is an indigenous tree, of medium size, rising in favorable situations to a height of 35 feet. The bark of the stem and large branches is rough, deeply furrowed, and grayish; that of the extreme branches or twigs is smooth and beautifully green. The leaves, which are alternate, petiolate, and downy when young, vary much in their form and size even upon the same tree. Some are oval and entire, others have a lobe on one side, but the greater number are three-lobed. The flowers, which appear before the leaves, are small, of a pale greenish-yellow color, and disposed in racemes which arise from the branches below the leaves and have linear bracts at their base. The fruit is an oval drupe, about as large as a pea, of a deep blue color when ripe, and supported on a red pedicel, enlarged at the extremity into a cup for its reception. For the microscopical character of the root and bark, see E. S. Bastin, *A. J. P.*, June, 1895. See also *Ph. Rev.*, 1899, 450.

The sassafras is common throughout the eastern United States, and extends into Mexico. The fresh flowers have a slightly fragrant odor, and almost all parts of the plant are more or less aromatic. The best time for collecting the pith is after the occurrence of frost in autumn, and the same is the case also with the bark of the root.

Bark of Sassafras Root.—As found in commerce, this is usually in small irregular fragments, sometimes invested with a brownish cork, sometimes partially or wholly freed from it, of a reddish or rusty cinnamon hue, very brittle, and presenting when freshly broken a lighter color than that of the exposed surfaces. The living bark is nearly white, but becomes colored, on exposure, immediately after collection. It is officially described as "in irregularly transversely curved or quilled pieces, from 1 to 15 cm. in length and from 1 to 4 mm. in thickness; outer surface orange-brown, nearly smooth and marked with more or less irregular ridges; inner surface light to dark reddish-

brown, obscurely short-striate; fracture short with a thin reddish-brown corky layer and a yellowish-white inner bark; odor aromatic; taste slightly mucilaginous, astringent, aromatic and somewhat pungent. The powder is light reddish-brown; when examined under the microscope it exhibits numerous starch grains and prominent, characteristic bast-fibers; starch grains either single or 2- to 4-compound, the individual grains being more or less spherical or polygonal and frequently with a distinct cleft, from 0.003 to 0.02 mm. in diameter, some of the swollen or altered grains attaining a diameter of 0.03 mm.; bast-fibers spindle-shaped, occasionally very irregular in outline, with sharply pointed ends, from 0.15 to 0.4 mm. in length, about 0.025 mm. in diameter, and with very thick, strongly lignified walls, the lumina being frequently nearly obliterated; parenchyma cells containing either starch grains or irregular yellowish-red masses of tannin and becoming bluish-black upon the addition of ferric chloride T.S.; fragments of wood few, with large, thin-walled tracheæ marked by simple pores and associated with rather thin-walled wood-fibers. Sassafras yields not more than 30 per cent. of ash." *U. S.*

According to Reinsch, the bark contains a heavy and light volatile oil, camphorous matter, fatty matter, resin, wax, a peculiar decomposition product of tannic acid called *sassafrid*, tannic acid, gum, albumen, starch, lignin, and salts. (See *Oleum Sassafras*, page 790.) The sassafrid bears some analogy to cinchonic red, and, like it, appears to be a derivative of the tannin, which exists in much larger proportion in the fresh bark than in that long kept. (Procter, *A. J. P.*, 1866, p. 490.) Owing to its volatile oil and tannic acid, the bark of sassafras root is an aromatic stimulant and astringent. It is used almost exclusively as an adjuvant to other more efficient medicines, the flavor of which it improves, while it renders them more acceptable to the stomach. The volatile oil may be used as an aromatic. In overdoses it is capable of producing marked narcotic poisoning, and it is said to act upon the lower animals as a narcotic. John Bartlett has reported several cases in which its use apparently caused abortion.

Sassafras Pith (*Sassafras medulla*) was recognized by the U. S. VIII, and is at present included in the N. F. IV. It occurs in "subcylindrical, often curved or coiled pieces, from 2 to 10 cm. in length and from 2 to 5 mm. in diameter; very light in weight; externally whitish, occasionally with small fragments of adhering wood; fracture short. Odor slight; sassafras-like; taste mucilaginous. When examined under the microscope, transverse sections of Sassafras Pith, mounted in phloroglucinol T.S. and hydrochloric acid, show nearly isodiametric cells with large intercellular spaces, the walls being more or less lignified and provided with numerous simple pores; mounts made in water show the separation of a thin layer of mucilage from the inner walls of the cells, characterized by the gradual disappearance of the pores. Macerate 0.5 Gm. of Sassafras Pith with 25 mils of cold distilled water for several hours and filter it through purified cotton; a mucilaginous solution is obtained which does not give a precipitate upon the addition of an equal volume of alcohol." *N. F.*

It abounds in a gummy matter, which it readily imparts to water, forming a limpid mucilage, which is not precipitated by alcohol, but has much less tenacity than that of gum arabic and will not answer as a substitute in the suspension of insoluble substances. This mucilage is much employed as a soothing application in inflammation of the eyes, and forms an agreeable and useful drink in *dysenteric, catarrhal,* and *nephritic* diseases. It may be prepared by adding a drachm of the pith to a pint of boiling water.

Dose, of sassafras bark, one to two drachms (3.9–7.7 Gm.).

SCAMMONIÆ RADIX. U. S., Br.

SCAMMONY ROOT Scam. Rad.

(scăm-mō'nī-æ rā'dĭx)

"The dried root of *Convolvulus Scammonia* Linné (Fam. *Convolvulaceæ*), yielding not less than 8 per cent. of the total resins of Scammony Root." *U. S.* "Scammony Root is the dried root of Convolvulus Scammonia, *Linn.*" *Br.*

As the resin of scammony is obtained in Oriental countries by a somewhat tedious process, it has been very difficult to obtain sufficient quantities of the genuine article for use in medicine. The British Pharmacopœia long ago solved the question by making official *scammony root* from which the resin is prepared. The U. S. P. IX following this precedent and for the same reason has introduced scammony root. There seems to be little doubt, however, that the natural exudation has properties which make it a more desirable medicine than the extracted resin. (*C. D.*, lxix, p. 864.) On the other hand, the therapeutic committee of the British Medical Association states that the natural exudation possesses no advantages over the resin. (*P. J.*, 1908, xxvii, p. 811.) Heuisler states that the extracted resin of true scammony root as well as the resin obtained from Mexican scammony (*Ipomœa Orizabensis*) are sold for "virgin" scammony. (*Proc. Md. Ph. Assoc.*, 1908, p. 35.)

Scammony root is officially described as follows: "Cylindrical or somewhat tapering, from 10 to 25 cm. in length and from 1 to 4.5 cm. in thickness; externally grayish- to reddish-brown; usually distinctly twisted, deeply longitudinally furrowed, marked by distinct root-scars, otherwise nearly smooth except for the lenticels and abraded cork, the upper portion terminated usually by a number of short stem branches; hard and heavy; fracture tough, irregular with projecting wood-fibers; internally somewhat mottled, showing yellowish, porous wood-wedges separated by whitish parenchyma containing starch and resin, bark thin; odor slight, re-

sembling that of jalap; taste very slightly sweet, becoming slightly acrid. Under the microscope, sections of Scammony Root show a corky layer consisting of from 2 to 10 rows of cells with thin, yellowish-brown lignified walls; an outer cortex with numerous stone cells occurring singly or in small groups, the walls being moderately thick, porous and not strongly lignified; parenchyma with numerous starch grains and monoclinic prisms of calcium oxalate; fibro-vascular bundles numerous, circular or elliptical with a well developed wood consisting of large tracheæ surrounded by slightly lignified wood-fibers; phloem or sieve prominent in which are included large resin ducts; the parenchyma, both in and surrounding the bundles, more or less collapsed and containing either starch or calcium oxalate crystals. The powder is light grayish-brown; when examined under the microscope it exhibits starch grains from 0.003 to 0.018 mm. in diameter, mostly single, occasionally 2- to 4-compound, the grains showing occasionally a central cleft; calcium oxalate crystals numerous, in monoclinic prisms from 0.01 to 0.045 mm. in length; fragments of leptomes or sieve with accompanying yellowish-brown resin cells; tracheæ mostly with reticulate thickenings and simple or bordered pores and associated with short wood-fibers having prominent oblique pores; stone cells of variable shape and varying from 0.04 to 0.11 mm. in length, the walls being from 0.006 to 0.012 mm. in thickness, slightly lignified and traversed with prominent, often branching pores; lignified cork cells relatively few.

"**Assay.**—Proceed as directed under *Jalapa*, using 10 Gm. of Scammony Root in No. 60 powder." *U. S.*

"Brownish-grey or yellowish-grey, tapering or nearly cylindrical, varying usually from two to eight centimetres, or more, in diameter. Frequently contorted and longitudinally furrowed; enlarged at the crown, and bearing the remains of slender aerial stems. Fracture very coarsely fibrous; internally light or dark grey. In transverse section, numerous rounded wood-bundles distributed throughout a paler ground-tissue in which dark resin cells can be distinguished with a lens; in the parenchymatous tissue abundant, characteristic starch grains. Characteristic odor; taste at first somewhat sweet, afterwards slightly acrid. Yields to *alcohol* (90 per cent.) a resin which has the properties described under 'Scammoniæ Resina.'" *Br.*

The wood consists of compressed pale brown, coarsely porous, usually subdivided fibers in a parenchymatous tissue similar to the bark. For microscopic structure, see *Dragendorff's Jahresbericht*, 1875.

The root of the *male jalap* (*orizaba root, Mexican scammony, Purgo macho*) has recently largely replaced in commerce the scammony root on account of its containing a much larger percentage of resin chemically indistinguishable from that of scammony. The Levant or true scammony root, it is said, averages a little under 9 per cent. of resin, while the Mexican root usually yields over 15 per cent. Male jalap occurs in transverse pieces one-half to an inch in thickness and two to four inches in diameter or in the case of the smaller roots in pieces three or four inches long sometimes obliquely cut, the transverse slices show concentric rings with protruding coarse fibers which at once distinguishes it from the true scammony in which the vascular bundles are scattered.

Large quantities of a false scammony root of unknown botanical origin have appeared in the London market. The root is 2 to 3 inches in diameter with a thin, brittle, blackish-brown bark, and on transverse section six or seven rings of wood. It is odorless and tasteless. (See *P. J.*, May, 1901, 596.)

Mexican Scammony Root.—Mexican scammony root has been identified by E. M. Holmes as being undoubtedly the root of *Ipomœa orizabensis*, and is described as follows: The appearance is quite characteristic and quite different from that of scammony root. It occurs mostly in transverse slices, showing concentric rings, from which coarse fibers protrude on both of the transverse surfaces. The sections are mostly those of the larger portion of the root, and vary from two to three inches or more in diameter, but are only about one-half to three-quarter inch in thickness. The smaller roots are about one inch or so in diameter, but are frequently three or four inches long; a few pieces are obliquely cut. The concentric arrangement of the vascular bundles at once distinguishes it from the root of *Convolvulus Scammonia*, in which they are scattered and somewhat rounded, forming isolated strands, in the softer tissue. It appears that during 1903 there was an importation of over 3000 bags, which sold readily to the German makers of scammony resin. Analyses made showed from 6.4 to 22.2 per cent. of resin, but most of it yielded about 17 per cent. While chemically there appears to be no difference between scammony resin and the resin of *Ipomœa orizabensis*, it remains to be ascertained if they are identical in their physiological action. At the request of Holmes, Harold Dean determined the amount of resin in a specimen and, in a separate paper, gives the method employed and the results, as follows: The drug was powdered, exhausted by percolation with alcohol (90 per cent.), the greater part of the alcohol distilled off, and the resulting strong tincture poured into three times its volume of water. The resin separated as a mass of honey-like consistence. It was well washed with boiling water until the washings were free from sugar and from color, and then dried on a water bath until the weight was constant. The yield of resin amounted to 18.5 Gm. from 100 Gm. of the powdered drug; this is the highest percentage yet recorded from this source. The dried resin was pale brown, and almost entirely soluble in ether, the insoluble portion from 18.5 Gm. weighing less than 0.25 Gm. It had the general characteristics of scammony resin. The powdered drug, dried at

100° C. (212° F.), yielded 9.89 per cent. of ash. (*P. J.*, March 5, 1904, 226, 327.)

Uses.—Scammony root in substance is not used medicinally, but solely for making resin of scammony.

Off. Prep.—Resina Scammoniæ, *U. S.* (*Br.*); Tinctura Jalapæ Composita (from Resin), *Br.*; Pilulæ Aloes, Hydrargyri et Scammonii Composita (from Resin), *N. F.*; Pilulæ Colocynthidis Compositæ (from Resin), *N. F.*; Pilulæ Coloeynthidis et Hyoscyami (from Resin), *N. F.*; Tinctura Jalapæ Composita (from Resin), *N. F.*

SCILLA. U. S., Br.

SQUILL Scill.

(sçĭl'lą)

"The fleshy, inner scales of the bulb of the white variety of *Urginea maritima* (Linné) Baker (Fam. *Liliaceæ*), cut into pieces and carefully dried. Preserve Squill in tightly-closed containers, in a dry place. If made into the official tincture and assayed biologically, the minimum lethal dose should not be greater than 0.006 mil of tincture, or the equivalent in tincture of 0.0000005 Gm. of ouabain, for each gramme of body-weight of frog." *U. S.*

"Squill is the bulb of Urginea Scilla, *Steinh.*, divested of its dry membranous outer scales, cut into slices, and dried. When powdered should be kept quite dry over quicklime." *Br.*

Squills; Scille, *Fr. Cod.*; Bulbus Scillæ, *P. G.*; Meerzwiebel, *G.*; Scilla, *It.*; Escila (Bulbo de), Cebolla albarrana, *Sp.*

Urginea maritima (*Urginea Scilla* Steinh.) is a perennial plant, with fibrous roots proceeding from the bottom of a large bulb, which sends forth several long, lanceolate, pointed, somewhat undulated, shining, deep-green leaves. From the midst of the leaves a round, smooth, succulent flower-stem rises, from one to three feet high, terminating in a long, close spike of whitish flowers. These are destitute of calyx, and stand on purplish peduncles, at the base of each of which is a linear, twisted, deciduous floral leaf. The squill grows on the sea coast of Spain, France, Italy, Greece, and the other countries bordering on the Mediterranean. The bulb is the official portion. It is generally dried for use, but is sometimes imported in the recent state packed in sand.

Properties.—The fresh bulb is pear-shaped, from 15 to 30 cm. in diameter, weighing as much as 5 or 6 pounds, and consists of fleshy scales attenuated at their edges, closely applied over each other, and invested by exterior scales so thin and dry as to appear to constitute a membranous coat. There are two varieties, distinguished as the *red* and the *white squill*. In the former the exterior coating is of a deep reddish-brown color, and the inner scales have a whitish rosy or very light pink epidermis, with a yellowish-white parenchyma; in the latter the whole bulb is white. They do not differ in medicinal virtue. The bulb abounds in a viscid, very acrid juice, which causes it to inflame and even excoriate the skin when much handled. By drying, this acrimony is very much diminished, with little loss of medicinal power. The bulb loses about four-fifths of its weight in the process. Vogel found 100 parts of fresh squill to be reduced to 18 by desiccation. The process is somewhat difficult, in consequence of the mucilaginous character of the juice. The bulb is cut into thin transverse slices, and the pieces dried separately by artificial or solar heat. The outer and central scales are rejected, the former being dry and destitute of activity, the latter too fleshy and mucilaginous.

Dried squill, as found in commerce, is "in irregular, more or less curved, somewhat flattened pieces, from 0.5 to 5 cm. in length, yellowish-white, somewhat translucent, nearly smooth and lustrous with slight projections of fibro-vascular bundles; brittle when dry and somewhat flexible when damp; odor slight; taste bitter and acrid. Under the microscope, sections of the scales of Squill show on the upper and lower surface a thin-walled epidermal layer, a mesophyll of nearly isodiametric or slightly elongated thin-walled cells and occasionally show in alcoholic or glycerin mounts spheroidal aggregates of a carbohydrate; numerous more or less rectangular cells containing mucilage and bundles of raphides of calcium oxalate, the latter from 0.075 to 1.0 mm. in length; fibro-vascular bundles few and isolated, with spiral or reticulate tracheæ. Occasionally some of the parenchyma cells contain a few somewhat spherical starch grains. The powder is light yellow, with a tendency to cake in moist atmosphere and consisting of very irregular fragments; when examined under the microscope it exhibits numerous single crystals and bundles of long raphides of calcium oxalate; fragments of thin-walled, colorless parenchyma, frequently with dark intercellular spaces due to the inclusion of air; fragments with spiral or reticulate tracheæ are occasionally found. Squill yields not more than 8 per cent. of ash.

Examined by the microscope, the bulb is seen to be pervaded by innumerable minute acicular crystals of calcium oxalate. According to Hartwich, the mucilage occurs either in the form of large drops, filling the parenchymatous cells, or as masses enclosing the raphides. For an elaborate microscopic study, with plates, see *A. Pharm.*, July, 1889. Water distilled from it had neither taste nor odor, and was drunk by Vogel to the amount of six ounces without effect. When kept in a dry place, squill retains its virtues for a long time; but if exposed to moisture it soon becomes mouldy.

"**Assay.**—For a method for assaying Squill see Biological Assays (Part III)." *U. S.*

"In curved, yellowish-white, somewhat translucent strips, from about two and a half to five centimetres long, frequently tapering towards both ends; tough and slightly flexible while moist, but brittle and easily pulverisable when dry. Almost inodorous; taste disagreeably bitter. Ash not more than 5 per cent." *Br.*

The virtues of squill are extracted by alcohol, but apparently only in part by water. It has been analyzed by Vogel, J. H. Marais, Lebourdais, Tilloy, Merck, and by Schmiedeberg (*Zeit. Physiol. Chem.*, 111, 112) with varying results. The bitter principle, not yet obtained pure, is *scillitin*. Merck, however, obtained three compounds of this class—*scillipicrin*, *scillitoxin*, and *scillin*. Jarmersted (*A. E. P. P.*, 11, 22) obtained a glucoside which he called *scillain*, but which seems to be identical with scillitoxin.

Ewins (*J. P. and Ex. T.*, 1912, ii, p. 155) separated from the squill two active principles, although neither of them in crystallizable form. The first is water soluble glucoside, which is fatal to the frog in doses of 0.03 Gm. for a 25 gramme frog. The second is a resinous body, very slightly soluble in water, but readily so in alcohol. Fatal dose for a frog is 0.06. Besides these they found a trace of caffeine. These authors state and it is generally acknowledged that the so-called active principles of squill which are found upon the market are not true principles but are impure bodies.

Schmiedeberg found a peculiar mucilage, analogous to dextrin, which he calls *sinistrin*, $(C_6H_{10}O_5)_n$. It is white, easily soluble in water, insoluble in alcohol, lævo-rotatory; on boiling with dilute sulphuric acid it yields levulose and an inactive sugar of reducing properties. The mucilage is not affected by saliva or diastase. This last statement, however, was contradicted by F. Kurtz (*A. J. P.*, 1894, 246), who says that diastase acts upon it, producing a reducing sugar. Kurtz also obtained a reducing sugar (probably dextrose) along with the gum direct by extracting the bulb with hot alcohol. S. Wanizewski (*A. J. P.*, 1893, 498) found *scillinine*, soluble in alcohol, but insoluble in water and in chloroform; *scillapicrine*, soluble in both water and alcohol, and *scillamarine*, soluble in both chloroform and alcohol. The bulbs of *Scilla maritima* also yield a slightly colored liquid oil of unpleasant odor when distilled in a current of steam. (*Husemann's Pflanzenstoffe*, 2d ed., p. 406.)

Uses.—Squill belongs to that series of drugs, commonly known as the digitalis group, which have for their characteristic properties the power of slowing and strengthening the pulse, of contracting the blood vessels, and in toxic doses causing systolic spasm of the frog's heart. (See *Digitalis*, p. 408.) While it in many regards closely resembles digitalis in its physiological action, it is notable for the strong degree of vasomotor action and for its local irritant effect. Probably by virtue of its effects on the circulation, but also largely because of its local irritant action upon the renal epithelium, squill is one of the most active diuretics among this group of drugs. Indeed it is so stimulating to the kidney that in overdose it is capable of causing an acute inflammation of this organ. When given in large dose, partly because of the central emetic effect which is characteristic of the digitalis group, but largely because of its local irritant influence upon the stomach, it produces severe nausea and even vomiting. In overdoses it has been known to cause hypercatharsis, strangury, bloody urine, and fatal inflammation of the stomach and bowels.

While squill is capable of exercising all the beneficial effects of digitalis in chronic *heart disease*, because of its action upon the alimentary canal it is rarely employed for this condition unless associated with *dropsy*. Because of its stimulant action upon the kidney as well as upon the heart, it is peculiarly useful for the evacuation of edematous infusions due to weakness of the heart, and is also sometimes of service in the ascites of *hepatic cirrhosis*. When, however, there is active inflammation of the kidney it must be used with great caution if at all. Like other emetic drugs, if given in sufficient doses to nauseate it tends to increase in the bronchial secretions and is occasionally used as an expectorant in *bronchitis* and *spasmodic croup*. Because of its potent action upon the circulation its use for this purpose, however, is not to be encouraged.

Neither water nor dilute acetic acid entirely extract the activity of squill. The only liquid preparations, therefore, which thoroughly represent the drug are those made with alcohol, of which the tincture is probably the better.

When given in substance it is most conveniently administered in the form of pill.

Dose, of squill, from one to two grains (0.065–0.13 Gm.).

Off. Prep.—Acetum Scillæ, *U. S., Br.;* Fluidextractum Scillæ, *U. S.;* Oxymel Scillæ, *Br.;* Pilula Ipecacuanhæ cum Scilla, *Br.;* Pilula Scillæ Composita, *Br.;* Syrupus Scillæ, *U. S., Br.* (from vinegar); Syrupus Scillæ Compositus, *U. S.* (from fluidextract); Tinctura Scillæ, *U. S., Br.;* Mistura Pectoralis Stokes (from Fluidextract), *N. F.;* Oxymel Scillæ (from Vinegar), *N. F.;* Pilulæ Digitalis, Scillæ et Hydrargyri, *N. F.*

SCOPARII CACUMINA. Br.

BROOM TOPS

(scō-pā'rī-ī că-cū'mĭ-nă)

"Broom Tops are the fresh and the dried tops of Cytisus scoparius, *Link*." *Br.* "The dried top of *Cytisus Scoparius* (Linné) Link (Fam. *Leguminosæ*)." *N. F.*

Scoparius, *N. F.*; Herba Scoparii, Spartium; **Irish or Scotch Broom**, Besom, Genêt à balais, *Fr.*; Gemeine Besenginster, Besenginster, Besenkraut, Pfriemenkraut, *G.*

Cytisus scoparius is a common European shrub, cultivated as a sand-binder and locally naturalized on the Atlantic Coast from Nantucket to Virginia. It is a low, densely branched shrub, from three to eight feet high, with numerous straight, pentangular, bright green, very flexible branches, and small, oblong, glabrous leaves, usually ternate, but on the upper part of the plant sometimes simple. The flowers are numerous, papilionaceous, large, showy, of a golden-yellow color, and solitary upon short

axillary peduncles. The seeds are contained in a compressed legume, which is hairy at the sutures. It is essential that true broom be carefully distinguished from *Spanish broom* (*Spartium Junceum*), since a number of cases of poisoning have occurred from the substitution of the dried flowers of Spartium for those of broom. (See Part II.)

The whole plant has a bitter, nauseous taste, and, when bruised, a strong, peculiar odor. The tops of the branches are used in medicine. They are in "thin, flexible, branched twigs, from 2 to 3 mm. in thickness, five-angled; externally dark green, nearly glabrous, with numerous reddish-brown cork patches; internally yellowish, fracture short-fibrous, that of thicker pieces tough and splintery, upper leaves sessile, with often only one obovate leaflet present in small amount or absent. Odor slight, on bruising more distinct and peculiar; taste disagreeable, bitter. Scoparius yields not more than 5 per cent. of ash." *N. F. IV.*

"Stem dark green, with long, straight, slender, alternate branches; the latter, like the upper part of the stem, winged, tough, flexible, and glabrous. Leaves, when present, small, sessile, and simple above, stalked and trifoliate below. Odor of the fresh tops, especially when bruised, characteristic; the dry tops almost inodorous." *Br.*

The seeds are reported to be used sometimes, and to be as active as the tops. Water and alcohol extract their active properties. According to Cadet de Gassicourt, the flowers contain volatile oil, fatty matter, wax, chlorophyll, yellow coloring matter, tannin, a sweet substance, mucilage, albumen, and lignin. Stenhouse has separated from them two principles, *scoparin,* $C_{21}H_{22}O_{10}$ (Goldschmidt and Himmelmayer (*Ap. Ztg.,* 1893, 566) give the following formula of scoparin: $C_{10}H_{16}O_8(OH)(OCH_3)$), and an alkaloid, *sparteine,* $C_{15}H_{26}N_2$. The former is in stellate crystals, easily dissolved by boiling water and alcohol, and is obtained by purifying a yellow gelatinous substance deposited upon the evaporation of the decoction. It is only slightly soluble in cold water, more readily in hot water with greenish light yellow color, easily soluble in aqueous ammonia and caustic and carbonated alkalies. It is decomposed by heat. When fused with potassium hydroxide it yields, according to Hlasiwetz, phloroglucin and protocatechuic acid. Sparteine was obtained by distillation from the mother waters of the scoparin. It is a colorless liquid, having a peculiar bitter taste, and all the properties of a volatile alkaloid. It is heavier than water, and boils at 288° C. (550.4° F.) if distilled in a current of hydrogen gas. It dissolves only slightly in water, but takes up some water itself. In contact with water it becomes opalescent. It turns yellowish on distillation in air, but can be distilled colorless in an atmosphere of carbon dioxide. It is colorless, but becomes brown by exposure to light; it has at first an odor of aniline, but this is altered by rectification. It readily neutralizes acids and forms crystallizable salts, which are extremely bitter. Its sulphate occurs in colorless crystals, and is freely soluble in water. (See *P. J.,* June 28, 1879; also *Sparteinæ Sulphas.*) By the action of potassium dichromate and sulphuric acid, *oxysparteine,* $C_{15}H_{24}N_2O$, is formed, and by the action of hydrogen dioxide upon this, a deliquescent *trioxysparteine,* $C_{15}H_{24}N_2O_3$, is obtained; if the hydrogen dioxide acts upon sparteine itself, *dioxysparteine,* $C_{15}H_{24}N_2O_2$, is formed as a solid, crystallizing in prisms melting at 128.5° C. (263.3° F.). Zinc and hydrochloric acid reduce sparteine to *hydrosparteine,* $C_{15}H_{28}N_2$, a thick liquid boiling at from 281° to 284° C. (537.8°–543.2° F.). (Schmidt, *Pharmaceutische Chemie,* 3te Auf., Bd. ii, 1276.)

Uses.—Scoparius is diuretic and cathartic, and in large doses emetic, and has been employed with advantage in *dropsy.* Cullen prescribed it in the form of decoction, made by boiling half an ounce of the fresh tops in a pint of water down to half a pint, of which he gave a fluidounce (30 mils) every hour until it operated by stool or urine. The seeds may be given in powder, in the dose of from ten to fifteen grains (0.65–1.0 Gm.). A fluidextract is official in the N. F. IV (see Part III).

Scoparin probably represents the diuretic and purgative influences of scoparius, although its physiological and therapeutic properties have not as yet been sufficiently investigated. For description of the effects of *sparteine,* see *Sparteinæ Sulphas.*

Oxysparteine, $C_{15}H_{24}N_2O$.—This is an alkaloidal oxidation product of sparteine, originally described by F. Ahrens (*Ber. d. Chem. Ges.,* 1891). It occurs in white, somewhat hygroscopic needles, melting at about 84° C. (183.2° F.), soluble in water, alcohol, ether, and chloroform. It has been found by Hurthle(*A. E. P. P.,* 1892) to be a cardiac stimulant, decreasing the pulse rate, but markedly increasing the arterial pressure and heart work. The hydrochloride, which occurs in large needles (often consolidated together) and is very soluble in water, has been used hypodermically by von Oefele in cases of *heart failure.* The dose is half a grain (0.032 Gm.), rapidly increased to one and a half grains (0.096 Gm.). The system is said soon to become accustomed to it.

Dose, of scoparius, ten to fifteen grains (0.65–1.0 Gm.).

Off. Prep.—Infusum Scoparii, *Br.;* Succus Scoparii, *Br.*

SCOPOLAMINÆ HYDROBROMIDUM. U. S. (Br.)

SCOPOLAMINE HYDROBROMIDE Scopolamin. Hydrobrom. [Scopolamine Bromide]

(skō-pō-lą-mĭ'næ hȳ-drō-brō'mĭ-dŭm)

"The hydrobromide [$C_{17}H_{21}O_4NHBr + 3H_2O = 438.15$] of lævorotatory scopolamine, also known as hyoscine, obtained from various plants of the *Solanaceæ.* Preserve it in well-closed

containers, protected from light." *U. S.* "Hyoscine Hydrobromide, $C_{17}H_{21}NO_4$, HBr,$3H_2O$, is the hydrobromide of an alkaloid, hyoscine or scopolamine, obtained from various plants of the natural order Solanaceæ." *Br.*

Hyoscinæ Hydrobromidum, *Br., U. S., VIII;* Hyoscine Hydrobromide; Bromhydrate d'Hyoscine, *Fr.;* Scopolaminum hydrobromicum, *P. G.;* Skopolaminhydrobromid, *G.;* Hyoscinum Hydrobromicum; Hydrobromate of Hyoscine, Scopolamine Hydrobromide; Bromhydrate d'Hyoscine, *Fr.;* Hyoscinhydrobromid, Bromwasserstoffsaures Hyoscin, *G.*

Scopolamine, $C_{17}H_{21}O_4N$, is found in the leaves and seeds of *Hyoscyamus niger, Duboisia myoporoides, Scopola japonica, Atropa Belladonna* and other solanaceous plants. When pure, it forms a syrupy liquid. The best salt for practical use is the hydrobromide, which is in "colorless, transparent, rhombic crystals, sometimes of large size; odorless; slightly efflorescent. *Great caution must be used in tasting it, and then only in dilute solutions.* One Gm. of Scopolamine Hydrobromide dissolves in 1.5 mils of water and in 20 mils of alcohol at 25° C. (77° F.); slightly soluble in chloroform; insoluble in ether. Its aqueous solution (1 in 20) is neutral or at most only slightly acid to litmus. When anhydrous it melts between 190° and 192° C. (374° and 377.6° F.). The specific rotatory power of the salt, determined in an aqueous solution containing the equivalent of 5 Gm. of anhydrous Scopolamine Hydrobromide in 100 mils of solution at 25° C. (77° F.), is from −22° to −25.75° in a 100 mm. tube (see Part III, Test No. 21). Add about 0.01 Gm. of the salt to 5 drops of nitric acid and evaporate it to dryness in a porcelain dish on a water bath; the residue yields a violet color upon the addition of alcoholic potassium hydroxide T.S. Silver nitrate T.S. produces in the aqueous solution of the salt a yellowish-white precipitate insoluble in nitric acid. Shake 2 mils of chloroform with 1 mil of an aqueous solution of the salt (1 in 20) to which a few drops of chlorine water have been added; the chloroform assumes a brownish color. When dried to constant weight at 100° C. (212° F.) it loses not more than 13 per cent. of its weight. It also loses its water of crystallization slowly over sulphuric acid. No weighable ash remains on incinerating 0.1 Gm. of Scopolamine Hydrobromide. The addition of a few drops of ammonia water T.S. to 1 mil of an aqueous solution of the salt (1 in 20) causes no turbidity; the addition of potassium hydroxide T.S. to another portion of 1 mil of the aqueous solution causes only a whitish, transient turbidity (*foreign alkaloids*). Add 0.05 mil of tenth-normal potassium permanganate V.S. to 15 mils of an aqueous solution of the salt (1 in 100); the solution is not completely decolorized within five minutes (*apoatropine*). The solution of about 0.1 Gm. of the salt in 1 mil of sulphuric acid is not more than faintly yellow (*carbonizable impurities*). Add a drop of nitric acid to this solution; an orange color is produced, due to the liberation of bromine, but no deep red color fading to orange is noticeable (*morphine*)." *U. S.*

"Small, colorless, transparent, non-deliquescent rhombic crystals. Soluble in 4 parts of *water.* Loses about 12 per cent. of its weight when dried at 100° C. (212° F.). Yields the *reactions* characteristic of bromides. An aqueous solution (5 in 100) yields with *solution of sodium hydroxide* a white precipitate soluble in excess of the reagent, but no precipitate with *solution of ammonia.* The alkaloid removed from the ammoniacal solution by shaking with *chloroform,* separating and evaporating the chloroformic solution, when dissolved in *diluted hydrochloric acid,* yields with *solution of auric chloride* a yellow precipitate, which, recrystallised from *water* acidified with *hydrochloric acid* and dried, melts at 198° to 200° C. (388.4°–392° F.). Treated with *nitric acid* as described under 'Atropina' a violet color is developed. No appreciable ash." *Br.*

E. Schmidt (*Ap. Ztg.,* 1891, 522) believes that the hyoscine hydrobromide of commerce is essentially hydrobromide of *scopolamine,* $C_{17}H_{21}NO_4$. This view has been confirmed by O. Hesse (*Ann. Ch. Ph.,* 1893, 304), and the British Pharmacopœia defines hyoscine as an alkaloid contained in different solanaceous plants, while the German Pharmacopœia changed the title to "Scopolaminum Hydrobromicum." The U. S. Pharmacopœia (8th Rev.) introduced Scopolaminæ Hydrobromidum as a separate title, but referred to Hyoscinæ Hydrobromidum for the description and tests, declaring them to be identical substances. *Atroscine,* an optically inert isomer of scopolamine, was found by Hesse in variable amount in the hyoscine hydrobromide of commerce. For further information on the chemistry of solanaceous alkaloids, see *Belladonnæ Radix,* p. 221.

Uses.—The older investigations into the effects of scopolamine upon the bodily functions are in many regards confusingly contradictory because of the failure to realize the difference in the physiological effects of *racemic* and *lævo-scopolamine.* While these two varieties of the alkaloid possess qualitatively the same physiological properties their actions are quantitatively so different that it is not to be wondered that different pharmacologists obtain such varying results. Lævo-scopolamine (the variety recognized by the U. S. P.) is paralyzant to the peripheral ends of the so-called autonomic nerves acting in this regard precisely like atropine, although less powerful. By virtue of this action it dilates the pupil, causes dryness of the throat and of the skin, accelerates the heart's action, etc. It differs strikingly from atropine however, in that it is not stimulant to the medullary centers and therefore does not increase the respiration nor elevate the blood pressure; and also in that it appears to act frequently as a cerebral depressant and tends to promote sleep. In some persons this sleep which it produces is interrupted or attended with a kind of low muttering delirium, recalling the mental confusion of atropine poisoning. A striking feature of the effects of large doses of scopolamine is the loss of memory for events which happened while under its influence. It has slight

analgesic properties, but according to the researches of Hauchold (*Z. E. P. T.*, 1910, vii, p. 743) greatly enhances the effect of other narcotics such as morphine or urethane. In large dose it is depressant to the respiratory center and apparently also in some degree to the motor ganglia of the spinal cord. The racemic scopolamine—sometimes known as atroscine—according to the studies of Cushny (*A. E. P. P.*, 1912, lxx, p. 433), differs from the optically active alkaloid only in being much less powerful in its effects upon the autonomic nerves. When locally applied it will cause dilatation of the pupil, but except in very large doses, it has no effect upon the pulse rate and scarcely any upon the secretions. Its action upon the central nervous system is about equal to that of the lævo-scopolamine.

The most important use of scopolamine is as a cerebral sedative. In ordinary *insomnias* it is usually much less efficient than the narcotics of the aliphatic group but is often useful as an adjuvant in the severer types of sleeplessness, such as seen in *delirium tremens*. In the *manias* it often acts most happily and in some cases even seems to exercise some curative influence. For the relief of *pain* it is rarely useful by itself, but may be advantageously combined with morphine. It is often of value as a symptomatic remedy in various forms of nervous excitement, such as is seen in *hysteria* or *neurasthenia*. It is probably its action upon the intellectual centers which make it so useful a drug in the treatment of *alcoholic* and other *drug habits*.

In a variety of other conditions of nervous excitement scopolamine has been found clinically useful, although its mode of action is not always clear, thus in *epilepsy*, while by itself of little avail, it greatly increases the effects of bromides; in *paralysis agitans* it is one of the most valuable drugs we possess; it is also useful to allay *sexual excitement* as *nymphomania* and *spermatorrhea*, and Hotz (*D. M. W.*, 1908) reports good results even in *tetanus*. As a mydriatic it is much quicker and less permanent in its effects than atropine and is therefore often used to paralyze accommodation in correcting errors of refraction.

In 1900 Schneiderlin, under the misapprehension that scopolamine was stimulating to the respiratory center, and would therefore antagonize depressant effects of morphine, introduced the use of a combination of these alkaloids as a means of producing surgical anesthesia. Under the catchy name of "*Twilight Sleep*" this method of anesthesia has been used to a large extent not only for surgical operations, but in obstetrics, either by itself or as a preliminary to the use of chloroform or ether. As the sole means of producing unconsciousness for surgical operations the *scopolamine-morphine anesthesia* is certainly not to be recommended as a routine measure. Not only is the anesthesia unsatisfactory in a very large proportion of cases, but the method has given an extraordinarily high mortality. In 1906, H. C. Wood, Jr. (*Amer. Med.*, xii, p. 544), collected statistics of two thousand cases showing a mortality of 1 in 221 anesthesias, and Avarffi subsequently (*J. A. M. A.*, 1910, liv) in six thousand anesthesias found a mortality of 1 in 150. In obstetrical practice while it is difficult to estimate the relative danger to the mother, the danger to the child seems to be distinctly greater than after either chloroform or ether. Avarffi found in the reports of a thousand cases over 17 per cent. of embarrassed respiration in the new-born infant. The question, however, of whether the use of scopolamine as a preliminary to ether anesthesia is advantageous or not is, as yet, a matter of great difference of opinion. While it is undoubted that the quantity of ether under such circumstances is less than that ordinarily required, it is not certain whether the danger is consequently diminished or not.

The ordinary dose of scopolamine ranges from 1/200 to 1/100 of a grain and occasionally even somewhat more. Many persons, however, are excessively susceptible to its influence and even these quantities may cause toxic symptoms. While scopolamine poisoning very rarely ends fatally, the symptoms are often extremely alarming. There are marked disturbances of intellection, sometimes an active delirium resembling that of atropine poisoning and at others simply complete disorientation. Many cases present marked somnolence, but in others this may be lacking. At times the pupils are dilated, the pulse rate accelerated and there is dryness of the mouth with a peculiar husky character to the voice apparently due to laryngeal paralysis, but these symptoms are often absent or very mild, presumably dependent upon the variety of the alkaloid. The condition rarely requires active treatment but if there is serious embarrassment of the respiration strychnine may be used; it is usually better not to employ any drugs for the relief of the delirium, although if very active small doses of paraldehyde and bromides may be employed.

Dose, one-two-hundredth to one-eightieth of a grain (0.0003–0.0008 Gm.).

SENEGA. U. S. (Br.)

SENEGA Seneg. [Senega Snakeroot, Seneca Snakeroot]

(sĕn'ẹ-gạ)

"The dried roots of *Polygala Senega* Linné (Fam. *Polygalaceæ*), without the presence or admixture of more than 5 per cent. of stems and other foreign matter." *U. S.* "Senega Root is the dried root of Polygala Senega, *Linn.*" *Br.*

Senegæ Radix, *Br.*; Rattlesnake Root, Mountain Flax, Senega or Seneca Root, Radix Polygalæ Virginianæ; Polygala de Virginie, *Fr. Cod.*; Radix Senegæ, *P. G.*; Senegawurzel, Klapper-Schlangenwurzel, *G.*; Poligala Virginiana, *It.*; Poligala de virginia (Raiz de), *Sp.*

Besides *P. Senega*, two other species have attracted some attention in Europe—*P. amara* and *P. vulgaris*—as remedies in chronic pectoral affections; but, as they are not natives of this country, and are never used by practi-

tioners here, they do not merit particular notice.

A senega which was first used in Japan, and which has been referred by some writers to *P. japonica,* by others to *P. tenuifolia,* has been examined by Reuter, who finds in it 0.8 per cent. of resin, traces of methyl salicylate, and 8.8 per cent. of an oil which has somewhat the odor of patchouli. For description of other species of *Polygala* see Part II.

Polygala Senega has a perennial branching root, from which several erect, simple, smooth, round, leafy stems annually rise, from nine inches to a foot in height. The stems are occasionally tinged with red or purple below, but are green near the top. The leaves are alternate or scattered, lanceolate, pointed, smooth, bright green on the upper surface, paler beneath, and sessile or short petiolate. The flowers are small and white, and form a close spike at the summit of the stem. The calyx is their most conspicuous part. It consists of five sepals, two of which are wing-shaped, white, and larger than the others. The corolla is small and closed. The capsules are small, much compressed, obcordate, two-valved and two-locular, with two oblong-ovate, blackish, hairy seeds, slightly longer than the lobes of the caruncle. In *P. alba* Nutt, the seeds are silky and about twice the length of the caruncle lobes.

Polygala Senega extends over most of the United States and Southern Canada, east of the Rocky Mountains. At one time it was largely collected in Canada and the Northeastern Atlantic states; when this supply was exhausted, Kentucky and the States West and Southwest of it were invaded; then Wisconsin and the Northwestern States, from which with Western Canada the commerce at present derives its chief supply. There are two varieties of the plant, the typical *P. Senega,* the form found in the Northeastern United States, and the variety *latifolia* (T. and G.) which extends from Maryland and Pennsylvania to Michigan and Tennessee. This variety is distinguished by its height (from ten to twenty inches) and its very large, ovate or ovate-lanceolate leaves, which taper towards each end and attain a length of four inches. The root of commerce seems to be obtained from both varieties. It is brought into market in bales weighing from fifty to four hundred pounds. See True (*Ph. Era,* 1913, xlvi, p. 68).

Owing to the extensive use of senega considerable interest is manifested in the cultivation of the plant. Hood reports to have demonstrated that it can be successfully cultivated. (*Vermont Sta. Rept.,* 1907, p. 371.) It has also been grown by the Bureau of Plant Industry, U. S. Dept. of Agriculture.

Properties.—Senega is officially described as "usually in broken pieces; when entire slenderly conical, more or less tortuous, somewhat branched, from 3 to 15 cm. in length and from 2 to 10 mm. in thickness and bearing a few rootlets; crown knotty with numerous buds and short stem-bases; externally brownish-yellow, the crown rose-tinted, longitudinally wrinkled, frequently marked by a keel; fracture short, wood pale yellow, usually excentrically developed; odor peculiar, penetrating; taste sweetish, afterwards acrid. Under the microscope, transverse sections of Senega usually show a characteristic excentric development of wood, the central cylinder varying in outline from elliptical or ovate to irregularly fan-shaped, and being surrounded by an unevenly developed cortex which is thickest next to the broadest strands of wood and where the wood-wedges are narrow and the medullary rays very broad, the cortical parenchyma occupies a very narrow zone of the cross-section; in older roots a corky layer of from 4 to 5 rows of tangentially elongated, light yellowish or yellowish-brown cells; outer bark of about 20 rows of cells on one side of the root and only 10 or less on the other, the cells having slightly thickened walls and containing a colorless or pale yellow, amorphous substance, which is liberated in the form of large globules on the addition of a drop of potassium hydroxide T.S.; inner bark, the cells in radial rows, consisting of parenchyma, small groups of sieve tissue and medullary rays, the latter from 1 to 3 cells wide; all the cells in this zone show a collenchymatous thickening of the walls and contain an amorphous substance similar to that found in cells of the outer bark; woody layer of tracheæ with bordered pores, wood-fibers with oblique simple pores, tracheids, and medullary rays, the latter being rather indistinct and resembling the wood-fibers; tissues of the central layer of wood colored yellowish- or reddish-brown on the addition of a drop of potassium hydroxide T.S. The powder is yellowish-gray to light yellowish-brown, odor penetrating, slightly sternutatory; when examined under the microscope it exhibits a mixture of fragments of parenchyma containing oily globules and wood-fibers with tracheæ; wood-fibers, non-lignified and with oblique simple pores, from 0.175 to 0.25 mm. in length; tracheæ with simple and bordered pores and about 0.175 mm. in length; medullary ray cells somewhat lignified and with large simple pores. Extract 10 Gm. of powdered Senega by means of a Soxhlet apparatus, using 50 mils of ether containing 2 drops of hydrochloric acid. Continue the extraction during four or five hours and then add sufficient ether to make the liquid measure 50 mils. Take 25 mils of this solution and evaporate it on a water bath to dryness; the residue weighs not less than 0.3 Gm., and upon dissolving it in 10 mils of chloroform, transferring the solution to a test tube and adding 5 mils of sulphuric acid to form an underlying layer, a reddish-brown color is produced at the zone of contact, and the sulphuric acid shows a slightly green fluorescence after the mixture has stood for twenty-four hours. Pour 10 mils of the original ethereal solution into a beaker containing 10 mils of water and warm the mixture on a water bath until the ether has evaporated; the aqueous solution, upon filtering and adding a few drops of ferric chloride T.S.,

becomes a bright pinkish purple. Senega yields not more than 5 per cent. of ash." *U. S.*

"Greyish or brownish-yellow, slender, usually from five to ten centimetres long, with a knotty crown bearing the bases of numerous, slender, aerial stems; frequently curved or contorted, sparingly branched, keeled, sometimes transversely wrinkled. Fracture short. In transverse section, a horny translucent cortex free from starch grains and a white, often irregularly developed, wood. Characteristic odor; taste at first sweet, afterwards acrid." *Br.*

Holm describes the pharmacognosy of senega root and the morphology of the plant in *M. R.*, 1907, xvi, p. 155. Hartwich has made a very interesting observation in that he has found starch occasionally present in official senega. (*Apoth.-Ztg.*, xxvi, p. 84.) Hartwich has also described two false senegas. (*S. W. P.*, xlvi, pp. 537 and 749.) The pharmacognosy of the drug has been well elaborated by Tunmann in *Ph. Zentralh.*, xlix, p. 61. Muller describes and figures senega and a number of the drugs that have been used as adulterants of this drug or as occasional contaminations. (*Pharm. Praxis.*, vii, p. 309.)

Senega root varies somewhat in appearance according to the locality from which it is derived, and local varieties are recognized in commerce. In *Southern senega* the roots are very small, while in *Manitoba senega* they are large and thick, dark in color, and often have purple markings about the crown. The official senega is often known in commerce as *Southern senega,* or *small senega,* the roots seldom attaining the size of an ordinary lead-pencil, and four to five hundred of the dried roots being required to make a pound.

Since 1870 the so-called *Northern, White, False,* or *Large senega* has been sent into the American market from Wisconsin, Minnesota, and further west. It is much larger than true senega, probably eighty to one hundred to the pound. The knot at the top of the root is from one to three inches in diameter; below it the root abruptly contracts to from half an inch to an inch in diameter; it is usually from eight to ten inches long, more fleshy and much less contorted than true senega, nearly free from small rootlets, but breaking up below into from four to eight descending branches; very light-colored, with the ligneous portion thick and regular, and in the circular outlines of the section, with the keel rudimental or not rarely altogether absent. The taste is similar to that of true senega, but somewhat more mucilaginous and less rapidly acrid. In structure, false senega root is very similar to the true root; it has, indeed, been asserted that there are anatomical differences between the two senegas, but O. Linde (*P. J.*, xvi, 724) has been unable to make out any such differences. According to L. E. Sayre (*A. J. P.*, Sept., 1897), it is not possible to distinguish the two drugs when powdered. For description of the roots of a number of species of Polygala see *Flora*, Jan., 1886, and *D. C.*, 1901, 26. False Senega was thought to be the product of *Polygala Boykinii* Nuttall, or of *P. alba* Nuttall, whose habitat extends from the mountains of Texas to western British America, but Farwell (*M. R.*, 1907, xvi, 221) believes it is from the *P. Senega*, as it has the characteristic keel-like ridge of the official drug. The properties of senega as well as the medicinal virtues of the root, are extracted by boiling water and by alcohol. Diluted alcohol is an excellent solvent.

Senega root was analyzed by Gehlen, Peschier of Geneva, Feneulle of Cambray, Dulon d'Astafort, Folchi, and Trommsdorff, and subsequently by Quevenne. The virtues of senega appear to reside chiefly, if not exclusively, in the acrid principles called *senegin,* $C_{17}H_{28}O_{10}$, and *polygalic acid,* $C_{19}H_{30}O_{10}$. These principles resemble saponin very closely and are recognized as distinct. Quevenne obtained polygalic acid by the following process: Powdered senega is exhausted by alcohol of 33°, and so much of the alcohol is distilled off as to bring the resulting tincture to the consistence of syrup. The residue is treated with ether in order to remove the fatty matter. The liquid upon standing deposits a precipitate, which is separated by filtration and is then mixed with water. To the turbid solution thus formed alcohol is added, which facilitates the production of a white precipitate, consisting chiefly of polygalic acid. The liquid is allowed to stand for several days, that the precipitate may be fully formed. The supernatant liquid being decanted, the precipitate is drained upon a filter, and, being removed while yet moist, is dissolved by the aid of heat in alcohol of 36°. The solution is boiled with purified animal charcoal, and filtered while hot. Upon cooling, it deposits the principle in question in a state of purity. Thus obtained, polygalic acid is a white powder, inodorous, and of a taste at first slight, but soon becoming pungent and acrid, and producing a very painful sensation in the throat. It is fixed, unalterable in the air, inflammable, soluble in water slowly when cold and rapidly with the aid of heat, soluble in all proportions in boiling absolute alcohol, which deposits most of it on cooling, quite insoluble in ether and in the fixed and volatile oils, and possessed of the properties of reddening litmus and neutralizing the alkalies. Quevenne found it, when given to dogs, to occasion vomiting, and much embarrassment in respiration, and in large quantities to destroy life. Dissection exhibited evidences of inflammation of the lungs, and frothy mucus was found in the stomach, œsophagus, and superior portion of the trachea, showing the tendency of this substance to increase the mucous secretion, and explaining in part the beneficial influence of senega in croup. (*J. P. C.*, xxii, 449, and xxiii, 227.) Bolley showed that this active principle was resolvable by hydrochloric acid into glucose and a peculiar substance called *sapogenin.* Rochleder (*Chem. Cb.*, 1867, p. 925) confirmed this view of the identity of polygalic acid and saponin.

Christophson (*J. P. C.*, 1874) and Schneider (*A. Pharm.*, [3], 7, 394) have thoroughly

established the existence of saponin in senega root. According to the researches of Trommsdorff and Schneider, saponin is contained solely in the bark, the woody tissues being inert. (See *Quillaja*, p. 1035.) L. Reuter (*A. Pharm.*, 1889, 309 and 452) finds that the constituents of senega root are fixed oil and resin, traces of volatile oil (a mixture of valeric ether and methyl salicylate), sugar (7 per cent.), which seems to develop to a greater extent upon standing, senegin or saponin (from 2 to 5 per cent.), yellow coloring matter, and malates. The quantity of methyl salicylate varied in different samples from 0.25 to 0.33 per cent. See also Schroeder's analysis. (*A. J. P.*, 1896, 178.) Methyl salicylate occurs in very many, if not all, of the species of the genus Polygala. (See paper by Kremers and James, *Ph. Rev.*, xvi.) Kain (*Ph. Ztg.*, 1898, 562) states that he has discovered a lævo-rotatory glucoside distinguished from saponin by its mild taste, solubility in absolute alcohol, and in its not giving a precipitate with barium hydroxide.

Senega yields its virtues to water, cold or hot, and to boiling alcohol, and the extracts obtained by means of these liquids have the sensible properties of the root. But under the influence of heat a portion of the acrid principle unites with the coloring matter and coagulated albumen, and thus becomes insoluble in water. In forming an aqueous extract, the infusion should be prepared by percolation, as it is thus most concentrated, and consequently requires less heat in its evaporation. In preparing the infusion, the temperature of the water should not exceed 40° C. (104° F.). Experience has thoroughly proved the value of the use of an alkali in small proportion in making galenical preparations of senega, it prevents gelatinization and combines with the active principles. (See *Fluidextractum Senegæ*, page 499.)

The roots of *Panax quinquefolius* L., or ginseng, were at one period frequently mixed with those of senega, but are easily distinguishable by their shape and taste. The roots of *Gillenia trifoliata* (L.), Moench., and *Asclepias Vincetoxicum* L. (*P. J.*, ix, 411), and of *Triosteum perfoliatum* L. (see Part II), are noted as occurring in commercial senega; they are readily detected by the absence of the keel-like line.

Uses.—Senega owes what therapeutic virtues it possesses to its saponins. (See *Quillaia.*) These by their local irritant action upon the mucous membrane of the stomach tend to cause nausea, thereby increasing the secretions of the sweat glands and especially of the bronchial glands. For this reason the drug has been used as an expectorant in various forms of *bronchitis* and in *asthma*. In overdose it is capable of acting as an irritant poison producing violent vomiting and purging. Polygalic acid may be employed in doses of from one-fourth to one grain (0.016–0.065 Gm.), administered in the form of either pill or capsule.

For a formula for its preparation, see also *A. J. P.*, 1860, 150.

Dose, from fifteen to twenty grains (1.0–1.3 Gm.).

Off. Prep.—Infusum Senegæ, *Br.;* Fluidextractum Senegæ, *U. S.;* Syrupus Senegæ (from Fluidextract), *U. S.;* Tinctura Senegæ, *Br.;* Syrupus Scillæ Compositus (from Fluidextract), *U. S.;* Mistura Pectoralis, Stokes (from Fluidextract), *N. F.;* Syrupus Cimicifugæ Compositus (from Fluidextract), *N. F.*

SENNA. U. S. (Br.)

SENNA Senn.

(sĕn'nạ)

"The dried leaflets of *Cassia acutifolia* Delile, known in commerce as Alexandria Senna, or of *Cassia angustifolia* Vahl, known in commerce as India Senna (Fam. *Leguminosæ*), without the presence or admixture of more than 10 per cent. of stem tissues, pods, seeds and other impurities." *U. S.* "Senna Leaves are the dried leaflets of Cassia acutifolia, *Delile*, and of Cassia angustifolia, *Vahl.* Known in commerce as Alexandrian senna, and Tinnevelly senna." *Br.*

Sennæ Folia, *Br.;* Senna Leaves; Séné, *Fr. Cod.;* Feuilles de Séné, *Fr.;* Folia Sennæ, *P. G.;* Sennesblätter, *G.;* Sena, *It.;* Sen, *Sp.*

The plants which yield *senna* belong to the genus Cassia, of which several species contribute to furnish the drug. These were confounded by Linnæus and comprised in a single species, which he named *Cassia Senna.* Since his time the subject has been more thoroughly investigated, especially by Delile, who accompanied the French expedition to Egypt and had an opportunity of examining the plant in its native country. Besides the official species, it is probable that *C. lanceolata* of Forskhal and *C. æthiopica* of Guibourt contribute towards commercial senna. The leaves of a number of species of Cassia are utilized like senna leaves in the respective countries in which they grow, among which may be mentioned *C. marilandica* L.; *C. cathartica* Mart.; *C. rugosa* Don.; *C. splendida* Vog.; *C. lævigata* Willd.; *C. multijuja* Rich.; *C. Chamæcrista* L.; and *C. montana* Hayne. Farwell asserts that *Cassia marilandica* and other American species of Cassia have been offered in large lots and sold as senna. (*M. R.*, xvii, p. 35.)

Cassia acutifolia is a small undershrub, two or three feet high, with a straight, woody, branching, whitish stem; but, according to Landerer, the senna plant attains the height of eight or ten feet in the African deserts. The leaves are alternate and pinnate, with glandless petioles, and two small narrow pointed stipules at the base. The leaflets, of which from four to six pairs belong to each leaf, are almost sessile, oval-lanceolate, acute, oblique at their base, nerved, from half an inch to an inch long, and of a yellowish-green color. The flowers are yellow, and in axillary spikes. The fruit is a flat, elliptical, obtuse, membranous, smooth, grayish-brown, bivalvular legume, about an inch long and half an inch broad, scarcely if at all curved, and

divided into six or seven cells, each containing a hard, heart-shaped, ash-colored seed. *C. acutifolia* grows wild in great abundance in Upper Egypt, Nubia, Sennaar, and other parts of Africa. This species furnishes the greater part of the variety known in commerce by the name of Alexandria senna.

Cassia angustifolia as usually grown is annual, but with care it may be made to live through the year, and then assumes the character of an undershrub. It has an erect, smooth stem, and pinnate leaves, with from four to eight pairs of leaflets. These are nearly sessile, lanceolate, obscurely mucronate, oblique at the base, smooth above and somewhat downy beneath, with the veins turned inward so as to form a wavy line immediately within the edge of the leaflet. The most striking character of the leaflet is its length, which varies from 2 to 5 cm. The petioles are without glands; the stipules minute, spreading and semi-hastate. The flowers are bright yellow, and arranged in axillary and terminal racemes rather longer than the leaves. The legume is oblong, membranous, tapering abruptly at the base, rounded at the summit, and 4 to 5 cm. long by about 1.5 cm. broad. This plant is found in Southern Arabia and on the coast of East Africa from Mozambique to the Somali land. It has been said to grow in the interior of India, and is cultivated at Tinnevelly for medicinal use.

Cassia obovata Colladon, possesses a rather shorter stem than that of *C. acutifolia*, rising to the height of only a foot and a half. The leaves have from five to seven pairs of leaflets, which are obovate, very obtuse, sometimes mucronate. The flowers are in axillary spikes, of which the peduncles are longer than the leaves of the plant. The legumes are very much compressed, curved almost into the kidney form, of a greenish-brown color, and covered with a very short down, which is perceptible only by the aid of a magnifying glass. They contain from eight to ten seeds. This species grows wild in Syria, Egypt, Senegambia, and Jamaica. (*P. J.*, Sept., 1867.) It has been cultivated successfully in Italy, Spain, and the West Indies. It is said to be no longer gathered for senna, although its leaflets and pods have been found in Alexandria senna.

C. lanceolata of Forskhal, found by that author growing in the deserts of Arabia, is admitted by Lindley and others as a distinct species. Some difference of opinion, however, exists upon this point. De Candolle considered it a variety of the *C. acutifolia* of Delile, from which it differs chiefly in having leaflets with glandular petioles, and, as Forskhal's description preceded that of Delile, he designated the species by the name of *C. lanceolata*. Forskhal's plant has been supposed by some to be the source of the India or Mocha senna, but the leaflets in this variety are much longer than those of *C. lanceolata*, from which the plant differs also in having no gland on the petiole. Niebuhr informs us that he found the Alexandria senna growing in the Arabian territory of Abu-Arisch, whence it is taken by the Arabs to Mecca and Jedda. This is probably the *C. lanceolata* of Forskhal. It is highly probable that this species is the source of a variety of senna which has been brought to this market under the name of *Mecca senna*.

Cassia æthiopica of Guibourt (*C. ovata* of Mérat), formerly confounded with *C. acutifolia*, is considered by Lindley to be a distinct species. It grows in Nubia, Fezzan, to the south of Tripoli, and probably, according to Guibourt, throughout Ethiopia. It is from this plant that the *Tripoli senna* of commerce is derived.

Several varieties of this valuable drug are known in commerce. Of these, four have been received in America—the Alexandria, the Tripoli, the India, and the Mecca senna—but only two are recognized by the Pharmacopœia, which are officially described as follows:

"**Alexandria Senna.**—Usually unbroken, occasionally in fragments, leaflets inequilaterally lanceolate or lance-ovate, from 2 to 3.5 cm. in length and from 6 to 10 mm. in breadth, having extremely short, stout petiolules; acutely cuspidate, entire, subcoriaceous, brittle, pale green or grayish-green, sparsely and obscurely hairy, especially beneath, the hairs appressed; odor characteristic, taste somewhat mucilaginous and bitter. Pods few, broadly elliptical, somewhat reniform, dark green, thin and membranous.

"**India Senna.**—Leaflets usually unbroken, from 2 to 5 cm. in length and from 6 to 14 mm. in breadth, usually more abruptly pointed than those of Alexandria Senna, yellowish-green and smooth above, paler beneath; in odor and taste closely resembling Alexandria Senna. Pods few, elliptical, more or less reniform and from 4 to 5 cm. in length. Powdered Alexandria Senna is light green; when examined under the microscope it exhibits non-glandular hairs, 1-celled, conical, often curved, from 0.1 to 0.35 mm. in length, walls thick and papillose; calcium oxalate in rosette aggregates, from 0.009 to 0.01 mm. in diameter, and in 4- to 6-sided prisms, about 0.015 mm. in length, usually in crystal fibers; stomata broadly elliptical, about 0.02 mm. in long diameter. In India Senna the powder is slightly darker green than that of Alexandria Senna and the hairs are similar but relatively fewer. Mix 0.5 Gm. of powdered Senna with 10 mils of an alcoholic solution of potassium hydroxide (1 in 10), boil the mixture for about two minutes, dilute it with 10 mils of water and filter. Now acidify the filtrate with hydrochloric acid, shake it with ether; remove the ethereal layer and shake it with 5 mils of ammonia water; the latter is colored pinkish-red or bluish-red. Senna yields not more than 12 per cent. of ash. The yield of ash insoluble in hydrochloric acid is not more than 3 per cent. of the Senna taken." *U. S.*

"Pale greyish-green or yellowish-green, thin, brittle; usually from two to four centimetres long, the leaflets of Alexandrian senna being usually smaller than those of Tinnevelly senna; lanceolate, or oval-lanceolate, acute, entire, and unequal at the base. Surface finely pubescent

or nearly glabrous; veins on the under surface distinct. Epidermis of both surfaces consisting of polygonal cells and bearing one-celled, thick-walled, warty hairs together with stomata, each stoma being enclosed between two cells with their long axes parallel to the ostiole. The powdered Leaves greenish-yellow, exhibiting, in addition to the characteristic epidermis, stomata, and hairs, elongated palisade cells and grouped sclerenchymatous fibres accompanied by prismatic crystals of calcium oxalate. Ash not more than 12 per cent." *Br.*

1. ALEXANDRIA SENNA.—This variety of senna is gathered in extreme Upper Egypt and the Soudan, and thence sent to Assouan at the First Cataract of the Nile, whence it finds its way into commerce through Cairo, Suakim, Suez and Alexandria. Two crops are produced annually, one in the spring and one in the autumn. The plants are first cut, then dried, and then the stripped-off leaves and pods are packed in crude bales, in which several species of senna are represented in varying proportion, the predominating species being *C. acutifolia.* Formerly there was an intentional mixture of the product of Cassia acutifolia with the leaflets of *C. obovata,* brought from other parts of Egypt, and even from Syria, with the leaves of *Cynanchum oleæfolium* (*C. Argel* of Delile, *Solenostemma Argel* Hayne), known commonly by the name of *argel* or *arguel,* and sometimes with those of *Tephrosia apollinea* of De Candolle, a leguminous plant growing in Egypt and Nubia. According to M. Royer, the proportions in which the three chief constituents of this mixture were added together were five parts of *C. acutifolia,* three of *C. obovata,* and two of *Cynanchum.* Thus prepared, the senna was again packed in bales, and transmitted to Alexandria. But at present there is much more uniformity in the constitution of Alexandria senna. This variety of senna is often called in French pharmaceutical works *séné de la palthe,* a name derived from an impost formerly laid upon it by the Ottoman Porte. A parcel of Alexandria senna, as it was formerly brought to market, consisted of the following ingredients: (1) the leaflets of *C. acutifolia,* characterized by their acute form, and their length, almost always less than an inch; (2) the leaflets of *C. obovata,* known by their rounded very obtuse summit, which is sometimes furnished with a small projecting point, and by their gradual diminution in breadth towards their base; (3) the pods, broken leafstalks, flowers, and fine fragments of other parts of one or both of these species; (4) the leaves of *Cynanchum oleæfolium,* which are distinguishable by their length, almost always more than an inch, their greater thickness and firmness, the absence of any visible lateral nerves on their under surface, their somewhat lighter color, and the regularity of their base. In this last character they strikingly differ from the genuine senna leaflets, which, from whatever species derived, are always marked by obliquity at their base, one side being inserted in the petiole at a point somewhat lower than the other, and at a different angle. Discrimination between this and the other ingredients is of some importance, as the Cynanchum must be considered an adulteration. It is said by the French writers to produce hypercatharsis and much irritation of the bowels, but was found by Christison and Mayer to occasion griping and protracted nausea, with little purgation. The flowers and fruit of the Cynanchum were also often present, the former white and in small corymbs, the latter an ovoid follicle rather larger than an orange-seed. Besides the above constituents of Alexandria senna, it occasionally contained leaflets of genuine senna, much longer than those of the *acutifolia* or *obovata,* equalling in this respect the Cynanchum, which they also somewhat resembled in form. They were distinguishable, however, by their greater thinness, the distinctness of their lateral nerves, and the irregularity of their bases. The leaflets and fruit of *Tephrosia apollinea,* which have been an occasional impurity in this variety of senna, may be distinguished, the former by their downy surface, their obovate-oblong, emarginate shape, their parallel unbranched lateral nerves, and by being usually folded longitudinally; the latter, by its dimensions, being from an inch to an inch and a half long, and only two lines broad. In Europe, Alexandria senna was formerly adulterated with the leaflets of *Colutea arborescens* L., or bladder senna, and the leaves of *Coriaria myrtifolia* L., a poisonous plant of Southern Europe. An account of these plants is given in PART II.

The leaflets of the Coriaria are ovate-lanceolate, grayish-green with a bluish tint, and are readily known, when not too much broken up, by their strongly-marked mydrib and two lateral nerves running from the base nearly to the summit. They are free from hairs and do not contain crystals of calcium oxalate. Another addition to Alexandria senna has been detected by Lacroix of Mâcon, France, in the leaves of the *Globularia Turbith* (*Globularia Alypum* Linn.), which seem to have taken the place of the *Colutea arborescens,* because more closely resembling the senna leaflet. The leaves of the Globularia are spatulate, much enlarged towards the upper end, rounded at the extremity, but always terminating in a short sharp point. Besides, they are brown, thick, firm, and hard to the touch, while those of the Colutea are green, very thin, and soft. They have an acrid, very bitter taste, but are without nauseous odor. They are asserted to be cathartic, but milder than senna, and capable of being substituted for it in twice the dose. (*J. P. C.,* 4e sér., i, 413.)

The so-called *Aden senna* which Holmes states to be active, is composed of small, broad, not very acute, hairy leaves, and is believed to be obtained from *C. holosericea* Fres. A false senna from Madras has been identified by E. M. Holmes as the product of *Cassia montana* Hayne. The leaflets are about the size of the Tinnevelly senna, but are distinguishable by obtuse or rounded ends which are with distinct mucronate, the tip is, however, often broken off and absent

from individual leaves; by the obtuse angles of the lateral veins and by the presence of a well marked network of veins of the under surface; further, the color of the upper surface is distinctly browner than of the Tinnevelly leaflet. The whole leaves of *Cassia montana* have from 10 to 15 pairs of leaflets, while the Tinnevelly senna has only from 6 to 8 pairs. In the drug this character can usually be made out by noticing the number of scars on the rachis. For a microscopic description of powder, see H. G. Greenish, *P. J.*, lvi, 694. In detecting the adulteration of senna, the apothecary may avail himself not only of the general physical characteristics of the leaves, but also of the fact that while the senna leaf, containing no tannic acid, does not precipitate ferric chloride, most leaves used in adulteration do alter the ferric solution. The microscopic characteristics of the false leaves, though varying greatly, are almost always very different from those of senna. In the senna leaflets the epidermis from the upper and under surface is very similar. The stomata are numerous; the epidermal hairs are unicellular and deciduous, leaving, when detached, a base which has the appearance of an annular pad, around which the neighboring cells seem to radiate. The parenchyma of the cell has a thick epidermis, and is divided into three layers, the uppermost and lowest of which consist of palisade tissue, and are separated by a zone of very small, rounded, parenchymatous cells. Rosette aggregate crystals of calcium oxalate are scattered throughout the parenchyma, and prismatic crystals, one in each cell, occur clustered around the bast tissue of the principal veins.

For a microscopical description of Alexandria senna, see *Proc. A. Ph. A.*, 1882, p. 238.

2. India Senna.—This variety is in Europe sometimes called *Mocha senna,* probably because obtained originally from that port. It derives its name of India senna from the route by which it reaches us. Though produced in Arabia, it is brought to this country and Europe from Calcutta, Bombay, and possibly other ports of Hindostan. It consists of the leaflets of *Cassia elongata,* with some of the leafstalks and pods intermixed. The eye is at once struck by the great length (about two inches) and comparative narrowness of the leaflets, so that the variety may be readily distinguished. The pike-like shape of the leaflet has given rise to the French name of *séné de la pique.* Many of the leaflets have a yellowish, dark-brown, or blackish color, probably from exposure after collection, and the variety has commonly in mass a characteristic dull tawny hue. It is generally considered inferior in purgative power. Leaflets of a senna resembling the Indian were brought by Livingstone from Southern Africa, where the plant grows abundantly. (*P. J.*, xvii, 499.)

A variety of India senna has reached this country which is a product of Hindostan, being cultivated at Tinnevelly, and probably other places in the south of the Peninsula. The plant was originally raised from seeds obtained from the Red Sea, and is the same as that from which the common Indian senna is derived. The drug is exported from Madras to England, where it is known by the name of *Tinnevelly senna.* It is a fine unmixed variety, consiting of unbroken leaflets, from one to two or more inches long, and sometimes half an inch in their greatest breadth, thin, flexible, and of a fine green color. T. B. Groves, however, states as the result of his experiments that Tinnevelly senna contains only two-thirds as much of the active principle as does the Alexandrian. (*P. J.*, Oct., 1868, p. 292.)

Much study has been given to the question of distinguishing the powder of Alexandria and India senna by means of the microscope. (See papers by Sayre, *A. J. P.*, 1896, 1897; Schneider, *Am. Drug.*, 1897; Denniston, *Ph. Rev.*, vol. xvi.) As a result of these studies it is asserted that it is possible to take advantage of the greater hairiness of the Alexandria senna as a practical distinction, it being alleged that a fragment of the epidermis of Alexandria leaf contains twice as many hairs as does a similar sized shred of epidermis from the India senna. It is especially proposed to count the number of epidermal cells between two hairs or their scars, the average distance of the hairs from one another being in the Alexandria senna three epidermal cells, and in the India six cells. Advantage may also be taken of the difference in the neighboring cells of the stomata; in the majority of stomata, in each case, there are two of the neighbor-cells, but in India senna the proportion is one having three neighbor-cells to seven having two, and in the Alexandria the proportion is one having three to two having two.

3. Tripoli Senna.—Genuine Tripoli senna consists in general exclusively of the leaflets of one species of Cassia, formerly considered to be a variety of *C. acutifolia,* but now admitted to be distinct, and named *C. æthiopica.* The leaflets, however, are much broken up, and it is probably on this account that the variety is usually less esteemed than the Alexandrian. The aspect given to it by this state of comminution, and by the uniformity of its constitution, enables the eye at once to distinguish it from the other varieties of senna. The leaflets, moreover, are shorter, less acute, thinner, and more fragile than those of *C. acutifolia* or Alexandria senna, and their nerves are much less distinct. The general opinion at one time was that it was brought from Sennaar and Nubia to Tripoli in caravans; but, it is reasonably asked by Fée, how could it be afforded at a cheaper price than the Alexandrian, if thus brought on the backs of camels a distance of eight hundred leagues through the desert. It is probably collected at Fezzan, immediately south of Tripoli.

4. Mecca Senna is still imported under the name of *Arabian* or *Bombay Senna,* and is obtained from both wild and cultivated plants of *Cassia angustifolia.* The best drug is obtained from British India, great care being taken in its garbling. Much of the commercial article

is of a dark brown color. The leaflets are oblong-lanceolate, on the average longer and narrower than those of *C. acutifolia,* and shorter than those of *C. elongata.* The variety in mass sometimes has a yellowish or tawny hue, more like that of India than like that of Alexandria senna and may be the product of the *C. lanceolata* of Forskhal. Landerer speaks of a valuable variety of senna, characterized by the large size of the leaflets, and sold under the name of Mecca senna, which he says comes from the interior of Africa.

Commercial senna is prepared for use by *garbling,* or picking out the leaflets, and rejecting the leafstalks, the impurities, and the leaves of other plants. The pods are also rejected by some apothecaries. (See *Senna Fructus.*)

The market for senna is gradually changing. For years the drug used in the United States was imported from London or European ports. At the present time, the importations into the United States are largely direct from Egypt. The amount of senna annually exported is about 8000 bales of each of the varieties. Owing to the failure of the crops at certain seasons, the price of senna is very high, and what is known as "broken" senna is found upon the market and sold for the genuine article. This is done with the sanction of the government. In addition, what is known as "senna siftings," which contain large amounts of sand and other foreign matter, have been offered, and these have caused the government inspectors a large amount of trouble. There is considerable difference in the actual constituents of the two sennas, and it would seem advisable for the Pharmacopœia to restrict the drug to one species or else to include them under two separate titles. This principle has been followed by the German Pharmacopœia, as well as the Swiss Pharmacopœia, which restrict the official drug to the Indian senna, or that derived from *Cassia angustifolia.* Indian senna is known commercially as Tinnevelly senna, and this name should probably have been used in the Pharmacopœia. Alexandria senna is occasionally admixed with the leaflets of *C. obovata* Coll. (*Bull. Soc. roy. d. pharm. Brux.,* liii, p. 169). For description of these leaves, see page 991. In addition to admixture of senna with the leaflets of *Cassia marilandica* it is stated that the leaves of *Ailanthus glandulosa* have been found admixed. A very interesting and characteristic test for genuine senna depends upon the sublimation of its oxymethylanthraquinone, which is always a constituent, and this may be further confirmed by testing the sublimed material with a drop of one of the solutions of the alkalies which will show a red-colored test. (*Pharm. Prax.,* v, p. 435.)

Constituents.—The odor of senna is faint and sickly; the taste slightly bitter, sweetish, and nauseous. Water and diluted alcohol extract its active principles. Pure alcohol extracts them but imperfectly. (Bley and Diesel, *Ph. Cb.,* Feb., 1849, p. 126.) The leaves are said to yield about one-third of their weight to boiling water. The infusion is of a deep reddish-brown color, and has the odor and taste of the leaves. When exposed to the air for a short time, it deposits a yellowish insoluble precipitate, supposed to result from the union of extractive matter with oxygen. The nature of this precipitate, however, is not well understood. Decoction also produces some change in the principles of senna, by which its medicinal virtues have been supposed to be impaired, but some experiments of B. Heerlein would seem to show that this opinion is incorrect. An extract prepared by boiling down an infusion, redissolving the residue, and again boiling down to a solid consistence, was found to operate actively in a dose equivalent to a drachm of the leaves. (*Ph. Cb.,* 1851, p. 909.) To diluted alcohol it imparts the same reddish-brown color as to water, but rectified alcohol and ether, digested upon the powdered leaves, become of a deep olive-green.

Lassaigne and Feneulle first isolated a substance to which they gave the name of *cathartin,* but it proved to be a mixture; Bley and Diesel (*Ph. Cb.,* 1849, p. 126) isolated a yellow coloring matter, which they called *chrysoretin,* but which Martius identified as *chrysophan;* Ludwig (*A. Pharm.* (2), cix, p. 42, and cxc, p. 69) obtained two bitter principles, *sennapicrin* and *sennacrol,* the first insoluble, the second soluble in ether; but the active purgative principle was first discovered in 1866 by Dragendorff and Kubly (*Viertelj. f. Prakt. Pharm.,* 16, pp. 96 and 337), who found it to be a glucoside of weak acid character, and named it *cathartic acid.* Thos. B. Groves, in 1868 (*P. J.,* 1869, p. 196), unaware of Dragendorff and Kubly's discovery, isolated the same principle, and found for it the same reactions. For a method of preparing cathartic acid, by Ralph Stockman, see *P. J.,* 1885, p. 740. Its formula is given as $C_{180}H_{96}N_2SO_{82}$, and by boiling its alcoholic solution with acids it yields *cathartogenic acid* and sugar. Gensz (*A. J. P.,* 1893, 334), who prepared it later by the method of Kubly and Stockman, gave the formula $C_{30}H_{36}NO_{18}$. It is amorphous, difficultly soluble in cold water, readily soluble in boiling water. The best solvent is a 30 to 40 per cent. alcohol; ether, benzene, chloroform, and petroleum ether are without solvent action. Alkalies with heat decompose it. It is prepared by partially precipitating with alcohol infusion of senna, concentrating to a syrupy consistence *in vacuo,* filtering, treating the filtrate with a large proportion of absolute alcohol, and repeatedly dissolving in water, and precipitating by alcohol the precipitate thus obtained. It is purified by submitting it (dissolved in moderately strong hydrochloric acid) to dialysis on a diaphragm of parchment paper, cathartic acid having strong colloidal properties. Groves found that ammonium cathartate purged moderately in the dose of three and three-quarters grains, with considerable griping, and that of certain mixed cathartates seven and a half grains purged violently, with much griping and sickness, and continued to act through most of a day. He considers four grains a fair dose.

It should be given in connection with an aromatic and a saline cathartic. *Magnesium cathartate* is soluble. The salts of this acid in aqueous solution are decomposed and rendered inert by long exposure to heat in contact with the air. (Groves, *P. J.*, Oct., 1868, 200–1.) Dragendorff and Kubly also found chrysophanic acid in small proportions, the two substances, *sennacrol* and *sennapicrin,* previously mentioned, and a peculiar non-fermentable saccharine principle, with the formula $C_{21}H_{44}O_{19}$, which they named *cathartomannite.* (*J. P. C.*, 4e sér., v.) A. Seidel proposes the name of *sennit* for catharto-mannite, and gives a process for its preparation in *A. J. P.*, 1885. In 1900 Tschirch and Hiepe made a comprehensive investigation of the chemical constituents of senna in which they found that the active principles belonged to the oxymethylanthraquinone group of glucosides, yielding emodin upon decomposition. From the aqueous percolate they extracted, besides *cathartic acid,* a crystalline body, giving the same reactions as *sennanigrin* and having the composition $C_{14}H_{10}O_5$. From the weak ammoniacal percolate they obtained *anthraglucosennin,* which, however, is composed of several distinct substances, for on treating it with ether, a portion enters solution and another remains undissolved; then the ether-soluble portion, if boiled with toluene and the solution poured on petroleum benzin, precipitates *sennaemodin,* while *sennachrysophanic acid* remains in solution and may be obtained on evaporation; the portion insoluble in toluene is a body which the authors have named *glucosennin.* Its composition agrees with the formula $C_{22}H_{18}O_8$, and it is possibly an emodin glucoside. From the portion of anthraglucosennin insoluble in ether, *sennaisoemodin* is obtained by treatment with acetone and shaking the resultant solution with petroleum benzin. The acetone solution retains a substance which the authors have named *sennarhamnetin.* Finally, the portion of anthraglucosennin remaining undissolved after treatment with ether and acetone is a black body which resembles in this and other respects aloe-nigrin. *Sennanigrin,* however, yields on treatment with alcoholic potassium hydroxide, sennaemodin and sennachrysophanic acid. (*A. Pharm.*, Aug. 31, 1900, 427, 448.)

Some results of experiments on the properties of senna which more particularly concern the pharmacist are noted in a paper contained in the *J. P. C.* (Janv., 1874, p. 80), and require to be mentioned here, because they tend to fix certain points which are left undetermined in the above statement. An extract made by evaporating in the air an aqueous infusion of senna possesses but partially the purgative properties of the leaves. If the extract be redissolved in a large quantity of water, and the solution be again evaporated, the extract now obtained will be quite inert. It follows that a prolonged decoction of senna destroys its cathartic powers. The presence of an alkali in the decoction increases the rapidity of the destruction. An infusion of senna in lime water, heated to the boiling point, and then deprived of lime by a stream of carbon dioxide, becomes inert. An infusion of senna, made to boil after the addition of potassium hydroxide, and then neutralized by an acid, is also inert. The mineral acids destroy the purgative powers of senna, but less energetically than the alkalies; the vegetable acids exercise the same power but feebly. Concentrated alcohol does not dissolve the active principle, which is soluble in cold water. It was Heerlein who first determined the complete want of purgative power in the pure alcoholic extract of senna. Nevertheless, this extract possesses in a high degree the odor and taste of senna, and, taken internally, without purging, imparts a deep-yellow color to the urine, which the alkalies change to red. The leaves exhausted by alcohol have all their purgative effect, but lose the power of affecting the urine so that an alkaline solution shall color it red. These facts prove that chrysophanic acid is not the purgative principle of senna. The fact that alcohol removes the odor and taste of senna without affecting its purgative action may sometimes be advantageously applied in cases in which the taste of senna is extremely offensive. L. Siebold, after experimenting with senna leaves washed with alcohol, arrived at the following conclusions: (1) Strong spirit does not remove any of the active principle from senna leaves; (2) the therapeutic action of cathartic acid is assisted by one or more of the constituents yielded by senna to strong alcohol, though these constituents produce no purgative effect when taken alone; (3) senna exhausted by alcohol is a reliable and pleasant purgative, but somewhat weaker in its action than the unexhausted leaves. Tutin reports the analysis of the water soluble portion of an alcoholic extract of Tinnevelly senna as containing (1) salicylic acid, (2) rhein ($C_{15}H_8O_6$), (3) kaempferol (1:3:4 trihydroxyflavonol), (4) aloe-emodin ($C_{15}H_{10}O_5$), (5) kaempferin ($C_{28}H_{30}O_6$), a glucoside of kaempferol, (6) glucosides of rhein and aloe-emodin, (7) a magnesium salt of an unidentified organic acid, (8) a sugar. The water insoluble portion contained (1) myricyl alcohol, (2) a phytosterol ($C_{27}H_{46}O$), (3) a phytosterolin ($C_{33}H_{56}O_6$), (4) palmitic and stearic acids, besides a small amount of essential oil.

Incompatibles.—Many substances produce precipitates with the infusion of senna, but it does not follow that they are all medicinally incompatible, as they may remove only inert ingredients. Cathartic acid is precipitated by infusion of galls and solution of lead subacetate. Lead acetate and tartar emetic which disturb the infusion, have no effect upon the solution of this substance.

Uses.—Senna was first used as a medicine by the Arabians. It was noticed in their writings as early as the ninth century, and the name itself is Arabic. Like the other cathartics of the anthraquinone series, its action is chiefly upon the lower bowel, and is therefore especially suitable in *habitual costiveness.* It increases the peristaltic movements of the colon by its local action upon the intestinal wall. The tendency to gripe may be obviated by combining it with aromatics

or with a saline laxative. The coloring matter of senna is absorbable, and twenty or thirty minutes after the ingestion of the drug it appears in the urine and may be recognized by a red color on the addition of ammonia. It is asserted also that the milk of nursing women acquires purgative properties after the administration of senna. Under the name of *cathartin* there is upon the market a mixture of the salts of cathartic acid which may be used in doses of from three to six grains (0.2–0.4 Gm.). *Sennax* is the name applied to the water-soluble glucoside of senna, and is marketed in tablets each one of which contains 0.075 Gm.

Dose, of senna, one-half to two drachms (2.0–7.7 Gm.).

Off. Prep.—Confectio Sennæ, *Br., N. F.;* Fluidextractum Sennæ, *U. S.;* Infusum Sennæ, *Br.;* Infusum Sennæ Compositum, *U. S.;* Pulvis Glycyrrhizæ Compositus, *U. S., Br.;* Syrupus Sennæ (from Fluidextract), *U. S., Br.;* Tinctura Sennæ Composita, *Br.;* Mistura Sennæ Composita (from Infusion), *Br.;* Syrupus Sarsaparillæ Compositus (from Fluidextract), *U. S.;* Elixir Cascaræ Sagradæ Compositum (from Fluidextract), *N. F.;* Elixir Catharticum Compositum (from Fluidextract), *N. F.;* Species Laxativæ, *N. F.;* Syrupus Ficorum Compositus, *N. F.;* Syrupus Sennæ Aromaticus, *N. F.;* Syrupus Sennæ Compositus, *N. F.*

SENNÆ FRUCTUS. Br.

SENNA PODS

(sĕn'næ frūc'tŭs)

"Senna Pods are the dried ripe fruits of Cassia acutifolia, *Delile,* and of Cassia angustifolia, *Vahl.*" *Br.*

Senna pods, while regarded as an adulterant in the U. S. P. IX in that the quantity is restricted, are official in the Br. Pharm. They are described as follows: "About five centimetres long, and from two to two and a half centimetres wide; broadly oblong or somewhat reniform; pale green; brownish in the centre above the seeds; very flat; rounded at the base, slightly mucronate at the apex. Pericarp papery. Seeds obovate-cuneate, flattened. Odor and taste slight." *Br.*

Uses.—They were preferred by the Arabian and mediæval physicians of Europe to the leaves, while Pereira states that they are much milder in their operation than the leaflets. This has been explained by the researches of E. F. Salmon, who has found that they contain about 25 per cent. more cathartic acid and emodin than the leaves, but no resinous principle or volatile oil. (*P. J.,* Oct., 1889.) The griping of senna being largely due to the resin, it is *a priori* to be expected that the pods would act more kindly than the leaves. A. W. Macfarlane has found this to be actually the case. From six to twelve pods for the adult, or from three to six for the young or very aged, infused in a claret-glass of cold water, in his experience, act very mildly but very thoroughly upon the whole intestine.

Dose, from one-half to one drachm (2.0–3.9 Gm.).

SERPENTARIA. U. S. (Br.)

SERPENTARIA Serpent. [Virginia Snakeroot, Texas Snakeroot]

(sĕr-pĕn-tā'rĭ-ă)

"The dried rhizome and roots of *Aristolochia Serpentaria* Linné, known in commerce as Virginia Snakeroot, or of *Aristolochia reticulata* Nuttall, known in commerce as Texas Snakeroot (Fam. *Aristolochiaceæ*), without the presence or admixture of more than 10 per cent. of the stems or other foreign matter." *U. S.* "Serpentary Rhizome is the dried rhizome and roots of Aristolochia Serpentaria, *Linn.,* and of Aristolochia reticulata, *Nutt.*" *Br.*

Serpentariæ Rhizoma, *Br.,* Serpentary Rhizome; Virginia Serpentaria, Virginia Snakeroot, Snakeweed, Pelican-flower, Snagrel, Sangrel, Radix Colubrina, Radix Viperina; Serpentary, Sangree; Serpentaire de Virginie, *Fr. Cod.;* Couleuvrée de Virginie, *Fr.;* Virginische Schlangenwurzel, *G.*

Many species of Aristolochia have been employed in medicine. Their supposed possession of emmenagogue properties has given origin to the name of the genus. Several of the nonofficial species are described in Part II.

Aristolochia Serpentaria is an herbaceous plant, with a short rhizome and numerous slender roots. Several stems often rise from the same rhizome. They are about eight or ten inches in height, slender, round, flexuose, jointed at irregular distances, and frequently reddish or purple at the base. The leaves are oblong-cordate, acuminate, entire, of a pale yellowish-green color, and supported on short petioles. The flowers proceed from the joints near the root, and stand singly on long, slender, round, jointed peduncles, which are sometimes furnished with one or two small scales, and bend downward so as nearly to bury the flower in the earth or decayed leaves. The tube of the calyx is curved like the letter S, enlarged at the base (ovary) and at its throat, the short limb being obtusely three-lobed. The anthers—six or twelve in number—are sessile, attached to the under part of the stigma, which is fleshy and from three to six-lobed. The fruit is an hexangular, six-celled capsule, containing several small flat seeds. The plant grows in rich shady woods from Connecticut west to Michigan and Missouri and south to Florida and Louisiana, abounding in the valley of the Ohio and in the mountainous regions of our interior. It flowers in May and June. The root is collected in Western Pennsylvania, West Virginia, Ohio, Indiana, and Kentucky. It is usually in bales containing about one hundred pounds, and is often mixed with the leaves and stems of the plant, and with adhering dirt. For an account of *A. hirsuta,* see 18th ed., *U. S. D.,* p. 1222. On account of the rather large use of serpentaria the drug is becoming scarcer and some attempts at cultivation

have been made. (See *Proc. A. Ph. A.*, 1905, liii, p. 275, and *West. Drug.*, xxvii, p. 775.)

A. hastata (Nuttall.) Duchartre.—This is now considered to be nothing more than a variety of *A. Serpentaria,* from which it differs in having hastate, acute, somewhat cordate leaves, and the lip of the corolla ovate. It flourishes on the banks of the Mississippi, in the Carolinas, and elsewhere. Its root scarcely differs from that of the official plant, and is frequently mixed with it, as is proved by the presence of the characteristic hastate leaves in the parcels brought into market.

A. reticulata was probably first observed by Nuttall, as a specimen labelled "*A. reticulata,* Red River," in the handwriting of that botanist, is contained in the Herbarium of the Academy of Natural Sciences of Philadelphia. From a root similar to that of *A. Serpentaria* numerous short, slender, round, flexuose, jointed stems arise, usually simple, but sometimes branched near the root. The older stems are slightly villous, the young densely pubescent. The leaves, which stand on very short villous petioles, are round or oblong-cordate, obtuse, reticulate, very prominently veined, and villous on both sides, especially upon the veins. From the lower joints of the stem four or five hairy, jointed peduncles proceed, which bear small leafy villous bracts at the joints, and several flowers on short pedicels. The flowers are small, purplish, and densely pubescent, especially at the base and on the ovary. The hexangular capsule is deeply sulcate. This species grows from Virginia to Louisiana, Texas, Arkansas, and Oklahoma.

Properties.—Serpentaria is officially described as follows: "Rhizome in both commercial varieties oblique, subcylindrical, more or less curved, from 10 to 30 mm. in length and from 1 to 2 mm. in diameter; externally dark brown, upper portion with short stem-bases and from lower and lateral portions arise numerous, long, thin, nearly straight, yellowish-brown roots; fracture short; internally yellowish-white, wood with broad, excentric wedges; odor terebinthinate; taste bitter, aromatic. Under the microscope, transverse sections of the rhizome of both commercial varieties of Serpentaria show an outer layer of epidermal cells; a cortex of from 10 to 15 rows of parenchyma; inner bark sometimes showing strongly lignified bast-fibers, either single or distributed in a more or less interrupted circle; a xylem of broad wood-wedges separated by broad medullary rays about 8 cells wide, the walls being strongly lignified and with numerous simple pores; pith excentric, composed of polygonal cells, the walls being lignified and porous. Starch in the cells of cortical parenchyma, medullary rays and pith. The root in transverse section shows a compact, 4- to 6-rayed stele, and a large starch-bearing cortical area. The stem in transverse section shows an interrupted circle of from 6 to 10 fibro-vascular bundles, a cortex with a prominent continuous ring of strongly lignified cells, and a few non-glandular hairs. The powder is grayish-brown; when examined under the microscope it exhibits numerous starch grains, single and 2- to 4-compound, the individual grains being more or less spherical or plano-convex and frequently with a central cleft, from 0.003 to 0.014 mm. in diameter; lignified elements numerous, consisting of tracheæ, wood-fibers, medullary ray cells and pith cells; a few non-glandular hairs of the stem are occasionally present." *U. S.*

"Rhizome of Aristolochia Serpentaria tortuous and slender, about two centimetres long and three millimetres thick; on the upper surface the remains of slender, aerial stems, and on the under surface numerous wiry interlacing roots, often about seven centimetres long. Both rhizome and roots dull yellowish-brown. Characteristic odor; taste strong, camphoraceous, bitter. Ash not more than 10 per cent. Rhizome and roots of Aristolochia reticulata resemble the foregoing, but are longer and thicker, and the roots are straighter." *Br.*

Holm has published an illustrated article on the pharmacognosy of serpentaria, including the morphology of the stems and leaves. (*M. R.*, xvi, p. 276.)

Texas serpentaria contains a larger percentage of volatile oil than does the other variety of the drug. The color of serpentaria, which in the recent root is yellowish, becomes brown on keeping.

The roots of *Spigelia marilandica* are sometimes found associated with serpentaria. They may be distinguished by the absence of the bitter taste, and, when the stem and foliage are attached, by the peculiar character of these parts. (See *Spigelia.*) We have seen the young roots of *Polygala Senega* mixed with serpentaria. Independently of their difference in odor and taste, they may be distinguished by being simple, and by a projecting line running from one end to the other of the root. Another adulteration was detected by P. S. Milleman of Chicago, who found in a parcel a large quantity of "golden seal" (*Hydrastis canadensis*). The rhizomes, with rootlets attached, were from a quarter of an inch to an inch in length, and about one-eighth of an inch in diameter, but at the present time (1917) on account of the high price of senega and hydrastis neither admixture is likely to occur.

The root yields all its virtues to water and alcohol, producing with the former a yellowish-brown infusion, with the latter a bright greenish tincture, rendered turbid by the addition of water. Chevallier found in the root a volatile oil, a yellow bitter principle, soluble in water and alcohol, resin, gum, starch, albumen, lignin, and various salts. Bucholz obtained from 1000 parts, 5 of a green fragrant volatile oil, 28.5 of a yellowish-green resin, 17 of extractive matter, 181 of gummy extract, 624 of lignin, and 144.5 of water. The active ingredients are probably the volatile oil and the yellow bitter principle of Chevallier, which that chemist considers analogous to the bitter principle of quassia; alkaline solution of cupric tartrate shows, moreover, the presence of a glucose sugar. The volatile oil

passes over with water in distillation, rendering the liquid milky, and impregnating it with the odor of the root. The volatile oil has been carefully investigated by J. C. Peacock (*A. J. P.*, 1891, 257). He found it to contain a terpene, $C_{10}H_{16}$, boiling at 157° C. (314.6° F.), of sp. gr. 0.865 (probably pinene); a compound ester boiling at 211° C. (411.8° F.), sp. gr. 0.9849, which on saponification yielded borneol, $C_{10}H_{18}O$, and a crystalline acid; a fraction boiling at from 239° to 240° C. (462.2°–464° F.), sp. gr. 0.9888, and of the composition $C_{18}H_{20}O$; and some green or bluish-green fluorescent oil in small quantity, which decomposes even when distilled under reduced pressure. The borneol ester constitutes about 60 per cent. of the oil. A principle called *aristolochine*, obtained from *A. Clematitis* and the roots of *A. rotunda* and *A. longa*, was investigated by Jul. Pohl. (*A. E. P. P.*, xxix.) He obtained it as a yellow crystalline mass, soluble in chloroform, ether, acetone, acetic anhydride, and alcohol, insoluble in petroleum benzin, benzene, and carbon disulphide, almost insoluble in cold water, slightly soluble in hot water. An ultimate analysis gave for its composition $C_{32}H_{32}O_{13}N$. O. Hesse obtained from the root of *Aristolochia argentina* an alkaloid to which he gives the name *aristolochine*, but has furnished no formula; a principle, *aristolin*, $C_{15}H_{28}O_3$; *physosterin palmitate*, in white scales, fusing at 82° C. (179.6° F.); and a mixture of acids to which he gives the names *aristic acid*, $C_{18}H_{18}NO_7$, *aristidic acid*, $C_{17}H_{10}(CH_3)NO_7$, and *aristolic acid*, $C_{15}H_{13}NO_7$.

The resinous *aristinic* acid has been obtained from a number of species of the genus *Aristolochia*, notably by Walz from *A. Clematitis*, by Chevallier from *A. Serpentaria*, by Dymock and Warden from *A. indica*, by Hesse from *A. argentina*, by Hooper from *A. bracteata*. Hooper has also obtained a closely alied, if not identical, resinous acid from the aristolochiaceous plant *Bragantia Wallichii*, besides an alkaloid, which, under the name of *Alpam*, has long been used in Western India as an antidote to snake venom. The allied species, *Bragantia tomentosa* of Blume, is said to be employed in Java as an emmenagogue.

Uses.—Serpentaria is a feeble stimulant tonic. Too largely taken, it occasions nausea, griping pains in the bowels, sometimes vomiting and dysenteric tenesmus. It has been recommended in *intermittent fevers*, and may be serviceable as an adjunct to quinine. It is sometimes given in *dyspepsia*. The dose of fluidextract is from twenty minims to half a fluidrachm (1.3 to 1.8 mils). According to Pohl, aristolochine in sufficient dose produces in the higher animals violent irritation of the gastrointestinal tract and of the kidneys, with death in coma from respiratory paralysis.

Dose, fifteen to thirty grains (1 to 2 Gm.).

Off. Prep.—Tinctura Cinchonæ Composita, *U. S., Br.;* Fluidextractum Serpentariæ, *N. F.;* Tinctura Serpentariæ, *N. F., Br.*

SERUM ANTIDIPHTHERICUM, U. S.

ANTIDIPHTHERIC SERUM Ser. Antidiph. [Diphtheria Antitoxin]

(sē'rŭm ăn'tĭ-dĭph-thĕr'i-cŭm)

"A fluid, having a potency of not less than 250 antitoxic units per mil, separated from the coagulated blood of the horse, *Equus Caballus* Linné (Fam. *Equidæ*), or other large domestic animal, which has been properly immunized against diphtheria toxin. It must be kept in sealed glass containers in a dark place, at a temperature between 4.5° and 15° C. (40° and 59° F.)" *U. S.* "The blood serum of horses which have been immunized against the diphtheria poison." *P. G.*

Serum Antidiphthericum, *P. G.;* Diphtherie-heil-serum, *G.;* Serum antidiphterique, *Fr.;* Siero antidifterico, *It.;* Suero antidifterico, *Sp.*

The antitoxic property of the blood serum of animals immunized by the inoculation of bacterial toxins was discovered in 1890 by Behring and Kitasato (*D. M. W.*, Nos. 49, 50, 1890). The great practical therapeutic value of diphtheria antitoxin was demonstrated independently by Behring and Roux and announced in papers read before the International Congress of Hygiene and Demography which met in Budapest in 1894.

Only the serum of the blood is used in medicine for prophylactic or curative purposes, although other body juices contain the active principle. The antitoxin has never been isolated in pure form. It is precipitated with the globulins and is believed to be allied to the enzymes. The antitoxin globulin retains its properties more persistently than the allied globulins with which it is associated. That is, it is more resistent to deleterious influences, more stable and more soluble than the other globulins found in blood serum. As we lack definite knowledge of the true chemical nature of the active principle contained in antitoxic serums, the antitoxin is variously spoken of as antikörper (G.) or antibodies, free receptors (Ehrlich), cytases (Metchnikoff), etc. Of the several antitoxins known, diphtheria and tetanus antitoxins are the only ones recognized by the U. S. Pharmacopeia. These are the only ordinary diseases caused solely by a soluble toxin; in other words, in these two diseases, not the bacteria themselves, but the poison which they excrete, produce the severe symptoms and frequent fatalities. And these two toxins, in the animal body, each give rise to an antitoxin which may be therapeutically or prophylactically efficient. Each antitoxin is specific; that is, neutralizes the poison of the particular infection which was inoculated into a suseeptible animal to produce it. While diphtheria antitoxin is used for other diseases, it is specific only in neutralizing the poisons produced by the diphtheria bacillus. Diphtheria antitoxin is sometimes normally present in small amounts in the blood serum of horses, man, and other animals.

Preparation.—Diphtheria antitoxin is made

by injecting the diphtheria poison (toxin) into horses. The horses are injected either subcutaneously or intravenously; usually the former method is preferred. Horses are selected because, on account of their size, a large amount of blood may readily be obtained, and because the serum of the horse is more easily borne by the human organism in large quantities than that of some other animals. Behring originally employed dogs and sheep with success; Aronson preferred the goat; Roux was the first to use the horse.

The antitoxin is produced by a vital reaction of the cells of the body caused by the stimulation of the toxin. Just which cells of the body take most active part in the production of the antitoxin is not exactly clear. Metchnikoff believed this power lies almost solely with the phagocytes, while Ehrlich believed that any of the body cells, but especially the connective tissue cells, play the most important role. The followers of Ehrlich and Metchnikoff have built up two divergent schools of thought to account for antitoxin immunity. It is interesting to note that both schools place the nutrition and metabolism of the cell at the groundwork of antitoxin production.

The toxin is made by growing a virulent culture of the diphtheria bacillus in an alkaline nutrient bouillon at about 37° C. (98.6° F.). This culture, when five to seven days old, is filtered through unglazed porcelain or diatomaceous earth in order to remove the bacterial cells. The clear filtrate, containing the soluble poisons elaborated by the growth and multiplication of the bacilli, is the *diphtheria toxin.* The horse is inoculated with increasing amounts of the toxin. At first very small amounts are used, but even these usually cause a local and constitutional reaction, swelling and edema at the site of inoculation, fever and derangement of appetite. These symptoms pass away in a few days, when a larger quantity of toxin is then inoculated, and this process is continued until within a few months the horse is able to withstand the subcutaneous inoculation of as much as a liter of a strong toxin with perhaps less local and general disturbance than is caused by the first treatment with a very small fraction of this amount.

As the doses of toxin given to the horse increase, the amount of antitoxin in the blood gradually increases until, after three to six months of treatment, the horse's blood usually contains from 200 to 400 units of antitoxin to the milliliter. The production of stronger antitoxin serums depends upon the horse and not upon the treatment. Some horses react actively and produce very high potency serums for long times; others cannot be induced to give a serum containing more than 150 to 200 units per milliliter. After a variable period (from several months to years) the horse loses the power of reaction, so that despite active treatment the immunizing power of the blood serum steadily diminishes. The horse is bled from the external jugular vein by means of a trocar and cannula. The blood is drawn into long sterile cylindrical tubes or other vessels and allowed to clot. The clear serum collects and in a few days is drawn off by a pipette. This clear albuminous fluid, passed through a filter which excludes bacteria, constitutes the Serum Antidiphthericum of the Pharmacopœia.

Preservatives.—The antitoxin in the blood serum neutralizes the toxin when the two are brought into contact, but the antitoxic serum does not prevent the growth of the bacteria themselves. Diphtheria bacilli grow and multiply well in diphtheria antitoxic serum. In other words, diphtheria antitoxin is a good culture medium for bacteria of all kinds. The greatest care must therefore be taken to prevent contamination. The serum may be kept sterile indefinitely only by means of the most exacting bacteriological precautions. It is sometimes marketed without the addition of an antiseptic substance, but this practice has been largely discontinued for the following reasons: (1) The technic required to prevent slight accidental contamination during the process of preparation and bottling is arduous; (2) there is danger of the introduction of serious contamination by unskilled persons who use the serum; (3) the addition of a small amount of certain preservatives is harmless. The serums made by the American manufacturers generally contain cresol (0.4 per cent.) phenol (0.5 per cent.), or chloroform (to saturation).

Properties.—Antidiphtheric Serum is officially described as "A yellowish or yellowish-brown, transparent or slightly turbid liquid, with sometimes a slight granular deposit; nearly odorless, or having an odor due to the presence of an antiseptic used as a preservative.

"Antidiphtheric Serum gradually loses in potency, the loss in one year varying between 10 per cent. and 30 per cent. The serum must come from healthy animals, must be sterile, must be free from toxins or other bacterial products, and must not contain an excessive amount of preservative (not more than 0.5 per cent. of phenol or cresol, when either of these is used), and the total solids must not exceed 20 per cent. Serum of a lower potency than 250 units per mil must not be sold or dispensed. Only such Sera may be sold or dispensed as have been prepared and propagated in establishments licensed by the Secretary of the Treasury of the United States.

"The United States law requires that each container of Serum sold or dispensed by licensed establishments shall bear upon the label, in addition to the name of the serum, the name, address, and license number of the manufacturer, and the date beyond which the product cannot be expected to yield its specific results. The label must also contain the laboratory number of the Serum and the total number of antitoxic units claimed for the contents of the container.

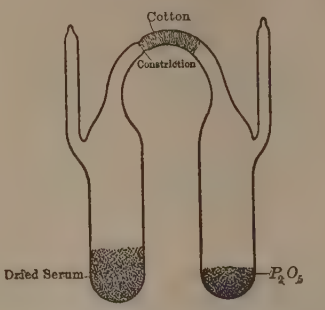
"The standard of strength, expressed in units of antitoxic power, shall be that established by the United States Public Health Service." *U. S.*

Tests.—The Immunity Unit. The strength

of antidiphtheric serum is expressed in immunity units. The unit is a measure of strength, not of volume. The official unit for this country is the antitoxic power contained in a definite quantity of the standard serum prepared and dispensed by the Hygienic Laboratory of the U. S. Public Health Service in accordance with the Law of July 1, 1902. The American standard was based on Ehrlich's normal serum made at the K. Institut für Experimentelle Therapie, Frankfurt a. Main, Germany. It is difficult to define the immunity unit in a brief sentence. A proper understanding of it may only be had from a study of the theoretical considerations involved (see "The immunity unit for standardizing diphtheria antitoxin," Bulletin No. 21, Hygienic Laboratory, U. S. Public Health Service, Washington, 1905.) The unit may be defined as the neutralizing power possessed by an arbitrary quantity of a diphtheria antitoxic serum kept under special conditions to prevent deterioration in an authorized laboratory. The test by which the strength of antitoxin contained in a unit is measured is a physiological one and depends upon the neutralization of the toxin by the antitoxin. This neutralization can only be determined by injecting the toxin and antitoxin mixtures into guinea pigs, which animals are highly susceptible to the diphtheria bacillus and its poisons.

The preparation and preservation of the standard serum is encompassed by many technical difficulties. A high-grade serum is selected. This is given a preliminary test to determine its potency. The serum is now reduced to dryness by evaporation in vacuo. Special apparatus is used to accomplish this evaporation quickly and at the same time to prevent contamination. The dried serum must be kept guarded under special conditions to prevent deterioration. The oxygen of the air must be excluded in order to retard the process of oxidation, which rapidly alters the antibodies, especially under the influence of light. The standard serum is, therefore, always kept under a vacuum and in absolute darkness in the Hygienic Laboratory of the U. S. Public Health Service. The serum must be perfectly dry. It is therefore kept under the influence of phosphoric anhydride, P_2O_5.

Further, the serum is kept in a specially built ice-box maintained at the constant temperature of 5° C. (41° F.) by means of circulating brine. The dried official serum is preserved in a small glass apparatus consisting of two parts connected by means of a glass tube, as shown in the accompanying illustration. The serum is placed in one portion of the apparatus and phosphoric anhydride, which is a very powerful dehydrating substance, in the other. The air is exhausted as much as possible by means of a high vacuum and the apparatus hermetically sealed. Several hundred such tubes are prepared, each one containing a weighed quantity of the powdered serum. From this arrangement, it will be seen that the powdered serum is kept dry, free from contact with the oxygen of the air, guarded against the action of light, and preserved at a constant low temperature. Once every two or three months, or whenever it is desired to prepare the standard solution, one of these bulbs is broken and 1 gramme of the serum carefully



U-shaped tubes used for preserving the standard serum. Half size.

weighed and dissolved in a solution made by mixing physiological saline solution (0.85 per cent.) one part, and pure glycerin two parts.

Testing the Standard Serum.—This glycerinated solution of blood serum is now accurately compared with previous standard solutions in terms of the immunity unit. This comparison is made by means of the test (L +) dose of toxin. The L + dose of a toxin is that quantity which when mixed with one immunity unit of serum is just able to kill a 250 gram guinea pig on the fourth day (about 96 hours). In the commercial testing of serums in order to have a coefficient of safety it is better to require the pig to live.

Testing the Toxin.—The toxin is a complex substance composed, according to Ehrlich, of several poisons, *e.g., toxin, toxoid, toxone* and *epitoxonoid.* The diphtheria toxin is first investigated biologically by adding varying quantities of the poison to the immunity unit and inoculating the mixtures into a series of guinea pigs. In this way, it is very evident, as Ehrlich has shown, that two limits, boundaries or zones are always shown, which are of the greatest importance in determining the nature and composition of the poison. Each of these limits is designated by the letter L, from *limes,* a boundary or zone. These limits are known respectively as L_o (O = nil) and L + (+ = death).

By L_o is meant that quantity of poison which just neutralizes or saturates one immunity unit as shown at the necropsy done forty-eight hours after the subcutaneous injection of the mixture into the guinea pig. The reaction at the site of inoculation at this examination must be hardly noticeable. Theoretically the L dose of toxin must unite with and neutralize just 200 "combining units" of antitoxin. A "combining unit" of antitoxin is in theory one two-hundredth of an immunity unit, and is supposed to contain enough antitoxin to just neutralize one fatal guinea pig dose of a pure toxin which is all poison without the comparatively inert (but antitoxin-neutralizing) toxoids and toxones. The

L_o dose, therefore, contains just 200 minimal lethal doses of a theoretically pure poison.

By L+ is meant the smallest quantity of toxin of which when mixed with one immunity unit of antitoxin there is left unneutralized a quantity to kill the animal on the fourth day. As defined by Ehrlich the L+ dose is that quantity of poison which, despite the antibodies contained in one immunity unit of serum, contains a sufficient excess of poison to cause the death of the guinea pig within the course of four days.

In studying the constitution of the diphtheria poison it is also necessary to determine its absolute toxicity with the greatest possible precision. The absolute toxicity of the diphtheria poison is expressed as the minimal lethal dose (MLD), sometimes spoken of as the minimal fatal dose (MFD), and occasionally simply as the lethal dose. The minimal lethal dose may be readily defined as the smallest quantity of toxin which will surely kill every guinea pig weighing 250 grammes in the course of four days, or at the latest, five days. As Ehrlich has pointed out, such a quantity may kill some of the animals sooner, that is, within thirty-six to forty-eight hours. A quantity of diphtheria poison that will kill every guinea pig, without exception, acutely within thirty-six to forty-eight hours contains more than the minimal lethal dose. The L+ dose is a much more definite and constant measure than the MLD. It does not show the irregularities or present the difficulties met with in determining the absolute toxicity of the poison. On account of the importance of the L+ and the L_o doses the following simplified tables taken from actual experiments are given to show just how the two are made:

Test to determine the L+ dose of a toxin.

	Result.
1 immunity unit + 0.19 mil toxin	Invariably causes late paralysis, never acute death.
1 immunity unit + 0.20 mil toxin	Sometimes causes late paralysis and sometimes acute death.
1 immunity unit + 0.21 mil toxin	Always causes acute death about the fourth day.
1 immunity unit + 0.22 mil toxin	Always causes acute death, usually on the second or third day.

The L+ dose of this toxin is, therefore, just 0.21 mil.

Tests to determine the L_o dose of a toxin.

	Result at autopsy 48 hours after inoculation.
1 immunity unit + 0.14 mil toxin	No visible reaction.
1 immunity unit + 0.15 mil toxin	No visible reaction.
1 immunity unit + 0.16 mil toxin	Slightest possible congestion about carbon particles or no reaction.
1 immunity unit + 0.17 mil toxin	Apparent reaction at site of inoculation.
1 immunity unit + 0.18 mil toxin	Injection and œdema at site.
1 immunity unit + 0.19 mil toxin	Injection and œdema at site.

The L_o dose of this toxin, therefore, is 0.16 mil.

Concentrated Serums.—At the present time the greater part of the diphtheria antitoxin used in the United States is concentrated. (See *Serum Antidiphthericum Purificatum*, U. S.). The processes used are due to Gibson and Banzhaf of the New York City Board of Health, and depend on precipitation of the globulin fractions with ammonium sulphate and subsequent purification and solution by dialysis. Sodium chloride and preservative are added and sterilization effected by filtration through a Berkefeld filter. The concentrated antitoxin solution thus prepared contains from two to three times the proportion of protein present in normal serum. Tests show that the artificially concentrated antitoxin kept in small vials in an ice box, preserves its potency as well as the ordinary antitoxin serum. Therapeutically the comparative results obtained are identical. Local irritation, rashes etc., seem to be less frequent and severe when this concentrated or "refined" antitoxin is administered, because for the same antitoxic unitage the product contains less of the protein substances which cause reactions.

Legal Requirements.—All diphtheria antitoxin sold in interstate commerce in this country must comply with the regulations made in accordance with the Law approved July 1, 1902, entitled "An Act to regulate the sale of viruses, serums, toxins, and analogous products in the District of Columbia, to regulate interstate traffic in said articles, and for other purposes." It is illegal to sell, barter, or exchange diphtheria antitoxin made in one State or Territory or the District of Columbia in another State or Territory or the District of Columbia unless the following salient points of the law have been complied with: 1. The product must be plainly marked with the proper name of the article contained therein: 2. The label on the package must plainly state the name and address of the manufacturer. 3. The package must be plainly labeled with the license number issued by the Secretary of the Treasury. 4. The date beyond which the contents cannot be expected, beyond reasonable doubt, to yield specific results, must be given on the label or package. The execution of the law rests with the Surgeon-General of the U. S. Public Health Service. Annual inspections of all licensed manufacturers are made by officers of the above named service. From time to time products of each licensed manufacturer are

bought on the open market and examined in the Hygienic Laboratory of the Public Health Service at Washington for purity and potency.

Uses.—Diphtheria antitoxin is a true specific for diphtheria if it is given in sufficient quantity and sufficiently early in the disease. The very unfavorable results obtained in England in 1895 in the treatment of *diphtheria* with serum were due, according to the report of the Lancet Commission (*L. L.*, July 19, 1896), in a great majority of cases, to the uses of serum too weak to produce therapeutic results. Experimental researches, for example, the very careful work of Madsen in Copenhagen in 1896, showed that for therapeutic purposes weak serum is of very little value. Equally disappointing results will be obtained if the antitoxin is administered after the toxine has damaged the cells. The early use of the remedy is of the greatest importance. No time should be lost, not even delay in waiting for bacteriological confirmation. As soon as diphtheria is suspected, 10,000 units of antitoxin should at once be injected into the subcutaneous or intramuscular tissue. The reliable figures given in the tables below, collected by Dieudonné (*Schutzimfung und Serum Therapie*) shows conclusively the great practical value of diphtheria antitoxin and emphasizes the importance of administering the remedy early.

Author.	Total number of cases.	Mortality per-centage.	First day	Second day.	Third day.	Fourth day.	Fifth day.	Sixth day.	After the sixth day.	Unknown.
Welch	1489	14.2	2.3	8.1	13.5	19.0	29.3	34.1	33.7	17.6
Hilbert	2428	18.3	2.2	7.6	17.1	23.8	33.9	34.1	38.2	....
Collective investigations of the American Pædiatric Society	5794	12.3	4.9	7.4	8.8	20.7	35.3	....	....	....
Collective investigations in the Austrian Health Department	1103	12.6	8.0	6.6	9.8	25.5	28.8	30.7	21.0	31.8
Collective investigations of the German Imperial Board of Health	9581	15.5	6.6	8.3	12.9	17.0	23.2	....	26.9	....

It will be seen from this table that every hour's delay lessens the chance of successful treatment. In cases treated within the first twenty-four hours of the onset of the disease the mortality is very small. "The bacteriological investigations of diphtheria in the United States" by William Welch (*Am. J. M. S.*, vol. 108, p. 427), show that 1115 cases of diphtheria treated in the first three days of the disease yielded a mortality of 8.5 per cent., whereas 546 cases in which the antitoxin was first injected after the third day of the disease a mortality of 27.8 per cent. resulted. Welch's statistics gathered from the hospitals of the world show conclusively that the antitoxin treatment produces "an apparent reduction of case mortality of 55.8 per cent." In Boston, a city which has suffered severely from diphtheria and where the antitoxin treatment has been particularly thorough, the reduction in the death rate has been striking. In the Boston City Hospital the death rate between 1888 and 1894 was only once below 40 per cent.; since 1895, when antitoxin was introduced, it has not once reached 15 per cent. (J. H. McCallum). Numerous statistics from all parts of the world upon the effect of the antitoxin treatment of diphtheria are practically unanimous in showing the good results of this remedy. The great value of diphtheria antitoxin is perhaps most strikingly seen in the laryngeal cases (*"membranous croup"*).

The standard curative dose is 10,000 units administered at once, though mild cases require less and severe ones more—particularly if not seen at the early stage. The entire amount needed should be given at one dose, intravenously if the case is urgent. A vein at the bend of the elbow may be punctured with the injection needle under aseptic precautions, and the antitoxin slowly introduced. Fortunately the serum is usually harmless even when injected in large quantities. The remedy should always be given by the hypodermic, intramuscular, or intravenous method. Strict asepsis must be observed. The liquid may be injected under the skin of any part of the body where the subcutaneous tissue is loose. The back, near the angle of the scapula, is a favorite site for inoculation; sometimes the flank or abdominal walls are chosen. The intramuscular route is more rapid and hence more effective than the subcutaneous; the heavy muscularature of the buttocks is usually chosen for this method. If improvement is not manifest after a few hours more antitoxin should be given, though this implies that the first dose was too small. It is the early administration rather than the large quantity which is most efficient. The exhibition of the remedy by the mouth or per rectum is practically valueless.

Diphtheria antitoxin is just as valuable for prophylaxis as for curative purposes. The passive immunity produced by the inoculation of the antitoxic serum does not last very long. The transitory nature of the immunity afforded by prophylactic injections is probably dependant upon the fact that the antitoxin-bearing horse serum, being a foreign protein, is broken down in the human body and excreted by the kidneys. The usual prophylactic dose is 1000 units. If the exposure to the infection continues the dose should be repeated in two weeks, but the second dose of antitoxin is more rapidly eliminated than the first. The antitoxin in the blood neutralizes the toxin elaborated by the bacilli growing on the mucous membrane of the throat, but has no

deleterious effect upon the bacteria themselves. The micro-organisms in this situation may continue to grow and remain virulent for months. This is the explanation of occasional failures of the antitoxin to prevent a subsequent attack of the disease.

Though the serum is usually harmless, sometimes urticaria, localized erythema and joint pains follow its administration. These symptoms commonly pass away without untoward consequences. The serum appears not to irritate the kidneys, even when injected into the tissues in very large amounts. Very rarely sudden death immediately follows the injection of diphtheria antitoxin. The cause of this unfortunate result is hypersusceptibility to horse serum. Such an accident may be avoided where it is feared on account of horse asthma or other evidence of sensitiveness, by the injection first of 0.1 mil of the serum and doubling the dose each half hour if no untoward symptoms develop, until the whole amount has been given. In any case, however, the danger from diphtheria is greater than the danger from serum reaction (anaphylaxis), and the antitoxin should not be withheld.

Diphtheric antitoxin gradually loses its strength, especially when kept under unfavorable conditions of light, temperature, etc. The loss in one year is usually from 10 to 30 per cent.; however, a serum will retain considerable antitoxic potency after years. Except for its diminished potency an old serum is quite as good as one freshly prepared; so that in an emergency or in order to save time an old serum may be administered, provided it remains uncontaminated.

Dose, prophylactic, 1000 to 2000 units; curative, 5000 to 20,000 units.

SERUM ANTIDIPHTHERICUM PURIFICATUM. U. S.

PURIFIED ANTIDIPHTHERIC SERUM Ser. Antidiph. Purif. [Antidiphtheric Globulins, Concentrated Diphtheria Antitoxin, Diphtheric Antitoxin Globulins, Refined and Concentrated Diphtheria Antitoxin]

(sē′rŭm ăn′-tĭ-dĭph-thĕr′ĭ-cŭm pū-rĭ-fĭ-cā′tŭm)

"A solution in physiological solution of sodium chloride of certain antitoxic substances obtained from the blood serum or plasma of the horse, *Equus Caballus* Linné (Fam. *Equidæ*), or other large domestic animal, which has been properly immunized against diphtheria toxin. After the serum or plasma from the immunized animal has been collected the antitoxin-bearing globulins are separated from the other constituents of the serum or plasma and dissolved in water; and sufficient sodium chloride is then added to make a solution containing from 0.6 to 0.9 per cent. of the salt. It has a potency of not less than 250 antitoxic units per mil. It must be kept in sealed glass containers in a dark place, at a temperature between 4.5° and 15° C. (40° and 59° F.)." *U. S.*

In the United States, this concentrated antitoxin has almost entirely supplanted the plain antidiphtheric serum, on account of the convenience of giving the same bulk in a smaller amount of fluid, and on account of the somewhat lessened tendency to urticaria after its use. Sterility is secured by careful filtration through bacteria-excluding filters.

For preparation, preservatives, tests, uses, see *Serum Antidiphthericum,* U. S.

Properties.—"A transparent, or slightly opalescent liquid, with sometimes a slight granular or ropy deposit, nearly odorless, or having an odor due to the presence of the antiseptic used as a preservative. The liquid is sometimes more or less viscous. The serum must come from healthy animals, must be sterile, must be free from toxins or other bacterial products, and must not contain an excessive amount of preservative (not more than 0.5 per cent. of phenol or cresol, when either of these is used), and the total solids must not exceed 20 per cent. Serum of a lower potency than 250 units per mil must not be sold or dispensed. Purified Antidiphtheric Serum must comply with the requirements for loss of potency, control, labeling, and standard for potency under *Serum Antidiphthericum.*" *U. S.*

Dose, prophylactic, 1000 to 2000 units; curative, 5000 and 20,000 units.

SERUM ANTIDIPHTHERICUM SICCUM. U. S.

DRIED ANTIDIPHTHERIC SERUM Ser. Antidiph. Sicc. [Dried Diphtheria Antitoxin]

(sē′rŭm ăn′-tĭ-dĭph-thĕr′ĭ-cŭm sĭc′cŭm)

"Dried Antidiphtheric Serum is obtained by the evaporation of either Antidiphtheric Serum or Purified Antidiphtheric Serum in a vacuum over sulphuric acid or other desiccating agent, or by passing over it a current of warm air freed from bacteria. It has a potency of not less than 4000 units per gramme. It must be kept in hermetically sealed, amber-colored glass containers free from air, at a temperature between 4.5° and 15° C. (40° and 59° F.), preferably in a dark place." *U. S.*

"Dried highly potent diphtheria antitoxin, which contains at least 5000 units in 1 gram, and has received no antiseptic or other addition; it is preserved in vacuum tubes." *P. G.*

Though the dried antitoxin retains its potency a much longer time than does the liquid serum, it is difficult to bring into solution for administration and the necessity of making such a solution strictly sterile without injuring the antitoxin imposes great inconvenience. For these reasons the dried product is little used in the United States.

Preparation, tests, uses, see *Serum Antidiphthericum,* U. S.

Properties.—"The Dried Serum is either in the form of orange or yellowish flakes or small lumps, or as a yellowish-white powder, without odor. The Serum is soluble in nine parts of distilled water, but the solution is opalescent and slightly viscous; it may be dissolved more readily in larger amounts of distilled water or physiological solution of sodium chloride. Immediately before use the Serum must be dissolved in

recently boiled and cooled distilled water under the most rigid aseptic conditions. The solution must be used immediately and if there should be any serum or solution remaining, it must be discarded. Dried Antidiphtheric Serum if kept as directed does not lose in potency, as does the liquid serum. It must comply with the requirements for control and labeling under *Serum Antidiphthericum* and the standard of strength, expressed in units of antitoxic power, shall be that established by the United States Public Health Service." *U. S.*

Preservative.—No antiseptic is added to the dry serum for the reason that bacterial multiplication cannot take place in a perfectly dry medium. Therefore, the double precaution must be taken that the serum be preserved entirely dry (hermetically sealed in vacuum), and that it be dissolved under rigid asepsis and used immediately.

Dose, prophylactic, 1000 to 2000 units; curative, 5000 to 20,000 units.

SERUM ANTITETANICUM. U. S.

ANTITETANIC SERUM Ser. Antitetan.
[Tetanus Antitoxin]

(sē'rŭm ăn-tĭ-tĕ-tăn'ĭ-cŭm)

"A fluid, having a potency of not less than 100 units per mil, separated from the coagulated blood of the horse, *Equus Caballus* Linné (Fam. *Equidæ*), or other large domestic animal, which has been properly immunized against tetanus toxin. It must be kept in sealed glass containers in a dark place, at a temperature between 4.5° and 15° C. (40° and 59° F.)." *U. S.*

"The blood-serum of horses which have been immunized against the tetanus poison." *P. G.*

Tetanus-Heilserum, *G.*; Serum Antitetanique, *Fr.*; Siero Antitetanico, *It.*; Suero Antitetanico, *Sp.*

The discovery of tetanus and diphtheria antitoxins was simultaneous, Behring, who worked principally on diphtheria, and Kitasato who worked on tetanus publishing their results together (*D. M. W.*, Nos. 49, 50, 1890) from the Hygienic Institute in Berlin under Robert Koch. In general the method of preparation is the same as that described under *Serum Antidiphthericum.* The purified and dried tetanus toxin is the most powerful poison known, the fatal dose for mice being as low as 0.000,000,05 gramme. There are at least two toxins produced by the tetanus bacillus—*tetano-spasmin,* which causes the muscular contractions typical of the disease, and *tetano-lysin,* which destroys the red corpuscles of the blood. The former is by far the more important, giving the symptoms of rigidity (*e.g.,* lockjaw), and tonic convulsions by which the disease is recognized in man and animals, and causing the high mortality. This poison is absorbed by the end-plates of the nerves in muscle, and travels up these motor nerves to the ganglion cells of the central nervous system. It is the passage along the nerves which occupies the greater part of the time of the incubation period.

Preparation.—The chief difference in method of preparation from that used in the case of diphtheria antitoxin lies in the fact that the tetanus bacillus belongs to the group of bacteria known as obligatory anaerobes, that is, those which thrive only in the absence of oxygen—and in the further fact that the poison formed by the tetanus bacillus is very unstable and rapidly loses in strength under ordinary conditions. The former difficulty is overcome by growing in deep vessels containing specially prepared broth which has been freshly heated to drive off the oxygen; and the latter by using the toxin soon after preparation or by storing it under special conditions.

Properties.—"A yellowish or yellowish-brown, transparent, or slightly turbid liquid with sometimes a slight granular deposit; nearly odorless, or having an odor due to the presence of the antiseptic used as a preservative. Antitetanic Serum gradually loses in potency, the loss being greater at higher than at lower temperatures. The Serum must come from healthy animals, must be sterile, must be free from toxins or other bacterial products, and must not contain an excessive amount of preservative (not more than 0.5 per cent. of phenol or cresol, when either of these is used), and the total solids must not exceed 20 per cent. Serum of a lower potency than 100 units per mil must not be sold or dispensed. Only such Sera may be sold or dispensed as have been prepared and propagated in establishments licensed by the Secretary of the Treasury of the United States. The United States law requires that each container of Serum sold or dispensed by licensed establishments shall bear upon the label, in addition to the name of the Serum, the name, address and license number of the manufacturer and the date beyond which the contents cannot be expected to yield its specific results. The label must also contain the laboratory number of the Serum and the total number of antitoxic units claimed for the contents of the container. The standard of strength, expressed in units of antitoxic power, shall be that established by the United States Public Health Service." *U. S.*

This serum was not included in the U. S. P. VIII because of the lack of a satisfactory standard. Since then, however, such a standard has been established. (The Standardization of Tetanus Antitoxin, by M. J. Rosenau and John F. Anderson, *Hyg. Lab. Bull.,* No. 43, U. S. P. H. S., March, 1908.) This method of standardization is distinct from any previously in use, but, since its adoption in this country, has come to be used to a large extent outside the United States as well. As with diphtheria antitoxin, the ultimate standard unit is a definite amount of dried serum kept under special condition at Washington. The technic of the preparation, storage, weighing, and solution of this antitoxin is the same as in the case of the diphtheria standard. The medium of measurement, however, is a standardized toxin which is likewise dried and preserved in vacuum tubes in the absence of moisture, and sent out to the establishments in various parts of the world

manufacturing tetanus antitoxin. On account of the hygroscopic quality of this dried poison and its extreme instability in the presence of moisture, it is necessary that the tubes be kept after opening in a vacuum desiccating chamber at a low temperature and protected from light. For each use the powder must be weighed quickly on delicate balances and computation made for gain in weight due to absorption of moisture. Any deterioration in the toxin may be detected by testing with the standard antitoxin or by ascertaining the minimal lethal dose (MLD), which is stated for each tube of toxin when sent out.

The animal used for testing tetanus antitoxin by the American standard is the guinea pig. The standard weight is 350 grammes, and the test dose of the toxin when mixed with one-tenth unit of antitoxin, should kill the guinea pig in about ninety-six hours.

Tetanus antitoxin, as well as all similar products, is tested for sterility by planting in suitable culture media and incubating for a number of days, and for presence of toxin, excess of preservative, or other deleterious content, by animal inoculation.

For other legal requirements, see *Serum Antidiphthericum,* U. S.

Uses.—Tetanus antitoxin has achieved its great success as a preventive rather than as a curative measure. Though in times of peace *tetanus* is not a common disease, the tetanus bacillus is ubiquitous and in its spore form, very long lived; its relative infrequence as a cause of sickness and death is due to the excellence of the bodily defenses against it. As explained above, the tetanus bacillus requires an absence of oxygen to thrive; this is not obtained unless the organism is introduced deep below the surface of the skin or under a tight covering, is accompanied by other organisms which absorb the oxygen, or has necrotic tissue as a nutrient. Even if so introduced, the natural antagonism of the body fluids or the wandering cells of the blood may render the invasion harmless. There is abundant evidence, however, that when the above conditions are favorable to its development, the tetanus bacillus produces a high mortality among wounded, and that this mortality is due to the toxin alone. Aside from the occasional tetanus infection when an ordinary wound is contaminated with dirt, and the cases of tetanus neonatorum now fortunately obsolete with the advent of asepsis in labor and in treatment of the umbilical cord, there are three large causes of tetanus: Fourth of July wounds—the laceration from explosion at short range driving contaminated material deep into the tissues; operation and wounds of horses—since horse manure is one of the most prolific sources of the tetanus bacillus; the wounds of warfare, particularly on cultivated terrain. In each of these three classes we have evidence of the value of tetanus antitoxin as a preservative.

In St. Louis, where tetanus had been common following Independence Day, the institution of serum treatment in 1904 was followed by entire absence of tetanus among those so treated. For the whole United States, where the growing use of tetanus antitoxin has been paralleled with decreasingly violent celebrations, the reduction in fatality is striking, the deaths from tetanus having fallen from 406 in 1903 to 1 in 1915, while the ratio of deaths from tetanus to total deaths from fireworks has fallen from 1 in 1.15 (406 out of 466) to 1 in 30, thus indicating that the tetanus prophylaxis has outstripped the general measures of safety.

The veterinary use of tetanus antitoxin in this country has repeatedly eliminated the disease among horses where it had previously been endemic. In France tetanus following operations on horses had been extremely common until the use of antitoxin was instituted, when the tetanus ceased except in the practise of those veterinarians who did not use the antitoxin.

All observers in the European war hospitals agree that when tetanus antitoxin was difficult to procure, in the early part of the war, the mortality from tetanus was high; but when properly standardized potent serum became available and was thoroughly administered, tetanus was rare. Though official statistics are not yet published, it seems clear from late military experience that in all wounds except the slight ones which heal quickly, the prophylactic injection of tetanus antitoxin should be repeated at weekly intervals until the wound is healed and wounded soldiers should receive a prophylactic dose when operated upon, even though the original wound had closed.

The results with tetanus antitoxin as a curative agent in the presence of the developed disease are not so brilliant, some surgeons questioning its value under these conditions. Intensive treatment, however, particularly intraspinal injection, apparently gives a lower death rate than is usual with tetanus treated without antitoxin. The technic for intraspinal medication is described under *antimeningococcus serum* in Part II.

For prophylaxis, then, 1500 units should be injected subcutaneously in case of any wound contaminated with dirt, caused by an explosive, or accompanied by severe mutilation of tissue. This injection should be repeated at weekly intervals until the wound has healed. It is also important that all such wounds receive thorough surgical attention, with wide opening and cleansing, removal of tissue likely to necrose, and repeated antiseptic dressings. For treatment, about 5000 units should be given intraspinally as promptly as possible, and 10,000 units intravenously at the same time; unless the serum is of low viscosity, it may well be diluted with sterile salt solution for intraspinous injection. The intraspinal dose may be repeated daily and the larger dose repeated subcutaneously a few days later to keep the blood saturated with antitoxin. The powdered antitoxin is sometimes used as a dusting powder on wounds, but absorption in this method is uncertain; chief reliance in prophylaxis must be placed in subcutaneous injection.

Hypersusceptibility to horse serum should be guarded against in the use of tetanus antitoxin as in the case of diphtheria antitoxin. The deterioration of the two serums is also similar.

SERUM ANTITETANICUM PURIFICATUM. U. S.

PURIFIED ANTITETANIC SERUM Ser. Antitetan. Purif. [Antitetanic Globulins, Concentrated Tetanus Antitoxin, Refined and Concentrated Tetanus Antitoxin, Tetanus Antitoxin Globulins]

(sē'rŭm ăn-tĭ-tē-tăn'ĭ-cŭm pū-rĭ-fī-cā'tŭm)

"A solution in physiological solution of sodium chloride of certain antitoxic substances obtained from the blood serum or plasma of the horse, *Equus Caballus* Linné (Fam. *Equidæ*), or other large domestic animal, which has been properly immunized against tetanus toxin. After the serum or plasma from the immunized animal has been collected, the antitoxin-bearing globulins are separated from the other constituents of the serum or plasma and dissolved in water; and sufficient sodium chloride is then added to make a solution containing from 0.6 to 0.9 per cent. of the salt. It has a potency of not less than 100 units per mil. It must be kept in sealed glass containers in a dark place, at a temperature between 4.5° and 15° C. (40° and 59° F.)." *U. S.*

As with diphtheria antitoxin, this concentrated serum is usually preferred to the unconcentrated on account of the reduction in bulk and the lessened amount of the proteins of horse-serum for a given unitage value.

Preparation, preservatives, tests, uses, see *Serum Antitetanicum,* U. S.

Properties.—"A transparent or slightly opalescent liquid, with sometimes a slight granular or ropy deposit; nearly odorless, or having an odor due to the presence of the antiseptic used as a preservative. The liquid is sometimes more or less viscous. The serum must come from healthy animals, must be sterile, must be free from toxins or other bacterial products, and must not contain an excessive amount of preservative (not more than 0.5 per cent. of phenol or of cresol, when either of these is used), and the total solids must not exceed 20 per cent. Serum of a lower potency than 100 units per mil must not be sold or dispensed. Purified Antitetanic Serum must comply with the requirements for loss of potency, control, labeling and standard for potency under *Serum Antitetanicum.*" *U. S.*

Dose, prophylactic, 1500 units; curative, 5000 to 20,000 units.

SERUM ANTITETANICUM SICCUM. U. S.

DRIED ANTITETANIC SERUM Ser. Antitetan. Sicc. [Dried Tetanus Antitoxin]

(sē'rŭm ăn-tĭ-tē-tăn'ĭ-cŭm sĭc'cŭm)

"Dried Antitetanic Serum is obtained by the evaporation of either Antitetanic Serum or Purified Antitetanic Serum in a vacuum, over sulphuric acid or other desiccating agent, or by passing over it a current of warm air freed from bacteria. It has a potency of not less than 1000 units per gramme. It must be kept in hermetically sealed amber-colored glass containers, free from air, at a temperature between 4.5° and 15° C. (40° and 59° F.), preferably in a dark place." *U. S.*

"Dried tetanus antitoxin which has received no antiseptic or other addition; it is preserved in vacuum tubes." *P. G.*

As with dried diphtheria antitoxin, dried tetanus antitoxin has the advantage of retaining full potency longer than the liquid forms, and the disadvantage of being difficult to bring into solution. The dried powdered tetanus antitoxin, however, has one additional use, as a local application to wounds; this treatment should be supplemented by subcutaneous injection of the liquid antitoxin or dissolved powder, since the amount absorbed from the wound is uncertain.

Preparation, tests, uses, see *Serum Antitetanicum,* U. S.

Properties.—"Dried Antitetanic Serum is either in the form of orange or yellowish flakes or small lumps, or a yellowish-white powder, without odor. The serum is soluble in nine parts of distilled water, but the solution is opalescent and slightly viscous; it may be dissolved more readily in larger amounts of distilled water or physiological solution of sodium chloride. For use, the serum must be dissolved in recently boiled and cooled distilled water under the most rigid aseptic conditions. The solution must be used immediately and, if there should be any serum or solution remaining, it must be discarded. Dried Antitetanic Serum if kept as directed does not lose in potency, as does the liquid serum. It is sometimes used as a dusting powder or for local application to infected wounds. It must comply with the requirements for control and labeling under *Serum Antitetanicum* and the standard of strength, expressed in units of antitoxic power, shall be that established by the United States Public Health Service." *U. S.*

Preservative.—No antiseptic is added to the dry serum for the reason that bacterial multiplication cannot take place in a perfectly dry medium. Therefore the double precaution must be taken that the serum be preserved entirely dry (hermetically sealed in vacuum) and that it be dissolved under rigid asepsis and used immediately.

Dose, prophylactic, 1500 units; curative, 5000 to 20,000 units.

SEVUM BENZOATUM. Br.

BENZOATED SUET

(sē'vŭm bĕn-zō-ā'tŭm)

"Prepared Suet, 1000 *grammes;* Benzoin, in coarse powder, 30 *grammes.* Melt the Suet, add the Benzoin, and maintain at a temperature of 60° C. (140° F.), for one hour, stirring frequently; strain, and stir until nearly cold. In

India, Benzoated Suet should be employed in making the official preparations for which Benzoated Lard (Adeps Benzoatus) is directed to be used." *Br.*

It is also official in the N. F. IV under the title *Sevum Benzoinatum* (see Part III).

SEVUM PRÆPARATUM. U. S., Br.

PREPARED SUET Sev. Præp. [Mutton Suet Sevum, U. S. 1890]

(sē'vŭm præ-pą-rā'tŭm)

"The internal fat of the abdomen of the sheep (*Ovis aries* Linné, Fam. *Bovidæ*), purified by melting and straining. Preserve Prepared Suet in well-closed vessels impervious to fat. It must not be used after it has become rancid." *U. S.* "Prepared Suet is the purified internal fat of the abdomen of the sheep, Ovis aries, *Linn.*" *Br.*

Sevum, *U. S.* 1890; Sebum Ovillum; Mutton-Suet, Prepared Mutton Tallow; Suif de Mouton, *Fr. Cod.*; Graisse de Mouton, *Fr.*; Sebum ovile, *P. G.*; Hammeltalg, Talg, Schöpsentalg, Unschlitt, *G.*; Grasso di Moutone, Grasso duro, *It.*; Sebo de carnero, *Sp.*

Suet is the fat of the sheep, taken chiefly from about the kidneys. It is prepared by cutting the fat into pieces, melting it with a moderate heat, and straining it through linen or flannel. In order to avoid too great a heat, the crude suet is sometimes purified by boiling it in a little water. Mutton suet is of a finer consistence, and requires a higher temperature for its infusion, than any other animal fat. It is very white, sometimes brittle, inodorous, of a bland taste, insoluble in water, and nearly so in alcohol. Boiling alcohol, however, dissolves it, and deposits it upon cooling. It consists, according to Chevreul, of stearin, palmitin, and olein, containing approximately 70 per cent. of stearin and palmitin and 30 per cent. of olein. These principles are described under the *Olea Fixa* (page 727). It is officially described as "a white, solid fat, nearly inodorous, and having a bland taste when fresh, but becoming rancid on prolonged exposure to the air. It is insoluble in water or cold alcohol; it dissolves in 44 parts of boiling alcohol, in about 60 parts of ether, and slowly dissolves in 2 parts of purified petroleum benzin. From its solution in the latter, when allowed to stand in a stoppered flask, it slowly separates in a crystalline form. An alcoholic solution of Prepared Suet is neutral or slightly acid to litmus paper moistened with alcohol. Prepared Suet melts between 45° and 50° C. (113° and 122° F.) and congeals between 37° and 40° C. (98.6° and 104° F.). One Gm. of Prepared Suet, dissolved in 50 mils of hot alcohol, and a few drops of phenolphthalein T.S. added, requires not more than 0.6 mil of tenth-normal potassium hydroxide V.S. to produce a pink color (*free acid*). Saponification value: not less than 193 nor more than 200 (see Part III, Test No. 9). Iodine value: not less than 33 nor more than 48 (see Part III, Test No. 8)." *U. S.*

"Firm, white, unctuous. Nearly inodorous; taste bland. *Saponification value* 192 to 195; *iodine value* 33 to 46; *acid value* not more than 2.0; melting point 45° to 50° C. (113°–122° F.); *refractive index* at 60° C. (140° F.), 1.4490 to 1.4510. In India, Prepared Suet should be employed in making the official preparations for which Prepared Lard (Adeps Præparatus) is directed to be used." *Br.*

E. Dieterich examined a large number of samples of mutton and beef suet, and found that they were without exception acid and that neutral suet does not exist. The melting point of mutton suet is between 48.5° and 50.5° C. (119.3°–122.9° F.); that of beef suet, between 47.5° and 48° C. (117.5°–118.4° F.). The specific gravity of mutton suet lies between 0.937 and 0.952; that of beef suet, between 0.943 and 0.952. (*A. Pharm.*, 1887, 496.)

Off. Prep.—Sevum Benzoatum, *Br.*

SINAPIS ALBA. U. S.

WHITE MUSTARD Sinap. Alb. [Yellow Mustard]

(si-nā'pĭs ăl'bą)

"The ripe seeds of *Sinapis alba* Linné (Fam. *Cruciferæ*), without the presence or admixture of more than 5 per cent. of other seeds or other foreign matter. Preserve powdered White Mustard in tightly-closed containers." *U. S.*

Sinapis Albæ Semina, *Br.* 1898; White Mustard Seeds; Yellow Mustard Seed; Moutarde blanche, *Fr. Cod.*; Semen Erucæ, *P. G.*; Weisser Senfsamen, Weisser Senf, *G.*; Senape bianca, *It.*; Mostaza blanca, *Sp.*

Neither black nor white mustard is any longer official in the British Pharmacopœia.

Yellow or *white mustard* is a native of Europe and is extensively cultivated, being occasionally spontaneous, in the United States. The commercial supplies are obtained from England, Holland, Germany and California.

Properties.—The official description of white mustard is as follows: "Sub-globular, from 1.5 to 2.5 mm. in diameter; testa yellowish, nearly smooth; embryo yellowish, oily, with two large cotyledons; inodorous, taste mildly pungent, acrid. The powder is light yellowish or pale brownish-yellow, developing a slight odor when moistened; when examined under the microscope it exhibits numerous tissues of the embryo containing small aleurone grains and a fixed oil, the latter forming in large globules on the addition of hydrated chloral T.S.; fragments of seed-coat comparatively few, nearly colorless, with small, characteristic stone cells and large epidermal cells, the outer walls being mucilaginous. The powder contains few or no starch grains. White Mustard does not yield allyl isothiocyanate upon distillation with steam (distinction from *Black Mustard*). White Mustard yields not more than 9 per cent. of ash." *U. S.*

For an illustrated monograph on the pharmacognosy of white mustard, see Winton and Moeller, "*Microscopy of Vegetable Foods.*" The only adulterant of white mustard are the seeds of the white Indian *colza*, obtained from *Brassica campestris* Sarson (L.) Prain. They are

distinguished in having a more pronounced ridge over the radicle. Under the microscope the seeds have an indistinct epidermis, the collenchymatous subepidermal layer is wanting, and the palisade cells are quite large compared with white mustard. For further information see *Sinapis Nigra.*

SINAPIS NIGRA. U. S.

BLACK MUSTARD Sinap. Nig. [Brown Mustard]

(sī-nā'pĭs nī'grą)

"The ripe seeds of *Brassica nigra* (Linné) Koch (Fam. *Cruciferæ*), without the presence or admixture of more than 5 per cent. of other seeds or other foreign matter. Preserve powdered Black Mustard in tightly-closed containers." *U. S.*

Sinapis Nigræ Semina *Br.* 1898; Black Mustard Seeds; Semina Brassicæ; Moutarde noire, *Fr. Cod.*; Moutarde, *Fr.*; Semen Sinapis, *P. G.*; Senfsamen, Schwarzer Senf.; Senape nera, *It.*; Mostaza (Semilla de), *Sp.*

Linnæus described two genera, Brassica and Sinapis, and subsequent botanists have greatly disagreed as to whether they should be considered identical or not. The revisers of the U. S. P. have adopted the opinion of Engler and Prantl and of Britton and Brown, that the two genera are distinct. The genus Sinapis differs from Brassica in that the pods of the former are terminated by a long, flat, sword-like beak, whereas in Brassica the beak is cylindrical or conical.

Common or black mustard (*Brassica nigra*), is an annual plant, with a stem three or four feet in height, divided and subdivided into numerous spreading branches. The leaves are petiolate and variously shaped. Those near the root are large, rough, lyrate-pinnate, and unequally toothed, those higher on the stem are smooth, and less lobed, and the uppermost are entire and narrow. The flowers are small, yellow, and stand closely together upon peduncles at the upper part of the branches. The pods are smooth, erect, nearly parallel with the branches, quadrangular, and furnished with a slender beak; seeds numerous, dark brown.

The white mustard is also annual. It is rather smaller than the preceding species. The lower leaves are deeply pinnatifid, the upper sublyrate, and all irregularly toothed, rugged, with stiff hairs on both sides, and pale green. The flowers are in racemes, with yellow petals, and linear, green calycine leaflets. The pods are spreading, bristly, rugged, roundish, swelling in the position of the seeds, ribbed, and provided with a very long ensiform beak.

Both sinapis alba and Brassica nigra are natives of Europe and cultivated in our gardens, and *B. nigra* has become naturalized in some parts of this country. Their flowers appear in June. The seeds are kept in the pharmacies, both whole and in the state of very fine powder as prepared by the manufacturers for the table. The latter is sometimes mixed with spices and ground into a smooth paste with water in a mill resembling a paint mill, and then is known as *French mustard.*

The seeds of *Brassica ibertifolia,* according to O. Harz, are sometimes sold as true white mustard seed. He examined some obtained from Bavaria, which had been returned by customers to the dealers on account of their bitter and disagreeable taste. He furnishes characteristic microscopical tests for distinguishing the false from the true mustard seed. His statement, however, that powdered white mustard seed when mixed with water is odorless, and that the false gives off a strong odor of essential oil of mustard, would seem to be a good reason, if correct, for preferring the false seed. (*P. J.,* 1887, 478.)

The *Brassica juncea* (L.) Coss. (*Sinapis juncea* L.), is extensively grown in India, and its seeds are largely exported to Europe. The same plant is also cultivated in Southern Russia. The seeds afford a very fine yellow mustard flour, and, according to Paul Birkenwald, yield 1.67 parts per hundred of volatile oil, against 1.89 parts per hundred by the true black mustard seed. (*S. W. P.,* 1888.)

Black mustard seeds are officially described as "ellipsoidal or irregularly spheroidal, from 1 to 1.6 mm. in diameter; testa deep reddish-brown, sometimes yellowish-brown and with a grayish tinge, minutely pitted or reticulate; embryo greenish-yellow or dark yellow, oily, with two large cotyledons; odor when dry, slight, on moistening very irritating; taste strongly pungent and acrid. The powder is light brown or greenish-brown; on moistening developing a strongly pungent, irritating, characteristic odor; when examined under the microscope it exhibits numerous tissues of the embryo, the cells containing small aleurone grains and a fixed oil, the latter forming in large globules on the addition of hydrated chloral T.S.; fragments of seed-coat conspicuous, with large, polyhedral, dark yellow areas, enclosing small, yellowish stone cells, each of the latter with a dark lumen. The powder contains few or no starch grains. Black Mustard, upon distillation with steam, yields allyl isothiocyanate (distinction from *White Mustard*). Black Mustard yields not more than 9 per cent. of ash." *U. S.*

Both white and black mustard afford a powder, which has a somewhat unctuous appearance, and cakes when compressed. This is commonly called *flour of mustard,* or simply *mustard,* and is prepared by crushing and pounding the seeds and then sifting them, the purest flour being obtained by a second sifting. Both the black and the white seeds are used in its preparation. Formerly it was adulterated with wheat flour colored by turmeric, to which cayenne pepper was added to render the mixture sufficiently hot. Pure mustard powder contains very few starch granules, but was formerly adulterated with farinaceous powders; the U. S. P. VIII required that White or Black Mustard should conform to the following test: "If 1 Gm. of powdered White (or Black) Mustard be exhausted by slow percolation with alcohol, and the marc mixed with 200 Cc. of water and

heated to boiling, and if, after cooling, sufficient cold water be added to make the mixture measure 1000 Cc., the addition of 4 Cc. of tenth-normal iodine V.S. should not produce a dark blue color (limit of *starch*)." *U. S. VIII.*

The epidermis of white mustard seeds contains a mucilaginous substance which is extracted by boiling water. An excellent basic monograph on the pharmacognosy of black mustard is that given by Winton and Moeller in "*The Microscopy of Vegetable Foods.*" Tschirch and Oliva have made a comparative study of the seeds of the Cruciferæ, with special reference to the variations found in the seed-coat of the several species of mustard. (*S. W. P.*, xliii, p. 614.) Spaeth gives the results of chemical and microscopical study of the mustards and some of their adulterants in *Ph. Zentralh.*, xlix, p. 698. Carles has also contributed a valuable article on the pharmacognosy of the different mustard seeds and the commercial varieties of mustard flour in *J. P. C.*, 1913, pp. 438 and 535. The most common adulteration of black mustard is *charlock*, which is the seeds of *Brassica arvensis* (L.) Ktze. This plant is especially abundant in the Northwestern part of the United States and the Dakota mustard contains varying mixtures of brown mustard and charlock. The presence of charlock is very easily determined by the use of a solution of chloral hydrate which changes the color of the palisade cells to a crimson red.

When bruised or powdered, both kinds of mustard impart their active properties wholly to water, but in a very slight degree to alcohol. They yield upon pressure a fixed oil, called *oil of mustard*, of a greenish-yellow color, little odor, and a mild not unpleasant taste; and the portion which remains is even more pungent than the unpressed seeds. The fixed oil of mustard consists of the glycerin compounds of stearic, oleic, and *erucic* or *brassic* acid, $C_{22}H_{42}O_2$, a homologue of oleic acid. Small quantities of *behenic* acid, $C_{22}H_{44}O_2$, also occur in oil of black mustard. This fixed oil is a yellow non-drying oil of from 0.915 to 0.920 sp. gr. at 15° C. (59° F.), solidifying at from –12° to —16° C. (10.4–3.2° F.). It has been long known that black mustard seeds yield by distillation with water a very pungent volatile oil, containing sulphur. Guibourt conjectured, and Robiquet and Boutron proved, that this oil does not pre-exist in the seeds, but is produced by the action of water. Hence the absence or very slight degree of odor in the seeds when bruised in a dry state, and their pungency when water is added. It seemed reasonable to suppose that the reaction in this case was similar to that exercised by water upon bitter almonds (see *Amygdala Amara*), and this has been proved to be the fact by the experiments of Simon, Bussy, Boutron, and Frémy. The composition and peculiar decompositions of the volatile oil of black mustard have already been described. (See *Oleum Sinapis Volatile.*)

A principle was extracted by Will from white mustard seed, with the aid of alcohol. It has been named *sinalbin*, and has the formula $C_{30}H_{44}N_2S_2O_{16}$. It is decomposed, after the analogy of sinigrin (potassium myronate), into *acrinyl sulphocyanate*, C_7H_7OCNS, *sinapine bisulphate*, $C_{16}H_{25}NSO_9$, and sugar, $C_6H_{12}O_6$, an albuminoid substance being formed at the same time. "The acrinyl sulphocyanate (C_7H_7OCNS) is a very active principle, oily, insoluble in water, not volatile. It may be obtained by causing ether to act on the product of the decomposition of sinalbin. Treated by an alkali and then neutralized by an acid, it colors ferric chloride red." (*J. P. C.*, Avril, 1872, 327.)

The analyses of mustard seeds and mustard flour given in the table below, are by Piesse and Stansell. (*Analyst*, 1880, p. 161.)[1]

[1] Analyses of Mustard.

	White Mustard, whole seeds.		White Mustard, ground.		Brown Mustard, whole seeds.	Brown Mustard ground.	
	Yorkshire.	Cambridge.	Superfine.	Fine.	Cambridge.	Superfine.	Fine.
Moisture	9.32	8.00	6.30	5.78	8.52	4.35	4.52
Fatty oil	25.56	27.51	37.18	35.74	25.54	36.96	38.02
Cellulose	10.52	8.87	3.90	4.15	9.01	3.09	2.06
Sulphur	0.99	0.93	1.33	1.22	1.28	1.50	1.48
Nitrogen	4.54	4.49	5.05	4.89	4.38	4.94	5.01
Albuminoids	28.37	28.06	31.56	30.56	26.50	29.81	30.25
Myrosin and albumin	5.24	4.58	7.32	6.67	5.214	6.46	6.78
Soluble matter	27.38	26.29	36.31	36.60	24.22	31.14	32.78
Volatile oil	0.06	0.08	0.03	0.04	0.047	1.437	1.50
Potassium myronate	.....	.....	.....	.....	1.692	5.141	5.366
Ash	4.57	4.70	4.22	4.31	4.98	5.04	4.84

According to F. W. Widmayer (*D. C.*, 1904, 8), the oil from yellow seed is of a greenish-yellow color, that of the brown seed a much darker shade. Both have but little odor and a mild, not unpleasant taste. Mustard seed oil is a semi-drying oil. The analytical data showing maximum and minimum results by M. L. Tolman and L. S. Munson on five samples are as follows: Specific gravity at 15.5° C. (59.9° F.), 0.9147 to 0.9193; Butyrorefractometer reading (15.5° C. (59.9° F.)), 74.5 to 76.5; Index of refraction at 15.5° C. (59.9° F.), 1.4750 to 1.4762; Maumené number 61.4 to 79.4; Specific temperature reaction 130.9 to 190.3; Hübl number,

98.4 to 113.0; Saponification value, 173 to 182.8; Melting point of fatty acids, 20.8 to 21.5° C. 69.4°–70.7° F.); Free fatty acids oleic, 0.13 to 1.13 per cent.; Solidification from –8° to –18° C. (17.6° to –0.4° F.). One remarkable feature of this oil is its penetrating or diffusing power. Barrels that will hold olive, cotton seed, or petroleum oil or even new oil or alcohol barrels invariably leak on being filled with it, and it is said by one who has had extensive experience in the mustard business that it has been known to come through a tank which had stood a pressure of 80 pounds of steam. (*D. C.*, 1904, 8.)

J. U. Lloyd has proposed standards for black and white mustard seed, mainly directed towards limiting the proportion of starch; the latter is not a constituent of ripe mustard seed, but commercial mustard nearly always contains starch, due to starch-bearing seeds accidentally present in the mustard seed, or to fraudulent admixture. (*A. J. P.*, 1898, 433.) Dieterich (*Ph. Ztg.*, Oct. 3, 1900, 767) proposed an assay for mustard seed, mustard oil and mustard paper.

Uses.—Mustard seeds swallowed whole operate as a laxative, and have acquired some reputation as a remedy in *dyspepsia*, and in other affections attended with torpid bowels and deficient excitement. The white seeds are preferred, and are taken in the dose of a tablespoonful (15.5 Gm.) once or twice a day, mixed with molasses, or previously softened and rendered mucilaginous by immersion in hot water. They probably act in some measure by mechanically stimulating the bowels. The powder, commonly called simply mustard, in the quantity of from one to two teaspoonfuls (3.9–7.7 Gm.), is an efficient and prompt—although unpleasant—stimulant emetic, especially valuable in *narcotic poisoning*. As a condiment mustard acts as a stimulant to the gastric mucous membrane, increasing according to Gottlieb (*A. E. P. P.*, 1894, xxxiii, 261), also the pancreatic secretion. By virtue of this stimulant action it will sometimes relieve obstinate *hiccough*.

But mustard is most valuable as a rubefacient. Mixed with water in the form of a cataplasm, and applied to the skin, it very soon produces redness with burning pain, which in less than an hour usually becomes insupportable. When a speedy impression is not desired, especially when the sinapism is applied to the extremities, the powder should be diluted with an equal, or double, portion of wheat flour. Care should be taken not to allow the application to continue too long, as vesication with obstinate ulceration, and even sphacelus, may result. This caution is particularly necessary when the patient is insensible and the degree of pain can afford no criterion of the sufficiency of the action. In making a mustard plaster the admixture of alcohol, vinegar, or other fluid than water, should be avoided as hindering the development of the volatile oil. The volatile oil is powerfully rubefacient, and capable of producing speedy vesication, but certainly is less controllable than is the mustard poultice. For external application as a rubefacient, 10 to 20 drops of the oil may be dissolved in a fluidounce of alcohol, or 6 or 8 drops in a fluidrachm of almond or olive oil. (See *Linimentum Sinapis Compositum*, N. F., Part III.) To form a *sinapism* it has been recommended to mix 20 drops of the volatile oil with a gelatinous mass made by heating together 3.5 drachms of glycerin and 5 drachms of starch. Lebaigue proposes applying to one sheet of paper a concentrated solution of *potassium myronate*, and to a second a concentrated solution of *myrosin*, and drying them. When used, the leaves are to be moistened and placed to the surface, one over the other. Volatile oil of mustard is formed by the reaction of the two principles, and a sinapism is obtained. (*J. P. C.*, Août, 1868, p. 118.) The volatile oil of mustard has been given internally in *colic*, two drops being incorporated with a six-ounce mixture, and half a fluidounce (15 mils) given for a dose. In overdoses it is highly poisonous, producing gastro-enteric inflammation, and probably perverting the vital processes by pervading the whole system. Its odor is perceptible in the blood, and is said to impart the smell of horse-radish to the urine. A *spirit of mustard* may be prepared by macerating, for two hours, 250 parts of powdered black mustard with 500 parts of cold water, then adding 120 parts of alcohol of 86 per cent., and distilling over 120 parts of spirit.

Dose, of mustard seed, one to two drachms (3.9–7.7 Gm.).

Off. Prep.—Emplastrum Sinapis, *U. S.*

SODII ACETAS. U. S.

SODIUM ACETATE Sod. Acet.

(sō'dĭ-ī ăˈçę-tăs)

"It contains not less than 59.97 per cent. nor more than 62.96 per cent. of anhydrous sodium acetate, corresponding to not less than 99.5 per cent. of the crystallized salt [$NaC_2H_3O_2 + 3H_2O = 136.07$]. Preserve it in well-closed containers." *U. S.*

Acetate of Soda; Acetas Sodicus (Natricus), Terra Foliata Tartari Crystallisata, Terra Foliata Tartari; Acétate de Soude Cristallisé, *Fr. Cod.*; Natrium Aceticum, *P. G.*; Natriumacetat, Essigsaures Natron, *G.*; Acetato di Sodio, *It.*

Sodium acetate may be easily prepared by adding crystals of sodium carbonate to acetic acid until it is neutralized, filtering, concentrating the solution, and crystallizing. It is prepared in the large way in the manufacture of crude pyroligneous acid, for the purpose of being decomposed, so as to yield the official acetic acid, by the action of sulphuric acid. The steps of the process by which it is made from the crude acid have been given under *Acidum Aceticum*.

Properties.—It is officially described as in "colorless, transparent, monoclinic prisms, or as a granular, crystalline powder; odorless, or having a faint, acetous odor. It has a cooling, saline taste. Efflorescent in warm, dry air. One Gm. of Sodium Acetate dissolves in 0.8 mil of

water and in 19 mils of alcohol at 25° C. (77° F.). An aqueous solution of the salt (1 in 20) is neutral or slightly alkaline to litmus or phenolphthalein T.S. When heated to about 58° C. (136.4° F.), the salt begins to liquefy. At about 120° C. (248° F.) it becomes anhydrous; at a higher temperature it is decomposed, with the evolution of inflammable, empyreumatic vapors, leaving a black residue of sodium carbonate and carbon, which imparts to a non-luminous flame an intensely yellow color, shows an alkaline reaction with litmus, and effervesces with acids. Add 0.1 Gm. of the salt to 1 mil of sulphuric acid and 1 mil of alcohol and warm; ethyl acetate is formed, recognizable by its odor. A saturated aqueous solution of the salt is not rendered turbid by the addition of sodium bitartrate T.S. (*potassium*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of the salt meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"**Assay.**—Proceed as directed under the Assay for alkali salts of organic acids (see Part III, Test No. 6). It shows not less than 59.97 per cent. nor more than 62.96 per cent. of $NaC_2H_3O_2$.

"Each mil of half-normal sulphuric acid V.S. used corresponds to 0.04101 Gm. of $NaC_2H_3O_2$. Each gramme of Sodium Acetate corresponds to not less than 14.62 mils nor more than 15.35 mils of half-normal sulphuric acid V.S." *U. S.*

Sodium acetate, when crystallized, consists of one acetic acid molecule, one atom of sodium and 3 molecules of water.

Uses.—Sodium acetate is diuretic, acting much like potassium acetate, but is rarely used as a medicine. It is employed principally to yield acetic acid by the action of sulphuric acid. In prescribing this salt, the fact, first noticed by Violette, should not be forgotten, that the mixture of equal parts of it and potassium nitrate, if heated, explodes with great violence. (*N. R.*, April, 1873.)

Dose, twenty grains to two drachms (1.3–7.7 Gm.).

SODII ARSENAS. U. S.

SODIUM ARSENATE Sod. Arsen. [Arsenas sodii, P. I.]

(sō'dĭ-ī ăr'sẹ-năs)

"It contains not less than 58.98 per cent. nor more than 61.92 per cent. of anhydrous sodium arsenate (di-sodium ortho-arsenate), corresponding to not less than 99 per cent. of the crystallized salt [$Na_2HAsO_4 + 7H_2O = 312.08$]. Preserve it in well-closed containers." *U. S.*

Natrum Arsenicum, Arsenias Natricus (Sodicus); Sodium Arseniate; Arseniate of Soda; Arséniate de Soude, *Fr. Cod.*; Natriumarsenat, Arsensaure Natron, *G.*; Arseniato bisodico, *It.*; Arseniato sodico, *Sp.*

In the U. S. P. the crystallized and anhydrous salts are official, while the anhydrous salt is the only one recognized in the Br. authority. The exsiccated salt is to be preferred as the crystallized arsenate is apt to contain varying proportions of water of crystallization. The U. S. P. obviates the consequent uncertainty of dosage by inserting an assay provision.

The process for this salt was first made official by the Br. Pharmacopœia of 1864, and by the U. S. Pharmacopœia of 1870. (See *U. S. D.*, 19th edition, page 1127.) In the process, the arsenious acid (arsenic trioxide) is converted into arsenic acid at the expense of the nitric acid of sodium nitrate, and then combines with the sodium of both salts, carbon dioxide, nitrous fumes being given off. The reaction seems to be as follows:

$$As_2O_3 + 2NaNO_3 + Na_2CO_3 + H_2O = 2Na_2HAsO_4 + N_2O_3 + CO_2$$

According to Higgins, the gases emitted in this process contain more or less arsenic—an inconvenience which may be avoided by first dissolving the arsenious acid in a solution of sodium hydroxide, and then adding the nitrate. The calcination should be performed in a reverberatory furnace. The gases which escape up the chimney are now free from arsenic, and consist only of ammonia and nitrous vapors. (*J. P. C.*, 4e sér., ii, 177.)

Properties.—Sodium arsenate is in "colorless, transparent, monoclinic prisms; odorless. Efflorescent in dry air, and somewhat deliquescent in moist air. *Great caution must be used in tasting it and then only in very dilute solutions.* One Gm. of Sodium Arsenate dissolves in 1.5 mils of water at 25° C. (77° F.); also in about 1 mil of boiling water; slightly soluble in alcohol at 25° C. (77° F.); nearly insoluble in boiling alcohol. When gently heated, the salt loses five molecules of water, and is converted into a white powder. At a higher temperature it loses all of its water of crystallization; when strongly heated, the salt fuses, and at a red heat it is converted into pyroarsenate. Sodium Arsenate responds to the tests for identity and purity prescribed under *Sodii Arsenas Exsiccatus* when taken in proportionate amount.

"**Assay.**—Dissolve about 0.5 Gm. of Sodium Arsenate, accurately weighed, in 25 mils of distilled water, heat the solution to 80° C. (176° F.), and add 10 mils of hydrochloric acid and 3 Gm. of potassium iodide. Allow the mixture to stand for fifteen minutes at 80° C. (176° F.), then cool and titrate it with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 58.98 per cent. nor more than 61.92 per cent. of Na_2HAsO_4.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.0092985 Gm. of Na_2HAsO_4. Each gramme of Sodium Arsenate corresponds to not less than 63.44 mils nor more than 66.59 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

Anhydrous sodium arsenate has the composition Na_2HAsO_4; in crystals it sometimes contains 12 molecules of water, equal to 53.73 per cent. of its weight. According to the official formula, this salt crystallizes with 7 molecules of water, or 40.39 per cent. "The latter salt loses 40.38 per cent. of its weight when dried

at 300° F. (148.9° C.), becoming anhydrous. An aqueous solution of 12.4 grains of anhydrous arsenate of sodium, acidulated with acetic acid, requires not less than 34 grains of acetate of lead for complete precipitation." *Br.* 1885. If the temperature of a solution of the salt be kept at 30° C. (86° F.), crystals will be deposited which contain 4 molecules of water. J. Lefort examined 10 different samples of the salt, obtained from as many different sources, and found their water of crystallization to vary from 44.05 to 57.45 per cent. (*J. P. C.*, 1880, 487.)

Uses.—Sodium arsenate possesses the therapeutic properties of arsenic. (See *Arseni Trioxidum.*) It is usually exhibited in solution. According to H. N. Moyer it is less irritating to the stomach than the more frequently used potassium arsenite. It is also occasionally employed hypodermically.

Pearson's Arsenical Solution, Liquor Sodii Arsenatis Pearson, N. F. (see Part III), is one-tenth the strength of U. S. P. IX *Liquor Sodii Arsenatis,* see page 658. Pearson's solution is used in Europe especially for the purpose of the preparation of arsenical baths in the treatment of *rheumatoid arthritis.*

Dose, of crystallized sodium arsenate, one-twentieth to one-eighth of a grain (0.003–0.008 Gm.).

Off. Prep.—Liquor Sodii Arsenatis (from Dried Salt), *U. S., Br.;* Sodii Arsenas Exsiccatus, *U. S.;* Liquor Sodii Arsenatis Pearson, *N. F.*

SODII ARSENAS EXSICCATUS. U. S. (Br.)

EXSICCATED SODIUM ARSENATE Sod. Arsen. Exsic.

(sō'dĭ-ī ăr'sẹ-năs ĕx-sĭc-cā'tŭs)

"It contains, when dried to constant weight at 150° C. (302° F.), not less than 98 per cent. of Na_2HAsO_4 (185.97). Preserve it in well-closed containers." *U. S.*

Sodii Arsenas Anhydrosus, *Br.*, Anhydrous Sodium Arsenate; Natrium Arsenicum Exsiccatum; Dried (anhydrous) Arsenate of Soda; Arséniate de Soude desséché, *Fr.;* Getrocknetes Natriumarsenate, *G.*

"Sodium Arsenate, in crystals, *a sufficient quantity.* Break the crystals into small fragments, and allow them to effloresce at a temperature between 40° and 50° C. (104° and 122° F.) until they are completely disintegrated; then gradually increase the temperature to 150° C. (302° F.) and continue the drying until the product ceases to lose weight. Reduce it to a fine powder, and transfer it to dry, well-closed containers." *U. S.*

"Anhydrous Sodium Arsenate is obtained by exposing to a temperature of 150° C. (302° F.) crystallised sodium arsenate, which may be prepared by treating with water the product of the fusion of arsenious anhydride with sodium nitrate and sodium carbonate. It contains not less than 98 per cent. of pure anhydrous di-sodium hydrogen arsenate, Na_2HAsO_4." *Br.*

For properties see also *Sodii Arsenas.*

Properties.—It is officially described as "an odorless, amorphous, white powder. It is slightly hygroscopic. *Great caution must be used in tasting it and then only in very dilute solutions.* One Gm. of Exsiccated Sodium Arsenate dissolves in 3.1 mils of water at 25° C. (77° F.); also in about 1.3 mils of boiling water; slightly soluble in alcohol at 25° C. (77° F.); nearly insoluble in boiling alcohol. Its aqueous solution (1 in 20) is alkaline to litmus. It imparts an intensely yellow color to a non-luminous flame. An aqueous solution of the salt (1 in 20) yields a white precipitate with barium chloride T.S., and a dark red precipitate with silver nitrate T.S.; both of these precipitates are soluble in nitric acid. Add 5 mils of tenth-normal silver nitrate V.S. to 2 mils of an aqueous solution of the salt (1 in 20) and redissolve the precipitate with the aid of a slight excess of ammonia water; no black precipitate of reduced silver appears on boiling for one minute (*arsenite*). Add 1 mil of ammonium sulphide T.S. to 5 mils of an aqueous solution of the salt (1 in 100); no dark coloration appears (*lead, copper, or iron*)." *U. S.*

"A white powder. Soluble in 6 parts of *water;* slightly soluble in *alcohol* (90 per cent.). Aqueous solution alkaline to *litmus.* Yields the *reactions* characteristic of sodium and of arsenates. When 0.25 gramme is dissolved in 25 millilitres of *water,* and to the solution 3 grammes of *potassium iodide* and 25 millilitres of *hydrochloric acid* are added, not less than 26.3 millilitres of *N/10 solution of sodium thiosulphate* are required to decolorise the iodine liberated. Yields no characteristic *reactions* for lead, copper, iron, aluminium, calcium, carbonates, chlorides, nitrates, or sulphates. Loses not more than 2 per cent. of its weight when dried at 150° C. (302° F.) (limit of moisture)." *Br.*

"**Assay.**—Dissolve about 0.3 Gm. of Exsiccated Sodium Arsenate, dried to constant weight at 150° C. (302° F.) and accurately weighed, in 25 mils of distilled water, in a glass-stoppered bottle, heat the solution to 80° C. (176° F.) and add 10 mils of hydrochloric acid and 3 Gm. of potassium iodide. Allow the mixture to stand in the stoppered bottle for fifteen minutes at 80° C. (176° F.), then cool and titrate it with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows, in the dried salt, not less than 98 per cent. of Na_2HAsO_4.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.0092985 Gm. of Na_2HAsO_4. Each gramme of Exsiccated Sodium Arsenate, previously dried, corresponds to not less than 105.4 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

Uses.—Dried or exsiccated sodium arsenate is useful when it is desired to exhibit the salt in pill form, but differs in no way in its physiological action from sodium arsenate.

Dose, one-fortieth to one-fifteenth of a grain (0.0016–0.004 Gm.).

SODII BENZOAS. U. S., Br.

SODIUM BENZOATE Sod. Benz.

(sō'dĭ-ī bĕn'zō-ās)

"It contains, when dried to constant weight at 110° C. (230° F.), not less than 99 per cent. of $NaC_7H_5O_2$ (144.04). Preserve it in well-closed containers." *U. S.* "Sodium Benzoate may be obtained by neutralizing benzoic acid with sodium carbonate. It contains not less than 96 per cent. of pure sodium benzoate, $NaC_7H_5O_2$." *Br.*

Sodæ Benzoas; Benzoate of Soda; Benzoate de Soude, *Fr. Cod.;* Natrium Benzoicum, Natriumbenzoat, Benzoesaures Natron, *G.;* Benzoato di sodio, *It.;* Benzoato sodico, *Sp.*

Sodium benzoate is easily made by adding benzoic acid to a concentrated hot solution of sodium carbonate or bicarbonate until effervesence ceases, and allowing the solution to cool and crystallize. R. Rother, in order to avoid annoyances in the effervescence mixes four ounces of benzoic acid and two and three-fourths ounces of sodium bicarbonate in an evaporating dish with from two to four fluidounces of alcohol; when a uniform mixture is produced, from three to six fluidounces of water are added, heat applied gently, and the powder granulated.

Properties.—It is officially described as "a white, amorphous, granular or crystalline powder; odorless, and having a sweetish taste. It is permanent in the air. One Gm. of Sodium Benzoate dissolves in 1.8 mils of water and in 61 mils of alcohol at 25° C. (77° F.), also in 1.4 mils of boiling water. An aqueous solution of Sodium Benzoate (1 in 20) is neutral or slightly alkaline to litmus. When heated, the salt melts, emits vapors having the odor of benzoic acid, then chars, and finally leaves a residue of sodium carbonate and carbon. To a non-luminous flame it imparts an intensely yellow color. Add a few drops of ferric chloride T.S. to an aqueous solution of the salt (1 in 20); a flesh-colored precipitate is deposited. Diluted hydrochloric or sulphuric acid produces in a concentrated aqueous solution of the salt a voluminous white precipitate of benzoic acid. Acidulate 10 mils of an aqueous solution of the salt (1 in 50) with hydrochloric acid and filter; the filtrate does not respond to the Test for heavy metals (see Part III, Test No. 3)." *U. S.*

"A white subcrystalline, or amorphous powder. Inodorous, or with a faint odor of benzoin; taste unpleasant, sweetish, saline. Soluble in 2 parts of *water,* and in 24 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of sodium. An aqueous solution (1 in 10) is slightly alkaline to *litmus,* gives a pale reddish precipitate with *T. Sol.* of *ferric chloride,* and yields with *diluted hydrochloric acid* a crystalline precipitate of benzoic acid. Loses not more than 4 per cent. of its weight when dried at 110° C. (230° F.). 1 gramme of this dried salt heated to redness till gases cease to be evolved leaves an alkaline residue which, treated with *water,* filtered, and well washed, yields a clear solution requiring for neutralisation not less than 13.7 or more than 13.9 millilitres of *N/2 solution of sulphuric acid.* Yields no characteristic *reactions* for copper, iron, potassium, or carbonates, and not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million." *Br.*

"**Assay.**—Dry the salt to constant weight at 110° C. (230° F.) and proceed as directed under the Assay for alkali salts of organic acids (see Part III, Test No. 6). It shows, in the dried salt, not less than 99 per cent. of $NaC_7H_5O_2$.

"Each mil of half-normal sulphuric acid V.S. used corresponds to 0.07202 Gm. of $NaC_7H_5O_2$. Each gramme of Sodium Benzoate, previously dried, corresponds to not less than 13.75 mils of half-normal sulphuric acid V.S." *U. S.*

Elias Elvove (*A. J. P.,* 1912, p. 298) proposes a new method for the assay of sodium benzoate and for all salts of potassium, sodium, and lithium with organic acids. It is based upon the decomposition of the salt with an excess of normal sulphuric acid and the subsequent cautious ignition to destroy organic matter and eliminate excess of sulphuric acid, leaving as a residue a normal sulphate of the basic element from the weight of which the purity of the original compound may be calculated.

Uses.—Sodium benzoate is used in the treatment of *rheumatism,* either of the acute or chronic type. Its mode of action in these conditions is apparently similar to that of the salicylates, although it is usually a less efficacious remedy. It has also been used in the treatment of *lithemia* and *gouty conditions* but with less convincing benefit. It is of service also as a urinary antiseptic, but the ammonium salt is generally preferred. Although benzoic acid is a powerful germicide the neutral salts are only feebly so. According to Doepner a 1 per cent solution of sodium benzoate has only a slight retarding influence upon the growth of the bacteria; on the other hand, Herter (*J. A. M. A.* 1910, liv) states that one-fifth of one per cent. has a perceptible inhibiting action. It is probable that the strong effects of sodium benzoate as a food preservative are due to a partial liberation of benzoic acid by the acidulous matters of the food stuff to which it is added. It is quite certain that an acid condition of the urine very greatly increases its efficacy as a urinary antiseptic.

Dose, from fifteen to thirty grains (1.0–2.0 Gm.).

Off. Prep.—Liquor Antisepticus, *N. F.;* Liquor Antisepticus Alkalinus, *N. F.;* Sodii Boro-Benzoas, *N. F.*

SODII BENZOSULPHINIDUM. U. S.

SODIUM BENZOSULPHINIDE Sod. Benzosulphin. [Sodium-Saccharin, Soluble Saccharin]

(sō'dĭ-ī bĕn-zō-sŭl-phĭ-nĭ'dŭm)

"The sodium salt [$NaC_7H_4O_3NS+2H_2O$= 241.14] of benzosulphinide. Preserve it in well-closed containers." *U. S.*

This salt may be prepared by the careful neutralization of sodium carbonate solution with benzosulphinide or so-called insoluble saccharin, and the subsequent concentration of the solution and crystallization of the salt. "Sodium Benzosulphinide occurs in colorless, rhombic prisms or as a white, crystalline powder; odorless or having a faint aromatic odor and an intensely sweet taste, even in dilute solutions; somewhat efflorescent. One Gm. of Sodium Benzosulphinide dissolves in 1.2 mils of water, and in about 50 mils of alcohol at 25° C. (77° F.). An aqueous solution of the salt (1 in 10) is neutral or only slightly alkaline to litmus, but produces no red color with phenolphthalein T.S. On incineration the salt leaves a residue consisting chiefly of sodium sulphate. Mix 10 mils of an aqueous solution of the salt (1 in 10) with 1 mil of hydrochloric acid; a crystalline precipitate of benzosulphinide is produced. Add a few drops of ferric chloride T.S. to 10 mils of an aqueous solution of the salt (1 in 20) previously acidulated with from 3 to 5 drops of acetic acid; no pink or violet precipitate is produced (*benzoate or salicylate*). In other respects it responds to the tests for identity and purity under *Benzosulphinidum*, omitting the melting point and the tests for ash, benzoic acid or salicylic acid." *U. S.*

Uses. — Sodium benzosulphinide is useful solely as a sweetening agent in those conditions, such as *diabetes, gout, obesity,* etc., in which sugar is objectionable. It has the advantage over the anhydride (see *Benzosulphinidum*) of being more freely soluble.

Dose, one-fourth to three grains (0.016–0.2 Gm.).

SODII BICARBONAS. U. S., Br.

SODIUM BICARBONATE Sod. Bicarb.

(sō'dĭ-ī bī-cär'bo-nās)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99 per cent. of $NaHCO_3$ (84.01). Preserve it in well-closed containers, in a cool place." *U. S.* "Sodium Bicarbonate may be obtained by exposing crystals of sodium carbonate to carbon dioxide, or by the interaction of sodium chloride and ammonium bicarbonate. It contains not less than 98.5 per cent. of pure sodium hydrogen carbonate, $NaHCO_3$." *Br.*

Natrium Carbonicum Acidulum; Bicarbonas Sodicus; Bicarbonate of Soda, Soda Saleratus, Acid Sodium Carbonate; Sodium Hydrogen Carbonate; Carbonate (Bi) de Soude, *Fr. Cod.;* Sel de Vichy, *Fr.;* Natrium Bicarbonicum, *P. G.;* Natriumbicarbonat, Doppeltkohlensaures Natron, *G.;* Bicarbonato di sodio, *It.;* Bicarbonato sodico, *Sp.*

Two kinds of sodium bicarbonate were formerly official—one, which is known by the title of this article, and which, to comply with the tests, must not have more than one per cent. of impurity, and the other, "commercial bicarbonate," which must contain at least 95 per cent. of pure bicarbonate. Formerly to obtain a salt which would comply with the official test it was necessary to purify the commercial salt, and the process of the U. S. Pharm. 1870 will be found as serviceable as any to accomplish this purpose. The U. S. Pharm. 1890 recognized only the purer salt, having dismissed *Sodii Bicarbonas Venalis.* Sodium bicarbonate must now contain 99 per cent. of the pure salt, and the quality of the commercial salt has greatly improved in late years.

Immense quantities of sodium bicarbonate were formerly imported from Great Britain, but the importation has ceased because of the development of the industry in this country. It is now made of excellent quality by the Pennsylvania Salt Manufacturing Co., at Natrona, Pa., using cryolite as raw material; and by the Solvay Process Co., of Geddes, near Syracuse, N. Y., using the ammonia-soda process; and the Michigan Alkali Co., of Wyandotte, Mich., and the Mathison Alkali Co., of Saltville, Va., from brine.

In the United States Pharmacopœia of 1860 a process for making sodium bicarbonate was given but it has since been abandoned, as the salt can be made much more economically on the large scale. The process consists in treating crystallized sodium carbonate, contained in suitable chambers, with carbon dioxide gas until the carbonate has taken up another molecule of carbon dioxide. It is formed by the union of neutral carbonate, Na_2CO_3, with carbon dioxide gas, CO_2, in the presence of water, H_2O, according to the following reaction:

$$Na_2CO_3 + CO_2 + H_2O = 2HNaCO_3$$

two molecules of the bicarbonate being generated. The necessary water is obtained through the liberation of the water of crystallization of the carbonate; in fact, provision has to be made for the escape of the excess by placing the crystals upon perforated bottoms.

Properties.—"Sodium Bicarbonate is a white, opaque powder; odorless, and having a cooling, mildly alkaline taste. It is permanent in dry air, but slowly decomposed in moist air. One Gm. of Sodium Bicarbonate dissolves in 10 mils of water at 25° C. (77° F.); insoluble in alcohol. An aqueous solution of Sodium Bicarbonate (1 in 20) when freshly prepared with cold distilled water, without shaking, is slightly alkaline to litmus. The alkalinity increases by standing, agitation, or increase in temperature. When heated above 15° C. (59° F.), an aqueous solution of the salt gradually loses carbon dioxide, and at boiling temperature the salt is entirely converted into normal sodium carbonate. When heated, the salt is decomposed into normal sodium carbonate, water, and carbon dioxide, and at 100° C. (212° F.) the loss is about 36.5 per cent. of its weight. At a bright red heat the residue fuses. To a non-luminous flame it imparts an intensely yellow color. An aqueous solution of the salt effervesces strongly with acids. No odor of ammonia is evolved on heating Sodium Bicarbonate in a test tube. Dissolve 1 Gm. of the salt in 20 mils of distilled water at 25° C. (77° F.); it yields a clear and colorless solution, leaving no residue. Dissolve 1 Gm. of the salt without agitation in 20 mils

of distilled water at a temperature not exceeding 15° C. (59° F.) and add 0.2 mil of normal hydrochloric acid and 2 drops of phenolphthalein T.S.; a red tint does not appear immediately (*carbonate*). An aqueous solution of the salt (1 in 50), mixed with a slight excess of hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3).

Assay.—Mix about 3 Gm. of Sodium Bicarbonate, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed, with 25 mils of distilled water and titrate with normal sulphuric acid V.S., methyl orange T.S. being used as indicator. It shows, in the dried salt, not less than 99 per cent. of $NaHCO_3$.

"Each mil of normal sulphuric acid V.S. used corresponds to 0.08401 Gm. of $NaHCO_3$. Each gramme of Sodium Bicarbonate, previously dried, corresponds to not less than 11.78 mils of normal sulphuric acid V.S." *U. S.* "A white powder, or small, opaque, monoclinic crystals. Taste saline. Soluble in 11 parts of *water*. Yields the *reactions* characteristic of sodium and of bicarbonates. 1 gramme requires for neutralization not less than 11.7 or more than 11.9 millilitres of *N/1 solution of sulphuric acid*. Yields no characteristic *reactions* for copper, iron, aluminium, calcium, sulphites, or thiosulphates, and not more than the slightest *reactions* for chlorides, sulphates, or ammonium. *Lead limit* 5 parts per million. *Arsenic limit* 2 parts per million. When 1 gramme of Sodium Bicarbonate is dissolved in 20 millilitres of cold *water*, without shaking, and 0.2 millilitre of *N/1 solution of sulphuric acid* and 2 drops of *solution of phenolphthalein* are added, no red color is immediately developed (limit of carbonate). The addition of *T. Sol. of ferric chloride* to the aqueous solution acidified with *hydrochloric acid* causes no red coloration (absence of thiocyanates).

"20 grammes of Sodium Bicarbonate are neutralized by 16.7 grammes of Citric Acid, and by 17.8 grammes of Tartaric Acid." *Br.*

The salt furnished by the manufacturers almost always comes up to the requirements of the Pharmacopœias. The presence of carbonate may be known by a decided alkaline taste and reaction, by a cold solution of the salt yielding a precipitate with magnesium sulphate, and by a solution in 40 parts of water affording, without agitation, an orange-colored or reddish-brown precipitate with corrosive sublimate. E. Kuhlmann recommends rosolic acid as the best test for detecting monocarbonate; if a small fragment be placed in a solution of sodium bicarbonate, the liquid remains perfectly colorless even after a quarter of an hour if the salt be pure; but if it contain from one to four per cent. of monocarbonate a rose-red color will be produced after a few moments, and *immediately* in the presence of larger quantities, rapidly changing them to purple-red. (*A. Pharm.*, 1887, p. 72.)

When the solution is exposed to heat, the salt gradually parts with carbon dioxide, and, at the temperature of 100° C. (212° F.), is converted into sesquicarbonate, $Na_2CO_3.NaHCO_3.2H_2O$. At red heat the second equivalent of carbon dioxide is expelled, and the anhydrous carbonate is left.

Sodium thiosulphate has been detected in small amount in European sodium bicarbonate by E. Mylius, who supersaturated the suspected bicarbonate in solution with sulphuric acid, and added a little pure zinc, when the odor of hydrogen sulphide was produced. A slight trace of arsenic was also discovered in the sodium bicarbonate. (*A. Pharm.*, 1886, p. 598.) F. B. Power subsequently examined samples of American bicarbonate, and found them all free from thiosulphate and arsenic; he detected, however, traces of chlorides, ammonia, and monocarbonate in the commercial salt. (*Ph. Rund.*, 1887, p. 35.)

Uses.—Sodium bicarbonate is used in medicine solely for the purpose of overcoming hyperacidity either of the stomach, blood, or urine. In cases of gastric conditions attended with increased acidity, whether due to fermentation or oversecretion in the acid glands, it is one of the most useful remedies we possess. It has the advantage over the carbonates of being more palatable and less irritant to the gastric mucosa. In cases of diminished alkalinity of the general system the so-called *acidosis*, such as is seen in *diabetic coma*, the intravenous injection of large doses of bicarbonate of soda offers greater hope of relief than any other mode of treatment. For this purpose large doses are required; Labbé and Carrié (*Rev. Internat. de Med.*, 1911, p. 250) administered daily for several days 15 grammes intravenously and 20 grammes by the mouth in a case of diabetic coma. For the purpose of diminishing excessive acidity of the urine, as in *rheumatic* or *gouty conditions*, while the drug is frequently employed it has no advantage over the citrate and is more liable to disturb digestion.

In pharmacy it is widely employed for making effervescent powders.

Dose, for an adult, from ten grains to a drachm (0.65–3.9 Gm.), taken most conveniently in a glass of carbonic acid water.

Off. Prep.—Trochisci Sodii Bicarbonatis, *U. S.* (*Br.*); Liquor Sodæ et Menthæ, *N. F.*

SODII BORAS. U. S. (Br.)

SODIUM BORATE Sod. Bor. [Borax, Sodium Tetraborate, Sodium Pyroborate]

(sō'dĭ-ī bō'răs)

"It contains not less than 52.32 per cent. nor more than 54.92 per cent. of anhydrous sodium borate (sodium biborate or tetraborate), corresponding to not less than 99 per cent. of the crystallized salt [$Na_2B_4O_7 + 10H_2O = 382.16$]. Preserve it in well-closed containers." *U. S.* "Purified Borax may be obtained from native borax; it may also be obtained by boiling native calcium borate with solution of sodium carbonate, and contains not less than 98.9 per

cent. of sodium pyroborate, $Na_2B_4O_7,10H_2O$." *Br.*

Borax Purificatus, *Br., P. G.*; Purified Borax; Sodæ Biboras, Biborate of Sodium; Sodium Biborate, Natrium Biboricum (Biboracicum), Boras Sodicus; Borate de Soude, *Fr. Cod.*; Borax, Bauracon, Sel de Perse, *Fr.*; Borax, Borsaures Natron, *G.*; Borato di sodio, Borace, *It.*; Borato sodico, Borax, *Sp.*

Borax was known to the ancients; but its chemical character was first ascertained by Geoffroy in 1732. It exists in nature, and may be obtained by artificial means. It occurs in several localities in Europe, in Peru, and in beds, associated with calcium borate, in the district of Iquique, in the republic of Ecuador. This mineral (*boronatrocalcite*), which has become an article of commerce, and is considerably used as a substitute for borax, contains, according to T. L. Phipson, 34 per cent. of water, 11.95 of soda, 14.45 of lime, 34.71 of boric acid, 1.34 of chlorine, 1.10 of sulphuric acid, 0.60 of silica, and 2 of sand, and may be considered as a compound essentially of one molecule of crystallized sodium borate and two molecules of calcium borate, with two molecules of water. It is said also to contain usually some iodine and bromine. (G. Sims.) Borax has long been known to occur in certain lakes of Thibet and Persia, from which it was obtained by spontaneous evaporation. It constituted the impure borax called in commerce *tincal*.

Several sources of borax have been developed within the limits of the United States. The existence of a borax lake in California was first made known by J. A. Veatch, who visited it in September, 1856, and, upon examining its waters, found borax among its constituents. The borax lake is a small offset of a large sheet of water, called Clear Lake, which is situated in the midst of a volcanic region, about 36 miles from the Pacific, and about 100 miles north of San Francisco. This lake supplied large quantities of borax to commerce, but in 1868 operations practically ceased at Borax Lake. More recently attention has been attracted to Searles Lake, in San Bernardino County, where potash salts occur with the borax and soda salts. This is now being worked for both potash and borax by concentration and fractional crystallization.

At present the chief supply of American borax comes from the more easily worked deposits in the sandy deserts about Death Valley, southeast of Pyramid Lake, in Nevada, in the Slate Range district, San Bernardino Co., and the Saline Valley, Inyo Co., California. In order to reduce as much as possible the cost of transportation before the present railway facilities, the boraxes of the Pacific coast were made usually of high quality, and the so-called "*boracic acid glass*," one pound of which is equal to three pounds of ordinary borax, was prepared. For an interesting description of the Slate Range district, see *Chem News*, 1886, 245. The most important deposits which are worked in California are the *colemanite* (*calcium borate*) deposits twelve miles northeast of Daggett, in the Mojave Desert. The formation (one hundred feet or more in width) has been traced for fully ten miles. The colemanite is readily dissolved by sodium carbonate solution, when the borax crystallizes out.

The production of borate in California for 1915 amounted to 67,004 tons. Only two other countries supply any considerable amount of borate minerals: Chili, which, in 1912, produced 43,356 tons of calcium borate, and Italy, which, in 1912, produced 2309 tons of crude boric acid.

Preparation.—Borax is made for the European market by the direct combination of *native boric acid* with soda. The acid is found abundantly in the crater of Vulcano, one of the Lipari Islands, but principally in a volcanic region of Tuscany occupying a space of ten or twelve miles. Within this region are found numerous hillocks and fissures, the latter of which emit hot aqueous vapor containing boric acid and certain gases. Around one or several of these fissures a circular basin of masonry is built, which is filled with water and called a lagoon. By the jets of vapor constantly breaking through it, the water becomes gradually impregnated with boric acid and heated. A series of such lagoons are made to communicate with each other on the declivity of a hill, and the lowest to discharge itself into a reservoir, where the solution is allowed to rest and deposit mechanical impurities. From this reservoir the solution is made to pass into leaden evaporating pans, heated by the natural vapor, where it receives sufficient concentration to fit it for being conducted into wooden tubs, where it is allowed to cool and crystallize. The crude acid, thus obtained contains, on an average, 84 per cent. of boric acid, the impurities consiting chiefly of alum, the double ammonium and magnesium sulphate, and calcium sulphate. The seven works in the neighborhood of Castelnuovo in Tuscany, belonging to Count Larderel, were producing, in 1878, over three millions of kilogrammes. Vulcano yielded 4000 kilogrammes of boric acid yearly. The crude acid is converted into borax by dissolving it to saturation in a solution of sodium carbonate, heated by steam, and the liquor, after boiling, is allowed to stand for ten or twelve hours. It is then drawn off into wooden vessels lined with lead, where it crystallizes. The impure crystals thus obtained are refined by dissolving in water heated by steam, adding sodium carbonate to the solution, and crystallizing. The merit of introducing the process for obtaining artificial borax belongs to Cartier and Payen, who succeeded in establishing its manufacture in France. According to Veatch, boric acid exists in the sea water on the coast of California.

Another method of neutralizing the Italian boric acid is practised in England. Instead of combining the acid and alkali in solution, the manufacturer mixes the acid in a solid state with a proper proportion of soda ash, and exposes the mixture to the heat of a reverberatory furnace, provision being made for the collection of a large quantity of ammonia, which is always present in the crude acid and escapes during the process. The remaining operations are similar to those performed in the prepara-

tion of sodium carbonate from the cake. (*A. J. P.*, 1867, p. 339.)

Properties.—Borax is a white salt, occurring in "colorless, transparent, monoclinic prisms, or as a white powder; odorless, and having a sweetish, alkaline taste. It is slightly efflorescent in warm dry air. One Gm. of Sodium Borate dissolves in 15 mils of water, and in about 1 mil of glycerin at 25° C. (77° F.); also in 0.6 mil of boiling water; insoluble in alcohol. An aqueous solution of the salt (1 in 20) is alkaline to litmus and turns turmeric paper reddish-brown. If the solution has been acidulated with hydrochloric acid, turmeric paper remains unchanged at first, but on drying becomes brownish-red, and this color is temporarily changed to greenish-black by moistening with ammonia water. When heated, the salt at first loses part of its water of crystallization, then melts, and, when further heated, swells and forms a white porous mass. At a red heat it loses all of its water of crystallization and fuses to a colorless glassy mass. To a non-luminous flame it imparts an intensely yellow color. Form a bead of borax on a platinum wire, dip it in glycerin, and hold it in a non-luminous flame; a transient, bright green color appears. An aqueous solution of the salt (1 in 20) does not effervesce with acids (*carbonate or bicarbonate*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of the salt meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"**Assay.**—Dissolve about 5 Gm. of Sodium Borate, accurately weighed, in 100 mils of distilled water and titrate the solution with normal hydrochloric acid V.S., methyl orange T.S. being used as indicator. It shows not less than 52.32 per cent. nor more than 54.92 per cent. of $Na_2B_4O_7$.

"Each mil of normal hydrochloric acid V.S. used corresponds to 0.1010 Gm. of $Na_2B_4O_7$. Each gramme of Sodium Borate corresponds to not less than 5.18 mils nor more than 5.44 mils of normal hydrochloric acid V.S." *U. S.*

"Transparent colorless crystals, sometimes slightly effloresced, with a weak alkaline reaction. Taste saline, alkaline. Soluble in 25 parts of *water*, and in 1 part of *glycerin;* insoluble in *alcohol* (90 per cent.). Colors flame intensely yellow. Its aqueous solution, acidified with *hydrochloric acid,* turns *turmeric paper* brown. A hot saturated solution, acidfied with a mineral acid, deposits, as it cools, crystals of boric acid, the solution of which in *alcohol* (90 per cent.) burns with a green flame. 2 grammes dissolved in *water* require for neutralisation 10.4 millilitres of *N/1 solution of sulphuric acid, solution of methyl-orange* being used as indicator; and if to this neutralised solution an equal volume of *glycerin* is added, 20.8 millilitres of *N/1 solution of sodium hydroxide* are required for neutralisation, *solution of phenolphthalein* being used as indicator. Yields no characteristic *reactions* for copper, iron, or calcium, and not more than the slightest *reactions* for chlorides or sulphates. *Lead limit* 5 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Above a red heat it melts into a limpid liquid, which, after cooling, concretes into a transparent solid, called *glass of borax,* much used as a flux in assays with the blowpipe. Borax has been found in the English market adulterated to the extent of 20 per cent. with sodium phosphate. This may be detected by exposing the suspected borax to the heat of a drying-room for a few hours, when the phosphate, if present, will effloresce, and may be picked out. Commercial borax is used as a flux in metallurgical operations; as the basis of the enamel so much applied to iron utensils, glazed brick, and much china, earthenware, and tiling; in the laundry with starch to impart a gloss to linen; by the meat packers of the United States (1000 tons yearly) as an antiseptic for meat intended for export to countries whose laws permit its presence, and very largely in soaps and toilet preparations and in detergent powders.

Borax has the property of rendering cream of tartar very soluble in water, and forms a combination with it called *soluble cream of tartar,* which is sometimes used in medicine. This preparation attracts moisture from the air, and is soluble in its own weight of cold and half its weight of boiling water. (See *Potassii Bitartras.*) R. F. Fairthorne states that borax is more soluble in water if sugar has been added to it. (*A. J. P.*, March, 1881.) Soluble cream of tartar may be made by substituting boric acid for the borax. *Boric acid soluble cream of tartar* was directed by the French Codex of 1837, and was made by the following formula. Four hundred parts of cream of tartar and 100 of the acid are dissolved in a silver basin, at the boiling temperature, in 2400 parts of water. The solution is kept boiling until the greater part of the water is consumed. The fire is then moderated, and the solution continually stirred while the evaporation proceeds. When the matter has become very thick, it is removed by portions, which are flattened in the hand, completely dried by the heat of a stove, powdered, and kept in well-stoppered bottles. This form of soluble cream of tartar is more soluble than that made with borax. According to E. Robiquet, in order to obtain soluble cream of tartar, made with boric acid, of good quality, it is necessary to use a large quantity of water, and to boil for a long time. By proceeding thus, the boric acid undergoes a molecular modification, equivalent to a change from the crystallized to the vitreous condition, and a preparation readily and totally soluble in cold water is insured. The product should not be powdered, but kept in large grains. (*J. P. C.*, xxi, 197.) Borax is incompatible with the salts of the alkaloids; in warm solution it decomposes hydrated chloral.

Composition.—Borax has the formula $Na_2B_4O_7 + 10H_2O$. It ordinarily crystallizes in monoclinic prisms, and contains ten molecules of water (*prismatic borax*); but a variety of the salt exists which crystallizes in octahedrons, and contains only five molecules of water (*octahedral borax*). The latter is obtained in the artificial production of borax by crystallizing from a

concentrated solution at a temperature between 60° and 80° C. (140° and 176° F.). When a solution of borax is evaporated at 100° C. (212° F.), the salt is left as a transparent, amorphous, brittle mass, containing four molecules of water. (Schweitzer.) Borax is looked upon as having the following probable composition, $2NaBO_2$. $B_2O_3.10H_2O$.

Sodium borate (neutral).—A soluble borate may be made by adding boric acid to a hot concentrated aqueous solution of sodium biborate or borax until it has a neutral reaction; crystals separate which have been erroneously described under the name sodium tetraborate. They are transparent, fragile, and glassy; it is found in commerce in glass-like masses. It is soluble in cold water, but more soluble (70 per cent.) in hot water. It is probably a mixture and not a true compound. Sodium metaborate, $NaBO_2H_2O$, is also known as neutral sodium borate and several compounds of this salt with free metaboric acid, HBO_2, are also known but are little used.

Boric acid may be obtained artificially by decomposing a hot saturated solution of borax with sulphuric acid, which unites with the soda to form sodium sulphate and sets free the acid. As thus obtained it is in white, shining, scaly crystals, characterized by the property of imparting a light-green color to the flame of burning alcohol. Boric acid has the formula H_3BO_3, and is now official. (See *Acidum Boricum.*) *Boron* is a non-metallic element, which, like carbon, is found to exist in two allotropic states, designated amorphous, and crystallized boron, corresponding severally to amorphous carbon and to the diamond. Crystallized boron is very brilliant, and of different colors, from garnet-red to a nearly colorless honey-yellow. Its density is 2.68, and its hardness very great, approximating that of the diamond. Amorphous borax of a density almost equal to that of the crystalline variety has been obtained and is now used because of its high resistance to the electric current.

Uses.—The action of borax and of boric acid upon the animal system are identical. The effects of borax are, however, very feeble, Cyon having found that in daily doses of three drachms borax exerts no perceptible influence upon the dog. Nevertheless, in sufficient amount it exerts a depressing influence upon the heart as well as upon the spinal centers, and a number of instances of poisoning from it have been reported. The symptoms have varied somewhat, but in most if not all the cases there have been great depression of spirits, fall of bodily temperature, a very feeble pulse—rapid or slow—and an erythematous eruption accompanied with much swelling of the parts, and especially affecting the lower extremities, and followed by exfoliation; nausea, violent vomiting, and hiccough have been present in some cases; ecchymoses have been noted; the mind usually remains clear until late in the poisoning, but death has been preceded by coma, with disturbances of the respiration, and involuntary discharges. The continued use of borax has produced "*borism*," which is characterized by gastric irritation, a peculiar absence of fatty matter and of moisture from the skin, and various skin eruptions, especially eczema, reddish papules with squamous desquamating borders, seborrheic acne, and scarlatiniform plaques.

The only systemic purpose for which borax is at present employed is in the treatment of *epilepsy*, but in a careful test made on a large scale in the epileptic ward of the Philadelphia Hospital, by H. C. Wood many years ago, it was found to have little or no influence upon that disorder, and these unfavorable conclusions have been confirmed by Yoedicke (*Med. Klin.*, 1912, p. 2020), who found that only a small percentage of cases seemed to be benefited by it.

Borax even in saturated solution is not at all germicidal, but it does possess slight antiseptic properties. According to Miquel the antiseptic strength is 1 in 14, which would be approximately a saturated solution at ordinary temperatures. It is widely employed as an antiseptic wash for *ulcers* and *abscesses*, but especially for inflammatory conditions of the mucous membranes, such as *conjunctivitis*, *stomatitis*, *cystitis*, *vaginitis*, and the like. It is probable that its beneficial action in these conditions is due more to its innocuousness than to its antibacterial powers. Because of its alkalinity it is a valuable detergent, especially for cleansing mucous membranes. It is also of service as a urinary antiseptic for administration by the mouth, especially when the urine is too highly acid; being eliminated unchanged it tends to alkalinize the urine.

Dose, ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Glycerinum Boracis, *Br.;* Mel Boracis, *Br.;* Liquor Antisepticus Alkalinus, *N. F.;* Liquor Sodii Boratis Compositus, *N. F.;* Mel Rosæ et Sodii Boratis, *N. F.;* Mel Sodii Boratis, *N. F.;* Sodii Boro-Benzoas, *N. F.*

SODII BROMIDUM. U. S., Br.

SODIUM BROMIDE Sod. Brom.

(sō′dĭ-ĭ brō′mĭ-dŭm)

"It contains, when dried to constant weight at 100° C. (212° F.), not less than 98.5 per cent. of NaBr (102.92). Preserve it in well-closed containers." *U. S.* "Sodium Bromide may be obtained in the same manner as Potassium Bromide, sodium carbonate being used in place of potassium carbonate. When dried at 110° C. (230° F.) it contains not less than 99 per cent. of pure sodium bromide, NaBr." *Br.*

Bromure de Sodium, *Fr. Cod.;* Natrium bromatum, *P. G.;* Natriumbromid, Bromnatrium, *G.;* Bromuro di sodio, *It.;* Bromuro sodico, *Sp.*

This salt contains a larger proportion of bromine than does potassium bromide, on account of the lower atomic weight of sodium, sodium bromide containing about 77 per cent. of bromine, while potassium bromide contains about 10 per cent less. It is a trifle more soluble in water and alcohol. It may be made by the

same process that is employed for potassium bromide, substituting sodium carbonate for potassium carbonate. According to Castelhaz, it is best made by transforming bromine into ammonium bromide, separating any iodine present as iodide by crystallization from the mother waters, and decomposing the ammonium bromide with sodium carbonate. The solution should be evaporated by heating carefully. (*A. J. P.*, xlii, 509.)

Properties.—It occurs in "colorless or white, cubical crystals, or as a white, granular powder; odorless, and having a saline taste. The salt absorbs moisture from the air without deliquescing. One Gm. of Sodium Bromide dissolves in 1.1 mils of water and in 16 mils of alcohol at 25° C. (77° F.). An aqueous solution of the salt (1 in 20) is neutral or faintly alkaline to litmus. When heated to a bright red heat, the salt fuses without decomposition, and at a somewhat higher temperature it volatilizes. To a nonluminous flame it imparts an intensely yellow color. Silver nitrate T.S., added to an aqueous solution of the salt (1 in 10), produces a yellowish-white precipitate, insoluble in nitric acid or in a moderate excess of ammonia water. Dissolve 1 Gm. of the salt in 10 mils of distilled water and add 0.1 mil of tenth-normal sulphuric acid V.S.; no color is produced by the subsequent addition of a drop of phenolphthalein T.S., even after boiling (*alkali*). Add a few drops of ferric chloride T.S. and 1 mil of chloroform to 10 mils of an aqueous solution of the salt (1 in 20), and shake the mixture; the chloroform does not acquire a violet tint (*iodide*). Drop 1 mil of diluted sulphuric acid on about 1 Gm. of the powdered salt; no yellow color appears at once (*bromate*). Ten mils of an aqueous solution of the salt (1 in 20), when acidulated with hydrochloric acid, is not rendered turbid by the addition of 1 mil of potassium sulphate T.S. (*barium*); another 10 mil portion, acidulated with hydrochloric acid, is not rendered more than slightly turbid by barium chloride T.S. (*sulphate*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Proceed as directed under the Assay for bromides (see Part III, Test No. 5), using about 0.4 Gm. of Sodium Bromide, dried to constant weight at 100° C. (212° F.), and accurately weighed. It shows, in the dried salt, not less than 98.5 per cent. of NaBr.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.010292 Gm. of NaBr. Each gramme of Sodium Bromide, previously dried, corresponds to not less than 95.7 mils nor more than 98.3 mils of tenth-normal silver nitrate V.S." *U. S.*

"Small, white, cubic crystals, or a white granular powder, somewhat deliquescent. Taste saline, somewhat bitter. Soluble in 1.5 parts of *water*, and in 16 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of sodium and of bromides. Loses not more than 5 per cent. of its weight when dried at 110° C. (230° F.). 0.5 gramme of this dried salt, dissolved in *water*, requires for complete precipitation not less than 48.1 or more than 48.9 millilitres of *N/10 solution of silver nitrate*. Yields no characteristic *reactions* for copper, iron, aluminium, zinc, calcium, magnesium, potassium, ammonium, carbonates, cyanides, bromates, or iodates, and not more than the slightest *reactions* for chlorides, iodides, or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Uses.—The physiological and therapeutic properties of sodium bromide are precisely similar to those of potassium bromide. (See page 890.) Because of the depressant effects of potassium on the heart when injected into the blood stream some believe that sodium bromide is preferable in cases of circulatory weakness. It appears to be somewhat less prone to disturb the stomach than the potassium salt and is usually to be preferred.

Dose, ten to sixty grains (0.65–3.9 Gm.).

Off. Prep.—Elixir Sodii Bromidi, *N. F.*; Elixir Trium Bromidorum, *N. F.*; Syrupus Bromidorum, *N. F.*

SODII CACODYLAS. U. S.

SODIUM CACODYLATE Sod. Cacodyl.

(sō′dĭ-ī că-cō-dȳ′lăs)

"Sodium dimethylarsenate [$Na(CH_3)_2AsO_2$ = 160.01], with a somewhat variable amount of water of crystallization. It contains not less than 72 per cent. nor more than 75 per cent. of $Na(CH_3)_2AsO_2$. Preserve it in well-closed containers." *U. S.*

This compound is prepared by heating together potassium acetate and arsenic trioxide which yields a distillate containing *cacodyl*, $As_2(CH_3)_4$, and *cacodyl oxide*, $As_2(CH_3)_4O$. This mixture is treated with an oxidizing agent which produces cacodylic acid, $(CH_3)_2AsO.OH$, which is then neutralized with sodium hydroxide, concentrated and crystallized.

"Sodium Cacodylate occurs as white, odorless, deliquescent prisms or as a granular powder. One Gm. of Sodium Cacodylate dissolves in about 0.5 mil of water and in about 2.5 mils of alcohol at 25° C. (77° F.). A solution of 2 Gm. of Sodium Cacodylate in 50 mils of distilled water requires not more than 0.5 mil of tenth-normal acid V.S. or tenth-normal alkali V.S. to render it neutral to phenolphthalein T.S. It melts in its water of crystallization at about 60° C. (140° F.), and becomes anhydrous at 120° C. (248° F.). The salt burns with a bluish flame, emitting a garlic-like odor. The salt imparts an intensely yellow color to a non-luminous flame. A mixture of a few drops of an aqueous solution of the salt (1 in 100) with 2 mils of hypophosphorous acid, allowed to stand in a stoppered tube, develops the odor of cacodyl within one hour. No turbidity is produced in 10 mils of an aqueous solution of the salt (1 in 20) by 1 mil of calcium chloride T.S., either in the cold or on heating (*monomethylarsenate*). No turbidity is produced in 5 mils of an aqueous solution of the

salt (1 in 20) by 2 mils of magnesia mixture T.S. within one hour (*arsenate or phosphate*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). Separate portions of an aqueous solution of the salt (1 in 50), acidulated with nitric acid, are not rendered turbid at once by silver nitrate T.S. (*chloride*) or by barium chloride T.S. (*sulphate*).

"**Assay.**—Dissolve about 2.5 Gm. of Sodium Cacodylate, accurately weighed, in distilled water, render the solution neutral to phenolphthalein T.S., if necessary, and then titrate with normal hydrochloric acid V.S., using methyl orange T.S. as indicator. It shows not less than 72 per cent. nor more than 75 per cent. of $Na(CH_3)_2AsO_2$.

"Each mil of normal hydrochloric acid V.S. used corresponds to 0.1600 Gm. of $Na(CH_3)_2AsO_2$. Each gramme of Sodium Cacodylate corresponds to not less than 4.5 mils nor more than 4.7 mils of normal hydrochloric acid V.S." *U. S.*

Uses.—Although cacodylic acid was employed as a therapeutic remedy by Jochheim in 1864, its popularity as a remedy may be dated from the writings of Gautier (*B. A. M.*, 1899, p. 604), since which time the salts of this acid have been used to a large extent in a number of conditions, chiefly those in which arsenic has been found to be of value.

Arsenic, like other poisonous elements, when bound up into a complex organic molecule in such a way that it does not ionize, no longer exercises its characteristic effects upon the bodily functions. Such a molecule is seen in cacodyl and various of its derivatives, such as sodium cacodylate. Although, in themselves, the cacodylates are relatively inert, in the course of their passage through the system they are in part slowly demethylized and yield more or less arsenious acid. For this reason they are capable of exercising the therapeutic effects of the inorganic forms of arsenic. Heffter (*A. E. P. P.*, xlvi, p. 230) has shown that a small, and not always constant proportion, ranging between two and three per cent. of the ingested dose of the arsenic is split off in the system, and eliminated in an inorganic form. This view is also sustained by the clinical study of Dawes and Jackson. (*J. A. M. A.*, 1907, xlviii, p. 2090.)

The range of demonstrated therapeutic usefulness of cacodylic acid is similar to that of arsenic. Its early popularity was achieved chiefly in the treatment of skin diseases, especially *psoriasis,* and in *tuberculosis.* In the latter condition it seems to act precisely as does arsenic, simply by improving the general nutritive state of the patient. There is also much clinical evidence of its value in various forms of *anemia, leukemia, asthma, chronic bronchitis, malaria,* and various other conditions in which arsenic is useful. It is especially employed in those conditions, such as *pernicious anemia,* in which it is desired to give very large doses of arsenic; Dawes (*J. A. M. A.*, 1911) reports a number of cases of this intractable infection which have been apparently cured, one having shown no symptoms for over three years. It has also been employed in *syphilis,* but the experimental investigations of Nichols (*J. A. M. A.*, 1911, lvi, p. 492) seem to demonstrate that it has no direct action upon the spirochetæ. It has also been employed in experimental *trypanosomiasis* (see Pflugholt, *M. M. W.*, 1910) with hopeful results. Besides the above conditions, it has been tried in the treatment of *carcinoma, leprosy,* and *pellagra,* but not to sufficient extent to allow of a positive conclusion as to its value. Although, as stated above, it is probable that cacodylic acid possesses no virtues which are not inherent in arsenic, it deserves recognition as a useful remedial agent. Its advantages over arsenous acid lie not merely in the fact of its lower toxicity, but especially in that it can be given hypodermically. If it be reduced in the system and arsenic eventually liberated, this change will not begin until after the remedy has passed the stomach, and probably does not occur to any large extent until after absorption, so that a comparatively large amount of arsenic can be introduced through the alimentary canal with little danger of deranging digestion. When given by the mouth, however, it generally imparts such a strong garlicky odor to the breath that this method of exhibiting the drug is rarely available.

Dose, one-fourth of a grain to two grains (0.016–0.13 Gm.).

SODII CARBONAS. Br.

SODIUM CARBONATE

(sō′dĭ-ī cär′bo-năs)

"Sodium Carbonate may be obtained from sodium chloride by interaction with ammonium bicarbonate, ignition, and subsequent crystallisation. It contains not less than 99 per cent. of pure sodium carbonate, $Na_2CO_3,10H_2O$." *Br.*

Carbonate of Soda, Sal Soda, Washing Soda; Natrium Carbonicum, *P. G.*; Carbonas Sodicus, Sal Sodæ; Carbonate de Soude pur cristallisé, *Fr. Cod.*; Einfach Kohlensaures Natron, Kohlensaures Natron, Soda, *G.*; Carbonato di sodio, *It.*; Carbonato sodico cristalizado, *Sp.*

Sodium carbonate is official in the U. S. P. IX only as *Sodii Carbonas Monohydratus.* (See page 1023.)

Native soda, sometimes called *natron,* is found in various parts of the world and exists either in the surface earth, which often exhibits a saline efflorescence, or in solution in small lakes, from which it is extracted by taking advantage of the drying up of the water during the heats of summer. (See *U. S. D.*, 19th edition, page 1136.)

Sodium carbonate is made from common salt by the older or Leblanc process in two steps; first, by converting the salt by sulphuric acid into sodium sulphate, and, secondly, by decomposing the sulphate by calcium carbonate and charcoal at a high temperature, so as to yield sodium carbonate. The chemical reactions may be summarized as follows:

$$2NaCl + H_2SO_4 = Na_2SO_4 + 2HCl$$
$$Na_2SO_4 + CaCO_3 + C_4 = Na_2CO_3 + CaS + 4CO$$

Within the last few decades a process has been put in practice which has given so much satisfaction in its results that it has superseded the hitherto unequalled process of Leblanc. It is designated the *ammonia-soda* process, and is based on the fact that when carbon dioxide is passed into a solution of common salt in aqueous ammonia a double decomposition occurs, and the slightly soluble sodium bicarbonate is precipitated:

$$NH_3 + CO_2 + NaCl + H_2O = HNaCO_3 + NH_4Cl$$

From the mother liquor containing the sal-ammoniac, if deemed advisable, the ammonia may be withdrawn by the action of lime, and serve in the renewal of the operation. The sodium bicarbonate is reduced by heat to the carbonate, and the carbon dioxide thus obtained serves to convert the ammonia into the ammonium bicarbonate necessary in the proceeding. The waste product here is calcium chloride, which takes with it all the chlorine of the salt originally used. Therefore if the ammonia-soda process were to replace the Leblanc process, hydrochloric acid and chlorine would have to be made independently, and would become much dearer than at present. To obviate this objection to the ammonia-soda process and to produce hydrochloric acid as one product of the same process, the late Walter Weldon proposed to use magnesia instead of lime in the decomposing of the sal-ammoniac. This would leave magnesium chloride instead of calcium chloride. From the magnesium chloride the chlorine can be obtained as follows:

$$MgCl_2 + H_2O = 2HCl + MgO$$

Steam will liberate hydrochloric acid from the magnesium chloride. This process is carried out practically at Salindres in France, although its economy is not definitely established.

A still more promising suggestion is that of the distinguished chemist Ludwig Mond of Brunner, Mond & Co., who are the chief English manufacturers of ammonia-soda. He proposes to freeze out the ammonium chloride from the mother liquors by artificial refrigeration, sublime it, and pass the vapor over magnesia, whereby the hydrochloric acid is retained in combination with the magnesia as magnesium chloride, while the ammonia passes on. The magnesium chloride is then heated in a current of air, when it is split up into chlorine and magnesia.

The reaction between ammonium bicarbonate and sodium chloride, upon which the ammonia process was founded, was first discovered by Dyar and Hemming about 1838, but it was only in 1863 that Ernest Solvay, a Belgian chemist, made it a practical success. The advantages of this method are that the sodium chloride is directly transformed into sodium carbonate, that in the precipitation sodium is the only metal thrown down, and that the preparation is therefore remarkably pure, that it is entirely exempt from the compounds of sulphur, that the amount of product is very large, that the apparatus used is very simple, that there is a great saving of fuel and of labor, and, finally, that no unwholesome gases are diffused in the atmosphere, interfering with the health of the workmen and the community. Schloesing and Rolland have observed that in the double decomposition between ammonium bicarbonate and sodium chloride a certain portion only—about two-thirds—undergoes the change. This is explained by Bauer, who finds that the reaction is limited by another in an inverse direction. Thus, if ammonium bicarbonate and sodium chloride yield sodium bicarbonate and ammonium chloride (hydrochlorate of ammonia), these, put together, inversely yield ammonium bicarbonate and sodium chloride. An equilibrium is thus established, and the mixture preserves a constant composition, at the point where the two reactions take place at the same time. (*J. P. C.*, Sept., 1874.)

Another source of sodium carbonate has been discovered in *cryolite*, a mineral existing in great abundance on the coast of Greenland, and largely imported into this country by a manufacturing company which enjoys to a certain extent a monopoly of the mineral under the Danish authorities. Cryolite consists mainly of a double aluminum and sodium fluoride, containing in 100 parts 13 of aluminum, 34 of sodium, and 53 of fluorine. Sodium carbonate is obtained by heating cryolite with lime, whereby calcium fluoride is formed, while the sodium and aluminum combine to form a sodium aluminate, a weak salt, which is dissolved out by lixiviation. The soda is converted into carbonate by passing carbon dioxide under pressure through the solution, and the alumina, separated from the soda, becomes insoluble, and is deposited. (*A. J. P.*, Jan., 1868, p. 71.) Cryolite is also largely used in Denmark and Germany in the preparation of sodium carbonate and of alumina, the latter of which is employed in the manufacture of alum and aluminum.

Besides the preparation of sodium carbonate, cryolite is employed for other important purposes. Within recent years it has become quite important as a flux for the electrolytic production of aluminum by the Hall and similar processes. (See *Alumen.*) Its only known locality, at least in large amount, is Greenland, where it is found on the southwest coast, near Cape Farewell, existing in beds, of which one is said to be eighty feet thick and three hundred long. It is imported by the "Pennsylvania Salt Manufacturing Company" into Philadelphia in immense quantities. It is a handsome mineral, hard, brittle, and translucent, sometimes almost transparent, but generally of a frosty whiteness, which probably suggested its name of *cryolite* or *kryolite*, from the Greek κρύος, *frost*. Though homogeneous in great degree, it exhibits here

and there in its substance dark spots, sometimes mere specks, sometimes of considerable size, which appear to be crystalline centers of substances mixed with it at the time of solidification, such as galena, ferrous carbonate, copper and iron pyrites, etc.

The different kinds of impure sodium carbonate, whether barilla, kelp, or soda-ash, being exceedingly variable in composition, it is important to determine by assay the amount of alkali which they contain. These various forms of carbonated soda are largely consumed in dyeing and bleaching, and in the manufacture of soap and glass.

Soda-ash is in white or gray masses, and contains about half its weight of foreign salts, consisting of sodium chloride and sodium sulphate.

Properties.—"Transparent, colorless, rhombic crystals, efflorescent. Taste strongly alkaline. Soluble in 2 parts of *water*. Aqueous solution strongly alkaline to *litmus*. Free from the impurities enumerated under 'Sodii Bicarbonas.' When heated it liquefies and then dries, losing 62.9 per cent. of its weight. 1 gramme requires for neutralisation not less than 13.8 millilitres of *N/2 solution of sulphuric acid. Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million. 20 grammes of Sodium Carbonate are neutralised by 9.8 grammes Citric Acid, and by 10.5 grammes of Tartaric Acid." *Br.*

This salt presents an anomaly in its solubility, as ascertained by Henri Loewel; it is more soluble in water at 36.1° C. (97° F.) than at its boiling point. Sodium carbonate is insoluble in alcohol. The most usual impurities in it are sodium sulphate and common salt, which may be detected by converting it into a nitrate and testing separate portions of this severally with barium chloride and silver nitrate. Common salt is seldom entirely absent, but good specimens are free from sodium sulphate. When badly prepared it is liable to contain sodium sulphide, which may be detected by the production of the odor of hydrogen sulphide upon dissolving the salt in water. Sodium carbonate is incompatible with acids, which decompose it with effervescence, acidulous salts, lime water, ammonium chlorid, and earthy and metallic salts. When crystallized it contains ten molecules of water. It is thus perceived that this salt, when crystallized, contains two-thirds of its weight of water; but the quantity actually present in it, as found in commerce, is variable, being dependent on the extent to which it may have undergone efflorescence. To obtain pure sodium carbonate for the purpose of a test, J. Lawrence Smith of Louisville, Ky., recommends that sodium oxalate should be prepared from the common carbonate, and then decomposed by heat.

Uses.—Soda being the natural alkali of the blood and other liquids of the human organism, its influence upon that organism in disease is very slight. In the experiments of Gradeau the injection of 107 grains of sodium carbonate directly into the blood of a dog produced practically no symptoms, and in the studies of Münch upon the effect on the human system of the continuous exhibition for a few days of large amounts of soda the results were almost entirely negative. The chief influence of the salt is upon certain of the liquid excretions. Thus, the urine becomes distinctly alkaline, without, however, so far as we know, there being any distinct change in its general constituents. The experiments of Lewaschen prove that soda salts given to dogs with biliary fistula increase very markedly the liquidity of the bile and diminish the percentage of solids in it. These experiments are in accord with clinical experience, which shows that the alkaline sodium salts, given one to two hours after meals in full dose, are of decided value in the treatment of *gall-stones* and various affections associated with excessive acidity of the biliary secretion. On account of its having no general effect upon the system, soda and its carbonates are superior to potassium as simple alkaline remedies. When, therefore, it is desired to overcome *acidity of the stomach or intestines*, or to render acid urine alkaline, these preparations are very available. The bicarbonate is, however, usually preferred to the carbonate as being less likely to irritate the stomach. Alkaline sodium salts are also employed with advantage, internally and externally, in *skin diseases*, especially those of a papulous and scaly character. A lotion suitable for these cases may be formed by dissolving from two to three drachms of the carbonate in a pint of water. For a bath, from eight to sixteen ounces of the salt may be dissolved in the necessary quantity of water. In recent *burns* without much destruction of the skin, the free application of a saturated solution will usually give immediate relief. When swallowed in an overdose, it acts as an irritant poison. The best antidotes are the fixed oils, acetic acid, and lemon juice.

Dose, from five to thirty grains (0.32–2.0 Gm.).

SODII CARBONAS EXSICCATUS. Br.

EXSICCATED SODIUM CARBONATE

(sō'dĭ-ī cär'bo-năs ĕx-sĭc-cā'tŭs)

"Exsiccated Sodium Carbonate is obtained by heating Sodium Carbonate until it loses nearly 63 per cent. of its weight. It contains not less than 95 per cent. of pure anhydrous sodium carbonate, Na_2CO_3." *Br.*

Dried Carbonate of Soda; Exsiccated Sodium Carbonate; Carbonate de Soude sec du commerce, *Fr. Cod.*; Natrium carbonicum siccum, *P. G.*; Getrocknetes Natriumcarbonat, Entwässerte Soda, *G.*; Carbonato sodico seco, *Sp.*

The dried sodium carbonate (*Natrium Carbonicum Siccum*) of the *P. G. V* contains about 75 per cent. of anhydrous sodium carbonate and corresponds to the formula $Na_2CO_3 + 2H_2O$. This is not as stable a form as the U. S. P. monohydrated salt.

Sodium carbonate contains ten molecules of water of crystallization, and, when heated, readily undergoes aqueous fusion. Upon continuing the heat, the water is driven off, and a white porous mass remains, which is easily reduced to powder. Dried sodium carbonate is in the form of a white powder, and differs in nothing from the crystallized, except in being devoid of water of crystallization. (See *Sodii Carbonas.*) It is officially described as "a whitish powder. Taste strongly alkaline. Yields the *reactions* characteristic of sodium and of carbonates. 1 gramme requires for neutralisation not less than 17.9 millilitres of *N/1 solution of sulphuric acid. Lead limit* 25 parts per million. *Arsenic limit* 5 parts per million." *Br.* (See *Sodii Carbonas Monohydras.*)

Uses.—This preparation has the advantage over the common carbonate that it admits of being made into pills, in consequence of being in the dried state. As the water of crystallization forms more than half of the crystallized carbonate, the dose of the dried salt must be reduced in proportion. For the medicinal properties of this salt, see *Sodii Carbonas.*

Dose, two to ten grains (0.13–0.65 Gm.) may be given three times a day, in the form of pill prepared with soap and aromatics.

SODII CARBONAS MONOHYDRATUS. U. S.

MONOHYDRATED SODIUM CARBONATE
Sod. Carb. Monohyd.

(sō′dĭ-ī căr′bo̤-năs mō-no̤-hȳ-drā′tŭs)

"It contains not less than 99.5 per cent. of $Na_2CO_3 + H_2O$ (124.02). Preserve it in well-closed containers." *U. S.*

Preparation.—This salt was introduced into the U. S. P. VIII, upon the recommendation of Coblentz and Frerichs, on account of its much greater stability when compared with sodium carbonate; it contains but one molecule of water of crystallization, while the ordinary carbonate contains ten; as it is almost impossible to keep the carbonate without efflorescing, it became difficult to use it for chemical or pharmaceutical purposes without previously determining the quantity of water present. Coblentz ascertained by experiment that by exposure in an open vessel, monohydrated sodium carbonate gained the first week 0.14 per cent. of moisture, this increased to 0.16 per cent. by the second week. It is prepared by heating and crystallizing sodium carbonate at a temperature above 35° C. (95° F.). As it can be prepared commercially at a low price of excellent quality and is in the form of granular crystals its introduction into the Pharmacopœia has proved a great convenience. It may be used in the place of sodium carbonate.

Properties.—It is officially described as "a white, crystalline, granular powder; odorless, and having a strongly alkaline taste. When exposed to the air, under ordinary conditions, it absorbs only a slight percentage of moisture; exposed to warm, dry air at or above 50° C. (122° F.), the salt effloresces, and at 100° C. (212° F.) it becomes anhydrous. One Gm. of Monohydrated Sodium Carbonate dissolves in 3 mils of water, and in 7 mils of glycerin at 25° C. (77° F.); also in 1.8 mils of boiling water; insoluble in alcohol. An aqueous solution of the salt (1 in 10) is strongly alkaline to litmus and phenolphthalein T.S., and effervesces with acids. An aqueous solution of the salt imparts an intensely yellow color to a non-luminous flame. An aqueous solution of the salt (1 in 50), mixed with a slight excess of hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3).

"Assay.—Dissolve about 2.5 Gm. of Monohydrated Sodium Carbonate, accurately weighed, in about 25 mils of distilled water and titrate with normal sulphuric acid V.S., methyl orange T.S. being used as indicator. It shows not less than 99.5 per cent. of $Na_2CO_3 + H_2O$.

"Each mil of normal sulphuric acid V.S. used corresponds to 0.06201 Gm. of $Na_2CO_3 + H_2O$. Each gramme of Monohydrated Sodium Carbonate corresponds to not less than 16.05 mils of normal sulphuric acid V.S." *U. S.*

Uses.—Monohydrated sodium carbonate can be used for the same purposes that sodium carbonate can, in the proportion of 1 of the former to 2.3 of the latter. (See *Sodii Carbonas,* page 1022.) For internal use it may replace the exsiccated sodium carbonate, being nearly identical with it in composition. (See *Sodii Carbonas Exsiccatus,* page 1023.)

Dose, two to ten grains (0.13–0.65 Gm.).

SODII CHLORIDUM. U. S., Br.

SODIUM CHLORIDE **Sod. Chlorid.**

(sō′dĭ-ī ȼhlō′rĭ-dŭm)

"It contains, when dried to constant weight at 110° C. (230° F.), not less than 99 per cent. of NaCl (58.46). Preserve it in well-closed containers." *U. S.* "Sodium Chloride, NaCl, may be obtained by purifying common salt." *Br.*

Chloruretum Sodicum, Sal Commune, s. Culinare; Table Salt; Muriate of Soda, Sea Salt, Salt; Chlorure de Sodium purifié, *Fr. Cod.;* Hydrochlorate de Soude, Sel commun, Sel de Cuisine, Sel marin, *Fr.;* Natrium Chloratum, *P. G.;* Natriumchlorid, Chlornatrium, Kochsalz, *G.;* Cloruro di sodio, Sal commune, *It.;* Cloruro sodico, Sal comun, *Sp.*

This mineral production, so necessary to mankind, is universally distributed over the globe, and is the most abundant of the native soluble salts. Most animals have an instinctive relish for it, and from its frequent presence in the solids and fluids of the animal economy, it may be supposed to perform an important part in assimilation and nutrition.

Natural State.—Common salt exists in nature either in the solid state or in solution. In the solid state, called *rock salt, fossil salt,* and *sal gemmæ,* it is often found forming extensive beds, and even entire mountains, from which it is extracted in blocks or masses by mining operations. Its geological position

is very constant, it occurring almost invariably in secondary formations, associated with clay and gypsum. In solution it exists in certain springs and lakes, and in the waters of the ocean. The principal salt mines are found in Poland, Hungary, and Russia; in various parts of Germany and Austria, particularly the Tyrol; in Cheshire, England; in Spain; in various parts of Asia and Africa; in Turk's island near St. Domingo; and in Peru and other countries of South America. There are but few mines in the United States where rock salt is produced—at present, one in Louisiana, two in Kansas, and a group operated by one company in the western part of the State of New York; but there are numerous salt springs, which either flow naturally or are produced artificially by sinking wells to various depths in places where salt is known to exist. These are found principally in Missouri, Kentucky, Illinois, Ohio, Michigan, Pennsylvania, Virginia, West Virginia, and New York. In the last-mentioned State the springs are the most productive, the chief ones being situated at Salina, Montezuma, and Galen. In West Virginia an important salt region exists, extending fifteen miles on both sides of the Great Kanawha River, and in Michigan in the counties of Huron, Bay, Wayne, and Saginaw extensive salt wells are worked. California is the only one of the United States in which sea water is utilized for salt production by solar evaporation; this is done extensively at San Diego Bay. The production in the United States in 1915 amounted to 38,231,496 barrels of 280 pounds each.

Rock salt is always transparent or translucent; but it often exhibits various colors, such as red, yellow, brown, violet, blue, etc., which are supposed to be derived from iron and manganese.

Extraction.—Mines of salt are worked in two ways. When the salt is pure, it is merely dug out in blocks and thrown into commerce. When impure, it is dissolved in water, and extracted afterwards from the solution by evaporation. When the salt is naturally in solution, the mode of extraction depends upon the strength of the brine and the temperature of the place where it is found. When the water contains from 14 to 15 per cent. of the salt, it is extracted by evaporation in open pans or vacuum pans provided with crystallizing boxes. If, however, it contains only 2, 3, 4, or 5 per cent., the salt is obtained in a different manner. If the climate be warm, it may be procured by spontaneous evaporation, effected by the heat of the sun; if temperate, by a peculiar mode of evaporation, to be mentioned presently, and the subsequent application of artificial heat.

Sea water is a weak saline solution, containing approximately 2.7 per cent. of common salt, which is extracted by the agency of solar heat in warm countries. Salt thus obtained is called *bay salt*. The extraction is conducted in Europe principally on the shores of the Mediterranean, the waters of which are saltier than those of the open ocean. The mode in which it is performed is by letting the sea water into shallow dikes, lined with clay, and capable, after having been filled, of being shut off from the sea. In this situation the heat of the sun gradually concentrates the water, and the salt is deposited. About 40,000 tons a year are thus made at San Diego, California, the only place in the United States where solar evaporation is carried out. In temperate climates, weak brines are first concentrated in buildings called *graduation houses*. These are rough wooden structures open on the sides, ten or eleven yards high, five or six wide, and three or four hundred long, and containing an oblong pile of brushwood somewhat smaller than the building itself. The brine is pumped up into troughs full of holes, placed above the brushwood, upon which it is allowed to fall, and in its descent, it becomes minutely divided. This operation, by greatly increasing the surface of the brine, promotes its evaporation; and, being repeated several times, the solution is at last brought to the requisite degree of strength to permit of its final concentration in iron boilers by artificial heat.

A very interesting and valuable article describing the American salt industry and very well illustrated with photographs will be found in the *American Food Journal* for December, 1916.

Properties.—Sodium chloride is white, without odor, and of a peculiar taste called saline. It is usually crystallized in cubes; but by quiet evaporation it often assumes the form of hollow quadrangular pyramids, or hopper-shaped crystals, consisting of an aggregation of cubes. It is officially described as follows: "Sodium Chloride occurs as colorless, transparent, cubical crystals, or as a white, crystalline powder; odorless, and having a purely saline taste. It is usually slightly hygroscopic. One Gm. of Sodium Chloride dissolves in 2.8 mils of water, and in 10 mils of glycerin at 25° C. (77° F.); also in 2.7 mils of boiling water; slightly soluble in alcohol. An aqueous solution of the salt (1 in 10) is neutral to litmus. When heated the salt decrepitates. At a red heat it fuses, and at a white heat it is slowly volatilized and partly decomposed. To a non-luminous flame it imparts an intensely yellow color. With silver nitrate T.S. an aqueous solution of the salt (1 in 20) yields a white, curdy precipitate, insoluble in nitric acid, but readily soluble in ammonia water. An aqueous solution of Sodium Chloride does not respond to the Test for heavy metals (see Part III, Test No. 3). Separate portions of 10 mils each of an aqueous solution of Sodium Chloride (1 in 100), after the addition of 1 mil of ammonia water, show no immediate turbidity upon the addition of ammonium oxalate T.S. (*calcium*) or of sodium phosphate T.S. (*magnesium*). Digest 2 Gm. of the finely powdered salt for three hours with 25 mils of warm alcohol, cool the mixture and remove the undissolved salt by filtration. Evaporate the filtrate to dryness, dissolve the residue in 5 mils of distilled

water, add 1 mil of chloroform, and cautiously introduce, drop by drop, with constant agitation, chlorine T.S. which has been diluted with twice its volume of distilled water. The chloroform does not acquire a violet, yellow, or orange color (*iodide or bromide*).

"**Assay.**—Proceed as directed under the Assay for chlorides (see Part III, Test No. 5), using about 0.25 Gm. of Sodium Chloride, dried to constant weight at 110° C. (230° F.) and accurately weighed. It shows, in the dried salt, not less than 99 per cent. of NaCl.

"Each mil of tenth-normal silver nitrate V.S. corresponds to 0.005846 Gm. of NaCl. Each gramme of Sodium Chloride, previously dried, corresponds to not less than 169.3 mils of tenth-normal silver nitrate V.S." *U. S.*

"Small, white, crystalline grains, or transparent, cubic crystals, free from moisture. Taste saline. Soluble in 3 parts of *water*. Yields the *reactions* characteristic of sodium and of chlorides. Yields no characteristic *reactions* for potassium, bromides, or iodides, and not more than slight *reactions* for calcium, magnesium, or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million. 20 millilitres of an aqueous solution (1 in 20) are not immediately colored blue by 0.5 millilitre of *solution of potassium ferrocyanide* (limit of iron)." *Br.*

S. Hill (*Ph. Post.*, 1912, p. 37) states that the flame test for potassium in sodium chloride is unreliable, especially as a great deal of the blue glass gives fallacious results owing to its unsuitability. He recommends the use of *Koevenagel's reagent* of *cobalt sodium hexanitrite*, which produces a yellow precipitate in potassium solutions as dilute as 1-2000.

When pure, salt undergoes no change in the air; but when contaminated with magnesium chloride, as not unfrequently happens, it is deliquescent. Exposed to a gradually increasing heat, it first decrepitates from the presence of interstitial moisture, next melts, and finally volatilizes in white fumes with but partial decomposition. It is decomposed by several of the acids, particularly sulphur and nitric, which disengage vapors of hydrochloric acid; by potassium carbonate with the assistance of heat; and by silver nitrate and mercurous nitrate. In contact with iron, in the presence of air and moisture, it undergoes decomposition. It is decomposed by steam excessively heated, with the escape of hydrochloric acid and an alkaline residue. Several varieties of common salt are distinguished in commerce, as *stored salt, fishery salt, bay salt*, etc.; but they are characterized by the size and compactness of the grains, and not by any difference in composition.

Sodium chloride is incompatible with mercurous, lead, and silver salts with the formation of the corresponding insoluble metallic chloride.

Composition.—Common salt, in its pure state, consists of one atom of chlorine and one of sodium. It contains no water of crystallization. The common salt of commerce, besides pure sodium chloride, contains, generally speaking, insoluble matter, and usually more or less calcium and magnesium sulphates and calcium and magnesium chlorides. When pure, it is not precipitated by sodium carbonate, barium chloride, or potassium ferrocyanide. Calcium chloride is generally present in very small amount; but the magnesium chloride sometimes amounts to 28 parts in 1000. Calcium sulphate is usually present, constituting variously from 1 to 23½ parts in 1000, and magnesium sulphate is sometimes present and sometimes absent. To separate the earths, a boiling solution of sodium carbonate must be added as long as any precipitate is formed. The earths will form as carbonates, and must be separated by filtration, and the sodium sulphate and sodium chloride resulting from the double decomposition will remain in solution. The sodium sulphate may then be decomposed by the cautious addition of barium chloride, avoiding excess, which will generate sodium chloride and insoluble barium sulphate.

Uses.—Although sodium chloride, like other salines, is capable of exercising a diuretic and cathartic action, because of its rapid diffusibility it is much inferior to many other substances. Common salt has for many years been a household remedy in the treatment of *hemoptysis* in doses of one teaspoonful (3.9 Gm.) taken dry. The observations of Belden (*Z. E. P. T.*, 1909, vii, p. 290) lend support to this employment; he found that although when mixed with the blood outside of the body it had no effect, when administered either by the stomach or by injection it increased the coagulability of the blood. He believed the effect to be due to alteration in the concentration of the blood. Externally applied in solution it is stimulant and may be used either locally or generally. Locally it has been employed in the form of fomentations in *sprains* and *bruises*. Salt baths are used for their tonic and exciting effect in various diseases, especially when attended with weakness of the circulation. A pound of salt to four gallons of water forms a solution of about the strength of sea water and suitable for a bath. (See also under *Aqua*, p. 164.) Because of its physiological inertness sodium chloride is the substance generally preferred to increase the density of water when for any reason it is desired to inject that fluid directly into the vein (see *Liquor Sodii Chloridi Physiologicus*).

The uses of common salt in domestic economy as a condiment and an antiseptic are well known.

Dose, as a cathartic, from two drachms to half an ounce (7.7–15.5 Gm.); as an emetic, from half an ounce to an ounce (15.5–31 Gm.), dissolved in four or five times its weight of water. It is frequently used as a clyster, two tablespoonfuls in a pint of water.

Off. Prep.—Liquor Sodii Chloridi Physiologicus, *U. S.*; Sal Carolinum Factitium, *N. F.*; Sal Carolinum Factitium Effervescens, *N. F.*; Sal Kissingense Factitium, *N. F.*; Sal Kissingense Factitium Effervescens, *N. F.*; Sal Vichyanum Factitium, *N. F.*; Sal Vichyanum Factitium Effervescens, *N. F.*; Sal Vichyanum Factitium Effervescens cum Lithio, *N. F.*

SODII CITRAS. U. S.

SODIUM CITRATE Sod. Cit.

(sō'dĭ-ī cī'trăs)

"It contains not less than 98 per cent. of $Na_3C_6H_5O_7 + 2H_2O$ (294.07). Preserve it in well-closed containers." *U. S.*

Citrate of Soda; Citras Sodicus; Citrate de Soude, *Fr.*; Natrium Citricum; Natriumcitrat, Citronsaures Natron, *G.*

Preparation.—The official salt is the normal salt of citric acid and sodium, there being three possible combinations owing to the tri-fold basicity of citric acid. It may be made by adding to a hot aqueous solution of 59 parts of citric acid an aqueous solution of 53 parts of monohydrated sodium carbonate, neutralizing, evaporating, and crystallizing.

Properties.—It is officially described as "in small crystals or as a white, granular powder; odorless, and having a cooling, saline taste. One Gm. of Sodium Citrate dissolves in 1.3 mils of water at 25° C. (77° F.); also in 0.6 mil of boiling water; insoluble in alcohol. An aqueous solution of Sodium Citrate (1 in 20) is slightly alkaline to litmus but is not reddened by 1 drop of phenolphthalein T.S. When heated to about 150° C. (302° F.), the salt loses all of its water of crystallization; on ignition at a red heat, it carbonizes and emits inflammable gases which have a very pungent, acrid odor, and a residue remains which is alkaline to litmus and strongly effervesces with acids. To a non-luminous flame, the salt imparts an intensely yellow color. Mix 10 mils of an aqueous solution of the salt (1 in 20) with 10 mils of calcium chloride T.S.; the liquid remains clear until it is boiled, when a white, granular precipitate is produced. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of the salt meets the requirements of the Test for arsenic (see Part III, Test No. 1).

Assay.—Proceed as directed under the Assay for alkali salts of organic acids (see Part III, Test No. 6). It shows not less than 98 per cent. of $Na_3C_6H_5O_7 + 2H_2O$.

"Each mil of half-normal sulphuric acid V.S. used corresponds to 0.04901 Gm. of $Na_3C_6H_5O_7 + 2H_2O$. Each gramme of Sodium Citrate corresponds to not less than 20 mils of half-normal sulphuric acid V.S." *U. S.*

Uses.—Sodium citrate, like the potassium salt, is oxidized in the system and appears in the urine in the form of a carbonate, and may therefore be used to overcome excessive acidity of the urine. Lichtwitz (*Th. M.*, 1911, xxv, p. 81) recommends it especially in the treatment of *diabetic acidosis* instead of the carbonates. When added to the blood outside of the body it prevents coagulation, presumably by the formation of non-ionizing calcium citrate. In the same way it prevents the curdling of milk by rennin, the sodium caseinate which is formed by this ferment after the addition of the citrate being soluble. According to Robertson and Burnett (*J. P. Ex. T.*, 1912, lix), when administered in large doses to mammals it causes severe symptoms by depriving the tissues of ionizable calcium. While it has been experimentally shown that the administration of sodium citrate by the mouth may delay the coagulability of the blood, it is improbable that any severely toxic symptoms can be caused by its oral administration.

Sodium citrate may be used for the various purposes to which potassium citrate is put (see *Potassium Citrate*), but is probably somewhat less efficient as a diuretic or diaphoretic. It is widely employed in the modification of cow's milk for infant feeding for the purpose of preventing the formation of large hard curds. For this purpose from one to two grains of the salt may be added to each ounce of milk used in the mixture. It has also been highly lauded by Weaver (*New Orleans Med. and Surg. Journ.*, lxc) in the treatment of *pneumonia*. Wright reported remarkable results from its use as a local application for *furunculosis*. *Wright's solution* consists of sodium citrate, 2 grains, sodium chloride, 20 grains, water, 1 ounce; cotton saturated with this solution is placed over the boil and covered with waxed paper to prevent evaporation.

Dose, fifteen to sixty grains (1.0–3.9 Gm.).

SODII CITRO-TARTRAS EFFERVESCENS. Br.

EFFERVESCENT SODIUM CITRO-TARTRATE

(sō'dĭ-ī cī'trō-tär'trăs ĕf-fĕr-vĕs'cĕns)

"Sodium Bicarbonate, in powder, 510 *grammes;* Tartaric Acid, in powder, 270 *grammes;* Citric Acid, in powder, 180 *grammes;* Refined Sugar, in powder, 150 *grammes.* Mix the powders thoroughly; place the mixture in a dish or pan of suitable form heated to between 90° and 105° C. (194° and 221° F.). When the mixture, by aid of careful manipulation, has assumed a granular character, separate it into granules of uniform and convenient size by means of suitable sieves. Dry the granules at a temperature not exceeding 55° C. (131° F.). The product weighs about one thousand grammes." *Br.*

The object of this combination is to furnish sodium citrate and tartrate in a convenient and portable form. As the water has been driven off by heat, no reaction takes place until dissolved in water, when the two acids combine with the soda of the bicarbonate to produce sodium tartrate and citrate, and the carbon dioxide escapes with brisk effervescence. It is in this form that the preparation is intended to be used.

It may be mixed with unpleasant salines whose taste it hides by effervescence. In full dose it has a laxative action similar to that of Seidlitz powders.

Dose, one to two drachms (3.9–7.7 Gm.), which may be taken in a small wineglassful or more of water, and repeated occasionally as required.

SODII CYANIDUM. U. S.

SODIUM CYANIDE Sod. Cyanid.

(sō′dĭ-ī cȳ-ăn-ī′dŭm)

"It contains not less than 95 per cent. of Na CN (49.01). Preserve it in well-closed containers, protected from light." *U. S.*

NOTE.—Sodium Cyanide replaces potassium cyanide of the U. S. P. VIII.

Sodium cyanide may be made by various processes, all of which are analogous to those for the potassium salt. (See *Potassii Cyanidum.*) One of the most recent methods, however, is by the fusion of calcium cyanide with sodium carbonate, $NC.NCCa + Na_2CO_3 = 2NaCN + CaCO_3$.

Potassium cyanide has been very extensively used in the arts and was often adulterated. In addition to this, its excessive tendency to absorb moisture has caused it to be replaced by sodium cyanide, which, on account of the lower atomic weight of sodium, makes it technically stronger weight for weight in the content of hydrocyanic acid. In addition to this, the higher price and scarcity during the European War of potassium salts have justified the introduction of sodium cyanide into the U. S. P. IX.

"Sodium Cyanide occurs in the form of white, opaque, amorphous pieces, or as a white, granular powder; odorless when perfectly dry; deliquescent in the air and exhaling the odor of hydrocyanic acid. *Great caution must be used in handling this salt.* It is freely soluble in cold water. An aqueous solution of the salt (1 in 20) is strongly alkaline to litmus, and emits the odor of hydrocyanic acid. At a low red heat the salt fuses. To a non-luminous flame it imparts an intensely yellow color. A few drops of a solution of the salt (1 in 20) yield with silver nitrate T.S. a white precipitate, which is soluble in an excess of the solution of Sodium Cyanide, and in ammonia water. Shake 5 mils of a solution of the salt (1 in 20) with a few drops each of ferrous sulphate T.S. and of ferric chloride T.S., and then add a slight excess of hydrochloric acid; a blue precipitate (iron ferrocyanide) is produced. In 5 mils of an aqueous solution of the salt (1 in 10) a drop of ferric chloride T.S. followed by 2 mils of diluted hydrochloric acid produces neither a dark blue color (*ferrocyanide*) nor a red color (*sulphocyanate*).

"**Assay.**—Dissolve about 0.45 Gm. of Sodium Cyanide, accurately weighed, in 25 mils of distilled water, add 4 mils of ammonia water, 3 drops of potassium iodide T.S. and titrate with tenth-normal silver nitrate V.S. to the production of a permanent precipitate. It shows not less than 95 per cent. of NaCN.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.009802 Gm. of NaCN. Each gramme of Sodium Cyanide corresponds to not less than 96.9 mils of tenth-normal silver nitrate V.S." *U. S.*

Uses.—Sodium cyanide acts upon the system as does prussic acid. (See *Acidum Hydrocyanicum Dilutum.*) It is rarely used as a medicine. Five grains of it may be regarded as a usual fatal dose (see Venghauss, *A. Pharm.*, clii, p. 138), although smaller doses may occasionally take life. Sodium cyanide has the power of dissolving silver oxide and may be used for the removal of silver nitrate stains from clothing. According to Guthrie, a solution of three grains (0.2 Gm.) to the ounce (30 mils), dropped in the eye every other day, will remove olive colored stains from the conjunctiva caused by silver nitrate.

Owing to the large use of the cyanides for the recovery of gold and other technical purposes, numerous accidental cases of poisoning have occurred. The symptoms and treatment of these are precisely the same as outlined under *Acidum Hydrocyanicum.*

Dose, one-eighth of a grain (0.008 Gm.).

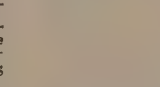
SODII GLYCEROPHOSPHAS. U. S.

SODIUM GLYCEROPHOSPHATE Sod. Glycerophos. [Sodium Glycerinophosphate]

(sō′dĭ-ī glȳ-cę-rō-phŏs′phăs)

"Hydrated Sodium Glycerophosphate containing not less than 68 per cent. of the anhydrous salt [$Na_2C_3H_7PO_6$ or $C_3H_5(OH)_2PO_4Na_2 = 216.10$]." *U. S.*

Sodium glycerophosphate which formerly existed as a pasty mass can now be found in commerce in solid plates or scales which renders it more convenient for pharmaceutical use. It is made by treating glycerophosphoric acid with sodium hydroxide in a manner similar to the process for calcium glycerophosphate. The official sodium glycerophosphate is the normal salt having the following structural composition, exclusive of water of hydration:



The theoretical acid salt has never been prepared in a solid form. The special salt, like the calcium salt of the same acid (which see), is found in several commercial forms, varying in the amount of water of hydration present. Some of these are solid and others liquid. As is the case with the calcium salt, greater solubility is conferred upon the product by the presence of a small proportion of some organic acid such as citric or lactic.

It is officially described as "white, monoclinic plates or scales, or as a white powder, having a saline taste; odorless. It is very soluble in cold or hot water; nearly insoluble in alcohol. An aqueous solution of the salt (1 in 20) is alkaline to litmus and to phenolphthalein T.S. When strongly heated the salt is decomposed, evolving inflammable vapors, and at a red heat is converted into sodium pyrophosphate. Dissolve 1 Gm. of Sodium Glycerophosphate in 10 mils of distilled water and add 3 drops of phenolphthalein T.S.; the red color produced is

discharged by the addition of 1.5 mils of tenth-normal sulphuric acid V.S. (*free alkali*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). Add an equal volume of cold ammonium molybdate T.S. to 10 mils of an aqueous solution of the salt (1 in 20); no precipitate is formed within one hour (*phosphates*). On heating this mixture a yellow precipitate is formed. Triturate 1 Gm. of the salt with 20 mils of dehydrated alcohol, filter the mixture, evaporate the filtrate on a water bath and dry the residue for one hour at a temperature not exceeding 70° C. (158° F.); the weight of this residue does not exceed 0.01 Gm. (*alcohol-soluble impurities*).

"**Assay.**—Dissolve about 3 Gm. of the salt, accurately weighed, in 30 mils of distilled water and titrate with half-normal hydrochloric acid V.S., using methyl orange T.S. as indicator. It shows not less than 68 per cent. of $Na_2C_3H_7PO_6$.

"Each mil of half-normal hydrochloric acid V.S. used corresponds to 0.10805 Gm. of $Na_2C_3H_7PO_6$. Each gramme of Sodium Glycerophosphate corresponds to not less than 6.29 mils of half-normal hydrochloric acid V.S." *U. S.*

Uses.—The glycerophosphates have been used in medicine on the supposition that being more nearly allied chemically to the form in which phosphorus is found in the body, they would be more easily utilized in conditions of depraved phosphorus nutrition and thereby aid in the upbuilding of nerve strength. It seems well established that when taken by the mouth they are absorbed unchanged but, according to Marfori (*A. E. P. P.*, Schmiedeberg Festsch., 1908, p. 378), when injected subcutaneously they are rapidly excreted by the kidneys. The glycerophosphoric acid absorbed from the alimentary tract is retained for some days but is slowly decomposed in the body, being eliminated through the urine as inorganic phosphate. It is probable that the system is capable of utilizing a portion of the glycerophosphoric acid, synthesizing from it the complex organic bodies in which phosphorus exists in the tissues. But the same thing is true of sodium phosphate. Whether glycerophosphate has any higher nutritive value than inorganic phosphates is extremely doubtful. Forbes (*Ohio Technical Bull.* No. 6, 1914), in an elaborate research upon swine, reaches the conclusion that there is no fundamental differences in the nutritive values of the glycerophosphates and phosphates, except that the former are less likely to disturb the digestive tract. In a review of the literature on this subject for the Council on Pharmacy and Chemistry, Marshall (*J. A. M. A.*, 1915, lxiv, p. 573) concluded "that organic phosphorus is of no more value as a food than inorganic." Granting this be true, however, does not necessarily disprove their therapeutic utility. It is possible to conceive that the unbroken molecule of glycerophosphoric acid, circulating in the blood, may in some way exercise a stimulating action on the metabolism of the central nervous system. While there is considerable clinical evidence of the value of the glycerophosphates in various conditions of depraved metabolism, such as *neuralgia, neurasthenia, senility, Graves's disease,* etc., the testimony is not unanimous. We must regard, therefore, the value of sodium glycerophosphate as a remedy in conditions of general debility as still *sub judice.* It has the advantage over the calcium salt that being soluble it may be administered in liquid form.

Dose, ordinarily ten to thirty grains (0.65–2.0 Gm.), although much larger quantities may be given safely.

Off. Prep.—Liquor Sodii Glycerophosphatis, *U. S.;* Elixir Calcii et Sodii Glycerophosphatum (from Solution), *N. F.;* Elixir Glycerophosphatum Compositum (from Solution), *N. F.*

SODII HYDROXIDUM. U. S.

SODIUM HYDROXIDE Sod. Hydrox. [Sodium Hydrate, Caustic Soda, U. S. 1890]

(sō'dī-ī hȳ-drŏx'ĭ-dŭm)

"It contains not less than 90 per cent. of Na OH (40.01). Preserve it in well-closed containers. If bottles are used as containers they must be made of hard glass." *U. S.* "Sodium Hydroxide of commerce purified by means of alcohol." *Br.,* 1914 Appendix.

Soda Caustica; Hydrate of Soda; Natrium Causticum, s. Hydricum; Soude caustique, *Fr. Cod.;* Natron, Aetznatron, *G.;* Soda caustica, *It.;* Hidrato sodico, *Sp.*

The solution of *sodium hydroxide,* being a solution of the caustic alkali, yields it on evaporation in the solid state. Metallic vessels are used in consequence of the chemical action of soda on earthenware or porcelain, and the product is directed to be kept in green glass bottles because these resist its action better than those of white glass. Sodium hydroxide is usually poured into cylindrical moulds to harden, or allowed to solidify in mass, and broken into irregular fragments.

Sodium hydroxide, sodium hydrate, or "caustic soda," of commerce, occurs in hard grayish-white rods or cakes, deliquescent, very alkaline and corrosive. It affords the reactions characteristic of sodium. It usually contains as impurities alumina, carbonates, chlorides, phosphates, and sulphates.

Purified Sodium Hydroxide may be obtained by dissolving caustic soda in ethylic alcohol, filtering the solution, evaporating it to dryness in a silver dish, occasionally adding distilled water during the evaporation. The residue is *Purified Sodium Hydroxide.* It should yield no characteristic reaction with the tests for phosphates or sulphates, and not more than the slightest reactions with the tests for carbonates. It is not quite free from alumina.

Sodium hydroxide has been made on a large scale by simply modifying the Leblanc process (see *Sodii Carbonas*), so that more coal is added in the black-ash fusion, when carbonate is reduced to hydroxide with the liberation of car-

bon monoxide by the action of the quick-lime, the reactions being:

$$CaCO_3 + C = CaO + 2CO$$
$$Na_2CO_3 + CaO + H_2O = 2NaOH + CaCO_3$$

It is also made like the corresponding compound, caustic potash, by the decomposition of sodium carbonate in solution by quick-lime. (See *Liquor Sodii Hydroxidi.*) Ammonia soda ash when causticised yields a purer caustic than Le Blanc soda as it is freer from sulphur impurities. It may also be purified from carbonate, and from lime salts and other impurities, as the potassium hydroxide is purified by treatment with alcohol, which dissolves the alkali, but leaves the salts insoluble. (See *Sodii Carbonas,* page 1021.) H. A. Frasch devised a method for caustic soda in which nickel hydroxide acts upon sodium chloride in the presence of an excess of ammonia; a double nickel-ammonium chloride ($Ni(NH_3)_2Cl_2 + 4NH_3$) separates as a violet, crystalline mass leaving caustic soda in the solution. Both the nickel and the ammonia are regenerated.

The manufacture of caustic soda by electrolytic means from brine in the United States has developed very greatly within the last few years.

Properties.—It is officially described as in "dry, white, or nearly white, fused masses, or sticks, hard and brittle, showing a crystalline fracture; odorless. *Great caution is necessary in using it,* as it rapidly destroys organic tissues. Exposed to the air, it deliquesces, absorbs carbon dioxide, and becomes covered with a coating of carbonate. One Gm. of Sodium Hydroxide dissolves in 0.9 mil of water at 25° C. (77° F.); also in about 0.3 mil of boiling water; very soluble in alcohol. A solution of Sodium Hydroxide even when greatly diluted is strongly alkaline to litmus. When introduced into a non-luminous flame, it imparts to it an intensely yellow color. An aqueous solution of Sodium Hydroxide (1 in 20) is clear and colorless (*organic matter or insoluble impurities*), and, after being acidulated with acetic acid, it yields no precipitate on the addition of an excess of tartaric acid T.S., or upon the addition of a few drops of sodium cobaltic nitrite T.S. (*potassium*). An aqueous solution of Sodium Hydroxide (1 in 50), slightly acidulated with hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Dissolve in a 500 mil graduated flask about 10 Gm. of Sodium Hydroxide, accurately weighed in a glass-stoppered weighing-bottle, in 250 mils of distilled water, which has previously been boiled and cooled, and add 15 mils of barium chloride T.S. Fill the flask to the mark with distilled water, which has previously been boiled and cooled, and thoroughly agitate the liquid. Filter it through a dry filter into a dry flask (rejecting the first 20 mils) and titrate 100 mils of the clear filtrate with normal hydrochloric acid V.S., using phenolphthalein T.S. as indicator. It shows not less than 90 per cent. of NaOH.

"Each mil of normal hydrochloric acid V.S. used corresponds to 0.04001 Gm. of NaOH. Each gramme of Sodium Hydroxide corresponds to not less than 22.5 mils of normal hydrochloric acid V.S." *U. S.*

Sodium hydroxide as found in commerce is in grayish-white fragments, opaque, brittle, and extremely corrosive. It is deliquescent, very soluble in water, soluble in alcohol, and possessed of all the alkaline properties of potassium hydroxide, from which it differs in imparting a yellow color to flame, and in not giving in solution a yellow precipitate with platinic chloride or a crystalline precipitate with tartaric acid in excess. When heated it melts, and at an intense heat evaporates. Though deliquescent, like potassium hydroxide, it does not, like that alkali, become permanently liquid, but forms a paste, which after a time effloresces. The difference in this respect between the two alkalies is owing to the circumstance that, while both are converted into carbonates by uniting with the carbon dioxide of the air, potassium hydroxide forms a deliquescent and sodium hydroxide an efflorescent salt. It is apt to contain 20 or 25 per cent. of water and impurities originating from the sodium carbonate used in preparing the solution from which it is made. The official volumetric assay permits the presence of 10 per cent. of water and impurities, but limits the fixed impurities to 2 per cent.

If the solution be colored brown by hydrogen or ammonium sulphide, the presence of lead may be suspected, derived probably from the glass vessels in which it has been kept. It may be used for making the solution of sodium hydroxide extemporaneously. (See *Liquor Sodii Hydroxidi.*)

Uses.—Sodium hydroxide is rarely employed as an internal remedy. Its most important medical use is as a caustic for the same class of cases in which potassium hydroxide is employed. (See page 901.) It has the advantage over the latter of being less deliquescent and is probably milder. Under the name of *London Paste* there was formerly used for the destruction of diseased tonsils in the London Throat Hospital a combination made by triturating together equal parts of caustic soda and unslaked lime.

Off. Prep.—Liquor Sodii Hydroxidi, *U. S.;* Soda cum Calce, *N. F.*

SODII HYPOPHOSPHIS. U. S., Br.

SODIUM HYPOPHOSPHITE Sod. Hypophos.

(sō'dĭ-ī hȳ-pǫ-phŏs'phĭs)

"It contains not less than 98 per cent. of $NaPH_2O_2 + H_2O$ (106.07). Preserve it in well-closed containers. Caution should be observed in dispensing Sodium Hypophosphite, as an explosion is liable to occur when it is triturated or heated with nitrates, chlorates or other oxidizing agents." *U. S.* "Sodium Hypophosphite may be obtained by the interaction of sodium carbonate and calcium hypophosphite. When dried at 110° C. (230° F.) it contains not less than

97 per cent. of pure sodium hypophosphite, $NaPH_2O_2$." *Br.*

Natrium Hypophosphorosum, Hypophosphis Sodicus; Hypophosphite of Soda; Hypophosphite de Soude, *Fr. Cod.*; Unterphosphorigsaures Natron, *G.*; Hipofosfito sodico, *Sp.*

Preparation.—*Sodium hypophosphite* is prepared by mixing solutions of calcium hypophosphite and monohydrated sodium carbonate, in the proportion of eight ounces of the former dissolved in five pints of water to six of the latter in two pints of water. Double decomposition takes place, with the formation of calcium carbonate and sodium hypophosphite, of which the latter is held in solution and the former is precipitated.

$$Ca(H_2PO_2)_2 + Na_2CO_3 = 2NaH_2PO_2 + CaCO_3$$

After filtration to separate the calcium carbonate, the solution is evaporated to a pellicle, and then stirred constantly until the salt granulates, the heat being continued. If required quite pure, the granulated salt is dissolved in official alcohol, and the liquid, having been evaporated to a syrupy consistence, is set aside to crystallize.

Sometimes sodium hypophosphite explodes with violence during the evaporation of its solution. This was ascribed to the use of too high a temperature; but the same accident has occurred when the heat was applied by means of a water bath. (See *A. J. P.*, 1860, p. 87.) In the *Chemical News* (No. 31, p. 46), Tuson stated that, though he had superintended the manufacture of large quantities of calcium and sodium hypophosphites, he had never witnessed anything like an explosion; but the heat employed in evaporation had never approached 100° C. (212° F.), and this is probably the true explanation. Caution, therefore, should be observed to evaporate at a low temperature.

Properties.—"Sodium Hypophosphite occurs as small, colorless, transparent, rectangular plates of a pearly luster, or as a white, granular powder; odorless, and having a saline taste. It is deliquescent on exposure to moist air. One Gm. of Sodium Hypophosphite dissolves in 1 mil of water at 25° C. (77° F.); also in about 0.15 mil of boiling water; soluble in alcohol, slightly soluble in dehydrated alcohol, and freely soluble in glycerin at 25° C. (77° F.); freely soluble in boiling alcohol. An aqueous solution of Sodium Hypophosphite (1 in 20) is neutral or slightly alkaline to litmus. When heated in a test tube, the salt at first loses its water of crystallization, and upon further heating is decomposed, evolving spontaneously inflammable hydrogen phosphide, which burns with a bright yellow flame. To a non-luminous flame the salt imparts an intensely yellow color. When an aqueous solution of the salt (1 in 20), acidulated with hydrochloric acid, is added drop by drop with agitation to an excess of mercuric chloride T.S., a white precipitate of mercurous chloride is formed. Upon the further addition of the Solution of Sodium Hypophosphite, the precipitate becomes gray from reduction to metallic mercury. A solution of 1 Gm. of the salt in about 10 mils of distilled water requires not more than 1.5 mils of tenth-normal hydrochloric acid V.S. for neutralization, methyl orange T.S. being used as indicator. Heat 5 mils of an aqueous solution of the salt (1 in 5) in a test tube with 0.5 mil of diluted hydrochloric acid on a water bath for thirty minutes; no offensive odor is developed. Measure 5 mils of an aqueous solution of the salt (1 in 25) into a beaker containing 3 mils of nitric acid, diluted with about 10 mils of distilled water, and evaporate the mixture to dryness on a water bath; the residue meets the requirements of the Test for arsenic (see Part III, Test No. 1). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). Add magnesia mixture T.S. to 10 mils of an aqueous solution of the salt (1 in 20), made alkaline with ammonia water; it is not affected within one minute (*phosphate*).

"**Assay.**—Dissolve about 1 Gm. of Sodium Hypophosphite, accurately weighed, in 10 mils of distilled water, add 10 mils of nitric acid and evaporate the solution to dryness on a water bath. Then add 5 mils of nitric acid and again evaporate to dryness on a water bath. Dissolve the residue in 20 mils of distilled water, add a drop of phenolphthalein T.S. and sufficient special potassium hydroxide T.S. (see Reagents) to produce a pink color, and then dilute to exactly 100 mils with distilled water. Transfer 10 mils of this solution to a 100 mil graduated flask, add 50 mils of tenth-normal silver nitrate V.S. and proceed from this point as directed in the assay under *Sodii Phosphas*. It shows, in the dried salt, not less than 98 per cent. of $NaPH_2O_2 + H_2O$.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.0035357 Gm. of $NaPH_2O_2 + H_2O$. Each gramme of Sodium Hypophosphite corresponds to not less than 277.2 mils of tenth-normal silver nitrate V.S." *U. S.*

"White granules, deliquescent. Taste bitter, nauseous. Soluble in 1 part of *water* and in 30 parts of *alcohol* (90 per cent.); insoluble in *ether*. Yields, when heated, spontaneously inflammable hydrogen phosphide and hydrogen. Yields the *reactions* characteristic of sodium, Rapidly attacked by oxidising agents. Its solution yields with a warm aqueous solution of *copper sulphate* a red precipitate of cuprous hydride, which on boiling evolves hydrogen. Yields no characteristic *reactions* for copper, iron, aluminium, zinc, calcium, magnesium, potassium, or ammonium, and not more than the slightest *reactions* for carbonates, chlorides, or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million. Loses not more than 2 per cent. of its weight when dried at 110° C. (230° F.). When the salt thus dried is assayed by the process described under 'Calcii Hypophosphis' not more than 28 millilitres of *N/10 solution of sodium thiosulphate* are required to decolorise the iodine liberated, corresponding to not less than 97 per cent. of pure sodium hypophosphite, $NaPH_2O_2$." *Br.*

The solubility of sodium hypophosphite is increased by the addition of hypophosphorus acid. As the soluble salts of mercury and silver are reduced by the hypophosphites, they are, of course, incompatible with sodium hypophosphite in prescriptions. With calcium hypophosphite, all the soluble sulphates and carbonates produce precipitates.

Uses.—This preparation is as useless as the other hypophosphites. (See *Syrupus Hypophosphitum Compositus.*)

Dose, ten to twenty grains (0.65–1.3 Gm.), three times a day.

Off. Prep.—Emulsum Olei Morrhuæ cum Hypophosphitibus, *U. S.;* Syrupus Hypophosphitum, *U. S.;* Elixir Cinchonæ Alkaloidorum et Hypophosphitum, *N. F.;* Elixir Hypophosphitum, *N. F.;* Elixir Hypophosphitum et Ferri, *N. F.;* Elixir Sodii Hypophosphitis, *N. F.;* Emulsum Olei Morrhuæ cum Hypophosphitibus, *N. F.;* Liquor Hypophosphitum, *N. F.;* Liquor Hypophosphitum Compositum, *N. F.;* Syrupus Calcii et Sodii Hypophosphitum *N. F.;* Syrupus Hypophosphitum Compositus, *N. F.;* Syrupus Sodii Hypophosphitis, *N. F.*

SODII INDIGOTINDISULPHONAS. U. S.

SODIUM INDIGOTINDISULPHONATE Sod. Indigotin. [Indigo Carmine]

(sō′dĭ-ī ĭn-dĭ-gō-tĭn-dī-sŭl′phŏ-nās)

"Chiefly the sodium salt [$C_{16}H_8O_2N_2(SO_3Na)_2 = 466.22$] of indigotindisulphonic acid." *U. S.*

Indigotin, commonly called *indigo blue,* $C_{16}H_{10}N_2O_2$, is a neutral, tasteless, dark blue powder, insoluble in water. When this is acted upon by sulphuric acid it forms disulphindigotic (sulpho-coerulic) acid, $C_{16}H_8N_2O_2(HSO_3)_2$. This acid is neutralized by sodium and the official salt is produced. This is known as indigo-carmine, soluble indigo, coeruline and other similar descriptive names.

It is officially described as follows: "Sodium Indigotindisulphonate occurs as a blue powder or as a dark purple paste. Before applying the following tests to the paste, deprive it of water by drying it to constant weight at 100° C. (212° F.). When compressed, it acquires a coppery luster. Sodium Indigotindisulphonate is sparingly soluble in water, yielding a dark blue solution; almost insoluble in alcohol. The addition of nitric acid, bromine water, or chlorine water to an aqueous solution of the salt (1 in 200) discharges the blue color. The blue color is also discharged by warming this solution with sodium hydroxide and zinc dust or with stannous chloride T.S. Dissolve 1 Gm. of Sodium Indigotindisulphonate, previously dried to constant weight at 100° C. (212° F.), in 200 mils of distilled water, filter the solution through counterbalanced filters, wash the filters and residue with distilled water until the washings cease to be colored blue, and dry at 100° C. (212° F.). The dry, insoluble residue remaining on the filter does not exceed 2 per cent. Boil about 0.2 Gm. of Sodium Indigotindisulphonate for two minutes with 10 mils of distilled water, cool, and then triturate the solution with small portions of bromine water until the blue color disappears. On now adding a few drops of potassium iodide T.S. to the liquid, no blue color is produced (*starch or starch iodide*). Add 15 mils of solution of hydrogen dioxide and 10 mils of sodium hydroxide T.S. to about 0.2 Gm. of the salt, shake the mixture until the blue color disappears, then evaporate the liquid to about 10 mils, cool, acidulate with hydrochloric acid, and add a few drops of ferrous sulphate T.S.; no blue color is produced (*iron ferricyanide or ferrocyanide*)." *U. S.*

This salt is used as a dye and also as a microscopic stain and in certain chemical reagents both for qualitative and quantitative tests. It is official for the purpose of coloring the tablets of corrosive sublimate (see *Toxitabellæ Hydrargyri Chloridi Corrosivi,* U. S.).

SODII IODIDUM. U. S., Br.

SODIUM IODIDE Sod. Iod.

(sō′dĭ-ī ī-ŏd′ĭ-dŭm)

"It contains, when dried to constant weight at 100° C. (212° F.), not less than 99 per cent. of NaI (149.92). It contains not more than 7 per cent. of moisture. Preserve it in well-closed containers." *U. S.* "Sodium Iodide may be obtained from iodine and sodium hydroxide by a process similar to that employed in making Potassium Iodide, the salt being crystallised at a temperature not lower than 20° C. (68° F.). When dried at 110° C. (230° F.) it contains not less than 99 per cent. of pure sodium iodide, NaI." *Br.*

Iodure de Sodium, *Fr. Cod.;* Natrium Jodatum, *P. G.;* Natriumjodid, Jodnatrium, *G.;* Yoduro sodico, *Sp.*

Preparation.—This iodide may be prepared either by treating a solution of sodium hydroxide with iodine, or by double decomposition between ferrous iodide and sodium carbonate, precisely as potassium iodide is obtained by the corresponding processes for that salt.

Properties.—It is a very soluble white salt, crystallizing in anhydrous cubes from a hot solution, and in oblique rhombic prisms, with two molecules of water, by spontaneous evaporation. It is officially described as in "colorless, cubical crystals, or as a white, crystalline powder; odorless, and having a saline taste. In moist air Sodium Iodide deliquesces, or at first cakes and then deliquesces, and frequently undergoes decomposition, assuming a brown tint. One Gm. of Sodium Iodide dissolves in 0.55 mil of water, about 2 mils of alcohol, and in 1 mil of glycerin at 25° C. (77° F.); also in 0.4 mil of boiling water. An aqueous solution of Sodium Iodide (1 in 20) is neutral or slightly alkaline to litmus. When strongly heated, the salt melts, and at a bright red heat it is slowly volatilized and partly decomposed. To a non-luminous flame it imparts an intensely yellow color. Add

1 mil of ferric chloride T.S., diluted with an equal volume of distilled water, to 5 mils of an aqueous solution of the salt (1 in 20); and shake the mixture with 5 mils of chloroform; the latter acquires a violet color. Dissolve 1 Gm. of the salt in 10 mils of distilled water, and add 0.15 mil of tenth-normal sulphuric acid V.S.; no red color is produced by the addition of a drop of phenolphthalein T.S. (*alkali*). A solution of 1 Gm. of the salt in 1 mil of distilled water yields no precipitate with 1 mil of sodium bitartrate T.S. (*potassium*). Dissolve 0.5 Gm. of the salt in 10 mils of distilled water, which has been previously boiled and cooled, and add 2 drops of diluted sulphuric acid (free from sulphurous or nitrous acid), no distinct, yellow color appears within half a minute (*iodate*), and no turbidity occurs (*thiosulphate*). Add 5 mils of potassium hydroxide T.S. and about 0.2 Gm. of aluminum wire to a solution of 1 Gm. of Sodium Iodide, in 5 mils of distilled water contained in a test tube of about 40 mils capacity. Insert a pledget of purified cotton in the upper portion of the test tube, and place a piece of moistened red litmus paper over its mouth. On heating the tube and contents upon a water bath for fifteen minutes, no blue coloration of the paper is discernible (*nitrate or nitrite*). Ten mils of an aqueous solution of the salt (1 in 20), acidulated with hydrochloric acid, is not rendered turbid by the addition of 1 mil of potassium sulphate T.S. (*barium*); another 10 mil portion of an aqueous solution (1 in 20), acidulated with hydrochloric acid, is not rendered more than slightly turbid by a few drops of barium chloride T.S. (*sulphate*). Heat gently 5 mils of an aqueous solution of the salt (1 in 10) with 1 drop of ferrous sulphate T.S., 1 drop of ferric chloride T.S., and 0.5 mil of potassium hydroxide T.S.; no blue color appears after acidulating the mixture with hydrochloric acid (*cyanide*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). When dried to constant weight at 100° C. (212° F.), it loses not more than 7 per cent. of its weight (*moisture*).

"**Assay.**—Proceed as directed under the Assay for iodides (see Part III, Test No. 5), using about 0.5 Gm. of Sodium Iodide, previously dried to constant weight at 100° C. (212° F.), and accurately weighed. It shows, in the dried salt, not less than 99 per cent. of NaI.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.014992 Gm. of NaI. Each gramme of Sodium Iodide, previously dried, corresponds to not less than 66 mils nor more than 67.7 mils of tenth-normal silver nitrate V.S." *U. S.*

"A white crystalline powder, deliquescent. Taste saline and somewhat bitter. Soluble in less than 1 part of *water* and in 3 parts of *alcohol* (90 per cent.). Yields the *reactions* characteristic of sodium and of iodides. Loses not more than 5 per cent. of its weight when dried at 110° C. (230° F.); 0.5 gramme of this dried salt requires for complete precipitation not less than 33.0 or more than 33.9 millilitres of *N/10 solution of silver nitrate*. Yields no characteristic *reactions* for copper, iron, aluminium, calcium, magnesium, potassium, ammonium, bromates, cyanides, carbonates, or iodates, and not more than the slightest *reactions* for bromides, chlorides, or sulphates. *Lead limit* 10 parts per million. *Arsenic limit* 5 parts per million." *Br.*

Sodium iodide possesses the same incompatibilities as the other soluble iodides. It produces insoluble precipitates with mercurous, lead and silver salts and even weak oxidizing agents liberate iodine from it when in solution.

Uses.—Sodium iodide has the same therapeutic effects as the other iodides. (See *Iodum.*) It is said to be better borne by the stomach than potassium iodide, although it contains 8 per cent. more iodine. Pfannenstill (*D. M. W.*, 1911, p. 2420) asserts that by the conjoint internal administration of large doses of sodium iodide and hydrogen peroxide externally, a local liberation of free iodine may be obtained at the point of application of hydrogen dioxide. He recommends this method of treatment, especially in *tuberculous ulcers* of the mucous membrane and in *lupus*. His method has received some confirmation, and Reuterskiold (*Cb. Chir.*, 1911, p. 985) has found it of service in various surgical conditions, such as *osteomyelitis, cellulitis, infected leg ulcers*, etc.

Dose, five to thirty grains (0.32–2.0 Gm.).

Off. Prep.—Syrupus Ferri et Mangani Iodidi, *N. F.*

SODII NITRIS. U. S., Br.

SODIUM NITRITE Sod. Nitris.

(sō'dĭ-ī nī'trĭs)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 95 per cent. of $NaNO_2$ (69.01). Preserve it in well-closed containers." *U. S.* "Sodium Nitrite may be obtained by fusing sodium nitrate with metallic lead. It contains not less than 95 per cent. of pure sodium nitrite, $NaNO_2$." *Br.*

Nitrite of Sodium, Nitrite of Soda; Nitrite de Soude, *Fr.*; Salpetrigsaures Natron, *G.*

Preparation.—According to M. A. Darbon, it is made on a large scale as follows: Sodium nitrate is melted in large cast iron vessels, whereby hygroscopic water is removed and a part of the iodides and iodates, still present, are decomposed. At 310° C. (590° F.) the nitrate begins to fuse. It is heated to 400° to 420° C. (752°–788° F.), and pure metallic lead in thin sheets is gradually added, the mass being constantly stirred, about 280 parts of lead being necessary for 100 parts of sodium nitrate used. The lead must be as free as possible from other metals and antimony particularly must be absent. When all the lead has been added, care having been exercised to prevent overheating, the stirring must be kept up for some time, and the melted mass is then, by means of a cast iron

ladle, run in the form of thin threads into water with constant stirring.

In this process, besides the nitrite, about 1 per cent. of sodium hydroxide is produced, which in its turn dissolves a portion of lead, and has to be removed during the subsequent purification, either by nitric acid or by lead nitrate or sulphuric acid. The crude products are a solution containing the nitrite, undecomposed saltpetre, sodium hydroxide holding lead in solution, the soluble impurities of the sodium nitrate, such as sodium chloride, etc., and a residue consisting of lead oxide, a little metallic lead, and a certain proportion of lead peroxide. The solution strained from the residue, with the washings, is diluted to about 6° to 8° B., neutralized with nitric acid as long as a precipitate is formed, separated from this precipitate, concentrated to 42° to 45° B. while warm, and then left to crystallize—the crystals requiring possibly recrystallization. The pure crystals are separated by a centrifugal machine, washed, dried and packed in cylinders of double thickness of parchment paper. (*Chem. News*, Sept. 22, 1899, 146.) A more satisfactory process as used at present is by heating sodium nitrate with quicklime and passing in a current of SO_2.

$$NaNO_3 + CaO + SO_2 = NaNO_2 + CaSO_4$$

Properties.—It is officially described as in "white, or nearly white, opaque, fused masses, or sticks, as colorless, transparent, hexagonal crystals, or as a granular powder; odorless, and having a mild, saline taste. When exposed to the air, the salt deliquesces and is gradually oxidized to sodium nitrate, and becomes unfit for use. One Gm. of Sodium Nitrite dissolves in 1.5 mils of water at 25° C. (77° F.); sparingly soluble in alcohol; very soluble in boiling water. An aqueous solution of Sodium Nitrite (1 in 10) is slightly alkaline to litmus. When heated the salt melts, and at a red heat is decomposed, yielding oxygen, nitrogen, nitrogen dioxide, and sodium oxide. To a non-luminous flame it imparts an intensely yellow color. Mix 5 mils of an aqueous solution of the salt (1 in 10) with 5 drops of potassium iodide T.S. and add 5 drops of hydrochloric acid; iodine is liberated, and nitrogen dioxide gas escapes with effervescence. Dissolve 0.5 Gm. of the salt in 25 mils of diluted hydrochloric acid, evaporate the solution to dryness and dissolve the residue in 25 mils of distilled water, adding a few drops of diluted hydrochloric acid; 10 mils of the resulting solution does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Dissolve about 1 Gm. of Sodium Nitrite, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed in a stoppered weighing-bottle, in sufficient distilled water to make 100 mils, and add 10 mils of this solution, from a pipette, to a solution consisting of 50 mils of tenth-normal potassium permanganate V.S., 100 mils of distilled water and 5 mils of sulphuric acid. In adding the sodium nitrite solution, immerse the tip of the pipette beneath the surface of the permanganate mixture. Warm the liquid to 40° C. (104° F.), allow it to stand for five minutes and then titrate with tenth-normal oxalic acid V.S. It shows, in the dried salt, not less than 95 per cent. of $NaNO_2$.

"Each mil of tenth-normal potassium permanganate V.S. used corresponds to 0.0034505 Gm. of $NaNO_2$. Each gramme of Sodium Nitrite, previously dried, corresponds to not less than 275.3 mils of tenth-normal potassium permanganate V.S." *U. S.*

"A white crystalline powder, deliquescent. Taste saline. Soluble in 1.5 parts of *water*. Yields the *reactions* characteristic of sodium and nitrites. 0.1 gramme dissolved in *water* decolorises not less than 27.5 millilitres of *N/10 solution of potassium permanganate*, the solution being maintained slightly acid. Aqueous solution neutral or only slightly alkaline to *litmus;* gives no precipitate on the addition of *diluted sulphuric acid* (absence of lead). *Arsenic limit* 5 parts per million." *Br.*

Uses.—The injection of a nitrite into the circulation produces an increase in the rate of the pulse with a marked fall of blood pressure. At the same time if the dose has been sufficient there develops motor weakness and diminution of reflex activity. After toxic doses the breathing becomes rapid and often of dyspneic character, the mucous membranes of a peculiar slate color, and convulsions may occur. The acceleration of the heart rate is due to a depressant action upon the cardio-inhibitory center in the medulla. The fall of blood pressure is due to a dilatation of the arteries through a direct action upon the muscular coat of their walls. The vessels of the lungs do not share in this action, for H. C. Wood, Jr. (*J. Ex. M.*, 1911, xiv), has shown that the pulmonary artery is contracted rather than dilated. As was first shown by H. C. Wood (*Am. J. M. S.*, July, 1871), the motor weakness and diminished reflexes are the result of an action upon the spinal cord. The increased breathing is not due to any action upon the respiratory center, but is a response to the deprivation of the system for oxygen which is brought about through chemical alteration of the coloring matter of the blood. Whether the new compound formed is identical with methemoglobin, which results from the action of a number of poisons, or not is at present uncertain, but it is a so much more stable compound than oxyhemoglobin that the system is unable to obtain sufficient oxygen to maintain normal functions.

Of the various compounds which liberate the nitrite ion in the system and produce the physiological results described above, those official are amyl nitrite, glyceryl nitrate, ethyl nitrite, and sodium nitrite. The difference between the effects of these drugs is chiefly in their rapidity and duration. The influence of amyl nitrite may be perceived usually within 30 seconds after

its administration, and lasts for from 5 to 10 minutes, that of nitroglycerin being within 1 or 2 minutes, and rarely endures more than one-half hour, sodium nitrite manifests its action in from 5 to 10 minutes and lasts for about 2 hours. (See Wallace and Ringer, *J. A. M. A.*, 1909, liii, 1629.)

The most important use of sodium nitrite is for the purpose of reducing arterial pressure in threatened *apoplexy*, certain types of *chronic nephritis*, the early stages of *arterial degenerations*, and other conditions of too *high blood-pressure*. In arterio-sclerosis, after actual degenerative changes have taken place in the walls of the blood vessels, although widely employed it is incapable of much benefit because when the muscular tissue is replaced by connective tissue the drug can no longer cause dilatation of the arteries. On the other hand, in those forms of too high blood pressure in which there is no degenerative change in the walls of the vessels it is one of the most valuable drugs we possess to cause a temporary reduction. It has the great advantage over nitroglycerin in the longer duration of its effects. In convulsive disorders the nitrites are useful only for immediate effects and for this purpose the other preparations are superior to the sodium salt.

Because of its deliquescence sodium nitrite can be prescribed only in solution and should always be given well diluted, but even with the greatest care it will very often cause such marked gastric disturbance as to interdict its use.

Dose, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Spiritus Ætheris Nitrosi, *U. S.*

SODII PERBORAS. U. S.

SODIUM PERBORATE Sod. Perbor.

(sō'dĭ-ī pẹr-bō'răs)

"It contains not less than 9 per cent. of available oxygen, corresponding to about 86.5 per cent. of $NaBO_3 + 4H_2O$ (154.06). Preserve it in well-closed containers, in a cool place." *U. S.*

Sodium perborate is made by decomposing sodium peroxide with acid under a patented process.

In the presence of water, this salt undergoes decomposition with the formation of hydrogen dioxide and sodium metaborate, the resulting solution being slightly alkaline in reaction.

$$NaBO_3 + H_2O = H_2O_2 + NaBO_2$$

In the dried state, sodium perborate, if pure, is permanent in the air. Commercial varieties of sodium perborate yield from 5 per cent. to 10 per cent. of free oxygen.

"Sodium Perborate occurs as white, crystalline granules or as a powder; odorless, and having a saline taste. It is stable in cool and dry air, but is decomposed with the evolution of oxygen in warm or moist air. Sodium Perborate is soluble in water. A saturated aqueous solution of the salt is alkaline to litmus or phenolphthalein T.S. In aqueous solution the salt is decomposed into metaborate and hydrogen dioxide, the solution gradually evolving oxygen. Oxygen is evolved more rapidly if the solution is warmed. The salt imparts an intensely yellow color to a non-luminous flame. Turmeric paper, if moistened with an aqueous solution of the salt which has been acidulated with hydrochloric acid, becomes brown in color, particularly on drying; on moistening the dried test paper with ammonia water, the color is changed to greenish-black. Agitate a mixture of 1 mil of an aqueous solution of the salt (1 in 50), 1 mil of diluted sulphuric acid, a few drops of potassium dichromate T.S., and 2 mils of ether; the ether acquires a blue color. Strongly heat 0.5 Gm. of the salt in a platinum crucible, and dissolve the residue in 25 mils of distilled water with the aid of a few drops of hydrochloric acid; 10 mils of the resulting solution does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Dissolve about 0.25 Gm. of the salt, accurately weighed, in a mixture of 50 mils of distilled water and 10 mils of diluted sulphuric acid and titrate the solution with tenth-normal potassium permanganate V.S. It shows not less than 9 per cent. of available oxygen.

"Each mil of tenth-normal potassium permanganate V.S. used corresponds to 0.0008 Gm. of available oxygen. Each gramme of Sodium Perborate corresponds to not less than 112.5 mils of tenth-normal potassium permanganate V.S." *U. S.*

Sodium perborate has been supplied under various trade names, as *peroxigen, peroxydol,* etc. Under the trade name of *Pergenol* has also been introduced a mixture of sodium perborate and sodium bitartrate. This is asserted to correspond to 12 per cent. of hydrogen dioxide, so that the preparation of a solution corresponding to the official solution of hydrogen dioxide requires one part of pergenol and three of water. *Perboral* is a mixture of the perboric acid and para-iodo-sulfonic acid. According to Jaubert (*B. M. J.*, 1905), *perborax* has the formula $Na_2B_4O_8 + 10H_2O$.

Uses.—Sodium perborate is used as a means of obtaining the therapeutic effects of hydrogen dioxide. According to Herbol (*D. M. W.*, 1908, p. 1092), a 2 per cent. solution of sodium perborate is equivalent in germicidal activity to an 0.4 per cent. solution of hydrogen dioxide. In *wounds* or *ulcers* it may be used in solution or as a dusting powder. For the preparation of antiseptic mouth wash it has the advantage over the solution of the dioxide of hydrogen of being alkaline instead of acid. It has also been employed in various skin diseases, especially in *acne vulgaris*. Herzfeld (*J. A. M. A.*, 1911, lvii, p. 6113) has used it not only as an antiseptic dressing in infected wounds, chronic ulcers, or diabetic gangrene, but as a hemostatic in epistaxis and other local bleedings. It may be employed either as a dusting powder or as a solution in strengths of from 2 per cent. upwards. It is rarely used internally.

Dose, one to three grains (0.065–0.2 Gm.).

SODII PHENOLSULPHONAS. U. S.

SODIUM PHENOLSULPHONATE Sod. Phenolsulph. [Sodii Sulphocarbolas, U. S. 1890, Sodium Sulphocarbolate]

(sō'dĭ-ī phē-nŏl-sŭl'phọ-năs)

"It contains not less than 83.64 per cent. nor more than 87.82 per cent. of anhydrous sodium phenolsulphonate (sodium paraphenolsulphonate), corresponding to not less than 99 per cent. of the crystallized salt [$NaC_6H_5O.SO_3 + 2H_2O = 232.14$]. Preserve it in well-closed containers." *U. S.*

Sodii Sulphocarbolas, *Br.*, *U. S.* 1890; Sodium paraphenolsulphonate; Sodium Sulphophenate; Sulfophénate de Soude, *Fr.*; Phenolsulfosaures Natrium, Phenylschwefelsaures Natron, *G.*

Sodium phenolsulphonate may be made by mixing equal parts of pure phenol and strong sulphuric acid, whereby *paraphenol sulphonic acid* (*sulphocarbolic acid*), $C_6H_4(HSO_3)OH$, is produced. The mixed liquids must be subjected to a temperature of 55° C. (131° F.) for several days, and then twenty parts of water should be added. Two parts of barium carbonate are added to the liquid, a little at a time, carefully graduating the quantity until effervescence ceases. The liquid is now allowed to stand to permit the precipitation of barium sulphate, and of any carbonate which might be present, and the liquor filtered. The solution of *barium phenolsulphonate* is decomposed by adding sodium carbonate until precipitation ceases, when the liquid is filtered from the barium carbonate, and the sodium phenolsulphonate may be obtained by evaporating the filtrate and crystallizing.

Properties.—"Sodium Phenolsulphonate occurs as colorless, transparent, rhombic prisms or crystalline granules; odorless, and having a cooling, saline, bitter taste. It is somewhat efflorescent in dry air. One Gm. of Sodium Phenolsulphonate dissolves in 4.2 mils of water, 140 mils of alcohol and in about 5 mils of glycerin at 25° C. (77° F.); also in 0.8 mil of boiling water and 13.5 mils of boiling alcohol. An aqueous solution of Sodium Phenolsulphonate (1 in 10) is neutral to litmus. When heated slightly above 100° C. (212° F.) the salt loses all of its water of crystallization and becomes white. At a higher temperature it chars, emits inflammable vapors having the odor of phenol, and finally leaves a residue consisting chiefly of sodium sulphate. To a non-luminous flame it imparts an intensely yellow color. A diluted solution of the salt (1 in 100) is rendered pale violet by ferric chloride T.S., but remains clear; barium chloride T.S. leaves the solution of the original salt clear, but if the salt is ignited, and the residue dissolved in distilled water, the same reagent produces in the filtered solution a copious, white precipitate. Add bromine T.S. to 10 mils of an aqueous solution of the salt (1 in 100); a permanent yellow color but neither turbidity nor precipitation is produced within two minutes (*phenol*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3).

Assay.—Dissolve about 0.25 Gm. of Sodium Phenolsulphonate, accurately weighed, in 50 mils of distilled water, add 50 mils of tenth-normal bromine V.S. and 5 mils of hydrochloric acid. Allow the mixture to stand for fifteen minutes, then add 2 Gm. of potassium iodide dissolved in 5 mils of distilled water, and subject the solution to residual titration with tenth-normal sodium thiosulphate V.S., using starch T.S. as indicator. It shows not less than 83.64 per cent. nor more than 87.82 per cent. of $NaC_6H_5O_4S$.

"Each mil of tenth-normal bromine V.S. used corresponds to 0.004903 Gm. of $NaC_6H_5O_4S$. Each gramme of Sodium Phenolsulphonate corresponds to not less than 170.6 mils nor more than 179.1 mils of tenth-normal bromine V.S." *U. S.*

Uses.—The phenol sulphonates, or sulphocarbolates as they are commonly called, were introduced into medicine with the idea of obtaining the antiseptic action of carbolic acid in a non-toxic form, for it is well known that the combination of sulphuric acid with phenol destroys its toxicity. But it has been shown by Withers that the phenol sulphonates are not possessed of any antiseptic power. The claim which has been made that they are decomposed in the intestinal tract with the liberation of phenol is not supported by any scientific evidence and seems *a priori* improbable. There is neither sufficient clinical nor scientific evidence of the value of this drug in medicine. Sodium phenolsulphonate is, however, still employed as an intestinal antiseptic.

Dose, five to ten grains (0.32–0.65 Gm.).

SODII PHOSPHAS. U. S., Br.

SODIUM PHOSPHATE Sod. Phos. [Sodium Orthophosphate]

(sō'dĭ-ī phŏs'phăs)

"It contains not less than 39.25 per cent. nor more than 44.00 per cent. of anhydrous sodium phosphate (di-sodium-ortho-phosphate), corresponding to not less than 99 per cent. of the crystallized salt [$Na_2HPO_4 + 12H_2O = 358.24$]. Preserve it in well-closed containers, in a cool place." *U. S.* "Sodium Phosphate may be obtained by the interaction of sodium carbonate and the solution of acid calcium phosphate produced on mixing bone-ash and sulphuric acid. It contains not less than 99.5 per cent. of pure di-sodium hydrogen phosphate, $Na_2HPO_4,12H_2O$." *Br.*

Medicinal Tribasic Sodium Phosphate, Phosphate of Soda; Disodium Hydrogen Phosphate; Phosphas Sodicus (Natricus) Sal Mirabile Perlatum; Phosphate de Soude, *Fr. Cod.*; Natrium Phosphoricum, *P. G.*; Natriumphosphat, Phosphorsaures Natron, *G.*; Fosfato bisodico, *It.*; Fosfato sodico, *Sp.*

A process for this salt is no longer official; for that of the U. S. P., 1870, see *U. S. Disp.*, 19th edition, page 1151.

The incombustible part of bones is obtained by burning them to whiteness, and consists of neutral calcium phosphate, called bone phosphate, associated with some calcium carbonate, etc. When this is mixed with sulphuric acid,

the calcium carbonate is entirely decomposed, giving rise to effervescence. The calcium phosphate undergoes partial decomposition; the greater part of the lime, being detached, precipitates as calcium sulphate, while the phosphoric acid, set free, combines with the undecomposed portion of the phosphate, and remains in solution as an acid calcium phosphate, holding dissolved a small portion of the calcium sulphate. In order to separate the acid phosphate from the precipitated mass of calcium sulphate, boiling water is added to the mixture, the whole is strained, and the sulphate washed as long as acid phosphate is removed, which is known by the water passing through in an acid state. The different liquids which have passed the strainer, consisting of the solution of acid calcium phosphate, are mixed and allowed to stand, and by cooling a portion of calcium sulphate is deposited, which is removed by decantation. The bulk of the liquid is now reduced by evaporation, and, in consequence of the diminution of the water, a fresh portion of calcium sulphate is deposited, which is separated by subsidence and decantation as before. The acid calcium phosphate solution, being heated, is now saturated by means of a hot solution of sodium carbonate. The calcium carbonate is separated by a new filtration, and the filtered liquor, which is a solution of sodium phosphate, is evaporated so as to crystallize.

The reactions are as follows:

$$Ca_3(PO_4)_2 + 2H_2SO_4 = 2CaSO_4 + Ca(H_2PO_4)_2$$

$$Ca(H_2PO_4)_2 + 2Na_2CO_3 = 2Na_2HPO_4 + Ca CO_3 + CO_2 + H_2O$$

In the U. S. process of 1870 the calcined bone is to the acid as 10 to 6; in the Br. process of 1867 as 10 to 6½ nearly. The proportion recommended by Berzelius is as 10 to 6.66. The acid, in the former official process, was added to the calcined bone in the concentrated state, and afterwards diluted with more or less water. In the process given by Berzelius it is first diluted with twelve times its weight of water. All the writers state that sodium phosphate crystallizes more readily by allowing its solution to be slightly alkaline, and a remarkable fact is, that a neutral solution, when it crystallizes, leaves a supernatant liquid which is slightly acid and uncrystallizable. Hence it is necessary, after getting each successive crop of crystals, to render the mother water slightly alkaline, before it will furnish an additional quantity.

Funcke, a German chemist, has given the following cheap and expeditious method for obtaining sodium phosphate. To the powdered calcined bone, diffused in water, sufficient diluted sulphuric acid is added to decompose all the calcium carbonate which it contains. When the effervescence ceases, the matter is treated with nitric acid, which dissolves the calcium phosphate and leaves the sulphate. The nitric solution of the phosphate is then treated with sodium sulphate, equal in quantity to the bone employed, and after the reaction is completed, the nitric acid is recovered by distillation. In consequence of a double decomposition, calcium sulphate and sodium phosphate are formed, the latter of which is separated by water, and crystallized in the usual manner.

Properties.—The medicinal sodium phosphate, according to the U. S. Pharmacopœia IX is in "large, colorless, monoclinic prisms, or as a granular, crystalline salt; odorless, and having a cooling, saline taste. The crystals effloresce in the air. One Gm. of Sodium Phosphate dissolves in 2.7 mils of water at 25° C. (77° F.); insoluble in alcohol. An aqueous solution of Sodium Phosphate (1 in 10) is alkaline to litmus and phenolphthalein T.S. When heated to about 40° C. (104° F.) the salt fuses, yielding a colorless liquid; at 100° C. (212° F.) it loses all of its water of crystallization and at a red heat is converted into sodium pyrophosphate. It imparts an intensely yellow color to a non-luminous flame. An aqueous solution of the salt (1 in 20) yields a white, crystalline precipitate with magnesia mixture T.S. Not more than a slight turbidity appears on dissolving 1 Gm. of the salt in 20 mils of distilled water (*calcium or aluminum*). No effervescence occurs on the addition of hydrochloric or nitric acid to a solution of the salt (*carbonate*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of the salt meets the requirements of the Test for arsenic (see Part III, Test No. 1). Add a few drops of silver nitrate T.S. to 10 mils of an aqueous solution of the salt (1 in 20), previously mixed with 5 mils of diluted nitric acid; not more than an opalescence is produced (*chloride*)." *U. S.*

"Transparent, colorless, rhombic prisms, efflorescent. Taste saline. Soluble in 7 parts of *water*, the solution being slightly alkaline to *litmus*. Yields the *reactions* characteristic of sodium and of phosphates. 5 grammes dissolved in 50 millilitres of *water* require for neutralisation not less than 13.9 millilitres of *N/1 solution of sulphuric acid, solution of methyl orange* being used as indicator. Yields no characteristic *reactions* for potassium, ammonium, carbonates, or chlorides, and not more than the slightest *reaction* for sulphates. *Lead limit* 5 parts per million. *Arsenic limit* 5 parts per million." *Br.*

"Assay.—Introduce about 0.4 Gm. of Sodium Phosphate, accurately weighed, into a 100 mil graduated flask, dissolve it in 10 mils of distilled water, add 50 mils of tenth-normal silver nitrate V.S. and agitate the mixture well. Then gradually add zinc oxide (see page 1692) in small portions until the liquid is neutral to litmus. Then add distilled water to make 100 mils, agitate the mixture thoroughly, filter through a dry filter, rejecting the first 20 mils of filtrate, collect 50 mils of the subsequent filtrate, add 2 mils of nitric acid and 2 mils of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium sulphocyanate V.S. to

the production of a permanent red color. It shows not less than 39.25 per cent. nor more than 44 per cent. of Na_2HPO_4.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.004735 Gm. of Na_2HPO_4. Each gramme of Sodium Phosphate corresponds to not less than 82.9 mils nor more than 92.9 mils of tenth-normal silver nitrate V.S." *U. S.*

Before the blowpipe, sodium phosphate at first undergoes the aqueous fusion, and afterwards, at a red heat, melts into a globule of limpid glass, which becomes opaque on cooling. It is liable to adulteration, sometimes containing sodium carbonate, from this salt having been added in excess in its preparation, in which case it will effervesce with acids. If it contain sodium sulphate, or any other soluble sulphate, the precipitate caused by barium chloride will be a mixture of barium sulphate and phosphate, and will not be totally soluble in nitric acid. A. B. Lyons found a specimen which consisted almost entirely of sodium sulphate. (*A. J. P.*, 1875, 371; see also *N. R.*, April, 1877.) Barium chloride will detect sodium carbonate also, by producing a precipitate of barium carbonate, soluble with effervescence in nitric acid. If a chloride be present, the *yellow* precipitate caused by silver nitrate will be a mixed one of silver chloride and phosphate, not entirely soluble in the same acid. The salt is incompatible with soluble salts of lime, with which it gives a precipitate of calcium phosphate, and with neutral metallic solutions. It is found in several of the animal secretions, particularly the urine. For an elaborate article upon the methods of determining the percentage of phosphates present in a substance, see *Chem. News*, Oct., 1874, 200. Samples of sodium phosphate have been found in commerce contaminated with arsenic in dangerous quantities. The official test to detect arsenic should always be applied to sodium phosphate. (*C. D.*, June 30, 1900, 1073; *Am. Drug.*, Aug. 27, 1900, 103.)

The medicinal sodium phosphate is one of the three sodium salts of tribasic phosphoric acid, H_3PO_4. In this salt two of the three replaceable hydrogen atoms have been replaced by sodium, so that its formula is HNa_2PO_4, which then crystallizes out with 12 molecules of water. Its complete formula is then $HNa_2PO_4 + 12H_2O$. When gently heated, it loses its water of crystallization (see *Sodii Phosphas Exsiccatus*) and at a red heat the salt is converted into *sodium pyrophosphate*, $Na_4P_2O_7$. (See *Sodii Pyrophosphas.*)

Uses.—Sodium phosphate was introduced into practice about the year 1800 by Pearson of London. In doses of from one to two ounces (31 to 62 Gm.) it is a mild purgative, and, from its pure saline taste, is well adapted to the cases of children, and of persons of delicate stomach. In smaller doses it has been considerably used, generally in connection with other phosphates, to meet any real or supposed deficiency of phosphates in the system, and for this purpose it is well adapted by its ready solubility. It is widely believed that it exerts, especially in children, an extraordinary influence upon the hepatic secretion. It is therefore employed in *constipation* where the stools are light in color, in infantile *diarrhea*, with *white or green stools*, and sometimes with *jaundice*, these evidences of deficient or disordered bile are said to quickly yield to small doses of sodium phosphate, the passages assuming their healthy yellow color, and the attendant disease generally disappearing. It probably, however, possesses only the virtues of the other saline laxatives.

Dose, as a laxative from one to four drachms (3.9–15.5 Gm.); as a hepatic stimulant from twenty to forty grains (1.3–2.6 Gm.) may be given, dissolved in water, after meals.

Off. Prep.—Sodii Phosphas Effervescens (from Dried Salt), *U. S., Br.;* Sodii Phosphas Exsiccatus, *U. S.;* Liquor Sodii Phosphatis Compositus, *N. F.*

SODII PHOSPHAS ACIDUS. Br.

ACID SODIUM PHOSPHATE

(sō'dĭ-ī phŏs'phās ă'cĭ-dŭs)

"Acid Sodium Phosphate may be obtained by the combination of di-sodium hydrogen phosphate with phosphoric acid. It contains not less than 70 per cent. of pure sodium di-hydrogen phosphate, NaH_2PO_4." *Br.*

Sodium Di-hydrogen Phosphate: Sodium Biphosphate: Monsodium Hydrogen Phosphate.

This salt which has been introduced into medicine and is found as a commercial article, is sometimes known as *primary sodium phosphate* or *monosodium orthophosphate*. It is prepared by adding the proper molecular proportions of the ordinary disodium orthophosphate and phosphoric acid according to the following reaction:

$$Na_2HPO_4 + H_3PO_4 = 2NaH_2PO_4.$$

This salt is not only used in medicine, but is employed in the manufacture of baking powders in which it plays the part of the acidic element in liberating CO_2 from $NaHCO_3$.

It is described in the British Pharmacopœia, 1914, as "transparent, colorless, rhombic crystals, or in crystalline powder. Taste saline, acid. Readily soluble in *water*, the solution being acid to *litmus*. Yields the *reactions* characteristic of sodium and of phosphates. 1 gramme dissolved in a mixture of 10 millilitres of *water* and 10 millilitres of *glycerin* requires for neutralisation not less than 5.8 millilitres of *N/1 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator. Yields no characteristic *reactions* for potassium and ammonium, and not more than the slightest *reactions* for sulphates or chlorides. *Lead limit* 5 parts per million. *Arsenic limit* 2 parts per million." *Br.*

Uses.—The acid sodium phosphate is used in medicine for the purpose of increasing the acidity of the urine, especially in certain types

of *cystitis*. It may be prepared extemporaneously by treating the neutral phosphate with phosphoric acid; to prepare it extemporaneously about 32 parts of the official phosphoric acid is required for each 100 parts of the official neutral sodium phosphate in solution.

Dose, from fifteen to thirty grains (1–2 Gm.) repeated as often as may be necessary.

SODII PHOSPHAS EFFERVESCENS. U. S., Br.

EFFERVESCENT SODIUM PHOSPHATE Sod. Phos. Eff.

(sō′dĭ-ī phŏs′phăs ĕf-fẹr-vĕs′cẹnṣ)

Sodæ Phosphas Effervescens; Effervescent Phosphate of Soda; Natrium Phosphoricum Effervescens; Phosphate de Soude effervescent, *Fr.*; Brausendes Natriumphosphat, *G.*

* "Exsiccated Sodium Phosphate, in fine powder, *two hundred grammes* [or 7 ounces av., 24 grains]; Sodium Bicarbonate, dried and powdered, *four hundred and seventy-seven grammes* [or 16 ounces av., 361 grains]; Tartaric Acid, dried and powdered, *two hundred and fifty-two grammes* [or 8 ounces av., 389 grains]; Citric Acid, unefflouresced crystals, *one hundred and sixty-two grammes* [or 5 ounces av., 313 grains], to make about *one thousand grammes* [or 35 ounces av., 120 grains]. Powder the Citric Acid and mix it intimately with the exsiccated sodium phosphate and tartaric acid, then thoroughly incorporate the sodium bicarbonate. Place the mixed powders on a plate of glass or in a suitable dish, in an oven heated to between 93° and 104° C. (199.4° and 219.2° F.). Manipulate the mixture carefully with a wooden spatula, and, when it has become moist, rub it through a No. 6 tinned-iron sieve, and dry the granules at a temperature not exceeding 54° C. (129.2° F.). Immediately transfer the salt to suitable containers and seal them tightly. Care must be taken to prevent the salt from coming in contact with air containing moisture." *U. S.*

"Sodium Phosphate, in crystals, 500 *grammes;* Sodium Bicarbonate, in powder, 500 *grammes;* Tartaric Acid, in powder, 270 *grammes;* Citric Acid, in powder, 180 *grammes.* Dry the Sodium Phosphate until it has lost about 60 per cent. of its weight; powder the dried salt and mix it with the other ingredients. Place the whole in a dish or pan of suitable form heated to between 90° and 105° C. (194° and 221° F.). When the mixture, by aid of careful manipulation, has assumed a granular character, separate it into granules of uniform and convenient size by means of suitable sieves. Dry the granules at a temperature not exceeding 55° C. (131° F.). The product weighs about one thousand grammes." *Br.*

This salt, introduced in the Br. Add. 1885, and into the U. S. P. VIII and IX, affords a pleasant means of giving sodium phosphate.

Dose, one-fourth to one-half ounce (7.7–15.5 Gm.).

SODII PHOSPHAS EXSICCATUS. U. S.

EXSICCATED SODIUM PHOSPHATE Sod. Phos. Exsic.

(sō′dĭ-ī phŏs′phăs ĕx-sịc-cā′tŭs)

"It contains, when dried to constant weight at 110° C. (230° F.), not less than 98 per cent. of Na_2HPO_4 (142.05). Preserve it in well-closed containers." *U. S.*

* "Sodium Phosphate, *a convenient quantity.* Allow the crystals to effloresce for several days in warm air, at a temperature of from 25° to 30° C. (77°–86° F.), then continue the drying in an oven, raising the temperature very gradually until 100° C. (212° F.) has been reached, and maintaining this temperature until the salt ceases to lose weight. Powder and sift the residue and transfer it to well-closed containers." *U. S.*

Properties.—"Exsiccated Sodium Phosphate is a white powder which absorbs moisture readily, and which, after allowance is made for the loss of water of crystallization, conforms to the reactions and tests under *Sodii Phosphas.* One Gm. of Exsiccated Sodium Phosphate dissolves in 8.1 mils of water at 25° C. (77° F.); also in 1.1 mils of boiling water; insoluble in alcohol.

Assay.—Exsiccated Sodium Phosphate, when quantitatively estimated by the assay method under *Sodii Phosphas,* using about 0.15 Gm. of the salt, previously dried to constant weight at 110° C. (230° F.) and accurately weighed, shows, in the dried salt, not less than 98 per cent. of Na_2HPO_4.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.004735 Gm. of Na_2HPO_4. Each gramme of Exsiccated Sodium Phosphate, previously dried, corresponds to not less than 207 mils of tenth-normal silver nitrate V.S." *U. S.*

Uses.—This salt was introduced in this form for use in making effervescent sodium phosphate. Forty parts of exsiccated sodium phosphate represent about 100 parts of crystallized sodium phosphate (see *Sodii Phosphas*), although in damp atmosphere it absorbs water readily and may contain from 10 to 25 per cent. The water content should always be determined before it is used in any important preparation. It is not used medicinally unless in combination.

Off. Prep.—Sodii Phosphas Effervescens, *U. S.*

SODII SALICYLAS. U. S., Br.

SODIUM SALICYLATE Sod. Salicyl.

(sō′dĭ-ī săl-ị-cȳ′lăs)

"It contains, when dried to constant weight at 100° C. (212° F.), not less than 99.5 per cent. of $NaC_7H_5O_3$ (160.04). Preserve it in well-closed containers, protected from heat and light." *U. S.* "Sodium Salicylate may be obtained by the interaction of salicylic acid and sodium carbonate. It contains not less than 99.5

per cent. of pure sodium salicylate, $NaC_7H_5O_3$." *Br.*

Salicylate of Soda; Salicylate de Soude, *Fr. Cod.;* Natrium salicylicum, *P. G.;* Natriumsalicylat, *G.;* Salicilato di sodio, *It.;* Salicilato sodico, *Sp.*

This salt is prepared by mixing 100 parts of pure salicylic acid with sufficient water to form a paste, and then with 104 parts of pure crystallized sodium carbonate (U. S. P. 1890) (uneffloresced) in a glass or porcelain vessel; carbon dioxide will be evolved, and sodium salicylate will remain in solution. The liquid may be strained through thoroughly washed muslin, if necessary, and heated in an evaporating dish until the carbon dioxide is expelled. If alkaline to litmus paper, enough salicylic acid must be added to be slightly in excess, and the solution is then evaporated at a low heat to dryness. If the acid be not in excess, the salt will not be white, but gray or lead-colored.

Properties.—Pure sodium salicylate is a "white, micro-crystalline powder, or in scales, or as an amorphous powder; colorless or having not more than a faint pink tinge; odorless, or having a faint, characteristic odor and a sweet, saline taste. One Gm. of Sodium Salicylate dissolves in 0.9 mil of water and in 9.2 mils of alcohol at 25° C. (77° F.); very soluble in boiling water or in boiling alcohol; soluble in glycerin. An aqueous solution of Sodium Salicylate (1 in 10) when freshly made is colorless or nearly colorless, and neutral or slightly acid to litmus. When heated the salt is decomposed, giving off inflammable vapors and an odor of phenol, and finally leaving a residue of sodium carbonate and carbon. To a non-luminous flame it imparts an intensely yellow color. Add a few drops of ferric chloride T.S. to an excess of a concentrated aqueous solution of Sodium Salicylate (1 in 4); a dark red color and a precipitate are produced. In a solution of the salt (1 in 100) a deep violet-blue color is produced. Diluted hydrochloric acid or sulphuric acid produces a voluminous, white precipitate in a concentrated aqueous solution of the salt. Add 1 mil of hydrochloric acid to a solution of 1 Gm. of Sodium Salicylate in 20 mils of distilled water and filter the liquid; the filtrate does not decolorize 2 drops of tenth-normal iodine V.S. (*sulphite or thiosulphate*). Add a slight excess of hydrochloric acid to an aqueous solution of the salt (1 in 50), and filter; the filtrate does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Proceed as directed under the Assay for alkali salts of organic acids (see Part III, Test No. 6), using about 2 Gm. of Sodium Salicylate, previously dried to constant weight at 100° C. (212° F.) and accurately weighed. It shows, in the dried salt, not less than 99.5 per cent. of $NaC_7H_5O_3$.

"Each mil of half-normal sulphuric acid V.S. used corresponds to 0.08002 Gm. of $NaC_7H_5O_3$. Each gramme of Sodium Salicylate, previously dried, corresponds to not less than 12.43 mils of half-normal sulphuric acid V.S." *U. S.*

"Small colorless scales, or tabular crystals with a pearly lustre. No odor; taste sweetish, unpleasant, saline. Soluble in 1 part of *water*, but this solution, when allowed to stand, is liable to deposit crystals of the salt containing 6 molecules of water of crystallisation; soluble in 6 parts of *alcohol* (90 per cent.). Solutions neutral or faintly acid to *litmus*. Carbonises when heated, leaving finally a white ash which effervesces with acids and imparts an intense yellow color to flame. *T. Sol. of ferric chloride* colors a dilute solution violet. 2 grammes, heated to redness till gases cease to be evolved, leave an alkaline residue which, when treated with *water*, filtered, and well washed, yields a clear solution requiring for neutralisation not less than 24.8 millilitres of *N/2 solution of sulphuric acid.* When to a concentrated aqueous solution excess of *diluted nitric acid* is added, a precipitate is produced which, collected, washed, and dried, responds to the tests described under 'Acidum Salicylicum,' and the filtrate yields not more than the slightest *reactions* for sulphates or chlorides. *Lead limit* 10 parts per million. *Arsenic limit* 2 parts per million. 50 to 100 grammes kept in a closed vessel for several days do not evolve the slightest odor of phenol. Dissolves without coloration or effervescence in *sulphuric acid* (absence of certain organic impurities and of carbonates)." *Br.*

Sodium salicylate is incompatible with antipyrine, forming, when mixed in powder, a liquid mixture.

Uses.—The action of sodium salicylate upon the economy, and its therapeutic use, are precisely those of salicylic acid, except that the salt is not locally irritating, and, being soluble, is more rapidly absorbed. When salicylic acid is administered, it is mostly converted into sodium salicylate before it is absorbed into the blood. One drachm of the salt contains about fifty grains of the acid.

Dose, from ten to thirty grains (0.65–2.0 Gm.).

Off. Prep.—Caffeinæ Sodio-Salicylas, *N. F.;* Elixir Sodii Salicylatis, *N. F.;* Elixir Sodii Salicylatis Compositum, *N. F.;* Liquor Antisepticus, *N. F.;* Liquor Ferri Salicylatis, *N. F.*

SODII SULPHAS. U. S., Br.

SODIUM SULPHATE Sod. Sulph. [Glauber's Salt]

(sō'dĭ-ī sŭl'phăs)

"It contains not less than 43.64 per cent. nor more than 48 per cent. of anhydrous sodium sulphate, corresponding to not less than 99 per cent. of the crystallized salt [$Na_2SO_4 + 10H_2O = 322.23$]. Preserve it in well-closed containers, in a cool place." *U. S.* "Sodium Sulphate, $Na_2SO_4,10H_2O$, may be obtained by the interaction of sodium chloride with sulphuric acid," *Br.*

Sulphate of Soda; Sulfas Sodicus (Natricus), Sal mirabile Glauberi; Vitriolated Soda, Glauber's Salt; Sulfate de Soude purifié, *Fr. Cod.;* Sel de Glauber, *Fr.;* Natrium Sulfuricum, *P. G.;* Natriumsulfat, Schwefelsaures Natron, Glaubersalz, *G.;* Solfato di Sodio, *It.;* Sulfato Sodico, Sal admirabile de Glaubero, *Sp.*

Sodium sulphate, in small quantities, is extensively diffused in nature, and is obtained artificially in several chemical operations. It exists in solution in many mineral springs, among which may be mentioned those of Cheltenham and Carlsbad, and it is found combined with calcium sulphate constituting a distinct mineral. Many ponds containing this salt are found in the country between Santa Fé and the head waters of the Arkansas, and on the route to the Rocky Mountains. Sodium Sulphate occurs in abundant deposits, in conjunction with sodium carbonate, in Wyoming. As an artificial product, sodium sulphate is formed in the processes for obtaining hydrochloric acid and chlorine, and in the preparation of ammonium chloride from ammonium sulphate and common salt. It may also be procured from sea water, in which it is present.

Immense quantities of sodium sulphate are made by decomposing common salt by sulphuric acid, in the manufacture of soda-ash and sodium carbonate (see *Sodii Carbonas*), in both the Leblanc and the Hargreave's processes. So far from the generated hydrochloric acid being a product of much value, its absorption in a convenient way, so as to avoid the nuisance of its escape into the atmosphere in a gaseous state, is an object of importance to the manufacturer. (See *Acidum Hydrochloricum.*) At Strassfurt sodium sulphate is produced extensively by utilizing the mother liquors from the treatment of carnallite or kilderite, which still contains about 25 per cent. of magnesium sulphate and 50 per cent. of sodium chloride.

The residue of the process for obtaining chlorine by the action of sulphuric acid and manganese dioxide on common salt is a mixture of sodium sulphate and manganous sulphate. Large quantities of this residue are formed in manufacturing chlorinated lime (bleaching powder), and the sodium sulphate in it, roughly purified, supplies a part of the salt consumed in making soda-ash and sodium carbonate.

The process for obtaining ammonium chloride from ammonium sulphate and common salt forms another source of sodium sulphate. By double decomposition, sodium sulphate and ammonium chloride are formed, and by exposing the mixed salts to heat, the ammonium chloride sublimes, and the sodium sulphate remains behind. (See *Ammonii Chloridum.*)

Properties.—Sodium sulphate is in "large, colorless, transparent, monoclinic prisms, or granular crystals; odorless, and having a bitter, saline taste. The salt effloresces rapidly in the air. One Gm. of Sodium Sulphate dissolves in slightly over 1 mil of water at 25° C. (77° F.); insoluble in alcohol; soluble in glycerin; when heated to about 33° C. (91.4° F.) it melts in its water of crystallization. An aqueous solution of the salt (1 in 10) is neutral to litmus. When gently heated the salt fuses, and, on continuing the heat to 100° C. (212° F.), it loses all of its water of crystallization (about 56 per cent.). At a red heat, the anhydrous salt fuses without decomposition. To a non-luminous flame it imparts an intensely yellow color. An aqueous solution of Sodium Sulphate (1 in 20) yields with barium chloride T.S. a white precipitate insoluble in hydrochloric acid. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of the salt meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"**Assay.**—Dissolve about 1 Gm. of Sodium Sulphate, accurately weighed, in 100 mils of distilled water, acidulate the solution with hydrochloric acid and heat it to boiling. Gradually add an excess of hot barium chloride T.S., heat for thirty minutes on a water bath, collect the precipitate of barium sulphate on a filter, wash it until silver nitrate T.S. no longer produces an opalescence in 2 mils of the filtrate acidulated with nitric acid, dry, ignite, and weigh it. It corresponds to not less than 43.64 per cent. nor more than 48 per cent. of Na_2SO_4.

"Each gramme of Sodium Sulphate corresponds to not less than 0.717 Gm. nor more than 0.789 Gm. of $BaSO_4$." *U. S.*

"In transparent monoclinic prisms; efflorescent. Taste bitter, saline. Soluble in 3 parts of *water;* insoluble in *alcohol* (90 per cent.). Loses about 55.9 per cent. of its weight when dried at 100° C. (212° F.). Yields the *reactions* characteristic of sodium and of sulphates. 1 gramme dissolved in *water* acidified with *hydrochloric acid* yields, on the addition of excess of *solution of barium chloride,* a white precipitate which, washed and dried, weighs about 0.724 gramme. Yields no characteristic *reactions* for iron, magnesium, potassium, ammonium, or carbonates, and not more than the slightest *reactions* for chlorides. *Lead limit* 5 parts per million. *Arsenic limit* 2 parts per million." *Br.*

When recently prepared it is beautifully transparent; but on exposure to the air it effloresces, and the crystals become covered with an opaque white powder. After long exposures it undergoes complete efflorescence, and falls into powder with loss of more than half its weight. A supersaturated solution of sodium sulphate will remain without crystallizing at ordinary temperatures, even though containing several times the weight of the salt that will be dissolved at the same degree of heat. But the solution instantly forms into a crystalline mass upon adding to it a fragment of the same salt crystallized, or other substances that have been exposed to the air, or upon abruptly placing it in contact with the air.

When crystallized sodium sulphate is subjected to heat it dissolves in its water of crystallization, then dries, and afterwards by the application of a red heat melts with the loss of 55½ per cent. of its weight. Coppet has ascertained that there are two varieties of the anhydrous sulphate—one in which the salt is deprived of its water at ordinary temperature, the other in which the desiccation is effected at a heat above that of 33° C. (91.4° F.). The two differ in their relation to the crystalliza-

tion of the salt, the former causing immediate crystallization when thrown into a supersaturated solution, the second not. Occasionally it contains an excess of acid or alkali, which may be discovered by litmus or turmeric paper. Common salt may be detected by silver nitrate; a salt of iron by potassium ferrocyanide. This salt is not subject to adulteration. It is incompatible with potassium carbonate, calcium chloride, the salts of barium, lead acetate and subacetate, and with silver nitrate if the solutions are strong. It consists of two atoms of sodium combined with the group SO_4 characteristic of sulphates, and crystallizes with ten molecules of water, $Na_2SO_4 + 10H_2O$.

Uses.—Sodium sulphate in doses of from half an ounce to an ounce (15.5–31 Gm.) is an efficient hydragogue cathartic; in smaller doses, an aperient and diuretic. When in an effloresced state, the dose must be reduced one-half, on account of its having lost about one-half of its weight of water. Sodium sulphate is much less used than formerly, having been almost entirely superseded by magnesium sulphate, which is less disagreeable to take and milder in its action. Its nauseous taste, however, may be disguised by the admixture of a little lemon juice or cream of tartar, or by the addition of a few drops of sulphuric acid. It is an ingredient in the artificial Cheltenham salt. (See Part II.) D. de Luca has found sodium sulphate remarkably efficient in removing *stains* or *opacity* of the *cornea,* if applied in the form of powdered crystals directly to the eyeball twice daily. (*J. P. C.,* Sept., 1867.) The only uses of sodium sulphate in the arts are to make sodium carbonate and some kinds of glass. It has no U. S. official preparations.

Dose, two drachms to an ounce (7.7–31 Gm.).

Off. Prep.—Sodii Sulphas Effervescens, *Br.;* Sal Carolinum Factitium, *N. F.;* Sal Carolinum Factitium Effervescens, *N. F.*

SODII SULPHAS EFFERVESCENS. Br.

EFFERVESCENT SODIUM SULPHATE

(sō′dĭ-ī sŭl′phăs ĕf-fẹr-vĕs′cẹns)

Sodæ Sulphas Effervescens; Effervescent Sulphate of Soda; Natrium Sulfuricum Effervescens; Brausendes Natriumsulfat, *G.*

"Sodium Sulphate, in crystals, 500 *grammes;* Sodium Bicarbonate, in powder, 500 *grammes;* Tartaric Acid, in powder, 270 *grammes;* Citric Acid, in powder, 180 *grammes.* Dry the Sodium Sulphate until it has lost about 55 per cent. of its weight; powder the dried salt, and mix it with the other ingredients. Place the whole in a dish or pan of suitable form, heated to between 90° and 105° C. (194° and 221° F.). When the mixture, by aid of careful manipulation, has assumed a granular character, separate it into granules of uniform and convenient size by means of suitable sieves. Dry the granules at a temperature not exceeding 55° C. (131° F.). The product weighs about one thousand grammes." *Br.*

It is used as an effervescent laxative, in the *dose* of from one-fourth to one-half ounce (7.7–15.5 Gm.) dissolved in cold water and taken while effervescing.

SODII SULPHIS. Br.

SODIUM SULPHITE

(sō′dĭ-ī sŭl′phĭs)

"Sodium Sulphite may be obtained by the interaction of sulphurous acid and sodium carbonate. It contains not less than 94 per cent. of pure sodium sulphite, $Na_2SO_3,7H_2O$." *Br.*

Natrium Sulfurosum, Sulfis Sodicus (Natricus); Sulfite de Soude, *Fr.;* Natriumsulfit, Schwefligsaures Natron, *G.*

This salt may be prepared by passing sulphurous acid gas into a solution of sodium carbonate, and evaporating out of contact of the air. The sulphurous acid unites with the soda of the carbonate to form sodium sulphite, and the carbon dioxide escapes. After sufficient concentration, the solution is allowed to cool, and the salt crystallizes. A better way, however, is to dissolve a convenient weight of sodium carbonate in a small quantity of water, then pass the sulphurous acid gas through the solution until it is completely saturated, and acid sodium sulphite is formed. The addition of an equal weight of sodium carbonate forms a solution of the neutral sulphite, which is to be evaporated and crystallized. On exposure the salt gradually changes into a sulphate.

Sulphuric acid added to the solution gives rise to an odor of burning sulphur, owing to the escape of sulphurous acid, and the liquid remains transparent, indicating the absence of calcium. Sodium sulphite consists of two atoms of sodium combined with the group SO_3, characteristic of sulphites, and crystallized with seven molecules of water, $Na_2SO_3 + 7H_2O$. For methods of determining sodium carbonate in sodium sulphite by C. E. Caspari and M. R. Moffat the reader is referred to *Proc. A. Ph. A.,* 1902; also *West. Drug.,* 1904, 59. Sodium sulphite has been replaced in the U. S. P. by the more stable exsiccated salt, which see.

Properties.—"Colorless, transparent, monoclinic prisms, efflorescent in dry air. Inodorous; taste saline and sulphurous. Soluble in 2 parts of *water;* insoluble in *alcohol* (90 per cent.). Yields the *reactions* characteristic of sodium and of sulphites. Aqueous solution neutral or faintly alkaline to *litmus;* on the addition of *hydrochloric acid* evolves sulphur dioxide, but does not become cloudy (absence of thiosulphate). 0.3 gramme dissolved in 30 millilitres of *N/10 solution of iodine* yields a solution which requires for complete decolorisation not more than 7.6 millilitres of *N/10 solution of sodium thiosulphate. Arsenic limit* 5 parts per million." *Br.*

Uses.—According to the experiments of L. Pfeiffer (*A. E. P. P.,* xxvii), the sulphites are capable of causing death by paralyzing the heart and also the respiratory and other motor

nerve centers, but are so rapidly and completely changed into the sulphates that unless given in enormous amount they exert very little influence upon the system; 96.5 per cent. of the sulphite was regained from the urine as a sulphate, and 86 per cent. passed out in five hours after ingestion. But according to Kionka (*D. M. W.*, 1902, xxviii, p. 89) even in doses comparable to those used in the preservation of food the prolonged use produced in dogs serious symptoms of intoxication. Although the experiments of Sternberg have demonstrated that sodium sulphite has no germicidal powers, it appears to be distinctly toxic to the more highly organized fungoid parasites. It has been used in cases of *yeasty vomiting* with remarkable success. The matter vomited in these cases contains two microscopic fungi, called Sarcina ventriculi and Torula cerevisiæ. The remedy was first used at the suggestion of Graham of London, who supposed that the sulphurous acid, necessarily extricated from the salt in the stomach by the acid of the yeasty matter, would destroy the parasites. Sodium sulphite is sometimes used locally, especially in that species of *aphthous sore mouth* which is attributed to a parasitic vegetable. The wash may be made of a drachm of the salt to a fluidounce of water. It is said that the solution acts with surprising rapidity, a single application of it sometimes removing the disease in 24 hours. Astrié, an Italian physician, has proposed this salt as a remedy for the constitutional effects of mercury, when used in excess, on the ground that it has the power of rendering the metal soluble. It also has been largely given internally as an antizymotic (see *Sodii Thiosulphas*), but without general success.

Dose, of sodium sulphite, fifteen to sixty grains (1.0–3.9 Gm.).

SODII SULPHIS EXSICCATUS. U. S.

EXSICCATED SODIUM SULPHITE Sod. Sulphis. Exsic.

(sō′dĭ-ī sŭl′phĭs ĕx-sĭc-cā′tŭs)

"It contains not less than 90 per cent. of Na_2SO_3 (126.07). Preserve it in well-closed containers, in a cool place." *U. S.*

This salt may be readily prepared from the crystallized salt by heating the latter at a temperature slightly above 100° C. (212° F.) until an anhydrous residue of constant weight remains. It is more uniform in water content than the crystalline salt, which was official in the U. S. P. VIII.

It is officially described as follows: "Exsiccated Sodium Sulphite occurs as a white powder; odorless, and having a cooling, saline, sulphurous taste. Exposed to the air, it is slowly oxidized to sulphate. One Gm. of Sodium Sulphite dissolves in 3.2 mils of water at 25° C. (77° F.); sparingly soluble in alcohol. An aqueous solution of the salt (1 in 10) is alkaline to litmus. At a red heat, the salt fuses to a reddish-yellow mass of sodium sulphate and sodium sulphide. To a non-luminous flame the salt imparts an intensely yellow color. Upon the addition of hydrochloric acid to the salt, sulphur dioxide is liberated, which is recognized by its odor, and by its blackening a strip of paper moistened with mercurous nitrate T.S. held in the escaping gas. Dissolve 1 Gm. of Exsiccated Sodium Sulphite in 10 mils of diluted hydrochloric acid and heat the solution sufficiently to expel the gases; the liquid does not become turbid (*thiosulphate*). Dissolve 1 Gm. of the salt in 20 mils of diluted hydrochloric acid, evaporate the solution to dryness, and dissolve the residue in 50 mils of distilled water. Ten mils of this solution does not respond to the Test for heavy metals (see Part III, Test No. 3). Add 3 mils of nitric acid to 5 mils of an aqueous solution of the salt (1 in 25), cautiously evaporate the solution to dryness on a water bath, and treat the residue with a few mils of distilled water and filter the liquid. On evaporating the filtrate and washings to dryness, this residue meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"Assay.—Add about 0.3 Gm. of Exsiccated Sodium Sulphite, accurately weighed, to 50 mils of tenth-normal iodine V.S. in a glass-stoppered flask, agitate the mixture until complete solution results and titrate with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 90 per cent. of Na_2SO_3.

"Each mil of tenth-normal iodine V.S. used corresponds to 0.006304 Gm. of Na_2SO_3. Each gramme of Exsiccated Sodium Sulphite corresponds to not less than 142.8 mils of tenth-normal iodine V.S." *U. S.*

A. H. Clark (*Drug. Circ.*, 1914, p. 457) has reported at length upon the keeping qualities of the anhydrous salt in comparison with the hydrated crystalline form. His conclusions are in favor of the greater stability of the dehydrated salt.

Uses.—Dried sodium sulphite is used for the same purposes and in the same manner as the crystalline, except it is a little more than twice as strong and must be used in correspondingly small amounts.

Dose, eight to thirty grains (0.5–2.0 Gm.).

SODII THIOSULPHAS. U. S.

SODIUM THIOSULPHATE Sod. Thiosulph.
[Sodii Hyposulphis, U. S. 1890, Sodium Hyposulphite]

(sō′dĭ-ī thī-o-sŭl′phās)

"It contains not less than 63.07 per cent. nor more than 67.48 per cent. of anhydrous sodium thiosulphate, corresponding to not less than 99 per cent. of the crystallized salt [$Na_2S_2O_3 + 5H_2O = 248.22$]. Preserve it in well-closed containers." *U. S.*

Hyposulphite of Soda; Natrum Subsulfurosum (Hyposulfurosum); Hyposulphis Sodicus; Hyposulphite de Soude, *Fr., Cod.*; Sulfite sulfuré de Soude, *Fr.*; Natrium thiosulfuricum, *P. G.*; Natriumthiosulfat, Unterschwefligsaures Natron, *G.*; Hiposulfito sodico, *Sp.*

This salt is used in the United States and

British Pharmacopœias as a test, and for the formation of the *Volumetric Solution of Sodium Thiosulphate*. It is found only in the Appendix of the Br. It is readily prepared, according to Walchner, by mixing a pound of dry sodium carbonate, in fine powder, with five ounces of sulphur, heating the mixture gradually in a porcelain vessel until the sulphur melts, and stirring the agglutinated mass, still kept hot, in order that every portion of it may come in contact with the air. The sodium sulphide first formed is thus converted into sodium sulphite. This is dissolved in water, and the filtered solution being boiled with sulphur becomes one of sodium thiosulphate, from which, after filtration and concentration, the salt is deposited in crystals. The latter part of the reaction is as follows:

$$Na_2SO_3 + S = Na_2S_2O_3$$

It may be obtained also by digesting the solution of sodium sulphite at a high temperature, but short of ebullition, with finely divided sulphur. It is made also by oxidizing sodium hydrosulphide, according to the following reaction:

$$2NaHS + 2O_2 = 2Na_2S_2O_3 + H_2O$$

Thiosulphuric acid exists only in combination, and its salts were formerly considered simply as sulphuretted sulphites. The true hyposulphurous acid, according to theory, would be H_2SO_2, while $H_2S_2O_3$ is more properly *thiosulphuric* acid, as it differs from sulphuric acid by the replacement of one oxygen atom by one sulphur atom.

Inasmuch as Schützenberger discovered the true hyposulphurous acid, H_2SO_2, exact chemical usage would demand that we give the distinguishing name thiosulphuric to what was formerly called hyposulphurous. Schützenberger himself called the newly-discovered acid *hydrosulphurous*, but this is not characteristic, and the correct name for "sodium hyposulphite" is *sodium thiosulphate*.

Properties.—It is officially described as in "colorless, transparent, monoclinic prisms; odorless, and having a cooling, afterwards bitter taste. It is permanent in the air below 33° C. (91.4° F.), but efflorescent in dry air above that temperature; slightly deliquescent in moist air. One Gm. of Sodium Thiosulphate dissolves in 0.5 mil of water at 25° C. (77° F.); insoluble in alcohol; at boiling temperatures it is rapidly decomposed. An aqueous solution of the salt (1 in 10) is neutral or faintly alkaline to litmus. When rapidly heated the salt melts. When heated slowly until it is effloresced, and afterwards to 100° C. (212° F.), it undergoes partial decomposition, loses all of its water of crystallization, and at red heat is decomposed, sulphur being liberated, while a residue of sodium sulphide and sodium sulphate remains. To a non-luminous flame it imparts an intensely yellow color. An aqueous solution of Sodium Thiosulphate readily dissolves many compounds of silver (chloride, bromide, iodide, oxide, etc.) and discharges the color of a solution of iodine or of starch iodide. Add a few drops of ferric chloride T.S. to 5 mils of an aqueous solution of the salt (1 in 10); a dark violet color is produced which disappears rapidly upon agitation. The addition of sulphuric or hydrochloric acid to an aqueous solution of Sodium Thiosulphate liberates sulphur dioxide (recognized by its odor, and by its blackening a strip of paper moistened with mercurous nitrate T.S. held in the escaping gas); a white precipitate of sulphur is also formed (distinction from *sulphite or bisulphite*). An aqueous solution of the salt (1 in 20) is not rendered turbid by the addition of ammonium oxalate T.S. (*calcium*). Add 10 mils of diluted hydrochloric acid to 1 Gm. of the salt, evaporate it to dryness on a water bath, heat the residue with 50 mils of distilled water and filter. Ten mils of this filtrate does not respond to the Test for heavy metals (see Part III, Test No. 3). Add 3 mils of nitric acid to 5 mils of an aqueous solution of the salt (1 in 25), evaporate the solution cautiously to dryness on a water bath, treat the residue with a few mils of distilled water, filter the liquid and evaporate the filtrate and washings to dryness; the residue meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"**Assay.**—Dissolve about 1 Gm. of Sodium Thiosulphate, accurately weighed, in about 20 mils of distilled water and titrate with tenth-normal iodine V.S., starch T.S. being used as indicator. It shows not less than 63.07 per cent. nor more than 67.48 per cent. of $Na_2S_2O_3$.

"Each mil of tenth-normal iodine V.S. used corresponds to 0.015814 Gm. of $Na_2S_2O_3$. Each gramme of Sodium Thiosulphate corresponds to not less than 39.9 mils nor more than 42.7 mils of tenth-normal iodine V.S." *U. S.*

Its solution dissolves silver chloride and all water-insoluble compounds of that metal, except the sulphide, and that resulting from the decomposition of a silver salt by light. Though without action on potassium iodide, it dissolves iodine, decomposes iodic acid with liberation of iodine, and destroys the blue color of starch iodide. (Brande and Taylor.) In dissolving iodine it forms with it sodium iodide and sodium tetrathionate, as represented by the formula

$$2(Na_2S_2O_3) + I_2 = (NaI)_2 + Na_2S_4O_6$$

It dissolves also lead sulphate and iodide, and calcium sulphate, much more freely than does water. (*J. P. C.*, 1864, 363.) Its relations to iodine render it valuable as a means of estimating the quantity of free iodine, for which purpose it is used in the Pharmacopœias in the form of a *volumetric solution*. In consequence of its peculiar solvent properties, it is much used in photography. The photographers employ it for the purpose of dissolving the unchanged silver iodide or bromide from the plate after the action of the light, and thus fixing the image already formed. It is also largely used as an "*antichlor*" in the paper manufacture, to free the paper pulp from the excess of chlorine used

in the bleaching. One of the most delicate tests is that of iodine with starch. The blue color produced by the mixture of very small quantities of these two substances in solution is instantly discharged by a solution containing a trace of the thiosulphate. If zinc or iron is dipped into an acidified solution of the thiosulphate, the liberated hydrogen at once reduces the sulphurous oxide which is in the solution to hydrogen sulphide, recognizable by lead acetate paper. This test will serve to show even traces of thiosulphate.

Uses.—Probably because of its confusion with the hyposulphite, sodium thiosulphate is recommended by many authorities in the treatment of various parasitic *diseases of the skin* and in yeasty fermentation in the stomach. It is not probable that the thiosulphate possesses any medicinal virtues, although sodium hyposulphite is certainly an active remedy. Trousseau (*R. T.*, 1905, p. 136) has recommended sodium thiosulphate in five per cent. solution as a topical application in *blepharitis* and *conjunctivitis*.

Dose, ten to twenty grains (0.65–1.3 Gm.), three times a day simply dissolved in water, or in the form of syrup. For external use a drachm may be dissolved in a fluidounce of water.

SODIUM

SODIUM

(sō'dĭ-ŭm)

"The metal sodium as met with in commerce. It should be preserved in well-stoppered bottles under mineral naphtha." *Br.*, 1898.

Sodium, *Fr.*; Natrium, Natronmetall, *G.*; Sodio, *It.*, *Sp.*

Sodium is a peculiar metal, the hydroxide of which is known as the alkali "soda." It was discovered by H. Davy in 1807, who obtained it in small quantity by decomposing the alkali by the agency of galvanic electricity. Sodium was formerly prepared on a large scale by igniting an intimate mixture of dry sodium carbonate, coal, and chalk. The amount of metal obtained by this method is, however, not over 40 per cent. of the theoretical result. A much improved process was next brought out by Castner (*J. Soc. Chem. Ind.*, 1887, 174), in which an iron carbide, or a mixture of fine iron and coke, is used to reduce the caustic soda, according to the reaction:

$$6NaOH + FeC_2 = 2Na_2CO_3 + 6H + Fe + 2Na$$

The reduction of the sodium hydroxide takes place at a temperature of about 800° C. (1472° F.), and is carried out in steel crucibles, each of which holds 5.6 kilos of sodium hydroxide and 1.97 kilos of carbide. The product of the reaction consists of about 4.85 kilos of sodium carbonate and 0.933 kilo of metallic sodium. This latter collects in a receiver connected with the top of the crucible, while the sodium carbonate is dissolved out from the residue and is causticized preparatory to being used again. This process in turn has been replaced by the electrolytic processes. The most successful of these is that of Castner, who uses an electrolyte of fused sodium hydroxide in an iron pot or crucible with an anode of iron and a cathode of copper. The sodium is reduced at a comparatively low temperature, and is ladled from the vessel into moulds. The process is carried out at present on a large scale by the Niagara Electro-Chemical Co., and at Oldbury, England, and several places in Germany.

Sodium is a soft, malleable, ductile solid, of a silver-white color. It possesses the metallic luster in a high degree, when protected from the action of the air, by which it is quickly tarnished and oxidized. Its sp. gr. is 0.97, and its fusing point 95.6° C. (204° F.). Its chemical affinities resemble those of potassium, but are less energetic. Like potassium, it has a strong attraction for oxygen. When thrown upon cold water it instantly fuses into a globule without inflaming, and traverses the surface in different directions with rapidity; on warm water it inflames. In both cases the water is decomposed, hydrogen is liberated, and sodium hydroxide generated. Like potassium, if exposed with a bright surface to the air, it undergoes a slow combustion, which renders it luminous in the dark. It combines with oxygen to form the monoxide, Na_2O, and a peroxide, Na_2O_2. This latter oxide is always formed when the metal is burned in the open air. It is officially described as "A soft metal, rapidly oxidizing in the air, but showing a bright metallic surface when freshly cut. It violently attacks water or alcohol (90 per cent.), with evolution of hydrogen, little or no insoluble matter remaining. It imparts an intense yellow color to flame. Each gramme very cautiously added to water affords a solution which should require for neutralization at least 42.6 cubic centimetres of the volumetric solution of sulphuric acid." *Br.*

Sodium is a constituent of many important medicinal preparations. Sodium salts are characterized by communicating to the blowpipe flame a rich yellow color, and by not being precipitable by any reagent except potassium metantimoniate. Sodium monoxide consists of two atoms of sodium and one atom of oxygen. This reacts with water to form sodium hydroxide (caustic soda),

$$Na_2O + H_2O = 2NaOH$$

The dioxide (or peroxide), Na_2O_2, is now manufactured on a large scale from the metal, and used as a substitute for hydrogen peroxide in bleaching processes. It forms a canary-yellow powder, which decomposes rapidly in the presence of moisture.

Uses.—Sodium occurs in the human body in larger amount than any other metal. It is the most nearly inert physiologically of all the earths. It is, therefore, the base of choice when

it is desired to obtain the effect of an acid radical, as an iodide, bromide or nitrite. For the effects of massive doses of sodium, see *Sodii Carbonas.*

SPARTEINÆ SULPHAS. U. S

SPARTEINE SULPHATE Spartein. Sulph.

(spär-tē-ĭ'næ sŭl'phăs)

"The sulphate [$C_{15}H_{26}N_2.H_2SO_4 + 5H_2O$ = 422.39] of sparteine, a liquid alkaloid obtained from *Cytisus Scoparius* (Linné), Link (Fam. *Leguminosæ*). Preserve it in well-closed containers, protected from light." *U. S.*

Sulfate de Spartéine, *Fr. Cod.*; Sparteinum Sulphuricum; Sparteinsulfat, Schwefelsaures Spartein, *G.*; Sulfato de esparteina, *Sp.*

This alkaloidal salt, prepared from Scoparius (see page 985) is officially described as in "colorless, rhombohedral crystals, or as a crystalline powder; odorless, and having a slightly saline and somewhat bitter taste. It is hygroscopic. One Gm. of Sparteine Sulphate dissolves in 1.1 mils of water and in 3 mils of alcohol at 25° C. (77° F.); insoluble in chloroform or ether. Its aqueous solution (1 in 20) is neutral or acid to litmus. Add 25 mils of ether and a few drops of diluted ammonia water, avoiding an excess, to about 0.1 Gm. of Sparteine Sulphate in a test tube, then add to the mixture an ethereal solution of iodine (1 in 50) until the liquid, when shaken, turns from an orange to a dark reddish-brown color. After a short time, the bottom and sides of the test tube will be coated with minute, dark greenish-brown crystals. Barium chloride T.S. produces a white precipitate insoluble in hydrochloric acid when added to an aqueous solution of Sparteine Sulphate. Incinerate about 1 Gm. of Sparteine Sulphate; not more than 0.1 per cent. of ash remains. A solution of about 0.1 Gm. of the salt in 2 mils of sulphuric acid is colorless (*readily carbonizable organic impurities*). Shake about 0.1 Gm. of Sparteine Sulphate in a test tube with 5 mils of potassium hydroxide T.S., the liquid at first becomes turbid, and small, colorless or nearly colorless drops of sparteine gradually collect on the surface. Suspend a strip of moistened red litmus paper in the mouth of a test tube, and apply a gentle heat; the test paper gradually acquires a blue color, but no odor of ammonia is perceptible (*ammonium salts*). A mixture of about 0.1 Gm. of Sparteine Sulphate, 0.5 mil of chloroform and 0.5 mil of alcoholic half-normal potassium hydroxide V.S. does not emit an odor of phenylisocyanide on heating (*aniline*)." *U. S.*

G. Marque (*J. P. C.*, xxx, 555) states that if a small quantity of sparteine sulphate be mixed with about one-third of its weight of chromium trioxide, and gently heated in a porcelain dish, the mass will soon turn green and emit a strong odor resembling coniine. Moureu and Villier (*Bull. Soc. Chim.*, 1903 (6), 12, 545) confirm Stenhouse's formula for sparteine sulphate, $C_{15}H_{26}N_2.H_2SO_4 + 5H_2O$. (For description of *Oxysparteine,* see Part II.)

Uses.—The statements of different investigators both clinical and pharmacological, concerning the effects of sparteine have been so extraordinarily contradictory that they are at present impossible of reconciliation; one is perforce driven to the belief that the different investigators did not have the same principle. It has been variously claimed to accelerate and to slow the pulse rate, to increase and to diminish the contractile power of the heart, to arrest the heart in systole and in diastole, to raise the blood pressure or to lower it, and finally to have no effect on the circulation whatsoever. Again it is claimed by some that it diminishes, and by some that it increases the quantity of urine, and by others that it has no effect upon the kidney. These discrepancies cannot be harmonized on the ground of difference in dosage. For review of the extensive literature upon the subject, the reader is referred to McNider (*Southern Med. Journ.*, 1910, iii, p. 498), and to Pilcher and Sollmann (*J. P. Ex. T.*, 1915, vi, p. 373). It has been used clinically in the treatment of various forms of cardiac disorders, such as *endocarditis,* but especially in such functional derangements as *nervous palpitation,* the *tachycardia of Grave's disease,* etc. It has also been employed as a diuretic in *dropsies,* especially when due to cardiac lesions. The doses recommended by various authors have ranged from one-sixth of a grain to as high as two grains (0.010–0.13 Gm.).

SPIGELIA. U. S.

SPIGELIA [Pinkroot]

(spĭ-gē'lĭ-ą)

"The dried rhizome and roots of *Spigelia marilandica* Linné (Fam. *Loganiaceæ*), without the presence or admixture of more than 10 per cent. of stems or other foreign matter." *U. S.*

Maryland, Carolina or Indian Pink, Worm-grass, Wormweed, American worm-root, Star-bloom; Spigelie du Maryland, *Fr.*; Marylandische Spigelie, Spigelie, *G.*; Spigelia, *It.*

Two species of *spigelia* have attracted attention as anthelmintics—*S. Anthelmia* L., of South America and the West Indies, and *S. marilandica* L. of this country. *Spigelia Anthelmia* L., of South America is an annual plant, from one or two feet in height, with thin, shortly petioled leaves, those of the lower stem being lanceolate, those above varying from very broadly lanceolate to ovate, with a distinct tendency to a rhomboidal outline and attaining a length of over four inches. It is much used as an anthelmintic in its native country, and its rhizome is said to have appeared in the European markets. The only specimens which we have seen, however, have been the whole dried plant, of which the attached rhizomes are much smaller and the rootlets much finer than in the North American species. It is affirmed that in overdoses this rhizome is a powerful poison, which has caused death not only in the domestic animal but also in man.

The *Carolina pink* (*Spigelia marilandica*) is

an herbaceous perennial plant. The stems, several of which rise from the same rhizome, are simple, erect, four-sided, nearly smooth, and from twelve to twenty inches high. The leaves are opposite, sessile, ovate-lanceolate, acuminate, entire, and smooth, with the veins and margins slightly pubescent. Each stem terminates in a one-sided spike, and supports from four to twelve flowers with very short peduncles. The calyx is persistent, with five long, subulate, slightly serrate leaves, reflexed in the ripe fruit. The corolla is funnel-shaped, and much longer than the calyx, with the tube inflated in the middle, and the border divided into five acute, spreading segments. It is of a rich carmine color externally, paler at the base, and orange-yellow within. The edges of the segments are slightly tinged with green. The stamens, though apparently very short, and inserted into the upper part of the tube between the segments, may be traced down its internal surface to the base. The anthers are oblong, heart-shaped; the ovary superior, ovate; the style about the length of the corolla, and terminating in a linear fringed stigma projecting considerably beyond it. The capsule is double, consisting of two cohering, globular, one-celled portions, with many seeds.

The plant is a native of our Southern and Southwestern States, being seldom found north of the Potomac. It grows in rich soils on the borders of woods, and flowers from May to July. The rhizome and roots are the only portions recognized in the Pharmacopœias. The drug was formerly collected in Georgia and the neighboring States by the Creek and Cherokee Indians, who disposed of it to the white traders. After the emigration of the Indians, the supply of spigelia from this source very much diminished, and at one time it nearly if not quite ceased. But a new source of supply was opened from the Western and Southwestern States, and it is now again obtainable. The commercial supplies being so restricted, some attention has been given to the cultivation of the plant. The Bureau of Plant Industry, U. S. Department of Agriculture, Washington, D. C., has grown spigelia under shade, and Miss Henkel states that it is readily cultivated in Georgia. (*D. C.*, lvi, p. 132.)

No drug has had a commercial history like spigelia. For twenty years or more it was largely substituted by *Ruellia ciliosa* Pursh. Sanders reported examining 57 samples of pinkroot which were obtained from various sections of the country and none were genuine. (*Jour. A. Ph. A.*, 1912, p. 502.) To Prof. Greenish (*A. J. P.*, 1891, p. 226) belongs the credit for the first pharmacognostic description of this common substitute, although he incorrectly attributed it to *Phlox carolina* L. (*P. ovata* L.). He pointed out that it was distinguished by the fact that it contained stone cells and cystoliths of calcium carbonate. Greenish's work was confirmed by Holm (*A. J. P.*, 1906, p. 553) and by Stockberger (*Ph. Rev.*, 1907, p. 2). His false identification continued in literature for several years, probably owing to the statements of the large drug houses which make a specialty of collecting American drugs. (*Proc. A. Ph. A.*, 1909, p. 1171.) The presence of *Phlox ovata* L. in commercial lots of spigelia has not been confirmed, and Kraemer illustrates the pharmacognosy of the rhizome and roots of this drug in *A. J. P.*, 1910, p. 470. Moser, however, affirms that *Phlox ovata* and *P. glaberrima* L. are frequently collected and sold as spigelia. (*A. J. P.*, 1909, p. 576.) Among some of the adulterants which have been identified are the rhizomes of goldenseal and caulophyllum, although a large variety of rhizomes are no doubt more or less intermixed.

Properties.—Pinkroot is officially described as "rhizome horizontal or slightly oblique, more or less flexuous, somewhat branched, from 1.5 to 5 cm. in length and from 2 to 5 mm. in diameter; externally dark brown, slightly annulate, with scars of bud scales, the upper surface knotty from approximate stem-bases, bearing cup-shaped scars; from the lower and lateral portions arise numerous, long, rather coarse, sparingly branched, brittle roots; fracture short, internally differentiated into three nearly equal zones of pith, wood and bark; odor slightly aromatic; taste bitter, pungent. Few if any of the roots exhibit thin, terminal portions with the bark stripped from the slender strands of wood. Stems usually attached to the upper portion of the rhizome, nearly cylindrical, attaining a length of 6 cm. and a diameter of 3 mm., light grayish-brown to purplish-brown, nodes annulate, marked by opposite leaf-scars. Under the microscope, transverse sections of the rhizome of Spigelia show a dark brown, more or less exfoliated epidermal layer; a cortex composed of from 10 to 15 rows of starch-bearing parenchyma; a distinct zone of sieve tissue from 0.075 to 0.15 mm. in width; a compact woody area composed of tracheæ and tracheids which are hardly distinguishable from each other, both kinds of vessels being marked with bordered pores; an internal sieve closely resembling the sieve in the bark; and a pith composed of fairly uniform, nearly polygonal, thin-walled cells, more or less filled with small starch grains. Transverse sections of the root show a large cortex, the cells of which are more or less filled with small starch grains and a central stele of 6 or 8 radial fibro-vascular bundles, which in the older roots are united by a strong development of lignified cells. The stem in transverse section is distinguished from the rhizome by a narrower woody zone, the tracheæ having spiral thickenings, and by a nearly uninterrupted circle of non-lignified bast-fibers in the bark. The powder is grayish-brown; when examined under the microscope it exhibits starch grains generally numerous, at times, however, few, spherical or slightly angular, from 0.002 to 0.006 mm. in diameter; fragments of lignified tracheæ and tracheids conspicuous; fragments of tracheæ with spiral thickening relatively few; bast-fibers few, very long, non-lignified; occasional fragments of the red-

dish-brown epidermal cells. Spigelia yields not more than 10 per cent. of ash." *U. S.*

The virtues of spigelia are extracted by boiling water. The root, analyzed by Feneulle, yielded a fixed and volatile oil, a small quantity of resin, a bitter substance supposed to be the active principle, a mucilaginous saccharine matter, albumen, gallic acid, the malates of potassium and calcium, etc., and woody fiber. The principle upon which the virtues of the root are thought to depend is brown, of a bitter nauseous taste, like that of the purgative matter of the leguminous plants, and when taken internally produces vertigo and a kind of intoxication. An analysis of the root by R. H. Stabler yielded as results a bitter uncrystallizable principle upon which the virtues of the medicine are supposed to depend, a little volatile oil, tannic acid, inert extractive, wax, resin, lignin, and salts of sodium, potassium, and calcium.

The active principle is a volatile alkaloid discovered by W. L. Dudley (*Am. Chem.*, vol. i, p. 150), who, on the contrary, found that the active principle of spigelia is a volatile alkaloid. He made it by distilling the ground root with milk of lime over a paraffin bath, and collecting the distillate in hydrochloric acid. After evaporation to dryness, the residue is taken up with alcohol and crystallized out of solution. He compared the reactions of this alkaloid, which he called *spigeline*, with those of nicotine, coniine, and lobeline. Spigeline yields a brownish-red precipitate with a solution of iodine in potassium iodide, a white crystalline precipitate with potassio-mercuric iodide, and a white flocculent precipitate with meta-tungstic acid. Boorsma (*P. J.*, 1898, 89) found 0.0005 Gm. of *spigeline* to be lethal to guinea pigs.

Uses.—The activity of spigelia is somewhat diminished by time. Spigelia is generally considered among the most powerful anthelmintics, especially esteemed against the *round-worm*. In the ordinary dose it usually produces little sensible effect on the system; more largely given it acts as a cathartic, though unequal and uncertain in its operation; in overdoses it is said to cause vertigo, dimness of vision, dilated pupils, spasms of the facial muscles and of the eye-lids, and even general convulsions. The death of two children who expired in convulsions was attributed to it by Chalmers. H. A. Hare (*Med. News*, March, 1887) has found that in the lower animals it produces symptoms similar to those just described, namely, dilatation of the pupil, exophthalmia, strabismus, progressive muscular weakness of spinal origin, cardiac depression, and death from failure of respiration. The narcotic effects are said to be less likely to occur when the medicine purges, and to be altogether obviated by combining it with cathartics. The danger from its employment cannot be great, as it is in very general use in the United States, in both regular and domestic practice, and we never hear at present of serious consequences. Its effects upon the nervous system have been erroneously conjectured to depend on other roots sometimes mixed with the genuine. The vermifuge properties of spigelia, first learned from the Cherokee Indians, were made known to the medical profession by Lining, Garden, and Chalmers, of South Carolina.

It may be given in substance or infusion, or as the fluidextract. The infusion may be made by macerating half a troyounce of the root in a pint of boiling water. It is usually combined with senna or some other cathartic, to insure its action on the bowels. A preparation much sold under the name of *worm tea* consists of spigelia, senna, manna, and savin, mixed together, in various proportions, to suit the views of different individuals.

Dose, of the powdered root, for an adult, one or two drachms (3.9–7.7 Gm.), to be repeated morning and evening for several days successively, and then followed by a brisk cathartic.

Off. Prep.—Fluidextractum Spigeliæ, *U. S.*

SPIRITUS

SPIRITS

(spĭr'ĭ-tŭs)

Alcoolats, *Fr.*; Geiste, *G.*; Spirito, *It.*

Spirits, as the term is here used, are alcoholic solutions of volatile principles formerly in general procured by distillation, but now frequently prepared by simply dissolving the volatile principle in alcohol or diluted alcohol. The distilled spirits are prepared chiefly from aromatic vegetable substances, the essential oils of which rise with the vapor of alcohol and condense with it in the receiver. Some of the oils, however, will not rise at the temperature of boiling alcohol, but may be distilled with water. In this case it is necessary to employ diluted alcohol or proof spirit, with the water of which the oil comes over in the latter part of the process. As the proof spirit of commerce is often impregnated with foreign matters, which give it an unpleasant flavor, it is better to use alcohol which has been carefully rectified, and to dilute it with the due proportion of water, as directed by the U. S. Pharmacopœia. In preparing the spirits, care should be taken to avoid the color and empyreumatic flavor arising from the decomposition of the vegetable matter by heat. Sufficient water must, therefore, be added to cover the vegetable matter after the alcohol shall have been distilled, and, as a rule, the heat should be applied by means of a water bath, or of steam. The aromatic should be macerated for some days with the alcohol before being submitted to distillation, as the oil, being thus dissolved, rises more readily with the spirituous vapor than when confined in the tissue.

The aromatic spirits are used chiefly to impart a pleasant odor and taste to mixtures, and to correct the nauseating and griping effects of other medicines. They serve also as carminatives in *flatulent colic*, and as agreeable stimulants in *debility of the stomach*.

SPIRITUS ÆTHERIS. U. S., Br.

SPIRIT OF ETHER Sp. Æth. [Hoffmann's Drops]

(spĭr'ĭ-tŭs æ'thẹ-rĭs)

Liquor Anodynus Mineralis Hoffmanni; Ether officinal alcoolisé, *Fr. Cod.;* Ether sulfurique alcoolisé, Liqueur d'Hoffmann, *Fr.;* Spiritus Ætherеus, *P. G.;* Aetherweingeist, Hoffmannsche Tropfen, *G.;* Etere con alcool, Liquore anodino di Hoffmann, *It.;* Eter sulfuricq alcoholizado, Licor anodino mineral de Hoffmann, *Sp.*

* "Ether, *three hundred and twenty-five mils* [or 10 fluidounces, 475 minims]; Alcohol, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the ether with a sufficient quantity of alcohol to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.* "Ether, 500 *millilitres;* Alcohol (90 per cent.), 1000 *millilitres.* Mix. Specific gravity 0.802 to 0.806." *Br.*

This preparation is merely ether diluted with about twice its volume of alcohol. Although introduced into the U. S. P., 1880, it does not seem to have been employed to any extent, and it might have been dropped with advantage at a later revision. The corresponding preparation of the German Pharmacopœia contains less ether, being made of one part of ether to three parts of alcohol, both by weight. Prepared with materials of proper strength, its sp. gr. is 0.802 to 0.806. *Br.*

The spirit of ether is used chiefly as a carminative in *flatulent colic.* Although not so frequently employed as the former U. S. P. *compound spirits of ether,* which is now official in the N. F. (see *Spiritus Ætheris Compositus,* Part III), it has all the therapeutic virtues of that preparation. It may also be employed as a diffusible heart stimulant. The Compound Spirit of Ether is commonly known as *Hoffmann's Anodyne.*

Dose, one to three fluidrachms (3.75–11.25 mils).

SPIRITUS ÆTHERIS NITROSI. U. S., Br.

SPIRIT OF NITROUS ETHER Sp. Æth. Nitros. [Sweet Spirit of Nitre]

(spĭr'ĭ-tŭs æ'thẹ-rĭs nī-trō'sī)

"An alcoholic solution of ethyl nitrite [$C_2H_5NO_2 = 75.05$], containing not less than 3.5 per cent. nor more than 4.5 per cent. of $C_2H_5NO_2$. Preserve it in small, well-stoppered, dark amber-colored bottles, in a cool and dark place, remote from fire." *U. S.* "Spirit of Nitrous Ether is an alcoholic solution containing not less than 1.52 or more than 2.66 per cent. by weight of ethyl nitrite, together with aldehyde and other allied substances. It should be kept in well-closed vessels; preferably in a cool dark place, and in small amber bottles." *Br.*

Spiritus Nitri Dulcis; Spiritus Ætheris Nitrici; Spiritus Nitrico-æthereus; Ether Azoteux Alcoolisé, Liqueur anodine nitreuse, *Fr.;* Spiritus Ætheris nitrosi, *P. G.;* Versüsster Salpetergeist, *G.;* Etere nitroso officinale, Spirito d'etere nitroso, *It.;* Espiritu de nitro dulce, *Sp.*

* "Sodium Nitrite, *one hundred grammes* [or 3 ounces av., 231 grains]; Sulphuric Acid, *forty mils* [or 1 fluidounce, 169 minims]; Monohydrated Sodium Carbonate, *six-tenths of a gramme* [or 9 grains]; Potassium Carbonate, completely deprived of water by heating, *three grammes* [or 46 grains]; Alcohol, Water, each, *a sufficient quantity.* Mix the sulphuric acid with *one hundred and twenty mils* [or 4 fluidounces, 28 minims] of water, cool the liquid, add *eighty-five mils* [or 2 fluidounces, 420 minims] of alcohol previously diluted with an equal volume of water, and introduce the solution into a 1000 mil [or 2 pint] flask, surrounded by a mixture of ice and water. Dissolve the sodium nitrite in *two hundred and eighty mils* [or 9 fluidounces, 225 minims] of water, filter, and, having poured the filtrate into a separatory funnel, allow the liquid to slowly drop into the flask containing the acid mixture. When all has been added and the reaction is complete, allow any crystals which may have formed to settle at the bottom of the flask, and decant the cold mixture of ethyl nitrite and aqueous solution quickly to the previously cooled separatory funnel, and draw off and discard the aqueous liquid. Wash the separated ethyl nitrite, first, with *twenty mils* [or 325 minims] of ice-cold water, and then remove any traces of acid by washing it with *fifteen mils* [or 243 minims] of ice-cold water, in which the monohydrated sodium carbonate has previously been dissolved. Carefully separate the ethyl nitrite from the aqueous liquid, and agitate it in a well-stoppered bottle with the potassium carbonate to remove traces of water. Then cool the liquid, decant, and pour the ethyl nitrite immediately into a tared bottle containing *five hundred grammes* [or 17 ounces av., 279 grains] of alcohol. Ascertain the weight of the ethyl nitrite poured into the alcohol by noting the increase in weight of the tared bottle and contents, and then add enough alcohol to make the mixture weigh *twenty-two times* the weight of the ethyl nitrite added. Lastly, transfer the product to small, well-stoppered, dark, amber-colored bottles, and keep these in a cool place, remote from fire." *U. S.*

"Nitric Acid, 150 *millilitres;* Sulphuric Acid, 100 *millilitres;* Copper of commerce, in wire or turnings, 100 *grammes;* Alcohol (90 per cent.), *a sufficient quantity.* To one thousand millilitres of the Alcohol add gradually the Sulphuric Acid, and then one hundred and twenty-five millilitres of the Nitric Acid, stirring constantly. Transfer the mixture to a retort or flask, in which the fragments of copper have been placed, and to which is attached an efficient condenser with a receiver containing one thousand millilitres of the Alcohol. Surround the receiver with ice-cold water and distil gently at a temperature which is at first about 77° C. (170.6° F.), and rises to 80° C. (176° F.), but does not exceed 82° C. (179.6° F.), until the volume of liquid in the receiver has been increased to sixteen hundred millilitres. Then allow the contents of the retort to cool, introduce the remaining twenty-five millilitres of Nitric Acid, and resume the distillation as before, until the liquid in the receiver has been increased to seventeen hundred

millilitres. Mix this liquid with one thousand millilitres of the Alcohol, or with as much as will make the product contain 2.66 per cent. by weight of ethyl nitrite when tested as described in the following paragraph." *Br.*

The official spirit of nitrous ether is a mixture of nitrous ether or ethyl nitrite, $C_2H_5NO_2$, and alcohol (rectified spirit). For many years, spirit of nitrous ether was made by acting on alcohol with nitric acid, and the present British process and that of the U. S. P., 1880, are constructed on this plan. The U. S. P. VIII and IX processes differed essentially; in these, the use of nitric acid was abandoned, sodium nitrite being substituted as the source of the nitrous compound. Ethyl nitrite is readily generated by the reaction of nitric acid with alcohol; and it matters not whether the alcohol be mixed with nitric acid directly, or with the materials for generating it, namely, nitre and sulphuric acid.

In the U. S., 1860, process, which was modelled after the plan of Squibb, the nitric acid and alcohol were directly mixed in a retort. The liquid condensed in the receiver was mixed with potassium carbonate, and again distilled, in order to free it from the acid which had come over with the nitrous ether, and, being too strong was diluted with alcohol, and thus brought to the state of *spirit* of nitrous ether. It was a great improvement over the formula of earlier Pharmacopœias, and had the merit of insuring a preparation of more uniform strength. But in the Pharmacopœia of 1870 the British process was substituted, as even better than it.

The U. S., 1880, process differed in several particulars from those formerly official. Copper was no longer used. The use of this metal originated with Redwood, under the impression that the nitrous radical was liberated by it and enabled to unite more readily with the ethyl of the alcohol, to form ethyl nitrite. Upon the small scale the copper served a useful purpose in controlling and moderating the reaction, but excellent results have been obtained by substituting broken glass, and quite as large a yield of ethyl nitrite is obtained. The nitric acid was not added in two portions, but the whole quantity was mixed with the sulphuric acid and alcohol at first. This was an improvement. The direction to "heat rapidly, by means of a water-bath, until strong reaction occurs and the temperature reaches 80° C. (176° F.)," was likely to cause loss in the hands of the inexperienced through excessive action, and inability to condense all the vapor of ethyl nitrite which would be suddenly generated. A temperature of 72° C. (161.6° F.) was amply sufficient to start the reaction, and as soon as effervescence took place the heat should have been *at once removed,* and not reapplied until the reaction slackened, so that a uniform and not an excessive reaction might be maintained. The greatest change was, however, in purifying the distillate by agitating it with ice cold distilled water, separating the ethereal layer and mixing it with alcohol, so that the finished product should contain 5 per cent. by weight of the crude ethyl nitrite. A thoroughly effective method of separating ethyl nitrite from its solution in alcohol and water is yet to be discovered. Some manufacturers agitate the distillate with a saturated solution of calcium chloride to separate the ethyl nitrite, and the British Pharmacopœia once used this method as a test.

The U. S. P., 1890, process overcame these objections by generating the nitrous compound necessary to effect the combination with ethyl by acting on sodium nitrite with sulphuric acid in the presence of alcohol, the violence of the reaction being controlled by diluting both the sulphuric acid and the alcohol with water, and by using an aqueous solution of the nitrite. A very thorough means of refrigeration had to be used, on account of the extreme volatility of the distillate, and because evolution of ethyl nitrite commenced before all the sulphuric acid was added and without the use of any other heat than that generated by the chemical reaction. Heat was not applied until the reaction became slower, and then only very moderately and capable of being instantly withdrawn if necessary. The advantages of this process are that the production of aldehyde and acetic ether is avoided, through the absence of nitric acid, and pure ethyl nitrite is easily obtained. Sodium nitrite can be procured of standard purity, although the impurities in the commercial salt do not affect the character of the ethyl nitrite. The use of alkaline nitrites in making ethyl nitrite is not new, as both potassium and sodium nitrites have been employed, Feldhaus, Dunstan, Dymond, and others having published processes; Frerichs, of St. Louis, used the method on a large scale, and C. O. Curtman and E. L. Patch, of Boston, also recommended its employment. (See *Am. Drug.,* 1893, p. 171.) An improvement was made in the U. S. P. VIII process and in the cold processes previously proposed by reversing the order of mixing the liquids in the flask; in the former pharmacopœial process the acid solution was dropped slowly into the sodium nitrite solution and alcohol; this caused some loss of ethyl nitrite with evolution of nitrogen tetroxide, on the other hand, in the present official cold process if carefully conducted with sufficient refrigeration, the production of ethyl nitrite takes place uniformly and slowly with very little loss. The great advantage, however, in this process consists in the avoidance of distillation and use of heat in preparing this very volatile product.

The present British formula rejects the sodium nitrite process, but introduces under *Liquor Ethyl Nitritis* (see page 632) a solution made by decomposing sodium nitrite in the presence of alcohol, and diluting the ethyl nitrite produced, with alcohol containing a little glycerin. It is unfortunate that both preparations were not made of the same strength, the solution containing 3 per cent., the spirit only 2 per cent., of ethyl nitrite; the solution contains no aldehyde, but the spirit is permitted to contain aldehyde and other substances.

Assay.—The U. S. P. and the Br. Ph. quantitative test is based on Allen's method, differing only in the relative quantities of the reagents. (See p. 1051; also paper by Curtman, *Proc. Missouri Pharm. Assoc.*, July, 1892; *A. J. P.*, 1898, 273.)

"Transfer about 40 mils of Spirit of Nitrous Ether, which has been previously shaken with 0.5 Gm. of powdered potassium bicarbonate, to a tared, 100 mil measuring flask, and weigh it accurately. Add sufficient alcohol to bring the volume to exactly 100 mils and mix thoroughly. Introduce into a nitrometer (see Part III, Gasometric Estimation) exactly 10 mils of the alcoholic solution, follow it by 10 mils of potassium iodide T.S., and afterwards by 5 mils of diluted sulphuric acid. When the volume of gas has become constant (within thirty to sixty minutes), note the volume of gas collected. Multiply this volume in mils by 0.307, and divide the product by one-tenth of the weight in grammes of the Spirit of Nitrous Ether taken. At standard temperature and pressure, the quotient represents the percentage of ethyl nitrite in the liquid. The temperature correction is one-third of 1 per cent. of the total percentage just found for each degree, additive if temperature is below, subtractive if above, 25° C. (77° F.). The barometric correction is four-thirtieths of 1 per cent. of the total percentage just found for each mm., additive if above, subtractive if below, 760 mm." *U. S.*

Allen's Test for Ethyl Nitrite.—A nitrometer should be filled with strong brine, and 5 mils of the sample to be tested should be placed in the cup of the nitrometer, and allowed to enter through the tap, taking care that no air gets in at the same time. Five mils of a strong solution of potassium iodide is next allowed to enter, and this is followed by about 5 mils of dilute sulphuric acid. Effervescence immediately ensues, and, if the tube be vigorously agitated at intervals, the reaction will be complete in five minutes, when the level of the liquid in the two limbs of the nitrometer is adjusted, and the volume of nitrogen dioxide gas read off. If the volume of gas evolved be small, another 5 mils of the sample should be let into the nitrometer, and the agitation repeated. The reaction is:

$$(C_2H_5)NO_2 + KI + H_2SO_4 = (C_2H_5)OH + KHSO_4 + I + NO$$

When strictly accurate results are not required, the volume of gas need not be corrected for variations of pressure, temperature, and tension of aqueous vapor, and if these considerations be omitted the calculation will be much simplified. Thus, if 0.030 gramme of nitrogen dioxide (representing 0.075 gramme of $C_2H_5NO_2$) under the *ordinary* conditions of pressure and temperature be taken to measure 23.55 mils, then

$$\frac{\text{volume of gas in mil} \times 0.3185}{\text{measure of sample in mil} \times \text{density of sample}} = \text{percentage by weight of } C_2H_5NO_2$$

If the density of the sample be omitted from the equation, the result will be the number of grammes of ethyl nitrite per 100 mils of the sample.

The nitrometer method has been proved to give very good results with pure sodium nitrite (prepared from silver nitrite) employed in known amount. The results with spirit of nitrous ether are somewhat higher than those given by Eykman's method, the difference being least when sodium chloride is employed in the latter process and time is given for the ferrous solution to react thoroughly on the solution of ethyl nitrite. The results by the iodide method are almost certainly more accurate than those by Eykman's process. With most specimens of sweet spirit of nitre a considerable amount of nitric oxide is produced (and iodine liberated) before adding the acid, the reaction probably depending on the presence of free acid in the sample. The results obtained in the nitrometer are remarkably constant, and the method furnishes a very easy means of assaying sweet spirit of nitre with considerable accuracy, which is further increased if a correction of 1.5 mils (= 0.0048 gramme of $C_2H_5NO_2$) be made for solubility of the gas. The process has the advantage of great ease and rapidity, and actually measures the nitrous compounds present in the sample, instead of leaving their proportions to be inferred from a more or less complex reaction, such as the reduction of permanganate, and others.

Theory of the Production of Nitrous Ether, etc.—The reaction in the U. S. P. IX process may be expressed as follows:

$$2C_2H_5OH + 2NaNO_2 + H_2SO_4 = 2C_2H_5NO_2 + Na_2SO_4 + 2H_2O$$

Alcohol, sodium nitrite, and sulphuric acid when brought in contact yield ethyl nitrite, sodium sulphate, and water.

The nitric acid process may be explained as follows: One molecule of nitric acid, by reacting with one molecule of alcohol, forms one molecule of nitrous acid, one molecule of aldehyde, and one molecule of water, thus:

$$HNO_3 + C_2H_6O = HNO_2 + C_2H_4O + H_2O$$

The nitrous acid, as soon as formed, reacts with a second molecule of alcohol, so as to form one molecule of nitrous ether or ethyl nitrite, with separation of one molecule of water, according to the reaction:

$$C_2H_5.OH + HNO_2 = C_2H_5NO_2 + H_2O$$

In the process of the British Pharmacopœia the nitric acid is converted into nitrous acid by the reducing action of metallic copper and sulphuric acid, the reaction being:

$$HNO_3 + Cu + H_2SO_4 = HNO_2 + CuSO_4 + H_2O$$

The nitrous acid now reacts with the alcohol as in the previous reaction, so as to produce the nitrous ether. The object of using the sulphuric acid is to economize the nitric acid.

Properties of Ethyl Nitrite.—*Pure* ethyl nitrite is pale yellow, has the combined odor of apples and Hungary wine, boils at 18° C. (64.4°

F.), and has the sp. gr. 0.900 at 15.5° C. (60° F.). The density of its vapor is 2.627. Litmus is not affected by it. When it is mixed with an alcoholic solution of potassium hydroxide, potassium nitrite and alcohol are formed, without producing a brown color, showing the absence of aldehyde. It is soluble in 48 parts of water, and in all proportions in alcohol or rectified spirit. It is highly inflammable, and burns with a white flame without residue. The impure ether, as formerly obtained by the Edinburgh and Dublin processes for subsequent dilution to form sweet spirit of nitre, boiled at 21.1° C. (70° F.), and had the density of 0.886 at 4.4° C. (40° F.). The specific gravity assigned to it by the Edinburgh College was 0.899. Mixed with an alcoholic solution of potassium hydroxide, it became dark brown, with production of *aldehyde resin.* This discoloration showed the presence of aldehyde. When kept, it became acid in a short time, as shown by litmus, and nitric oxide was given off, which often caused the bursting of the bottle. Its tendency to become acid was rendered greater by the action of the air, and depended on the absorption of oxygen by the aldehyde, which thereby became oxidized to acetic acid.

Ethyl nitrite in hermetically sealed glass tubes is found in commerce, affording a ready means of preparing small quantities of spirit of nitrous ether, which deteriorates on keeping; as pure ethyl nitrite boils at 18° C. (64.4° F.) the tubes should be cooled and opened and the liquid immediately diluted with the proper quantity of alcohol to make spirit of nitrous ether, or they should be kept in a cool place until used. Clarence M. Kline, of Philadelphia, originated this method of protecting ethyl nitrite. Nitrous ether, or *ethyl nitrite,* is formed by the combination of nitrous acid with the radical ethyl, and its formula is $C_2H_5.NO_2$. In its pure and concentrated state it is never used in medicine. (See *Liquor Ethyl Nitritis,* p. 632.)

Properties of Spirit of Nitrous Ether.—This is "a clear, mobile, volatile and inflammable liquid of a pale yellow or faintly greenish-yellow tint, having a fragrant, ethereal, and pungent odor free from acridity, and a sharp, burning taste. When freshly prepared, or even after being kept for some time with but little exposure to light and air, it is neutral to dry litmus paper. When long kept or after having been exposed to light and air, it acquires an acid reaction. Effervescence must not result when a crystal of potassium bicarbonate is added. Specific gravity: not above 0.823 at 25° C. (77° F.). Immerse a test tube half filled with the Spirit in a water bath heated to 65° C. (149° F.) until it has acquired that temperature; the Spirit distinctly boils upon the addition of a few small pieces of broken glass. Mix 10 mils of the Spirit with 5 mils of potassium hydroxide T.S., previously diluted with 5 mils of distilled water; the mixture assumes a yellow color which does not turn decidedly brown within twelve hours (*aldehyde*)." *U. S.*

"A transparent liquid, having a very faint yellowish tinge. Peculiar penetrating apple-like odor; taste characteristic. Specific gravity 0.838 to 0.842. When Spirit of Nitrous Ether is carefully poured on an acidified strong aqueous solution of *ferrous sulphate* contained in a test-tube, a deep olive-brown coloration is produced at the surface of contact of the two liquids, widening as the tube is gently shaken. Does not effervesce, or only very slightly, when shaken with *sodium bicarbonate* (limit of acid). 10 millilitres mixed with 5 millilitres of *N/1 solution of sodium hydroxide* and 5 millilitres of *water* assume a yellow color, which does not become brown on standing twelve hours (limit of aldehyde). 1 volume shaken briskly at intervals during five minutes in a brine-charged nitrometer, with 1 volume of *solution of potassium iodide* and 1 volume of *diluted sulphuric acid,* yields at 15.5° C. (60° F.) and normal pressure not less than 4 or more than 7 volumes of nitric oxide gas, corresponding to not less than 1.52 or more than 2.66 parts by weight of ethyl nitrite in 100 parts by weight of the Spirit." *Br.*

Impurities and Tests.—Spirit of nitrous ether, when made by the nitric acid process, is never quite free from aldehyde, and, if the distillation be too long continued, it is prone to contain a good deal of this substance, which afterwards becomes acetic acid by absorbing oxygen. The change goes on rapidly if the preparation be insecurely kept. Aldehyde, if in considerable proportion, may be detected by its imparting a pungent odor and an acrid flavor, and by the spirit assuming a brown tint on adding a weak solution of potassium hydroxide, owing to the formation of aldehyde resin (see official test). Another test for aldehyde, though less reliable, is the addition of an equal volume of sulphuric acid to the sweet spirit of nitre. If the sample is good, the change of color will be slight; if it contains much aldehyde, it will become dark-colored. Acetic acid, as well as other acids (usually nitrogen acids) that may happen to be present, may be discovered by the taste, by their acting on litmus strongly, and by their decomposing the alkaline carbonates or bicarbonates with effervescence. Nitrogen acids are known by their coloring blue a piece of paper previously dipped into tincture of guaiac. These acids operate injuriously by their chemical reactions with other substances, when spirit of nitre is prescribed in mixtures. Thus, they liberate iodine from potassium iodide, gradually decolorize compound infusion of rose, and in the compound mixture of iron hasten the conversion of ferrous oxide into ferric oxide. To obviate these effects, Harvey, of Leeds, keeps sweet spirit of nitre standing on crystals of potassium bicarbonate, and states that, if the preparation be of full strength, no appreciable portion of the alkali will be dissolved. (*P. J.,* Jan., 1842.) When acid sweet spirit of nitre is rectified from calcined magnesia, it becomes acid again in a short time, but, according to Klauer, when rectified from neutral potassium tartrate it continues unchanged for months. A deep olive color with

ferrous sulphate shows the presence of a nitrogen acid.

According to Bastick, sweet spirit of nitre contains about one-fifth of one per cent. of anhydrous hydrocyanic acid, when made from nitrous ether formed by acting upon alcohol with nitrous acid evolved by the action of starch on nitric acid, according to the process of Liebig. In making sweet spirit of nitre on a large scale, Squibb found that hydrocyanic acid vapors were produced if the heat happened to rise too high, and the ester ceased to be formed. Schoor and G. B. Schmidt found that, after a careful distillation, hydrocyanic acid could be detected in the residue left in the retort to the amount of 0.977 per cent., while the distillate contained but an insignificant trace. (*Ph. Ztg.*, No. 37; *N. R.*, Sept., 1880.)

Alcohol and water have often been fraudulently added to sweet spirit of nitre. These additions were at one time difficult to detect, but the official tests now afford a ready means of ascertaining its quality and strength.

The pharmacist should note specially that the U. S. P. IX requires this Spirit to be preserved in small, well-stoppered, dark, amber-colored bottles, in a cool and dark place. The former custom of keeping it in partially filled shop bottles in the regular stock must be abandoned if the preparation is to be dispensed of official strength. This is no hardship as the stock can be filled into small bottles at the time it is made and will then be ready for dispensing.

Kebler, Palkin, and Ewing in the *J. A. Ph. A.*, 1916, p. 514, record the results of many experiments conducted with a view to determining the stability of spirit of nitrous ether and the causative factors of its deterioration. They conducted twelve series of experiments covering all possible store conditions and the assays show conclusively that when properly made and carefully kept, this preparation is much more stable than is popularly supposed, and will keep much longer than the average pharmacist would keep it, without undergoing any material change.

In the *J. A. Ph. A.*, 1916, p. 1327, Englehardt and Winters suggest a new method of estimation of the ethyl nitrite, based upon Dietzes potassium chlorate method as used in the Netherland Pharmacopœia, which avoids the use of the nitrometer and barometer and gives very good results.

Uses.—Sweet spirits of nitre possesses the physiological properties of the other nitrites (see *Sodii nitris*). Its inhalation produces acceleration of the pulse with the characteristic leaden purplish color of the lips, mouth and finger tips, followed by flushing of the face, giddiness, nausea, muscular debility, and violent headache. It is rarely employed, however, to produce the full physiological action of the nitrites its chief employment being to relax the blood vessels of the skin and thereby increase the flow of sweat. It is an extremely popular diaphoretic in mild *fevers*, especially in children. Because of its action on the circulation it also at times exercises a diuretic influence.

Dose, one-half to one fluidrachm (1.8–3.75 mils).

Off. Prep.—Mistura Glycyrrhizæ Composita, *U. S.*; Mistura Copaibæ, *N. F.*; Mistura Copaibæ et Opii, *N. F.*

SPIRITUS AMMONIÆ AROMATICUS. U. S., Br.

AROMATIC SPIRIT OF AMMONIA Sp. Ammon. Arom.

(spĭr'ĭ-tŭs ăm-mō'nĭ-æ ăr-ō-măt'ĭ-cŭs)

Spiritus Ammoniæ Compositus; Spirit of Sal Volatile; Alcoolat ammoniacal aromatique, *Fr. Cod.*; Aromatischer Ammoniakgeist, *G.*

* "Ammonium Carbonate, in translucent pieces, *thirty-four grammes* [or 1 ounce av., 87 grains]; Ammonia Water, *ninety mils* [or 3 fluidounces, 21 minims]; Oil of Lemon, *ten mils* [or 162 minims]; Oil of Lavender, *one mil* [or 16 minims]; Oil of Myristica, *one mil* [or 16 minims]; Alcohol, *seven hundred mils* [or 23 fluidounces, 321 minims]; Distilled Water, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. To the ammonia water, contained in a flask, add *one hundred and forty mils* [or 4 fluidounces, 352 minims] of distilled water, and afterwards the ammonium carbonate reduced to a moderately fine powder. Close the flask and agitate the contents until the ammonium carbonate is dissolved and allow it to stand for twelve hours. Introduce the alcohol into a graduated bottle of suitable capacity, add first the oils, then gradually the solution of ammonium carbonate, and afterwards enough distilled water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Set the liquid aside during twenty-four hours in a cool place, occasionally agitating it, and then filter through paper, in a well-covered funnel. Preserve the product in glass-stoppered bottles, in a cool place." *U. S.*

"Ammonium Carbonate, 100 *grammes;* Strong Solution of Ammonia, 200 *millilitres;* Oil of Nutmeg, 15 *millilitres;* Oil of Lemon, 20 *millilitres;* Alcohol (90 per cent.), 3000 *millilitres;* Distilled Water, 1500 *millilitres*. Place the Oil of Lemon, Oil of Nutmeg, and Alcohol with the Distilled Water in a retort; distil three thousand five hundred millilitres; then distil and separately collect an additional two hundred and twenty-five millilitres. Place the latter, together with the Ammonium Carbonate and the Strong Solution of Ammonia, in a bottle holding rather more than five hundred millilitres; securely cork the bottle and gently warm it in a water-bath to 60° C. (140° F.), shaking from time to time until all the salt has dissolved. Filter the resulting solution when cold through cotton wool, and gradually mix the filtrate with the portion first distilled." *Br.*

In both of these formulas ammonium carbonate and uncombined ammonia are used; but

they differ in the relative proportion of the materials and the mode of conducting the process. The U. S. spirit is a mere solution of the ingredients in alcohol diluted with a small proportion of water, while the British contains so much of the ingredients as may rise in distillation and be condensed with the seven pints of spirit that result. The strength of the former is definite, that of the latter more or less indefinite, as a portion of the materials must be left behind. The advantage arising from distillation, however, the avoidance of discoloration, is one which is well worth considering, although the spirit will always grow darker with age. The present preparation differs from that formerly official in the substitution of oil of myristica for oil of pimenta, it having been shown that oil of pimenta increased the tendency of the spirit to darken. Commercial oil of myristica frequently has a terebinthinate odor. Much care is needed to select for this preparation volatile oils that are fresh and of good quality. The translucent official ammonium carbonate, which is a mixture of bicarbonate and carbamate, does not dissolve in alcohol; the bicarbonate precipitates, and the carbonate, $NH_4HCO_3 + NH_4OH = (NH_4)_2CO_3 + H_2O$, dissolves. The object of the addition of free ammonia in the official process is to convert the insoluble bicarbonate into the carbamate, and it is directed that these shall be allowed to stand during *twelve hours* while this change is taking place. The effloresced ammonium carbonate of commerce having parted with some of its ammonia is a bicarbonate; hence, when it is used, unless more than the official proportion of the ammonia water be added, some of the ammonium salt will remain in the precipitate as ammonium bicarbonate.

The difficulty of precipitation which so many pharmacists complain of is thus explained. It is a useful precaution to permit the ammonium carbonate and ammonia water to remain in contact for twelve hours before diluting with the other ingredients; this will secure the entire conversion of the bicarbonate, and obviate the precipitation above noted. In addition to this, it is officially directed to set the mixed liquid aside, for twenty-four hours, before final filtration. It is officially described as "a nearly colorless liquid when freshly prepared, but gradually acquiring a yellow color. It has the pungent odor and taste of ammonia. Specific gravity: about 0.900 at 25° C. (77° F.)." *U. S.*

"A nearly colorless transparent liquid. Odor and taste pungent and ammoniacal. Specific gravity 0.888 to 0.893. 20 millilitres require for neutralisation 25.4 millilitres of *N/1 solution of sulphuric acid*, corresponding to 2.16 grammes of ammonia, NH_3, in 100 millilitres of the Spirit. When 20 millilitres are mixed with 50 millilitres of *water* and excess of *solution of barium chloride*, the mixture heated to 70° C. (158° F.), the precipitate collected, washed until free from alkali, and dissolved in 20 millilitres of *N/1 solution of hydrochloric aicd*, the solution thus obtained, after being boiled and cooled, requires for neutralisation not less than 7.2 or more than 8 millilitres of *N/1 solution of sodium hydroxide*, corresponding to not less than 2.35 or more than 2.51 grammes of acid ammonium carbonate and ammonium carbamate, calculated together as $N_3H_{11}C_2O_5$, in 100 millilitres of the Spirit." *Br.*

In handling this preparation on the large scale, copper vessels must never be used, as the preparation has a solvent effect upon the film of tarnish which is always present and thereby becomes contaminated, sometimes with the development of a bright green color. When this occurs, the preparation must either be thrown away or redistilled in a glass apparatus.

Uses.—Aromatic spirits of ammonia is much more widely used than the simple spirit because of its grateful taste and odor. It is used to correct *hyperacidity of the stomach* when not associated with inflammatory changes in the mucous membrane of that organ, and especially when there is *nausea* or *sick headache*. By virtue of its local irritant effect upon the mucous membrane of the stomach it will often reflexly excite the medulla and thereby relieve the feeling of *faintness*. It has, however, been enormously misapplied as a heart stimulant; as pointed out elsewhere (see *Aqua Ammoniæ*) although ammonia is a stimulant to the circulation it can act only when injected hypodermically.

Dose, thirty minims to a fluidrachm (1.8–3.75 mils), sufficiently diluted.

Off. Prep.—Mistura Sennæ Composita, *Br.;* Tinctura Guaiaci Ammoniata, *U. S.;* Tinctura Valerianæ Ammoniata, *U. S.;* Liquor Sodæ et Menthæ, *N. F.;* Tinctura Kino et Opii Composita, *N. F.*

SPIRITUS AMMONIÆ FŒTIDUS. Br.

FETID SPIRIT OF AMMONIA

(spĭr'ĭ-tŭs ăm-mō'nĭ-æ fœt'ĭ-dŭs)

Alcoolat ammoniacal fétide, Essence antihystérique, *Fr.;* Ammoniakalischer Stinkasantgeist, *G.*

"Asafetida, 75 *grammes;* Strong Solution of Ammonia, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres*. Break the Asafetida into small pieces, and macerate it in a closed vessel in seven hundred and fifty millilitres of the Alcohol for twenty-four hours; distil until alcoholic vapors cease to be condensed; mix the distillate with the Strong Solution of Ammonia, and add sufficient Alcohol to produce the required volume." *Br.*

This is an alcoholic solution of the volatile oil of asafetida mixed with strong solution of ammonia, and is an energetic nervous stimulant and antacid, adapted to certain *hysterical conditions* associated with gastric weakness and acidity. It is one of the preparations formerly recognized by the British Colleges, and reinstated after having been dropped from the first British Pharmacopœia.

"A nearly colorless, transparent liquid with a strong odor of ammonia and of asafetida. Specific gravity 0.842 to 0.850. 25 millilitres require for neutralisation not less than 40 milli-

litres of *N/1 solution of sulphuric acid,* corresponding to not less than 2.72 grammes of ammonia, NH_3, in 100 millilitres of the Spirit." *Br.*

This preparation combines the carminative effect of asafetida with the antacid properties of ammonia. It may be used in gastric or intestinal *flatulence.*

Dose, thirty minims to a fluidrachm (1.8–3.75 mils), to be largely diluted when administered.

SPIRITUS AMYGDALÆ AMARÆ. U. S.

SPIRIT OF BITTER ALMOND Sp. Amygd. Amar.
[Essence of Bitter Almond]

(spĭr'ĭ-tŭs ą-mŷg'dą-læ ą-mā'ræ)

Alcoolé d'essence amande amere, *Fr.;* Bittermandelgeist, *G.*

* "Oil of Bitter Almond, *ten mils* [or 162 minims]; Alcohol, *eight hundred mils* [or 27 fluidounces, 24 minims]; Distilled Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the oil in the alcohol, and add enough distilled water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Note: This Spirit is intended for medicinal use; it must not be used for flavoring foods." *U. S.*

Although the U. S. P. states that "this spirit is intended for medicinal use; it must not be used for flavoring foods," *U. S.,* it has little medicinal virtue except for its flavor. Because of the hydrocyanic acid in the oil of bitter almond this preparation will contain approximately 0.03 per cent. of that acid and hence cannot be used incautiously. It would have been better to have replaced this spirit with a solution of benzaldehyde.

Dose, from two to eight minims (0.12–0.5 mil).

Off. Prep.—Elixir Anisi, *N. F.*

SPIRITUS ANISI. U. S., Br.

SPIRIT OF ANISE Sp. Anisi

(spĭr'ĭ-tŭs ą-nī'sī)

Essence of Anise; Teinture d'essence d'anis vert, *Fr. Cod.;* Anisgeist, *G.*

* "Oil of Anise, *one hundred mils* [or 3 fluidounces, 183 minims]; Alcohol, *a sufficient quantity* to make *one thousand mils* [or 33 fluidounces 6½ fluidrachms]. Mix the oil with sufficient alcohol to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.* "Oil of Anise, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

Dose, as a stomachic and carminative, from twenty to sixty minims (1.3–3.75 mils), properly diluted.

SPIRITUS ARMORACIÆ COMPOSITUS. Br.

COMPOUND SPIRIT OF HORSERADISH

(spĭr'ĭ-tŭs ăr-mǫ-rā'cĭ-æ cǫm-pŏs'ĭ-tŭs)

Esprit (alcoolat) de Raifort composée, Alcoolat antiscorbutique, *Fr.;* Zusammengesetzter Meerrettiggeist, *G.*

"Horseradish Root, scraped, 125 *grammes;* Dried Bitter-Orange Peel, bruised, 125 *grammes;* Nutmeg, bruised, 3 *grammes;* Alcohol (90 per cent.), 625 *millilitres;* Distilled Water, 750 *millilitres.* Macerate the Horseradish Root in the Distilled Water for one hour, add the other ingredients, and distil one thousand millilitres. Specific gravity 0.917 to 0.927." *Br.*

This may be used advantageously as an addition to diuretic remedies, in *dropsy* attended with debility, especially in the case of drunkards.

Dose, from one to four fluidrachms (3.75–15 mils).

SPIRITUS AURANTII COMPOSITUS. U. S.

COMPOUND SPIRIT OF ORANGE Sp. Aur. Co.

(spĭr'ĭ-tŭs âu-răn'tĭ-ī cǫm-pŏs'ĭ-tŭs)

Teinture d'essence d'orange, *Fr. Cod.;* Esprit d'orange composée, *Fr.;* Zusammengesetzter Orangegeist, *G.*

* "Oil of Orange, *two hundred mils* [or 6 fluidounces, 366 minims]; Oil of Lemon, *fifty mils* [or 1 fluidounce, 331 minims]; Oil of Coriander, *twenty mils* [or 325 minims]; Oil of Anise, *five mils* [or 81 minims]; Alcohol, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix them. Keep the product in completely filled, well-stoppered bottles, in a cool and dark place." *U. S.*

This compound spirit has been introduced for the purpose of producing the orange flavor in making the official aromatic elixir (page 411), and in various N. F. elixirs. It will be found by physicians to be a useful and fragrant addition to prescriptions.

Off. Prep.—Elixir Aromaticum, *U. S.*

SPIRITUS CAJUPUTI. Br.

SPIRIT OF CAJUPUT

(spĭr'ĭ-tŭs căj-ŭ-pū'tī)

Teinture (alcoolé) d'essence de Cajeput, Alcoolé d'essence de Cajeput, *Fr.;* Cajeputgeist, *G.*

"Oil of Cajuput, 100 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

For an account of the medicinal properties and uses of oil of cajuput, of which this is simply an alcoholic solution, see *Oleum Cajuputi.*

Dose, from five to twenty minims (0.3–1.3 mils), properly diluted.

SPIRITUS CAMPHORÆ. U. S., Br.

SPIRIT OF CAMPHOR Sp. Camph.

(spĭr'ĭ-tŭs căm'phǫ-ræ)

"*One hundred mils* of Spirit of Camphor yields not less than 9.5 Gm. nor more than 10.5 Gm. of camphor." *U. S.*

Tinctura Camphoræ, *U. S.* 1850; Tincture of Camphor; Alcohol Camphoratus; Teinture de camphre concentrée, *Fr. Cod.;* Esprit de Camphre, Alcool camphré, *Fr.;* Spiritus Camphoratus, *P. G.;* Kamphergeist, *G.*

* "Camphor, *one hundred grammes* [or 3 ounces av., 231 grains]; Alcohol, *a sufficient quantity,* to make *one thousand mils* [or 33

fluidounces, 6½ fluidrachms]. Dissolve the camphor in *eight hundred mils* [or 27 fluidounces, 24 minims] of alcohol, filter through paper, and pass enough alcohol through the filter to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

"Camphor, 100 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. Specific gravity, 0.845 to 0.850. *Optical rotation* at 15.5° C. (60° F.), not less than + 4°." *Br.*

"Add 0.05 Gm. of anhydrous potassium carbonate to 5 mils of Spirit of Camphor; the potassium carbonate does not liquefy or adhere to the bottom of the vessel (*added water*).

"**Assay.**—Fill a two hundred millimeter polariscope tube with the Spirit of Camphor and take the mean of four or more readings of the rotation, beginning at zero each time. The temperature correction for each degree is half a minute, additive if above, subtractive if below, 25° C. (77° F.). Evaporate 60 mils of the Spirit of Camphor in a dish, on a water bath, and when the camphor begins to solidify stir it with a glass rod until dry. Then transfer the camphor to a watch glass, cover it with an inverted funnel and place the watch glass on wire gauze 10 cm. above a Bunsen burner having a flame 4 cm. high. When the camphor has all sublimed, dissolve 2.5 Gm. of the sublimate in sufficient alcohol (which must be of about 95 per cent. by volume) to make exactly 25 mils and take the mean of four or more polariscope readings as before. The minutes of rotation of the Spirit of Camphor divided by the minutes of rotation of the control test just made, and this multiplied by 10, shows the number of grammes of camphor in 100 mils of the Spirit of Camphor." *U. S.*

For another method of assay of spirit of camphor, see *Ph. Centralh.*, 1901, 472.

The camphor content of the spirit is easily obtained by the official method when a polariscope is available, but the detection of the addition of water is a more difficult task. This has been worked out by Maiden and Elliot, and the results of the method published in the *J.A. Ph. A.*, 1914, p. 91.

Spirit of camphor is an excellent preparation, much used locally in liniments and internally in *diarrhea,* and in *hysteria* and other forms of *nervous excitement.* Dilution with water precipitates the camphor, but when as in many cases it is desired to combine it with aqueous preparations, by dropping it into brandy or whisky and then adding water an eligible preparation is obtained; or the spirit of camphor may be dropped upon sugar and then mixed with water.

Dose, from ten to thirty minims (0.6–1.8 mils).

Off. Prep.—Lotio Ammoniacalis Camphorata, *N. F.;* Mistura Opii et Chloroformi Composita, *N. F.;* Mistura Opii et Rhei Composita, *N. F.;* Tinctura Kino et Opii Composita, *N. F.;* Tinctura Pectoralis, *N. F.*

SPIRITUS CHLOROFORMI. U. S., Br.

SPIRIT OF CHLOROFORM Sp. Chlorof.

(spĭr'ĭ-tŭs ċhlō-rō-för'mī)

Chloric Ether, Spirit of Chloric Ether, *Br.;* Alcoolé de Chloroforme, *Fr.;* Chloroformspiritus, *G.*

* "Chloroform, *sixty mils* [or 2 fluidounces, 14 minims]; Alcohol, *a sufficient quantity* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the chloroform with sufficient alcohol to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.* "Chloroform, 50 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve." *Br.*

It is to be regretted that the name Chloric Ether has been retained as a synonym in the British Pharmacopœia, 1914. There would be some reason for naming a mixture of chloroform and ether by the title chloric ether, but to use the term for an alcoholic solution of chloroform must inevitably cause confusion.

Chloric ether of the older works was a solution of variable strength of chloroform in alcohol, and was used as a general anesthetic. The practice has, however, very properly been abandoned, and the spirit of chloroform is now used as an internal remedy, especially in cases of *gastro-intestinal spasm* or *pain,* in which it acts as a local agent. The official aromatic elixir is an agreeable vehicle for its administration.

Dose, from ten to sixty minims (0.6–3.75 mils).

SPIRITUS CINNAMOMI. U. S., Br.

SPIRIT OF CINNAMON Sp. Cinnam.

(spĭr'ĭ-tŭs cĭn-nạ-mō'mī)

Teinture (alcoolé) d'essence de Cannelle, Esprit de Cannelle, *Fr.;* Zimmtspiritus, *G.;* Spirito di cannella, *It.*

* "Oil of Cinnamon, *one hundred mils* [or 3 fluidounces, 183 minims]; Alcohol, *a sufficient quantity* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the oil with sufficient alcohol to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

"Oil of Cinnamon, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

The spirit of cinnamon is an agreeable aromatic cordial.

Dose, from ten to thirty minims (0.6–1.8 mils) in water.

SPIRITUS GLYCERYLIS NITRATIS. U. S. (Br.)

SPIRIT OF GLYCERYL TRINITRATE, SPIRIT OF NITROGLYCERIN Sp. Glyceryl. Nit.

[Spiritus Glonoini, U. S. 1890, Spirit of Glonoin]

(spĭr'ĭ-tŭs glĭċ-ẹ-rĭ'lĭs nī-trā'tĭs)

"An alcoholic solution containing not less than 1 per cent. nor more than 1.1 per cent. of $C_3H_5(NO_3)_3$ (227.07). Preserve it in well-stoppered bottles in a cool, dark place, remote from fire.

Great care must be exercised in dispensing, handling, packing, transporting, and storing this Spirit, since a dangerous explosion may result if any considerable quantity of it is spilled, and the alcohol wholly or partly lost by evaporation. If, through accident, it is spilled, a solution of potassium hydroxide must be poured over it at once to effect partial decomposition." *U. S.*

Liquor Trinitrini, *Br.*; Solution of Trinitrin; Liquor Nitroglycerini; Solution of Nitroglycerin; Liquor Glonoini; Solution of Glonoin; Nitroglyceringeist, Glycerintrinitratlösung, *G.*

"Trinitroglycerin of commerce, 1 *gramme;* Alcohol (90 per cent.), sufficient to produce 100 *millilitres.* Dissolve." *Br.*

This official spirit was first introduced into the U. S. P. 1890 with the view of furnishing a satisfactory form for the administration of nitroglycerin.

The British Liquor Trinitrini is practically identical. Abundant precautions are included, which should on no account be neglected. The official description is as follows: "A clear, colorless liquid, having the odor of alcohol. *Caution must be exercised in tasting it,* since even a small quantity is liable to produce a violent headache. The same effect is produced when it is applied to the skin. It is neutral to litmus. Specific gravity: 0.814 to 0.820 at 25° C. (77° F.). Heat about 10 mils of Spirit of Glyceryl Trinitrate on a water bath with 1 mil of potassium hydroxide T.S. until the alcohol is evaporated, and then heat a portion of the residue with about 0.5 Gm. of potassium bisulphate; the pungent odor of acrolein is evolved. Dissolve the remainder of the residue in 2 mils of distilled water acidulated with diluted sulphuric acid, add a few drops of diphenylamine T.S. and pour the solution upon 2 mils of sulphuric acid in a test tube so as to form a separate layer; a dark blue color is produced at the zone of contact. Mix 10 mils of the Spirit with 11 mils of distilled water, both previously cooled to 15° C. (59° F.); a clear solution results. On now adding 2 mils more of distilled water, the mixture, at 15° C. (59° F.), becomes turbid. Weigh accurately not more than about 5 mils of the Spirit, allow it to evaporate spontaneously in a tared dish protected from dust, and dry the residue to constant weight in a desiccator, over sulphuric acid. The weight of the residue corresponds to not less than 1 per cent. nor more than 1.1 per cent. of the weight of Spirit taken." *U. S.*

"A clear colorless liquid, neutral to *litmus.* Specific gravity 0.840. A mixture of 10 millilitres with an equal volume of *water,* cooled to 15.5° C. (60° F.), remains clear, but the further admixture of 1 millilitre of *water* causes opacity (presence of a due amount of glyceryl trinitrate). On further diluting with *water* and setting aside the mixture, there is deposited a liquid of oily consistence, one drop of which, absorbed by paper and struck with a hammer on a hard surface, explodes. This Solution contains 1 gramme of trinitroglycerin in 100 millilitres; 110 minims contain 1 grain." *Br.*

For a method of assaying this spirit, by Chas. Rice, see *Am. Drug.,* 1895, 6; also Nagelvoort's method, *A. J. P.,* 1894, 527. F. W. Heyl and J. F. Staley review the various methods for the estimation of nitroglycerin and give comparative results of the assay of a large number of preparations and tablets. (*A. J. P.,* 1914, p. 195.) On account of the importance of nitroglycerin as a therapeutic agent, we append the following:

Nitroglycerin. Trinitrine. Glonoin. Glyceryl Trinitrate. $C_3H_5(NO_3)_3$.—When glycerin is gradually added in small portions at a time to a mixture of one part of strong nitric acid and three to four parts of concentrated sulphuric acid, and at a temperature kept low by artificial refrigeration, it is converted into a bright yellow liquid, which has remarkable explosive properties and has received the name at the head of this article. Nitroglycerin was discovered in the year 1846 by Sobrero of Turin, who called it *pyroglycerine.* It was afterwards made a subject of study by de Vrij of the Netherlands, Gladstone, and Kopp, but did not attract general attention until 1867, when Alfred Nobel, a Swedish engineer, suggested its use for explosive purposes by mixing it with inert substances like kieselguhr or infusorial earth to make the product commercially known as *dynamite.* It is a yellow liquid (said to be colorless or slightly yellowish when pure); of a sp. gr. from 1.525 to 1.6; inodorous; of a sweet, pungent, aromatic taste; very slightly soluble in water, but readily soluble in ether, alcohol, and methylated spirit; not freezing above −15.5° C. (4° F.) when quite pure, according to J. R. Wagner, but, as it occurs in commerce, solidifying by continued exposure to a temperature of 8° C. (46.4° F.), and assuming the form of long needles, which it is dangerous to handle, as they explode violently when gently broken. In the liquid state the mere contact of flame does not inflame or explode it; but concussion, or touching it with a red-hot iron, explodes it with great vehemence. Detonating mixtures, or exploding gunpowder, in its near vicinity, produce the same effect. By keeping, it undergoes partial decomposition, and in confined vessels the pressure of the accumulated gases which result is sometimes so great as to cause its explosion upon the slightest concussion. Its explosive force greatly exceeds that of gunpowder. According to Nobel, one volume of the fluid yields on explosion 10,384 volumes of gas, while one volume of gunpowder yields only 800 volumes. It has, therefore, been much employed in blasting rocks, in mining, quarrying, road making, etc., and its economical advantages have kept it in extensive use, notwithstanding the danger.

Nitroglycerin is formed by the introduction of the nitro-group (NO_3) in place of the three replaceable hydrogen atoms of the glycerin formula, according to the reaction:

$$C_3H_5(OH)_3 + 3(HNO_3) = C_3H_5.(NO_3)_3 + 3(H_2O)$$

E. Kopp gives the following as his method of

preparing nitroglycerin on the spot where it is needed. First, fuming nitric acid of the sp. gr. 1.51 to 1.53 is mixed with twice its weight of the strongest sulphuric acid. At the same time commercial glycerin, free from lead and lime, is evaporated in a pot to 30° or 31° Baumé, so that on cooling it shall have a syrupy consistence. Into 3300 grammes of the acid mixture, contained in a glass or porcelain capsule placed in a trough of cold water, 500 grammes of the prepared glycerin are slowly poured with constant stirring, great care being taken to prevent any sensible heating of the mixture. The whole is then to be left for five or ten minutes, after which the mixture is to be poured into five or six times its volume of cold water to which a rotatory motion has been given. The nitroglycerin precipitates rapidly in the form of a heavy liquid, which is separated by decantation, then washed with a little alkaline water which is decanted; it is then put into bottles. In this state it still contains a little acid and water, but these do not interfere with its use as an explosive agent if it is promptly used. Latterly it has also been prepared by mixing 3½ parts of sulphuric acid of 1.83 sp. gr. with 1 part of potassium nitrate, and cooling this, when potassium sulphate will crystallize out. The acid drained off from this is peculiarly adapted for the formation of nitroglycerin, which then takes place rapidly and without so much dangerous development of heat.

The sulphuric acid plays no part in the reaction and acts simply as a dehydrating agent. Nitroglycerin, being an ester, is readily saponified and rendered harmless when brought into contact with alkali hydroxides even in the cold. The reaction is as follows: $C_3H_5(NO_3)_3 + 3KOH = C_3H_5(OH)_3 + 3KNO_3$.

A complete and well illustrated article on nitroglycerin manufacture will be found in Molinari's Industrial Organic Chemistry, p. 223.

Uses.—The effects of nitroglycerin upon the system are precisely similar to those of the nitrites (see *Sodii Nitris*). According to the observations of Wallace and Ringer (*J. A. M. A.*, 1909, lii, p. 1629) the effects of one and one-half minims of the spirits of nitroglycerin come on within two or three minutes after taking by the mouth and endure for about one-half hour. The amount of the drug required to affect the system varies extraordinarily in different individuals. Murrell (*L. L.*, 1879, i, p. 80), has reported violent effects from one or two minims of the 1 per cent. solution. On the other hand, Kolipinski (*M. News*, 1890) reports a case in which two drachms of the official solution were taken without serious symptoms (amount somewhat doubtful). It is probable that many of these cases in which large quantities have been ingested the drug was of inferior quality. Nitroglycerin is a volatile substance and unless evaporation is guarded against its preparations lose potency. The tablet triturates of nitroglycerin which are frequently employed, are especially liable to deterioration. The spirit of glyceryl nitrate is used in the same class of cases as sodium nitrite, but is employed where rapidity of action is important, as in *angina pectoris, threatened apoplexy, asthma, strychnine poisoning,* and the like. It has been enormously misused as a cardiac stimulant in various forms of collapse; it should be remembered that its effect is always to lower blood pressure and it can do no good in any form of circulatory failure. It has been highly recommended in *hemoptysis,* its action being attributable to the consentaneous dilatation of the abdominal and contraction of the pulmonary vessels.

According to Ebright (*J. A. M. A.*, 1914, lxii, p. 201), workers in dynamite factories are subject to chronic nitroglycerin poisoning. The most characteristic symptom of this intoxication is throbbing headache, at times so violent that the patient may become maniacal. The pain is made worse by lying down and is not alleviated by either acetphenetidin or morphine. After some time the workers in these factories appear to develop an immunity to the poisoning.

Dose, of the spirit, from one to two minims (0.06–0.12 mil).

SPIRITUS JUNIPERI. U. S., Br.

SPIRIT OF JUNIPER Sp. Junip.

(spĭr'ĭ-tŭs jū-nĭp'ẹ-rī)

Teinture d'essence de Genièvre, *Fr. Cod.*; Spiritus Juniperi, *P. G.*; Wachholderspiritus, *G.*

* "Oil of Juniper, *fifty mils* [or 1 fluidounce, 331 minims]; Alcohol, *a sufficient quantity* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the oil with sufficient alcohol to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

"Oil of Juniper, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter. This Spirit is of twice the strength of the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

This spirit is used chiefly as an addition to diuretic infusions. It is about 33 per cent. stronger than the spirit official before 1890.

Dose, from thirty to sixty minims (1.8–3.75 mils).

SPIRITUS JUNIPERI COMPOSITUS. U. S.

COMPOUND SPIRIT OF JUNIPER Sp. Junip. Co.

(spĭr'ĭ-tŭs jū-nĭp'ẹ-rī cọm-pŏs'ĭ-tŭs)

Teinture (alcoolé) d'essence de Genièvre composée, *Fr.*; Zusammengesetzter Wachholderspiritus, *G.*

* "Oil of Juniper, *eight mils* [or 130 minims]; Oil of Caraway, *one mil* [or 16 minims]; Oil of Fennel, *one mil* [or 16 minims]; Alcohol, *fourteen hundred mils* [or 47 fluidounces, 162 minims]; Water, *a sufficient quantity,* to make *two thousand mils* [or 67 fluidounces, 301 minims]. Dissolve the oils in the alcohol, and gradually add enough water to make the product measure *two thousand mils* [or 67 fluidounces, 301 minims]." *U. S.*

This spirit is a useful addition to diuretic in-

fusions and mixtures in debilitated cases of *dropsy*. It corresponds very closely to Holland gin.

Dose, from two to four fluidrachms (7.5–15 mils).

SPIRITUS LAVANDULÆ. U. S., Br.

SPIRIT OF LAVENDER Sp. Lavand.

(spĭr'ĭ-tŭs lą-văn'dŭ-læ)

Teinture (alcoolé) d'essence de Lavande, *Fr.*; Spiritus Lavandulæ, *P. G.*; Lavandelspiritus, *G.*

* "Oil of Lavender, *fifty mils* [or 1 fluidounce, 331 minims]; Alcohol, *a sufficient quantity* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the oil with sufficient alcohol to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

"Oil of Lavender, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

Spirit of lavender is used widely as a perfume, and as an ingredient in other preparations. The perfume usually sold under the name of *lavender water* is not a distilled spirit, but an alcoholic solution of the oil, with the addition of other odorous substances. The following is given by Brande as one of the most approved recipes for preparing it. "Take of rectified spirit five gallons, essential oil of lavender twenty ounces, essential oil of bergamot five ounces, *essence of ambergris* [made by digesting one drachm of ambergris and eight grains of musk in half a pint of alcohol] half an ounce. Mix." The Br. spirit is double the strength of the U. S. preparation. It is a grateful stimulant and carminative when administered in sweetened water.

Dose, of the U. S. Spirit, from ten to thirty minims (0.6–1.8 mils); of the Br. Spirit, five to twenty minims (0.3–1.3 mils).

Off. Prep.—Mistura Ferri Composita, *N. F.*

SPIRITUS MENTHÆ PIPERITÆ. U. S., Br.

SPIRIT OF PEPPERMINT Sp. Menth. Pip. [Essence of Peppermint]

(spĭr'ĭ-tŭs mĕn'thæ pĭp-ẹ-rĭ'tæ)

Teinture d'essence de Menthe, *Fr. Cod.*; Spiritus Menthæ Piperitæ, *P. G.*; Pfefferminzspiritus, Englische Pfefferminzessenz, *G.*; Alcohol de menta piperita, *Sp.*

* "Oil of Peppermint, *one hundred mils* [or 3 fluidounces, 183 minims]; Peppermint, bruised, *ten grammes* [or 154 grains]; Alcohol, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Macerate the peppermint leaves, freed as much as possible from stems, during one hour in *five hundred mils* [or 16 fluidounces, 435 minims] of water and then strongly express them. Mix *eight hundred mils* [or 27 fluidounces, 24 minims] of alcohol with the oil, add the macerated leaves and enough alcohol to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms], macerate the mixture during six hours, with frequent agitation, and then filter it. Preserve the product in amber-colored bottles." *U. S.*

"Oil of Peppermint, 100 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

The distilled spirit has no advantage over a simple solution of the oil in alcohol; and this mode of preparing it has been adopted both in the U. S. and British Pharmacopœias. The American spirit is green in color, but the British is almost colorless. P. H. Utech suggests the maceration of the peppermint in water for two hours, washing and draining, before adding to the solution of the oil; water soluble matter is removed and a more permanent green color produced. He recommends the same treatment for the spearmint in making spirit of spearmint, and the U. S. P. IX adopted this plan. It has long been popularly used under the name of *essence of peppermint.* The spirit of peppermint affords a convenient method of administering a dose of the volatile oil, being of such a strength that when dropped on loaf-sugar it may be taken without inconvenience.

Dose, ten to thirty minims (0.6–1.8 mils), given as just mentioned, or mixed with sweetened water.

SPIRITUS MENTHÆ VIRIDIS. U. S.

SPIRIT OF SPEARMINT Sp. Menth. Vir.

(spĭr'ĭ-tŭs mĕn'thæ vīr'ĭ-dĭs)

Tinctura Olei Menthæ Viridis, *U. S.* 1850; Essence of Spearmint; Grüne Minzessenz, *G.*

* "Oil of Spearmint, *one hundred mils* [or 3 fluidounces, 183 minims]; Spearmint, bruised, *ten grammes* [or 154 grains]; Alcohol, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Macerate the spearmint leaves, freed as much as possible from stems, during one hour in *five hundred mils* [or 16 fluidounces, 435 minims] of water and then strongly express them. Mix *eight hundred mils* [or 27 fluidounces, 24 minims] of alcohol with the oil, add the macerated leaves and enough alcohol to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms], macerate the mixture during six hours, with frequent agitation, and then filter it. Preserve the product in amber-colored bottles." *U. S.*

The remarks made on the Spirit of Peppermint are equally applicable here.

Dose, ten to thirty minims (0.6–1.8 mils).

SPIRITUS MYRISTICÆ. Br.

SPIRIT OF NUTMEG [Essence of Nutmeg]

(spĭr'ĭ-tŭs mў-rĭs'tĭ-cæ)

Teinture (alcoolé) d'essence de Muscade, *Fr.*; Muskatspiritus, *G.*

"Oil of Nutmeg, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

It is used chiefly for its flavor. Spirit of nutmeg was not retained in the U. S. P. IX. It was made in the U. S. P., 1890, by dissolving 50 mils of nutmeg in 950 mils of alcohol. (See *Oleum Myristicæ.*)

Dose, from five to twenty minims (0.3–1.3 mils).

SPIRITUS RECTIFICATUS. Br.

ALCOHOL (90 PER CENT.) [Rectified Spirit]

(spĭr'ĭ-tŭs rĕc-tĭ-fĭ-cā'tŭs)

"Alcohol (90 per cent.) is a mixture of ethyl hydroxide and water, containing in 100 parts by volume 90 parts by volume of ethyl hydroxide, C_2H_5OH; and is obtained by the distillation of fermented saccharine liquids." *Br.*

"A colorless, transparent, very mobile and inflammable liquid. Characteristic pleasant odor; taste strongly spirituous, burning. Specific gravity 0.8337. Contains 85.68 per cent. by weight of ethyl hydroxide, C_2H_5OH, and 14.32 per cent. by weight of water. Burns with a blue smokeless flame. Leaves no residue on evaporation (absence of non-volatile matter). Remains clear when mixed with *water* (absence of oily or resinous substances). A little exposed on clean white filter paper leaves no unpleasant smell after the alcohol has evaporated (absence of fusel oil and allied impurities). 100 millilitres, with 2 millilitres of *N/10 solution of silver nitrate,* exposed for twenty-four hours to bright light and then decanted from the black powder which has formed, undergo no further change when again exposed to light with more *N/10 solution of silver nitrate* (absence of more than traces of amylic alcohol and of other organic impurities). When mixed with half its volume of an aqueous solution (1 in 5) of *sodium hydroxide,* the mixture does not immediately darken in color (absence of more than traces of aldehyde). No immediate darkening in color is caused by the addition of *solution of ammonia* (absence of tannin, excess of aldehyde, and other organic impurities). On mixing Alcohol (90 per cent.) and *water,* contraction of volume and rise of temperature occur. When such a mixture is prescribed in the British Pharmacopœia, the cooled liquid should be employed." *Br.*

For further information concerning this liquid, the reader is referred to *Alcohol,* page 103, and also to the text under the article *Alcohol Dilutum,* page 104.

SPIRITUS ROSMARINI. Br.

SPIRIT OF ROSEMARY

(spĭr'ĭ-tŭs rŏs-mą-rī'nī)

Spiritus Anthos; Teinture d'essence de Romarin, *Fr. Cod.;* Rosmarinspiritus, *G.;* Alcohol de romero, *Sp.*

"Oil of Rosemary, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve. When not clear, shake with a little *powdered talc* and filter." *Br.*

This spirit is not official in the United States Pharmacopœia IX. It is a grateful perfume, and is used chiefly as an odorous ingredient in lotions and liniments.

STAPHISAGRIA. U. S. (Br.)

STAPHISAGRIA Staphisag. [Stavesacre]

(stăph-ĭ-sā'grĭ-ą)

"The ripe seeds of *Delphinium Staphisagria* Linné (Fam. *Ranunculaceæ*), without the presence or admixture of more than 2 per cent. of foreign vegetable matter." *U. S.* "Stavesacre Seeds are the dried ripe seeds of Delphinium Staphisagria, *Linn.*" *Br.*

Staphisagriæ Semina, *Br.;* Semen Staphisagriæ, Staphidiagriæ or Pedicularis; Stavesacre Seeds; Staphisaigre, *Fr. Cod.;* Stephanskörner, Läusekörner, *G.;* Stafisagria, *It.*

Delphinium Staphisagria L., or stavesacre, is a handsome, annual or biennial plant, one or two feet high, with a simple, erect, downy stem, and palmate, five- or seven-lobed leaves, supported on hairy petioles. The flowers are bluish or purple, in terminal racemes, with pedicels twice as long as the flower, and bracteoles inserted at the base of the pedicel. The sepals are five in number, irregular, petal-like, the upper one being spurred at the base. The petals are four, irregular, the two upper having long spurs which are inclosed in the spur of the calyx, the two lower having short claws. The pistils form a many seeded pod or capsule in fruit.

The plant is a native of the south of Europe. E. M. Holmes calls attention to the remarkable fact that the plant in the English botanic gardens hitherto considered to be *Delphinium Staphisagria* is in reality another species, *i.e., Delphinium pictum* Willd. The author accounts for the absence of the true plant in botanic gardens partly by the fact that it is only half-hardy in Great Britain, while *D. pictum* is hardy, and partly by the reason that the illustrations in several works on medicinal plants—even in Bentley and Trimen's "Medicinal Plants"—are incorrect or unreliable. The two species are distinguished as follows: *D. Staphisagria* has very hairy stems, glandular hairs being mixed with the long spreading soft hairs; flowers that when well-developed have an ultramarine blue tint; a calyx with very short or almost obsolete spur; carpels containing only four or five seeds. *D. pictum* Willd., has shorter soft hairs, but no glandular hairs on the stems; the flowers are of a pale lilac color; the spur is as long as the calyx segments; each carpel contains ten or twelve seeds, and these are only half the size of those of *D. Staphisagria.* The true *D. Staphisagria* extends from Teneriffe around both the northern and southern coasts of the Mediterranean to Asia Minor. It is quite possible, therefore, that varieties having blossoms of different tints may occur. The evidence obtainable, however, goes to show that the form of the plant from which the seed of commerce is obtained has clear blue flowers. (*Y. B. P.,* 1899, 390.) For description of other species of this genus, see *Delphinium,* Part II.

Properties.—The seeds of stavesacre are officially described as "irregularly triangular, flattened, or somewhat tetrahedral, one side being convex, from 4 to 7 mm. in length and from 3 to 6 mm. in breadth; externally dark brown, becoming lighter with age, and coarsely reticulate; easily cut, showing a somewhat light brown, oily endosperm, enclosing a small embryo at the pointed end; odor slight, disagreeable; taste intensely bitter and acrid. Under the microscope, transverse sections of Staphisagria show an outer layer of nearly tabular, thick-walled, non-lignified cells, some being extended centrifugally, and forming the reticulations of the seed-coat; 2 or 3 rows of parenchyma cells with more or less irregular thin walls; a thin layer of very small, thick-walled cells with numerous, lattice-like or reticulate pores; endosperm large, composed of polygonal cells enclosing small aleurone grains and fixed oil, the latter forming in large globules on the addition of hydrated chloral T.S." *U. S.*

"Irregularly triangular or obscurely quadrangular, arched, blackish-brown when fresh, but becoming dull greyish-brown on keeping. Surface wrinkled and deeply pitted; kernel soft, whitish, oily. No marked odor; taste nauseous, bitter and acrid." *Br.*

The seeds of the field larkspur (*D. Consolida* L.) and of *D. Ajacis* L. are being largely used in place of the official staphisagria; in fact, they are recognized in the National Formulary. These are readily distinguished, being about 2 mm. in length and of a black or blackish-brown color.

The virtues of staphisagria are extracted by water and alcohol. Analyzed by Lassaigne and Feneulle it yielded a brown and a yellow bitter principle, a volatile oil, about 30 per cent. of a fixed oil, albumen, a nitrogenous substance, a mucilaginous saccharine matter, mineral salts, and a peculiar alkaloid called *delphinine,* which exists in the seeds combined with an excess of malic acid. Marquis, in Dragendorff's laboratory in 1877, isolated the following four alkaloids: *delphinine,* $C_{22}H_{35}O_6N$, a crystallizable alkaloid, of bitter taste, weak alkaline reaction, soluble in alcohol, ether, and chloroform; *delphinoidine,* $C_{42}H_{68}O_7N_2$, amorphous, soluble in ether, alcohol, chloroform, reaction strongly alkaline, fusing point from 110° to 120° C. (230°–248° F.); *delphisine,* $C_{27}H_{46}O_4N_2$, crystallizing in warty aggregations, soluble in ether, alcohol, and chloroform; *staphisagrine,* $C_{22}H_{33}O_5N$, only obtained amorphous, difficultly soluble in water and ether, easily soluble in alcohol and chloroform, of bitter taste, fusing point 90° C. (194° F.), of alkaline reaction in alcoholic solution. If delphinine be rubbed up with an equal quantity of malic acid, and some drops of concentrated sulphuric acid added, there will be produced an orange-red color passing into rose, growing deeper after some hours, and finally changing from the edges to violet, and at last becoming cobalt blue. (Tattersall, *Chem. News,* 41.) It is stated that no other alkaloid and no other organic acid, except malic, affords this reaction. (*Pflanzenstoffe,* 2d ed., 1884, 617.) The total amount of alkaloids is about 1 per cent. According to Charalampi Kara-Stojanow (*In. Dis.,* Dorpat, 1890), delphinine and *delphisine* have the same composition, $C_{31}H_{49}O_7N$, crystallize from their solutions in ether and petroleum benzin in identical forms, and have their melting points at 189° and 191° C. (372.2° and 375.8° F.), while *delphinoidine* has the formula $C_{25}H_{12}O_4N$. Ahrens (*Ap. Ztg.,* 1899, 361) obtained from the residue of the seeds of *D. staphisagria,* from which delphinine, delphinoidine, delphisine and staphisagrine had been extracted, the alkaloid *staphisagroine* (*Ber. d. Chem. Ges.,* 1899, 1581). For Katz's process for extracting delphinine, see *Ph. Ztg.,* 1900, 735.

Uses.—The seeds were formerly used as an emetic and cathartic, but have been abandoned in consequence of their violence. A strong tincture has been employed as an embrocation in *rheumatism.* The ointment is used to destroy *lice* and the *itch-mite.* Staphisagria should never be used internally, and when it is applied externally, care should be exercised not to put it on an abraded surface, but only upon the unbroken epidermis. In some countries the seeds are used like Cocculus Indicus to intoxicate fish.

When given in poisonous doses to the lower animals, *delphinine* produces excessive salivation, followed by violent and repeated vomiting, great disturbance of respiration, failure of heart action, gradual enfeeblement of voluntary motion and of sensation, and a peculiar fibrillary spasm of the muscles of the abdomen, which is said to be characteristic of the poisoning. Elevation of temperature and glycosuria have both been noticed; death is said to occur always from failure of respiration, though the heart is greatly enfeebled and finally ceases in diastole. According to Gauthier, the period of depression of the heart and of sensibility is preceded by one of excitement. The pupils are dilated and the motor nerve finally paralyzed. (*L. M. R.,* Oct., 1887.) Turnbull, in his work *On the Medical Properties of the Ranunculaceæ,* states that pure delphinine may be given to the extent of three or four grains a day, in doses of half a grain each, without exciting vomiting, and without producing much intestinal irritation, though it sometimes purges. In most instances it proves diuretic, and gives rise to sensations of heat and tingling in various parts of the body. Externally, it acts like veratrine, but, according to Turnbull, produces more redness and burning and less tingling than that substance. He has employed it in *neuralgia, rheumatism* and *paralysis.* It may be applied by friction, in the form of ointment or alcoholic solution, in proportions varying from ten to thirty grains of the alkaloid to an ounce of the vehicle, and the friction should be continued till a pungent sensation is produced. Turnbull probably had an impure alkaloid; the doses just mentioned would not be safe with a pure delphinine.

Staphisagrine is said to act like delphinine, except that it does not depress the heart so much

or produce fibrillary contractions. Although cases of human poisonings have occurred with staphisagria, we know of none in which the result has been fatal. The symptoms are similar to those produced in the lower animals. Kobert states that the alkaloids of staphisagria all resemble aconitine in their action, but that delphinoidine has some narcotic action.

Off. Prep.—Fluidextractum Staphisagriæ, *U. S.;* Unguentum Staphisagriæ, *Br.*

STILLINGIA. U. S.

STILLINGIA Stilling. [Queen's Root]

(stĭl-lĭn'gĭ-ą)

"The dried roots of *Stillingia sylvatica* Linné (Fam. *Euphorbiaceæ*). Preserve Stillingia in tightly-closed containers, adding a few drops of chloroform or carbon tetrachloride, from time to time, to prevent attack by insects." *U. S.*

Silver Leaf, Queen's Delight, Yaw Root; Stillingie, *Fr., G.*

Stillingia sylvatica is an indigenous perennial plant, commonly called *Queen's delight,* with herbaceous stems, two or three feet high, and alternate, sessile, oblong or lanceolate-oblong, obtuse serrulate leaves, tapering at the base, and accompanied with stipules. The staminate and pistillate flowers are distinct upon the same plant. They are yellow, and arranged in the form of a spike, of which the upper part is occupied by the male, the lower by the female flowers. The staminate florets are scarcely longer than the bracteal scales. The plant grows in pine barrens from Maryland to Florida and west to Kansas and Texas, flowering in May and June. When wounded it emits a milky juice.

Properties.—The root, which is the part used, is large, thick, and woody. It is officially described as "entire, terete, unequally tapering, rarely branched, usually in pieces attaining a length of 40 cm. and from 0.5 to 3 cm. in diameter, externally reddish-brown, longitudinally wrinkled; fracture very fibrous; internally the bark is light reddish-brown, thick, spongy, finely fibrous, with numerous resin cells and easily separable from the porous, radiate wood; odor distinct; taste bitter, acrid and pungent. The powder is pinkish-brown or light reddish-brown; when examined under the microscope it exhibits numerous starch grains from 0.005 to 0.035 mm. in diameter, mostly single, very variable in shape, and usually with a central cleft; numerous fragments, with more or less tabular secretion cells, containing a reddish-brown, amorphous, resinous substance; fragments of tracheæ mostly with simple pores and associated with wood-fibers, the walls being very thin, lignified and possessing numerous, transverse, slit-like simple pores; bast-fibers long, narrow, the walls thick and slightly lignified; fragments of reddish-brown cork cells; occasionally crystals of calcium oxalate in rosette aggregates about 0.035 mm. in diameter. Stillingia yields not more than 5 per cent. of ash." *U. S.*

The odor is slight, peculiar, and somewhat oleaginous, but in the recent root is said to be strong and acrimonious. The taste is bitterish and pungent, leaving an impression of disagreeable acrimony in the mouth and fauces. Holm gives an excellent illustrated article on the pharmacognosy of stillingia in *Merck's Rep.,* xx, p. 412. W. Saunders has obtained from the root a volatile oil, which he found to possess the odor, taste, and peculiar acrimony of the root in a high degree. He procured six and a quarter ounces from five pounds of the dried root. It had a thick consistence, and required the addition of alcohol to render it fit for manipulation. Wm. Bichy (*A. J. P.,* 1885, p. 529) found an alkaloid which he named *stillingine.* It was obtained as an amorphous powder, volatilizable on heating, forming a sulphate in fine scale-like crystals.

Uses.—In large doses stillingia is emetic and cathartic, but is rarely used for these purposes. Smaller quantities have been supposed to exercise an alterative effect upon the system and are used in *syphilitic* and *scrofulous* conditions. The drug is probably, however, without any real value.

Dose, half a drachm to a drachm (2.0–3.9 Gm.).

Off. Prep.—Fluidextractum Stillingiæ, *U. S.;* Elixir Corydalis Compositum (from Fluidextract), *N. F.;* Fluidextractum Stillingiæ Compositum, *N. F.;* Syrupus Stillingiæ Compositus, *N. F.*

STRAMONIUM. U. S. (Br.)

STRAMONIUM Stramon. [Jamestown Weed, Jimson Weed]

(strą-mō'nĭ-ŭm)

"The dried leaves of *Datura Stramonium* Linné, or of *Datura Tatula* Linné (Fam. *Solanaceæ*), without the presence or admixture of more than 10 per cent. of stems or other foreign matter, and yielding not less than 0.25 per cent. of the total alkaloids of Stramonium." *U. S.* "Stramonium Leaves are the dried leaves of Datura Stramonium, *Linn.*" *Br.*

Stramonii Folia, *Br., U. S.* 1890—Stramonium Leaves; Herba Stramonii; Thornapple Leaves; Thorn, Devil's or Mad Apple, Apple of Peru, Stink-weed, Jamestown (Jimson) Lily, Devil's Trumpet, Derotry; Stramoine ou Pomme-épineuse, *Fr. Cod.;* Feuilles de Stramoine, *Fr.;* Folia Stramonii, *P. G.;* Stechapfelblätter, *G.;* Stramonio, *It.;* Estramonio (Hoja de), *Sp.*

The *thornapple* (*Datura Stramonium*) is an annual plant, of rank and vigorous growth, usually about three feet high, but in a rich soil attains a height of six feet or more. The root is large, whitish, and furnished with numerous rootlets. The stem is erect, round, smooth, somewhat shining, simple below, dichotomous above, with numerous spreading branches. The leaves are petiolate, five or six inches long, of an ovate-triangular form, irregularly sinuated and toothed at the edges, unequal at the base, dark green on the upper surface, and pale beneath. The flowers are large, axillary, solitary, and peduncled, having a tubular, pentangular, five-

toothed calyx, and a funnel-shaped corolla with a long tube, and a wavy plaited border, terminating in five acuminate teeth. The upper portion of the calyx falls with the deciduous parts of the flower, leaving its base, which becomes reflexed and remains attached to the fruit. This is a large, fleshy, roundish-ovate, four-valved, four-locular capsule, thickly covered with sharp spines, and containing numerous seeds, attached to a longitudinal placenta in the center of each locule. It opens at the summit. There are two varieties of this species of Datura, one with a green stem and white flowers, the other with a dark reddish stem minutely dotted with green, and purplish flowers striped with deep purple on the inside. The latter is now considered as a distinct species, being the *D. Tatula* of Linnæus. The properties of both are the same.

It is doubtful to what country this plant originally belonged. Many European botanists refer it to North America, while we in return trace it to the old continent. Nuttall considers it as having originated in South America or Asia, and it is probable that its native country is to be found in some part of the East. It is said to grow wild, abundantly in Southern Russia, from the borders of the Black Sea eastward to Siberia. Its seeds, being retentive of life, are taken in the earth put on shipboard for ballast from one country to another, not infrequently springing up upon the passage, and thus propagating the plant in all regions which have any commercial connection. In the United States it is found everywhere in the vicinity of cultivation frequenting dung heaps, the road sides and commons, and other places where a rank soil is created by the deposited refuse of towns and villages. Its flowers appear from May to July or August, according to the latitude. Where the plant grows abundantly, its vicinity may be detected by the rank odor which it diffuses to some distance around. Notwithstanding the abundance of the plant, it is being cultivated in order to obtain a drug which shall be of uniform quality. The Bureau of Plant Industry, U. S. Department of Agriculture, has conducted experiments on a large scale. Several hundred pounds of leaf were grown, cured by artificial heat in a tobacco barn, and marketed at a price in advance of the highest quoted figure. Mitlacher has reported his observations on the cultivation of stramonium in *Zeit. Oest. Apoth.*, 1, p. 391. Miller has conducted comparative experiments on *D. Stramonium* and *D. Tatula.* (*A. J. P.*, lxxiv, p. 446.)

All parts of it are medicinal. The leaves, seeds, and root were formerly recognized by the U. S. P., the leaves and seed in the U. S. P., 1890, but in the U. S. P. VIII and IX the seeds were not included and the leaves alone are official under the title *Stramonium.* The leaves may be gathered at any time from the appearance of the flowers till the autumnal frost. In this country the plant is generally known by the name of *Jamestown* (*vulgo, Jimson*) *weed*, derived probably from its having been first observed in the neighborhood of that old settlement in Virginia. In India *Datura alba, D. ferox,* and *D. fatuosa* are employed as poisons. The last has been admitted to the Br. (See *Daturæ Folia.*) Under the names of *Man t'o lo fa, Wan t'o lo hua,* and *Nau yeung fa,* the Chinese use as a medicine the flowers of the *Datura alba;* according to Frank Browne, they contain 0.485 per cent. of hyoscine, free from other alkaloids. *El Bethene,* a Datura of the Sahara Desert, is capable of causing delirium, coma, and death, and it is probable that all the species of the genus are poisonous. A. R. L. Dohme (*Proc. A. Ph. A.*, 1894, 231) examined stramonium to determine the value in alkaloid of the various parts of the plant; he found that, in general, the fresh parts yielded more than the dried parts; the stems contained the most alkaloid, the seeds next, then the leaves, and the roots the least of all.

The *fresh leaves* when gruised emit a fetid narcotic odor, which they lose upon drying. Their taste is bitter and nauseous. These properties, together with their medicinal virtues, are imparted to water and alcohol. Water distilled from them, though possessed of their odor in a slight degree, is destitute of their active properties. They contain, according to Promnitz, 0.58 per cent. of gum, 0.6 of extractive, 0.64 of green starch, 0.15 of albumen, 0.12 of resin, 0.23 of saline matters, 5.15 of lignin, and 91.25 of water. The leaves, if carefully dried, retain their bitter taste. They are officially described as "usually much wrinkled and either loose or more or less matted together; laminæ when entire from 2 to 30 cm. in length, having petioles from 0.5 to 8 cm. in length; inequilaterally ovate, summits acute or acuminate, bases unequal, one side extending from 3 to 12 mm. below the other, margins sinuate, toothed or angled, the teeth being few, acute or acuminate and with rounded sinuses; frequently with numerous circular perforations which may have become filled with cork; upper surfaces dark green, sparsely hairy, especially upon the veins, lower surfaces light green; odor distinct, heavy and narcotic; taste unpleasant, nauseous. Stems cylindrical, usually flattened, attaining a length of 30 cm. and a diameter of 7 mm.; longitudinally wrinkled, occasionally with 1 or more deep furrows, light greenish-brown to purplish-brown. The powder is brownish-green; upon clearing the fragments with hydrated chloral T.S. and examining under the microscope, it shows numerous elliptical stomata, about 0.025 mm. in length, and surrounded usually with 3 neighboring cells; cells of the mesophyll containing numerous small chloroplastids; calcium oxalate either in rosette aggregates, from 0.01 to 0.02 mm. in diameter, or in rod-like crystals, or in the form of sphenoidal micro-crystals; non-glandular hairs few, characteristic, 2- to 4-celled, attaining a length of 0.5 mm., the basal cell about 0.04 mm. in width, some of the cells more or less collapsed, the outer walls with numerous, slight, centrifugal projections; glandular hairs few, with 1- to 2-celled stalks and usually 2- to 4-celled,

glandular heads; tracheæ annular or spiral, fragments of the tracheal wall frequently detached. Stem fragments show large annular or spiral tracheæ which occasionally are thickened, with simple or bordered pores and associated with wood parenchyma; fragments with long, narrow unequally thickened collenchymatous cells; parenchyma with sphenoidal micro-crystals; wood-fibers occasional; bast-fibers absent. Stramonium yields not more than 20 per cent. of ash." *U. S.*

J. S. Ward has found commercial stramonium leaves freely adulterated with those of *Carthamus helenioides* and *Xanthium Strumarium.* (*P. J.*, lxvi, 326.) For a paper on the structure of the leaves of *D. Stramonium, Atropa Belladonna,* and *Hyoscyamus niger* by Schlotterbeck and van Zwaluwenburg, see *Proc. A. Ph. A.*, 1897, 202. Holm has published an illustrated article on the morphology of stramonium. (*M. R.*, xxii, p. 162.) Rosenthaler has subjected the leaves of stramonium to pyro-analysis and obtained a distinctive and characteristic sublimate. (*B. P. G.*, xxi, p. 530.)

The following are some of the more common synonyms used to designate stramonium seeds: *Stramonii Semina, Stramonium Seed, Semen Stramonii,* P. G.; *Semences* (*Graines*) *de Stramoine,* Fr.; *Stechapfelsamen,* G., which were formerly official. The *seeds* are small, kidney-shaped, pitted and wrinkled, flattened on the sides, of a dark-brown almost black color, inodorous unless bruised, and of the bitter, nauseous taste of the leaves, with some degree of acrimony. The testa is dull brownish-black, hard, and encloses a cylindrical curved embryo, which is embedded in a whitish oily albumen. They are much more energetic in their action on the system than are the leaves. Hirtz and Hopp inferred from their experiments that one part of an extract prepared from them was equal in strength to five parts of an extract prepared in precisely the same manner from the leaves. (*Ann. Thér.*, 1862, p. 22.)

Geiger and Hesse succeeded in isolating an alkaloid, to which the name *daturine* was given, and which Trommsdorff has repeatedly procured by their process. Von Planta (*A. J. P.*, 23, p. 38) found that daturine was identical with atropine, and this result has since been confirmed; but Ladenburg (*Ber. d. Chem. Ges.*, 13, p. 909) found that *Datura Stramonium* contains two alkaloids, which he designated as *heavy daturine* and *light daturine.*

The more difficultly soluble heavy daturine fuses at 113.5° to 114° C. (236.3°–237.2° F.), and must be considered as a mixture of *atropine* and *hyoscyamine.* It yields a gold salt fusing between 135° and 150° C. (275° and 302° F.), out of which, by crystallization repeated six times and by rejection each time of the mother liquor, is obtained hyoscyamine gold-chloride fusing at 158° to 160° C. (316.4°–320° F.). From the mother liquors by evaporation is obtained nearly pure atropine gold chloride fusing at 135° to 140° C. (275°–284° F.). If the heavy daturine be repeatedly crystallized out of dilute alcohol, pure atropine can be isolated from it, fusing at 113.5° to 114.5° C. (236.3°–238.1° F.), and yielding a lusterless gold salt fusing at 135° to 139° C. (275°–282.2° F.). The light daturine is the alkaloid which Ladenburg and Meyer in a previous study had shown to be identical with hyoscyamine. Hence *Datura Stramonium* contains the two alkaloids *atropine,* $C_{17}H_{23}O_3N$, and *hyoscyamine,* isomeric with the other, which *Atropa Belladonna* also contains. (*A. J. P.*, 1884, 440.) The mother liquors from which hyoscyamine is obtained yield a difficultly crystallizable base, first called hyoscine, but now known as *scopolamine.* Its gold salt is more difficultly soluble than the gold salts of atropine and hyoscyamine, and affords a means of separation. The base, when purified, can be crystallized out of ether in colorless crystals, melting at 59° C. (138.2° F.). Its formula is $C_{17}H_{21}O_4N$, and it is decomposed by boiling with baryta water into *scopolin,* $C_8H_{13}NO_2$, and *atropic acid,* $C_9H_8O_2$. (Schmidt, *Pharm. Chemie,* 3te Auf., ii, 1339.)

Gérard (see *J. P. C.*, 1892, 8) studied *daturic acid* obtained from stramonium seed. D. Holde has, by means of benzene, extracted from stramonium seed 16.7 per cent. of a fixed oil. (*P. J.*, lxx, p. 90.) This has been examined by J. M. Baird and F. E. Sleeper, see *Proc. A. Ph. A.*, 1903, 324.

Assay of Stramonium.—"Proceed as directed under *Belladonnæ Radix,* page 222, using 15 Gm. of Stramonium, in No. 60 powder, increasing the amount of water to be added after maceration to 25 mils, and, before titration, treating the final residue twice with 5 mils of ether, evaporating to dryness each time.

"Each mil of tenth-normal sulphuric acid consumed corresponds to 28.92 milligrammes of the total alkaloids of Stramonium." *U. S.*

"Ovate, petiolate, usually from ten to fifteen centimetres long, often unequal at the base; margin sinuate-dentate, apex acuminate. Upper surface dark greyish-green; under surface paler, and minutely wrinkled. Walls of the epidermal cells sinuous; stomata on both surfaces; on the lower surface, especially of young leaves, curved multicellular hairs with thin, warty walls, and also glandular hairs with unicellular or multicellular stalks; in the mesophyll numerous cluster-crystals of calcium oxalate. Characteristic odor; taste bitter, unpleasant. Ash not more than 18 per cent." *Br.*

Uses.—Stramonium is so similar to belladonna in the symptoms produced by it in small or large doses, in its toxicity and its general physiological and therapeutic action, that the two drugs are practically identical. Furthermore, they are about the same strength in activity, so the preparations may be used in similar doses. Stramonium has been employed in all the conditions for which belladonna is more commonly used, but has acquired special repute in the treatment of *asthma,* this probably being due to the fact that the practice of smoking *Datura ferox* in that disease was introduced into Great Britain from the East Indies by

General Gent, and that afterwards the English species was substituted for that employed in Hindostan. Formerly the roots were chiefly used, but at present the dried leaves are exclusively employed. The beneficial effect is doubtless due to the presence of atropine which paralyzes the endings of the pulmonary branch of the vagus, thus relieving the bronchial spasm, for Gunther (*W. K. W.*, 1911, p. 748) has shown that the smoke from a stramonium cigarette containing 1.25 Gm. of stramonium leaves contains as much as 0.5 Mgm. of atropine. The leaves may be made up into cigarettes or smoked in a pipe, either with or without a mixture of tobacco; more commonly, however, the coarsely ground leaves are mixed with equal parts of potassium nitrate, in order to increase combustion, and burned in a saucer.

Death is said to have been produced by the free use of the India *Datura ferox*, but it seems hardly possible that the species which is found in North America would produce such a result.

The seeds are more powerful than the leaves. The seeds were once officially recognized, but the presence of a large amount of fixed oil made it difficult to extract them or to make stable preparations from them and the leaves have taken their place. They may be given in the dose of one-half to one grain (0.032–0.065 Gm.) twice a day; an extract made by evaporating the decoction, in one-quarter or one-half the quantity. The inspissated juice of the fresh leaves was formerly very commonly prescribed; but the alcoholic extract is now almost exclusively used, the dose being half a grain (0.032 Gm.). (See *Extractum Stramonii.*)

Dose, of the leaves, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Extractum Stramonii (Pilular and Powdered), *U.S.;* Tinctura Stramonii, *U. S., Br.;* Unguentum Stramonii (from Pilular Extract), *U. S.;* Fluidextractum Stramonii, *N. F.*

STRONTII BROMIDUM. U. S., Br.

STRONTIUM BROMIDE Stront. Brom.

(strŏn'tĭ-ī brō'mĭ-dŭm)

"It contains not less than 98 per cent. of $SrBr_2 + 6H_2O$ (355.57). Preserve it in well-closed containers." *U. S.* "Strontium Bromide may be obtained by neutralising dilute hydrobromic acid with strontium carbonate, evaporating and crystallising. It contains not less than 97 per cent. of pure strontium bromide, $SrBr_2,6H_2O$." *Br.*

Bromure de Strontium, *Fr. Cod.;* Strontiumbromid, *G.;* Bromuro Estroncico, *Sp.*

This salt, made official in the U. S. P., 1890, may be made by burning strontium in bromine vapor, by dissolving strontium carbonate in hydrobromic acid, or by substituting hydrobromic acid for hydrochloric acid in the latter part of the process given for preparing strontium salts. (See page 1066.)

Properties.—"Strontium Bromide occurs as colorless, transparent, hexagonal crystals; odorless, and having a bitter, saline taste. The salt deliquesces in moist air but effloresces in very dry air. One Gm. of Strontium Bromide dissolves in 0.35 mil of water at 25° C. (77° F.); soluble in alcohol; insoluble in ether. Its aqueous solution (1 in 20) is neutral to litmus. When quickly heated, the crystals at first melt, and at above 180° C. (356° F.) lose all of their water of crystallization. To a non-luminous flame the salt communicates a crimson color. Silver nitrate T.S. added to an aqueous solution of the salt (1 in 10) produces a yellowish-white precipitate, insoluble in nitric acid or in a moderate excess of ammonia water. With calcium sulphate T.S. an aqueous solution of the salt (1 in 20) slowly forms a white precipitate of strontium sulphate, insoluble in dilute acids; the precipitation occurs more quickly with diluted sulphuric acid or a readily soluble sulphate. Add a few drops of ferric chloride T.S. and 1 mil of chloroform to 10 mils of an aqueous solution of the salt (1 in 20) and shake the mixture; the chloroform does not acquire a violet tint (*iodine*). Drop 1 mil of diluted sulphuric acid upon about 1 Gm. of the powdered salt; no yellow color appears at once (*bromate*). Dissolve 1 Gm. of Strontium Bromide and 1 Gm. of sodium acetate in 5 mils of distilled water, and render the solution slightly acid by the addition of from 3 to 5 drops (or a sufficient quantity) of diluted acetic acid. The solution, upon the addition of 5 drops of potassium dichromate T.S. and agitation, does not become cloudy within three minutes (*barium*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3).

"**Assay.**—Proceed as directed under the Assay for bromides (see Part III, Test No. 5), using about 0.8 Gm. of Strontium Bromide, accurately weighed. It shows not less than 98 per cent. of $SrBr_2 + 6H_2O$.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.017778 Gm. of $SrBr_2 + 6H_2O$. Each gramme of Strontium Bromide corresponds to not less than 55.1 mils nor more than 56.6 mils of tenth-normal silver nitrate V.S." *U. S.*

"White acicular crystals, deliquescent. Taste saline, slightly bitter. Soluble in less than 1 part of *water*, and in *alcohol* (90 per cent.). Yields the *reactions* characteristic of bromides; an aqueous solution slowly deposits a crystalline precipitate on the addition of *solution of calcium sulphate*. A solution of 1 gramme in *water*, to which 5 millilitres of *solution of sodium acetate* and 3 millilitres of *acetic acid* have been added, does not become cloudy on the addition of 1 millilitre of *solution of potassium chromate* (absence of barium). 1 gramme dissolved in *water* requires for complete precipitation not less than 54.6 or more than 57 millilitres of *N/10 solution of silver nitrate*. 0.5 gramme moistened with *sulphuric acid* and gently ignited leaves a white residue weighing not less than 0.250 gramme. *Lead limit* 20 parts per million. *Arsenic limit* 5 parts per million." *Br.*

For further tests, see *Proc. A. Ph. A.*, 1897, 608.

Uses.—Strontium bromide has been strongly commended as a substitute for potassium bromide in the treatment of *epilepsy* and allied conditions. It depends for its action on the nervous system upon the presence of bromine in it, and appears to act upon the nervous centers in much the same manner as does the corresponding salt of potassium. Its influence upon the general nutrition is much more favorable than is that of the potassium salt, and it is much less apt to produce the disagreeable effects of bromism. Moreover, it is less irritating to the gastro-intestinal mucous membranes, on which, indeed, it often seems to exert a beneficial influence. For these reasons many cases of epilepsy tolerate it much better than they do other bromides. In the experience of H. C. Wood, however, it seemed to be in its anticonvulsive influence among the least powerful and certain of its class. Possibly this result has been due to Wood not having employed it in sufficient dose, he never having administered more than two drachms a day, while the French observers affirm that it may be given with great advantage in the daily dose of three drachms. Strontium bromide is further stated by Sée to have an extraordinary influence in the reduction of the excretion of sugar in *diabetes*, and to be a valuable remedy in the treatment of *gastric dilatation* and *catarrh*.

Dose, fifteen to thirty grains (1–2 Gm.).

STRONTII IODIDUM. U. S.

STRONTIUM IODIDE Stront. Iod.

(strŏn'tĭ-ī ī-ŏd'ĭ-dŭm)

"It contains not less than 99 per cent. of $SrI_2 + 6H_2O$ (449.57). Preserve it in small, amber-colored, glass-stoppered bottles, carefully protected from light." *U. S.*

Iodure de Strontium, *Fr.*; Strontiumjodid, *G.*

This official salt may be made by evaporating a solution of hydriodic acid saturated with strontium hydroxide or carbonate.

Properties.—"Strontium Iodide occurs as colorless, transparent, hexagonal plates, as a white, granular powder, or in crystalline crusts; odorless, and having a bitter, saline taste. It is deliquescent, and is colored yellow by exposure to air and light. One Gm. of Strontium Iodide dissolves in about 0.2 mil of water at 25° C. (77° F.); soluble in alcohol; slightly soluble in ether. Its aqueous solution (1 in 20) is neutral or slightly alkaline to litmus. When cautiously heated, the crystals melt and gradually lose their water of crystallization. At a red heat, the salt is decomposed, losing iodine and leaving a residue of strontium oxide. To a non-luminous flame it imparts a crimson color. When calcium sulphate T.S. is added to an aqueous solution (1 in 10) it slowly forms a white precipitate of strontium sulphate, insoluble in dilute acids; the precipitation occurs more quickly with diluted sulphuric acid or a readily soluble sulphate. Add 1 mil of ferric chloride T.S. to 5 mils of an aqueous solution of the salt (1 in 20); iodine is liberated, which imparts a violet color to chloroform, when shaken with it. Dissolve 1 Gm. of Strontium Iodide and 1 Gm. of sodium acetate in 5 mils of distilled water, and render the solution slightly acid by the addition of from 3 to 5 drops (or a sufficient quantity) of diluted acetic acid. The solution, upon the addition of five drops of potassium dichromate T.S. and agitation, does not become cloudy within three minutes (*barium*). Gently heat 5 mils of an aqueous solution of the salt (1 in 10) with 1 drop of ferrous sulphate T.S., 1 drop of ferric chloride T.S., and 0.5 mil of potassium hydroxide T.S.; no blue color appears after acidulating the mixture with hydrochloric acid (*cyanide*). An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). Dissolve 0.3 Gm. of the salt in 5 mils of distilled water, add an excess of silver nitrate T.S. and a few drops of nitric acid; filter, digest the precipitate with 5 mils of ammonia water and filter. On saturating the filtrate with nitric acid, not more than a slight turbidity is produced (*chloride or bromide*).

"**Assay.**—Proceed as directed under the Assay for iodides (see Part III, Test No. 5), using about 1 Gm. of Strontium Iodide, accurately weighed. It shows not less than 99 per cent. of $SrI_2 + 6H_2O$.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.022478 Gm. of $SrI_2 + 6H_2O$. Each gramme of Strontium Iodide corresponds to not less than 44 mils of tenth-normal silver nitrate V.S." *U. S.*

Uses.—This salt has been brought forward as a means of obtaining the alterative influence of an iodide without irritating the intestinal tract or depressing the general nutrition. It contains about 56.5 per cent. of iodine, and, although its actual value has scarcely as yet been made out, may be substituted for potassium iodide in various diseases.

Dose, five to fifteen grains (0.32–1.0 Gm.).

STRONTII SALICYLAS. U. S.

STRONTIUM SALICYLATE Stront. Salicyl.

(strŏn'tĭ-ī săl-ĭ-cȳ'lăs)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99 per cent. of $Sr(C_7H_5O_3)_2 + 2H_2O$ (397.74). Preserve it in well-closed containers, protected from heat and light." *U. S.*

Strontium Salicylicum; Salicylate de Strontium, *Fr.*; Salicylsaures Strontium, Strontiumsalicylat, *G.*

Preparation.—This salt is made by adding 10 parts of salicylic acid to 100 parts of hot water and then adding 5.3 parts of pure strontium carbonate, filtering, evaporating and crystallizing.

Properties.—It is officially described as "a white, crystalline powder; odorless, and having a somewhat sweet, saline taste. One Gm. of

Strontium Salicylate dissolves in 19 mils of water, and in 61 mils of alcohol at 25° C. (77° F.); also in 3.7 mils of boiling water and in 14 mils of boiling alcohol. When heated, the salt is decomposed, giving off inflammable vapors and an odor of phenol, and finally leaving a residue of strontium carbonate and carbon. To a non-luminous flame it imparts a crimson color. An aqueous solution of the salt (1 in 30) is colorless. With calcium sulphate T.S. an aqueous solution of the salt (1 in 20) slowly forms a white precipitate of strontium sulphate, insoluble in dilute acids. Add a few drops of ferric chloride T.S. to an excess of a concentrated aqueous solution of Strontium Salicylate; a dark red color and a precipitate are produced; in an aqueous solution of the salt (1 in 100) a deep violet-blue color is produced. Diluted hydrochloric acid produces a voluminous, white precipitate of salicylic acid in a concentrated aqueous solution of the salt. Add 1 mil of diluted sulphuric acid to 10 mils of an aqueous solution of Strontium Salicylate (1 in 50) and filter; the filtrate does not respond to the Test for heavy metals (see Part III, Test No. 3). Agitate 2 Gm. of Strontium Salicylate with 10 mils of diluted acetic acid, heat the mixture, cool, and then filter. The filtrate, upon the addition of 5 drops of potassium dichromate T.S., does not become cloudy within three minutes (*barium*).

"**Assay.**—Introduce into a platinum crucible about 2 Gm. of Strontium Salicylate, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed, and thoroughly carbonize it at a temperature not exceeding red heat. Dissolve the residue in 30 mils of half-normal hydrochloric acid V.S., and submit it to residual titration with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows, in the dried salt, not less than 99 per cent. of $Sr(C_7H_5O_3)_2 + 2H_2O$.

"Each mil of half-normal hydrochloric acid V.S. used corresponds to 0.099435 Gm. of $Sr(C_7H_5O_3)_2 + 2H_2O$. Each gramme of Strontium Salicylate, previously dried, corresponds to not less than 9.96 mils of half-normal hydrochloric acid V.S." *U. S.*

Uses.—Strontium salicylate when taken internally is slowly decomposed in the alimentary canal with the liberation of salicylic acid, which acid or its educts can be detected in the urine shortly after administration. As a salicylate, the strontium salt is of especial value in subacute *rheumatic* affections, acting more slowly and persistently than most of the other allied salts, and having much less tendency to disturb the digestion. Blankenhorn (*J. A. M. A.*, 1916, lvi, p. 331) from comparative studies in twenty-three cases of various diseases, has come to the conclusion that the toxic dose of strontium is the same as that of sodium salicylate, and that the strontium salt has no advantage in any way. It may be administered in capsule or in solution.

Dose, five to thirty grains (0.32–2.0 Gm.).

STRONTIUM

STRONTIUM

(strŏn'tĭ-ŭm)

$Sr = 87.63$

Strontium belongs to the alkaline earth-group of metals along with barium and calcium. It is a yellow metal, of the sp. gr. 2.5, somewhat harder than lead, and is sufficiently malleable to be hammered out into thin plates. It oxidizes quickly on exposure to air, and hence must be kept under naphtha, like the alkali metals. It has so far been prepared only in a small way by electrolysis from the chloride or the hydroxide, the best procedure being that of Bunsen and Matthiessen.

For the preparation of pure salts, Barthe and Falières found that the following method permits the preparation of pure strontium salts with comparative ease, and has the advantages that no heat is necessary, and that the chemicals employed need not be pure.

Dissolve natural strontium carbonate (or the sulphide obtained by reduction of the sulphate) in just sufficient diluted hydrochloric acid (1 to 5); it will be an advantage if some of the carbonate or sulphide remains undissolved. The clear liquid, which contains calcium, barium, and strontium salts, besides small quantities of iron, aluminum, and magnesium, is decanted from the deposit, and a small excess of ammonia added, which precipitates iron and alumina. To the filtrate is added an excess of sulphuric acid; the precipitate consisting of strontium, barium, and calcium sulphates, is washed repeatedly by decantation with water containing from 1 to 2 per cent. of sulphuric acid, and finally with distilled water. This will remove all traces of magnesium and calcium sulphate. The precipitate is next treated in the cold with an excess of a solution of ammonium or potassium carbonate (1 to 10), stirring frequently for two days, and finally washing with distilled water by decantation. The mixture of carbonate and sulphate is treated with diluted hydrochloric acid, which dissolves strontium carbonate and traces of baryta. After allowing it to stand for twenty-four hours the clear liquid is decanted and filtered through a filter previously washed with diluted hydrochloric acid. To the perfectly clear filtrate are added 200 Gm. of hydrochloric acid per liter, and then from 2 to 3 Gm. of precipitated strontium sulphate, which may contain barium sulphate; stirring frequently for several hours. The strongly acid liquid dissolves a little strontium sulphate (about 0.25 per cent.), but in proportion as the strontium is dissolved the barium takes hold of the sulphuric acid, while an equivalent quantity of strontium chloride is formed. The strontium sulphate being in excess will insure the final elimination of all the barium. The filtrate is evaporated to dryness, the salt dissolved in three times its weight of distilled water, allowed to stand for twenty-four hours, filtered, evaporated to crystallization, and dried. The crystals showed in

the spectroscope only the lines of strontium. (*Bull. Soc. Chim.*, 1892, 104.)

Strontium nitrate is largely used for making *red fire* in pyrotechnics; the salt is made by dissolving strontium carbonate in diluted nitric acid, evaporating the solution and crystallizing.

Uses.—At one time the strontium salts were deemed to be highly toxic, but in 1890 Laborde (*C. R. S. B.*, 1890, ii) showed that this belief was due to the fact that the earth had been contaminated with barium salts and that pure strontium was no more injurious than potassium. When a salt of strontium is taken by the mouth probably only small amounts of the metal are absorbed. The fact that it is excreted chiefly by the intestinal glands (Mendel and Thatcher, *A. J. Phys.*, 1904, xi, 5) makes it difficult to determine whether the salt found in the feces has been absorbed and re-excreted, or whether it is simply due to non-absorption. Even after hypodermic administration only traces of the metal appear in the urine. Wood and Arnold (*Phila. Monthly Medical Journal*, April, 1899) have shown that when introduced into the blood stream the strontium salts exercise a marked stimulating effect upon both the heart and arterial muscles, which are secondarily depressed by toxic doses. It causes also an increase in the contractions of the voluntary muscles with delay in their relaxation. Taken by the mouth, however, it is so slowly absorbed that it is improbable that enough can be introduced into the system to exercise any influence. According to Mendel and Thatcher, small quantities are stored up in the bones replacing a part of the calcium.

The salts of strontium, especially *strontium lactate*, were at one time extensively employed in the treatment of *chronic Bright's disease*. The remarkable claim was made for them that not only did they have a valuable diuretic effect, but that they exercised a beneficial effect upon the kidney, causing marked diminution in the excretion of albumin. Later experience, however, has not justified the earlier enthusiasm, and the use of the metal, except as a carrier of therapeutically active acids, has almost dropped out of vogue. By some it is believed that the strontium salts are less liable to disturb digestion. Especially has this been urged in regard to the salicylate, but in the experiments of Blankenhorn (*J. A. M. A.*, 1916, lvi, 331), there was no difference in the effects of the strontium and sodium salicylate.

STROPHANTHINUM. U. S.

STROPHANTHIN Strophanthin.

(strō-phan-thĭ'nŭm)

"A glucoside or mixture of glucosides obtained from *Strophanthus Kombe* Oliver (Fam. *Apocynaceæ*). Preserve it in well-closed containers, protected from light." *U. S.*

Strophantine, *Fr. Cod.*; Strophanthin, *G.*

Preparation.—*Strophanthin* may be prepared by Fraser's process of depriving the ground seeds of fatty oil by percolation with petroleum benzin, making a tincture from the marc with 70 per cent. alcohol, distilling, evaporating and treating the extract with water; this solution is then filtered and the filtrate precipitated with tannic acid; the precipitate is washed, mixed with litharge, dried and exhausted with alcohol; by adding ether to the alcoholic liquid, strophanthin is precipitated. For an improved method, see Rowe, *J. A. Ph. A.*, 1916, v, 1183.

Properties.—It is officially described as "a white or yellowish powder containing varying amounts of water, which it does not lose entirely without decomposition. It is permanent in the air. *Great caution must be used in tasting it and then only in very dilute solutions.* Strophanthin is very soluble in water and in diluted alcohol, less soluble in dehydrated alcohol; nearly insoluble in chloroform, ether, or benzene. Its solutions are neutral to litmus and are dextrorotatory. Sulphuric acid added to Strophanthin produces an emerald-green color, changing to brown. Add a trace of ferric chloride T.S. and a few mils of sulphuric acid to an aqueous solution of Strophanthin; a red-brown precipitate is produced which turns dark green after one or two hours. No weighable ash remains on incinerating 0.1 Gm. of Strophanthin. A solution of 0.1 Gm. of Strophanthin in 15 mils of distilled water, when mixed with 5 mils of hot alkaline cupric tartrate V.S., produces no precipitate; but on heating an aqueous solution to 70° C. (158° F.), with a small amount of dilute hydrochloric acid (1 in 20) it is hydrolized into strophanthidin, which precipitates, and a sugar which remains in solution. The latter is capable of reducing alkaline cupric tartrate V.S." *U. S.*

For further details of the various kinds of strophanthin and their properties, see *Strophanthus* and *Acocanthera* (Part II).

Uses.—Strophanthin fully represents the therapeutic properties of strophanthus. While occasionally used by the mouth it is usually reserved where it is desirable to administer the drug by injection. On account of its intense local irritant effect the hypodermic injection is not to be recommended, the drug may, however, be thrown into the muscle substance or better, directly into a vein. In cases of severe *circulatory failure*, such as that seen in *pneumonia* and other infectious diseases, in *collapse* from *ether anesthesia*, and in *uremia*, striking results are often obtained by the intravenous injection of strophanthin. Bailey (*J. P. Ex. T.*, 1909, i, p. 349) finds the treatment of the utmost value as an emergency measure in broken compensation of *heart disease*, but not suitable for continuous use.

The confusion concerning the identity of the various strophanthins, as well as the extraordinary difference in their activity according to the channel of administration, has given rise to great diversity of statement as to the proper dosage of these glucosides. A long summary of the literature on this subject is given in *Merck's Report* for 1912, as a result of which the conclusion is reached that when given in-

travenously G-strophanthin is nearly twice as strong as the K-strophanthin (the official), but that when exhibited by the mouth G-strophanthin is very much weaker than the official. The conclusions reached from this article are that the maximum *daily* dose of these glucosides should not exceed for G-strophanthin, intravenously, one sixty-fourth of a grain (0.001 Gm.), by mouth, one-half grain (0.032 Gm.). Of the K-strophanthin intravenously, one-fortieth grain (0.0016 Gm.), by mouth, one-twentieth of a grain (0.003 Gm.).

For a discussion of the various strophanthins, see *Strophanthus.*

Dose, one two-hundredth of a grain (0.0003 Gm.).

STROPHANTHUS. U. S. (Br.)

STROPHANTHUS Strophanth.

(strō-phăn-thŭs)

"The dried, ripe seeds of *Strophanthus Kombe* Oliver, or of *Strophanthus hispidus* De Candolle (Fam. *Apocynaceæ*), deprived of the long awns. If made into the official tincture and assayed biologically the minimum lethal dose should not be greater than 0.00006 mil of tincture, or the equivalent in tincture of 0.0000005 Gm. of ouabain, for each gramme of body weight of frog. Preserve Strophanthus in tightly-closed containers, adding a few drops of chloroform or carbon tetrachloride, from time to time, to prevent attack by insects." *U. S.* "Strophanthus Seeds are the dried ripe seeds of Strophanthus Kombé, *Oliver,* freed from the awns." *Br.*

Strophanthi Semina, *Br.;* Strophanthus Seeds; Strophantus, *Fr. Cod.;* Semen Strophanti, *P. G.;* Strophanthussamen, *G.;* Strofanto, *It.;* Estrofanto (Semilla de), *Sp.*

Strophanthus continues to have considerable interest among pharmacognosists and pharmacologists. There is no fixed principle of agreement in the several pharmacopœias. Meyer (*A. Pharm.,* 1908, p. 51) very correctly states that it is for the pharmacologist and therapeutist to determine the relative values of each of the seeds before it is possible to determine whether one specis may be substituted for another. In Germany the needs of *Strophanthus hispidus* are preferred because of their guaranteed purity. (*Ber. d. D. Pharm. Ges.,* xviii, p. 284.) On the other hand, the British Pharmacopœia, the French Codex and the Swiss Pharmacopœia confine their official definitions to *S. Kombe.* The U. S. Pharmacopœia alone recognizes both species, the *S. hispidus* being added because of the arguments that have been advanced in this country as to the efficacy of these seeds. The literature in recent years on the question of strophanthus has been quite voluminous. Some of the more interesting articles being the following: Thoms (*Arb. a. d. Pharm. Inst. d. Univ. Berlin,* 1905, p. 74); Gilg (*Ibid.,* p. 59); Pabisch (*Zeit. Oest. Apoth. Ver.,* xlvii, p. 509); Gilg (*B. P. G.,* xviii, p. 284); Hartwich (*Ap. Ztg.,* xxvi, p. 94).

According to Engler and Prantl, there are twenty-eight recognized species of the genus found in Africa and Asia, extending to China, the East Indies, and the Philippines. The commercial drug is often largely composed of the seeds of other than the recognized official species, and may contain the seeds from related genera, especially those of *Kickxia africana* Benth. The seeds of *Kickxia africana* are without hairs, spindle-shaped, not flattened, twisted into an S-like shape, and with the base and the summit of the seed alike in their forms. On cross-section the cotyledons are seen much folded, while those of the strophanthus lie parallel one upon the other. The transverse section of the kickxia seed, when treated with concentrated sulphuric acid, first turns brown, then red, while the seeds of both kinds of strophanthus take on a green color. According to Stapf, the plant represents a new genus and should be known as the *Funtumia africana;* the only other species of the genus, *F. elastica,* yields India rubber.

The seeds of all the species of strophanthus apparently possess hairs that have a characteristic thickened base somewhat resembling those of nux vomica seeds. The seeds of various species of the genus strophanthus are used for the preparation of arrow poison in Africa, at Kombé in the Manganja country, in the Gaboon district, and in Guinea and Senegambia. In Gaboon this poison is called *inée, onaye,* or *onage.* (See also *Acocanthera,* PART II.) The plant which yields the arrow poison of Kombé was first brought to Europe by Sir John Kirke and described as a new species by Oliver, of Kew, under the name of *S. Kombe.* There can be no doubt that much of the Strophanthus of commerce is yielded by other species. *S. Kombe* grows solely in East Africa, as far as is known, so that all of the drug coming from West Africa must be yielded by other species. The tracing of the origin of the seeds is made more difficult by the fact that in Africa seeds from different regions are mixed before shipment. The seeds of *S. hispidus* enter commerce, as do also those of *S. glaber, S. emini,* and *S. courmontii.* (*P. J.,* 1899, lxiii, p. 321.) A white woolly strophanthus is said to be yielded by *S. Nicholsoni,* a species first characterized by Holmes (*P. J.,* 1897, lix, 208). *S. gratus* of Sierre Leone also contributes its seeds; also *S. glaber* contains *ouabain,* which, according to Karsten, is identical with strophanthin. (*C. R. A. S., cxxvi,* 346.)

Sharp (*P. J.,* 1912, lxxxviii, p. 159) has found that the seeds of the *S. courmontii* are about one-fourth as poisonous to frogs as those of the *S. Kombe,* but their physiological effects are of a similar type. The seeds of the *S. emini* Asch, he found to be almost without action upon the frog's heart. The seeds of the *S. Thalloni* and of the *S. Tarmentosus* A. D. C., are also active.

S. hispidus when by itself takes the form of a bush, but usually occurs as a woody climber inhabiting the forests between the coasts and the center of the African continent. It reaches

to the tops of the highest trees, coiling on the ground, and hanging in festoons from tree to tree. The stem is several inches in diameter. The flowers are cream-colored, yellow at the base, purplish-spotted above. They are grouped in terminal cymes. The lobes of their gamopetalous corollas are prolonged into very narrow tail-like ends being nine or more inches in length. They last but a short time during the months of October and November. The fruit, a pair of follicles from 10 to 17 inches long, is ripe in June, and is gathered by the natives, who scrape off the husks (epicarp and mesocarp) before drying, and preserve the more leathery internal inner covering (endocarp) with the enclosed seeds; hence the pods as they appear in commerce are smooth and of a tawny color. The seeds themselves are covered with long comose hairs, which, being deciduous, are apt to be lost before the escape of the seed from the pod. In preparing the arrow poison, the natives are said to pound the seeds deprived of their hairs to a pulp, add the adhesive sap of another plant, and simply smear the mixture for six inches along the point of the arrow. Game wounded by such an arrow is said to be rarely able to move a hundred yards, and the flesh is eaten without bad effect. Karsten has examined the *root* of Strophanthus hispidus and found that it contained *trigonelline, choline* and *strophanthin* in such small proportions that it will probably never be commercially valuable. (*B. P. G.,* 1902; 12, 241.)

Properties.—Strophanthus occurs in commerce either in pods or as clean seeds. Helbing states (*P. J.,* March, 1887) that he has found the seeds to constitute about 37 per cent., the pod (endocarp) 37 per cent., and the hairs about 25 per cent., and says that the quality of the pods may be determined by examining the color of the pappus. If this is white and bright, the seeds and pods are in good condition.

At present strophanthus seeds are much less mixed than formerly. In 1892 Hartwich classified commercial strophanthus seeds (*A. Pharm.,* 1892, 401), in the following groups: (1) The official products yielded by *S. hispidus* or *S. Kombe,* which contain strophanthin and no crystals of calcium oxalate. (2) Those resembling the official seeds, but of different habitat—viz., Mozambique and Sierre Leone. (3) Those which contain calcium oxalate crystals, but no strophanthin—viz., Senegal, Lagos, Niger, German East Africa, Togoland, and Baol of Senegal. (4) A very hairy seed from the Upper Niger. The hairs vary in color from a silky white to brown; the embryo contains calcium oxalate crystals, but the seeds do not contain strophanthin. (5) Seeds which are said to be glabrous, but possess hairs in the region of the raphe. These include those from Lagos and Zambesi, and contain neither calcium oxalate crystals nor strophanthin. In 1896 S. E. Jelliffe stated that there are in the American market two hairy seeds, the product respectively of *S. hispidus* (Kombe) and *S. asper,* and one smooth seed, *S. gratus* of the Gaboon. (See *D. C.,* 1896, 101.) The seeds of *S. Gratus* are recommended by E. Gilg as more easily recognized than the others and because it yields strophanthin more readily in crystalline form. (*B. P. G.,* 1904, 90.) There are two chief varieties both of which are now official.

The more important of the rarer varieties of strophanthus are composed of seeds which at one time were much mixed in Africa before exportation with those of *S. Kombe* and *S. hispidus* and are the products of two species, *S. glabra* and *S. Thalloni.* The seeds of *S. glabra* are about 13 to 16 Mm. long from 3 to 4½ Mm. wide, and from 1 to 1½ Mm. thick. They are lanceolate with a rounded or truncated base and a long attenuate apex. The ventral face is flat or concave, the dorsal being convex, and possesses sometimes a small keel near the shaft. The surface is glabrous, of a dull waxy appearance; the color varies from an ochre-yellow to a fawn or cinnamon; the odor is characteristic; the fracture is horny and the taste extremely bitter. The hairs of the awn are about 7 Cm. in length, numerous, silky, white, and when viewed in a mass yellowish or grayish. The seed coat is relatively thin; the albumen is thick and cartilaginous; the embryo is not thick, the radicle is as long as in *S. hispidus* or *S. Kombe.* With concentrated sulphuric acid the color changes from yellow to rose and finally to violet. For an elaborately illustrated article on the histology of *S. Kombé,* by P. E. F. Perredes, see *W. C. R. L.,* No. 15; see also *B. P. G.,* 1904, 104, 120.

The seeds of *S. gratus* (Wall et Hook.) Franch, are characterized by their uniform and reliable activity and it has been suggested that they may replace advantageously those of *S. Kombe.* They are obtained from plants growing in the Senegal and Congo, the same region in which *S. hispidus* is found. According to Gilg the seeds are spindle-shaped, being at the basis more or less rounded, although sometimes truncate. In the upper portion, they are sharply angular, sometimes being winged and gradually tapering at the summit. Externally the seeds are of a characteristic yellow or yellowish-brown. They vary in length from 11 to 19 Mm., in breadth from 3 to 5 Mm., and in thickness from 1 to 1.3 Mm. In taste they are strongly and persistently bitter. On the addition of sulphuric acid to microscopic sections the latter are colored reddish or of a rose tint, changing to a deep red or violet.

The seeds of *S. Thalloni* are very long and narrowly spindle shaped, tapering above and below, and covered with numerous brownish hairs. A smooth blackish-brown Strophanthus seed is said to be sent into commerce from Indo-Malaya.

The seeds of *S. Courmontii* are 8 to 14 Mm. in length, 2.5 to 3.5 Mm. in breadth and 1 to 2 Mm. in thickness; of a distinctly lanceolate form and decidedly brown color, often with the hairs rubbed off, but having a golden sheen when these remain, while the tint is dull and

reddish when they are absent. The ridge on the ventral surface is indistinct and the arrangement of the hairs in longitudinal rows is not as apparent as in the official seed. They also contain crystals of calcium oxalate in abundance, which have been stated by some observers to be entirely absent from *S. Kombe* and *S. hispidus* but are in fact there in very small amount. The seeds of *S. elemi* are grayish-green in hue and contain crystals of calcium sparingly in the embryo. The statement of E. M. Holmes (*P. J.*, lxiv) that the seeds of *S. Kombe* and *S. hispidus* give with sulphuric acid a greenish reaction, while those of *S. Courmontii* give a reddish, and *S. elemi* a yellowish-brown changing into reddish, seems not to be absolutely accurate, for while the seed albumen of *S. Kombe* always gives the greenish reaction the cotyledons frequently are mottled with red and rarely give an entirely red reaction. (Perredes.)

Strophanthus is officially described as "lance-ovoid, flattened and obtusely edged; from 7 to 20 mm. in length, about 4 mm. in breadth and about 2 mm. in thickness; externally of a light fawn color with a distinct, greenish tinge, silky lustrous from a dense coating of closely appressed hairs (*S. Kombe*); or light to dark brown, nearly smooth and sparingly hairy (*S. hispidus*), bearing on one side a ridge running from about the center to the summit; fracture short and somewhat soft, the fractured surface whitish and oily; odor heavy when the seeds are crushed and moistened; taste very bitter. Under the microscope, sections of *Strophanthus Kombe* show a seed-coat composed of several layers of more or less collapsed, thin-walled cells and from the epidermal layer arise numerous non-glandular hairs, which are from 0.2 to 0.8 mm. in length, usually more or less bent, thin-walled, and slightly lignified at the base; in the rhaphe occurs a tangentially elongated fibro-vascular bundle having numerous spiral tracheæ; endosperm of from 9 to 30 rows of more or less polygonal cells with slightly thickened walls and containing small aleurone grains, a fixed oil, and strophanthin, the latter being colored bright green upon the addition of sulphuric acid; in the center occur two large plano-convex cotyledons having a distinct epidermal layer, a few fibro-vascular bundles and numerous parenchyma cells containing aleurone grains, a fixed oil, and occasionally a small amount of strophanthin. Sections of *S. hispidus* resemble those of *S. Kombe*, the hairs being fewer and the bases more strongly lignified. The powder is grayish-brown to dark brown; odor distinct; when examined under the microscope it exhibits chiefly thin-walled parenchyma cells and fragments of long, thin-walled hairs, the latter relatively few in *S. hispidus;* mounts made with hydrated chloral T.S. show numerous oil globules; upon the addition of sulphuric acid many of the fragments of the endosperm may be colored greenish. Strophanthus yields not more than 5 per cent. of ash." *U. S.*

The seeds of *S. Kombe* are described in the British Pharmacopœia as "oval, acuminate, about fifteen millimetres long and four millimetres broad; flattened, narrowed towards the base, which is obtuse; covered with silky appressed hairs; provided on one side with a longitudinal ridge running from the centre to the apex; of a greenish-fawn color. Kernel white and oily; cotyledons straight; endosperm narrow; in the seed-coats not more than an occasional crystal of calcium oxalate. Characteristic odor; taste very bitter. *Sulphuric acid* diluted with one-fifth of its volume of *water* colors the endosperm, and sometimes the cotyledons, dark green (presence of strophanthin)." *Br.*

Assay.—"For a method of assaying Strophanthus, see Biological Assays (Part III)." *U. S.*

The U. S. P. recognizes the biological assay as the only satisfactory method.

The Qualitative Examination of Strophanthus Seeds.—C. Hartwich (*A. Pharm.*, 1892) declares the usual course for the qualitative examination of strophanthus seeds—as the external appearance, the bitter taste, and the few chemical tests—insufficient, and recommends a microscopical test for strophanthin to supplement the usual tests. In the examination of a great variety of strophanthus seeds some were found to contain starch, which is rarely present in the commercial article.

For the valuation of the seeds the presence of strophanthin may be ascertained in the following manner. A thin cross-section of the seed is placed on a glass slide and covered with a drop of concentrated sulphuric acid. The endosperm at least should assume an intense green color, which is easily seen with a hand-glass. Often the green is preceded momentarily by a blue color. The cotyledons are also colored green, but generally less intensely than the endosperm. Gradually the color changes through blue into red, and after one-quarter to one hour it disappears. In seeds which contain but little strophanthin the endosperm alone is colored green, while the embryo is colored yellow and then red, or only the epidermis and the adjacent cells are colored in addition. For testing the tincture three drops are taken, and for the extract a piece a little larger than a pin head. In either case mix the drug with a half-drop of ferric chloride solution and three drops of sulphuric acid. A brown precipitate is formed which is distinctly green after one hour, and should retain the color for fully three hours.

Chemical Properties.—Hardy and Gallois obtained from strophanthus two crystalline principles. One, a glucoside, they call *strophanthin;* the second, an alkaloid, they name *inœine.* The first-named appears to be the active principle of the poison. (*J. P. C.*, 3e sér., xxv, p. 176.) T. R. Fraser describes more fully the glucoside strophanthin. (*P. J.*, 1886, July 23.) When heated with dilute sulphuric aicd it yields glucose and *strophanthidin,* which is insoluble in water, is very soluble in alcohol, and has a strongly bitter taste. In a subsequent study Fraser (*A. J. P.,*

1889, p. 532) has found strophanthin difficult to separate, but obtained it pure by a somewhat tedious process, depending upon the formation of a tannate and subsequent decomposition by lead oxide. It yielded upon analysis results corresponding to the formula $C_{30}H_{34}O_{10}$. Thoms (*Ber. d. Chem. Ges.*, 1898, 534) obtained pure strophanthin. Arnaud gives its formula as $C_{31}H_{48}O_{12}$; this was confirmed by Kohn and Kulisch and has been adopted by the French Codex. Feist gives its composition as $C_{40}H_{66}O_9$. Thoms found that the strophanthins as obtained from different species differ somewhat in chemical composition and properties and he proposes to designate them as follows: *k-strophanthin* when obtained from *S. Kombe; g-strophanthin* (*S. gratus*), *e-strophanthin* (*S. Emini*), *h-strophanthin* (*S. hispidus*). To g-strophanthin he gives the formula $C_{30}H_{46}O_{12} + 9H_2O$. G. strophanthin seems to be identical with *ouabain* (see *Acocanthera*, Part II). *Strophanthidin* has the formula $C_{23}H_{32}O_7 + 1\frac{1}{2}H_2O$. Strophanthidin, the product of decomposition of the glucoside, is described as having an intensely bitter taste and a neutral reaction, and as being very slightly soluble in water, moderately soluble in cold and freely in warm alcohol. It crystallizes with great readiness. No alkaloid was detected, but in the lead precipitate from an aqueous solution of the alcoholic extract a compound was found of strongly acid reaction and freely soluble in water, to which the name of *kombic acid* has been given. The experiments of Fraser have shown that the active principle of strophanthus is most abundant in the seeds, but that it is contained also in the follicles and the hairs. Pharmaceutical preparations of the drug should, therefore, be made from the separated seeds, while the pericarp and the hairs may be employed for the manufacture of strophanthin. For methods of assaying strophanthus see *D. C.*, 1900, 132.

After reviewing all of the proposed assay methods for this drug, Lampart and Mueller (*A. Pharm.*, ccli, 609) proposed a method based upon the preliminary extraction of the drug with absolute alcohol, the removal of oil from the percolate with petroleum ether, the conversion of the glucosides into strophanthidin by boiling with hydrochloric acid and the subsequent extraction with chloroform, weighing, and calculating to strophanthin by multiplying by the factor 2.187. The authors received the Hagen Bucholz prize of the German Apothecaries Society for this work.

Uses.—As was first shown by Thomas R. Fraser (*J. A. P.*, vii, p. 141), strophanthus belongs to that group of cardiac poisons of which digitalis is the type. Its effects upon the circulation are so similar to that drug (see page 408), that it is only necessary to note the points of difference. Strophanthus is somewhat more rapid in its action and decidedly less permanent than digitalis; it causes relatively less reduction of the pulse rate and is generally believed to have less influence on the vasomotor mechanism. It appears to be absorbed from the intestinal tract with much less regularity than digitalis and therefore is less certain in its effects. Besides its action upon the circulation, strophanthus has a marked influence on intestinal peristalsis, according to Magnus (*A. G. P.*, 1905, cviii, p. 1) causing increased peristalsis and tone and under certain conditions tetanic spasm of the intestines. Probably because of this action it frequently produces diarrhea when used clinically. According to the early researches of Fraser it exercises a similar influence on all forms of muscle tissue including voluntary muscles. It is by some believed that strophanthus has a direct stimulating effect upon the kidney and is superior to digitalis as a diuretic, but the evidence in favor of this view is far from convincing. While it possesses some local anesthetic powers it is so highly irritant that it is practically unavailable for this effect.

Strophanthus is used in medicine solely for its influence on the circulation, especially in cases of *chronic heart weakness*. It is of value in exactly the same class of cases in which digitalis is employed and, although more likely to cause digestive disturbances, is frequently useful as an alternative or adjuvant to that drug. By some it is believed to be especially indicated in those cases complicated with dropsies, because of a belief in a greater diuretic power. In cases of threatening urgency the effects of strophanthus upon the circulation can be obtained almost immediately by means of the intravenous injection of its active principle (see *Strophanthinum*).

The question of the relative variability of potency in strophanthus as compared to digitalis cannot as yet be definitely answered. Although certain German investigators have claimed that strophanthus is more subject to wide range in power, Hatcher and Bailey (*J. A. M. A.*, 1909, lii, p. 5) have found that the tincture of strophanthus is much more uniform in this country than the tincture of digitalis.

Dose, of strophanthus, one-fourth to one grain (0.016–0.065 Gm.).

Off. Prep.—Extractum Strophanthi, *Br.*; Tinctura Strophanthi, *U. S.*, *Br.*

STRYCHNINA. U. S., Br.

STRYCHNINE Strych.

(strȳch-nī'nạ)

"An alkaloid [$C_{21}H_{22}O_2N_2 = 334.20$] obtained from nux vomica, and also obtainable from other seeds of the *Loganiaceæ*. Preserve it in well-closed containers." *U. S.* "Strychnine, $C_{21}H_{22}N_2O_2$, is an alkaloid, obtained from the seeds of Strychnos Nux-vomica, *Linn.*, and other species of Strychnos." *Br.*

Strychnia, *U. S.* 1870; Strychninum; Strychnine, *Fr. Cod.*; Strychnin, *G.*; Stricnina, *It.*; Estricnina, *Sp.*

The U. S. and Br. Pharmacopœias very properly omit processes for preparing this alkaloid, as it can be made profitably only by the

manufacturing chemist on a large scale. (See U. S. D., 17th ed., p. 1295.)

J. F. Molyn proposed, previously to the extraction of strychnine, to subject nux vomica to fermentation, by which the saccharine and gummy matters of the seeds are decomposed, and lactic acid is formed, which decomposes the strychnine and brucine igasurates, producing with these bases very soluble lactates. For the particulars of this process, see *A. J. P.*, xix, 99, and for other processes see U. S. D., 14th ed., p. 1456.

The bean of St. Ignatius yields strychnine more easily and more largely than nux vomica. If thought desirable, brucine may be in great measure separated from the strychnine of commerce, by dissolving the latter in very dilute nitric acid, filtering, and concentrating. Brucine nitrate crystallizes in short, thick, dense prisms grouped together; strychnine nitrate in radiated tufts of long, light, capillary needles. By gentle agitation of the liquid, the latter salt is suspended and may be poured off, leaving the former. The alkaloids may be obtained by dissolving the salts in water, and precipitating with ammonia.

Properties.—As usually found in commerce, strychnine is a white or grayish-white powder. When rapidly crystallized from its alcoholic solution, it has the form of a white, granular powder; when slowly crystallized, that of elongated octohedra, or rhombic prisms with pyramidal summits. It is officially described as in "colorless, transparent, prismatic crystals, or as a white, crystalline powder; odorless, permanent in the air. *Great caution must be used in tasting it and then only in very dilute solutions* which are exceedingly bitter. One Gm. of Strychnine dissolves in 6420 mils of water, 136 mils of alcohol, 5 mils of chloroform, and in 180 mils of benzene at 25° C. (77° F.); also in 3100 mils of boiling water, and 34 mils of boiling alcohol; very slightly soluble in ether. Its saturated solutions are alkaline to litmus and are lævorotatory. Sulphuric Acid containing 1 per cent. of ammonium vanadate produces with Strychnine a deep violet-blue color, changing to a deep purple, and finally to a cherry-red. A solution of about 0.1 Gm. of Strychnine in 2 mils of sulphuric acid is not more than pale yellow (*readily carbonizable organic impurities*), but on adding a fragment of potassium dichromate, a deep blue color is momentarily produced, changing to deep violet, then to purplish-red, cherry-red, and finally to orange or yellow. Incinerate about 1 Gm. of Strychnine; not more than 0.1 per cent. of ash remains. One mil of a mixture of equal volumes of nitric acid and distilled water, added to about 0.1 Gm. of Strychnine, may produce a yellow, but not a red or reddish color (*brucine*)." *U. S.*

"Colorless, transparent, prismatic crystals, permanent in the air. Very slightly soluble in *water*, but sufficiently soluble to impart an intensely bitter taste; soluble in about 150 parts of *alcohol* (90 per cent.). *Sulphuric acid* forms with it a colorless solution which, on the addition of *nitric acid*, acquires not more than a faint pink color (limit of brucine). When a small fragment is dissolved in 2 or 3 drops of *sulphuric acid* on a white porcelain plate and a crystal of *potassium bichromate* is slowly moved through the solution, an intense violet color is produced, passing to red and yellow. No appreciable ash." *Br.*

It melts like a resin, is decomposed at a comparatively low temperature, and entirely dissipated at a red heat. Guy obtained a crystalline sublimate, at a heat but a few degrees below that at which it begins to change color and undergo decomposition. Its melting point has been given as 284° C. (543° F.), but, according to Flückiger, in small portions it melts as low as 225° C. (437° F.) and can with care be sublimed without decomposition. According to Waddington, when heated to decomposition it emits a most suffocating odor, resembling the odor of asphaltum. (*P. J.*, March, 1868, p. 413.) Fused with an excess of potassium hydroxide, it yields, according to Goldschmied (*Ber. d. Chem. Ges.*, 15, p. 1977), *indol*, C_8H_7N, and when distilled with zinc dust it yields a *dimethyl pyridine*, C_7H_9N, and *carbazol*, $C_{12}H_9N$. The volatile oils dissolve it freely. Petroleum benzin dissolves 0.607 per cent. of it, and amyl alcohol 0.55 per cent. (Dragendorff, *J. P. C.*, 4e sér., iv, 473.) It has an alkaline reaction on test-paper, and forms salts with the acids. Nitric acid does not redden it if perfectly pure, but often reddens it as found in commerce, in consequence of the presence of brucine. Eugène Marchand proposed the following test by which a very minute proportion of strychnine may be detected. If a little of the alkaloid be rubbed with a few drops of concentrated sulphuric acid containing one-hundredth of nitric acid, it will be dissolved without change of color; but if the least quantity of lead peroxide be added to the mixture, a magnificent blue color will be instantly developed, which will pass rapidly into violet, then gradually to red, and ultimately become yellow. (*J. P. C.*, 3e sér., iv, 200.) Otto recommended as a test a minute quantity of solution of potassium dichromate, which, added to the solution of strychnine in concentrated sulphuric acid, produces a splendid violet color. (*A. J. P.*, xix, 77.) A similar change of color is produced, according to E. W. Davy, by substituting a strong solution of potassium ferricyanide (red potassium prussiate) for that of potassium dichromate. (*A. J. P.*, xxv, 414.) It appears that any substance capable of yielding nascent oxygen readily will serve to develop the characteristic violet color, when applied after the addition of sulphuric acid. According to Wm. Copney, the least efficacious agent is potassium chlorate, a much better is lead dioxide, a still better is manganese dioxide, and the best of all is potassium dichromate, and the general result of numerous experiments, recently made, is that the last-mentioned agent is the most effec-

tive. The sulphuric acid must be of not less sp. gr. than 1.84. The play of colors, according to Copney, is first blue, then purple, then crimson, which is followed by red and green, the latter sometimes giving place to yellow. It is stated that the 1-500,000th part of a grain may be detected. (See *A. J. P.*, xxviii, 459.) On the other hand, some chemists have found difficulties with the potassium dichromate test. Thus, Brieger (*Jahresb.*, 1850, p. 617) found that, unless the substance was first moistened with sulphuric acid and the dichromate added to it subsequently, the reaction of strychnine was interfered with by quinine, morphine, and especially by sugar. Sonnenschein (*Fresenius's Zeitschrift*, ix, p. 495) found that ceroso-ceric oxide was much more sensitive as a reagent to use with sulphuric acid for strychnine than potassium dichromate. This fact we can confirm from experience. It gives a blue color lasting longer, which then becomes violet, and then a permanent cherry-red. Vanadio-sulphuric acid (1 part of ammonium vanadate dissolved in 200 parts of pure sulphuric acid of 1.84 sp. gr.) is colored by strychnine at first violet-blue, passing into violet, and finally cinnabar-red. On dilution with water this color remains rose-red. According to Dragendorff, the color persists when as little as 0.001 milligramme of strychnine is used.

A reaction, more sensitive than the sulphuric acid and potassium dichromate test for detecting strychnine and sensitive to 0.01 Mgm. of the alkaloid, is proposed by G. Guerin (*P. J.*, xciii, p. 83) as follows: The alkaloidal residue is dissolved in 2 or 3 drops of sulphuric acid and then 2 or 3 Mgm. of manganese carbonate is added. On stirring, a blue color, gradually changing to violet and finally to pink, is produced. Landerer has found that solid iodic acid or potassium iodate heated gently with strychnine gives rise to a beautiful violet color, gradually passing to red, which remains unchanged for many days. (*A. J. P.*, March, 1861, p. 110.)

Wm. T. Wenzell states that, when very minute quantities of the alkaloid are being dealt with, much the best plan is to prepare a reagent by dissolving in 2000 grains of sulphuric acid one grain of potassium permanganate. The alkaloid, during the evaporation of its acidulated solution on the porcelain, collects in the margins of the film, and the smallest possible dot of the reagent is to be placed so that its margin comes in contact with that of the film. In this way, Wenzell affirms, he was able to detect 1-900,000th part of strychnine. (*A. J. P.*, xlii, 385.) Some doubt was thrown upon the value of this test by experiments which seemed to prove that the presence of morphine in excess, especially in connection with organic matter, so far modified or disguised the action of the test upon strychnine as to prevent the appearance of the characteristic color, but subsequent and carefully conducted experiments by Robert P. Thomas satisfactorily determined that the conclusions in relation to the effects of morphine were erroneous, and that whether alone or associated with organic matters, in small or in large quantity, it does not prevent the operation of this color-test if carefully applied. (*Am. J. M. S.*, Oct., 1861, and 1862, 1340; also *J. Am. C. S.*, 1894, No. 12.) J. U. Lloyd in his novel "Stringtown on the Pike" used in an interesting manner a color reaction which he had discovered that produced a color which might deceive some who were working on a toxicological investigation in strychnine poisoning. *Lloyd's reaction* consists in adding sulphuric acid to a mixture of 1 part of hydrastine and 4 parts of morphine and adding a little potassium dichromate in the manner in which the color test for strychnine is made; colors are produced which somewhat resemble those given by strychnine, but a careful toxicologist could not be deceived. A controversy ensued upon the announcement of the reaction, participated in by Williams, Mayer, Wangerin, Wharton, and others, the result of which proved that the value of the official color test of strychnine had not been seriously assailed. (See *D. C.*, 1901, 28, 48; Proc. *N. Y. State Pharm. Assoc.*, 1901, 252; *Amer. Drug.*, 1903, 66.)

Strychnine consists of carbon, hydrogen, nitrogen, and oxygen and has the formula $C_{21}H_{22}O_2N_2$. The salts of strychnine are for the most part soluble and crystallizable. Their solution is decomposed by the alkalies and their carbonates, and by tannic but not by gallic acid, and is not affected by ferric salts. They are precipitated by the solution of iodine in potassium iodide, and the precipitate, though soluble in alcohol, is insoluble in the diluted acetic and hydrochloric acid of the U. S. Pharmacopœia. (Fairthorne, *A. J. P.*, xxvii, 212.)

Strychnine is likely to contain impurities, of which the chief, besides brucine, are coloring matter and lime or magnesia. The two latter impurities are left behind when the adulterated alkaloid is incinerated in the open air. Pure strychnine leaves no ash under these circumstances. Brucine is detected by the red color which it yields with nitric acid. Neither this nor sulphuric acid colors strychnine—a test which distinguishes it from several other alkaloids.

Uses.—Strychnine is a stimulant to the whole central nervous system. The effects upon the brain are usually not well marked but in some individuals wakefulness often follows its use and the increased acuity of the special senses is further evidence of its stimulant action upon the cerebrum. The most direct symptom caused by strychnine is violent convulsions. These have been shown by McGuigan and Becht (*J. P. Ex. T.*, 1916, viii, 143), to be due to a simultaneous stimulation of both motor and sensory ganglia of the spinal cord. In the medulla the centers which show a special evidence of the stimulating effect of strychnine, are those governing respiration and vasomotion. While the increase in respiration caused by strychnine is not as great in the normal animal as after

some other drugs, it seems to possess an extraordinary power of overcoming the effects of depressant poisons. Clinically it is perhaps the most reliable respiratory stimulant which we possess. During the strychnic convulsion there is great rise in the blood pressure. This is due in large part to the violent spasm of the muscles and consequent asphyxia, but even when the convulsions are prevented by the previous injection of curare the drug still produces a distinct rise in the arterial pressure, indeed in doses too small to cause convulsions there is still evidence of a stimulation of the vasomotor center. The experiments of Pilcher and Sollman (*J. P. Ex. T.,* 1915, vi, p. 331), indicate that the effect is due largely to an increased irritability of the center so that it responds abnormally powerfully to any exciting influence. The effect of the drug upon the heart is not clearly understood. Although La Franca (*Z. E. P. T.,* 1911, ix, p. 436) found that strychnine increased the irritability and conductivity of the heart muscle the scientific evidence of any direct influence upon the heart is far from convincing. In large toxic dose strychnine causes a paralysis of the motor nerves similar to that produced by curare but it is improbable that this action can play any part in strychnine poisoning in the human being.

The convulsant effects of strychnine naturally suggest its use in *paralysis* but a moment's thought must convince anyone that in most forms of palsies it is incapable of benefit. When the loss of power depends upon the actual destruction of motor cells, as after apoplexy or poliomyelitis, it is evident that the drug can do no good because what does not exist cannot be stimulated. Or when there is a failure in the conducting power of the nerve, as in peripheral neuritis, it is equally manifest that excitation of the spinal cells is futile. Indeed in spinal paralyses much harm may be done by irritating the inflamed tissue in the neighborhood of the area of destruction. On the other hand when the paralysis is due to the effect of depressant poisons circulating in the blood, as, for instance, in certain types of *chronic lead poisoning,* strychnine may prove of the utmost value. Like other bitters strychnine improves the appetite and digestion, but it has been enormously misused as a "general tonic." It is to be remembered that strychnine is essentially a stimulant leading to an increased functional activity with an expenditure, rather than a storing up, of reserve power. Such slight tonic effects as it may possess are due to the improved digestion and circulation. There is a common belief among clinicians that strychnine increases the peristaltic activity of the intestinal tract and hence it is frequently added to laxative mixtures, but the experimental evidence on this point is contradictory.

As a circulatory stimulant strychnine is useful in a wide variety of conditions such as *surgical shock, collapse* from hemorrhage, *poisoning* by such depressants as ether, chloroform, or alcohol, and the adynamic stages of *infectious fevers.* In some forms of *chronic heart disease,* especially in *myocarditis,* despite the failure of pharmacologists to explain its modus operandi it seems to be clinically useful. Its value in *chronic bronchitis* in old and feeble subjects is probably also to be attributed to its effects upon the circulation. As a respiratory stimulant it is especially valuable in narcotic poisoning, as by opium or chloral. Strychnine is also asserted to be of much service in toxic *amblyopias,* especially that due to nicotine poisoning.

For ordinary purposes the dose of strychnine ranges from one-sixtieth to one-twentieth of a grain (0.0011–0.003 Gm.) but under many circumstances much larger quantities may be safely administered. Especially when used for its influence upon the circulation is it essential to give large doses. Many of the clinical reports of failure to influence the circulation with strychnine have doubtless been due to too small doses, thus Lucas (*American Journ. Dis. of Children,* 1914, vii) found that it required at least one-tenth of a grain to cause an appreciable change in the blood pressure. While others have reported distinct effects from somewhat smaller dose, the use of one-fortieth or one-thirtieth of a grain with the idea of having any marked influence upon the circulation is a delusion. In many cases it is essential to push the strychnine until marked exaggeration of the reflexes or even twitchings of the muscle afford a warning that the patient is approaching the toxic stage.

Poisoning.—The symptoms of strychnine poisoning come on usually with great suddenness and violence. Often without warning of any kind a patient falls in a violent convulsion. The convulsions are usually tonic in character, but are interrupted with periods of almost complete relaxation. They involve all the muscles of the body and are brought on by the slightest sensory impulses. During the spasm the body is rigid, usually arched backwards in the position of opisthotonos, the arms flexed, the face drawn into the *risus sardonicus.* Consciousness is not affected except as the result of the asphyxiation. During the period of convulsion the muscles of the chest are so firmly fixed that respiration is impossible and death may occur as the result of asphyxiation. In some cases, however, the fatal termination may be deferred for some hours and finally be the result of exhaustion. The ordinarily fatal dose probably lies between one-half and one grain, although much larger quantities may be recovered from under proper treatment. In the treatment of strychnine poisoning it is to be remembered that the convulsions are of reflex origin and therefore all manipulations which are capable of furnishing the sensory stimulus must be sedulously avoided. For this reason no attempt should be made to empty the stomach; death has occurred during a convulsion brought on by the effort to pass a stomach tube. As a chemical antidote potassium permanganate is

probably to be preferred, although Fantus (*J. A. M. A.*, 1915, lxiv) has reported favorable results in the lower animals from the use of Lloyd's reagent (silicated earth), and compound solution of iodine or tannic acid are also of value. The most important therapeutic measure is the control of the convulsions. For this purpose chloroform is probably the most efficient remedy. This drug should be administered to the stage of surgical anesthesia after which chloral hydrate and potassium bromide may be given to continue the sedative effect. Amyl nitrite is also a useful agent because of the rapidity of its action; during the height of the convulsion, when there is no respiration, 3 to 5 minims may be given hypodermically.

In an investigation of the members of the pyridine series of bases by C. Greville Williams and W. H. Waters (*Proc. Roy. Soc.*, xxxii, p. 162, 1881), they found that β lutidine (dimethyl-pyridine, C_7H_9N) was antagonistic to strychnine and an apparent antidote. When injected into frogs already under the influence of strychnine, it arrested the convulsions; or if given first and then followed by a fatal dose of strychnine, it prevented the appearance of the tetanus. (Blyth, *Poisons, their Effects and Detection*, 1884, p. 319.)

Strychnine should never be prescribed in liquid form in combination with bromides, iodides, or chlorides, for fear of forming the insoluble strychnine hydrobromide, hydriodide, or hydrochloride. Several cases of poisoning have occurred through neglect of this precaution. A. B. Lyons (*A. J. P.*, Oct., 1877) records a case of poisoning through the patient's receiving in the last dose the greater portion of the strychnine hydrobromide, which had crystallized out.

Dose, one-sixtieth to one-fifteenth of a grain (0.0011–0.004 Gm.).

Off. Prep.—Syrupus Ferri Phosphatis cum Quinina et Strychnina, *Br.;* Elixir Ferri Pyrophosphatis, Quininæ et Strychninæ, *N. F.;* Elixir Pepsini, Bismuthi et Strychninæ, *N. F.;* Liquor Hypophosphitum Compositus, *N. F.;* Liquor Strychninæ Acetatis, *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ, *N. F.;* Pilulæ Aloini, Strychninæ et Belladonnæ Compositæ, *N. F.;* Pilulæ Antidyspepticæ, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arseni Fortiores, *N. F.;* Pilulæ Ferri, Quininæ, Strychninæ et Arseni Mites, *N. F.;* Pilulæ Laxativæ Compositæ, *N. F.;* Syrupus Ferri, Quininæ et Strychninæ Phosphatum, *N. F.;* Syrupus Hypophosphitum Compositus, *N. F.*

STRYCHNINÆ HYDROCHLORIDUM. Br.

STRYCHNINE HYDROCHLORIDE

(strȳch-nī'næ hȳ-drō-chlō'rī-dŭm)

"Strychnine Hydrochloride, $C_{21}H_{22}N_2O_2$,HCl,$2H_2O$, is the hydrochloride of the alkaloid strychnine." *Br.*

Strychninum Hydrochloricum; Hydrochlorate of Strychnine, *Br.*, 1885; Chlorhydrate de Strychnine, *Fr.;* Strychninhydrochlorid, Salzsaures Strychnin, *G.*

This salt of strychnine was made official for the first time in the Br. Ph. 1898; it is used in making *Liquor Strychninæ Hydrochloridi.* (See p. 661.) It is described as in "small, colorless, prismatic crystals. Soluble in 60 parts of *water.* Aqueous solution neutral to *litmus;* taste intensely bitter. Loses from 7 to 9 per cent. of its weight when dried at 110° C. (230° F.). Responds to the tests enumerated under 'Strychnina,' and yields the *reactions* characteristic of chlorides. No appreciable ash." *Br.*

In its physiological and therapeutic action, strychnine hydrochloride is equivalent to strychnine though slightly weaker.

Dose, one-sixtieth to one-fifteenth of a grain (0.0011–0.004 Gm.).

Off. Prep.—Injectio Strychninæ Hypodermica, *Br.;* Liquor Strychninæ Hydrochloridi, *Br.*

STRYCHNINÆ NITRAS. U. S.

STRYCHNINE NITRATE Strych. Nit.

(strȳch-nī'næ nī'trăs)

"The nitrate [$C_{21}H_{22}O_2N_2.HNO_3 = 397.21$] of the alkaloid strychnine. Preserve it in well-closed containers, protected from light." *U. S.*

Azotate de Strychnine, *Fr. Cod.;* Nitrate de Strychnine, *Fr.;* Strychninum nitricum, *P. G.;* Strychninnitrat, Salpetersaures Strychnin, *G.;* Nitrato di stricnina, *It.*

Preparation.—This salt may be made by dissolving a sufficient quantity of the alkaloid strychnine in diluted nitric acid until it is neutralized, evaporating the solution and crystallizing the strychnine nitrate.

Properties.—It is officially described as in "colorless, glistening needles, or as a white, crystalline powder; odorless, permanent in the air. *Great caution must be used in tasting it and then only in very dilute solutions* which are exceedingly bitter. One Gm. of Strychnine Nitrate dissolves in 42 mils of water, 150 mils of alcohol, 50 mils of glycerin, and in 105 mils of chloroform at 25° C. (77° F.); also in 9 mils of boiling water and 77 mils of alcohol at 60° C. (140° F.); insoluble in ether. Its saturated aqueous solution is neutral or only slightly acid to litmus and is lævorotatory. A solution of the salt, when poured carefully into a test tube upon a layer of sulphuric acid containing diphenylamine in solution, develops a blue color at the zone of contact. When the salt is heated with hydrochloric acid, a bright red color is produced. In other respects it responds to the tests for identity and purity under *Strychnina.*" *U. S.*

Uses.—Strychnine nitrate has no advantage over the other soluble salts of strychnine.

Dose, one-sixtieth to one-fifteenth of a grain (0.0011–0.004 Gm.).

Off. Prep.—Syrupus Phosphatum cum Quinina et Strychnina, *N. F.*

STRYCHNINÆ SULPHAS. U. S.

STRYCHNINE SULPHATE Strych. Sulph.

(strȳch-nī'næ sŭl'phās)

"The sulphate $[(C_{21}H_{22}O_2N_2)_2.H_2SO_4 + 5H_2O = 856.56]$ of the alkaloid strychnine. Preserve it in well-closed containers." *U. S.*

Strychniæ Sulphas, *U. S.*, 1870; Strychninum Sulphuricum; Sulfate de Strychnine, *Fr. Cod.*; Schwefelsaures Strychnin, Strychninsulfat, *G.*; Sulfato de estricnina, *Sp.*

Preparation.—A process for this salt is no longer official. Two forms of *strychnine sulphate* are known, the acid sulphate, or commercial sulphate, and the official or neutral sulphate. Commercial strychnine sulphate, $C_{21}H_{22}O_2.N_2H_2SO_4 + 2H_2O$, crystallizes in needles. The water is expelled at 150° C. (302° F.). To prepare the neutral sulphate $(C_{21}H_{22}O_2N_2)_2.H_2SO_4$, a solution of the acid sulphate is divided into two equal portions: one of these portions is precipitated by ammonia, and the precipitate is added to the other part of the solution and the mixture boiled. On cooling, the liquid deposits the neutral salt in transparent prisms containing 5 molecules of H_2O. The crystals melt and become anhydrous at 200° C. (392° F.). By the spontaneous evaporation of an aqueous solution of the salt, transparent pyramids belonging to the quadratic system are obtained. According to Rammelsburg, these crystals contain 6 molecules of H_2O. (*Ber. d. Chem. Ges.*, 1881, p. 1231; *N. R.*, Jan., 1882.)

Properties.—This salt is in "colorless or white, prismatic crystals or as a white, crystalline powder; odorless, and efflorescent in dry air. *Great caution must be used in tasting it and then only in very dilute solutions* which are exceedingly bitter. One Gm. of Strychnine Sulphate dissolves in 32 mils of water, 81 mils of alcohol and in 220 mils of chloroform at 25° C. (77° F.); also in 7 mils of boiling water and 26 mils of alcohol at 60° C. (140° F.); freely soluble in glycerin; insoluble in ether. Its saturated aqueous solution (1 in 50) is neutral or only slightly acid to litmus. Barium chloride T.S. produces in a solution of the salt a white precipitate, insoluble in hydrochloric acid. When dried to constant weight at 100° C. (212° F.) it loses not more than 11 per cent. of its weight. In other respects Strychnine Sulphate responds to the tests for identity and purity under *Strychnina*." *U. S.*

The chief advantage of this preparation over strychnine is its much greater solubility in water. Owing to the presence of sulphuric acid and water of crystallization in this salt, it contains but about 75 per cent. of strychnine, and the proportionate dose would be therefore somewhat greater than that of the alkaloid. For a process for making *strychnine arsenite*, see *U. S. D.*, 19th edition, page 1196.

Dose, one-sixtieth to one-fifteenth of a grain (0.0011–0.004 Gm.).

Off. Prep.—Elixir Cinchonæ Alkaloidorum, Ferri, Bismuthi, et Strychninæ, *N. F.*; Elixir Cinchonæ Alkaloidorum, Ferri et Strychninæ, *N. F.*; Elixir Ferri, Quininæ et Strychninæ, *N. F.*; Elixir Quininæ Valeratis et Strychninæ, *N. F.*

STYRAX. U. S. (Br.)

STORAX [Liquid Storax]

(stȳ'răx)

"A balsam obtained from the wood and inner bark of *Liquidambar orientalis* Miller (Fam. *Hamamelidaceæ*)." *U. S.* "Prepared Storax is a viscid balsam obtained from the wounded trunk of Liquidambar orientalis, *Mill.*, purified by solution in alcohol, filtration, and evaporation of the solvent." *Br.*

Styrax Præparatus, *Br.*; Prepared Storax; Styrax Liquidus, Balsamum Storacis, Balsamum Styracis, Balsamum Styrax Liquidus; Styrax liquide, *Fr. Cod.*; Styrax, *P. G.*; Storax, Flüssiger Storax, *G.*; Storace liquido, *It.*; Estoraque liquido, *Sp.*

All species of the genus Liquidambar as well as those of a related genus, *Altingia*, yield *storax*. The product most valued, however, is that obtained from *L. orientalis* Miller.

The *oriental sweet-gum* (*Liquidambar orientalis*) is a tree from twenty to forty feet high. The palmate leaves have each of their divisions obscurely three-lobed, and are serrate, perfectly smooth, bright green and shining on the upper and pale on the under surface. The tree is a native of Asia Minor, in the southwestern parts of which it forms large forests. It yields the so-called *liquid storax*.

According to the researches of Moeller, storax is a pathological rather than a physiological product; when the young wood is injured secretion reservoirs are formed in which the storax is produced. (*O. Z.*, 1.) In collecting the drug the outer bark is first heavily bruised, so as to injure the inner bark, and after a time the outer bark having been removed the inner bark is scraped off. According to Maltass, this inner bark is first pressed cold in horse-hair bags, after which hot water is thrown over the bags and they are again pressed. Lieutenant Campbell states that the inner bark is first boiled with water, and, a portion of the balsam which rises having been skimmed off, is then pressed so as to extract the remainder. The residuary bark, after expression, is dried in the sun, and employed in various parts of Turkey for fumigation. It is the drug known in commerce as *Storax bark* or *Cortex Thymiamatis*. (Hanbury, *P. J.*, 1857, xvi, 463.) The balsam is sent in casks to Constantinople, Smyrna, and other ports of the Levant.

Several kinds of storax have been described. The purest was the *storax in grains*, which was in whitish, yellowish-white, or reddish-yellow tears, about the size of a pea, opaque, soft, adhesive, and capable of uniting so as to form a mass. Another variety, formerly called *styrax calamita*, from the circumstance, it is supposed, that it was brought wrapped in the leaves of a kind of reed, consisted of dry and brittle masses, formed of yellowish agglutinated tears, in the interstices of which was a brown or reddish matter. The French call it *storax amygdaloïde*,

This and the preceding variety had a pleasant odor like that of vanilla. Neither of them, however, is now found in the markets. It is probable that one or both of these varieties may have been the product of *Styrax officinale.* A third variety, which was formerly seen in commerce, *styrax calamita,* was in brown or reddish-brown masses of various shapes, light, friable, yet possessing a certain degree of tenacity, and softening under the teeth. Upon exposure, it becomes covered upon the surface with a white efflorescence of styracin. It evidently consisted of sawdust, united with a portion of the balsam. As found in commerce, it was usually in the state of a coarse, soft, dark-colored powder, mingled with occasional light friable lumps of various sizes, and containing very little of the balsam. When good, it should yield, upon pressure between hot plates, a brown resinous fluid having the odor of storax. Hanbury states that some of this variety is prepared at Trieste, Venice, and Marseilles, by mixing the residue of the liquid-ambar bark remaining after expression, and reduced to coarse powder, with genuine liquid storax. (*P. J.,* April, 1863.)

American Storax, Liquidambar styraciflua, or *Sweet Gum* of our Southern States.—Its geographical range reaches into Mexico, and it yields a storax-like product in an abundance proportionate to the heat of the climate. A specimen from Guatemala is described by Flückiger and Hanbury as a yellow, opaque resin, of honey-like consistence, becoming transparent, amber-colored, and brittle by exposure to the air, and having a rather terebinthinous balsamic odor and but little taste. Sometimes it occurs as a thick golden-brown fluid. It contains cinnamic acid and styracin. (*A. J. P.,* 1874, p. 161.) It is soluble in alcohol, and has been gathered to a considerable extent in the United States for the preparation of chewing gum. The resins of *Liquidambar formosana* and *L. altigiana* are known in Eastern commerce. *Malay storax* is an aromatic resinous product obtained from the *Altingia excelsa* Noronha (*L. altigiana* Bl.) It is sometimes called *rasamala resin* and contains tannic acid besides a very minute amount of cinnamic and benzoic acids.

A fourth variety, which, under the name of *liquid storax,* is the one commonly used, is a semi-fluid, adhesive substance, brown or almost black upon the surface exposed to the air, but of a slightly greenish-gray color within, and of an odor somewhat like that of balsam of Peru, though less agreeable. It is kept in jars.

Properties.—The storax used by pharmacists should correspond to the following official description and tests: "Storax is a semi-liquid, grayish, sticky, opaque mass, depositing on standing a heavy, dark brown stratum; transparent in thin layers, and having a characteristic odor and an acrid taste. It is heavier than water. It is insoluble in water, but completely soluble (with the exception of accidental impurities) in an equal weight of warm alcohol; almost completely soluble in ether, acetone, benzene, or carbon disulphide. When heated on a water-bath, Storax becomes more fluid, and if it is then agitated with warm, purified petroleum benzin, the supernatant liquid, on being decanted and allowed to cool, is not darker than pale yellow and deposits white crystals of cinnamic acid and cinnamic esters. The separated crystals evolve the odor of benzaldehyde when heated with diluted sulphuric acid and potassium permanganate. Incinerate about 0.5 Gm. of Storax; not more than 1 per cent. of ash remains. Dissolve about 10 Gm. of Storax, accurately weighed, in 20 mils of hot alcohol; the undissolved residue, after washing it on a filter with hot alcohol and drying at 100° C. (212° F.), does not exceed 2.5 per cent. The combined filtrate and washings, after the evaporation of the alcohol at a temperature not exceeding 60° C. (140° F.) and drying the residue for one hour at 100° C. (212° F.), leave a brown, transparent, semi-liquid product representing not less than 60 per cent. of the weight of Storax taken; this product is soluble in ether, with the exception of a few flakes, but only partially soluble in purified petroleum benzin. Dissolve about 1 Gm. of Storax, purified as described above, and accurately weighed, in 50 mils of alcohol, add 0.5 mil of phenolphthalein T.S., and titrate with half-normal alcoholic potassium hydroxide V.S. The acid value so obtained is not less than 56 nor more than 85 (see Part III, Test No. 10). Mix about 1 Gm. of Storax, purified as described, and accurately weighed, in a 250 mil flask with 50 mils of purified petroleum benzin, add 25 mils of half-normal alcoholic potassium hydroxide V.S. and allow the mixture to stand twenty-four hours, with frequent shaking. Then add 0.5 mil of phenolphthalein T.S. and titrate with half-normal hydrochloric acid V.S. It shows a saponification value of not less than 170 nor more than 230 (see Part III, Test No. 9)." *U. S.*

"Brownish-yellow, viscous, transparent in thin layers. Entirely soluble in *alcohol* (90 per cent.) and in *ether.* Odor and taste agreeable and balsamic. Boiled with *solution of potassium chromate* and *sulphuric acid* it evolves an odor of benzaldehyde. Loses not more than 5 per cent. of its weight when heated in a thin layer on a water-bath for one hour. *Acid value* not less than 60 or more than 90; *ester value* not less than 100 or more than 146. Yields not less than 20 per cent. by weight of cinnamic acid when tested by the following process:—Dissolve 2.5 grammes of the Storax in 25 millilitres of *N/2 alcoholic solution of potassium hydroxide,* boil for one hour under a reflux condenser, neutralise with *N/2 solution of sulphuric acid,* remove the alcohol by evaporation, and dissolve the residue in 50 millilitres of *water. Shake* this aqueous solution with 20 millilitres of *ether;* after separation remove the ethereal layer, wash it with 5 millilitres of *water* and add the washings to the aqueous solution, rejecting the ethereal liquid. Acidify the aqueous solution with *diluted sulphuric acid* and shake it with four successive portions, each of 20 millilitres, of *ether.* Mix the ethereal solutions, wash with

a few millilitres of *water,* transfer to a flask and distil off the ether. To the residue add 100 millilitres of *water* and boil vigorously for fifteen minutes under a reflux condenser. Filter the solution while hot, cool to 15.5° C. (60° F.), and collect on a tared filter the crystals of cinnamic acid that have separated. Repeat the extraction of the residue with the filtrate at least three times, or until no more cinnamic acid is removed. Press the filter paper and crystals between blotting paper, dry in a desiccator over *sulphuric acid,* and weigh. Add to the weight of the crystals so ascertained 0.03 gramme (representing the average amount of cinnamic acid remaining dissolved in the aqueous liquid). The total weight is not less than 0.5 gramme." *Br.*

As found in commerce, storax is usually so much adulterated as to require purification before it can be used, and in both Pharmacopœias processes were formerly given. Whenever not originally pure enough for use, it should be dissolved in alcohol, the solution strained, and the alcohol distilled off to a certain extent, and then completely evaporated at a gentle heat. Among the substances used in the adulteration of storax is turpentine. To detect it Hager employed the following method. He liquefied the resin, in a tube, by means of a water bath, added half its volume of absolute alcohol, and hastened the solution by agitation; he then treated it with several volumes of benzin. This operation was repeated twice. The liquors obtained were then evaporated, in a tared vessel, and there was secured, for pure storax, a colorless residue (45 to 55 per cent.), with a light-blue opalescence; for that mixed with turpentine, a residue more considerable, yellowish, and having the terebinthinate odor. (*J. P. C.,* Fév., 1876, p. 161.) The quality of storax at present on the market appears to be very much inferior to what it was a few years ago. It is stated (*P. J.,* 1911, lxxxvii, p. 86) that whereas in 1907 the commercial storax averaged about 19 per cent. of cinnamic acid with an acid number of 68.9, that upon the market in 1911 contained only about 2.5 per cent. of cinnamic acid, and had an acid number around 100. It is not improbable that this deterioration is due to the extraction of cinnamic acid before it is marketed.

Storax melts with a moderate heat, and, when the temperature is raised, takes fire and burns with a white flame, leaving a light, spongy, carbonaceous residue. It imparts its odor to water, which it renders yellow and milky. Its active constituents are dissolved by alcohol and ether. Neumann obtained from 480 grains of storax 120 of aqueous extract, and from an equal quantity 360 grains of alcoholic extract. Containing volatile oil and resin, and yielding benzoic or cinnamic acid by distillation, it is entitled to rank as a balsam.

The most abundant constituent of storax is probably *storesin,* $C_{36}H_{55}(OH)_3$, discovered in 1877 by W. von Miller. This is present in two forms, designated respectively alpha and beta, both free and in the form of a cinnamic ester. Storesin is an amorphous substance, melting at 168° C. (334.4° F.), readily soluble in petroleum benzin. *Cinnamic esters of phenylpropyl, cinnamic ester of ethyl, cinnamic ester of benzyl,* and especially *cinnamate of cinnamyl,* $C_9H_7O_2$. C_9H_9, the so-called *styracin* of Bonastre, have also been observed. This last compound can be removed by ether, benzene, or alcohol after the separation from the resin of the cinnamic acid; it is insoluble in water, and volatile only in superheated steam. It crystallizes in tufts of long rectangular prisms, which melt at 38° C. (100.4° F.), but frequently do not solidify readily. By concentrated solution of potassium hydroxide, it is resolved into a cinnamate and cinnamic alcohol (*styrone*), $C_9H_{10}O$, which latter is not present in liquid storax. The yield of *cinnamic acid* varies from 6 to 12 per cent., or even, according to Löwe, as much as 23 per cent. of crystallized cinnamic acid can be obtained. The acid dissolves abundantly in ether, alcohol, or hot water, slightly in cold water; it is inodorous, but has an acrid taste. It fuses at 133° C. (271.4° F.), and boils at 290° C. (554° F.). Another minor constituent of storax is a fragrant substance melting at 65° C. (149° F.), and possessing the odor of vanillin, which Rump (*Ber. d. Chem. Ges.,* 1878, 1034) identified. Miller also shows that water removes from the drug a little free benzoic acid. There is further found in liquid storax a hydrocarbon, C_8H_8, first prepared by Simon in 1839, which exists in the resin as a liquid, and also in a polymeric form as a solid. The former, called *styrol, styrene,* or *cinnamene styrene,* has a sp. gr. of 0.924, and a boiling point of 146° C. (294.8° F.). It is a colorless, mobile liquid, possessing the odor and burning taste of liquid storax. It has since been formed synthetically, and has been recognized as *phenylethylene,* $C_6H_5.CH=CH_2$. When heated for a considerable time to 100° C. (212° F.), or for a shorter period to 200° C. (392° F.), it is converted without change of composition into the colorless, transparent solid *metastyrol,* which, unlike styrol, is not soluble in alcohol or in ether. Lastly, there has been found in liquid storax, by J. H. van t'Hoff (1876), about 0.4 per cent. of a pleasant-smelling lævo-rotatory oil of the formula $C_{10}H_{16}O$. (*Pharmacographia,* 2d ed., 274 and 275.) Tschirch and L. v. Itallie (*A. Pharm.,* Sept., 1901, 506) state that styrax contains free cinnamic acid, vanillin, styrol, styracin, cinnamic acid-ethyl ester, cinnamic acid-phenylpropyl ester and storesinol partly free and partly as cinnamic acid ester.

Uses.—Styrax is a stimulating expectorant and feeble antiseptic, which was at one time used in various *pulmonic catarrhs,* also in *gonorrhea* and *leucorrhea,* but at present is very seldom used except as a constituent of the compound tincture of benzoin. Externally, mixed with two or three parts of olive oil, liquid storax was found by H. Schultze, of Magdeburg, to be very effective as a local remedy in scabies.

Dose, ten to twenty grains (0.65–1.3 Gm.).

Off. Prep.—Tinctura Benzoini Composita, *U. S., Br.*

SUCCI

JUICES

(sŭc'cī)

Sucs végétaux, *Fr.*; Pflanzensäfte, *G.*

Though introduced to professional notice by Squire in the year 1835, and subsequently used by many practitioners, the juices were recognized but once by the U. S. Pharmacopœia (1870). They consist of the expressed juices of fresh plants, preserved by the addition of one-third of their bulk of alcohol. Considering the great inequality in strength, and, of course, the uncertainty in operation, of fresh juices themselves, varying according to the soil, climate, mode of cultivation, season, and the age of the plant, it may be questioned whether they merit the prominence which has been given them in the past.

SUCCUS LIMONIS. Br.

LEMON JUICE

(sŭc'cus lĭ-mō'nĭs)

"Lemon Juice is the freshly expressed juice of the ripe fruit of Citrus Medica, *Linn.*, var. β Limonum, *Hook. f.*" *Br.*

Limonis Succus, *U. S. P. VIII;* Succus Citri; Suc de Citron (de Limon), *Fr. Cod.;* Citronensaft, Limonensaft, *G.;* Succo di limone, *It.;* Zumo de limon, *Sp.*

We are supplied with lemons and limes chiefly from the West Indies, the Mediterranean and California. Though the former of these fruits only is directed by the Br., lime juice is recognized by the N. F., and both kinds are employed indiscriminately for most medicinal purposes, and the lime affords a juice at least equal, in proportional quantity and acidity, to that obtained from the lemon.

The seed of the lime contains 58 per cent. of fixed oil, which is said to equal in flavor the best olive oil. Its tendency to resist rancidity is reputed to be very great. (*B. C. D.*, 1894, 411.) Lime juice is official in the N. F. IV under the title of *Succus Citri* (see Part II).

As lemons rapidly deteriorate on keeping, if exposed to the air, the suggestions of protecting them by dipping them in melted paraffin, or by using a varnish of shellac dissolved in alcohol, made by George Mee, of London, are not without value. Mee found that lemons thus covered with varnish continued sound for a period of many months. (See *A. J. P.*, 1866, p. 474.)

The juice is the part for which the fruit is most esteemed. It is sharply acid, with a peculiar grateful flavor, and consists chiefly of water, citric acid (from 6 to 10 per cent.), gum and sugar (from 3 to 4 per cent.), and inorganic salts (2.28 per cent.). It sometimes has in it a little volatile oil, derived by pressure from the rind. It is "a slightly turbid, yellowish liquid. Taste sharply acid. Specific gravity 1.030 to 1.040. 20 millilitres require for neutralisation not less than 20 and not more than 25.7 millilitres of *N/1 solution of sodium hydroxide*, corresponding to a proportion of not less than 7 and not more than 9 grammes of citric acid in 100 millilitres. The residue obtained on evaporation, dried at 110° C. (230° F.), yields not more than 3 per cent. of ash. 100 millilitres of Lemon Juice are neutralised by about 11.4 grammes of Potassium Bicarbonate, by about 9.5 grammes of Sodium Bicarbonate, and by about 16.5 grammes of Sodium Carbonate." *Br.*

The U. S. P. IX does not recognize lemon juice; the U. S. P. VIII provided the following tests: "It reddens blue litmus paper and should contain from 7 to 9 per cent. of citric acid. If a few drops of barium chloride T.S. be added to filtered Lemon Juice, no turbidity or white precipitate should be produced (absence of *sulphuric acid* or *sulphates*). If an equal volume of sulphuric acid containing a few drops of alcohol be added to Lemon Juice, and the liquid heated, no odor of acetic ether should be developed (absence of *acetic acid*). Upon the addition of solution of potassium acetate (1 in 3) and alcohol in excess, no white crystalline precipitate should form after allowing the liquid to stand fifteen minutes (absence of *tartaric acid*). At least 10 mils of normal potassium hydroxide V.S. should be required to neutralize 10 mils of Lemon Juice, phenolphthalein T.S. being used as indicator." *U. S. VIII.*

As lemons cannot always be obtained, the juice is often kept in a separate state, but, from its liability to spontaneous decomposition, it speedily becomes unfit for medicinal use, and, though various means have been resorted to for its preservation, it can never be made to retain for any length of time its original flavor unaltered. One of the most effectual methods of preserving the juice is to allow it to stand for a short time after expression, until a coagulable matter separates, then to filter, and introduce it into glass bottles, with a stratum of almond oil or other sweet oil upon its surface. It will keep still better if the bottles containing the filtered juice be permitted, before being closed, to stand for fifteen minutes in a vessel of boiling water. Another mode is to add one-tenth of alcohol and to filter. The juice may also be preserved by concentrating it either by evaporation with a gentle heat, or by exposure to a freezing temperature, which congeals the aqueous portion and leaves the juice much stronger than before. When used, it may be diluted to the former strength, but though the acid properties are retained, bottled lemon juice is frequently found to be preserved with sulphur dioxide, which dissolves in it to form sulphurous acid. The presence of this preservative interferes with some of its pharmaceutical uses and such a product should not be employed for medicinal purposes. The flavor of the juice is found to have been deteriorated. Lemon syrup is another form in which the juice is preserved.

The proportion of citric acid in lemon juice varies greatly, ranging from 4.5 to nearly 9 per cent. Stoddart found the acidity to diminish rapidly with the advance of summer, with little change in the sp. gr. of the juice. (*P. J.*, Oct., 1868.) H. H. Robins, after examining large consignments of lemons, states that the average

yield of citric acid taken from a year's receipts was 35.23 grains in a fluidounce. (*C. D.*, 1896, 742.) A solution of tartaric acid in water, with the addition of a little sulphuric acid, and flavored with the oil of lemon, has been fraudulently substituted for lemon juice, particularly as an antiscorbutic on long voyages, for which purpose it is quite useless. An application of the test for tartaric and sulphuric acids will at once detect the fraud.

The proportion of citric acid in lime juice is required by the N. F. IV to be not less than 5 Gm. nor more than 10 Gm. to each 100 mils. It is required to be free from sulphuric acid, but is permitted to contain 0.04 Gm. of SO_2 in each 100 mils. Other preservatives are prohibited as are also artificial colors.

Uses.—Lemon juice is refrigerant, and, properly diluted, forms a refreshing and agreeable beverage in *febrile* and *inflammatory affections*. It may be given with sweetened water in the shape of lemonade, or may be added to the mildly nutritive drinks, such as albumen water, barley water, etc., usually administered in *fevers*. It is also much employed in the formation of those diaphoretic preparations known by the names of *neutral mixture* and *effervescing draught*. (See *Mistura Potassii Citratis*, p. 654.) One of the most beneficial applications of lemon juice is to the prevention and cure of *scurvy*, for which it may be considered almost a specific. For this purpose, ships destined for long voyages should always be provided with a supply of the preserved juice. In England every foreign-going ship is required by law to take such a supply of lemon or lime juice that every seaman shall have a daily allowance of an ounce after having been ten days at sea. Its antiscorbutic effects have been found to be due to the presence of one of a class of chemical activators called *vitamines*. It has been employed with advantage in *acute rheumatism* in doses of from one to four fluidounces (30–120 mils) from four to six times a day. Locally applied it acts as an astringent and has been used with benefit in *pruritus of the scrotum*, in *uterine hemorrhage* after delivery, in *sunburn*, and as a gargle in *diphtheritic sore throat*.

Off. Prep.—Syrupus Limonis, *Br.*; Trochiscus Acidi Carbolici, *Br.*

SUCCUS SCOPARII. Br.

JUICE OF BROOM

(sŭc'cŭs scō-pā'rĭ-ī)

Suc de Genet à Balais, *Fr.*; Besenginstersaft, *G.*

"Bruise fresh Broom Tops; press out the juice; to every three volumes of juice add one volume of Alcohol (90 per cent.); set aside for seven days; filter." *Br.*

In large doses this juice is prone to disturb the stomach and bowels. It is more appropriately used as an adjuvant to other diuretics than alone.

Dose, as a diuretic, one to two fluidrachms (3.75–7.5 mils).

SUCCUS TARAXACI. Br.

JUICE OF TARAXACUM

(sŭc'cŭs tą-răx'ą-cī)

Suc de Pissenlit, *Fr.*; Löwenzahnwurzelsaft, Löwenzahnsaft, *G.*

"Bruise Taraxacum Root; press out the juice; to every three volumes of juice add one volume of Alcohol (90 per cent.); set aside for seven days; filter." *Br.*

Dose, two fluidrachms to half a fluidounce (7.5–15.0 mils).

SULPHONETHYLMETHANUM. U. S. (Br.)

SULPHONETHYLMETHANE Sulphonethylmeth. [Trional]

(sŭl-phōn-ĕ-thўl-męth-ā'nŭm)

"Diethylsulphonemethylethylmethane [$C_8H_{18}S_2O_4$ or $(CH_3)(C_2H_5)C(SO_2C_2H_5)_2 = 242.28$]. Preserve it in well-closed containers." *U. S.*

"Methylsulphonal, or diethyl-sulphone-methyl-ethyl-methane, $C_8H_{18}S_2O_4$, is an oxidation product of the mercaptol resulting from the condensation of ethyl-methyl-ketone with ethyl-mercaptan." *Br.*

Methylsulphonal, *Br.*; Methylsulphonal; Trionalum; Diethylsulphone-methylethylmethane; Trional, *Fr. Cod.*; Diéthylsulfone-méthyléthyl-méthane, *Fr.*; Methylsulfonalum *P. G.*; Methylsulfonal, Trional, *G.*; Trional, *Sp.*

Preparation.—*Sulphonethylmethane* is made by passing hydrochloric acid gas to saturation through a mixture of ethyl mercaptan and methyl ethylketone, then oxidizing the condensation product (methyl-ethyl-ketone mercaptol) by treating it with a weak solution of potassium permanganate; the compound is purified by repeated crystallization from its solutions in boiling water.

Sulphonethylmethane (or trional) and tetronal are substances which are members of the group of disulphones to which sulphonal belongs and are respectively *diethylsulphon-methylethyl-methane* and *diethylsulphon-diethyl-methane*. Their relationship to sulphonal (diethylsulphondimethyl-methane) will be readily seen by a comparison of formulas.

Sulphonal.	Trional.	Tetronal.
$C\begin{cases}SO_2C_2H_5\\SO_2C_2H_5\\CH_3\\CH_3\end{cases}$	$C\begin{cases}SO_2C_2H_5\\SO_2C_2H_5\\CH_3\\C_2H_5\end{cases}$	$C\begin{cases}SO_2C_2H_5\\SO_2C_2H_5\\C_2H_5\\C_2H_5\end{cases}$

Properties.—It is officially described as in "colorless, lustrous, odorless, crystalline scales, which have a bitter taste in aqueous solution. One Gm. of Sulphonethylmethane dissolves in 200 mils of water at 25° C. (77° F.); more soluble in boiling water; soluble in alcohol or ether. Its saturated aqueous solution is neutral to litmus. It melts between 74° and 76° C. (165.2° and 168.8° F.); at a higher temperature it is decomposed with the evolution of sulphur dioxide. Heat about 0.1 Gm. of Sulphonethylmethane with an equal weight of powdered charcoal in a

dry test tube; the characteristic, unpleasant odor of mercaptan is developed. Incinerate about 2 Gm. of Sulphonethylmethane; not more than 0.05 per cent. of ash remains. About 1 Gm. of Sulphonethylmethane dissolved in 50 mils of boiling distilled water develops no odor. Ten mil portions of this solution, after cooling and filtering, when tested separately, show no turbidity at once on the addition of a few drops of barium chloride T.S. (*sulphate*) or a few drops of silver nitrate T.S. (*chloride*). Twenty mils of the cold filtrate from the preceding test does not at once decolorize 0.05 mil of tenth-normal potassium permanganate V.S. (*readily oxidizable impurities*)." *U. S.*

"A white crystalline powder; taste slightly bitter. Soluble in 320 parts of *water,* somewhat more soluble in dilute *alcohol.* Melting point from 76° to 76.5° C. (168.8°–169.7° F.). At a red heat it decomposes with evolution of sulphur dioxide. When heated with *anhydrous sodium acetate* hydrogen sulphide is liberated. When boiled with *water* no offensive odor is developed (absence of mercaptan and merceaptol). 100 millilitres of a cold saturated aqueous solution do not immediately decolorise 1 drop of an aqueous solution (1 in 1000) of *potassium permanganate* (limit of readily oxidisable substances). No appreciable ash." *Br.*

The name methylsulphonal certainly appears to be a misnomer, as the product differs from sulphonal by the substitution of an ethyl group for one of the two methyl groups of sulphonal.

Uses.—The group of sulphone derivatives was introduced into medicine by Baumann in 1892. Two of them are recognized by the Pharmacopœia, sulphonethylmethane and sulphonmethane. These compounds are depressants to the higher cerebral centers. Although when given in very large dose they produce in the lower animals paresis and tremors, in quantities anywhere approaching the therapeutic dose they have almost no effect on man save to produce sleep. They are both characterized by the slowness of absorption and persistence of their action, although sulphonethylmethane is not quite so slow in its effects as sulphonmethane.

While in single dose they are relatively safe somnifacients, when used continuously over long periods of time they give rise to serious forms of intoxication. This generally starts with constipation and vague neurasthenic pains. In the fully developed stage chronic sulphone poisoning is characterized by obstinate constipation with scaphoid abdomen, cramp-like pains in the extremities, ataxia, insomnia, and a peculiar discoloration of the urine which ranges from a faint pinkish hue to a deep port wine red. This discoloration is due to the presence of a pigment known as *hematoporphyrin,* which is probably derived from decomposition of the blood. The urine is also usually highly acid and may contain albumen and tube casts. The prognosis in chronic sulphone poisoning is always grave. In the treatment it is essential to open the bowels as promptly as possible; for this the most powerful purgatives are usually required, and their action may be assisted by high enemata. In order to hasten the elimination of the poison large quantities of water should be administered, both by mouth and by hypodermoclysis. The free use of alkalies has been recommended with the idea of correcting the acidity of the system; sodium bicarbonate may be added to physiological salt solution for hypodermic injection. Symptom treatment is rarely of any efficacy.

There appears to be no recorded case of fatal acute poisoning by trional. Sixty grains (3.9 Gm.) are said to have produced hematoporphyrinuria, but one hundred and twenty grains (7.7 Gm.) have been recovered from without very serious symptoms. Although trional is less prone than is sulphonal to cause chronic poisoning, a number of cases have occurred.

Sulphonethylmethane is used in medicine solely as a somnifacient. In doses of from fifteen to twenty grains (1.0–1.3 Gm.) it usually causes sleep in from a half to an hour without unpleasant after effects. It may be administered as a powder, stirred up in half a glass of water, or enclosed in a gelatin capsule.

Dose, ten to twenty grains (0.65–1.3 Gm.).

SULPHONMETHANUM. U. S. (Br.)

SULPHONMETHANE Sulphonmeth.

(sŭl-phōn-mĕth-ā'nŭm)

"Diethylsulphonedimethylmethane [$C_7H_{16}S_2O_4$ or $(CH_3)_2C(SO_2C_2H_5)_2 = 228.27$]. Preserve it in well-closed containers." *U. S.* "Sulphonal, or dimethyl-methane-diethyl-sulphone, $C_7H_{16}S_2O_4$, may be obtained by oxidising mercaptol." *Br.*

Sulphonal, *Br.;* Diethylsulphon-dimethyl-methane; Acétone-diéthylsulfone, *Fr. Cod.;* Sulfonalum, *P. G.;* Sulfonal, *G.;* Sulfonale, *It.;* Sulfonal, *Sp.*

Preparation.—This compound belongs to the class of disulphones, to which belong also trional and tetronal. (See page 1080.) It may be made by the following processes. When anhydrous mercaptan (ethyl sulphydrate) and anhydrous acetone are mixed and a stream of dry hydrochloric acid gas passed through, the liquid gradually becomes turbid and separates into two layers, the upper being mercaptol (dithioethyldimethylmethane, the lower, diluted hydrochloric acid. The mercaptol is separated, washed, and then oxidized with potassium permanganate, the liberated oxygen converting the mercaptol into sulphonal. It may also be prepared by the action of ethyl chloride on sodium thiosulphate, the resulting sodium ethyl thiosulphate being converted into ethyl mercaptan and acid sodium sulphate by the action of water. This conversion is made to take place in the presence of alcohol, hydrochloric acid, and acetone, the ethyl mercaptan being condensed to mercaptol, which is oxidized by potassium permanganate, sulphonal being the result. It forms heavy colorless prismatic crystals, melting at 125.5° C. (257.9° F.), which are not very soluble in cold water, but more readily in boiling water, and in alcohol and alcoholic ether. A

characteristic test is to fuse the sulphonal in a small dry test-tube, heat to about 280° C. (536° F.), and to the clear liquid add pyrogallic (or gallic) acid. The liquid becomes brown and gives off the characteristic odor of mercaptan or sulphur alcohol. Heating with potassium cyanide or even with powdered charcoal will effect the same decomposition.

Properties.—It is officially described as in "colorless, inodorous, and nearly tasteless prismatic crystals, or as a crystalline powder. One Gm. of Sulphonmethane dissolves in 365 mils of water, 60 mils of alcohol, 11 mils of chloroform, and in 64 mils of ether at 25° C. (77° F.); also in 16 mils of boiling water and 3 mils of boiling alcohol; soluble in benzene. It melts between 124° and 126° C. (255.2° and 258.8° F.). In other respects it responds to the tests for identity and purity under *Sulphonethylmethanum.*" *U. S.*

The British Pharmacopœia gives the following description:

"Colorless prismatic crystals. No odor; nearly tasteless. Soluble in 450 parts of cold *water,* in 15 parts of boiling *water,* and in 80 parts of *alcohol* (90 per cent.). Melting point 125° C. (257° F.). Aqueous solution neutral to *litmus.* When mixed with an equal weight of *potassium cyanide* and heated, the odor of mercaptan is evolved, and when to the solution of the product in *water* excess of *hydrochloric acid* and a few drops of *T. Sol. of ferric chloride* are added, a reddish color is developed. Evolves hydrogen sulphide when gradually heated with *anhydrous sodium acetate.* Yields no characteristic *reactions* for chlorides or sulphates. No appreciable ash." *Br.*

Uses.—The action of sulphonmethane upon the system is similar to that of sulphonethylmethane. It generally requires, however, somewhat larger doses to produce sleep and its effects come on more slowly. Although usually not followed by disagreeable after effects, there sometimes remains some mental confusion and lassitude the following day. For some unknown reason it does not act happily in cases of heart disease and there have been reported sudden deaths in patients suffering from cardiac weakness following the use of sulphonal. It is best administered in the form of a powder stirred up in a glass of hot water or milk; it should never be exhibited in pill form.

Because of the seriousness of the chronic poisoning by this drug (see under *Sulphonethylmethane*)—the mortality is upwards of 75 per cent.—and the insidiousness of its onset, sulphonal should never be used without interruptions for more than a week or ten days. Acute poisoning by sulphonal is rare, but Knapp has reported a case in which 450 grains produced death after unconsciousness lasting three days. Even after therapeutic doses occasionally a measles-like rash appears.

Dose, from ten to forty grains (0.65–2.6 Gm.).

SULPHUR LOTUM. U. S.

WASHED SULPHUR Sulphur Lot.

(sŭl'phŭr lō'tŭm)

"Washed Sulphur, when dried to constant weight in a desiccator over sulphuric acid, contains not less than 99.5 per cent. of S (32.07)." *U. S.*

Flores Sulphuris Loti; Soufre Sublimé Lavé, *Fr. Cod.;* Sulphur Depuratum, *P. G.;* Gereinigter Schwefel, Gereinigte Schwefelblumen, *G.;* Solfo sublimato e levato, *It.;* Azufre lavado, *Sp.*

* "Sublimed Sulphur, *one hundred grammes* [or 3 ounces av., 231 grains]; Ammonia Water, *ten mils* [or 162 minims]; Water, *a sufficient quantity.* Pass the sublimed sulphur through a No. 30 sieve, mix it thoroughly with *one hundred mils* [or 3 fluidounces, 183 minims] of water, add the ammonia water, and set the mixture aside for three days in a closed vessel, agitating occasionally. Then add *one hundred mils* [or 3 fluidounces, 183 minims] of water, transfer the mixture to a strainer, and wash the sulphur with water until the washings cease to impart a blue color to red litmus paper. Then allow it to drain, press the residue strongly, dry it rapidly at a moderate heat in a drying closet, pass it through a No. 30 sieve, and keep it in well-closed containers." *U. S.*

Sublimed sulphur is frequently contaminated with small quantities of sulphuric acid and other impurities, and the object of the ammonia in the above process is to neutralize the acid, the salt being subsequently washed out and to remove any arsenical contamination. (See *Sulphur Sublimatum.*)

Properties.—It is officially described as "a fine, yellow powder, without odor or taste. It responds to the solubility and identity tests under *Sulphur Sublimatum.* Agitate 2 Gm. of Washed Sulphur with 10 mils of distilled water and filter; the filtrate is neutral to litmus (*acid or alkali*). The amount of residue left after volatilizing or igniting a weighed portion of dried Washed Sulphur does not exceed 0.5 per cent. Digest 0.5 Gm. of Washed Sulphur for three hours with 10 mils of ammonia water, filter the liquid, and evaporate the clear filtrate to dryness on a water bath. Then add 1 mil of nitric acid, and again evaporate to dryness. This residue meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"**Assay.**—When dried to constant weight in a desiccator over sulphuric acid and assayed by the method under *Sulphur Sublimatum,* it shows, in the dried product, not less than 99.5 per cent. of S.

"Each gramme of Washed Sulphur, previously dried, corresponds to not less than 7.243 Gm. of barium sulphate." *U. S.*

For description of chemical and therapeutic properties, see *Sulphur Sublimatum.*

Dose, one to three drachms (3.9–11.6 Gm.).

Off. Prep.—Pulvis Glycyrrhizæ Compositus, *U. S.;* Unguentum Sulphuris, *U. S.;* Sulphuris Iodidum, *N. F.;* Trochisci Sulphuris et Potassii Bitartratis, *N. F.*

SULPHUR PRÆCIPITATUM. U. S., Br.

PRECIPITATED SULPHUR Sulphur Præc. [Lac Sulphuris, Milk of Sulphur]

(sŭl'phŭr præ-cĭp-ĭ-tā'tŭm)

"Precipitated Sulphur, when dried to constant weight in a desiccator over sulphuric acid, contains not less than 99.5 per cent. of S (32.07)." *U. S.* "Precipitated Sulphur is obtained by the action of hydrochloric acid upon a solution prepared by boiling together sulphur and lime in water." *Br.*

Magisterium Sulphuris; Soufre précipité, *Fr. Cod.*; Lait de Soufre, *Fr.*; Sulfur præcipitatum, *P. G.*; Schwefelmilch, *G.*; Solfo precipitato, *It.*

* "Sublimed Sulphur, *one hundred grammes* [or 3 ounces av., 231 grains]; Calcium Oxide, *fifty grammes* [or 1 ounce av.,.334 grains]; Hydrochloric Acid, Water, each, *a sufficient quantity.* Slake the calcium oxide, and mix it thoroughly with *five hundred mils* [or 16 fluidounces, 435 minims] of water. Add the sublimed sulphur, previously sifted, and, after thorough mixing, add *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of water, and boil the mixture in a porcelain or glass vessel during one hour, stirring or agitating the mixture very frequently, and replacing the water lost by evaporation. Then cover the vessel, and permit the contents to cool and become clear by subsidence. Carefully draw off the clear solution, and filter the remainder. To the united liquids add gradually and with constant stirring hydrochloric acid, previously diluted with an equal volume of water, until the liquid is nearly neutralized, but still retains an alkaline reaction and a yellow color. Collect the precipitate on a strainer, and wash it until the washings are neutral to litmus and cease to give a precipitate upon the addition of ammonium oxalate T.S. Then dry the product rapidly, and keep it in well-closed containers." *U. S.*

The process for *precipitated sulphur* was not changed in the last revision. The Br. Pharm. in its official definition outlines the method used in the U. S. preparation.

In the U. S. process three molecules of calcium oxide react with six atoms of sulphur to form two molecules of calcium disulphide and one of calcium thiosulphate (hyposulphite);

$$3CaO + (S_2)_3 = 2CaS_2 + CaS_2O_3$$

On the addition of the hydrochloric acid, six atoms of sulphur are precipitated (four from the two molecules of calcium disulphide and two from the one molecule of calcium thiosulphate), and the calcium and oxygen unite with the hydrochloric acid, so as to form calcium chloride and water, according to the reaction:

$$2CaS_2 + CaS_2O_3 + 6HCl = 3CaCl_2 + 3H_2O + (S_2)_3$$

This rationale is not exactly applicable to the British process of 1885, in which the proportion of the sulphur to the lime employed was greater than in that of the U. S. Pharm., and on account of this greater excess of sulphur the reaction takes place as follows:

$$3CaO + (S_2)_6 = 2CaS_5 + CaS_2O_3$$

a calcium pentasulphide being formed. Hydrochloric acid is the most eligible precipitant for the sulphur, as it gives rise to calcium chloride, which is a very soluble salt and is easily washed away. Sulphuric acid is wholly inadmissible, as it generates calcium sulphate, which, from its sparing solubility, becomes necessarily intermingled with the precipitated sulphur. According to Schweitzer, the best material from which to precipitate the sulphur is potassium sulphide, formed by boiling sulphur with potassium hydroxide. Otto, of Brunswick, finds that potassium sulphide is likely to contain copper sulphide, and therefore he prefers calcium sulphide.

Properties.—Precipitated sulphur is in friable lumps, of a white color, with a pale yellowish-green tint, and consisting of finely divided particles slightly cohering, or, as officially described, is "a fine, amorphous powder, of a pale yellow color, without odor or taste. Agitate 2 Gm. of Precipitated Sulphur with 10 mils of distilled water and filter; the filtrate is neutral to litmus (*acid or alkali*). It responds to the solubility and identity tests under *Sulphur Sublimatum.* It is more readily and completely soluble in carbon disulphide than other forms of sulphur. The amount of residue left after volatilizing or igniting a weighed portion of dried Precipitated Sulphur does not exceed 0.3 per cent. Digest 1 Gm. of Precipitated Sulphur for three hours with 10 mils of ammonia water and filter the liquid. Evaporate the clear filtrate to dryness on a water bath, add 1 mil of nitric acid, and again evaporate to dryness. This residue meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"**Assay.**—When dried to constant weight in a desiccator over sulphuric acid and assayed by the method under *Sulphur Sublimatum,* it shows, in the dried product, not less than 99.5 per cent. of S. Each gramme of Precipitated Sulphur, previously dried, corresponds to not less than 7.243 Gm. of barium sulphate." *U. S.*

"A greyish-yellow, soft powder, free from grittiness and from the odor of hydrogen sulphide. Under the microscope it is seen to consist of opaque globules, without any admixture of crystalline matter. Burns with a blue flame, forming sulphur dioxide, and leaving not more than 0.5 per cent. of fixed residue. When 10 grammes are mixed with *water,* filtered, and thoroughly washed, the mixed filtrate and washings require for neutralisation not more than 2 millilitres of *N/10 solution of sodium hydroxide* (limit of acidity). *Arsenic limit* 5 parts per million." *Br.*

The German test, that 1 Gm. of precipitated sulphur should dissolve in 5 Gm. of carbon disulphide, is trustworthy, according to Fittinger. Precipitated sulphur is entirely dissipated by heat; water boiled with it should not redden litmus. When recently prepared, it is devoid of

taste, but possesses a peculiar odor. When long exposed, in a moist state, to the air, it becomes strongly contaminated with sulphuric acid. From its color it was formerly called *lac sulphuris*, or *milk of sulphur*. It is insoluble in water, but dissolves in a boiling solution of potassium hydroxide, and in oil of turpentine by the aid of heat. When of a brilliant white color, the presence of calcium sulphate may be suspected, in which case the preparation will not be wholly volatilized by ignition. If pure, it communicates a harsh feel when rubbed between the fingers, owing to the friction of the particles. Precipitated sulphur differs from sublimed sulphur in being in a state of more minute division, and in its amorphous condition, sublimed sulphur being crystalline.

Colloidal sulphur, which is said to be physiologically much more active than ordinary sulphur, may be produced by passing H_2S into a solution of SO_2 and, after decantation, adding distilled water to the precipitated sulphur, which readily dissolves, and may be freed from SO_2 by subsequent dialysis. This aqueous solution contains about six grains to the fluidounce of colloidal sulphur.

Uses.—Precipitated sulphur possesses medicinal properties similar to those of sublimed sulphur. Its state of extreme division renders it more readily suspended in liquids. A form easily suspended in water may be prepared by adding to the calcium polysulphide solution a solution of casein. The precipitated sulphur carries with it a little casein which communicates through its colloidal effect suspending properties to the sulphur. It is sometimes selected for forming sulphur ointments; these are lighter in color and smoother than those made with sublimed sulphur.

Dose, one to three drachms (3.9–11.6 Gm.).

Off. Prep.—Confectio Sulphuris, *Br.;* Trochiscus Sulphuris, *Br.;* Pasta Betanaphtholis, *N. F.;* Pasta Zinci Sulphurata, *N. F.*

SULPHUR SUBLIMATUM. U. S., Br.

SUBLIMED SULPHUR Sulphur Sublim.
[Flowers of Sulphur]

(sŭl'phŭr sŭb-lĭ-mā'tŭm)

"It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 99.5 per cent. of S (32.07)." *U. S.* "Sublimed Sulphur may be obtained from native sulphur or sulphides." *Br.*

Flores Sulphuris; Brimstone; Soufre Sublimé, *Fr. Cod.;* Fleur (Crême) de Soufre, *Fr.;* Sulfur sublimatum, *P. G.;* Schwefel, Schwefelblumen, Schwefelblüthe, *G.;* Solfo sublimato, *It.;* Azufre sublimado, Azufre, *Sp.*

Natural States.—Sulphur is very generally disseminated throughout the mineral kingdom, and is almost always present, in minute quantity, in animal and vegetable matter. Among vegetables, it is present in volatile oil of mustard and other cruciform plants. It occurs in the earth either native or in combination. When native it is found in masses, translucent or opaque, or in the powdery form mixed with various earthy impurities. In combination it is usually united with certain metals, as iron, lead, mercury, antimony, copper, and zinc, forming compounds called sulphides. *Native sulphur* is most abundant in volcanic countries, and is hence called *volcanic sulphur*. Productive mines of sulphur are found in Sicily, but the output has declined in recent years. In 1915 it was 334,974 metric tons. Sulphur exists as a mineral in widely separated localities and in quantities in the Western United States. Two hundred miles south of Salt Lake City there is a deposit of sulphur two thousand feet square and of an unknown thickness, shafts having been sunk sixty feet without reaching the bottom. This sulphur is said to be free from arsenic and antimony and is a surface deposit. Much sulphur has been found in Mount Humboldt, Nevada, and Sulphur Mountain, as it is called, in the Yellowstone National Park, is largely composed of the mineral. The only localities in the United States in which sulphur is actively mined at present, however, are in Calcasieu Parish, La., where the Union Sulphur Company is now operating on an extensive scale, and a sulphur deposit underlying a quicksand is being mined by the Frasch process, and at Freeport and other localities in Texas. A double-walled iron pipe is driven through the quicksand into the sulphur bed, and steam having been sent down between the walls of the pipe, the melted sulphur is raised in the inner pipe. An annual production of 375,000 tons is now maintained by the Union Sulphur Company, and this can be increased readily from the wells already opened. Sulphur exists in large quantities in various localities in Japan, and 24,647 tons from there was received in the United States in 1915 for consumption on the Pacific coast.

Sicilian sulphur is usually extracted from the sulphur-containing earth by heating in covered mounds known as *calcaroni*, and collecting the melted sulphur or by extraction from the earth by superheated steam under several atmospheres pressure. In Louisiana it is pumped from the wells in a melted state of 99.9 per cent. purity.

The process of purifying the crude Sicilian sulphur consists in distilling the crude sulphur from a large cast iron still, set in brickwork over a furnace and furnished with an iron head. The head has two lateral communications, one with a chamber of brick work, the other with an iron receiver immersed in water, which is constantly renewed to cool it sufficiently to cause the sulphur to condense in the liquid form. When the tube between the still and the receiver is shut, and that communicating with the chamber is open, the sulphur condenses on its walls in the form of an impalpable powder, and constitutes *sublimed sulphur*, or *flowers of sulphur*. If, on the other hand, the communication with the chamber be closed, and that with the receiver open, the sulphur will condense in the latter in the fused state, and, when cast in

cylindrical moulds, forms the *roll sulphur* of commerce.

In the island of Anglesea, and at Swansea, Wales, large quantities of sulphur are obtained from imported Spanish copper pyrites in the process for extracting the metal. The furnaces in which the ore is roasted are connected with chambers in which the volatilized sulphur is condensed.

A process for separating pure sulphur from the residue of the manufacture of soda (calcium sulphide), proposed by Max Schaffner, has been used in most of the soda factories of Germany, and has been introduced, to a greater or less extent, in England, France, and Belgium. We shall confine ourselves to an outline. The process is divided into three parts: *first*, the preparation of the *soda solution* by heaping up the soda residue in the air, whereby oxidation takes place, and polysulphides and thiosulphates are formed, which are extracted by lixiviation; *secondly*, the solution thus obtained is decomposed in close stone or iron vessels, by hydrochloric acid, which decomposes the polysulphides and thiosulphates, with precipitation of sulphur; and, *thirdly*, the sulphur is obtained pure by fusing it under water, with steam and a pressure of 1¾ atmospheres. Calcium chloride remains in solution, gypsum is suspended, and the addition of a little milk of lime neutralizes any free acid present, and with the sulphur forms calcium sulphide, which dissolves whatever arsenic sulphide may be present, leaving the sulphur free from impurities. This collects in the bottom of the kettle, and is drawn off into moulds. From 60 to 65 per cent. of pure sulphur is thus obtained from the soda residue. A. M. Chance (*J. Soc. Chem. Ind.*, 1888, p. 162) has described a process which after several years of experiment has been perfected, and seems likely to solve definitely the problem of sulphur recovery, if, as stated, 95 per cent. of the sulphur can be either recovered as brimstone or burned in sulphur furnaces for the manufacture of sulphuric acid. Chance passes limekiln gases (carbon dioxide and nitrogen) into the vats of alkali waste, liberating thereby the sulphur as hydrogen sulphide. This mixed with nitrogen goes into another vessel of alkali waste, when H_2S and CaS unite to form $Ca(HS)_2$, a calcium sulphydrate, while the nitrogen is allowed to escape. The $Ca(HS)_2$ is now decomposed by a fresh quantity of CO_2, and thus liberates a double quantity of hydrogen sulphide. This is so pure that when mixed with the requisite quantity of air and passed over anhydrous ferric oxide at a dull red heat the hydrogen is burned, liberating the sulphur, according to the reaction:

$$H_2S + O = H_2O + S$$

The sulphur can be obtained either in the sublimed or in the fused form, according to the temperature of the chamber.

Crude foreign sulphur has come to this country principally from Messina, in Sicily, and the ports of Italy, but in recent years Japanese sulphur has been received on the Pacific coast. Roll sulphur and the flowers are often brought from Marseilles. Good Sicilian sulphur does not contain more than 3 per cent. of impurity, consisting chiefly of earths. The Louisiana sulphur the extraction of which is described on page 1084 enters commerce, having the purity of 99.9 per cent. Crude sulphur is employed by the manufacturers of sulphuric acid, and, as it is very variable in quality, it becomes important to ascertain its value. This may be done by drying a given weight of it and submitting it to combustion. The weight of the incombustible residue, added to that lost in drying, gives the amount of impurity.

Properties.—Sulphur is a non-metallic element, existing in several allotropic states. In its ordinary state it is a brittle solid, of a pale yellow color, permanent in the air, and exhibiting a crystalline texture and shining fracture. It has a slight taste, and a perceptible odor when rubbed. When pure its sp. gr. is about 2, but it varies a little in density in its different allotropic states. Occasionally, from impurity, its sp. gr. is as high as 2.35. It is a poor conductor of heat, and becomes negatively electric by friction. The melting point of sulphur varies with its allotropic state, which is readily altered by heat. Pure sulphur melts and sublimes at 114.5° C. (238° F.). If heated above its melting point, it undergoes, in proportion to the heat applied, a progressive change, which will cause it, upon slow cooling, to solidify at a temperature lower than that at which it was melted; and if it be remelted it will be found to have a higher melting point than before. Melted sulphur is perfectly limpid, and of a bright yellow color. When sulphur is melted, and, after partial cooling, the crust formed on its surface is pierced, and the fluid portion poured out, it may be obtained in slender monoclinic crystals, constituting an allotropic condition of the element. This variety, however, gradually passes back into the more permanent variety found in nature. When sulphur is heated above its melting point, it becomes deeper in color and less fluid. At 200° C. (392° F.) it has a deep brown color, and is so viscid that it cannot be poured from the containing vessel. If the temperature be still further increased, the sulphur resumes its fluidity, but retains its brown color. Finally, when the temperature reaches 448.4° C. (839° F.), it boils, forming a yellow vapor, and may be distilled. If melted sulphur, heated above 200° C. (392° F.), is suddenly cooled by being poured out into water, it becomes a reddish-brown plastic mass, with alteration of properties, called *soft sulphur* (*viscid sulphur*), which constitutes another allotropic variety, and is employed in taking impressions of medals, etc. This form of sulphur resumes the hard state, but not its original color, after the lapse of a few days, or suddenly if heated to 100° C. (212° F.). Sulphur is insoluble in water, but soluble in alkaline solutions, petroleum, rectified coal naphtha, the fixed oils, oil

of turpentine and other volatile oils, alcohol and ether, chloroform, and carbon disulphide. One of its best solvents is carbon disulphide, from solution in which it crystallizes generally in rhombic octahedra, forms belonging to a different system from the monoclinic prisms obtained by crystallizing melted sulphur by cooling. Hence sulphur is said to be dimorphous. Eugène Pelouze has observed that the oils obtained by distilling the tar from gas works dissolve most sulphur at a temperature near their boiling point, and, if a saturated solution at this heat were to be allowed to cool, it would deposit sulphur in a crystalline form, and M. C. Wiedmann has suggested the application of this property to extraction of sulphur from native sulphur earths and ores, and from the residue of coal-gas works. (*A. J. P.*, June, 1871, p. 267.)

The allotropic states of sulphur have been studied chiefly by Brodie, Magnus and Weber, and Berthelot. These states are induced, for the most part, by heat, and are distinguished by the crystalline form of the sulphur, and by its solubility or non-solubility in carbon disulphide. *Insoluble sulphur* is the name given to that part of the soft sulphur which is left undissolved by the disulphide, amounting to between one-third and nearly one-half of the former. Brodie was unable to determine the melting point of this sulphur, but found it considerably above 120° C. (248° F.), or the melting point of prismatic sulphur. Flowers of sulphur contain about one-third of their weight of insoluble sulphur.

According to Marès, sulphur mixed with calcium carbonate, in the presence of the organic matters of the soil, is converted at first into hydrogen sulphide, then, under the influence of air and porous bodies, into sulphuric acid, finally into calcium sulphate, but Egidio Pollacer, on the contrary, thinks that sulphur in contact with calcium carbonate passes very readily into sulphuric acid, and then to calcium sulphate, independently of organic matters, and without being preliminarily changed into hydrogen sulphide, and this opinion he supports by several experiments. (*J. P. C.*, Oct., 1874, p. 330.)

Sulphur takes fire at about the temperature of 148.8° C. (300° F.), and burns with a blue flame, combining with the oxygen of the air, and giving rise to sulphurous oxide, SO_2. The combinations of sulphur are numerous, and are among the most powerful chemical agents. It forms with oxygen four oxides, *sulphurous oxide* (*sulphur dioxide*), SO_2 *sulphuric oxide* (*sulphur trioxide*), SO_3, *sulphur sesquioxide*, S_2O_3, and *sulphur heptoxide*, S_2O_7. The first two of these oxides, by their union with water, form *sulphurous acid*, H_2SO_3, and *sulphuric acid*, H_2SO_4, respectively. There are also known *hyposulphurous acid*, H_2SO_2, the corresponding oxide of which is not known, and in combination *thiosulphuric acid* (frequently spoken of as hyposulphurous acid), $H_2S_2O_3$, *persulphuric acid*, $H_2S_2O_8$, and a series of acids, $H_2S_2O_6$, $H_2S_3O_6$, $H_2S_4O_6$, and $H_2S_5O_6$, called the *thionic series*. It forms with hydrogen, hydrogen sulphide (hydrosulphuric acid or sulphuretted hydrogen), and with the metals, various *sulphides*. Some of the sulphides are analogous to oxyacids, others to basic hydroxides; and these different sulphides, by combining with one another, form compounds which, from their analogy to salts, are called Berzelius *sulphosalts*.

Sulphur, when obtained by roasting the native sulphide, sometimes contains arsenic, and is thereby rendered poisonous. Sicilian sulphur, being volcanic, is not subject to this impurity. The common English roll sulphur is sometimes made from iron pyrites, and is then prone to contain orpiment (arsenic trisulphide). This impurity may be detected by heating the suspected sulphur with nitric acid. The arsenic, if present, will be converted into arsenic trioxide, and the nitric solution, diluted with water, neutralized with sodium carbonate, and acidulated with hydrochloric acid, will give a yellow precipitate of arsenic pentasulphide with a stream of hydrogen sulphide. A precipitate may be more readily obtained from the nitric solution if, after neutralization, sulphurous acid be added, which will convert the arsenic acid into arsenous acid. This is more easily decomposed by the hydrogen sulphide, but the precipitate obtained will now be the trisulphide. Sulphur, when perfectly pure, is wholly volatilized by heat, and soluble without residue in oil of turpentine. According to Playfair, a solution of sodium nitro-prusside is a delicate test for the alkaline sulphides, producing with them a violet tint. Bailey of West Point, employed the same test for detecting sulphur in any compound. The substance suspected to contain it is fused with sodium carbonate, with the addition of carbonaceous matter if necessary. If sulphur be present it will be converted into sodium sulphide, and upon the addition of a small portion of the fused mass to a drop of the nitro-prusside the characteristic violet tint will be produced.

Sublimed sulphur, usually called *flowers of sulphur* (*flores sulphuris*), is "a fine, yellow powder, having a slight, characteristic odor, and a faintly acid taste. Sublimed Sulphur is practically insoluble in water and nearly insoluble in alcohol; it is slightly soluble in ether; soluble or partially soluble in carbon disulphide, chloroform, or olive oil. At about 115° C. (239° F.) it fuses to a yellow, mobile fluid, which upon further heating becomes dark and viscid. In the air it burns to sulphur dioxide, characterized by its odor. The amount of residue left after volatilizing or igniting a weighed portion of well-dried Sublimed Sulphur does not exceed 0.5 per cent.

"**Assay.**—Transfer about 1 Gm. of Sublimed Sulphur, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed, to a flask containing 50 mils of a 10

per cent. solution of potassium hydroxide. Boil the mixture until the liquid is of a transparent, golden-yellow color and then dilute it with distilled water to make a volume of exactly 250 mils. Oxidize 25 mils of this diluted solution by the addition of solution of hydrogen dioxide in excess (using about 50 mils), and heat on a water bath for thirty minutes. Then acidulate the liquid with hydrochloric acid, and dilute it with 100 mils of distilled water. Now heat it to boiling and add hot barium chloride T.S., in small portions, to the resulting liquid until no further precipitation takes place. Heat this mixture on a water bath for thirty minutes, collect the resulting precipitate on a filter, wash, dry, ignite, and weigh the barium sulphate. Carry out a blank determination, using the same amount of all of the reagents but omitting the Sulphur, and before making the final calculation deduct the amount of barium sulphate thus obtained from that obtained in the assay. It shows, in the dried product, not less than 99.5 per cent. of S.

"Each gramme of Sublimed Sulphur, previously dried, corresponds to not less than 7.243 Gm. of barium sulphate." *U. S.*

"A slightly gritty powder of a bright greenish-yellow color. Odorless and tasteless. Under the microscope it is seen to consist of irregular angular particles mixed with almost opaque globules. Burns with a blue flame, forming sulphur dioxide, and leaving not more than 0.25 per cent. of fixed residue. When 10 grammes are mixed with *water*, filtered, and thoroughly washed, the mixed filtrate and washings require for neutralisation not more than 5 millilitres of *N/10 solution of sodium hydroxide* (limit of acidity). *Arsenic limit* 5 parts per million." *Br.*

It is always contaminated with a little sulphuric acid, which is formed at the expense of the oxygen of the air contained in the subliming chambers. Accordingly, it always reddens litmus, and, if the acid is present in considerable quantity, sometimes cakes. It may be freed from acidity by careful washing with diluted ammonia water. (See *Sulphur Lotum.*)

Uses.—Elemental sulphur is free from local effect and is so insoluble that it cannot be absorbed, and hence exercises no effect upon the system. When taken into the alimentary canal, however, a portion of it unites to form hydrogen sulphide, which is an active agent. By virtue of its local irritant action upon the mucous membrane the latter substance provokes intestinal peristalsis and therefore sulphur exercises a laxative influence. The movements produced by it are soft, generally without griping, and it is a frequently used laxative in cases of *hemorrhoids*. A certain amount of the hydrogen sulphide formed may be absorbed; indeed it is asserted that the sweat of persons taking sulphur will cause a black deposit of sulphide upon silver coins. Although the therapeutic properties of hydrogen sulphide have not been clearly determined, sulphur has been widely used as an alterative, especially in *chronic rheumatism* and *gout*. Besides this, a portion of the sulphide will be eliminated through the mucous membrane of the respiratory tract and sulphur may therefore exercise a beneficial action in *chronic bronchitis* and *asthma*.

The most important uses, however, of sulphur are external. When brought in contact with the skin, especially in the presence of alkalies, a similar union of sulphur with hydrogen takes place as in the intestines. The alkaline sulphide thus formed is an active poison to various pathogenic parasites and sulphur is therefore a useful remedy in such diseases as *scabies*, *ringworm*, and *favus*. Besides this effect the sulphides by their local stimulating effect tend to overcome congestion in the skin and they have the power of softening the horny elements. For one or the other of these effects sulphur is a valuable remedy in a number of non-parasitic diseases of the skin, especially *acne*, *psoriasis*, *seborrhea*, etc. Locally it may be employed either in the form of a suspension or in an ointment in strengths of from 5 to 20 per cent. It is often incorporated in soaps. For local application the precipitated sulphur is the best because of its finely divided state. For internal administration either the washed or precipitated sulphur may be employed.

Under the names of *sulfidal* and *sulfoform* a soluble *colloidal sulphur* has been introduced. This is asserted by Joseph (*Derm. Cb.*, 1913) and others to be superior to the official sulphur in the treatment of skin diseases. It is used in strengths of from 2 to 20 per cent. See under *Sulphur Precipitatum* for method of preparation.

According to Hannon of Brussels, *soft sulphur*, recently prepared, possesses valuable therapeutic properties, not as a laxative, but as a stimulant to the circulation, lungs, and skin, far more active than ordinary sulphur. The *dose* of soft sulphur is from twenty to fifty grains (1.3–3.2 Gm.), given in the form of pill. It has also been successfully employed for filling the hollows of *carious teeth*. (*P. J.*, xvii, 330.) Sublimed sulphur has been used with extraordinary success in South Africa and the Philippines in the treatment of *amœboid dysentery*. It acts probably by killing the amœba. It may be given in divided doses up to two hundred grains (13 Gm.) a day.

Much sulphur is consumed in the arts, principally in the manufacture of gunpowder and of sulphuric acid.

Dose, one to three drachms (3.9–11.6 Gm.).

Off. Prep.—Antimonium Sulphuratum, *Br.;* Confectio Sulphuris, *Br.;* Emplastrum Hydrargyri, *Br.;* Potassa Sulphurata, *Br.;* Pulvis Glycyrrhizæ Compositus, *Br.;* Sulphur Lotum, *U. S.;* Sulphur Præcipitatum, *U. S.;* Sulphuris Iodidum, *Br.;* Unguentum Sulphuris, *U. S., Br.;* Liquor Calcis Sulphuratæ, *N. F.;* Petroxolinum Sulphuratum, *N. F.;* Petroxolinum Sulphuratum Compositum, *N. F.;* Unguentum Sulphuris, *N. F.;* Unguentum Sulphuris Alkalinum, *N. F.;* Unguentum Sulphuris Compositum, *N. F.*

SUMBUL. U. S.

SUMBUL [Musk-root]

(sŭm'bŭl)

"The rhizome and roots of *Ferula Sumbul* (Kauffmann) Hooker filius (Fam. *Umbelliferæ*)." *U. S.*

Sumbul Radix, *Br.;* Racine de Sumbul, *Fr.;* Sumbulwurzel, Moschuswurzel, *G.*

Under the name of *sumbul* or *jatamansi,* a root has long been used in India, Persia, and other parts of the East, as a perfume, an incense in religious ceremonies, and medicinally. It was the root of a then unknown plant, supposed to be umbelliferous, and, from the character of the root, to grow in low wet places. The plant is said to inhabit no part of British India, but the regions to the north and east of it, as Nepaul, Bootan, Pucharia, etc. The root is taken northward to Russia, and reaches the rest of Europe through Petrograd. The physicians of Moscow and Petrograd were the first to employ it on the continent of Europe. Granville first introduced it to the notice of the profession in Great Britain and in this country. It has also been imported into England from India, whither it was brought from a great distance. The plant which is now recognized by the U. S. P. as the source of the sumbul is the *Ferula Sumbul* Hooker fil.

Ferula Sumbul was first discovered by the Russian Fedschenko in 1869, growing at an elevation of 3000 feet in the mountains which separate Russian Turkestan from Bucharia. In 1871 it was described by Kauffmann, who erected a new genus on characters dependent upon the enormous size of the vittæ in the immature fruit. The plant has been cultivated in the Moscow botanical gardens, and, less successfully, at Kew, and it has been found that the vittæ almost disappear in ripening, and do not afford a good generic character. The plant is a large umbellifer, reaching a height of eight feet, and having a solid, cylindrical, slender stem, which in the upper part gives origin to about twelve slender divaricate branches. The root-leaves are two and a half feet long, with short, channelled, broadly dilated, completely clasping petioles. They are triangular in outline, tripinnate, with the alternate divisions fine. The stem-leaves rapidly decrease in size until they become mere sheathing bracts. The flowers are polygamous, the fruit from three-eighths to one-half inch long by one-fourth inch wide; the mericarps oblong-oval, dorsally much compressed, thin, with three faint, thread-like, dorsal ridges; no dorsal vittæ, and commissural ones collapsed. J. E. Aitchison states (*Tr. Linn. Soc.,* ser, 2, *Bot.,* 69) that the root of *Ferula suaveolens,* which has only a faint musky odor, is one of the kinds exported from Persia to Bombay by the Persian Gulf.

Properties.—Sumbul is officially described as "in transverse segments, attaining a length of 10 cm. and a diameter of 7 cm.; externally light brown to dark brown, longitudinally wrinkled and showing in the upper portions a smooth, grayish, epidermal layer, occasionally with the short stem-bases attached; fracture short, fibrous, spongy; internally light yellow or brownish-yellow, arrangement of wood irregular and with yellowish-brown or blackish resinous patches frequently extending over the entire ends of the segments; odor peculiar, musk-like; taste bitter and somewhat aromatic. The powder is grayish-brown; when examined under the microscope it exhibits numerous, irregular, brownish-black fragments and well-defined isolated tracheæ, the latter with distinct end-walls, and mostly with reticulate thickenings and from 0.03 to 0.1 mm. in width; occasional fragments of polygonal epidermal cells with yellowish-brown walls; numerous, nearly colorless, yellowish-brown and reddish-brown fragments consisting of a granular substance in which the cellular structure is not well defined; long, narrow fragments consisting of more or less collapsed leptome or sieve tissue; occasional fragments of well-defined parenchyma with a few, nearly spherical starch grains, from 0.003 to 0.012 mm. in diameter." *U. S.*

The root has been analyzed by Reinsch and other German chemists, and found to contain volatile oil, two balsamic resins, one soluble in alcohol, the other in ether; wax, gum, starch, a bitter substance soluble in water and alcohol, and an acid which was named *sumbulic acid,* but which Riecker and Reinsch showed to be *angelic acid,* $C_5H_8O_2$, accompanied by a little valeric acid, $C_5H_{10}O_2$. Solution of potassium hydroxide is said to convert the resin into the potassium salt of an acid called *sumbulamic,* but which has not been sufficiently investigated. The musk-like odor seems to be connected with the balsamic resins, and probably depends on some principle associated with them not yet isolated. The volatile oil, of which 0.33 per cent. is yielded by distillation, has a taste like that of peppermint. On dry distillation it yields a bluish oil which contains *umbelliferone.* Philip H. Utech (*A. J. P.,* 1893, p. 465) has extracted and purified the resin soluble in alcohol. He obtained it as a soft, whitish, translucent resin which, on drying at 110° C. (230° F.), yielded a clear, transparent, amber-colored product having a bitter taste and the aromatic odor of the root. It constituted 6.1 per cent. of the drug. J. H. Hahn (*Proc. Penna. Ph. Assoc.,* 1896, 75) found 17.25 per cent. of fixed oil in sumbul.

A proximate analysis reported by Heyl and Hart (*A. J. P.,* Dec., 1916, p. 546, shows the following results: Moisture, 10.17 per cent.; starch, 7.70 per cent.; pentrosans, 10.60 per cent.; crude fiber, 17.15 per cent.; protein, 5.50 per cent.; dextrin, 1.40 per cent.; ash, 6.50 per cent.; sucrose, 1.64 per cent.; reducing sugar, 0.51 per cent., volatile oil, 1.10 per cent.; resins, 17.1 per cent. Alkaloids were not detected. The volatile oil did not show the presence of sulphur. *Umbelliferon* was detected, as was also

betaine. Vanillic acid ($C_8H_8O_4$) was identified in the resinous portion and a phytosterol was also recognized as being present. Acetic, butyric, angelic and tiglic acids were among the volatile acids, while among the non-volatile acids were oleic, linoleic, tiglic, cerotic, palmitic and stearic.

Uses.—Sumbul is supposed to have a quieting influence on the nervous system and is used in the treatment of various *hysterical* conditions. By many it is believed to have an especial relation to the pelvic organs and it is widely employed in *dysmenorrhea* and allied disorders. It has also been used as a stimulant to mucous membranes not only in *chronic dysenteries* and *diarrheas,* but in *chronic bronchitis,* especially with *asthmatic* tendency, and even in *pneumonia.*

Murawieff, of Russia, prepares the resin, which he considers to be the active principle, by macerating the root first in water, and then in a solution of sodium carbonate, washing it well with cold water, drying it, treating it with alcohol, filtering the tincture, adding a little lime and again filtering, separating the lime by sulphuric acid, agitating with animal charcoal, again filtering, distilling off nearly all the alcohol, mixing the residuum with water, driving off the remaining alcohol, and, finally, washing the precipitate with cold water, and drying it.

Half an ounce of a tincture produced narcotic symptoms, such as confusion of the head, a tendency to snore, even when awake, feelings of tingling, etc., with a strong odor of the medicine from the breath and skin, which continued for a day or two and gradually passed off. (*N. R.,* Oct., 1874, p. 309.)

Dose, one-half drachm to two drachms (2.0–7.7 Gm.).

Off. Prep.—Fluidextractum Sumbul, *U. S.;* Extractum Sumbul, *U. S.;* Tinctura Sumbul, *N. F.*

SUPPOSITORIA. U. S.

SUPPOSITORIES

(sŭp-pŏs-ĭ-tō′rĭ-ă)

Suppositoires, *Fr. Cod.;* Suppositoria, *P. G.;* Suppositorien, Stuhlzäpfchen, *G.;* Supositorios, *Sp.*

Suppositories are solid bodies usually intended to be introduced into the rectum with a view either of evacuating the bowels by irritating the mucous membrane of the rectum, or of producing a specific effect on the neighboring parts or on the system at large. Suppositories are also made for vaginal or urethral administration. They fulfil the same indications as enemata, and are sometimes preferable from the facility of their application, and, when the object is to produce the peculiar effect of a medicine, from the smallness of their bulk, which facilitates retention. Their form may be cylindrical, conical, or spherical, the last being preferable when the bulk is small, or they may be in the shape of the modified cone with a tapering base, as recommended by H. S. Wellcome. (*Proc. A. Ph. A.,* 1893, p. 103.) They should be of such a consistence as to retain their shape, but so soft as to incur no risk of wounding the rectum. For laxative purposes the suppository may be from one to three inches long, and about as thick as a common candle; with a view to the specific effects of medicines it should be considerably smaller, as in this case it is important that the medicines should be retained and the irritative influence of distention avoided. Soap is not unfrequently employed in this way as a laxative. A. B. Taylor, of Philadelphia, in 1852 called attention to cacao butter as the best base for suppositories, having more exactly the requisite degree of consistence and fusibility than any combination of suet, spermaceti, wax, etc., that could be employed. (*A. J. P.,* 1852, p. 211.) Experience has proved the correctness of his views. It has been thought necessary to use wax, spermaceti, or some other substance having a comparatively high fusing point, in order to render the suppository sufficiently firm. Continued experience has, however, demonstrated that, except in the warmest weather, or in the case of camphor, phenol, the essential oils, and similar medicinal substances, even the commercial cacao butter will suffice. It is said that cacao butter is usually adulterated with some other fat which melts at a low temperature, and that if a pure article can be obtained any substance to increase its hardness is never required. When such a material is employed, wax is usually selected, although cetaceum is preferable. If not more than 10 per cent. of the spermaceti is added, the value of the suppository is not very materially affected, although it melts more slowly, and consequently requires a longer time to act, than when the butter of cacao is used alone. Suppositories containing a considerable percentage of wax melt so slowly in the rectum as to be comparatively useless, or they may fail altogether to soften down, and be finally passed from the anus unchanged.

A critical study and contribution to the literature of suppository bases has been published by Bruno Solomon (*Ph. Ztg.,* 1913, p. 502), who classifies them in general as (1) cacao butter, (2) fat and wax combinations, (3) glycerin and gelatin, agar, soap, etc. He prepares what he calls a *mother mass* of gelatin 50, distilled water 100, and glycerin 100. From this, modifications with agar-agar and soap, etc., may be subsequently prepared with the minimum of effort.

A very good method of mixing the oil of theobroma with the hardening material is by grating with an ordinary tin grater, such as used in kitchens, and mixing the coarse powders before melting, and W. G. Ewing has proposed rubbing the powders and the medicinal substance in a mortar together, dividing the plastic mass, and shaping it with the fingers. It is better to shape them with a spatula, and roll them upon a pill tile with a little lycopodium. This plan, although having its advantages, is, however, not equal to the official one of melting the ingredients and running them

into moulds. Extemporaneous moulds, made by rolling paper into cones about an inch long, may be used, but are much less convenient than permanent metallic moulds. The tendency of the hardened suppositories to adhere to the moulds may be overcome more or less perfectly by dusting the moulds with lycopodium powder, or greasing them well with olive oil, but it is far better to rely upon the natural contraction of the mass, caused by thoroughly cooling the moulds. Wm. B. Addington (*A. J. P.*, 1873, p. 257) advises lining the moulds with tin foil. The difficulty may also be met by the use of moulds that open lengthwise, which are now used almost exclusively in preference to individual moulds, and Chas. E. Dwight commends very highly the substitution of plaster of Paris moulds for the metallic ones commonly employed. The mould must be very cold, so as to chill the melted liquid at once and prevent any separation of its ingredients by gravity. It has been proposed to condense the powdered ingredients of suppositories in a cold mould. (*A. J. P.*, 1875, p. 79.) It has also been recommended to form the excipient into the required shape, and then, while it is still soft, make an excavation from the base upward, into which the medicine may be introduced, and afterwards enclosed by a little of the cacao butter. But, as one of the objects of the excipient is an equable diffusion of the medicine, to prevent irritation, this method would be inapplicable to substances in any degree locally irritant.

J. Percy Remington has devised a suppository mould made of soft vulcanized rubber, it is used in the same manner as that employed for a metal mould, the advantage being mainly the facility of removal when the suppository is cold, a slight pressure with a twisting motion causes the soft rubber mould to open, and the suppository to drop out easily. (*Proc. New Jersey Pharm. Association*, 1906.)

The inventive genius of pharmacists has been industriously applied to the construction of suppository moulds, and there are now many varieties; the principle is much the same in all, however, but for convenience they may be classed as follows: 1. Individual moulds; these were among the first to be used. Half a dozen conical, hard-metal moulds, or made of paper, tin-foil, etc., are retained in an upright position in a tray containing ice-water. (See *A. J. P.*, 1861, p. 5; 1863, p. 228; 1867, p. 121; 1868, p. 52; 1870, pp. 296, 392; *Proc. A. Ph. A.*, 1902, 501.) 2. Moulds which consist of two solid pieces of metal, hinged or temporarily joined, so that when the suppository is thoroughly cooled the parts may be separated and the suppository dropped out. (See *A. J. P.*, 1871, pp. 488, 563; 1874, pp. 192, 246; 1875, pp. 98, 202; 1877, p. 569; 1879, pp. 184, 277; and *Proc. A. Ph. A.*, 1893, p. 103; 1902, 757.) 3. Soft rubber moulds. (See *Proc. New Jersey Pharm. Assoc.*, 1906.) 4. Moulds designed to be used through compression; more or less powerful. (*N. R.*, June, 1879, Jan. and March, 1880; also *Proc. A. Ph. A.*, 1897, p. 442.)

The weight—*i.e.*, the size—of rectal suppositories should vary according to the purposes for which they are employed. When they are to be used for infants and children, they should weigh from five to ten grains. The Br. Pharm., in conformity with the recommendation of H. B. Brady (*P. J.*, 1866, p. 544; 1868, p. 321; and 1871, pp. 193, 488, 563), adopts the weight of fifteen grains. Experience has shown this to be the most useful size, and the U. S. P. 1880 adopted it, but the U. S. P. (9th Rev.) directed the weight to be thirty grains. The papers of Brady upon the subject of suppositories may be consulted with advantage; also a series of articles by several other authors in *A. J. P.*, 1871.

The U. S. P. IX directs as follows: "Suppositories are solid bodies of various weights and shapes, adapted for introduction into the different orifices of the human body, and melting or softening at body heat. The vehicles usually employed are oil of theobroma, glycerinated gelatin, or sodium stearate. For suppositories made with oil of theobroma the following general processes may be employed: Take of the Medicinal Substance, *the prescribed quantity;* Oil of Theobroma, grated, *a sufficient quantity.* Reduce the medicinal substance, if dry, to a very fine powder, or, if an extract, soften it with an appropriate liquid, then mix it thoroughly in a mortar with about an equal weight of grated oil of theobroma, and incorporate the remainder of the oil of theobroma until a homogeneous, plastic mass is obtained, adding, if necessary, a small quantity of expressed oil of almond. Roll the mass on a graduated tile until a cylinder of the proper length is formed, divide this into the required number of equal parts, and with a spatula, or other mechanical aid, form them into the desired shape. If the process of cold compression is preferred, mix the medicinal substance in a suitable mortar with about an equal weight of grated oil of theobroma, as above directed, then thoroughly incorporate it with the remainder of the oil of theobroma, previously finely grated, chilling the mortar, if necessary, to preserve the pulverulent form of the mixture. Transfer the powdered mass to the cylinder of an appropriate suppository compresser and by the use of this apparatus prepare the desired number of compressed suppositories. If the process of fusion is preferred, mix the medicinal substance with about an equal weight of grated oil of theobroma, as above directed, then thoroughly incorporate it with the remainder of the oil of theobroma, previously melted by a gentle heat, in a suitable vessel provided with a lip; then allow it to cool to about 38° C. (100.4° F.), and, when the mixture begins to congeal, pour it immediately into suitable well-cooled moulds. Keep the moulds at a freezing temperature until the suppositories have hardened and are ready to be removed. For suppositories containing hydrated

chloral, phenol, or other substances which soften the vehicle, raise the melting point of the oil of theobroma by the addition of from 10 to 15 per cent. of spermaceti, but the melting point must not be raised above 37° C. (98.6° F.). For suppositories made with glycerinated gelatin the following process may be used: Take of the Medicinal Substance, *the prescribed quantity;* Glycerinated Gelatin, Glycerin, Water, each, *a sufficient quantity.* Mix the medicinal substance, if solid and soluble in water or glycerin, or if a miscible liquid, with a little water, and add sufficient glycerin to make the weight of the mixture one-half that of the finished mass. Then thoroughly incorporate it with an equal weight of melted glycerinated gelatin, and pour it at once into suitable moulds which have been greased with a small quantity of petrolatum. Cool the moulds thoroughly before removing the suppositories. Moulds for urethral suppositories should be warmed sufficiently before pouring the mass to facilitate the proper filling of the mould. Suppositories having a firmer consistence may be prepared by substituting mucilage of acacia for a portion of the water or glycerin. If the medicinal substance is insoluble in water or glycerin, thoroughly levigate it in a warm mortar with a sufficient quantity of glycerin to make the weight of the mixture one-half that of the finished mass. Then thoroughly incorporate it with an equal weight of melted glycerinated gelatin, and pour it into suitable moulds as above directed. With bulky powders about one-half of the glycerin may be replaced with water before levigation. Glycerinated gelatin suppositories should be protected against the effects of heat, moisture and dry air by keeping them in tightly-closed containers in a cool place. *Rectal Suppositories* should be cone-shaped, and when made from oil of theobroma should weigh about *two grammes. Urethral Suppositories (Bougies)* should be pencil-shaped, pointed at one extremity, and either *seven centimeters* in length, weighing about *two grammes,* or *fourteen centimeters* in length, weighing about *four grammes,* when made with glycerinated gelatin. If prepared with oil of theobroma they should weigh about one-half the above quantities. *Vaginal Suppositories* should be globular or oviform in shape, and weigh about *ten grammes* if made with glycerinated gelatin, and about *four grammes* if made with oil of theobroma." *U. S.*

The U. S. Pharmacopœia gives no detailed formulæ for suppositories, except in one case, *Suppositoria Glycerini.*

Suppositories are used in medicine (1) for the purpose of obtaining the systemic action of drugs after their absorption, (2) for the local effects of their ingredients. There is an old superstition among the medical profession that systemically acting drugs introduced per rectum have more effect upon the pelvic organs than when given by the mouth, and suppositories of opium, belladonna, etc., are habitually recommended in the treatment of diseases of the bladder and uterus. This view, however, is patently erroneous. The per rectum channel of exhibiting systemically acting drugs may, however, be of service in those cases in which deleterious influence upon the stomach is feared. Speaking in a general way, quantities of about double the dose exhibited by the mouth may be given in the form of suppositories. As a means of obtaining the local action of astringents, anesthetics, or antiseptics, upon the mucous membrane of the rectum suppositories are very valuable.

SUPPOSITORIA ACIDI CARBOLICI. Br.

PHENOL SUPPOSITORIES

(sŭp-pŏs-ĭ-tō'rĭ-ă ăç'ĭ-dī kăr-bŏl'ĭ-cī)

Carbolic Acid Suppositories; Suppositories d'acide Phénique, *Fr.;* Phenol-suppositorien, *G.*

"Phenol, 0.8 gramme; White Beeswax, 0.5 gramme; Oil of Theobroma, *a sufficient quantity* for twelve suppositories each weighing about one gramme. Dissolve the Phenol in the Oil of Theobroma, previously melted, add the White Beeswax, and pour the melted mixture into suitable moulds; or let the mixture cool and then divide it into twelve equal parts, and press each into a conical or other convenient form for a suppository. Each of these Suppositories contains 0.067 gramme (about 1 grain) of Phenol." *Br.*

These suppositories may be used to obtain the local anesthetic and antiseptic effect of phenol. The wax is needed to offset the tendency to liquefy.

SUPPOSITORIA ACIDI TANNICI. Br.

TANNIC ACID SUPPOSITORIES

(sŭp-pŏs-ĭ-tō'rĭ-ă ăç'ĭ-dī tăn'nĭ-cī)

Suppositories de Tannin, *Fr.;* Tanninsuppositorien, Tannin-Stuhlzäpfchen, *G.*

"Tannic Acid, 2.4 *grammes;* Oil of Theobroma, *a sufficient quantity* for twelve suppositories each weighing about one gramme. Melt the Oil of Theobroma; triturate the Tannic Acid intimately with a little of the Oil, and add to the remainder; stir well; as the mixture begins to thicken pour it into suitable moulds; or let the mixture cool and then divide it into twelve equal parts, and press each into a conical or other convenient form for a suppository. Each of these Suppositories contains 0.2 gramme (about 3 grains) of Tannic Acid." *Br.*

As it is hardly conceivable that a rectal dose of less than five grains should be wanted for the adult, the U. S. preparation of 1870 was of the latter strength (*i.e.,* five grains). The benzoated lard formerly added by the British authorities with a view of preventing rancidity has been omitted. The remedy is especially applicable to cases of *piles* and *prolapsus of the rectum.*

SUPPOSITORIA BELLADONNÆ. Br.

BELLADONNA SUPPOSITORIES

(sŭp-pŏs-ĭ-tō'rĭ-ă bĕl-lă-dŏn'næ)

Suppositoires de belladone, *Fr.*; Belladonnasuppositorien, *G.*

"Liquid Extract of Belladonna, 1.7 *millilitres;* Oil of Theobroma, *a sufficient quantity* for twelve suppositories each weighing about one gramme. Evaporate the Liquid Extract of Belladonna to a syrupy consistence; mix with the Oil of Theobroma, previously melted; as the mixture begins to thicken pour it into suitable moulds; or let the mixture cool and then divide it into twelve equal parts, and press each into a conical or other convenient form for a suppository. Each of these Suppositories contains, approximately, 0.001 gramme (about 1/60 grain) of the alkaloids of Belladonna Root." *Br.*

SUPPOSITORIA GLYCERINI. U. S., Br.

SUPPOSITORIES OF GLYCERIN Supp. Glycerin.

(sŭp-pŏs-ĭ-tō'rĭ-ă glĭç-ĕ-rĭ'nī)

Suppositoires de Glycérin, *Fr.*; Glycerinsuppositorien, *G.*

* "Glycerin, *thirty grammes* [or 1 ounce av., 25.5 grains]; Monohydrated Sodium Carbonate, *five-tenths of a gramme* [or 7.7 grains]; Stearic Acid, *two grammes* [or 31 grains]; Water, *five mils* [or 81 minims], to make *ten rectal suppositories.* Dissolve the monohydrated sodium carbonate in the water and add it to the glycerin contained in a suitable vessel placed in a water bath in such a way that the vessel is well down in the boiling water and its contents protected as much as possible from the steam of the bath. Add the stearic acid and heat the mixture for fifteen minutes or until the carbon dioxide ceases to be evolved, and the liquid is clear. Then pour the melted mass into suitable moulds, remove the suppositories when they are completely cold, and preserve them in tightly-stoppered glass vessels in a cool place." *U. S.*

"Gelatin, cut small, 14 *grammes;* Glycerin, 70 *grammes;* Distilled Water, *a sufficient quantity.* Soak the Gelatin in the Distilled Water for five minutes, or until thoroughly softened; drain well, add the Glycerin, dissolve on a water-bath and evaporate until the mixture weighs one hundred grammes. Pour the product into suitable moulds having capacities corresponding to two, four, or eight grammes of the Suppository, or of such other capacities as may be required. Each of these Suppositories contains 70 per cent. by weight of Glycerin." *Br.*

These were official for the first time in the U. S. P. 1890. Glycerin suppositories have come into extensive use, the object being to introduce glycerin into the rectum with a minimum amount of other ingredients. Stearic acid was selected on account of its forming with sodium carbonate the hardest soap attainable, thus permitting the introduction of a suppository containing at least 90 per cent. of glycerin, the water, added to dissolve the monohydrated sodium carbonate, and some of the glycerin being evaporated during the manipulation. This process was perfected by J. P. Remington. (See *Practice of Pharmacy,* 6th ed.) The British method, on account of the use of gelatin, permits the presence of only 70 per cent. of glycerin, the suppository not being firm enough for convenient application, and, in addition, the method of hydrating the gelatin is faulty. (*C. D.*, 1898, 831.) Instead of wrapping the suppositories in tin foil it will be found more satisfactory to insert each one in a small glass tube of the proper size, corked at both ends, or in small individual cylindrical vials. Some protection from the moisture in the air is necessary because of the hygroscopic character of glycerin. (See *P. J.*, 1893, 63; 1895, 182; *Am. Drug.*, 1894, 91; *West. Drug.*, 1894, 141; *A. J. P.*, 1895, 599.)

Uses.—Glycerin suppositories are very much used to produce fecal discharges in *constipation.* They act by locally irritating the mucous membrane of the rectum, and are often satisfactory, though never really purgative. As an occasional remedy they are useful, but their habitual employment is probably injurious to the mucous membrane.

SUPPOSITORIA IODOFORMI. Br.

IODOFORM SUPPOSITORIES

(sŭp-pŏs-ĭ-tō'rĭ-ă ĭ-ŏd-ō-fŏr'mī)

Suppositoires d'Iodoforme, *Fr.*; Jodoformsuppositorien, *G.*

"Iodoform, in powder, 2.4 *grammes;* Oil of Theobroma, *a sufficient quantity* for twelve suppositories each weighing about one gramme. Proceed as directed for Suppositoria Acidi Tannici. Each of these Suppositories contains 0.2 gramme (about 3 grains) of Iodoform." *Br.*

These suppositories are valuable in cases of rectal inflammation and irritation. It is often possible by their use in *dysentery* to avoid the use of opium to a greater or less extent. They are especially serviceable to relieve the pain and itching of *hemorrhoids.*

SUPPOSITORIA MORPHINÆ. Br.

MORPHINE SUPPOSITORIES

(sŭp-pŏs-ĭ-tō'rĭ-ă mör-phī'næ)

Suppositoires de Morphine, Suppositoires morphinés, *Fr.*: Morphinumsuppositorien, Morphin-Stuhlzäpfchen, *G.*

"Morphine Hydrochloride, 0.2 *gramme;* Oil of Theobroma, *a sufficient quantity,* for twelve suppositories each weighing about one gramme. Proceed as directed for Suppositoria Acidi Tannici. Each of these Suppositories contains 0.017 gramme (about ¼ grain) of Morphine Hydrochloride." *Br.*

These may be used to obtain the systemic effects of morphine when, for any reason, it is undesirable to exhibit that drug by mouth.

SUPPOSITORIA PLUMBI COMPOSITA. Br.

COMPOUND LEAD SUPPOSITORIES

(sŭp-pŏs-ĭ-tō'rĭ-ă plŭm'bī cŏm-pŏs'ĭ-tă)

Suppositoires de Plomb composés, Suppositoires de Plomb opiacés, *Fr.*; Zusammengesetzte Bleisuppositorien, *G.*; Stuhlzäpfchen von Opium und Bleizucker, *G.*

"Lead Acetate, in powder, 2.4 *grammes;* Opium, in powder, 0.8 *gramme;* Oil of Theobroma, *a sufficient quantity,* for twelve suppositories each weighing about one gramme. Proceed as directed for Suppositoria Acidi Tannici. Each of these Suppositories contains 0.2 gramme (about 3 grains) of Lead Acetate, and 0.067 gramme (about 1 grain) of Opium." *Br.*

This irrational combination is occasionally used in *diarrhea* or *hemorrhoids.*

SUPRARENALUM SICCUM U. S.

DRIED SUPRARENALS Supraren. Sicc. [Glandulæ Suprarenales Siccæ U. S. VIII, Desiccated Suprarenal Glands]

(sūp-ră-rē-nā'lŭm sĭc'cŭm)

"The suprarenal glands of animals which are used for food by man, cleaned, dried, freed from fat, and powdered, and containing not less than 0.4 per cent. nor more than 0.6 per cent. of epinephrine, the active principle of the suprarenal gland. One part of Dried Suprarenals represents approximately 6 parts of fresh glands, free from fat. If assayed biologically *one gramme* of Dried Suprarenals contains the equivalent of *ten milligrammes* of lævo-methylaminoethanol-catechol." *U. S.*

The suprarenal glands are small organs found in all mammals, situated in the neighborhood of the kidney. When freed of their fat and dried they may be pulverized. This is a "light yellowish-brown, amorphous powder, having a slight, characteristic odor; partially soluble in water. Dried Suprarenals contain not more than 7 per cent. of moisture, and the yield of ash does not exceed 7 per cent.

"**Assay.**—Add 0.005 Gm. of finely powdered manganese dioxide and 10 mils of distilled water to 0.01 Gm. of Dried Suprarenals; thoroughly shake the mixture several times during one hour and filter. Compare the color of the filtrate in a test tube or in any convenient manner, with the color of cobaltous chloride T.S. and diluted gold chloride T.S. (see Reagents, Part III) combined as follows: Mix 1.85 mils of cobaltous chloride T.S. with 0.95 mil of diluted gold chloride T.S. and 7.2 mils of distilled water; the color corresponds to 0.2 per cent. of epinephrine in the filtrate obtained above; 2.95 mils of cobaltous chloride T.S. with 1.25 mils of diluted gold chloride T.S. and 5.8 mils of distilled water corresponds in color to 0.4 per cent. of epinephrine; 4.05 mils of cobaltous chloride T.S. with 1.35 mils of diluted gold chloride T.S. and 4.6 mils of distilled water corresponds in color to 0.6 per cent. of epinephrine; 5.15 mils of cobaltous chloride T.S. with 1.55 mils of diluted gold chloride T.S. and 3.3 mils of distilled water corresponds in color to 0.8 per cent. of epinephrine. The percentages of epinephrine indicated by the above color standards are based upon the maceration of 0.01 Gm. of the Dried Suprarenals in 10 mils of distilled water, as directed above, and filtering. In samples containing more than 0.8 per cent. of epinephrine, 0.005 Gm. of the Dried Suprarenals may be taken, in which case the percentage stated above, as indicated by the color standards, should be doubled. The standard color solutions keep unchanged, if sealed in glass tubes. For a method of assaying Dried Suprarenals, see Biological Assays (Part III)." *U. S.*

It will be noted that the chemical and biological assays differ; the latter requiring the presence of 1 per cent. of active principle, the former only 0.5 per cent. How this discrepancy is to be reconciled surpasses conjecture.

Seidel and Fenger (*U. S. Hygienic Lab. Bull.* No. 100, 1914) have found that the percentage of epinephrine in the suprarenal gland of the beef runs distinctly higher than those of either sheep or swine, varying in the beef glands from 0.4 to 1 per cent., in hogs and sheep from 0.1 to 0.4.

Uses.—An aqueous solution of the dried suprarenals will produce all the effects described under *adrenalin* (see p. 94), but because of its greater convenience the alkaloid is universally preferred. There are one or two conditions, however, in which the whole drug is to be preferred. Foremost among these is that syndrome known as *Addison's disease.* According to S. Solis-Cohen, the administration of the suprarenal gland by the mouth every two or three hours is sufficient to prevent the occurrence of the *asthmatic paroxysm.*

Locally, the suprarenals may be used in solutions of the extract in the proportion of 5 to 25 per cent. As these solutions form excellent culture media for bacteria they are not permanent unless an antiseptic is added.

Dose, three to ten grains (0.2–0.65 Gm.).

SYRUPI.

SYRUPS

(sy-rŭ'pī)

Sirops, *Fr. Cod.*; Sirupi, *P. G.*; Sirupe, *G.*; Sciroppi, *It.*; Jarabe, *Sp.*

Syrups are concentrated solutions of sugar in aqueous fluids, either with or without medicinal impregnation. When the solution is made with pure water, it is named *syrup* or *simple syrup;* when made with water charged with one or more medicinal agents, it is called in general terms a *medicated syrup,* and receives its special designation from the substance or substances added.

Medicated syrups are prepared by dissolving sugar in infusions, vinegars, decoctions, expressed juices, fermented liquors, or simple aqueous solutions, or by adding a medicating substance, like a tincture or a fluidextract, to simple syrup. When the active matter of the vegetable is not readily soluble in water, is associated with soluble matter which it is desirable to avoid, or is volatilized or decomposed by a heat of 100° C. (212° F.), it is sometimes ex-

tracted by diluted alcohol, the spirituous ingredient of which is subsequently driven off.

The process of percolation has been applied for the solution of the sugar and is offered as an alternative process in a number of official preparations. This process offers several advantages over the older methods. The amount of labor attending the operation is greatly reduced, no heat is employed so that volatile constituents are not injured, and the finished syrup is filtered and protected from the usual contaminations attending straining, etc. For the mode of properly conducting this process the reader is referred to page 1095.

The quality and quantity of the sugar employed are points of importance. Official granulated sugar should be employed and although the commercial grades are usually of good quality it is possible to secure a sugar of better grade, known as "druggists' dry granular" or "crystal A," which is obtained from the first runnings from the bone-black filters. In this sugar the crystals are large and the syrup is unusually free from yellowish tint, even in a heavy strata. The syrup made from this sugar is often sold as "Rock Candy Syrup."

In relation to the quantity of sugar, if in too small proportion, fermentation is apt to occur; if too abundant, crystallization. The Pharmacopœial formula calls for 850 Gm. of sugar to make 1000 mils of syrup, the amount of water required being about 465 mils. A somewhat smaller quantity will answer where an acid, such as lemon juice or vinegar, is used.

As it is desirable, in many instances, that the active matters should be in as concentrated a state as possible in the syrup, it is often necessary to evaporate a large proportion of the aqueous fluid in which they are dissolved. This may be done either before the addition of the sugar or afterwards. In either case care is requisite not to apply a heat too great or too long continued, lest the active principles should be injured. The use of concentrated pharmaceutical preparations, such as tinctures and fluidextracts, as the source of medication, has largely replaced other methods. The proper point of concentration for syrups which are prepared on a large scale by boiling is best ascertained by the use of that variety of Baumé's hydrometer called a *saccharometer*. This should stand at 30° in boiling syrup—30.5° in hot weather and at 35° in the syrup when it is cool. Another very accurate, though less ready, method is to ascertain the sp. gr. by weighing a portion of the liquid. Syrup, when boiling, should have a sp. gr. of about 1.261; at 25° C. (77° F.) about 1.313; this is the specific gravity of the official syrup. A third method of ascertaining the proper point of concentration is by the thermometer, which, in boiling syrup of the proper consistence, stands at 105° C. (221° F.). This indication is founded on the fact that the boiling point of syrup rises with the increase of its density.

When carefully prepared with the best refined sugar, syrups made by the hot process or by agitation in the cold usually require no other clarification than to remove any scum which may rise to their surface upon standing, and to pour them off from any dregs which may subside. But, as the sugar employed is seldom free from impurities, it may be best, as a rule, to remove the scum as it rises during the heating process, and to strain the syrup while hot through muslin or flannel. The percolation process avoids this necessity. Should syrups at any time lack the due degree of transparency, they may be filtered through paper if a hot water funnel is used, or, when likely to be injured by this treatment, may be clarified by other mechanical means, as mentioned under the head of *Syrupus*. The vicious habit practised not long ago by sugar refiners of "blueing" sugars by the use of ultramarine and other coloring agents cannot be too strongly deprecated, and it is a great benefit to pharmacy that this practice has been discontinued by most sugar refiners. (See *A. J. P.*, 1901, 119.)

The medicated syrups are liable to undergo various alterations, according to their nature and mode of preparation. The acid syrups, when too much boiled, often show a copious white deposit, which is invert sugar produced by the action of the acid upon the sugar. Even at ordinary temperatures, acids slowly convert common sugar into invert sugar, which, being less soluble than the former, is often deposited in the form of crystalline grains. Excessive acidity soon causes a darkening of the syrup, due to caramelization of the sugar. Syrups containing too little sugar are subject to fermentation, in consequence of the presence of yeast cells. Those which contain too much, deposit a portion in the crystalline state, and the crystals, attracting the sugar remaining in solution, gradually weaken the syrup, and render it liable to the same change as when originally made with too little sugar. The want of due proportion of saccharine matter frequently also gives rise to mouldiness, when air has access to the syrup. It is said that syrups enclosed, while they are still hot, in bottles which are not full are apt to ferment, but if in well filled bottles they will generally keep better. When syrups undergo the vinous fermentation, they become covered at the surface with froth, produced by the disengagement of carbon dioxide, and acquire a vinous odor from the presence of alcohol, while their consistence is diminished by the loss of a portion of the sugar, which has been converted into that liquid. When the quantity of alcohol has increased to a certain point, the fermentation ceases, or goes on more slowly, owing to the preservative influence of the alcohol. Such syrups should never be used for pharmaceutical purposes, as no amount of reboiling can render them fit for use.

The percolation method for preparing syrups has come into general use. For some syrups it is to be preferred to the usual method of heating, and all syrups which contain a volatile

principle, or one likely to be injured by heat, are preferably made by *percolation*. L. Orynski (*D. C.*, March, 1871) first drew attention to the subject. The details of the official method are given below. It was first recommended that a small piece of sponge should be used to close the lower orifice of the percolator, but this has advantageously been replaced by purified cotton. Some experience is necessary in adjusting the cotton, but the proper degree of pressure is soon learned.

To be successful in using the process, care in several particulars must be exercised. (1) The percolator should be cylindrical or semi-cylindrical, and cone-shaped as it nears the lower orifice. (2) The sugar must be coarse, else it will form into a compact mass, which the liquid cannot permeate. (3) The sponge or pledget must be introduced with care. If pressed too tightly in, it will effectually stop the process; if inserted too loosely, the liquid will pass too rapidly, and will, in consequence, be weak and turbid (not properly filtered). See also a practical paper on this subject in *A. J. P.*, Jan., 1881, by G. H. Chas. Klie, and *Bull. Pharm.*, 1902, 1248. For a paper on *Fruit Syrups*, see *West. Drug.*, 1902, 182; *Proc. Penn. Pharm. Assoc.*, 1903, 196.

Syrups may be made (without heat) *rapidly* by putting the ingredients in a churn and agitating briskly.

"Rock Candy Syrup," the evaporated mother liquor left after crystallizing sugar in the form of large crystals, called "rock candy," has come largely into use in America. It varies much in quality as made by various manufacturers, and often contains added glucose. It should never be used indiscriminately or for making the official syrups, and it should always be carefully tested before being used for any purpose. (See analyses by L. F. Kebler, in *A. J. P.*, 1895, 143.)

At best, syrups are apt to change, and various measures have been proposed for their preservation, but the best plan is to make small quantities of syrups at a time, and to keep them, unless when wanted for immediate use, in bottles quite full and well stoppered, which should be put in the cellar or other cool place. Glycerin is often used to aid in the preservation of syrups; in special cases this may be advantageous, but the solvent properties of glycerin must be remembered, and the finished preparation may possess properties (due to the glycerin) which are not found in syrups made without glycerin, and which may therefore be injurious in prescriptions. (See *West. Drug.*, 1898, 444.)

SYRUPUS. U. S., Br.

SYRUP [Sirup, Simple Syrup]

(sy-rŭ'pŭs)

Syrupus Simplex; Syrupus Sacchari s. Albus; Sirop de Sucre, *Fr. Cod.*; Sirop simple, *Fr.*; Sirupus simplex, *P. G.*; Weisser Sirup, *G.*; Sciroppo semplice, *It.*; Jarabe simple, *Sp.*

* "Sugar, in dry crystalline granules, *eight hundred and fifty grammes* [or 29 ounces av., 430 grains]; Distilled Water, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Place at the bottom of a glass percolator of suitable size, a layer of purified cotton about one-half inch in thickness, well fitted to the sides of the percolator, and moisten it with a little distilled water. Introduce the sugar into the percolator, make its surface level without shaking or jarring, then carefully pour upon it *four hundred and fifty mils* [or 15 fluidounces, 104 minims] of distilled water and regulate the flow of the liquid, if necessary, so that it passes out in rapid drops. Return the first portion of the percolate until it runs through clear and, when all of the liquid has passed, follow it by distilled water, added in portions, so that all of the sugar may be dissolved and the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly. Syrup may also be prepared in the following manner: Dissolve the sugar with the aid of heat in *four hundred and fifty mils* [or 15 fluidounces, 104 minims] of distilled water, raise the temperature to the boiling point, strain the liquid, and pass enough distilled water through the strainer to make the product, when cold, measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly. Syrup thus prepared has a specific gravity of about 1.313 at 25° C. (77° F.)." *U. S.*

"Refined Sugar, 1000 *grammes;* Distilled Water, sufficient to produce 1500 *grammes*. Heat together until dissolved; add sufficient Distilled Water to produce the required weight. Specific gravity 1.330. *Optical rotation* + 56° to + 58°." *Br.*

This syrup, when properly prepared, is inodorous, of a sweet taste without peculiar flavor, thick, viscid, nearly colorless, and perfectly transparent. It sometimes requires straining through muslin or it may be filtered through a pledget of cotton or often through paper.

From the observations of Maumené, it appears that a solution of pure cane sugar, when long kept, undergoes a molecular change analogous to that produced by the reaction of weak acids, the saccharine liquid becoming brown when boiled with potassium hydroxide. But, as this phenomenon is exhibited alike by uncrystallizable sugar and by glucose, the experiment does not determine which of those forms of saccharine matter has been produced. (*C. R. A. S.*, xxxix, 914.) Procter observed a similar change in simple syrup which had been kept in his cabinet for six years. (*A. J. P.*, xxvii, 430.) Schaeuffele, having noticed, on one occasion, in the preparation of simple syrup, that the foam exhibited a singular blue color, while a part of the cane sugar was rapidly transformed into the uncrystallizable variety, made investigations as to the cause, and was led to the conclusion that it was the presence of indigo in the loaves of sugar, introduced with the view of giving brilliancy and whiteness, but this conclusion was erroneous, as it is well known that *ultramarine*, and not indigo, was formerly used for this pur-

pose. The presence of a blue coloring matter in sugar was frequently noticed in this country; syrup made from such sugar was not colorless, and in a short time deposited a dark-colored sediment. Colorless "rock candy" forms an excellent source for pure syrup (the broken crystals can be procured cheaply from the manufacturers), and syrup entirely free from impurities is required in making such preparations as syrup of hydriodic acid, syrup of ferrous iodide, etc. Joseph L. Mayer (*J. A. P. A.*, 1916, p. 712) shows that it is unfair to assume that commercial glucose is present as an adulterant of syrup, simply because it contains reducing sugar, for in a series of experiments conducted by him, working with both cold process and hot process syrups, the amount of invert sugar found after standing for one year, ranged from about 8 per cent. to over 40 per cent., depending entirely on the length of time of standing. The grade of granulated sugar known as "crystal A" or as "Druggists' Dry Granular," referred to on page 1094, is used with success in some parts of the country where it can be readily obtained. It is crystallized from the first runnings from the bone-black filters.

Syrup is very useful in the formation of pills and mixtures, and in various other pharmaceutical operations in which sugar in solution is required.

The U. S. syrup is practically identical with that formerly official, being a trifle stronger, the sp. gr. being given as 1.313 at 25° C. (77° F.). That of the Br. syrup is 1.330 at 15.5° C. (60° F.), probably adapted to the climate of Great Britain, which is not so cold in winter as is ours, at least in the Northern and Middle States.

SYRUPUS ACACIÆ. U. S.

SYRUP OF ACACIA Syr. Acac.

(sy-rŭ'pŭs ą-cā'cĭ-æ)

Syrupus Gummosus; Sirop de Gomme, *Fr. Cod.*; Gummisirup, *G.*; Sciroppo di gomma arabica, *It.*; Jarabe de goma, *Sp.*

* "Acacia, in selected pieces, *one hundred grammes* [or 3 ounces av., 231 grains]; Sugar, *eight hundred grammes* [or 28 ounces av., 96 grains]; Distilled Water, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Place the acacia in an enameled or porcelain dish, and add *four hundred and thirty mils* [or 14 fluidounces, 259 minims] of distilled water, and stir occasionally until the acacia is dissolved; then, having added the sugar, place the dish on a water bath and apply heat, gradually increasing the temperature until the water in the water bath boils. Maintain this temperature for fifteen minutes, and stir the syrup from time to time until the sugar is dissolved. Strain the syrup while hot, add sufficient distilled water, recently boiled, to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms], and transfer it, while yet hot, into small bottles which have been rinsed with boiling water and heated in an oven at 160° C. (320° F.) for from fifteen to thirty minutes. Close the bottles tightly with rubber stoppers which have been just previously boiled in water for thirty minutes and cap them with paper." *U. S.*

In the 18th edition of this work the process of the U. S. P., 1890, was condemned because of the tendency of the mucilage of acacia to spoil and thus make an unreliable syrup; the U. S. P. (9th Rev.) provides for a practically permanent preparation by the sterilization of the syrup, the containers, and the stoppers. This syrup is useful in the preparation of mixtures, pills, and troches, and is a good demulcent; but, unfortunately, the proportion of the gum to the sugar is too small to meet all the indications calling for the conjoint use of these substances. To avoid fermentation, C. B. Mann commends the use of one fluidounce of glycerin and seven fluidounces of water as the solvent. If the mucilage of acacia be made with chloroform water or a trace of chloroform be added to syrup of acacia, fermentation is measurably retarded, but the present official method is satisfactory for the purpose.

Off. Prep.—Syrupus Morphinæ et Acaciæ, *N. F.*

SYRUPUS ACIDI CITRICI. U. S.

SYRUP OF CITRIC ACID Syr. Acid. Cit.

(sy-rŭ'pŭs ăç'ĭ-dī cĭt'rĭ-cī)

Sirop d'Acide citrique, *Fr. Cod.*; Citronensauresirup, *G.*

* "Citric Acid, *ten grammes* [or 154 grains]; Distilled Water, *ten mils* [or 162 minims]; Tincture of Lemon Peel, *ten mils* [or 162 minims]; Syrup, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the citric acid in the distilled water and add the solution to *nine hundred and fifty mils* [or 32 fluidounces, 59 minims] of syrup, mixing it well. Then add the tincture of lemon peel, shake the mixture, and add enough syrup to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly and preserve it in containers which have been previously washed with boiling water. This preparation must not be dispensed unless it is free from moulds and fermentation products." *U. S.*

This is more uniform in its character, keeps better, and is more readily prepared than lemon syrup, but does not equal it in flavor, if the latter be well made. If long kept it is prone to acquire a musty taste, and to deposit invert sugar copiously, in consequence of the action of the acid on the cane sugar. It is much employed as an agreeable and refrigerant addition to drinks, especially carbonic acid water. Tincture of fresh lemon peel is used in this syrup instead of spirit of lemon which was used in the process of the U. S. P., 1890; spirit of lemon is no longer official and the tincture is preferable as a flavoring agent. Tartaric acid, on account of its greater cheapness, has not infrequently been substituted for the citric acid; but the syrup made with it does not keep so well, and is more apt to be irritating to the stomach.

SYRUPUS ACIDI HYDRIODICI. U. S., Br.

SYRUP OF HYDRIODIC ACID Syr. Acid. Hydriod.

(sy-rŭ'pŭs ăç'ĭ-dī hȳ-drī-ŏd'ĭ-cī)

"*One hundred mils* of Syrup of Hydriodic Acid contains not less than 1.3 Gm. nor more than 1.45 Gm. of HI (127.93)." *U. S.*

Sirop d'Acide Iodhydrique, *Fr.;* Jodwasserstoffsirup, *G.*

* "Diluted Hydriodic Acid, *one hundred and twenty-five mils* [or 4 fluidounces, 109 minims]; Distilled Water, *three hundred mils* [or 10 fluidounces, 69 minims]; Syrup, *five hundred and seventy-five mils* [or 19 fluidounces, 212 minims], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix them." *U. S.*

"Diluted Hydriodic Acid, 100 *grammes;* Distilled Water, 50 *millilitres;* Syrup, sufficient to produce 1000 *millilitres.* Mix." *Br.*

An unprotected aqueous solution of hydriodic acid is unstable, the iodine being in time always liberated, rendering it irritant and unfit for internal administration, and as it has been proved that syrup protects the acid efficiently, the 1880 Committee of Revision introduced the Syrup of Hydriodic Acid, with the view of furnishing a preparation which should remain, if carefully preserved, for a long time unchanged. The process for this syrup was changed at the U. S., 1890, revision. The "Buchanan" method of producing hydriodic acid by the decomposition of potassium iodide with tartaric acid was employed, the resulting acid potassium tartrate being crystallized out by the use of diluted alcohol and a reduced temperature. Decomposition and the discoloration due to the separation of a trace of iodine were obviated by the use of a small quantity of potassium hypophosphite; this in contact with tartaric acid is decomposed, and the trace of hypophosphorus acid generated is sufficient to protect the solution of hydriodic acid from change, the very small quantity of acid potassium tartrate produced at the same time crystallizing out with the rest of the salt in the diluted alcohol. In the U. S. P. IX the syrup is made by adding diluted hydriodic acid to water and syrup, it having been proved that diluted hydriodic acid could be made so as to be reasonably permanent (see *Acidum Hydriodicum Dilutum,* page 31), but the principal advantage is that the syrup can now be made extemporaneously as needed for prescriptions. Diluted simple syrup has been proved to make a more permanent syrup of hydriodic acid than syrup of official strength. So-called syrup of hydriodic acid is found in the market in which glycerin is the principal diluting constituent. The substitution of glucose for syrup is also practised, the reason being given that the presence of glucose prevents discoloration. (*Proc. A. Ph. A.,* 1897, 221.)

Properties.—Syrup of hydriodic acid is officially described as "a transparent, colorless, or not more than pale straw-colored, syrupy liquid; odorless, and having a sweet and acidulous taste. Specific gravity: about 1.215 at 25° C. (77° F.). Mix 5 mils of Syrup of Hydriodic Acid with a few drops of starch T.S. and add three drops of chlorine water; the liquid acquires a deep blue color. No blue color is produced in the Syrup by starch T.S. alone (*free iodine*).

"**Assay.**—Introduce exactly 25 mils of Syrup of Hydriodic Acid into a flask, dilute it with 100 mils of distilled water, add 40 mils of tenth-normal silver nitrate V.S., agitate the mixture, add 5 mils of diluted nitric acid and 2 mils of ferric ammonium sulphate T.S. and titrate with tenth-normal potassium sulphocyanate V.S. It shows, in each 100 mils, not less than 1.3 Gm. nor more than 1.45 Gm. of HI.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.012793 Gm. of HI." *U. S.*

Uses.—Syrup of hydriodic acid possesses the general therapeutic properties of the alkaline iodides, and is used by various practitioners to obtain alterative effects in *scrofula* and similar disorders. As it contains 1.4 per cent. by weight of absolute hydriodic acid, for practical purposes a teaspoonful may be said to represent about 0.75 of a grain of iodine or a little over 1 grain of potassium iodide. It is evident that the doses in which it is usually administered—from twenty to forty minims (1.3–2.5 mils)—are too small. It should be well diluted at the time of administration, to prevent the possibility of injury to the teeth.

Dose, from one to two fluidrachms (3.75–7.5 mils).

SYRUPUS AROMATICUS. Br.

AROMATIC SYRUP

(sy-rŭ'pŭs ăr-ŏ-măt'ĭ-cŭs)

Sirop Aromatique, *Fr.;* Aromatischer Sirup, *G.*

"Tincture of Orange, 250 *millilitres;* Cinnamon Water, 250 *millilitres;* Syrup, 500 *millilitres.* Mix the Tincture of Orange and Cinnamon Water; shake the mixture with a little *powdered talc;* filter; add the Syrup." *Br.*

This preparation of the Br. Ph., 1898, is practically a simple elixir (see *Elixir Aromaticum,* p. 433); it has been introduced mainly as a vehicle or adjuvant.

SYRUPUS AURANTII. U. S., Br.

SYRUP OF ORANGE Syr. Aurant.

(sy-rŭ'pŭs âu-răn'tĭ-ī)

Syrup of Orange Peel; Sirop d'Ecorce d'Orange amère, *Fr. Cod.;* Sirupus Aurantii Corticis, *P. G.;* Pomeranzenschalensirup, Orangenschalensyrup, *G.;* Sciroppo di arancio amaro, *It.;* Jarabe de corteza de naranja amarga, *Sp.*

* "Tincture of Sweet Orange Peel, *fifty mils* [or 1 fluidounce, 331 minims]; Citric Acid, *five grammes* [or 77 grains]; Purified Talc, *fifteen grammes* [or 231 grains]; Sugar, *eight hundred and twenty grammes* [or 28 ounces av., 405 grains]; Distilled Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Triturate the Purified Talc in a mortar with the tincture, add gradually

four hundred mils [or 13 fluidounces, 252 minims] of distilled water, filter, and add sufficient distilled water through the filter to obtain *four hundred and fifty mils* [or 15 fluidounces, 104 minims] of filtrate; in this filtrate dissolve the citric acid and sugar by agitation without heat, and add sufficient distilled water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly." *U. S.*

"Tincture of Orange, 125 *millilitres;* Syrup, sufficient to produce 1000 *millilitres.* Mix." *Br.*

The U. S. P. IX process is an improvement over all preceding formulas as the flavor is derived from the tincture of fresh orange peel and the alkaline magnesium carbonate of the U. S. P. VIII, which modified the flavor, has been replaced by inert talc, the latter being used as a distributing and filtering medium. The British preparation, which is a mere mixture of the tincture with syrup, is inferior. The syrup has an agreeable, slightly acid flavor, for which it is alone employed. For a process by E. E. Williams, using powdered pumice to disintegrate the orange peel, see *D. C.,* 1898, 125.

SYRUPUS AURANTII FLORUM. U. S. (Br.)

SYRUP OF ORANGE FLOWERS Syr. Aurant. Flor.

(sy-rŭ'pŭs âu-răn'tĭ-ī flō'rŭm)

Syrupus Aurantii Floris, *Br.;* Sirop de Fleur d'Oranger, *Fr. Cod.;* Pomeranzenblüthensirup, *G.;* Jarabe de azahar, *Sp.*

* "Sugar, *eight hundred and fifty grammes* [or 29 ounces av., 430 grains]; Orange Flower Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the sugar in *four hundred and fifty mils* [or 15 fluidounces, 104 minims] of orange flower water by agitation, without heat, add enough orange flower water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms], mix thoroughly and strain. Syrup of orange flowers may also be made in the following manner: Prepare a percolator in the manner described under *Syrupus.* Pour *four hundred and fifty mils* [or 15 fluidounces, 104 minims] of orange flower water upon the sugar, return the first portions of the percolate until it runs through clear, and, when all the liquid has passed, follow it by orange flower water, until the sugar is all dissolved and the product measures *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly." *U. S.*

"Orange-flower water of commerce, undiluted, 150 *millilitres;* Refined Sugar, 300 *grammes;* Syrup, sufficient to produce 1000 *millilitres.* Mix the orange-flower water with the Refined Sugar in a closed vessel; stand in a moderately warm place, shaking occasionally till dissolved; then add sufficient Syrup to produce the required volume." *Br.*

The second U. S. process, by percolation, will be preferable here. This syrup is used chiefly for flavoring mixtures.

SYRUPUS CALCII LACTOPHOSPHATIS. U. S., Br.

SYRUP OF CALCIUM LACTOPHOSPHATE Syr. Calc. Lactophos.

(sy-rŭ'pŭs căl'cĭ-ī lăc-tŏ-phŏs-phā'tĭs)

Sirop de Lactophosphate (phospholactate) de chaux, *Fr.;* Calciumphospholactatsirup, *G.;* Jarabe de lactofosfato calcico, *Sp.*

* "Precipitated Calcium Carbonate, *twenty-five grammes* [or 386 grains]; Lactic Acid, *sixty mils* [or 2 fluidounces, 14 minims]; Phosphoric Acid, *thirty-six mils* [or 1 fluidounce, 104 minims]; Stronger Orange Flower Water, *fifty mils* [or 1 fluidounce, 331 minims]; Sugar, *six hundred and fifty grammes* [or 22 ounces av., 406 grains]; Glycerin, *fifty mils* [or 1 fluidounce, 331 minims]; Distilled Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. To the lactic acid, mixed with *one hundred mils* [or 3 fluidounces, 183 minims] of distilled water, gradually add the calcium carbonate, stirring until solution is effected. Then add the phosphoric acid, previously diluted with *fifty mils* [or 1 fluidounce, 331 minims] of distilled water, and stir until the precipitate first formed is dissolved. Add *one hundred mils* [or 3 fluidounces, 183 minims] of distilled water, filter the solution, mix the stronger orange flower water with the filtrate, add the glycerin, and dissolve the sugar in the mixed liquids by agitation; then add enough distilled water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] and strain." *U. S.*

"Calcium Lactate, 75 *grammes;* Concentrated Phosphoric Acid, 45 *millilitres;* Orange-flower water of commerce, undiluted, 25 *millilitres;* Refined Sugar, 700 *grammes;* Distilled Water, sufficient to produce 1000 *millilitres.* Mix the Calcium Lactate with four hundred millilitres of the Distilled Water, add the Concentrated Phosphoric Acid and stir until solution is complete, then add the orange-flower water, dissolve the Refined Sugar in the mixture without the aid of heat, and add sufficient Distilled Water to produce the required volume; filter." *Br.*

The U. S. P., 1880, syrup was almost identical with the preparation proposed by William Neergaard. Freshly precipitated calcium phosphate is soluble in lactic acid, and this preparation was such a solution protected from change and rendered more agreeable to the taste by the addition of sugar and orange flower water. As made by this formula it will usually be found to contain a precipitate of a gelatinous character, which gradually forms in the course of a few days or weeks; the means commonly used to prevent this precipitation is the addition of a fluidrachm of hydrochloric acid to a pint of the syrup—hydrochloric acid being a better solvent for calcium phosphate than is lactic acid. The U. S. P. in the last three revisions has prepared calcium lactate by dissolving calcium carbonate in lactic acid and subsequently adding phosphoric acid. Precipita

tion can be avoided by the addition of a trace of hydrochloric acid. The process of percolation to dissolve the sugar may be advantageously substituted here for that of agitation. The syrup is sometimes prepared by dissolving two hundred grains of calcium lactophosphate (which is now furnished by the manufacturing chemists) in a pint of syrup flavored with orange flower water, a fluidrachm of hydrochloric acid being added to prevent precipitation. The British syrup, 1914, is made by dissolving calcium lactate in phosphoric acid. The syrup affords an excellent means of administering calcium phosphate.

Dose, from two to four fluidrachms (7.5–15.0 mils), representing from three to six grains of the lime salt.

Off. Prep.—Elixir Cinchonæ Alkaloidorum, Ferri, et Calcii Lactophosphatis, *N. F.;* Syrupus Calcii Lactophosphatis et Ferri, *N. F.*

SYRUPUS CASCARÆ AROMATICUS. Br.

AROMATIC SYRUP OF CASCARA

(sy-rŭ'pŭs kăs'cą-ræ ăr-ǫ-măt'į-cŭs)

Sirop aromatique de Cascara Sagrada, *Fr.;* Aromatischer Amerikanisch-Faulbaumrindensirup, *G.*

"Liquid Extract of Cascara Sagrada, 400 *millilitres;* Tincture of Orange, 100 *millilitres;* Alcohol (90 per cent.), 50 *millilitres;* Cinnamon Water, 150 *millilitres;* Syrup, sufficient to produce 1000 *millilitres.* Mix." *Br.*

This was a new syrup in the Br. Pharm., 1898. It forms a convenient means of administering cascara, the alcohol being added to aid its preservation.

Dose, from one-half to two fluidrachms (1.8–7.5 mils).

SYRUPUS CHLORAL. Br.

SYRUP OF CHLORAL

(sy-rŭ'pŭs ċhlō'rąl)

Sirop de Chloral, *Fr. Cod.;* Chloralhydratsirup, *G.;* Jarabe de hidrato de cloral, *Sp.*

"Chloral Hydrate, 200 *grammes;* Distilled Water, 200 *millilitres;* Syrup, sufficient to produce 1000 *millilitres.* Dissolve the Chloral Hydrate in the Distilled Water; add sufficient Syrup to produce the required volume. 10 millilitres of this Syrup contain 2 grammes of Chloral Hydrate; 1 fluid drachm contains 10.9 grains." *Br.*

Dose, one to two fluidrachms (3.75–7.5 Gm.).

SYRUPUS CODEINÆ PHOSPHATIS. Br.

SYRUP OF CODEINE PHOSPHATE

(sy-rŭ'pŭs cō-dę-ī'næ phŏs-phā'tĭs)

Sirop de Codéine, *Fr. Cod.;* Kodeinsirup, *G.;* Sciroppo di codeina, *It.;* Jarabe de codeina, *Sp.*

"Codeine Phosphate, 5 *grammes;* Distilled Water, 15 *millilitres;* Syrup, sufficient to produce 1000 *millilitres.* Dissolve the Codeine Phosphate in the Distilled Water; add sufficient Syrup to produce the required volume. 10 millilitres of this Syrup contain 0.05 gramme of Codeine Phosphate; 1 fluid drachm contains 0.27 grain." *Br.*

This syrup is intended to furnish a convenient method of using codeine phosphate. A syrup of codeine, made from the sulphate is official in the N. F. (see *Syrupus Codeinæ,* Part III).

Dose, one-half to two fluidrachms (1.8–7.5 mils).

SYRUPUS FERRI IODIDI. U. S., Br.

SYRUP OF FERROUS IODIDE Syr. Ferr. Iod. [Ferri iodidi syrupus P. I.]

(sy-rŭ'pŭs fĕr'rī ī-ŏd'į-dī)

"A syrupy liquid containing not less than 4.75 per cent. nor more than 5.25 per cent. of FeI_2 (309.68). Preserve it in completely filled, tightly-stoppered bottles." *U. S.*

Syrup of Iodide of Iron; Sirop d'Iodure de fer, *Fr. Cod.;* Syrupus Ferri Jodati, *P.G.;* Eisenjodürsirup, *G.;* Sciroppo di protojoduro di ferro, *It.;* Jarabe de yoduro ferroso, *Sp.*

* "Iron, in the form of fine, bright wire, and cut into small pieces, *twelve and five-tenths grammes* [or 193 grains]; Iodine, *forty-one and five-tenths grammes* [or 1 ounce av., 203 grains]; Diluted Hypophosphorous Acid, *twenty mils* [or 325 minims]; Sugar, *five hundred and seventy-five grammes* [or 20 ounces av., 123 grains]; Distilled Water, *a sufficient quantity,* to make *one thousand grammes* [or 35 ounces av., 120 grains]. Introduce the iron and iodine into a flask of thin glass, having a capacity of about *five hundred mils* [or 1 pint], add to it *one hundred and fifty mils* [or 5 fluidounces, 35 minims] of distilled water. Shake the mixture occasionally, checking the reaction, if necessary, by placing the flask in cold water, and, when the solution has acquired a greenish color, and has lost the odor of iodine, heat it to boiling and add at once *fifty grammes* [or 1 ounce av., 334 grains] of the sugar; when this has dissolved, filter the solution into the remainder of the sugar contained in a porcelain dish. Rinse the flask and iron wire with *one hundred and twenty-five mils* [or 4 fluidounces, 109 minims] of distilled water and pass the washings through the filter into the sugar. Stir the mixture with a glass rod or a porcelain spatula, heating the liquid on a water bath until complete solution is effected, and, having passed the syrup through a clean muslin strainer into a tared bottle, add the diluted hypophosphorous acid, and sufficient distilled water to make the product weigh *one thousand grammes* [or 35 ounces av., 120 grains]." *U. S.*

"Iron, in wire, 15.0 *grammes;* Iodine, 41.4 *grammes;* Distilled Water, 75.0 *millilitres;* Glucose, 100.0 *grammes;* Syrup, sufficient to produce 1000.0 *grammes.* Add the Iron and the Iodine to fifty millilitres of the Distilled Water

in a flask; shake occasionally, cooling if necessary. When the reaction is completed add the Glucose, heat on a water-bath for five minutes, mix, and while still hot filter into a tared vessel containing part of the Syrup. Rinse the flask and wash the filter-paper with the remaining twenty-five millilitres of the Distilled Water heated to boiling; add sufficient Syrup to produce the required weight." *Br.*

W. G. Toplis (*Proc. Penna. Pharm. Assn.*, 1916, p. 243) substitutes Ferrum Reductum for the card teeth officially directed in this process, with the result that the solution can be effected, ready for filtration, in less than ten minutes, working with the official proportions.

These preparations furnish solutions of ferrous iodide rendered more permanent by sugar. The iodine should be dry, for, if moist, as commercial iodine often is, less ferrous iodide will be formed and the syrup will be proportionally weaker. In both processes a large excess of iron is taken. A moderate excess is useful in preventing the solution of ferrous iodide from undergoing any change from the absorption of oxygen during filtration, before it comes in contact with the sugar. The method adopted in the Pharmacopœia of 1880, of filtering the unprotected solution of ferrous iodide into the sugar contained in an open porcelain dish, and afterward straining the syrup through linen, was directly opposed to the experience of many practical pharmacists, and to the views which had been hitherto held of the action of the air upon the solution of ferrous iodide, and although with care, in skilful hands, oxidation may have been avoided, nothing was gained in time. In the U. S. P. IX process a small quantity of sugar is added to the solution of ferrous iodide before filtering, but the principle change was in the reduction of the strength of the finished syrup to 5 per cent. of ferrous iodide, which is *one half the quantity of ferrous iodide* that was in the former official syrup (10 per cent.). The strength of 5 per cent. is that recommended by the Brussels International Conference for the unification of the formulas for Potent Remedies.

Properties.—It is officially described as "a transparent, pale yellowish-green, syrupy liquid, having a sweet, strongly ferruginous taste and a slightly acid reaction. Specific gravity: about 1.35 at 25° C. (77° F.). Add a few drops of potassium ferricyanide to 5 mils of Syrup of Ferrous Iodide; a blue precipitate is produced. Mix 5 mils of Syrup of Ferrous Iodide with a few drops of starch T.S. and add three drops of chlorine water; the liquid acquires a deep blue color. No blue color is produced in the Syrup by starch T.S. alone (*free iodine*).

" **Assay.**—Dilute about 10 Gm. of Syrup of Ferrous Iodide, accurately weighed, with 30 mils of distilled water, add 50 mils of tenth-normal silver nitrate V.S., and 5 mils of nitric acid and heat on a water bath until the precipitate of silver iodide is yellow. Cool, add 2 mils of ferric ammonium sulphate T.S., and determine the residual silver nitrate by titration with tenth-normal potassium sulphocyanate V.S. It shows not less than 4.75 per cent. nor more than 5.25 per cent. of FeI_2.

" Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.015484 Gm. of FeI_2. Each gramme of Syrup of Ferrous Iodide corresponds to not less than 3.07 mils nor more than 3.4 mils of tenth-normal silver nitrate V.S." *U. S.*

" When 5 grammes of the Syrup are diluted with 20 millilitres of *water,* acidified with *nitric acid* and mixed with 20 millilitres of *N/10 solution of silver nitrate,* not less than 3.5 or more than 4.2 millilitres of *N/10 solution of ammonium thiocyanate* are required to produce a permanent red coloration, *solution of ferric sulphate* being used as indicator, corresponding to not less than 4.9 and not more than 5.1 grammes of ferrous iodide, FeI_2, in 100 grammes of the Syrup. 10 millilitres of this Syrup contain about 0.7 gramme of ferrous iodide; 1 fluid drachm contains 3.75 grains. It is of the strength required by the International Agreement, and is approximately of two-thirds the strength of the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

In regard to the former U. S. syrup, E. S. Wayne observed that, when kept for some time, it occasionally deposited invert sugar, into which the cane sugar was converted through the agency of hydriodic acid. According to J. M. Maisch, the solution was decomposed not only by light, but also by the action of atmospheric oxygen in bottles partly filled and frequently opened. The oxidation of the iron and the evolution of the iodine were accelerated by the action of light, when the solution was thus insecurely kept; but when the altered solution was transferred to air-tight bottles completely filled, and exposed to the direct light of the sun, it resumed its transparency, and its original tint was restored, or its color rendered much lighter. After this restoration the solution could not be the same, and it is probably that it contained some ferric iodate. The removal of the apparent defects of a solution of ferrous iodide by the action of sunlight is, therefore, not an admissible expedient, because it changes the nature of the solution. The same may be said of the addition of tartaric or citric acid, which has been proposed for clearing the discolored syrup. Syrup of ferrous iodide is rendered brown by sulphuric acid, and emits violet vapors when heated.

Syrup of ferrous iodide will on long keeping become permanently discolored through the action of hydriodic acid on the sugar, which causes caramelization, an effect frequently observed in syrups containing citric, tartaric, or other acids. This discoloration must not be confounded with that due to the liberation of iodine. J. F. Judge (*A. J. P.*, 1876, p. 159) recommended hypophosphorous acid in small proportions to restore the pale green color, and of all the additions that have been proposed this is unquestionably the least objectionable and the

most effective. (*Y. B. P.*, 1885, p. 484.) Charles Rice preserved syrup of ferrous iodide successfully on the large scale by storing it in vessels having a stopcock at the bottom and pouring a small quantity of pure olive oil upon the surface to protect from oxidation. A. G. Hammer proposed the addition of syrup to a boiling solution of ferrous iodide before filtering from the excess of iron, and attributes the success in preservation to the fact that a portion of the cane sugar is converted into grape sugar which he believes has greater powers in preventing change. (*Pharm.*, 1876, p. 99.) Glycerin has been proposed as a substitute for sugar in this preparation; it answers the same purpose, but it may be doubted whether more effectually. Glucose or solution of grape sugar has been repeatedly recommended as superior to ordinary syrup for use in this preparation; when the glucose is pure, it is superior as a preservative.

When the syrup is concentrated it becomes brown, and when evaporated to dryness forms a mass which may be called *saccharine ferrous iodide,* and which is not entirely soluble again, a little ferric oxide being left. This saccharine iodide, being protected by the sugar it contains, is not liable to the objections which apply to the pure solid salt (see *Ferrous Iodide,* Part II), and may be made into pills. (See *U. S. D.*, 19th edition, page 1225, for *Ferri Iodidum Saccharatum.*)

Notes on examination of market samples and conclusions and recommendations as to methods of preservation, keeping qualities, etc., have been published by the following authors: L. A. Brown, *Proc. Ky. Ph. Assn.*, 1914, 61; W. C. Alpers, *J. A. Ph. A.*, 1914, 420; G. M. Beringer, *J. A. Ph. A.*, 1914, 970.

Uses.—Syrup of ferrous iodide combines the alterative action of iodine with the hematinic action of iron. It is a popular remedy in chronic types of *tuberculosis,* especially in the *scrofula* of children. It has, however, no advantage over an extemporaneous combination of an iodine with ferruginous tonic, and has the drawback that the dose of either ingredient cannot be altered singly.

Dose, for an adult, ten to forty minims (0.6–2.5 mils); for a child of two years, two to eight minims (0.12–0.5 mil).

SYRUPUS FERRI PHOSPHATIS. Br.

SYRUP OF FERROUS PHOSPHATE

(sy-rŭ'pŭs fĕr'rī phŏs-phā'tĭs)

Sirop de Phosphate de Fer, *Fr.*; Eisenphosphatsirup, *G.*

"Iron, in wire, 8.6 *grammes;* Concentrated Phosphoric Acid, 62.5 *millilitres;* Syrup, 700.0 *millilitres;* Distilled Water, sufficient to produce 1000.0 *millilitres.* Dilute the Concentrated Phosphoric Acid with an equal volume of Distilled Water in a small flask; add the Iron and heat very gently until dissolved. Filter into the Syrup, and pass sufficient Distilled Water through the filter to produce the required volume. 10 millilitres of this Syrup contain 0.17 gramme of anhydrous ferrous phosphate; 1 fluid drachm contains 1 grain." *Br.*

The process for this syrup of the Br. Pharmacopœia has been greatly improved. H. W. Jones (*P. J.*, 3d ser., v, 541) proposed a formula in which the phosphate was made directly from metallic iron and phosphoric acid. R. Wright (*P. J.*, 1893, 191) improved the formula, and this method is superior to the cumbersome process of preparing a precipitate of ferric phosphate, and dissolving it in phosphoric acid. The syrup is a solution of ferrous phosphate protected by sugar. The sp. gr. is about 1.270. (Umney.) For its properties and uses, see *Ferri Phosphas,* page 471.

Dose, from one to two fluidrachms (3.75–7.5 mils).

SYRUPUS FERRI PHOSPHATIS CUM QUININA ET STRYCHNINA. Br.

SYRUP OF PHOSPHATE OF IRON WITH QUININE AND STRYCHNINE

(sy-rŭ'pŭs fĕr'rī phŏs-phā'tĭs cŭm quī-nī'nă ĕt strȳch-nī'nă)

Syrupus Ferri, Quininæ et Strychninæ Phosphatum, Syrup of the Phosphates of Iron, Quinine, and Strychnine, *N. F.*; Easton's Syrup; Sirop Tonique d'Easton, *Fr.*; Eisenphosphatsirup mit Chinin und Strychnin, Eastonscher Sirup, *G.*

"Iron, in wire, 8.60 *grammes;* Concentrated Phosphoric Acid, 62.50 *millilitres;* Strychnine, in powder, 0.57 *gramme;* Quinine Sulphate, 14.80 *grammes;* Syrup, 700.00 *millilitres;* Distilled Water, sufficient to produce 1000.00 *millilitres.* Dilute the Concentrated Phosphoric Acid with an equal volume of Distilled Water in a small flask; add the Iron and heat very gently until dissolved; add the solution to the Strychnine and Quinine Sulphate previously triturated with thirty millilitres of the Distilled Water; when solution is complete filter the Syrup, and pass sufficient Distilled Water through the filter to produce the required volume. 10 millilitres of this Syrup contain 0.17 gramme of anhydrous ferrous phosphate, 0.148 gramme of Quinine Sulphate, and 0.057 gramme of Strychnine; 1 fluid drachm contains 1 grain of anhydrous ferrous phosphate, 4/5 grain of Quinine Sulphate, and 1/32 grain of Strychnine." *Br.*

This syrup is not official in the U. S. P. IX. In the U. S. P. VIII it was made by diluting the glycerite with syrup, but as the glycerite did not prove to be a permanent preparation, the syrup could not be depended upon as containing the full proportion of the active ingredients. The British Pharm., 1914, retained the syrup of the previous Pharmacopœia unchanged, and the N. F. IV introduced the formula of the U. S., 1890.

Uses.—This syrup has the medicinal activities of its ingredients, but is a very ineligible preparation, and has not even an agreeable taste to excuse its polypharmacy. It is known

as *Easton's Syrup, Aitkin's Syrup, Syrup of the Three Phosphates*, and *Syrup of Triple Phosphates.*

Dose, one to two fluidrachms (3.75–7.5 mils).

SYRUPUS GLUCOSI. Br.

SYRUP OF GLUCOSE

(sy-rŭ'pŭs glu-cō'sī)

"Glucose, 250 *grammes;* Syrup, 500 *grammes.* Mix, by the aid of gentle heat." *Br.*

Sirop de Glycose, *Fr.;* Glykosesirup, *G.*

This was a new preparation of the Br. Ph., 1898. It may be used as a vehicle for syrups which contain chemical salts liable to discoloration through the action of light, but its principal use is to take the place of *treacle* or molasses so much used in British pharmacy as a pill excipient. (See *Pilulæ,* p. 859.)

SYRUPUS HYPOPHOSPHITUM. U. S.

SYRUP OF HYPOPHOSPHITES Syr. Hypophos.

(sy-rŭ'pŭs hȳ-pŏ-phŏs-phī'tŭm)

Syrupus Calcii Hypophosphitis Compositus; Sirop d'Hypophosphite de Chaux composé, Sirop de Hypophosphites, *Fr.;* Hypophosphitsirup, *G.*

* "Calcium Hypophosphite, *forty-five grammes* [or 1 ounce av., 257 grains]; Potassium Hypophosphite, *fifteen grammes* [or 231 grains]; Sodium Hypophosphite, *fifteen grammes* [or 231 grains]; Diluted Hypophosphorous Acid, *two mils* [or 32 minims]; Glycerin, *fifty mils* [or 1 fluidounce, 331 minims]; Sugar, *six hundred grammes* [or 21 ounces av., 72 grains]; Distilled Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Triturate the hypophosphites with *five hundred mils* [or 16 fluidounces, 435 minims] of distilled water, until they are dissolved, add the diluted hypophosphorous acid, filter the liquid and pass enough distilled water through the filter to make the filtrate measure *five hundred and forty mils* [or 18 fluidounces, 125 minims]. To this add the glycerin and sugar, dissolve the latter by agitation without heat, and finally add enough distilled water, through the filter, to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Strain if necessary." *U. S.*

The determination of the total phosphorus content, which is the best that can be done toward estimating the value of this preparation, is the most readily accomplished by a modification of the method of Jewett, proposed by Barnard and McAbee (*J. A. P. A.,* 1914, 1505), which consists in oxidizing 2 Gm. of the sample with nitric acid and subsequently estimating as phosphomolybdate. Examinations of commercial samples revealed the fact that most of them were far below the theoretical phosphorus content for the official syrup.

This syrup is a simple solution of calcium, sodium, and potassium hypophosphites, in water, protected by sugar, and flavored with the tincture of fresh lemon peel. The calcium hypophosphite will usually not entirely dissolve; hence the direction to use hypophosphorous acid to complete the solution. Percolation will no doubt be preferred by many to agitation, for dissolving the sugar. It has been stated that the sulphuretted odor sometimes noticed in this syrup is due to the decomposition of sulphates or sulphites (present as impurities in the salts) by the hypophosphorous acid. (*P. J.,* 1895, 143.) Each fluidrachm of the syrup contains about two and a half grains of calcium hypophosphite, and not quite one grain each of the sodium and potassium salts. This syrup affords an excellent means of administering the hypophosphites.

Dose, from one to three fluidrachms (3.75–11.25 mils).

SYRUPUS IPECACUANHÆ. U. S.

SYRUP OF IPECAC Syr. Ipecac.

(sy-rŭ'pŭs ĭp-ę-căc-ū-ăn'hæ)

Sirop d'Ipécacuanha, *Fr. Cod.;* Sirupus Ipecacuanhae, *P. G.;* Brechwurzelsirup, Ipecacuanhasirup, *G.;* Sciroppo di ipecacuanha, *It.;* Jarabe de ipecacuana, *Sp.*

* "Fluidextract of Ipecac, *seventy mils* [or 2 fluidounces, 176 minims]; Acetic Acid, *ten mils* [or 162 minims]; Glycerin, *one hundred mils* [or 3 fluidounces, 183 minims]; Sugar, *seven hundred grammes* [or 24 ounces av., 303 grains]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dilute the fluidextract of ipecac with *three hundred mils* [or 10 fluidounces, 69 minims] of water to which the acetic acid has previously been added, and mix them thoroughly by shaking, and set the liquid aside in a cool place for twenty-four hours. Then filter, and pass enough water through the filter to make the filtrate measure *four hundred and fifty mils* [or 15 fluidounces, 104 minims]. To this filtrate add the glycerin, dissolve the sugar in the mixed liquids, and add enough water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly, and strain, if necessary. Syrup of Ipecac may also be made in the following manner: Prepare a percolator in the manner described under *Syrupus.* Mix the filtrate obtained as directed in the preceding formula with the glycerin, pour the mixture upon the sugar, return the first portions of the percolate, until it runs through clear, and, when all the liquid has passed, follow it with water, until the sugar is all dissolved and the product measures *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly." *U. S.*

The present U. S. syrup is made in accordance with the suggestions of Laidley of Richmond, Va., who found the syrup, as formerly prepared, to spoil on keeping. (*A. J. P.,* xxvi, 103, and July, 1879.) (See a practical paper on this subject by A. Robbins in *A. J. P.,* Aug., 1879.) The substitution of glycerin for a por-

tion of the syrup in the U. S. process is an improvement, but the addition of the very small quantity of Acetic Acid is of questionable utility. For formulæ in which the drug ipecac is employed, the reader may consult *A. J. P.*, 1870, p. 127; 1871, p. 104; May, 1881.

If strictly official fluidextract of ipecac is used in making this syrup, and the process is carried out in all its details, the syrup will remain transparent; but if commercial fluidextract is used, or if the fluidextract has not been very carefully made, it will be necessary to modify the process somewhat to secure a transparent syrup. This may be effected by allowing the diluted fluidextract in the official process for making this syrup to remain for two or three days in a cool place before filtering, and adding to the sugar.

One fluidounce of this syrup should contain the virtues of about thirty grains of ipecac.

Although this syrup possesses all the virtues of ipecac, it is used almost exclusively as a nauseating expectorant in *acute bronchitis*.

Dose, for an adult, as an expectorant, from fifteen to thirty minims (0.9–1.8 mils); as an emetic, half a fluidounce (15 mils).

SYRUPUS LACTUCARII. U. S.

SYRUP OF LACTUCARIUM Syr. Lactucar.

(sy-rŭ'pŭs lăc-tū-cā'rĭ-ī)

Sirop de Lactucarium, *Fr.*; Lactucariumsirup, *G.*

* "Tincture of Lactucarium, *one hundred mils* [or 3 fluidounces, 183 minims]; Glycerin, *two hundred mils* [or 6 fluidounces, 366 minims]; Citric Acid, *one gramme* [or 15 grains]; Orange Flower Water, *fifty mils* [or 1 fluidounce, 331 minims]; Syrup, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the tincture of lactucarium with the glycerin, add the orange flower water in which the citric acid has been previously dissolved, and filter, if necessary. Finally, add a sufficient quantity of syrup to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly." *U. S.*

The only disadvantage of this syrup is the slight petroleum-like taste which seems to be inseparable from lactucarium preparations made by extracting the resinous principles with petroleum benzin; the new tincture of lactucarium, notwithstanding all the care that can be given to the purification of the petroleum benzin, will still hold a trace of the benzin-residue flavor, which it communicates to the syrup. The recommendations made by various pharmaceutical writers to add a solution of an alkali to cloudy syrup of lactucarium, in order to make it transparent, are inadmissible, for Aubergier has conclusively shown that alkalies destroy the bitter principles of lactucarium.

Jos. W. England and N. D. Streeter both prefer to make the syrup directly from the lactucarium. For processes, see *A. J. P.*, 1883, pp. 393, 593.

Louis Emanuel presents an interesting contribution on the subject in the *Proc. P. P. A.*, 1912, p. 151, in which all processes as well as the product are criticised.

This syrup for half a century has been largely used on the assumption that it possessed properties similar to those of opium without the habit-forming tendency of the latter, and Aubergier's syrup has been in great vogue in Europe and to a less extent in this country. After the passage of the Food and Drugs Act in 1906, the Aubergier preparations of lactucarium were found to contain a declaration on the label of the presence of morphine. In France it is evident that lactucarium had failed to sustain its reputation, for the French Codex introduced Sirop de Lactucarium Opiacé (1884), which contained alcoholic extract of lactucarium, with the addition of one-half the proportion of extract of opium. This was an official recognition of the feeble character of lactucarium, and inasmuch as many persons used the syrup as a substitute for opium or morphine, the fact remained that thousands were deceived and in many cases the opium habit was established. We are of the opinion that lactucarium and its preparations should no longer receive recognition. The formula for Aubergier's syrup will be found in the *U. S. D.*, 19th edition, page 1230.

Dose, two to three fluidrachms (7.5–11.25 mils).

SYRUPUS LIMONIS. Br.

SYRUP OF LEMON

(sy-rŭ'pŭs lĭ-mō'nĭs)

Syrupus Succus Citri; Sirop de Limon (de Citron), Sirop de suc de Limon (de citron), *Fr.*; Citronensirup, Citronensaftsirup, *G.*; Jarabe de limon, *Sp.*

"Lemon Peel, in thin slices or grated, 20 *grammes;* Alcohol (90 per cent.), *a sufficient quantity;* Lemon Juice, 500 *millilitres;* Refined Sugar, 760 *grammes*. Macerate the Lemon Peel in thirty millilitres of the Alcohol for seven days; press; filter; add sufficient of the Alcohol to produce forty millilitres. In the Lemon Juice, clarified by subsidence or filtration, dissolve the Refined Sugar by the aid of gentle heat; cool; add the forty millilitres of alcoholic liquid; mix." *Br.*

The U. S. P. 1880 syrup of lemon was dropped at the 1890 revision; as it is frequently used, the process is appended.

"Lemon Juice, recently expressed and strained, *forty parts* [or seventeen fluidounces]; Fresh Lemon Peel, *two parts* [or one ounce av.]; Sugar, in coarse powder, *sixty parts* [or twenty-eight ounces av.]; Water *a sufficient quantity*, to make *one hundred parts* [or about two pints]. Heat the Lemon Juice to the boiling point; then add the Lemon Peel, and let the whole stand, closely covered, until cold. Filter, add enough Water through the filter to make the filtrate weigh *forty parts* [or measure seventeen fluidounces], dissolve the Sugar in the filtered liquid

by agitation, without heat, and strain." *U. S.* 1880.

The addition of lemon peel to the preparation is an improvement, but the internal white portion of the peel should be carefully removed before adding to the hot lemon juice, or the finished syrup will have a bitter taste. (See *Limonis Cortex.*) This syrup forms a cooling and grateful addition to beverages in *febrile complaints,* and serves to conceal the taste of saline purgatives in solution.

SYRUPUS PICIS LIQUIDÆ. U. S.

SYRUP OF TAR Syr. Pic. Liq.

(sy-rŭ'pŭs pī'cĭs lĭq'uĭ-dæ)

Syrupus cum aquâ piceâ; Syrupus Piceus; Sirop de Goudron, *Fr. Cod.*; Theersirup, *G.*; Jarabe de brea, *Sp.*

* "Tar, *five grammes* [or 77 grains]; Alcohol, *fifty mils* [or 1 fluidounce, 331 minims]; Magnesium Carbonate, *ten grammes* [or 154 grains]; Sugar, *eight hundred and fifty grammes* [or 29 ounces av., 430 grains]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the tar in the alcohol, add the magnesium carbonate and *fifty grammes* [or 1 ounce av., 334 grains] of sugar, and after thorough trituration add *four hundred and ten mils* [or 13 fluidounces, 415 minims] of water. Stir the mixture occasionally during two hours and then filter it, returning the filtrate to the filter until the liquid is clear. Dissolve the remainder of the sugar in the clear filtrate obtained from the treatment of the tar, and strain the syrup, adding sufficient water through the strainer to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Syrup of Tar may also be made in the following manner: Prepare a percolator in the manner described under *Syrupus.* Pour the clear filtered liquid obtained from the treatment of the tar as directed above upon the remainder of the sugar, return the first portions of the percolate until it runs through clear, and, when all the percolate has passed, follow it with water until the sugar is all dissolved and the product measures *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly." *U. S.*

In many sections of our country this syrup has been largely used. The process of the U. S. P. IX is an improvement on the one formerly official; the proportion of tar being reduced from 75 Gm. to 5 Gm. It is similar to the U. S. P. VIII process except that the washing of the tar to remove acid constituents has been omitted because these would not be present in a tar which conforms to the U. S. P. tests. The tar is dissolved in alcohol, magnesium carbonate and a little sugar added, the mixture filtered, and more sugar dissolved with the aid of a gentle heat. This syrup affords an excellent method of administering small quantities of tar in the milder forms of subacute or chronic *bronchitis.*

Dose, from one to two fluidrachms (3.75–7.5 mils).

SYRUPUS PRUNI VIRGINIANÆ. U. S., Br.

SYRUP OF WILD CHERRY Syr. Prun. Virg.

(sy-rŭ'pŭs prū'nī vĭr-gĭn-I-ā'næ)

Syrup of Virginian Prune, *Br.* 1898; Sirop d'Ecorce de Cerisier, *Fr.*; Wildkirschenrindensirup, *G.*

* "Wild Cherry Bark in No. 20 powder, *one hundred and fifty grammes* [or 5 ounces av., 127 grains]; Sugar, *eight hundred grammes* [or 28 ounces av., 96 grains]; Glycerin, *fifty mils* [or 1 fluidounce, 331 minims]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the glycerin with *two hundred mils* [or 6 fluidounces, 366 minims] of water, moisten the wild cherry bark with *one hundred mils* [or 3 fluidounces, 183 minims] of this mixture, pack it firmly in a cylindrical percolator and pour the remaining *one hundred and fifty mils* [or 5 fluidounces, 35 minims] of the menstruum upon it. When the glycerin-water menstruum has disappeared from the surface of the drug, add sufficient water to saturate the powder and leave a stratum above it. Close the lower orifice, and, having closely covered the percolator, allow the drug to macerate for twenty-four hours. Then allow the percolation to proceed slowly, gradually adding water as a menstruum until the percolate measures *five hundred mils* [or 16 fluidounces, 436 minims]. Dissolve the sugar in the percolate by agitation without heat, strain and pass enough water through the strainer to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly. Syrup of Wild Cherry may also be made in the following manner: Prepare a percolator in the manner described under *Syrupus.* Pour the percolate obtained as directed in the preceding formula upon the sugar, return the first portions of the percolate until it runs through clear, and, when all the liquid has passed, follow it with water, until the sugar is all dissolved and the product measures *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly. This Syrup should be stored in non-metallic, tightly-closed containers, in a cool place, as it rapidly loses hydrocyanic acid even under the most favorable conditions." *U. S.*

"Wild Cherry Bark, in No. 20 powder, 150 *grammes;* Refined Sugar, in coarse powder, 750 *grammes;* Glycerin, 65 *millilitres;* Distilled Water sufficient to produce 1000 *millilitres.* Moisten the Wild Cherry Bark with Distilled Water; set aside for twenty-four hours in a closed vessel; pack in a percolator; percolate with Distilled Water until four hundred and fifty millilitres have been collected; dissolve the Refined Sugar in the percolated liquid, without heat; add the Glycerin and sufficient Distilled Water to produce the required volume." *Br.*

The British Pharmacopœia introduced this syrup into the 1898 edition. The process is modelled after the U. S. formula.

The U. S. process affords a handsome syrup

with the virtues of the bark unimpaired by the injurious effects of heat. It is based upon a formula proposed by Procter and Turnpenny in *A. J. P.*, xiv, 27. The introduction of the glycerin into the receiving bottle instead of mixing it with the menstruum was dropped in the process of the U. S. P., which, in our opinion, is a mistake. The glycerin is not needed in the menstruum to increase the astringency of the syrup but it serves a useful purpose in keeping the infusion from decomposing and precipitating a reddish, insoluble substance in the receiving bottle. This syrup should never be made by adding fluidextract to simple syrup, as the fluidextract is likely to vary greatly in quality, and frequently precipitates when mixed with syrup, the syrup when made by the above process is far superior in flavor. It is largely used as a vehicle for cough mixtures.

Dose, one to four fluidrachms (3.75–15.0 mils).

SYRUPUS RHEI. U. S., Br.

SYRUP OF RHUBARB Syr. Rhei

(sy-rŭ'pŭs rhē'ī)

Sirop de Rhubarbe, *Fr.*; Sirupus Rhei, *P. G.*; Rhabarbersirup, Rhabarbersaft, *G.*

* "Fluidextract of Rhubarb, *one hundred mils* [or 3 fluidounces, 183 minims]; Spirit of Cinnamon, *four mils* [or 65 minims]; Potassium Carbonate, *ten grammes* [or 154 grains]; Water, *fifty mils* [or 1 fluidounce, 331 minims]; Syrup, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the spirit of cinnamon with the fluidextract of rhubarb, and add the potassium carbonate previously dissolved in the water, and gradually add this mixture to enough syrup to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

"Rhubarb, in No. 20 powder, 70.0 *grammes;* Oil of Coriander, 0.5 *millilitre;* Refined Sugar, 840.0 *grammes;* Alcohol (90 per cent.), 280.0 *millilitres;* Distilled Water, sufficient to produce 1000.0 *millilitres.* Mix two hundred and seventy millilitres of the Alcohol with three times its volume of Distilled Water. Moisten the Rhubarb with seventy millilitres of this diluted alcohol and set aside for twenty-four hours in a closed vessel; pack in a percolator; pass the remainder of the diluted alcohol slowly through the moistened powder; evaporate the percolate to four hundred and seventy-five grammes; filter; dissolve the Refined Sugar in the filtrate by the aid of heat; cool; add the Oil of Coriander dissolved in ten millilitres of the Alcohol; mix, and finally add sufficient Distilled Water to produce the required volume." *Br.*

The Br. process is a troublesome and imperfect method.

The U. S. syrup differs from that official before 1890 in several particulars, and, in our opinion, it is greatly improved; the activity of the rhubarb and the corrigent effects of the cinnamon are both secured without impairing the appearance of the finished syrup, while the simplicity of the manipulation must commend the process to all. In the Br. Pharm. 1914 oil of coriander replaced coriander fruit official in the former pharmacopœia.

The official syrup is a mild cathartic, adapted for use with infants, to which it may be given in the dose of a fluidrachm (3.75 mils).

Dose, for adults, two to three fluidrachms (7.5–11.25 mils).

SYRUPUS RHEI AROMATICUS. U. S.

AROMATIC SYRUP OF RHUBARB Syr. Rhei Arom. [Spiced Syrup of Rhubarb]

(sy-rŭ'pŭs rhē'ī ăr-ǫ-măt'ĭ-cŭs)

Sirop de Rhubarbe aromatique, *Fr.*; Gewürzter Rhabarbersaft, *G.*

* "Aromatic Tincture of Rhubarb, *one hundred and fifty mils* [or 5 fluidounces, 35 minims]; Potassium Carbonate, *one gramme* [or 15 grains]; Syrup, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the potassium carbonate in the tincture and add this to sufficient syrup to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly." *U. S.*

A small amount of alkali is added here to prevent the syrup from becoming turbid.

The *aromatic syrup of rhubarb* is a warm stomachic laxative, too feeble for adult cases, but well calculated for the bowel complaints of infants; which are so frequent in our cities during the summer season, and as a remedy for which this preparation, or one analogous to it, has been long in use, under the name of *spiced syrup of rhubarb.* The dose for an infant with *diarrhea* is a fluidrachm (3.75 mils), repeated every two hours until the passages indicate by their color that the medicine has operated. It should be borne in mind that the syrup, as prepared by the present formula, contains one-seventh of diluted alcohol, which, though not injurious in most cases in which this syrup is used, might render it too stimulating in some instances of diarrhea in the very young infant.

Dose, one to three fluidrachms (3.75–11.25 mils).

SYRUPUS RHŒADOS. Br.

SYRUP OF RED POPPY

(sy-rŭ'pŭs rhœ'ą-dŏs)

Sirop de Coquelicot, *Fr. Cod.*; Sirop de Pavot rouge, *Fr.*; Klatschrosensaft, *G.*

"Red-Poppy Petals, 260 *grammes;* Refined Sugar, 720 *grammes;* Alcohol (90 per cent.), 50 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres.* Add the Red-Poppy Petals gradually to four hundred millilitres of Distilled Water kept hot upon a water-bath, stir frequently, and afterwards, the vessel being removed, infuse for twelve hours. Then press out the liquid; strain; add the Refined Sugar,

and dissolve by the aid of heat. When nearly cold, add the Alcohol, and sufficient Distilled Water to produce the required volume." *Br.*

The object of introducing the petals into water heated by a water bath is that they may shrink by being scalded, as otherwise they could not be completely immersed in the quantity of water directed. After this has been accomplished, they should be immediately removed from the fire, lest the liquor become too thick and ropy. The fine red color of this syrup is its only recommendation. It is very liable to ferment; according to Enders, this can be obviated by evaporating the recently prepared syrup to dryness, keeping the powdered residue in well-stoppered bottles, and dissolving it, as wanted, in four-fifths of its weight of water.

Dose, as stated in the Br. Pharmacopœia, one-half to one fluidrachm (1.8–3.75 mils).

SYRUPUS ROSÆ. Br.

SYRUP OF ROSE

(sy-rŭ'pŭs rō'sæ)

Syrup of Roses, *Br.;* Syrupus Rosarum Rubrarum; Syrup of Red Rose; Sirop de Rose rouge, *Fr.;* Rosensirup, *G.*

Syrup of Rose was deleted from the U. S. P. IX, but the process was introduced into the National Formulary IV (see Part III).

"Dried Red-Rose Petals, 50 *grammes;* Refined Sugar, *a sufficient quantity;* Distilled Water, boiling, 500 *millilitres.* Infuse the Red-Rose Petals in the Distilled Water for two hours; strain; press; heat the infusion to the boiling point; filter; add to the filtrate twice its weight of Refined Sugar and dissolve by the aid of heat." *Br.*

Syrup of rose is mildly astringent, but is valued most for its fine red color, on account of which it is occasionally added to mixtures. The color is developed by the small amount of diluted sulphuric acid which is added.

Dose, a fluidrachm (3.75 mils).

SYRUPUS SARSAPARILLÆ COMPOSITUS. U. S.

COMPOUND SYRUP OF SARSAPARILLA
Syr. Sarsap. Co.

(sy-rŭ'pŭs săr-sa-pa-rĭl'læ cŏm-pŏz'ĭ-tŭs)

Syrupus Sudorificus; Sirop de Salsepareille composé, *Fr. Cod.;* Sirop sudorifique, *Fr.;* Zusammengesetzter Sarsaparillsirup, *G.;* Jarabe de zarzaparrilla compuesto, *Sp.*

* "Fluidextract of Sarsaparilla, *two hundred mils* [or 6 fluidounces, 366 minims]; Fluidextract of Glycyrrhiza, *fifteen mils* [or 243 minims]; Fluidextract of Senna, *fifteen mils* [or 243 minims]; Oil of Sassafras, *two-tenths of a mil* [or 3 minims]; Oil of Anise, *two-tenths of a mil* [or 3 minims]; Methyl Salicylate, *two-tenths of a mil* [or 3 minims]; Alcohol, *nineteen and four-tenths mils* [or 314 minims]; Syrup, *seven hundred and fifty mils* [or 25 fluidounces, 173 minims]; to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the fluidextracts and add the alcohol, in which the methyl salicylate and the oils have been dissolved. Gradually add this solution to the syrup and mix thoroughly." *U. S.*

An important change was made in this compound syrup in the U. S. P. 1890, through the substitution of fluidextracts and volatile oils for the drugs used in the U. S. P. 1880 process. It was further improved in the U. S. P. VIII by doubling the amount of volatile oils. The present syrup is not perfectly transparent, but the U. S. P., 1890, syrup had the same fault. The simplicity of the present formula is a welcome improvement.

In the original edition of the U. S. Pharmacopœia, published in 1820, a process for a syrup of sarsaparilla was adopted, intended to present the famous French *sirop de cuisinier.* This process has been variously modified from time to time, but the present preparation possesses any possible therapeutic virtues of the original preparation.

Uses.—The *compound syrup of sarsaparilla* is a senseless survival of an ancient superstition. As pointed out elsewhere in this work, it is improbable that sarsaparilla possesses any therapeutic virtue, and even if it did the proportion in the compound syrup is too small to exert any effect upon the system. While the syrup has a pleasant flavor, owing to the licorice and volatile oils it contains, as a vehicle it would be improved by omitting the sarsaparilla and the senna.

Corrosive sublimate, which is often given in connection with this syrup, is said to be completely decomposed by it, being converted into calomel. Samuel Kennedy (*Ph. Rec.,* 1888, p. 201) showed that when corrosive sublimate was dissolved in this syrup precipitation invariably occurred; if an equal amount of sodium chloride was added, precipitation was greatly retarded. Lepage of Gisors, proposes as a substitute potassium iodohydrargyrate, which he has found not to undergo decomposition. (See *Potassio-mercuric Iodide,* Part II.)

Dose, of the syrup, half a fluidounce (15 mils), equivalent to somewhat less than a drachm (3.9 Gm.) of the root, to be taken three or four times a day.

Off. Prep.—Syrupus Bromidorum, *N. F.*

SYRUPUS SCILLÆ. U. S., Br.

SYRUP OF SQUILL. Syr. Scill.

(sy-rŭ'pŭs sçĭl'læ)

Syrupus Aceti Scillæ; Sirop de Scille, *Fr.;* Meerzwiebelsirup, *G.*

* "Vinegar of Squill, *four hundred and fifty mils* [or 15 fluidounces, 104 minims]; Sugar, *eight hundred grammes* [or 28 ounces av., 96 grains]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the sugar in the vinegar of squill with the aid of a gentle heat, then strain the syrup and, when the liquid is cold,

add enough water, through the strainer, to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly." *U. S.*

"Vinegar of Squill, 175 *millilitres;* Refined Sugar, 650 *grammes;* Distilled Water, sufficient to produce 1000 *grammes.* Mix the Vinegar of Squill with an equal volume of Distilled Water. In the mixture dissolve the Refined Sugar by the aid of gentle heat; add sufficient Distilled Water to produce the required weight." *Br.*

The present British formula is almost identical with U. S. IX, and differs from that of 1864 in taking the vinegar already formed, instead of preparing it as the first step of the process. Vinegar of Squill of the Br. Pharm. 1914 is double the strength of that formerly official. The heating should be performed as quickly as possible, to prevent undue loss of acetic acid.

This syrup is much employed as an expectorant, especially in combination with a solution of tartarized antimony. It is incompatible with ammonium carbonate, but not with ammonium chloride.

Dose, about a fluidrachm (3.75 mils).

SYRUPUS SCILLÆ COMPOSITUS. U. S.

COMPOUND SYRUP OF SQUILL Syr. Scill. Co. [Hive Syrup]

(sy-rŭ'pŭs sĕ-ĭl'lē kŏm-pŏz'ĭ-tŭs)

Coxe's Hive Syrup; Sirop de Scille composé, *Fr.;* Zusammengesetzter Meerzwiebelsirup, *G.*

* "Fluidextract of Squill, *eighty mils* [or 2 fluidounces, 338 minims]; Fluidextract of Senega, *eighty mils* [or 2 fluidounces, 338 minims]; Antimony and Potassium Tartrate, *two grammes* [or 31 grains]; Distilled Water, *ten mils* [or 162 minims] Syrup, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the antimony and potassium tartrate in the distilled water with the aid of heat, add this solution to *seven hundred and fifty mils* [or 25 fluidounces, 173 minims] of syrup and mix thoroughly. Then gradually add the fluidextracts, previously mixed, and finally, sufficient syrup to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

This is intended as a substitute for the popular preparation called *Coxe's hive syrup,* from which it differs chiefly in containing sugar instead of honey. Prepared as originally directed in the Pharmacopœia, it invariably fermented from the want of sufficient concentration. This defect was corrected many years ago when sugar was substituted for honey, in consequence of the uncertain consistence and constitution of the latter. The present formula is a decided improvement, fluidextracts of squill and senega being used. Percolation has been found very well adapted for dissolving the sugar and producing a transparent syrup. The present U. S. P. process has the merit of simplicity, but, unfortunately, the fluidextract of squill is never a wholly satisfactory preparation.

The name Coxe's hive syrup, which is meaningless because it is not used in the treatment of *hives,* is said to owe its origin to a period when croup, for which the remedy is often used, was known popularly as "hives."

Compound syrup of squill combines the virtues of senega, squill, and tartar emetic, of the last of which it contains about one grain in a fluidounce. It is emetic, diaphoretic, expectorant, and frequently cathartic, and may be given with advantage in mild cases of simple *croup,* also in the latter stages of severe cases when the object is to promote expectoration. The dose of this syrup is, for children, from two to twenty minims (0.12–1.3 mils), according to the age, and it may be repeated in cases of croup every fifteen or twenty minutes until it causes vomiting.

Dose, for adults as an expectorant, from twenty to thirty minims (1.3–1.8 mils).

SYRUPUS SENEGÆ. U. S.

SYRUP OF SENEGA Syr. Seneg.

(sy-rŭ'pŭs sĕn'ē-gæ)

Sirop de Polygala, *Fr.;* Sirupus Senegae, *P. G.;* Senegasirup, *G.*

* "Fluidextract of Senega, *two hundred mils* [or 6 fluidounces, 366 minims]; Syrup, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the fluidextract with sufficient syrup to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*

The syrup affords a very convenient mode of exhibiting senega in pectoral complaints. Owing to the pectinous principle present in senega, the syrup made directly from the root as in the process of 1870 was always turbid. It has been frequently pointed out that the addition of an alkali renders the syrup transparent, and the 1890 process directed the use of a small quantity of ammonia water, although, if the fluidextract of senega which contains alkali be used as in the U. S. P. IX, this addition is unnecessary. This syrup may be given as a nauseating expectorant.

Dose, one or two fluidrachms (3.75 or 7.5 mils).

SYRUPUS SENNÆ. U. S., Br.

SYRUP OF SENNA Syr. Senn.

(sy-rŭ'pŭs sĕn'næ)

Sirop de Séné, *Fr.;* Sirupus Sennae, *P. G.;* Sennasirup, *G.*

* "Fluidextract of Senna, *two hundred and fifty mils* [or 8 fluidounces, 218 minims]; Oil of Coriander, *five mils* [or 81 minims]; Syrup, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the oil of coriander with the fluidextract of senna and add sufficient syrup to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly." *U. S.*

"Senna Leaves, 440.0 *grammes;* Oil of Coriander, 0.2 *millilitre;* Alcohol (90 per cent.), 2.0

millilitres; Refined Sugar, 540.0 *grammes;* Alcohol (20 per cent.), 760.0 *millilitres.* Moisten the Senna Leaves with four hundred and forty millilitres of the Alcohol (20 per cent.); pack tightly in a vessel which can afterwards be closed; set aside for three days; press strongly; reserve the liquid obtained; break up the marc; moisten it with one hundred and sixty millilitres of the Alcohol (20 per cent.); set aside for twenty-four hours; press strongly; add the liquid obtained to the portion previously reserved; break up the marc; mix it with the remainder of the Alcohol (20 per cent.); set aside for three hours; press again; evaporate the resulting liquid until it is reduced to such a volume that when added to the reserved liquid the whole measures four hundred and forty millilitres. Mix the evaporated liquid with the reserved liquid; heat the product in a covered vessel to 82° C. (179.6° F.) for a few minutes; set aside for twenty-four hours; filter, and pass Distilled Water through the filter until the filtrate measures four hundred and forty millilitres; add the Refined Sugar, and dissolve in a covered vessel by the aid of gentle heat; cool; add the Oil of Coriander dissolved in the Alcohol (90 per cent.); mix." *Br.*

The process was improved in the U. S. P. VIII by simply adding the fluidextract and oil of coriander to syrup, and this process has been retained in the Ninth Revision.

Dose, of the U. S. syrup of senna, for an adult, from one to four fluidrachms (3.75–15.0 mils); of the Br. syrup from one to two fluidrachms (3.75–7.5 mils).

SYRUPUS TOLUTANUS. U. S., Br.

SYRUP OF TOLU Syr. Tolu.

(sy-rŭ'pŭs tŏl-ū-tā'nŭs)

Sirop de Baume de Tolu, *Fr. Cod.;* Sirop balsamique, *Fr.;* Tolubalsamsirup, *G.;* Jarabe de balsamo de Tolu, *Sp.*

* "Tincture of Tolu, *fifty mils* [or 1 fluidounce, 331 minims]; Magnesium Carbonate, *ten grammes* [or 154 grains]; Sugar, *eight hundred and twenty grammes* [or 28 ounces av., 405 grains]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Rub the tincture of tolu in a mortar with the magnesium carbonate and *sixty grammes* [or 2 ounces av., 51 grains] of the sugar. Then gradually add *four hundred and thirty mils* [or 14 fluidounces, 259 minims] of water, with constant trituration, and filter. Dissolve the remainder of the sugar in the clear filtrate, with the aid of a gentle heat, strain the syrup while hot, and add sufficient water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Syrup of tolu may also be made in the following manner: Prepare a percolator in the manner described under *Syrupus.* Pour the filtrate obtained as directed in the preceding formula upon the remainder of the sugar, return the first portions of the percolate until it runs through clear, and, when all of the liquid has passed, follow it with water, until all of the sugar is dissolved and the product measures *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly." *U. S.*

"Balsam of Tolu, 25 *grammes;* Refined Sugar, 660 *grammes;* Distilled Water, sufficient to produce 1000 *grammes.* Add four hundred grammes of the Distilled Water, boiling, to the Balsam of Tolu; cover lightly and heat on a water-bath for half an hour, stirring frequently. Remove; add Distilled Water, if necessary, so that the liquid, when cold, measures four hundred millilitres. Filter the solution, add the Refined Sugar, dissolve by the aid of a water-bath, and finally add sufficient Distilled Water to produce the required weight." *Br.*

The U. S., 1890, process for this syrup was more satisfactory than that formerly official. It was practically a return to the U. S., 1870, method (based on Finley's process, substituting precipitated calcium phosphate for magnesium carbonate, and using a freshly made strong tincture for the official tincture of tolu.

The U. S. Pharmacopœia VIII and IX process reintroduced magnesium carbonate with much advantage, and has the further improvement of using the official tincture of tolu instead of making the latter from the balsam by a special process. In the British process the soluble principles of the balsam are extracted by boiling it with water, but with great waste of the material, as the water dissolves but a small portion of the active matter. To obviate this waste, the same portion of balsam is, according to Brande, usually employed in successive operations, and it long continues to impart odor and taste to boiling water. W. H. Hostelley's modification is as follows: For making twenty-five ounces of syrup, take one ounce of balsam of tolu, one pound of granulated sugar, and water which has been previously filtered through animal charcoal, enough to make twenty-five ounces; rub the tolu to a fine powder, aided by some of the sugar, and mix this with the remainder of the granulated sugar; now prepare a percolator by placing a piece of cotton in the neck, pack the powder in it, pour in the filtered water, and receive twenty-five ounces of percolate. (*A. J. P.,* 1887, p. 290.) Syrup of tolu is used chiefly to impart its agreeable flavor to mixtures. If a stronger preparation is desired, tincture of tolu may be added in the desired quantity, directing the bottle to be shaken.

Dose, one to four fluidrachms (3.75–15.0 mils).

SYRUPUS URGINEÆ. Br.

SYRUP OF URGINEA

(sy-rŭ'pŭs ür-gĭ'nē-ą)

"Vinegar of Urginea, 175 *millilitres;* Refined Sugar, 650 *grammes;* Distilled Water, sufficient to produce 1000 *grammes.* Mix the Vinegar of Urginea with an equal volume of Distilled Water. In the mixture dissolve the Refined Sugar by the aid of gentle heat; add sufficient Distilled Water to produce the required weight." *Br.*

This syrup corresponds to the Syrup of Squill of the British Pharmacopœia and is used for the same purpose.

Dose, one-half to one fluidrachm (1.8–3.75 mils).

SYRUPUS ZINGIBERIS. U. S., Br.

SYRUP OF GINGER Syr. Zingib.

(sy-rŭ'pŭs zĭn-gĭb'ẹ-rĭs)

Sirop de Gingembre, *Fr.;* Ingwersirup, *G.*

* "Fluidextract of Ginger, *thirty mils* [or 1 fluidounce, 7 minims]; Alcohol, *twenty mils* [or 325 minims]; Magnesium Carbonate, *ten grammes* [or 154 grains]; Sugar, *eight hundred and twenty grammes* [or 28 ounces av., 405 grains]; Water, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the fluidextract of ginger and the alcohol, then triturate the liquid in a mortar with the magnesium carbonate and *sixty grammes* [or 2 ounces av., 51 grains] of the sugar. Then gradually add *four hundred and thirty mils* [or 14 fluidounces, 259 minims] of water, with constant trituration, and filter. Dissolve the remainder of the sugar in the clear filtrate, with the aid of a gentle heat, strain the syrup while hot, and add sufficient water to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Syrup of Ginger may also be made in the following manner: Prepare a percolator in the manner described under *Syrupus.* Pour the filtrate obtained as directed in the preceding formula upon the remainder of the sugar, return the first portions of the percolate until it runs through clear, and, when all the liquid has passed, follow it with water, until all of the sugar is dissolved and the product measures *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix thoroughly." *U. S.*

"Ginger, in powder, 25 *grammes;* Alcohol (90 per cent.), *a sufficient quantity;* Syrup, sufficient to produce 1000 *millilitres.* Prepare fifty millilitres of a strong tincture of the Ginger by the *process of percolation* with the Alcohol. To this add sufficient of the Syrup to produce the required volume." *Br.*

The U. S. P. process has been improved by the addition of magnesium carbonate as an aid in distributing the resinous fluidextract so as to facilitate its solution in water. It is practically a return to the U. S. 1870 method.

The British syrup, being made by the simple incorporation of the tincture with syrup, has of course all the strength of the ginger, but is inferior to the U. S. preparation in appearance and flavor. The old plan of using water as the menstruum for the drug has been abandoned, as the syrup thus made is encumbered with mucilage and starch, and consequently rendered more liable to decomposition. In order that the preparation may be of the proper strength, it is necessary that the fluidextract should have been made with the best ginger and with the official menstruum. The syrup of ginger is much used as a warm stomachic addition to tonic and purgative infusions or mixtures, and to impact flavor particularly to carbonic acid water.

Dose, one to four fluidrachms (3.75–15.0 mils).

TABELLÆ TRINITRINI. Br.

TRINITRIN TABLETS

(tă-bĕl'læ trī-nī'trĭ-nī)

Tablets of Nitroglycerin.

"Trinitrin Tablets are tablets of chocolate each weighing 0.300 gramme and containing 0.0005 gramme (0.5 milligram) of the trinitroglycerin of commerce. Each of these Tablets contains 0.5 milligram (approximately 1/130 grain) of the trinitroglycerin of commerce." *Br.*

A pill of nitroglycerin, made with althea and confection of rose, is recognized by the N. F. (see Part III). They afford a convenient mode of exhibiting glyceryl nitrate, but because of its volatility are apt to lose their strength on keeping.

Dose, one to two tablets.

TALCUM PURIFICATUM. U. S.

PURIFIED TALC Talc. Purif.

(tăl'cŭm pū-rĭ-fĭ-cā'tŭm)

"A purified, native, hydrous magnesium silicate sometimes containing a small amount of aluminum silicate." *U. S.*

Talcum, *U. S. VIII,* Talc purifié, *Fr.;* Gereinigter Talk, *G.;* Talcum Venetum; Soapstone; Talc, *Fr. Cod.;* French Chalk; Creta Gallica; Talc de Venise, Craie de Briancon, *Fr.;* Talcum, *P. G.;* Talk, Talkstein, Speckstein, *G.*

Talc is a native hydrous magnesium silicate which is found in various parts of the world, especially in France, Italy, and the United States. An especially high quality is obtained in New York, Vermont, Virginia, and North Carolina. The production of talc in the United States amounted, in 1915, to 166,336 tons, and of soapstone to 20,555 tons.

It is frequently associated with ferrous oxide, alumina, and lime. It occurs in irregular masses of a greenish-gray color, having a peculiar wax-like appearance of the surface, and giving when rubbed a greasy sensation to the skin. It is odorless, tasteless, and insoluble in water or in dilute solutions of the acids or alkaline hydroxides. It is largely used in the arts, especially in the manufacture of paper when it is used as a filler. For medicinal purposes it is reduced to a fine powder, and purified by washing with hydrochloric acid. The present pharmacopœia gives no process for its purification. That of the U. S. VIII was as follows:

"Talc, in fine powder, *five hundred grammes* [or 17 ounces av., 279 grains]; Hydrochloric Acid, *seventy-five cubic centimeters* [or 2 fluidounces, 257 minims]; Water, *a sufficient quantity.* Mix the powdered Talc with about *twenty-five hundred cubic centimeters* [or 5 pints] of boiling Water, gradually add *fifty*

cubic centimeters [or 1 fluidounce, 331 minims] of the Hydrochloric Acid, and boil the mixture during fifteen minutes, then allow it to stand for fifteen minutes. Decant, and reject the supernatant liquid containing the finer particles of Talc in suspension, and again boil the residue with *twenty-five hundred cubic centimeters* [or 5 pints] of Water, mixed with the remainder of the Hydrochloric Acid, and allow it to stand for fifteen minutes. Again decant, and reject the finer suspended particles, and wash the coarser residue with Water by repeated decantation, until a portion of the wash-water, after filtering and acidifying with nitric acid, fails to become opalescent upon the addition of silver nitrate test solution. Then transfer the magma to a close linen or muslin strainer, allow it to drain, and dry it at 110° C. (230° F.)." *U. S. VIII.*

Purified Talc is intended to replace magnesium carbonate, calcium phosphate, and other absorbent powders used to aid filtration, it having the advantage of insolubility, although its absorbent properties are deficient in comparison with magnesium carbonate. As much of the talc sold commercially has been bolted for use in toilet powders it is too fine for use as a filtering medium; the fine particles passing through the pores of the filter paper. For this reason the U. S. P. directs talc for filtering to be not finer than a No. 100 powder.

An interesting and valuable communication on the subject of filtering media is contributed to the *J. A. Ph. A.*, 1916, p. 506, by W. L. Scoville. In it he gives experimental data of the comparison of paper pulp, talc, infusorial earth and Fuller's earth, in filtering aqueous solutions of alkaloids. He says that of the media experimented with, Fuller's earth is the only one producing any marked change in the filtrate, and that it removes from 22 to 100 per cent. of alkaloidal substances from solution, depending upon the alkaloid and whether the liquid is acid, alkaline, or neutral. The "Mechanism of Filtration" is the title of an article by Hatchek (*J. S. C. I.*, 1908, p. 538), in which the effect of various filtering media is scientifically discussed and diagrammatically illustrated.

Properties.—It is officially described as follows: "Purified Talc is a very fine, white or grayish-white powder, which adheres to the skin, is quite free from grittiness and is slippery to the touch; it is odorless and tasteless. Mix 0.5 Gm. of Purified Talc with about 2 Gm. each of anhydrous sodium and potassium carbonates, heat the mixture in a platinum crucible until fusion is complete, and treat the resulting fused mass with hot distilled water. Then neutralize the liquid with diluted sulphuric acid, add 10 mils more of the diluted acid and evaporate the mixture until white fumes of sulphuric acid anhydride are evolved. Add 20 mils of distilled water, boil the mixture and filter; an insoluble residue of *silica* remains. The addition of ammonia water and ammonium chloride to the filtrate may produce a white gelatinous precipitate of *aluminum hydroxide*, and the filtrate from this mixture on the addition of sodium phosphate T.S. yields a white crystalline precipitate of magnesium ammonium phosphate. Purified Talc, when subjected to ignition at red heat, loses not more than 5 per cent. of its weight. Boil 10 Gm. of Purified Talc with 50 mils of distilled water for one-half hour, adding water from time to time to maintain approximately the original volume. It yields a filtrate which is neutral to litmus, and one-half of this filtrate, when evaporated and dried at 110° C. (230° F.), yields not more than 0.005 Gm. of residue (*soluble substances*). The remaining half of this filtrate, after slightly acidulating with hydrochloric acid, does not yield a blue color upon the addition of potassium ferrocyanide T.S. (*iron*). NOTE.—Purified Talc, when used as a filtering medium, should not be finer than a No. 100 powder." *U. S.*

Uses.—Purified talc is used pharmaceutically (see above) and as a protecting, soothing powder to the skin. When in very fine powder it forms the basis of many of the proprietary toilet and infant powders, and is very valuable as a dusting powder in *intertrigo, prickly heat, pruritus,* and other conditions of dermal irritation.

TAMARINDUS. Br.

TAMARIND

(tăm-ą-rĭn'dŭs)

"Tamarinds are the fruits of Tamarindus indica, *Linn.*, freed from the brittle outer part of the pericarp and preserved with sugar." *Br.* The preserved pulp of the fruit of *Tamarindus indica* Linné (Fam. *Leguminosæ*)." *N. F.*

Fructus Tamarindorum; Tamarinier, *Fr. Cod.;* Tamarin Pulpe brute de Tamarins, *Fr.;* Pulpa Tamarindorum cruda, *P. G.;* Tamarindemnus, Tamarinden, *G.;* Tamarindo, *It.;* Tamarindo (Pulpa de), *Sp.*

The tamarind tree (*Tamarindus indica*) is the only species of this genus. It rises to a great height, sends off numerous spreading branches, and has a beautiful appearance. The trunk is erect, thick, and covered with a rough, ash-colored bark. The leaves are alternate and pinnate, composed of many pairs of opposite leaflets, which are almost sessile, entire, oblong, obtuse, unequal at their base, about half an inch long by a sixth of an inch broad, and of a dark-green color. The flowers, which are in small lateral racemes, have a yellowish calyx, and yellow petals beautifully variegated with red veins. The fruit is a broad, compressed, reddish ash-colored pod, much curved, from two to six inches long, with numerous brown, flat, quadrangular seeds, contained in loculi formed by a tough membrane. Exterior to this membrane is a light-colored acid pulpy matter, between which and the shell are several somewhat branched tough ligneous strands, running from the stem to the extremity of the pod, the attachment of which they serve to strengthen. The shells are fragile and easily separated.

The tree appears to be a native of the East and West Indies, Egypt, and Arabia, though believed by some to have been imported into America. Barth, the African traveller, found it abundant in the interior of Africa. De Candolle was doubtful whether the East and West India trees are of the same species. It is stated by writers that the pods of the former are much larger than those of the latter, and have a greater number of seeds, the East India tamarinds containing six or seven, those from the West Indies rarely more than three or four; but this seems not to be correct.

Calcutta appears to be the chief emporium for the tamarinds of the European markets. Tamarinds are also sent from the West Indies and Ecuador to England; when from this source they are preferred. The latter are known as American tamarinds, and are obtained from *T. indica,* var. *occidentalis* Gärtn. They are of a light brown color, less cohesive and possess less acidity than the tamarinds from the Old World. Tamarinds are brought to us chiefly from the West Indies, where they are prepared by placing the pods, previously deprived of their shells, in layers in a cask, and pouring boiling syrup over them. A better mode, sometimes practised, is to place them in stone jars, with alternate layers of powdered sugar. They are said to be occasionally prepared in copper boilers. In the East Indies tamarinds are often prepared for market by stripping off the outer shell and pressing the pulpy interiors into a mass; sometimes they are packed as in the West Indies.

Properties.—Fresh tamarinds, which are sometimes, though rarely, brought to this country, have an agreeable, sour taste, without any mixture of sweetness. In the United States they are usually met with only in the preserved state, this is a dark-colored adhesive mass, consisting of syrup mixed with the pulp, membrane, strong, somewhat branching fibres or string-like strands, and seeds of the pod, and having a sweet acidulous taste. The brown, flattish, quadrangular seeds, each enclosed in a tough membrane, should be hard, clean, and not swollen, the string-like fibers tough and entire, and the odor without mustiness. Tamarind is officially described as "a reddish-brown, moist, sugary mass, containing strong branched fibres, and brown, shining seeds, each enclosed in a tough membrane. Taste agreeable, subacid. The pulp yields no characteristic *reactions* for copper." *Br.*

"A pulpy mass of a light reddish-brown color, changing with age to a dark brown, containing some branching fibers and numerous reddish-brown, smooth, oblong or quadrangular, compressed seeds, each enclosed in a tough membrane. Odor distinct; taste sweet and agreeably acid." *N. F.*

From the analysis of Vauquelin, it appears that in 100 parts of the pulp of tamarinds, independently of the sugar added to them, there are 9.40 parts of citric acid, 1.55 of tartaric acid, 0.45 of malic acid, 3.25 of potassium bitartrate, 4.70 of gum, 6.25 of pectin, 34.35 of parenchymatous matter, and 27.55 of water. K. Müller, after analyzing nine commercial varieties, states that only traces of citric and malic acids are present, but that tartaric acid and acid potassium tartrate are present in considerable amount. Copper may often be detected in preserved tamarinds, derived from the boilers in which they are prepared. Its presence may be ascertained by the reddish coat which it imparts to the blade of a spatula or other steel implement immersed in the tamarinds.

Uses.—Tamarinds are laxative and refrigerant, and infused in water form a highly grateful drink in febrile diseases. Convalescents often find the pulp a pleasant addition to their diet, and useful when a laxative action is desirable. It is sometimes prescribed in connection with other mild cathartics. Though frequently given with infusion of senna to cover its taste, it is said to weaken its purgative power, and the same observation has been made of its influence upon the resinous cathartics in general. For a formula for *fluidextract of tamarind,* see *Nat. Drug.,* 1892, 101.

Dose, from a drachm to an ounce (3.9–31 Gm.).

Off. Prep.—Confectio Sennæ, *Br., N. F.*

TARAXACUM. U. S. (Br.)

TARAXACUM Tarax. [Dandelion]

(tą-răx'ą-cŭm)

"The dried rhizome and roots of *Taraxacum officinale* Weber (Fam. *Compositæ*). Preserve the thoroughly dried drug in tightly-closed containers, adding a few drops of chloroform or carbon tetrachloride, from time to time, to prevent attack by insects." *U. S.* "Taraxacum Root is the fresh root of Taraxacum officinale, *Wiggers.* Collected in the autumn." *Br.*

Taraxaci Radix, *Br.,* Taraxacum Root; Dandelion Root, Blowball, Milk, Witch, or Yellow Gowan, Lion's-tooth, Cankerwort; Pissenlit, Dent de Lion, *Fr. Cod.;* Radix Taraxaci cum herba, *P. G.;* Löwenzahn, *G.;* Tarassaco, *It.;* Taraxacon, Diente de Leon, *Sp.*

The dandelion is an herbaceous plant, with a perennial fusiform root. The leaves, which spring immediately from the short upright rhizome, are long, pinnatifid, generally runcinate, with the divisions toothed, smooth, and of a fine green color. The common name of the plant was derived from the fancied resemblance of its leaves to the teeth of a lion. The flower-stem rises from the midst of the leaves, six inches or more in height. It is erect, simple, naked, smooth, hollow, fragile, and terminated by a large golden-colored flower, which closes in the evening and expands with the returning light of the sun. The involucre is smooth and double, with the outer scales bent downward. The florets are very numerous, ligulate, and toothed at their extremities. The receptacle is flat and naked. The pappus is stipulate, and at the period of maturity is disposed in a spherical form, and is so light and feathery as to

be easily borne away by the wind, with the achene attached. Another plant resembling the common dandelion, the achenes of which, however, are narrower and bright red or reddish brown, known as the *red-seeded dandelion*, is the product of *T. erythrospermum*, Andrz., and is supposed by some to be naturalized from Europe.

The common dandelion, *Taraxacum officinale*, grows spontaneously in widely separated parts of the globe. It is abundant in this country, adorning our grass plots and pasture grounds with its bright yellow flowers, which, in moist places, show themselves with the first opening of spring, and continue to appear until near the close of summer. In India the plant is cultivated in various parts of the country, and its root collected for use between the months of September and February. (*P. J.*, Dec. 1871, 523.) All parts of the plant contain a milky bitterish juice, which exudes when they are broken or wounded. The leaves, when very young and blanched by the absence of light during their growth, are tender and not unpleasant to the taste, and are sometimes used as a salad. When older and of their natural color, they are medicinal, but the leaves of the wild plant in various stages of its early growth are used for salads by those who have cultivated a taste for this vegetable. The Pharmacopœias recognize only the root. It should be full grown when collected, and should be employed in the recent state, as it is then most active. It does not, however, as stated by Duncan, lose nearly all its bitterness by drying, and the root dug up in the warmer seasons might, if dried with care, be employed with propriety in the succeeding winter. The juice of the root is thin and watery in the spring; milky, bitter, and spontaneously coagulable in the latter part of summer and autumn, and sweet and less bitter in the winter when affected by the frost. The months of July, August, and September are, therefore, the proper periods for collecting it.

Henry Barton, of Brighton, England, prepared the juice from the flower-stalks by crushing and pressure, adding 25 per cent. of spirit, and, after allowing it to stand for some weeks in glass bottles, filtering to separate a very small quantity of deposit, and setting aside for use. According to Barton, it remains bright, and retains its characteristic taste. Though not so rich in solid constituents as the juice of the root, yet, having an equal bitterness, it is probably not less efficacious as a medicine, if it be true, as stated by Bentley, that the efficacy of the medicine does not depend solely on the amount of its solid constituents, but principally if not entirely on the bitter principle it contains. Barton stated that the juice is certainly one of the best preparations of taraxacum. (*A. J. P.*, 1872, p. 509.)

Properties.—The official description of Taraxacum follows: "Cylindrical or somewhat flattened, gradually tapering, usually in broken pieces, from 6 to 15 cm. in length and from 5 to 15 mm. in thickness; externally brown or blackish-brown, longitudinally wrinkled, having numerous root and rootlet-scars; crown simple or branched with numerous leaf-bases showing annulate markings; odor slight or inodorous; taste bitter. Under the microscope, transverse sections of the root of Taraxacum show a porous, pale yellow wood from 1 to 4 mm. in diameter, surrounded by a light brown bark from 2 to 6 mm. in thickness, the latter composed of concentric layers of lacticiferous vessels and sieve tissues, alternating with whitish inulin-bearing parenchyma. The rhizome portions show a small pith. The powder is light brown; when examined under the microscope it exhibits parenchyma cells which are large, thin-walled and contain irregular masses of inulin; fragments with yellowish-brown lacticiferous vessels; tracheæ reticulate; intermediate fibers non-lignified, with irregular, simple and oblique pores. Taraxacum yields not more than 10 per cent. of ash." *U. S.* "Fresh root frequently three decimetres or more long, and twelve millimetres or more thick, smooth and yellowish-brown externally, whitish within. Fracture short, the exposed surface showing a small yellow porous wood, surrounded by a thick nearly white cortex exhibiting a variable number of irregular concentric rings, from which a milky juice exudes. Inodorous; taste bitter." *Br.*

Taraxacum should be free from the root of *Cichorium Intybus* Linné, which closely resembles it, but is usually paler, more bitter, and has the milk vessels in radiating lines. The drug consists in part of the rhizome which shows from ten to fifteen fibro-vascular bundles surrounded by the parenchyma-tissue of the pith, the diameter of which in some instances exceeds the thickness of the woody zone several times. In other respects the structure of the rhizome resembles the root, the concentric arrangement of the laticiferous ducts in particular excluding any possibility of mistaking the specimens for chicory, etc. (*Am. Drug.*, 1887, p. 2.) The active properties of taraxacum are yielded to water by boiling, and do not appear to be injured in the process. Dragendorff obtained from the root gathered in October and dried at 100° C. (212° F.) 24 per cent. of *inulin* and some sugar. The root gathered in March from the same place yielded 1.74 per cent. of inulin, 17 of uncrystallizable sugar, and 18.7 of *levulin*. This last-named substance, discovered by Dragendorff, has the same composition as inulin, but dissolves in cold water, and is devoid of any rotatory power. Mannite, which has been found in the infusion of the root, has been demonstrated by Smith, of Edinburgh, not to pre-exist in the root, but to be formed by spontaneous changes consequent on exposure.

A crystallizable principle has been extracted from the juice of the root by Pollex, who has named it *taraxacin*. It is bitter and somewhat acrid, fusible, but not volatile, sparingly soluble in cold water, but very soluble in boiling water, alcohol, and ether. It is obtained by boiling the milky juice in distilled water, filtering the concentrated liquor, and allowing

it to evaporate spontaneously in a warm place. The taraxacin crystallizes, and may be purified by repeated solution and crystallization in alcohol or water. Kromayer (*A. Pharm.* (2), cv, 6) also obtained taraxacin, and, in addition, a second crystalline principle, *taraxacerin*, $C_8H_{16}O$, insoluble in water, but soluble in alcohol. According to Vogel, the intra-cellular substance of the root consists chiefly of pectose, which is the result of a metamorphosis of the substance constituting the membrane of the cells. L. E. Sayre found that the yield of taraxacin varies in roots collected at different seasons. (See *Proc. A. Ph. A.*, 1893, 1894, 1895, 1896, 1897.)

F. B. Power (*C. D.*, 1912, p. 822) contributed the results of some investigations of this drug, in which he states that besides inulin, resin and sugar, no definite substances have previously been isolated. The *taraxacin* of Polex (1839), and the *taraxacerin* of Kromayer (1861), to which was assigned the formula $C_{30}H_{50}O_5$, are both alleged to be definite mixtures. Power found in the air dried English root, an enzyme, essential oil, oily resin, fatty acids, including *melissic*, and *p-hydroxy-phenylacetic acid*, which had never before been isolated from a plant.

The roots of various plants have been largely substituted for dandelion in England and on the Continent by the herb gatherers, and we are informed that fraudulent substitution is not unfrequent, in this country, of the root of *Cichorium Intybus*, or *chicory*. It is rare to find chicory mixed with dandelion, the former being usually boldly substituted for the latter.

Uses.—Taraxacum was formerly supposed to possess cholagogic as well as diuretic powers. It has been used in various conditions accompanied with congested or *torpid liver*. There is, however, no sufficient reason for believing it possesses any therapeutic virtues. The dried root is sometimes mixed, in powder, with ground coffee, the taste of which covers that of the dandelion. It is roasted and powdered and then prepared in the same manner.

Dose, one to three drachms (3.9–11.6 Gm.).

Off. Prep.—Fluidextractum Taraxaci, *U. S.* (*Br.*); Extractum Taraxaci, *U. S., Br.;* Succus Taraxaci, *Br.;* Elixir Gentianæ Glycerinatum, *N. F.;* Elixir Taraxaci Compositum, *N. F.*

TEREBENUM. U. S., Br.

TEREBENE Tereben.

(tĕr-ĕ-bē′nŭm)

"A liquid consisting of dipentene and other hydrocarbons, obtained by the action of concentrated sulphuric acid on oil of turpentine. Preserve it in well-closed containers, protected from light." *U. S.* "Terebene is a mixture of dipentene and other hydrocarbons, obtained by shaking oil of turpentine with successive quantities of sulphuric acid until optically inactive, and then distilling in a current of steam." *Br.*

Térébène, *Fr.;* Tereben, *G.*

This substance is produced by the action of sulphuric acid upon oil of turpentine. The sulphuric acid must be added gradually to the cooled oil of turpentine, in the proportion of one part of acid to twenty parts of oil, and after a day's standing the mixture is heated to boiling. After cooling, the oily layer is removed, freed from acid by calcium carbonate, and rectified. The terebene so obtained boils at 156° C. (312.8° F.), is optically inactive and of rather pleasant odor. Some cymol is always produced at the same time, and by continued action of the acid the terebene is said to be entirely converted into cymol and colophene. Jayne and Chase, however, from a study of a number of samples of commercial terebenes (*A. J. P.*, 1887, p. 65), conclude that the boiling point of the true terebene is much higher, 173° to 180° C. (343.4°–356° F.). They found an inactive camphor, boiling at about 200° C. (392° F.) (probably borneol), to be formed also, and the residue left on rectifying was principally *colophene*.

Properties.—*Terebene* is officially described as "a colorless, thin liquid, having a rather agreeable, thyme-like odor, and an aromatic, somewhat terebinthinate taste. One mil of Terebene dissolves in 3 mils of alcohol at 25° C. (77° F.); slightly soluble in water. On exposure to light and air Terebene gradually becomes resinified, and acquires an acid reaction. Specific gravity: 0.860 to 0.865 at 25° C. (77° F.). It boils between 160° and 172° C. (320° and 341.6° F.). Terebene does not redden blue litmus paper which has been moistened with alcohol. Its optical rotation does not exceed +0.3° in a 100 mm. tube at 25° C. (77° F.) (*unaltered oil of turpentine*). After the determination of the boiling point, transfer the residue remaining in the distilling flask to a dish, by means of ether, and evaporate the liquid on a water bath; any residue remaining does not exceed 1 per cent. of the original weight of Terebene taken (*rosin*)." *U. S.*

"A colorless liquid. Agreeable odor; taste aromatic and terebinthinate. Specific gravity from 0.862 to 0.866. Soluble in 5 parts of *alcohol* (90 per cent.). *Optical rotation* at 15.5° C. (60° F.), +1° to −1°. Distils between 156° and 180° C. (312.8° and 356° F.), leaving only a slight viscous residue (absence of excess of resin). Not more than 15 per cent. distils below 165° C. (329° F.)." *Br.*

Power and Kleber (*Ph. Rund.*, 1894, 18) stated that pinene is not obtained by the action of sulphuric acid on oil of turpentine, that the U. S. P., 1890, boiling points 156° to 160° C. (312.8°–320° F.) should be 170° to 185° C. (338°–365° F.), and that the sp. gr. should be 0.855 instead of 0.862; also that terebene consists mainly of *dipentene* and *terpinene* with some cymol and camphene.

Uses.—Terebene is a valuable stimulant expectorant, first recommended by William Murrell (*B. M. J.*, Dec., 1885), in that form of *chronic bronchitis* often known as *winter cough*. It is very useful not only in cases of chronic bronchitis, but also in the *acute* disease, after the earlier stages have passed by. It probably exerts upon other mucous membranes the same

action that it does upon that of the lungs, and it has been employed with asserted good results in *dyspepsia,* especially in the flatulent intestinal variety, and may be used in chronic or subacute inflammation of the genito-urinary tract. Its action upon the general system has not been investigated, but probably resembles that of oil of turpentine. It may be given in emulsion, or by dropping into half a teaspoonful of sugar. It is also sometimes administered in pastils or lozenges. It has been used by atomization, with asserted good results. Murrell (*B. M. J.,* July 24, 1884) states that terebene is an active antiseptic and germicide, one part in four hundred and fifty being able to keep in check the action of the yeast plant, and one part in five hundred having a very perceptible influence on the development of bacilli and paramœcia.

Dose, two to eight minims (0.12–0.5 mil).

TEREBINTHINA CANADENSIS. Br.

CANADA TURPENTINE

(tĕr-ę-bĭn'thĭ-nạ căn-ạ-dĕn'sĭs)

"Canada Turpentine is the oleo-resin obtained from Abies balsamea, *Mill.*" *Br.*

Canada Balsam, Balsam of Fir; Balsamum Canadense; Baume du Canada, *Fr. Cod.;* Térébenthine du Canada, *Fr.;* Canadischer Terpentin, *G.*

The term *turpentine* is usually applied to certain vegetable juices, liquid or concrete, which consist of resin combined with a peculiar volatile oil, called *oil of turpentine.* They are generally procured from different species of pine, fir, or larch, though other trees afford products which are known by the same general title, as, for instance, *Pistacia Terebinthinus* L., which yields the Chian turpentine. Some French writers extend the name of turpentine to other juices consisting of resin and essential oil, without benzoic or cinnamic acid, as copaiba, balm of Gilead, etc. We shall describe particularly, in this place, the turpentines which are either now official or have recently ceased to be so. A brief botanical view of the plants from which they are respectively derived will be in accordance with the plan of this work. It is proper to observe first that the family Coniferæ includes about three hundred and fifty species. These may be divided into two sub-orders, as Engler and Prantl suggest—viz., *Pinoideæ* and *Taxoideæ.* Lindley had previously recommended a similar sub-division, but considered each subgroup as deserving of family rank, and gave them the names Pinaceæ and Taxaceæ, which is commonly followed by the authors of Manuals of Botany. The *Pinoideæ* may be further subdivided into the (A) *Abietineæ,* including Araucaria, Pinus, Cedrus, Larix, Picea, Tsuga, Abies, Sequoia, Taxodium, etc.; and (B) *Cupressineæ,* which include Thuja, Juniperus, etc. The *Taxoideæ* include Ginkgo, Taxus, etc.

The genus Pinus is represented by about seventy species, which are widely distributed throughout the northern hemisphere of both continents. The principal centers of distribution of the species of this genus are in the Western United States (twenty-five species), Eastern United States (thirteen species), and the highlands of Mexico. It is one of the most important genera from an economic standpoint. The following species yield valuable timber: *P. palustris, P. Strobus, P. echinata, P. Lambertiana, P. ponderosa, P. monticola, P. heterophylla, P. sylvestris, P. Laricio, P. nepalensis, P. Thunbergii,* and *P. densiflora.* Turpentine is obtained chiefly from the Eastern American *P. palustris* and *P. heterophylla;* it is also obtained from *P. Pinaster* and *P. halepensis* of the Mediterranean basin, and from the Himalayan *P. Roxburghii.* The edible seeds (*Pine Nuts*) of several species yield important articles of human food, the best being produced by the nut pines of Western North America, by *P. pinea* of the Mediterranean, *P. Cembra* of Europe and Asia, and *P. gerardiana* of Northwestern India. *Pine wool,* a coarse fiber manufactured from the leaves of *P. Laricio, P. sylvestris,* and other European species, is used to stuff mattresses and cushions, and woven with animal wool, is made into hospital and military blankets and into underclothing which are reputed to possess medicinal properties. In the Southern United States carpets are woven from the leaves of *P. palustris.* The bark of several species contains sufficient tannin to make them valuable for tanning leather.

1.—*Pinus palustris* Mill. (*P. australis* Michx. *f.*).—The names by which the tree is known in the Southern States are *long-leaved pine, yellow pine, Southern pine, hard pine, Virginia pine,* and *pitch pine;* but the first is the most appropriate. The leaves occur three in a group, being from ten to fifteen inches long, subtended at the base by a conspicuous scaly sheath from one to one and a half inches long. The leaves are crowded at the ends of the branches. The cones are terminal, conical, and armed with a short recurved spine.

This pine is a very large indigenous tree, growing in dry, sandy soils, from the southern part of Virginia to the Gulf of Mexico. Its mean elevation is sixty or seventy feet, and the diameter of its trunk about fifteen or eighteen inches for two-thirds of its height. The leaves are about a foot in length, of a brilliant green color, and united in bunches at the ends of the branches. This tree furnishes by far the greater proportion of the turpentine, tar, etc., consumed in or exported from the United States. (See *Pix Liquida.*)

2.—*Pinus Tæda* L.—This is the *loblolly* or *old field pine* of the Southern States. "Leaves in threes, elongated, with elongated sheaths; strobiles oblong-conical, deflexed, shorter than the leaf; spines inflexed."

It is abundant in Virginia, where it occupies the lands exhausted by cultivation. It exceeds eighty feet in height, has a trunk two or three feet in diameter, and expands into a wide spreading top. The leaves are about six inches long, and of a light green color. It yields turpentine in abundance, but the quantity is less

than that which flows from the preceding species.

3.—*Pinus sylvestris* L. *Scotch Pine, Norway Pine, Scotch Fir.*—Leaves in pairs, rigid; strobiles ovate-conical, of the length of the leaves; scales linear-oblong, the ends much thickened, their exposed parts (apophysis) oblique, rhomboidal, with a transverse ridge and central tubercle.

This tree, when of full size, is eighty feet high, with a trunk four or five feet in diameter. It inhabits Scotland and the northern and mountainous parts of Europe. It yields a considerable proportion of the common European turpentine.

4.—*Pinus Pumilio* Haenke (*P. montana* Mill.).—This pine is known in gardens under several names which are given to the forms occurring in the different mountain ranges over which it is spread. Beissner, in his *Handbuch der Nadelholzkunde,* considers *P. Pumilio* Haenke, a synonym of *P. montana* Mill., whereas in the *Index Kewensis* the latter is brought under the former. Most authors agree with De Candolle and Beissner in bringing *P. Pumilio* Haenke, under *P. montana* Mill. The latter is a small tree, with decumbent or knee-like more or less erect branches, which are covered with a dark colored persistent bark. The leaves occur two in a sheath, each of which is from one to two inches long, straight, or scythe-shaped, with obtuse apex; both sides are dull green and slightly glaucous. The cones are ovoid, about one and a half inches long, with a pyramidal protuberance on each scale on the outer or exposed side. It is found in the sub-alpine regions of Central Europe at elevations between 4000 and 8000 feet; also on the Carpathian Mountains at from 4000 to 5500 feet. From its branches by spontaneous exudation or by cutting off their ends, *Hungarian balsam* is obtained. A volatile oil is obtained from its leaves (see *Oleum Pini Pumilionis*).

Pinus Pinaster Solander (*P. maritima* Poir.), which is found in the southern and maritime parts of Europe, yields much of the turpentine, pitch, and tar consumed in France, and is admitted among the official plants in the French Codex. *Pinus Lambertiana* of California, produces by exudation a saccharine matter which has been found to contain a peculiar sweet principle called *pinite.* (*C. R. A. S.,* Sept., 1855.) *Pinus Sabiniana* Dougl., known as *nut-pine* or *digger-pine* (because the nut is largely consumed by the Digger Indians), yields, on being notched, a turpentine whose volatile oil is extensively used in California under the name of *abietene.* The *Pinus rigida,* or *pitch pine* of this country, and probably others besides those mentioned, are sometimes employed in the preparation of tar. *Pinus Teocoty* Cham. et Schlecht., yields a turpentine known as *Mexican* or *Brea turpentine,* which is used in Mexico.

Abies.—The genus Abies is represented by about twenty-three species, which are distributed in the New World from Labrador and the valley of the Athabasca River to the mountains of North Carolina and from the mountains of Alaska to the highlands of Guatemala, and in the Old World from Siberia and the mountains of Central Europe to Southern Japan, the Himalayas, Asia Minor, and the mountains of Northern Africa. The species of this genus yield soft, perishable woods and balsamic exudations, which are employed in medicine and the arts.

Abies balsamea (L.) Mill., (*A. balsamifera* Michaux).—"Leaves solitary, flat, emarginate or entire, glaucous beneath, somewhat pectinate, sub-erect above, recurved spreading; cones cylindrical, erect; bracts abbreviate, obovate, conspicuously mucronate, sub-serrulate."

This is the *American silver fir,* or *balm of Gilead tree,* inhabiting Canada, Nova Scotia, Maine, and the mountainous regions farther south. It is an elegant tree, seldom rising more than forty feet, with a tapering trunk, and numerous branches, which diminish in length in proportion to their height and form an almost perfect cone. The leaves are six or eight lines long, inserted in rows on the sides and tops of the branches, narrow, flat, rigid, bright green on their upper surface, and of a silvery whiteness beneath. The cones are large, erect, nearly cylindrical, of a purplish color, and covered with a resinous exudation, which gives them a glossy, rich, and beautiful appearance. It is from this tree that the *Canada balsam* is obtained.

Several other species of Abies are important. The *A. Picea* Lindl. (*Abies pectinata* of De Candolle, *Pinus picea* of Linnæus), or *European silver fir,* growing in the mountainous regions of Switzerland, Germany, and Siberia, yields the *Strassburg turpentine* (*Térébenthine d'Alsace* or *des Vosges*), which is much used in some parts of Europe. By the distillation of its cones with water it also affords a variety of oil of turpentine called in France *essence de templine.* By boiling the young branches of the allied *Picea Mariana* (Mill.), B. S. P. (*Pinus nigra* Link.), or *black* or *bog spruce* of this country, and evaporating the decoction, the *essence of spruce* is prepared. It is a thick, molasses-like liquid, with a bitterish, acidulous, astringent taste, and is used for making *spruce beer.* (See *U. S. D.,* 19th edition, page 1244.)

Abies Fraseri, Lindley.—This species, commonly called *double fir,* occurs at high elevations in the mountains of Tennessee and North Carolina. The tree is noted for its hardiness, and is used for ornamental purposes. It is also said to have been used to furnish a balsam of fir similar to that obtained from *A. balsamea,* but the data concerning this are obscure.

Russian White Pitch, "belji var," "Sos nowaja Smold," which probably derived from the Siberian Fir, *Abies Pichta* Forb. (*Picea obovata* Ledeb.), contains, according to A. Tschirch, two free resin acids, the amorphous, *beljiabiennic acid,* $C_{13}H_{20}O_2$, and the crystalline, *belpiabietinic acid* besides *belpiresene,* $C_{13}H_{36}O$ and an essential oil. (*A. Pharm.,* Nov., 1902.)

Larix.—The genus Larix has eight recognized species, which are now widely distributed over

the sub-arctic and mountainous regions of the northern hemisphere, ranging from the Arctic Circle to the mountains of Pennsylvania in the New World and to latitude 30° in the Old World. The species produce hard, durable, valuable timber; turpentine, which is sometimes used in medicine; tar; bark rich in tannin; and a peculiar manna-like substance.

Larix decidua Mill. (*Larix europæa* De Cand.).—"Leaves fascicled, deciduous; cones ovate-oblong; margins of the scales reflexed, lacerated; bracts panduriform." The *European larch* is a large tree inhabiting the mountains of Siberia, Switzerland, Germany, and the east of France. It yields the *Venice turpentine* of commerce, and a peculiar sweetish substance called in France *Briançon manna,* which exudes spontaneously and concretes upon its bark. When the larch forests of Russia take fire, a juice exudes from the trunk during their combustion, which concretes and is called *Orenburg gum.* It is wholly soluble in water.

Coniferin is a term which has been given to a principle discovered by Hartig in the cambium of several of the Coniferæ. The species in which it has been found are *Pinus Strobus* and *P. Cembra, Picea Abies* and *A. pectinata,* and *Larix Europæa,* and it probably exists in many others. It is obtained by removing the outer bark, scraping the cambium from the surface of the wood, subjecting this to pressure, boiling the viscid juice to coagulate the albuminous substances, filtering, and evaporating the filtered liquid to one-fifth of its volume. The coniferin is deposited in crystals. The mother-water is very sweet, and contains a saccharine substance closely allied to cane sugar. The crystals are purified by dissolving them in water, decolorizing by animal charcoal, and finally crystallizing from weak alcohol. Coniferin was chemically examined by M. W. Kubel, and later by Tiemann and Haarmann, who proved that it is a glucoside and as crystallized from the juice has the composition $C_{16}H_{22}O_8 + 2H_2O$. When treated with dilute acids or ferments it is decomposed as follows: $C_{16}H_{22}O_8 + H_2O = C_6H_{12}O_6 + C_{10}H_{12}O_3$. When this latter compound is oxidized (or coniferin itself) by potassium dichromate and sulphuric acid, *vanillin* is obtained, $C_6H_3(OH)\begin{cases}OCH_3\\CHO\end{cases}$. Vanillin has been thus made commercially, but is now made preferably from the eugenol of oil of cloves or from benzoin.

In Japan, the exudation from the *Pinus densiflora* Sieb. et Zucc., and that from the *Pinus Thunbergii* Parl. are used under the respective names of *akamatsu* and *kuromatsu.* They are said to contain about 18 per cent. of oil and 81 per cent. of resin. The distilled oil is bright and colorless, having an odor somewhat different from that of the European oil of turpentine. It boils at from 155° to 156° C. (311°–312.8° F.), and has a specific gravity of a little under 0.87. Its index of polarization is from 55° to 61° (dextrogyrate). The resin cannot be distinguished from the European. A turpentine closely resembling the French oil is produced in Burmah from the *Pinus Khasya* Royle, and *Pinus Merkusii* Jungh. et De Vries. (See *P. J.,* lvi, 1896, 370.)

Pistacia.—See *Mastiche.*

Pistacia Terebinthus L. is a small tree of the family Anacardiaceæ, with numerous spreading branches, bearing alternate, pinnate leaves, which consist of three or four pairs of ovate-lanceolate, entire, acute, smooth, and shining leaflets, with an odd one at the end. The male and female flowers are dicœcious, small, and in branching racemes. It is a native of Barbary and Greece, and flourishes in the islands of Cyprus and Chio, the latter of which has given its name to the *Chian turpentine* obtained from the tree. A gall produced upon this plant by the puncture of an insect has been used in Eastern Europe in pectoral affections.

We shall treat of the several varieties of turpentine under distinct heads.

1. White Turpentine.

Terebinthina, *N. F. IV;* **Thus Americanum,** *Br.;* **Common Frankincense; Térébenthine de Boston,** *Fr.;* **Terebinthina communis; Térébenthine de Bordeaux ou Térébenthine commune,** *Fr. Cod.;* **Terebinthina,** *P.G.;* **Terpentin, Gemeiner Terpentin,** *G.;* **Trementina comune,** *It.;* **Trementina de pina,** *Sp.*

"A concrete oleoresin obtained from *Pinus palustris* Miller, and from other species of *Pinus* (Fam. *Pinaceæ*)." *N. F. IV.*

Turpentine, or as it is more frequently called, white turpentine, was deleted from the U. S. VIII and the Br. Pharm., 1914. It was introduced in the N. F. IV as an ingredient in *compound rosin cerate,* or Deshler's salve, which was official in the U. S. VIII.

This variety of turpentine is derived chiefly from the *Pinus Palustris* and the *P. Tæda.* It occurs in the sap wood and is obtained by making incisions through the bark and wood and collecting the exudation in cavities or boxes made lower down on the trunk, from which it is dipped into barrels or other receptacles. It gradually thickens and ultimately acquires a soft solid consistence. White turpentine as found in commerce "occurs in yellowish, opaque masses, lighter internally, sticky and more or less glossy, brittle in the cold. Odor and taste characteristic. It is freely soluble in alcohol, ether, chloroform, or glacial acetic acid. Its alcoholic solution is acid to litmus." *N. F.* The following test is of value in testing the purity of turpentine:

"Dissolve about 1 Gm. of Turpentine, accurately weighed, in 25 mils of alcohol and collect the insoluble residue, if any, on a filter which has been dried at 100° C. (212° F.) and weighed. Then wash the residue and filter with about 25 mils of alcohol and dry at 100° C. (212° F.). The weight of the residue does not exceed 2 per cent. (*mechanical impurities*)." *N. F.*

In former times, large quantities were collected in New England, but the turpentine trees

of that section have long been entirely exhausted, and our commerce has been until recently almost exclusively supplied from North Carolina and the southeastern parts of Virginia. Latterly attention was turned to the collection of this valuable product of Georgia and Florida, and now an abundant supply is derived from the vast pine forests which occupy the southern portion of our country bordering on the Gulf of Mexico.

During the winter, deep notches or excavations of the capacity of about three pints are made in the trunk of the tree three or four inches from the ground, and for about three feet above these so-called "boxes" the tree is deprived of its bark and some of the wood scraped off. Into these the turpentine or "crude" begins to flow about the middle of March, and continues to flow throughout the warm season, slowly at first, rapidly in the middle of summer, and more slowly again in the autumn, the tree being scraped every eight or ten days to prevent clogging. The liquid is removed from the "boxes" as they fill, and transferred into casks, where, if left, it gradually thickens, and ultimately acquires a soft solid consistence, but most of it is separated at once by distillation into the rosin and the volatile oil of turpentine.

When a tree is boxed, it is weakened and falls easily before the wind. To obviate the former destructive method, Herty has devised "the cup and gutter system." (See *Bulletin No. 40, Bureau of Forestry.*) By this method a small incision is made through the bark and a strip of galvanized iron is inserted. The turpentine flows along this strip and is caught in an earthenware receptacle much resembling a medium-sized flower pot inserted upon the tree. While this method increases the yield of turpentine, it has not been generally adopted. Large quantities of turpentine are prepared directly from the wood of the trees which have been destroyed by the older or box method of collecting the oleoresin. "Wood" turpentine is not recognized as equivalent to "turpentine" by the Pure Food and Drugs Act, and must be labelled as "Wood Turpentine." The latter has a peculiar odor and is not used in medicine but is widely used in the arts.

White turpentine, as found in commerce, is yellowish white, of a peculiar somewhat aromatic odor, and a warm, pungent, bitterish taste. It is somewhat translucent, and of a consistence varying with the temperature. In the middle of summer it is almost semi-fluid and very adhesive; though brittle in the winter it is often so firm and hard as to be incapable of being made into pills without heat. "In yellowish, opaque masses, brittle in the cold; lighter internally, sticky and more or less glossy; odor and taste terebinthinate. The alcoholic solution of Turpentine has an acid reaction." *U. S. VIII.*

Exposed to the air it ultimately becomes perfectly hard and dry. In the recent state it affords about 17 per cent. of volatile oil. (See *Oleum Terebinthinæ.*) It is likely to contain small pieces of bark, wood, or other impurity. Tschirch and Koritschoner found the following constituents in white turpentine: *palabiennic acid*, $C_{13}H_{20}O_2$, 5 per cent.; *palabietinic acid*, $C_{20}H_{30}O_2$, which is crystalline, 6 to 7 per cent.; *α-* and *β-palabietinolic acids*, together 53 to 57 per cent. Both the latter are amorphous and are separated by the differing solubility of their lead salts. All the acids are soluble in sodium hydroxide solution. The portion of the resin insoluble in NaOH solution consists of essential oil, 20 to 22 per cent., and *paloresene*, 10 per cent., with traces of a bitter principle. The essential oil has a characteristic turpentine-like odor. The sp. gr. is 0.864. (See *Oleum Terebinthinæ.*) It is dextrogyrate, while the resin itself and palabietinic acid are lævogyrate. The authors have furthermore examined *Russian white pitch*, a product known as "belji var," and probably derived from the Siberian fir. (*A. Pharm.*, Nov., 1902.)

2. Common European Turpentine.

Térébenthine de Bordeaux, *Fr. Cod.*; Térébenthine commune, *Fr.*; Gemeiner Terpentin, *G.*; Trementina comune, *It.*; Trementina comun, *Sp.*

This is the *Terebinthina vulgaris* of the old London Pharmacopœia. It is furnished by several species of pine, but chiefly by *P. sylvestris* L. and *P. Pinaster* Soland. For details as to the varieties of European turpentine and the methods of procuring them, consult *A. J. P.*, 1878, 69, 479; *Proc. A. Ph. A.*, xxiv, 203; *P. J.*, viii, 283; x, 447. From the latter tree it is obtained largely in the maritime districts of the southwest of France, especially in the department of the Landes, and is exported from Bordeaux. Hence it is called in commerce *Bordeaux turpentine.* It is procured by making incisions into the trunk, or removing portions of the bark, and receiving the juice which flows out, in small troughs, or in holes dug at the foot of the tree. It is purified by heating, and filtering it through straw, or by exposing it to the sun in a barrel, through holes in the bottom of which the melted turpentine escapes. Thus prepared, it is whitish, turbid, thickish, and separates, upon standing, into two parts, one liquid and transparent, the other of a consistence and appearance like that of thickened honey. As found in European commerce, it often consists wholly of this latter portion. It speedily hardens on exposure in thin layers to the air. The most liquid specimens are completely solidified by the addition of one part of magnesia to thirty-two parts of the turpentine. (*J. P. C.*, xxv, 499.) Tschirch and Bruening (*A. Pharm.*, 1900, ccxxxvii, 630) find this oleoresin to have the following composition: 6 to 7 per cent. of *pimarinic acid*, $C_{14}H_{22}O_2$; 8 to 10 per cent. of *pimaric acid*, $C_{20}H_{30}O_2$; 48 to 50 per cent. of *alpha- and beta-pimarobic acids*, $C_{18}H_{26}O_2$; 5 to 6 per cent. of *bordoresin*, together with traces of *succinic acid.* The acid resins are soluble in sodium hydroxide solution, the pimarinic acid being separable from the other two by its property of forming with ammonium carbonate a water-soluble double salt. The volatile oil consists of two fractions, the

larger fraction, amounting to about 85 per cent. of the whole, distilling easily. It is scarcely ever given internally, but furnishes large quantities of oil of turpentine and rosin. We do not import it into this country. The substance which the French call *galipot*, or *barras*, is that portion of the turpentine which concretes upon the trunk of the tree when wounded, and is removed during the winter. (Thénard.) This, when purified by melting with water and straining, takes the name of *yellow* or *white pitch*, or *Burgundy pitch*. When turpentine, whether the European or the American, has been deprived of its oil by distillation, the resin which remains is called *rosin*, and sometimes *colophony*, from the Ionian city of Colophon, where it was formerly prepared. It is the official rosin (*resina*), and is sometimes called yellow rosin (*resina flava*). White rosin (*resina alba*) is prepared by incorporating this, while in fusion, with a certain proportion of water. (See *Resina*.) Tar (*pix liquida*) is the product extracted from the wood by slow combustion and chemically altered by heat. Common pitch (*pix nigra*, or *resina nigra*) is the solid residue left after the evaporation by boiling of the liquid parts of tar.

3. Canada Turpentine.

Baume du Canada, *Fr. Cod.*; Canadischer Balsam, Canadischer Terpentin, *G.*; Trementina del Canada, *It.*

Terebinthina Canadensis, U. S., Br., is collected in Canada and the State of Maine from the *Abies balsamea*, by breaking the vesicles which naturally form upon the trunk and branches, and receiving their liquid contents in a bottle. "Pale yellow or greenish-yellow, transparent, viscous. Agreeable terebinthinate odor; taste feebly bitter and acrid. Dries very slowly to a transparent varnish when exposed to the air. Solidifies when mixed with about one-sixth of its weight of *heavy magnesia* moistened with a little *water*." *Br.*

"It is completely soluble in ether, chloroform, or benzene." *U. S. VIII.*

For a paper on its miscibility in alcohol, by J. E. Morrison, see *Proc. A. Ph. A.*, 1894, 309. By time and exposure it becomes thicker and more yellow, and finally solid. It is usually brought into market in bottles under the name of *Canada balsam* or *balsam of fir*. Under the microscope the hard balsam is found to be entirely free from any granular or crystalline structure. In Europe it is sometimes called *balm of Gilead*, from its supposed resemblance to that celebrated medicine. The term *balsam*, as at present understood, is improperly applied to it, as it contains no benzoic or cinnamic acid, and is in fact a true turpentine, consisting chiefly of resin and volatile oil. Bonastre obtained from 100 parts of Canada turpentine 18.6 parts of volatile oil, 40.0 of resin easily dissolved by alcohol, 33.4 of sub-resin of difficult solubility in that fluid, 4.0 of caoutchouc similar to sub-resin, and 4.9 of bitter extractive and salts, besides traces of acetic acid. Flückiger found in 100 parts 24 parts of an essential oil, $C_{10}H_{16}$, with a very small proportion of an oxygenated oil, 60 parts of a resin soluble in boiling alcohol, and 16 parts of a resin soluble only in ether. (*Pharmacographia*, 2d ed., 614.) Emmerich obtained by fractional distillation of the oil, *bornyl* or *terpinyl acetate*, *pinene*, and a fragrant liquid resembling oil of lemon. (*A. J. P.*, 1895, 135. See also a paper by Hunkel, *A. J. P.*, 1895, 9.) The chief distinction between it and *Strassburg turpentine*, which is sometimes sold for it in commerce, is in the odor.

According to Tschirch, Wiegel and Bruening, Canada turpentine contains about 63 per cent. of acid resins, from 23 to 24 per cent. of volatile oil, and from 11 to 12 per cent. of indifferent resin. The acid portion consists of four acids, of which one—*canadinic acid*, $C_{19}H_{34}O_2$—obtained by treating the oleoresin with ammonium carbonate, with which it combines; a small amount of crystalline *canadolic acid*, $C_{19}H_{28}O_2$, and two amorphous isomeric acids—α- and β-*canadinolic acids*, $C_{19}H_{30}O_2$—which constitute the main portion of the acid resins. The indifferent resin has the formula $C_{21}H_{40}O$. The greater part of the volatile oil boils between 160° and 167° C. (320° and 332.6° F.). (*A. Pharm.*, 1900, Aug. and Sept., 401, 411 and 487.)

Abies Menziesii Lind.—From this a *Balsam of Fir* of the Pacific Slope, has been obtained; it is a turpentine similar to Canada balsam and is extensively sold under the names *Oregon Balsam* or Oregon Balsam of Fir. Roberts and Becker (*Proc. P. P. A.*, 1913, p. 328) state that Canada balsam is thicker than Oregon balsam, dries to a solid, transparent film, while Oregon balsam remains sticky, has a lower acid value than Oregon balsam, and solidifies when mixed with 20 per cent. of magnesium oxide, which Oregon balsam does not.

4. Venice Turpentine.

Terebinthina Laricis, *N. F. IV*; Larch Turpentine, Térébenthine de Venise, *Fr. Cod.*; Térébenthine de Mélèze, *Fr.*; Venetianischer Terpentin, *G.*; Trementina di Venezia, *It.*; Trementina de alerce, Trementina de Venecia, *Sp.*

"A viscid oleoresin obtained from *Larix europœa* De Candolle (Fam. *Pinaceæ*)." *N. F.*

"*Venice turpentine* is a nearly transparent, yellowish or yellowish-green, thick liquid, heavier than water, and having a distinctive odor and a bitter characteristic taste. Completely soluble in alcohol, glacial acetic acid, acetone, or chloroform. Almost entirely soluble in petroleum benzin with the separation of a light flocculent deposit. One part of Venice turpentine dissolves completely and forms a clear solution in 3 parts of 80 per cent. alcohol. It may possess a slight, greenish fluorescence when viewed by reflected light but exhibits no violet or purple fluorescence (*rosin oil*). Dissolve 5 Gm. of Venice turpentine in 25 mils of alcohol, add a few drops of phenolphthalein T.S. and render the solution slightly alkaline by the addition of a 10 per cent. solution of

potassium hydroxide. The resulting solution is clear and transparent and no separation of oily drops occurs (*rosin oil*). Its acid number is not more than 80 when determined as directed in the U. S. Pharmacopœia IX." *N. F.*

This turpentine was named from the circumstance that it was formerly an extensive article of Venetian commerce. It is procured in Switzerland, and in the French province of Dauphiny, from the *Larix decidua* (*L. europæa*), which grows abundantly upon the Alps and the Jura Mountains. The peasants bore holes into the trunk about two feet from the ground, and conduct the juice by means of wooden gutters into small tubs placed at a convenient distance. It is afterwards purified by filtration through a leather sieve. Genuine Venice turpentine is a viscid liquid, the consistence of honey, flowing with difficulty, cloudy or imperfectly transparent, yellowish or slightly greenish, of a strong not disagreeable odor, and a warm bitterish, and acrid taste. It does not readily concrete on exposure, is not solidified by one-sixteenth of magnesia, and is entirely soluble in alcohol. (Guibourt, *J. P. C.*, xxv, 500.) H. Beckurts and W. Brueche found the specific gravity at 15° C. (59° F.) from 1.060 to 1.190; acid number from 76 to 101 (Kremel found from 68 to 70.3); ester number from nothing to 6; saponification number from 81 to 101, and the iodine number from 137 to 149. (*A. Pharm.*, 1892, ccxxx, 83.) It yields on an average 15 per cent. of essential oil, of the composition $C_{10}H_{16}$, which has been found to be nearly pure *pinene*. The residual resin is soluble in two parts of warm alcohol of 57 per cent., and more copiously in absolute alcohol.

Tschirch and Wiegel investigated the constituents of Larch Turpentine. According to these investigators, this oleoresin contains from 60 to 64 per cent. of acid resins soluble in soda, from 20 to 22 per cent. of volatile oil, and from 14 to 15 per cent. of indifferent resin. The acid resins consist mainly of two isomeric amorphous bodies, *a*- and *b*-larinolic acid, $C_{18}H_{28}O_2$, and a smaller quantity of the crystalline *laricinolic acid*, $C_{20}H_{30}O_2$. The greater portion of the volatile oil boils between 155° and 170° C. (311° and 338° F.); a smaller quantity of higher boiling sesquiterpene commencing to boil at 190° C. (374° F.). The recently distilled oil has the sp. gr. 0.872, and possesses a characteristic turpentine odor. It is soluble in all proportions in alcohol and other solvents. (*A. Pharm.*, 1900, Aug. and Sept., 401, and 411, 487.) What is sold under the name of Venice turpentine, in commerce, is usually quite brown, and is a factitious substance, prepared by dissolving rosin in oil of turpentine. According to G. Fabris the nature of these spurious Venice turpentines can readily be detected by dissolving 5 Gm. of the sample in 20 mils of 95 per cent. alcohol, adding a few drops of phenolphthalein and sufficient of a 10 per cent. solution of potassium hydroxide to render it alkaline. With genuine Venetian turpentine a clear solution is obtained, while the spurious drug yields a turbid solution, from which, on standing, drops of oily resin separate.

5. Chian Turpentine.

Térébenthine de Chio, *Fr. Cod.*; Cyprischer Terpentin, *G.*; Trementina Cipria, *It.*

This variety of turpentine is collected chiefly in the island of Chio, or Scio, from the *Pistacia Terebinthus*, and it is said that the whole annual product of the island is only about two hundred and twenty-four pounds. During the summer the juice flowing spontaneously, or from incisions in the bark, falls upon smooth stones, or bundles of twigs, placed at the foot of the tree, from which it is procured by boiling and straining. After straining it is again boiled with a little water until all the water is evaporated, when it is finally poured into a vessel of cold water and kneaded. At first it is of a dirty yellow color, but after kneading it becomes quite white. (*P. J.*, xvi, 385.) The annual product of each tree is very small, and the turpentine, therefore, commands a high price even in the place where it is procured. Very little of it reaches this country. It is said to be frequently adulterated with the other turpentines. It is a thick, tenacious liquid, of a greenish-yellow color, or it occurs as a viscid opaque mass. The odor is peculiar, penetrating, and more agreeable than that of the other substances of the same class. The taste is mild, without bitterness or acrimony. Flückiger found nearly 14½ per cent. of essential oil, which contained a small quantity of an oxygenated oil. It leaves a glutinous residue when treated with strong alcohol. (Guibourt.) Its alcoholic solution does not redden litmus paper. (Martindale.) On exposure, liquid Chian turpentine speedily thickens, and ultimately concretes into a translucent solid, yellowish or yellowish-brown when in small pieces, greenish-brown in mass.

The odor of Chian turpentine is variously described. As the only tests we now have of the purity of the drug are its physical characteristics, and of these the odor is the most important, we give the following description by Wm. Martindale. (*P. J.*, April, 1880.) Chian turpentine "has when fresh a distinctive odor, slightly like the pinaceous turpentines, but much more agreeable and aromatic, according to some resembling citron and jasmine; but there is always a background smell like that of mastic, which becomes more developed and distinct with age, when it has lost the more volatile portion, the essential oil. According to Pereira, the turpentine-like odor is combined with the odor of fennel, and Guibourt says, when kept in a covered glass vessel the odor is strong and agreeable, analogous to that of fennel or the resin of elemi. It probably loses this rapidly. A specimen, bearing Guibourt's name, in the Ph. Society's Museum, has now no trace of it, but the mastic odor is very persistent. If the fennel odor be very evident in it I should fear the sample was not genuine, as in a statement made in the *Lancet* the writer says what is sold as Chian turpentine 'is either greatly adulterated or a wholly factitious article, manufactured from black resin, Canada balsam, and the essen-

tial oils of fennel and juniper. The taste of genuine Chian turpentine resembles that of mastic; it is agreeable and free from the characteristic bitterness and acridity of the pinaceous turpentines."

Besides the turpentines mentioned, various others are noticed in books on Materia Medica, though not found in commerce in this country. There are the *Strassburg turpentine,* much used in France, and obtained from the *Abies Picea* (*Abies pectinata* of De Candolle), or European silver fir, which grows on the mountains of Switzerland and Germany and bears a close resemblance, as well in its appearance as in its product, to *Abies balsamea* of Canada; the *Russian turpentine,* from *Pinus sylvestris;* the *Damara turpentine,* which speedily concretes into a very hard rosin, and is derived from *Pinus Damaris* Lam., the *Agathis damara* of Richard, growing in the East India islands; the *cowrie* or *cowdie* resin, procured by incision from another species of Agathis, *A. australis,* in New Zealand; and the *Dombeya turpentine,* a glutinous, milky-looking fluid, of a strong odor and taste, derived from the *Araucaria Dombeyi* of Richard, also called *Dombeya excelsa,* which inhabits Chili.

Finnan Turpentine, the oleoresin of *Pinus sylvestris,* is found by Tschirch and Niederstadt to consist of: 1.5 per cent. *silveolic acid,* $C_{14}H_{20}O_2$; 58 to 60 per cent. of *α-silvinolic acid,* $C_{15}H_{26}O_2$, and *β-silvinolic acid* ($C_{14}H_{24}O_2$); 20 to 21 per cent. of *resene;* 15 per cent. of volatile oil; and traces of bitter principle and succinic acid. Silveolic acid is crystalline; *α-* and *β-*silvinolic acids are both amorphous. The volatile oil has the sp. gr. 0.840 at 15° C. (59° F.), is soluble in all proportions in alcohol, ether, and chloroform, and is neutral when recently distilled, but becomes acid when exposed to the air. (*A. Pharm.,* 1901, ccxxxix, 167.)

Jura Turpentine.—A. Tschirch and E. Bruening have determined the following constituents of the oleoresin of *Picea vulgaris:* From 2 to 3 per cent. of *picea-pimarinic acid,* $C_{18}H_{30}O_2$; from 1.5 to 2 per cent. of *picea-pimaric acid,* $C_{20}H_{30}O_2$; from 48 to 50 per cent. of *α-* and *β-picea-pimarolic acid,* $C_{25}H_{44}O_2$; from 32 to 33 per cent. of volatile oil; from 10 to 12 per cent. of resene, $C_{21}H_{36}O$; and traces of succinic acid, coloring matter and bitter principle. (*A. Pharm.,* 238, Nov. 10, 1900, 616.)

Tschirch and Weigel (*A. Pharm.,* 1900, Aug. and Sept., 401, 411, 487) investigated Strassburg turpentine—the oleoresin of *Abies Picea;* it contains from 8 to 10 per cent. of an acid resin, *abieninic acid,* $C_{13}H_{20}O_2$; from 1.5 to 2 per cent. of a crystalline acid resin, *abietolic acid,* $C_{20}H_{28}O_2$; from 46 to 50 per cent. of two amorphous isomeric acid resins, *α-* and *β-abietinolic acid,* $C_{16}H_{24}O_2$; from 12 to 16 per cent. of a neutral resin, *abieto-resin;* and from 28 to 30 per cent. of volatile oil, together with traces of succinic acid, bitter principle, coloring matter, moisture and impurities. The oil when recently distilled has the sp. gr. 0.860, boiling between 148° and 165° C. (298.4° and 329° F.); the major fraction distils between 162° and 163° C. (323.6° and 325.4° F.). It has a greenish fluorescence and a lemon-like odor. When the oleoresin is distilled with potassium hydroxide a pleasant rose or orange-flower odor is developed, possibly due to the liberation of a fragrant alcohol.

Properties.—The turpentines resemble one another in odor and taste, though distinguished by shades of difference. Liquid at first, they become thick and gradually solid by exposure, in consequence partly of the volatilization, partly of the oxidation of their essential oil. They are rendered more liquid or softened by heat, and at a high temperature take fire, burning with a white flame and much smoke. Water extracts only a minute proportion of their volatile oil. They are almost wholly soluble in alcohol and ether, and readily unite with the fixed oils. They yield by distillation a volatile oil, called *oil of turpentine,* the composition of which is essentially uniform, it being composed of several terpenes (pinene, dipentene, and sylvestrene) of the formula $C_{10}H_{16}$, the residue consisting exclusively of rosin. (See *Oleum Terebinthinæ* and *Resina.*) Both the cones and leaves of *Abies Picea* yield oils known respectively as *pine cone oil* and *pine needle oil.* According to *Schimmel's Report* for April, 1897, they both contain pinene, limonene, and bornyl acetate. The oil from *Pinus sylvestris,* known as *fir oil,* also contains bornyl acetate to the amount of 12 per cent., according to *Schimmel's Report* for October, 1897, 47. On the other hand, the oil from *Larix Europæa,* known as *larch needle oil,* contains 8.1 per cent. of bornyl acetate and 6.14 per cent. of free borneol. (*Ibid.,* 61.)

Schiff affirms that the odor of turpentine is due to the presence of a product of oxidation, probably a camphoric aldehyde, $C_{10}H_{16}O_3$, which, with the odor, may be removed by shaking the turpentine with sodium bisulphite. A non-odorless turpentine may also be obtained by washing with solution of sodium hydroxide and distilling in an atmosphere of carbon dioxide. From the experiments of Faure, of Bordeaux, it appears that some of the liquid turpentines, like copaiba, may be solidified by the addition of magnesia. (*Journ. de Chim. Méd.,* 1830, 94.) According to Thierry, the same result is obtained by the addition of one part of calcium hydroxide to thirty-two parts of common European turpentine. (*J. P. C.,* 3e sér., i, 315.) Crouzel (*P. J.,* 1892, 11) found tannin in the bark of *P. Pinaster,* associated with a peculiar reddish-yellow coloring matter, representing tannin in the process of formation.

Ed. Hirschsohn made experiments with the object of determining a reliable method for distinguishing artificial turpentine from the common, natural turpentine and larch turpentine, this becomes possible by the difference in the solvent effect of official ammonia water and alcohol, sp. gr. 0.863 at 15.6° C. (60° F.), upon them, under the conditions indicated in the following table:

Kind of Turpentine	Ammonia Solution (sp. gr. 0.960), 1 p. turpentine and 5 p. ammonia solution.	Alcohol (sp. gr. 0.863), 1 p. turpentine and 3 p. alcohol.
Venice turpentine	Is not disintegrated; produces a milky fluid in the water-bath.	Yields a nearly clear solution.
Common turpentine	Easily disintegrated, forming a milky mixture, then gelatinous; becomes clear in the water-bath.	Large quantities are deposited, but the mixture becomes clear in the water-bath.
Artificial turpentine	Is disintegrated, becomes clear in the water-bath for a moment, then turbid.	Turbid solution and precipitation; turbid in the water-bath with precipitation.

A mixture of common turpentine with larch (Venice) turpentine is recognized by the turbidity of, and precipitate from, the solution of 1 Gm. of the sample in 3 Gm. of alcohol sp. gr. 0.863. The same occurs if the common is replaced by artificial turpentine, but the latter is differentiated by ammonia, from the fact that in the presence of 20 to 30 per cent. of common turpentine the sample is easily disintegrated, and the solution becomes clear in the water bath, while in the presence of artificial turpentine the behavior is the same as with the pure Venice turpentine. (*Ph. Centralh.*, Nov. 26, 1903, 825 to 828.)

Uses.—The physiological activities of turpentines depend upon their volatile oils. They are so inconvenient of administration, and so variable in their activity that at present they are very rarely, if ever, used internally by regular practitioners of medicine. For an account of their physiological and therapeutic properties, see *Oleum Terebinthinæ*, p. 792. If given at all they should be administered in emulsion. Chian turpentine has been recommended as a specific in *cancer*, given in emulsion in doses of five grains (0.32 Gm.), increased *pro re nata*, and also applied locally. It is probably without value. Turpentine vapor baths have been found useful in the treatment of *chronic rheumatism;* they may be given by simply evaporating oil of turpentine in the ordinary cabinet or other vapor bath, or by driving the vapor through the fine branches and leaves of a terebinthinate plant. They probably differ in their action from the simple hot vapor bath by the stimulation of the skin due to the local action of the turpentine, and by the copious sweating which they produce. The bath should always be so arranged that the terebinthinate vapor is not inhaled by the patient.

Dose, twenty to thirty grains (1.3–2.0 Gm.).

TERPINI HYDRAS. U. S.

TERPIN HYDRATE Terpin. Hyd.

(tẹr-pī'nī hȳ'drăs)

"The hydrate [$C_{10}H_{18}(OH)_2 + H_2O$ = 190.18] of the dihydric alcohol terpin. Preserve it in well-closed containers, in a cool place." *U. S.*

Terpine, *Fr. Cod.;* Dihydrate de Térébenthène, Hydrate de Terpilène, *Fr.;* Terpinum hydratum, *P. G.;* Terpinhydrat, *G.;* Terpina, *Sp.*

In making terpin hydrate a mixture of four parts of rectified oil of turpentine, three parts of alcohol (sp. gr. 0.863), and one part of nitric acid is put in large, shallow porcelain dishes and allowed to stand for three or four days. The crystals which have formed are then collected and allowed to drain thoroughly; they are then pressed between sheets of absorbent paper, and crystallized from a cold solution in 95 per cent. of alcohol. The product is about 12 per cent. of the original turpentine oil. E. T. Hahn proposed the use of methyl alcohol (sp. gr. 0.801) in place of alcohol, in making terpin hydrate. (*A. J. P.*, 1897, 73.)

The anhydrous *terpin* $C_{10}H_{18}(OH)_2$, obtained from it by the loss of water has the characters of a glycol. Dipentene dihydrochloride is its hydrochloric acid ether. By the loss of water the terpin then becomes *terpineol*, $C_{10}H_{17}(OH)$, a liquid with an aromatic odor resembling lilac, and finally yields dipentene, terpinene, or terpinolene, according to the conditions of its treatment. Bouchardat and Voiry obtained terpineol in crystals which melt at 35° C. (95° F.) and remain in superfusion for long periods. (*Ann. Ch. Ph.*, 1893, 103.) For Wallach's researches on crystallized terpineol, see *P. J.*, 1893, 2.

L. Krentmann states that good results are obtained by replacing the alcohol in the process with hydrogen dioxide solution and subjecting the mixture poured into shallow dishes to light and air. The temperature should be carefully regulated so that the range will be between 15° and 20° C. (59° and 68° F.).

Terpin hydrate is officially described as in "colorless, lustrous, rhombic prisms, nearly odorless, and having a slightly aromatic and somewhat bitter taste. Efflorescent in dry air. One Gm. of Terpin Hydrate dissolves in about 200 mils of water, 13 mils of alcohol, 135 mils of chloroform and in 140 mils of ether at 25° C. (77° F.); also in about 34 mils of boiling water, 3 mils of boiling alcohol, and in about 1 mil of boiling glacial acetic acid. Heated slowly to about 100° C. (212° F.) it sublimes in fine needles. When quickly heated, it melts between 115° C. and 117° C. (239° and 242.6° F.), with the loss of water. It also loses its water of crystallization slowly over sulphuric acid. Add a few drops of sulphuric acid to a hot aqueous solution of Terpin Hydrate; the liquid becomes turbid and develops a strongly aromatic odor. Incinerate about 2 Gm. of Terpin Hydrate; not more than 0.05 per cent. of ash remains. Terpin Hydrate has no odor of

turpentine, and its saturated, hot, aqueous solution is not acid to litmus." *U. S.*

The pharmacy of terpin hydrate seems to be much misunderstood if one may judge by the liquid preparations on the market purporting to contain amounts of terpin hydrate impossible to be held in solution by the alcoholic strength of the preparation. It requires about 40 per cent. of alcohol in the finished preparation to hold in solution an amount of terpin hydrate corresponding to one grain to each fluidrachm.

Uses.—Terpin was first physiologically investigated by Lépine, in 1855, who found it to act both upon the mucous membranes and upon the nervous system in a manner similar to the oil of turpentine. It has since been used in *chronic bronchitis* and in the advanced stages of *acute bronchitis*, especially when the secretion is unusually free; also in *chronic cystitis* and *gonorrhea*.

Dose, two to five grains (0.13–0.32 Gm.), from four to six times a day, in pill or in emulsion.

Off. Prep.—Elixir Terpini Hydratis, *N. F.*; Elixir Terpini Hydratis et Diacetylmorphinæ, *N. F.*; Elixir Terpini Hydratis et Codeinæ, *N. F.*

TERRA SILICEA PURIFICATA. U. S.

PURIFIED SILICEOUS EARTH Ter. Sil. Purif. [Purified Kieselguhr, Purified Infusorial Earth]

(tĕr'rą sĭ-lĭ'cē-ą pū-rĭ-fī-cā'tą)

"A form of silica (SiO_2 = 60.30) consisting of the frustules and fragments of diatoms, purified by boiling with diluted hydrochloric acid, washing and calcining. It does not contain more than 10 per cent. of moisture. Preserve it in tightly-closed containers." *U. S.*

"Purified Siliceous Earth is a very bulky and very fine powder, white or of a pale light gray or pale buff color, without odor or taste. It readily absorbs moisture and will retain about four times its weight of water without the mixture becoming fluid. It is insoluble in water, acids or dilute alkaline solutions. Boil 10 Gm. of Purified Siliceous Earth with 50 mils of distilled water and filter the mixture; the filtrate is colorless and neutral to litmus. When ignited its color is not darkened (organic impurities) nor does it lose more than 10 per cent. of its weight (*moisture*). Add 1 Gm. of Purified Siliceous Earth to 25 mils of diluted hydrochloric acid; no effervescence occurs (*carbonate*) and, after boiling, and filtering, the filtrate is colorless, and separate portions, when tested, yield no precipitate with barium chloride T.S. (*sulphate*) and no blue color with potassium ferrocyanide T.S. (*iron*). Digest 1 Gm. of Purified Siliceous Earth, for fifteen minutes, with 20 mils of diluted hydrochloric acid and filter. Ten mils of the filtrate, when evaporated to dryness and ignited, does not leave a residue weighing more than 0.005 Gm." *U. S.*

Kieselguhr, infusorial earth or diatomaceous earth, as it is sometimes called, is found as a natural deposit of greater or lesser purity in many parts of the world. It should not be confounded with kaolin whose chemical composition and physical properties are quite distinct. It has wide-spread technical uses on account of its many valuable physical properties. On account of its high absorbent power and inertness, it is used to absorb nitroglycerin in the manufacture of dynamite. It is also used in transporting sulphuric acid without danger, as it forms a pulverulent compound consisting of seventy-five per cent. of sulphuric acid. It is used in fireproofing and insulating work on account of its incombustibility and non-conductivity. Its principal use in pharmacy is as a filtering medium for which it is very well suited in many ways (see *Talcum Purificatum*). It is also used in making dermatologic pastes.

THEOBROMINÆ SODIO-SALICYLAS. U. S. (Br.)

THEOBROMINE SODIO-SALICYLATE Theobrom. Sodio-Sal.

(thē-ō-brō-mĭ'næ sō-dĭ-ō-săl-ĭ-cȳ'lăs)

"Sodium theobromine [$C_7H_7O_2N_4Na$ = 202.10] and sodium salicylate [$NaC_7H_5O_3$ = 160.04], in approximately molecular proportions. It yields, when dried to constant weight in a desiccator over sulphuric acid, not less than 46.5 per cent. of theobromine [$C_7H_8O_2N_4$ = 180.10]. Preserve it in well-closed containers." *U. S.*

"Theobromine and Sodium Salicylate, $Na_2C_{14}H_{12}N_4O_5$, may be obtained by combining sodium hydroxide, theobromine, and sodium salicylate in molecular proportions. Should be preserved in stoppered, amber-colored bottles." *Br.*

Theobrominæ et Sodii Salicylas, Theobromine and Sodium Salicylate, *Br.*; Diuretin.

This compound, known also as *diuretin*, and also as *theonasal*, was the first of the soluble compounds of theobromine introduced into medicine.

Theobromine is a *dimethylxanthin* (dimethyloxypurin) isomeric with theophylline and differing in the location of the methyl groups which in theophylline are in the 1–3 position and in theobromine are in the 3–7 position. It is found in cacao beans in amounts ranging from 0.9 to 3.0 per cent., and in very much smaller amounts in kola nuts. It is also related to caffeine, which is a *tri-methyl xanthin*.

"Theobromine Sodio-Salicylate is a white, odorless powder, of a sweetish, saline, and somewhat alkaline taste. It gradually absorbs carbon dioxide from the air with the liberation of theobromine, becoming partially insoluble in water. One Gm. of Theobromine Sodio-Salicylate dissolves in 1 mil of water at 25° C. (77° F.); slightly soluble in alcohol. An aqueous solution of Theobromine Sodio-Salicylate (1 in 20) is colorless and clear or at most opalescent, and is strongly alkaline to litmus and phenolphthalein T.S. When ignited Theobromine Sodio-Salicylate yields a residue which colors a non-luminous flame intensely yellow and

effervesces with acids. An aqueous solution of Theobromine Sodio-Salicylate (1 in 100), slightly acidulated with acetic acid, becomes violet on the addition of ferric chloride T.S. Dissolve 1 Gm. of Theobromine Sodio-Salicylate in 10 mils of distilled water in a separator, add a few mils of sodium hydroxide T.S. and shake the mixture with 10 mils of chloroform. The residue obtained after the evaporation of the separated chloroform layer, when dried to constant weight at 80° C. (176° F.), does not exceed 0.005 Gm. (*caffeine*). About 0.1 Gm. of Theobromine Sodio-Salicylate dissolves in 2 mils of sulphuric acid without effervescing (*sodium carbonate*) and without producing more than a slight color (*organic impurities*)." *U. S.*

"A white amorphous powder. No odor; taste sweetish and alkaline. Soluble in 1 part of *water;* soluble in *alcohol* (90 per cent.); insoluble in *ether,* and in *chloroform.* Aqueous solution (1 in 4) alkaline to *litmus* and colorless; when acidified with *acetic acid* yields a violet coloration with *T. Sol. of ferric chloride;* when neutralised with *hydrochloric acid* gives a white precipitate of theobromine, and the filtrate from this, on the addition of more of the acid, gives a precipitate of salicylic acid; the precipitated theobromine, washed with a little *water,* yields, when treated with *potassium chlorate* and *hydrochloric acid* as described under 'Caffeina,' a purple color. The aqueous solution also yields precipitates with *T. Sol. of mercuric chloride,* with solutions of alkaloidal salts, and with *N/10 solution of iodine.*" *Br.*

"**Assay.**—Dissolve about 2 Gm. of Theobromine Sodio-Salicylate, previously dried to constant weight in a desiccator over sulphuric acid, and accurately weighed, in 10 mils of warm distilled water, and titrate the solution with normal hydrochloric acid V.S., phenolphthalein T.S. being used as indicator. Not more than 5.5 mils of normal hydrochloric acid V.S. is required to neutralize 2 Gm. of Theobromine Sodio-Salicylate. The solution should now be slightly alkaline to litmus or be made so by the addition of one or two drops of very dilute ammonia water. Allow it to stand at from 20° to 25° C. (68°–77° F.) for three hours, stirring occasionally, then transfer the precipitate of theobromine obtained to a dried and weighed filter of 9 cm. diameter, and wash the precipitate and filter with four successive portions of 5 mils each of ice-cold distilled water, afterwards dry the filter and contents at 100° C. (212° F.) and weigh. To the weight of precipitate thus obtained add for each 2 Gm. of salt, 0.13 Gm. (the approximate quantity of theobromine remaining in the liquid and washings). The sum corresponds to not less than 46.5 per cent. of the weight of dried Theobromine Sodio-Salicylate taken.

"About 0.05 Gm. of the precipitate obtained in the preceding assay, when evaporated to dryness on a water bath with 1 mil of hydrochloric acid and about 0.1 Gm. of potassium chlorate, leaves a reddish-yellow residue, which becomes purple on moistening with a drop of ammonia water. Another portion of about 0.2 Gm. of the precipitate, when slowly heated, volatilizes without melting and without leaving a weighable residue." *U. S.*

"Yields not less than 40 per cent. of theobromine and 35 per cent. of salicylic acid when tested by the following process: Dissolve 2 grammes of the Salicylate of Theobromine and Sodium in 10 millilitres of warm *water,* slightly acidify with *diluted hydrochloric acid,* add *solution of ammonia* until the reaction is faintly alkaline, and set aside for three hours at about 15.5° C. (60° F.), stirring frequently. Collect the precipitated theobromine on a tared filter, wash twice with 10 millilitres of *water,* dry at 100° C. (212° F.), and weigh the precipitate; it weighs not less than 0.8 gramme. Acidify the filtrate and washings with *hydrochloric acid,* shake with two successive quantities, each of 10 millilitres, of *ether,* evaporate the mixed ethereal solutions, dry the residue at 60° C. (140° F.), and weigh; it weighs not less than 0.7 gramme." *Br.*

Uses.—The effects of theobromine upon the system are very similar to those produced by caffeine except that it has relatively little influence upon the central nervous system. Because of this fact it is much less liable to produce wakefulness—although in some sensitive individuals it does act as a cerebral stimulant—and is not useful as a respiratory stimulant. The most important effect of theobromine upon the system is an increase in the secretion of urine. The mechanism of this action is doubtless the same as that of caffeine. Theobromine also is a powerful stimulant to the voluntary muscles, but because of its feeble effect upon the central nervous system is less useful than caffeine for the purpose of overcoming fatigue. It is used in medicine as a diuretic, especially in cases of *dropsy.* It is superior to caffeine in that because of its feeble influence over the central nervous system much larger doses can be administered than are permissible with caffeine.

Dose, from five to ten grains (0.32–0.65 Gm.), repeated at short intervals up to thirty or forty grains (2.0–2.6 Gm.) in 24 hours.

THEOPHYLLINA. U. S.

THEOPHYLLINE Theophyll. [Dimethylxanthine]

(thē-ō-phy̆l-lī'nạ)

"An organic base [$C_7H_8O_2N_4 + H_2O$ or 1 : 3 $C_5H_2(CH_3)_2O_2N_4 + H_2O = 198.12$], isomeric with theobromine. It is found in small amounts in the leaves of *Thea sinensis* Linné (Fam. *Ternstræmiaceæ*) and is also prepared synthetically." *U. S.*

Theophylline belongs to a group of organic compounds related to uric acid and known as diureides or xanthin bases. It is also known as 1–3, dimethyl, 2–6, dioxypurine, and differs from caffeine in having one less methyl group. It forms crystalline salts with hydrochloric and nitric acids and with a number of metallic

chlorides. It forms a soluble compound with sodium hydroxide. Caffeine may be prepared from it by methylation. It is prepared from the mother liquors of caffeine manufacture by precipitating a sparingly soluble silver compound which is later decomposed by hydrogen sulphide. The amount found naturally in tea is so small that most of the commercial product is of synthetic origin. It is made from ethyl cyanoacetate, which is the starting point for the synthesis of a number of the xanthine bases.

Properties.—"Theophylline occurs as a white, crystalline powder; odorless and having a bitter taste. It is permanent in the air. One Gm. of Theophylline dissolves in 100 mils of water and 80 mils of alcohol at 25° C. (77° F.). It is more readily soluble in hot water; sparingly soluble in ether. It is readily soluble in solutions of the alkali hydroxides and in ammonia water. A saturated aqueous solution of Theophylline is neutral to litmus. It melts between 269° and 272° C. (516.2° and 521.6° F.). Dissolve about 0.01 Gm. of Theophylline in 1 mil of hydrochloric acid in a porcelain dish, add 0.1 Gm. of potassium chlorate, evaporate the solution to dryness on a water bath and invert the dish over a vessel containing a few drops of ammonia water; the residue acquires a purple color which is destroyed by fixed alkalies. An aqueous solution of Theophylline yields a precipitate with tannic acid T.S. which is soluble in an excess of the reagent. Dissolve about 0.5 Gm. of Theophylline in 5 mils of potassium hydroxide T.S. and add 15 mils of a solution containing 0.5 Gm. of sulphanilic acid and 5 mils of hydrochloric acid in 100 mils of distilled water and then add 5 mils of an aqueous solution of sodium nitrite (1 in 200). When this mixture is brought nearly to boiling and sodium hydroxide T.S. is added, drop by drop, a blood red color is produced (distinction from *caffeine or theobromine*). A clear solution is produced when about 0.2 Gm. of Theophylline is dissolved in 5 mils of sodium hydroxide T.S. or in 5 mils of ammonia water (distinction from *caffeine, theobromine, or paraxanthine*). Theophylline loses not more than 9.5 per cent. of its weight when dried to constant weight at 100° C. (212° F.). Incinerate about 0.1 Gm. of Theophylline; no weighable ash remains. About 0.2 Gm. of Theophylline dissolves in 5 mils of sulphuric acid without producing more than a faint yellow color (*organic impurities*)." *U. S.*

Uses.—In its effects upon the system, theophylline acts almost the same as its isomer, theobromine (see p. 1123), and is used in medicine for precisely the same purposes. It appears, however, to be somewhat more irritant to mucous membrane, and is therefore more actively diuretic and also more likely to produce gastric disturbances. When used continuously over considerable periods of time the primary diuretic influence of theophylline may disappear, and the quantity of the urine return to its former low level, this despite increased doses of the drug. The explanation of this clinical observation is not yet forthcoming.

This drug is used almost exclusively in the form of one of its soluble compounds (see *Theocine Compounds,* Part II).

Dose, three to five grains (0.2–0.32 Gm.).

THYMOL. U. S., Br.

Thymol

(thȳ′mŏl)

"A phenol [$C_{10}H_{14}O$ or $C_6H_3(CH_3)(OH)(C_3H_7)$ 1:3:4 = 150.11] occurring in the volatile oil of *Thymus vulgaris* Linné (Fam. *Labiatæ*) and in some other volatile oils. Preserve it in well-closed containers." *U. S.* "Thymol, or isopropyl-metacresol, $C_{10}H_{14}O$, is a substance obtained from the volatile oils of Thymus vulgaris, *Linn.,* Monarda punctata, *Linn.,* and Carum copticum, *Benth. and Hook. f.* Purified by recrystallisation from alcohol." *Br.*

Acidum Thymicum; Thymic Acid; Thymol, Acide Thymique, *Fr. Cod.;* Thymolum, *P. G.;* Thymol, Thymiansaure, Thymolkampher, *G.;* Timolo, *It.;* Timol, *Sp.*

This substance has attracted considerable attention from its possession of antiseptic properties analogous to those of phenol, salicylic acid and creosote, with which it is also analogous in composition. It may be obtained by submitting the volatile oils of several plants to a prolonged refrigeration, under the influence of which it crystallizes. Thus, it has been obtained from *Monarda didyma* Linn., *M. punctata* and *Carum copticum* Benth. et Hook. *Ocimum viride* Willd., a plant which is used in Liberia as an antiperiodic, and is said to be especially valuable owing to the fact that when growing in a room it will drive mosquitoes out of the apartment, as well as the medicinally active *O. gratissimum* of India, probably depend for their activities upon thymol. (*Proc. A. Ph. A.,* xxvi, 168.) Thymol is obtained from any of the oils in which it occurs by distilling off from these the larger part of the hydrocarbons and adding warm sodium hydroxide solution to the residue, which combines with the thymol. The mixture is diluted after a time with hot water, which causes the unattacked oil to rise to the top. From the sodium hydroxide solution hydrochloric acid sets the thymol free. This collects as an oily layer, which on cooling will crystallize if a crystal of thymol is added.

Properties.—Thymol boils at 220° to 230° C. (428°–446° F.). It is very slightly soluble in water, but is very soluble in alcohol, and more freely in proportion to the concentration of the menstruum. It is dissolved by ether and the fixed oils, and has no rotatory power as regards polarized light. The alkalies unite with it to form soluble salts. Like creosote, it has the property of combining with animal tissues and thus protecting them against putrefaction. Its formula is $C_{10}H_{14}O$, or $C_6H_3\begin{cases}OH\\CH_3\\C_3H_7\end{cases}$; while *thymene,* with which it is associated in the oil, is a hydrocarbon, isomeric with the oil of

turpentine, and having the composition $C_{10}H_{16}$. As its formula indicates, it is a *propyl-cresol;* and it has been made synthetically by Widmann from cuminol (isopropyl benzaldehyde). This is first nitrated, then by means of phosphorus pentachloride the oxygen of the aldehyde group replaced by chlorine, the nitro group reduced, the chlorine replaced by hydrogen, and the amide group replaced by hydroxyl. The successive changes are thus indicated:

$$C_6H_4\begin{cases}C_3H_7\\COH\end{cases} \text{ to } C_6H_3\begin{cases}NO_2\\C_3H_7\\COH\end{cases}$$

$$C_6H_3\begin{cases}NO_2\\C_3H_7\\CHCl_2\end{cases} \text{ to } C_6H_3\begin{cases}NH_2\\C_3H_7\\CHCl_2\end{cases}$$

$$C_6H_3\begin{cases}NH_2\\C_3H_7\\CH_3\end{cases} \text{ to } C_6H_3\begin{cases}OH\\C_3H_7\\CH_3\end{cases}$$

A process has been patented by M. Dinesman for making *synthetic thymol* from *p* cymol (see *Ph. Centralh.,* Oct., 1901, 650).

Thymol is described in the U. S. P. "as in large, colorless, translucent, rhombic prisms, having an aromatic, thyme-like odor, and a pungent, aromatic taste, with a very slight caustic effect upon the lips. One Gm. of Thymol dissolves in 1010 mils of water, about 1 mil of alcohol, 0.7 mil of chloroform, 1.5 mils of ether, and in 1.7 mils of olive oil at 25° C. (77° F.); soluble in glacial acetic acid or in fixed or volatile oils. Its alcoholic solution (1 in 20) is neutral to litmus and is optically inactive. As a solid it is heavier than water, but when liquefied by fusion it is lighter than water. It melts between 48° and 51° C. (118.4° and 123.8° F.), remaining liquid at a considerably lower temperature. When it is triturated with about an equal weight of camphor or menthol, the mixture liquefies. When a very small crystal of Thymol is dissolved in 1 mil of glacial acetic acid, and then 6 drops of sulphuric acid and 1 drop of nitric acid are added, the liquid assumes a deep bluish-green color by reflected light. Heat about 1 Gm. of Thymol in a test tube in a water bath with 5 mils of a 10 per cent. solution of sodium hydroxide; a clear, colorless, or pale red solution is formed, which becomes darker on standing, without the separation of oily drops. Upon the addition of a few drops of chloroform to this solution and agitating the mixture, a violet color is produced. Volatilize about 2 Gm. of Thymol on a water bath; not more than 0.05 per cent. of residue remains. An alcoholic solution of Thymol (1 in 20) is not colored violet by ferric chloride T.S. (*phenol*)." *U. S.*

"Large, oblique prismatic crystals, sinking in water at 15.5° C. (60° F.). Melting point from 50° to 51° C. (122°–123.8° F.). Completely volatilised on a water-bath. Odor recalling that of thyme; taste pungent, aromatic. Almost insoluble in *water;* freely soluble in *alcohol* (90 per cent.), in *ether,* and in *solution of sodium hydroxide.* A solution of Thymol in half its volume of *glacial acetic acid,* warmed with an equal volume of *sulphuric acid,* assumes a reddish-violet color." *Br.*

Uses.—Thymol was originally introduced as a disinfectant for the same range of purposes for which phenol is employed. The advantage claimed for it was a more agreeable odor. Its drawbacks are its strong local irritant effect and its sparing solubility in water. Concerning its antibacterial powers the findings of different investigators have been contradictory, thus Cooper (*B. M. J.,* 1912, i, p. 1235) finds that in the presence of organic matter it is eight times as powerful as phenol and in the absence of organic matter twenty-five times as strong. On the other hand Schmidt (*Z. P. C.,* 1910, lxvi, p. 412) asserts that it has no germicidal value against vigorous bacteria. It is probably superior to phenol in antibacterial power. It is to-day rarely employed as a surgical disinfectant, but is an ingredient in many of the antiseptic mixtures intended for use upon mucous cavities, such as the National Formulary *Antiseptic Solution.* Its value for these purposes, however, is greatly reduced because of its powerful local irritant action; it is scarcely possible to apply it in stronger solution than one part in a thousand without considerable discomfort. Thymol is also used as a gastro-intestinal disinfectant in *fermentative gastritis, enteritis,* and similar conditions. For this purpose it may be given in doses of two to five grains (0.13–0.32 Gm.) several times a day. Perhaps the most important modern use of thymol is as a vermifuge. It is efficient against the *tape-worm* and probably all forms of intestinal parasites, but is especially employed against the *hook-worm.* For this purpose it is necessary to use it in such large doses that there is danger of poisoning unless absorption be guarded against. The method employed by the Porto Rican Commission as reported by Schultz (*J. A. M. A.,* 1911, lvii, p. 1102) was as follows: If the patient be fairly robust, from fifteen to thirty grains (1–2 Gm.) were given mixed with an equal quantity of sugar of milk, and administered on an empty stomach; this dose is repeated in two hours, and two hours later followed by a vigorous purge, either magnesium sulphate or compound cathartic pills. It is essential that the intestines be as empty as possible as the presence of various foodstuffs encourages absorption. Castor oil should be avoided as the cathartic for a similar reason. The symptoms of thymol poisoning are nausea, vomiting, headache, ringing in the ears, dizziness, muscular weakness, thready pulse, and fall of bodily temperature.

Dose, two to fifteen grains (0.13–1.0 Gm.).

Off. Prep.—Cataplasma Kaolini, *N. F.;* Liquor Antisepticus, *N. F.;* Liquor Antisepticus Alkalinus, *N. F.;* Nebula Aromaticus, *N. F.;* Nebula Thymolis, *N. F.;* Petroxolinum Sulphuratum Compositum, *N. F.;* Pulvis Antisepticus, *N. F.*

THYMOLIS IODIDUM. U. S.

THYMOL IODIDE Thymol. Iod.

(thȳ-mō'lĭs ī-ŏd'ĭ-dŭm)

"Chiefly dithymol-diiodide [$C_{20}H_{24}O_2I_2$ or $(C_6H_2.CH_3.C_3H_7.OI)_2 = 550.03$]. It contains, when dried to constant weight in a desiccator over sulphuric acid, not less than 43 per cent. of iodine (I = 126.92). Preserve it in well-closed containers, protected from light." *U. S.*

Dithymoldiiodide; Aristol; Aristolum; Diiododithymol, *Fr. Cod.*; Dithymol Biiodé, *Fr.*; Dithymoljodid, Aristol, Annidalin, Thymotol, *G.*; Aristol, *Sp.*

Preparation.—*Thymol Iodide* contains about 45 per cent. of iodine; it is the product of the condensation of two molecules of thymol and the substitution of the hydrogen in the hydroxyl group in each by iodine. It may be prepared by decomposing a solution of iodine in potassium iodide by an alcoholic solution of thymol. For process, see *A. J. P.*, 1891, 175; *Proc. A. Ph. A.*, 1891, 572; *Bull. Pharm.*, 1891, 260. The Cincinnati Academy of Pharmacy published the following formula for thymol iodide: Thymol, 50 Gm.; potassium iodide, 58 Gm.; sodium hydroxide, 50 Gm.; water, to make 500 mils; solution of chlorinated soda, to make 3000 mils. Dissolve the thymol, potassium iodide, and sodium hydroxide in sufficient water, add the solution of chlorinated soda, collect the precipitate on a filter and wash it with water until it is free from chlorides. Remove the precipitate and dry it carefully at a temperature not exceeding 20° C. (68° F.). Reduce it to powder and keep it in a well-stoppered dark bottle. (*Am. Drug.*, 1898, 130.) The French Codex directs that two solutions be made, one by dissolving 16 Gm. of sodium hydroxide and 15 Gm. of thymol in sufficient water to make the solution measure 300 mils. The other solution is made by dissolving 60 Gm. of iodine and 80 Gm. of potassium iodide in enough water to make the solution measure 300 mils, the latter solution is added gradually to the alkaline solution of thymol with constant stirring; the resulting brown precipitate is washed with water and the product dried between 40° and 50° C. (104° and 122° F.).

Properties.—Thymol Iodide occurs as "a reddish-brown or reddish-yellow bulky powder with a very slight, aromatic odor. Thymol Iodide is insoluble in water or glycerin; slightly soluble in alcohol at 25° C. (77° F.); readily soluble in chloroform, ether, collodion or in fixed or volatile oils, leaving a slight residue. It is not soluble in solution of sodium hydroxide, either cold or warm. When heated with concentrated sulphuric acid, it is decomposed with the separation of iodine. Dried to constant weight in a desiccator over sulphuric acid, it loses not more than 5 per cent. of its weight. Incinerate about 0.5 Gm. of Thymol Iodide in a porcelain crucible at a temperature not exceeding a low red heat; not more than 1.5 per cent. of ash remains. Shake about 0.1 Gm. of Thymol Iodide for one minute with 20 mils of distilled water and filter. The filtrate does not become more than opalescent on the addition of a few drops of nitric acid and silver nitrate T.S. (*halogen salts*). Shake about 0.5 Gm. of Thymol Iodide with 10 mils of distilled water and filter the mixture; the filtrate is not alkaline to litmus (*alkalies*), nor is it colored blue upon the addition of a few drops of starch T.S. (*free iodine*).

Assay.—Mix thoroughly about 0.25 Gm. of Thymol Iodide, previously dried to constant weight in a desiccator over sulphuric acid and accurately weighed, with about 3 Gm. of anhydrous sodium carbonate. Cover the mixture with about 1 Gm. more of anhydrous sodium carbonate and heat it moderately, in a crucible, gradually increasing the heat, but not exceeding a dull redness, until the mass is completely carbonized. When sufficiently cooled, extract the residue with boiling distilled water and wash it on a filter with boiling distilled water until the washings cease to produce an opalescence with silver nitrate T.S. Heat the combined washings, which measure about 150 mils, on a water bath and add an aqueous solution of potassium permanganate (1 in 20) in small portions, until the hot liquid remains permanently pink. Then add just enough alcohol to remove the pink tint, cool the liquid to room temperature, and dilute it to 200 mils. Mix it well and then filter through a dry filter, rejecting the first 50 mils of filtrate. To 100 mils of the subsequently clear filtrate add about 1 Gm. of potassium iodide (free from iodate) and an excess of diluted sulphuric acid, and titrate the liberated iodine with tenth-normal sodium thiosulphate V.S., adding starch T.S. near the end of the titration. It shows, in the dried Thymol Iodide, not less than 43 per cent. of I.

"Each mil of the tenth-normal sodium thiosulphate V.S. used corresponds to 0.002115 Gm. of I. Each gramme of Thymol Iodide corresponds to not less than 203.3 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

Osseward (*Proc. A. Ph. A.*, 1901, 176) obviates the difficulty of obtaining smooth ointments of thymol iodide (which most dispensers have experienced when proceeding in the usual way) by adding sufficient ether to 1 oz. of thymol iodide placed in a dry mortar, to form a paste, then stirring in 1 oz. of olive oil until a smooth paste is obtained; the ether can be dissipated during the stirring, and this 50 per cent. mixture used in making ointments by incorporating with fatty substances.

Uses.—Thymol iodide is used as a non-toxic and non-irritant dusting powder for *wounds*. It has the same range of usefulness for this purpose as iodoform over which it has the great advantage of being comparatively odorless. According to Shamberg and Kolmer (*J. A. M. A.*, 1914, lxii, p. 1950), it restrains the growth of *Staphylococcus aureus* when present in the proportion of 0.5 per cent. Despite, however, its superiority in direct antiseptic action to iodoform, it is not held in as high esteem by most surgeons. It is also used as a dusting

powder in various moist *skin diseases,* such as weeping eczemas, and Daxenberger (*Heilkunde,* 1908) recommends a 10 per cent. solution in olive oil as a local application in *atrophic rhinitis* and *fissure in ano* as well as various *skin diseases.*

Dose, from two to three grains (0.13–0.2 Gm.).

THYROIDEUM SICCUM. U. S., Br.

DRIED THYROIDS Thyroid. Sicc. [Glandulæ Thyroideæ Siccæ, U. S. VIII Desiccated Thyroid Glands]

(thȳ-roi-dē'ŭm sĭc'cŭm)

"The thyroid glands of animals which are used for food by man, freed from connective tissue and fat, dried and powdered, and containing not less than 0.17 per cent. nor more than 0.23 per cent. of iodine (I = 126.92) in thyroid combination. One part of Dried Thyroids corresponds to approximately 5 parts of the fresh glands." *U. S.* "Dry Thyroid is a powder prepared from the fresh and healthy thyroid glands of the sheep. Remove the external fat and connective tissue from the thyroid glands taken from the sheep immediately after killing. Cut the glands across, and reject any which contain cysts, are hypertrophied, or are otherwise abnormal. Mince finely the healthy glands, and dry at a temperature of 30° to 40° C. (86°–104° F.); powder the dried product; remove all fat by washing with *petroleum spirit;* again dry the residue." *Br.*

Dry Thyroid; Getrocknete Schilddrüsen, *G.*

Desiccated thyroid glands were introduced into the U. S. P. VIII for the first time; the British Pharmacopœia introduced this preparation in the 1898 and 1914 editions. The process for dry thyroid is given above; the objection to its use is that the powder may contain bacteria, or even ptomaines, if great care is not used in its preparation; it is also stated that glycerin does not dissolve all of the thyroiodin which is the principal active constituent, and "Thyroid Solution" cannot be thoroughly representative.

See *Liquor Thyroidei,* Br., 1898, *U. S. Disp.,* 19th edition, page 740.

Properties.—Dry thyroid is officially described as "a yellowish, amorphous powder, having a slight, characteristic odor. Dried Thyroids must be free from iodine in inorganic or any other form of combination than that peculiar to the thyroid. Dried Thyroids contain not more than 6 per cent. of moisture and the yield of ash does not exceed 5 per cent.

"Assay.—Mix 1 Gm. of Dried Thyroids in a nickel crucible of about 125 mils capacity, with 15 Gm. of a mixture composed of 138 parts by weight of anhydrous potassium carbonate, 106 parts of anhydrous sodium carbonate and 75 parts of potassium nitrate. Spread an additional 5 Gm. of this fusion mixture evenly over the surface. Heat the crucible over a free Bunsen flame until no further carbonization is observed, cool it and dissolve the residue in about 150 mils of distilled water, warming to hasten solution. Transfer this solution to an Erlenmeyer flask, of about 500 mils capacity and add approximately 50 mils, or its equivalent, of a fresh solution of chlorinated soda (containing 2.4 per cent. of chlorine by weight). Now treat the mixture with enough phosphoric acid, diluted with an equal volume of distilled water, to produce an appreciable yellow tint of free chlorine, then add 10 mils more of the phosphoric acid diluted with an equal volume of distilled water, and boil the contents of the flask for one-half hour or until the volume has been reduced to about 150 mils. Cool the liquid, add 10 mils of an aqueous solution of potassium iodide (1 in 100) and titrate the liberated iodine with freshly prepared two-hundredth-normal sodium thiosulphate V.S., starch T.S. being used as indicator just before the end of the reaction. It shows not less than 0.17 per cent. nor more than 0.23 per cent. of I.

"Each mil of two-hundredth-normal sodium thiosulphate V.S. used corresponds to 0.1058 milligramme of I derived from the Thyroid Glands used. Each gramme of Dried Thyroids corresponds to not less than 16.07 mils nor more than 21.74 mils of two-hundredth-normal sodium thiosulphate V.S." *U. S.*

"A light, dull-brown powder, with a very faint meat-like odor and taste; free from any flavor of putrescence. Liable to become damp on exposure to the air, and to deteriorate." *Br.*

Many preparations of the thyroid glands are upon the market, most of which are powders or so-called standardized extracts. The active principles have not been isolated in such a state of purity as to admit of accurate description.

The chemical nature of the active principle of thyroid gland is unknown. The substance isolated by Baumann (*Z. P. T.,* 1895, xxi) and called by him *thyro-iodine* (*iodothyrin*), is by many believed to represent the activities of the gland. But while it undoubtedly possesses many of the properties of thyroid gland there is strong evidence that it will not set aside all of the symptoms of thyroidectomy. Moreover it does not appear to be, strictly speaking, a chemical individual since it may contain varying proportions of iodine. Pick and Pilenes (*Z. E. P. T.,* 1909, vii, p. 518), prepare a *thyroglobulin* by macerating the thyroid gland in normal salt solution and precipitating after some weeks the globulins with ammonium sulphate which they assert will set aside fully developed myxedema. *Iodoglobulin* is apparently simply an aqueous extract of the thyroid gland. E. C. Stanford (*Y. B. P.,* 1898, p. 354) gives the following process for preparation of *thyroglandin* which is practically the same thing as iodoglobulin.

"The thyroid glands, freed from fat and minced, are first macerated in four to five times their weight of cold water, using ice if necessary in summer to keep down the temperature to 10° C. (50° F.), for twenty-four hours, and this maceration is repeated. The solutions are filtered off and evaporated to dryness at a tem-

perature not exceeding 100° C. (212° F.). The extract is powdered, and represents the iodo-globulin and a small proportion of saline matter. The residue from the cold water maceration is boiled for one hour with a 1 per cent. solution of sodium hydroxide (in the proportion of 1 per cent. of sodium hydroxide to the original weight of the glands). The solution is allowed to cool to deposit the fat, and filtered off. This solution is then carefully neutralized with hydrochloric acid and evaporated to dryness at 100° C. (212° F.); the residue, which contains all the thyroiodin, is then powdered and mixed with the iodo-globulin obtained in the first process. The resulting powder is thyroglandin."

Beebe finds in thyroglobulin a substance which he calls *thyroprotein*, and believes to be the active principle. Whatever be the precise nature of this active principle, it is apparent that it is an iodine-containing body, and although the quantity of iodine does not furnish an altogether trustworthy guide to the quality of thyroid body, a sample of the drug with a low content of organic iodine may be rejected as of inferior quality.

Kendall (*J. Bi. Chem.*, 1915, xx, 501) claims to have separated the iodine-containing principle of the thyroid in a crystalline form. He believes it to be a diiodo-dihydroxy-indol. Its melting point is 220° C. (428° F.), and it contains 60 per cent. of iodine. It produces tachycardia, loss of weight, and nervous irritability. The effective dose is very small; in a cretin weighing forty pounds a dose of 11 Mgm. distributed over a period of fourteen days caused an increase in the pulse rate from 90 to 140.

Uses.—It has been proved upon the human being by Kocher, of Berne, and upon monkeys by Horsley, of London, that the removal of the thyroid body is followed by the production of increasing weakness, associated with swelling of the body, enlargement and thickening of the skin, mucoid exudation into the subcellular tissue, and a very extraordinary slowing of all functions—a condition which progresses until the subject sinks into a state of complete apathy, with subnormal temperature and failure of all vital functions. This congeries of symptoms is the same as that previously described under the name of *myxœdema* by Ord.

It is probable that when the secretion of the thyroid gland is diminished to a slight extent, not sufficient to give rise to myxedematous symptoms, there is more or less modification in various functions of the body. On the other hand, the administration of thyroid gland to normal animals or men causes well marked symptoms which we may speak of as the physiological action of thyroid. There is strong reason to believe that the symptoms of Graves's disease are due to an excessive secretion of the thyroid gland.

The single dose of thyroid produces no very obvious changes in the bodily functions, although Asher and Flack (*Z. B.*, 1911, lv, p. 83) have shown that there is an increased irritability of the vasomotor center; that is, that the response both to pressor and depressor influences is greater than normal. The most marked result following the continued use of the thyroid gland is a diminution in the bodily weight. Simultaneously with the loss of weight there is an increase in the output of nitrogenous and phosphatic elements of the urine indicating an augmented protein catabolism. The increase in the nitrogenous elimination is not, however, sufficient to account for the loss in bodily weight; it has been estimated that from one-sixth to one-third of the loss of weight can be attributed to the increased destruction of protein tissue. The natural conclusion is that there is an even greater oxidation of the adipose tissue of the body. This view is confirmed by the experiments of Magnus-Levy (*D. M. W.*, 1896), who has demonstrated a great increase in the amount of carbonic acid expired. There are also more or less marked changes in the blood, the most being an increase in the mononuclear leukocytes either with or without an increase in the total number of white corpuscles. Hunt and Seidell (*J. P. Ex. T.*, 1910, ii, p. 15) have shown that thyroid feeding alters the resistance of mice to certain poisons, diminishing the susceptibility to acetonitril, but increasing that to morphine. They have suggested this reaction as a test of the activity of samples of the drug.

Among the conditions for which thyroid gland has been found clinically useful stand pre-eminent those states which are due to an absence of its secretion. These symptoms when occurring in adult life, either as the result of degenerative changes in the gland or of unwise surgical procedures, are known as *myxedema*, but when due to a congenital absence are called *cretinism*. In these cases, especially the congenital group, most striking improvement follows the continued use of thyroid feeding. As the thyroid failure is usually permanent it is necessary to continue the use of the drug throughout the patient's life. Our knowledge of the effects of thyroid feeding would seem to strongly indicate the use of the drug in the treatment of *obesity*. Unfortunately, however, although there is in the majority of cases a rapid loss of weight under the thyroid treatment for a short period of time, the system soon becomes inured to the action of the drug, and despite its continued use even in ascending doses the patient may regain the lost weight. It is, however, often of service in conjunction with the dietetic and hygienic measures suitable for this class of cases, but much harm has been done by the proprietary anti-fat remedies containing thyroid as the active ingredient. It is by far too powerful a drug to be used except under medical supervision. As pointed out above, the thyroid gland also has apparently some relation with the sexual organs, and it has been found clinically useful in certain uterine disorders, notably *metrorrhagia*. There are few diseases, either chronic or acute, in which the thyroid gland has not been recommended. Among those conditions in which its value is more or less substantiated may be mentioned diseases of the bones,

as *ununited fractures, osteomalacia,* and *rheumatoid arthritis,* certain skin diseases especially *psoriasis, hay fever, asthma, cancer, hemophilia,* etc.

In view of the uncertainty concerning the nature of the active principle of this drug we believe that it is much better to use the official dried gland than any of the many proprietary preparations. In myxedema it is generally well to begin with relatively large doses, about five grains (0.32 Gm.) until the accumulated symptoms due to the prolonged lack of thyroid secretion have abated, and afterwards continue the use of the drug in smaller quantities. For other conditions it is generally well to begin with smaller doses, two or three grains (0.13–0.2 Gm.), three times a day, gradually increasing if necessary, until palpitation of the heart or excessive nervousness indicates that the physiological limit or the therapeutic purpose is obtained. In any case, during the administration of the drug the occurrence of any of the symptoms of hyper-thyroidism should be the immediate signal for the withdrawal of the drug.

Among the various preparations of thyroid upon the market may be mentioned *iodothyrin* (*thyro-iodine*). As this appears commercially it is diluted with milk sugar to a strength equal to that of the fresh gland. The dose is ten to thirty grains (0.65–2.0 Gm.). *Thyroprotein,* standardized to contain 0.33 per cent. of iodine. *Thyraden,* dose two to eight grains (0.13–0.5 Gm.). *Thyrein,* said to be identical with iodothyrin. *Thyroidin,* a commercial preparation corresponding to the official dried gland. *Thyreoidin* Notkin, dose, one-sixth grain (0.01 Gm.). It is said also to be useful for hypodermic administration in the form of a one-half per cent. solution. *Thyron* or *tyron,* prepared by treating thyroid gland with tannic acid.

Dose, of dried thyroids, from two to five grains (0.13–0.32 Gm.).

TINCTURA ACONITI. U. S., Br.

TINCTURE OF ACONITE Tr. Aconit. [Aconiti tinctura P. I.]

(tĭnc-tū'rą ăc-o-nī'tī)

"*One hundred mils* of Tincture of Aconite yields not less than 0.045 Gm. nor more than 0.055 Gm. of the ether-soluble alkaloids of aconite. If assayed biologically the minimum lethal dose should not be greater than 0.0004 mil for each gramme of body weight of guinea-pig." *U. S.* "Tincture of Aconite contains in 100 millilitres 0.04 gramme of the ether-soluble alkaloids of Aconite Root." *Br.*

Tinctura Aconiti Radicis, *U. S.* 1870; Tincture of Aconite Root; Teinture de racine d'Aconit, *Fr. Cod.*; Tinctura Aconiti, *P. G.*; Akonittinktur, Eisenhuttinktur, *G.*; Tinctura di aconito, *It.*; Tintura alcoholica de aconito, *Sp.*

* "Aconite, in No. 60 powder, *one hundred grammes* [or 3 ounces av., 231 grains], to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P, as modified for assayed tinctures (see page 1160), using a mixture of *seven volumes* of alcohol and *three volumes* of water as the menstruum and adjusting the volume of the finished Tincture so that each *one hundred mils* contains 0.05 Gm. of the ether-soluble alkaloids of aconite." *U. S.*

"Aconite Root, in No. 40 powder, 150 *grammes;* Alcohol (70 per cent.), *a sufficient quantity.* Moisten the powder with seventy-five millilitres of the Alcohol, and produce, by the *percolation process,* one thousand millilitres of a strong tincture. Determine the proportion of ether-soluble alkaloids present in this strong tincture, by evaporating one hundred millilitres to dryness in a shallow porcelain evaporating basin, and proceeding as directed under 'Aconiti Radix.' Dilute the remainder of the strong tincture with sufficient of the Alcohol to produce a Tincture of Aconite containing 0.04 gramme of ether-soluble alkaloids in 100 millilitres of the Tincture. Examined by the foregoing process Tincture of Aconite is found to contain in 100 millilitres 0.04 gramme of the ether-soluble alkaloids of Aconite Root. *Limit of error* 0.002 gramme in excess or defect. This Tincture is of approximately the same strength as the Tinctura Aconiti of the International Agreement, and about twice as strong as the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

Assay. U. S. P. IX.—"Evaporate 150 mils of Tincture of Aconite at a temperature not exceeding 75° C. (167° F.), until it measures about 20 mils. Add 10 Gm. of purified sawdust (see Reagents, Part III) to this liquid, incorporate it thoroughly and then continue the evaporation until the sawdust is dry. Transfer the impregnated sawdust to a 250 mil flask, add 150 mils of ether and proceed as directed in the assay under *Belladonnæ Radix,* page 222, fourth line of the Assay, modifying the process there given by using the ammonia water with a small quantity of distilled water to rinse out the dish in which the mixture was evaporated, and use ether only in the final extraction of the alkaloids. Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 64.539 milligrammes of the ether-soluble alkaloids of aconite. For an alternative method of assaying Tincture of Aconite, see Biological Assays (Part III)." *U. S.*

Robinson (*A. I. M.,* 1915, xv, p. 645) has found that the substance separated by the U. S. P. method of assaying aconite and giving the chemical test for aconitine, had a minimal lethal dose at least forty-five times as much as that of crystalline aconitine. This fact emphasizes the necessity of physiological standardization of aconite. For description of biological assay, see *Aconitum.*

The old tincture of the U. S. Pharmacopœia, 1890, had seven times the strength of the British, and the title was changed from *Tinctura Aconiti Radicis* to *Tinctura Aconiti* in the U. S., 1880, revision. It was much stronger than the Tincture of Aconite Leaves, which is still used occasionally, and made of the strength of two troyounces of powdered aconite leaves in a pint of diluted alcohol, and too much caution cannot

be observed to avoid mistaking one tincture for the other. A very important change was made in the strength of Tincture of Aconite in the U. S. P. VIII. The former 35 per cent. tincture was replaced by a tincture of 10 per cent., which is now the strength of the official tincture, 1914. A chemical assay process was also appended and the U. S. P. IX further recommends a biological standard and assay. The latter is desirable because faulty manipulation or storage changes the aconitine to inert bodies, and this would not be detected by the chemical assay. In preparing it, each step of the process must be carefully attended to. The root should be thoroughly comminuted, and very carefully packed in the percolator, and the displacing menstruum very gradually added. Tartaric acid which was formerly used in accordance with the researches of Duquesnel in the U. S., 1880, tincture has been abandoned, as it was found to be unnecessary. For a paper on Tincture of Aconite, by M. I. Wilbert, see *Proc. A. Ph. A.*, 1902, 348. The external use of the tincture requires care, as serious symptoms have followed its too free employment. (Case, *B. M. S. J.*, Feb., 1872, 74.)

Fleming's Tincture of Aconite.—This should always be expressly designated when prescribed. It is considerably stronger than the official; and several deaths have occurred from the use of it. The following is Fleming's formula: Take of the root, carefully dried and finely powdered, *sixteen (troy) ounces;* Alcohol, *sixteen fluidounces.* Macerate for four days, put into a percolator, and add alcohol until twenty-four fluidounces are obtained. Not more than two drops of this should be given as a commencing dose, to be increased till its peculiar effects are experienced.

Dose, U. S. tincture, 3–10 min. (0.2–0.6 mil); Br. tincture, 5–15 min. (0.3–0.9 mil); if frequently repeated, 2–5 min. (0.12–0.3 mil).

TINCTURA ALOES. U. S.

TINCTURE OF ALOES Tr. Aloes

(tĭnc-tū'rą ăl'ō-ēs)

Teinture (alcoolé) d'Aloés, *Fr. Cod.;* **Tinctura Aloës,** *P. G.;* **Aloetinktur,** *G.;* **Tinctura alcoholica de acibar,** *Sp.*

* "Aloes, in No. 40 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Glycyrrhiza, in No. 40 powder, *two hundred grammes* [or 7 ounces av., 24 grains] to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), using diluted alcohol as the solvent." *U. S.*

Tincture of aloes was deleted from the Br. Pharm., 1914. The process of the previous British Pharmacopœia is appended.

"Extract of Barbados Aloes, *½ ounce* (Imperial) or 25 grammes; Liquid Extract of Liquorice, 3 *fl. ounces* (Imp. meas.) or 150 cubic centimetres; Alcohol (45 per cent.), *a sufficient quantity.* Place the Extract of Barbados Aloes in a closed vessel with *sixteen fluid ounces* (Imp. meas.) or eight hundred cubic centimetres of the Alcohol; set aside for forty-eight hours, occasionally shaking until dissolved; add the Liquid Extract of Liquorice; filter; pass sufficient of the Alcohol through the filter to produce *one pint* (Imp. meas.) or one thousand cubic centimetres of the Tincture." *Br.*, 1898.

The strength of the British tincture, 1898, was only one-fourth that of the U. S. tincture. The formula of the U. S. (8th Rev.) directed glycyrrhiza instead of extract of licorice, but has returned to the process of maceration for its preparation. Ménière says of the tincture of aloes that it deposits crystals of aloin, which adhere to the sides of the bottle, and in the upper part of it a yellow resinous matter is seen.

Dose, as a purgative, from two to four fluidrachms (7.5–15.0 mils); as a laxative, from one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA ALSTONIÆ. Br.

TINCTURE OF ALSTONIA

(tĭnc-tū'rą ăl-stōn'i-æ)

"Alstonia, in No. 20 powder, 125 *grammes;* Alcohol (60 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

This tincture represents whatever therapeutic properties alstonia bark may possess. It is used in *malaria.*

Dose, one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA ARNICÆ. U. S. (Br.)

TINCTURE OF ARNICA Tr. Arnic. [Tinctura Arnicæ Florum, U. S. 1890]

(tĭnc-tū'rą är'nĭ-çæ)

Tinctura Arnicæ Florum, *Br.*, Tincture of Arnica Flowers; Teinture (alcoolé) de Fleur d'Arnica, Teinture d'Arnica, *Fr. Cod.;* Tinctura Arnicae, *P. G.;* Arnikatinktur, *G.;* Tintura di Arnica, *It.;* Tintura alcoholica de arnica, *Sp.*

* "Arnica, in No. 20 powder, *two hundred grammes* [or 7 ounces av., 24 grains]; Diluted Alcohol, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Moisten the drug with *five hundred mils* [or 16 fluidounces, 435 minims] of diluted alcohol, transfer it to a percolator, and, without pressing the powder, allow it to stand well covered for twenty-four hours, then pack it with moderate pressure and allow the percolation to proceed slowly, pouring on additional diluted alcohol as needed. When the percolate measures *two hundred and fifty mils* [or 8 fluidounces, 218 minims] stop the flow, macerate the drug for an additional twenty-four hours, and then continue the percolation until the total percolate measures *five hundred mils* [or 16 fluidounces, 435 minims]. Again interrupt the percolation, macerate the drug for another twelve hours and afterwards collect an additional *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of percolate. Again macerate the drug for twelve hours and then allow the percolation to proceed slowly, pouring on sufficient diluted alcohol to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of Tincture." *U. S.*

"Arnica Flowers, in No. 20 powder, 100

grammes; Alcohol (45 per cent.), sufficient to produce 1000 *millilitres*. Moisten the powder with two hundred *millilitres* of the Alcohol, and complete the *percolation process.*" *Br.*

The U. S. IX and Br. Pharm., 1914, have dropped arnica root and tincture of arnica flowers alone represents arnica in both Pharmacopœias. *Tincture* of *Arnica Root,* Br., 1898, was made by percolating 50 grammes powdered arnica rhizome with 70 per cent. alcohol, until one thousand mils were obtained. Tincture of arnica root was solely intended for internal administration and confusion arose from the similarity in names.

The U. S. P. tincture of arnica differs from that official in 1870 in the menstruum selected, which is now diluted alcohol in place of alcohol. The change was advocated by numerous pharmaceutical writers, and there is no question of the ability of the menstruum to exhaust the arnica flowers, if they are tightly packed in the percolator. The principal objection to the change is the greater difficulty that will be experienced in mixing the tincture with liniments containing oily and alcoholic liquids.

Either alone, or diluted with water, soap liniment, etc., tincture of arnica is often applied popularly to *bruises, sprains, tumors* and local *rheumatic pains,* under the impression that it has extraordinary healing powers. It probably acts merely as a counter-irritant. On some skins it produces a violent eczematous inflammation. If given internally, the *dose* would be from ten to thirty minims (0.6–1.8 mils), increased until some effect was produced.

Dose, of the British tincture of the root, twenty minims to half a fluidrachm (1.3–1.8 mils).

TINCTURA ASAFŒTIDÆ. U. S. (Br.)

TINCTURE OF ASAFETIDA Tr. Asafœt.

(tĭnc-tū'rą ăs-ą-fœt'ĭ-dæ)

Tinctura Asafetidæ, *Br.;* Teinture (alcoolé) d'Asafœtida, *Fr. Cod.;* Asanttinktur, Stinkasanttinktur, *G.;* Tinctura alcoholica de asafetida, *Sp.*

* "Asafetida, bruised, *two hundred grammes* [or 7 ounces av., 24 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), using alcohol as the solvent." *U. S.*

"Asafetida, bruised, 200 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Macerate the Asafetida in a closed vessel with *seven hundred and fifty millilitres* of the Alcohol for seven days, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

This tincture becomes milky on the addition of water, in consequence of the separation of the resin.

Dose, thirty minims to a fluidrachm (1.8–3.75 mils).

Off. Prep.—Mistura Magnesii, Asafœtidæ et Opii, *N. F.*

TINCTURA AURANTII AMARI. U. S. (Br.)

TINCTURE OF BITTER ORANGE PEEL Tr. Aurant. Amar.

(tĭnc-tū'rą âu-răn'tĭ-ī ą-mā'rī)

Tinctura Aurantii, *Br.;* Tincture of Orange; Teinture (alcoolé) d'Ecorce d'Orange amère, *Fr.;* Tinctura Aurantii, *P. G.;* Pomeranzentinktur, Pomeranzenschalentinktur, *G.*

* "Bitter Orange Peel, in No. 40 powder, *two hundred grammes* [or 7 ounces av., 24 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using a mixture of *three volumes* of alcohol and *two volumes* of water as the menstruum." *U. S.*

"Fresh Bitter-Orange Peel, cut small, 250 *grammes;* Alcohol (90 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

It is the peel of the Seville orange that is directed in this process, and the outer part only is active. The substitution of fresh for dried orange peel was proposed in England, and its propriety considerably discussed. (See *P. J.,* Nov. 9, 1872, also April 4, 1874.) Indeed, it met with so much favor as to be introduced in the 1885 revision of the British Pharmacopœia, and was used in the *Tinctura Aurantii Recentis,* Br.; but in the Br. Pharm., 1898, the name was changed to *Tinctura Aurantii.* The two tinctures differ also because of the fact that the Br. "orange peel" is only of the outer layer, while the U. S. includes also the inner, white, portion of the rind. The U. S. tincture has a greenish-brown color and a bitterish taste, the latter due to the presence of hesperidin from the inner layer of the rind. The Br. tincture of orange more closely resembles the U. S. *Tinctura Aurantii Dulcis* in sensible properties. The tincture of bitter orange peel is employed as a grateful addition to infusions, decoctions, and mixtures.

Dose, from one to two fluidrachms (3.75–7.5 mils).

Off. Prep.—Syrupus Aromaticus, *Br.;* Syrupus Aurantii, *Br.;* Elixir Aurantii Amari, *N. F.*

TINCTURA AURANTII DULCIS. U. S.

TINCTURE OF SWEET ORANGE PEEL Tr. Aurant. Dulc.

(tĭnc-tū'rą âu-răn'tĭ-ī dŭl'cĭs)

Teinture de Zeste d'Orange douce, *Fr.;* Apfelsinenschalentinktur, *G.*

* "Sweet Orange Peel, grated from the fresh fruit, *five hundred grammes* [or 17 ounces av., 279 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), macerating the drug in *one thousand mils* of alcohol and completing the preparation with alcohol. Use purified cotton as the filtering medium." *U. S.*

This tincture was designed to furnish a highly

flavored alcoholic preparation of orange and has no medicinal properties. It is used as a pleasant adjuvant and flavoring agent.

Off. Prep.—Syrupus Aurantii, *U. S.*

TINCTURA BELLADONNÆ FOLIORUM. U. S. (Br.)

TINCTURE OF BELLADONNA LEAVES Tr. Bellad. Fol. [Belladonnæ tinctura P. I.]

(tĭnc-tū'rą bĕl'lą-dŏn'næ fō-lī-ō'rŭm)

"*One hundred mils* of Tincture of Belladonna Leaves yields not less than 0.027 Gm. nor more than 0.033 Gm. of the total alkaloids of belladonna leaves." *U. S.* "Tincture of Belladonna contains in 100 millilitres 0.035 *gramme* of the alkaloids of Belladonna Leaves." *Br.*

Tinctura Belladonnæ, *Br., U. S. P.* 1880; Tincture of Belladonna; Teinture de feuille de Belladone, *Fr. Cod.;* Belladonnatinktur, *G.;* Tintura alcoholica de belladonna, *Sp.*

* "Belladonna Leaves, in No. 60 powder, *one hundred grammes* [or 3 ounces av., 231 grains], to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P, as modified for assayed tinctures (see page 1160), using diluted alcohol as the menstruum and adjusting the volume of the finished Tincture so that each *one hundred mils* contains 0.03 Gm. of the total alkaloids of belladonna leaves." *U. S.*

"Belladonna Leaves, dried and in No. 20 powder, 100 *grammes;* Alcohol (70 per cent.) sufficient to produce 1000 *millilitres.*

"Moisten the Belladonna Leaves with one hundred millilitres of the Alcohol, and complete the *percolation process.* Determine the proportion of alkaloids contained in the tincture so prepared by the Br. process below." *Br.*

"**Assay.**—Evaporate 100 mils of Tinctura of Belladonna Leaves on a water bath until it measures about 10 mils, transfer the evaporated liquid to a separator, and proceed as directed in the assay under *Fluidextractum Belladonnæ Radicis,* page 486, second line of the Assay, beginning with the words 'add 10 mils,' modifying the process there given by increasing the ammonia water to 5 mils which, with about 5 mils of distilled water, is to be used in divided portions to rinse out the dish in which the mixture was evaporated; before titrating treat the residue twice with 5 mils of ether, evaporating to dryness each time." *U. S.*

"Evaporate 100 millilitres in an evaporating basin on a water-bath until it measures about 10 millilitres, add, if necessary, sufficient *alcohol* (90 per cent.) to dissolve any separated substance and transfer to a separator, rinsing the dish with a little *water.* Add 10 millilitres of *water,* 20 millilitres of *chloroform,* and 2 millilitres of *solution of ammonia.* Shake well and separate the chloroformic layer. Repeat the extraction with two successive portions of 10 millilitres of *chloroform.* Mix the chloroformic solutions, and shake them with 10 millilitres of *N/1 solution of sulphuric acid* diluted with twice its volume of *water.* Separate the chloroformic solution. Repeat the shaking with a further 10 millilitres of the acidified water. Mix the acid solutions, add 20 millilitres of *chloroform* and 4 millilitres of *solution of ammonia.* Shake well, draw off the chloroformic solution into a beaker, and repeat the extraction with two further portions, each of 10 millilitres, of *chloroform.* Allow the mixed chloroformic solutions to evaporate, dry the residue on a water-bath for thirty minutes, dissolve it in 10 millilitres of *N/20 solution of sulphuric acid* and titrate with *N/20 solution of sodium hydroxide,* using *tincture of cochineal* as indicator. Deduct the number of millilitres of alkaline solution required from 10, and multiply the difference by 0.01446; the product will be the weight in grammes of the alkaloids contained in 100 millilitres of the tincture. This quantity should be not less than 0.035 gramme. Should the tincture contain more than this proportion it must be diluted with the necessary quantity of Alcohol (70 per cent.).

"Examined by the foregoing process, Tincture of Belladonna is found to contain in 100 millilitres 0.035 gramme of the alkaloids of Belladonna Leaves. *Limit of error* 0.002 gramme in excess or defect. This Tincture contains seven-tenths of the proportion of alkaloids contained in the Tincture of Belladonna of the British Pharmacopœia, 1898. It may be used when the Tinctura Belladonnæ of the International Agreement is required." *Br.*

In the U. S. P., 1890, the name of this tincture was changed to *Tinctura Belladonnæ Foliorum,* for the sake of greater precision. In the U. S. P. VIII its strength was reduced to 10 per cent. to conform to the International Protocol standard.

The tincture is an efficient preparation when made from the recently dried leaves and assayed by the official process.

Dose, from five to fifteen minims (0.3–0.9 mil).

TINCTURA BENZOINI. U. S.

TINCTURE OF BENZOIN Tr. Benz.

(tĭnc-tū'rą bĕn-zo-ī'nī)

Teinture (alcoolé) de Benjoin, *Fr. Cod.;* Tinctura Benzoës, *P. G.;* Benzoëtinktur, *G.;* Tintura di benzoino, *It.;* Tintura alcoholica de benjui, *Sp.*

* "Benzoin, in No. 40 powder, *two hundred grammes* [or 7 ounces av., 24 grains]; to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), using alcohol as the solvent." *U. S.*

This tincture was introduced into the Pharmacopœia chiefly for the purpose of adding to ointments to prevent rancidity. This, however, is bad pharmaceutical practice and is hardly ever followed.

Dose, fifteen to thirty minims (0.9–1.8 mils).

TINCTURA BENZOINI COMPOSITA. U. S., Br.

COMPOUND TINCTURE OF BENZOIN Tr. Benz. Co.

(tĭnc-tū'rą bĕn-zo-ĭ'nī cŏm-pŏs'ĭ-tą)

Tinctura Balsamica, Balsamum Commendatoris, Elixir Traumaticum; Friars' Balsam; Teinture (alcoolé) balsamique, *Fr. Cod.;* Baume du Commandeur de Permes, *Fr.;* Persischer Wundbalsam, *G.*

* "Benzoin, in No. 40 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Aloes, in No. 40 powder, *twenty grammes* [or 308.6 grains]; Storax, *eighty grammes* [or 2 ounces av., 360 grains]; Balsam of Tolu, *forty grammes* [or 1 ounce av., 180 grains]; to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), using alcohol as the solvent." *U. S.*

"Benzoin, in powder, 100 *grammes;* Prepared Storax, 75 *grammes;* Balsam of Tolu, 25 *grammes;* Aloes, 20 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.*

"Macerate the Benzoin, Storax, Balsam of Tolu, and Aloes with eight hundred millilitres of the Alcohol in a closed vessel for two days, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

Compound tincture of benzoin now contains 10 Gm. of benzoin to each 100 mils instead of 12 as in the U. S. P., 1890.

Uses.—Compound tincture of benzoin is chiefly employed both for its antiseptic and protective effect as a local application to minor *wounds, chapped hands* or *nipples, indolent ulcers,* etc. It is the *balsamum traumaticum* of the older Pharmacopœias, and may be considered as a simplified form of certain complex compositions, such as *baume du commandeur, Wade's balsam, Balsam de Maltha, Friar's balsam, Jesuit's drops, Turlington's balsam,* etc., which were formerly in great repute, and are still esteemed by the people, as pectorals and vulneraries. The compound tincture of benzoin is precipitated by water. A variety of *court plaster* is made by applying to black silk, by means of a brush, first a solution of isinglass, and afterwards an alcoholic solution of benzoin.

It is occasionally employed internally as a stimulating expectorant in *chronic bronchitis.* More frequently it is used as an inhalant by adding a teaspoonful of the tincture to a pint of hot water and breathing the vapors; this mode of treatment is especially useful in the early stages of *acute bronchitis.* It has also been recommended in *chronic dysentery* with the idea that it would exercise its local action upon the ulcerated surface of the colon, but is of doubtful utility.

Dose, fifteen to sixty minims (0,9–3.75 mils).

TINCTURA BERBERIDIS. Br.

TINCTURE OF BERBERIS

(tĭnc-tū'rą bęr-bĕr'ĭ-dĭs)

"Berberis, in No. 60 powder, 100 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.*

"Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.* This tincture is used as a bitter tonic.

Dose, one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA BUCHU. Br.

TINCTURE OF BUCHU

(tĭnc-tū'rą bū'ċhū)

Teinture (alcoolé) de Buchu, *Fr. Cod.;* Teinture de Bucco, *Fr.;* Buchutinktur, *G.*

"Buchu Leaves, in No. 20 powder, 200 *grammes;* Alcohol (60 per cent.) sufficient to produce, 1000 *millilitres.* Moisten the powder with two hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture has the virtues of buchu leaves.

Dose, from one to two fluidrachms (3.75–7.5 mils), either simply diluted with water or as an addition to the infusion of the leaves.

TINCTURA CALUMBÆ. U. S., Br.

TINCTURE OF CALUMBA Tr. Calumb.

(tĭnc-tū'rą cą-lŭm'bæ)

Tinctura Colombo; Teinture (alcoolé) de Colombo, *Fr. Cod.;* Kolombotinktur, *G.;* Tintura alcoholica de colombo, *Sp.*

* "Calumba, in No. 20 powder, *two hundred grammes* [or 7 ounces av., 24 grains]; to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), packing the moistened drug moderately, and using a mixture of *three volumes* of alcohol and *two volumes* of water as the menstruum." *U. S.*

"Calumba Root, in No. 20 powder, 100 *grammes;* Alcohol (60 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

This tincture was doubled in strength at the U. S. P. (VIII) in order to bring it into the class of 20 per cent. non-potent tinctures. The British tincture 1914 retains the strength of 10 Gm. of drug in each 100 mils.

Joseph Ince recommends that the tincture be prepared from the root as found in commerce, without further slicing or powdering it. Made as he proposes, the tincture is clear and bright; while if the powdered root is used it will be very turbid, even after filtration. (*P. J.,* xiv, 491.) No. 20 powder is now directed instead of the No. 50 powder used in older Pharmacopœias. Tincture of calumba may be added to tonic infusions or decoctions, to increase their stimulant power, but, like all the other bitter tinctures, should be used with caution.

Dose, of the U. S. tincture one-half to one fluidrachm (1.8–3.75 mils), of the Br. tincture one to two fluidrachms (3.75–7.5 mils).

TINCTURA CANNABIS. U. S. (Br.)

TINCTURE OF CANNABIS Tr. Cannab. [Tinctura Cannabis Indicæ, U.S.P. VIII]

(tĭnc-tū'rą căn'ną-bĭs)

"When assayed biologically Tincture of Cannabis produces incoördination when administered to dogs in a dose of not more than 0.3 mil per kilogramme of body weight." *U. S.*

Tinctura Cannabis Indicæ, *Br.*; Tincture of Indian Hemp; Tincture of Hemp; Teinture (alcoolé) de Chanvre de l'Inde, *Fr. Cod.*; Indischhanftinktur, *G.*

* "Cannabis, in No. 40 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P, as modified for assayed tinctures (see page 1160), using alcohol as the menstruum, and adjusting the volume of the finished Tincture to conform with the above biological standard." *U. S.*

"Extract of Indian Hemp, 50 *grammes;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Dissolve." *Br.*

"Assay.—Proceed as directed under Biological Assays (Part III)." *U. S.* (Also see *Cannabis*, p. 279).

Tincture of cannabis is assayed by tests upon dogs and it is generally advisable, for this purpose, to concentrate the tincture to about one-fourth its bulk. Care should be observed in the process of evaporation that the temperature does not rise above 60° C. (140° F.).

The American reader must take care not to confound the Indian Hemp here referred to with *Apocynum cannabinum*, known by the same name in this country. The term "Indian Hemp" should be dropped entirely, as its continued use has been the cause of at least one fatal mistake. The strength of the present tincture is about 33 per cent. less than that of the 1890 tincture.

Dose, ten to thirty minims (0.6–1.8 mils), to be gradually increased until some effects are experienced.

Off. Prep.—Tinctura Chloroformi et Morphinæ Composita, *Br.* Mistura Chloroformi et Morphinæ Composita. *N. F.*

TINCTURA CANTHARIDIS. U. S. (Br.)

TINCTURE OF CANTHARIDES Tr. Canthar. [Cantharidis tinctura P.I.]

(tĭnc-tū'rą cąn'thăr'ĭ-dĭs)

Tinctura Cantharidini, *Br*; Tincture of Cantharidin; Tincture of Spanish Flies; Teinture (alcoolé) de Cantharide, *Fr. Cod.*; Tinctura Cantharidum, *P. G.*; Spanischfliegentinktur, *G.*; Tinctura di cantaridi, *It.*; Tinctura alcoholica de cantaridas, *Sp.*

* "Cantharides, in No. 60 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Alcohol, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Place the cantharides in a strong tin container, which has a capacity of not less than *two thousand mils* [or 67 fluidounces, 301 minims]. Add *one thousand mils* of alcohol, agitate the mixture thoroughly, and insert in the opening of the can a tightly fitting cork through which passes a glass tube, not less than 6.4 mm. in diameter and 75 cm. in length. Place the can in a water bath and maintain a temperature of from 50° to 55° C. (122°–131° F.) for twenty-four hours with frequent agitation. Then remove it from the water bath, pour the contents into a cylindrical percolator, in the neck of which has been placed a pledget of purified cotton, allow the percolation to proceed, and, after the liquid has disappeared from the surface and ceased to drop from the percolator, gradually pour on sufficient alcohol to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of Tincture." *U. S.*

"Cantharidin, 0.1 *gramme;* Chloroform, 10.0 *millilitres;* Alcohol (90 per cent.) sufficient to produce, 1000.0 *millilitres.* Dissolve the Cantharidin in the Chloroform, and add sufficient of the Alcohol to produce the required volume. This tincture contains approximately one-seventh of the proportion of Cantharidin contained in the Tinctura Cantharidis of the International Agreement; it contains approximately the same proportion of Cantharidin as the Tinctura Cantharidis of the British Pharmacopœia, 1898." *Br.*

An improvement was made in this tincture in the 1880 revision by substituting alcohol for diluted alcohol. It is frequently used in mixtures of castor oil and alcohol in the so-called hair tonics, and when made with diluted alcohol turbidity results. The official tincture is double the strength of that of the U. S. P. 1890 and is now in conformity with the provisions of the International Protocol. It is the most convenient form for the internal use of Spanish flies, the virtues of which it possesses to their full extent. (See *Cantharis.*) If made with diluted alcohol, when long kept it deposits fatty matter, cantharidin in rhomboidal tables, and other crystals of a quite different form. It is occasionally employed externally as a rubefacient; but its liability to vesicate should be taken into consideration. The British tincture, 1914, is made by dissolving the blistering principle, cantharidin, in chloroform and alcohol. It is about the strength of the tincture of the Br. Pharm., 1898.

Dose, of the U. S. tincture, one to three minims (0.06–0.2 mil); of the Br., two to five minims (0.12–0.3 mil).

TINCTURA CAPSICI. U. S., Br.

TINCTURE OF CAPSICUM Tr. Capsic.

(tĭnc-tū'rą căp'sĭ-cī)

Tincture of Cayenne Pepper; Teinture (alcoolé) de Piment des Jardins, *Fr.*; Tinctura capsici, *P. G.*; Spanischpfeffertinktur, *G.*

* "Capsicum, in No. 50 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using a mixture of *ninety-five volumes* of alcohol and *five volumes* of water as the menstruum." *U. S.* "Capsicum, in No. 20 powder, 50 *grammes;* Alcohol (60 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

The U. S. P. tincture is double the strength of the British. The alcoholic strength of the menstruum is of unusual proportions, 19 volumes of alcohol to 1 volume of water, the reason for this is that, on account of oleoresinous constituents of capsicum, alcohol is required and on account of a small quantity of a constituent

soluble in water and insoluble in alcohol a little water must be added to the menstruum to prevent cloudiness. It is used in atonic conditions of the stomach, especially in *alcoholic gastritis.* It may also be used locally in various sluggish conditions of the throat and for the various purposes for which red pepper is applicable. (See *Capsicum.*) Applied by means of camel's-hair pencil to the *relaxed uvula,* it sometimes produces contraction and relieves prolapsus of that part.

Dose, of the U. S. tincture, five to ten minims (0.3–0.6 mil); of the Br. preparation, ten to twenty minims (0.6–1.3 mils).

Off. Prep.—Tinctura Chloroformi et Morphinæ Composita, *Br.;* Mistura Chloroformi et Morphinæ Composita, *N. F.;* Mistura Opii et Chloroformi Composita, *N. F.;* Mistura Opii et Rhei Composita, *N. F.*

TINCTURA CARDAMOMI. U. S.

TINCTURE OF CARDAMOM Tr. Cardam.

(tĭnc-tū'rą cär-dą-mō'mī)

Teinture (alcoolé) de Cardamome, *Fr.;* Kardamomentinktur, *G.*

* "Cardamom Seed, in No. 40 powder, *one hundred and fifty grammes* [or 5 ounces av., 127 grains], to make *onè thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using diluted alcohol as the menstruum." *U. S.*

The strength of this tincture was doubled in the U. S. P. (VIII) in order to bring it into the 20 per cent. class; it is an agreeable but strong aromatic, and may be advantageously added to tonic and purgative infusions.

Dose, one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA CARDAMOMI COMPOSITA. U. S., Br.

COMPOUND TINCTURE OF CARDAMOM Tr. Cardam. Co.

(tĭnc-tū'rą cär-dą-mō'mī cǫm-pŏş'ĭ-tą)

Teinture de Cardamome composée, *Fr.;* Zusammengesetzte Kardamomentinktur, *G.*

* "Cardamom Seed, in No. 40 powder, *twenty grammes* [or 308.6 grains]; Saigon Cinnamon, in No. 60 powder, *twenty-five grammes* [or 386 grains]; Caraway, in No. 40 powder, *twelve grammes* [or 185 grains]; Cochineal, in No. 60 powder, *five grammes* [or 77 grains]. To make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), macerating the mixed powders in *seven hundred and fifty mils* [or 25 fluidounces, 173 minims] of a mixture of *fifty mils* [or 1 fluidounce, 331 minims] of glycerin and *nine hundred and fifty mils* [or 32 fluidounces, 59 minims] of diluted alcohol and completing the preparation by using first the remainder of the mixture prepared as directed above and then diluted alcohol." *U. S.* "Cardamom Seeds, in No. 20 powder, 14 *grammes;* Caraway Fruit, in No. 20 powder, 14 *grammes;* Cinnamon Bark, in No. 20 powder, 28 *grammes;* Cochineal, in No. 20 powder, 7 *grammes;* Glycerin, 100 *millilitres;* Alcohol (45 per cent.) sufficient to produce 1000 *millilitres.* Moisten the mixed powders with fifty millilitres of the Alcohol, and prepare, by the *percolation process,* eight hundred and fifty *millilitres* of tincture. Add the Glycerin and sufficient of the Alcohol to produce the required volume." *Br.*

In this tincture and the one immediately preceding, the proportion of cardamom seems to be reduced, but official cardamom seed now means the seed recently removed from the capsules.

This is a very agreeable aromatic tincture, occasionally used as a carminative, but more frequently as an addition to mixtures, infusions, etc., which it renders pleasant to the taste and acceptable to the stomach. It is one of the most highly prized vehicles, not merely because of its pleasant flavor, but also on account of its beautiful color. The substitution of glycerin in the U. S. formula of 1880 for the honey formerly used was an improvement, as it increases the stability of the preparation.

Dose, one to two fluidrachms (3.75–7.5 mils).

TINCTURA CASCARILLÆ. Br.

TINCTURE OF CASCARILLA

(tĭnc-tū'rą căs-cą-rĭl'læ)

Teinture (alcoolé) de Cascarille, *Fr. Cod.;* Kaskarilltinktur, *G.*

"Cascarilla, in No. 40 powder, 200 *grammes;* Alcohol (70 per cent.) sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred and fifty *millilitres* of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture has the properties of cascarilla, but is seldom, if ever, used in this country.

Dose, from thirty minims to two fluidrachms (1.8–7.5 mils).

TINCTURA CHIRATÆ. Br.

TINCTURE OF CHIRETTA

(tĭnc-tū'rą ċhĭ-rā'tæ)

Tincture of Chirata; Teinture (alcoolé) de Chirette, *Fr.;* Chirettatinktur, *G.*

"Chiretta, in No. 40 powder, 100 *grammes;* Alcohol (60 per cent.) sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture is used as a bitter tonic. Although no longer recognized by the U. S. P., it is still prescribed in this country. The tincture of the U. S. 1890 was of twenty per cent. strength.

Dose, from one to two fluidrachms (3.75–7.5 mils), three or four times a day.

TINCTURA CHLOROFORMI ET MORPHINÆ COMPOSITA. Br.

COMPOUND TINCTURE OF CHLOROFORM AND MORPHINE

(tĭnc-tū'rą ¢hlō-rǫ-fōr'mī ĕt mör-phī'næ cǫm-pŏs'ĭ-tą)

"Chloroform, 75 *millilitres;* Morphine Hydrochloride, 10 *grammes;* Diluted Hydrocyanic Acid, 50 *millilitres;* Tincture of Capsicum, 25 *millilitres;* Tincture of Indian Hemp, 100 *millilitres;* Oil of Peppermint, 2 *millilitres;* Glycerin, 250 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres.* Mix the Chloroform, Tincture of Capsicum, Tincture of Indian Hemp, Oil of Peppermint, and Glycerin, with four hundred and fifty *millilitres* of the Alcohol, and dissolve the Morphine Hydrochloride in the mixture; add the Diluted Hydrocyanic Acid, and sufficient of the Alcohol to produce the required volume. This Compound Tincture contains in 1 millilitre 7.5 centimils of Chloroform, 1 centigram of Morphine Hyrochloride, and 5 centimils of Diluted Hydrocyanic Acid; it contains in 10 minims ¾ minim of Chloroform, ⅓ grain of Morphine Hydrochloride, and ½ minim of Diluted Hydrocyanic Acid." *Br.*

This is the official substitute for *chlorodyne,* the well-known British nostrum. It does not differ from the process of the Br. Pharm. 1898, except that the oil of peppermint was increased from 1.5 mils to 2 mils. It is much stronger than the *Mistura Opii et Chloroformi Composita* of the N. F. IV (see Part III).

Dose, from five to fifteen minims (0.3–0.9 mil).

TINCTURA CINCHONÆ. U. S., Br.

TINCTURE OF CINCHONA Tr. Cinch.

(tĭnc-tū'rą cĭn-¢hō'næ)

"One hundred mils of Tincture of Cinchona yields not less than 0.8 Gm. nor more than 1 Gm. of the alkaloids of cinchona." *U. S.* "Tincture of Cinchona contains in 100 millilitres 1 gramme of the alkaloids of Red Cinchona Bark." *Br.*

Tinctura Cinchonæ Flavæ; Tincture of Yellow Cinchona; Tincture of Peruvian Bark; Teinture (alcoolé) de Quinquina jaune, *Fr. Cod.;* Tinctura Chinæ, *P. G.;* Chinatinktur, *G.;* Tintura di china, *It.*

* "Cinchona, in No. 40 powder, *two hundred grammes* [or 7 ounces av., 24 grains]; to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P, as modified for assayed tinctures (see page 1160), using as the first menstruum a mixture of *seventy-five mils* [or 2 fluidounces, 257 minims] of glycerin, *six hundred and seventy-five mils* [or 22 fluidounces, 396 minims] of alcohol, and *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of water and completing the percolation with a mixture of *two volumes* of alcohol and *one volume* of water. Then adjust the volume of the finished Tincture so that each *one hundred mils* contains 0.9 Gm. of the alkaloids of cinchona." *U. S.*

"Red Cinchona Bark, in No. 40 powder, 200 *grammes;* Alcohol (70 per cent.), a sufficient quantity. Moisten the powder with two hundred *millilitres* of the Alcohol; set aside for seven days in a closed vessel; percolate with more of the Alcohol, until seven hundred *millilitres* of percolate have been collected; press the marc; add the expressed liquid to the percolate; set aside for twenty-four hours; filter.

"Take ten millilitres of the strong tincture so prepared, and determine the proportion of alkaloids contained in it by the process described under 'Extractum Cinchonæ Liquidum.' Add to the bulk of the strong tincture such a quantity of the Alcohol that 100 millilitres of the resulting Tincture contain 1 gramme of the alkaloids of Red Cinchona Bark. Examined by the process described under 'Extractum Cinchonæ Liquidum' Tincture of Cinchona is found to contain in 100 millilitres 1 gramme of the alkaloids of Red Cinchona Bark. *Limit of error* 0.05 gramme in excess or defect." *Br.*

Assay.—"Evaporate 25 mils of Tincture of Cinchona on a water bath until it measures about 15 mils, add 10 Gm. of purified sawdust (see Reagents, Part III), incorporate this thoroughly and then continue the evaporation at a temperature not exceeding 80° C. (176° F.) until it is dry. Transfer the impregnated sawdust to a 500 mil flask, and proceed as directed in the assay under *Cinchona,* page 350, fourth line of the Assay, modifying the process there given by increasing the ammonia water to 10 mils and using this in divided portions to rinse the dish in which the mixture was evaporated; then add the rinsings to the flask." *U. S.*

This tincture is very properly made with a large proportion of bark, as in the bitter tinctures it is important that the alcohol should bear as small a proportion to the tonic principle as possible. Even when strongest, however, it cannot, in ordinary cases, be given in doses sufficiently large to obtain the full effect of the bark, without stimulating too highly. The tincture of the Br. Pharm. 1898 and 1914 is now made from 70 per cent. alcohol instead of the old menstruum 50 per cent., and is assayed so that it has a definite strength (100 mils containing 1 Gm. of alkaloids); these are undoubted improvements. A deposit is apt to form in the tincture when kept, consisting chiefly of cinchonic red holding probably a portion of the alkaloids in combination. This was found by J. Adams to be perfectly dissolved by heat, though it uniformly reappeared on the cooling of the tincture. The addition of diluted sulphuric acid did not cause its solution, and, even though it was removed by filtering the tincture, the deposition was afterwards renewed. (*P. J.,* April, 1868, 470.) In reference to a mode of obviating in some measure this tendency to deposition, the reader is referred to the statements of M. Vauflart on the subject of deposition in the tinctures prepared by percolation. A. B. Taylor, in experimenting on this subject, prepared a tincture in which the menstruum consisted of two parts of alcohol, one part of water,

and one part of glycerin, and which was kept three months without undergoing deposition. (*A. J. P.*, Jan. 1865, 50.) This suggested the addition of glycerin to the official formula, and there can be no doubt that the tincture has been thereby improved, experience having demonstrated the utility of glycerin in liquid preparations of cinchona. Tincture of cinchona is rarely employed, but may be used as a tonic.

Dose, from one to two fluidrachms (3.75–7.5 mils).

Off. Prep.—Tinctura Cinchonæ Composita, *Br.*

TINCTURA CINCHONÆ COMPOSITA. U. S., Br.

COMPOUND TINCTURE OF CINCHONA Tr. Cinch. Co.

(tĭnc-tū'rą cĭn-ȼhō'næ cǫm-pŏs'ı̣-tą)

"*One hundred mils* of Compound Tincture of Cinchona yields not less than 0.4 Gm. nor more than 0.5 Gm. of the alkaloids of cinchona." *U. S.* "Compound Tincture of Cinchona contains in 100 millilitres 0.5 gramme of the alkaloids of Red Cinchona Bark." *Br.*

Compound Tincture of Peruvian Bark; Huxham's Tincture of Bark; Teinture de Quinquina composée, Elixir fébrifuge d'Huxam, *Fr.*; Tinctura Chinæ Composita, *P. G.*; Zusammengesetzte Chinatinktur, *G.*

* "Red Cinchona, in No. 40 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Bitter Orange Peel, in No. 40 powder, *eighty grammes* [or 2 ounces av., 360 grains]; Serpentaria, in No. 60 powder, *twenty grammes* [or 308.6 grains], to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P, as modified for assayed tinctures (see page 1160), using as the first menstruum a mixture of *seventy-five mils* [or 2 fluidounces, 257 minims] of glycerin, *six hundred and seventy-five mils* [or 22 fluidounces, 396 minims] of alcohol and *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of water and completing the percolation with a mixture of *two volumes* of alcohol and *one volume* of water. Then adjust the volume of the finished Tincture so that each *one hundred mils* contains 0.45 Gm. of the alkaloids of cinchona." *U. S.*

"**Assay.**—Proceed as directed in the assay under *Tinctura Cinchonæ,* page 1136, modifying the process there given by using 50 mils of the Compound Tincture instead of 25 mils of the tincture there directed." *U. S.*

"Dried Bitter-Orange Peel, bruised, 50 *grammes;* Serpentary Rhizome, in No. 40 powder, 25 *grammes;* Cochineal, in powder, 3 *grammes;* Tincture of Cinchona, 500 *millilitres;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Mix the solid ingredients with five hundred millilitres of the Alcohol; set aside in a closed vessel for seven days, shaking frequently; strain, and then press; mix the two liquids thus obtained; add the Tincture of Cinchona, and sufficient of the Alcohol to produce the required volume; set aside for twenty-four hours; filter. Examined by the process described under 'Extractum Cinchonæ Liquidum' Compound Tincture of Cinchona is found to contain in 100 millilitres 0.5 gramme of the alkaloids of Red Cinchona Bark. *Limit of error* 0.05 gramme in excess or defect." *Br.*

This is the preparation commonly known by the name of *Huxham's tincture of bark.* It differs from that official in the U. S. P., 1890, only in the alcoholic strength of the menstruum, which is now about in the proportion of 2.7 volumes of alcohol to 1 volume of water; it was formerly 3 volumes of alcohol to 1 volume of water. The use of glycerin is an improvement, precipitation being thus largely prevented. In the U. S. P. VIII the drugs are not directed in the powdered state, the intention being to mix the drugs together and then to reduce the mixture to a *uniform* powder; in this way the volatile principles in the Serpentaria and Orange Peel are retained, and thorough exhaustion by percolation is secured. In the U. S. P. IX this principle was omitted probably on account of the difficulty of its execution. The process for the British tincture (1898) presents some novel features. Half of the quantity of the tincture is first made from four of the ingredients; this is then mixed with an equal bulk of tincture of cinchona. The reason for this was probably to avoid assaying a mixed product during the process; but the final test has to deal with the finished tincture, and the utility of the whole method is doubtful. Compound tincture of cinchona is an excellent bitter tonic, useful for its local effect on the stomach but too feeble in the principles of cinchona to serve when the systemic action of the drug is required.

Dose, one to two fluidrachms (3.75–7.5 mils).

Off Prep.—Gargarisma Guaiaci Composita, *N. F.*

TINCTURA CINNAMOMI. U. S., Br.

TINCTURE OF CINNAMON Tr. Cinnam.

(tĭnc-tū'rą cĭn-ną-mō'mī)

Teinture (alcoolé) de Cannelle, *Fr. Cod.*; Tinctura Cinnamomi, *P. G.*; Zimmttinktur, *G.*; Tinctura alcoholica de canela, *Sp.*

* "Saigon Cinnamon, in No. 50 powder, *two hundred grammes* [or 7 ounces av., 24 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using a mixture of *seventy-five volumes* of glycerin, *six hundred and seventy-five volumes* of alcohol, and *two hundred and fifty volumes* of water as the menstruum." *U. S.*

"Cinnamon Bark, in No. 40 powder, 200 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with two hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

The British and the U. S. tinctures are now of the same strength. This tincture has the aromatic and astringent properties of cinnamon, and may be used as an adjuvant to cretaceous mixtures and astringent infusions or decoctions.

By long keeping it is prone to gelatinize and become unfit for use. According to Greenish, this can be prevented by using a menstruum composed of six parts of alcohol and two parts of water. (*P. J.*, Feb. 1872, 641). Glycerin is now used in the menstruum for this purpose. It is an agreeable flavoring to other tinctures and because of its astringent powers is especially used in *diarrhea* mixtures.

Dose, one to two fluidrachms (3.75–7.5 mils).

Off. Prep.—Elixir Taraxaci Compositum, *N. F.;* Mistura Rhei Alkalina, *N. F.*

TINCTURA COCCI. Br.

TINCTURE OF COCHINEAL

(tĭnc-tū'rą cŏc'cī)

Teinture (alcoolé) de Cochenille, *Fr. Cod.;* Cochenilletinktur, *G.*

"Cochineal, in powder, 100 *grammes;* Alcohol (45 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

This is valued chiefly for imparting color to liquid preparations; four or five per cent. of this tincture will give a deep red color. (See *Coccus.*)

Dose, from twenty minims to a fluidrachm (1.3–3.75 mils).

TINCTURA COLCHICI SEMINIS. U. S. (Br.)

TINCTURE OF COLCHICUM SEED Tr. Colch. Sem.

[Colchici tinctura P. I.]

(tĭnc-tū'rą cŏl'çhį-cī sĕm'į-nīs)

"*One hundred mils* of Tincture of Colchicum Seed yields not less than 0.036 Gm. nor more than 0.044 Gm. of colchicine." *U. S.*

Tinctura Colchici, *Br.;* Tincture of Colchicum; Tinctura Colchici, *U. S.* 1890; Teinture (alcoolé) de semence de Colchique, *Fr. Cod.;* Tinctura Colchici, *P. G.;* Zeitlosentinktur, *G.;* Tintura alcoholica de colquico, *Sp.*

* "Colchicum Seed, in No. 50 powder, *one hundred grammes* [or 3 ounces av., 231 grains], to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P, as modified for assayed tinctures (see page 1160), using a mixture of *three volumes* of alcohol and *two volumes* of water as the menstruum and adjusting the volume of the finished Tincture so that each *one hundred mils* contains 0.04 Gm. of colchicine." *U. S.*

"Colchicum Seeds, in No. 30 powder, 100 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with fifty millilitres of the Alcohol, and complete the *percolation process.* This Tincture is of approximately the same strength as the Tinctura Colchici of the International Agreement, and is of one-half the strength of the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

Assay.—"Evaporate 150 mils of Tincture of Colchicum Seed on a water bath to about 20 mils, transfer it to a 50 mil graduated flask and rinse the evaporating dish with about 10 mils of distilled water, in divided portions. Then add 10 mils of solution of lead subacetate, shake the mixture thoroughly, add enough distilled water to make 50 mils and pour this into a 500 mil flask. Now add 250 mils of recently boiled distilled water, using part of the water to rinse the 50 mil flask, and proceed as directed in the assay under *Colchici Semen,* page 371, twelfth line of the Assay, beginning with the words 'filter off 200 mils.'" *U. S.*

The strength of this tincture was lowered to 10 Gm. per 100 mils in the U. S. P. VIII and IX to comply with the rule adopted for potent tinctures. An assay process was also appended.

It was at one time supposed that the tincture was quite as effective made from the unbruised as from the bruised seeds, but the opinion has been shown to be erroneous. (*A. J. P.*, xxvi, 120.) See also a paper by N. Rosenwasser, *Ibid.*, 1877, 436. Subsequently L. I. Morris showed that if the whole seeds were *digested* with hot diluted alcohol they could be perfectly exhausted. (*A. J. P.*, 1881, p. 6.) Maisch recommended, as a convenient method of comminuting the seeds, to macerate them for two or three days in a portion of the menstruum, then to remove them and bruise them in a clean iron mortar, taking care that none of the menstruum or of the seeds should be wasted. (*A. J. P.*, xxviii, 514.)

This tincture possesses the properties of colchicum, and may be given whenever that medicine is indicated, but the fluidextract, containing less alcohol, is generally preferred.

Dose, from fifteen to thirty minims (0.9–1.8 mils), to be repeated with caution.

TINCTURA CUBEBÆ. Br.

TINCTURE OF CUBEBS

(tĭnc-tū'rą cū-bĕ'bæ)

Teinture (alcoolé) de Cubèbe, *Fr. Cod.;* Kubebentinktur, *G.*

"Cubebs, in No. 20 powder, 200 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

The U. S. P. has not recognized this tincture for many years, but it is official in the N. F. (see Part III). While this tincture represents the therapeutic virtue of cubeb, it is an inelegant form of administering that drug.

Dose, one to two fluidrachms (3.75–7.5 mils).

TINCTURA DATURÆ SEMINUM. Br.

TINCTURE OF DATURA SEEDS

(tĭnc-tū'rą dă-tū'ræ sē'mĭ-nŭm)

"Datura Seeds, in No. 20 powder, 250 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the bruised Datura Seeds with two hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture well represents the activities of *datura*.

Dose, five to fifteen minims (0.3–0.9 mil).

TINCTURA DIGITALIS. U. S., Br.

TINCTURE OF DIGITALIS Tr. Digit.
[Digitalis tinctura P. I.]

(tĭnc-tū'rą dĭg-ĭ-tā'lĭs)

"If assayed biologically the minimum lethal dose should not be greater than 0.006 mil of the Tincture, or the equivalent in Tincture of 0.0000005 Gm. of ouabain, for each gramme of body weight of frog." *U. S.*

Tincture of Foxglove; Teinture (alcoolé) de Digitale, *Fr. Cod.*; Tinctura Digitalis, *P. G.*; Fingerhuttinktur, *G.*; Tintura di digitale, *It.*; Tintura alcoholica de digital, *Sp.*

* "Digitalis, in No. 60 powder, *one hundred grammes* [or 3 ounces av., 231 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using a mixture of *three volumes* of alcohol and *one volume* of water as the menstruum." *U. S.*

"**Assay.**—For a method of assaying Tincture of Digitalis, see Biological Assays (Part III)." *U. S.*

"Digitalis Leaves, in No. 20 powder, 100 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres*. Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process*. This Tincture is of approximately the same strength as the Tinctura Digitalis of the International Agreement, and is of four-fifths the strength of the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

For method of biological assay of this tincture, see *Digitalis*.

It seems well established that the tincture of digitalis deteriorates more rapidly than well-kept leaves. The rate of deterioration of the tincture is probably from 10 to 20 per cent. a year, although it may be higher under unfavorable conditions. There is much evidence that a tincture of digitalis made with 60 or 70 per cent. of alcohol retains its activity better than that made with more dilute spirit; hence the wisdom of increasing the strength of alcohol. According to Focke, light accelerates the change. For literature upon this subject, see Eberhardt and Eldred. (*J. A. Ph. A.*, 1914, iii, p. 38.)

Tincture of digitalis probably represents the crude drug better than any other official preparation. The beginning dose is ordinarily from five to fifteen minims (0.3–0.9 mil) three or four times a day, increased cautiously as circumstances demand. Very much larger single doses may be employed, thus as high as a fluidrachm may occasionally be given at a dose if not repeated.

It should be remembered that, as with most of the tinctures, one minim is equivalent to about two drops.

Dose, from five to thirty minims (0.3–1.8 mils).

TINCTURA ERGOTÆ AMMONIATA. Br.

AMMONIATED TINCTURE OF ERGOT

(tĭnc-tū'rą ęr'gŏ-tæ ąm-mō-nĭ-ā'tą)

Tinctura Secalis Cornuti Ammoniata; Teinture Ammoniacale de Seigle Ergoté, *Fr.*; Ammoniakalische Mutterkorntinktur, *G.*

"Ergot, in No. 20 powder, 250 *grammes;* Solution of Ammonia, 100 *millilitres;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres*. Mix the Solution of Ammonia with nine hundred millilitres of the Alcohol; moisten the powder with one hundred millilitres of this mixture, and percolate with the remainder; press the marc; mix the expressed liquid with the percolate; add sufficient of the Alcohol to produce the required volume; set aside for twenty-four hours; filter." *Br.*

This is a new official tincture of the Br. Ph., 1898; it differs from the tincture recommended by the British Pharmaceutical Conference in the use of solution of ammonia in place of aromatic spirit of ammonia.

Dose, from one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA FERRI CHLORIDI. U. S. (Br.)

TINCTURE OF FERRIC CHLORIDE Tr. Ferr. Chlor.

(tĭnc-tū'rą fĕr'rī ęhlō'rĭ-dī)

"A hydro-alcoholic solution containing ferric chloride [$FeCl_3 = 162.22$] (about 13 per cent.), corresponding to not less than 4.48 per cent. of Fe. Protect Tincture of Ferric Chloride from light." *U. S.*

Tinctura Ferri Perchloridi, *Br.*; Tincture of Chloride of Iron; Tincture Ferri Muriatis; Tincture of Perchloride of Iron; Tincture of Muriate of Iron; Tinctura Ferri Sesquichloridi; Teinture de Perchlorure de fer, *Fr.*; Eisenchloridtinktur, *G.*

* "Solution of Ferric Chloride, *three hundred and fifty mils* [or 11 fluidounces, 401 minims]; Alcohol, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix the solution with enough Alcohol to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms], then transfer the Tincture to an amber-colored, glass-stoppered bottle and keep it for at least three months before dispensing." *U. S.*

"Strong Solution of Ferric Chloride, 250 *millilitres;* Alcohol (90 per cent.), 250 *millilitres;* Distilled Water, sufficient to produce 1000 *millilitres*. Mix." *Br.*

This tincture does not differ materially from that official in 1880, the change due to making one by weight and the other by volume, and the rounding of the figures, causing a difference in specific gravity—the U. S. P., 1880, tincture having the sp. gr. 0.980 and the U. S. P., 1890, tincture that of 0.960, the latter thus being slightly lighter. In the U. S. P. VIII the quantity of Solution of Ferric Chloride used in making 1000 mils of the tincture was increased from 250 mils to 350 mils on account of the reduction in strength of the solution from

13 per cent. of metallic iron to 10 per cent. This increases the specific gravity to about 1.00. The strength of the new tincture, in ferric chloride, remains practically the same as the 1890 preparation.

The U. S. formula of 1870 appeared, in respect to the precise method of proceeding, to be copied from that of E. R. Squibb, published in *A. J. P.* (1857, p. 290). Iron wire was chosen as the form of iron to be used, because it is generally the purest. This, which was in very slight excess, was first treated with a portion of the hydrochloric acid, which formed with it ferrous chloride, with the escape of hydrogen, producing effervescence. The action was allowed to go on spontaneously until effervescence ceased, and was then aided by heat, which caused the saturation of the acid used. The solution being filtered, the remainder of the hydrochloric acid was added, and afterwards the nitric acid gradually, the liquid having been heated to the boiling point before the latter addition. The nitric acid was decomposed, with the escape of nitrous fumes producing effervescence, while, through the influence of a portion of its oxygen and the additional portion of hydrochloric acid, the ferrous chloride was converted into ferric chloride, the conversion being completed when the effervescence ceased and the previous green color had been changed to a reddish-brown. The precise reactions by which these changes are effected have been explained elsewhere. (See *Ferri Chloridum*, page 464, and *Liquor Ferri Chloridi*, page 634.) In the revision of 1870 the process was divided into two parts, and a new preparation, *Liquor Ferri Chloridi*, introduced. When this is added to the alcohol, the latter reacts gradually with the acid, producing a small proportion of an ester which gives a peculiar flavor to the tincture and probably modifies in some degree its influence on the system. For this reason it is preferable to keep the tincture a year before dispensing, and the official direction is to keep it at least three months.

Properties.—Tincture of ferric chloride is officially described as "a bright, amber-colored liquid, having a slightly ethereal odor, a very astringent, styptic taste, and an acid reaction. Specific gravity: about 1.00 at 25° C. (77° F.). The Tincture yields a brownish-red precipitate with ammonia water, a blue precipitate with potassium ferrocyanide T.S., and a white precipitate, insoluble in nitric acid, with silver nitrate T.S. After the Tincture has been exposed for some time to daylight, it yields a greenish or greenish-blue color with potassium ferricyanide T.S. (presence of some *ferrous salt*, due to reduction). Add a clear crystal of ferrous sulphate to a cooled mixture of equal volumes of concentrated sulphuric acid and a diluted portion of the Tincture (1 in 10); the crystal does not become brown, nor is a brownish-black zone developed around it (*nitric acid*).

"**Assay.**—Evaporate to dryness in a porcelain dish on a water bath about 5 mils of Tincture of Ferric Chloride, accurately weighed in a tared weighing-bottle. Add 2 mils of hydrochloric acid and 5 mils of solution of hydrogen dioxide to the residue and again evaporate the mixture to dryness. Dissolve this residue in 25 mils of distilled water, transfer the solution to a 250 mil glass-stoppered flask, mix it with 3 mils of hydrochloric acid and about 1 Gm. of potassium iodide, and allow the mixture to stand for thirty minutes at a temperature of 40° C. (104° F.). Cool the solution, add 100 mils of distilled water and titrate the liberated iodine with tenth-normal sodium thiosulphate V.S. It shows not less than 4.48 per cent. of Fe.

"Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.005584 Gm. of Fe. Each gramme of Tincture of Ferric Chloride corresponds to not less than 8 mils of tenth-normal sodium thiosulphate V.S." *U. S.*

The tincture is decomposed by the alkalies, alkaline earths and their carbonates, astringent vegetable infusions, and mucilage of acacia, which produces with it a brown semi-transparent jelly. All these substances are, therefore, incompatible with it in prescriptions.

Bestucheff's tincture, which is much used in Europe, is simply a solution of ferric chloride in a mixture of one measure of ether and three measures of alcohol. (See *Tinctura Ferri Chloridi Etherea*, N. F. IV.)

Uses.—Tincture of chloride of iron has in the past been attributed with curative properties verging on the mystical. Thus it has been supposed to exercise a specific action in *erysipelas*, *diphtheria*, and other infectious diseases. Its value in these states, however, is, to say the least, questionable. In *Bright's disease* it has been used not only for its chalybeate effect but with the idea that its astringent action would lessen the quantity of albumin in the urine. As it is an active coagulant of albumin, however, it cannot exist in the blood and therefore can never reach the kidney unchanged; any beneficial effect which may follow its employment in diseases of the kidney is of the same nature as that which is produced by other preparations of iron, namely, an enrichment of the hemoglobin content of the blood. In *anemias* it acts as a chalybeate, but is inferior to many other salts of iron. In the first place a dose of fifteen minims represents only approximately 0.7 grain of iron. In the second place, because of its high astringency and local irritant effect it cannot be administered in large quantities without producing disturbances in the stomach. Locally it is valuable as an astringent in *hemorrhages* and passive congestions of the mucous membrane. Mixed with equal parts of glycerin and water it may be applied by means of a swab with benefit in various types of *pharyngitis*. Its use as a gargle is not to be recommended as its acidity makes it injurious to the teeth.

Dose, five to thirty minims (0.3–1.8 mils), which may be gradually increased.

Off. Prep.—Liquor Ferri et Ammonii Acetatis, *U. S.*

TINCTURA GAMBIR COMPOSITA. U. S. (Br.)

COMPOUND TINCTURE OF GAMBIR Tr. Gambir Co. [Compound Tincture of Pale Catechu To replace Tincture Catechu Composita, U. S. 1890, Compound Tincture of Catechu]

(tĭnc-tū′rą găm′bĭr cọm-pŏș′ĭ-tą)

Tinctura Catechu, *Br.;* Tincture of Catechu; Teinture (alcoolé) de Cachou, *Fr. Cod.;* Tinctura Catechu, *P. G.;* Katechutinktur, *G.*

* "Gambir, in No. 50 powder, *fifty grammes* [or 1 ounce av., 334 grains]; Saigon Cinnamon, in No. 50 powder, *twenty-five grammes* [or 386 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), using diluted alcohol as the solvent." *U. S.*

"Catechu, in powder, 200 *grammes;* Cinnamon Bark, bruised, 50 *grammes;* Alcohol (45 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

The name of this tincture was changed at the 1880 revision, so that it more accurately indicated its composition than did its former name. In the U. S. P. (8th Rev.) the name was again changed to Tinctura Gambir Composita. This was due to the introduction of gambir in place of catechu (see *Gambir*). The present tincture is one-half the strength of the U. S. P., 1890, compound tincture of catechu. Cinnamon has been present in the tincture of catechu of former Pharmacopœias in the same relatively large proportion—2 parts of cinnamon to 3 parts of catechu—and this disproportion has been usually overlooked. The present tincture contains 2 parts of gambir to 1 part of cinnamon. The British tincture (1898) was increased to 20 per cent. in the proportion of catechu, and is now four times the strength of the U. S. tincture. This is a grateful astringent tincture, useful in all cases to which catechu is applicable and in which small quantities of spirit are not objectionable. It may often be advantageously added to cretaceous mixtures in *diarrhea.* It may be given with sweetened water or some mucilaginous liquid, or in port wine when this is not contra-indicated. It sometimes gelatinizes when kept, and becomes unfit for use.

Dose, of the U. S. tincture of gambir, two to four fluidrachms (7.5–15.0 mils); of the British tincture of catechu, one-half to two fluidrachms (1.8–7.5 mils).

Off. Prep.—Tinctura Pectoralis, *N. F.*

TINCTURA GELSEMII. U. S., Br.

TINCTURE OF GELSEMIUM Tr. Gelsem.

(tĭnc-tū′rą ǧęl-sĕm′ĭ-ī)

Teinture (alcoolé) de Gelsemium, *F.;* Gelsemiumtinktur, *G.*

* "Gelsemium, in No. 60 powder, *one hundred grammes* [or 3 ounces av., 231 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using a mixture of *sixty-five volumes* of alcohol and *thirty-five volumes* of water as the menstruum." *U. S.*

"Gelsemium Root, in No. 40 powder, 100 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with fifty millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture has proven a valuable addition, and will be preferred to the fluidextract for internal administration, as it is safer, and can be used more satisfactorily in extemporaneous combination. The menstruum of the U. S. P., 1890, and VIII and IX processes is weaker than that formerly official, alcohol having been replaced by alcohol diluted with water in the proportion of 65 to 35. For Farr and Wright's method of estimating this tincture, see *C. D.,* 1892, 263.

Dose, from five to twenty minims (0.3–1.3 mils).

TINCTURA GENTIANÆ COMPOSITA. U. S., Br.

COMPOUND TINCTURE OF GENTIAN Tr. Gentian. Co.

(tĭnc-tū′rą ǧĕn-tĭ-ā′næ cọm-pŏș′ĭ-tą)

Teinture (alcoolé) de Gentiane Composée, *Fr.;* Zusammengesetzte Enziantinktur, *G.*

* "Gentian, in No. 40 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Bitter Orange Peel, in No. 40 powder, *forty grammes* [or 1 ounce av., 180 grains]; Cardamom Seed, in No. 40 powder, *ten grammes* [or 154 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), packing it moderately and using as the first menstruum a mixture of *one hundred mils* [or 3 fluidounces, 183 minims] of glycerin, *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol and *four hundred mils* [or 13 fluidounces, 252 minims] of water and completing the percolation with diluted alcohol." *U. S.*

"Gentian Root, cut small and bruised, 100.0 *grammes;* Dried Bitter-Orange Peel, bruised, 37.5 *grammes;* Cardamom Seeds, in powder, 12.5 *grammes;* Alcohol (45 per cent.), 1000.0 *millilitres.* Prepare by the *maceration process.*" *Br.*

There has always been difficulty from precipitation in this tincture; glycerin has been added to the menstruum to overcome this annoyance, but it is only partially successful. This is an elegant bitter, much used in *dyspepsia,* and as an addition to tonic mixtures in debilitated states of the digestive organs. There is, however, much danger of its abuse by alcoholics, especially in chronic cases.

Dose, one to two fluidrachms (3.75–7.5 mils).

TINCTURA GUAIACI. U. S.

TINCTURE OF GUAIAC Tr. Guaiac.

(tĭnc-tū′rą guaĭ′ą-cī)

Tinctura Guajaci; Teinture (alcoolé) de Résine de Gayac, *Fr.;* Guajaktinktur, *G.*

* "Guaiac, in No. 40 powder, *two hundred grammes* [or 7 ounces av., 24 grains], to make

one thousand mils [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), using alcohol as the solvent." *U. S.*

Although this tincture can be prepared by percolation if care and skill are used, maceration is doubtless preferable.

This tincture is given in *chronic rheumatism* and *gout,* in the dose of from one to three fluidrachms three or four times a day. As it is precipitated by water, it is most conveniently administered in mucilage, sweetened water, or milk, by which the separated guaiac is held in temporary suspension, although it is almost impossible, without actual emulsification, to prevent the resinous material from separating and forming a coating on the inner surface of the bottle. Schär recommends tincture of guaiac as a reagent to detect the presence of ozonizing bodies. (*Ph. Rund.,* 1894, 254.)

Dose, one fluidrachm (3.75 mils) three times a day.

Off. Prep.—Mistura Guaiaci, *N. F.*

TINCTURA GUAIACI AMMONIATA. U. S., Br.

AMMONIATED TINCTURE OF GUAIAC Tr. Guaiac. Ammon.

(tĭnc-tū'rą guaĭ'ą-cī ąm-mō-nī-ā'tą)

Ammoniated Tincture of Guaiacum; Tinctura Guaiaci Composita; Teinture (alcoolé) de Gayac ammoniacale, *Fr.*; Ammoniakalische Guajaktinktur, *G.*

* "Guaiac, in No. 40 powder, *two hundred grammes* [or 7 ounces av., 24 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), using aromatic spirit of ammonia as the solvent." *U. S.*

"Guaiacum Resin, in powder, 200 *grammes;* Oil of Nutmeg, 3 *millilitres;* Oil of Lemon, 2 *millilitres;* Strong Solution of Ammonia, 75 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Mix the Strong Solution of Ammonia with seven hundred millilitres of the Alcohol; add the Guaiacum Resin; set aside in a closed vessel for forty-eight hours, shaking frequently; filter; dissolve the Oil of Lemon and Oil of Nutmeg in the filtrate, and pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

The British Pharmacopœia, 1898, improved the process for this tincture by abandoning the distilled aromatic spirit of ammonia used as a menstruum by the former British authority and substituting alcohol containing solution of ammonia and volatile oils, the proportion of oil of lemon having been reduced 60 per cent.

This tincture is celebrated in the treatment of *chronic rheumatism,* and is frequently also used in *amenorrhea.* It is more stimulating, and is probably more effectual, than the preceding on account of the presence of the alkali. It is precipitated by water, and should be administered emulsified with gum, so that the guaiac may be held in suspension.

Dose, from one to two fluidrachms (3.75–7.5 mils).

Off. Prep.—Gargarisma Guaiaci Composita, *N. F.*

TINCTURA HAMAMELIDIS. Br.

TINCTURE OF HAMAMELIS

(tĭnc-tū'rą hăm-ą-mĕl'ĭ-dĭs)

Teinture (alcoolé) de Hamamélis, *Fr.*; Hamamelistinktur, *G.*; Tinctura alcoholica de hamamelis, *Sp.*

"Hamamelis Bark, in No. 20 powder, 100 *grammes;* Alcohol (45 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with fifty millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

Dose, from thirty to sixty minims (1.8–3.75 mils).

TINCTURA HYDRASTIS. U. S., Br.

TINCTURE OF HYDRASTIS Tr. Hydrast. [Tincture of Golden Seal]

(tĭnc-tū'rą hȳ-drăs'tĭs)

"*One hundred mils* of Tincture of Hydrastis yields not less than 0.36 Gm. nor more than 0.44 Gm. of the ether-soluble alkaloids of hydrastis." *U. S.*

Teinture (alcoolé) de Hydrastis, *Fr.*; Hydrastistinktur, *G.*; Tintura alcoholica de hidrastis, *Sp.*

* "Hydrastis, in No. 60 powder, *two hundred grammes* [or 7 ounces av., 24 grains], to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P, as modified for assayed tinctures (see page 1160), using a mixture of *two volumes* of alcohol and *one volume* of water as the menstruum and adjusting the volume of the finished Tincture so that each *one hundred mils* contains 0.4 Gm. of the ether-soluble alkaloids of hydrastis." *U. S.*

"Assay.—Evaporate 50 mils of Tincture of Hydrastis on a water bath until it measures about 10 mils, transfer the evaporated liquid to a separator, and proceed as directed in the assay under *Fluidextractum Belladonnæ Radicis,* page 486, second line of the Assay, beginning with the words "add 10 mils," modifying the process there given by using the ammonia water with about 5 mils of distilled water, in divided portions, to rinse out the dish in which the Tincture was evaporated. Use only ether as the immiscible solvent throughout the assay and dry the residue at 100° C. (212° F.) to constant weight, instead of titrating it. The weight of the residue represents the amount of ether-soluble alkaloids in 50 mils of Tincture of Hydrastis." *U. S.*

"Liquid Extract of Hydrastis, 100 *millilitres;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Mix." *Br.*

The British tincture is half the strength of that of the U. S. P. IX.

This tincture is useful in combination with other tinctures, or as an addition to extem-

poraneous mixtures where the fluidextract would not be so eligible.

Dose, from one to two fluidrachms (3.75–7.5 mils).

TINCTURA HYOSCYAMI. U. S., Br.

TINCTURE OF HYOSCYAMUS Tr. Hyosc. [Tincture of Henbane Hyoscyami tinctura P. I.]

(tĭnc-tū'rą hȳ-ǫs-cȳ'ą-mī)

"*One hundred mils* of Tincture of Hyoscyamus yields not less than 0.0055 Gm. nor more than 0.0075 Gm. of the alkaloids of hyoscyamus." *U. S.*

Teinture (alcoolé) de Jusquiame, *Fr.*; Bilsenkrauttinktur, *G.*; Tintura alcoholica de beleno, *Sp.*

* "Hyoscyamus, in No. 60 powder *one hundred grammes* [or 3 ounces av., 231 grains], to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P, as modified for assayed tinctures (see page 1160), using diluted alcohol as the menstruum and adjusting the volume of the finished Tincture so that each *one hundred mils* contains 0.0065 Gm. of the alkaloids of hyoscyamus." *U. S.*

"Assay.—Evaporate 250 mils of Tincture of Hyoscyamus on a water bath to about 10 mils, transfer the evaporated liquid to a separator, and proceed as directed in the assay under *Fluidextractum Belladonnæ Radicis,* page 486, second line of the Assay, beginning with the words "add 10 mils," modifying the process there given by increasing the ammonia water to 5 mils which, with 5 mils of distilled water, is to be used, in divided portions, to rinse the dish in which the Tincture was evaporated; before titrating treat the residue twice with 5 mils of ether, evaporating to dryness each time." *U. S.*

"Hyoscyamus Leaves, in No. 20 powder, 100 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

The strength of the British tincture (1898) was slightly reduced (20 per cent.) in order to bring it into the class of tinctures having the maximum dose of a fluidrachm. The strength was also reduced in the U. S. P. VIII and IX from 15 to 10 Gm. per 100 mils, and an assay process appended. The Br. and U. S. tinctures are now of the same strength.

This tincture possesses the activities of hyoscyamus. When it purges, as it sometimes does, it may be united with a very small proportion of tincture of opium.

Dose, one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA IODI. U. S. (Br.)

TINCTURE OF IODINE Tr. Iodi.

(tĭnc-tū'rą ī-ō'dī)

"An alcoholic solution of iodine and potassium iodide. *One hundred mils* contains not less than 6.5 Gm. nor more than 7.5 Gm. of I (126.92) and not less than 4.5 Gm. nor more than 5.5 Gm. of KI (166.02)." *U. S.*

Tinctura Iodi Mitis, *Br.*; Weak Tincture of Iodine; Tinctura Iodi Fortis, *Br.*; Strong Tincture of Iodine; Tinctura Iodinii, *U. S.*, 1870; Teinture (alcoolé) d'iode, *Fr. Cod.*; Tinctura Jodi, *P. G.*; Jodtinktur, *G.*; Solucion alcoholica de yodo, *Sp.*

* "Iodine, *seventy grammes* [or 2 ounces av., 205 grains]; Potassium Iodide, *fifty grammes* [or 1 ounce av., 334 grains]; Distilled Water, *fifty mils* [or 1 fluidounce, 331 minims]; Alcohol, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the potassium iodide in the distilled water contained in a bottle graduated to *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]; add the iodine and agitate the mixture until solution is effected. Then add sufficient alcohol to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of Tincture, and mix thoroughly." *U. S.*

"Assay for Potassium Iodide.—Evaporate 10 mils of Tincture of Iodine in a tared porcelain dish on a water bath and gently heat the residue over a Bunsen flame to volatilize the iodine; it leaves a residue weighing not less than 0.45 Gm. nor more than 0.55 Gm., which corresponds to the identity tests under *Potassii Iodidum.*

"Assay for Iodine.—Mix 5 mils of the Tincture with 25 mils of distilled water and titrate the solution with tenth-normal sodium thiosulphate V.S.; it requires not less than 25.6 mils nor more than 29.6 mils of tenth-normal sodium thiosulphate V.S. for complete decoloration.

"Each mil of tenth-normal sodium thiosulphate V.S. corresponds to 0.012692 Gm. of I." *U. S.*

In the British Pharmacopœia 1914 an important change was made in the names of the liquid preparations of iodine. The name has been changed from Tinctura Iodi to Tinctura Iodi Mitis, but the strength remains the same. Liquor Iodi Fortis now becomes Tinctura Iodi Fortis. The strength has been slightly increased.

Weak Tincture of Iodine (*Br.*).

"Iodine, 25 *grammes;* Potassium Iodide, 25 *grammes;* Distilled Water, 25 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve the Potassium Iodide and Iodine in the Distilled Water; add sufficient of the Alcohol to produce the required volume." *Br.*

"10 millilitres of the Tincture, diluted with 20 millilitres of *water,* require for decolorisation not less than 19.2 or more than 19.8 millilitres of *N/10 solution of sodium thiosulphate.* This Weak Tincture contains 0.025 gramme of Iodine in each millilitre; 1 minim contains about 1/44 grain. It is not of the same strength as the Tinctura Iodi of the International Agreement. It contains the same proportion of Iodine as the Tinctura Iodi of the British Pharmacopœia, 1898." *Br.*

Strong Tincture of Iodine (*Br.*).

"Iodine, 100 *grammes;* Potassium Iodide, 60

grammes; Distilled Water, 100 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Dissolve the Potassium Iodide and the Iodine in the Distilled Water; add sufficient of the Alcohol to produce the required volume." *Br.*

"Five millilitres of the Tincture, diluted with 20 millilitres of *water,* require for decolorisation not less than 38.4 or more than 39.6 millilitres of *N/10 solution of sodium thiosulphate.* This Strong Tincture contains 0.1 gramme of Iodine in each millilitre; 1 minim contains about 1/11 grain. It is of approximately the same strength as the Tinctura Iodi of the International Agreement. It contains approximately the same proportion of Iodine as the Liquor Iodi Fortis of the British Pharmacopœia, 1898. *Br.*

An important change was made in the formula of tincture of iodine in the U. S. P. VIII by the addition of about 5 per cent. of potassium iodide; this improvement not only permits the dilution of the tincture with water without precipitating the iodine, so that the tincture can now be administered internally, but it also particularly increases the stability of the tincture.

When tincture of iodine made as in previous pharmacopœias by solution of iodine (alone) in alcohol was allowed to stand subjected to varying conditions for two months, the loss in iodine was as high as 7 per cent.; on the other hand the loss in iodine with tincture containing 5 per cent. of potassium iodide was not appreciable in the same length of time under similar treatment. The addition of potassium iodide also causes the iodine to dissolve rapidly in the alcohol, and in the U. S. P. IX formula, a small amount of water aids solution. The compound solution of iodine made with water is retained, and is most suitable for internal administration. (See *Liquor Iodi Compositus.*) The iodine should be thoroughly dried before being weighed out. The tincture should be kept in well-stoppered bottles, in order to prevent the evaporation of the alcohol. It should never be dispensed in cork-stoppered vials, because of the destructive action of the iodine on the cork; rubber or glass stoppers should be used.

L. F. Kebler (*J. Ind. & E. C.,* 1913, p. 484) reports the results of analyses of a number of samples collected in pharmacies in the District of Columbia in which the iodine content ranged from 1.97 Gm. to 9.26 Gm. in 100 mils and the potassium iodide content from 0.0 to 6.82 Gm. in 100 mils.

J. W. Mardin (*J. A. P. A.,* 1913, p. 1464) gives a method of determining the alcohol in this preparation by a series of factors based upon the alternations in sp. gr. produced respectively by potassium iodide and iodine and gives tables which may be consulted for the determination by this method.

Properties.—The tincture has a deep brown color. One grain of iodine is contained in about fifteen minims, or thirty drops. It is at present less used internally than it formerly was, in consequence of an impression that it is apt to irritate the stomach. Water decomposes the tincture when it contains no potassium iodide and it is supposed that when this is swallowed the iodine is precipitated upon the mucous membrane. Besides, the tincture undergoes a gradual change when long kept, owing, according to Guibourt, to a reaction between the alcohol and the iodine. A portion of the latter is supposed to take hydrogen from the former, producing hydriodic acid, which dissolves another portion of the iodine to form iodized hydriodic acid, while the place of the hydrogen in the alcohol is supplied by iodine, giving rise to ethyl iodide and similar products. The new products have an agreeable odor and are soluble in water; and consequently the tincture gradually loses by time the property of being precipitated on dilution. A. Göpel found the change to be so slow, when the tincture is kept in the dark and at a low temperature, that in three months a specimen thus treated had lost but one per cent. of iodine. Commaille confirmed the labors of the last-mentioned investigator. Subsequent experiments have, however, given results somewhat at variance with those of Guibourt. Carles found that after exposure in a transparent glass flask to diffuse daylight for ten months, the tincture contained only one-twelfth per cent. of hydriodic acid. He was also unable to find any of the ethyl iodide which, according to Guibourt, is formed simultaneously with the acid. (*P. J.,* 3d ser., v. 88.)

Uses.—Tincture of iodine is now employed almost exclusively for its local effects. It is a powerful local irritant acting somewhat slowly but with great persistence. If applied too freely it will produce an acute dermatitis with desquamation of the cuticle. It is a favorite remedy as a counter-irritant in inflammations of the joint, especially when of a more or less chronic type, thus it is widely employed in *sprains* after the stage of acute inflammation has subsided, in *chronic rheumatism, arthritis deformans, gout, chilblains, myalgias,* and the like. In *scrofulous glands* and chronic rheumatic conditions it is often applied with the idea of obtaining the local counter-irritant effect as well as the constitutional action of the iodine from absorption through the skin. While it is true that if evaporation is guarded against perceptible amounts of iodine may be absorbed, after the application of the tincture to the skin as ordinarily employed, the quantity taken up by the system is insignificant. The irritant action of tincture of iodine is also made use of for the obliteration of serous cavities, as in the radical cure of *hydrocele* or *ovarian dropsies.*

As pointed out on page 592, iodine is a powerful germicide and within the last few years the tincture of iodine has become a valuable addition to the surgeon's armamentarium against infections. It is used for the purpose of sterilizing the skin, before operation or for hypodermic injections, for disinfecting *wounds* and in infections of accessible mucous membranes as of the nose and throat. It is also employed as a local remedy in the treatment

of *erysipelas,* but its application requires some caution and it is better to surround the inflamed surface with a border of the tincture, embracing a portion of both the sound and diseased skin with the idea of preventing the progress of the inflammation, than to attempt a complete cure by covering the whole surface affected.

Under the title of *colorless tincture of iodine* (*Tinctura Iodi Decolorata*) various combinations manufactured from tincture of iodine have been prepared. These preparations are calculated to mislead practitioners, for they contain no free iodine and therefore have not the therapeutic virtues of the official tincture, but are variable mixtures consisting principally of ammonium iodide and various other compounds of iodine. (See *Tinctura Iodi Decolorata,* N. F. IV, Part III.)

The former German tincture contains in addition some ethyl iodide, triethyl-ammonium iodide, and traces of sodium iodide and sulphate. Luc has found the inhalation of the fumes from slightly warmed tinctures very useful in *coryza.*

Lugol's solution (*Liquor Iodi Compositus,* page 646) is a much preferable preparation for the internal administration of iodine. Debauque, an apothecary of Mons, has ascertained that tannic acid has the property of rendering iodine soluble in water, and states that an ounce of syrup of orange-peel in four or six ounces of water will form a clear solution with a quantity of tincture of iodine containing five or six grains of the medicine. (*J. P. C.,* 3e sér., xx, 34.)

Dose, one to five minims (0.06–0.3 mil).

TINCTURA JALAPÆ. Br.

TINCTURE OF JALAP

(tĭnc-tū′rą ją-lā′pæ)

Teinture (alcoolé) de Jalap, *Fr. Cod.;* Jalapentinktur, *G.*

"Jalap, in No. 40 powder, 200 *grammes;* Alcohol (70 per cent.), *a sufficient quantity.* Moisten the powder with one hundred millilitres of the Alcohol; pack in a percolator; gradually add more of the Alcohol until six hundred millilitres of percolate have been collected; press the marc; add the expressed liquid to the percolate; set aside for twenty-four hours; filter. Determine the amount of Jalap Resin present in ten millilitres of the strong tincture so prepared by the process described under 'Jalapæ Resina,' and dilute the remainder of the strong tincture with sufficient of the Alcohol to produce a Tincture of Jalap containing 1.5 grammes of the Resin in 100 millilitres. When 10 millilitres of the Tincture, concentrated by evaporation, are mixed with eight times their volume of *water,* the resin thus separated, washed with *water* and dried at a gentle heat, weighs not less than 0.145 or more than 0.155 gramme." *Br.*

This tincture is no longer official in the U. S. Pharmacopœia, but is in the N. F. IV (see Part III). The tincture of jalap of the U. S. P. 1870 was made by percolating six troy-ounces of powdered jalap with a mixture of two measures of alcohol and one of water, until two pints of tincture were obtained.

This tincture is now prepared on the basis of proportion of resin, not of crude drug, as formerly. It possesses the medicinal virtues of jalap, and is sometimes added to cathartic mixtures.

Dose, one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA JALAPÆ COMPOSITA. Br.

COMPOUND TINCTURE OF JALAP

(tĭnc-tū′rą ją-lā′pæ cŏm-pŏs′ĭ-tą)

"Jalap, in No. 40 powder, 80 *grammes;* Scammony Resin, in powder, 15 *grammes;* Turpeth, in No. 40 powder, 10 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the mixed powders with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture is also official in the N. F. IV (see Part III). It is a harsh but active purgative, capable of producing serious effects if given in over-dose.

Dose, one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA KALADANÆ. Br.

TINCTURE OF KALADANA

(tĭnc-tū′rą kă-lą-dā′næ)

"Kaladana, in No. 40 powder, 200 *grammes;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This is a new tincture of the British Pharmacopœia 1914. It is used as a cathartic in doses of one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA KINO. U. S., Br.

TINCTURE OF KINO Tr. Kino

(tĭnc-tū′rą kī-nō)

Teinture (alcoolé) de Kino, *Fr. Cod.;* Kinotinktur, *G.*

* "Kino, *one hundred grammes* [or 3 ounces av., 231 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Place the kino in a capacious flask and pour on it *five hundred mils* [or 16 fluidounces, 435 minims] of boiling water. Agitate the mixture thoroughly, then heat it on a water bath, containing boiling water, for one hour, shaking it frequently. Allow the liquid to cool, add enough recently boiled water to make the product measure *five hundred mils* [or 16 fluidounces, 435 minims] and then add *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol. Stopper the flask, set it aside in a cool place for twenty-four hours and then decant the mixture through cheese cloth. Preserve it in a cool and dark place, in small bottles, tightly corked." *U. S.*

"Kino, in powder, 100 *grammes;* Glycerin, 150 *millilitres;* Distilled Water, 250 *millilitres;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Mix the Glycerin and the Distilled Water; rub the Kino in a mortar with a sufficient quantity of the mixture to form a smooth paste, gradually adding the remainder of the mixture; transfer to a closed vessel; add five hundred millilitres of the Alcohol; set aside for twelve hours, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

Much inconvenience is caused by the tendency of this tincture to gelatinize and gradually lose its astringency. The present official formula is believed to furnish a tincture free from this objection. It is probable that different specimens of kino vary in their tendency to gelatinize. Groves states that fresh kino will not gelatinize, and Martindale that the Australian kino is much more prone to do so than the East India drug. The air has some effect, for if this be entirely excluded the tincture will keep for a long time without undergoing the change. It should be introduced, when prepared, into very small bottles, which should be kept well corked and be opened only when wanted for use. J. D. Wood obtains a handsome preparation, which he believes to keep well and not gelatinize, by using a menstruum of 2 parts of alcohol sp. gr. 0.835, and 1 part each of water and glycerin.

L. Meyers Connor gets rid of the gelatinizing property by using magnesium carbonate in making the tincture, but it is very probable that a large part of the kino-tannic acid is removed at the same time. (*A. J. P.,* xlv, 260.) P. F. Smith of Louisville, furnished the following formula: "Take of Kino *one ounce and a half;* Ground Logwood *half an ounce;* Diluted Alcohol *a sufficient quantity.* Moisten the Logwood with a portion of the Diluted Alcohol, and introduce it into a displacement apparatus. Dissolve the Kino by triturating with successive portions of Diluted Alcohol, and percolate the solution through the Logwood until a pint of tincture is obtained." We have used this process and have not noticed gelatinization to take place in any instance. Sugar added in equal proportions with the kino employed has been recommended as a preventive of gelatinization, and R. Rother claims permanence for the following formula: Powder one and a half troyounces of kino and half a troyounce of catechu, mix them, add ten fluidounces of water, heat for ten or fifteen minutes with constant stirring, and let the mixture cool. Add water to make the mixture twelve fluidounces, and then add four fluidounces of alcohol. Pour the mixture into a bottle containing sixty grains of filter-paper, shake the whole well at intervals, and strain the tincture after twenty-four hours. (*A. J. P.,* 1886, 333.)

An important change in the process of the U. S. Pharmacopœia VIII was the employment of heat. This was due to the researches of Edmund White (*P. J.,* 1903, May, 644, and Nov., 702), who with David Hooper believes that the gelatinization of tincture of kino is due to an enzyme or oxydase present in the kino; the activity of this is destroyed by heat. Tincture of kino is one of the most frequently prescribed astringents, especially in the treatment of *diarrhea.*

Dose, one to two fluidrachms (3.75–7.5 mils).

Off. Prep.—Tinctura Kino et Opii Composita, *N. F.*

TINCTURA KRAMERIÆ. Br.

TINCTURE OF KRAMERIA

(tĭnc-tū'rą krą-mē'rī-æ)

Tincture of Rhatany; Teinture (alcoolé) de Ratanhia, *Fr. Cod.;* Tinctura Ratanhiæ, *P. G.;* Ratanhiatinktur, *G.*

Tincture of krameria was deleted from the U. S. P. IX, but retained in the Br. Pharm. 1914 and added to the N. F. IV (see Part III). The British tincture closely resembles the former U. S. P. preparation.

"Krameria Root, in No. 40 powder, 200 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

It is stated that the tincture made from Pará rhatany furnishes a clear solution on the addition of water, while that from Peruvian root yields a turbid mixture.

The same precaution should be observed in keeping this tincture as is recommended for tincture of kino. It is a good preparation in cases which admit of the use of small quantities of alcohol.

Dose, one or two fluidrachms (3.75 or 7.5 mils).

TINCTURA LACTUCARII. U. S.

TINCTURE OF LACTUCARIUM Tr. Lactucar.

(tĭnc-tū'rą lăc-tū-cā'rĭ-ī)

Teinture (alcoolé) de Lactucarium, *Fr.;* Lactucariumtinktur, *G.*

* "Lactucarium, *five hundred grammes* [or 17 ounces av., 279 grains]; Glycerin, *two hundred and fifty mils* [or 8 fluidounces, 218 minims]; Alcohol, Purified Petroleum Benzin, Diluted Alcohol, Water, each, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Beat the lactucarium with clean sand, in an iron mortar, to a coarse powder, and then transfer it to a bottle; add *two thousand mils* [or 67 fluidounces, 301 minims] of purified petroleum benzin, cork the bottle tightly, and set it aside for forty-eight hours, frequently agitating the mixture. Pour the mixture on a double filter, cover the funnel, and, when the liquid has passed through the filter, wash the residue gradually with *fifteen hundred mils* [or 50 fluidounces, 345 minims] of purified petroleum benzin, and allow the lactucarium to dry by exposing it to a current of air. When it is dry and free from the odor of benzin, reduce it to a powder, using more sand, if necessary, and pack it moderately in a conical percolator. Mix the

glycerin with *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of water, and *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol, and gradually pour this mixture on the powder. When the liquid begins to drop from the percolator, close the lower orifice, and having closely covered the percolator, macerate for twenty-four hours. Then allow the percolation to proceed slowly, gradually adding first the remainder of the menstruum, and then diluted alcohol until the drug is exhausted. Reserve the first *seven hundred and fifty mils* [or 25 fluidounces, 173 minims] of the percolate, evaporate the remainder on a water bath, at a temperature not exceeding 70° C. (158° F.), until it measures *two hundred and fifty mils* [or 8 fluidounces, 218 minims], and mix this with the reserved portion. Filter the mixed liquids and wash the filter with sufficient diluted alcohol to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of Tincture." *U. S.*

This tincture was first official in the U. S. 1890. It is based on the formula of J. L. Lemberger, who recommended the extraction of the resinous inert lactucerin by treatment with petroleum benzin. Great care must be observed to use *purified* petroleum benzin, as it is almost impossible to get rid of the odor and taste of petroleum in the finished preparation if the ordinary benzin be used. It is as useless as the other preparations of lactucarium.

Dose, half to one fluidrachm (1.8–3.75 mils).

Off. Prep.—Syrupus Lactucarii, *U. S.*

TINCTURA LAVANDULÆ COMPOSITA. U. S., Br.

COMPOUND TINCTURE OF LAVENDER Tr. Lavand. Co. [Compound Spirit of Lavender]

(tĭnc-tū'rą lą-văn'dŭ-læ cŏm-pŏs'ĭ-tą)

Spiritus Lavandulæ Compositus, *U. S.* 1870; Lavender Drops; Teinture (alcoolé) de Lavande composée, *Fr.*; Zusammengesetzte Lavendeltinktur, *G.*

* "Oil of Lavender, *eight mils* [or 130 minims]; Oil of Rosemary, *two mils* [or 32 minims]; Saigon Cinnamon, in No. 50 powder, *twenty grammes* [or 308.6 grains]; Clove, in No. 50 powder, *five grammes* [or 77 grains]; Myristica, in No. 50 powder, *ten grammes* [or 154 grains]; Red Saunders, in No. 50 powder, *ten grammes* [or 154 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), macerating the powders in a mixture of *seven hundred and fifty mils* [or 25 fluidounces, 173 minims] of alcohol, in which the oils have been dissolved, and *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of water. Complete the preparation with a mixture of *three volumes* of alcohol and *one volume* of water." *U. S.*

"Oil of Lavender, 5.0 *millilitres;* Oil of Rosemary, 0.5 *millilitre;* Cinnamon Bark, bruised, 10.0 *grammes;* Nutmeg, bruised, 10.0 *grammes;* Red Saunders Wood, rasped, 20.0 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000.0 *millilitres.* Macerate the solid ingredients and the Oils with nine hundred millilitres of the Alcohol for seven days, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

The compound tincture of lavender of the U. S. Pharmacopœia is nearly twice the strength of the British preparation, although it is made with a menstruum weaker in alcohol. When properly prepared it is an excellent preparation to be used for *gastric uneasiness, nausea,* and *flatulence.*

Dose, from thirty minims to a fluidrachm (1.8–3.75 mils).

TINCTURA LIMONIS CORTICIS. U. S. (Br.)

TINCTURE OF LEMON PEEL Tr. Limon. Cort.

(tĭnc-tū'rą lĭ-mō'nĭs cŏr'tĭ-cĭs)

Tinctura Limonis, *Br.;* Tincture of Lemon; Teinture (alcoolé) de Zeste de Citron, *Fr.;* Citronenschalentinktur, *G.*

* "Lemon Peel, grated from the fresh fruit, *five hundred grammes* [or 17 ounces av., 279 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), macerating the drug in *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of alcohol and completing the preparation with alcohol. Use purified cotton as the filtering medium." *U. S.*

"Lemon Peel, cut small, 250 *grammes;* Alcohol (90 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

Tincture of lemon peel was a new official preparation of the U. S. P. VIII. Spirit of lemon made from oil of lemon was abandoned, because the poor quality of the oil with which it was likely to be made caused it to have a terebinthinate flavor. The 50 per cent. tincture made by macerating fresh lemon peel in alcohol was proposed by Scoville and the present formula produces a very satisfactory preparation.

This tincture was doubled in strength at the 1898 revision of the Br. Pharm., but is now only about one-half the strength of the U. S. tincture. It is made with strong alcohol instead of proof spirit formerly used. It forms a grateful aromatic addition to tonic infusions, etc.

Dose, from one to two fluidrachms (3.75–7.5 mils).

Off. Prep.—Syrupus Acidi Citrici, *U. S.*

TINCTURA LOBELIÆ. U. S.

TINCTURE OF LOBELIA Tr. Lobel. [Lobeliæ tinctura P. I.]

(tĭnc-tū'rą lo-bē'lĭ-æ)

Teinture (alcoolé) de Lobélie enflée, *Fr. Cod.;* Tinctura Lobeliae, *P. G.;* Lobelientinktur, *G.;* Tintura di lobelia, *It.;* Tintura alcoholica de lobelia, *Sp.*

* "Lobelia, in No. 50 powder, *one hundred grammes* [or 3 ounces av., 231 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process

P (see page 1160), using diluted alcohol as the menstruum." *U. S.*

The strength of this tincture is the same as that of the U. S. P. VIII, which is one-half that of the U. S. 1890. For method of assay, see *C. D.*, 1893, 454; also *P. J.*, 1895, 141. It possesses the emetic and narcotic properties of lobelia, and is much used in *asthma.* A saturated tincture is strongly recommended by A. Livezey as a local application in *erysipelas,* and in the *eczematous eruption* of *Rhus poisoning.* (*B. M. S. J.*, lv, 262.)

Dose, as an expectorant, fifteen to thirty minims (0.9–1.8 mils).

TINCTURA LOBELIÆ ÆTHEREA. Br.

ETHEREAL TINCTURE OF LOBELIA

(tĭnc-tū'rą lo-bē'lĭ-æ æ-thē'rę-ą)

Teinture éthérée de Lobélie enflée, *Fr.*; Ätherische Lobelientinktur, *G.*

"Lobelia, in No. 40 powder, 200 *grammes;* Spirit of Ether, sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred *millilitres* of the Spirit of Ether, and complete the *percolation process.*" *Br.*

It should be noted that this tincture is twice the strength of the U. S. tincture and the International Protocol.

Dose, from five to fifteen minims (0.3–0.9 mils).

TINCTURA MOSCHI. U. S.

TINCTURE OF MUSK Tr. Mosch.

(tĭnc-tū'rą mŏs'ḳhī)

Teinture (alcoolé) de Musc, *Fr. Cod.*; Moschustinktur, *G.*; Tintura di muschio, *It.*; Tintura alcoholica de almizcle, *Sp.*

* "Musk, *five grammes* [or 77 grains]; Alcohol, *forty-five mils* [or 1 fluidounce, 250 minims]; Water, *forty-five mils* [or 1 fluidounce, 250 minims]; Diluted Alcohol, *a sufficient quantity,* to make *one hundred mils* [or 3 fluidounces, 183 minims]. Triturate the musk with the water gradually added until a smooth mixture is obtained; transfer this to a bottle and allow the mixture to macerate for twenty-four hours; then add the alcohol and macerate the mixture for six days, with occasional agitation. Transfer this mixture to a plain paper filter, and, when the liquid has drained off completely, wash the residue on the filter with sufficient diluted alcohol to make *one hundred mils* [or 3 fluidounces, 183 minims] of Tincture." *U. S.*

This tincture was reduced in strength about one-half in the U. S. P. 1890, on account of the greatly increased cost of musk. This change, in our opinion, was ill-advised, and does not secure the main object, as the patient will have to take double the dose, even if the alcohol be therapeutically contraindicated. The process has been arranged so as to make the end-product 100 mils, as very few pharmacists will require 1000 mils of tincture of musk. Musk will yield its virtues to the above menstruum if the process be followed; if wanted for its odor it will be economy to add a minim of solution of sodium hydroxide to the water used to rub the musk into a smooth paste. Care should be especially taken to use pure grain musk in this preparation.

Dose, from thirty minims to two fluidrachms (1.8–7.5 mils).

TINCTURA MYRRHÆ. U. S., Br.

TINCTURE OF MYRRH Tr. Myrrh.

(tĭnc-tū'rą mŷr'rhæ)

Teinture (alcoolé) de Myrrhe, *Fr. Cod.*; Tinctura Myrrhae, *P. G.*; Myrrhentinktur, *G.*; Tintura di mirra, *It.*; Tintura alcoholica de mirra, *Sp.*

* "Myrrh, in moderately coarse powder, *two hundred grammes* [or 7 ounces av., 24 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), using alcohol as the solvent." *U. S.*

"Myrrh, in coarse powder, 200 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Macerate the Myrrh with eight hundred millilitres of the Alcohol in a closed vessel for seven days, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

The strength of this tincture was increased 60 per cent. at the revision of the British Pharmacopœia (1898) and is now equivalent to the U. S. preparation.

Official alcohol is preferable to diluted alcohol as a solvent of myrrh, because it forms a perfectly clear tincture, which is not attainable with the latter menstruum. The addition of water to the tincture renders it turbid. According to E. B. Shuttleworth (*A. J. P.*, xliii, 369), the gum which is left behind in making the tincture may be utilized for making mucilage. The tincture of myrrh is used solely as a local application to stimulate *indolent and foul ulcers, spongy gums, aphthous sore mouth,* and *ulcerations of the throat.*

Dose, from fifteen to thirty minims (0.9–1.8 mils).

TINCTURA NUCIS VOMICÆ. U. S., Br.

TINCTURE OF NUX VOMICA Tr. Nuc. Vom. [Strychni tinctura P. I.]

(tĭnc-tū'rą nū'cĭs vŏm'ḭ-çæ)

"*One hundred mils* of Tincture of Nux Vomica yields not less than 0.237 Gm. nor more than 0.263 Gm. of the alkaloids of nux vomica." *U. S.* "Tincture of Nux Vomica contains in 100 millilitres 0.125 gramme of strychnine." *Br.*

Teinture (alcoolé) de Noix vomique, *Fr. Cod.*; Tinctura Strychni, *P. G.*; Brechnusstinktur, Krähenaugentinktur, *G.*; Tintura di noce vomica, *It.*; Tintura alcoholica de nuez vomica, *Sp.*

* "Nux Vomica, in No. 40 powder, *one hundred grammes* [or 3 ounces av., 231 grains], to make about *one thousand millilitres* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P, as modified for assayed

tinctures (see page 1160), using a mixture of *three volumes* of alcohol and *one volume* of water as the menstruum and adjusting the volume of the finished Tincture so that each *one hundred mils* contains 0.25 Gm. of the alkaloids of nux vomica. The rate of flow for the percolate should not exceed ten drops per minute." *U. S.*

"Liquid Extract of Nux Vomica, 50 *millilitres;* Distilled Water, 150 *millilitres;* Alcohol (90 per cent.), sufficient to produce 600 *millilitres.* Mix; filter if necessary. Examined by the process described under 'Extractum Nucis Vomicæ Liquidum,' Tincture of Nux Vomica is found to contain in 100 millilitres 0.125 gramme of strychnine. *Limit of error* 0.005 gramme in excess or defect. This Tincture contains in each millilitre 1.25 milligrams of strychnine; each fluidrachm contains about 1/16 grain. It contains approximately the same proportion of strychnine as the Tinctura Nucis Vomica of the International Agreement, and one-half of that contained in the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

Assay.—"Evaporate 100 mils of Tincture of Nux Vomica on a water bath until it measures about 10 mils, transfer the evaporated liquid to a separator, and proceed as directed in the assay under *Fluidextractum Belladonnæ Radicis,* page 486, second line of the Assay, beginning with the words 'add 10 mils,' modifying the process there given by using 5 mils of ammonia water with a little distilled water, in divided portions, to rinse the dish in which the Tincture was evaporated and by dissolving the residue in 10 mils of tenth-normal sulphuric acid V.S. instead of 5 mils.

"Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 36.4 milligrammes of the alkaloids of nux vomica." *U. S.*

In the U. S. VIII this tincture was made from the extract, the object being to secure a more reliable and definite tincture than was possible under the process official prior to 1890; for this reason 2 per cent. of the standardized extract was directed to be dissolved in a mixture of 3 volumes of alcohol and 1 volume of water. On account of the very tough structure of nux vomica, percolation was accomplished usually with varying results. The amount of extract present in the percolate was to some extent a measure of its activity; hence, if a weighed portion of the percolate was evaporated to dryness, and the percentage of dry extract noted, it was easy to calculate the amount present in the whole quantity. The standard for Tincture of Nux Vomica was changed in the U. S. P. IX from 0.1 Gm. of strychnine in 100 mils to 0.25 Gm. in 100 mils of the alkaloids of nux vomica and instead of making the tincture from a definite quantity of extract of nux vomica percolation of the powdered drug is used. It is true that the tincture must be assayed, and the pharmacist, for this reason, must depend on the manufacturer for his supply, as it is unprofitable to assay small quantities of the tincture. We believe that more uniform results were obtained for the U. S. P. VIII tincture than will be for that of the U. S. P. IX, although the U. S. P. IX process is supposed to give a product of a more uniform color, which was the principal defect in the U. S. P. VIII product.

The British Pharmacopœia standardizes the liquid extract (see page 496), and makes its tincture from it of such strength that 100 mils shall contain 0.125 Gm. of strychnine. R. Rother (*A. J. P.,* Jan., 1883), after experimenting with various substances, found that sodium chloride aided greatly in softening the bassorin-like substance in which the alkaloidal principles of nux vomica are embedded, and he proposes its use by adding it to the menstruum of diluted alcohol in the proportion of 120 grains to the pint (see *U. S. D.,* 16th ed., p. 1527).

The amount of strychnine in this tincture is so small that it is not to be recommended for producing the systemic effects of that alkaloid. Its most important use is as a bitter tonic in *gastric atony.*

Dose, of the tincture, ten to thirty minims (0.6–1.8 mils), to be increased if necessary.

Off. Prep.—Elixir Phosphori et Nucis Vomicæ, *N. F.*

TINCTURA OLIVERI CORTICIS. Br.

TINCTURE OF OLIVER'S BARK

(tĭnc-tū'rą ŏl-ĭ-vē'rī cŏr'tĭ-cīs)

"Oliver's Bark, in No. 40 powder, 100 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with fifty millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture has been used in Australia for a number of years and is now official in the Br. Pharm. 1914. It possesses the properties of an aromatic like cinnamon.

The *dose* is from one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA OPII. U. S., Br.

TINCTURE OF OPIUM Tr. Opii [Laudanum Opii tinctura P. I.]

(tĭnc-tū'rą ō'pĭ-ī)

"*One hundred mils* of Tincture of Opium yields not less than 0.95 Gm. nor more than 1.05 Gm. of anhydrous morphine." *U. S.* "Tincture of Opium contains in 100 millilitres 1 gramme of morphine, calculated as anhydrous." *Br.*

Tinctura Thebaica, Tinctura Meconii, Tinctura Extracti Opii; Teinture d'Extrait d'Opium, *Fr. Cod.;* Teinture (alcoolé) d'Opium, Teinture thébaïque, *Fr.;* Tinctura Opii Simplex, *P. G.;* Einfache Opiumtinktur, *G.;* Tintura di oppio, *It.;* Tintura alcoholica de opio, *Sp.*

* "Granulated Opium, *one hundred grammes* [or 3 ounces av., 231 grains]; Alcohol, Water, Diluted Alcohol, each, *a sufficient quantity,* to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]; Heat *four hundred mils* [or 13 fluidounces, 252 minims] of water to

boiling, and pour it on the granulated opium contained in a tared vessel, and weigh; then stir the mixture occasionally during twelve hours, restore the original weight by the addition of water, add *four hundred mils* [or 13 fluidounces, 252 minims] of alcohol, pour the mixture into a bottle, and continue the maceration for forty-eight hours, occasionally shaking the mixture. Then transfer the mixture to a percolator, return the first portion of the percolate until it runs through clear, and, when the original menstruum has ceased to drop, continue the percolation slowly, gradually adding sufficient diluted alcohol to make the percolate measure *nine hundred and fifty mils* [or 32 fluidounces, 59 minims]. Assay a portion of this percolate, as directed below, and, from the morphine content thus determined, ascertain by calculation the amount of anhydrous morphine in the remainder of the liquid and adjust the volume of the finished Tincture so that each *one hundred mils* contains 1 Gm. of anhydrous morphine." *U. S.*

U. S. Assay.—"Evaporate 80 mils of Tincture of Opium on a water bath until the alcohol is all removed. Then proceed as directed in the assay under *Opium,* page 817, twenty-third line of the Assay, beginning with the word 'Transfer.' The result of the assay indicates the amount of morphine obtained from 40 mils of the Tincture of Opium." *U. S.*

"Opium, 200 *grammes;* Alcohol (90 per cent.), Distilled Water, of each, *a sufficient quantity.* Rub the Opium to a paste with five hundred *millilitres* of Distilled Water, previously heated to at least 90° C. (194° F.); set aside for six hours; add five hundred *millilitres* of the Alcohol; mix thoroughly; set aside in a covered vessel for twenty-four hours; strain, and then press; mix the two liquids thus obtained; set aside for twenty-four hours; filter. Determine the proportion of morphine, calculated as anhydrous, in the strong tincture so prepared by the following process:

Br. Assay.—"Pour 40 millilitres of the liquid into a porcelain dish; evaporate on a water-bath until the volume is reduced to about 10 millilitres; mix the residual liquid in a mortar with 1 gramme of freshly slaked *lime;* dilute the mixture with *water* to 41 millilitres; set aside for half an hour, stirring from time to time. Filter off 25 millilitres of the liquid (representing 25 millilitres of the strong tincture) through a plaited filter, having a diameter of about one decimetre, into a convenient vessel; add 2.5 millilitres of *alcohol* (90 per cent.) and 15 millilitres of *ether;* shake the mixture; add 1 gramme of *ammonium chloride;* shake well and frequently during half an hour; set aside for twelve hours for the morphine to separate. Counterbalance two small filters; place one within the other in a small funnel in such a way that the triple fold of the inner filter shall be superposed upon the single fold of the outer filter; wet them with *ether;* remove the ethereal layer of the liquid in the vessel as completely as possible by means of a small pipette, and transfer it to the filter; rinse the vessel with 8 millilitres of *ether,* again transferring the ethereal layer, by means of the pipette, to the filter; wash the filter with a total amount of 5 millilitres of *ether* added slowly, and in portions; let the filter dry in the air; pour upon it the liquid in the bottle, in portions, in such a way as to transfer the granular crystalline morphine as completely as possible to the filter. When all the liquid has passed through, wash the remainder of the morphine from the vessel with *morphinated water.* Wash the crystals with *morphinated water* until the washings are free from color; allow the filter to drain and dry it, first at 60° C. (140° F.), and finally at 115° C. (239° F.) for two hours. Weigh the crystals in the inner filter, counterbalancing by the outer filter. Take 0.2 gramme of the crystals, and titrate, with *N/10 solution of sulphuric acid,* as directed under 'Opium.' Add to the weight of anhydrous morphine obtained, as indicated by the titration, 0.025 gramme, a proportion representing the average loss of morphine during the process. Having thus ascertained the proportion of morphine, calculated as anhydrous, present in 25 millilitres of the strong tincture, dilute the remainder of the latter with sufficient of a mixture of Alcohol (90 per cent.) and Distilled Water, in equal volumes, to produce Tincture of Opium containing 1 gramme of morphine, calculated as anhydrous, in 100 millilitres. Examined by the foregoing process, Tincture of Opium is found to contain in 100 millilitres 1 gramme of morphine, calculated as anhydrous. *Limit of error* 0.05 gramme in excess or defect. This Tincture contains in 100 millilitres 1 gramme of morphine, calculated as anhydrous; 110 minims contain 1 grain of the same. It is of approximately the same strength as the Tinctura Opii of the International Agreement, and is about one-third stronger than the corresponding preparation of the British Pharmacopœia, 1898. Tincture of Opium may be prepared with any variety of opium containing a known percentage of morphine, calculated as anhydrous, provided that the percentage is not less than seven and a half, and provided that the resulting Tincture of Opium responds to the foregoing test." *Br.*

The proportion of opium in these formulas is the same, the finished tincture in both U. S. and Br. Pharmacopœias containing 1 Gm. of anhydrous morphine in 100 mils. The Br. Pharm., 1914, does not direct opium *in powder,* but relies upon an assay to bring the product to a uniform strength. The drying and granulating of the opium are clearly useful provisions, as they insure greater uniformity in the strength of the tincture. Crude opium contains variable proportions of water, and laudanum prepared from a moist specimen will be weaker than that prepared from an equal weight of the dried. The granulation insures the previous drying of the drug, and is thus useful independently of the greater facility which it gives to the action of the menstruum; it is, however, often neglected. Deviation from the official strength

in so important a preparation is certainly a great evil. There can be little doubt, we think, that the present U. S. formula insures a more complete exhaustion of the opium than did the former simple procedure of maceration for six days, while the saving in time is apparent. Granulated opium is preferred to powdered opium because of the greater facility of extraction. Opium in fine powder cannot be readily percolated with diluted alcohol, but if it be mixed with an equal weight of an insoluble powder like purified talc there will be no difficulty; percolation will necessarily be slow, but this is just what is required to secure thorough exhaustion.

In the United States and Great Britain this tincture is universally known by the name of *laudanum*. As this term was formerly applied to other preparations of opium, and still continues to be so applied on the continent of Europe, the tincture is sometimes distinguished by the epithet *liquidum*, which, however, is seldom used in this country. *Tinctura Thebaica* is another title by which the preparation is known.

About two-thirds of the opium used in the preparation of the tincture are dissolved, the residue consisting chiefly of inert matter, but containing traces of morphine. According to the requirements of the Pharmacopœia, 10 minims of this tincture will contain about one-tenth of a grain of morphine. Because of the other narcotic principles of opium, however, the clinical effects are somewhat stronger; the narcotic action of ten minims of the tincture of opium (0.6 mil) is nearly equivalent to one-sixth of a grain (0.01 Gm.) of morphine. Its action differs slightly from that of pure morphine, it being more constipating and more nauseating. As pointed out under opium the other alkaloids present seem to lessen the depressant effect of morphine upon the respiratory center so that the crude drug is a somewhat safer form of narcotic than pure opium.

The tincture of opium is probably the best of the official preparations where the effects of the whole drug are desired. It should be recollected that a fluidrachm of laudanum will yield on an average about one-hundred and twenty drops. When long kept with occasional exposure to the air, it becomes thick from the evaporation of a portion of the alcohol and the deposition of solid matter. If given in this state, it often acts with unexpected energy, and death has resulted in infants from doses which would have been entirely safe if the tincture had not been concentrated in this way.

Dose, five to ten minims (0.3–0.6 mil).

Off. Prep.—Linimentum Opii, *Br.;* Tinctura Camphoræ Composita, *Br.;* Tinctura Opii Ammoniata, *Br.;* Linimentum Opii Compositum, *N. F.;* Lotio Plumbi et Opii, *N. F.;* Mistura Camphoræ Acida, *N. F.;* Mistura Carminativa, *N. F.;* Mistura Copaibæ et Opii, *N. F.;* Mistura Magnesiæ, Asafœtidæ et Opii, *N. F.;* Mistura Opii et Chloroformi Composita, *N. F.;* Mistura Opii et Rhei Composita, *N. F.;* Mistura Opii et Sassafras, *N. F.;* Tinctura Kino et Opii Composita, *N. F.;* Tinctura Pectoralis, *N. F.*

TINCTURA OPII AMMONIATA. Br.

AMMONIATED TINCTURE OF OPIUM

(tĭnc-tū'rą ō'pĭ-ī ąm-mō-nĭ-ā'tą)

Scotch Paregoric; Teinture d'Opium ammoniacale, *Fr.;* Ammoniakalische Opiumtinktur, *G.*

"Tincture of Opium, 100 *millilitres;* Benzoic Acid, 20 *grammes;* Oil of Anise, 5 *millilitres;* Solution of Ammonia, 200 *millilitres;* Alcohol (90 per cent.) sufficient to produce 1000 *millilitres*. Dissolve the Oil of Anise and the Benzoic Acid in six hundred millilitres of the Alcohol; add the Tincture of Opium and the Solution of Ammonia; mix; filter; add sufficient of the Alcohol to produce the required volume. This Tincture contains in 100 millilitres 0.1 gramme of morphine, calculated as anhydrous; 110 minims contain about 1/10 grain of the same. It contains approximately one-tenth less morphine than that contained in the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

This is an old preparation of the Edinburgh Pharmacopœia, formerly used in Scotland under the name of *Paregoric Elixir*. It differs, however, both in composition and in strength, from the very popular preparation known as Paregoric in the United States.

Dose, from thirty minims to a fluidrachm (1.8–3.75 mils).

TINCTURA OPII CAMPHORATA. U. S. (Br.)

CAMPHORATED TINCTURE OF OPIUM Tr. Opii Camph. [Paregoric, Opii tinctura benzoici P. I.]

(tĭnc-tū'rą ō'pĭ-ī cămp-phọ-rā'tą)

Tinctura Camphoræ Composita, *Br.;* Compound Tincture of Camphor; Paregoric Elixir; Elixir parégorique; *Fr. Cod.;* Teinture (alcoolé) d'Opium Camphrée, *Fr.;* Tinctura Extracti Opii Camphorata, Elixir Paregoricum, Tinctura Opii benzoïca, *P. G.;* Benzoësaurehaltige Opiumtinktur, *G.*

* "Powdered Opium, *four grammes* [or 62 grains]; Benzoic Acid, *four grammes* [or 62 grains]; Camphor, *four grammes* [or 62 grains]; Oil of Anise, *four mils* [or 65 minims], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process M (see page 1160), macerating the above ingredients in a mixture of *forty mils* [or 1 fluidounce, 169 minims] of glycerin and *nine hundred and fifty mils* [or 32 fluidounces, 59 minims] of diluted alcohol. Complete the preparation with diluted alcohol." *U. S.*

"Tincture of Opium, 50 *millilitres;* Benzoic Acid, 5 *grammes;* Camphor, 3 *grammes;* Oil of Anise, 3 *millilitres;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres*. Dissolve the Benzoic Acid, Camphor, and Oil of Anise in nine hundred *millilitres* of the Alcohol; add the Tincture of Opium and sufficient of the Alcohol to produce the required volume; filter if necessary. This Compound Tincture contains

in 10 millilitres 5 milligrammes (0.005 gramme) of morphine, calculated as anhydrous; and in each fluid drachm about one thirty-seventh of a grain of the same. It contains approximately one-tenth more morphine than the Tinctura Opii Benzoica of the International Agreement, and one-tenth more than was contained in the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

This is the well-known *paregoric.* It is widely employed with the idea that it is a mild anodyne for the relief of *cough, nausea,* and abdominal *pains.* As its narcotic effects depend, however, entirely upon the opium which it contains its mildness is due solely to the fact that it is usually given in relatively small doses. In *diarrheas* the effect of the opium is somewhat enhanced by the camphor. The superstition that it is especially suited for children is senseless; if morphine be indicated for infants the alkaloid itself is just as useful if given in equivalent dose. One-half a fluidounce (15 mils) of either the United States or British tincture contains about nine-tenths of a grain of powdered opium.

Dose, for an infant, from five to twenty minims (0.3–1.3 mils); for an adult, from one to four fluidrachms (3.75–15.0 mils).

For a description of *Bateman's drops* and *Godfrey's cordial,* see *Tinctura Pectoralis* (Part III) and *Mistura Opii et Sassafras* (Part III), respectively.

Off. Prep.—Mistura Glycyrrhizæ Composita, *U. S.;* Mistura Pectoralis, Stokes, *N. F.*

TINCTURA OPII DEODORATI. U. S.

TINCTURE OF DEODORIZED OPIUM Tr. Opii Deod.

(tĭnc-tū'ra ō'pī-ī dę-ō-dǫ-rā'tī)

"*One hundred mils* of Tincture of Deodorized Opium yields not less than 0.95 Gm. nor more than 1.05 Gm. of anhydrous morphine." *U. S.*

Deodorized tincture of opium, *U. S.* 1880; Teinture (alcoolé) d'Opium sans odeur, *Fr.;* Desodorirte Opiumtinktur, *G.*

* "Granulated Opium, *one hundred grammes* [or 3 ounces av., 231 grains]; Purified Petroleum Benzin, *seventy-five mils* [or 2 fluidounces, 257 minims]; Alcohol, *two hundred mils* [or 6 fluidounces, 366 minims]; Water, *a sufficient quantity,* to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Heat *five hundred mils* [or 16 fluidounces, 435 minims] of water to boiling, and pour it on the granulated opium contained in a suitable vessel, stirring the mixture frequently during twenty-four hours. Then transfer the mixture to a percolator, return the first portion of the percolate until it runs through clear, and, when the original menstruum has ceased to drop, continue the percolation slowly, gradually adding water until the opium is practically exhausted. Concentrate the percolate, by evaporation on a water bath, until it measures *one hundred and fifty mils* [or 5 fluidounces, 35 minims]; cool, transfer it to a bottle, add *sixty-five mils* [or 2 fluidounces, 95 minims] of purified petroleum benzin, stopper, and shake the mixture frequently during ten minutes. Separate the benzin layer and repeat the shaking out with the remainder of the purified petroleum benzin, carefully and completely separating the benzin layer each time. Allow the aqueous liquid to evaporate spontaneously in a warm place until the odor of benzin has almost disappeared, remove the last traces by cautiously heating on a water bath and then add *six hundred mils* [or 20 fluidounces, 138 minims] of water. Filter the liquid, add the alcohol and wash the residue on the filter with sufficient water to make the product measure *nine hundred and fifty mils* [or 32 fluidounces, 59 minims]. Assay a portion of this filtrate as directed below, and, from the morphine content thus determined, ascertain by calculation the amount of anhydrous morphine in the remainder of the liquid and adjust the volume of the finished tincture so that each *one hundred mils* contains 1 Gm. of anhydrous morphine.

"**Assay.**—Proceed as directed in the assay under *Tinctura Opii.*" *U. S.*

A liquid extract is first made from granulated opium in which are left behind all the ingredients of opium insoluble in water; and this, being well shaken with purified benzin, is further deprived of all the principles soluble in this fluid, including narcotine and the noxious odorous matter. The purified benzin is then entirely separated, and, the residue having been dissolved in water, the solution is filtered, and mixed with enough alcohol to preserve it. It had been repeatedly recommended by several pharmacists to replace the ether used in the U. S. P., 1890, process with petroleum benzin, which removes the narcotine just as well as does the ether, and has the merit of being much cheaper. The objection, however, was that benzin almost invariably leaves a trace of a taste and an odor like those of petroleum, and hence it is not fitted for use in a remedy used almost exclusively internally, but the employment of purified petroleum benzin in the U. S. P. IX should obviate this objection. Patch found that acetone, which had been suggested as a substitute for ether, was open to the same objection as petroleum benzin.

Frederick T. Gordon (*A. J. P.,* 1900, 576) recommends an improved process for preparing tincture of deodorized opium in which he proposes paraffin in place of ether for deodorizing the aqueous extract of opium. The opium, in a granulated condition, is extracted with water practically as directed by the Pharmacopœia. The first 300 mils of percolate from 100 Gm. of drug are received, the subsequent portions are evaporated to 200 mils, and the two portions, being mixed, are heated to 82° C. (180° F.). Then 150 Gm. of paraffin U. S. P. are added, and when this has melted the mixture is shaken thoroughly for five or ten minutes and set aside to cool. When the paraffin has hardened, the crust is broken and the aqueous opium solution poured out, the under side of the paraffin

crusts being washed with a little water and the washings added to the decanted liquid, which is brought to 800 mils. To this, 200 mils of alcohol are added and finally enough water to make 1000 mils of finished product. The paraffin removes the narcotine and odorous matter, but none of the morphine (the latter existing in the opium, as is well known, as meconate, and this is insoluble in the melted paraffin). Wm. S. White also proposes the use of melted paraffin in preparing the tincture of deodorized opium instead of the inflammable benzin authorized by the U. S. P. He states that 70 Gm. of paraffin to each liter of the preparation is sufficient, and all that is necessary is to warm the evaporated extract, add the melted paraffin, agitate well and allow to stand over night, when the paraffin may readily be removed as a solid cake. He states also that the morphine obtained in assaying the tincture made by this method is remarkably white and pure. (*J. A. Ph. A.*, 1913, p. 939.) A. E. Ebert (*A. J. P.*, 1902, 157) prefers gasoline to benzin and objects to the use of paraffin, or paraffin oils because of their liability to dissolve some of the morphine; he recommends a *concentrated liquid opium* to be used in making the various galenical opium preparations. This tincture is practically equivalent in therapeutic effect to the simple tincture of opium and is by many preferred because of its less offensive odor. The experiments of Macht, however (see *Opium*), indicate that the presence of narcotine is advantageous as it tends to neutralize the depressant action of the opium upon the respiratory center.

Dose, five to ten minims (0.3–0.6 mil).

Off. Prep.—Tinctura Ipecacuanhæ et Opii, *N. F.*

TINCTURA PHYSOSTIGMATIS. U. S.

TINCTURE OF PHYSOSTIGMA Tr. Physostig. [Tincture of Calabar Bean]

(tĭnc-tū′rą phȳ-sǫ-stĭg′mą-tĭs)

"*One hundred mils* of Tincture of Physostigma yields not less than 0.013 Gm. nor more than 0.017 Gm. of the alkaloids of physostigma." *U. S.*

Teinture (alcoolé) de fève du Calabar, *Fr.;* Kalabarbohnentinktur, *G.*

• "Physostigma, in No. 50 powder, *one hundred grammes* [or 3 ounces av., 231 grains], to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a tincture by Type Process P, as modified for assayed tinctures (see page 1160), using alcohol as the menstruum and adjusting the volume of the finished tincture so that each *one hundred mils* contains 0.015 Gm. of the alkaloids of physostigma.

"**Assay.**—Evaporate 150 mils of Tincture of Physostigma on a water bath until it measures about 20 mils, add 10 Gm. of sawdust purified (see Reagents, Part III), to the liquid and incorporate it thoroughly. Continue the evaporation on a water bath until the mixture is dry, then transfer the impregnated sawdust to a 250 mil flask, and proceed as directed in the assay under *Physostigma,* page 850, third line of the Assay, beginning with the words 'and add 150 mils of ether,' modifying the process there given by using the solution of sodium bicarbonate, in divided portions, to rinse the evaporating dish." *U. S.*

This tincture was reduced from 15 Gm. (U. S. P., 1890) to 10 Gm. of drug per 100 mils in the U. S. P. VIII and an assay process appended; the U. S. P. IX has retained this strength. This *tincture of Calabar Bean* is much weaker than that proposed by Fraser, which was nearly as strong as a fluidextract—five minims representing three grains of the drug.

Dose, of the official tincture, from ten to thirty minims (0.6–1.8 mils).

TINCTURA PICRORHIZÆ. Br.

TINCTURE OF PICRORHIZA

(tĭnc-tū′rą pĭc-rō-rhī′zæ)

"Picrorhiza, cut small and bruised, 250 *grammes;* Alcohol (45 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

Although "this Tincture is of twice the strength of the corresponding preparation of the Indian and Colonial Addendum, 1900," *Br.,* the proportion of alcohol in this tincture is too large for it to be available as an antiperiodic; it is used as a bitter tonic.

Dose, one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA PODOPHYLLI. Br.

TINCTURE OF PODOPHYLLUM

(tĭnc-tū′rą pŏd-ǫ-phȳl′lī)

Teinture (alcoolé) de Résine de Podophyllum, *Fr.;* Podophyllintinktur, *G.*

"Podophyllum Resin, 36.5 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Add the Podophyllum Resin to nine hundred *millilitres* of the Alcohol, and set aside for twenty-four hours, shaking occasionally; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

The introduction of this tincture is of doubtful utility.

Dose, five to fifteen minims (0.3–0.9 mil).

TINCTURA PODOPHYLLI INDICI. Br.

TINCTURE OF INDIAN PODOPHYLLUM

(tĭnc-tū′rą pō-dō -phȳl′lī ĭn′dĭ-cī)

"Indian Podophyllum Resin, 36.5 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Add the Indian Podophyllum Resin to nine hundred millilitres of the Alcohol, and set aside for twenty-four hours, shaking occasionally; filter; pass sufficient of the Alcohol

through the filter to produce the required volume." *Br.*

This has been introduced to afford a substitute in the Asiatic provinces for the tincture of podophyllum.

Dose, five to fifteen minims (0.3–0.9 mil).

TINCTURA PRUNI VIRGINIANÆ. Br.

TINCTURE OF WILD CHERRY

(tĭnc-tū'rą prū'nī vĭr-ĝĭn-ĭ-ā'næ)

Tincture of Virginian Prune; Teinture (alcoolé) d'Ecorce de Cerisier, *Fr.*; Wildkirschenrindentinktur, *G.*

"Wild Cherry Bark, in No. 20 powder, 200 *grammes;* Alcohol (90 per cent.), 565 *millilitres;* Distilled Water, 365 *millilitres;* Glycerin, 100 *millilitres.* Mix the powder with the Distilled Water; set aside in a closed vessel for twenty-four hours; add the Alcohol, and complete the *maceration process;* add the Glycerin to the product." *Br.*

This was a new official tincture of the Br. Pharm., 1898; its utility is doubtful. The English name has been changed from Virginian Prune to Wild Cherry in the Br. Pharm., 1914. The use of the glycerin serves to retard precipitation.

Dose, from one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA PYRETHRI. U. S., Br.

TINCTURE OF PYRETHRUM Tr. Pyreth. [Tincture of Pellitory]

(tĭnc-tū'rą pȳ-rē'thrī)

Teinture (alcoolé) de Pyrèthre (racine), *Fr. Cod.*; Bertramwurzeltinktur, *G.*

* "Pyrethrum, in No. 50 powder, *two hundred grammes* [or 7 ounces av., 24 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using alcohol as the menstruum." *U. S.*

"Pyrethrum Root, in No. 40 powder, 200 *grammes;* Alcohol (70 per cent.), sufficient to produce, 1000 *millilitres.* Moisten the powder with one hundred and fifty millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture is a powerful local irritant, and is an ingredient in several well-known mouth and tooth washes. For its uses, which are purely external, see *Pyrethrum.*

TINCTURA QUASSIÆ. U. S. Br.

TINCTURE OF QUASSIA Tr. Quass.

(tĭnc-tū'rą quas'sĭ-æ)

Teinture (alcoolé) de Quassie Amère, *Fr.*; Quassiatinktur, *G.*

* "Quassia, in No. 50 powder, *two hundred grammes* [or 7 ounces av., 24 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using a mixture of *one volume* of alcohol and *two volumes* of water as the menstruum." *U. S.*

"Quassia Wood, rasped, 100 *grammes;* Alcohol (45 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

The strength of this tincture was doubled in the U. S. P. VIII and is twice that of the present British tincture. It may be employed as an addition to tonic infusions or mixtures. It has the advantage that, being free from tannin, it may be given in conjunction with salts of iron.

Dose, one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA QUILLAIÆ. Br.

TINCTURE OF QUILLAIA

(tĭnc-tū'rą quĭl-lā'iæ)

Teinture (alcoolé) d'Ecorce de Quillaya, *Fr.*; Seifenrindentinktur, *G.*

Tincture of quillaja was deleted from the U. S. P. IX, but is now official in the N. F. IV. (see Part III).

"Quillaia Bark, in No. 20 powder, 50 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with twenty-five millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture is almost exclusively used as an emulsifying agent. Its medicinal activity, however, limits its use. (See *Quillaja,* p. 928.) The British tincture is only one-fourth the strength of the preparation.

Dose, from one-half to one fluidrachm (1.8–3.75 mils).

TINCTURA QUININÆ. Br.

TINCTURE OF QUININE

(tĭnc-tū'rą quĭ-nī'næ)

Teinture (alcoolé) de Quinine, *Fr.*; Chinintinktur, *G.*

"Quinine Hydrochloride, 20 *grammes;* Tincture of Orange, 1000 *millilitres.* Dissolve." *Br.*

Quinine sulphate was replaced in this preparation by the hydrochloride in the 1885 Br. Pharmacopœia, because, as pointed out by Wright (*Y. B. P.*, 1884, 537), the sulphate was not always soluble in the proportion of tincture of orange peel ordered.

Dose, a fluidrachm (3.75 mils) (about equal to one and one-tenth grains of quinine hydrochloride).

TINCTURA QUININÆ AMMONIATA. Br.

AMMONIATED TINCTURE OF QUININE

(tĭnc-tū'rą quĭ-nī'næ ąm-mō-nĭ-ā'tą)

Teinture Ammoniacale de Quinine, *Fr.*; Ammoniakhaltige Chinintinktur, *G.*

"Quinine Sulphate, 20 *grammes;* Solution of Ammonia, 100 *millilitres;* Alcohol (60 per cent.), 900 *millilitres.* Mix the Solution of Ammonia with the Alcohol; add the Quinine Sulphate; shake until a clear solution is produced; set aside for three days; filter." *Br.*

Dose, one fluidrachm (3.75 mils), representing about one and one-tenth grains of quinine sulphate.

TINCTURA RHEI. U. S. (Br.)

TINCTURE OF RHUBARB Tr. Rhei

(tĭnc-tū'ra rhē'ī)

Tinctura Rhei Composita, *Br.*, Compound Tincture of Rhubarb; Teinture (alcoolé) de Rhubarbe, *Fr. Cod.*; Rhabarbertinktur, *G.*; Tintura di rabarbaro, *It.*

* "Rhubarb, in No. 40 powder, *two hundred grammes* [or 7 ounces av., 24 grains]; Cardamom Seed, in No. 40 powder, *thirty grammes* [or 1 ounce av., 25.5 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using a mixture of *one hundred mils* [or 3 fluidounces, 183 minims] of glycerin, *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol and *four hundred mils* [or 13 fluidounces, 252 minims] of water as the first menstruum and completing the percolation with diluted alcohol." *U. S.*

"Rhubarb, in No. 20 powder, 100.0 *grammes;* Cardamom Seeds, in No. 20 powder, 12.5 *grammes;* Coriander Fruit, in No. 20 powder, 12.5 *grammes;* Glycerin, 100.0 *millilitres;* Alcohol (45 per cent.) sufficient to produce 1000.0 *millilitres.* Moisten the solid ingredients with one hundred millilitres of the Alcohol, and prepare, by the *percolation process,* eight hundred and fifty millilitres of tincture. Add the Glycerin, and sufficient of the Alcohol to produce the required volume." *Br.*

This tincture was doubled in rhubarb and cardamom strength in the U. S. P. (8th Rev.). The tincture of rhubarb on standing deposits a yellow precipitate. This has been shown by James T. King (*A. J. P.,* xlii) to be in most cases largely composed of chrysophanic acid. He proposed to remedy this by the use of a stronger alcohol, or, as recommended by J. B. Moore (*A. J. P.,* xlv, 306), by the substitution of glycerin for a portion of the alcohol. We have not found that either of these plans entirely prevents precipitation, although glycerin is an aid in this direction.

Dose, from one to two fluidrachms (3.75–7.5 mils).

Off. Prep.—Mistura Opii et Rhei Composita, *N. F.*

TINCTURA RHEI AROMATICA. U. S.

AROMATIC TINCTURE OF RHUBARB Tr. Rhei Arom.

(tĭnc-tū'ra rhē'ī ăr-o-măt'ĭ-ca)

Teinture (alcoolé) de Rhubarbe aromatique, *Fr.*; Aromatische Rhabarbertinktur, *G.*

* "Rhubarb, in No. 40 powder, *two hundred grammes* [or 7 ounces av., 24 grains]; Saigon Cinnamon, in No. 40 powder, *forty grammes* [or 1 ounce av., 180 grains]; Clove, in No. 40 powder, *forty grammes* [or 1 ounce av., 180 grains]; Myristica, in No. 40 powder, *twenty grammes* [or 308.6 grains], to make *one thousand mils* [or 33 fluidounces. 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using a mixture of *one hundred mils* [or 3 fluidounces, 183 minims] of glycerin, *five hundred mils* [or 16 fluidounces, 435 minims] of alcohol and *four hundred mils* [or 13 fluidounces, 252 minims] of water as the first menstruum and completing the percolation with diluted alcohol." *U. S.*

This is the tincture which is used in making the aromatic syrup of rhubarb. It is preferable to separate the preparations, as it is occasionally desirable to prescribe the tincture without the admixture with syrup, while the pharmacist will always prefer to make the tincture in quantity and keep it on hand, since it is permanent, and add to it syrup to make the aromatic syrup when needed.

Dose, for an adult, from one-half to one fluidrachm (1.8–3.75 mils).

Off. Prep.—Syrupus Rhei Aromaticus, *U. S.*

TINCTURA SANGUINARIÆ. U. S.

TINCTURE OF SANGUINARIA Tr. Sanguin. [Tincture of Blood Root]

(tĭnc-tū'ra săn-guĭ-nā-rĭ-æ)

Teinture (alcoolé) de Sanguinaire, *Fr.*; Blutwurzeltinktur, *G.*

* "Sanguinaria, in No. 60 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Hydrochloric Acid, *ten mils* [or 162 minims]; Alcohol, Water, each, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix *six hundred mils* [or 20 fluidounces, 138 minims] of alcohol with *four hundred mils* [or 13 fluidounces, 252 minims] of water. Moisten the drug with a mixture of the hydrochloric acid and *thirty mils* [or 1 fluidounce, 7 minims] of this menstruum, transfer it to a percolator, and, without pressing the powder, allow it to stand, well covered, for six hours; then pack it firmly and pour on enough menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for twenty-four hours. Then allow the percolation to proceed slowly, pouring on sufficient menstruum made of alcohol and water, in the same proportion as before, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of Tincture." *U. S.*

This tincture was reduced from 15 Gm. (U. S. P, 1890) to 10 Gm. of drug, per 100 mils, in the U. S. P. VIII and IX.

A precipitate will generally be found deposited upon the sides and bottoms of bottles containing this tincture. W. J. McConn (*A. J. P.,* 1884, p. 505) recommended the addition of an alkaline citrate, preferably potassium citrate, as a preventive. He found sanguinarine in the precipitate. See also Homerberg and Beringer (*A. J. P.,* 1913, lxxxv, p. 394). The official menstruum now contains hydrochloric acid, with a view of preventing precipitation. This tincture is emetic in the *dose* of from three to four fluidrachms (11.25–15 mils); but it is rather intended to act as an expectorant or an alterative, for which purpose from fifteen to sixty minims (0.9–3.75 mils) may be given.

TINCTURA SCILLÆ. U. S., Br.

TINCTURE OF SQUILL Tr. Scill.

(tĭnc-tū'rą sçĭl'læ)

"If assayed biologically the minimum lethal dose should not be greater than 0.006 mil of Tincture, or the equivalent in Tincture of 0.0000005 Gm. of ouabain, for each gramme of body weight of frog." *U. S.*

Teinture (alcoolé) de Scille, *Fr. Cod.*; Meerzwiebeltinktur, *G.*; Tintura alcoholica de escila, *Sp.*

* "Squill, in No. 20 powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Alcohol, Water, each, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Moisten the drug with sufficient menstruum, prepared by mixing *three volumes* of alcohol and *one volume* of water, and macerate it in a closed vessel in a moderately warm place for twenty-four hours, stirring occasionally. Then transfer it to a percolator, shake it down evenly without packing and pour on enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for twenty-four hours. Then allow the percolation to proceed slowly, gradually adding sufficient of the same menstruum to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of Tincture.

"**Assay.**—For a method of assaying Tincture of Squill, see Biological Assays (Part III)." *U. S.*

"Squill, bruised, 200 *grammes;* Alcohol (60 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

Tincture of Squill was reduced from the strength of 15 Gm. (U. S. P. 1890) to 10 Gm. of drug, per 100 mils, U. S. P. VIII and IX). This tincture yields a grayish, rose-colored, very bitter and acrid deposit, consisting of silky tufts. (Ménière.) The tincture represents the virtues of squill probably better than any other official preparation.

Dose, from ten to twenty minims (0.6–1.3 mils) (from twenty to forty drops).

TINCTURA SENEGÆ. Br.

TINCTURE OF SENEGA

(tĭnc-tū'rą sĕn'ę-gæ)

Teinture (alcoolé) de Polygala de Virginie, *Fr.*; Senegatinktur, *G.*

"Senega Root, in No. 40 powder, 200 *grammes;* Alcohol (60 per cent.), sufficient to produce, 1000 *millilitres.* Moisten the powder with two hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

The Br. Pharm. 1898 increased the strength of this preparation 60 per cent. The tincture is efficient, but it is hardly needed while recourse can be had to the fluidextract or the syrup.

Dose, from thirty minims to two fluidrachms (1.8–7.5 mils).

TINCTURA SENNÆ COMPOSITA. Br.

COMPOUND TINCTURE OF SENNA

(tĭnc-tū'rą sĕn'næ cǫm-pŏs'ĭ-tą)

Elixir Salutis; Teinture (alcoolé) de Séné composée, Teinture de Séné aromatique, Elixir de Salut, *Fr.*; Zusammengesetzte Sennatinktur, *G.*

"Senna Leaves, in No. 20 powder, 200 *grammes;* Caraway Fruit, in No. 20 powder, 25 *grammes;* Coriander Fruit, in No. 20 powder, 25 *grammes;* Glycerin, 100 *millilitres;* Alcohol (45 per cent.), sufficient to produce 1000 *millilitres.* Moisten the solid ingredients with two hundred and fifty millilitres of the Alcohol, and prepare, by the *percolation process,* eight hundred and fifty millilitres of tincture. Add the Glycerin and sufficient of the Alcohol to produce the required volume." *Br.*

The Br. Pharm. 1898 increased the proportion of senna in this preparation 60 per cent.

This tincture is the *elixir salutis* of the old Pharmacopœias. It is a warm cordial purgative, useful in *costiveness* attended with flatulence, and in *atonic gout,* especially when occurring in intemperate persons. It is also added to cathartic infusions and mixtures. Tincture of senna yields a yellow scaly deposit, containing white crystals of calcareous salts. (Ménière.)

Dose, from two to four fluidrachms (7.5–15 mils).

TINCTURA SERPENTARIÆ. Br.

TINCTURE OF SERPENTARY

(tĭnc-tū'rą sęr-pęn-tā'rĭ-æ)

Teinture (alcoolé) de Serpentaire de Virginie, *Fr.*; Schlangenwurzeltinktur, *G.*

"Serpentary Rhizome, in No. 40 powder, 200 *grammes;* Alcohol (60 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with two hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

Tincture of Serpentaria was doubled in strength in the U. S. P. VIII, but is now transferred to the N. F. (see Part III). This tincture is little other than a feebly aromatic, alcoholic stimulant. The Br. Pharm. 1898 increased the strength of this preparation 60 per cent.

Dose, thirty minims to two fluidrachms (1.8–7.5 mils).

TINCTURA STRAMONII. U. S., Br.

TINCTURE OF STRAMONIUM Tr. Stramon.

(tĭnc-tū'rą strą-mō'nĭ-ī)

"*One hundred mils* of Tincture of Stramonium yields not less than 0.0225 Gm. nor more than 0.0275 Gm. of the total alkaloids of stramonium." *U. S.*

Tincture of Stramonium Leaves; Teinture (alcoolé) de Stramoine (feuille), *Fr. Cod.*; Stechapfelblättertinktur, *G.*

* "Stramonium, in No. 60 powder, *one hundred grammes* [or 3 ounces av., 231 grains], to

make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P, as modified for assayed tinctures (see page 1160), using diluted alcohol as the menstruum and adjusting the volume of the finished Tincture so that each *one hundred mils* contains 0.025 Gm. of the total alkaloids of stramonium.

"**Assay.**—Evaporate 100 mils of Tincture of Stramonium on a water bath until it measures about 10 mils, transfer the evaporated liquid to a separator, and proceed as directed in the assay under *Fluidextractum Belladonnæ Radicis*, page 486, second line of the Assay, beginning with the words 'add 10 mils,' and modifying the process there given by using the ammonia water and about 5 mils of distilled water in addition to rinse the dish in which the Tincture was evaporated; before titrating treat the residue twice with 5 mils of ether, evaporating to dryness each time." *U. S.*

"Stramonium Leaves, in No. 20 powder, 200 *grammes;* Alcohol (45 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with two hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

This tincture is now made from Stramonium leaves instead of the seeds as directed by the U. S. P. 1890, and the strength made 10 Gm. of drug, per 100 mils, instead of 15 Gm., as in the U. S. P. 1890, and an assay has been appended. The Br. Pharm. 1898 increased the strength of this preparation 60 per cent., but changed the form of the drug from seeds to leaves. The British tincture is now double the strength of the U. S. P. tincture.

Dose, from ten to twenty minims (0.6–1.3 mils); of the British tincture, five to ten minims (0.3–0.6 mil).

TINCTURA STROPHANTHI. U. S., Br.

TINCTURE OF STROPHANTHUS Tr. Strophanth. [Strophanthi tinctura P. I.]

(tĭnc-tū'rą strǫ-phăn'thī)

"If assayed biologically the minimum lethal dose should not be greater than 0.00006 mil of Tincture, or the equivalent in Tincture of 0.0000005 Gm. of ouabain, for each gramme of body weight of frog." *U. S.*

Teinture (alcoolé) de Strophantus Kombé, *Fr. Cod.;* Tinctura Strophanthi, *P. G.;* Strophanthustinktur, *G.;* Strophanthussamentinktur, *G.;* Tinctura di strofanto, *It.;* Tintura alcoholica de estrofanto, *Sp.*

* "Strophanthus, in No. 40 powder, *one hundred grammes* [or 3 ounces av., 231 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Pack the drug in a cylindrical percolator and slowly percolate it with purified petroleum benzin until a few drops of the percolate, evaporated from filter paper, no longer leaves a greasy stain; then remove the strophanthus from the percolator and expose it to the air until it is dry and the odor of benzin has disappeared. Prepare a Tincture from this dried drug by Type Process P (see page 1160), using alcohol as the menstruum, but allow the moistened drug to macerate for forty-eight hours before starting the percolation, instead of twenty-four hours as directed in Type Process P.

"**Assay.**—For a method of assaying Tincture of Strophanthus, see Biological Assays (Part III)." *U. S.*

"Strophanthus Seeds, in No. 30 powder, dried at 45° C. (113° F.), 100 *grammes;* Ether, *a sufficient quantity;* Alcohol (70 per cent.), sufficient to produce 1000 *millilitres.* Pack the powder in a percolator; moisten with the Ether, and macerate for twenty-four hours; then allow percolation to proceed, continuing the addition of the Ether until the liquid passes through colorless. Remove the marc from the percolator, and dry it, gradually heating it to 50° C. (122° F.). Again reduce it to powder, repack in the percolator, and moisten with the Alcohol. Macerate for forty-eight hours, then pour on successive quantities of the Alcohol, percolating slowly, until five hundred millilitres of percolate are obtained; add sufficient of the Alcohol to produce the required volume. This Tincture is made with four times the proportion of Strophanthus Seeds ordered for the corresponding preparation of the British Pharmacopœia, 1898. It is of approximately the same strength as the Tinctura Strophanthi of the International Agreement, but in the case of the latter Tincture, the seeds are not treated with ether for the removal of fat and resins." *Br.*

Strophanthus seeds are reduced to powder with great difficulty. E. R. Squibb bruises them (after drying perfectly) in an iron mortar with broken glass. (*Ephem.,* vol. iii, 1252.) Made by either the U. S. or Br. process, the tincture is usually slightly cloudy when first prepared, but on standing soon becomes clear. The use of petroleum benzin in the U. S. P. IX and ether in the Br. P. for the preliminary exhaustion of the drug is to effect the removal of the fixed oil which interferes with the stability of the preparation unless previously removed.

Uses.—The tincture of strophanthus fully represents the crude drug and may be used for all the purposes for which strophanthus is serviceable. It is apparently a stable preparation and although somewhat subject to variations in potency, according to Hatcher and Bailey (*J. A. M. A.,* 1909, lii, p. 5) is much more uniform in strength than tincture of digitalis.

Dose, three to eight minims (0.2–0.5 mil)

TINCTURA TOLUTANA. U. S., Br.

TINCTURE OF TOLU Tr. Tolu. [Tolu Tincture]

(tĭnc-tū'rą tō-lū-tā'ną)

Tincture of Balsam of Tolu; Teinture (alcoolé) de Baume de Tolu, *Fr. Cod.;* Tolubalsamtinktur, *G.*

* "Balsam of Tolu, *two hundred grammes* [or 7 ounces av., 24 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process

M (see page 1160), using alcohol as the solvent." *U. S.*

"Balsam of Tolu, 100 *grammes;* Alcohol (90 per cent.), sufficient to produce, 1000 *millilitres.* Dissolve the Balsam of Tolu in eight hundred *millilitres* of the Alcohol; filter; pass sufficient of the Alcohol through the filter to produce the required volume." *Br.*

This tincture was doubled in strength in the U. S. P. VIII. The British tincture (1914) is half the strength of the U. S. P. tincture.

The tincture of tolu has the properties of the balsam, and may be employed as an addition to expectorant mixtures in *chronic bronchitis,* but the proportion of alcohol is too large to allow of its advantageous use in some cases. It is used in preparing the syrup of tolu. In smaller quantities it is often employed to flavor cough mixtures. It is precipitated by aqueous liquids.

Dose, one-half to two fluidrachms (1.8–7.5 mils).

Off. Prep.—Syrupus Tolutanus, *U. S.*

TINCTURA URGINEÆ. Br.

TINCTURE OF URGINEA

(tĭnc-tū'rą ür-gĭ'nē-æ)

"Urginea, bruised, 200 *grammes;* Alcohol (60 per cent.), 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

This tincture was introduced into India and is intended to be used in place of squill.

The *dose* is five to fifteen minims (0.3–0.9 mil).

TINCTURA VALERIANÆ. U. S.

TINCTURE OF VALERIAN Tr. Valer.

(tĭnc-tū'rą vą-lē-rĭ-ā'næ)

Teinture (alcoolé) de Valériane, *Fr. Cod.;* Tinctura Valerianæ, *P. G.;* Baldriantinktur, *G.;* Tinturo di valeriana, *It.*

* "Valerian, in No. 40 powder, *two hundred grammes* [or 7 ounces av., 24 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using a mixture of *three volumes* of alcohol and *one volume* of water as the menstruum." *U. S.*

The proportion of alcohol was increased in the U. S. 1890 tincture, to prevent precipitation, and this strength has been retained in the present revision. It is now three parts of alcohol to one part of water. The tincture possesses the properties of valerian, but cannot be given in some cases, so as to produce the full effects of the root, without stimulating too highly, in consequence of the large proportion of spirit. It deposits on standing a black, very cohesive precipitate, with starch, and a yellow extractive matter. (Ménière.)

Dose, one to four fluidrachms (3.75–15.0 mils).

TINCTURA VALERIANÆ AMMONIATA. U. S., Br.

AMMONIATED TINCTURE OF VALERIAN Tr. Valer. Ammon.

(tĭnc-tū'rą vą-lē-rĭ-ā'næ ąm-mō-nĭ-ā'tą)

Tinctura Valerianæ Composita; Teinture de Valériane ammoniacale, *Fr.;* Ammoniakalische Baldriantinktur, *G.*

* "Valerian, in No. 40 powder, *two hundred grammes* [or 7 ounces av., 24 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using aromatic spirit of ammonia as the menstruum." *U. S.*

"Valerian Rhizome, in No. 40 powder, 200 *grammes;* Oil of Nutmeg, 3 *millilitres;* Oil of Lemon, 2 *millilitres;* Solution of Ammonia, 100 *millilitres;* Alcohol (60 per cent.), 900 *millilitres.* Mix the liquid ingredients, and, using the mixture as a menstruum, prepare by the *maceration process.*" *Br.*

The proportion of valerian was increased 60 per cent. in the Br. Pharm. 1898, and the aromatic spirit of ammonia replaced by alcohol, solution of ammonia, and volatile oils.

The ammonia in this preparation is thought to assist the solvent powers of the alcohol, while it co-operates with the valerian in medicinal action. The quantity of valerian was very judiciously increased one-third in the U. S. revision of 1880. The tincture is employed as an antispasmodic in *hysteria* and other *nervous diseases.*

Dose, from thirty minims to a fluidrachm (1.8–3.75 mils).

TINCTURA VALERIANÆ INDICÆ AMMONIATA. Br.

AMMONIATED TINCTURE OF INDIAN VALERIAN

(tĭnc-tū'rą vą-lē-rĭ-ā'næ ĭn'dĭ-cæ ąm-mō-nĭ-ā'tą)

"Indian Valerian Rhizome, in No. 40 powder, 200 *grammes;* Oil of Nutmeg, 3 *millilitres;* Oil of Lemon, 2 *millilitres;* Solution of Ammonia, 100 *millilitres;* Alcohol (60 per cent.), 900 *millilitres.* Mix the liquid ingredients, and, using the mixture as a menstruum, prepare by the *maceration process.*" *Br.*

This tincture was introduced into the Br. Pharm. 1914 to be used in India and elsewhere in place of ammoniated tincture of valerian.

Dose, thirty minims to one fluidrachm (1.8–3.75 mils).

TINCTURA VERATRI VIRIDIS. U. S.

TINCTURE OF VERATRUM VIRIDE Tr. Verat. Vir. [Tinctura Veratri, U. S. VIII]

(tĭnc-tū'rą vę-rā-'trī vĭ'rĭ-dĭs)

Tincture of Green Hellebore; Tincture of American Hellebore; Teinture (alcoolé) de Vératre, *Fr.;* Tinctura Veratri, *P. G.;* Nieswurzeltinktur, *G.*

* "Veratrum Viride in No. 60 powder, *one hundred grammes* [or 3 ounces av., 231 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type

Process P (see page 1160), using alcohol as the menstruum." *U. S.*

The U. S. tincture of American hellebore of 1890 was of the same strength as *Norwood's tincture,* which was prepared by its author from fresh drug (240 grains for each fluidounce of alcohol), and was supposed to be saturated. The U. S. P. 1890 tincture was made from dried and powdered veratrum (40 Gm. in 100 mils strength) but was reduced by the U. S. P. VIII from 40 per cent. to 10 per cent. in order that it might conform with the recommendations of the Brussels Congress concerning potent tinctures (see *Tincturæ*). This action has resulted in increasing the use of the fluidextract, which is a better preparation. The U. S. P. IX has returned to the exclusive use of veratrum viride. Veratrum album was also recognized in the U. S. P. VIII.

Dose, of U. S. tincture, ten to thirty minims (0.6–1.8 mils).

TINCTURA ZINGIBERIS. U. S., Br.

TINCTURE OF GINGER Tr. Zingib. [Tincture of Jamaica Ginger]

(tĭnc-tū'ra zĭn-gĭb'ẹ-rĭs)

Teinture (alcoolé) de Gingembre, *Fr. Cod.;* Tinctura Zingiberis, *P. G.;* Ingwertinktur, *G.*

* "Jamaica Ginger, in No. 30 powder, *two hundred grammes* [or 7 ounces av., 24 grains], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Prepare a Tincture by Type Process P (see page 1160), using alcohol as the menstruum. Evaporate 10 Gm. of Tincture of Ginger to dryness in a tared dish on a water bath; the yield of residue does not exceed 2 per cent. When treated with 20 mils of cold distilled water, not more than 15 per cent. of this residue dissolves. Evaporate 10 mils of Tincture of Ginger to dryness in a small flask. Add 5 mils of half-normal alcoholic potassium hydroxide V.S. and boil the mixture gently for thirty minutes under a reflux condenser. Remove the condenser and evaporate the alcohol on a water bath. Then add 50 mils of distilled water to the residue, agitate the mixture, filter it and transfer the aqueous filtrate to a separatory funnel and shake it out with 25 mils of ether. Evaporate the separated ether solution spontaneously by adding it, a few drops at a time, to the center of a watch glass. Cautiously apply the tip of the tongue to the dry residue; the taste should be slightly camphoraceous but not sharp or bitingly-pungent (*capsicum or similar pungent substitute*). It contains about 90 per cent. of $C_2H_5.OH$ by volume." *U. S.*

"Ginger, in No. 40 powder, 100 *grammes;* Alcohol (90 per cent.), sufficient to produce 1000 *millilitres.* Moisten the powder with one hundred millilitres of the Alcohol, and complete the *percolation process.*" *Br.*

The strength of this tincture was reduced at the 1880 revision one-third, to bring it into the 20 per cent. class; this is not a disadvantage, however, in view of the introduction of the fluidextract, and the dose is not now inconveniently large.

The tincture of the British Pharmacopœia is still too weak in the proportion of ginger. In consequence of the mucilaginous matter contained in ginger, the tincture made with diluted alcohol or proof spirit is apt to be turbid, and the drug is incompletely exhausted of its resinous and oily constituents. Alcohol or rectified spirit is, therefore, properly preferred. Official Jamaica ginger only should be used; for, while a darker-colored preparation is made when the inferior varieties are substituted, the apparent increase in strength is due to coloring matter, and not to the presence of a larger amount of volatile oil or resin.

The tincture of ginger is a useful carminative, and may often be beneficially added to tonic and purgative infusions or mixtures in debilitated states of the alimentary canal. It is in this country largely used for the preparation of a syrup of ginger, for which purpose, however, the fluidextract is official, and is better even than the strong tincture of the Br. Pharmacopœia 1885, which was dropped at the 1898 revision.

Dose, eight to forty minims (0.5–2.5 mils).

Off. Prep.—Acidum Sulphuricum Aromaticum, *U. S., Br.*

TINCTURÆ.

TINCTURES

(tĭnc-tū'ræ)

Teintures (Alcooliques) Alcoolés, *Fr.;* Tinkturen, *G.;* Tinture alcooliche, *It.;* Tinturas alcoholicas, *Sp.*

Tinctures, in the pharmaceutical sense of the term, are alcoholic solutions of medicinal substances, prepared by maceration, digestion, or percolation. Solutions in spirit of ammonia and ethereal spirit are embraced under the same denomination, but are severally distinguished by the titles of *ammoniated tinctures* and *ethereal tinctures.* The advantages of alcohol as a menstruum are that it dissolves principles which are sparingly, or not at all, soluble in water, and contributes to their preservation when dissolved, while it leaves behind some inert substances which are dissolved by water. In no instance, however, is dehydrated alcohol employed. Because of the slight amount of water in it, official alcohol dissolves more or less of substances which are insoluble in dehydrated alcohol, while its solvent power in relation to bodies soluble in that fluid is sufficient for all practical purposes. Diluted alcohol or proof spirit is often preferable to official alcohol, as it is capable of extracting a larger proportion of those active principles of plants which require an aqueous menstruum, while at the same time it is strong enough to prevent spontaneous decomposition. and has the advantages of being cheaper and less stimulating, although a few tinctures when prepared with weak alcoholic menstrua undergo some deterioration in time, in consequence of acetous fermentation taking place in the alcoholic fluid. The best preventive is to keep

them in full and well-closed bottles, at a low temperature. The diluted alcohol of the different Pharmacopœias is not of the same strength; that of the United States consists of equal volumes of official alcohol and water, and has the sp. gr. of about 0.936 at 15.56 C. (60° F.), while the British has four official diluted alcohols—70, 60, 45, and 20 per cent. Alcohol, or rectified spirit, is preferred as a solvent when the substance to be extracted or dissolved is nearly or quite insoluble in water, as in the instances of resins, guaiac, camphor, and the essential oils. The presence of water is here injurious, not only by diluting the menstruum, but also by exercising an affinity for the alcohol which interferes with its solvent power. Thus, water added to an alcoholic solution of one of these bodies produces a precipitate by abstracting the alcohol from it. Diluted alcohol, or proof spirit, is employed when the substance is soluble both in alcohol and in water; or when one or more of the ingredients are soluble in the one fluid and one or more in the other, as in the case of vegetable bodies which contain extractive or tannin, or the natural salts of the alkaloids, or gum united with resin or volatile oil. As these include the greater number of medicines from which tinctures are prepared, diluted alcohol is most frequently used. In the preparation of the tinctures, the drug should be dry, and properly comminuted by being bruised, sliced, or pulverized. It is usually better in a moderately fine than in a very fine powder; the proper degree depends, however, upon the ease with which the menstruum extracts the soluble principles. The recommendations of the International Protocol included the use of 70 per cent. alcohol for the various tinctures, but as this has not proven to be the best menstruum for some drugs, the U. S. P. has not always followed the suggestion.

In the U. S. P. IX the general article on tinctures is as follows:

"Tinctures are alcoholic preparations made by extracting the valuable principles from drugs by the use of appropriate menstrua or solvents. Tincture of ferric chloride and tincture of iodine are exceptional, not being made by extraction; they are alcoholic solutions of chemical substances. Tinctures of potent drugs are made of the strength of *ten grammes* [or 154 grains] of drug in *one hundred mils* [or 3 fluidounces, 183 minims] of tincture. The other tinctures vary in the proportion of drug in the finished tincture. Tinctures are made by percolation with few exceptions. Maceration or solution is preferred when from its physical character the drug is not suitable for percolation. The majority of official tinctures are prepared under one or the other of the two type processes described, and in each formula directions are given as to the process to be followed with such modifications as may be necessary. A number of drugs require special manipulation for the preparation of satisfactory tinctures, and for these the formulas in full will be found in the text. Where it has been found possible and desirable to standardize the tinctures a rubric and assay have been added. Tinctures should be stored in tightly-stoppered bottles, kept in a cool place, and protected from light.

Type Process P—Percolation.

"Moisten the powdered drug or mixed drugs designated in the formula with a sufficient quantity of the prescribed menstruum to render it evenly and distinctly damp, transfer it to a percolator, and, without pressing the powder, allow it to stand well-covered for six hours; then pack it firmly, unless otherwise directed, and pour on enough of the menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for twenty-four hours. Then allow the percolation to proceed slowly, gradually adding sufficient of the menstruum to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of finished tincture.

"*Modification for Assayed Tinctures.*—In Tinctures that are directed to be assayed, allow the percolation to proceed until the percolate measures *nine hundred and fifty mils* [or 32 fluidounces, 59 minims]. Assay a sample of this percolate as directed and from the alkaloidal content thus determined, ascertain by calculation the amount of alkaloids in the remainder of the liquid and add to this enough of the menstruum to make the finished Tincture conform to the required alkaloidal standard.

Type Process M—Maceration.

"Macerate the drug or mixed drugs designated in the formula in a stoppered container, in a moderately warm place, with *seven hundred and fifty mils* [or 25 fluidounces, 173 minims] of the prescribed solvent (unless a different amount is specified in the formula). Continue the maceration with frequent agitation during three days or until the drug is practically extracted, transfer the mixture to a filter and, when the liquid has drained off completely, gradually wash the residue on the filter with enough of the solvent to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms] of finished tincture." *U. S.*

The British Pharmacopœia in the *Appendix IX* (see Part III) has provided detailed instruction for both percolation and maceration processes.

Tinctures were at one time universally prepared by maceration or digestion. Our own Pharmacopœia formerly directed maceration at ordinary temperatures, and extended the period to two weeks. In several instances in which maceration is ordered in the U. S. Pharmacopœia, maceration for three days is directed, but the Br. process requires seven days. When circumstances require that the tincture should

be speedily prepared, digestion may be resorted to. Care should always be taken to keep the vessels well stoppered, in order to prevent the evaporation of the alcohol. The materials should be frequently shaken during the digestion or maceration, and this caution is especially necessary when the substance acted on is in the state of powder. The tincture should not be used until the maceration is completed, when it should be separated from the dregs either by simply filtering it through paper, or, when force is requisite, by expressing it through linen, and filtering.

The plan of preparing tinctures by percolation has been extensively adopted, and has been found to answer well when skilfully executed. In the present edition of our Pharmacopœia, percolation has been adopted as the rule, maceration being directed in some instances in which it was deemed preferable.

The method of making tinctures by diluting fluidextracts, except in a few special cases, is not to be recommended. The menstruum directed for the fluidextract is most frequently not identical with that used for the tincture, and precipitation of active constituents often ensues when this easy method is employed. Owing to the larger dose of the tinctures, and consequently less degree of concentration, a larger proportion of water can be used in their menstrua than in fluidextacts, and this is a distinct advantage, as tinctures are frequently prescribed in combination with aqueous solutions.

Another mode of exhausting medicines by spirit has been proposed by H. Burton. It consists in suspending in the solvent, immediately under its surface, the solid matter contained loosely in a bag. The liquid in contact with the bag, becoming heavier by impregnation with the matters dissolved, sinks to the bottom; its place is supplied with a fresh portion, which in its turn sinks, and thus a current is established, which continues until the solid substance is exhausted or the liquid saturated. During the maceration the bag should be occasionally raised above the surface of the liquor in the bottle, allowed to drain, and then again immersed. It is asserted that the period of maceration is much shortened in this way. For this mode of preparing tinctures Samuel Gale has proposed the use of a cylindrical stoneware vessel with a diaphragm capable of being supported at different heights by projections from the inner surface of the jar, with corresponding notches in the diaphragm, to permit its easy passage to the lower ledges. The material is to be placed upon the diaphragm and kept covered with the menstruum.

Tinctures prepared by adding alcohol to the expressed juices of plants have been long in use on the continent of Europe, and have been brought into notice in Great Britain. They are sometimes called in England *preserved vegetable juices.* This method of preparing tinctures has, however, been abandoned by both the U. S. and Br. Pharmacopœias. Preserved juices are often energetic, yet it is obvious that tinctures prepared from the fresh plant must be still more so, as they contain necessarily not only the soluble active matter of the juice, but also that which, when the juice is expressed, is left in the solid residue of the plant. For further information see *U. S. D.*, 19th ed., p. 1293.

A process for making tinctures from fresh drugs was official in the U. S. P. VIII. It was deleted from the U. S. P. IX, but introduced into the National Formulary IV under the heading *Tincturæ Medicamentorum Recentium* as follows:

"Tinctures of fresh drugs, when not otherwise directed, are to be prepared according to the following general formula: The Fresh Drug, cut, bruised, or crushed, *five hundred grammes* [or 17 ounces av., 279 grains]; Alcohol, *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Macerate the drug with the alcohol in a closed vessel in a moderately warm place during fourteen days, with occasional stirring; then strongly express the liquid and filter it through paper." *N. F.*

Tinctures should be kept in bottles accurately stoppered, in order to prevent evaporation, which might in some instances be attended with serious inconvenience, by increasing their strength beyond the official standard.

Medicines which act in small doses are most conveniently administered in tinctures, as the proportion of alcohol in which they are dissolved is insufficient to produce an appreciable effect. Those which must be given in large doses should be cautiously employed in this form, lest the injury done by the menstruum should more than counterbalance their beneficial operation. This remark is particularly applicable to chronic cases, in which the use of tinctures is apt to lead to the formation of habits of intemperance. The tinctures of the weaker medicines are more frequently given as adjuvants of other remedies than with the view of obtaining their own full effects upon the system.

In the revision of the Pharmacopœia of 1890, wherever practicable, the proportion of drug to finished tincture was made either 20, 15, 10, or 5 Gm. per 100 mils. Progressive pharmacy demands greater uniformity and simplicity in the processes, and hence in the U. S. P. VIII and IX practically all of the tinctures have been brought into two classes, 20 and 10 Gm. of drug per 100 mils. The potent tinctures, which contained mainly 15 Gm. of drug per 100 mils in the U. S. P. 1890, were reduced to 10 Gm. per 100 mils in order to comply with the recommendations of the Brussels Conference of 1902 for the unification of the strength of Potent Remedies.

A tabulated comparison of the tinctures of the P. G. IV and P. G. V as to sp. gr., extractive percentage and alkaloidal content, is available for those to whom it would be of value in the Yearbook of the *A. Ph. A.*, 1913, p. 84.

TOXITABELLÆ HYDRARGYRI CHLORIDI CORROSIVI. U. S.

POISON TABLETS OF CORROSIVE MERCURIC CHLORIDE Toxitabel. Hydrarg. Chlor. Corr. [Corrosive Sublimate Tablets Bichloride Tablets]

(tŏx-ĭ-tă-bĕl'læ hȳ-drär'gy-rī ċhlō'rĭ-dī cŏr-rǫ-sī'vī)

"Tablets of an angular shape (not discoid), each having the word "POISON" and the skull and cross bones design distinctly stamped upon it. Each tablet weighs about 1 Gm. and contains not less than 0.45 Gm. nor more than 0.55 Gm. of corrosive mercuric chloride ($HgCl_2$); the remainder consisting chiefly of sodium chloride (NaCl). The tablets are to be colored blue, preferably with sodium indigotindisulphonate. Poison Tablets of Corrosive Mercuric Chloride are to be dispensed in securely stoppered glass containers on the exterior of which is placed a red label bearing the word "POISON" and a statement indicating that the Tablets contain the required amount of corrosive mercuric chloride.

"Assay.—Proceed as directed under *Hydrargyri Chloridi Corrosivum,* using one tablet and washing the sulphide with distilled water until the filtrate is colorless and 5 mils of the washings, acidulated with nitric acid, yields no turbidity on the addition of a few drops of silver nitrate T.S. The weight of the mercuric sulphide obtained, multiplied by 1.167, indicates its equivalent in corrosive mercuric chloride. Tablets of Corrosive Mercuric Chloride may also be assayed as directed under the Electrolytic Method (see Part III, Test No. 4). Each tablet shows not less than 0.45 Gm. nor more than 0.55 Gm. of $HgCl_2$." *U. S.*

Uses.—The convenience of tablets of corrosive sublimate for the preparation of antiseptic solutions and their wide use, has led to the introduction of such a tablet into the Pharmacopœia. Because of the large number of cases of poisoning through the inadvertent swallowing of these tablets, in the place of compressed tablets of certain drugs which may have a somewhat similar appearance, it has become highly desirable that these tablets be made in such a form as to render such a mistake less liable. A variety of suggestions for this purpose have been made; among the most popular shapes are the oblong or coffin-shaped, and the triangular tablets. As the solution formed by these tablets is colorless, in order that the solution shall not be confounded with harmless drugs, the tablets are directed to be colored blue by the addition of sodium indigotindisulphonate, or other dye.

A bluish color is greatly preferable to a pink dye, which is sometimes used, not only because it is less liable to be confused with reddish colored drugs but because various confections are often colored red. Despite these precautions, however, it is probable that cases of poisoning by mercuric chloride, either accidental or intentional, will continue to occur from time to time. The physician, therefore, should exercise the greatest reserve in allowing tablets of corrosive sublimate to get into the hands of his patients and the pharmacist should be exceedingly careful in selling and dispensing them. The official tablet contains 0.5 Gm. (8.0 grains) of corrosive sublimate; one of them dissolved in one pint of water (500 mils) makes a solution of 1 to 1000. The addition of sodium chloride in these tablets aids in the solution of the mercuric chloride.

TRAGACANTHA. U. S., Br.

TRAGACANTH Trag. [Gum Tragacanth]

(trăg-ą-căn'thą)

"The spontaneously dried gummy exudation from the stems of *Astragalus gummifer* Labillardière, or from other Asiatic species of *Astragalus* (Fam. *Leguminosæ*)." *U. S.* "Tragacanth is a gummy exudation obtained by incision from Astragalus gummifer, *Labill.,* and some other species of Astragalus. Known in commerce as Syrian tragacanth." *Br.*

Gummi Tragacanthæ vel Astragalorum; Gomme Adragante, *Fr. Cod.*; Tragacantha, *P. G.*; Tragant, Traganth, *G.*; Gomma adragante, Dragante, *It.*; Gomo tragacanto, *Sp.*

Numerous species belonging to this genus yield a gummy matter having the properties of *tragacanth.* The drug known in commerce by that name was at first erroneously supposed to be obtained from *A. Tragacantha* of Linnæus (*A. massiliensis* of Lamarck), which grows in Southern Europe and Northern Africa and is now said to yield no gum. It was afterwards ascribed, on the authority of Tournefort, to a species (*A. creticus* of Lamarck) which grows in Crete and Ionia, and on that of Olivier, to *A. verus,* which inhabits Asia Minor, Armenia, and Northern Persia. Labillardière described a species by the name of *A. gummifer* which he found growing on Mount Libanus in Syria, and from which tragacanth exudes, though not that of commerce. Only recently it has been denied that *Astragalus gummifer* is the source of tragacanth. (*Cons. and Tr. Rep.,* 1910, p. 728.)

Sieber denies that any of the above-mentioned species yields the official tragacanth, which he ascribes to *A. aristatus,* growing in Anatolia, especially upon Mount Ida, where the gum is most abundantly collected. This plant, however, is not the *A. aristatus* of Villars, which, according to Sibthorp, furnishes tragacanth in Greece. (Mérat and De Lens.) Lindley received two specimens of plants, said to be those which furnish tragacanth in Turkestan, one of which proved to be *A. gummifer* of Labillardière which was said to yield a white variety, and the other a new species, which he called *A. strobiliferus,* and which was said to yield a red and inferior product. The fact seems to be that the commercial drug is collected from various sources; and it is affirmed that all the species of Astragalus with thorny petioles are capable of producing it. These form a natural group, and so closely resemble one another that botanists have found some difficulty in distinguishing them. They are very abundant on the mountains of Asia Minor, and, according

to information received by M. J. Léon Soubeiran from Balansa, a scientific traveller who derived his knowledge from personal observation, the gum-producing species are closely analogous to the *A. creticus* of Lamarck. It is in the Anti-Taurus range that the gum is chiefly collected. Transverse incisions are made, near the base of the stem, into the medullary tissues, which alone yield the gum. This exudes very slowly, flowing at night, and ceasing during the day; two weeks usually elapse before the pieces are large enough for collection. The shape of the pieces is influenced by the rapidity of the exudation, and the lines on their surface indicate the daily concretion. The section Tragacantha of the genus Astragalus includes the principal species which yield gum tragacanth.

According to Haussknecht, tragacanth is yielded by the following species of Astragalus: *A. adscendens* Boiss. et Haussk. (Southern Persia); *A. leioclados* Boiss. (in Middle and Western Persia, by Ispahan and Hamadan); *A. brachycalyx* Fisch. (Kurdistan and Luristan); *A. gummifer* Labill. (widely distributed from Lebanon to Armenia and in the northern regions of the Euphrates and Tigris); *A. microcephalus* Willd. (the same as *A. gummifer* Labill., and also in Asia Minor); *A. pycnocladus* Boiss. et Haussk. (particularly in Western Persia); *A. stromatodes* Bge. (in Achyr Dagh, in Northern Syria); *A. kurdicus* Boiss. (Aintab). Other species that yield a tragacanth gum are *A. heratensis* Bge., of the Khorasan Mountains, which yields a gum known as "kutira," and *A. Parnassi* Boiss., var. *cyllenea*, found on the mountains of Peloponnesus.

Harris states that the best Smyrna tragacanth is produced in Asia Minor. It is not, however, collected in the immediate vicinity of Smyrna, but comes from Karahissar, Jalowadsch, and even farther in the interior, where the plant grows wild. This kind of gum consists of white, yellow, and red, hardened pieces, which have become congealed after oozing out of the bush or tree in the hot sun of a Levantine summer. The gum is secured in a similar manner as opium by an incision in the branch. This is done in the spring and summer of each year, and the gum is usually scraped in September, when the first rains begin to fall. During the last twenty years the gum tragacanth trade of Smyrna has decreased. It has been estimated that the trade has fallen from 600,000 pounds to 55,000 pounds in that length of time. (*Oil, Paint and Drug Reporter*, lxxiii, p. 633.)

Properties.—Tragacanth is odorless and nearly tasteless. It occurs either in flaky, leaf-like pieces, irregularly oblong or roundish, or in tortuous vermicular filaments, rounded or flattened, rolled up or extended, of a whitish, yellowish-white, or slightly reddish color, marked by parallel lines or ridges, somewhat translucent, and resembling horn in appearance. In commerce certain varieties of tragacanth are recognized and usually known by the name of the locality from which they have been produced or through which they have entered commerce. The ordinary tragacanth, tragacanth in sorts, sometimes known as *traganton*, occurs in irregular pieces; Smyrna tragacanth appears usually in broad thick flakes, yellowish or brownish; Syrian tragacanth, in thin, ribbon-like, white flakes, is said really to be obtained in Kurdistan and Persia. Tragacanth is officially described as "in flattened, lamellated fragments varying from ribbon-shaped bands to long and linear pieces, which may be either straight or spirally twisted, and from 0.5 to 2.5 mm. in thickness; whitish to light brown in color, translucent and horny; fracture short; rendered more easily pulverizable by heating to 50° C. (122° F.); inodorous; taste insipid, mucilaginous. Under the microscope, sections made from Tragacanth, previously softened in water, and mounted in glycerin, show the lamellæ of mucilaginous walls and a few starch grains, the latter being mostly spherical and single, occasionally 2- to 3-compound, the individual grains from 0.003 to 0.025 mm. in diameter and colored blue with iodine. Indian Gum, derived from plants of uncertain origin, upon similar treatment and examination, shows numerous threads of a granular substance, sometimes the hyphæ of a fungus and chains of bacteria, and occasional fragments of a yellowish-brown or reddish-brown color, containing lignified wood-fibers, a few rosette aggregates of calcium oxalate, from 0.02 to 0.03 mm. in diameter, and a few spherical starch grains, from 0.003 to 0.007 mm. in diameter. Add 1 Gm. of Tragacanth to 50 mils of distilled water; it swells and forms a smooth, nearly uniform, stiff, opalescent mucilage free from cellular fragments. Indian Gum upon similar treatment forms an uneven mucilage containing a few reddish-brown fragments, and on stirring separates in the form of coarse, uneven strings. Shake 2 Gm. of Tragacanth with 100 mils of water until fully swollen and free from lumps, and then add 2 Gm. of powdered sodium borate and shake the mixture thoroughly until the salt is dissolved; the mucilage does not lose its transparency, nor exhibit any change in consistence, and on pouring is not slimy or stringy, even after standing twenty-four hours (*foreign gums*). Boil 1 Gm. of Tragacanth with 20 mils of water until a mucilage is formed, then add 5 mils of hydrochloric acid and again boil the mixture for five minutes; it develops no pink or red color (*Indian Gum*). The powder is whitish; forming with water a translucent mucilage and under the microscope exhibiting numerous starch grains, from 0.003 to 0.025 mm. in diameter, varying from spherical to elliptical, with occasional 2- to 4-compound grains, many of the grains being swollen and more or less altered, due to the drying of the Tragacanth before powdering. Powdered Indian Gum shows numerous fragments of lignified vegetable tissue. Tragacanth yields not more than 3.5 per cent. of ash." *U. S.*

"Thin flattened flakes, irregularly oblong, or more or less curved, marked on the surface by concentric ridges. Frequently two and a half

centimetres long, and twelve millimetres wide. White or pale yellowish-white, somewhat translucent. Horny, fracture short. Inodorous; almost tasteless. Sparingly soluble in *water,* but swelling into a gelatinous mass, which may be tinged violet or blue by *N/10 solution of iodine.* Ash not more than 4 per cent." *Br.*

It is hard and more or less fragile, but difficult of pulverization, unless exposed to a freezing temperature, or thoroughly dried, and powdered in a heated mortar at the temperature of 50° C. (122° F.). Its sp. gr. is 1.384. Introduced into water, it absorbs a certain proportion of that liquid, swells very much, and forms a soft adhesive paste, but does not dissolve. If agitated with an additional quantity of water, this paste forms a uniform mixture; but in the course of one or two days the greater part separates, and is deposited, leaving a portion dissolved in the supernatant fluid. Tragacanth is wholly insoluble in alcohol. It appears to be composed of two different constituents, one soluble in water and resembling gum arabic, the other swelling in water, but not dissolving. To separate the soluble from the insoluble part requires agitation with separate portions of water; the solutions are to be decanted and filtered, and the process is to be continued until water ceases to dissolve anything.

Von Sandersleben reported the discovery that when heated with dilute acids tragacanth acquired reducing properties, and formed, along with much syrup, *arabinose,* which crystallized. (Tollens, *Handbuch der Kohlenhydrate,* 1888, 218.) The explanation of this observation, now generally accepted, is that in tragacanth, like some other gums, part of the arabic acid is present in soluble form, mostly combined with bases, while another part is present in insoluble form, and is known as *traganthin.* This latter, however, under the influence of certain enzymes, is converted into the soluble form. (Lippmann, *Chemie der Zuckerarten,* 2te Auf., 1895, 925.) C. O'Sullivan states that tragacanth consists of cellulose, the portion insoluble in boiling water, cold dilute acids, and alkalies; also *soluble gum,* yielding a series of gum acids of the nature of *geddic acid,* and which are called *polyarabinon-trigalactan-geddic acids;* starch granules; bassorin, which yields *a-tragacanthan-xylan-bassoric acid, xylan-bassoric acid* and *bassoric acid.* (*Proc. Chem. Soc.,* 1901.) Examined by Kützing by means of the microscope, tragacanth was found to consist of organized cells. (See *A. J. P.,* xxv, 37.) In conformity with this statement is the remarkable fact, discovered by Hugo von Mohl and confirmed by Wigand, that tragacanth is not a secretion of the plant, but the result of the transformation of the cells of the pith and those of the medullary rays which traverse the ligneous part of the stem and older branches. (*A. J. P.,* xxxi, 243.)

It is stated by S. H. Maltass that tragacanth is adulterated, in the Levant, with worthless gums brought from Armenia and Caramania, which, as they are originally of a dark color and destitute of the flaky form of the genuine gum, are broken into small fragments and whitened by means of lead carbonate before being mixed with the tragacanth. Hanbury states, in confirmation of this, that he has detected lead in the *small tragacanth* imported into London. (*P. J.,* xv, 20.) Gum tragacanth has been recently admixed with and substituted by Indian gum, the product of *Cohlospermum gossypium* (Fam. *Bixaceæ*). This occurs in vermiform or rounded tears having a dull, rough surface. It is detected by the official tests. The powdered drug is not only adulterated with the Indian gum, but with powdered acacia, dextrin, wheat and cornstarch. Payet gives a test for the detection of acacia in powdered tragacanth which depends on the brown color produced by the oxidase of the former when brought in contact with an aqueous solution of guaiacol in the presence of hydrogen dioxide. (*Ann. de Chim. Analyt.,* x, p. 63.)

Uses.—Tragacanth is demulcent, but, on account of its difficult solubility, is not often given internally. The great viscidity which it imparts to water renders it useful for the suspension of heavy insoluble powders, and it is also employed in pharmacy to impart consistence to troches, for which it answers better than does gum arabic, and in making emulsions, although for these purposes it is inferior to acacia. It is also used for its demulcent action in *pharyngitis* by allowing a piece of the gum to dissolve slowly in the mouth. It is officially employed as the basis of many of the troches.

Off. Prep.—Glycerinum Tragacanthæ, *Br.;* Mucilago Tragacanthæ, *U. S., Br.;* Pulvis Tragacanthæ Compositus, *Br.;* Glyceritum Tragacanthæ, *N. F.*

TRINITROPHENOL. U. S. (Br.)

TRINITROPHENOL Trinitrophen. [Picric Acid]

(trī-nī-trō-phē′nŏl)

"Trinitrophenol [$C_6H_3O_7N_3$ or $C_6H_2(OH)(NO_2)_3$ 1 : 2 : 4 : 6 = 229.05]. Preserve it in well-stoppered bottles, in a cool place, remote from fire.

"*Caution.*—For safety in transportation it is usually mixed with about 20 per cent. of water. Before applying the tests described below, dry the Trinitrophenol to constant weight in a desiccator over sulphuric acid." *U. S.* "Picric Acid may be obtained by the action of nitric acid and sulphuric acid on phenol, and contains not less than 99 per cent. of tri-nitro-phenol, $C_6H_2(NO_2)_3OH$." *Br.*

Acidum Picricum, *Br.;* Acidum Picricum; Carbazotic Acid; Trinitrophenol; Nitrophenic Acid, C_6H_2.

It is obtained by the action of nitric acid on indigo, silk, leather, wool, aloes, benzoin, Australian gum, and other substances, or, as the name indicates, from phenol (carbolic acid). It may be cheaply prepared by adding coal tar creosote (impure phenol) gradually to strong nitric acid and heating, when, on standing, the picric acid will crystallize out; but in practice it is now almost always made by dissolving crys-

tallized phenol in strong sulphuric acid, and adding either nitric acid or sodium nitrate to the resultant phenolsulphonic acid. The reaction is as follows:

$$C_6H_5OH + H_2SO_4 = C_6H_4OH.HSO_3 + H_2O$$
$$C_6H_4OH.HSO_3 + 3HNO_3 = C_6H_2OH(NO_2)_3 + H_2SO_4 + 2H_2O$$

It is in pale yellow shining scales, fusing at 122.5° C. (252.5° F.) and subliming undecomposed. It is soluble in water, to which it gives a strong yellow color and very bitter taste. Its salts crystallize readily, and explode when heated. The potassium salt is so sparingly soluble that an alcoholic solution of the acid may be used as a test for this alkali. It is largely used in dyeing, producing magnificent yellow colors, and, in connection with indigo or Prussian blue, different shades of green. The salts which picric acid forms with potassium and sodium are yellow and bitter, and are much used in the arts. They are, however, violent explosives, and as such have produced very serious consequences. Picric acid itself it also a powerful explosive which is used in modern warfare, not as a propellant, but as the exploding charge in shells, a detonator being necessary to explode it. A saturated aqueous solution of picric acid is a very delicate test for albumin. (See *Esbach's Reagent,* Part III.) *Ammonium picrate* is universally preferred for internal use. It crystallizes in rhombic scales, which are somewhat more soluble than the corresponding potassium salt.

"Trinitrophenol occurs in pale yellow, rhombic prisms or scales; odorless, and having an intensely bitter taste. It explodes when heated rapidly and when subjected to percussion. One Gm. of Trinitrophenol dissolves in 78 mils of water, 12 mils of alcohol, 35 mils of chloroform, 65 mils of ether, and in 10 mils of benzene at 25° C. (77° F.); also in 15 mils of boiling water. An aqueous solution of Trinitrophenol is acid to litmus. It melts between 121° and 123° C. (249.8° and 253.4° F.). An aqueous solution of Trinitrophenol (1 in 100) has a yellow color, which becomes darker on the addition of alkalies, and red on the addition of ammonium sulphide T.S. or a solution of an alkaline cyanide. Add a few drops of barium chloride T.S. to 10 mils of an aqueous solution of Trinitrophenol (1 in 100); the liquid does not at once become opalescent (*sulphate*). Dissolve 2 Gm. of Trinitrophenol in 50 mils of benzene, collect the insoluble residue, if any, on a small filter which has been dried at 100° C. (212° F.) and weighed. Wash the residue and filter with benzene until the washings are colorless. The residue, dried at 100° C. (212° F.), does not exceed 0.2 per cent." *U. S.*

"Bright yellow crystalline powder. Inodorous; taste very bitter. Soluble in 90 parts of *water,* and in 10 parts of *alcohol* (90 per cent.), forming intensely yellow solutions which stain the skin yellow. Melting point 122° C. (251.6° F.). 2 grammes dissolved in hot *water* require for neutralisation 17.3 millilitres of *N/2 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator." *Br.*

Uses.—Trinitrophenol is germicidal, astringent, and apparently stimulates epithelial growth. According to Ehrenfried (*J. A. M. A.,* 1911, lvi, p. 412), a saturated aqueous solution (1.2 per cent.), destroys the *Bacillus pyocyaneus* in less than one minute and the *Staphyloccocus pyogenes aureus* in two minutes, while in the experiments of Schamberg and Kolmer (*L. L.,* 1911, ii, p. 1397) it showed itself four times as active as phenol. Internally trinitrophenol is comparatively feeble in its effects upon the system. It is absorbed probably as a sodium salt and eliminated chiefly through the urine to which it imparts an intense yellow color. After large doses the skin and mucous membranes are also stained yellow. In toxic quantities it causes in the lower animals destruction of the red blood corpuscles, but this effect has not been reported in man. The symptoms of poisoning as observed in human beings have been vomiting, diarrhea, the matters ejected being stained yellow, strangury and often anuria; in severe cases stupor with convulsions followed by collapse have also been noted. A very common symptom even after not extremely large doses is itching of the skin frequently associated with an eczematous eruption. Ehrenfried states that there is no fatal case of picric acid poisoning upon record, but 15 to 30 grains are sufficient to cause toxic symptoms. It should be remembered that the drug may be absorbed after its local application in sufficient quantities to produce constitutional effects.

Internally picric acid has been used in the treatment of *trichinosis* and *malaria,* but is probably without any value. It is capable of destroying intestinal parasites either *tapeworm* or *roundworm,* but has no advantage over other vermifuges. The practical value of trinitrophenol in medicine is as a local agent. While by some used as an antiseptic dressing for superficial *wounds,* it is especially prized in *burns* of the first and second degree and is also useful for its astringent and antiseptic action in *ulcers* with free discharge. Wilcox (*Archives of Pedriatics,* 1913, xxx) recommends it very highly in the treatment of various skin diseases, especially acute *eczema, intertrigo,* and *herpes labialis.* In local *hyperidrosis,* especially of the feet, it has long been recognized as a standard remedy. Picric acid is also highly recommended by a number of ophthalmologists in the treatment of *injuries of the cornea,* due to caustic agents, such as quick-lime and the mineral acids. It has also been employed in simple *conjunctivitis* and in *trachoma.* For the latter purpose Ohlemann (*Wochens. f. Ther. u. Hyg. d. Auges,* 1910, p. 103) recommends a 2 per cent. ointment which is applied directly to the lid, after previous cocainization if necessary.

For surgical purposes from one-half to one per cent. is generally used. In skin diseases the aqueous solution may be either painted over the lesion or sometimes gauze moistened with the

solution applied. In sweating feet a dusting powder containing 2 per cent. of picric acid with talc is sometimes used. The great drawback of the remedy is its powerful staining properties.

In skin diseases when the epiderm is unbroken it may be desirable to use stronger solutions in which case a hydro-alcoholic menstruum is employed.

Picric acid poisoning is quite common among workers engaged in the manufacturing of high explosives. In some cases this is manifested by dermatitis, often quite severe and resistant to treatment. The inflammation of the skin in these cases bears a strong resemblance to that seen in ivy poisoning and at times is accompanied with marked constitutional disturbances, such as headache, loss of appetite, nose bleed, and fever. There is in many of these cases more or less leukocytosis. In other patients the symptoms are chiefly gastro-intestinal; abdominal cramps, diarrhea, vomiting and headache being the most common manifestations. The inhalation of the dust by these workers produces a bronchitis accompanied with a dry hacking cough, often with expectoration of blood, and signs of irritation of the throat.

Dose, one-half to one grain (0.032–0.065 Gm.).

TRITICUM. U. S. (Br.)

TRITICUM Tritic. [Couch Grass Dog Grass]

(trĭt'ĭ-cŭm)

"The dried rhizome and roots of *Agropyron repens* (Linné) Beauvois (Fam. *Gramineæ*), gathered in the spring." *U. S.* "Couch Grass is the dried rhizome of Agropyron repens, *Beauv.*, freed from remains of leaves and rootlets." *Br.*

Agropyrum, *Br.;* Rhizoma Graminis; Radix Graminis; Quick-grass, Quitch, Scotch-grass, Twitch-grass, Witch-grass, Quickens; Chiendent officinal ou Petit chiendent, *Fr. Cod.;* Queckenwurzel, Grasswurzel, *G.;* Grama (Rizoma de), *Sp.*

This grass, originally a native of Europe, now abounds in meadows and cultivated grounds in the Northern United States, where it is often very troublesome as a weed. It is specifically characterized by its creeping rootstock, the leaves being flat, thin and finely veined, and the flowering glumes being glabrous or scabrous. It is probable that the rhizome of a number of other grasses share the medicinal properties of *Agropyron repens.* Of these the Scotch or Bermuda grass, *Capriola Dactylon* (L.) Kuntze, is probably as effective as the official species.

Much spurious triticum has appeared upon the market recently. Most of it can be readily distinguished from the official drug by the presence of starch in the spurious article.

Properties.—Triticum is officially described as follows: "Usually in pieces from 4 to 12 mm. in length and from 1 to 2.5 mm. in diameter; externally light yellow or yellowish-brown, longitudinally furrowed, smooth, lustrous, nodes with circular leaf-scars, a few root-scars and occasional slender roots; fracture tough, fibrous; internally lemon-yellow and with a large, hollow pith; odor slight, aromatic; taste sweetish. Roots filiform, irregularly branching, attaining a length of about 5 cm. and not more than 0.5 mm. in thickness, light brown or yellowish-brown, frequently covered with long root hairs. Under the microscope, transverse sections of Triticum show a single layer of strongly lignified epidermal cells; a hypodermis of from 3 to 6 rows of more or less polygonal cells with strongly lignified walls; a cortex of from 10 to 16 rows of thin-walled parenchyma cells, occasionally with nearly spherical starch grains about 0.005 mm. in diameter, or with irregular masses of a more or less soluble carbohydrate; among the parenchyma cells and near the hypodermis occur small, widely separated fibro-vascular bundles, each with a closed sheath of sclerenchymatous fibers; an endodermis, the lateral and inner walls of the cells moderately thickened, strongly lignified and somewhat porous; several layers of sclerenchymatous fibers immediately inside the endodermal ring, in which are imbedded an interrupted circle of collateral fibro-vascular bundles having large tracheæ; adjoining these are usually 8 to 10 rows of parenchyma cells with a few fibro-vascular bundles and a pith in which the parenchyma cells are more or less broken or absent. The powder is light yellowish; consisting of irregular, lignified fragments; numerous fragments showing tracheæ with annular or spiral thickenings or marked with simple pores and associated with long, narrow, rather thin-walled, strongly lignified sclerenchymatous fibers; fragments of epidermis made up of cells rectangular in outline, the longer walls considerably thickened, strongly lignified and marked with numerous transverse pores; ends of epidermal cells usually separated from each other by a very narrow cell with thin walls and few pores; numerous fragments of parenchyma rectangular in outline and with thin, porous walls. Triticum yields not more than 3 per cent. of ash." *U. S.*

"Rhizome pale yellow, rigid, from two to two and a half millimetres in diameter, usually in pieces from three to six millimetres long. Strongly furrowed longitudinally, hollow except at the nodes. Contains no starch. No odor; taste slightly sweet." *Br.*

The morphology of triticum has been described by Holm (*M. R.,* xix, p. 65). Kebler reports (*A. J. P.,* 1909, p. 75) the adulteration of triticum with Bermuda grass, by which he means probably *Capriola Dactylon* (L.) Kze., a grass which is naturalized in the United States from Europe and apparently widely distributed.

The Austrian Pharmacopœia has a requirement of not less than 30 per cent. of aqueous extractive for this drug.

Uses.—Triticum is never exhibited for the purpose of affecting the general system, but only for its influence upon the genito-urinary organs. It is much used by some surgeons in *irritable bladder,* and also in *cystitis.* It is one of the least stimulant of the remedies of its class, and may be employed very freely. In Europe its decoction is said to be used to a

considerable extent as a diluent and slightly nutritious drink. It may be taken *ad libitum*, or the fluidextract may be given in doses of a fluidrachm (3.75 mils) every three hours in five or six ounces of water.

Off. Prep.—Fluidextractum Tritici, *U. S.;* Decoctum Agropyri, *Br.;* Extractum Agropyri Liquidum, *Br.*

TRITURATIO ELATERINI. U. S.

TRITURATION OF ELATERIN

(trĭt-ū-rā′tĭ-ō ĕl-ą-tę-rī′nī)

Pulvis Elaterini Compositus, *Br.*, 1898; Compound Powder of Elaterin; Trituration d'Elatérine, *Fr.;* Elaterintrituration, *G.*

* "Elaterin, *ten grammes* [or 154 grains]; Sugar of Milk, in moderately fine powder, *ninety grammes* [or 3 ounces av., 76 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Mix them thoroughly by trituration (see *Triturationes*)." *U. S.*

The Br. Pharm., 1898, included Compound Powder of Elaterin, which was identical with the Trituration of Elaterin, except in strength; the U. S. P. trituration contains 10 per cent. of elaterin, the British powder 2½ per cent. It is not recognized by the Br. 1914.

This is probably the best representative of the class of triturations that could be selected for introduction into the national authority. Elaterium is at best a substance of variable quality, while the active principle is a definite product, and accurate dosage can be secured more effectually through the use of this trituration than by the employment of commercial elaterium.

Dose, from one-fourth to one grain (0.016–0.065 Gm.).

TRITURATIONES. U. S.

TRITURATIONS

(trĭt-ū-rā-tĭ-ō′nēȿ)

Triturations, *Fr.;* Triturationen, *G.*

"Unless otherwise directed, Triturations are to be prepared according to the following formula. * Take of the Substance, *ten grammes* [or 154 grains]; Sugar of Milk, in moderately fine powder, *ninety grammes* [or 3 ounces av., 76 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Weigh the substance and the sugar of milk separately; then place the substance, previously reduced, if necessary, to a moderately fine powder, in a mortar; add about an equal measure of sugar of milk, mix well by means of a spatula, and triturate the powders thoroughly together. Then add fresh portions of the sugar of milk, from time to time, until the whole is added, and continue the trituration after each addition until the substance is intimately mixed with the sugar of milk and reduced to a fine powder." *U. S.*

This general formula has been introduced into the Pharmacopœia in order that a definite and uniform method be authorized of making a class of powders which has come into use in various sections of our country. While the necessity of giving recognition to the class may be questioned by many, the importance of securing uniformity in composition is evident.

TROCHISCI.

TROCHES

(trǫ-ȼhĭs′cī)

Tabellæ; Lozenges; Tablettes, *Fr. Cod.;* Pastilli, Rotulae, *P. G.;* Pastillen, Plätzchen, Tabletten, *G.;* Pastiglie, *It.;* Tabletas, *Sp.*

Troches or *lozenges* are small, dry, solid masses, usually of a flattened shape, consisting for the most part of powders incorporated with sugar and mucilage. They are designed to be held in the mouth and dissolved slowly in the saliva, and are, therefore, adapted for the administration of those medicines only which do not require to be given in large quantities and which are destitute of any very disagreeable flavor.

Lozenges were formerly much more used and more skilfully prepared in Europe than in this country, but at present those manufactured here are fully equal to the imported lozenges. Tragacanth, from the greater tenacity of its mucilage, is better suited for their formation than gum arabic. The following directions for preparing them are taken from the *Dictionnaire des Drogues.* A mucilage of tragacanth is first prepared with cold water and strained. With this the powders, including sugar, are thoroughly mixed by rubbing upon a marble slab, and are thus formed into a paste, which is spread out by means of a roller upon the surface of the marble, previously powdered over with a mixture of sugar and starch. The thickness of the mass is rendered uniform by a frame upon which the ends of the roller rest. The upper surface is now dusted with sugar and starch, and the mass is divided into small cakes by means of a punch. These cakes are placed upon paper, and, having been exposed to the air for twelve hours, are carried into a drying room moderately heated. When perfectly dry, they are thrown upon a sieve to separate the sugar and starch, and are then enclosed in boxes. Lozenges may be prepared from almost any medicine which it is advisable to administer in this form. The following typical formula may be found useful.

Take citric acid, in powder, a drachm; powdered sugar eight ounces; oil of lemon twelve minims; mucilage of tragacanth a sufficient quantity. Form them in the manner above directed into troches of twelve grains each. Lozenges are sometimes made by saturating blank lozenges with aromatic spirits. Currant paste or jelly has come into use of late years largely as a basis for troches. For formulas for lozenges with currant paste basis, see *U. S. D.*, 19th edition, page 1297.

Lozenges of a cylindrical shape are extensively used, having a basis of licorice, gum, and sugar, and the manufacture of these is now an important industry. Franklin C. Hill devised an improved machine for making Licorice and

Wistar's Lozenges. (See *A. J. P.*, 1874, 401.) For Slocum's and Harrison's improved forms of lozenge boards, rollers, etc., see *A. J. P.*, 1879, 589; 1880, 255. A. D. Marcy figured an instrument for shaping troches in *N. R.*, Feb., 1882.

The Br. Pharmacopœia, 1914, adopted four bases for lozenges, as follows: fruit basis, rose basis, simple basis, and tolu basis. It will be noticed that in the British formulas the quantity of active ingredients for each lozenge is stated and the kind of basis indicated. This is done merely to avoid repetition.

PREPARATION WITH FRUIT BASIS.

"Take five hundred times the quantity of the drug ordered for one lozenge. Mix it with 6.5 grammes of Tragacanth and 26 grammes of Refined Sugar, both in fine powder. Add sufficient of the black-currant paste of commerce to produce 650 grammes, beat into a uniform mass, divide into 500 equal lozenges and dry in a hot-air chamber at a moderate temperature." *Br.*

PREPARATION WITH ROSE BASIS.

"Take five hundred times the quantity of the drug ordered for one lozenge. Treat it as described under 'Preparation with Simple Basis,' previously mixing with the Refined Sugar 0.025 millilitre of Oil of Rose." *Br.*

PREPARATION WITH SIMPLE BASIS.

"Take five hundred times the quantity of the drug ordered for one lozenge, mix it with 496 grammes of Refined Sugar and 19.5 grammes of Gum Acacia, both in fine powder. Make the mixture into a paste with 35 millilitres of Mucilage of Gum Acacia and a sufficient quantity of Distilled Water, divide into 500 equal lozenges and dry in a hot-air chamber at a moderate temperature." *Br.*

PREPARATION WITH TOLU BASIS.

"Take five hundred times the quantity of the drug ordered for one lozenge; dissolve such salts of alkaloids as may be ordered in 10 millilitres of Distilled Water; mix the solution with 482 grammes of Refined Sugar and 19.5 grammes of Gum Acacia, both in fine powder. Incorporate 10 millilitres of Tincture of Balsam of Tolu, and any other drugs ordered for the lozenges. Make into a paste with 35.5 millilitres of Mucilage of Gum Acacia and a sufficient quantity of Distilled Water; divide into 500 equal lozenges and dry in a hot-air chamber at a moderate temperature." *Br.*

TROCHISCUS ACIDI BENZOICI. Br.

BENZOIC ACID LOZENGE

(trō-ĸĭs'cŭs ăç'ĭ-dī bĕn-zō'ĭ-cī)

Tablettes de l'Acide Benzoique, *Fr.*; Benzoesäurepastillen, *G.*

"Benzoic Acid, 0.03 *gramme.* Mix with the *Fruit Basis* to form a Lozenge." *Br.*

This is a stimulant and antiseptic lozenge useful in *chronic pharyngitis,* and other passive congestions of the buccal cavity.

TROCHISCUS ACIDI CARBOLICI. Br.

PHENOL LOZENGE

(trō-ĸĭs'cŭs ăç'ĭ-dī căr-bŏl'ĭ-cī)

Tablettes de l'Acide Phénique, *Fr.*; Phenolpastillen, *G.*

"Phenol, in powder, 15 *grammes;* Refined Sugar, in powder, 500 *grammes;* Gum Acacia, in powder, 45 *grammes;* Tragacanth, in powder, 15 *grammes;* Lemon Juice, 45 *millilitres.* Mix. Divide into five hundred lozenges. Dry them in a hot-air chamber at a moderate temperature. Each lozenge contains 0.03 gramme of Phenol, or approximately one-half grain. It is of one-half the strength of the corresponding preparation of the British Pharmacopœia, 1898." *Br.*

This lozenge affords an excellent means of obtaining the antiseptic and local anodyne effect of phenol in *acute pharyngitis, stomatitis,* and similar infections of the mouth and throat.

TROCHISCI ACIDI TANNICI. U. S. (Br.)

TROCHES OF TANNIC ACID Troch. Acid. Tann.

(trō-ĸĭs'cī ăç'ĭ-dī tăn'nĭ-cī)

Trochiscus Acidi Tannici, *Br.*, Tannic Acid Lozenge; Tannin Lozenges; Tablettes de Tannin, *Fr.*; Tanninpastillen, *G.*

* "Tannic Acid, *six grammes* [or 92.5 grains]; Sugar, in fine powder, *sixty-five grammes* [or 2 ounces av., 128 grains]; Tragacanth, in fine powder, *two grammes* [or 31 grains]; Stronger Orange Flower Water, *a sufficient quantity,* to make *one hundred troches.* Rub the powders together until they are thoroughly mixed; then form a mass with stronger orange flower water, and divide it into *one hundred troches.*" *U. S.*

"Tannic Acid, 0.03 *gramme.* Mix with the *Tolu Basis* to form a Lozenge." *Br.* (See above.)

These are useful in *relaxation of the uvula,* and in *chronic angina,* being allowed slowly to dissolve in the mouth. Each U. S. troche contains about one grain (0.065 Gm.) of the acid; the Br. about half a grain (0.032 Gm.).

TROCHISCI AMMONII CHLORIDI. U. S.

TROCHES OF AMMONIUM CHLORIDE Troch. Ammon. Chlor.

(trō-ĸĭs'cī ăm-mō'nĭ-ī ĸlō'rĭ-dī)

Tablettes de Chlorhydrate d'Ammoniaque, *Fr.*; Chlorammoniumpastillen, *G.*

* "Ammonium Chloride, in fine powder, *ten grammes* [or 154 grains]; Extract of Glycyrrhiza, in fine powder, *twenty grammes* [or 308.6 grains]; Tragacanth, in fine powder, *two grammes* [or 31 grains]; Sugar, in fine powder, *forty grammes* [or 1 ounce av., 180 grains]; Syrup of Tolu, *a sufficient quantity,* to make

one hundred troches. Rub the powders together until they are thoroughly mixed; then, form a mass with syrup of tolu, and divide it into *one hundred troches.*" *U. S.*

Each troche contains about one and a half grains (0.096 Gm.) of ammonium chloride.

These troches are largely used in *congested conditions of the pharynx and larynx.*

TROCHISCUS BISMUTHI COMPOSITUS. Br.

COMPOUND BISMUTH LOZENGE

(trō-ghĭs'cŭs bĭs-mū'thī cŏm-pŏs'ĭ-tŭs)

Troches of Bismuth; Tablettes de Sous-nitrate de Bismuth, *Fr. Cod.*; Bismuthpastillen, *G.*

"Bismuth Oxycarbonate, 0.15 *gramme;* Heavy Magnesium Carbonate, 0.15 *gramme;* Precipitated Calcium Carbonate, 0.30 *gramme.* Mix with the *Rose Basis* to form a Lozenge." *Br.* (See p. 1168.)

These may be used to obtain the effects of bismuth subcarbonate on the stomach, as well as of the magnesium and calcium carbonates as an antacid, two or more being administered for a dose. They may also be found useful in *chronic inflammation of the throat and œsophagus.*

TROCHISCUS CATECHU. Br.

CATECHU LOZENGE

(trō-ghĭs'cŭs că'tē-chū)

"Catechu, 0.06 *gramme.* Mix with the *Fruit Basis* to form a Lozenge." *Br.*

This lozenge was introduced into the Br. Pharm., 1914. It is mildly astringent.

TROCHISCI CUBEBÆ. U. S.

TROCHES OF CUBEB Troch. Cubeb.

(trō-ghĭs'cī cū-bē'bæ)

Tablettes de Cubèbe, *Fr.*; Kubebenpastillen, *G.*

* "Oleoresin of Cubeb, *two grammes* [or 31 grains]; Oil of Sassafras, *one mil* [or 16 minims]; Extract of Glycyrrhiza, in fine powder, *twenty-five grammes* [or 386 grains]; Acacia, in fine powder, *twelve grammes* [or 185 grains]; Syrup of Tolu, *a sufficient quantity,* to make *one hundred troches.* Rub the powders together until they are thoroughly mixed; then add the oleoresin and the oil, and incorporate them with the mixture. Lastly, form a mass with syrup of tolu, and divide it into *one hundred troches.*" *U. S.*

Each lozenge contains one-third of a grain (0.021 Gm.) of the oleoresin of cubeb, being about one-fourth the strength of the lozenge of 1870, and one-half the strength of the 1890 troches. The preparation is intended chiefly for effect upon the fauces and other parts of the upper alimentary passages, and may be used advantageously in some cases of *chronic cough,* and in *ulceration* or *chronic inflammation of the fauces.*

TROCHISCUS FERRI REDACTI. Br.

REDUCED IRON LOZENGE

(trō-ghĭs'cŭs fĕr'rī rē-dăc'tī)

Tablettes de Fer Réduit par l'Hydrogène, Tablettes de Fer, *Fr.*; Eisenpastillen, *G.*

"Reduced Iron, 0.06 *gramme.* Mix with the *Simple Basis* to form a Lozenge." *Br.* (See p. 1168.)

From one to three of the lozenges may be taken for a dose.

TROCHISCUS GUAIACI RESINÆ. Br.

GUAIACUM RESIN LOZENGE

(trō-ghĭs'cŭs guaĭ'ă-cī rē-sĭ'næ)

Tablettes de Résine de Gayac, *Fr.*; Guajakharzpastillen, *G.*

"Guaiacum Resin, 0.2 *gramme.* Mix with the *Fruit Basis* to form a Lozenge." *Br.* (See p. 1168.)

TROCHISCUS IPECACUANHÆ. Br.

IPECACUANHA LOZENGE

(trō-ghĭs'cŭs ĭp-ē-căc-ū-ăn'hæ)

Tablettes d'Ipécacuanha, *Fr. Cod.*; Brechwurzelpastillen, *G.*; Pastiglie d'ipecacuana, *It.*

"Ipecacuanha Root, in powder, 0.015 *gramme.* Mix with the *Simple Basis* to form a Lozenge." *Br.* (See p. 1168.)

These are useful expectorant lozenges in *catarrhal complaints.*

TROCHISCUS KINO EUCALYPTI. Br.

EUCALYPTUS KINO LOZENGE

(trō-ghĭs'cŭs kī'nō eū-că-lŷp'tī)

Eucalyptus Gum Lozenge, Red Gum Lozenge; Tablettes de Kino d'Eucalypte, *Fr.*; Eucalyptuskinopastillen, *G.*

"Eucalyptus Kino, 0.06 *gramme.* Mix with the *Fruit Basis* to form a lozenge." *Br.* (See p. 1168.)

TROCHISCUS KRAMERIÆ. Br.

KRAMERIA LOZENGE

(trō-ghĭs'cŭs krą-mē'rĭ-æ)

Krameria Lozenge, Rhatany Lozenge; Tablettes de Ratanhia, *Fr.*; Ratanhiapastillen, *G.*

"Extract of Krameria, 0.06 *gramme.* Mix with the *Fruit Basis* to form a Lozenge." *Br.* (See p. 1168.)

These are astringent troches, which may be used in *chronic angina.*

TROCHISCUS KRAMERIÆ ET COCAINÆ. Br.

KRAMERIA AND COCAINE LOZENGE

(trō-ghĭs'cŭs krą-mē'rĭ-æ ĕt cō-cą-ĭ'næ)

Rhatany and Cocaine Lozenge; Tablettes de Ratanhia et de Cocaine, *Fr.*; Ratanhia- und Cocain-pastillen, *G.*

"Extract of Krameria, 0.060 *gramme;* Cocaine Hydrochloride, 0.003 *gramme.* Mix with

the *Fruit Basis* to form a Lozenge. This Lozenge contains 0.003 gramme of Cocaine Hydrochloride, or approximately 1/20 grain." *Br.* (See p. 1168.)

TROCHISCUS MORPHINÆ. Br.

MORPHINE LOZENGE

(trō-ḳĭs'cŭs mör-phĭ'næ)

Tablettes de Chlorhydrate de Morphine, Tablettes de Morphine, *Fr.;* Morphinpastillen, *G.*

"Morphine Hydrochloride, 0.002 *gramme.* Mix with the *Tolu Basis* to form a Lozenge. This Lozenge contains 0.002 gramme of Morphine Hydrochloride, or approximately 1/32 grain." *Br.* (See p. 1168.)

This is an undesirable preparation, as the local action of morphine is insignificant. Any sedative effect in *cough* will be due to the systemic absorption of the drug.

TROCHISCUS MORPHINÆ ET IPECACUANHÆ. Br.

MORPHINE AND IPECACUANHA LOZENGE

(trō-ḳĭs'cŭs mör-phĭ'næ ĕt ĭp-ē-căc-ū-ăn'hæ)

Tablettes de Morphine et d'Ipécacuanha, *Fr.;* Morphinpastillen mit Brechwurzel; Morphin- und Brechwurzel-pastillen, *G.*

"Morphine Hydrochloride, 0.002 *gramme;* Ipecacuanha Root, in powder, 0.006 *gramme.* Mix with the *Tolu Basis* to form a Lozenge. This Lozenge contains 0.002 gramme of Morphine Hydrochloride, or approximately 1/32 grain." *Br.* (See p. 1168.)

This tablet is used as an expectorant. Its effects are the same as would be those of its ingredients if administered in solution. Each lozenge contains one-thirtieth of a grain (0.002 Gm.) of morphine salt, and one-tenth of a grain (0.006 Gm.) of ipecacuanha.

TROCHISCI POTASSII CHLORATIS. U. S. (Br.)

TROCHES OF POTASSIUM CHLORATE Troch Pot. Chlorat.

(trō-ḳĭs'cī pō-tăs'sĭ-ī ḳhlō-rā'tĭs)

Trochiscus Potassii Chloratis, *Br.;* Potassium Chlorate Lozenge, Chlorate of Potash Lozenges; Tablettes de Chlorate de Potasse, *Fr. Cod.;* Kaliumchloratpastillen, Pastillen von Chlorsaurem Kali, *G.;* Pastiglie di clorato di potassio, *It.;* Tabletas de clorato potasico, *Sp.*

* "Potassium Chlorate, in fine powder, *fifteen grammes* [or 231 grains]; Sugar, in fine powder, *sixty grammes* [or 2 ounces av., 51 grains]; Tragacanth, in fine powder, *three grammes* [or 46 grains]; Water, *a sufficient quantity,* to make *one hundred troches.* Mix the sugar with the tragacanth by trituration in a mortar; then transfer the mixture to a sheet of paper, and by means of a bone or wooden spatula mix it with the potassium chlorate, being careful to avoid unnecessary trituration or pressure, which might cause the mixture to ignite or explode. Lastly form a mass with water and divide it into *one hundred troches.*" *U. S.*

"Potassium Chlorate, 0.2 *gramme.* Mix with the *Rose Basis* to form a Lozenge." *Br.* (See p. 1168.)

These lozenges are employed as mildly stimulant and astringent in cases of *sore throat,* although in commercial usage the official troches are almost entirely replaced by compressed tablets of potassium chlorate.

TROCHISCUS SANTONINI. Br.

SANTONIN LOZENGE

(trō-ḳĭs'cŭs săn-tō-nĭ'nī)

Trochisci Santonini, *U. S. VIII;* Troches of Santonin; Tablettes de Santonine, *Fr. Cod.;* Pastilli Santonini, *P. G.;* Santoninpastillen, *G.;* Pastiglie de santonina, *It.;* Tabletas de santonina, *Sp.*

"Santonin, 0.06 *gramme.* Mix with the *Simple Basis* to form a Lozenge." *Br.* (See p. 1168.)

Troches of santonin were deleted from the U. S. P. IX, but are official in the N. F. IV (see Part III).

The U. S. P. VIII process was faulty in the direction that the santonin should be in fine powder, an error which has been continued in the N. F. The longer the absorption of santonin is delayed in the intestines the more prolonged and consequently the more effective is its vermicidal influence. As soon as it is absorbed it ceases to act upon the worm, and becomes a more or less deleterious substance in the system. A dose of santonin in crystals which is not poisonous may become somewhat toxic when given in fine powder. The proportion of crystals in the lozenge mass (2½ per cent.) is not sufficient to prevent the formation of a good lozenge from a pharmaceutical point of view. The National Formulary lozenge contains about half a grain (0.032 Gm.) of santonin. The Br. formula calls for about one grain (0.065 Gm.).

Dose, for an adult, of the Br. lozenge, from one to three lozenges; of the N. F., two to six.

TROCHISCI SODII BICARBONATIS. U. S.

TROCHES OF SODIUM BICARBONATE Troch. Sod. Bicarb.

(trō-ḳĭs'cī sō'dĭ-ī bī-căr-bō-nā'tĭs)

Trochiscus Sodii Bicarbonatis, *Br.;* Sodium Bicarbonate Lozenge; Trochisci Natri Bicarbonici; Tablettes de Bicarbonate de Soude, *Fr. Cod.;* Pastilles de Vichy, Pastiles digestives, *Fr.;* Natronpastillen, Natriumbicarbonatpastillen, *G.;* Pastiglie di bicarbonato di sodio, *It.;* Tabletas de bicarbonato sodico, *Sp.*

* "Sodium Bicarbonate, *eighteen grammes* [or 278 grains]; Sugar, in fine powder, *fifty-four grammes* [or 1 ounce av., 396 grains]; Myristica, freshly grated, *one gramme* [or 15 grains]; Mucilage of Tragacanth, *a sufficient quantity,* to make *one hundred troches.* Triturate the myristica with the sugar, gradually added, until they are reduced to a fine powder, and mix this intimately with the sodium bicarbonate; then form a mass with the mucilage of tragacanth and divide it into *one hundred troches.*" *U. S.*

The U. S. troche contains about three grains (0.2 Gm.) of the alkaline salt. They may be employed to correct acid conditions of the mouth, or of the stomach. From one to six may be given for a *dose.*

TROCHISCUS SULPHURIS. Br.

SULPHUR LOZENGE

(trō-ghĭs'cŭs sŭl'phū-rĭs)

Tablettes de Soufre, *Fr. Cod.*; Schwefelpastillen, *G.*

"Precipitated Sulphur, 150 *grammes;* Acid Potassium Tartrate, in powder, 30 *grammes;* Refined Sugar, in powder, 275 *grammes;* Gum Acacia, in powder, 30 *grammes;* Tincture of Orange, 30 *millilitres;* Mucilage of Gum Acacia, 30 *millilitres.* Mix the Tincture of Orange with the powders; add the Mucilage of Gum Acacia to form a suitable mass. Divide into five hundred Lozenges. Dry them in a hot-air chamber at a moderate temperature. Each Lozenge contains 0.3 gramme of Precipitated Sulphur, or approximately 5 grains." *Br.*

These lozenges were first introduced into the "Additions" to the British Pharmacopœia 1885.

Dose, from one to six lozenges. (See *Sulphur Sublimatum,* p. 1087.)

TURPETHUM. Br.

TURPETH

(tür-pĕ'thŭm)

"Turpeth is the dried root and stem of Ipomœa Turpethum, *R.Br.*" *Br.*

Turpeth Root, Indian Jalap, Trivrit, Nisoth.

Ipomœa Turpethum (*operculina* Turpethum (L.) Peter) (Fam. *Convolvulaceæ*) is a convolvulaceous plant which is found throughout India, China, Ceylon, Australia, and is occasionally cultivated in botanical gardens as an ornamental plant. There are two varieties, viz., *Sveta* or white turpeth, and *Kirshna* or black turpeth, the former being preferred as a mild cathartic. The black variety is said to be a powerful drastic. (Watt, "*Dictionary of the Economic Products of India.*")

According to Mérat and De Lens, the root itself formerly came into commerce, but at present turpeth consists of the root and stem of the plant cut into short lengths, usually from 1.5 to 5 cm. in diameter; the central woody portion is often removed by splitting the bark on one side. The pieces are cylindrical, somewhat twisted and externally of a dull gray color. A transverse section shows a porous central wood surrounded by a broad cortical portion, containing yellowish-brown resin cells, lactiferous vessels and crystals of calcium oxalate. The fracture is short in the cortex and fibrous in the central portion. The drug has a faint odor and a nauseous taste, which is perceptible only after it has been some time in the mouth.

"In cylindrical pieces of varying length, from one to five centimetres wide, often split on one side and deprived of the central portion; longitudinally furrowed; dull grey or brown. Fracture of the bark short, of the wood fibrous; internally usually pale grey. In transverse section, a porous wood surrounded by a thick bark in which abnormal wood-bundles are frequently present. Slight odor; taste nauseous, slowly developed." *Br.*

Boutron-Chalard found in turpeth root, resin, a fatty substance, volatile oil, albumen, starch, a yellow coloring matter, lignin, salts, and ferric oxide. (*J. P. C.*, viii, 121.) The root contains 10 per cent. of resin. (Andouard, *Ann. Thér.*, 1866, 118.) According to Spirgatis this resin is a glucoside, *turpethin,* $C_{76}H_{128}O_{36}$ like that of other Convolvulaceæ, insoluble in ether, but soluble in alcohol, to which it imparts a brown color not removable by animal charcoal. To obtain it pure, the alcoholic solution is concentrated; the resin precipitated by, and afterwards boiled with, water, then dried, reduced to powder, digested with ether, and finally redissolved by absolute alcohol and thrown down by ether. After being treated several times in this way, it is obtained in the state of a brownish resin, yielding on pulverization a gray powder, which strongly irritates the mucous membrane of the nostrils and mouth, and is fusible at 182.2° C. (360° F.). It is inflammable, burning with a smoky flame and emitting irritant vapors. With strong bases it acts like jalapin, takes up water, and is transformed into a soluble acid, *turpethic acid,* $C_{34}H_{60}O_{18}$, while with dilute acids it is decomposed into *turpetholic acid,* $C_{16}H_{32}O_4$, and glucose. (*J. P. C.*, 4e sér., i, 236.)

Turpeth root is purgative, somewhat less powerful than jalap, and rather slow in its action.

Dose, five to twenty grains (0.32–1.3 Gm.).

Off. Prep.—Tinctura Jalapæ Composita, *Br.*

ULMUS. U. S.

ELM [Elm Bark Slippery Elm]

(ŭl'mŭs)

"The bark of *Ulmus fulva* Michaux (Fam. *Ulmaceæ*), deprived of the outer corky layer and dried." *U. S.*

Red Elm, Moose-elm, and Indian Elm; Cortex Ulmi Interior, Ulmi Cortex; Orme Fauve, *Fr. Cod.*; Ecorce d'Orme, *Fr.*; Ulmenrinde, Rüsterrinde, *G.*

The *slippery elm* (*Ulmus fulva*), is a lofty tree, fifty or sixty feet in height, with a trunk fifteen or twenty inches in diameter. The bark of the trunk is brown, that of the branches rough and whitish. The leaves are petiolate, oblong-ovate, acuminate, nearly equal at the base, unequally serrate, pubescent, and very rough on both sides. The buds, a fortnight before their development, are covered with a dense russet down. The flowers, which are apetalous, appear before the leaves, are sessile, and in clusters at the extremities of the young shoots. The clusters of flowers are surrounded by scales, which are downy like the buds. The calyx is also downy. The stamens are five, short, and of a pale rose color. The fruit is a membranaceous capsule or samara, enclosing in

the middle one round seed, destitute of fringe.

Ulmus fulva is indigenous, growing in all parts of the United States north of the Carolinas, but most abundantly west of the Alleghany Mountains. It extends westward to the Dakotas and northward to western Quebec and Lake Huron. It flourishes in open, elevated situations, and requires a firm, dry soil. From the *white elm* (*U. americana* L.) it is distinguished by its rough branches, its larger, thicker, and rougher leaves, its downy buds, and the character of its flowers and seeds. Its period of flowering is in April. The inner bark, separated from the cortex, is the part used. Large quantities are collected in the Lower Peninsula of Michigan.

Fremontia californica Torr., or *California Slippery Elm,* is not botanically allied to *Ulmus fulva;* its bark is said, however, to have the same properties as slippery elm bark, and to be used for a similar purpose.

Properties.—Elm bark is officially described as follows:

"Usually in bundles consisting of flat, oblong pieces, about 30 cm. in length and from 10 to 15 cm. in width; outer surface of a light brown or buff color with occasional dark brown patches of adhering cork, longitudinally striate and with detachable bundles of bast-fibers, and colored blackish upon the addition of a very diluted iodine T.S.; inner surface light yellowish-brown, nearly smooth and finely striate, only slightly darkened upon the addition of a very diluted iodine T.S.; fracture fibrous with projecting bast-fibers, the broken surface porous, due to the large mucilage cells; odor distinct; taste mucilaginous. The powder is very light brown; under the microscope it shows mostly fibrous fragments, and a finely granular portion made up of small starch grains, the latter being immediately colored bluish-black upon the addition of iodine T.S.; starch grains mostly spherical or more or less polygonal, usually about 0.003 mm. in diameter, but also attaining a diameter of 0.025 mm.; bast-fibers very long, about 0.02 mm. in diameter, with rather thin, slightly lignified walls; calcium oxalate in monoclinic prisms, mostly in crystal fibers, the individual crystals from 0.01 to 0.025 mm. in diameter; fragments of large mucilage cells with adhering starch grains. Macerate 1 Gm. of powdered Elm with 40 mils of distilled water for an hour and forcibly strain; the solution is of a mucilaginous consistence." *U. S.*

Ulmus abounds in mucilaginous matter, which it readily imparts to water. The mucilage is precipitated by solutions of lead acetate and subacetate, but not by alcohol. It contains a variety of tannin which colors iron solutions green, in amount about 6.5 per cent. according to Rink, or, according to Davy, a little less than 3 per cent.

Much of the bark brought into the market is of inferior quality, imparting comparatively little mucilage to water. It has the characteristic odor of the genuine bark, but is much less fibrous and more brittle, breaking abruptly when bent, instead of being capable, like the better kinds, of being folded lengthwise without breaking. To what this inferiority is owing, whether to difference in the species or the age, or to circumstances in the growth of the tree producing it, we are unable to state. Ground elm bark is said to be adulterated, usually with substances containing starch. Roberts found commercial specimens which possessed considerable of a brownish outer bark still adhering to them. One specimen was partly mouldy and had considerable adhering wood. (*Proc. Penn. Ph. Assoc.,* 1913, p. 85.) The following test, devised by Geo. M. Beringer, seems to have practical value: Ten grains of ground or pulverized elm bark, thoroughly shaken with one fluidounce of water, will, if pure and of good quality, in fifteen minutes form a thick jelly-like mass of a fawn color.

C. W. Wright, of Cincinnati, in a communication to the *Western Lancet,* states that slippery elm bark has the property of preserving fatty substances from rancidity, and that this fact was known to the Indians, who prepared bear's fat by melting it with the bark, in the proportion of a drachm of the latter to a pound of the former, keeping them heated together for a few minutes, and then straining off the fat. Wright tried the same process with butter and lard, and found them to remain perfectly sweet for a long time. (*A. J. P.,* xxiv.)

Uses.—Elm bark is an excellent demulcent, applicable to all cases in which this class of medicines is employed. It is especially recommended in *dysentery, diarrhea,* and *diseases of the urinary passages.* Its mucilage is reputed to be nutritious.

It is commonly used as a drink in the form of infusion. (See *Mucilago Ulmi.*) The powder may be used stirred in hot water, with which it forms a mucilage more or less thick according to the proportion added. The bark also serves as an emollient application in cases of *external inflammation.* For this purpose the powder may be formed into a poultice with hot water, or the bark itself may be applied, previously softened by boiling. McDowell, of Virginia, recommended slippery elm bark for the dilatation of *fistulas* and *strictures* (*Med. Examiner,* i, 244); subsequently H. R. Storer, of Boston, used it advantageously for *dilating the os uteri* (*B. M. S. J.,* liii, 300), and A. Abbe of the same place, succeeded in curing with it a case of *stricture of the rectum* (*B. M. S. J.,* liv, 349).

Off. Prep.—Trochisci Ulmi, *N. F.*

UNGUENTA.

OINTMENTS

(ụn-guĕn'tạ)

Pommades, Onguents, *Fr.;* Salben, *G.:* Pomatas, Unguentos, *It.;* Pomadas, Unguentos, *Sp.*

These are fatty substances, softer than cerates, of a consistence like that of butter, and such that they may be readily applied to the skin by inunction. When ointments are prepared

by merely mixing medicinal substances with simple ointment, hydrous wool-fat, lard, or petrolatum, care should be taken, if the added substance be a powder, that it be brought to the finest possible state of division before being incorporated with the unctuous matter. If soluble in water or in alcohol, it may often be advantageously rubbed with a little of one of these liquids. Gritty matter should not be allowed to enter these preparations. When an extract is added, if not uniformly soft, it should be made so by trituration with water or alcohol, according to its nature. Many of the ointments become rancid if long kept, and should, therefore, be prepared in small quantities at a time, or only when wanted for use. The tendency to rancidity may be in a considerable degree counteracted by imbuing the unctuous vehicle with benzoin, or with poplar buds, as recommended by Deschamps (*A. J. P.*, xv, 260); but care should be taken that there be no therapeutic objection to the admixture. Elm bark is said to have the same effect. (See p. 1172.) According to Geisler, ten drops of spirit of nitrous ether, incorporated with an ounce of ointment, will overcome the disagreeable fatty odor. (*Ph. Cb.*, 1847, 927.) Hydrous wool-fat or lanolin, petrolatum, and glycerite of starch are now used as vehicles for ointments. (See *Adeps Lanæ Hydrosus, Petrolatum,* and *Glyceritum Amyli.*) In the selection of a vehicle for an ointment it is important to consider the object for which the ointment is to be used. Lanolin is a natural emollient of the skin, composed of cholesterin and other substances.

Glycelæum is an oleaginous compound of finely powdered almond meal 1 part, glycerin 2 parts, and olive oil 6 parts. It was proposed by T. B. Groves, *C. D.*, Sept. 14, 1867, as a substitute for plasma and other fatty bodies, and has no doubt advantages, one of which is the facility with which it can be removed from the skin by a wet sponge. It has been proposed to substitute glycerin for oils and fats in the preparation of ointments, either wholly or in part; but ointments thus prepared are altogether unfit for application by inunction, as a portion of the glycerin remains upon the skin, producing a rough sensation of adhesiveness, very different from the softness caused by oleaginous matter, and in some skin diseases glycerin in an ointment would be positively injurious.

The cerates having been abolished as a class in the British Pharmacopœia, a few of the individual articles have been transferred to the ointments, making the definition of the latter class of preparations, as given above, not exactly applicable to all the individual substances at present included among them in that Pharmacopœia. We consider no substance to be strictly entitled to the name of ointment which is not of such a consistence as to adapt it to application to the skin by friction or inunction. Ointments should be dispensed in glass, porcelain, or queensware pots or jars, or, if for temporary use, in tight wooden boxes. We have used a very convenient method of dispensing soft ointments by introducing them into compressible tubes. These tubes are similar to those used for holding artists' colors, and have the advantage of shielding the ointment from the oxidizing action of the air while allowing the use of the desired quantity. Vanderkleed and Heidlberg (*Proc. P. P. A.*, 1913, p. 312) state that the only satisfactory method of determining whether or not the proper degree of subdivision has been attained is by the use of the microscope, and call attention to some of the precautionary measures which should be taken in order to obtain correct results. Their article is illustrated by numerous photographic representations of ointments of different degrees of fineness. For a classification of ointments in accordance with their therapeutic use, by C. S. N. Hallberg, see *West. Drug.*, 1900, 652.

Uses.—Ointments are used either for their local effects upon the skin or as a means of introducing drugs into the system through endermic absorption. The effects of fat-like substances upon the skin are due in part to their softening or emollient properties, and in part to the protection of the epiderm from the air, bacteria, or friction; they may also serve as carriers of antiseptic or other medicaments which influence pathological conditions of the skin. It is manifest that different qualities for an ointment base are desirable according to the purpose for which it is intended. Thus if it is intended to protect the skin the choice should fall on a substance which is not irritant nor readily absorbed nor liable to become liquid at a body temperature. On the other hand, for endermic administration one should choose a base which easily penetrates the skin. Concerning this last factor there has been a considerable amount of experimental investigation with not altogether harmonious results. The most widely used method has been to rub into the skin ointments made with various bases containing some substance easily demonstrable in the urine, and then determining the proportion of the medicament eliminated. Hirschfeld and Pollio (*Arch. f. Derm. u. Syph.*, 1904, lxxii, p. 163) found that the iodides were absorbed readily in ointments made with petrolatum or lard, but almost not at all from ointments made from wool fat. Bourjet (*Th. M.*, 1893) found that salicylic acid was absorbed readily from ointments made with true fats but poorly in those made with petrolatum or glycerin as the base. Sauerland (*Biochem. Zeit.*, 1912, xl, p. 56) in an elaborate research found that with vaseline, 40 per cent., with lard, 26 per cent., and with wool-fat, 18 per cent. of the iodine of iothion was absorbed through the skin; likewise methyl salicylate was absorbed in the same order, although in much smaller proportions. On the other hand, spirosal, a glycol salicylate, was absorbed scarcely at all from a lard ointment, but in fair amounts from either wool-fat or vaseline. Gardiner (*B. M. J.*, 1912, i, p. 238) rubbed ointments containing various stains into the shaven skin of guinea pigs and then examined the skin microscopically to ob-

serve the depth of penetration. He found that olive oil penetrated more deeply than any substance with which he experimented, but that goose grease and lard also penetrated well. Petrolatum remained limited to the very superficial portions of the skin. Wool-fat, while it penetrated somewhat more deeply than petrolatum, was noticeably behind lard. Wild (*B. M. J.*, 1911, ii, p. 161) employed a very different method to study this subject. He rubbed pure ointment bases into the skin for a measured time and then scraped off what was left on the skin and weighed. The difference between the quantity taken and that recovered he considered to represent the amount absorbed. He found that petrolatum was absorbed practically not at all, that of lard or olive oil about 15 per cent., and of hydrous wool-fat about 20 per cent., but that the absorption of the latter was noticeably less if it was deficient in water. While the evidence quoted is somewhat contradictory and it is probable that some ointment bases are better for one drug and some for another, yet it seems to us that in a general way the conclusion is justified that where absorption is desired lard is probably the best of the official ointment bases.

UNGUENTUM. U. S.

OINTMENT Ung. [Simple Ointment]

(ŭn-guĕn′tŭm)

Unguentum Adipis, *U. S.* 1860; Unguentum Simplex; Pommade simple, *Fr.*; Unguentum cereum, *P. G.*; Wachssalbe, *G.*

* "White Wax, *two hundred grammes* [or 7 ounces av., 24 grains]; Benzoinated Lard, *eight hundred grammes* [or 28 ounces av., 96 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Melt the white wax, add the benzoinated lard, and heat gently until liquefied; then stir the mixture until it congeals. For use in southern latitudes and during the warm season in other localities, 50 Gm. of the benzoinated lard (or more if necessary) may be replaced by an equal quantity of white wax." *U. S.*

Yellow wax was used in this ointment in the U. S. P., 1890, and objection was made to the color of the ointment. It has been very properly replaced by white wax in the U. S. P. VIII and IX, and the lard is now benzoinated.

This is emollient, and is occasionally employed as a mild dressing to blistered or excoriated surfaces, but more frequently as a vehicle, it being the basis of several official ointments.

UNGUENTUM ACIDI BORICI. U. S., Br.

OINTMENT OF BORIC ACID Ung. Acid. Bor.

(ŭn-guĕn′tŭm ăç′ĭ-dī bō′rĭ-cī)

Pommade de l'Acide Borique, *Fr.*; Unguentum Acidi Borici, *P. G.*; Borsalbe, *G.*

* "Boric Acid, in fine powder, *one hundred grammes* [or 3 ounces av., 231 grains]; Paraffin, *fifty grammes* [or 1 ounce av., 334 grains]; White Petrolatum, *eight hundred and fifty grammes* [or 29 ounces av., 430 grains], to make about *one thousand grammes* [or 35 ounces av., 120 grains]. Melt the paraffin, add the white petrolatum, and heat gently until liquefied. Then gradually add the hot liquid to the boric acid, contained in a warm mortar, triturating thoroughly, and stir the mixture until it congeals." *U. S.*

"Boric Acid, in powder, 10 *grammes;* Paraffin Ointment, white, 90 *grammes.* Melt the Paraffin Ointment; sift in the Boric Acid; stir until cold." *Br.*

Theodore Faber (*Ph. Ztg.*, 1914, p. 163) finds that boric acid in ointments may be readily and accurately estimated by the method of Jörgensen, in which it is converted into glycerin boric acid and estimated by titration with normal potassium hydroxide volumetric solution, as in the official method for estimating boric acid, the operation being carried out at a temperature sufficiently high to melt the fat, the presence of which may be disregarded.

This ointment was introduced into the U. S. P. (8th Rev.); it closely resembles the British ointment.

Uses.—This ointment probably has no superiority over plain white petrolatum. The prevalent belief that it has antiseptic properties because of the boric acid in it has no scientific support.

UNGUENTUM ACIDI SALICYLICI. Br.

SALICYLIC ACID OINTMENT

(ŭn-guĕn′tŭm ăç′ĭ-dī săl-ĭ-cŷl′ĭ-cī)

Pommade d'Acide Salicylique, *Fr.*; Salicylsalbe, *G.*

"Salicylic Acid, in powder, 2 *grammes;* Paraffin Ointment, white, 98 *grammes.* Melt the Paraffin Ointment; sift in the Salicylic Acid; stir until cold." *Br.*

UNGUENTUM ACIDI TANNICI. U. S.

OINTMENT OF TANNIC ACID Ung. Acid. Tann.

(ŭn-guĕn′tŭm ăç′ĭ-dī tăn′nĭ-cī)

Pommade d'Acide tannique, Pommade de Tannin, *Fr.*; Tanninsalbe, *G.*

* "Tannic Acid, *twenty grammes* [or 308.6 grains]; Glycerin, *twenty grammes* [or 308.6 grains]; Ointment, *sixty grammes* [or 2 ounces av., 51 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Dissolve the tannic acid in the glycerin with the aid of a gentle heat, and mix the solution thoroughly with the ointment, avoiding the use of iron utensils." *U. S.*

Ointment of Tannic Acid was doubled in strength at the U. S. P., 1890, revision. It is an excellent application in many cases of *piles* and *prolapsus ani*, also for *flabby ulcers.*

UNGUENTUM ACONITINÆ. Br.

ACONITINE OINTMENT

(ŭn-guĕn′tŭm ăc-ŏn-ĭ-tī′næ)

Pommade d'Oléate d'Aconitine, Pommade d'Aconitine, *Fr.*; Akonitinoleatsalbe, Akonitinsalbe, *G.*

"Aconitine, 2 *grammes;* Oleic Acid, 16 *grammes;* Prepared Lard, 82 *grammes.* Tritu-

rate the Aconitine with the Oleic Acid, and gently warm the mixture until dissolved; add the Prepared Lard; mix. This Ointment contains 2 per cent. of Aconitine. (See Appendix XII, Part III, *Unguenta.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

For the uses of this preparation the reader is referred to the articles on *Aconitum* and *Aconitina.* Care must be taken not to apply it too freely nor to an abraded or ulcerated surface, lest it produce serious constitutional effects.

UNGUENTUM AQUÆ ROSÆ. U. S., Br.

OINTMENT OF ROSE WATER Ung. Aq. Ros.

(ụn-guĕn'tŭm ă'quæ rō'şæ)

Rose Water Ointment; Unguentum Emolliens; Cold-cream, Ceratum Galeni, Galen's Cerate, *Fr. Cod.*: Cérat cosmétique, Crême froide, *Fr.*; Unguentum leniens, *P. G.*; Cold Cream, *G.*

* "Spermaceti, *one hundred and twenty-five grammes* [or 4 ounces av., 179 grains]; White Wax, *one hundred and twenty grammes* [or 4 ounces av., 102 grains]; Expressed Oil of Almond, *five hundred and sixty grammes* [or 19 ounces av., 330 grains]; Sodium Borate, in fine powder, *five grammes* [or 77 grains]; Stronger Rose Water, *one hundred and ninety grammes* [or 6 ounces av., 307 grains], to make about *one thousand grammes* [or 35 ounces av., 120 grains]. Reduce the spermaceti and the white wax to fine pieces and melt them on a water bath, add the expressed oil of almond and stir, continuing the heat until the mixture is uniform. Dissolve the sodium borate in the stronger rose water warmed on a water bath to the temperature of the melted wax and fat, and add the warm solution gradually to the melted mixture, stirring it rapidly and continuously until it congeals and becomes of uniform consistence. Ointment of Rose Water must be free from rancidity. If the Ointment has been chilled, warm it slightly before attempting to incorporate other ingredients with it." *U. S.*

"Rose Water, 20.0 *millilitres;* White Beeswax, 18.0 *grammes;* Purified Borax, 1.0 *gramme;* Almond Oil, 61.0 *grammes;* Oil of Rose, 0.1 *millilitre.* Melt the White Beeswax in the Almond Oil; add, with constant stirring, the Borax previously dissolved in the Rose Water; add the Oil of Rose, and continue to stir until cold." *Br.*

In the U. S. P., 1890, process the proportion of stronger rose water was greatly reduced—*i.e.*, from 30 to 20 per cent.; this makes a more stable preparation, but in our opinion the usefulness of the ointment has been curtailed by the reduction, its soft consistence being one of its most valuable characteristics. Sodium borate was added to increase its whiteness; its presence may, however, prove objectionable when the ointment is used as a basis in prescriptions, by reacting with some of the ingredients ordered by the physician. The U. S. P. VIII formula was retained with but slight changes in the U. S. P. IX. The manipulation was somewhat modified to increase uniformity of the product.

This preparation is a white, very soft, and elegant ointment, deriving a grateful odor from the rose water, which remains incorporated with the other constituents if kept enclosed in glazed vessels. We have found it an improvement to add oil of rose in the proportion of one drop to eight ounces, and, when made in the official quantity, to use an instrument known as the "Dover egg-beater" for giving it the desired creamy appearance. In larger amounts an ice cream churn is well adapted for this purpose. It is a pleasant, cooling application to irritated and excoriated surfaces, and may be used with great advantage for *chapped lips* and *hands*, so frequent in cold weather. It is a preparation of very early origin and is sometimes known by the name of Galen's Cerate. "Cold" cream is not recognized in the U. S. Pharmacopœia IX as an official synonym for ointment of rose water. This course became necessary because of the large number of unofficial ointments of varying composition popularly exploited as cold creams, and these were frequently dispensed, when physicians' prescriptions directed Ointment of Rose Water. The commercial cold creams must be made from substances which are not liable to rancidity, and paraffin oil, liquid petrolatum, white petrolatum, etc., largely form the basis of such, but the official ointment is to be preferred for use in prescriptions. W. C. Alpers furnishes the following formula for a cold cream which is more permanent than the official ointment. One hundred and fifty parts of white wax is melted in 600 parts of paraffin oil with the aid of a gentle heat; 9 parts of borax is dissolved in 240 parts of water; the two fluids are brought to a uniform temperature, not exceeding 60° C. (140° F.), and the aqueous solution is poured into the oily one in a continuous stream, stirring gently for a minute or two; then 1 part of oil of geranium and a little oil of rose are added while stirring, and the product while still warm is poured into jars. The cold cream so obtained is white, soft and smooth, pleasantly odorous, keeps well in the heat of summer and the cold of winter, and becomes only slightly thinner in summer. As the ointment is liable to become rancid when long kept, and the water to separate upon exposure, Joseph Laidley has proposed the substitution for the rose water of oil of rose and glycerin, the former in the proportion of two drops, the latter in that of four fluidrachms, the quantity of spermaceti being increased by two drachms. (*A. J. P.*, xii, 119.) For some purposes the substitution is useful, but the official preparation is preferable for *chapped hands*, as the glycerin frequently leaves an unpleasant sensation of stickiness on the skin.

UNGUENTUM ATROPINÆ. Br.

ATROPINE OINTMENT

(ụn-guĕn'tŭm ăt-rọ-pĭ'næ)

Pommade d'Oléate d'Atropine, Pommade d'Atropine, *Fr.*; Atropinoleatsalbe, Atropinsalbe, *G.*

"Atropine, 2 *grammes;* Oleic Acid, 8 *grammes;* Prepared Lard, 90 *grammes.* Triturate the

Atropine with the Oleic Acid, and gently warm the mixture until dissolved; add the Prepared Lard; mix. This Ointment contains 2 per cent. of Atropine. In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

For the uses of this ointment, see *Belladonna* and *Atropina*, p. 222 and p. 207. Caution must be observed that the ointment shall not come in contact with abraded, ulcerated, or wounded surfaces, and that it be not applied too freely to sound skin.

UNGUENTUM BELLADONNÆ. U. S., Br.

BELLADONNA OINTMENT Ung. Bellad.

(ụn-guĕn'tŭm bĕl-lą-dŏn'næ)

Pommade Belladonée, *Fr. Cod.*; Pommade de Belladone, *Fr.*; Belladonnasalbe, Tollkirschensalbe, *G.*

* "Pilular Extract of Belladonna Leaves, *ten grammes* [or 154 grains]; Diluted Alcohol, *five mils* [or 81 minims]; Hydrous Wool-fat, *thirty grammes* [or 1 ounce av., 25.5 grains]; Benzoinated Lard, *fifty-five grammes* [or 1 ounce av., 411 minims], to make about *one hundred grammes* [or 3 ounces av., 231 grains]. Triturate the extract with the diluted alcohol until a smooth mixture is obtained; with this incorporate the hydrous wool-fat; then add the benzoinated lard and mix thoroughly." *U. S.*

"Liquid Extract of Belladonna, 80 *millilitres;* Benzoated Lard, 60 *grammes;* Wool Fat, 20 *grammes.* Evaporate the Liquid Extract of Belladonna on a water-bath until it is reduced to twenty grammes; mix with the Benzoated Lard and Wool Fat. This Ointment contains 0.6 per cent. of the alkaloids of Belladonna Root. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoinated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

This is a convenient form for the external application of extract of belladonna. Care must be taken in preparing it that the extract employed have the due consistence, and, if dry and lumpy, it may be restored to the proper state by rubbing it with a little water in a heated mortar. The use of diluted alcohol, as now officially directed, is still better.

UNGUENTUM CANTHARIDINI. Br.

CANTHARIDIN OINTMENT

(ụn-guĕn'tŭm cạn-thăr-ị-dĭ'nī)

Unguentum Irritans, Unguentum ad Fonticulos; Pommade Epispastique (jaune, verte), *Fr. Cod.*; Onguent de Cantharides, *Fr.*; Unguentum Cantharidum, *P. G.*; Spanischfliegensalbe, *G.*; Unguento de cantaridas, *Sp.*

"Cantharidin, 0.1 *gramme;* Chloroform, 10.0 *millilitres;* Benzoated Lard, 290.0 *grammes.* Dissolve the Cantharidin in the Chloroform; add the solution to the Benzoated Lard, previously melted; stir until cold. This Ointment contains 0.033 per cent. of Cantharidin, which is approximately two-thirds of the proportion of Cantharidin contained in the Unguentum Cantharidis of the British Pharmacopœia, 1898. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

Cantharidin ointment of the Br. Pharm., 1914, is made by dissolving cantharidin, the blistering principle of Spanish flies, in chloroform and incorporating the solution in benzoated lard. This should make an effective ointment.

It should be recollected that this ointment is intended as a dressing for blisters, not to produce vesication. The U. S. Committee of Revision wisely deleted this preparation many years ago, as it was frequently prescribed under the impression that it was equal in strength to the cerate, in fact, identical with it, and disappointment resulted. Such a preparation should be left to extemporaneous prescription. *Dupuytren's ointment,* employed as a local application to *prevent the loss of hair,* was made by macerating a drachm of Spanish flies in a fluidounce of alcohol, and incorporating one part of the tincture thus formed with nine parts of lard.

UNGUENTUM CAPSICI. Br.

CAPSICUM OINTMENT

(ụn-guĕn'tŭm căp'sị-cī)

Pommade de Piment des Jardins, *Fr.*; Spanisch-Pfeffersalbe, *G.*

"Capsicum Fruit, bruised, 25 *grammes;* Hard Paraffin, 10 *grammes;* Soft Paraffin, 75 *grammes;* Prepared Lard, 10 *grammes.* Digest on a water-bath for one hour, stirring occasionally; strain; stir until cold. (See Appendix XII, Part III, *Unguenta.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

This is an active counter-irritant which may be used in the place of liquid liniments in *sprains, bruises, rheumatism,* and other inflammations.

UNGUENTUM CETACEI. Br.

SPERMACETI OINTMENT

(ụn-guĕn'tŭm cẹ-tā'cẹ-ī)

Pommade de baleine, *Fr.*; Walrathsalbe, *G.*

"Spermaceti, 20 *grammes;* White Beeswax, 8 *grammes;* Liquid Paraffin, 72 *grammes.* Melt together, and stir until cold." *Br.*

This ointment is employed as a mild dressing for *blisters, wounds,* and *excoriated surfaces,* or as the basis for carrying more active ingredients. It should be made in small quantities at a time, as it is apt to become rancid when long kept.

UNGUENTUM CHAULMOOGRÆ. Br.

CHAULMOOGRA OINTMENT [Gynocardia Ointment]

(ụn-guĕn'tŭm châul-mōōg'ræ)

"Chaulmoogra Oil, 10 *grammes;* Hard Paraffin, 40 *grammes;* Soft Paraffin, white, 50 *grammes.* Melt the Hard and Soft Paraffins to-

gether; add the Chaulmoogra Oil; stir until cold." *Br.*

This is intended for its local effects; it is not suitable for obtaining the systemic actions of chaulmoogra oil. (See *Oleum Chaulmoogra.*)

UNGUENTUM CHRYSAROBINI. U. S., Br.

CHRYSAROBIN OINTMENT Ung. Chrysarobin.

(ụn-guĕn'tŭm ȼhrȳs-ą-rọ-bī'nī)

Pommade de Chrysarobine, Pommade de Poudre de Goa, *Fr.*; Chrysarobinsalbe, Goapulversalbe, *G.*

* "Chrysarobin, *six grammes* [or 92.5 grains]; Benzoinated Lard, *ninety-four grammes* [or 3 ounces av., 138 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Triturate the chrysarobin with the benzoinated lard previously melted, and heat the mixture on a water bath for twenty minutes with occasional stirring; then strain and stir until it congeals." *U. S.*

"Chrysarobin, in powder, 4 *grammes;* Soft Paraffin, 96 *grammes.* Triturate the Chrysarobin with a portion of the Soft Paraffin until smooth; gradually add the remainder, mixing thoroughly by trituration." *Br.*

This ointment was reduced one-half in strength at the U. S. P., 1890, revision, but was slightly increased in strength in the U. S. P. IX; it is now about one-third stronger than the British ointment. It is a valuable agent in *psoriasis, ringworm,* and other *diseases of the skin,* but has the great drawback of leaving a permanent stain upon the linen. It is preferably made by dissolving the chrysarobin in a little hot benzene, mixing this rapidly with a portion of the melted lard, and subsequently stirring before adding the rest of the lard.

UNGUENTUM COCAINÆ. Br.

COCAINE OINTMENT

(ụn-guĕn'tŭm cō-cą-ī'næ)

Pommade d'Oléate de Cocaine, *Fr.*; Cocainoleatsalbe, *G.*

"Cocaine, 4 *grammes;* Oleic Acid, 16 *grammes;* Prepared Lard, 80 *grammes.* Triturate the Cocaine with the Oleic Acid, and gently warm the mixture until the alkaloid is dissolved; add the Prepared Lard; mix. This Ointment contains 4 per cent. of Cocaine. (See Appendix XII, Part III, *Unguenta.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

UNGUENTUM CREOSOTI. Br.

CREOSOTE OINTMENT

(ụn-guĕn'tŭm crē-ọ-sō'tī)

Pommade Créosotée, Pommade de Créosote, *Fr.*; Kreosotsalbe, *G.*

"Creosote, 10 *grammes;* Hard Paraffin, 40 *grammes;* Soft Paraffin, white, 50 *grammes.* Melt the Hard and Soft Paraffins together; add the Creosote; stir until cold." *Br.*

The British ointment is more than twice as strong as that official in the U. S. P., 1870, which was made by mixing half a fluidrachm of creosote with a troyounce of lard. For the use of this ointment, see *Creosotum.* It may sometimes be advantageously diluted with lard when found to irritate.

UNGUENTUM DIACHYLON. U. S.

DIACHYLON OINTMENT Ung. Diachyl.

(ụn-guĕn'tŭm dī-ăȼh'y-lŏn)

Unguentum Plumbi Hebræ; Hebra's Lead Ointment; Ongueat Diachylon, Pomade de Diachylon, *Fr.*; Unguentum diachylon, *P. G.*; Bleipflastersalbe, Diachylonsalbe, *G.*

* "Lead Plaster, *fifty grammes* [or 1 ounce av., 334 grains]; Oil of Lavender, *one gramme* [or 15 grains]; White Petrolatum, *forty-nine grammes* [or 1 ounce av., 319 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Melt together the lead plaster and the white petrolatum by applying a gentle heat, strain the mixture, allow it to cool but not congeal, add the oil of lavender, and stir the Ointment until it is cold." *U. S.*

This ointment has been largely used by dermatologists in *eczema* and other *skin diseases.* It is frequently called "*Unguentum Diachylon Hebræ,*" on account of its extensive use by Hebra, of Vienna. Vulpius states that the ointment used at Hebra's clinic, made according to the following formula, is very superior and will keep for weeks: Twenty parts of litharge are heated with sufficient water and eighty parts of olive oil until the reaction is completed, when one part of oil of lavender is added to the strained and cooling mass.

Our experience with the ointment made by the latter formula is that the tendency to rancidity constitutes its greatest objection, and in warm weather it is impossible to keep it longer than a few days. If even slightly rancid, it is unfit for use in most cases. A. Deringer (*Ph. Z. R.,* 1880, p. 103; *A. J. P.,* Sept., 1880) recommended the following modification: Dissolve 200 grammes of lead acetate in 1 liter of distilled water and 300 grammes of white Marseilles soap in 1½ liters of distilled warm water, filter both solutions, mix, wash the resulting precipitate frequently with distilled water, and, after removing the moisture from it as much as possible, melt 1 part of it together with 1½ parts of the best olive oil with a steam evaporating apparatus, and triturate into a white, smooth ointment in a mortar, which then possesses all the excellent mild and healing properties of Hebra's ointment. (See *Emplastrum Plumbi,* page 415.)

Eisner's modification, approved by L. A. Duhring, is as follows: One part of freshly precipitated (from lead acetate) pure white lead hydroxide is rubbed with two parts of water, and mixed well with six parts of the best Lucca olive oil. It should be stirred for about two hours over a hot water bath, and cooled with constant stirring until the proper

consistence is obtained. While cooling, a drachm of oil of lavender is to be added to each half-pound of ointment. (*M. T. G.*, May 7, 1881.)

UNGUENTUM EUCALYPTI. Br.

EUCALYPTUS OINTMENT

(ụn-guĕn'tŭm eū-cạ-lўp'tī)

Pommade d'Eucalypte, *Fr.*; Eukalyptussalbe, *G.*

"Oil of Eucalyptus, 10 *grammes;* Hard Paraffin, 40 *grammes;* Soft Paraffin, white, 50 *grammes.* Melt the Hard and Soft Paraffins together; add the Oil of Eucalyptus; stir until cold." *Br.*

This ointment is used as a stimulant to indolent *ulcers* and in *skin diseases.*

UNGUENTUM GALLÆ. U. S., Br.

NUTGALL OINTMENT Ung. Gall.

(ụn-guĕn'tŭm găl'læ)

Gall Ointment; Ointment of Galls; Pommade de Noix de Galle, *Fr.*; Galläpfelsalbe, *G.*

* "Nutgall, in very fine powder, *twenty grammes* [or 308.6 grains]; Ointment, *eighty grammes* [or 2 ounces av., 360 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Rub the nutgall with the ointment, gradually added, until they are thoroughly mixed. Avoid the use of metallic utensils." *U. S.*

"Galls, in powder, 20 *grammes;* Benzoated Lard, 80 *grammes.* Triturate the Galls with a portion of the Benzoated Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

Care should be taken to have the nutgall in very fine powder and thoroughly sifted. This ointment is used chiefly in *piles* and *prolapsus ani,* and in *flabby* or *indolent ulcers.*

Off Prep.—Unguentum Gallæ cum Opio, *Br.*

UNGUENTUM GALLÆ CUM OPIO. Br.

GALL AND OPIUM OINTMENT

(ụn-guĕn'tŭm găl'læ cŭm ō'pĭ-ō)

"Gall Ointment, 92.5 *grammes;* Opium, in powder, 7.5 *grammes.* Triturate the Opium with a portion of the Gall Ointment until smooth; gradually add the remainder, mixing thoroughly by trituration. This Ointment contains 7.5 per cent. of Opium." *Br.*

This combination of galls and opium is sometimes employed for *hemorrhoids.* From two to four per cent. of camphor is sometimes added.

UNGUENTUM HAMAMELIDIS. Br.

HAMAMELIS OINTMENT

(ụn-guĕn'tŭm hăm-ạ-mĕl'ĭ-dĭs)

Pommade de Hamamélis, *Fr.*; Hamamelissalbe, *G.*

"Liquid Extract of Hamamelis, 10 *millilitres;* Wool Fat, 60 *grammes;* Soft Paraffin, 30 *grammes.* Mix by trituration in a warm mortar." *Br.*

This was one of the "Additions" to the British Pharmacopœia, 1885, and afterwards introduced into the Br. Pharm., 1898, 1914. It is, in our opinion, of doubtful utility, but may be applied to *sprains.*

UNGUENTUM HYDRARGYRI. U. S., Br.

MERCURIAL OINTMENT Ung. Hydrarg.

(ụn-guĕn'tŭm hў-drär'gў-rī)

Mercury Ointment; Unguentum Mercuriale, s. Neapolitanicum; Pommade mercurielle à parties égales, Onguent mercuriel double, Onguent Napolitain, *Fr. Cod.*; Pommade napolitaine, *Fr.*; Unguentum Hydrargyri Cinereum, *P. G.*; Graue Quecksilbersalbe, *G.*

* "Mercury, *five hundred grammes* [or 17 ounces av., 279 grains]; Oleate of Mercury, *twenty grammes* [or 308.6 grains]; Prepared Suet, *two hundred and thirty grammes* [or 8 ounces av., 49 grains]; Benzoinated Lard, *two hundred and fifty grammes* [or 8 ounces av., 358 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Triturate the oleate of mercury in a warm mortar with the mercury added gradually, and when the globules are completely divided and distributed, set it aside for about fifteen minutes. Melt the lard and suet, allow the mixture to partially cool, add about *twenty-five grammes* [or 386 grains] of it to the mercurial mixture, and continue the trituration until globules of mercury are no longer visible under a lens magnifying ten diameters. Then add the remainder of the lard and suet and mix thoroughly." *U. S.*

Assay.—"Weigh 10 Gm. of Mercurial Ointment in a tared dish, melt it, then remove it from the fire and add 50 mils of warm purified petroleum benzin. Stir the mixture well, allow the mercury to settle completely, and decant the benzin. Wash the residue with successive portions of 10 mils each of warm purified petroleum benzin until it is entirely free from fatty matter, carefully retaining all of the separated Mercury in the dish, and allowing all traces of the benzin to evaporate. Add to the residue 10 mils of diluted hydrochloric acid, heat it gently and stir with a glass rod until the mercury collects in a globule. Pour off the acid, warm the mercury with a little distilled water, dry the globule on bibulous paper, and weigh. The separated mercury weighs not less than 4.9 Gm. nor more than 5.1 Gm." *U. S.*

"Mercury, 30 *grammes;* Benzoated Lard, 65 *grammes;* Prepared Suet, 5 *grammes.* Triturate until metallic globules cease to be visible. This Ointment is of approximately three-fifths the strength of the corresponding preparation of the British Pharmacopœia, 1898; it is of the same strength as the Unguentum Hydrargyri of the International Agreement. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

The U. S. P. IX ointment contains 50 per cent.

of mercury which was the strength of the Br. Pharm., 1898, ointment. In the Br. Pharm., 1914, the strength was reduced to 30 per cent. (corresponding with the International Protocol); but the title was not changed. The U. S. P. VIII introduced diluted mercurial ointment, 30 per cent. (See *Unguentum Hydrargyri Dilutum.*)

The U. S. official formula is particularly adapted to the extemporaneous preparation of this ointment, it having been shown that the extinguishment of the mercury is facilitated by the use of oleate of mercury, while its presence undoubtedly adds to the efficiency of the ointment. Oleic acid was suggested by Leo Eliel (see *Indiana Pharmacist,* 1888) in the proportion of 1 per cent. for the extinction of the mercury. The addition of 4 per cent. of compound tincture of benzoin aids in the preservation of the ointment. The trituration should not be accompanied with pressure, a light, rapid motion of the pestle being most effective. In the preparation of mercurial ointment, care is requisite that the mercury should be completely extinguished. The trituration is usually performed upon the large scale in a marble mortar, as it is difficult to keep iron so clean as not to impart more or less oxide to the ointment. The mercury is known to be extinguished when a portion of the mass, rubbed upon paper, exhibits no metallic globules under a magnifying glass of ten diameters. The operation cannot be considered as satisfactorily accomplished when the globules are invisible merely to the naked eye. To facilitate the process, which is very tedious, the addition of various substances has been proposed, calculated to hasten the disappearance of the metal. (For the details of many of these older processes see *U. S. D.,* 19th ed., p. 1310.)

E. R. Squibb prepared this ointment by succussion in an apparatus which agitates the mixture of fats and mercury until the metal is extinguished. When prepared with lard alone, the ointment is liable, in hot weather, to become so soft as to allow the metal to separate. Hence the official use of suet, and even a larger proportion might be employed, during the summer season. Christison states that the better plan is not to complete the process by a continuous trituration, but to operate for a short time every day and allow the ointment in the meantime to be exposed to the air. But so much time and labor are required in this process that the ointment is preferably made by machinery on the large scale. The fatty matters, kept in the fluid state by a heat of about 37.7° C. (100° F.), are triturated with the metal by means of two iron balls which are driven rapidly around in a circular trough by steam power. The extinguishment of the mercury is thus effected in about twelve hours. In buying from the manufacturer, great care should be exercised by the pharmacist, as much of the commercial ointment contains less than the official percentage of mercury. Indeed, it is sometimes found in the market without a trace of mercury, having been made by mixing up lamp black with rancid lard and suet until the proper tint is obtained. A method of preparing mercurial ointment proposed by Orosi is to precipitate metallic mercury, in the pulverulent form, from a solution of corrosive sublimate, by an excess of stannous chloride, with the addition of hydrochloric acid, and, having poured off the supernatant fluid, washed the precipitate with warm water, and dried it between bibulous paper, to incorporate it with the prescribed proportion of lard. To prevent the precipitated mercury from running into globules, it is recommended to cover with fat the interior of the vessel in which the precipitation takes place. For an account of many expedients that have been proposed to facilitate the extinguishment of the metal, see a paper by Dieterich. (*A. J. P.,* 1880.)

Mercurial ointment has when freshly prepared a bluish color, which becomes darker with age. It has been thought to contain the mercury in the state of mercurous oxide, but most of the metal can be separated by methods not calculated to reduce the oxide, and it is now generally admitted that by far the greater part of it exists in a state of minute division and not of chemical combination. It has been shown, however, that the metal is slightly oxidized, and the change of color which the ointment undergoes with age is attributable to further oxidation. If the ointment be kept long melted in a narrow vessel, metallic mercury subsides, and an oily liquid floats upon the surface. After this has been filtered so as to separate everything undissolved, it is blackened by hydrogen sulphide, and yields a trace of mercurial oxide to acetic acid. Christison states that he has examined various samples of the ointment, and never failed to detect mercurial oxides, and he has inferred from his observations that the oxide amounts to rather more than 1 per cent. But the proportion is variable, according to the age and mode of preparation of the ointment. It scarcely admits of a doubt that the mercurial oxide formed enters into chemical combination with the lard or one of its fatty acids. Donovan advanced the idea that the medicinal activity of the ointment depended exclusively on this compound of the lard with the mercurial oxide. An ointment made by merely mixing lard and black mercurial oxide has not the same effect, however, because there is no chemical union between the ingredients. But upon exposing such a mixture to a temperature of 176.6° C. (350° F.), and continually agitating it for two hours, he found that every ounce of lard dissolved and combined with twenty-one grains of oxide, and the resulting compound was proved to be equally effectual with the common ointment, and capable of being introduced into the system in one-third of the time. It has been proposed to substitute an ointment thus prepared for that made according to the official directions, as being more manageable and of more uniform strength. Care, however, would be required in preparing it to avoid a temperature either too high or too low, as the former might decompose the oxide, and

the latter would be insufficient to effect its union with the lard. There would be danger, also, that the lard might be rendered irritant by the influence of the heat, or if subjected to high summer temperatures will become unequal in strength in consequence of the settling of the metallic ingredient. The inference is that, after long standing, the contents of the jar should be triturated, so as to restore an equable strength, before being dispensed or always kept in a cool place. (*A. J. P.*, xvi, 2.)

Uses.—Mercurial ointment, when rubbed upon the surface of the body, produces, in consequence of its absorption, the general effects of mercury upon the system, but is used almost exclusively in the treatment of *syphilis*. Half to one drachm may be used at each application. It has also been employed as a resolvent in local affections, as in the case of *venereal buboes*, and of *chronic glandular swellings*, with the thought that it may operate directly by being applied in the course of the absorbents passing through the enlarged glands.

It is best absorbed if applied over those areas of the body where the skin is thin, as the bend of the elbows or knees, or the groins. The friction should on each occasion be continued till the ointment is not visible on the skin. When frequently rubbed upon the same part, it is prone to produce a disagreeable eruption, which interferes with its continued application, and it is therefore advisable to apply it to different parts if used on successive days. Mercurial ointment has been employed, with some success, to prevent the maturation of the *small pox pustule*, and the consequent pitting. For this purpose it may be applied to the face or other part, thickly spread on patent lint or muslin, care being taken to prevent the access of air to the covered part. To be successful it must be applied before the third or fourth day of the eruption. The ointment has been recommended also in *erysipelas* and in *chilblains*. Potassium iodide rubbed with mercurial ointment is said to promote the separation of the mercury in the form of globules (*J. P. C.*, 3e sér., x, 356); but the effect will not take place if the iodide has been throughly dried and well powdered and the ointment is added to it in small portions at a time. (*Ibid.*, x, 421.)

Off. Prep.—Linimentum Hydrargyri, *Br.;* Unguentum Hydrargyri Compositum, *Br.;* Unguentum Hydrargyri Dilutum, *U. S.*

UNGUENTUM HYDRARGYRI AMMONIATI. U. S., Br.

OINTMENT OF AMMONIATED MERCURY Ung. Hydrarg. Ammon. [White Precipitate Ointment]

(ụn-guĕn'tŭm hȳ-drär'gy-rī ạm-mō-nī-ā'tī)

Unguentum Præcipitati Albi; Ointment of White Precipitate; Pommade de Chloramidure de Mercure, *Fr.;* Unguentum Hydrargyri Album, *P. G.;* Weisse Quecksilbersalbe, *G.*

* "Ammoniated Mercury, in very fine powder, *ten grammes* [or 154 grains]; White Petrolatum, *fifty grammes* [or 1 ounce av., 334 grains]; Hydrous Wool-Fat, *forty grammes* [or 1 ounce av., 180 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Rub the ammoniated mercury with an equal weight of the melted white petrolatum, then add the remainder of the melted white petrolatum, mix thoroughly with the hydrous wool-fat, and stir the mixture until it congeals." *U. S.*

"Ammoniated Mercury, in powder, 5 *grammes;* Benzoated Lard, 95 *grammes*. Triturate the Ammoniated Mercury with a portion of the Benzoated Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. This Ointment is of approximately one-half the strength of the corresponding preparation of the British Pharmacopœia, 1898. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

The Br. Pharm., 1914, reduced the strength of this ointment one-half. Used chiefly as a stimulant and parasiticide in cutaneous eruptions, such as *scabies, ringworm, chronic eczema,* and *porrigo.*

UNGUENTUM HYDRARGYRI COMPOSITUM. Br.

COMPOUND MERCURY OINTMENT

(ụn-guĕn'tŭm hȳ-drär'gy-rī cọm-pŏs'ị-tŭm)

Pommade mercurielle comosée, *Fr.;* Kamper Quecksilbersalbe, *G.*

"Mercury Ointment, 40 *grammes;* Yellow Beeswax, 24 *grammes;* Olive Oil, 24 *grammes;* Camphor, in flowers, 12 *grammes*. Mix the Yellow Beeswax, Olive Oil, and Mercury Ointment with the aid of heat; add the Camphor; triturate until cold. This Ointment is of approximately three-fifths the strength of the corresponding preparation of the British Pharmacopœia, 1898. (See Appendix XII, Part III, *Unguenta,* and *Oleum Olivæ*)." *Br.*

The addition of camphor to mercurial ointment has been thought to soften it and promote absorption of the mercury, but that it has such an effect is very doubtful.

UNGUENTUM HYDRARGYRI DILUTUM. U. S.

DILUTED MERCURIAL OINTMENT Ung. Hydrarg. Dil. [Blue Ointment Hydrargyri unguentum P. I.]

(ụn-guĕn'tŭm hȳ-drär'gy-rī dī-lū'tŭm)

* "Mercurial Ointment, *six hundred grammes* [or 21 ounces av., 72 grains]; Petrolatum, *four hundred grammes* [or 14 ounces av., 48 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Mix them thoroughly. For use in southern latitudes or during the warm season in other localities, 50 Gm. of the petrolatum (or more, if necessary) may be replaced by an equal quantity of yellow wax.

"**Assay.**—Proceed as directed in the assay under *Unguentum Hydrargyri.* The separated mercury weighs not less than 2.9 Gm. nor more than 3.1 Gm." *U. S.*

This ointment was introduced into the U. S. P. (8th Rev.) to correspond to the recommenda-

tions of the International Conference; it should be kept in a cool place in the summer, as otherwise the mercury may separate on account of the softening of the fatty vehicle.

A substitute for *blue ointment* has been proposed by a French pharmacist, which is made as follows: 23.5 Gm. of mercuric chloride is triturated with 8.1 Gm. of sodium sulphocyanate and enough lanolin and petrolatum to make 100 Gm. The sulphocyanate reduces the mercuric chloride with the production of metallic mercury in a finely divided state and the resulting preparation is said to be very similar in its effect to blue ointment and to be much more easily prepared. (*Bull. Pharm.*, 1914, 306.)

UNGUENTUM HYDRARGYRI IODIDI RUBRI. Br.

MERCURIC IODIDE OINTMENT

(ụn-guĕn'tŭm hȳ-drär'gy-rī ī-ŏd'ī'dī rū'brī)

Ointment of Mercuric Iodide; Ointment of Red Iodide of Mercury; Pommade d'Iodure Mercurique, Pommade de Deutoiodure de Mercure, *Fr.*; Jodquecksilbersalbe, *G.*

"Red Mercuric Iodide, in powder, 4 *grammes;* Benzoated Lard, 96 *grammes.* Triturate the Red Mercuric Iodide with a portion of the Benzoated Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

This ointment is employed as a dressing to indolent *scrofulous* and *syphilitic ulcers.*

UNGUENTUM HYDRARGYRI NITRATIS. U. S., Br.

OINTMENT OF MERCURIC NITRATE Ung. Hydrarg. Nit. [Citrine Ointment]

(ụn-guĕn'tŭm hȳ-drär'gy-rī nī-trā'tĭs)

Ointment of Nitrate of Mercury; Unguentum Citrinum; Unguentum Hydrargyri Citrinum; Pommade Citrine, *Fr. Cod.*; Onguent Citrin, Pommade de Nitrate de Mercure, *Fr.*; Quecksilbernitratsalbe, Gelbe Quecksilbersalbe, *G.*

* "Mercury, *seven grammes* [or 108 grains]; Nitric Acid, *seventeen and five-tenths grammes* [or 271 grains]; Lard, free from water, *seventy-six grammes* [or 2 ounces av., 298 grains], to make about *one hundred grammes* [or 3 ounces av., 231 grains]. Warm the lard in a capacious porcelain dish until it has just melted, or to about 45° C. (113° F.). Add *seven grammes* [or 108 grains] of the nitric acid all at once and continue the heat until the characteristic reaction is complete. Hold an inverted glass funnel over the dish to protect the operator from any lard spurting from the dish during the reaction. Withdraw the heat immediately after the rapid rise of froth which accompanies the end reaction and cool the treated lard, stirring it until it assumes a bright citrine color. Dissolve the mercury in the remainder of the nitric acid, warming it if necessary to prevent crystallizing, and mix the solution with the previously prepared lard. All contact with metallic utensils or containers must be avoided." *U. S.*

"Mercury, 10 *grammes;* Nitric Acid, 30 *millilitres;* Prepared Lard, 40 *grammes;* Olive Oil, 70 *grammes.* Dissolve the Mercury in the Nitric Acid without the aid of heat, shaking gently from time to time. Heat the Prepared Lard and Olive Oil together on a sand-bath, so that the mixture when transferred to a heated earthen jar, capable of holding ten times the quantity, is at a temperature of about 150° C. (302° F.). Add the cold mercurial solution very gradually, stirring constantly with a glass or wooden spatula to promote the disengagement of fumes. Keep the mixture at a temperature of not less than 90° C. (194° F.) until frothing ceases, then stir until cold. (See Appendix XII, Part III, *Unguenta,* and page 779, *Oleum Olivæ.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

The formula for this ointment was changed in the U. S. P. (8th Rev.) by replacing the lard oil with lard; this in our opinion is not an improvement, as the present ointment is too hard in cold weather and more disposed to granulate than the ointment of the U. S. P. 1890. The introduction of a diluted citrine ointment into the Pharmacopœia similar to the one in the British Pharmacopœia would prove a great convenience.

The chemical changes which take place in the preparation of this ointment are not precisely known. They differ somewhat according to the circumstances under which the operation is performed; for example, according to the proportion and strength of the acid, the nature of the fatty matter, and the degree of heat employed. In the British process and that of the U. S. P. 1870 the mercury, in the first step of the process, is converted into a mixture of mercuric and mercurous nitrate by the addition of nitric acid in excess, with the loss of some of the free nitric acid through deoxidation. When the acid mercurial solution is added to the fatty matter, a reaction takes place, which results in the fat being oxidized at the expense of the free nitric acid, nitrogen dioxide and nitrogen tetroxide being at the same time liberated, and the olein of the fat is converted into elaidin, which change is recognized by the beautiful orange color of the fat. But the degree to which these changes take place is influenced greatly by the temperature to which the mixture is exposed. If this be low, there is little or no escape of gas; if elevated, there is a copious evolution of nitrous fumes. In the former case the changes are obviously less considerable than in the latter.

As formerly prepared, this ointment, though at first beautifully yellow and of the proper consistence, soon began to change, acquiring in time a dirty-greenish and mottled color, and becoming so hard and friable as to be unfit for use unless mixed with lard. These results were ascribed to various causes, and many different modifications of the process were pro-

posed in order to obviate them. The present official process was based on Rother's formula (*A. J. P.*, xlii, 420), and the value of this process lies principally in the fact that the olein of the oil is first converted into elaidin by the addition of nitric acid alone and the application of heat, and when the reaction has ceased and the basis of citrine ointment, as it might be called, is prepared, and nearly cold, the mercurial solution is added. In this way decomposition of the mercuric nitrate is avoided, as it is not subjected to heat, and the result is an ointment which will retain its color and consistence a long time. The drying vegetable oils appear, like olive oil, to be converted by nitrous acid or mercuric nitrate into elaidin, and it was a fair inference that they might be employed advantageously in the preparation of citrine ointment. Accordingly, Fessenden of North Carolina, stated, in an inaugural essay, that he substituted linseed oil for the neat's-foot oil, and succeeded in obtaining a perfectly good and durable ointment. Faliéres has found the oil of the ground nut (*Arachis hypogæa*) to answer very well. (*P. J.*, 1873, p. 1031.) Purified cotton seed oil makes an excellent vehicle. Washed butter has been used as the fat.

In the British process, when the fatty matter and the mercurial solution are mixed, care must be taken that the heat applied be not too great. Gas is extricated at 82.2° C. (180° F.), and at 100° C. (212° F.) escapes so abundantly that the mixture boils over unless the vessel is very large. (Alsop.) Besides, if the heat be too great, a portion of the mercury will be reduced, and the color of the ointment impaired. When large quantities of materials are operated upon, the reaction which occurs produces of itself a sufficient heat, but in ordinary cases the temperature should be kept at about 87.7° C. (190° F.) by means of a water bath, and if it exceed 96.1° C. (205° F.) should be reduced. It should always be sufficient to produce a copious extrication of gas. The ointment should be prepared in a glass, porcelain, or well-glazed earthen vessel, and a glass rod or a wooden spatula should be employed for stirring the mixture. Under no circumstances should an iron or steel spatula or stirrer be used in its preparation, because of the discoloration due to the action of the acid upon the iron.

The U. S. P. IX process is well adapted to small lots of the ointment but the reaction is too violent for large quantities. When large amounts are to be prepared mix the melted lard and acid in an earthenware crock of at least twice the size required to hold the ointment, place it in a water bath and warm it until the reaction begins. Then withdraw most of the heat and allow the reaction to proceed for some hours or until complete. Finally incorporate the solution of mercuric nitrate. If the reaction should become too violent it may be checked by adding cold water which will afterwards separate.

Uses.—This ointment is much and very advantageously employed, as a stimulant and alterative application, in *porrigo* or *tinea capitis*, *impetigo larvalis*, *psoriasis*, *sycosis*, *pityriasis*, certain forms of *chronic eczema*, and various other eruptive affections. It is an active parasiticide and antiseptic, highly stimulating and generally should be diluted with lard, unless in very sluggish cases. Some care is requisite in its use, to avoid the risk of salivation. When hard and friable, it must be rubbed up with fresh lard before it can be applied. An ointment prepared with lard and nitric acid, called *Alyon's ointment*, after the person who first prepared it, was formerly much used in cases similar to those in which the citrine ointment is now employed. The *ointment of nitric acid* of the former Edinburgh and Dublin Pharmacopœias was of this character.

Off. Prep.—Unguentum Hydrargyri Nitratis Dilutum, *Br.*

UNGUENTUM HYDRARGYRI NITRATIS DILUTUM. Br.

DILUTED MERCURIC NITRATE OINTMENT [Diluted Ointment of Nitrate of Mercury]

(ụn-guĕn'tŭm hȳ-drär'gy-rī nī-trā'tĭs dī-lū'tŭm)

"Mercuric Nitrate Ointment, 20 *grammes;* Soft Paraffin, yellow, 80 *grammes.* Mix by trituration." *Br.*

UNGUENTUM HYDRARGYRI OLEATI. Br.

MERCURIC OLEATE OINTMENT

(ụn-guĕn'tŭm hȳ-drär'gy-rī ō-lẹ-ā'tī)

Pommade d'Oléate Mercurique, *Fr.;* Quecksilberoleatsalbe, *G.*

"Oleated Mercury, 25 *grammes;* Benzoated Lard, 75 *grammes.* Mix by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

UNGUENTUM HYDRARGYRI OXIDI FLAVI. U. S., Br.

OINTMENT OF YELLOW MERCURIC OXIDE
Ung. Hydrarg. Oxid. Flav.

(ụn-guĕn'tŭm hȳ-drär'gy-rī ŏx'ĭ-dī flā'vī)

Yellow Mercuric Oxide Ointment; Pommade d'oxyde mercurique jaune, *Fr.;* Gelbe Quecksilberoxydsalbe, *G.*

* "Yellow Mercuric Oxide, in very fine powder, *ten grammes* [or 154 grains]; Water, *ten grammes* [or 154 grains]; Hydrous Wool Fat, *forty grammes* [or 1 ounce av., 180 grains]; Petrolatum, *forty grammes* [or 1 ounce av., 180 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Triturate the yellow mercuric oxide with the water until the mixture is perfectly smooth, then add the hydrous wool fat in divided portions, and incorporate thoroughly with the petrolatum. All contact with metallic utensils or containers must be avoided." *U. S.*

"Yellow Mercuric Oxide, in powder, 2 *grammes;* Soft Paraffin, yellow, 98 *grammes.* Triturate the Yellow Mercuric Oxide with a

portion of the Soft Paraffin until smooth; gradually add the remainder, mixing thoroughly by trituration." *Br.*

The unctuous vehicle of this ointment, without being so liquid as to allow the powder to subside, must yet melt at the heat of the body, and thus, when introduced into the eye, spread equably over the surface. It should, moreover, be as far as possible chemically indifferent to the oxide, and, while perfectly bland in its proper state, should not be liable to become irritating by rancidity.

Uses.—This is the least irritant of the official ointments of the mercurial salts. It possesses the disinfectant and local stimulating properties of the mercury preparations and is used in various skin diseases, especially in *eczema* of the auditory canal or eye-lid, and in *hordeolum.* The U. S. ointment generally requires dilution, the British being of a more frequently used strength.

UNGUENTUM HYDRARGYRI OXIDI RUBRI. Br.

RED MERCURIC OXIDE OINTMENT [Red Precipitate Ointment]

(ŭn-guĕn'tŭm hȳ-drär'gy-rī ŏx'ĭ-dī rū'brī)

Unguentum Præcipitati Rubri; Pommade d'oxyde rouge de Mercure, *Fr. Cod.*; Pommade de Lyon, Pommade de Précipité rouge, Baume ophthalmique rouge, *Fr.*; Unguentum Hydrargyri Rubrum, *P. G.*; Rothe Quecksilbersalbe, *G.*

"Red Mercuric Oxide, in powder, 10 *grammes;* Paraffin Ointment, yellow, 90 *grammes.* Melt the Paraffin Ointment; sift in the Red Mercuric Oxide; stir until cold." *Br.*

Red Precipitate Ointment was deleted from the U. S. P. IX but has been added to the N. F. (see Part III). It has been largely replaced in medical practice by Yellow Mercuric Oxide Ointment, which is a more desirable preparation.

The red mercuric oxide here referred to is that prepared from the nitrate and usually called *red precipitate.* It is important that the oxide should be thoroughly pulverized before being mixed with the lard, as otherwise it might prove injurious in cases of ophthalmia, in which it is sometimes used. When great care is taken to have the red oxide very finely pulverized, the color is more yellowish than is usual. This ointment loses its fine red color when long kept, probably in consequence of the conversion of the red oxide into the black, or its reduction to the metallic state. It is best to prepare it in small quantities at a time. The U. S. P. (8th Rev.) process was an improvement over the process of the U. S. P. 1890, particularly in the choice of the vehicle.

Ointment of red mercuric oxide is more highly stimulating than that of the yellow oxide. It is employed in *indolent and foul ulcers,* and *various skin diseases.* It is less frequently employed than the ointment of yellow mercuric oxide, because the latter can be made smoother and less irritating, and has the same chemical composition and properties. It may be diluted with lard if found too stimulating.

UNGUENTUM HYDRARGYRI SUBCHLORIDI. Br.

MERCUROUS CHLORIDE OINTMENT [Calomel Ointment]

(ŭn-guĕn'tŭm hȳ-drär'gy-rī sŭb-klō'rī-dī)

Unguentum Calomelanos, *Br.* 1864; Ointment of Subchloride of Mercury; Ointment of Calomel; Pommade de Chlorure Mercureux, Pommade de Calomel, Pommade de Calomélas, *Fr.*; Quecksilberchlorürsalbe, *G.*

"Mercurous Chloride, 20 *grammes;* Benzoated Lard, 80 *grammes.* Triturate the Mercurous Chloride with a portion of the Benzoated Lard, until smooth; gradually add the remainder, mixing thoroughly by trituration. This Ointment is of twice the strength of the corresponding preparation of the British Pharmacopœia, 1898. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

Uses.—While ointments of calomel are often of much value in the same class of cases for which the yellow oxide is employed, this ointment is far too strong. We believe ointments of this character might well be left to extemporaneous prescription.

UNGUENTUM IODI. U. S., Br.

IODINE OINTMENT Ung. Iodi

(ŭn-guĕn'tŭm ī-ō'dī)

Unguentum Iodinii, *U. S.* 1870; Pommade d'iodure de potassium ioduré, *Fr. Cod.*; Pommade d'Iode, *Fr.*; Jodsalbe, *G.*

* "Iodine, *four grammes* [or 62 grains]; Potassium Iodide, *four grammes* [or 62 grains]; Glycerin, *twelve grammes* [or 185 grains]; Benzoinated Lard, *eighty grammes* [or 2 ounces av., 360 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Triturate the iodine and potassium iodide in a glass mortar with the glycerin until dissolved, then gradually incorporate the benzoinated lard and mix thoroughly. All contact with metallic utensils or containers must be avoided. This Ointment must not be dispensed unless it has been recently prepared." *U. S.*

"Iodine, 4 *grammes;* Potassium Iodide, 4 *grammes;* Glycerin, 12 *grammes;* Prepared Lard, 80 *grammes.* Triturate the Iodine, Potassium Iodide, and Glycerin in a glass or porcelain mortar; add the Prepared Lard; mix thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

The object of the potassium iodide and water in the U. S. 1890 process was to bring the iodine into a state in which it may be equably incorporated with the lard. They were found to answer better in practice than the alcohol formerly used, but glycerin answers still better and is used in both Pharmacopœias.

Miles Shimer (*Proc. P. P. A.*, 1915, p. 304) suggests that by keeping the iodine, potassium iodide and glycerin already made up as a stock

solution, the dispensing of U. S. P. iodine ointment is much more expeditiously accomplished.

The proportion of potassium iodide was increased from 1 Gm. to 4 Gm. in the U. S. P. VIII and glycerin (12 per cent.) added. When rubbed upon the skin it imparts to it an orange color, which, however, slowly disappears with the absorption of the iodine.

Uses.—Ointment of Iodine is useful both for the local counter-irritant effect of the element and as a means of obtaining the constitutional action of the iodides. It is commonly believed that this ointment exercises a local resolvent action and it is therefore employed in various forms of *arthritis, goitre, scrofulous swellings of the glands,* and other *chronic tumefactions.* When continued for some time it occasionally produces a pustular eruption upon the portion of skin to which it is applied. It has also been recommended in *chilblains.* The ointment should be prepared only when wanted for use, for it undergoes change if kept, losing its deep orange-brown color, and becoming pale upon its surface, due to the combination of part of the iodine with the fat.

UNGUENTUM IODOFORMI. U. S., Br.

IODOFORM OINTMENT Ung. Iodof.

(ŭn-guĕn'tŭm ī-ō-dō-fôr'mī)

Pommade d'Iodoforme, *Fr.*; Jodoformsalbe, *G.*

* "Iodoform, in very fine powder, *ten grammes* [or 154 grains]; Benzoinated Lard, *ninety grammes* [or 3 ounces av., 76 grains], to make *one hundred grammes* [or 3 ounces av., 231 grains]. Triturate the iodoform thoroughly with about twice its weight of the benzoinated lard, then incorporate the remainder of the benzoinated lard." *U. S.*

"Iodoform, in powder, 10 *grammes;* Prepared Lard, 90 *grammes.* Triturate the Iodoform with a portion of the Prepared Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

It is important to have the iodoform in very fine powder, as officially directed, and, owing to the powerful odor of iodoform, it is usual to add oil of bitter almond or one of the other volatile oils, balsam of Peru, or a similar substance, to render the odor more bearable.

UNGUENTUM LANÆ COMPOSITUM. Br.

COMPOUND WOOL FAT OINTMENT [Emollient Ointment]

(ŭn-guĕn'tŭm lā'næ cŏm-pŏs'ĭ-tŭm)

"Prepared Lard, 40 *grammes;* Wool Fat, 40 *grammes;* Paraffin Ointment, 20 *grammes.* Melt together; stir until cold. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

The addition of the paraffin ointment to woolfat overcomes the stickiness which is so frequently an obstacle to the employment of that emollient.

UNGUENTUM MYROBALANI. Br.

MYROBALAN OINTMENT

(ŭn-guĕn'tŭm mȳ-rō-bă-lā'nī)

"Myrobalans, in powder, 20 *grammes;* Benzoated Lard, 80 *grammes.* Triturate the Myrobalans with a portion of the Benzoated Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

This is used as a local astringent.

Off. Prep.—Unguentum Myrobalani cum Opio, *Br.*

UNGUENTUM MYROBALANI CUM OPIO. Br.

MYROBALAN AND OPIUM OINTMENT

(ŭn-guĕn'tŭm mȳ-rō-bă-lā'nī cum ōp'ĭ-ō)

"Myrobalan Ointment, 92.5 *grammes;* Opium, in powder, 7.5 *grammes.* Triturate the Opium with a portion of the Myrobalan Ointment until smooth; gradually add the remainder, mixing thoroughly by trituration. This Ointment contains 7.5 per cent. of Opium." *Br.*

UNGUENTUM PARAFFINI. Br.

PARAFFIN OINTMENT

(ŭn-guĕn'tŭm păr-ăf-fī'nī)

Pommade de Paraffin, *Fr.*; Paraffinsalbe, *G.*

"Hard Paraffin, 27 *grammes;* Soft Paraffin, 70 *grammes;* White Beeswax, 3 *grammes.* Melt together; stir until cold. When Paraffin Ointment is used as the basis of white ointments it should be prepared with the white variety of Soft Paraffin; and when used for colored ointments it should be prepared with the yellow variety of Soft Paraffin. (See Appendix XII, Part III, *Unguenta.*)" *Br.*

This was recognized by the Br. Ph. 1898 for use as a vehicle in the exhibition of various medicaments.

UNGUENTUM PHENOLIS. U. S. (Br.)

OINTMENT OF PHENOL Ung. Phenol. [Unguentum Acidi Carbolici, U. S. 1890, Ointment of Carbolic Acid]

(ŭn-guĕn'tŭm phē-nō'lĭs)

Unguentum Acidi Carbolici, *Br.*; Pommade de Phénol, Pommade Phéniquée, Pommade d'Acide phénique, *Fr.*; Karbolsalbe, Phenolsalbe, *G.*; Carbolized Petrolatum.

* "Liquefied Phenol, *two and twenty-five hundredths grammes* [or 35 grains]; Ointment, *ninety-seven and seventy-five hundredths grammes* [or 3 ounces av., 196 grains], to make *one hundred grammes* [or 3 ounces av., 231

grains]. Add the liquefied phenol to the melted ointment and stir the mixture until it begins to congeal." *U. S.*

"Phenol, 3 *grammes;* Paraffin Ointment, white, 97 *grammes.* Melt the Paraffin Ointment; in it dissolve the Phenol; stir until cold." *Br.*

The quantity of phenol in this ointment was decreased from 10 per cent. in the U. S. P. 1880 to 5 per cent. in the 1890 revision, and has been further decreased to 2.25 per cent. in the U. S. P. IX. This is an improvement, for it is a very strong ointment, which for most purposes still requires dilution.

Its value as a disinfectant is greatly overestimated, for phenol exerts its full anti-bacterial powers only when in aqueous solution.

UNGUENTUM PICIS LIQUIDÆ. U. S., Br.

TAR OINTMENT Ung. Pic. Liq.

(ụn-guĕn'tŭm pī'cĭs lĭq'uị-dæ)

Pommade de Goudron, *Fr. Cod.;* Theersalbe, *G.*

* "Tar, *five hundred grammes* [or 17 ounces av., 279 grains]; Yellow Wax, *one hundred and fifty grammes* [or 5 ounces av., 127 grains]; Lard, *three hundred and fifty grammes* [or 12 ounces av., 151 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Melt the yellow wax, add the lard, and to the melted mixture add the tar, previously warmed, and incorporate thoroughly; strain through muslin, and stir the mixture until it congeals." *U. S.*

"Tar, 70 *grammes;* Prepared Lard, 5 *grammes;* Yellow Beeswax, 25 *grammes.* Melt together; stir until cold. (See Appendix XII, *Unguenta.*) In India, Prepared Suet (Sevum Præparatum) should be employed instead of Prepared Lard in making this Ointment." *Br.*

The formula for tar ointment in the U. S. P. 1890 differed from that formerly official in the use of yellow wax and lard in place of suet. The same ingredients were retained in the Eighth Revision, but the proportion of wax was slightly decreased, making the ointment somewhat softer in consistence. This ointment is highly useful as a stimulant application in various *scaly* and *scabby eruptions,* particularly in *psoriasis* and *chronic eczema* and also for its antiparasitic effect in *tinea capitis* or similar *skin diseases.* In the last-mentioned affection it should be applied night and morning, and in bad cases the patient should constantly wear a cap thickly coated internally with the ointment. In some cases it requires dilution with an equal quantity of lard to avoid irritation.

UNGUENTUM PLUMBI IODIDI. Br.

LEAD IODIDE OINTMENT

(ụn-guĕn'tŭm plŭm'bī ī-ŏd'ị-dī)

Lead Iodide Ointment; Pommade d'Iodure de Plomb, *Fr. Cod.;* Jodbleisalbe, *G.*

"Lead Iodide, in powder, 10 *grammes;* Benzoated Lard, 90 *grammes.* Triturate the Lead Iodide with a portion of the Benzoated Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

For the uses of this ointment, see *Plumbi Iodidum.* It is also official in the N. F. IV (see Part III).

UNGUENTUM PLUMBI SUBACETATIS. Br.

LEAD SUBACETATE OINTMENT

(ụn-guĕn'tŭm plŭm'bī sŭb-ă-cẹ-tā'tĭs)

Cerate of Subacetate of Lead was not admitted to the U. S. P. IX, but has been included in the N. F. IV (see Part III).

"Strong Solution of Lead Subacetate, 12.5 *grammes;* Wool Fat, 25.0 *grammes;* Hard Paraffin, 12.5 *grammes;* Soft Paraffin, 50.0 *grammes.* Melt together the Wool Fat and the Hard and Soft Paraffins; stir until nearly cold; add the Strong Solution of Lead Subacetate, and continue to stir until cold." *Br.*

The white petrolatum, wool fat and paraffin now used in this ointment are preferable to the lard and cottonseed oil formerly employed, as they are free from the great objections to the former official cerate, of proneness to rancidity, and discoloration. This cerate received the name by which it is commonly known from Goulard, by whom it was employed and recommended.

The ointment of subacetate of lead was formerly largely used in *excoriations, burns, scalds,* and *chilblains,* but is infrequently employed at present.

UNGUENTUM POTASSII IODIDI. Br.

POTASSIUM IODIDE OINTMENT

(ụn-guĕn'tŭm pọ-tăs'sĭ-ī ī-ŏd'ị-dī)

Ointment of Potassium Iodide; Pommade d'Iodure de Potassium, *Fr. Cod.;* Unguentum Kalii jodati, *P. G.,* Jodkaliumsalbe, Kaliumjodidsalbe, *G.*

"Potassium Iodide, 10.0 *grammes;* Potassium Carbonate, 0.6 *gramme;* Distilled Water, 9.4 *grammes;* Benzoated Lard, 80.0 *grammes.* Dissolve the Potassium Iodide and Potassium Carbonate in the Distilled Water; mix the solution, gradually, with the Benzoated Lard, in a slightly warmed mortar. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

The former ointments of potassium iodide became discolored by time in consequence of the liberation of iodine. This was due to rancidity in the lard, and the slightest change in the fat would produce some discoloration. It was prevented in the U. S. P. 1880 by the sodium thiosulphate, which also produces traces of sodium iodide and sulphur. The addition of potassium carbonate by the present Br. Pharmacopœia is made with the same object.

The *Bulletin de Pharmacie du Nord* recommended a concentrated solution of potassium iodide in glycerin as a basis for this ointment. One gramme of the salt is dissolved in two and a half grammes of hot glycerin, and the solution mixed with the fatty constituent in the proper proportion. The advantages of this method are that the ointment is free from crystals, and the salt more readily absorbed. The glycerin would probably not be objectionable in most cases, and potassium carbonate could be added, if desired. Ointment of potassium iodide is employed for the discussion of *goitres, scrofulous tumors,* and other *indolent swellings,* and is sometimes preferred to the ointment of iodine, as it does not, like that, discolor the skin. It does not, however, possess the antiseptic nor counter-irritant properties of the free iodine.

UNGUENTUM STAPHISAGRIÆ. Br.

STAVESACRE OINTMENT

(ụn-guĕn'tŭm stăph-ĭ-să'grĭ-æ)

Onguent de Staphisaigre, *Fr.*; Stephanskörnersalbe, *G.*

"Stavesacre Seeds, 20 *grammes;* Yellow Beeswax, 10 *grammes;* Benzoated Lard, 85 *grammes.* Crush the Stavesacre Seeds; digest the crushed seeds with the Benzoated Lard on a water-bath for two hours; strain and press through calico; melt the Beeswax in the liquid mixture; stir until cold. (See Appendix XII, Part III, *Unguenta.*) In India, Prepared Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

This ointment is but half the strength of that official in the British Pharmacopœia 1885; it is said to be non-irritant, and is largely used in Great Britain for destroying *body-lice,* also in *scabies* and *prurigo.*

UNGUENTUM STRAMONII. U. S.

STRAMONIUM OINTMENT Ung. Stramon.

(ụn-guĕn'tŭm strą-mō'nĭ-ī)

Pommade de Stramoine, *Fr.*; Stechapfelsalbe, *G.*

* "Pilular Extract of Stramonium, *ten grammes* [or 154 grains]; Diluted Alcohol, *five mils* [or 81 minims]; Hydrous Wool Fat, *twenty grammes* [or 308.6 grains]; Benzoinated Lard, *sixty-five grammes* [or 2 ounces av., 128 grains], to make about *one hundred grammes* [or 3 ounces av., 231 grains]. Triturate the extract with the diluted alcohol until a smooth mixture is obtained; with this incorporate the hydrous wool fat, then add the benzoinated lard, and mix thoroughly." *U. S.*

This is a more certain preparation than that of the former editions of the U. S. Pharmacopœia, which was made by boiling the fresh leaves in lard. The color of the ointment of the U. S. P. IX is different from that of the earlier Pharmacopœias, the greenish tint being due to the use of official extract of stramonium which is now made from the leaves instead of the seeds. For remarks by A. P. Sharp of Baltimore, on the preparation of this ointment, see *A. J. P.* (xxvii, 391). A useful anodyne application in *irritable ulcers, painful hemorrhoids,* and *bruises.*

UNGUENTUM SULPHURIS. U. S., Br.

SULPHUR OINTMENT Ung. Sulphur.

(ụn-guĕn'tŭm sŭl'phŭ-rĭs)

Pomatum Sulfuratum, Unguentum Sulfuratum Simplex; Pommade Soufrée, *Fr. Cod.*; Schwefelsalbe, *G.*

* "Sublimed Sulphur, *one hundred and fifty grammes* [or 5 ounces av., 127 grains]; Benzoinated Lard, *eight hundred and fifty grammes* [or 29 ounces av., 430 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Rub the sublimed sulphur with the benzoinated lard, gradually added, until they are thoroughly mixed." *U. S.*

"Sublimed Sulphur, 10 *grammes;* Benzoated Lard, 90 *grammes.* Triturate the Sublimed Sulphur with a portion of the Benzoated Lard until smooth; gradually add the remainder, mixing thoroughly by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

Washed sulphur was substituted in the U. S. P., 1890, for the sublimed sulphur of the former Pharmacopœia; the change was of questionable utility and the U. S. P. IX has again returned to the use of sublimed sulphur. It has been found that the acid products resulting from the slight decomposition in sublimed sulphur have value as parasiticides. In the U. S. P. VIII the percentage of sulphur was reduced one-half. Its disagreeable odor may be partially concealed by oil of lemon or oil of bergamot.

This ointment affords a ready means of obtaining the local action of sulphur. For discussion of its properties, see *Sulphur.*

UNGUENTUM ZINCI OLEATIS. Br.

ZINC OLEATE OINTMENT

(ụn-guĕn'tŭm zĭn'cī ō-lę-ā'tĭs)

Pommade d'oléate de zinc, *Fr.*; Zinkoleatsalbe, *G.*

"Zinc Sulphate, 30 *grammes;* Hard Soap, in shavings, 90 *grammes;* Distilled Water, boiling, Soft Paraffin, white, of each *a sufficient quantity.* Dissolve the Zinc Sulphate in sixty millilitres of the Distilled Water. Dissolve the Hard Soap in six hundred millilitres of the Distilled Water. Mix the solutions; heat to boiling; allow the melted zinc oleate so produced to rise to the surface; cool until it solidifies; pour off the aqueous liquid; boil the zinc oleate with successive quantities of Distilled Water until the washings afford not more than a slight *reaction* for sulphates; reduce the cake thus obtained to a coarse powder; dry at a temperature below 60° C. (140° F.); melt on a water-bath with an equal weight of the Soft Paraffin; stir until cold." *Br.*

This ointment was radically changed in the Br. Ph., 1898, revision; instead of using zinc oleate made from oleic acid and zinc oxide, a process is ordered which directs the zinc oleate to be made by double decomposition between zinc sulphate and sodium oleo-stearate (hard soap). The product is a white, fine precipitate; it is, however, not a pure oleate, but a zinc oleo-stearate or oleo-palmitate.

This preparation has therapeutic properties similar to those of the ointment of zinc oxide, but is a little more stimulating. It is especially useful in *chronic eczema* and similar *cutaneous eruptions.*

UNGUENTUM ZINCI OXIDI. U. S. (Br.)

OINTMENT OF ZINC OXIDE Ung. Zinc. Ox. [Zinc Ointment]

(ŭn-guĕn'tŭm zĭn'cī ŏx'ĭ-dī)

Unguentum Zinci, *Br.;* Ointment of Zinc; Unguentum de Nihilo Albo; Pommade d'Oxyde de Zinc, Cérat épulotique, *Fr.;* Unguentum Zinci, *P. G.;* Zinksalbe, *G.*

* "Zinc Oxide, in very fine powder, *two hundred grammes* [or 7 ounces av., 24 grains]; Benzoinated Lard, *eight hundred grammes* [or 28 ounces av., 96 grains], to make *one thousand grammes* [or 35 ounces av., 120 grains]. Rub the zinc oxide, which must be free from gritty particles, with about one-fourth of the melted benzoinated lard, in a previously warmed container, and with this incorporate the remainder of the benzoinated lard, previously melted. If necessary, strain the Ointment while warm, and stir it thoroughly until it congeals." *U. S.*

"Zinc Oxide, 15 *grammes;* Benzoated Lard, 85 *grammes.* Mix by trituration. (See Appendix XII, Part III, *Unguenta.*) In India, Benzoated Suet (Sevum Benzoatum) should be employed instead of Benzoated Lard in making this Ointment." *Br.*

The assay of this ointment for its zinc oxide content may be easily accomplished, according to J. L. Mayer (*Proc. N. Y. P. A.*, 1913, p. 226) by igniting a weighed portion of the ointment and weighing the resulting zinc oxide. Care should be taken after combustion has begun, to withdraw the burner and allow the sample to burn quietly until all inflammable matter is consumed. If the resulting oxide is not white in color it may be moistened with nitric acid and re-ignited. The same procedure will serve for the assay of ointment of zinc stearate.

The British ointment is weaker in the proportion of zinc oxide than that of the U. S. Pharmacopœia, the former containing about 15 per cent., the latter 20 per cent. *Commercial* zinc oxide should not be used, as it is usually gritty, and it is difficult to make a smooth ointment with it; the many expedients that have been suggested by various writers, such as the use of a paint mill or of a flat iron, or trituration with oil or with glycerin, are unnecessary if official zinc oxide is employed and the directions of the Pharmacopœia followed.

This ointment enjoys an extraordinary popularity in the treatment of all sorts of inflammatory conditions of the skin, as *eczema, sunburn, sore nipples, chapped hands,* etc. It owes its value in part to the emollient action of the lard and partly to the protective and mildly astringent action of zinc oxide.

Manufacturers have often replaced the lard in this ointment with petrolatum because of the difficulty in preserving the U. S. P. product, but this substitution is not desirable as the resulting ointment is not "drying" but remains moist. The official ointment, when applied to the skin, is quickly absorbed, leaving the zinc oxide as a protective coating. The ancient *unguentum tutiæ,* or *tutty ointment,* prepared from tutty, or impure zinc oxide, has almost been forgotten.

URANII NITRAS. U. S.

URANIUM NITRATE Uran. Nit. [Uranyl Nitrate]

(ū-rā'nĭ-ī nī'trās)

"It contains not less than 98 per cent. of $UO_2(NO_3)_2 + 6H_2O$ (502.62) (uranyl nitrate). Preserve it in well-closed containers, protected from light." *U. S.*

The salts of uranium are obtained from the mineral *uraninite* or *pitchblende,* which is noteworthy from the fact that it is the mineral in which Becquerel discovered radio-active properties in 1896, which led to further investigation and the subsequent discovery of radium by the Curies about four years later (see Part III). Pitchblende consists of mixed oxides of uranium and has the formula $UO_2.2UO_3$. The salts of uranium are really not true salts of the element but are compounds of the lower oxide UO_2, and are usually called uranyl salts. Upon treating solutions of these uranyl salts with sodium hydroxide solution a yellow precipitate of sodium uranate $Na_2U_2O_7$ is produced which is of technical use in producing a variety of glass, with a peculiar yellow fluorescence, known as uranium glass.

Uranium nitrate is officially described as follows: "Uranium Nitrate occurs in the form of light yellow prisms; odorless and having a bitter, astringent taste; somewhat efflorescent; radioactive. One Gm. of Uranium Nitrate dissolves in 1.2 mils of water at 25° C. (77° F.); freely soluble in alcohol or ether. Aqueous solutions of Uranium Nitrate are yellow and acid to litmus. Separate portions of an aqueous solution of the salt (1 in 20) yield, with sodium hydroxide T.S. or ammonia water, a yellow precipitate insoluble in an excess of the reagent but soluble in ammonium carbonate T.S.; with ammonium sulphide T.S. a dark brown precipitate; and with sodium phosphate T.S. a yellow precipitate. Mix 2 mils of the aqueous solution with an equal volume of sulphuric acid, cool the mixture, and add a crystal of ferrous sulphate; a dark brown color appears around the crystal. An aqueous solution of the salt does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of the salt (1 in 20) remains clear after the addition of an equal volume of ammonium car-

bonate T.S. (*alkaline earths*). Dilute 3 mils of this mixture to 10 mils with distilled water and add 10 mils of hydrogen sulphide T.S.; no color or precipitate is produced (*iron, manganese, or zinc*). A solution of 1 Gm. of Uranium Nitrate in 20 mils of distilled water, acidulated with 1 mil of diluted sulphuric acid, does not completely decolorize 0.1 mil of tenth-normal potassium permanganate V.S. (*uranous compounds*). An aqueous solution of the salt (1 in 100) does not at once produce a turbidity with barium chloride T.S. (*sulphate*).

"**Assay.**—Dissolve about 0.4 Gm. of the salt, accurately weighed, in 100 mils of distilled water, heat the solution to boiling, add ammonia water until no further precipitate is produced, and allow the precipitate to settle. Then wash the precipitate well on a filter with an aqueous solution of ammonium nitrate (1 in 100), and afterwards moderately ignite it in a platinum crucible, with free access of air, until the weight is constant. The urano-uranic oxide (U_3O_8) so obtained corresponds to not less than 54.8 per cent. of the weight of the salt taken, which is equivalent to not less than 98 per cent. of $UO_2(NO_3)_2 + 6H_2O$." *U. S.*

Uses.—Uranium nitrate has been used in the treatment of *diabetes mellitus* in *doses* of from one to two grains (0.065–0.13 Gm.). There is however, no sufficient reason to believe that it can influence the metabolism and any diminution which has followed its exhibition may be attributed to injury to the kidney. It is used as an indicator in the estimation of the urinary phosphates, as well as for other chemical purposes. It is incompatible with the alkaloids, chloral hydrate, salts of arsenous and phosphoric acids and changes the color of cochineal and its derivatives.

Dose, from one to two grains (0.065 to 0.13 Gm.).

URGINEA. Br.

URGINEA [Indian Squill]

(ür-gĭ'nē-ą)

"Urginea consists of the younger bulbs of Urginea indica, *Kunth,* collected soon after the plants have flowered, divested of their dry, outer, membranous coats, cut into slices, and dried. When powdered should be kept quite dry over quicklime." *Br.*

Urginea indica is a plant resembling *Urginea maritima.* It is easily distinguished from the latter in that the bulb when entire is scaly and not tunicated as the European Squill. Urginea indica grows in sandy soil near the sea coast throughout India and also extends to the lower Himalayas. The medicinal properties of the drug are apparently identical with the Squill of the Greeks. The outer coats are quite inert and should be removed as indicated in the definition of the Br. Pharm.

"Curved or sickle-shaped strips, separated or connected, several together, to a portion of the shortened axis; usually one to five centimetres long and five to ten millimetres wide; yellowish-white, fleshy, often longitudinally ribbed; tough when slightly moist, but brittle and pulverisable when dry. No odor; taste bitter and acrid." *Br.*

The bulbs of *Urginea indica* are rounded, conical or pear-shaped and about the size of an onion; tunicated, consisting of fleshy coats which enclose each other completely; color whitish; taste bitter and acrid. The bulbs of *Scilla indica* Baker, which were recognized by the Br. Add. 1900, differ in that they are not tunicated but made up of thick fleshy inbricated scales; otherwise, except that they are somewhat smaller, they resemble those of Urginea indica.

Uses.—The bulbs of Indian squill have long been used in India for purposes similar to that for which the official squill is employed in Europe and America, but no sufficient chemical examinations have been made to prove the identity of the Indian and European drugs.

Dose, one to three grains (0.065–0.2 Gm.).

Off. Prep.—Acetum Urgineæ, *Br.;* Oxymel Urgineæ (from Vinegar), *Br.;* Pilula Ipecacuanhæ cum Urginea, *Br.;* Pilula Urgineæ Composita, *Br.;* Syrupus Urgineæ, *Br.;* Tinctura Urgineæ, *Br.*

UVA URSI. U. S. (Br.)

UVA URSI [Bearberry]

(ū'vą ŭr'sī)

"The dried leaves of *Arctostaphylos Uva-ursi* (Linné) Sprengel (Fam. *Ericaceæ*), without the presence or admixture of more than 5 per cent. of stems or other foreign matter." *U. S.* "Bearberry Leaves are the dried leaves of Arctostaphylos Uva-ursi, *Spreng.*" *Br.*

Uvæ Ursi Folia, *Br.;* Barren Myrtle, Mountain Box, Rockberry; Kinnikinnic; Uva-ursi, Busserole, Raisin d'Ours, *Fr. Cod.;* Folia Uvae Ursi, *P. G.;* Bärentraube, Bärentraubenblätter, *G.;* Uva Ursina, *It.;* Gayuba, *Sp.*

The *uva ursi,* or *bearberry,* is a low evergreen shrub, with trailing stems, the young branches of which rise obliquely upward for a few inches. The leaves are scattered, upon short petioles, from half an inch to an inch long, obovate, or oblong-spatulate, acute at the base, obtuse at the apex, entire, with a rounded margin, thick coriaceous, smooth, shining, deep green on their upper surface, paler and covered with a net-work of veins beneath; furnished especially near the margin or near the midrib with minute hairs, which are usually abundant in young leaves, but may be few or absent in old leaves, especially those which have been much handled. The flowers, which stand on short reflexed peduncles, are in small clusters at the ends of the branches. The calyx is small, five-parted, reddish, and persistent. The corolla is ovate or urceolate, reddish-white, or white with a red lip, transparent at the base, contracted at the mouth, and divided at the margin into five short reflexed segments. The stamens are ten, with short filaments and bifid anthers; the ovary round, with a style longer than the stamens, and a simple stigma. The fruit is a small, round, depressed,

smooth, glossy red berry, with an insipid mealy pulp and five cohering seeds.

This humble but hardy shrub inhabits the northern latitudes and high mountains of Europe, Asia, and America. On the American continent it extends from Hudson's Bay as far southward as New Jersey and Pennsylvania, in some parts of which it grows in abundance. It prefers a barren soil, flourishing on gravelly hills and elevated sandy plains. The leaves are the only part used in medicine. They are imported from Europe, but are also collected within our own limits, and the market of Philadelphia is supplied to a considerable extent from New Jersey. They should be gathered in autumn, and only the green leaves selected. In Europe the uva ursi is adulterated with the inert leaves of the *Vaccinium Vitis-Idæa* L. (*Cowberry, Mountain Cranberry*); these may be distinguished by being obovate, having revolute margins which are sometimes slightly toothed, and the presence of fine blackish dots or bristly points upon their lower surface. Leaves of the *Chimaphila umbellata* (L.) Nutt., sometimes found among the uva ursi, may be readily detected by their greater length, their cuneiform-lanceolate shape, and their serrate edges.

Arctostaphylos glauca Lindl., *manzanita,* is a small tree or shrub indigenous in California, where it generally grows in dry and rocky places on the west of the mountain ranges. The leaves appear to possess properties similar to those of the official species. (See Flint, *A. J. P.,* 1873, p. 187.) The fruit of *A. arguta* Zucco, a Mexican species, is said to be a narcotic poison.

Properties.—Uva ursi is officially described as: "Usually more or less entire, laminæ obovate or oblong-spatulate, from 12 to 30 mm. in length and from 5 to 13 mm. in breadth; summits obtuse or rounded; margins entire, slightly revolute; bases cuneate, tapering into short, stout petioles; upper surfaces dark green, glabrous and shiny, finely reticulate; under surfaces yellowish-green and slightly pubescent, especially on the midribs; coriaceous, fracture short; odor aromatic, tea-like; taste astringent and somewhat bitter. The powder is olive green; under the microscope it shows irregular fragments; epidermal cells polygonal, those of the lower surface showing broadly elliptical stomata about 0.035 mm. in length, surrounded by from 5 to 8 neighboring cells; cells of mesophyll with chloroplastids and frequently irregular masses of a carbohydrate; fragments of fibro-vascular bundles with spiral tracheæ associated with narrow, strongly lignified sclerenchymatous fibers and frequently also with crystal fibers with monoclinic prisms, from 0.006 to 0.015 mm. in diameter; numerous fragments made up of cells having a yellowish-brown content which are colored a bluish-black upon the addition of ferric chloride T.S. Place 0.1 Gm. of powdered Uva Ursi on a watch crystal and cover with another watch crystal and gently heat the powder; a crystalline sublimate forms, consisting of long rods and feather-like aggregates which polarize light with a brilliant play of colors. Macerate 1 Gm. of powdered Uva Ursi with 10 mils of boiling water, shake the mixture occasionally until cold and then filter it; the filtrate yields a grayish-purple precipitate upon the addition of a few drops of ferrous sulphate T.S." *U. S.*

"Obovate or spatulate, about two centimetres long, yellowish-green, coriaceous, entire, shortly petiolate. Upper surface glabrous, shining, reticulate; veinlets depressed. Slight odor; taste very astringent." *Br.*

The commercial drug frequently consists of the entire plants and therefore contains a large quantity of stems. The latter should not be present, according to the official definition, in greater amount than five per cent. Farwell states that the leaves are sometimes very dark or blackish-green, which is probably due to carelessness in drying. (*M. R.,* xvii, p. 35.) Holm has contributed an interesting article on the morphology of the plant. (*M. R.,* xx, p. 95.)

Uva ursi leaves contain—besides tannic and gallic acids, bitter extractive resin, gum, fatty matter, and salts of potassium and calcium—two glucosides, *arbutin,* $C_{12}H_{15}O_7$, and *ericolin,* and a resinous principle, *urson.* The tannin is so abundant (6 or 7 per cent.) that the leaves are used for tanning in Russia.

Arbutin is somewhat widely diffused in the species of Ericaceæ, such as *Chimaphila umbellata* (L.) Nutt., *Chimaphila maculata* (L.) Pursh, *Epigæa repens* L., and *Gaultheria procumbens* L. Kawalier (*Chem. Gaz.,* 1853, p. 61) obtained it from uva ursi by precipitating the decoction with lead acetate, filtering, treating the liquid with hydrogen sulphide, again filtering, evaporating to the consistence of syrup, and allowing the product to stand for several days. This gradually assumed the form of a crystalline jelly, which, being placed upon linen so as to allow the mother liquor to drain off, and then pressed, yielded nearly colorless crystals, which were purified by solution in boiling water and treatment with animal charcoal. Arbutin thus obtained is in long, acicular, colorless crystals, united in tufts, and of a bitter taste. It is soluble in water, alcohol, and ether, unchanged apparently by a heat of 100° C. (212° F.), but fusible at 167° to 168° C. (332.6°–334.4° F.), without action on vegetable colors, and not precipitated by ferric salts or by lead acetate or subacetate. It is a glucoside, being resolvable by emulsin, or more rapidly by boiling with sulphuric acid, into glucose and *hydroquinone,* $C_6H_6O_2$ (*arctuvine* of Kawalier). The occurrence of methylhydroquinone among the products of decomposition led Hlasiwetz and Habermann to give the formula $C_{25}H_{34}O_{14}$ to arbutin, but Schiff showed that this was because arbutin was almost always accompanied by *methylarbutin,* $C_{12}H_{15}(CH_3)O_7 + H_2O$. This compound has been made synthetically by Schiff (*Ber. d. Chem. Ges.,* 1882, p. 1841) by acting upon arbutin with methyliodide and potassium hydroxide in methyl alcohol solution, and purely synthetically by Michael (*Ber. d. Chem. Ges.,* 1885, p. 118) by the action of methylhydroquinone and acetochlorhydrose. It is decomposed by dilute

acids into glucose and methylhydroquinone. Upon heating 1 part of arbutin with 8 parts of manganese oxide, 2 parts of sulphuric acid, and 1 part of water, it gives off the penetrating odor of quinone. The aqueous solution is rendered blue by a small quantity of solution of ferric chloride, and green by a larger quantity. No precipitate is produced by either acids or alkalies. It blackens ammoniacal solution of silver nitrate after boiling with diluted sulphuric acid, and throws down cuprous oxide from alkaline copper solutions upon heating. It dissolves in sulphuric acid, forming a colorless solution, turning red after a short time; a trace of nitric acid turns this solution yellow-brown. An aqueous solution (1 in 20) is not changed by hydrogen sulphide. A good test for arbutin is that of Julius Jungmann, as follows: When phosphomolybdic acid is added to a solution of arbutin previously rendered alkaline by ammonia or other alkali, a blue color is produced, which is deep when the solutions are strong, but observable even when they are very dilute. (*A. J. P.*, May, 1871, p. 204.)

After the extraction of arbutin there is obtained from the mother liquor *ericolin*, $C_{34}H_{56}O_{21}$. This is also found in many other ericaceous plants. It is glucosidal in nature and yields on decomposition, besides glucose, a volatile oil, *ericonol*. Another crystallizable principle has been discovered by Trommsdorf, who calls it *ursone*, $C_{30}H_{48}O_3$. It appears to be of a resinous character, although it can be obtained in silky needles, being tasteless and inodorous, insoluble in water, difficultly soluble in alcohol and ether, fusible, at a higher temperature volatilizable, and inflammable in the air. It is obtained by treating uva ursi with a very small quantity of ether by percolation, allowing the ether to evaporate, washing the crystalline extract with ether, and recrystallizing from alcohol. (*A. J. P.*, xxvii, 334.)

A. G. Perkin has obtained from the leaves of uva ursi a yellow coloring principle of the composition $C_{15}H_{10}O_7$, crystallizing in glistening yellow needles. On fusion with alkali, phloroglucinol and protocatechuic acid were formed. Though resembling quercetin in these points, it forms deep green solutions with diluted potassium hydroxide. (*A. J. P.*, 1898, 584.)

Uses.—Uva ursi is used to-day almost exclusively in the treatment of catarrhs of the urinary tract, especially *acute cystitis*. Although by some it is believed to exercise an astringent and alterative influence on these membranes, it is probable that its action is simply that of a mild antiseptic. Lewin (*V. A. P. A.*, 1883, xcii, p. 517) attributes its virtues to the arbutin which is decomposed in the system liberating hydroquinone. Bass, however (*Z. E. P. T.*, 1912, x, p. 120), is doubtful whether enough hydroquinone can appear in the urine to exercise any antiseptic effect. But whether or not its virtue is due to arbutin or some other principle, the clinical evidence is strong that uva ursi is a useful drug in these conditions. Formerly it was also employed in *gravel, nephritis, urethritis,* and *menorrhagia,* but has been largely abandoned. Because of the formation of hydroquinone in the body the urine often acquires a greenish color from the use of uva ursi.

Arbutin has been employed in medicine not only for its antiseptic effect but also as a diuretic in doses of from one to three grains (0.065–0.2 Gm.).

Dose, powdered uva ursi, from twenty grains to a drachm (1.3–3.9 Gm.), to be repeated three or four times a day; but the fluidextract is always preferred.

Off. Prep.—Fluidextractum Uvæ Ursi, *U. S.;* Infusum Uvæ Ursi, *Br.;* Elixir Buchu Compositum (from Compound Fluidextract of Buchu), *N. F.;* Fluidextractum Buchu Compositum, *N. F.*

VALERIANA. U. S. (Br.)

VALERIAN Valer.

(vą-lē-rī-ā′ną)

"The dried rhizome and roots of *Valeriana officinalis* Linné (Fam. *Valerianaceæ*)." *U. S.* "Valerian Rhizome is the dried rhizome and roots of Valeriana officinalis, *Linn.* Collected in the autumn." *Br.*

Valerianæ Rhizoma, *Br.;* Valerian Root; Radix Valerianæ Minoris, R. Valerianæ Sylvestris, R. Valerianæ Montanæ; Common, Garden, Cat's or Great Wild Valerian, All-heal, Summer Heliotrope, Herb Bennet, Vandal Root; Valériane officinale, *Fr. Cod.;* Racine de Valériane, Valériane, *Fr.;* Radix Valerianae, *P. G.;* Baldrian, Wilde Baldrianwurzel, Baldrianwurzel, *G.;* Valeriana, *It.;* Valeriana (Rizoma de), *Sp.*

For *Valerianæ Indicæ Rhizoma,* see p. 1192.

Official or *great wild valerian* (*Valeriana officinalis*) is a large, handsome, herbaceous plant, with a perennial rhizome, and an erect, round, channelled stem, from two to four feet high, furnished with opposite pinnate leaves, and terminating in flowering branches. The leaves of the stems are attached by short, broad sheaths; the radical leaves are larger and long petiolate. In the former the leaflets are lanceolate and partially dentate, in the latter elliptical and deeply serrate. The flowers are small, white or rose-colored, agreeably odorous, and disposed in terminal corymbs interspersed with pear-shaped bracts. The number of the stamens is three. The fruit is a capsule containing one oblong-ovate, compressed seed. The plant is a native of Europe, where it grows either in damp woods and meadows or on dry elevated grounds. As found in these different situations, it presents characters so distinct as to have induced some botanists to make two varieties. Dufresne makes four, of which three prefer marshy situations. The variety which affects a dry soil (*sylvestris* L. Ph.) is not more than two feet high, and is distinguished by its narrow leaves.

The valerian plant is cultivated to some extent in New England and New York, and in Europe, in England and Holland. In this country it will grow in light, well-prepared, and well-drained soil, and is propagated by dividing the roots in the fall and setting these portions

in rows about two feet apart. (*D. C.*, lvi, p. 134.) In Europe it appears to be grown in a clayey soil. (*Pac. Pharm.*, vii, p. 297.) Mitlacher reports on the results of his experiments on the cultivation of valerian. (*Zeit. Oest. Apoth. Ver.*, l, p. 459.)

Valeriana mexicana DC.—According to the *Nueva Farmacopea Mexicana*, the roots of this plant contain a large percentage of valeric acid, which they yield readily and economically. In Mexican commerce they are said to occur in slices or fleshy disks about four centimeters or more in diameter, or in voluminous tubercles. Externally the color is grayish-yellow, internally yellow; the odor is strong and disagreeable, the taste bitter. R. McLaughlin (*A. J. P.*, 1893, 329) found 3.3 per cent. of oil in the Mexican valerian root. (See also *Schim. Rep.*, April, 1897.)

Japanese Valerian. Kesso Root.—This, formerly believed to be the product of *Patrinia scabiosæfolia* Link, is now thought to be obtained from a variety of *V. officinalis*. It yields a volatile oil. (*P. J.*, xx, 837, xxi, 1069.) The rhizome sometimes known as *Valerianæ Radix Majoris* is obtained from *V. Phu* L., of Southern Europe, and Western Asia. It is from 4 to 6 inches long, ½ inch in thickness, brown, annulated with numerous yellowish roots, and a feeble, valerian-like odor and taste.

Properties.—The root should be collected in spring, before the stem begins to shoot, or in the autumn, when the leaves decay. It should be dried quickly, and kept in a dry place. It consists of numerous, long, slender, brittle, cylindrical, thick-barked rootlets, issuing from a tuberculated rhizome. It is officially described as: "Rhizome upright, from 2 to 4 cm. in length, and from 1 to 2 cm. in diameter, usually cut longitudinally into 2 to 4 pieces; externally yellowish-brown or dark brown, upper portion with stem-bases and frequently with a short horizontal branch or stolon, and from the outer surface arise numerous, slender, brittle roots; fracture of rhizome short and horny, internally light brown, with a thick bark and narrow central cylinder; odor pronounced, of valeric acid, becoming stronger upon aging; taste sweetish, camphoraceous and somewhat bitter. Under the microscope, transverse sections of the root of Valerian show a single epidermal layer of papillose cells, some being modified to root hairs; a hypodermal layer containing some secretion cells with suberized walls, and in which are usually numerous small, oily globules and occasionally small prismatic crystals; cortical parenchyma, the cells filled with starch, some of the cells near the hypodermis containing a few oil globules; an endodermis of thin-walled cells enclosing a central cylinder with usually 3 to 5 fibro-vascular bundles; tracheæ with simple and bordered pores. Older roots show a large pith of starch-bearing parenchyma, a secondary thickening in the fibro-vascular bundles and a periderm of a few layers of cells. Sections of the rhizome show a thin periderm, a cortical parenchyma with scattered fibro-vascular bundles, a layer of altered cells of the endodermis, numerous, more or less twisted, collateral fibro-vascular bundles and a large pith. The powder is light brown to grayish-brown; under the microscope it exhibits numerous starch grains, from 0.003 to 0.02 mm. in diameter, spherical, plano-convex, polygonal, 2- to 4-compound and each usually with a central cleft; tracheal fragments, the walls having simple and bordered pores or scalariform and reticulate thickenings, accompanied by narrow sclerenchymatous fibers, the walls being thin, porous, and strongly lignified; occasional fragments of epidermis with root hairs, and fragments of cork. Valerian yields not more than 20 per cent. of ash." *U. S.*

"Rhizome short, erect, entire or sliced, dark yellowish-brown externally, whitish internally. Roots numerous, about seven to ten centimetres long, of the same color as the rhizome, slender, brittle. Strong, characteristic, disagreeable odor; taste unpleasant, camphoraceous, slightly bitter. Ash not more than 10 per cent." *Br.*

The roots of *Valeriana Phu* L., and *V. dioica* L., are said to be sometimes mingled with those of the official plant. According to Ebermayer, in Germany various ranunculaceous roots are a dangerous adulterant of valerian; they may be readily detected by their want of the peculiar odor of the official root. According to M. O. Raveil, the valerian in the markets of Paris is largely adulterated with the roots of *scabious* (*Scabiosa succisa* L., and *S. arvensis* L.). They are shorter than the genuine root, with larger radicles, less rough, little or not at all striated, very brittle, with a white amylaceous fracture. The roots are inodorous in themselves, but are very apt to acquire odor from contact with the valerian. (*J. P. C.*, xxvi, 209.)

The odor in the fresh root is pleasantly aromatic, but in the dried is stronger and less agreeable. Cats are strongly attracted by it. The taste is at first sweetish, afterwards bitter and aromatic.

Trommsdorff found it to consist of 1.2 parts of volatile oil, 12.5 of a peculiar extractive matter, soluble in water, insoluble in ether and alcohol, and precipitated by metallic solutions, 18.75 of gum, 6.25 of a soft odorous resin, and 63 of lignin. Runge found in it a peculiar fixed acid, which produced with bases white salts, becoming green on exposure to the air. (*Chem. Gaz.*, No. 170, p. 452.) Of these constituents the most important is the *volatile oil*. It is of a pale greenish color, of the sp. gr. 0.934, with the pungent odor of valerian, and an aromatic taste. It becomes yellow and viscid by exposure. Bruylants (*Ber. d. Chem. Ges.*, 1878, p. 449) has obtained from oil of valerian, (1) a hydrocarbon or terpene, $C_{10}H_{18}$, boiling at 157° C. (314.6° F.); (2) a liquid compound, $C_{10}H_{18}O$, which by means of chromic acid affords common camphor, and formic, acetic, and valeric acids, which are met with in old valerian root, owing no doubt to the slow oxidation of the compound $C_{10}H_{18}O$; (3) a crystalline compound of the same composition, which in the root is probably combined with the three organic

acids mentioned, forming corresponding esters with them: (4) at from 285° to 290° C. (545°–554° F.), a greenish, syrupy oil, which when rectified is colorless, and seems to have the composition of a *borneol oxide*, $(C_{10}H_{17})_2O$. Schimmel & Co. (*Schim. Rep.*, April, 1897) summarize the most recent researches upon valerian oil from different sources. In the oil from Dutch and Thuringian roots, the amount varying from 0.5 to 1 per cent., they find pinene, camphene, borneol, bornyl formate, bornyl acetate, and *bornyl isovalerate*, together with a sesquiterpene and an alcohol, $C_{10}H_{20}O_2$. In the oil from Japanese roots (amounting to from 6 to 6.5 per cent.) (*Kesso oil*), they find pinene, camphene, dipentene, terpineol, borneol, bornyl acetate, bornyl isovalerate, and *kessyl acetate*. Trommsdorff ascertained the existence in the oil of *valeric acid*.

This acid is a colorless volatile liquid, of an oleaginous consistence, having an odor analogous to that of valerian, and a very strong, sour, disagreeable taste. It is soluble in thirty parts of water, and in all proportions in ether and alcohol. It combines with salifiable bases, forming soluble salts, which retain, in a diminished degree, the odor of the acid. (*J. P. C.*, xx, 316.) The acid does not pre-exist in the oil, but is produced by the decomposition of its borneol ester. Valeric acid is obtained by distilling the impure oil with magnesium carbonate, decomposing by sulphuric acid the magnesium valerate which remains, and again distilling. The following process by T. and H. Smith, of Edinburgh, avoids the inconvenience of distilling so bulky a root as valerian, while it answers the same purpose as that of Rabourdin. Boil the root for three or four hours with rather more than its bulk of water in which an ounce of sodium carbonate is dissolved for every pound of the root, replacing the water as it evaporates. Express strongly, and boil the residuum twice with the same quantity of water, expressing each time as before. Mix the liquids, add two fluidrachms of strong sulphuric acid for every pound of the root, and distil until three-fourths of the liquid have passed over. Neutralize this with sodium carbonate, concentrate the liquid, decompose the sodium valerate contained in it by sulphuric acid, and collect the valeric acid set free, by a separator, funnel, or by distillation. (*A. J. P.*, xvii, 253.) Lefort obtains the acid by the rapid oxidation of the volatile oil. He distilled 100 parts of the root with 500 of water, 10 of sulphuric acid, and 6 of potassium dichromate, and in this way procured a larger proportion of acid than by any other process. (*J. P. C.*, 3e sér., x, 194.)

Uses.—Valerian is used as a sedative to the higher nerve centers in conditions of *nervous unrest, hysteria, hypochondriasis, neuralgic pains*, and the like. The virtues of the plant seem to depend chiefly on the esters of valeryl which are contained in the volatile oil. According to Chevalier (*Nouv. Rem.*, 1912, xxix, p. 169), the volatile oil of valerian is a depressant to the whole central nervous system, including both the motor and psychical centers of the brain and the motor cells of the spinal cord. The esters contained in this drug are unstable bodies and in the process of drying largely oxidized with the formation of valeric acid. As the latter is practically without physiological action much of the virtue of the plant is lost during the drying process. Probably for this reason preparations of this drug are very uncertain in their activity and valerian has largely fallen into disrepute. Chevalier has introduced the juice of the fresh root which he asserts is a valuable remedy not only for the conditions mentioned above, but even as a narcotic in *insomnia* and an anticonvulsant in *epilepsy*. The dose of this juice, which has been introduced under the name of *energetene of valerian*, is one to three coffeespoonsful. It appears also to have some slight influence upon the circulation, slowing the heart and increasing its force, and causing a rise in blood pressure, and has been used in the treatment of *cardiac palpitations*.

Dose, twenty to forty grains (1.3–2.6 Gm.). The dose of the oil of valerian, which is occasionally employed, is four to five minims (0.25–0.3 mil).

Off. Prep.—Tinctura Valerianæ, *U. S.*; Tinctura Valerianæ Ammoniata, *U. S., Br.*; Fluidextractum Valerianæ, *N. F.*

VALERIANÆ INDICÆ RHIZOMA. Br.

INDIAN VALERIAN RHIZOME

(vạ-lē-rĭ-ā'næ ĭn'dĭ-cæ rhī-zō'mạ)

"Indian Valerian Rhizome is the dried rhizome and roots of Valeriana Wallichii, *DC.*" *Br.*

Valeriana Wallichii is a perennial herb growing in the temperate Himalayas and in the Khasia Mountains. The rhizome is more largely used as a perfume than in medicine. It is used in preparations for the hair and the dried rhizome is used as an incense. It is officially described as follows: "Rhizome curved, about five centimetres long, from five to ten millimetres thick, dull brown, with raised transverse leaf-scars, numerous prominent root-scars and a few thick roots; the crown bearing the remains of petioles. Fracture short. In transverse section, dark with a large pith and diffuse ring of small wood-bundles. Strong, characteristic, disagreeable odor; taste unpleasant, camphoraceous." *Br.*

According to Lindenberg (*Ph. Z. R.*, 1886), Indian valerian is practically identical in its composition with the European drug, but contains a slightly larger amount of volatile oil. It may be employed in the same class of cases as valerian.

Off. Prep.—Tinctura Valerianæ Indicæ Ammoniata, *Br.*

VANILLINUM. U. S.

VANILLIN Vanillin.

(vạ-nĭl-lĭ'nŭm)

"Methylprotocatechuic aldehyde [$C_8H_8O_3$ or $C_6H_3.OH.OCH_3.COH$ 4 : 3 : 1 = 152.06] occur-

ring naturally in vanilla, or prepared synthetically. Preserve it in well-closed containers, protected from light." *U. S.*

Vanilline, *Fr. Cod.*; Vanillin, Vanillekampher, Protocatechualdehydmethylaether, *G.*

Preparation.—*Vanillin* was first obtained from vanilla by Gobley, who, by exhausting vanilla with 85 per cent. alcohol, evaporating the resulting tincture to an extract, softening this with water, and agitating in a flask with ether so long as it gave color to that fluid, then evaporating the ethereal liquid and treating the residue with boiling water, obtained on the evaporation of the water a crop of crystals having the odor of vanilla. Purified by treatment with animal charcoal and recrystallization, the principle appeared in the form of colorless, long, four-sided needles terminated by two faces. It has a strong odor of vanilla, with a hot, biting taste, and is frequently seen in acicular crystals upon the external surface of the bean. This compound, for which Gobley proposed the name *vanillin*, is now recognized as the methyl-ether of protocatechuic aldehyde, $C_6H_3\begin{cases}OCH_3\\OH\\COH,\end{cases}$ or $C_8H_8O_3$, and is known to occur somewhat diffused in the vegetable kingdom, being found in the sugar beet and in the wood-tissue of many plants. It forms crystalline needles fusing at 80° to 81° C. (176°–177.8° F.), difficultly soluble in cold water, readily soluble in hot water, easily soluble in alcohol and ether, chloroform, and carbon disulphide. It oxidizes slowly in damp air to *vanillic acid*, $C_8H_8O_4$; when heated with diluted hydrochloric acid to 200° C. (392° F.), it breaks up into methyl chloride and protocatechuic acid. Tiemann and Haarmann (*Ber. d. Chem. Ges.*, 1874), who first ascertained the true character of vanillin, also found that it could be made synthetically from *coniferin*, a glucoside contained in the cambium layer of the pine. This coniferin, $C_{16}H_{22}O_8 + 2H_2O$, or the compound $C_{10}H_{12}O_3$, which with glucose results from its decomposition, is oxidized by sulphuric acid and potassium dichromate with the production of vanillin. Artificial vanillin was made in this way from coniferin under Tiemann and Haarmann's patents, and was made by Reimer and Tiemann from guaiacol by heating it with sodium hydroxide and chloroform, but it is now made from *eugenol*, $C_6H_3\begin{cases}OH\\OCH_3\\CH_2.CH:CH_2\end{cases}$. This on heating with alcoholic solution of potassium hydroxide is changed into *isoeugenol*, $C_6H_3\begin{cases}OH\\OCH_3\\CH:CH.CH_3\end{cases}$, and this is then oxidized, when *vanillin*, $C_6H_3\begin{cases}OH\\OCH_3\\CHO\end{cases}$ is formed. A larger yield is obtained if the isoeugenol is first acetylated, as the acetisoeugenol is more stable under the influence of oxidizing agents. The product acetvanillin is readily decomposed, with the liberation of the vanillin. The oxidation is effected by a variety of oxidizing agents. Sodium peroxide has been used with success, or more recently the isoeugenol sodium has been oxidized at the positive pole of an electrolytic cell, using an alkaline hydroxide as the cathode liquid. Oil of cloves is therefore used as a basis for the manufacture of artificial vanillin.

Properties.—It is officially described as "in fine, white, or only very slightly yellowish, crystalline needles, having the odor and taste of vanilla. One Gm. of Vanillin dissolves in 100 mils of water at 25° C. (77° F.); also in 16 mils of water at 80° C. (176° F.); freely soluble in alcohol, glycerin, chloroform, or ether. Its aqueous solution is acid to litmus and is optically inactive. It melts between 80° and 82° C. (176° and 179.6° F.). It is easily dissolved by aqueous solutions of the alkali hydroxides, and from the combinations thus formed it is precipitated at once by the addition of acids. An aqueous solution of Vanillin gives a blue color with ferric chloride T.S.; if the mixture is boiled, the blue color changes to brown, and on cooling a white, or nearly white, precipitate of dihydrodivanillin separates. Vanillin is extracted completely from its solution in ether by shaking with a saturated, aqueous solution of sodium bisulphite, from which it is precipitated by the addition of sulphuric acid. A cold aqueous solution of Vanillin gives, on the addition of lead acetate T.S., a white precipitate of a lead compound of vanillin, soluble in hot water. Incinerate about 2 Gm. of Vanillin; not more than 0.05 per cent. of ash remains. Warm about 0.1 Gm. of Vanillin with a concentrated alcoholic solution of sodium hydroxide, add a drop of chloroform and again warm; the odor of phenylisocyanide is not perceptible (*acetanilid*)." *U. S.*

A new qualitative test and colorimetric method for the quantitative estimation of vanillin has been described by Clarence Estes (*J. I. and E. C.*, 1917, p. 142) which depends upon the effect of the addition of solution of acid nitrate of mercury under certain conditions. A violet to violet-red color is produced, which is unlike that produced by any organic compound likely to be present as an accidental or interfering substance. The results of the application of the author's method directly to flavoring extracts of known composition agreed closely with the gravimetric figures.

Uses.—According to Grasset, vanillin produces in frogs spinal convulsions followed by paralysis due to a direct action upon both the spinal cord and motor nerves. It has been suggested as a stomachic and excito-motor given in doses of three-fourths of a grain (0.048 Gm.).

(*A. Pharm.*, Aug., 1896.) Neither it nor vanilla, however, are used for other than flavoring purposes. The fact that while the vanilla beans have steadily risen in price for a number of years that of the artificial vanillin has enormously fallen, indicates that as a flavoring agent vanillin is not equal to the natural product. It is said that articles flavored with it leave a peculiar, disagreeable after-taste and retain their flavor only a very short time.

Off. Prep.—Elixir Amygdalæ Compositum, *N. F.;* Elixir Vanillini Compositum (from Compound Spirit), *N. F.;* Spiritus Vanillini Compositus, *N. F.*

VERATRINA. U. S.

VERATRINE Veratrin. [Veratria]

(vĕr-ą-trī'ną)

"A mixture of alkaloids obtained from the seed of *Asagræa officinalis* (Chamisso and Schlechtendal) Lindley (Fam. *Liliaceæ*). Preserve it in well-closed containers, protected from light." *U. S.*

Vératrine, *Fr. Cod.;* Veratrinum, *P. G.;* Veratrin, *G.;* Veratrina, *It., Sp.*

No process is given in the U. S. P. IX for preparing veratrine and the Br. Pharm., 1914, deleted it. A process will be found in the *U. S. D.*, 19th edition, pages 1327 and 1328.

In the U. S. process of 1870 the first step is to obtain a tincture of cevadilla, which is evaporated to the consistence of an extract. This contains the veratrine combined with a vegetable acid, probably gallic, as it exists in the seeds. From the extract the alkaloid is dissolved by the acidulated water, which at the same time converts it in great measure into a sulphate, a small portion possibly remaining in the solution combined with an excess of the natural acid. The magnesia combines with the acids and throws down the veratrine, which is then taken up by alcohol and again yielded in a purer state by evaporation. To purify it still further, it is redissolved in water by the agency of sulphuric acid, is submitted to the action of animal charcoal, and is finally precipitated by ammonia. In the British process, the tincture was concentrated until it began to let fall a precipitate, and was then poured into water, which throws down the resin and oil with a portion of the coloring matter and retains the salt of veratrine. This is then decomposed by ammonia, and the precipitated veratrine is slightly washed with cold water to free it from adhering impurities. If much water be employed in the washing, a considerable portion of the veratrine will be lost, in consequence of impure veratrine being in some degree soluble in water. The remaining steps of the British process consist in the purification of the veratrine by forming a hydrochloride in solution, decolorizing this by animal charcoal and again precipitating by ammonia.

The U. S. process of 1870 is essentially that of Couërbe. The veratrine obtained by it, though not pure, is sufficiently so for medicinal use. A drachm of it, in this state, may be procured from a pound of cevadilla. Meissner, in 1819, applied the term *sabadilline* to an alkaloid extracted by him. Pelletier and Caventou had probably produced the same preparation when they announced the discovery of veratrine in the same year. This substance is the veratrine described as prepared by Couërbe's process. Couërbe, in 1834, announced the discovery of an additional alkaloid, to which he gave Meissner's old name of sabadilline, and Weigelin, in 1871, announced the discovery of a third alkaloid, which he called *sabatrine*. G. Merck, in 1855, obtained veratrine in a crystallized state by solution and separation from strong alcohol.

Wright and Luff (*J. Chem. S.*, 33, p. 338) have brought order from this confusion by a careful study of the whole subject. They found three alkaloids in sabadilla seeds: *cevadine*, $C_{32}H_{49}O_9N$ (the alkaloid hitherto known as the veratrine of Merck); *veratrine*, $C_{37}H_{53}O_{11}N$; and *cevadilline*, $C_{34}H_{53}O_8N$. Of these, the cevadine (formerly veratrine) forms, when crystallized from alcohol, needles or compact crystals which fuse at 205° C. (401° F.), effloresce rapidly in the air, and become opaque, are insoluble in water, easily soluble in alcohol and ether, and dissolve in warm concentrated hydrochloric acid with a dark violet color, which on boiling becomes intensely red. When heated with alcoholic potassium hydroxide they are decomposed into *methyl-crotonic* (*tiglinic*) *acid* and *cevine*, $C_{27}H_{43}O_8N$. The veratrine of Wright and Luff is obtained from the mother liquor of the cevadine by extraction with ether. It forms an uncrystallizable resinous mass, fusing at 180° C. (356° F.), but yields crystallized salts. Boiled with sodium hydroxide it is decomposed into *dimethyl-protocatechuic* (*veratric*) *acid* and *verine*, $C_{28}H_{45}O_8N$. Cevadilline remains after the extraction of the veratrine, insoluble in ether. It is also uncrystallizable, nearly insoluble in ether and in boiling benzene, but easily soluble in fusel oil.

Flückiger recognized only two of these alkaloids, and made them both of the composition $C_{32}H_{49}O_9N$. The first, which he called *cevadine*, he stated is decomposed by boiling with barium hydroxide when in alcoholic solution, and yielded products as follows:

$$C_{32}H_{49}O_9N + 2H_2O = C_5H_8O_2 + C_{27}H_{45}O_9N$$

The first of these products is *methyl-crotonic acid*, and the second is *cevine*. The other alkaloid he called *veratridine*, and gave its decomposition as follows:

$$2C_{32}H_{49}O_9N + 4H_2O = C_9H_{10}O_4 + C_{55}H_{92}O_{16}N_2 + 2H_2O$$

The first of these products is *dimethyl-protocatechuic acid*, and the second he called *veratroïn*. (Flückiger, *Pharm. Chem.*, 1888, ii, p. 532.) Merck still terms the cevadine of Wright and Luff veratrine, and prepares it in white crystals of the formula $C_{32}H_{49}O_9N$, fusing at 202° C. (395.6° F.). Frankforter (*A. J. P.*, 1897, 372) confirmed this formula, $C_{32}H_{49}O_9N.H_2O$, but gave to the purified veratrine the

melting point from 146° to 148° C. (294.8°–298.4° F.).

Two acids have also been found in sabadilla—the *sabadillic* or *cevadic acid* of Pelletier and Caventou, forming needle-like crystals fusing at 20° C. (68° F.), and the *veratric acid* of Merck, which Koerner showed to be dimethylprotocatechuic acid.

Properties.—Veratrine is officially described as "a white, or grayish-white, amorphous powder, odorless, but causing intense irritation and sneezing when even a minute quantity reaches the nasal mucous membrane. *Great caution must be used in tasting it.* It is slightly hygroscopic. One Gm. of Veratrine dissolves in 1760 mils of water, 2.8 mils of alcohol, 0.7 mil of chloroform, and in 4.2 mils of ether at 25° C. (77° F.); also in 1345 mils of water at 80° C. (176° F.); insoluble in petroleum benzin. Its alcoholic solution is alkaline to moistened litmus paper. Triturate about 0.05 Gm. of Veratrine with 2 mils of sulphuric acid in a glass mortar; the yellow or orange-red solution exhibits by reflected light a greenish fluorescence, which becomes more intense upon the addition of an equal volume of sulphuric acid. Upon standing, the solution gradually assumes a deep red color. Sulphuric acid, when heated with Veratrine, gives a cherry-red color. Sulphuric acid added to a mixture of one part of Veratrine and six parts of sugar produces a green color which changes to blue, and finally the mixture becomes colorless. No weighable ash remains on incinerating 0.1 Gm. of Veratrine. An alcoholic solution of Veratrine (1 in 20) remains clear after the addition of platinic chloride T.S. (*various foreign alkaloids*)." *U. S.*

Uses.—Probably because of its unfortunate name it has been assumed by some that veratrine represents the therapeutic virtues of veratrum. Its physiological action, however, differs greatly from that of veratrum, and if it possess any therapeutic usefulness it is certainly not for the conditions for which veratrum is employed.

Veratrine is an intense local irritant and somewhat locally anesthetic. Rubbed upon the skin it excites a sensation of warmth and a peculiar tingling. Sometimes an evanescent blush is produced and still more rarely an eruption upon the skin, but generally no decided signs of inflammation are evinced. When taken into the mouth it produces an almost insupportable sense of acrimony, and snuffed up the nostril it produces violent sneezing, and when taken into the stomach in large doses it causes violent vomiting, serous purging with intense burning in the mouth and throat and general muscular weakness. It is a powerful muscle poisoning and if given in sufficient dose in the lower animals it causes an extraordinary prolongation of the contraction of the striated muscles; the time required for relaxation of voluntary muscles may be 20 or 30 times as long as normal. A similar influence is exerted upon the ventricular muscles, at least in the frog, but the slowing of the heart rate seen in warm blooded animals seems to be due chiefly to stimulation of the cardio-inhibitory center. Death in mammals is generally due to depression of the respiration.

The only justifiable therapeutic use of veratrine is as an anodyne counter-irritant in *neuralgias* and various forms of *arthritis*. Even for this purpose it has no advantages sufficient to offset the dangers of systemic poison which might follow from its absorption.

Dose, one-thirtieth of a grain (0.002 Gm.).

Off. Prep.—Oleatum Veratrinæ, *N. F.;* Unguentum Veratrinæ, *N. F.*

VERATRUM VIRIDE. U. S.

VERATRUM VIRIDE Verat. Vir. [Green Hellebore, American Hellebore]

(vẹ-rā-trŭm vĭ'rĭ-dē)

"The dried rhizome and roots of *Veratrum viride* Aiton (Fam. *Liliaceæ*), without the presence or admixture of more than 5 per cent. of stems or other foreign matter." *U. S.*

Big or False Hellebore, Swamp Hellebore, Indian Poke, Itch-weed, Tickle-weed, Bugbane; Vératre vert, *Fr.;* Grüner Germer, *G.;* Vedegambre verdo, *Sp.*

In the several revisions of the U. S. Pharmacopœia, *veratrum* has been handled in a vacillating manner. In 1880 and 1890 the drug was restricted to that obtained from *V. viride*. In 1900 both *V. viride* and *V. album* were recognized, this being done for reason of the large importations of Veratrum (*V. album*) and there being no practical method of distinguishing between these two drugs. The U. S. Pharmacopœia IX has wisely restricted the definition, in the interest of uniform medicine, to *V. viride*. This, however, may offer some practical commercial difficulties as it is not always easy to differentiate its substitution by *V. album,* and certainly it is almost impossible to detect an admixture with the European drug.

That the two species are very closely allied, and the two rhizomes histologically, chemically, and toxicologically very similar is indisputable, but similiarity is not identity. The European plant seems to be more actively poisonous than is the American, and has been said by some chemists to contain a larger proportion of the alkaloids. It usually also has a distinctly greater action upon the intestinal tract and it is probable that the proportionate amounts of the alkaloids differ in the two species. The conclusions reached in an elaborate physiological research made by H. C. Wood and H. C. Wood, Jr., for the Committee of Revision of the U. S. VIII was that the drugs can scarcely be distinguished physiologically, but that the European plant is more likely to disturb the intestines and that in the absence of any cogent reason for recognizing *V. album,* veratrum viride should alone be retained.

The American hellebore, *Veratrum viride*, known also by the names of *Indian poke, poke root,* and *swamp hellebore,* has a perennial, thick, fleshy rhizome, the upper portion of which is tunicated, the lower solid, and beset with numerous whitish roots. The stem is annual, cy-

lindrical, striated, pubescent, and solid, from three to six feet in height, furnished with bright green leaves, and terminating in a panicle of greenish-yellow flowers. The leaves gradually decrease in size as they ascend. The lower are from six inches to a foot long, oval, acuminate, plaited, nerved, and pubescent, and embrace the stem at their base, thus affording it a sheath for a considerable portion of their length. Those on the upper part of the stem, at the origin of the flowering branches, are oblong-lanceolate. The panicle consists of numerous flowers, distributed in racemes with downy peduncles. Each flower is accompanied by a downy, pointed bract, much longer than its pedicel. The perianth consists of six oval acute segments, thickened on the inside at their base, with the three alternate segments longer than the others. The six stamens have recurved filaments and roundish two-lobed anthers. The ovary is ovoid, tri-carpellary; styles three and persistent. Some of the flowers have only the rudiments of pistils. Those on the upper end of the branchlets are barren, those below fruitful. The fruit is a three-lobed capsule, three-celled, and containing flat imbricated seeds. This indigenous species of veratrum inhabits swamps, wet meadows, and the banks of mountain streamlets. It is more abundant northward, but reaches as far south as Georgia. From May to July is the season for flowering. It is doubtful whether the rhizome should be collected in autumn or just before flowering. It should be thoroughly dried and carefully preserved, as otherwise it deteriorates.

Veratrum album L. (*V. viride* Roehl., but not *V. viride* Aiton.).—The specific difference between this plant, which is a native of Europe and Northern Asia, and *V. viride* of North America has been questioned by various botanists, but it is now generally acknowledged that the two species are distinct. (See *Index Kewensis;* also Engler and Prantl.) *V. album* resembles closely the American species, but is distinguished by its yellowish-white flowers. The rhizome of *V. nigrum* of Central Europe is said to be sometimes substituted for that of *V. album,* but is much smaller. According to the Pharmacographia, that of the Mexican species, *V. frigidum* Schl., exactly resembles that of *V. album.*

Properties.—As found in commerce, veratrum is usually in small pieces or fragments, but sometimes it comes whole or sliced, so that its characteristic form may be observed. In this condition it is seen to consist of a rhizome one to three inches in length by somewhat less than an inch in thickness where broadest, tapering to a very obtuse or truncated extremity, simple or divided, compact but light, of a dark-brown color externally, and either closely invested with numerous yellow rootlets often several inches long, or exhibiting marks on the surface whence they have been removed. When sliced, the cut surface is of a dingy-white color. The rootlets are from three to six inches long, about as thick as a large knitting needle, or somewhat thicker, obviously much shrunk in drying, and marked by numerous closely set indentations, which give them a characteristic appearance. Not unfrequently portions of the dried stem or leafstalks remain attached to the rhizome, which should always be rejected, as they were ascertained by Procter to be inert. (*A. J. P.,* 1864, p. 99.)

Veratrum Viride is officially described as follows: "Rhizome upright, obconical, usually cut longitudinally into 2 to 4 pieces, from 2 to 7 cm. in length and from 1.5 to 3 cm. in diameter, externally light brown to dark brown or brownish-black, frequently bearing at the summit numerous, closely arranged, thin leaf-bases, otherwise rough and wrinkled, somewhat annulate from scars of bud-scales and bearing in the outer portion numerous roots, the lower part more or less decayed; fracture hard and horny; internally yellowish or grayish-white, marked with numerous, irregular fibro-vascular bundles; inodorous but sternutatory; taste bitter and acrid. Roots nearly cylindrical, from 3 to 8 cm. in length and from 1 to 3 mm. in diameter; externally light brown to yellowish-brown, deeply transversely wrinkled; fracture short, bark whitish, very thick, enclosing a porous central cylinder. The powder is grayish-brown to dark brown, strongly sternutatory; under the microscope it exhibits numerous starch grains from 0.003 to 0.02 mm. in diameter, spherical or ellipsoidal, single or 2- to 3-compound, the individual grains being often swollen or otherwise more or less altered; calcium oxalate in raphides, from 0.015 to 0.15 mm. in length; fragments with tracheæ, the walls being more or less strongly lignified and marked with scalariform or reticulate thickenings, frequently containing a lemon-yellow substance and associated with narrow, slightly lignified, porous, sclerenchymatous fibers; reddish-brown or brownish-black cork fragments occasional." *U. S.*

It has been asserted that the color of *V. album* is much lighter than that of *V. viride,* but this certainly is practically incorrect, however it may apply to carefully preserved specimens. Very commonly the roots have been removed from commercial *V. album,* while in America they are generally allowed to remain on the rhizomes. According to R. H. Denniston, no microscopic differences can be detected in the rhizomes, but in the roots distinction is possible owing to the fact that directly beneath the epidermis in the *V. viride* the collenchyma region consists of but two or three rows of large, irregular and distorted cells, while in *V. album* this region is generally made up of seven to eight rows of rounded, thicker-walled and smaller cells, which are not in the least distorted. Any such test is, of course, inapplicable to the drug in powder. In the color test proposed by R. H. Denniston, sulphuric acid is added to the powder; with *V. album* a brick-red color, with *V. viride* an orange-red color, will be produced. Of course the test is of little value in determining the character of a powder, as it does not possess sufficient differentiation.

The pharmacognosy of *V. viride* has been well illustrated by Bastin (*A. J. P.,* 1895, p. 196). The structure of *V. album* has been presented by

Meyer (*Arch. d. Pharm.*, 1882, p. 81; and in "*Wissenschaftliche Drogenkunde*," vol. 2, p. 46). Rosenthaler has submitted veratrum to pyroanalysis and has obtained a sublimate which is in part crystalline and gives a yellowish-red color with sulphuric acid. (*Apoth. Zeit.*, xxviii, p. 991.)

Pelletier and Caventou, in 1819, found in the rhizome of *Veratrum album* a substance which they regarded as identical with the veratrine just announced by Meissner as contained in sabadilla seeds. Simon (*Ann. Ch. Ph.*, 24, p. 214), in 1837, found the alkaloid *jervine* also in *Veratrum album.* Bullock (*A. J. P.*, 1865, p. 321) found that while *Veratrum viride* contained at least two characteristic alkaloids, neither of these was veratrine. The alkaloids noted by Bullock were named in a former edition of this work *viridine* and *veratroidine.* Peugnet (*N. Y. M. R.*, 1872, p. 120), in 1872, showed the identity of the first of these with jervine, and this was confirmed by Mitchell (*A. J. P.*, 1874), who also made out a distinct alkaloid in *Veratrum album,* to which he applied the name of *veratralbine.* The veratroidine discovered by Bullock in *Veratrum viride* in 1865 was also found in *Veratrum album* by Tobien in 1877. In a paper published in the *A. J. P.*, April, 1876, Bullock expressed his doubt as to the existence of veratroidine as a distinct alkaloid, considering that it might have been only jervine admixed with resin. Here the matter rested until the elaborate researches of Wright and Luff (*J. Chem. S.*, xxxv, 405, 421) who found in *Veratrum album: jervine,* $C_{26}H_{43}O_2N + 2H_2O$, *rubijervine,* $C_{26}H_{43}O_2N$, *pseudojervine,* $C_{29}H_{43}O_7N$, *veratralbine,* $C_{28}H_{43}O_5N$ (?), and also traces of an alkaloid having sternutatory power (possibly *cevadine*). In *Veratrum viride* they found jervine, pseudojervine, cevadine, very little rubijervine, and traces of veratrine and veratralbine. Of these, rubijervine probably agrees with Bullock's veratroidine, although as prepared by Bullock in his earlier experiments it was undoubtedly mixed with resin, as the fusing point given 132.2° to 135° C. (270°–275° F.) is much lower than that given by Wright and Luff for their pure crystals, which fused at 236° C. (456.8° F.). Pseudojervine forms crystals very similar to those of jervine, but it fuses at 299° C. (570.2° F.), instead of 231° to 237° C. (447.8°–458.6° F.). Pehkschen (*A. J. P.*, 1891) finds *jervine* in both the Veratrum species. Obtained by recrystallization from absolute alcohol it forms snow-white crystals of the formula $C_{14}H_{22}O_2N$ (determined by the analysis of the base and of its hydrochloride and sulphate). It melts at 237.7° C. (460° F.), and is slightly lævogyre. He finds *veratroidine* (rubijervine of Wright and Luff), and gives it the formula $C_{32}H_{53}O_9N$ (determined both by analysis and by molecular weight determination). It melts at 149.2° C. (300.6° F.), and is optically inactive. He obtained, thirdly, an alkaloid in rhombic crystals, which is probably a purer form of Wright and Luff's *pseudojervine.* Its formula is $C_{29}H_{49}O_{12}N$. It melts at 259.1° C. (498.4° F.), and is optically inactive. No color reactions could be obtained with this base, but if the slightest quantity of veratroidine or jervine is added, color reactions agreeing with Wright and Luff's pseudojervine are obtained. A very small quantity of a fourth alkaloid (Wright and Luff's veratralbine) was obtained, but not enough to allow of present investigation. Salzberger (*A. J. P.*, 1891) obtained the three bases *jervine, rubijervine,* and *pseudojervine,* and two new ones, *protoveratrine* and *protoveratridine,* from the rhizome of *Veratrum album;* the first of these two bases has the formula $C_{32}H_{51}O_{11}N$, and crystallizes in microscopic four-sided plates, which melt with charring at 245° to 250° C. (473°–482° F.). The base is exceedingly poisonous and violently sternutatory. It is insoluble in water, benzene, and petroleum benzin, slightly soluble in chloroform, boiling 96 per cent. alcohol, and ether. Dilute acids, with the exception of acetic acid, dissolve it. *Protoveratridine,* $C_{26}H_{45}O_8N$, occurs as colorless four-sided plates, which melt at 265° C. (509° F.). It is not poisonous, and does not cause sneezing. It is almost insoluble in the common solvents, but is soluble in dilute acids. Worthington pointed out the presence of gallic acid and sugar in *Veratrum viride.*

Uses.—The various alkaloids present in veratrum act upon the system in very different manners, and none of them appears to exercise exactly the same action as the whole drug. According to H. C. Wood (*Phila. Medical Times,* 1874, iv, p. 737), jervine is a depressant to the respiratory center, to the vasomotor center, and to the heart muscle, and also lowers reflex activity by an effect upon the spinal cord, and rubijervine is chiefly a stimulant to the cardio-inhibitory mechanism, but has a more depressant action upon the respiratory center. According to Eden (*A. E. P. P.*, 1892, xxix, p. 440), small doses of protoveratrine stimulate cardiac inhibition thereby causing a lowering of the blood pressure. In large doses there is a secondary paralysis of inhibition accompanied by rise in the pressure. In large quantities it also exercises a poisonous effect upon the voluntary muscles similar to that of veratrine. Rubijervine is present in such small proportions (according to Breideman, *J. P.*, 1906, lxxxiv, 0.053 per cent.) and is so feeble a substance that it is improbable that it plays any part in the physiological action of the drug. Jervine, although present in larger quantities (0.34 per cent.), according to H. C. Wood, Jr., is less poisonous than the drug itself. Protoveratrine, although present in small amounts (0.06 per cent., according to Breideman), is an extremely toxic substance and is the most important of the ingredients at present known. It appears to differ, however, in some of its properties from the whole drug.

When a moderate dose of veratrum is introduced into the system, the most marked change produced is reduction in the rate of the pulse accompanied with a fall in the arterial pressure. At the same time there may be some slow-

ing in the respiration. With proper doses the slowing of the pulse is extreme and we have seen, in the lower animals, even complete arrest of the heart at this stage of the poisoning. The slowing of the pulse does not occur if the pneumogastric nerves have been divided previous to the injection of the drug, and is at once abolished either by section of these nerves or by the administration of atropine. It must be regarded, therefore, as due to stimulation of the cardio-inhibitory center. The reduction in the arterial tension in the normal animal may, therefore, be attributed to the slowing of the pulse. The conclusions of H. C. Wood, Jr. (*U. P. M. B.*, March, 1908), that contrary to the older views, veratrum does not lower arterial tone, have been confirmed by the experiments of Pilcher and Sollmann (*J. P. Ex. T.*, 1915, vii, p. 295) on animals and the observations of Collins (*A. I. M.*, 1915, xvi, pp. 54–58) on man. After toxic doses of veratrum there is a late paralysis of the intra-cardiac terminals of the pneumogastric nerve and consequent increase in the pulse rate with at first a rise of the blood pressure followed by a fall. This toxic fall in the blood pressure appears to be due to a direct depressant action upon the heart muscle. There is, following the toxic dose, also marked reduction in the respiratory activity, death being due eventually to failure of this function.

Veratrum was introduced into medicine about a century ago by the group of physicians who called themselves "eclectics." By them it was attributed with mysterious "adenagic" virtues and used in all sorts of inflammatory diseases. Later under the belief that it dilated the blood vessels and hence would relieve various local congestions, regular practitioners employed it largely in the treatment of *pneumonia, peritonitis,* and other sthenic *fevers.* While it is still employed to some extent in this type of disorder, our knowledge of its physiological action indicates that its true field of usefulness is rather in chronic, than in acute, diseases. Thus it is a very valuable agent for the reduction of excessively *high blood pressure* in *arteriosclerosis, interstitial nephritis,* and other conditions of hypertension; in cases with feeble myocardia it should be used cautiously because the stimulation of the cardio-inhibitory mechanism predisposes to cardiac dilatation. For the same purpose it is often employed in threatened *apoplexy,* in *chronic endocarditis,* especially in those in which there is considerable degree of cardiac hypertrophy, and in the so-called *irritable heart* seen in soldiers and athletes. In *exophthalmic goitre* and various other forms of *tachycardia* it is frequently of great service to reduce the pulse rate and prevent the heart exhausting itself in excessive activity. In certain of these conditions its line of usefulness more or less parallels that of digitalis. It differs, however, sharply from that drug, in that while digitalis tends to increase the tone of the heart muscle, veratrum rather diminishes cardiac tone. Veratrum has also been used widely by obstetricians in the treatment of *puerperal eclampsia.* Whether its benefit in this condition is to be attributed to a depressant action upon the motor cord, as some believe, or whether it be due to a lowering of the blood pressure, is as yet uncertain. The dose of veratrum must be gauged by the effect it produces; in general it may be said that if it does not slow the pulse no benefit will be received by the patient. The drug should therefore be pushed until evidence of its action is seen in the reduction of the pulse rate. Ordinarily from one to three minims (0.06–0.2 mil) of the fluidextract may be given every two or three hours until it manifests its action. It should be remembered, however, that in some cases the cardio-inhibitory mechanism is refractory to the action of the drug and no dose will slow the pulse, and if given incautiously it may do great harm. Fortunately in most instances if given in too large dose it will manifest its toxic action by nausea before any more serious symptoms are produced.

Toxicology.—The symptoms of veratrum poisoning are vomiting accompanied with great nausea and much retching. There is profound prostration with muscular weakness, the skin bedewed with perspiration and pale in color, the pulse, in the milder cases, or in the early stage of the severe cases, is extremely slow and easily compressible, later, in the severe types of poisoning, it may become rapid and irregular. The respirations are often shallow and sometimes stertorous. Frequently there is much complaint of dizziness and in a few cases there has been dilatation of the pupil with disturbance of vision. Because of the promptness with which vomiting comes on even very large single doses of veratrum may be recovered from, thus Buckingham (*A. J. M. S.*, 1865) reports a case in which recovery followed a teaspoonful of the fluidextract. But when repeated large doses have been taken, the poisoning is much more dangerous.

In the treatment of veratrum poisoning if the patient be vomiting it is well to give a couple of glasses of water in order to thoroughly cleanse the stomach, at the same time twenty grains (1.3 Gm.) of tannic acid may be exhibited as an imperfect chemical antidote. If for any reason vomiting has not occurred it should be at once provoked or the stomach washed out by means of a stomach pump. The patient must be kept in a horizontal position and should not be allowed to sit up to vomit. After washing out the stomach in the manner described above, efforts should be made to stop the vomiting by the use of counter-irritation over the epigastrium and the cautious employment of morphine. But since when the drug proves fatal death is due to the respiratory arrest the latter should not be given in too large doses. If seen in the early stages when the pulse is slow, atropine is a remedy of great value antagonizing the effect of the veratrum upon the pneumogastric nerve and at the same time checking the excessive sweating and stimulating the respiratory center. Other active respiratory stimulants, such as hypodermic injections of ammonia and strych-

nine, may be employed, and if the bodily temperature is low it should be maintained by the external application of heat.

Dose, one to two grains (0.065–0.13 Gm.).

Off. Prep.—Fluidextractum Veratri Viridis, *U. S.;* Tinctura Veratri Viridis, *U. S.*

VIBURNUM PRUNIFOLIUM. U. S. (Br.)

VIBURNUM PRUNIFOLIUM Viburn. Prun.
[Black Haw]

(vī-bŭr'nŭm prū-nĭ-fō'lĭŭm)

"The dried bark of *Viburnum prunifolium* Linné or of *Viburnum Lentago* Linné (Fam. *Caprifoliaceæ*), without the presence or admixture of more than 5 per cent. of wood or other foreign matter." *U. S.* "Black Haw is the dried bark of Viburnum prunifolium, *Linn.*" *Br.*

Virburnum, *Br.;* Stagbush, Sheep-berry.

Viburnum prunifolium is a tall, very handsome shrub, which is quite common in the Middle and Southern United States, east of the Mississippi, flowering in May and ripening in the early autumn its ovoid or oblong blackish fruit. It is specifically characterized by its acuminate, glabrous winter buds, by its acuminate, sharply serrulate, ovate leaves on long, slender, sometimes broadened and wavy margined petioles. Its sessile cymes are 2 to 5 inches broad and bear oval bluish-black drupes.

Viburnum Lentago L., *Sheep Berry, Sweet Viburnum,* resembles the previous species, but has the winter buds smaller, less acute and often reddish pubescent, and its leaves stouter petioled and not acuminate at the apex. Its geographical limit overlaps that of *V. prunifolium,* but extends much further westward and northward, even to Manitoba. The bark of *V. dentatum* L., or *Arrow wood,* is said to be sometimes substituted for the official drug. (For description of *V. opulus,* see Part II.)

Properties.—The bark is officially described as "in irregular, transversely curved or quilled pieces, from 1.5 to 6 cm. in length, and from 0.5 to 1.5 mm. in thickness; outer surface grayish-brown, or, where the outer cork has scaled off, brownish-red, longitudinally wrinkled; inner surface reddish-brown, longitudinally striated; fracture short but uneven, showing in bark which is young or of medium thickness, a dark brown cork, a brownish-red outer cortex, and a whitish inner cortex in which are numerous light yellow groups of sclerenchymatous tissues; odor slight; taste distinctly bitter and somewhat astringent. The powder is dark brown; under the microscope it exhibits numerous large stone cells, which are often elongated, thick-walled and strongly lignified; bast-fibers few, crystals of calcium oxalate from 0.015 to 0.035 mm. in diameter, occurring mostly in rosette aggregates, occasionally in crystal fibers; monoclinic prisms of calcium oxalate few." *U. S.*

"In quills or curved pieces, one to four millimetres thick; dull brown or reddish-brown. Outer surface longitudinally wrinkled or, in older bark, with shallow fissures and scaly; inner surface longitudinally striated, reddish-brown. Fracture granular. In transverse section, a dark brown outer portion and a whitish or reddish bast with numerous groups of sclerenchymatous cells. Slight odor; taste astringent and bitter." *Br.*

The morphology of viburnum prunifolium is well illustrated by Holm in *M. R.,* xxii, p. 35. Illustrations of the bark of the several species of viburnum are given in Kraemer's "*Scientific and Applied Pharmacognosy*"; also see *P. J.,* 1903, lxx, p. 197. Lloyd states that the bark of all native species of viburnum are collected by root diggers and sold under the name of black haw. (*Ph. Rev.,* xxiii, p. 333.) The bark of the root is preferred to that of the stem and the official definition formerly limited the drug to the root bark. Farwell reported the substitution of the genuine drug by the bark of some other species of viburnum than those specified by the Pharmacopœia. The bark is much darker than the official bark and consisted largely of stem bark. (*M. R.,* xvii, p. 35.)

Herman van Allen found the following constituents in viburnum: (1) a brown resinous body, of a very bitter taste, from which it was found impossible to separate the sugar; (2) a greenish-yellow resin or neutral principle of a bitter taste, slightly soluble in water, freely so in alcohol, called by Krämer *viburnin;* (3) valeric acid; (4) a tannic acid giving a greenish-black color with ferric salts; (5) oxalic acid; (6) citric acid; (7) malic acid; (8) sulphates; (9) calcium, magnesium, potassium, and iron chlorides. (*A. J. P.,* 1880, 443.) As the result of elaborate investigation, T. Shennan (*Royal Coll. Phys. Lab. Rep.,* Edinburgh, vi, 1897) concludes that the *Viburnum prunifolium* contains *viburnic—i.e.,* valeric—acid, and a non-volatile alkaloid which, however, he failed to obtain in a pure condition.

Viburnum has been used quite largely in the treatment of *dysmenorrhea, after-pains,* and other uterine disorders. Pilcher (*A. I. M.,* Jan., 1917), however, has shown that in the doses ordinarily employed it has no effect of any kind on the uterine muscle.

R. L. Payne, Jr., has found that when given in toxic amount to the lower animals viburnum produces muscular weakness, ending in complete paralysis with loss of reflex action, which he believes to be due to an influence upon the motor side of the spinal cord. In warm blooded animals there is also marked lowering of the arterial pressure, believed by Payne to be the result of a direct action of the drug upon the heart. Experiments of Payne have in a measure been confirmed by those of T. Shennan, but as the latter took six drachms of the fluidextract within thirty minutes, with no demonstrable effect except a doubtful decrease of the rate and force of the pulse, it is plain that the drug is very feeble.

The solid extract (*dose,* from three to ten grains (0.2–0.65 Gm.)) does not represent the drug completely, owing to loss of volatile acid;

so that the fluidextract should be preferred, in doses of from one-half to one fluidrachm (1.8–3.75 mils).

Dose, thirty to sixty grains (2.0–3.9 Gm.).

Off. Prep.—Extractum Viburni Prunifolii, *U. S.;* Fluidextractum Viburni Prunifolii, *U. S.* (*Br.*); Elixir Viburni Prunifolii (from Fluidextract), *N. F.*

VINA MEDICATA.

MEDICATED WINES

(vī-nạ mĕd-ĭ-cā′tạ)

Vins médicinaux, Œnolés, *Fr.;* Medicinische Weine, *G.*

All wines were deleted from the U. S. P. IX. The Committee of Revision realized that the time had come to use alcohol of various strengths and to drop the inconvenience of using a liquid for a menstruum of varying quality and which required standardization to bring it to a reasonably definite strength. Another contributory cause for the deletion was the ignoring by pharmacists of the specified varieties of wines which were known to conform to the official requirements. Most pharmacists used sherry wine for Vinum Album and port wine for Vinum Rubrum, although both of these were known to be fortified wines containing nearly 10 per cent. more alcohol than the maximum limit for the officially designated wines of those titles. Both the Br. Pharm. 1914 and the N. F. IV have retained sherry wine as a menstruum, and the former uses also an "Orange Wine" (see *Vinum Aurantii*, page 1201).

The reported advantages of wine as a pharmaceutical menstruum are that, in consequence of the alcohol it contains, it dissolves substances insoluble in water, and, to a certain extent, resists their tendency to spontaneous change, while at the same time it is less stimulating than strong or diluted alcohol, owing to its smaller proportion of alcohol. The acid which it usually contains serves in some instances to increase its solvent power. But most wines, particularly the light varieties, are liable to undergo decomposition, and even the strongest acquire such a liability from the principles which they extract from vegetable substances; so that medicated wines, though they keep much better than infusions or decoctions, are inferior in this respect to the tinctures. The proportion of alcohol, moreover, is not constant, and the preparations, therefore, made with them were formerly of unequal strength. In the choice of wine, the purest and most generous should be selected. The medicated wines, in consequence of their liability to change, should be prepared in small quantities, from wine of proper strength, and should be kept in a cool place. *Detannated wine* may be best made by digesting the wine with casein which has the advantages of milk, formerly used, without its diluting effect or the introduction of foreign and undesirable constituents. Gelatin has also been used successfully for the same purpose, but is somewhat inferior to casein, which is now obtainable either in the soluble or insoluble form. The former should be used and the latter form may be made soluble by the careful use of an alkali. Ferric hydroxide should never be used for detannating wines, for, while it successfully removes the tannin, it also removes other valuable constituents and the acid of the wine always takes up a little of the iron so that a slightly ferruginous preparation results, which is usually undesirable.

VINUM ANTIMONIALE. Br. (N. F.)

ANTIMONIAL WINE

(vī′nŭm ăn-tĭ-mō-nĭ-ă′lē)

Vinum Antimonii, *N. F. IV;* Wine of Antimony; Vin antimonié, Vin émétique, Vin stibié, *Fr.;* Vinum Stibiatum, *P. G.;* Brechwein, *G.;* Vino emetico, *Sp.*

Wine of Antimony was not admitted to the U. S. P. IX, but has been transferred to the N. F. IV, sherry wine replacing the white wine. The formula of the U. S. P. VIII is given herewith.

"Antimony and potassium tartrate, *four grammes* [or 62 grains]; boiling distilled water, *sixty-five mils* [or 2 fluidounces, 95 minims]; alcohol, *one hundred and seventy-five mils* [or 5 fluidounces, 440 minims]; white wine, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the antimony and potassium tartrate in the boiling distilled water. Add this solution to a mixture of the alcohol with *seven hundred and twenty-five mils* [or 24 fluidounces, 247 minims] of white wine; mix well, and allow the mixture to stand until it has cooled. Then filter and add sufficient white wine through the filter to make the liquid measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms.]"

"Tartarated Antimony, 4 *grammes;* Distilled Water, boiling, 40 *millilitres;* Sherry, sufficient to produce 1000 *millilitres.* Dissolve the Tartarated Antimony in the Distilled Water, and add sufficient Sherry to produce the required volume." *Br.*

The Br. Ph., 1914, and N. F. IV formulas contain about 2 grains of tartar emetic in the fluidounce.

Considerable difficulty is often experienced in effecting a solution of tartar emetic in wine, and precipitation is likely to occur after the solution has been effected. These results are undoubtedly due to the variability in the amount of tannic acid in wines of different type and quality. Paris stated that he had seen the decomposition of the tartar emetic so complete that no traces of the salt could be detected in the supernatant liquid. The difficulty was not avoided by the plan adopted in the U. S. Pharmacopœia VIII of first dissolving the antimonial in water and then adding the wine; for, even allowing that the solution may be accomplished, the same ingredients are present, and their mutual reaction must ultimately result in the same effects. The proper course is to select perfectly pure crystallized tartar emetic, and wine which is low in tannic acid content, to make a permanent solution.

The advantages of antimonial wine are that

it affords the means of administering minute doses of tartar emetic, and that it is more permanent than an aqueous solution of that salt, which is liable to spontaneous decomposition. It is used only as a diaphoretic or expectorant.

Dose, from ten to thirty minims (0.6–1.8 mils), given frequently.

VINUM AURANTII. Br.

ORANGE WINE

(vī'nŭm âu-răn'tī-ī)

Vin d'Ecorce d'orange amère, *Fr.;* Pomeranzenwein, *G.*

"Orange Wine is made by the fermentation of a saccharine solution to which Fresh Bitter-Orange Peel has been added." *Br.*

This is officially described as "a vinous liquid, having a golden sherry color, and a taste and aroma derived from the Bitter-Orange Peel. Contains from 12 to 14 per cent. by volume of ethyl hydroxide. Not more than slightly acid to *litmus.* When 50 millilitres are made alkaline with *solution of sodium hydroxide,* evaporated to a small bulk, acidified with *hydrochloric acid,* and shaken with *benzene,* the residue obtained on evaporating the benzene solution, when dissolved in *water,* does not assume a violet color on the addition of a drop of *T. Sol. of ferric chloride* (absence of salicylic acid). Yields not more than the slightest characteristic *reactions* for sulphites." *Br.*

This wine is used as a vehicle, and is the official menstruum for several Br. preparations.

VINUM COLCHICI. Br. (N. F.)

COLCHICUM WINE

(vī'nŭm cŏl'çhĭ-cī)

Vinum Colchici Cormi, *N. F. IV;* Wine of Colchicum corm; Vinum Colchici Radicis, U. S. 1890; Wine of Colchicum Root; Vin de Bulbe de Colchique, *Fr. Cod.;* Œnolé de Bulbe de Colchique; Zeitlosenknollenwein, *G.;* Vino con colchico, *It.*

"Colchicum Corm, in No. 20 powder, 200 *grammes;* Sherry, 1000 *millilitres.* Prepare by the *maceration process.*" *Br.*

The British, 1914, colchicum wine is only half the strength of the U. S., 1890, preparation. The latter was intended to be a saturated vinous tincture of colchicum. A wine of colchicum corm is also official in the N. F. IV (see Part III) but it is double the strength of the British wine, *i.e.,* 400 Gm. of corm per 1000 mils of wine. A wine made from the fresh bulb is occasionally imported from England, and is thought by some to be more efficacious than the official preparation. *Wine of Colchicum Seed,* also in the N. F. IV, is made by mixing together 10 mils of fluidextract of colchicum seed, 15 mils of alcohol, and 75 mils of sherry wine. In *gout* this wine is frequently given in connection with magnesium sulphate. It is a violent poison in overdoses. Two fluidrachms and a half (9.3 mils) of it are said to have caused death.

Dose, ten to forty minims (0.6–2.5 mils).

VINUM FERRI. Br.

IRON WINE

(vī'nŭm fĕr'rī)

Vinum Chalybeatum, s. Martiatum; Eisenwein, Stahlwein, *G.*

"Iron, in wire, 50 *grammes;* Sherry, 1000 *millilitres.* In a closed vessel partially immerse the Iron in the Sherry; continue the maceration until the filtered liquid responds to the following test:—Evaporate 50 millilitres to dryness, incinerate the residue, heat the ash with *hydrochloric acid* diluted with an equal volume of *water,* filter, wash the filter paper with *water,* and add to the mixed filtrate and washings excess of *solution of ammonia.* Collect the precipitate, wash, dry and ignite; the residue weighs not less than 0.089 or more than 0.215 gramme, representing a proportion of not less than 0.125 or more than 0.300 gramme of iron, calculated as iron, Fe, in 100 millilitres of the Wine." *Br.*

(See also *Vinum Ferri Citratis.*)

When wine is made to react on metallic iron with presence of air, the metal is oxidized, and then unites with the excess of acid of the potassium bitartrate, which is the characteristic salt of wines. The ferruginous salt, therefore, formed is iron and potassium tartrate, or the tartarated iron of the Br. Pharmacopœia, and this was the old method of preparing the Wine of Iron. But it is obvious that the strength in iron cannot be entirely uniform, as the quantity dissolved must depend on the proportion of the bitartrate in the wine, which is variable, and on various circumstances of the manipulation. In consideration of these objections, it was thought best, in the Br. formula of 1864, to substitute a simple solution in the wine, of the iron and potassium tartrate already formed, and to abandon the old tedious formula. But it is obvious that a solution of the ferruginous salt in wine is not exactly the same as the wine of iron prepared with the metal, as it contains the potassium bitartrate unaltered. For this and other reasons, the Br. Pharmacopœia has returned to the old method.

Dose, one to four fluidrachms (3.75–15.0 mils).

VINUM FERRI CITRATIS. Br. (N. F.)

WINE OF IRON CITRATE

(vī'nŭm fĕr'rī cĭ-trā'tĭs)

Vinum Ferri, *N. F. IV;* Wine of Iron; Vinum Chalybeatum, *Br.;* Wine of Ferric Citrate; Vin Chalybé, Œnolé ferrugineux, Vin ferrugineux, *Fr. Cod.;* Eisenwein, *G.*

"Iron and Ammonium Citrate, 18 *grammes;* Orange Wine, sufficient to produce 1000 *millilitres.* Dissolve. Shake occasionally for three days; filter." *Br.*

This wine was not admitted to the U. S. P. IX but was added to the N. F. IV (see Part III). The formula of the U. S. P. VIII is given herewith.

"Iron and Ammonium Citrate, *forty grammes* [or 1 ounce av., 180 grains]; Tincture

of Sweet Orange Peel, *sixty mils* [or 2 fluidounces, 14 minims]; Syrup, *one hundred mils* [or 3 fluidounces, 183 minims]; White Wine, *a sufficient quantity,* to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the iron and ammonium citrate in *seven hundred mils* [or 23 fluidounces, 321 minims] of White Wine. Add to this the tincture of sweet orange peel, and the Syrup, and, lastly, enough White Wine to make the product measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Set the mixture aside for two days; then filter through paper, in a well-covered funnel." *U. S. VIII.*

Dose of the Br. preparation, one to four fluidrachms (3.75–15.0 mils).

VINUM IPECACUANHÆ. Br. (N. F.)

IPECACUANHA WINE

(vī'nŭm ĭp-ę-căc-ū-ăn'hæ)

Wine of Ipecac; Vin (œnolé) d'Ipécacuanha, *Fr.;* Brechwurzelwein, *G.*

"Liquid Extract of Ipecacuanha, 50 *millilitres;* Sherry, 950 *millilitres.* Mix; set aside for forty-eight hours; filter." *Br.*

This wine was not admitted to the U. S. P. IX but was added to the N. F. IV (see Part III). The U. S. P. VIII process was as follows:

"Fluidextract of Ipecac, *one hundred mils* [or 3 fluidounces, 183 minims]; Alcohol, *one hundred mils* [or 3 fluidounces, 183 minims]; White Wine, *eight hundred mils* [or 27 fluidounces, 24 minims], to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix them. Set the mixture aside for two days; then filter through paper, in a well-covered funnel."

The wine of ipecac of the U. S. P. VIII and N. F. IV contains in a fluidounce the virtue of about 45 grains, the British, 1914, of only somewhat more than 22 grains. Wine of ipecac possesses all the medicinal properties of the root, and may be used as a substitute when it is desirable to administer the medicine in a liquid form. It is much used as an expectorant and a diaphoretic, and the effects of the Dover's powder may be obtained by combining it with a liquid preparation of opium.

VINUM QUININÆ. Br.

QUININE WINE

(vī'nŭm quĭ-nī'næ)

Vin (Œnolé) de Quinine, *Fr.;* Chininwein, *G.*

"Quinine Hydrochloride, 2 *grammes;* Orange Wine, 875 *millilitres.* Dissolve; filter if necessary." *Br.*

The Br. Ph., 1898, replaced quinine sulphate used in the 1885 process by quinine hydrochloride on account of the greater solubility of the latter. Each fluidounce contains one grain of quinine hydrochloride.

Dose, one-half to one fluidounce (15–30 mils).

VINUM XERICUM. Br., N. F.

SHERRY WINE Vin. Xeric.

(vī'nŭm xĕ'rĭ-cŭm)

"Sherry is a Spanish wine." *Br.* "An alcoholic liquid made by fermenting the juice of fresh ripe grapes, the fruit of cultivated species of *Vitis* Linné (Fam. *Vitaceæ*), freed from seeds, stems and skins, and fortifying with pure grape brandy. It contains not less than 16 per cent. nor more than 24 per cent. of C_2H_5OH, by volume, when estimated (for alcohol) as directed in the U. S. Pharmacopœia IX. Preserve it in well-closed casks or in well-stoppered bottles, in a cool place." *N. F. IV.*

"Pale yellowish-brown, containing not less than 16 per cent. by volume of ethyl hydroxide. Contains in 100 millilitres not less than 0.1 or more than 0.2 gramme of volatile acids, calculated as acetic acid, $HC_2H_3O_2$, and not less than 0.3 or more than 0.45 gramme of fixed acids, calculated as tartaric acid, $H_2C_4H_4O_6$, when tested by the following process:—(1) Titrate 25 millilitres of the Sherry with *N/5 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator, and note the number (*a*) of millilitres of the former solution required. (2) Introduce 25 millilitres of the Sherry with 25 millilitres of *water* into a flask capable of holding 200 millilitres and attach a condenser; add 0.5 gramme of *tannic acid,* and distil gently until about 25 millilitres have been collected. Then pass a current of steam through the residual liquid in the flask, and continue the distillation until about 200 millilitres in all have been collected. Titrate the distillate with *N/5 solution of sodium hydroxide, solution of phenolphthalein* being used as indicator. The number (*b*) of millilitres of the former solution required is not less than 2.1 or more than 4.2, representing a proportion of not less than 0.1 or more than 0.2 gramme of volatile acids, calculated as acetic acid, $HC_2H_3O_2$, in 100 millilitres of the Sherry. Deduct the number (*b*) of millilitres required in (2) from the number (*a*) of millilitres required in (1). The difference is not less than 5 or more than 7.5, representing a proportion of not less than 0.3 or more than 0.45 gramme of fixed acids, calculated as tartaric acid, $H_2C_4H_4O_6$, in 100 millilitres of the Sherry. When 50 millilitres of the Sherry are made alkaline with *solution of sodium hydroxide,* evaporated to a small bulk, acidified with *hydrochloric acid* and shaken with *benzene,* the residue obtained on evaporating the benzene solution, when dissolved in *water,* does not assume a violet color on the addition of a drop of *T. Sol. of ferric chloride* (absence of salicylic acid)." *Br.*

In the U. S. P. VIII two varieties of wine were officially recognized, respectively designated as *vinum album* and *vinum rubrum.* Although the descriptions and tests of both of these articles included only natural wines of low alcohol content (10 to 12 per cent.), most pharmacists continued to use sherry and port wine

respectively for the white and red wine, and as both sherry and port are fortified wines containing over 20 per cent. of alcohol, lack of conformity to official character of product in the class of preparations made from these wines was the rule rather than the exception. For this reason wine was deleted from the U. S. P. IX, but sherry has been admitted to the N. F. IV.

"Sherry Wine is a pale yellowish-brown or amber-colored liquid, having a pleasant, aromatic odor, free from yeastiness, and having a fruity, characteristic taste without excessive sweetness or acidity. Specific gravity: from 0.985 to 1.000 at 25° C. (77° F.). Evaporate 100 mils of Sherry Wine in a tared dish, on a water bath, and dry the residue to constant weight at 100° C. (212° F.); it weighs not less than 3 Gm. nor more than 7 Gm. Ignite this residue at a low temperature and burn it gradually to whiteness, moisten the ash with a small portion of ammonium carbonate T.S. and again carefully ignite; the ash weighs not less than 0.175 Gm. nor more than 0.5 Gm. Dilute 50 mils of Sherry Wine with 200 mils of distilled water; it requires for neutralization not less than 20 mils nor more than 40 mils of tenth-normal potassium hydroxide V.S., using phenolphthalein T.S. as indicator (*free acid*). Acidulate 50 mils of Sherry Wine with hydrochloric acid, heat and add an excess of barium chloride T.S. Collect the precipitate on a filter of known ash content, wash it thoroughly, dry, and ignite; the residue weighs not more than 0.034 Gm. (*sulphate*). To 10 mils of Sherry Wine add an equal volume of distilled water and 5 drops of ferric chloride T.S.; not more than a faint greenish-brown color appears (*tannic acid*). Add 10 mils of diluted sulphuric acid to 75 mils of Sherry Wine and shake out the mixture in a separator twice, using each time 20 mils of a mixture of equal volumes of purified petroleum benzin and ether. Transfer the separated benzin-ether solution to an evaporating dish, allow the solvent to evaporate spontaneously and dissolve the residue in 3 mils of distilled water; the solution does not have a sweet taste (*saccharin*) nor does it yield a violet color upon the addition of a few drops of a dilute solution of ferric chloride (1 in 200) (*salicylic acid*)." *N. F. IV.*

VIRUS VACCINICUM. U. S.

VACCINE VIRUS Virus Vaccin. [Glycerinated Vaccine Virus, Smallpox Vaccine, Jennerian Vaccine]

(vī'rŭs văc-cĭn'ĭ-cŭm)

"The pustules of vaccinia or cowpox from healthy vaccinated animals of the bovine species, removed and prepared under aseptic conditions." *U. S.*

Impfstoff, *G.*; Virus vaccin, *Fr.*; Vaccino, virus di vacca, *It.*; Vacuna, *Sp.*

Though constantly used by the medical profession for more than a century, this article is now first admitted into the United States Pharmacopœia in the Ninth Decennial Revision. Vaccination against smallpox is the oldest and the surest method of preventive medicine, directed against a specific disease. Its efficacy was first proven by Jenner in England in 1796, and soon corroborative evidence was supplied from America, notably by Waterhouse of Boston. Up to the middle of the nineteenth century, the vaccine material was commonly taken from the arm of a person previously vaccinated and thus carried on from patient to patient. At present the calf serves exclusively in this country as the animal for propagating the virus to be used on human subjects; the danger of transmitting some other latent disease of man at the same time is thus avoided. Other improvements which have occurred in the course of time are the use of the more potent pulp, instead of the lymph of the vesicle on the calf, and especially the use of glycerine as a preservative. The glycerine is allowed to act on the virus for a number of days before use, and by this means the bacteria, normally present on the skin of the calf from which the virus is taken, are very greatly reduced in number. Phenol and ether have also been used to obtain a nearly sterile vaccine. The dry vaccine point is no longer allowed to be sold in interstate traffic; this form of vaccine either contained a large number of organisms or was comparatively inert. Moist points are still used, but the preferable form of container is one in which the virus is sealed in glass, such as in a capillary tube; insertion by single incision or by rotary abrasion is thus made easy and the large areas of scarification avoided.

Preparation.—"The vaccine pulp should be thoroughly rubbed up in a mortar or passed through a special grinder, strained to remove coarse particles, and made into a smooth emulsion with a glycerin solution. Vaccine Virus gradually loses in potency, the loss being more rapid at high than at low temperatures. Preserve it at a temperature between 4.5° and 15° C. (40° and 59° F.), protected from light. Only such Vaccine Virus may be sold as has been prepared in establishments licensed by the Secretary of the Treasury of the United States. The law and the regulations demand that the following requirements be observed: No Vaccine shall be used from any animal having a communicable disease, or suspected of having a communicable disease, other than vaccinia; animals used for propagating Vaccine Virus must be under daily veterinary examination for a period of not less than seven days before vaccination, and as soon as the vaccine pulp is removed a necropsy shall be made on each animal and permanent records kept. Each lot of Vaccine Virus shall be examined to determine its freedom from pathogenic micro-organisms and a special examination must be made of each lot to determine the absence of tetanus spores or toxin, and permanent records must be kept of these examinations. The Virus must be marketed in sterile containers that comply with the requirements of the law and the regulations established by the United States Public Health Service. Each package of Vaccine Virus shall

bear upon the label the name, address, and license number of the manufacturer and the date beyond which the contents cannot be expected to yield their specific results. The label should also contain the laboratory number of the Virus." *U. S.*

The propagation of vaccine virus requires sterile laboratory equipment and careful technic throughout. The animals must be tuberculin tested, repeatedly inspected and kept very clean; the removal, grinding, and distribution of the vaccine into its final containers are strict aseptic operations.

Uses.—To appreciate what vaccination has done for mankind, it is necessary to consider the era before vaccination, when having had smallpox was one of the evidences of maturity, and the toll of lives yearly demanded by this disease was a constant drain on every class of humanity. In more recent times the regions where vaccination is little practiced are conspicuous for the number of pock-marked faces; opposition to vaccination was so general in Montreal that when in 1886 a Pullman car conductor brought smallpox from Chicago, an epidemic broke out which in nine months killed 3164 persons. As a contrast to this may be cited the experience of smallpox hospitals, where doctors, nurses, and attendants never having had smallpox are kept immune by vaccination. Smallpox among the unvaccinated is the most contagious disease known, yet vaccination is often too lightly regarded in that it is carelessly performed and no attention is given the patient after the operation. Any wound is liable to complications; a wound intentionally given should be particularly guarded against infection. Vaccination by scarification or cross-hatching, which forms an ulcerating area of appreciable extent—and the use of vaccination shields or other inappropriate after-care are the most frequent causes of sore arms. To vaccinate, the skin of the upper arm near the insertion of the deltoid muscle should be cleansed and dried. Soap and water, alcohol, or ether may be used for this purpose, but no stronger antiseptic should be applied. The cotton or cloth with which the skin is wiped should be sterile and nothing else allowed to touch the site. The capillary tube may be wiped with alcohol, the ends broken inside the bulb, and the glycerinated virus expelled by the bulb to form a line on the cleansed skin. Drawing the skin tight by grasping the arm beneath, a single incision about an inch long and parallel with the arm is made through the virus. This incision may be made with a flamed needle or other sterile instrument and should penetrate the papillary layer, but preferably not draw blood. The virus should be thoroughly rubbed into the incision with a smooth sterile instrument, such as the side of the needle. No other incision or cross scratching should be made unless there will be no opportunity for re-vaccination; in the latter case similar single incisions may be made on either side of the first and at least an inch away; other tubes should be used for this purpose. By this means the pustulation is limited so that large confluent crusts are not formed and deep ulceration with the tendency to secondary infection is avoided. Another method which produces even a smaller wound, but is surely successful only with very fresh virus is inoculation by the twisting abrasion. A dentist's drill (sterilized each time by flaming or other method) is used for this purpose. A slight twirling motion between the thumb and forefinger causes this instrument when pressed against the skin to give a shallow area denuded of epidermis, but without bleeding, no larger than a pinhead. To this the virus can be applied and rubbed in as above described. The vaccination area should dry (not in direct sunlight) for fifteen minutes or half an hour before being covered with clothing. The arm must be kept clean, dressed aseptically when the vesicle appears, and, when pustulation ensues, treated antiseptically. No dressing should be allowed to remain on the arm more than forty-eight hours. The arm should be seen by the physician on the third, sixth and ninth day at least, to determine the character of the reaction, and as often as may be necessary thereafter to insure rapid healing of the wound. It is preferable if the whole process can take place without the crust breaking. Vaccination is a surgical procedure and is worthy not only of the painstaking asepsis of a skilled physician, but of his intelligent after-care as well. If never previously vaccinated, the patient usually shows a papule about the fourth day, a vesicle about the fifth, and a pustule the eighth. Re-vaccination may be more rapid in its course, and correspondingly milder; in some cases a small papule is seen on the second day, subsiding without further progress. These abortive accelerated reactions may be taken as indicative of a degree of immunity.

The protection given by vaccination is relative, not absolute, and re-vaccination should be done when exposure to smallpox takes place or is threatened. All infants except in the presence of eczema or marasmus should be vaccinated before teething begins; re-vaccination should be performed before entering school and again at the age of fifteen.

Vaccine virus is the most rapidly deteriorating product likely to be carried by the pharmacist, and should be kept in the coldest part of an ice-box, at a temperature below 5° C. (41° F.).

XANTHOXYLUM. U. S.

XANTHOXYLUM Xanthox. [Prickly Ash Bark]

(xăn-thŏx'ȳ-lŭm)

"The dried bark of *Xanthoxylum americanum* Miller, known in commerce as Northern Prickly Ash Bark, or *Xanthoxylum Clava-Herculis* Linné, known in commerce as Southern Prickly Ash Bark (Fam. *Rutaceæ*)." *U. S.*

X. americanum: Toothache Tree, Angelica Tree, Suterberry, Pellitory Bark, Yellow-wood; Clavalier, Frêne épineux, *Fr.*, Zahnwehholz, Zahnwehrinde, *G.*

X. Clava-Herculis: Sea Ash, Hercules' Club, Pepper-wood.

Northern Prickly Ash (*Xanthoxylum americanum*) is a shrub from five to twenty-five feet in height, with alternate branches, which are covered with strong, sharp, scattered prickles. The leaves are alternate and pinnate, consisting of four or five pairs of leaflets, and an odd terminal one, with a common footstalk, which is sometimes prickly on the back, and sometimes unarmed. The leaflets are nearly sessile, ovate, acute, slightly serrate, and somewhat downy on their under surface.

The flowers, which are small and greenish, are disposed in sessile umbels near the origin of the young shoots. The plant is polygamous, some shrubs bearing both male and perfect flowers, others only female. The number of stamens is five, of the pistils three or four in the perfect flowers, about five in the pistillate. The capsules are stipitate, oval, punctate, of a greenish-red color, with two valves, and one oval blackish seed. This species of xanthoxylum is indigenous, growing in woods and in moist shady places throughout the Northern, Middle, and Western States. The flowers appear in April and May, before the foliage. The leaves and capsules have an aromatic odor, recalling that of oil of lemon.

Botanists are not agreed concerning the distinction of the genus Fagara from Xanthoxylum. Thus, the authors of the Index Kewensis consider the two genera identical, while Engler and Prantl separate them. The most important character separating them seems to be the absence of sepals in Xanthoxylum. Most of the species of the genus Fagara are tropical trees.

Z. Clava-Herculis L. [*Fagara Clava-Herculis* (L.) Small], or Southern Prickly Ash, varies in size from a large bush to a small tree. Its bark is armed with warty prickles, and large conical cork wings occur on the branches and the petioles. The alternate leaves have from seven to nine ovate-lanceolate, crenate-serrulate, unequal-sided leaflets, smooth and shining on the upper surface. It grows on dry soil, westward as far as Western Texas, and perhaps into Mexico, eastward to the Atlantic coast, and northward to Southern Virginia, especially affecting the coast region.

The fruits (*Prickly ash berries*) of both of the official species probably contain the same principles found in the barks. The dried berries are recognized by the N. F. under the name of *Xanthoxyli Fructus,* and are described in Part II.

There has been much confusion in regard to the nomenclature of the prickly ashes. *Aralia spinosa* L., or angelica tree, which grows in the Southern States, is occasionally confounded with *X. Clava-Herculis,* in consequence partly of being sometimes called, like the latter, *prickly ash.* Its bark is nearly smooth externally, is beset with slender prickles in transverse rows and has a taste different from that of *F. Clava-Herculis.* Besides the official trees, the bark of *F. flava* (Vahl), Frug. and Urban (*X. caribæum* S. Wats.), the *satin-wood* of semi-tropical Florida and the West Indies, has appeared in commerce under the name of *yellow Hercules club* or *yellow thorn.* This bark is thin, with an odor like that of Angustura bark, a bitter, disagreeable, acrid taste, and a canary-yellow color, which it imparts to the saliva when chewed. It would seem, also, that under the name of *prickly yellow wood, yellow wood,* or *fustic,* the products of other West Indian xanthoxylums and allied plants find their way into commerce.

Xanthoxylum veneficum Bailey, of Australia is, according to J. H. Maiden, a violent convulsive poison, 5 grains of the extract being a fatal dose for a cat. *Xanthoxylum scandens* is said to be used by the natives of Java as a fish poison, and according to Van der Haar, contains an alkaloid. (*P. J.*, 71, 134; 73, 814.)

Properties.—Although the bark of the Southern prickly ash was not recognized by the U. S. Pharmacopœia until the revision of 1880, as long ago as 1864 Bridges pointed out that it had entered commerce, and gave the physical characteristics separating it. (*Proc. A. Ph. A.*, xii, p. 270.) The characteristics of the two barks are very well given in the following official description.

"**Northern Prickly Ash Bark.**—In transversely curved fragments or quills, from 2 to 15 cm. in length; bark from 0.5 to 2 mm. in thickness; outer surface light gray to brownish-gray with grayish patches of foliaceous lichens bearing numerous small black apothecia; longitudinally wrinkled and with numerous whitish lenticels; the cork occasionally abraded, showing the yellowish or orange inner bark; inner surface yellowish-white, finely longitudinally striate and usually with numerous, bright, shining crystals; fracture short, uneven; odor slight; taste bitter, acrid, becoming pungent. Under the microscope, transverse sections of Northern Prickly Ash Bark show an outer corky layer consisting of from 4 to 20 rows of cells, the tangential walls being more or less thickened and lignified; a wide strata of collenchyma inside of the cork cambium composed of from 8 to 10 rows of tangentially elongated cells, with very thick walls and containing plastids; a more or less indistinct row of endodermal cells beneath which occur small groups of primary bast-fibers; the inner bark consists of numerous parenchyma cells among which are included large oil-secretion reservoirs, separated by medullary rays which are mostly one cell in width; the parenchyma cells as well as the oil-secretion reservoirs contain numerous colorless oily globules. Scrapings from either the inner or outer surface show numerous rod-shape crystals and flat prisms, from 0.015 to 0.25 mm. in length, which polarize light with a display of bright colors.

"**Southern Prickly Ash Bark.**—In transversely curved or irregular, oblong, flattened pieces, or in quills from 2 to 40 cm. in length, bark from 1 to 4 mm. in thickness; outer surface light gray to brownish-gray, marked by

numerous large, barnacle-shaped projections of cork, from 0.5 to 3.5 cm. in thickness, otherwise with numerous grayish patches of foliaceous lichens, bearing blackish apotheeia, and numerous, elliptical lenticels; inner surface light yellowish-brown to olive brown, obscurely longitudinally striate and free from crystals; odor and taste as in Northern Prickly Ash Bark. Under the microscope, transverse sections of Southern Prickly Ash Bark show a strong development of lignified cork occurring in the form of rings, the successive layers being separated by several rows of narrow tabular cells strongly thickened on the tangential walls; beneath the cork cambium occurs a thin layer of collenchyma followed by the outer tissues of the primary cortex and consisting of small groups of rather large stone cells and occasional, scattered groups of bast-fibers and parenchyma; the inner bark consists of parenchyma, a more or less indistinct leptome or sieve tissue among which are numerous, large, light yellowish oil-secretion reservoirs, medullary rays from 1 to 2 cells in width and occasional groups of stone cells and bast-fibers; starch grains numerous, nearly spherical, from 0.002 to 0.01 mm. in diameter, and occurring in the parenchyma cells and medullary rays; calcium oxalate chiefly in monoclinic prisms from 0.01 to 0.025 mm. in diameter, occurring in crystal fibers and in parenchyma cells of the primary cortex. Powdered Xanthoxylum is light grayish-brown, under the microscope it shows mostly irregular fragments of cork cells, nearly colorless and strongly lignified, fragments of parenchyma containing either small starch grains, oily globules or monoclinic prisms of calcium oxalate; stone cells in small groups with thick, colorless walls and containing frequently a reddish-brown substance; bast-fibers few and non-lignified. In the Northern Prickly Ash, the stone cells are usually absent, and the calcium oxalate crystals and the fragments of cork are relatively few." *U. S.*

Xanthoxylum is practically never adulterated, and hence the drug has never been studied very exhaustively. Kraemer illustrates the inner structure of the Southern prickly ash bark in his work on *"Scientific and Applied Pharmacognosy."* Recently the bark of a tropical American species, *X. Ochroxylum* D. C., has been the subject of a pharmocognostical study by Leprince. (*Repert. Pharm.*, 1912, xxiv, p. 215.)

W. L. Cliffe after careful examination demonstrated that the bark of Southern prickly ash exceeded that of the Northern prickly ash in active properties. (*A. J. P.*, 1901, 562.) In 1829, Edward Staples isolated from *X. americanum* a crystalline *xanthoxyline* which was again found by J. U. Lloyd in 1876. Subsequently, from the same plant Edward T. Moffet (*A. J. P.*, 1886, 417) obtained a supposed alkaloid in yellow crystals, soluble in alcohol and chloroform, insoluble in petroleum benzin, ether, and benzene. G. H. Colton (*A. J. P.*, 1880, p. 191) separated from the Southern prickly ash, tasteless, colorless, silky acicular crystals, soluble in alcohol, ether, and chloroform, less soluble in benzene, and insoluble in water. The identity of all these principles was assumed until E. G. Eberhardt (*A. J. P.*, 1890, 231) obtained from the Southern prickly ash a colorless crystalline principle agreeing in solubilities with that of Colton. On analysis it gave figures indicating the formula $C_{20}H_{19}O_6$ or $C_{30}H_{28}O_6$. At the same time he analyzed a sample of Lloyd's crystalline principle from *X. fraxineum* (*X. americanum* Mill.), which had been preserved in the cabinet of the Philadelphia College of Pharmacy, and found for it the formula $C_{20}H_{27}O_6$. Numerous reactions also indicated that the two principles were different. Thus, Lloyd's crystals dissolve in concentrated sulphuric acid with light red color, and on the addition of an excess of water produce a whitish precipitate which is taken up by chloroform; the crystals from the *X. Clava-Herculis,* dissolve in concentrated sulphuric acid with dark red color, and on dilution separate a purplish precipitate, which is not taken up by chloroform. Lloyd's principle melts, moreover, at 129.5° C. (265.1° F.), while Eberhardt's melts at 119° C. (246.2° F.). In 1863, J. D. Perrin separated from the Caribbean *Xanthoxylum Clava-Herculis* an alkaloid which he considered to be *berberine.* This had also been described as early as 1826 by Chevallier and Pelletan under the name of *xanthopicrite. X. senegalense* (*artar root*) was analyzed by Giacosa and Soave (*A. J. P.*, 1890, 500), who found a fixed oil, a neutral crystalline substance, melting at 120° C. (248° F.), and two alkaloids. The first of these they call *artarine,* and give to it the formula $C_{20}H_{17}O_4N$ (which makes it agree with *berberine*), or $C_{21}H_{23}O_4N$, in which case they consider that it may be *methylhydroberberine.* The second alkaloid, crystallizing in blood-red needles, they did not analyze.

Uses.—Xanthoxylum is stimulant, producing, when swallowed, a sense of heat in the stomach, with more or less general arterial excitement, and a tendency to diaphoresis. It is thought to resemble mezereum and guaiac in its remedial action, and is given in the same diseases. As a remedy in *chronic rheumatism,* it enjoys some reputation in this country. The bark, used as a masticatory, is a popular remedy for *toothache.* Xanthoxylum is capable of being used as a counter-irritant, and great relief is sometimes afforded in various forms of chronic pelvic disease in women by means of a hot pack, applied to the lower part of the trunk, of two to four ounces of fluidextract of xanthoxylum and an ounce of tincture of cayenne pepper to two quarts of water. A decoction prepared by boiling an ounce in three pints of water down to a quarter may be given in the quantity of a pint (473 mils), in divided doses, during the twenty-four hours.

Dose, fifteen to thirty grains (1–2 Gm.).

Off. Prep.—Fluidextractum Xanthoxyli, *U. S.;* Elixir Corydalis Compositum, *N. F.*

ZINCI ACETAS. U. S., Br.

ZINC ACETATE Zinc. Acet.

(zĭn'cī ă'cę-tăs)

"It contains not less than 83.16 per cent. nor more than 87.32 per cent. of anhydrous zinc acetate, corresponding to not less than 99.5 per cent. of the crystallized salt [$Zn(C_2H_3O_2)_2 + 2H_2O = 219.45$]. Preserve it in well-closed containers." *U. S.* "Zinc Acetate, $Zn(C_2H_3O_2)_2,2H_2O$, may be obtained by neutralising acetic acid with zinc carbonate." *Br.*

Acetas Zincicus; Acétate de Zinc, *Fr. Cod.;* Zincum Aceticum, *P. G.;* Zinkacetat, Essigsaures Zink, Essigsaures Zinkoxyd, *G.*

A process for this salt is no longer given in the U. S. P. In the U. S. process of 1870 zinc oxide—instead of the carbonate as in the Br. process—is acted upon directly by acetic acid. During the evaporation of the solution of the zinc acetate, a small portion of the acetic acid is lost; and hence the necessity of acidulating with a few drops of acetic acid before crystallizing. Though not economical, these processes have the recommendation of being easily performed, and of yielding a pure product. In relation to zinc acetate, see a paper by Ambrose Smith, *A. J. P.* (vii, 14).

Properties.—Zinc acetate is in "soft, white, six-sided, monoclinic plates, of a pearly luster, having a faintly acetous odor, and, in dilute solutions, an astringent, metallic taste. When exposed to the air, the salt gradually effloresces and loses some of its acid. One Gm. of Zinc Acetate dissolves in 2.3 mils of water and in 30 mils of alcohol at 25° C. (77° F.); also in 1.6 mils of boiling water and about 1 mil of boiling alcohol. Its aqueous solution is neutral or slightly acid to litmus. When heated, the salt is partially fused, losing water and acid. At a higher temperature it is decomposed, with evolution of inflammable and empyreumatic vapors, and leaving a residue consisting chiefly of zinc oxide. An aqueous solution of the salt (1 in 20) yields a white, gelatinous precipitate with potassium ferrocyanide T.S. and a white precipitate with ammonium sulphide T.S. Add 0.1 Gm. of the salt to 1 mil of sulphuric acid and 1 mil of alcohol and warm the mixture; ethyl acetate is formed, recognizable by its odor. Ammonium carbonate T.S., when added in small portions to an aqueous solution of the salt (1 in 20), produces at first a white precipitate, which redissolves completely upon the addition of an excess of the reagent. Ten mils of an aqueous solution of the salt (1 in 50), to which 1 mil of hydrochloric acid has been added, does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of the salt meets the requirements of the Test for arsenic (see Part III, Test No. 1).

"Assay.—Dissolve about 1 Gm. of Zinc Acetate, accurately weighed, in 100 mils of distilled water, render the solution slightly alkaline with ammonia water and warm it to 80° C. (176° F.). Completely precipitate the zinc as zinc sulphide by the addition of ammonium sulphide T.S. and warm the liquid on a water bath until the precipitate settles. Collect the latter on a filter, wash it with distilled water containing a few drops of ammonium sulphide T.S., then dissolve it in hot, dilute nitric acid (1 in 3), evaporate the solution to dryness in a tared platinum dish, ignite the residue and weigh it as zinc oxide. The amount of zinc oxide obtained corresponds to not less than 83.16 per cent. nor more than 87.32 per cent. of $Zn(C_2H_3O_2)_2$.

"Each gramme of Zinc Acetate corresponds to not less than 0.369 Gm. nor more than 0.387 Gm. of zinc oxide.

"Zinc Acetate may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

"Thin, translucent, colorless, crystalline plates, of a pearly lustre. Taste sharp and unpleasant. Soluble in 2.5 parts of *water.* Yields the *reactions* characteristic of zinc and of acetates. Yields no characteristic *reactions* for lead, copper, cadmium, iron, aluminium, calcium, magnesium, sodium, potassium, ammonium chlorides, or sulphates. *Arsenic limit* 5 parts per million. 0.5 gramme, tested as described under 'Zinci Sulphas,' yields a solution with not more than a faint pink coloration (limit of manganese)." *Br.*

The Br. Pharmacopœia (1898) gives in its formula for zinc acetate three molecules of water. Although the U. S. Pharmacopœia of 1880 adopted the formula giving to zinc acetate three molecules of water, Dibbit states that it contains but two molecules. Franchimont has confirmed this, and proved that both of these two molecules are lost at the temperature of 100° C. (212° F.). (*Ber. d. Chem. Ges.*, 1879, p. 11; *A. J. P.*, May, 1879.) The U. S. P. IX adopted this view, and recognize two molecules, and also the Br. Pharm. 1914. The precipitate thrown down by ammonia from the pure salt is entirely redissolved by an excess of the precipitant, but if ferric oxide be present it will be left undissolved. Zinc acetate is decomposed by the mineral acids, with the escape of acetous vapors.

Uses.—Zinc acetate is used almost exclusively as a local remedy. It is employed principally as an astringent collyrium in *ophthalmia,* and as an injection in *gonorrhea,* after the acute stage in these affections has passed. The strength of the solution usually prescribed is one or two grains to a fluidounce (0.065 or 0.13 Gm. to 30 mils) of distilled water.

ZINCI CARBONAS PRÆCIPITATUS. U. S. (Br.)

PRECIPITATED ZINC CARBONATE Zinc. Carb. Præc.

(zĭn'cī căr'bo-năs præ-cĭp-ĭ-tā'tŭs)

"Precipitated Zinc Carbonate is of somewhat variable chemical composition, corresponding to not less than 68 per cent. of ZnO (81.37)." *U. S.*

"Zinc Carbonate is a hydrated zinc carbonate, and may be obtained by the interaction of zinc sulphate and sodium carbonate." *Br.*

Zinci Carbonas, *Br.*, Zinc Carbonate; Zinci Carbonas Præcipitata, *U. S.* 1870; Carbonate of Zinc; Zincum Carbonicum, Carbonas Zincicus; Carbonate (sous-) de Zinc Hydraté, Hydrocarbonate de Zinc, *Fr. Cod.*; Carbonate de Zinc, *Fr.*; Zinkcarbonat, Kohlensaures Zinkoxyd, *G.*

Calamina, U. S. 1850, was dropped from the U. S. Pharmacopœia in 1860 on account of its impurities, and in the 1880 revision the formula for its substitute was also omitted. Calamine has again come into some use and is official in the N. F. IV as *Calamina Præparata* (*Lapis Calaminaris*). In the U. S. formula of 1870 a double decomposition takes place between zinc sulphate and sodium carbonate, resulting in the formation of sodium sulphate in solution, and basic zinc carbonate which is precipitated. Sodium carbonate is preferable to potassium carbonate for decomposing the sulphate, since the former gives rise to sodium sulphate, which is more easily washed away than the potassium sulphate derived from the latter. Boiling water is properly used in the process, in order to obtain a pulverulent precipitate, which is readily washed. If cold solutions are used, a gelatinous precipitate is formed, which is washed with difficulty. When a solution of zinc sulphate is precipitated by an excess of acid potassium carbonate, a normal zinc carbonate is obtained. With normal sodium carbonate, on the other hand, taken as a precipitant, a basic salt results.

Properties.—It is officially described as "an impalpable, white powder without odor or taste. It is permanent in the air. Precipitated Zinc Carbonate is insoluble in water or in alcohol; completely dissolved by diluted acids with copious effervescence; soluble in ammonia water and in ammonium carbonate T.S. When strongly heated, the salt loses water and carbon dioxide, and leaves a residue, which is yellow while hot, but becomes white on cooling. For making the following tests for identity, make a solution by adding 10 mils of diluted sulphuric acid and 10 mils of distilled water to 1.5 Gm. of Precipitated Zinc Carbonate, and, after effervescence has ceased, remove the undissolved excess by filtration. In portions of this solution a white gelatinous precipitate is produced by potassium ferrocyanide T.S., and a white precipitate by ammonium sulphide T.S. Another portion of this solution yields with ammonium carbonate T.S. a white precipitate, which redissolves completely in an excess of the reagent. Ten mils of a solution of the salt (1 in 50) made with the aid of a slight excess of hydrochloric acid does not respond to the Test for heavy metals (see Part III, Test No. 3). Mix 1 Gm. of the salt in a flask with 10 mils of boiling distilled water and add 2 drops of phenolphthalein T.S.; not more than 1 mil of tenth-normal hydrochloric acid V.S. is required to discharge any red color that may be produced (*alkali*).

Assay.—"Digest about 2 Gm. of Precipitated Zinc Carbonate, accurately weighed, with 50 mils of normal sulphuric acid V.S. until solution is complete; then titrate the excess of sulphuric acid with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 68 per cent. of ZnO.

"Each mil of normal sulphuric acid V.S. used corresponds to 0.040685 Gm. of ZnO. Each gramme of Precipitated Zinc Carbonate corresponds to not less than 16.8 mils of normal sulphuric acid V.S." *U. S.*

"White amorphous powder. No odor or taste. Insoluble in *water;* entirely soluble in *diluted nitric acid.* Yields the *reactions* characteristic of zinc and of carbonates. Yields no characteristic *reactions* for lead, copper, cadmium, iron, aluminium, calcium, magnesium, sodium, potassium, or ammonium, and not more than the slightest *reactions* for chlorides or sulphates. *Arsenic limit* 10 parts per million. 0.2 gramme, dissolved in *diluted sulphuric acid,* and tested as described under 'Zinci Sulphas,' yields a solution with not more than a faint pink coloration (limit of manganese)." *Br.*

If adulterated with chalk it will be only partly soluble in oxalic acid solution. Precipitated zinc carbonate is often sold under the incorrect name of *flowers of zinc,* a name which properly belongs only to the oxide, as obtained by combustion. When obtained from solutions of zinc sulphate and sodium carbonate it has a variable composition, as different hydrated basic carbonates are formed, according to the temperature used, etc.; the higher the temperature and the larger the quantity of water used, the more basic the carbonate becomes.

Uses.—This was introduced as a substitute for prepared calamine, but, as one of the important virtues of the native product was its pinkish color, the substitution is not a step in advance. It is used locally for much the same purpose as zinc oxide.

ZINCI CHLORIDUM. U. S., Br.

ZINC CHLORIDE Zinc. Chlor.

(zĭn'cī ȼhlō'rı̣-dŭm)

"It contains not less than 95 per cent. of $ZnCl_2$ (136.29). Preserve it in small, glass-stoppered bottles." *U. S.* "Zinc Chloride, $ZnCl_2$, may be obtained by the interaction of hydrochloric acid and zinc." *Br.*

Butter of Zinc; Chloruretum Zincicum; Chlorure de Zinc, *Fr. Cod.*; Zincum Chloratum, *P. G.*; Zinkchlorid, Chlorzink, *G.*; Cloruro zincico, *Sp.*

The British Pharmacopœia does not give a detailed process for making this salt; that of the Br. Pharm. 1885 follows:

"Take of Granulated Zinc *one pound* [avoirdupois]; Hydrochloric Acid *forty-four fluid ounces* [Imperial measure]; Solution of Chlorine *a sufficiency;* Carbonate of Zinc *half an ounce* [av.], or *a sufficiency;* Distilled Water *one pint* [Imp. meas.]. Put the Zinc into a

porcelain basin, add by degrees the Hydrochloric Acid previously mixed with the water, and aid the action by gently warming it on a sand-bath until gas is no longer evolved. Boil for half an hour, supplying the water lost by evaporation, and allow it to stand on a cool part of a sand-bath for twenty-four hours, stirring frequently. Test a few drops of the resulting liquid for iron or lead by adding excess of ammonia and then sulphydrate of ammonium, when a black precipitate will be produced if iron or lead be present.

In the latter case filter the remainder of the product into a gallon bottle, and pour in the solution of chlorine by degrees, with frequent agitation, until the fluid acquires a permanent odor of chlorine. Add the carbonate of zinc, in small quantities at a time, and with renewed agitation, until a brown sediment appears, and the whole of the iron or lead is thus precipitated. Filter through paper into a porcelain basin, and evaporate until a portion of the liquid, withdrawn on the end of a glass rod and cooled, forms an opaque white solid. Pour it out now into proper moulds, and when the salt has solidified, but before it has cooled, place it in closely-stoppered bottles. If no iron or lead be present, filter and evaporate, etc., at once." *Br.* 1885.

In the U. S. process of 1870 the zinc chloride is obtained by evaporating the previously formed solution. The British first prepares the zinc chloride in solution, and in order to get rid of the iron uses chlorine, which combines with the iron to form ferric chloride, and, zinc carbonate being added, the zinc combines with the chlorine to increase the product of zinc chloride, while ferric oxide is deposited and carbon dioxide is set free. As this preparation is used chiefly as a caustic, it is melted and cast into moulds as the last step in the Br. process. Rhighini prepares this chloride by double decomposition between solutions of barium chloride and zinc sulphate. Barium sulphate is precipitated, and zinc chloride remains in solution, from which it is obtained in white flaky crystals by due evaporation. As zinc sulphate is obtainable in considerable quantities as a cheap by-product in the washing of pyrites and other sulphide ores containing zinc, as well as from the so-called "pickle waste" solutions from brass foundries, this is sometimes used as a commercial source for the manufacture of zinc chloride. Finely ground salt is added to the zinc sulphate solution, and the mixture chilled, when the sodium sulphate produced by the reaction crystallizes out, leaving zinc chloride in solution.

Properties.—It is "a white, or nearly white, granular powder, or in porcelain-like masses, or moulded into pencils; odorless; *it is so intensely caustic as to make tasting dangerous,* unless the salt is dissolved in a large quantity of water. It is very deliquescent. One Gm. of Zinc Chloride dissolves in 0.25 mil of water, and in about 1.3 mils of alcohol at 25° C. (77° F.); freely soluble in glycerin. An aqueous solution of the salt (1 in 10) is acid to litmus. When heated to 115° C. (239° F.), Zinc Chloride fuses to a clear liquid. At a higher temperature it is partly volatilized in dense, white fumes, and partly decomposed, leaving a residue of zinc oxide. An aqueous solution of the salt (1 in 20) yields a white, gelatinous precipitate, with potassium ferrocyanide T.S. and a white precipitate with ammonium sulphide T.S. With silver nitrate T.S. an aqueous solution of the salt (1 in 20) yields a white, curdy precipitate insoluble in nitric acid but readily soluble in ammonia water. Mix an aqueous solution of the salt (1 in 20) with an equal volume of alcohol; a single drop of hydrochloric acid is sufficient to render 10 mils of the mixture perfectly clear (*oxychloride*). Completely precipitate the zinc from a solution of 1 Gm. of the salt in 50 mils of distilled water, by means of ammonium sulphide, filter, evaporate the filtrate, and gently ignite; not more than 0.004 Gm. of residue remains. Ten mils of an aqueous solution of the salt (1 in 50) to which 1 mil of diluted hydrochloric acid has been added does not respond to the Test for heavy metals (see Part III, Test No. 3). Add ammonium carbonate T.S., in small portions, to an aqueous solution of Zinc Chloride (1 in 20); the precipitate produced is white, and redissolves completely in an excess of the reagent. Add sufficient potassium hydroxide T.S. to 5 mils of an aqueous solution of the salt (1 in 10) to redissolve the precipitate which first forms, and then warm the solution; the odor of ammonia is not perceptible (*ammonium salts*). Ten mils of an aqueous solution of the salt (1 in 20), acidulated with 1 mil of hydrochloric acid, is not rendered more than slightly turbid by the addition of 1 mil of barium chloride T.S. (*sulphate*).

"**Assay.**—Proceed as directed under the Assay for chlorides (see Part III, Test No. 5), using about 0.3 Gm. of Zinc Chloride, accurately weighed, in a stoppered weighing-bottle. It shows not less than 95 per cent. of $ZnCl_2$.

"Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.0068145 Gm. of $ZnCl_2$. Each gramme of Zinc Chloride corresponds to not less than 139.4 mils of tenth-normal silver nitrate V.S." *U. S.*

"Colorless opaque rods or tablets, or in granules; very deliquescent and caustic. Almost entirely soluble in *water,* in *alcohol* (90 per cent.), and in *ether.* Yields the *reactions* characteristic of zinc and of chlorides. Yields no characteristic *reactions* for lead, copper, cadmium, iron, aluminium, calcium, magnesium, sodium, potassium, ammonium, or sulphates. *Arsenic limit* 5 parts per million. 0.25 gramme, tested as described under 'Zinci Sulphas,' yields a solution with not more than a faint pink coloration (limit of manganese)." *Br.*

When pure, it is wholly soluble in water, alcohol, and ether, but as prepared by the U. S. formula it contains some oxychloride,

which is left undissolved by water. According to Lassaigne, commercial zinc chloride sometimes contains as much as 12 per cent. of zinc arsenate, which, being insoluble in solution of zinc chloride, will be left undissolved when the chloride is treated with water. By filtration, therefore, it may be entirely separated. It yields with ammonium and potassium hydroxide a white precipitate, soluble in those reagents when added in excess. It tends to form basic insoluble compounds, the so-called *oxychlorides,* of which Sorel's mass, $Zn\begin{cases}OH\\Cl\end{cases}$, is an example.

These are used for cements and as a filling for teeth. The potassium and sodium carbonates also throw down white precipitates, which are not dissolved by an excess of the precipitants. Zinc chloride has a strong tendency to combine with organic bases, forming crystallizable compounds, as with strychnine, morphine, quinine, cinchonine, etc., in this respect resembling certain other metallic chlorides, as platinum, palladium, gold, and mercury chlorides. (*J. P. C.*, 4e sér., iii, 56.) When exposed to heat, zinc chloride first melts and then sublimes. It has been obtained in small deliquescent octahedrons of the formula $ZnCl_2 + H_2O$, by evaporating its hydrochloric acid solution to a syrup, and then adding a little concentrated hydrochloric acid. It consists of one atom of zinc and two of chlorine.

Uses.—Zinc chloride has been used internally in *scrofula, epilepsy, chorea,* and other nervous diseases, but is of little or no value. Its chief use has been as an escharotic in *cancerous affections.* As a caustic it has the advantage of not causing constitutional disorder from absorption. Canquoin prepared zinc chloride as an escharotic by thoroughly and quickly mixing it with wheat flour and water into a paste of four different strengths, containing severally an ounce of the chloride incorporated with two, three, four, and five ounces of flour, fifteen drops of water being added for every ounce of flour, or sufficient to form the paste. According to the French Codex, *Caustique au Chlorure de Zinc* (*Canquoin's Paste*) is prepared by dissolving 8 parts of zinc chloride in 1 part of cold water and incorporating a mixture of 6 parts of flour with 2 parts of zinc oxide.

P. Carles states that the official paste is too hygroscopic; he triturates in a mortar 10 grammes of fused zinc chloride with 2 grammes of 60 per cent. alcohol, and incorporates, with constant trituration, 15 grammes of wheat flour. This mass may be formed into cylinders of suitable size, and when once dry is but little affected by atmospheric humidity. (*L'Union Pharm.*)

It is applied in cakes from a twelfth to a third of an inch in thickness, and produces an eschar more or less deep (from a line to an inch and a half), according to the thickness and strength of the paste, the length of the application, and the nature of the part acted on. Canquoin's strongest paste is applied to lardaceous and fibro-cartilaginous structures; the second, to *carcinomatous tumors,* and very painful *cancers* which have not much thickness; and the third, to *cancerous affections* in persons who have a dread of the use of the knife. These preparations, applied to the skin denuded of its cuticle by means of a blister, excite in a few minutes a sensation of heat, and afterwards violent burning pain. The eschar, which is white, thick, and very hard, falls off, with the aid of an emollient poultice, between the eighth and twelfth days. In all cases the caustic is to be reapplied, after the falling off of the eschar, until the whole morbid structure is destroyed. When the skin is unbroken, it is usual to destroy not merely the cuticle, but the true skin also, by means of acid mercuric nitrate, to the extent to which the chloride is desired to operate. This is applied spread on lint, and the dressing is covered with a portion of cotton wadding, to absorb any discharge and to preserve a uniform temperature. The surrounding skin should be protected from the caustic by a thickly-spread dressing of simple cerate.

Felix's Caustic Paste (*L. L.*, vol. ii, 1887) is made according to the following formula: Starch, 37 grammes; Wheat Flour, 112 grammes; Mercuric Chloride, 1 gramme; Dry Zinc Chloride, 110 grammes; pure Iodol, 10 grammes; Croton Chloral, 10 grammes; Camphor Bromide 10 grammes; Crystallized Carbolic Acid, 10 grammes; Distilled Water, sufficient to form a stiff homogeneous paste. The hand should be wetted when applying it. The paste is allowed to remain on from six to twenty-four hours, according to the amount of eschar it is desired to form.

Instead of flour, Alex. Ure of Glasgow, mixes the chloride with pure anhydrous calcium sulphate in impalpable powder. He states that this has the advantages of furnishing a porous medium from which the escharotic gradually exudes into the morbid structure, and of forming afterwards, by acquiring a firmer consistence, an impervious case for the eschar. Cock of Guy's Hospital, has imitated this mode of preparing the chloride, so as to form a caustic which may be limited in its action and does not run. It may be prepared as a caustic seton by thickly covering a waxed cotton wick with Canquoin's caustic paste, and then rolling it out in the form of a cylinder, according to the plan of Ancrenis of Lyons. A thread is wound spirally around the cylinder to give it firmness.

In overdoses, zinc chloride acts as a corrosive poison, producing burning pain in the gullet and stomach, nausea and vomiting, cold sweats, depression of the pulse, and cramps of the legs. The antidotes are weak alkalies, or their carbonates, and, if these are not immediately at hand, soap. Zinc chloride is not used internally.

Zinc chloride is a useful disinfectant, being inexpensive and comparatively non-poisonous.

ZINCI OLEOSTEARAS. Br.

ZINC OLEOSTEARATE

(zĭn'cī ō-lē-ō-stē'ą-răs)

"Hard Soap, 200 *grammes;* Curd Soap, 100 *grammes;* Zinc Sulphate, 100 *grammes;* Distilled Water, *a sufficient quantity.* Dissolve the Soaps in one thousand five hundred millilitres of the Distilled Water by the aid of heat; add to the solution the Zinc Sulphate previously dissolved in two hundred millilitres of the Distilled Water. Collect the precipitate, wash it with Distilled Water until the washings are free from sulphates, dry it, and reduce it to a fine powder." *Br.*

It is officially described as "a white amorphous powder. Odor faint, resembling that of fat. Insoluble in *water,* in *alcohol* (90 per cent.), and in *ether.* Ash about 13 per cent. The ash, dissolved in *hydrochloric acid* and the solution neutralised, yields the *reactions* characteristic of zinc. When 0.5 gramme is heated with 0.5 millilitre of *hydrochloric acid* diluted with 0.5 millilitre of *water,* a mixture of fatty acids is liberated and floats on the surface of the aqueous liquid; this aqueous liquid, filtered, neutralised with *solution of ammonia,* treated with excess of *solution of ammonium hydrosulphide,* again filtered, evaporated to dryness, and the product gently ignited, leaves no appreciable residue (absence of fixed alkalies and of alkaline earths)." *Br.*

Uses.—Zinc oleostearate is used for the same purposes as zinc stearate.

ZINCI OXIDUM. U. S., Br.

ZINC OXIDE Zinc. Oxid.

(zĭn'cī ŏx'ĭ-dŭm)

"It contains, when freshly ignited, not less than 99 per cent. of ZnO (81.37)." *U. S.*
"Zinc Oxide, ZnO, may be obtained from metallic zinc by combustion in air." *Br.*

Flores Zinci; Oxydum Zincicum; Oxyde Zinc par voie sèche, Fleurs de Zinc, *Fr. Cod.;* Zincum Oxydatum, *P. G.;* Philosophenwolle, Zinkblumen, Zinkoxyd, *G.;* Oxido zincico, *Sp.*

Preparation.—The British Pharm., 1885, and the U. S. P., 1870, prepared the zinc oxide from the carbonate already formed. By referring to the article on Precipitated Zinc Carbonate, it will be found that it is obtained in the process from zinc sulphate, by the decomposing influence of sodium carbonate. Other methods of obtaining the zinc carbonate are by the mutual decomposition of the sodium chloride and carbonate and the ammonium sulphate and carbonate, but the former official plan is preferred. Lefort found it to furnish a carbonate which is washed with facility and is convertible by calcination into a pure oxide, readily reduced to an impalpable and very light powder. (*J. P. C.,* 3e sér., xi, 329.) It is, besides, more economical. The zinc carbonate, in whatever way obtained, is exposed to heat to drive off the carbon dioxide and water, in order to obtain the oxide. According to Mohr, a full red heat is not necessary, a temperature between 280° and 300° C. (536° and 572° F.) being sufficient. It is probable that an unnecessarily high heat injures the oxide as a therapeutic agent.

"Take of Precipitated Carbonate of Zinc *twelve troyounces.* Expose it, in a shallow vessel, to a low red heat until the water and carbonic acid are wholly expelled." *U. S.,* 1870.

Zinc oxide may be obtained by the combustion of the metal. Zinc melts at 433° C. (811.4° F.), and immediately becomes covered with a film of gray oxide. When the temperature reaches nearly to redness, it takes fire and burns with an intense white light, generating the oxide in the form of very light and white flocculi, resembling carded wool, which quickly fill the crucible, and are in part driven into the atmosphere by the current of air. One form of apparatus for the production of the oxide, as practically carried on, consists of a large muffle, heated to redness in a suitable furnace, and supplied with zinc from time to time as the combustion proceeds. The necessary draught of air is conveyed from the muffle by a tube passing through the top of the furnace and terminating in a vessel of water, in which the portion of oxide carried up by the current is retained. The resulting oxide is freed from particles of metallic zinc by being passed through a sieve. Zinc oxide has been very largely produced from calamine by the so-called "furnace and bag" process, at Bethlehem, Pa., by the Lehigh Zinc Company. The process is as follows: The ore is first ground fine by a stone crusher, and then carefully mixed with coal known as "buckwheat," next in grade to "pea." It is then transferred to the furnaces, of which there are fifty-four, with 1390 feet of grate-surface. Within these the mixed coal and ore are reduced by the direct action of heat and the cold blast upon a furnace bed having a multiplicity of small holes, each producing the reducing flame of the blow-pipe. The zinc oxide rises, and passes through a huge combustion flue to a large circular tower, 50 feet high, in which the oxide and ashes separate. The ashes being heavier than the oxide, the velocity of the fans which impel the product forward lifts the oxide to the top, and the ashes drop to the bottom. The oxide is forced onward through a cooling-room, size 80 by 40 feet, and heated to from 204.8° to 371.1° C. (400.5°–700° F.). Thence the oxide is blown through large flues into the "bag" room. This is in a large building, devoid of furniture, except bags of muslin, 45 feet long, in which the oxide is deposited. It is now very white, and, after being kiln-dried and bolted, is by heavy pressure reduced in bulk and barrelled, ready for shipment. The production direct from ore is available only when the latter is free from cadmium, as otherwise the zinc oxide would be contaminated with cadmium oxide.

Properties.—The official zinc oxide is described in the U. S. Pharmacopœia as "a very fine, amorphous, white or yellowish-white pow-

der, free from gritty particles, without odor or taste; it gradually absorbs carbon dioxide from the air. Zinc Oxide is insoluble in water or in alcohol; it dissolves without effervescence in dilute acids, also in ammonia water and in ammonium carbonate T.S. When strongly heated, it assumes a yellow color which disappears on cooling. For making the following tests for identity, digest 1.3 Gm. of Zinc Oxide, with occasional agitation, in a mixture of 10 mils of diluted hydrochloric acid and 10 mils of distilled water until the solution is saturated, then remove the undissolved Zinc Oxide by filtration. In portions of this filtrate a white, gelatinous precipitate is produced by potassium ferrocyanide T.S., and a white precipitate by ammonium sulphide T.S. Ten mils of a solution of Zinc Oxide (1 in 50), made with the aid of a slight excess of hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3). Mix 1 Gm. of Zinc Oxide in a flask with 10 mils of boiling distilled water and add 2 drops of phenolphthalein T.S.; not more than 1 mil of tenth-normal hydrochloric acid V.S. is required to discharge any red color that may be produced (*alkali*).

Assay.—"Digest about 1.5 Gm. of freshly ignited Zinc Oxide, accurately weighed, with 50 mils of normal sulphuric acid V.S. until solution is complete. Then titrate the excess of sulphuric acid with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 99 per cent. of ZnO.

"Each mil of normal sulphuric acid V.S. used corresponds to 0.040685 Gm. of ZnO. Each gramme of freshly ignited Zinc Oxide corresponds to not less than 24.3 mils of normal sulphuric acid V.S." *U. S.*

"A soft, white or nearly white, amorphous powder, becoming pale yellow when heated. No odor or taste. Yields the *reactions* characteristic of zinc. Soluble in *diluted hydrochloric acid* without the separation of any black particles. Yields no characteristic *reactions* for copper, cadmium, iron, aluminium, calcium, magnesium, sodium, potassium, ammonium, and only slight *reactions* for lead and carbonates. *Arsenic limit* 10 parts per million. 0.2 gramme, dissolved in *diluted sulphuric acid*, and tested as described under 'Zinci Sulphas,' yields a solution with not more than a faint pink coloration (limit of manganese)." *Br.*

As obtained by combustion, it is perfectly white. It dissolves in solution of potassium and sodium hydroxides, but not in their carbonates. Being anhydrous, it is insoluble in ammonia, but the impure oxide found in commerce, being generally hydrated, is soluble in that alkali. At a low white heat it fuses, and at full whiteness sublimes. When prepared by combustion it was formerly called *pompholix, nihil album, lana philosophica*, and *flowers of zinc*. Prepared by the old official process—namely, by precipitating zinc sulphate with ammonia—it contains the subsulphate, which may be detected by dissolving the oxide in nitric acid and adding barium nitrate T. S. which produces a white precipitate if a sulphate is present. Sometimes it is obtained by precipitating zinc chloride with ammonia, in which case the oxide contains subchloride, easily detected by silver nitrate. If it contains white lead or chalk, it will not be entirely soluble in diluted sulphuric acid, but an insoluble lead or calcium sulphate will be left. If iron be present, brownish-red flocks of ferric oxide will remain undissolved when the hydrochloric acid solution of the zinc oxide is treated with ammonia in excess.

The powder sold in commerce as zinc oxide is often very impure. Sometimes the carbonate is substituted for it, showing that the exposure to a red heat has been omitted. In this case the preparation will effervesce with acids. Some samples contain a large proportion of subsulphate, showing that the discarded but productive process of precipitating the solution of zinc sulphate by ammonia has been employed. Again, other samples contain oxychloride, which can be detected by adding silver nitrate T. S. to the nitric acid solution of the oxide. These impure oxides are pointed out by Redwood, of London, as occurring in the English market, and no doubt are sold in the United States. A sample of commercial zinc oxide is noticed in *N. R.*, Aug., 1878, which proved to be powdered gypsum. Unfortunately, a white oxide is preferred by purchasers, though whiteness is generally a sign of impurity; the yellowish-white official oxide should be exclusively used by pharmacists. There has been reported in Swiss commerce an unusual form of zinc oxide, which is in light loose powder that produces a lumpy ointment and which, when rubbed with two-thirds its weight of olive oil, does not form a paste as do the ordinary oxides, but remains as a dry powder.

Uses.—Zinc oxide has been used as an antispasmodic in *chorea, epilepsy,* and *whooping-cough,* but is probably of little value as a systemic remedy. It is also sometimes employed for its astringent and sedative properties in *diarrhea.* Its most important use, however, is as an application to excoriated surfaces and in various *skin diseases.* It owes its popularity to a combination of four qualities: it is non-toxic, protective, mildly astringent and probably antiseptic. It may be applied as a dusting powder—usually in conjunction with talcum—suspended in aqueous mixtures or in the form of ointment. (See *Unguentum Zinci Oxidi.*) It has also been used in *gonorrhea.* As a cosmetic it has the great advantage over the preparations of lead of not being poisonous.

Zinc oxide, prepared by combustion, called commercial zinc oxide, is extensively used in painting as a substitute for white lead, over which it has the advantage of not being discolored by hydrogen sulphide. It is stated that it has greater covering power as a color than white lead, 10 parts being equal to 13 of white lead. It is, however, dearer, so that the pure oxide has not replaced white lead. This form of oxide, even though pure, is often unsuited for medical uses, because of lack of

smoothness and the presence of gritty particles. There is an English preparation known as *Griffith's zinc white*, or *lithophone*, made by precipitating zinc sulphate by barium sulphide; it is, therefore, a mixture of zinc sulphide and barium sulphate. If this be roasted in a current of superheated steam the zinc sulphide will be converted into zinc oxide. This process has been patented in Germany by Meissner. (Wagner's *Chem. Technol.*, 11th ed., p. 159.)

Dose, two to five grains (0.13–0.32 Gm.), preferably in pill form.

Off. Prep.—Unguentum Zinci Oxidi, *U. S.* (*Br.*); Glycerogelatinum Zinci Durum, *N. F.*; Glycerogelatinum Zinci Molle, *N. F.*; Mulla Zinci, *N. F.*; Pasta Resorcinolis Fortis, *N. F.*; Pasta Resorcinolis Mitis, *N. F.*; Pasta Zinci, *N. F.*; Pasta Zinci Mollis, *N. F.*; Pasta Zinci Sulphurata, *N. F.*; Unguentum Picis Compositum, *N. F.*; Unguentum Resorcinolis Compositum, *N. F.*

ZINCI PHENOLSULPHONAS. U. S.

ZINC PHENOLSULPHONATE Zinc. Phenolsulph. [Zinc Sulphocarbolate]

(zĭn'cī phē-nŏl-sŭl'phŏ-năs)

"It contains not less than 73.7 per cent. nor more than 77.4 per cent. of anhydrous zinc phenolsulphonate, corresponding to not less than 99.5 per cent. of the crystallized salt [$(C_6H_5O.SO_3)_2Zn + 8H_2O = 555.72$]. Preserve it in small, well-closed containers." *U. S.*

Zinci Sulphocarbolas, *Br.* 1898; Zincum Sulphophenolicum; Zinc Paraphenolsulphonate; Sulphophénate de Zinc, *Fr.*; Phenolsulfosaures Zink, Sulfokarbolsaures Zink, *G.*

Properties.—It is officially described as in "colorless, transparent, rhombic prisms or tabular crystals or in granular form; odorless, and having an astringent, metallic taste. When exposed to the air the salt effloresces, and upon exposure to light and air may become slightly pink. One Gm. of Zinc Phenolsulphonate dissolves in 1.6 mils of water, and in 1.8 mils of alcohol at 25° C. (77° F.); also in 0.4 mil of boiling water. Its aqueous solution (1 in 10) is acid to litmus. When heated to 125° C. (257° F.), the salt loses all of its water of crystallization. At a higher temperature it chars, emitting inflammable vapors having the odor of phenol, and finally leaves an incombustible residue. An aqueous solution of the salt (1 in 20) yields a white, gelatinous precipitate with potassium ferrocyanide T.S., and a white precipitate with ammonium sulphide T.S. Ammonium carbonate T.S., when added in small portions to an aqueous solution of the salt (1 in 20), produces a white precipitate which redissolves completely upon the addition of an excess of the reagent. A dilute solution of the salt (1 in 100) is colored pale violet by ferric chloride T.S. The addition of a few drops of barium chloride T.S. to 10 mils of an aqueous solution of the salt (1 in 20), previously acidulated with 3 drops of hydrochloric acid, produces not more than a slight turbidity (*sulphate*). Ten mils of an aqueous solution of the salt (1 in 50), to which 1 mil of diluted hydrochloric acid has been added, does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of the salt meets the requirements of the Test for arsenic (see Part III, Test No. 1).

Assay.—"Dissolve about 1 Gm. of Zinc Phenolsulphonate, accurately weighed, in 100 mils of distilled water and proceed as directed in the assay under *Zinci Acetas*. The amount of zinc oxide obtained corresponds to not less than 73.7 per cent. nor more than 77.4 per cent. of $Zn(C_6H_5O_4S_2)_2$.

"Each gramme of Zinc Phenolsulphonate corresponds to not less than 0.146 Gm. nor more than 0.153 Gm. of ZnO.

"Zinc Phenolsulphonate may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

Uses.—Zinc phenolsulphonate has been employed as an antiseptic and astringent application to indolent or foul *ulcers*, and in subacute inflammations of the mucous membrane. The solutions used may be a little stronger than those of zinc sulphate employed for similar purposes. It has also been used as an intestinal antiseptic.

Dose, one to three grains (0.065–0.2 Gm.).

ZINCI STEARAS. U. S.

ZINC STEARATE Zinc. Stear.

(zĭn'cī stē'ăr-ăs)

"A compound of zinc with stearic acid and small, but variable proportions of palmitic acid, containing an amount of zinc corresponding to not less than 13 per cent. nor more than 15.5 per cent. of ZnO." *U. S.*

Stéarate de Zinc, *Fr.*; Zinkstearat, Stearinsaures Zinkoxyd, Talgsaures Zinkoxyd, *G.*

(See *Zinci Oleostearas*, Br., page 1211.)

Zinc stearate differs from the oleate of zinc of the U. S. P., 1890; the latter was of a soft ointment-like solid. It may be made by mixing a solution of sodium stearate with one of zinc acetate, at a temperature of 50° C. (122° F.), washing, and then drying the precipitate. For a process for zinc oleostearate by F. E. Niece in which he uses oleic and stearic acids and solution of zinc acetate, see *Proc. Penna. Pharm. Assoc.*, 1902, 135.

Properties.—It is officially described as "a fine, white, bulky powder, tasteless and having a faint, characteristic odor. Zinc Stearate is insoluble in water, alcohol or ether. The salt is neutral to moistened litmus paper. When heated, the salt fuses. At a higher temperature it is decomposed, giving off inflammable vapors and the odor of burning fat, and finally leaves a residue consisting chiefly of zinc oxide. Heat 1 Gm. of Zinc Stearate with a mixture of 25 mils of distilled water and 5 mils of hydrochloric acid; stearic acid is liberated and floats as an oily layer on the surface of the liquid. Boil 1 Gm. of Zinc Stearate with 25 mils of distilled water and 5 mils of hydrochloric acid, filter while hot and wash the filter with 25 mils of

hot water. Render the filtrate alkaline with ammonia water, warm it to 80° C. (176° F.), and add ammonium sulphide T.S. in excess, filter, evaporate the filtrate to dryness, and ignite the residue. Dissolve this residue in 10 mils of hot distilled water, filter, again evaporate, ignite, and weigh; not more than 1 per cent. of residue remains (*alkalies and alkali earths*). The insoluble residue of fatty acids obtained in the preceding test, when well washed, melts at a temperature not below 56° C. (132.8° F.).

Assay.—"Boil about 1 Gm. of Zinc Stearate, accurately weighed, with 50 mils of tenth-normal sulphuric acid V.S. for ten minutes and cool. Then titrate the excess of sulphuric acid with tenth-normal potassium hydroxide V.S., using methyl orange T.S. as indicator. It shows not less than 13 per cent. nor more than 15.5 per cent. of ZnO.

"Each mil of tenth-normal sulphuric acid V.S. used corresponds to 0.0040685 Gm. of ZnO. Each gramme of Zinc Stearate corresponds to not less than 32 mils nor more than 38.1 mils of tenth-normal sulphuric acid V.S." *U. S.*

Uses.—Zinc stearate is employed in *eczema, acne* and other cutaneous diseases, in the form of powder, or made into an ointment.

Off. Prep.—Unguentum Zinci Stearatis, *N. F.*

ZINCI SULPHAS. U. S., Br.

ZINC SULPHATE Zinc. Sulph.

(zĭn'cī sŭl'phăs)

"It contains not less than 55.86 per cent. nor more than 58.65 per cent. of anhydrous zinc sulphate, corresponding to not less than 99.5 per cent. of the crystallized salt [$ZnSO_4 + 7H_2O = 287.55$]. Preserve it in well-closed containers." *U. S.* "Zinc Sulphate, $ZnSO_4$, $7H_2O$, may be obtained by the interaction of diluted sulphuric acid and zinc." *Br.*

Sulfas Zincicus, Vitriolum Album; White Vitriol; Sulfate de Zinc officinal, *Fr. Cod.;* Zincum Sulfuricum, *P. G.;* Zinksulfat, Schwefelsaures Zinkoxyd, Weisser Vitriol, Galitzenstein, *G.;* Solfato di zinco, *It.;* Sulfato zincico, *Sp.*

The Pharmacopœias no longer give detailed processes for preparing this salt.

Strong sulphuric acid is but slightly acted upon by zinc, some hydrogen sulphide being evolved by the reduction of the acid; but when it is *diluted,* the acid is instantly decomposed, and, while hydrogen escapes with rapid effervescence, it is replaced by the zinc with the production of zinc sulphate. From this it will be perceived that *hydrogen* is a collateral product of the process. The proportion of the zinc to the strong acid in the process is as 4 to 5.53. The molecular weights give the ratio of 4 to 6 almost exactly—which indicates that the metal is somewhat in excess. If the materials are mixed at once, without any precaution, the effervescence of hydrogen is apt to be excessive, and to cause the overflowing of the liquid. This may be avoided by commencing the solution of zinc with a very dilute acid, which, as the action slackens, is made by degrees stronger and stronger by the addition, at intervals, of small portions of fresh acid. As the zinc of commerce generally contains iron, this would contaminate the product, unless precautions were taken to prevent it. Hence the addition of chlorine, which reacts with ferrous sulphate to form ferric sulphate and ferric chloride, which, upon the addition of zinc carbonate, yield sulphuric acid and chlorine to the zinc, ferric oxide being deposited and carbon dioxide set free. The former is separated by filtration, the latter escapes during the evaporation, the additional zinc sulphate crystallizes with that first formed, and the zinc chloride remains in the mother waters.

Preparation on the Large Scale.—Impure zinc sulphate, as it occurs in commerce, is called *white vitriol.* It is manufactured by roasting *blende* (native zinc sulphide) in a reverberatory furnace. This mineral, besides zinc sulphide, contains small quantities of iron, copper, and lead sulphides, and by roasting is converted, in consequence of the oxidation of its constituents, into zinc sulphate, mixed with iron, copper, and lead sulphate. The roasted matter is then lixiviated, and the solution obtained, after having been allowed to settle, is concentrated by evaporation, so that, on cooling, it may concrete into a white crystalline mass. In this state it always contains ferrous sulphate, and sometimes a small proportion of copper sulphate. It may be purified from these metals by dissolving it in water and boiling the solution with zinc oxide, which converts the iron and copper sulphates into zinc sulphate and the respective hydroxides of iron and copper. The purified solution is then decanted or filtered, and, after due evaporation, allowed to crystallize. It has generally been proposed to purify the white vitriol of commerce by digesting its solution with metallic zinc, under the impression that this is capable of precipitating all the foreign metals; but, according to Berzelius, though it will precipitate copper readily, it has no action on iron. F. Stolba recommends a process which has been used successfully for the purification of zinc sulphate by the use of zinc carbonate and zinc permanganate.

Properties.—Zinc sulphate is in "colorless, transparent, rhombic crystals, or as a granular, crystalline powder, without odor, and having an astringent, metallic taste. It is efflorescent in dry air. One Gm. of Zinc Sulphate dissolves in 0.6 mil of water, and in 2.5 mils of glycerin at 25° C. (77° F.); insoluble in alcohol. Its aqueous solution (1 in 10) is acid to litmus. When rapidly heated, the salt melts. When strongly ignited it is partly decomposed, losing both water and sulphuric acid. An aqueous solution of the salt (1 in 20) yields a white, gelatinous precipitate with potassium ferrocyanide T.S., and a white precipitate with ammonium sulphide T.S. and with barium chloride T.S. An aqueous solution of the salt (1 in 10) yields with ammonium carbonate T.S. a white precipitate, which redissolves completely in an excess of the reagent. Ten mils of an aqueous solution of Zinc Sulphate (1 in 50), after being

acidulated with 1 mil of diluted hydrochloric acid, does not respond to the Test for heavy metals (see Part III, Test No. 3). An aqueous solution of the salt meets the requirements of the Test for arsenic (see Part III, Test No. 1). An aqueous solution of Zinc Sulphate (1 in 20) is not colored pink by methyl orange T.S. (*free acid*). Add 2 drops of nitric acid to a solution of 1 Gm. of Zinc Sulphate in 20 mils of distilled water, follow with 0.2 mil of tenth-normal silver nitrate V.S. and filter the mixture. The subsequent addition of a few drops of tenth-normal silver nitrate V.S. to the filtrate produces no cloudiness or opalescence (*chloride*). Dissolve 1 Gm. of Zinc Sulphate in 50 mils of distilled water, precipitate the zinc completely with ammonium sulphide T.S., filter, evaporate the filtrate to dryness, and ignite; not more than 0.5 per cent. of residue remains (*alkali and alkali earth salts*).

Assay.—"Dissolve about 1 Gm. of Zinc Sulphate, accurately weighed, in 100 mils of distilled water and estimate the salt as zinc oxide by the method given in the assay under *Zinci Acetas*. The salt yields an amount of zinc oxide corresponding to not less than 55.86 per cent. nor more than 58.65 per cent. of $ZnSO_4$.

"Each gramme of Zinc Sulphate corresponds to not less than 0.2815 Gm. nor more than 0.2955 Gm. of ZnO. Zinc Sulphate may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

"Colorless, transparent, prismatic crystals. Taste metallic, styptic. Soluble in less than 1 part of *water*. Yields the *reactions* characteristic of zinc and of sulphates. Yields no characteristic *reactions* for lead, copper, cadmium, aluminium, calcium, magnesium, sodium, potassium, ammonium, or acetates, and not more than the slightest *reactions* for iron or chlorides. *Arsenic limit* 5 parts per million. When 0.5 gramme is dissolved in *water*, excess of *solution of ammonia* added, and the mixture allowed to stand, any precipitate that is obtained being filtered off and dissolved in *diluted nitric acid*, then this acid solution, diluted with *water* to about 15 millilitres and heated to boiling, does not acquire more than a faint pink coloration on the addition of 1 millilitre of *N/10 solution of silver nitrate* and 10 millilitres of an aqueous solution (1 in 10) of *ammonium persulphate* (limit of manganese)." *Br.*

Zinc sulphate is incompatible with alkalies and alkaline carbonates, sulphides, lime water, the soluble lead salts, and astringent infusions.

Composition.—Crystallized zinc sulphate consists of one sulphuric acid group, SO_4, one atom of zinc, and seven molecules of water. The *white vitriol* of commerce contains but three molecules of water.

The impure commercial variety of zinc sulphate is in the form of irregular white masses having some resemblance to lump sugar. The lumps usually exhibit, here and there on the surface, yellow stains, produced by ferric compounds. It is less soluble than the pure salt, on account of its containing less water by crystallization.

Uses.—Internally, zinc sulphate is, at present, employed only for its emetic action. Because of the promptness and certainty of its effect and its comparative freedom from danger it is one of the most valuable vomitants we possess in various *poisonings*. Externally, it is used as an active astringent, mild caustic, or disinfectant. Its solution constitutes a good styptic to bleeding surfaces, and is frequently resorted to as an injection in *fluor albus* and *gonorrhea*, and as a collyrium in *ophthalmia*, also as a stimulant application to *ulcers* both of the mucous membrane and of the skin. Simpson, of Edinburgh, employed dried zinc sulphate in the form of powder, paste, or ointment, as a powerful, rapid, manageable, and safe caustic in indurated inflammatory ulcers of the cervix uteri, in *lupus*, in *ulcerous forms of skin diseases*, and in removing *urethral caruncles, condylomata, warty excrescences*, etc. The dried salt should be finely levigated. The caustic paste is made by incorporating an ounce of the powder with a drachm of glycerin; and the caustic ointment, by thoroughly mixing the same quantity of the powder with two drachms of lard.

Zinc sulphate, in an overdose, acts as an irritant poison. Besides vomiting and incessant retching, it produces anxiety, distressing restlessness, and extreme prostration. Few cases are on record of fatal poisoning by this salt, the patient being generally relieved by its prompt expulsion in vomiting. Death is said to have been caused, however, by an ounce and a half. The treatment consists in the free administration of bland drinks, the use of opium to allay irritation, and the employment of the usual antiphlogistic remedies should symptoms of inflammation arise.

Dose, from one-fourth to one-half grain (0.016–0.032 Gm.); as an emetic, from ten to thirty grains (0.65–2.0 Gm.). When used as a collyrium, an injection, or a gargle, or as a wash for indolent ulcers, from one to three grains (0.065–0.2 Gm.) or more may be dissolved in a fluidounce (30 mils) of water. For medicinal purposes the crystallized salt only should be used.

Off. Prep.—Liquor Zinci et Alumini Compositus, *N. F.*; Liquor Zinci et Ferri Compositus, *N. F.*; Mistura Adstringens, *N. F.*; Pulvis Antisepticus, *N. F.*

ZINCI VALERAS. U. S. (Br.)

ZINC VALERATE Zinc. Valer.

(zĭn'cī văl'ę-rās).

"It contains not less than 99 per cent. of the crystallized salt [$Zn(C_5H_9O_2)_2 + 2H_2O = 303.55$]. Preserve it in small, well-closed containers." *U. S.* "Zinc Valerate, $Zn(C_5H_9O_2)_2$, $2H_2O$, may be obtained by saturating iso-valerianic acid with zinc carbonate, or by the interaction of zinc sulphate and sodium iso-valerianate." *Br.*

Zinci Valerianas, *Br.;* Zincum Valerianicum; Valerianas Zincicus; Valérianate de Zinc, *Fr. Cod.;* Valérate de Zinc, *Fr.;* Zincvalerianat, Baldriansaures Zinkoxyd, *G.;* Valerianato zincico, *Sp.*

The present Pharmacopœias do not give a method for preparing this salt; for former formulas, see *U. S. Dispensatory,* 19th edition, p. 1359.

Properties.—"Zinc Valerate occurs as white, pearly scales, or as a white powder having the odor of valeric acid, and a sweetish, astringent, and metallic taste. On exposure to the air, it slowly loses valeric acid and becomes partially insoluble in water. One Gm. of Zinc Valerate dissolves in 70 mils of water at 25° C. (77° F.), usually leaving an insoluble residue of basic salt; soluble in 22 mils of alcohol at 25° C. (77° F.). Its aqueous solution (1 in 100) is acid to litmus. When gently heated, the salt melts. At a higher temperature it is decomposed, giving off inflammable vapors, and finally leaving a residue consisting chiefly of zinc oxide. Dissolve 0.5 Gm. of Zinc Valerate in a mixture of 0.5 mil of hydrochloric acid and 9 mils of distilled water; the valeric (isovaleric) acid is liberated and floats as an oily layer on the surface of the liquid. Filter the mixture just prepared through a small, wetted filter; the clear filtrate diluted with distilled water to 25 mils does not respond to the Test for heavy metals (see Part III, Test No. 3). Heat 0.5 Gm. of Zinc Valerate with a mixture of 7.5 mils of distilled water and 5 mils of diluted sulphuric acid and filter; 5 mils of the filtrate meets the requirements for the Test for arsenic (see Part III, Test No. 1). Zinc Valerate dissolves in ammonium carbonate T.S. without leaving a residue. Triturate 0.5 Gm. of Zinc Valerate with 3 mils of distilled water and 0.2 mil of ferric chloride T.S., and filter; the filtrate does not show a red color (*acetate*). Add a concentrated, aqueous solution of copper acetate to a concentrated aqueous solution of Zinc Valerate; the mixture remains perfectly clear (*butyrate*).

Assay.—"Dissolve about 1 Gm. of Zinc Valerate, accurately weighed, in 100 mils of distilled water, with the aid of a few drops of hydrochloric acid, if necessary, and estimate the zinc as zinc oxide by the method given in the assay under *Zinci Acetas.* The salt yields an amount of zinc oxide corresponding to not less than 99 per cent. of $Zn(C_5H_9O_2)_2 + 2H_2O$.

"Each gramme of Zinc Valerate corresponds to not less than 0.265 Gm. of ZnO. Zinc Valerate may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

"White, pearly, tabular crystals. Disagreeable odor; taste metallic. Very slightly soluble in cold *water,* or in *ether;* soluble in hot *water,* and in *alcohol* (90 per cent.). Yields, when heated to redness, after moistening with a small quantity of *nitric acid,* not less than 26 or more than 27 per cent. of zinc oxide. Yields no characteristic *reactions* for lead, copper, cadmium, iron, aluminium, calcium, magnesium, sodium, potassium, ammonium, acetates, or carbonates, and not more than the slightest *reactions* for chlorides or sulphates. *Arsenic limit* 5 parts per million. When heated in a retort with *diluted sulphuric acid* it yields a distillate which, when added to *a solution of copper acetate,* does not immediately become turbid or opalescent, but forms after a short time oily drops, which gradually pass into a bluish-white crystalline deposit (absence of butyrates). 0.2 gramme of the zinc oxide obtained on incineration, dissolved in *diluted sulphuric acid,* and tested as described under 'Zinci Sulphas,' yields a solution with not more than a faint pink coloration (limit of manganese)." *Br.*

The salt, as obtained by the British, 1885, and U. S. P., 1870, formulas, contained one molecule of water; but when formed by saturating zinc carbonate, made into a paste with water, with valeric acid, it contains six molecules of water, and when dried at 50° C. (122° F.), perfectly resembles the official salt. (Wittstein.) Other authorities (Flückiger, *Pharm. Chem.,* and Roscoe and Schorlemmer's *Chem.,* vol. iii, Part I) gave the formula of the stable crystallized salt as $Zn(C_5H_9O_2)_2 + 2H_2O$. Zinc acetate impregnated with oil of valerian has been substituted for this salt; but at present, from the relative costliness of the oil, there is no inducement to this fraud. Zinc butyrate has been sold in Paris for the valerate, and is so like it as not to be distinguished by its physical properties. The two salts, however, may be differentiated by adding a concentrated solution of the acid of the suspected salt obtained by distillation with sulphuric acid, to a concentrated solution of copper acetate. If the acid be the butyric, its addition to the solution of the acetate will disturb the transparency of the latter, by the formation of a bluish-white precipitate; if it be the valeric, no change will be produced. (Larocque and Huraut, *J. P. C.,* 3e sér., ix, 430.)

Uses.—This salt has been used in *neuralgia, epilepsy,* and other nervous diseases, but is probably without therapeutic value. It has also been suggested for *diabetes insipidus.*

Dose, one to two grains (0.065–0.13 Gm.), repeated several times a day, and given in the form of pill.

Off. Prep.—Elixir Zinci Valeratis, *N. F.*

ZINCUM. U. S.

ZINC Zinc.

(zĭn'cŭm)

"It contains not less than 99 per cent. of Zn (65.37)." *U. S.*

Spelтrum; Zinc pur. *Fr. Cod.;* Speltre, Zinc, *Fr.;* Zink, *G.;* Zinco, *It.;* Zinc, *Sp.*

Zinc occurs native in two principal states, as a sulphide, called *blende,* and as a carbonate or silicate, to which the name of *calamine* is applied indiscriminately, although the name belongs properly only to the latter. In this country there are two additional ores that are worked

for zinc. Both occur at Franklin and Mine Hill, New Jersey, and are characteristic of those localities. They are the native oxide, called *red oxide* or *zincite*, and a mixture of zinc oxide with manganese and iron oxide, known as *franklinite*. Zinc has been detected in the vegetable kingdom in a peculiar violet, *Viola calamina*, growing on the calamine hills of Rhenish Prussia. It is largely produced in Belgium, Germany, and this country, the chief American localities being the southwestern section of Missouri, together with the neighboring counties of Kansas, the New Jersey localities before mentioned, Lehigh County, Pennsylvania, Virginia, Wisconsin and Montana. The metal is extracted generally from blende or calamine. This is roasted and mixed with charcoal powder, and the mixture heated in iron cylinders placed horizontally over a furnace. When the reduction of the zinc commences, iron receivers are adapted to the opening of the cylinder to condense the volatilized metal. The metal is then melted and run into moulds, and forms *spelter*, or the zinc of commerce. In this state it contains iron, and traces of lead, cadmium, arsenic, copper, sulphur, and charcoal. To purify it from these substances, it must be subjected to a second distillation in a crucible, furnished with a tube passing through its bottom and open at both ends, its upper extremity reaching a little more than half-way up the interior of the crucible, and its lower end terminating above a vessel of water. The impure zinc being placed in the crucible, the cover luted on, and the fire applied, the pure zinc is volatilized, and, passing down the tube by a descending distillation, condenses in the water below. In the arts zinc is purified sufficiently for commercial purposes without volatilization.

The production of spelter in the United States for the year 1914 amounted to 353,049 tons, and for 1915 to 489,519 tons, which is double the output in 1910. Previous to the European war Belgium produced about 200,000 tons a year and France about 64,000 tons; these are not, at present, available.

Properties.—Zinc has a bluish-white color, a peculiar taste, and a perceptible odor when rubbed. Its texture is laminated, and its fracture crystalline. Its malleability and ductility are not very great. When perfectly pure, it may be reduced to thin leaves at ordinary temperatures; but the zinc of commerce requires to be heated to a temperature between 100° and 148.8° C. (212° and 300° F.) to render it sufficiently malleable to be rolled into sheets. The softness of zinc is peculiar, as shown by the circumstance that it clogs the file when the attempt is made to reduce it to filings; and hence to have it in the divided form it is necessary to melt it, and triturate it at the moment of solidification. Subject to heat it fuses at 398° C. (748.4° F.). According to A. von Riemsdyk, it volatilizes to some extent before fusion at a temperature of 268.3° C. (515° F.). (*A. J. P.*, 1869, p. 424.) At full redness it boils, and in close vessels may be distilled over; but in open vessels it takes fire, and burns with a dazzling white flame, giving off dense white fumes. It dissolves in most of the acids with disengagement of hydrogen, and precipitates all the metals either in the metallic state or in that of oxide. It forms but one oxide (a monoxide) and but one sulphide. The monoxide is official, and has been described under another head. (See *Zinci Oxidum.*)

Zincum Granulatum, Br., 1885. *Granulated Zinc.*—"Take of Zinc of commerce *one pound.* Heat it in an earthen crucible, and immediately the metal is fused remove the crucible from the fire and pour the fluid in a thin stream into a vessel containing about two gallons of cold water. Drain off the water and dry the granulated zinc." *Br.*, 1885.

The official zinc is described as "a bluish-white metal, showing a crystalline fracture. It occurs in the form of thin sheets, or in irregular, granulated pieces, or moulded into thin pencils, or in powder, and having a specific gravity ranging from 6.9 when it is cast to 7.2 after it is rolled. It is dissolved by diluted sulphuric or hydrochloric acid with the evolution of hydrogen, usually leaving some insoluble residue. When heated above 100° C. (212° F.) and not above 150° C. (302° F.), the metal becomes malleable and ductile; above 200° C. (392° F.), it becomes sufficiently brittle to be (powdered in an iron mortar; at from 412° to 415° C. (773.6°–779° F.) it melts, and at 940° C. (1724° F.) it boils and may be readily distilled. Add 1 Gm. of Zinc to 25 mils of diluted sulphuric acid; the liberated hydrogen does not have a disagreeable odor, nor does it color a strip of paper moistened with lead acetate T.S. (*sulphur*), or with silver nitrate T.S. (*arsenic, antimony, and phosphorus*). The filtered solution is colorless, and yields a white gelatinous precipitate with potassium ferrocyanide T.S., and a white precipitate with ammonium sulphide T.S." *U. S.*

Assay.—"Dissolve about 1 Gm. of Zinc, accurately weighed, in a slight excess of hydrochloric acid and add sufficient distilled water to make 100 mils. Dilute 10 mils of the clear solution with distilled water to make 100 mils, render it slightly alkaline with ammonia water and subsequently treat it as directed in the assay for *Zinci Acetas* for the determination of zinc oxide. The metal yields an amount of zinc oxide corresponding to not less than 99 per cent. of Zn.

"Each gramme of Zinc corresponds to not less than 1.232 Gm. of ZnO. Zinc may also be assayed by the Electrolytic method (see Part III, Test No. 4)." *U. S.*

Zinc of good quality dissolves in diluted sulphuric acid, with the exception of a scanty grayish-black residue. If absolutely pure, it would be wholly dissolved. The solution is colorless, and yields white precipitates with potassium ferrocyanide and ammonium sulphydrate. Ammonia throws down from this solution a white precipitate, which is wholly dissolved when the alkali is added in excess. Zinc is extensively employed in the arts. It is the best metal that can be used, in conjunction with copper or carbon, for galvanic combinations.

Its solution in diluted sulphuric acid furnishes the readiest method for obtaining hydrogen. With copper it forms *brass*, and, in the form of *sheet zinc*, it is employed to cover the roofs of houses, to line sinks, put under stoves, and for other purposes. It is also applied to the covering of iron, to protect it from oxidation, in the same manner as tin, forming what is commercially known as *galvanized iron*. A fine powder, known as *zinc dust*, obtained by the condensation of zinc vapor in the distillation of zinc from its ores, is much used in chemical laboratories as a convenient reducing agent in many reactions. Zinc should never be used for culinary vessels, as it is soluble in the weakest acids. Zinc and its oxide are dissolved to a certain extent by water containing common salt, a double zinc and sodium chloride being produced in solution. (*J. P. C.*, Nov., 1867, p. 397.)

Zinc Nitrate is sometimes used as a caustic either in the form of *paste* or in *pencils*. Lefort prepares it by dissolving commercial zinc with heat in equal volumes of nitric acid and water, maintaining an excess of zinc, and concentrating until a slight basic precipitate is formed, which carries down any iron present. Boiling water is then added, and, when cool, the solution is filtered, and evaporated at a gentle heat until slight ebullition takes place; if then left to cool, it forms a cake, which should be broken up and drained in a glass funnel. Of the zinc nitrate so prepared, 100 grammes are dissolved in 50 grammes of water, and afterwards incorporated with 50 grammes of wheaten flour. This forms a homogeneous paste, which remains soft, spreads easily over surfaces without afterwards contracting, and does not spread at the edges through absorption of moisture. When made into cylinders, it should not be dried by heat, as it slightly decomposes and becomes yellow and friable; it may be kept dry by placing it in a tin box with some pieces of quicklime, but not in contact with them. (*L. M. R.*, June 18, 1873; *A. J. P.*, Dec., 1873.) Chas. Rice prepares pencils by pouring fused zinc nitrate into paper cylinders which are made by rolling paper around a lead-pencil and sealing with wax. The mixed *mercury and zinc cyanide* was originally suggested as a practical antiseptic by Lister, who claimed for it the advantages of being non-volatile, unirritating, insoluble in water, and soluble only in three thousand parts of blood serum; so that it is not easily washed off the gauze by discharge from wounds. Its germicidal value is said to be very slight, but its inhibitory power to be such that a one twelve-hundredth solution will permanently prevent putrefaction in animal fluids. (See *N. R.*, 1876, p. 44; also *Mercuric and Zinc Cyanide*, Part II.) *Cyanide gauze* may be made actively germicidal by impregnation with a solution of one to four thousand of corrosive sublimate.

The compounds of zinc are poisonous, but not to the same extent as those of lead. The zinc oxide, used in painting as a substitute for white lead, is said to be capable of producing a colic resembling that caused by lead, and called *zinc colic*. It attacks the workmen exposed to the dust of the oxide while engaged in packing it in barrels, and is said to yield to the remedies appropriate to the treatment of lead colic. This latter statement, however, is, to say the least, very questionable.

Uses.—Zinc is never used as a medicine in the metallic state, but is employed in this state to prepare zinc sulphate and zinc chloride, and the Reduced Iron of the Br. Pharmacopœia. In combination it forms a number of important preparations.

ZINGIBER. U. S., Br.

GINGER Zingib.

(zĭn'jĭ-bẽr)

"The dried rhizomes of *Zingiber officinale* Roscoe (Fam. *Zingiberaceæ*), the outer cortical layers of which are often either partially or completely removed. Preserve it in tightly-closed containers, adding a few drops of chloroform or carbon tetrachloride, from time to time, to prevent attack by insects." *U. S.* "Ginger is the scraped and dried rhizome of Zingiber officinale, *Roscoe*." *Br.*

Gingembre (gris et blanc), *Fr. Cod.*; Rhizoma Zingiberis, *P. G.*; Ingwer, *G.*; Zenzero, *It.*; Jengibre (Rizoma de), *Sp.*

There are about twenty species of the genus Zingiber, the commercial ginger being obtained from *Zingiber officinale*. According to Watt, this species is probably a native of tropical Asia, but is not known except in the cultivated state. It is now extensively cultivated in the tropical countries of both the Eastern and Western Hemispheres.

The ginger plant, *Zingiber officinale*, has a biennial or perennial, creeping rhizome, and an annual stem, which rises two or three feet in height, is solid, cylindrical, erect, and enclosed in an imbricated membranous sheathing. The leaves are lanceolate, acute, smooth, five or six inches long by about an inch in breadth, and stand alternately on the sheaths of the stem. The flower-stalk rises by the side of the stem from six inches to a foot, and, like it, is clothed with oval acuminate sheaths; but it is without leaves, and terminates in an oval, obtuse, bracteal, imbricated spike. The flowers are of a dingy yellow color, and appear two or three at a time between the bracteal scales. The flowers have an aromatic odor, and the stems when bruised are slightly fragrant; but it is in the rhizome that the virtues of the plant reside. This is fit to be dug up when a year old. The rhizome of the ginger is lifted from the soil by a single thrust of the fork at the time when the stems of the plant turn white, before the rhizome has begun to get tough and fibrous. The root is scalded in boiling water and rapidly dried, when it constitutes the *black* or ordinary ginger of commerce.

In Jamaica the so-called *white* or *Jamaica ginger* is produced by carefully peeling the fresh rhizomes so that only the epidermis is removed,

the cells immediately beneath the epidermis being the richest in volatile oil and resin. The peeled pieces are macerated sometimes in water and sometimes in lime juice, and not rarely the color of the ginger is improved by finally coating it with chalk. (See Kilmer, *A. J. P.*, 1898, p. 65; Harris, *P. J.*, 1909, xxix, p. 379.) An inferior white ginger is also produced in the East Indies. The thoroughness of desiccation is a matter of commercial importance. The moisture in ginger should not exceed 10 per cent., but in the poorer specimens may constitute one-fourth of the whole weight. In China the fresh ginger is rasped into a powder and as such dried. Formerly *East Indian ginger* was imported into the United States from Calcutta, while the *Jamaica* or *West Indian ginger* came usually through London. At present the cultivation of ginger is spread almost over the whole sub-tropical world, and the drug is produced in St. Lucia, Dominica and Africa, Cochin-China, Japan, etc. The world's production of ginger is estimated to be annually over 20,000,000 pounds. Of this nearly 4,000,000 pounds is annually exported from Jamaica, the United States using about 1,500,000 pounds. (*C. D.*, lxxvii, p. 489; *Cons. and Tr. Rep.*, 1910, p. 1085.)

In Martinique a ginger is said to be obtained by the cultivation of *Zingiber Zerumbet* Rosc. The ginger of Siam is said to be produced by *Alpinia Galanga*, and is the same drug, therefore, as the *Greater* or *Java Galanga Root*. The large, ordinary, *preserved ginger* of China is, according to C. Ford (*Kew Bulletin*, 1891) also the product of *A. Galanga*. It is made by boiling young, tender, carefully selected and decorticated rhizomes in syrup. Preserved ginger from the West Indies is made from the official plant. According to Hartwich and Swanlund, the rhizome of the *Zingiber Mioga*, which is cultivated in China and Japan, has a taste less pungent than that of the official ginger, and distinctly recalling bergamot. In commerce the varieties of ginger are known by the place of their production. African and Cochin ginger on an average yield more resin and volatile oil than do the older varieties.

The recent root is from one to four inches long, somewhat flattened on its upper and under surface, knotty, obtusely and irregularly branched or lobed, externally of a light ash color with circular rugæ, internally yellowish-white and fleshy. It sometimes begins to grow when kept in a damp atmosphere. The *common* or *black ginger* is of the same general shape, but has a dark ash-colored wrinkled epidermis, which, being removed in some places, exhibits patches of an almost black color, apparently the result of exposure. Beneath the epidermis is a brownish, resinous, almost horny cortical portion. The interior parenchyma is whitish, the cells being filled with starch. The powder is of a light yellowish-brown color. This variety is most extensively used. The *Jamaica* or *white ginger* is white or yellowish-white on the outside. The pieces are rounder and thinner, and afford when pulverized a beautiful yellowish-white powder.

The uncoated ginger of the East Indies resembles the Jamaica, but is darker, being gray rather than white. As the Jamaica commands a much higher price than even the uncoated East India production, the latter is occasionally altered to simulate the former. This is sometimes done by coating the exterior with calcium sulphate or carbonate, sometimes by bleaching with the fumes of burning sulphur or in other ways, by which not only the exterior but also the internal parts are rendered whiter than in the unprepared root. Powdered ginger which has been exhausted in the preparation of essence, technically known as "*spent ginger*," is used to a large extent in the adulteration of powdered ginger. Its detection without assay of some sort is almost impossible, unless so much is present as to sensibly alter the taste of the powder. Allen and Moor rely upon the proportion of cold water extract yielded and the soluble ash. Dyer and Gilbard state that the fixed ethereal extract is of little value, on account of its variability in genuine ginger, but that the extract obtained by alcohol after ether affords a valuable criterion. In genuine ginger the average yield is 2.9 per cent. while in spent ginger it is 1.2 per cent. They also affirm that in genuine ginger the ash produced is 2.7 per cent., in the exhausted ginger it is 0.3 per cent. A. Russell Bennett concludes that spent ginger can be detected by noting the alcoholic and cold water extracts and the soluble ash, affirming that ginger should yield not less than 5 per cent. of extract with 90 per cent. alcohol, 8.5 per cent. of cold water extract and 1.5 per cent. of soluble ash.

Commercial gingers are known as "scraped," "decorticated," and "coated." The "scraped" gingers are those from which the cortex has been removed in whole or in part by peeling, as seen in the Jamaica, Cochin and Japan varieties. In the "coated" gingers a portion of the outer natural layers are retained as in the African, Calcutta and Calicut varities. "Bleached" and "unbleached" gingers are also distinguished, the former being lighter in color due to careful washing or special treatment. All of the above varieties mentioned are recognized in the U. S. Pharmacopœia IX, and are described as follows:

"**Jamaica Ginger.**—Rhizomes free from the outer corky layers, in horizontal, laterally compressed, irregularly branched pieces, from 4 to 16 cm. in length; and from 4 to 20 mm. in thickness; externally light brown, longitudinally striate, ends of the branches with depressed stem-scars; fracture short-fibrous, mealy and resinous; internally yellowish to light brown, cortex thin, endodermis a thin yellow layer enclosing a large central cylinder with numerous groups of fibro-vascular bundles and yellowish oil cells; odor agreeably aromatic; taste aromatic and pungent.

"**African Ginger.**—Rhizomes with cork partly removed on the flattened sides, the patches without cork smooth and of a light brown color, the

portions with cork longitudinally or reticulately wrinkled and grayish-brown; fracture short or short-fibrous, internally lemon-yellow or dark bluish with yellowish oil-secretion cells and light yellow to reddish-brown resin cells; odor strongly aromatic; taste intensely pungent.

"**Calcutta Ginger.**—Rhizomes resembling the African Ginger, the branches or 'fingers' being somewhat larger, and with a considerable proportion of shriveled pieces, externally grayish-brown or grayish-blue; fracture short and mealy, or horny; internally light yellow or light brownish-yellow with numerous yellowish oil cells and yellowish-brown resin cells; odor aromatic; taste starchy and strongly pungent.

"**Calicut Ginger.**—Rhizomes resembling African Ginger, more of the periderm being usually removed; externally more or less uniformly light brown; fracture short or short-fibrous, and mealy; internally light-yellow or brownish-yellow with numerous yellowish oil and resin cells; odor aromatic; taste very pungent.

"**Cochin Ginger.**—Rhizomes with most of the corky layer removed on the flattened sides; externally light brown to grayish-yellow, fracture short and mealy; internally yellowish-white with numerous yellowish oil cells and brownish-red or blackish resin cells; odor aromatic; taste pungent but not so persistent as in the African variety.

"**Japanese Ginger.**—Rhizome somewhat resembling Cochin Ginger but usually with a thin coating of lime; externally nearly smooth or slightly wrinkled and of a whitish color; fracture short and very mealy; internally varying from a yellowish-white to light brown and with numerous brownish-red resin cells; odor aromatic; taste pungent.

"Powdered Ginger is light yellow, or light brown to dark brown; under the microscope it exhibits numerous starch grains varying greatly in form and size in the different varieties, being nearly spherical, ovoid, ellipsoidal or pear-shaped and frequently with a characteristic beak, usually from 0.005 to 0.04 mm., occasionally from 0.045 to 0.06 mm. in the long diameter; sclerenchymatous fibers long, thin-walled, non-lignified, with oblique pores and distinctly undulate on one side; oil-secretion cells with suberized walls and containing a light yellowish or yellowish-brown, oily substance; cork cells absent in the Jamaica variety. Introduce 4 Gm. of ground Ginger into a 200 mil flask, fill to the mark with distilled water, and agitate at half-hour intervals during eight hours. Then allow the mixture to stand for sixteen hours, and filter. Evaporate 50 mils of the filtrate, representing 1 Gm. of the drug, on a water bath, dry to constant weight at 100° C. (212° F.) and weigh; it yields not less than 8 per cent. of residue. Ginger yields not less than 2 per cent. of a non-volatile extract soluble in ether and not less than 4 per cent. of an extract soluble in alcohol. Ginger yields not more than 8 per cent. of ash." *U. S.*

"In flattish, irregularly branched pieces, usually from seven to ten centimetres long; each branch marked at its summit by a depressed scar. Fracture short with projecting fibres. Agreeable, aromatic odor; taste pungent. When 5 grammes of powdered Ginger are shaken with 100 millilitres of *alcohol* (90 per cent.) occasionally during twenty-four hours and filtered, 20 millilitres of the filtrate yield on evaporation not less than 0.050 gramme of residue dried at 100° C. (212° F.); and when 5 grammes are similarly treated with 100 millilitres of *water*, 20 millilitres of the filtrate yield not less than 0.085 gramme of residue dried at 100° C. (212° F.). Ash not more than 6 per cent.; and after deduction of that portion of the ash which is soluble in *water* not more than 1.5 per cent." *Br.*

The odor of ginger is aromatic and penetrating, the taste spicy, pungent, hot, and biting. These properties gradually diminish, and are ultimately lost, by exposure. The morphology and pharmacognosy of ginger have been studied by Meyer (*Wissenschaftliche Drogenkunde*, vol. ii, p. 64) and Tschirch and Oesterle (*Anatomischer Atlas.*, Lief. vi, p. 109). Kraemer and Sindall have published an article on the "Microscopical and Chemical Examination of the Different Varieties of Commercial Ginger" (*A. J. P.*, 1908, p. 303). Spaeth reports on the adulteration and detection of adulterants of ginger and asserts that the more common adulterants are flour, curcurma, linseed and rapeseed cake, cayenne pepper hulls, and extracted ginger. (*Zeitschr. f. Unters. d. Nahr. u. Genussm.*, x, p. 23.)

The use of capsicum in preparations of ginger is not infrequent. When present, it may be detected by the method described under tincture of ginger (see page 1159).

The virtues of ginger are extracted by alcohol. The peculiar flavor of the root appears to depend on the volatile oil, its pungency partly on the resinous or resino-extractive principle. A considerable quantity of pure white starch may be obtained from it. The volatile oil, examined by A. Papousek, was yellow, of the odor of ginger, and of a hot aromatic taste. Its sp. gr. was 0.893, and its boiling point 246.1° C. (475° F.). Deprived of water by distillation over phosphoric oxide, it consisted of carbon and hydrogen, with the formula $C_{10}H_{16}$, and therefore belongs to the terpenes. Tresh considers that the essential oil is mainly made up of a hydrocarbon, $C_{15}H_{24}$, or isomers of it, which boil at from 245° to 270° C. (473°–518° F.). (*P. J.*, No. 586, 1881.) Schimmel & Co. (*April*, 1897) state that the essential oil contains *camphene* and *phellandrene*, and hence the terpenes have the formula $C_{10}H_{16}$, as first stated. Flückiger obtained from one hundred and twelve pounds of Jamaica ginger four and a half ounces of the oil, or about one-fourth of one per cent. He states, however, that Schimmel & Co., of Leipsic, informed him that they obtained as much as 2.2 per cent. from good ginger. (*Pharmacographia*, 2d ed., p. 637.) H. von Soden and W. Rojahn (*Ph. Ztg.*, 1900, 414) obtained a new sesquiterpene from oil of gin-

ger by fractioning the saponified oil. They have named it *zingiberene.* It has the sp. gr. 0.872 at 15° C. (59° F.). Those pieces of ginger which are very fibrous, light and friable, or worm eaten, should be rejected. The commercial powder of ginger is very frequently adulterated, rice starch, powdered ginger which has been exhausted in making preparations, and even brick dust and chalk, being used, and the loss of pungency made good by the addition of capsicum or mustard.

Uses.—Ginger is a grateful stimulant and carminative, and is often given in *dyspepsia* and *flatulent colic.* It is an excellent addition to bitter infusions and tonic powders, imparting to them an agreeable, warming, and cordial operation upon the stomach. It is especially valuable in *alcoholic gastritis.* In the serous type of *diarrhea,* when due to a relaxed condition of the bowel, it is a remedy of much service but should not be employed in the presence of inflammatory conditions. The hot infusion is popularly employed under the name of "Ginger Tea" for its diaphoretic effect in *colds,* especially when accompanied with suppression of the menses. Externally it is rubefacient. Under the name of *"Essence of Ginger"* cheap alcoholic preparations of ginger were formerly sold and used as intoxicants. A number of cases of blindness produced by such use have been recorded, the amblyopia having been due to the large use of methyl alcohol in the making of these "essences." The infusion may be prepared by adding half an ounce of the powdered or bruised root to a pint of boiling water, and may be given in the dose of one or two fluidounces (30–60 mils).

Dose, ten to twenty grains (0.65–1.3 mils).

Off. Prep.—Fluidextractum Zingiberis, *U. S.;* Infusum Sennæ, *Br.;* Oleoresina Zingiberis, *U. S.;* Pilula Scillæ Composita, *Br.;* Pilula Urgineæ Composita, *Br.;* Pulvis Aromaticus, *U. S.* (*Br.*); Pulvis Jalapæ Compositus, *U. S.;* Pulvis Kaladanæ Compositus, *Br.;* Pulvis Opii Compositus, *Br.;* Pulvis Rhei Compositus, *U. S., Br.;* Pulvis Scammonii Compositus, *Br.;* Syrupus Zingiberis (from Fluidextract), *U. S., Br.;* Tinctura Zingiberis, *U. S., Br.;* Elixir Rubi Compositum, *N. F.;* Pulvis Aromaticus Rubifaciens, *N. F.;* Pulvis Myrciæ Compositus, *N. F.;* Tinctura Antiperiodica, *N. F.;* Tinctura Antiperiodica sine Aloe, *N. F.;* Tinctura Aromatica, *N. F.*

PART II

DRUGS AND MEDICINES NOT OFFICIAL

In the present section it is proposed to consider remedies which are not recognized in the United States or British Pharmacopœias, but which, on account of their use in domestic or professional medicine, their toxic properties, their history, or the probability that they may prove in the future remedies of power, or valuable products, require notice in an encyclopedic work like the United States Dispensatory. The limit of the present volume forbids an exhaustive description of all these substances, but the attempt is made to give at least the essential information and the key to the literature about almost everything used in medicine. The substances treated of in this part are not considered to be of as great importance as those found in Part I, and hence the type and arrangement of titles are different; experience has shown that this method helps to educate the reader to distinguish between official and unofficial substances.

Abrastol. *Asaprol. Calcium betanaphtholsulphonate. Calcinaphthol.—Calcium α-monosulphonate of β-naphthol,*

$$C_{10}H_6\begin{cases}OH\\SO_3\end{cases}\!\!>Ca + 3H_2O.$$
$$C_{10}H_6\begin{cases}SO_3\\OH\end{cases}$$

This is a pinkish powder, soluble in water and alcohol, and resembling the salicylates in its taste. It is neutral in reaction, readily soluble in alcohol and water, and not altered by heat. On exposure to light and air it tends to darken and become less soluble. It is incompatible with quinine salts, antipyrine, ferric salts, and potassium iodide, soluble carbonates and oxalates, and when rubbed with some of the synthetic drugs, exalgin, urethane, etc., it forms masses. Asaprol was originally brought forward by A. Stackler as a germicide, antipyretic, and antirheumatic in *rheumatism, typhoid fever,* etc. (*B. G. T.,* 1892.) Dujardin-Beaumetz (*B. G. T.,* Jan., 1894) found that when given by the mouth to rabbits in the dose of 0.25 Gm. per kilo it has no deleterious effect, although less than 1 Gm. per kilo proved fatal. It escapes from the kidneys in the form of *naphthol sulphuric ester,* which may be recognized by the dark blue coloration of the urine on the addition of ferric chloride. In acute *rheumatism,* Dujardin-Beaumetz believed that the remedy is equal to salicylates, and that it has the advantage of not producing tinnitus aurium or eruptions upon the skin. Buck (*Ther. Woch.,* 1897) confirms the value of asaprol in *rheumatism.* Moncorvo (*B. G. T.,* March and April, 1895) recommends it in *chorea* and in *malarial diseases.* He also affirms that, used locally, it is an excellent antiseptic, hemostatic, and cicatrizant. He uses it in aqueous solution, 1 to 4 per cent., or as an ointment with vaseline. He even asserts that a 1 per cent. solution applied to the periglotteal region will rapidly cure *whooping cough.* It has been used to a limited extent as a food preservative, particularly for beverages, and is prohibited by statute in a number of states. It is detected by the yellow coloration produced by mercuric nitrate T.S. when added to the residue obtained by shaking out the acidulated solution, of the substance suspected of containing it, with ether, and evaporating the ether on a watch glass. The *dose* of abrastol is from ten to thirty grains (0.6–1.9 Gm.) three times a day.

Abroma. *Abroma angustum* L. f. (Fam. *Sterculiaceæ.*)—Under the name of *Olutkombul,* the glutinous sap of this plant has long been used in India in *dysmenorrhea.* According to Sircar (*Indian Medical Gazette,* 1900) and other English practitioners, it is a very efficient remedy in congestive and neuralgic *dysmenorrhea* when given in doses of two drachms (7.7 Gm.) at the time of the first premonitory pains and continuing to the end. The fresh root is sometimes used. *Dose,* half a drachm (2 Gm.).

Abrus. *Abri Semina. Jequirity. Prayer Beads. Abrus Seeds. Abrus precatorius* L. (Fam. *Leguminosæ.*)—The seeds of this plant, which grows in India and also in Brazil, are employed in India as a standard weight by druggists and jewelers, and also for criminal poisoning. The seeds are ovoid, from 5 to 8 mm. in length, smooth, shiny and of a bright scarlet, having a black marking at the lower, or hilum, portion. They are said to be inert when taken whole into the stomach. They contain *abric acid,* $C_{21}H_{24}N_3O$, and, according to the researches of Sidney Martin (*P. J.,* Sept., 1887; *Proc. Roy. Soc.,* 1889, vol. xlvi), two proteid poisons, a paraglobulin and an albumose (together called *abrin*), which are almost identical in their physiological properties with principles found in snake venom, although less powerful. According

to Flexner, the toxic action of these substances also closely resembles that of true toxins, the most characteristic result being focal necroses in various organs. Flexner suggests that these in turn are due to a lesion in the blood-vessel walls caused by the abrin. (*J. Ex. M.*, 1897, vol. ii.) The ordinary lethal dose of abrin for animals is said to be 0.00001 Gm. per kilo of weight. (Consult *The Non-Bacillous Nature of Abrus Poisoning*, J. H. Warden and L. A. Waddel, Calcutta, 1884; Bufalini, *Ann. di Chim. e di Farm.*, No. 2, 1886; Kobert, *W. M. Bl.*, Nov., 1889.) The root of Abrus, known as *Indian liquorice*, possesses toxic properties like the seeds and should not be used in place of licorice. According to David Hooper, it contains *glycyrrhizin*. (*P. J.*, 1894.) Abrin is used in the treatment of certain chronic diseases of the eye, especially in *corneal opacities*, and *trachomatous pannus*. It excites a purulent inflammation of the conjunctiva, which appears to lead to an increase in the local circulation, provoking thereby an absorption of inflammatory exudates. The remedy is capable of great harm in unsuitable cases, and extreme caution must be employed in its use. The infusion of jequirity, which was formerly employed for this purpose, has been almost abandoned because it was liable to cause an uncontrollable inflammation which in some instances has entirely destroyed vision. The infusion of the crude drug was employed in strengths of from 2 to 20 per cent., which must be prepared at a temperature below 50° C. (112° F.). According to Ehrlich, the solution of abrin should not be stronger than one part in 500,000; any increase of strength must be made with great care. Both Ehrlich and Calmette succeeded in immunizing rabbits against abrin, and obtained an antitoxic serum. P. Römer (Graefe's *Archiv. f. Ophthal.*, vol. lii, 1901) has introduced two preparations: *jequiritol*, an abrin solution, sterilized, of four different strengths; *jequiritol serum*, which, as commercially supplied, has such immunizing power that 0.1 mil suffices to protect a white mouse from the effects of a hundredfold lethal dose of jequiritol when the latter and jequiritol serum are injected conjointly. (For details and methods of use, see *Th. M.*, May, 1902; *M. R.*, 1902; Kattwinkel, *Jequiritol*, Bonn, 1902; Seefelder, *Klinische monatsblätter*, 1905, p. 273; Schoen, *Hospitalstidende*, No. 37, p. 921.)

Absinthium. *N. F. IV. Wormwood.*—It was official in the U. S. P. 1890 and is now recognized by the National Formulary. The definition is as follows: "The dried leaves and flowering tops of *Artemisia Absinthium* Linné (Fam. *Compositæ*), without the presence of more than 5 per cent. of foreign matter." *N. F. IV.* Several species of Artemisia have enjoyed some reputation as medicines. The leaves of *A. Abrotanum* L., or *southernwood*, are reported by Craveri to contain a crystallizable alkaloid, *abrotine;* they were formerly employed as a tonic and anthelmintic. *A. pontica* L. has been substituted for common wormwood, but is weaker. *A. vulgaris* L., or *mugwort*, has been used in Germany in *epilepsy, chorea*, and *amenorrhea*. *A. ludoviciana* Nutt., a native of the southwestern regions of the United States, has been commended as a stimulant to the hair. (*A. J. P.*, 1872, p. 106.) In China, *moxa* is prepared from *A. chinensis* L. and *A. indica* Willd.

Wormwood, also known as *Madderwort, Wermuth, Mugwort, Mingwort* and *Warmot*, is a shrubby, more or less herbaceous, finely canescent plant, growing to a height of 2 to 4 feet. The leaves are 1 to 3 pinnately divided, the lobes being lanceolate or obovate, the basal leaves being petiolate while the floral ones are linear and entire; the flowers are all fertile, yellowish, and occur in hemispherical panicled heads. The plant is a native of Europe and is to some extent cultivated in the United States. It is now naturalized and rather common in eastern Canada to Pennsylvania, growing along roadsides and waste places. It should be gathered in July or August, during flowering.

The N. F. description is as follows: "Stems and leaves gray-green, finely silky-hairy and glandular throughout; largest leaves reaching 10 or 12 cm. in length, and of nearly equal breadth, on long petioles, two to three times pinnately lobed or divided, the ultimate segments oblong or obovate, obtuse, entire or slightly toothed; upper leaves becoming shorter petioled, small and narrower, the uppermost being only about 2 cm. in length and resembling the ultimate segments of the larger ones; heads racemose-paniculate, drooping on short peduncles, greenish-yellow, from 3 to 4 mm. in breadth, round-ovoid, the outer bracts linear-oblanceolate, obtuse, the inner broader and scarious-margined; receptacle hairy; outer flowers sometimes pistillate. Odor characteristic, aromatic; taste very bitter. The powdered drug is brownish to yellowish-green and, when examined under the microscope, exhibits numerous, characteristic, T-shaped, non-lignified hairs, consisting of a short, one- to four-celled stalk bearing a single apical cell attached near the center and up to 0.8 mm. in length and 0.035 mm. in width. Many of the hairs are more or less collapsed, twisted or broken; glandular hairs, some with one- or two-celled stalk, the glandular portions consisting of from four to eight secreting cells surrounded by a membrane; few simple hairs from the flowers, some of which are very long and up to 0.085 mm. in width; epidermal fragments with elliptical stomata, the latter up to 0.035 mm. in length; fragments of mesophyll and palisade cells containing chloroplastids; tracheæ mostly spiral, up to 0.035 mm. in width; few sclerenchymatous fibers, with thick, usually lignified walls and simple pores, up to 0.02 mm. in width; pollen grains few, somewhat spherical or triangular in outline, up to 0.03 mm. in diameter; calcium oxalate crystals in rosette aggregates about 0.01 mm. in diameter. Absinthium yields not more than 10 per cent. of ash." *N. F.*

The volatile oil (*oleum absinthii*) is usually dark green, sometimes yellow or brownish or even blue, having a strong odor of the plant, an acrid peculiar taste, and the sp. gr. 0.925 to 0.950. It is sometimes adulterated with alcohol, oil of turpentine, etc., which lessen its specific gravity. It is composed of: *thujone* (*absinthol*), which has the specific gravity 0.926, composition $C_{10}H_{16}O$, boiling point 200° C. (392° F.) to 205° C. (401° F.), and when heated with phosphorus pentasulphide or zinc chloride yields cymene ($C_{10}H_{14}$); thujyl alcohol ($C_{10}H_{18}O$), both free and as the esters of acetic, isovaleric, and palmitic acids; phellandrene and possibly pinene; cadinene; and a *blue oil* of as yet undetermined composition. (Gildemeister and Hoffmann, *Aetherische Oele*, 1899.) The *absinthic acid* found by Braconnot is said to be succinic acid. Caventou first obtained *absinthin* in an impure condition. (See U. S. D., 14th ed., p. 5.) P. Senger (*A. Pharm.*, 230, p. 94) has obtained absinthin as a yellow substance of an intensely bitter taste

melting at 55° C. (131° F.). He gives it the formula $C_{15}H_{20}O_4$ and considers it to be a glucoside, as on boiling with diluted sulphuric acid it yields dextrose and absinthic acid. Kromayer gives the formula for absinthin as $C_{40}H_{56}O_8 + H_2O$. Absinthin is soluble in water, alcohol, and ether and has been introduced into medicine for use in the treatment of *constipation* and *chlorosis*. *Dose*, one and one-half to three grains (0.1–0.2 Gm.). Adrian and Trillat isolated a new crystalline body ($C_{53}H_{51}O_{20}$) from wormwood by treating an alcoholic extract with amyl alcohol, the absinthin having been previously removed. They also isolated another crystalline principle, *anabsinthin*, $C_{18}H_{24}O_4$ (*P. J.*, 1899, 1, 75). The old *salt of wormwood* (*sal absinthii*) was impure potassium carbonate, made from the ashes of the plant.

Wormwood, which was formerly in vogue as a stomachic tonic, antiperiodic, and anthelmintic, is at present very seldom used. The volatile oil is an active narcotic poison. In dogs and rabbits from thirty to fifty drops (1.5–2.5 mils) of it will cause trembling, stupor, hebetude, and even insensibility; one to two fluidrachms (3.75–7.5 mils) of it causes violent epileptiform convulsions, with involuntary evacuations, unconsciousness, and stertorous breathing, which may or may not end in death. (Marcé, *B. G. T.*, Mai, 1864; Amory, *B. M. S. J.*, March, 1868, p. 83.) In man the oil acts similarly; a half ounce (15 mils) of it caused, in a male adult, insensibility, convulsions, foaming at the mouth, and a tendency to vomit; though the patient recovered under the use of emetics, with stimulants and demulcents. (*L. L.*, Dec. 6, 1862.) According to J. L. Corning, the volatile oil is a powerful local anesthetic, locally useful in *rheumatic pains*. Böhm and Kobert affirm that the oil escapes through the kidneys unchanged. *Dose*, of wormwood in substance, from twenty to forty grains (1.3–2.6 Gm.); of the infusion (one ounce in a pint of boiling water), from one to two fluidounces (30–60 mils); of the oil, one to two minims (0.06–0.12 mil).

Absinthe is a liqueur containing oils of wormwood, angelica, anise, and marjoram. According to Baudrimont, the *absinthe ordinaire* contains 47.66 per cent. of alcohol, the *demi-fine* 50 per cent., the *fine* 68 per cent., and the *absinthe Suisse* 80.66 per cent. The preparation, if manipulated properly, possesses naturally a bright green color, brought to an olive-green by slight addition of caramel coloring; but artificial coloring was formerly often resorted to, and indigo, turmeric, cupric acetate, and aniline green have been used to produce the proper shade. The importation of absinthe liqueur into the United States is now prohibited by law. *Absinthism* differs from ordinary alcoholism in its manifestations; its characteristic symptoms are restlessness at night, with disturbing dreams, nausea and vomiting in the morning, with great trembling of the hands and tongue, vertigo, and a tendency to epileptiform convulsions.

Acalypha. *Br. Add.* 1900.—The fresh and the dried herb, *Acalypha indica* L. This euphorbiaceous plant is said to have expectorant and emetic properties similar to those of ipecac, and also to be employed by the native Indian practitioners in the form of the fresh leaves as a poultice for *ulcers*, and as a suppository for *constipation* in children. The *Succus Acalyphæ*, Br. Add., 1900, is prepared by adding one volume of 90 per cent. alcohol to three volumes of the juice expressed from fresh leaves, with subsequent filtration. It is given in doses of from one to four fluidrachms (3.75–15 mils). The *liquid extract* (*Extractum Acalyphæ Liquidum*, Br. Add., 1900), made with a menstruum of 90 per cent. alcohol, is given in doses of from five to thirty minims (0.3–1.8 mils).

Acetal. *Acetol. Diethylacetal. Diethylaldehyde.* $C_6H_{14}O_2$ or $CH_3CH(OC_2H_5)_2$.—*Ethidene* (*Ethylidene*) *diethylic ether*, a limpid volatile liquid boiling at 103°–104° C. (219°–223° F.), sp. gr. 0.831 at 22° C. (71.6° F.), and produced by the imperfect oxidation of alcohol. Sparingly soluble in water, readily soluble in alcohol, is stated to be narcotic in the *dose* of thirty minims (1.8 mils). Used as a hypnotic in *doses* of two or three fluidrachms (8–12 mils), preferably in emulsion. The title Acetal is also given to a proprietary remedy for *headache*.

Acetonitrile. *Methyl Cyanide.* CH_3CN. (C_2H_3N).—This is a colorless liquid, with a characteristic odor, miscible with both water and alcohol, and prepared from acetamide with glacial acetic acid by heat. Although it is probable that it is partly broken up in the system, methyl cyanide is not highly toxic. According to Lang (*A. E. P. P.*, 1894, xxxiv, p. 24), the fatal dose for rabbits is about one gramme. About one-fifth of the cyanogen which is introduced in the radical may be recovered from the urine in the form of an alkaline sulpho-cyanide. Its chief importance lies in the fact that it has been suggested by Hunt (*A. I. P. T.*, 1904, xii, p. 44) as a means for the biological standardization of the thyroid gland. (See *Thyroideum Siccum.*)

Aceto-Ortho-Toluid. *Ortho-tolyl-acetamid.* $C_7H_7.NH.C_2H_3O$.—Colorless needles, easily soluble in hot water, alcohol, and ether; powerfully depressant to animal temperature, although feebly poisonous. Used as an *antipyretic* in *doses* of from three to eight grains (0.2–0.5 Gm.). (E. Barbarini, *T. Mod.*, 1892, 532.)

Aceto-Para-Toluid. $C_6H_4(CH_3)NH.C_2H_3O$.—Colorless crystals slightly soluble in water, used in doses of fifteen to thirty grains (1.0–2.0 Gm.) as an *antipyretic*.

Acetophenone. *Hypnone. Phenyl-methyl-ketone. Phenylmethylacetone.* C_8H_8O or $C_6H_5CO.CH_3$.—A colorless liquid, boiling at 200° C. (392° F.), sp. gr. 1.035, having a very tenacious, persistent odor, suggesting that of bitter almonds and jasmine, not inflammable, not soluble in water or in glycerin, but very soluble in alcohol, ether, chloroform, petroleum benzine, and also certain fixed oils, especially that of sweet almonds. It is made by distilling a mixture of calcium acetate and benzoate. It was originally proposed as a somnifacient but has been shown to be both uncertain as a hypnotic and toxic in its action. The researches of Regnier, confirmed by Kamensky, have demonstrated that it acts powerfully on nutrition, rapidly lessening the hemoglobin in the blood and causing loss of weight. Norman, however, claims excellent results from hypodermic injections of from five to twelve minims (0.3–0.7 mil) in *insanity*. (*J. M. S.*, xxxiii.) *Dose*, from three to ten minims (0.2–0.6 mil), although Rey has given as much as twenty-three minims (1.5 mils) without producing sleep. It is usually administered in solution in olive or almond oil (1 in 10) either in gelatin capsules or suspended in an emulsion.

Acetophenone-Paramidophenol Ether.—This substance, prepared by G. Vignolo, has been studied physiologically by F. Badano (*Arch. I. C. M.*, xxxvi, 1897), who finds that it powerfully reduces bodily temperature by lessening the heat

production; that in poisonous doses it causes the formation in the blood of methemoglobin, and kills by respiratory paralysis.

Acetopyrine. *Acopyrin. Pyrosal. Antipyrinæ Acetyl-salicylas.*—This occurs as a white, crystalline powder, having an odor resembling acetic acid; melting point 63°–65° C. (145.4°–151° F.); sparingly soluble in cold but freely in warm water; freely soluble in alcohol, chloroform, and in warm toluol; less so in ether and in petroleum benzin. It was originally introduced into medicine by Winterberg and Braun (*W. K. W.*, 1900, No. 39) as combining the activities of antipyrine and acetyl-salicylic acid, into which substances, according to W. Meitner (*St. P. M. W.*, xx, 1900), it is broken up in the stomach; the acetyl-salicylic acid undergoing further decomposition in the intestines. Acetopyrine has been much used as an analgesic in *migraine, sciatica, neuritis,* and also as an antipyretic in *typhoid* and other low fevers. It has also been employed as an antirheumatic, especially in subacute and chronic cases. Goldmann (*All. W. M. Z.*, April, 1901) claims that it is valuable in *bronchitis;* and Bolognesi (*B. G. T.*, March, 1901) recommends it in *gonorrhea.* Its physiological and therapeutic activities are probably those of its constituents. It may be given in *doses* of five to ten grains (0.32–0.65 Gm.), in capsules or suspended in water, and repeated up to thirty grains (2 Gm.) in the twenty-four hours when necessary. In fevers two doses may be given two hours apart about the time of the exacerbation. Its incompatibilities are the same as those of antipyrin, it being also incompatible with iron compounds and acids.

Acetylene. C_2H_2.—Acetylene was first prepared by Berthelot, who obtained it by passing the electric spark between carbon points in an atmosphere of hydrogen. It is now prepared on a large scale by the decomposition of carbides, like calcium carbide, with water according to the reaction:

$$CaC_2 + 2H_2O = C_2H_2 + Ca(OH)_2$$

The product so obtained is almost always contaminated with phosphine, and this should always be removed by washing the acetylene with bromine water. It is produced by a number of other methods involving the reduction of higher hydrocarbon and is produced to a limited extent when the flame of a bunsen burner or gas stove strikes back and burns at the base, giving rise to its characteristic odor, by which the condition of the burner is frequently detected.

Acetylene is a colorless gas of ethereal odor, slightly soluble in water, more readily in alcohol and ether, and most abundantly in acetone. It burns ordinarily with a very smoky flame, but from a burner with a fine slit gives a clear white flame. It forms an explosive mixture with air, also a series of explosive compounds with copper, silver, and other metals. These compounds are in reality the carbides of the respective metals, the formula of the copper compound being Cu_2C_2.

According to Mosso and Ottolengui (*Rendiconti Della R. Academia dei Lincei.*, 1896) acetylene gas is an active poison, causing death in the dog in about one minute through respiratory failure, and always producing a fatal result when present in the air in more than 20 per cent. Rosemann (*A. E. P. P.*, xxxvi, 1895) asserts that its toxic properties are very feeble, and that it has no action upon hemoglobin.

In Moissan's experiments from 40 to 79 per cent. of the vapor was necessary in the air breathed before toxic manifestations were produced (*C. R. A. S.*, cxxi), while Oliver found that no symptoms were caused so long as even a moderate amount of atmospheric air was maintained with the vapor, and when the animal was made to breathe pure acetylene gas the symptoms were very similar to, if not identical with, those of asphyxiation. (*B. M. J.*, 1898, i.)

Calcium carbide, CaC_2, from which acetylene is made, is prepared by melting a mixture of powdered lime and coke dust in an electrical furnace. It is a grayish-brown, dense substance having a crystalline metallic fracture and the specific gravity of 2.26. It evolves a peculiar odor when exposed to the atmosphere, due to the action of moisture which causes partial decomposition with the production of acetylene. When exposed to the air, it lumps, it becomes coated with a layer of calcium hydroxide, which to a great extent protects the interior of the lumps from further deterioration. Calcium carbide is not inflammable and one pound, if pure, yields 5.9 cubic feet of acetylene gas at 18° C. (64.4° F.). The production of calcium carbide throughout the world in 1909 was 280,000 tons, of which the United States and Canada produced 45,000 tons.

Acetylphenylhydrazin. $C_6H_5.(NH)_2.C_2H_3O$. —This substance, first introduced into medicine in an impure form, under the name of *pyrodin,* has since been used in an alleged pure condition under the name of *hydracetin.* It is chemically closely allied to acetanilid, which possesses only one imido-group, (NH); it is, as indicated by its name, hydrazin in which hydrogen atoms are replaced by phenyl and acetyl. It is made by heating together phenylhydrazin and glacial acetic acid, and purifying the product by recrystallization. It forms colorless, inodorous crystals, melting at 128.5° C. (263° F.), soluble in fifty parts of water and readily soluble in alcohol. Guttmann (*Pr. M. W.*, 1889) demonstrated that this substance is a powerful poison, seven and a half grains (0.5 Gm.) being sufficient to kill a rabbit, with a remarkable destruction of the red blood cells. He found it a powerful antipyretic, in *doses* of from one and a half to two and a half grains (0.096–0.16 Gm.) but believes it to be a very dangerous remedy on account of its action on the blood. Externally he considered it to be safe, and allied to pyrogallic acid in its influence upon *skin diseases;* but Basch (*L. L.*, 1890) has seen very violent poisoning from the use of a 10 per cent. ointment, without benefit to the *psoriasis.* On the other hand, Lemoine (*B. M.*, 1889) finds it, in *doses* of three-fourths of a grain (0.048 Gm.), a valuable remedy in the treatment of *hectic fever of phthisis,* reducing the temperature and checking night sweats. When the *dose* of two and a half grains (0.16 Gm.) per day is exceeded, violent symptoms (cyanosis) are apt to be produced.

Acetylsalicyl Amide. *Ethrisin. Arthrisin.*—This occurs as white crystals which are soluble in alcohol and acetic acid. It is intended for the treatment of *rheumatism.*

Achillea. *U. S.* 1870.—The flowering tops of *Achillea Millefolium* L. *Milfoil,* or *yarrow* is a perennial herb, very common both in Europe and America. It is from a foot to eighteen inches in height, and is specifically distinguished by its doubly pinnate, downy, minutely divided leaves, with linear, dentate, mucronate divisions, from which it derived the name of milfoil, by its furrowed stem and involucre, and by its dense

corymbs of whitish flowers, which appear throughout the summer, from June to September. The whole herb has medicinal properties. *Achillea nobilis*, L., and *A. moschata* Jacq., or *Iva* of Europe, are sometimes used as substitutes for *A. Millefolium*.

Both the flowers and leaves of *A. Millefolium* have an agreeable, though feeble, aromatic odor, which continues after drying, and a bitterish, astringent, pungent taste. The aromatic properties are strongest in the flowers, the astringency in the leaves. The plant contains a blue volatile oil, tannin, and a peculiar principle, *achillein*, which was discovered by Zanon. (*Ann. Ch. Ph.*, lviii, 21.) As analyzed by von Planta (*Ann. Ch. Ph.*, clv, 1870) its formula is $C_{20}H_{38}N_2O_{15}$. It occurs in a brownish-red mass of a strongly bitter taste, soluble in water, more feebly in alcohol, and not at all in ether. *Achilleic acid*, also discovered by Zanon, is affirmed by Hlasiwetz to be identical with aconitic acid. The oil, which may be obtained separately by distillation with water, has a beautiful azure-blue color, and the peculiar flavor of milfoil. Schimmel & Co. (*Ber. d. Chem. Ges.*, 1894, p. 50) found its most important constituent to be *cineol*, $C_{10}H_{18}O$. The high boiling blue portion is probably identical with the *azulein* of chamomile oil. *Ivaïn*, $C_{24}H_{42}O_5$, has also been isolated; it occurs as a dark-yellow resinous mass, insoluble in water, readily soluble in alcohol, and producing an intensely bitter solution.

The active principles of the drug are extracted both by water and alcohol. Milfoil is a mild aromatic sudorific tonic and astringent. Pappi states that *achillein* given in divided doses up to from thirty to seventy-five grains (2–5 Gm.) causes marked irregularity of the pulse. The infusion is sometimes used in acute *suppression of the menses*. The *dose* of achillea is thirty to sixty grains (1.9–3.9 Gm.); the volatile oil has been used in doses of ten to fifteen minims (0.6–1.0 mil).

Acitrin.—The ethyl ester of 2-phenyl-cinchoninic acid, $C_9NH_5(C_6H_5)COOC_2H_5$, is found in commerce under the name of *acitrin*. It occurs as a pale yellow, crystalline powder, without odor or taste. It is very slightly soluble in water, but more readily in alcohol or ether. It melts at 61° C. (141.8° F.).

It is used in the treatment of *gouty* and *rheumatic* affections in the same manner as phenyl-cinchonic acid. The *dose* is eight to fifteen grains (0.5–1 Gm.).

Acocanthera.—The Wa Nyika, the Wa Gyriama, and the Wa Kamba tribes of Eastern Africa, and the natives of Obok on the Gulf of Aden, prepare vegetable arrow poisons probably from different species of plants, although the names *wabayo* and *ouabaïo* seem to have been used as synonyms by missionaries and others sending the extract to Europe.

The botanical sources of these arrow poisons are uncertain. It is certain that several species of the apocynaceous genus *Acocanthera* are used for arrow poisons by the natives of Africa. Of the four principal species, *A. schimperi* B. and H. is found abundantly in the highlands of Abyssinia and throughout a great portion of Eastern Africa; *A. deflersii* Schwf., which resembles the last-named species closely, but, according to Schweinfurth, differs in that its flowers are larger, sweet-smelling and pure white, has been found in the neighborhood of Yemen; *A. ouabaïo* Arnaud is a native of Somaliland, and *A. venenata* Don, of South Africa. For details, see *A. de S.*, cvii, p. 1162; abs. in *J. P. C.*, 1889, p. 245. From *Acocanthera abyssinica* is prepared *Shashi-poison* of German Eastern Africa.

In 1882 Arnaud obtained from an unidentified species of the genus Acocanthera (which he named provisionally *A. Ouabaïo*), a crystalline glucoside, and in 1893 Lewin separated from the *Acocanthera Deflersii* an amorphous glucoside.

Owing to the imperfect identification of the plants from which the principles have been obtained, there has been much confusion in the names which have been applied to the principles which various investigators have separated from these arrow poisons. According to Lewin (*B. K. W.*, 1906, p. 1583), there are two glucosides found in the various species of acocanthera, one of which is crystalline, and the other amorphous. The amorphous substance, or, as it is generally known, *amorphous ouabain*, corresponds to the *abyssinin* of Briege (*A. I. P. T.*, 1903), and the *carissin* prepared by Bancroft from the *Carissa ovata* R. Br. (Fam. *Apocynaceæ*), an Australian plant. The *acocantherin* of Frazer he regards as identical with the crystalline ouabain of Arnaud, and probably is isomeric with the amorphous variety. It is generally conceded that the crystalline ouabain is chemically identical with the glucoside discovered by Thoms in the *Strophanthus gratus* (see page 1068). Its action seems to be precisely the same as that of strophanthus. Ouabain was apparently first employed clinically by Stadelmann (*B. K. W.*, 1906, vol. xliii, p. 1586), and has more recently been used by others with more or less success in the treatment of various forms of *cardiac weakness*. Stadelmann used an amorphous glucoside prepared by Merck from the wood of the *Acocanthera Schimperi*, in *doses* of from one three-hundredth to one two-hundredth of a grain (0.0002–0.0003 Gm.) three times a day.

Acoine. $HCl.C{=}NC_6H_4O(C_2H_5)$, $NHC_6H_4O(CH_3)$, $NHC_6H_4O(CH_3)$.

Di-para-anisyl-mono-phenetyl-guanidine-hydrochloride.—A white, crystalline powder, melting point 176° C. (348.8° F.), and soluble in water (six parts to one hundred). It is incompatible with iodine or alkaline iodides. Acoine was introduced as a local anesthetic by Trolldenier. (*Th. M.*, xiii; also *Zeit. T. M.*, 1901.) It has been specially used by ophthalmologists in a 1 per cent. aqueous solution, stronger solutions being very irritant or even corrosive. It is not absorbed through a normal conjunctiva, but when the epithelial covering is destroyed, or when the drug is injected into the sub-conjunctival tissues, it is said to act more powerfully than cocaine, and to be specially efficacious in the relief of deep-seated ocular pains. It is also actively antiseptic, the 1 per cent. solution remaining free from bacteria. Acoine has also been used with asserted excellent results in dentistry and in operations upon the nose. For dental purposes a 2 per cent. solution is preferred. One per cent. of common salt should be added to hypodermic solutions, which are preferably made with distilled water.

Acrolein. *Acrylic Aldehyde. Allyl aldehyde.* C_3H_4O. $CH_2{=}CH.CHO$.—Acrolein, a decomposition product of glycerin or glycerides, is a fluid which emits an intensely pungent odor, is soluble in two or three parts of water, and boils at 52.5° C. (126.5° F.). It is asserted by E. Koch and G. Fuchs (*Cb. B.*, 1899, xxvi) to be a valuable bactericide, but its exceedingly disagreeable odor and

tendency to undergo decomposition have prevented its coming into use. It is the cause of the irritating vapors given off when glycerin or fats are heated in air to the point of decomposition.

Actæa. *Actæa spicata*, L. *Baneberry. Herb Christopher. Radix Christophorianæ. Racine de Saint Christophe*, Fr. *Christophswurz, Wolfswurz*, G.—This is a perennial herbaceous plant (Fam. *Ranunculaceæ*) growing in the woods of mountainous regions from Japan to Central Europe as well as in Siberia. Its dark-brown, bitterish, somewhat acrid root resembles that of *Helleborus niger*, for which it is said to be occasionally substituted. It is an active emeto-purgative, capable of producing, when in overdose, dangerous effects. There are two American species which probably have medicinal properties similar to those of *A. spicata*,—namely, *A. alba* (L.) Mill., or *white cohosh*, and *A. rubra* (Ait.) Willd., or *red cohosh*, distinguished by the color of their berries. *Actæa racemosa* was the former name of the official *Cimicifuga racemosa*. (*Proc. A. Ph. A.*, 1858.)

Actinium.—This was discovered in 1899 in uranium pitch blend by De Bierne, and is asserted to be identical with the *anemium* of Giesel (De Bierne, *C. R. A. S.*, 1899, cxxix and 1904, cxxxix, p. 538). It has been used by Czerny and Caan (*M. M. W.*, 1911, p. 1801) in the treatment of various forms of *cancer*. They inject intramuscularly from one-sixth to two grains of actinium suspended in normal salt solution (0.01–0.12 Gm.).

It occurs commercially as a brownish-red powder, insoluble in water, but soluble in strong nitric or hydrochloric acids.

Actinomeris. *Verbesina helianthoides* Michx. (*Actinomeris helianthoides* Nutt.) (Fam. *Compositæ.*)—At one time known as *Gravel Weed, Diabetes Weed*, now known as *Sunflower Crownbeard*. It is a perennial herb growing in the thickets and on dry prairies from Ohio and Missouri to Texas and Georgia. The root is said to be largely used in Upper Georgia in *dropsy* and *chronic cystitis*. *Dose* of infusion (one ounce to a pint), one fluidounce (30 mils).

Adalin. *N. N. R.* 1917.—This remedy, which is *bromine-di-ethyl-acetyl-carbamid*, $C(C_2H_5)_2BrCONHCONH_2$, is a white, crystalline powder with a slightly bitter taste, almost insoluble in water. It melts at 116° C. (240.8° F.). According to Impens (*Ther. Geg.*, 1912, p. 158), it is slowly absorbed and partially broken up in the system, being eliminated both as an inorganic bromide and in the original form. It was introduced into medicine with the idea that it would combine the sedative effects of bromine with the narcotic action of the aliphatic series. The dose of bromine which is administered under this circumstance is, however, so small that it seems improbable that it could seriously modify the action of the drug, and the conclusions of Takeda (*A. I. P. T.*, 1911, xxi, p. 203), that its effects are due to the whole molecule, are probably correct. It is used in medicine as a somnifacient, nerve sedative and analgesic. As a hypnotic it is frequently useful in the milder forms of *sleeplessness*, but in severe cases is uncertain in its effects. The somnifacient dose should be from fifteen to twenty grains (1–1.3 Gm.). Adalin differs markedly from most of the other aliphatic narcotics in that it possesses distinct analgesic properties and is useful in *neuralgia* and various forms of neurotic *pains*. As a general nerve sedative it has been employed in *neurasthenia, hysteria, epilepsy, whooping cough*, and a host of other conditions accompanied with hyper-irritability of the central nervous system. The *dose* in these conditions is ordinarily from five to fifteen grains (0.2–0.9 Gm.). According to Finck (*Med. Klin.*, 1910, p. 1860), it may be given safely up to forty-five grains (2.9 Gm.) in the twenty-four hours.

Adamon.—Adamon is the dibromo-dihydro cinnamic acid ester of borneol. It is used as a sedative in *neurasthenia, hysteria* and other conditions of nervous erethism. According to Oppenheim (*D. M. W.*, 1913, p. 1103), it is especially valuable as an anaphrodisiac in *nymphomania*. *Dose*, eight to twelve grains (0.5–0.7 Gm.).

Adansonia. *Adansonia digitata*, L. *Baobab.*—A tree of enormous magnitude, belonging to *Bombaceæ*. It is a native of Africa, extending quite through that continent from Senegal to Abyssinia, and has been introduced into the West Indies. The leaves and bark of this tree abound in mucilage, and have little odor or taste. By the Africans the leaves are used as a diaphoretic, and the subacid pulp of the fruit in *dysentery*. Under the name of *cream-of-tartar tree* various trees have been described. Their fruits contain, or have been supposed to contain, potassium bitartrate. The most important of these is the *Adansonia Gregorii* F. Muell., of North Australia. Another cream-of-tartar fruit is yielded by a tree of South Africa, which, according to E. M. Holmes, is probably the *Adansonia madagascariensis* Baillon. This fruit has been examined by E. J. Millard (*P. J.*, April, 1890), who found that it contains no cream of tartar at all. It is probably identical with a cream-of-tartar fruit examined by F. L. Slocum. (*A. J. P.*, 1880). Heckel and Schlagdenhauffen (*Nouv. Rem.*, xxi, 487) have found in the fruit of the *Adansonia digitata* as much as 2 per cent. of free tartaric acid and 12 per cent. of potassium bitartrate. Duchassaing, of Guadeloupe, West Indies, and Pierre, of France, commended the bark of *A. digitata* highly as an antiperiodic. (*A. G. M.*, 3e sér., xxiii, 535.) It is said to be acceptable to the stomach, and to produce no other observable physiological effect than increase of appetite, increased perspiration, and perhaps diminished frequency of pulse. An ounce may be boiled in a pint and a half of water to a pint, and the whole taken in a day. (*J. P. C.*, 3e sér., xiii, 412 and 421.)

Adenanthera. *Adenanthera pavonina* L. *Zangavara.*—Rochebrune (*Toxicologie Africaine*) states that he has obtained from this plant a crystalline principle which resembles in its activity physostigmine, but does not affect the muscles.

Adenia. *Adenia venenata* Troost.—A climbing passion-flower of Africa, said by Schweinfurth to be used as a vesicant. (*P. J.*, March, 1874.) The *Adenium hongkii* is employed by the natives of the Soudan as an ordeal poison. Perrott and LePrince (*P. J.*, 1910, lxxxiv, p. 82) have separated an active principle which is neither glucosidal nor alkaloidal, and which has a strophanthin-like effect.

Adhatoda. *Br. Add.* 1900. (Fam. *Acanthaceæ.*)—The fresh and dried leaves of *Adhatoda Vasica* Nees. (*Justicia Adhatoda*, L.) "The fresh leaves are four or six inches (about ten to fifteen centimeters) long and about an inch and a half (nearly four centimeters) broad, they are opposite lanceolate, entire short petiolate, taper-pointed, smooth on both sides. The dried leaves are of a dull brownish-green color which becomes much

lighter when the leaves are powdered. They have a strong characteristic tea-like odor and a bitter taste." *Br. Add.*, 1900.

The leaves are stated to contain an alkaloid, *vasicine*, and an organic acid, *adhatodic acid* (see *Pharmacog. Indica*, vol. iii). Vasicine, isolated by Hooper, is soluble in water, sparingly in benzin and carbon disulphide, readily soluble in ether and chloroform. The claim is made for it that it exerts a powerful toxic influence upon lower forms of vegetable and animal life, and is not poisonous to the higher animals. The leaves are stated to be actively poisonous to frogs and are considerably used in India as an expectorant and antispasmodic, especially in the treatment of *asthma*. The Br. Add. recognized the *liquid extract* (*Extractum Adhatodæ Liquidum*, Br. Add., 1900), made with alcohol and given in doses of from twenty to sixty minims (1.3–3.75 mils); the freshly *expressed juice* (*Succus Adhatodæ*, Br. Add., 1900), *dose*, from one to four fluidrachms (3.75–15.0 mils); the *tincture* (*Tinctura Adhatodæ*, Br. Add., 1900), *dose*, from one-half to one fluidrachm (1.8–3.75 mils).

Adiantum. *Maidenhair.*—Tradition has attributed to various species of this genus of ferns valuable properties in chronic pulmonic *catarrhs*. *A. pedatum*, L., of America, *A. Capillus-Veneris*, L., of Europe, *A. lunulatum* Burm., of India, are the most important of these alleged medicinal species. The European species is sometimes employed on the Continent as an emmenagogue under the name of *polytrichi*, *polytrichon*, or *kalliphyllon*, and is given in the form of infusion, sweetened with sugar or honey, and a syrup prepared from it is said to be popular in France under the name of *sirop de capillaire*, and is official in the French Codex.

Adonis. *N. F. IV. Vernal Pheasant's Eye. Sommerteufelsauge*, G.—It is official in the N. F. IV, in which it is defined as "the dried, overground portion of *Adonis vernalis* Linné (Fam. *Ranunculaceæ*), without the presence of more than 5 per cent. of foreign matter." This ranunculaceous plant of Northern Europe and Asia has long been used as an abortifacient, while its rhizome sometimes occurs in commercial black hellebore as an adulteration. Linderos examined the leaves and found in them 10 per cent. of *aconitic acid*. (*Ann. Ch. Ph.*, 1876, 340.) Cervello, in 1882, obtained from the plant a glucoside, to which he gave the name of *adonidin*. For improved method of preparation, see *P. J.*, vol. xvi, 145, and *A. J. P.*, 1887, 609. This glucoside occurs in the form of a somewhat hygroscopic, canary-yellow powder of an intensely bitter taste; soluble in water, alcohol, and in amyl alcohol; insoluble in anhydrous ether, chloroform, oil of turpentine, or petroleum benzin. Its reaction is neutral. It reduces Fehling's solution, if previously heated with a few drops of hydrochloric acid. It exists in small quantities in all portions of the plant. For further details as to reactions, see *P. J.*, xv, 145. Podwyssotzki found commercial samples of adonidin to be mixtures of the active principle with other constituents of the plant. He gives the name of *picroadonidin* to the active principle, which he describes as an amorphous glucoside having an excessively bitter taste, possessing the properties of a cardiac poison in the highest degree, and being easily soluble in water and alcohol and entirely soluble in ether. (*P. J.*, xix, 1888, 346.) According to Fuckelman, confirmed by Mercier (*Nouv. Rem.*, 1914), commercial adonidin is a mixture of a neutral body with a hemolytic acid, *adonic acid*. Cervello states (*A. E. P. P.*, xv) that adonidin exists also in the *Adonis cupaniana* of Southern Europe, and F. Borgiotti affirms the value of *A. æstivalis*, L., in heart affections. (*D. M. Ztg.*, Aug., 1888.) Tahara asserts that the glucoside of *Adonis autumnalis*, L., is distinct, and calls it *adonin* ($C_{24}H_{40}O_9$) (*Ber. d. Chem. Ges.*, xxiv), while Y. Inoko (*A. E. P. P.*, xxviii) affirms that the glucoside of *A. amurensis* of Japan is also peculiar, and assigns to it the formula $C_{30}H_{40}O_9$, allied to adonidin, but much less powerful.

Merck has described an additional crystalline principle, which fuses at 102° C. (216° F.), is very soluble in water and warm alcohol, and crystallizes in clear needle-like prisms. It has a neutral reaction, does not reduce Fehling's solution, and is not colored brown by alkalies. Its analysis seems to indicate a formula $C_5H_{12}O_5$, and Merck considers that it is a hitherto undescribed pentatomic alcohol, and calls it *adonite*. Whether it be identical with the *adonidulcite* announced in a preliminary communication by Podwyssotzki shortly before his death, Merck is not able to state, as no details of fusing point, formula, or chemical reactions were given by the former. (*M. Bull.*, Jan., 1893.) E. Fischer (*Ber. d. Chem. Ges.*, 1893, 633) confirms the formula $C_5H_{12}O_5$ given by Merck, as well as the statement that it is a pentatomic alcohol; by oxidation with sodium hypobromite it is changed into *ribose*, $C_5H_{10}O_5$, which treated with sodium amalgam again yields adonite.

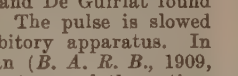
The National Formulary description is as follows: "Glabrous, with the exception of the younger portions, which may be slightly grayish-puberulent; stems from 15 to 50 cm. in length, thick, but soft and weak; shining, simple or branched, the branches mostly from near the base and similar to the main stem; naked below, except for some scale-like leaf-vestiges, densely leafy above; leaves from 2 to 4 cm. in length and two-thirds or more as broad, pinnately divided into several segments, the larger of which are again divided, the ultimate segments being narrowly linear, and acute; flowers terminal, yellow but usually drying to a cream color, from 3 to 6 cm. in breadth; sepals five, green or grayish-puberulent, more than half the length of the petals, oblong, obtuse, finely nerved; petals from five to twenty, oblong, obtuse, finely nerved; stamens indefinite; pistils numerous, in fruit forming an ovoid, obtuse, dense head of ovoid akenes, which are tipped with the very small, persistent styles. Odor faint; taste bitterish, afterward somewhat acrid. The powdered drug is grayish-green and, when examined under the microscope, exhibits numerous fragments of pith parenchyma, the cells with few simple pores, up to 0.05 mm. in width and 0.25 mm. in length; groups of long narrow sclerenchyma fibers, mostly with lignified walls from 0.005 to 0.007 mm. in thickness and having a few rounded or oblique simple pores; tracheæ spiral or with bordered pores and up to 0.017 mm. in width; epidermal cells from the stem and petiole, elongated in surface view and with elliptical stomata, the latter about 0.064 mm. in length; fragments of the epidermal tissue from the lamina of the leaf, composed of finely striated cells with wavy, vertical walls; associated with broadly elliptical stomata, the latter up to 0.047 mm. in length; brownish colored fragments from the scales at the base of the stem, composed of elongated cells with somewhat rounded ends and yellowish-brown walls; starch grains

and calcium oxalate crystals few or absent. Adonis yields not more than 12 per cent. of ash."

Adonidin belongs physiologically to the digitalis group. Although in Hare's experiments (*T. G.*, 1886) the frog's heart was arrested in diastole. Cervello (*A. E. P. P.*, xv) and De Guirlat found that the arrest is systolic. The pulse is slowed by stimulation of the inhibitory apparatus. In the experiments of Henrijean (*B. A. R. B.*, 1909, xxiii, p. 363) in the early stages of the action, electrical stimulation of the pneumogastric nerve produced an unwonted degree of retardation of the pulse rate, which would indicate an increased excitability of the peripheral ends of the nerves. All investigators are in accord that the slowing of the pulse is to a large extent abolished by section of the vagi, so that the inhibitory influence must be largely also of central origin. There occurs also a pronounced rise of the blood pressure, which, according to Hare, is due partly to a stimulant action upon the heart, and partly to an effect upon the vasomotor mechanism. In the more exact experiments of Henrijean, vaso-constriction appeared only late in adonidin poisoning. After large toxic doses, the heart becomes irregular, and the blood pressure falls. According to Kakowski (*A. I. P. T.*, xv, p. 21), adonidin differs from most of the other digitalis group in that it dilates the coronary arteries, while most of these drugs produce constriction.

Adonis vernalis was introduced as a cardiac tonic by Bubnow in 1879. Clinical experience confirms the conclusion of the pharmacologist, that it resembles digitalis in its action, and is a useful agent in the treatment of chronic *heart disease*. The advantages which have been claimed for it are, that it is more prompt in its action, and that it manifests less cumulative tendency than digitalis, but it appears to be less certain in its effect. Bechterew asserts that it is a useful remedy in *epilepsy* when used in conjunction with the bromides. The *dose* of adonis vernalis is from two to ten grains (0.12–0.6 Gm.), which may be given in the form of an infusion. The glucoside adonidin may be given in doses of one-twelfth to one-fourth of a grain (0.005–0.015 Gm.).

Æsculus. *Horse-chestnut.*—Chestnut (*Æsculus Hippocastanum*, L.) said to have been originally a native of Asia, but introduced about the middle of the sixteenth century into Europe, whence it has spread to this country. It is to this species that this article especially applies, though it is probable that any medicinal properties which the tree may have are shared by the other species of the genus. The seed or nut abounds in starch, but its bitter, disagreeable taste has prevented its general use as a food, although as long ago as 1856 starch was made from it in France, and recently a pleasant and nutritious article of diet is said to have been prepared by removing its bitter principle by means of alcohol. For analysis of the oil it contains, see Stillesen, *Proc. A. Ph. A.*, 1909, lvii, p. 201. In the leaves Rochleder found *quercitrin*, and a bitter principle, *esculin* (*æsculin*); and in the capsules of the fruit a peculiar acid, *capsulæsic acid* (*J. P. C.*, May, 1859; Aug., 1860). (For Rochleder's method of extracting esculin, see *U. S. D.*, 18th edition; for a second process, see *A. J. P.*, xliv, 400.) Esculin is in shining, white, prismatic crystals, inodorous, bitter, but slightly soluble in cold water, more soluble in boiling water, and very readily so in boiling alcohol and in alkaline solutions. Its solution, which is fluorescent, is precipitated by lead subacetate, and its formula, according to Schiff, is $C_{15}H_{16}O_9 + 1\frac{1}{2}H_2O$. When treated with dilute sulphuric acid, it is converted into grape sugar and a substance called *esculetin*, $C_9H_6O_4$, which is now known to be a *dioxycoumarin*,



Tannin is found in all parts of the tree, including the leaves as well as the bark and fruit. According to Rochleder, when pure, it is white and soluble in water, alcohol, and ether; becomes red by the absorption of oxygen; colors ferric salts green, but violet on the addition of a little alkali; fluorescent when it is in alkaline solution; in concentrated solution is precipitated, at least partially, by sulphuric, hydrochloric, and metaphosphoric acids, but not by acetic acid, and forms also, with potassium and sodium sulphites and ammonium sulphide, precipitates which are readily dissolved by dilute acetic acid. (*J. P. C.*, Jan., 1868, 72.)

The powdered kernel of the nut is a sternutatory. The extract of the wood has been used in dyeing silk black. The fixed oil, extracted from the kernels by ether, has been employed in France as a topical remedy in *rheumatism;* and the bark as an antiperiodic in doses of half an ounce (16 Gm.) in the twenty-four hours, given in the form of decoction. The flowers are stated to contain quercitrin. In the United States a decoction of the leaves is popularly employed for *whooping cough*, and to the seeds themselves, when "carried in the pocket of the patient," is attributed the marvellous property of curing *hemorrhoids*, *rheumatism*, etc. Esculin has also been administered in *malarial disorders*, in fifteen-grain (1 Gm.) *doses* repeated once during the intermissions. (*Ann. Thér.*, 1859, 1860.) The glucoside esculin has the property, like other fluorescent substances, of absorbing ultra violet rays which are then gradually given off. Because of these properties, it is used on the one hand, as a protective against the effects of sunlight and on the other as a means of continuing the effect of heliotherapy. Thus Freund has found it useful not only against *sunburn*, but as a prophylactic against *snow blindness* (*Zeit. f. Neuere Physikal. Med.*, 1908, ii), and Graham (*L. L.*, 1905, ii, p. 1769) recommends it in the Finsen light treatment of *lupus vulgaris* and similar conditions. For this purpose he injected five minims (0.3 mil) of a 2 or 3 per cent. solution immediately beneath the skin in the region to be treated by the light. Under the name of *zeozon* and *ultra-zeozon* there are upon the market pastes whose exact compositions are not stated but which are claimed to contain oxyderivatives of esculin.

The fruit of the *Æsculus pavia* L., or *Red Buckeye* of the Southern United States, is said to be an active convulsant. E. C. Batchelor (*A. J. P.*, xlv, 144) found in the cotyledons of the seeds about 2½ per cent. of a peculiar glucoside. *Æsculus glabra* Willd., the *Ohio Buckeye*, is asserted to be useful in *portal congestion*. (*N. P.*, ii, 21.)

Æthusa. *Fool's Parsley. Æthusa Cynapium*, L. (Fam. *Umbelliferæ.*)—A fetid herb naturalized from Europe and growing in waste places or cultivated grounds in the northern United States and Canada. In 1859, Walz stated that the fruit of the *Æthusa Cynapium* contains a volatile base similar to coniine. This statement has been confirmed by Power and Tutin (*J. Am. C. S.*, 1905, xxvii) who recovered, besides various inert mat-

ters, about one forty-thousandth of 1 per cent. of the volatile alkaloid. This plant has been variously attributed with poisonous properties, but Harley (*P. J.*, 1880, xi, p. 43) denies any noxious quality, and, in the experiments of Power and Tutin, the extract from five hundred grammes of the dry herb caused in a small dog, vomiting and salivation, but the animal entirely recovered.

Afridol. *Sodium hydroxymercuric toluylate. N. N. R.* 1916. $C_6H_3(CH_3)(COONa)HgOH$ 2:3:1. —This is an odorless, tasteless white powder, difficultly soluble in neutral or acid media, but soluble in ammoniacal solution containing ammonium chloride. It is said to be of value for rendering parts of the body antiseptic for surgical operations. It has also been recommended in the treatment of parasitic skin diseases, *acne*, *sycosis*, etc., the afridol soap being proposed for this purpose.

Agaric. *Agaricus Albus. White Agaric. Larch Agaric. Touchwood. Spunk. Tinder. Fungus purgatif*, Fr. *Larchenschwamm*, G.—It is defined in the National Formulary IV as "the dried fruit body of the fungus *Polyporus officinalis* Fries (Fam. *Polyporaceæ*) [growing on one or more species of *Pinus* Linné, *Larix* Adanson, and *Picea* Link (Fam. *Pinaceæ*)], deprived of its outer rind, and without the presence of more than 10 per cent. of foreign matter." The term Agaric is more properly applied, however, to the fungi of the genus Agaricus, but most medical writers and the N. F. limit it to the fungus from *Polyporus officinalis* Fries (*Boletus laricis* Jacquin; *B. purgans* Persoon), which is found upon the old trunks of the European larch and upon *Larix sibirica* Ledebour, of Asia. The same species is found on various coniferous trees in some of the western United States and British Columbia. It is of various sizes, from that of the fist to that of a child's head, or even larger, hard and spongy, externally brownish or reddish; but, as found in commerce, it is deprived of its exterior coat, and consists of a light, white, spongy, somewhat farinaceous, friable mass, which, though capable of being rubbed into powder upon a sieve, is not easily pulverized in the ordinary mode, as it flattens under the pestle. That which is most esteemed is said to be brought from Siberia; but it is probably produced wherever the European larch grows. It is described in the N. F. as in "light, fibrous, somewhat spongy pieces of irregular shape; grayish-white to pale brown externally; yellowish and resinous internally; fracture tough, fibrous; friable but difficult to powder. The powdered drug, examined under the microscope, shows numerous non-septate, narrow, mycelial threads and many cubical crystals of calcium oxalate from 0.01 to 0.02 mm. in diameter. It yields to boiling alcohol not less than 50 per cent. of a resinous extract. Agaric yields not more than 2 per cent. of a white ash, rich in phosphates." *N. F.* Wm. M. McPheeters (*St. L. M. S. J.*, x, 421) found a specimen brought from the Rocky Mountains decidedly cathartic in *doses* of twenty-four grains (1.6 Gm.).

Agaric has a sweetish, very bitter taste. It owes its medicinal virtues to *Agaric acid* (*N. N. R.*, 1916), which is also called *laricic* and *agaricinic acid*. This is a tribasic acid, $C_{19}H_{36}OH(CO OH)_3 + 1\frac{1}{2}H_2O$, occurring as an odorless, tasteless, micro-crystalline powder, melting at 141.5° C. (286.5° F.). According to J. Schmieder, agaric contains a small amount of soft resin, $C_{15}H_{20}O_4$, extracted with petroleum benzin, and from 4 to 6 per cent. of a fatty body, which is made up of (1) *agaricol*, $C_{10}H_{16}O$, fusing at 223° C. (433.4° F.); (2) *phytosterin*, $C_{26}H_{44}O$; (3) solid hydrocarbons, $C_{23}H_{46}$ and $C_{29}H_{54}$; (4) cetyl alcohol, $C_{16}H_{33}.OH$; (5) a liquid aromatic alcohol, $C_9H_{18}O$; (6) a fatty acid, $C_{14}H_{24}O_2$; and (7) ricinoleic acid, $C_{18}H_{34}O_3$. (Schmidt, *Lehrbuch der Pharm. Chem.*, ii, 3te Auf., 1528.) J. D. Riedel has produced two phenetidides of agaric acid, for which antipyretic and anhidrotic properties are claimed. (*Ph. Ztg.*, xlvii.) *Sodium, Lithium* and *Bismuth agaricinates* have been prepared and introduced into medicine.

According to Hoffmeister (*A. E. P. P.*, 1889, xxv, p. 189), in a moderate dose, agaric acid has no effect upon the system, except to paralyze the nerves of the sweat glands. When given in very large doses, it produced primary excitation of the medulla, followed by paralysis, increasing at first the blood pressure and the respiratory rate, which was followed by diminishing activity in both. The large doses also acted as an irritant to the stomach and intestine, causing vomiting and purging. The depressant action shown on the sweat glands was not shared by the other glands of the body. McCartney (*J. P. Ex. T.*, 1917, x, 83) offers the remarkable theory that its antihydrolic action is due to spasm of the muscular layer of the skin. The most important use of agaric is in the treatment of the *colliquative sweats* of wasting conditions, such as *phthisis*. Its value in these conditions has been abundantly confirmed by clinical experience. Aside from the solanaceous drugs, it is probably the most reliable remedy that we possess for this purpose. Rosenbaum has found the *fluid extract of agaric* (*Med. Klin.*, 1906) of service in various catarrhal conditions of the alimentary tract, even in *intestinal tuberculosis*.

Under the name of *agaricin* are marketed preparations containing the active *agaric acid*, with larger or smaller amount of impurities. The *dose* of the pure principle is from one-sixth to one-half of a grain (0.01–0.03 Gm.).

Thoerner obtained from *Agaricus atramentosus* crystalline, dark-brown scales, which he believed to be *dioxykinon*. (*Ber. d. Chem. Ges.*, 1878, 533.) According to T. L. Phipson, *Agaricus ruber* contains a rose-red coloring matter, *ruberin*, which appears bright-blue by transmitted light; being soluble in water, it is washed out of the head of the fungus by a heavy fall of rain. Ether extracts from the fungus a yellowish-white alkaloid, *agarythrine*, which has a bitter, afterwards burning taste, somewhat like aconitine; its chloride is soluble, but the sulphate insoluble in water, the latter dissolving in alcohol; it dissolves in nitric acid with red color, and is colored red by chlorinated lime and afterwards bleached. On agitating the solution of the alkaloid with ether, it is oxidized by the air to a red coloring matter, which is probably the cause of the red color of the surface of the fungus. (*Chem. News*, 1882, 199.) An agaric growing on the *Larix leptolepis*, and used in Japan as a sacred medicine under the name of *Toboshi* or *Eburiko*, has been found by Y. Inoko to contain agaric acid. (*Sei-I-Kwai*, April, 1891.)

Fungus chirurgorum. Boletus chirurgorum, Wundschwamm, G.—*Surgeon's agaric* is the product of *Polyporus fomentarius* (L.) Fries, which is found upon the oak and beech trees of Europe. It is shaped somewhat like the horse's foot, with a diameter of from six to ten inches. It is soft like velvet when young, but afterwards becomes hard and ligneous. It usually rests immediately upon

the bark of the tree, without any supporting footstalk. On the upper surface it is smooth, but marked with circular ridges of different colors, more or less brown or blackish; on the under surface, it is whitish or yellowish, and full of small pores; internally it is fibrous, tough, and of a tawny-brown color. It is composed of short tubular fibers compactly arranged in layers, one of which is added every year. The best is that which grows on the oak, and the season for collecting the fungus is August or September. It has neither taste nor odor. Among its constituents, according to Bouillon-Lagrange, are extractive, resin in very small proportion, nitrogenous matter also in small quantity, potassium chloride, and calcium sulphate, and in its ashes are found iron, and calcium and magnesium phosphate. It is prepared for use by removing the exterior rind or bark, cutting the inner part into thin slices, and beating these with a hammer until they become soft, pliable, and easily torn by the fingers. In this state it was formerly much used by surgeons for arresting *hemorrhage*, being applied with pressure. *P. ignarius* (L.) Fries and *P. marginatus* Fries yield similar products.

When prepared polyporus (so-called agaric) is steeped in a solution of nitre, and afterwards dried, it constitutes *spunk*, *punk*, or *tinder*, the *amadou* of the French, which occurs in flat pieces, of a consistence somewhat like that of very soft, rotten buckskin leather, of a brownish-yellow color, capable of absorbing liquids, and inflammable by the slightest spark. It is said to be prepared also from various other species of *Polyporus*, as *P. ungulatus*, *P. ribis*, etc.

Agathin. $C_6H_5.N(CH_3).N : CH.C_6H_4.OH$. *Salicyl-α-methyl-phenyl-hydrazine.*—This is obtained by the reaction of salicylic aldehyde upon α-methyl-phenyl-hydrazin. It is a yellowish crystalline substance, without odor or taste, is insoluble in water, soluble in alcohol and ether and melts at 74° C. (165.2° F.). It was proposed as a remedy by Israel Roos, and is said by E. Rosenbaum to act like salicylic acid. Although excellent results (see *D. M. Ztg.*, 1892, Nos. 50, 93) have been claimed for it in *neuralgia* and *rheumatism*, without unpleasant effects other than headache, in trials by H. C. Wood it did not seem serviceable. *Dose*, from five to ten grains (0.3–0.65 Gm.).

Agave. *Agave americana*, L. *American Agave. American Aloe. Maguey.* (Fam. *Amaryllidaceæ.*)—An evergreen succulent plant, indigenous to Florida, Mexico, and other parts of tropical America, and largely cultivated, chiefly for hedges, in the south of Europe, especially in Spain. Although the *Agave americana* is the best known form, botanists have described fifty species of the genus, which are indigenous to South America and the southern portions of North America, and many of which contribute to the economic products produced in that country from the agave plant. The number of these products is very great. *Sisal grass* or *sisal hemp* and *Tampico hemp*, also known as *Pita hemp* or *Pita fiber*, are the most important of the various fibers obtained from the agave leaves, though a number of other forms are locally known in Mexico. From a number of species of *Agave*, are produced in Mexico, large quantities of fermented liquors, known as *pulque*, and distilled liquors known as *mescal* or *tequila*. All of the pulque agaves have thick leaves. When they are about to bloom the central bud is cut out, leaving a large cavity into which the sap (*aguamiel* or *honey water*) exudes rapidly. At first clear green, yellowish or whitish, this sap soon by fermentation becomes milky and acquires a cider-like taste or, if the process is allowed to go on, is rapidly converted into vinegar. *Pulque* is said to contain about 7 per cent. of alcohol, and is very largely used as a beverage by the Mexicans, but its odor and taste are disagreeable to unaccustomed palates. The juice has in it an optically inactive reducing sugar, *agavose*, $C_{12}H_{22}O_{11}$. The leaves and roots and stocks of the agave contain saponin and are used in Mexico in the place of soap. The fresh juice is said to be laxative, diuretic, and emmenagogue, and in doses of two fluidounces (60 mils) useful in *scurvy*. The leaves are said to be used as counter-irritants, and Lenoble has found in them an acrid volatile oil. (*J. P. C.*, xv.) *Agave Gum* has been compared to gum arabic, but differs in containing a much larger proportion of lime, and in being only partially soluble in water, the soluble portions resembling pure gum, but the larger insoluble portions having all the characteristics of bassorin.

Agave virginica, L., which grows in our Southern States, is known in South Carolina by the name of *rattlesnake's master*, has a very bitter root, which is used, in the form of tincture, in *colic*.

Agelæa. *Agelæa Lamarckii* Planch.—Under the name of *Cephan-Mahi*, *Soandrou*, *Vahé-mainti*, this African plant is used as an anti-blenorrhagic. According to Rochebrune (*Toxicologie Africaine*), it contains a poisonous glucoside, *agelætoxine*.

Ageratum. *Ageratum conyzoides* L. (Fam. *Compositæ*), a Brazilian plant commonly known in cultivation as ageratum, is said by Barker Smith (*C. D.*, May 15, 1876) to be used as an emmenagogue.

Agrimonia. *Agrimonia Eupatoria*, L. *Common Agrimony. Herba Agrimoniæ. Aigremoine, Eupatoire des Grecs*, Fr. *Odermœning, Leberklette*, G. (Fam. *Roscaceæ.*)—This species of agrimony is a perennial herb, indigenous to Europe, and while somewhat resembling one or more species of Agrimonia growing in the United States, it differs, according to Britton, markedly in foliage and fruit from any of our species. Its stem, which rises from one to three feet in height, is hairy, furnished with interruptedly pinnate leaves, and terminated by a long simple spike of yellow flowers. Both the herb and root have been employed. A volatile oil may be obtained from the plant by distillation. Agrimony is a mild astringent and alterative. It also contains a bitter principle. *Dose*, one drachm (3.9 Gm.) or more. (See 16th ed., U. S. D.)

Ailanthus. *Ailanthus glandulosa* Desf. *Tree of Heaven. Chinese Sumach. Tree of the gods. Ailanto. Götterbaum*, G.—This well-known shade-tree, belonging to the Fam. *Simarubaceæ* in its general aspect and the character of its foliage, appears like a gigantic sumach, and was at one time considered to be a Rhus. In France it is cultivated for the sake of its leaves, upon which the Chinese silkworm is fed, and is known by the name of *Japan varnish* (*vernis de Japon*), from its having been mistaken for the true Japan varnish tree, which is a species of Sumach. (*P. J.*, vii, 370.) The powdered bark is of a greenish-yellow color, possesses a strong, narcotic, nauseating odor, in the fresh condition, and has a strongly bitter taste. When chewed, it is said to produce a general uneasiness, a sense of increasing weakness,

vertigo, cold sweats, with shivering and a sensation of nausea. It has been found to contain lignin, chlorophyll, a yellow coloring principle, a gelatinous substance (pectin), quassiin, an odorous resin, traces of a volatile oil, a nitrogenous fatty matter, and several salts. F. H. Davis detected traces of a crystallizable organic acid, but no alkaloid or glucoside. (*A. J. P.*, 1885, 600.) By the action of alcohol, there is obtained from the bark an *oleoresin* which has the consistence of tar, a very dark greenish-brown color, and in a high degree the odor and taste of the bark. Hetet found the bark to produce in dogs copious stools and the discharge of worms. The resin purged, but rarely acted as an anthelmintic. The powdered bark has been used successfully against the *tapeworm*. In China the bark is very popular as a remedy in *dysentery* and other *bowel complaints*. (*A. J. P.*, 1874, 276; *P. J.*, vii, 372.) *Dose*, from seven to thirty grains (0.45–2.0 Gm.). The oleoresin produces the same effect in a somewhat smaller dose, and keeps better than the bark, which loses its powers with age. (*J. P. C.*, March, 1859, 163.)

In India the bark of the *Ailanthus excelsa* Roxb. is used as a bitter tonic. It occurs in rough, dirty-green pieces. Narayan Daji found in it a bitter uncrystallizable principle and a bitter nitrogenous acid, *ailanthic acid*, to which he attributes medicinal virtues. (*P. J.*, Aug., 1870, Oct., 1876, June, 1877.) This acid is not used medicinally in this country.

Air. *Liquid Air.*—This substance is produced commercially for the manufacture of oxygen and nitrogen. In its manufacture air is subjected to a pressure of 200 atmospheres, then cooled by a salt and ice mixture, and suddenly allowed to expand to 20 atmospheres. This compression and expansion is repeated until the temperature reaches −189° C. (−308.2° F.), when most of the air liquefies. It is difficult to transport, owing to its tendency to return to gas, and is therefore usually used near the point of manufacture. It is usually a milky liquid, from the presence of solid carbon dioxide, but may be freed from CO_2 and becomes transparent and of a slightly bluish color. Substances such as rubber, meat, eggs, mercury, etc., when plunged into it are frozen in a few moments. When applied to the skin it freezes the parts and may be utilized as a local anesthetic for minor surgical operations. Taylor and McKenna (*Lancet*, 1909, ii, p. 1774) have used liquid air with good results in the treatment of *lupus erythematosus* and also for the destruction of *nævi*. The method of applying it is to wrap a piece of absorbent cotton around the end of a stick about ten inches long. This is immersed for a moment in liquid air and then pressed firmly against the part to be treated.

Ajowan. *Ajava. Ajwan.*—The ripe fruit of *Carum copticum* Benth. et Hook. (*Carum Ajowan* Benth. et Hook., *Ptychotis Ajowan* D. C.), an annual of the Fam. *Umbelliferæ*. It is cultivated in India, Egypt, Persia and Afghanistan. The fruits resemble those of parsley, but are distinguished by their odor. They yield 3 to 4 per cent. of volatile oil which contains from 45 to 55 per cent. of thymol. This oil is official in the B. P. (see *Oleum Ajowan*). The fruits also contain from 25 to 32 per cent. of a fixed oil and from 15 to 17 per cent. of protein, making them a very good cattle food. They are used in the form of an extract and water, viz.: *Extractum Ptychotis Liquidum* P.I. and *Aqua Ptychotis* P.I. The water known as *Omum water* is used in India in the treatment of *cholera*. The *dose* of the *Fluidextract of ajowan* is ten to thirty minims (0.6–2.0 mils).

Ajuga.—Of this genus *A. chamæpitys* (L.), or *Ground Pine; A. reptans*, L., *Mountain Bugle*, or *Common Bugle;* and *A. pyramidalis*, L., all of them European species, the last naturalized in America, have been used in medicine, and are probably mild astringents and tonics. The ground pine is said to contain a volatile oil, and has been used to some extent in *amenorrhea* and in various forms of *rheumatism*, in *doses* of from one to two drachms (3.9–7.7 Gm.). *Ajuga Iva*, L., of Sardinia, is said to be a depressomotor, an active bactericide, and an antiperiodic. (*A. I. B.*, xxxiv.)

Akazga. *Boundou. Quai. Ikaga. Icaya.*—An ordeal poison, largely used in a district on the west coast of Africa, extending far into the interior, north and south of the equator. The precise botanical character of the plant is unknown, but it is thought to belong to one of the *Loganiaceæ*. Thomas R. Fraser found in the plant an alkaloid, *akazgine*. The alcoholic extract or the alkaloid acts on the system similarly to nux vomica. (For further description, see *U. S. D.*, 19th ed., p. 1373 and also *A. J. P.*, March, 1867.)

Alangine.—This alkaloid, according to Scheriff, occurs in the bark of the stem and root of *Alangium Lamarckii* Thwaites (Fam. *Coruaceæ*), a shrub indigenous to the tropical forests of India and Burma. It is very bitter, soluble in alcohol, chloroform, and acetic ether, but insoluble in water. In small doses it acts as a febrifuge; in *doses* of fifty grains (3.2 Gm.) it is emetic.

Alanin (Alpha). $CH_3CH(NH_2)COOH$. *Propionic Glycocoll. Alpha-aminopropionic acid.*—Prepared from aldehyde ammonia by hydrocyanic and hydrochloric acid and forms white crystals that are soluble in alcohol and water. It is used as the basis for the preparation of alanin compounds.

Alanin Mercury. *Hydrargyri Amidopropionas. Mercury Amidopropionate.*—Lucca asserts that this compound may be administered internally or subcutaneously, in *doses* of from one-twelfth to one-sixth of a grain (0.005–0.01 Gm.). To prepare "alanin mercury," crystallized amidopropionic acid is dissolved in water, heated to boiling, and mercury added as long as it is dissolved. The filtrate is rapidly evaporated, and the compound then separates in white, crystalline needles.

Alantol. (*Pinguin.*) $C_{10}H_{16}O$.—Prepared by distillation from the root of *Inula Helenium* (*Elecampane*). It is a yellowish to a brownish-yellow liquid with a taste and odor similar to peppermint. It is insoluble in water and soluble in the immiscible solvents. It has been used in place of turpentine in *pulmonary tuberculosis*. *Dose*, one-sixth minim (0.01 mil) 10 times daily in pill or powder form.

Alboferrin. *Alboferine.*—A light-brown, odorless, non-hygroscopic and permanent powder consisting of a phospho-albumin preparation of iron, freely dissolving in cold water and possessing a slightly saline taste. Its composition is stated to be as follows: albumin, 90.14 per cent.; iron, 0.68 per cent.; phosphorus, 0.32 per cent.; amido nitrogen, 0.13 per cent., and mineral substances, 9.5 per cent. This preparation has been recommended by a number of German clinicians as a good ferruginous tonic in *anemia, scrofulosis, rickets*, and other diseased conditions. *Dose*, for

a child, fifteen to forty-five grâins (1–3 Gm.); for adults, forty-five to seventy-five grains (3–5 Gm.) a day.

Alchemilla. *Alchemilla vulgaris*, L. *Lady's Mantle.* (Fam. *Rosaceæ.*)—This astringent, bitterish perennial European herb was formerly employed in *diarrhea.* By the ancients it was highly esteemed; extraordinary powers were ascribed to it by the alchemists. (*P. J.*, 1885, 791.)

Alcornoque.—For an account of this bark, which has long since fallen into entire neglect, see 16th edition *U. S. D.*, p. 1545.

Aldehydes.—Aldehyde is a generic term that applies to a class of bodies holding an intermediate position between the alcohols and the acids derived from the former by oxidation. The word itself was coined from the Latin *al*cohol *dehyd*rogenatum, meaning alcohol deprived of hydrogen. They are generally prepared by the oxidation, by chromic acid, of the respective alcohols.

Anisic Aldehyde. Anisaldehyde.—Prepared from anethol by oxidation. Formula $C_6H_4(O.CH_3).CHO$.—A colorless liquid with an aromatic odor. Soluble in alcohol and ether. Boiling point 245°–246° C. (473°–474.8° F.). Sp. gr. 1.126 at 15° C. (59° F.). It is used in admixture with other odorous substances in perfumery, the addition of other odors being necessary to bring out the agreeable hawthorn odor of the aldehyde.

Butylic Aldehyde. (*Iso-butyryl aldehyde.*) $(CH_3)_2CH.CHO$.—A transparent, colorless, highly refractive liquid. Sp. gr. 0.797. Miscible with water and alcohol and possessing a pungent odor.

Ethyl Aldehyde. CH_3CHO. *Acetic Aldehyde. Ethylic Aldehyde. Aldehyde, Acetaldehyde. Aldéhyde acetique* (*vinique*), Fr.—This substance is commonly given the name "Aldehyde," which, being a generic name, is misleading and indefinite. The following formula for its preparation is given: One part of ethyl alcohol, of sp. gr. 0.842, and 1 part of potassium dichromate are introduced into a large tubulated retort, and 1⅓ parts of sulphuric acid dropped in through the tubulure. Sufficient heat is evolved to start the distillation, but heat must be applied towards the end. The distillate is slightly contaminated with acetic acid. If the aldehyde be desired pure, the distillate is to be mixed with twice its volume of ether, surrounded with cold water, and dry ammoniacal gas passed in to saturation. Aldehyde-ammonia crystallizes out. This is to be decomposed in a retort by a mixture of 3 parts of sulphuric acid and 4 parts of water, and the distillate rectified and dried by contact with calcium chloride. Aldehyde is a colorless, mobile, inflammable liquid, having a decidedly pungent, ethereal, and suffocating odor. Its sp. gr. is 0.790, and boiling point 22° C. (71.6° F.). It mixes in all proportions with water, alcohol, and ether, and is rapidly converted into acetic acid on exposure to the air, through absorption of oxygen. It possesses very marked anti-putrescent properties, meat being preserved for months by its 2 per cent. aqueous solution. The intoxication caused by it in animals is characterized by a very great loss of sensibility. It appears to paralyze the vagi, although its cardiac action is comparatively feeble. Upon the respiration it exerts a most powerful influence, in small doses quickening it, in large doses depressing it. The temperature is much diminished. Applied locally aldehyde is very irritating. (*M. T. G.*, Sept., 1875.)

Heptoic Aldehyde. Oenanthol. Heptanal. $C_6H_{13}CHO$.—A highly refractive liquid, colorless and possessing an agreeable aromatic odor. It is prepared from castor oil by heating and fractional distillation, and is soluble in alcohol and ether and slowly in water. It is used in perfumery and as the basis of the preparation of other odorous aldehyde compounds.

Iodaldehyde may be made by mixing together iodine, iodic acid, and a solution of aldehyde and separating by adding water. (See paper by P. Chautard, *P. J.*, 1886, 224.)

Paracuminic Aldehyde. Cuminol. Cumyl Hydride. $(C_6H_4)(CH_3)_2.CH.CHO$.—A yellowish oily fluid with a persistent strong odor and an acid burning taste. It is one of the constituents of Roman chamomile. It is soluble in alcohol and ether and has a sp. gr. of .9382 at 0° C. (32° F.).

Propylic Aldehyde. Propionic Aldehyde. $CH_3CH_2.CHO$.—A colorless liquid with a suffocating odor, soluble in water, and boiling at 48° C. (118.4° F.). It is claimed to be a powerful antiseptic and an effective preservative.

Valeric Aldehyde. Isovaleric aldehyde. $(CH_3)_2CH.CH_2.COCO$.—A colorless liquid with a pungent, apple-like odor. It is miscible in all proportions with alcohol and ether, boils at 92° C. (197.6° F.), and has a specific gravity of 0.804 at 15° C. (59° F.). It is used commercially as an artificial flavoring agent and in the art of perfumery. It was also proposed at one time as a hypnotic and sedative, but was later on abandoned.

A condensation product of Aldehyde is known as "*Aldol,*" $CH_3CH(OH)CH_2CHO$, and is exploited as a hypnotic and sedative. Like formaldehyde it will, on spontaneous evaporation, leave a solid residue of *Paradol*, a polymeric substance.

Aletris. *N. F. IV. Unicorn Root. Star Grass. Aletris farinosa* L. *Blazing Star. Mealy Starwort. Colic Root. Ague Root. Alétris farineux. Unicorn Root true*, Fr. *Mehlige Aletris*, G. (Fam. *Liliaceæ.*)—It is described in the N. F. as "the dried rhizome and roots of *Aletris farinosa* Linné (Fam. *Liliaceæ*). Rhizome horizontal or slightly oblique, nearly cylindrical or laterally compressed above, from 2 to 4 cm. in length and from 5 to 12 mm. in diameter; externally grayish-brown, upper portion with circular stem scars from 3 to 7 mm. in diameter and with numerous leaf bases, the sides and lower portion with numerous tough, wiry, whitish or reddish-brown roots which are more or less flexuose and provided with short branches; fracture short; internally light brown, cortex from 1 to 2 mm. in thickness, central cylinder with numerous twisted and branching fibro-vascular bundles. Odor slight, acetous; taste sweetish, somewhat bitter. Examined microscopically, the greater part of the drug is found to consist of parenchyma cells filled with spherical or ellipsoidal starch grains from 0.008 to 0.016 mm. in diameter. Some of the parenchyma cells contain raphides, the latter being from 0.025 to 0.045 mm. in length. The tracheæ are reticulate or provided with simple pores and around these are several layers of lignified cells with thick walls and simple, large oblique pores. The endodermis is composed of several layers of thick-walled and closely-lamellated cells of a deep yellow color and the cortex is readily separated. Aletris yields not more than 16 per cent. of ash." *N. F.* An indigenous perennial plant, the leaves of which spring immediately from the rhizome, and spread on the ground in the form of a star. This drug is often contaminated with other drugs collected by mistake for it, being most fre-

quently confused with *Helonias* species. The bitterness is extracted by alcohol, and the tincture becomes turbid upon the addition of water. The decoction is moderately bitter, but much less so than the tincture. It affords no precipitate with the salts of iron. (Bigelow.) In small doses of about ten grains (0.65 Gm.), it appears to be a simple, bitter tonic. In very large doses, it is said to be cathartic and emetic. It has been employed, with asserted benefit, in *colic, dropsy* and *chronic rheumatism. Aletrin,* a resinoid, is prepared by exhausting the drug with alcohol and evaporating the percolate to dryness, treating with water, and drying the residue; it is asserted to be a *uterine stimulant* in *doses* of from one to two grains (0.065–0.13 Gm.). *Dose,* of aletris, thirty grains (1.9 Gm.).

Aleudrin.—*Dichloroisopropyl alcohol carbamate,* $CH_2Cl.CHO(CONH_2).CH_2Cl$, a white, odorless, crystalline powder; melting at 82° C. (179.6° F.); sparingly soluble in water; readily dissolved by organic solvents.

According to Maass (*D. M. W.*, 1912, p. 1232), aleudrin exercises on the lower animals an hypnotic effect without influence upon temperature, circulation, or respiration. According to Burchard (*D. M. W.*, 1913, p. 1044), it has a marked analgesic action and is a useful remedy in *neuralgias* and other painful neuroses. It has also been used as a general sedative in various conditions of nervous excitation, such as *hysteria, chorea, mania,* etc. In full doses it has an hypnotic action and may be used in *insomnia.* The *dose* is from eight to twenty-five grains (0.5–1.5 Gm.).

Algarobilla, the pod of *Cæsalpinia brevifolia,* (Clos.) Benth. (Fam. *Leguminosæ*), a drug containing over 60 per cent. of tannin and a quantity of *ellagic acid,* is obtained from Chili. (Gehe's Report, *N. R.*, 1878, 332; *J. Chem. S.*, 1891, 918.)

Alisma. *Alisma Plantago-aquatica,* L. *Water Plantain. Plantain d'eau. Pain de grenouilles,* Fr. *Froschlöffel, Wasserwegerich,* G. (Fam. *Alismaceæ.*)—A perennial herbaceous plant, common to Asia, Europe, and the United States. The root has, when fresh, an odor like that of Florentine orris, but loses it when dried. Its taste is acrid and nauseous. It contains a pungent volatile oil and an acrid resin, to which all its virtues must be ascribed. The Calmucks in Russia are said to use it for food. The *leaves* are rubefacient, and will sometimes even blister. They have been recommended in *gravel* and *cystitis. Dose,* a drachm (3.9 Gm.).

Alkanet. *Anchusæ Radix. Alkanna Root, Alkanet Root, Orcanette,* Fr. *Spanish Bugloss. Alkannawurzel,* G.—This is the root of *Alkanna tinctoria* L., or *dyers' alkanet,* an herbaceous perennial plant, of the Fam. *Boraginaceæ,* growing in the Grecian Archipelago and the south of Europe, where it is cultivated. See E. M. Holmes, *P. J.*, 1897, p. 61. For an account of Syrian alkanet and allied plants, see *Proc. A. Ph. A.*, 1896, 565. Alkanet, as found in commerce, is in pieces 7 to 10 cm. long, and from 5 to 15 mm. thick, somewhat twisted, consisting of a dark-red, easily separable bark, and an internal ligneous portion, which is reddish externally, whitish near the center, and composed of numerous distinct, slender, cohering fibers. As it comes to us it is usually much decayed internally, very light, and of a loose, almost spongy texture. The fresh root has a faint odor, and a bitterish, astringent taste; but when dried it is nearly inodorous and insipid. Its coloring principle, which abounds mostly in the cortical part, is soluble in alcohol, ether, and the oils, to which it imparts a deep red color, but is insoluble in water. It may be obtained by first exhausting the root with water, and then treating it with a weak solution of potassium or sodium carbonate, from which the coloring principle may be precipitated by an acid. According to Pelletier, by whom it was discovered, it possesses acid properties, forming with the alkalies and earths neutral compounds, which are of a blue color, and soluble in alcohol and ether. Its weak acid character resembles that of alizarin, to which it is chemically related, as when distilled with zinc dust it yields *methyl-anthracene.* It has also received the names of *anchusin* and *alkannin.* The *anchusin* has been extracted and studied by C. J. S. Thompson. (*A. J. P.*, 1886, 409.) He finds it to vary in amount between 5.25 and 6.02 per cent. It is red, resin-like, insoluble in water, soluble in oils, alcohol, chloroform, and ether, and with a rich deep blue color in alkali hydroxides, the color changing again to crimson on addition of an acid. According to A. Gawalowski, the red coloring matter of alkanet root consists of two distinct bodies, the one turning blue, the other green by the action of alkalies. The first of these, *alkannic acid,* is extracted by ether and alcohol. The second, *anchusic acid,* is obtained by extraction with benzene. Both form characteristic colored salts. (*Ph. Ztg.*, 1902, 817.) Alkanet is somewhat astringent, and was formerly used in several diseases; but it is now employed exclusively for coloring oils, ointments, and plasters, which are beautifully reddened by one-fortieth of their weight of the root. The best way to use it with this object in view is to suspend the alkanet, after tying it in a piece of flannel, in the melted fat. A fine color is obtained by previously washing the alkanet with water and then thoroughly drying it before suspending it in the fat or oil. It is said also to be used in the preparation of spurious *port wine.* The *Oleum Hypericum,* formerly much used under that title or the name *Red Oil,* consisted of fixed oil colored with alkanet.

Allamanda.—*Allamanda cathartica,* L., is a shrub of the Fam. *Apocynaceæ,* growing in Porto Rico, the extract of whose bark is said to be an excellent hydragogue cathartic, in *doses* of from one to two grains (0.065–0.13 Gm.).

Alliaria. *Alliaria officinalis* Andrz. [*Sisymbrium Alliaria,* Scop. *Erysimum Alliaria,* L. *Alliaria Alliaria* (L.) Brit.] *Hedge Garlic.*—A perennial European herb, a native also of Northern Asia, and naturalized from Canada to Virginia, having an alliaceous odor when rubbed, and a bitterish, somewhat acrid taste. When eaten it communicates its odor to the breath. Wertheim obtained from the root a volatile oil, apparently identical with that of mustard. (*Ann. Ch. Ph.*, liii, 52.) The herb and seeds are esteemed diuretic, diaphoretic, and expectorant, and are used as external applications in *gangrenous affections,* and to promote *suppuration.*

Allophanic Acid. *Acidum Allophanicum.* $NH_2.CO.NH.CO.OH$.—This is a *urea-carbonic acid,* but occurs only in the form of salts and esters, as at the moment of liberation the acid splits into urea and carbonic acid gas. Its best known derivative is its amide, called *biuret.* Apparently it exercises no influence on the system of itself, but according to Overlach (*B. K. W.*, 1908, p. 1403) is valuable because it has the power of forming compounds with a number of substances of unpleasant taste and penetrating odor, and rendering them

much less disagreeable. For instance, santalol unites with allophanic acid to form a tasteless, dry, crystalline powder (having the composition $NH_2.CO.NH.COOC_{15}H_{23}$). The same is true of castor oil and of creosote.

The combination of santalol and the allophanic acid has been used in the treatment of *gonorrhea* under the name of *Allosan;* it represents about 72 per cent. of santalol. The *dose* is fifteen to thirty grains (1–2 Gm.).

Almatein.—This proprietary article is a condensation product of formaldehyde with hematoxylin and is given the concrete formula $CH_2O_2.(C_{16}H_{12}O_5)_2.CH_2$. It is a bright red, light powder, odorless and tasteless, insoluble in water, but soluble in dilute alkalies, alcohol or glycerin. Astalfoni (*Press. Med.*, 1908) finds that it has a powerful antiseptic action and is non-poisonous. It passes through the system unchanged, and is split up by the alkaline intestinal juices, with the slow liberation of formaldehyde, and is employed as an intestinal disinfectant. It has been used also as a dusting powder on *wounds* (Werndorff, *M. M. W.*, 1909), also dissolved in glycerin as an injection in cold *abscesses*. One drawback to its use is its staining powers. The *dose* for internal administration is from five to fifteen grains (0.3–0.9 Gm.).

Alnus. *Alder.*—Of this genus of small trees or bushes, *A. glutinosa* (L.) Medic., or *European Alder, Black Alder; A. rugosa* (Du Roi) K. Koch (*A. serrulata* Willd.), or *American Alder; A. incana* (L.) Willd., or *Tag Alder*, are tonic and astringent, and have been used in intermittent fever, the bark being the part employed. *A. glutinosa* has been used for dyeing and also for tanning. According to Eitner, the bark contains from 16 to 20 per cent. of tannic acid. The tannic acid, however, appears to differ from that of galls and oak bark, as, according to Stenhouse, it does not yield glucose when acted on by sulphuric acid. (*P. J.*, Dec., 1861.) F. Dreykorn and E. Reichardt, however, state that it is resolved by sulphuric acid into *alnine red* and sugar. (*A. J. P.*, xlii, 403.)

Alpha-naphthol. $C_{10}H_7OH$.—A coal tar constituent obtained in colorless prisms or powder of a disagreeable taste. It is sparingly soluble in water, but more soluble in alcohol and ether. It melts at 94° C. (201.2° F.), and boils at 278°–280° C. (532°–536° F.). In antiseptic action it is about equivalent to its isomer, beta-naphthol. It is used internally as an antiferment in five grain (0.3 Gm.) doses; in *typhoid fever* thirty to sixty grains (2–4 Gm.) a day. Externally it has been used in a 10 to 20 per cent. oily solution in *erysipelas, scarlet fever* and *smallpox*, as well as in various *skin diseases*. According to Maximovitch, alpha-naphthol has the same action upon pathogenetic germs as has beta-naphthol, having the superiority over the latter compound, however, of being less poisonous to the higher animals in proportion to its germicidal power. It may be used in the same strength of solution and the same dose as beta-naphthol. Alpha-naphthol has been proposed as a test for sugar in urine. Posner and Epenstein have studied the action of the test, and considered it to be free from many of the objections raised against other tests for sugar. The test depends upon the fact that a solution of sugar, in the presence of pure concentrated sulphuric acid and a solution of alpha-naphthol, gives a violet-colored reaction, due, according to Udransky, to the separation of furfurol. This reaction occurs not only with sugars, but with all carbohydrates and with certain albuminoids; hence *the urine must be free from albumin.* The test is said to be extremely sensitive, showing one-hundredth of one per cent. of sugar. The urine must always be previously diluted. *Winkler's test* for hydrochloric acid in the stomach is performed as follows: 5 Gm. of alpha-naphthol are dissolved in 100 mils of alcohol, to which is added from 0.5 to 1.0 Gm. of grape sugar. A mixture of the filtered gastric juice is then evaporated with a few drops of the reagent in a porcelain dish on a water bath; if free hydrochloric acid be present, a bluish-violet marginal zone will appear and rapidly become inky black. Various compounds of naphthol have been proposed in medicine. The substance recommended by Polaillon, under the name of *microcidin*, as being ten times more powerful than phenol and less toxic than beta-naphthol, is said to be *sodium naphthol.* (Helbing's *Mod. Mat. Med.*, 79.)

Alphol.—*Salicylic Ester of Alpha-naphthol, Alpha-naphthol salicylate,* $C_6H_4\begin{cases}OH\\COOC_{10}H_7\end{cases}$, is obtained by reaction between salicylic acid and alpha-naphthol. It is a white, crystalline powder, melting at 83° C. (181.4° F.). Soluble in alcohol, ether, and fixed oils; insoluble in water, decomposed in the alkaline secretions of the intestinal tract into alpha-naphthol and salicylic acid. It is incompatible with alkalies and with ferric compounds. Used as an antiseptic and antirheumatic. *Dose,* eight to fifteen grains (0.5–1.0 Gm.).

Alphozone. *Succinic Dioxide. N. N. R.* 1916. $(COOH.CH_2CH_2CO)_2O_2$.—This powerful oxidizing agent occurs as a fluffy, white, crystalline powder, the crystals being small, irregular plates. It is fairly soluble in water and alcohol, sparingly so in ether and insoluble in chloroform and benzene. It is devoid of odor and deteriorates slightly on exposure to air. It is employed for the germicidal and antiseptic properties of its oxygen, being used both externally and internally. Unlike hydrogen peroxide it does not effervesce on contact with pus. A 1 to 1000 solution in water is generally used externally.

Aluminum.—Under the name of *escalin*, a mixture of two parts of the finely powdered metallic aluminum with one part of glycerin has been employed by Klemperer (*Ther. Geg.*, May, 1907) as a substitute for the insoluble salts of bismuth, especially in the treatment of *gastric ulcers.* Sussman (*Ther. Geg.*, May, 1908) has also found this preparation useful in the treatment of *anal fissures.* It is marketed in the form of tablets, which when thrown into water disintegrate and yield on stirring a uniform suspension of the metal. Four of these tablets may be given at a dose, preferably on an empty stomach and repeated daily for three or four days. For description of physiological action of aluminum see p. 124.

Aluminum Acetate as well as the *subacetate* is largely employed in medicine. The deliquescent acetate may be made by the direct combination of hydrated alumina with acetic acid or by reaction between aluminum sulphate and lead acetate,

$$Al_2(SO_4)_3 + 3Pb(C_2H_3O_2)_2 = 3PbSO_4 + Al_2(C_2H_3O_2)_6.$$

The *neutral aluminum acetate* is a valuable astringent and antiseptic in *sore throat* and similar inflammatory conditions. It may be employed in the form of a gargle containing from 1 to 3 per cent. The relatively insoluble *basic acetate* is used as a dusting powder in *sweating feet*, in which it exercises both a dessicating and deodorizing influence, and in chronic *leg ulcers*,

weeping eczema, and the like. A solution containing 7.5 to 8 per cent. of *basic aluminum acetate* is official in the N. F. under the title *Liquor Alumini Subacetatis*, which is practically identical with the *Liquor Aluminii Acetici* P. G. This must not be confused with the *Liquor Alumini Acetatis* N. F. or *Burow's Solution*, which is the solution of the neutral acetate also used for much the same purposes. (See Part III). Stansburg (*Am. J. Surg.*, 1912, xxvi, p. 82) has found the N. F. solution of aluminum subacetate a valuable local application in *furunculosis*, *erysipelas* and *ivy poisoning*. He dilutes the solution with from seven to ten parts of water and saturates gauze with this solution and applies it over the diseased area.

Preparations asserted to contain the basic aluminum acetate have been introduced into therapeutics under the names of *lenicet* and *eston*. It seems probable, however, that the latter is a mixture of several aluminum salts. (See Friedlander, *Ap. Ztg.*, 1907, p. 819.) From eston is prepared two other compounds, one known as *formeston*, in which two of the acetyl radicals are replaced by formic acid, and the other *subeston*, which is a double basic acetate. These appear to be not only astringent, but also germicides of considerable power; Blasius (*Hyg. R.*, 1908, xviii, p. 941) finds that the saturated solution of eston, representing about 2 per cent., is fatal to most non-sporulating bacteria after thirty minutes' exposure.

Aluminum Acetico-tartrate. *Alsol.*—Under the name of alsol has been employed a 50 per cent. aqueous solution of the acetico-tartrate of aluminum. According to Aufrecht, this solution is a more powerful germicide than phenol. It has been found clinically valuable by Hanau and Pinner (*Med. Klin.*, 1909) wherever an antiseptic astringent is necessary, especially in the treatment of catarrhal conditions of the female genitalia. They applied it by means of gauze soaked in a 5 to 10 per cent. alsol solution. As a gargle or spray in *pharyngitis* and the like, it may be used in from 1 to 3 per cent. solution. A creamy solution of aluminum acetico-tartrate has been highly recommended by Lewitt (*Ther. Geg.*, 1910, p. 95) in the treatment of *pruritus*, *intertrigo*, *acne vulgaris*, and other skin diseases. A solution similar to alsol is recognized in the N. F. as *Liquor Alumini Acetico-tartratis* (see Part III).

Aluminum and Iron Sulphate. *Ferroso-Aluminic Sulphate. Sulphate of Aluminum and Iron.* $AlFe(SO_4)_2 + 12H_2O$.—This double salt was brought forward by Sir James Murray of Dublin, as an astringent, styptic, and vermifuge. His method of preparing it is not very clearly expressed, but it may be presumed to be formed by dissolving alumina and ferrous carbonate, both recently precipitated, in sulphuric acid, and evaporating the solution. Klauer states that it is produced in crystalline tufts when a solution of the component salts mixed with an excess of sulphuric acid is left to stand in a warm place. (*Watt's Dict.*, vol. v, 583.) Murray recommended it in *chronic dysentery*, *diarrhea*, *fluor albus*, and the *colliquative sweats* and *diarrhea* which attend *hectic fever* and *consumption*. Externally he found it a powerful styptic, useful as a gargle in *relaxation of the tonsils and uvula*, and in *salivation*, as an injection in *hemorrhages*, and as a wash for foul and flabby *ulcers*. *Dose*, from five to ten grains (0.32–0.65 Gm.), dissolved in some aromatic water.

Aluminum and Potassium Salicylate. *Alkasal. Alkasol.*—It is prepared by the combination of aluminum salicylate and potassium acetate with the use of heat. It is used for the same purposes as aluminum acetate.

Aluminum and Sodium Acetate. *Acetonal.* $Al_2(OH)_2.(C_2H_3O_2)_5Na$.—It is used as a 10 per cent. solution, and its equivalent can be prepared by dissolving 82 parts of sodium acetate in 4050 parts of liquor alumini acetatis *N. F.*

Aluminum Boroformate, $Al_2O_3B(OH)_3.H_2CO_2 + 5H_2O$, occurs in lustrous crystals, and may be prepared by introducing freshly precipitated alumina into a mixture of two parts of formic acid, one part of boric acid, and seven parts of water. The solution is evaporated and crystallized. Used as an antiseptic and astringent. (*Ph. Rund.*, 1894, 256.)

Aluminum Boro-tannate. *Cutal, Lutol.*—A brownish powder, insoluble in water, used as an astringent and disinfectant in diseases of the skin. It may be applied as an ointment or as a dusting powder.

Aluminum Boro-tartrate. *Boral.*—This is a crystalline substance, with a sweetish astringent taste, soluble in water. It is used, generally in powder form, as a local astringent in diseases of the nose and throat.

Aluminum Carbonate. $Al_2(CO_3)_2$.—This occurs in chalky white, easily pulverized, tasteless lumps. It is used as a mild antiseptic styptic in *croup*, *ocular affections*, *diarrhea*, etc. It is incompatible with acids, phosphates and lead acetate.

Aluminum Caseinate.—A yellowish-white, tasteless powder containing 5 per cent. of aluminum; insoluble in water, sparingly dissolved when macerated in saliva, and yielding aluminum to dilute acids. It was introduced by Rud. Meyer (*Ap. Ztg.*, Sept. 23, 1899, 566) as a remedy in *intestinal catarrh*, given in doses of four to five grains (0.26–0.32 Gm.). It is prepared as follows: Milk, freed from albumin by repeated heating to 62° C. (143.6° F.) and straining, and then sterilized, is precipitated with solution of aluminum subacetate (*Liquor Alumini Subacetatis*); the precipitate is washed completely with water, and after removing the water with alcohol, deprived of fat by means of ether. The product is dried at a moderate temperature, and while drying powdered.

Aluminum Chlorate, $Al(ClO_3) + 6H_2O$.—Under the name of *prophylacticum mallebrein* there has been introduced a solution which is stated to contain 25 per cent. of aluminum chlorate. It is claimed to have the property of detoxicating bacterial toxins and hence to be useful in certain infectious diseases, notably *diphtheria* and laryngeal *tuberculosis*. It is applied either as a spray or gargle in strengths of from 0.5 to 1 per cent.

Aluminum Chloride, *N. F. IV. Alumini Chloridum.*—According to the N. F., "it contains, when dried over sulphuric acid, $AlCl_3 + 6H_2O$ (241.58) corresponding to not less than 20.5 per cent. of aluminum oxide (Al_2O_3). Preserve it in well-closed containers." It "occurs as a white, or yellowish-white, deliquescent, crystalline powder; nearly odorless; taste sweetish and very astringent. One gramme dissolves in about 0.5 mil of water and in about 4 mils of alcohol at 25° C. (77° F.), also soluble in glycerin. An aqueous solution of the salt (1 in 10) is clear, and is acid to litmus. Separate portions of an aqueous solution of the salt (1 in 10) yield with silver nitrate T.S. a white curdy precipitate insoluble in nitric acid, with ammonia water a white gelatinous precipitate almost insoluble in an excess of ammonia

water, and with sodium hydroxide T.S. a white gelatinous precipitate completely soluble in an excess of the reagent. Ten mils of an aqueous solution of the salt (1 in 100), after the addition of 0.2 mil of barium chloride T.S., does not become cloudy within one minute (*sulphate*). The addition of 0.3 mil of potassium ferrocyanide T.S. to 20 mils of an aqueous solution of the salt (1 in 150) does not produce a blue coloration within one minute (*iron*). The addition of hydrogen sulphide T.S. to 10 mils of an aqueous solution of the salt (1 in 10) does not produce a white precipitate or turbidity (*zinc*). An aqueous solution of the salt does not respond to the Test for heavy metals (see *U. S. P.*, Test No. 3, Part III). An aqueous solution of the salt meets the requirements of the Test for arsenic (see *U. S. P.*, Test No. 1, Part III)."

Assay.—"Dissolve about 0.5 Gm. of the salt, previously dried in a desiccator and accurately weighed, in 100 mils of distilled water, add 1 Gm. of ammonium chloride and then precipitate the aluminum hydroxide by the addition of a slight excess of ammonia water to the boiling solution. Collect the precipitate on a filter, wash it with distilled water, dry, ignite thoroughly and weigh. The weight of the aluminum oxide so obtained is not less than 20.5 per cent. of the weight of the Aluminum Chloride taken for the assay." *N. F.* Externally it is used as an astringent and antiseptic, especially in *hyperidrosis*. Internally it has been employed in locomotor ataxia in *doses* of five grains (0.3 Gm.).

Aluminum Lactate.—Perutz (*M. M. W.*, 1913, p. 1261) has used solutions of aluminum lactate in strengths of from 0.1 to 2 per cent. for its astringent effect in *chronic gonorrhea, eczema, mercurial ptyalism*, etc. He was unable to demonstrate any direct antiseptic effect, but found that in suppurative conditions it exercises a beneficial influence. Under the trade name of *Fixin* a proprietary form of this salt has been suggested as a gastro-intestinal disinfectant.

Aluminum Oleate. $Al_2(C_{18}H_{33}O_2)_6$.—A white to a yellowish tenacious mass, soluble in alcohol and ether, and is used as an antiseptic in skin diseases.

Aluminum Phenolsulphonate. *Sozal. Aluminum sulphocarbolate.* $Al_2(C_6H_4HSO_4)_6$.—This forms a reddish-white powder of slight phenol odor and astringent taste. It is soluble in water and alcohol. Merck recommends it as a substitute for iodoform, especially commendable in *cystitic* and suppurating *ulcers*.

Aluminum Salicylate. *Salumin.* $Al(C_6H_4OH\,COO)_3$.—A reddish-white powder, insoluble in water and alcohol, but soluble in dilute alkalies. It is employed in nasal and throat affections by insufflation. *Ammoniated aluminum salicylate*, a yellowish, water-soluble powder, is also used in the same manner, and in solution is employed in *catarrh* and *ozena*, as a spray.

Aluminum Silicate.—An aluminum silicate sold under the name of *neutralon* has been recommended by Rosenheim and Ehrmann (*D. M. W.*, 1910, xxxvi, p. 111) in the treatment of *hyperchlorhydria* and *gastric ulcer*. Its value depends in part upon its protective action but also partly due to the fact that it is slowly decomposed by the hydrochloric acid forming an aluminum chloride which exercises a mild astringent effect. The *dose* is from one-half to one teaspoonful (2–4 Gm.) in half a glass of water, taken an hour before meals.

Aluminum Subformate. *Aluminum formate.* $Al(HCOO)_2OH$.—Under the name of *alformin*, a solution containing about 16 per cent. of aluminum subformate has been used as an astringent and disinfectant. In *pharyngitis*, five to ten drops of this solution may be added to a glass of water and used as a gargle.

Aluminum Subgallate. *Gallal.* $Al_4(C_7H_2O_5)_3 + 4H_2O$.—Basic aluminum gallate is an amorphous, brownish powder prepared from solutions of alum and sodium gallate. It is insoluble in water, but soluble in diluted acids. It is employed, chiefly in *ozena*, as an antiseptic astringent.

Aluminum Sulphate, *N. F. IV. Aluminum Sulphas.* $Al_2(SO_4)_3 + 16H_2O = 630.67$. *Sulfate d'Alumine*, Fr. *Aluminium sulfuricum*, P. G. *Aluminium sulfat, Schwefelsaure Thonerde*, G.—A process was given in the *U. S. P.*, 1870, for the preparation of this salt, but the 1880 Committee of Revision very properly omitted the process, merely giving a description and tests for the salt. It was not admitted to the U. S. IX but was introduced into the N. F. IV. It may be manufactured by various methods (see *U. S. D.*, 19th ed., p. 124), but is now obtained chiefly as one of the by-products in the manufacture of soda from cryolite or from bauxite. The American production, chiefly from bauxite, in 1914 amounted to 164,954 short tons, and importations to 2891 tons.

It contains not less than 99.5 per cent. of $Al_2(SO_4)_3 + 16H_2O$ and is thus described (N. F. IV): "Aluminum Sulphate occurs as a white crystalline powder, shining plates, or crystalline fragments; without odor, having a sweetish and afterwards an astringent taste; permanent in the air. One gramme dissolves in 1 mil of water at 25° C. (77° F.), more soluble in boiling water, but insoluble in alcohol. When gradually heated to about 200° C. (392° F.), it loses its water of crystallization (about 45.7 per cent. of its weight). An aqueous solution of the salt (1 in 20) is acid to litmus. Separate portions of an aqueous solution of the salt (1 in 20) yield with barium chloride T.S. a white precipitate insoluble in hydrochloric acid, and with sodium hydroxide T.S. a white gelatinous precipitate which is soluble in an excess of the alkali, but which is again separated on the addition of a sufficient amount of ammonium chloride T.S. Gently heat 1 Gm. of Aluminum Sulphate with 10 mils of sodium hydroxide T.S.; the liquid does not evolve the odor of ammonia. A filtered aqueous solution of the salt (1 in 10) does not become more than faintly opalescent within five minutes after the addition of an equal volume of tenth-normal sodium thiosulphate V.S. (*free acid*). The addition of 5 drops of potassium ferrocyanide T.S. to 20 mils of an aqueous solution of the salt (1 in 150), does not produce at once a blue coloration (*iron*). An aqueous solution of the salt does not respond to the Test for heavy metals (see *U. S. P.*, Test No. 3, Part III). An aqueous solution of the salt meets the requirements of the Test for arsenic (see *U. S. P.*, Test No. 1, Part III)."

Assay.—"Dissolve about 0.5 Gm. of Aluminum Sulphate, accurately weighed, in 100 mils of distilled water, add 1 Gm. of ammonium chloride and then precipitate the aluminum hydroxide by the addition of a slight excess of ammonia water to the boiling solution. Collect the precipitate on a filter, wash it with distilled water, dry, ignite thoroughly and weigh. The weight of the aluminum oxide so obtained is not less than 16.1 per cent. of the weight of the Aluminum Sulphate taken

for the assay, corresponding to not less than 99.5 per cent. of $Al_2(SO_4)_3 + 16H_2O$." *N. F. IV.*

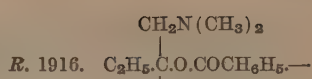
It has been employed in aqueous solution (20 grains in a fluidounce up to saturation *pro re nata*) as an antiseptic, detergent application to *foul ulcers*, and as an injection in *fetid discharges from the vagina*. Solution of aluminum sulphate is capable of dissolving a considerable quantity of recently precipitated gelatinous alumina. Such a solution, impregnated with benzoin, has been proposed by Mentel as a hemostatic, under the name of *benzoinated solution of alumina*. It resembles the *styptic liquid of Pagliari*. It is prepared by saturating with gelatinous alumina a solution made of eight ounces of aluminum sulphate dissolved in a pint of water. To the saturated solution six drachms of bruised amygdaloid benzoin are added, and the whole is kept at a temperature of about 65.5° C. (150° F.) for six hours, with occasional agitation, so that the liquid, after filtration, may have about the density 1.26. This liquid, put in a cool place for several days, so as to deposit some crystals of alum, forms the benzoinated solution, remarkable for its very sweet odor and astringent balsamic taste. Benzoinated solution of alumina, diluted in the proportion of from two to five fluidrachms to the pint of water, has been found useful as an injection in *leucorrhea*.

Aluminum Tannotartrate.—Yellowish-white lamellæ or powder, strongly astringent taste, soluble in two parts water. It has been employed as an insufflation or gargle in rhinolaryngological and other catarrhal affections. It is incompatible with iron compounds, phosphates and alkalies.

Alumnol. *Aluminum beta-naphthol-disulphonate.* $Al_2(C_{10}H_5(OH)(SO_3)_2)_3$. *Alumini naphthol sulphonas, N. N. R.* 1916.—A whitish, nonhygroscopic powder darkening slightly on exposure to air, easily soluble in cold water and very soluble in glycerin, slightly soluble in alcohol. Its aqueous solution has a slight bluish fluorescence, feeble acid reaction, and is colored blue by iron chloride. The solution of 40 per cent. is made with hot water and remains clear on cooling. Though it coagulates albumin, it is said to be dissolved in an excess of albumin, and, therefore, to be able to reach deep recesses of wounds.

It has been strongly recommended as an astringent and antiseptic in nasal, urethral, and other catarrhal inflammations. The strength of the solution employed varies from 1 per cent. in *gonorrhea* to 10 per cent. in *abscesses*. (See *B. K. W.*, 1892; *Dermatologen-Congress zu Wein*, 1892; *Th. M.*, 1892, 644.) Two to ten parts of alumnol mixed with ten parts of starch has been used by insufflation in cases of *laryngitis*. Alumnol, however, would appear to be very feeble and slowly acting as a germicide, a 1 per cent. solution requiring twenty-four hours to destroy bacilli of anthrax. As a surgical dressing from 1 to 2 per cent. solution may be used. In *infected wounds* the caustic 20 per cent. solution is employed. In diseases of the skin alumnol is used with talc or starch as a powder, or with lanolin as an ointmnet, the strength varying from 2 to 20 per cent. Its solutions are incompatible with caustic alkalies and alkaline carbonates, with albumen, gelatin solutions, soluble nitrates, silver salts, and other reducible salts. Rubbed with phenol it produces a plastic mass.

Alypin. *N. N. R.* 1916.



Alypin is 2-benzoxy-2-dimethyl-amino-methyl-1-dimethyl-amino-butane-hydrochloride. It bears a close relation to *Stovaine*, which see. Its preparation is a complicated process starting with ethyl magnesium bromide dissolved in ether and dichloracetone. It occurs as a crystalline hygroscopic powder, freely soluble in both water and alcohol, with a melting point of 169° C. (336.2° F.). Its solution will stand boiling for a period of five minutes. The *nitrate* of this same base has been also introduced, especially for the purpose of using in combination with silver salts.

Alypin has been employed as a substitute for cocaine in the production of surgical anesthesia either by local application or injecting into the subarachnoid space. It differs from cocaine in that it produces relaxation of the blood vessels, when applied locally, instead of constriction. According to Le Brocq (*B. M. J.*, March 27, 1909), alypin is about equally anesthetic to cocaine but is more highly toxic. Several cases of alypin poisoning have been reported of which at least two have ended fatally. The symptoms have been cyanosis, convulsions, stupor and arrest of respiration (see Lichtenstein, *Ther. Geg.*, 1914, xvi). Braun (*D. M. W.*, 1905) reports that it produces pronounced irritation at the point of injection, and this view has been confirmed by other investigators, especially as regards its ophthalmic use. As a local anesthetic it would, therefore, appear to have no advantages over the other preparations of its class. It has also been employed in doses of one-sixth to one-third of a grain (0.01–0.02 Gm.) for the relief of *vomiting*. As a local anesthetic it may be used in strengths of from 2 to 5 per cent. and its solutions in these strengths are stable but become moldy when further diluted. An alkali hydroxide or carbonate gives a precipitate with an aqueous solution of alypin, and mixed with calomel and dampened with alcohol it gives a black color.

Amapa Milk.—The milky sap of the bitter bark of *Plumeria Fallax* (Fam. *Apocynaceæ*), a Brazilian tree, has come into general use as a vermifuge and antimalarial, having been used and known by the natives of Brazil and South America from time immemorial. It is also used externally in the treatment of *cancerous sores*. *Dose*, for children, one minim for each year of age.

Amber. *Succinum. Ambre, Succin*, Fr. *Bernstein*, G.—Amber is a fossil resin, occurring generally in small detached masses, in alluvial deposits, in different parts of the world. According to Goefert, there are about fifty species of extinct coniferous trees of which amber represents the resinous exudation. It is found chiefly in East Prussia, either on the seashore, where it is thrown up by the Baltic, or underneath the surface. Large deposits occur in some lakes on the eastern coast of Courland, and an extensive bed of yellow amber was discovered in 1854, on sinking a well in the coal mines near Prague. The largest mass of amber yet found weighed thirteen pounds. Amber also occurs in considerable quantities near Catania, in Sicily. It is usually associated with lignite, and sometimes encloses insects and parts of plant tissues. In the United States, it was found at Cape Sable, Maryland, by Troost. In this

locality it is associated with lignite and iron pyrites. It has also been discovered in the greensand formation of Martha's Vineyard, Harrisonville, N. J., and elsewhere. The amber consumed in this country is brought from the ports of the Baltic. A mine of it is said to have been discovered near Rockwood in Australia.

It is a brittle solid, generally in small irregular masses, permanent in the air, having a homogeneous texture and vitreous fracture, and susceptible of a fine polish. It becomes negatively electric by friction. Its color is generally brownish-yellow, either light or deep, but is occasionally reddish-brown or bluish from staining with ferric phosphate. It has no taste, and is inodorous when cold, but exhales a peculiar, aromatic odor when heated. It is usually translucent, though occasionally transparent or opaque. Its sp. gr. is about 1.07. Water and alcohol scarcely act on it. When heated in the open air, it softens, melts at 286.7° C. (548° F.), swells, and at last inflames, leaving, after combustion, a small portion of ashes. Subjected to distillation in a retort furnished with a tabulated receiver, it yields, first, a yellow acid liquor, and afterwards a thin yellowish oil, with a yellow waxy substance, which is deposited in the neck of the retort and the upper part of the receiver. This waxy substance, exhausted by cold ether of the part soluble in that menstruum, is reduced to a yellow micaceous matter, identical with the *chrysen* of Laurent. A white, crystalline substance, identical with the *idrialin* of Dumas, may be separated from the micaceous substance by boiling alcohol. Both chrysen and idrialin are hydrocarbons. (Pelletier and Walter, *J. P. C.*, v, 60.) As the distillation proceeds, a considerable quantity of combustible gas is given off, which must be allowed to escape. By continuing the heat, the oil gradually deepens in color, until, towards the end of the distillation, it becomes black and of the consistence of pitch. The oil obtained is called *oil of amber* (*Oleum Succini*), and the acid liquor is a solution of impure *succinic acid*. Repeatedly distilled from nitric acid, amber yields an acid liquor, from which, after it has been neutralized with potassium hydroxide, ether separates pure camphor. (Doepping, *J. P. C.*, vi, 168.) Borneol is also obtained by distilling to dryness powdered amber with an extremely concentrated solution of potassium hydroxide. (G. Reich, *J. P. C.*, xiii, 33.)

Tschirch (*Harze und Harzbehälter*, 278) has made within recent years a careful study of amber. He finds the main constituents to be a *succinoabietic ether of borneol*, which is extracted by prolonged treatment with alcohol, and amounts to 30 per cent. of the amber, and the *succinic ester of succinoresinol*, which is insoluble in alcohol and makes up 70 per cent. of the amber. This latter compound holds a small amount of sulphur (about 0.47 per cent.).

Amber was held in high estimation by the ancients as a medicine, but at present is never so used. The *oil of amber* is an empyreumatic product which is prepared by destructive distillation of amber. The heat requisite for the complete decomposition of amber cannot be supported by a glass retort; and, in order that all the oil which it is capable of yielding may be collected, the distillation should be performed in a tubulated iron or earthenware retort, which may be placed immediately upon the fire; sand is added to prevent the amber from swelling too much. The oil may be separated from the acid liquor by means of the separating funnel. As first procured, it is a thick, very dark-colored liquid, of a peculiar, strong, empyreumatic odor. In this state it is occasionally employed as a liniment, but for internal use it should be rectified.

The U. S. Pharmacopœia of 1870, under the name of *Oleum Succini Rectificatum*, or *Rectified Oil of Amber*, gave the following process. "Take of Oil of Amber *a pint;* Water *six pints*. Mix them in a glass retort, and distil until four pints of Water have passed with the Oil into the receiver; then separate the Oil from the Water, and keep it in a well-stopped bottle." *U. S.*, 1870.

By successive distillations oil of amber becomes thinner and more limpid, till at length, it is obtained colorless. The first portions which distil are less colored than those which follow, and may be separated for keeping, while the remainder is submitted to another distillation. For practical purposes, however, the oil is sufficiently pure when once redistilled. As usually found in commerce, the rectified oil is of a light yellowish-brown or amber color. As first distilled it has an amber color, sp. gr. 0.903 at 15.6° C. (60° F.), and a boiling point from 170.5°–186.1° C. (339°–367° F.). (Ebert.) When quite pure it is said to be colorless, as fluid as alcohol, of the sp. gr. 0.758 at 23.8° C. (75° F.), and to boil at 85.5° C. (186° F.). It has a strong, peculiar, unpleasant odor, and a hot acrid taste. It imparts these properties in some degree to water, without being perceptibly dissolved. It is soluble in eight parts of alcohol of the sp. gr. 0.847, in five parts of the sp. gr. 0.825, and in all proportions in absolute alcohol, ether, chloroform, carbon disulphide, and the fixed oils. (Ebert.) On exposure to light and air, it slowly changes in color and consistence, becoming ultimately black and solid. It appears, when quite pure, to be a hydrocarbon of the terpene class. It is said to be sometimes adulterated with oil of turpentine, which may be detected by passing hydrochloric acid gas through the suspected oil. If pure it will remain wholly liquid; while oil of turpentine, if present, will give rise to the formation of a solid compound. (*P. J.*, xiii, 292.) It was officially described as "a colorless or pale yellow, thin liquid, becoming darker and thicker by age and exposure to air, having an empyreumatic, balsamic odor, a warm, acrid taste, and a neutral or faintly acid reaction. Sp. gr. about 0.920. It is readily soluble in alcohol. When mixed with fuming nitric acid, it acquires a red color, and, after some time, is almost wholly converted into a brown, resinous mass of a peculiar musk-like odor." *U. S.*, 1870.

Rectified oil of amber is stimulant and antispasmodic, and occasionally promotes the secretions, particularly that of urine. It has been employed with advantage in *amenorrhea*, *hysteria*, and *whooping cough*. The *dose* is from five to fifteen minims (0.3–0.9 mil), diffused in some aromatic water by means of sugar and gum arabic. Externally applied the oil is rubefacient.

Ambergris. *Ambra grisea* (*cinerea*). *Ambre, Ambre gris*, Fr. *Amber, Graue Ambra*, G.—This substance, which is found floating on the sea, particularly in the southern hemisphere, is now generally believed to be produced in the intestines of the *Physeter macrocephalus* L., or *sperm whale*. It is in roundish or amorphous pieces, usually small, but sometimes weighing as much as 50, 100, or even 200 pounds. These pieces are often composed of concentric layers. They are of various colors, usually gray, with brownish, yel-

low, and white streaks, often dark brown or blackish on the external surface. They are opaque, lighter than water, and of a consistence like that of wax. Ambergris has a peculiar aromatic agreeable odor, is almost tasteless, softens with the warmth of the hand, melts under 100° C. (212° F.), is almost completely volatilizable by heat, and is inflammable. It is insoluble in water, but is readily dissolved, with the aid of heat, by alcohol, ether, and the volatile and fixed oils. It consists chiefly of a peculiar fatty matter analogous to cholesterin, and denominated by Pelletier and Caventou *ambrein*. This may be obtained by treating ambergris with heated alcohol, filtering the solution, and allowing it to stand. Crystals of ambrein are deposited. It is incapable of forming soaps with the alkalies. When pure it has little or no odor. Beauregard and Gouchet believe that ambergris is a calculus composed of crystals of *ambrene* mixed with black pigment and star-coral débris. When fresh it is soft in consistence and disagreeable in odor. If kept for a year or two in air tight containers it loses its excrementitious odor and acquires the characteristic perfume for which it is valued, although its use in perfumery is more for the purpose of fixing delicate floral odors than for any odor which it contributes to the mixture itself. This change Beauregard believes is due to a microbe (*Spirillum recti physeteris*). (*C. R. A. S.*, cxxv, 254.) Ambergris is very frequently adulterated, and it then does not exhibit its ordinary odor, fusibility and volatility.

Ambergris was long regarded as a cordial and antispasmodic, somewhat analogous to musk, useful in *typhoid fevers*, and various nervous diseases. It formerly entered into many official preparations, and is still retained in some European pharmacopœias. The *French Codex* formerly directed a tincture to be prepared by macerating, for ten days, 100 parts of powdered ambergris with 1000 parts of alcohol of sp. gr. 0.864, expressing and filtering. Martin affirms that the tincture will keep better, deposit nothing, and have a more agreeable odor, if the ambergris, instead of being merely powdered in a mortar, be subjected to porphyrization, especially with the addition of washed sand. Heat, he says, should never be used in its preparation. (*J. P. C.*, 4e sér., i, 448.) It is, however, feeble as a remedy, and is chiefly used in perfumery. It is comparatively rare and very expensive, the black variety commanding a price of from $10 to $15 an ounce, while the white or gray variety costs in the neighborhood of twice that figure. *Dose*, five grains to a drachm (0.32–3.9 Gm.).

Ambrine.—The trade name for a French proprietary preparation which has been on the market for many years, but has come into prominence because of its large use during the European war in the treatment of *burns*. Similar preparations are on the market sold under the trade names *mulene, parresine, thermozine, hyperthermine,* etc. It is essentially solid paraffin with the addition of ingredients which increase its adhesiveness and plasticity. According to Leach, a similar preparation may be made by dissolving 5 drops of asphalt (asphalt varnish or *B. asphaltum*) in 1.5 mils of olive oil with the aid of heat, and incorporating the solution with 97.5 Gm. of melted paraffin (melting point 47.2° C. (117° F.). (*J. A. M. A.*, lxviii, p. 1498.) A number of other formulas have been proposed, among them paraffin, 96 per cent., and yellow wax, 4 per cent. The essential factor seems to be a melting point between 38° and 53° C. (100.4°–127.4° F.), a sterile product, sufficient strength to the film so that it may readily be lifted from the burn and a pliability which will prevent breaking if bent. In applying it to the burn the melted mixture is sprayed or painted over the area, to form a thin layer, absorbent cotton is then applied and afterwards more of the melted mixture. (Sollmann, *J. A. M. A.*, lxviii, p. 1037.)

Ambrosia. *Ambrosia trifida* L. *Ragweed, Roman Wormwood, Hog-weed, Bitter-weed, Ambrosie*, Fr. *Traubenkraut*, G. (Fam. *Compositæ.*)—This and another indigenous annual, *A. artemisiifolia* L., are deemed by the eclectics astringent and stimulant, and are given in low forms of *fever*. L. W. Schwab has found in *A. artemisiifolia* a bitter glucoside (*A. J. P.*, 1890), and Schimmel & Co. have obtained from it about 0.15 per cent. of a green volatile oil (sp. gr. 0.876). (*Schim. Rep.*, 1904, p. 96.) The pollen of this plant is also said to be one of the causes of *hay fever*. It is estimated that there are about 90,000,000 pollen grains in a gramme of ragweed pollen.

Amenyl.—Amenyl was first prepared by Freund and Heim. It is the hydrochloride of *methylhydrastimide*. It occurs as yellowish needles, melting at 227° C. (440.6° F.), soluble in hot water and alcohol. Amenyl has been used by Falk (*Th. M.*, 1909, p. 581) in the treatment of *amenorrhea*. In cases of functional amenorrhea, especially occurring during the period of puberty, he obtained good results, but in the more severe menstrual disturbances it was of little value. He believes that its action depends upon a dilatation of the blood vessels. The *dose* is one grain (0.065 Gm.).

Amidoacetal. $H_2N.CH_2CH(O.C_2H_5)_2$.—According to the experiments of A. Mallèvre (*A. Phys.*, xlix), this substance is an active poison, causing death in mammals by respiratory paralysis.

Amido-azotoluol.—Under the name of *epithermol* has been introduced a purified form of amido-azotoluol. It is asserted to have a marked power in stimulating the growth of epithelium and to be a useful application to aid the healing of skin over large *wound surfaces*, and *old ulcers*. It may be applied in the form of ointment containing 8 per cent. or in 4 per cent. alcoholic solution, or as a 10 per cent. dusting powder. Curbski (*Cb. Chir.*, 1910) has reported a case of poisoning from the use of this ointment in which the symptoms resemble those of aniline poisoning. According to Curschmann (*Th. M.*, 1911, p. 717) the acetylization of amido-azotoluol diminishes its toxicity and does not affect its therapeutic value. This preparation is on the market under the name of *azodermin*.

Amidophenols. *Derivatives of p-amidophenol*, $C_6H_4(OH)NH_2$.—In an elaborate series of experiments (*Cb. I. M.*, 1897) Treupel and Hinsberg find that derivatives from amidophenol are active as antipyretics in proportion as they are decomposed in the system, and that the decomposition is to be measured by the amount of indophenol in the urine. Among these substances is *dulcin*, called also *para-phenetolcarbamide* and *sucrol*,

$$CO\begin{cases} NH.C_6H_4.OC_2H_5 \\ NH_2 \end{cases}$$

which occurs in white, glittering, needle-like crystals, melting at from 173°–174° C. (343.4°–345.2° F.), soluble in 800 parts of cold and 55 of boiling

water, and 25 of alcohol, having a taste which is said to be two hundred times sweeter than sugar. (Dulcitol, the carbohydric alcohol related to gelatose, is sometimes assigned the name of "dulcin," and should not be confused with the amidophenol "dulcin" which possesses distinctly different characteristics.) It has been recommended as a substitute for sugar, in *diabetes*, and, on account of its solubility, to improve the flavor of castor, cod liver, or other oils. According to Treupel and Hinsberg, fifteen grains (1 Gm.) of it will reduce the temperature in fever about one degree Centigrade in the course of about three hours, and no unaltered dulcin is to be found in the urine, but indophenol.

Besides dulcin, Treupel and Hinsberg examined physiologically the following amidophenol derivatives: *Lactylamidophenolethylcarbonate, benzoylacetamidophenol, ethyldiacetamidophenol, oxyphenacetinsalicylate.*

The use of dulcin and other artificial sweetening agents as substitutes for cane sugar is prohibited by most food laws.

Aminol.—This is an antiseptic liquid, colorless, slightly turbid, and having the odor of trimethylamine. It is alkaline in reaction. Sp. gr. 1.01. It is obtained commercially from herring pickle. It is supposed to contain in each liter 1.5 Gm. calcium hydroxide, 3.5 Gm. sodium chloride, and 0.3 Gm. trimethylamine. A tablespoonful (15 mils) diluted with a fluidounce of water may be used for a lotion, gargle, or spray.

Ammi. *Ammi visnaga* Lam.—The fruit of this umbelliferous plant, indigenous in the countries around the Mediterranean, contains a crystalline principle, *kellin* (*C. R. A. S.*, August, 1879), which is said (*Union Méd.*, April, 1886) to act upon the heart and spinal cord. Mild antipyretic and antilithic properties have been attributed to the fruit.

Ammonium Anacardate. *Acid Ammonium Anacardate.*—This is the ammonium compound of beta and delta resinous acids of *Anacardium Occidentale.* (*Cashew Nut.*) It is a brownish mass, soluble in alcohol and decomposed by heat with liberation of ammonia. It is used as a hair dye and is incompatible with acids or acid salts and with lead acetate.

Ammonium Arsenate. *Ammonii Arsenas.* $(NH_4)_2HAsO_4$.—This salt is obtained in crystals by saturating a concentrated solution of arsenic acid with ammonia or ammonium carbonate, and allowing it to evaporate spontaneously. The crystals, which belong to the trimetric system, effloresce on exposure to the air, and lose half their ammonia. Its solution is alkaline. It has been used with advantage by Biett in several inveterate *diseases of the skin.* It is administered in solution, one grain of the salt in a fluidounce of distilled water; twenty to twenty-five minims (1.2–1.6 mils) of this solution may be given in divided portions in the course of the day.

The *arsenite of ammonia*, NH_4HAsO_2, a water-soluble, white powder, has also been used after the manner of and for the same purposes as the arsenate.

Ammonium Bicarbonate. *Acid Carbonate of Ammonium.* $H(NH_4)CO_3$.—This salt was brought into notice by Wm. Procter, with reference to its antacid properties. It is formed by exposure of the ordinary carbonate to the air, and is found in considerable quantities on the sides of casks in which that salt is imported, and less largely even in the bottles in which it is kept in commerce. For further information concerning this salt, see *U. S. D.*, 19th ed.

Ammonium Binoxalate. *Acid Ammonium Oxalate.* $NH_4H_2CO_4 + H_2O$.—Colorless trimetric crystals soluble in water and used solely for removing ink stains, and ecchymotic spots from the face.

Ammonium Bisulphite. NH_4HSO_3.—White crystals soluble in water and used internally in fermentative *dyspepsia* in ten to thirty grain (0.66–2.0 Gm.) doses and externally as a wash in *sore mouth* and *skin affections.* The *bisulphate*, NH_4HSO_4, colorless water-soluble crystals, has been given in fifteen to sixty grain (0.9–3.9 Gm.) doses in *gastric affections.*

Ammonium Borate. *Ammonium Metaborate.* $(NH_4HB_4O_7) + 3H_2O$.—Only the acid salt is known. By dissolving one part of boric acid in excess, in three parts of heated water of ammonia, sp. gr. 0.960, and allowing the solution to cool slowly, this salt is obtained in crystals. These are rhombic octahedrons, with truncated summits, and often truncated edges, and are semi-transparent. The taste of the salt is alkaline, and it has an alkaline reaction. On exposure, it effloresces, losing ammonia, and becoming in time the tetraborate. It is soluble in about twelve parts of water. (Gmelin, ii, 435.) Becker has used it with asserted great advantage in *stone in the bladder* and *renal colic.* Under its influence the urine becomes loaded with uric acid and the earthy phosphates. It is said also to be an excellent remedy in *chronic catarrh of the bladder.* It is believed by Becker to be the *ludus* of Paracelsus, which had a great reputation in the treatment of *urinary calculi. Dose*, ten to twenty grains (0.65–1.3 Gm.) every hour, in water sweetened with licorice. (*Journ. de Thérap. Méd.-Chir.*, Sept. 1, 1866.)

Ammonium Camphorate. *Ammonium Bicamphorate.* $NH_4HC_{10}H_{14}O_4 + 3H_2O$.—A white, crystalline powder soluble in water and possessing a sedative action on the nervous system. *Dose*, one to three grains (0.06–0.18 Gm.).

Ammonium Caseinate. *Ammonii Caseinas. Eucasinum. Casein-ammonium.*—A compound made by passing ammonia over casein until it is soluble in water, forming a nearly clear solution. In the form of a white or slightly yellow powder, almost without odor or taste. It is recommended as a dietetic, given in soups, chocolate, etc.

Ammonium Hypophosphite. *N. F. IV. Ammonii Hypophosphis.*—According to the N. F. "it contains, when dried to constant weight at 100° C. (212° F.), not less than 97.5 per cent. of $NH_4PH_2O_2$ (83.10). Preserve it in well-closed containers. It occurs in deliquescent, colorless, hexagonal plates, or as a granular powder, odorless and having a saline and bitter taste. One gramme dissolves in about 1 mil of water, and in about 20 mils of alcohol at 25° C. (77° F.); very soluble in boiling water or boiling alcohol. When heated, the salt is decomposed with the evolution of hydrogen phosphide, which is spontaneously inflammable. Dissolve 1 Gm. of Ammonium Phosphate in 20 mils of distilled water; the resulting solution is not more than slightly turbid (*calcium, aluminum*). Ten mils of an aqueous solution of the salt (1 in 100), acidulated with nitric acid, is not rendered more than slightly opalescent by silver nitrate T.S. (*chloride*). Ten mils of an aqueous solution of Ammonium Phosphate (1 in 100) mixed with 2 mils of hydrochloric acid is not rendered turbid at once by the

addition of a few drops of barium chloride T.S. (*sulphate*). An aqueous solution of the salt does not respond to the Test for heavy metals (see *U. S. P.*, Test No. 3, Part III). An aqueous solution of the salt meets the requirements of the Test for arsenic (see *U. S. P.*, Test No. 1, Part III)." *N. F.*

Assay.—"Transfer about 1 Gm. of Ammonium Phosphate, accurately weighed, to a distilling flask, dissolve it in 300 mils of distilled water and add 25 mils of an aqueous solution of sodium hydroxide (1 in 4). Connect the flask with a small glass condenser, the lower outlet tube of which is inserted beneath the surface of 50 mils of half-normal sulphuric acid V.S., contained in a flask of about 500 mils capacity, and distil the liberated ammonia into the acid. Titrate the excess of acid with half-normal potassium hydroxide V.S., using methyl orange T.S., as an indicator and calculate the percentage of ammonia in the salt. It shows not less than 20 per cent. of NH_3. Each mil of half-normal sulphuric acid V.S. used corresponds to 0.008515 Gm. of NH_3. Each gramme of Ammonium Phosphate corresponds to not less than 23.5 mils of half-normal sulphuric acid V.S." *N. F.* It possesses the therapeutic properties of the hypophosphites with the additional stimulating property of the ammonium. It is recommended by clinicians particularly in the latter stages of *bronchitis* and *laryngitis*. *Dose*, two to five grains (0.13–0.3 Gm.) every two or three hours.

Ammonium Nitrate. *Ammonii Nitras. U. S.* 1890. *Nitrate of Ammonia.* NH_4NO_3.—Ammonium nitrate may be prepared by treating commercial ammonium carbonate with nitric acid so long as effervescence takes place, or to saturation, filtering, and evaporating the solution. By careful evaporation and slow refrigeration the salt may be obtained in well-defined crystals. If crystallized after rapid concentration by boiling and sudden cooling, it forms long, flexible and elastic threads. If the solution be heated till all the water has been driven off and the fused mass kept at a temperature not exceeding 160° C. (320° F.), the commercial salt is produced. It is usually obtained as a by-product in the manufacture of other chemicals.

"Colorless crystals, generally in the form of long, thin, rhombic prisms, or in fused masses, without odor, having a sharp, bitter taste, and somewhat deliquescent. Soluble, at 15° C. (59° F.), in 0.5 part of water, and in 20 parts of alcohol; very soluble in boiling water, and in 3 parts of boiling alcohol. When gradually heated, it melts at 165°–166° C. (329°–330.8° F.); at a temperature between 230° and 250° C. (446°–482° F.) it is decomposed into nitrogen monoxide gas and water, leaving no residue. The aqueous solution of the salt is neutral to litmus paper, and when gently heated with potassium or sodium hydrate test-solution, it evolves the odor of ammonia. On heating the salt with sulphuric acid, it emits nitrous vapors." *U. S.*, 1890.

For further information concerning this salt, see *U. S. D.*, 19th ed., p. 1380.

For the mode of preparing nitrogen monoxide (hyponitrous oxide), or nitrous oxide gas, from ammonium nitrate, see *Nitrogen Monoxide*, p. 719.

Ammonium Persulphate, $(NH_4)_2S_2O_8$, is prepared by electrolyzing an acid solution of ammonium sulphate, and is a most efficient oxidizing agent in acid, neutral, or alkaline solutions. It occurs in small, colorless crystals, soluble in water. Its solution evolves oxygen when heated, and is used as an antiseptic and as a cheap and effective mouth wash. Ammonium persulphate is used in photography. In medicine it is chiefly valuable as forming the basis of *Klett's test* (*Chem. Ztg.*, 1900, p. 690) for indican in urine. To 10 mils (160 minims) of urine add 5 mils (80 minims) of 25 per cent. hydrochloric acid together with a crystal of ammonium persulphate, to which add chloroform, when a blue color develops in the latter.

Ammonium Phosphate. *N. F. IV, Br.*, 1898. *Ammonii Phosphas. Ammoniæ Phosphas. Phosphate of Ammonia. Phosphas Ammonicus. Phosphate d'Ammoniaque*, Fr. *Ammonium Phosphoricum. Phosphorsaures Ammoniak*, G. *Ammon. Phos.*—"It contains diammonium hydrogen phosphate [$(NH_4)_2HPO_4 = 132.13$] and ammonium dihydrogen phosphate [$NH_4H_2PO_4 = 115.09$], corresponding to not less than 20 per cent. of combined ammonia ($NH_3 = 17.03$). Preserve it in well-closed containers in a cool place." *N. F. IV.* "A salt, $(NH_4)_2HPO_4$, which may be obtained by neutralizing phosphoric acid with solution of ammonia." *Br.* (1898).

The *diammonium hydrogen phosphate* was formerly official, under the name of ammonium phosphate, in both the United States and British Pharmacopœias. The preparation recognized at present, by the N. F., is a mixture of this salt with the more acid ammonium di-hydrogen phosphate.

The process formerly given in the British Pharmacopœia involved treating diluted phosphoric acid with stronger ammonia water until the solution was slightly alkaline, then evaporating until crystals formed on cooling, ammonia being added from time to time in order to maintain constantly a slight excess of this base. Without such a precaution a portion of the more acid phosphate will be formed owing to the escape of the ammonia during the process of evaporation. This salt may also be made by saturating the excess of acid in acid calcium phosphate by means of ammonium carbonate. Calcium phosphate is precipitated and ammonium phosphate obtained in solution, which, being duly concentrated by a gentle heat, affords the salt in crystals upon cooling. The method of obtaining the acid calcium phosphate is given under the head of sodium phosphate. (See *Sodii Phosphas.*) Ammonium phosphate prepared in this way is a white salt, crystallizing in six-sided tables, derived from oblique quadrangular prisms, efflorescent, insoluble in alcohol, and soluble in four parts of cold water. The solution has an alkaline, somewhat saline taste, and an alkaline reaction, and gives off ammonia when heated.

The other acid phosphate, $NH_4H_2PO_4$, is obtained by boiling a solution of either of the other salts so long as ammonia escapes, and then crystallizing. Its crystals are four-sided prisms, permanent in the air, of an acid taste and reaction, and soluble in 5 parts of cold water. (Bridges.)

The ammonium phosphate of commerce is a mixture of these two phosphates and hence corresponds more closely with the N. F. definition.

The variety of phosphoric acid employed in this formula is the tribasic, which forms three salts with ammonia, one containing three atoms of ammonium without basic hydrogen, which is called the neutral phosphate, the second, two molecules of ammonium and one of basic hydrogen, forming an acid phosphate, and the third, one molecule of ammonium and two of basic hydrogen, forming also an acid phosphate. The second of these was

the one intended by the U. S. (1880) and British Pharmacopœias, and is represented by the formula $(NH_4)_2HPO_4$.

The description of this salt in the N. F. is as follows:

"Ammonium Phosphate occurs in colorless crystals, or as a white crystalline powder, losing ammonia on exposure to the air. One Gm. dissolves in about 4 mils of water; it is insoluble in alcohol. An aqueous solution (1 in 20) is neutral or alkaline to litmus. Separate portions of an aqueous solution of the salt (1 in 20) yield with magnesia mixture T.S. a white precipitate, with silver nitrate T.S., a yellow precipitate, and, upon warming with ammonium molybdate T.S., a yellow precipitate. Dissolve 1 Gm. of Ammonium Phosphate in 20 mils of distilled water; the resulting solution is not more than slightly turbid (*calcium, aluminum*). Ten mils of an aqueous solution of the salt (1 in 20), acidulated with nitric acid, is not rendered more than slightly opalescent by silver nitrate T.S. (*chloride*). Ten mils of an aqueous solution of Ammonium Phosphate (1 in 100) mixed with 2 mils of hydrochloric acid is not rendered turbid at once by the addition of a few drops of barium chloride T. S. (*sulphate*). An aqueous solution of the salt does not respond to the Test for heavy metals (see *U. S. P.*, Test No. 3, Part III). An aqueous solution of the salt meets the requirements of the Test for arsenic (see *U. S. P.*, Test No. 1, Part III)." *N. F.*

Assay.—"Transfer about 1 Gm. of Ammonium Phosphate, accurately weighed, to a distilling flask, dissolve it in 300 mils of distilled water and add 25 mils of an aqueous solution of sodium hydroxide (1 in 4). Connect the flask with a small glass condenser, the lower outlet tube of which is inserted beneath the surface of 50 mils of half-normal sulphuric acid V.S., contained in a flask of about 500 mils capacity, and distil the liberated ammonia into the acid. Titrate the excess of acid with half-normal potassium hydroxide V.S., using methyl orange T.S. as an indicator, and calculate the percentage of ammonia in the salt. It shows not less than 20 per cent. of NH_3. Each mil of half-normal sulphuric acid V.S. used corresponds to 0.008515 Gm. of NH_3. Each gramme of Ammonium Phosphate corresponds to not less than 23.5 mils of half-normal sulphuric acid V.S." *N. F.*

The British Pharmacopœia (1898) gave the following quantitative test: "When 2 grammes are dissolved in *water*, and *solution of magnesium ammonio-sulphate* is added in excess, a crystalline precipitate should be formed, which, after being well washed upon a filter with *solution of ammonia* diluted with an equal volume of *water*, and then dried and heated to redness, weighs 1.68 grammes." The amount of the residue, which is magnesium pyrophosphate, indicates the quantity of phosphoric acid contained in the salt. This quantitative test for phosphoric acid was for the purpose of identifying the di-ammonium hydrogen phosphate.

This salt was first brought to the notice of the profession as a remedy for *gout* and *rheumatism*, by T. H. Buckler (*A. J. M. S.*, 1846), and has since been so employed with apparently useful results.

Dose, from five to thirty grains (0.32–1.9 Gm.), three or four times a day, dissolved in a tablespoonful of water.

Ammonium Sulphate. *Ammonii Sulphas. U. S.* 1880. *Sulphate of Ammonium.* $(NH_4)_2SO_4$; 131.21. *Ammonium Sulphuricum. Sal Ammonium Secretum Glauberi. Sulfate d'Ammoniaque, Sel secret de Glauber*, Fr. *Schwefelsaures Ammon, Ammonium, Ammoniak*, G.—Gas liquor is distilled with lime and the gas received in sulphuric acid, which yields a purified product. Most of the ammoniacal liquor is worked up into ammonium sulphate at present. In the United States the production of ammonium sulphate has increased enormously in recent years, owing to the introduction of by-product coke ovens. In 1915 the production from this source was 197,000 tons, of which 50,700 tons additional were obtained from coal gas plants. The total value was $11,175,000. (*U. S. Geological Survey Report*). "Colorless, transparent, rhombic prisms, permanent in the air, odorless, having a sharp, saline taste and a neutral reaction. Soluble in 1.3 parts of water at 15° C. (59° F.) and in 1 part of boiling water; insoluble in absolute alcohol, but slightly soluble in alcohol of sp. gr. 0.817; when heated to about 140° C. (284° F.), the salt fuses, is gradually decomposed, and on ignition is wholly dissipated. The aqueous solution of the salt, when heated with potassa, evolves vapor of ammonia. With test-solution of chloride of barium it yields a white precipitate insoluble in hydrochloric acid. A 1 per cent. solution of the salt should not be blackened by test-solution of sulphide of ammonium (lead and iron), nor, when acidulated with nitric acid, should it be rendered more than opalescent by test-solution of nitrate of silver (limit of chloride)." *U. S.*, 1880. It is not used as a medicine, but enters into the composition of ammonium alum and the iron and ammonium sulphate, and is the principal source of ammonia gas used in chemical manufacturing, refrigeration, etc.

Ammonium Tartrate.—The neutral ammonium tartrate has been used by Clausen for the clearing up of *corneal opacities*. The eye is irrigated with a warm neutralized solution containing 5 per cent. of ammonium tartrate for twenty to thirty minutes two or three times a day.

Ammonium Uranate. *Ammonii Uranas.* $NH_4 U_2O_7 + (H_2O)_n + Aq$.—This is a reddish-yellow, amorphous powder, insoluble in the usual solvents. It has been used by Weil (*S. M.*, 1907, p. 573) with asserted favorable results in the treatment of *syphilis*. The remedy was administered in doses of five-sixth grain (0.05 Gm.), suspended in a liquid petrolatum, by intra-muscular injection. The strength of the suspension was 5 per cent. and the injections were made once a week. The treatment required on an average of two months. It is used in the arts for painting on porcelain.

Ammonium Urate. *Ammonii Uras.* $C_5H_3(NH_4)N_4O_3$.—This is an acid salt, and may be formed by digesting uric acid in solution of ammonia, or by adding sal ammoniac to the solution of other urates. Uric acid is frequently obtained from the dried and powdered excrements of the boa constrictor, and of other large snakes, by dissolving it in a weak solution of potassium hydroxide with the aid of heat, and precipitating the uric acid from the filtered solution by hydrochloric acid, added in excess. Ammonium urate is a white, amorphous, very sparingly soluble salt. It is a constituent of some varieties of guano. It has been used with asserted good effects externally in chronic *eczema*, in the form of an ointment (twenty grains to the ounce). (See 16th edition

U. S. D.) Neubauer found that when given internally to rabbits it causes increase in the urea, uric acid, and oxalates of the urine. (*Ranking's Abstract*, 1857.)

Amygdophenin. *Phenetidin Amygdalate.* $C_6H_4.OC_2H_5NH.CO.CH.OH.C_6H_5$. *Phenyl-glycol-phenetidin.*—This is a derivative of *p-amidophenol*, analogous to phenacetin. In constitution it is a light, crystalline, grayish-white powder, soluble with difficulty in water. It is obtained by the action of mandelic acid upon *p-phenetidin* in the presence of dehydrating agents. R. Stüve asserts that it is practically free from antipyretic properties; that it is an analgesic which is often useful in *neuralgias* and the pains of *spinal scleroses;* and that it is very useful in *rheumatism*, it having had more effect in some comparative trials than the salicylates. It is best administered in capsules, fifteen grains (1 Gm.), from three to six times a day.

Amyl Alcohol. *Alcohol Amylicum. Amylic Alcohol*, $C_5H_{11}OH$. *Hydrated Oxide of Amyl. Fousel Oil. Fusel Oil. Hydrate of Amyl. Grain Oil. Potato Spirit Oil. Alcool Amylique, Huile de Grain*, Fr. *Amylalcohol, Fuselöl*, G.—This alcohol is always present in the products of alcoholic fermentation, and, according to the experiments of L. Perdrix (*J. Chem. S.*, 1892, 90), the bacillus *B. amylozymicus* produces a fermentation in starch resulting in a large production of amyl alcohol. It is an ingredient in the ardent spirit obtained from various grains, but is most abundant in that procured from fermented potatoes. In grain spirit it is present in the proportion of about one part in five hundred by measure. When grain or potato whisky is distilled for the purpose of obtaining alcohol, the pure spirit will continue to come over for a certain time, after which, if the distillation be continued, a milky liquid will be obtained, which, upon standing, will be covered with a stratum of amyl alcohol. Subjected to distillation, the milky liquid will at first boil at a comparatively low temperature, and yield water and a little of the alcohol; but after a time the boiling point will rise to 132° C. (269.6° F.), when the amyl alcohol will come over pure, and by changing the receiver may be so collected.

Properties.—Amyl alcohol is an oily, colorless liquid, of a strong, characteristic odor, and an acrid, burning taste. As usually prepared it has a pale yellow color. Its sp. gr. is 0.818; that of its vapor 3.15. It boils at 132° C. (269.6° F.), and congeals at −25° C. (−13° F.) in the form of crystalline leaves. It is very sparingly soluble in water, but unites in all proportions with alcohol, ether, and essential oils. It dissolves iodine, sulphur, and phosphorus, and is a good solvent for fats, resins, camphor, and alkaloids. When dropped upon paper it does not leave a permanent greasy stain. It does not take fire like alcohol by the contact of flame, but requires to be heated to a temperature of about 54.5° C. (130° F.) before it begins to burn. Pasteur first observed that the ordinary amyl alcohol of fermentation was a mixture of two distinct alcohols, one present in smaller amount, optically active, levogyrate, and the other, the main portion, optically inactive. Their boiling points are very close, but they may be separated by the difference in solubility of the barium amyl-sulphates, and yield different sets of derivatives. (*C. R. A. S.*, 41, 296.) Heated with phosphoric acid, it loses a molecule of water, and forms a hydrocarbon, C_5H_{10}, homologous with ethylene, called *amylene* or *valerene*, which has been proposed as an anesthetic. According to Long and Linebarger, American fusel oil consists chiefly of active and inactive amyl alcohol, with some isobutyl alcohol, isopropyl and ethyl alcohols, and traces of normal propyl and normal butyl alcohols. (*Chem. News*, lxi, 185–187.) Amyl alcohol should not affect the color of litmus paper, previously moistened with water, should leave no fixed residue upon evaporation, should require to dissolve it about 40 parts of distilled water at 15° C. (59° F.), and should become not more than slightly turbid upon mixture with petroleum benzin (absence of more than a little alcohol, or water). (See *Amylene* below.) When subjected to oxidizing agents, it loses two atoms of hydrogen and gains one of oxygen, and becomes $C_5H_{10}O_2$, or *valeric acid*, the acid found in valerian. Hence the test given in the Br. Pharmacopœia of 1885: "Exposed to the air in contact with platinum-black, it is slowly oxidized, yielding valerianic (valeric) acid." This acid bears the same relation to amyl alcohol that acetic acid does to ethyl alcohol, and formic acid to methyl alcohol. The free amyl, $(C_5H_{11})_2$, has been isolated by E. Frankland. It is a colorless, transparent liquid, of the sp. gr. 0.7704. (*Chem. Gaz.*, March 15, 1850.) Its hydride, $C_5H_{11}H$, was discovered to be an energetic anesthetic by Simpson of Edinburgh. A mixture of amyl alcohol, green soap, phenol (1 per cent.) and water, under the trade name of *Amyl Karbol*, has a wide use in Europe as a disinfecting solution.

Crude fusel oil may be obtained from the alcohol distillers. Kent, of New York, found in it, as impurities, water, alcohol, acetic and valeric acids, oxide of iron, and an amyl compound analogous to *œnanthic ether*. Fusel oil has been used largely by the manufacturers of alkaloids as a solvent and in the preparation of *amyl acetate* (*pear oil, banana oil*), which is used in the manufacture of pyroxylin varnishes and smokeless powder and as a basis for the manufacture of isoprene, lately used in the manufacture of synthetic cacoutchouc. This manufacture of amyl acetate for solvent purposes now consumes the great bulk of the fusel oil obtained from the rectifiers.

Fusel oil was formerly recognized by both the United States and the British Pharmacopœias as an artificial source of valeric acid.

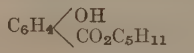
Amyl alcohol is a very active narcotic, and under the name of *Faints* (*feints*) is used in England and Northern Europe for the purpose of increasing the activity and prolonging the effects of ordinary liquors. In small doses it is said to be especially efficacious in controlling the nervous weakness and irritability of confirmed drunkards, while larger doses produce headache, giddiness, double vision, staggering, unconsciousness, fall of temperature, abolition of reflexes, muscular rigidity, followed by complete relaxation, pronounced cyanosis, and a peculiar odor from the breath suggesting that of a Jargonelle pear.

Horand has employed amyl alcohol for its disinfecting and dessicating action in inoperable *cancerous ulcers*. (*R. T.*, 1910.) He asserts that by the local application of from three to ten drops daily there is not only a disappearance of the odors, but often a shrinking in the size of the tumor, and considerable improvement in the general condition.

T. B. Futcher (*Am. Med.*, August, 1901, p. 210) has shown that both in animals and also in man, when taken in toxic doses, fusel oil affects profoundly the blood, causing methemoglobinuria,

also glycosuria, attended with the presence of combined glycuronic acid, and in some cases violent nephritis. The size of the fatal dose probably varies very much. It is affirmed that death occurred from the taking of a single fluidounce (30 mils), but in another case recovery resulted after six fluidounces (180 mils) had been swallowed.

Amyl Salicylate. *Salicylic Amylester. Amylenol.*



A colorless to a yellow refracting fluid, possessing an odor resembling that of salol, having the sp. gr. 1.065 at 15° C. (59° F.) and made by the action of chlorine on a solution of salicylic acid in amyl alcohol. It boils at 270° C. (518° F.). It is slightly dextrorotatory. Refractive index (20°) 1.505–1.507. The preparation dissolves in ether, alcohol, and chloroform, but it is almost insoluble in water. This substance has been proposed by B. Lyonnet (*R. T.*, lxviii, No. 2) as a substitute in *rheumatism* for methyl salicylate, over which it has the advantage of less pronounced odor and taste. It is also coming into wide use as a fixing agent for delicate odors in the perfumer's art. It is given internally usually in gelatin capsules, three to five minims (0.2–0.3 mils) each, eight or ten times a day. It has also been found very useful as a local application, one-half to one drachm (2.0–3.9 Gm.), being applied to rheumatic joints and covered with wax paper, or other impervious dressing. It is incompatible with acids or acid salts and with iron compounds.

Amyl Valerate. *N. N. R.* 1917. $C_4H_9COOC_5H_4$.—The isovaleric acid ester of iso-amyl alcohol. A colorless liquid having, when diluted with alcohol, in which it is very soluble, an odor of apples. Insoluble in water, sp. gr. 0.858; boiling point 188°–190° C. (370.4°–374° F.). It has been used in the place of valerian in the treatment of various nervous conditions.

Pouchet asserts that amyl valerate (*J. des Pr.*, 1899, 45) has the power of softening, or if present in sufficient quantity, of dissolving cholesterin, and recommends its use in the treatment of *gall-stones*. *Dose*, three to eight minims (0.2–0.5 mil). Technically it has been used as an artificial apple flavor.

Amylamine Hydrochloride, *Amylamine Chloride*, $C_5H_{11}NH_2HCl$, $C_5H_{13}N.HCl$, crystallizes either in efflorescent scales or in quadratic octahedrons. According to Dujardin-Beaumetz (*C. R. A. S.*, lxxvii, 1247), in small doses (from $^1/_{60}$–$^1/_{12}$ grain (0.001–0.005 Gm.) to a rabbit) this salt lowers the temperature and also the force and frequency of the pulse. In larger amounts it produces profound nervous disturbance, with tonic and clonic convulsions, ending often in death. In man, doses of from seven to fifteen grains (0.45–1.0 Gm.) diminish the pulse and temperature.

From amylamine hydrochloride by boiling with an excess of calcium chloride is formed *amyldichloramine*, a yellowish-green oily liquid, the smelling of which produces violent irritation of the mucous membrane of the nose, followed by severe headache and vertigo. According to the researches of Boinet (*Congrès Français de Méd.*, 1, 1894), it is not only a violent local irritant, but also a powerful centric poison, producing death by asphyxia. Boinet has also examined physiologically *propyldichloramine* and *isobutyldichloramine*, finding that they are similar in their toxic influence to amyldichloramine.

Amylene. *Valerene. Pentene.* C_5H_{10}.—This compound was alluded to under amyl alcohol. The name is given to the isomeric hydrocarbons of the olefin series, having the formula C_5H_{10}, of which five are possible. Amylene is prepared by distilling amyl alcohol with a concentrated solution of zinc chloride, which acts by dehydrating, withdrawing a molecule of water. The product is redistilled, and that which comes over first, constituting the more volatile part, is separately collected, and agitated with concentrated sulphuric acid, when the amylene, freed from water, will rise to the surface. Amylene is a colorless, very mobile liquid, having the density 0.655 at 10° C. (50° F.). Its boiling point is 34° C. (93.2° F.). Its odor is peculiar and disagreeable. It is soluble in alcohol and ether in all proportions, but very sparingly so in water. When pure it does not act on potassium, and is not colored by a prolonged contact with potassium hydroxide.

In 1857, Snow, of London, proposed amylene as an anesthetic. It was soon shown, however, to be dangerous, the French Academy of Medicine formally condemning it.

Amylene Hydroxide. Amylene Hydrate. Tertiary Amyl Alcohol. Dimethylethylcarbinol ($C_5H_{12}O$ or $(CH_3)_2C.(C_2H_5)OH$) is a clear, colorless liquid, of a strong, penetrating odor, soluble in eight parts of water, and miscible with alcohol, ether, chloroform, petroleum benzin, glycerin, and fixed oils in almost all proportions; sp. gr. 0.812 at 12° C. (53.6° F.).

In 1887, von Mering proposed the use of amylene hydroxide as a soporific, stating that it stood midway between hydrated chloral and paraldehyde, one drachm (3.9 Gm.) of hydrated chloral, two drachms (7.7 Gm.) of amylene hydroxide, and three drachms (11.6 Gm.) of paraldehyde being about equivalent in power. In cases of poisoning, reported by C. Dietz, by the amylene hydroxide, the symptoms were deep narcosis, dilated pupils, loss of corneal reflexes, slow, deep, irregular breathing, small, slow pulse, and fall of temperature. Amylene hydroxide is a safe, rapidly acting, and occasionally useful but not analgesic hypnotic, in doses of from thirty to forty minims (1.8–2.5 mils). According to Brackmann, confirmed by W. Niessen, it is very valuable in *diabetes insipidus*, lessening thirst and polyuria. Amylene hydrate has also been recommended for the relief of *epileptic* and *eclamptic convulsions*. *Dose*, fifteen minims (0.9 mil) morning and evening.

Pental. Trimethylethylene. β-isoamylene, $(CH_3)_2C=CH.CH_3$, or C_5H_{10}, is obtained from crude amylene, which consists of pentane (C_5H_{12}), pental (C_5H_{10}), and α- and γ-amylene. If the mixture be shaken with diluted sulphuric acid at a low temperature, −20° C. (−4° F.), the trimethylethylene and γ-amylene will be decomposed and amylsulphuric acid produced, which after dilution with water yields tertiary amyl alcohol and trimethylethylene; by fractional distillation the pental is obtained in a pure state.

Pental is a colorless, highly inflammable liquid; sp. gr. 0.678; boiling point 38° C. (100° F.). It was highly commended by W. Lombardino as an anesthetic of great practical value. H. C. Wood and David Cerna have, however, shown that pental acts upon the lower animals as a powerful cardiac depressant, and clinical experience has demonstrated that it is too dangerous for practical use.

Pentane.—Amyl hydride, $CH_3CH_2CH_2CH_2CH_3$, was discovered by E. Frankland of Manchester. It is a saturated hydrocarbon, and has been proved to be one of the light products in American petroleum, being the portion boiling at from 37°–39° C. (99°–102° F.) (Schorlemmer). Amyl hydride is a colorless, volatile, mobile liquid, possessing a fruity odor, and having no taste. It is one of the lightest liquids known, having the sp. gr. 0.626 at 17° C. (63° F.). It boils at 38° C. (100° F.), and the sp. gr. of its vapor is 2.5. It is very inflammable, and burns with a brilliant white flame. It is readily soluble in alcohol and ether, but insoluble in water. Belonging to the paraffin or saturated series of hydrocarbons, it is a very stable compound, resisting the action of fuming sulphuric acid and the most powerful oxidizing agents. This substance was proposed by Simpson as an anesthetic, but has not sustained the claims made for it. It is used as a solvent in analytical chemistry and as an illuminant in photometric determinations.

Amylene Carbamate.—Under the name *aponal* amylene carbamate $NH_2—CO—O—C(CH_3)(C_2H_5)—CH_3$ has been introduced as a somnifacient. It seems to be a drug of only moderate power but acting promptly and apparently without injurious after-effects. The *dose* is from eight to thirty grains (0.5–2 Gm.).

Amylene Chloral. *N. N. R.* 1916. *Dormiol. Methyl Butanol Chloral* (in 50 per cent. solution).

$$CCl_3.CH(OH)(OC_5H_{11})$$

—This is a compound formed by the union of chloral and amylene hydroxide. It is a colorless, oily fluid of sp. gr. 1.24, having a peculiar camphor-like odor and a cooling, pungent taste. It is insoluble in water but is miscible in all proportions with alcohol, ether, acetone, and fixed oils. Its incompatibilities are the same as those of chloral. There is a large amount of clinical evidence as to the value of dormiol in all forms of *insomnia* which are not dependent upon the existence of pain. It is employed largely in insane asylums, and the testimony is uniform that it acts favorably in about 70 per cent. of the cases, that it produces no disagreeable after-effects, and that when continuously exhibited it produces no chronic poisoning. It is further claimed that it may be used in cardiac cases when hydrated chloral would be dangerous. It acts promptly and produces a quiet sleep, which is often of very short duration; further, patients become rapidly accustomed to its use. *Dose,* ten to forty-five minims (0.6–2.9 mils). It may be given in capsules or emulsion, but it is well taken when dropped in cold water and quickly swallowed.

Amyloform is a patented chemical compound of formaldehyde and starch, introduced by Claassen as a substitute for iodoform. It is stated to be odorless, innocuous, and non-irritant. *Dextroform* is a similar compound, in which dextrin is used in place of starch. Dextroform is soluble in water and glycerin. Amyloform can be heated to 180° C. (356° F.) without decomposition, and therefore is readily sterilized. It is said to be non-poisonous, and has been used by Langgard, Krabbel, and others as a dusting powder in the treatment of infected *ulcers* and wounds of all kinds. It is said to act more energetically in lessening secretion and as a disinfectant than iodoform.

Amytin.—The ammonium salt of a mixture of sulphonated hydrocarbons prepared by the action of sulphuric acid on various hydrocarbons and subsequent treatment with ammonia. Under the name of amytin (*anytin, anysin*), Unna has introduced into medicine a 33 per cent. aqueous solution of *ichthyol-sulphonic acid,* which has the property of dissolving ichthyol, various ethereal oils, phenol, and camphor, forming solutions which are known by Unna as *Amytoles* (*anytoles*). Amytin is more or less irritant to the skin, and is affirmed to be useful in those skin diseases which need stimulation.

Anacahuite Wood.—In the year 1860 considerable quantities of this wood were imported from Mexico, into Germany, as a supposed remedy in *phthisis,* but it failed to sustain its first reputation. It is the product of *Cordia Boissieri* DC. (See *P. J.*, Dec., 1862, 272, with figure.)

Anacardium. *Anacardium occidentale* L. *West Indian Cashew-nut. Acajou à Pommes,* Fr. *Caschunuss,* G.—A small and elegant tree of the Fam. *Anacardiaceæ,* growing in the West Indies and other parts of tropical America. A gum exudes from the bark, which bears some resemblance to gum arabic, but is only in part soluble in water, and consists of true gum and bassorin. It is the *gomme d'acajou* of the French writers. Peckoldt describes *cashew gum* as occurring in hard, fragile pieces which are more or less transparent, yellowish-brown, and stalactite-shaped, and is as soluble in water as acacia. (*Zeit. Oest. Apoth. Ver.,* 1893, 501.) The fruit is a fleshy, pear-shaped receptacle, supporting at its summit a hard, shining, ash-colored, kidney-shaped nut, an inch or more in length and three-quarters of an inch broad, consisting of a pericarp having large balsam canals and of a sweet oily kernel which is now an article of commerce, as a food sold either in the raw state or roasted and salted. The receptacle is red or yellow, and of agreeable subacid flavor with some astringency. It is edible, and affords a juice which has been recommended in *uterine complaints* and *dropsy.* This juice is converted by fermentation into a vinous liquor, which yields by distillation a spirit used in making punch, and said to be powerfully diuretic. The black juice contained between their outer and inner shell of the nuts is extremely acrid and corrosive, producing, when applied to the skin, severe inflammation, followed by blisters or desquamation. Staedeler found in it two peculiar principles—*anacardic acid* and a yellow, oleaginous liquid, *cardol.* (See *J. P. C.,* 3e sér., xiii, 459.) The juice is used in the West Indies for the cure of *corns, warts, ringworms,* and obstinate *ulcers,* and even of *elephantiasis.* It is said to be sometimes applied to the face by women, in order to remove the cuticle, and produce a fresher and more youthful aspect. In a case of external poisoning which came under observation, in a lady who was exposed to the fumes of the roasting nuts, the face was so much swollen that for some time not a feature was discernible. (*N. J. Med. Rep.,* 1855, 187.) In the case of a boy the tongue, face, neck, hands, forearms, scrotum, etc., were red and enormously swollen, and very painful. The tincture of iodine was found useful as a local application. The black juice of the nut and a milky juice which flows from the tree after incision are used for almost indelibly marking linen. The *Oriental*

Cashew-nut or *Anacardium Orientale* is the fruit of *Semecarpus Anacardium*, L., a tree quite common in Southern Asia. It contains principles similar to the West Indian Cashew, and is also said to contain an alkaloid, *chuchunine*.

Anagallis. *Anagallis arvensis*, L. *Scarlet Pimpernel. Red Chickweed. Weather-glass. Mouron rouge*, Fr. *Gauchheil, Rothe Miere*, G. (Fam. *Primulaceæ.*)—An annual plant, growing in Europe and the United States. It has little odor, but a bitterish, somewhat acrid taste. The ancients esteemed it a counter-poison, and Orfila found three drachms of its extract to cause fatal gastro-enteritis in a dog. It has been recommended as a local application to old and ill-conditional *ulcers*, and has been used as a folk-remedy in *visceral obstructions, consumption, dropsy*, etc. J. A. Heintzelman obtained from it a volatile oil of a strong, peculiar odor, a pungent and somewhat acrid taste, and the sp. gr. 0.987. Four drops (0.25 mil) of it produced intense headache and nausea, lasting for twenty-four hours, with pains throughout the body. According to Daccomo and Tommasoli, anagallis contains an active ferment, which rapidly digests raw meat. (*Rassegna di Sci. Med.*, 1892, No. 4.) *A. cœrulea* (Schreb.) Ledeb., having blue petals, is a variety of *A. arvensis*, and shares its medicinal properties.

Anagyris. *Anagyris fœtida*, L. (Fam. *Leguminosæ.*)—Hardy and Gallois have separated from *Anagyris fœtida* an alkaloid, *anagyrine*. Parthiel and Spasski found that the crude alkaloid could be separated into *cytisine*, $C_{11}H_{14}N_2O$ and *anagyrine*, $C_{15}H_{22}N_2O$; the latter is not obtainable in crystalline form; it forms a brittle, resinous-like mass easily reducible to a yellowish powder, but rapidly absorbs moisture and becomes sticky. It volatilizes at 245° C. (473° F.). (*Arch. d. Pharm.*, 244, No. 1, 1906, 20.) It forms, however, a crystalline hydrobromide.

Anagyrine hydrobromide, which has the formula $C_{14}H_{18}N_2O_2HBr$, occurs in colorless or faintly yellow crystals and soluble in water. Anagyrine, according to Loewi (*A. I. P.*, vol. vii, p. 66), is physiologically related to lobeline, acting primarily upon the nerve endings as a paralyzant and later upon nerve centers, but having no direct influence upon the muscles. It lessens the cardiac frequency and decreases the force of the systole in the frog, but is said in the mammal to have very little influence upon the blood pressure, death occurring through respiratory paralysis.

Analgen. *Ortho-ethoxy-monobenzoyl-amido-quinoline. Benzanalgene. Quinalgene. Labordin.* $C_{18}H_{16}N_2O_2$. $C_9H_5.(OC_2H_5)NH(CO.C_6H_5)N$.—The name analgen was first given to the acetyl derivative, but it was found that the benzoyl radical gave a more desirable product, and this is now made exclusively and the name analgen applied to it. It is in colorless crystals, insoluble in water, soluble in hot alcohol, melting point 208° C. (406° F.).

First produced and brought forward by Vis as an antipyretic, analgesic, and antirheumatic remedy, it was subsequently investigated by Maass (*Z. K. M.*, xxviii, 1895), who found that in sufficient dose it depresses the heart and the reflexes, finally causing convulsions with loss of power, and death by centric paralysis of respiration. Both it and its derivative, *oxyethylamidoquinoline*, act upon the peripheral nerves as local anesthetics. The fatal dose for the lower animals was found by Maass to be three grammes per kilo. The continuous use of small doses produces emaciation, feebleness, and lessening of the reflexes. In cases of fever it causes active depression of temperature, often with free sweating, and usually decrease in the urinary secretion, and especially of the nitrogenous elimination. After chronic poisoning in the lower animals fatty degeneration was found in the liver and kidneys. The urine of patients taking it is said to become red, owing to the presence of *oxyethylamidoquinoline urate*. In *headaches* and the other nervous disturbances of *neurasthenic* individuals it is said to act well without affecting digestion. It is said also to relieve the pain of organic diseases, and to be distinctly anti-malarial. (See *B. A. M.*, xxxvi.) *Dose*, eight to fifteen grains (0.5–1.0 Gm.), up to forty-five grains (0.3 Gm.) a day if required; best administered in capsule or in acidulated water.

Anchietea. *Anchietea salutaris* St. Hil. *Cipo Suma. Cipo Carneiro. Pirageia.* (Fam. *Violaceæ.*)—The bark of the root of this Brazilian plant contains *anchietine*, an alkaloid isolated by Peckoldt. (*Ber. d. Chem. Ges.*, 1897, p. 98.) It is used in Brazil in treating *scrofula, erysipelas*, and *eczema*. Given in *doses* of two drachms (7.7 Gm.), it acts as an aperient, while three drachm (11.6 Gm.) doses produce vomiting.

Anchusa. *Anchusa officinalis*, L. *Bugloss. Ox-tongue.* (Fam. *Boraginaceæ.*)—The root, leaves, and flowers of this European biennial plant were at one time recognized by the U. S. Pharmacopœia, but probably are practically devoid of medicinal properties. In France the *Anchusa italica*, which is there known as *buglosse*, is substituted for *A. officinalis* and is still in popular use as a diaphoretic and diuretic.

Andrographis. *Br. Add.* 1900. *Andrographis paniculata* Nees. (Fam. *Acanthaceæ.*)—Under the name of *Kiryat* this plant is stated to be used to some extent in India as a bitter tonic, having similar properties to chiretta. It appears scarcely to enter commerce at all, although exposed in the shops of the herbalists. (See *B. P. C.*, p. 122.) The Br. Add., 1900, recognized the *infusion* (*Infusum Andrographidis*, one ounce to a pint), *dose*, one-half to one fluidounce (15–30 mils); the *concentrated liquor* (*Liquor Andrographidis Concentratus*), *dose*, one-half to one fluidrachm (1.8–3.75 mils); and the *tincture* (*Tinctura Andrographidis*), *dose*, one-half to one fluidrachm (1.8–3.75 mils).

Andromeda. *Oxydendrum arboreum* (L.) DC., (*Andromeda arboreum* L.), *Sour Wood*, or *Sorrel-tree*, grows in the valleys of the Alleghanies, from Pennsylvania to Florida and west from Indiana to Louisiana. The decoction of the leaves was at one time used as a pleasantly acidulous drink in fevers. The powder of the leaves and buds of *Leucothoë racemosa* (L.) A. Gray (*Andromeda racemosa* L.) is said to be a powerful errhine.

J. F. Eykman, of Japan, found a poisonous glucoside, *asebotoxin*, in *Andromeda* (*Pieris*) *japonica*. (*N. R.*, 1882, 290.) In 1883, Plügge separated from *Andromeda japonica* a colorless, crystallizable, poisonous principle, *andrometoxin*. Subsequently he found that various ericaceous plants contain it. (*A. Pharm.*, xxvi; also *A. J. P.*, 1889.) It exists in *Azalea indica* and *Rhododendron maximum* L., and has been found by De Zaayer (*Chem. Ztg.*, July, 1887) in *Rhododendron ponticum*, and in *Kalmia angustifolia* L., and *K. latifolia* L.; also in *Monotropa uniflora* L., by A. J. M. Lasché (*Ph. Rund.*, Sept., 1889). It occurs in acicular crystals, melting at from 228° to 229° C. (442°–

444° F.), soluble in alcohol, amyl alcohol, chloroform, ether, benzene, much more soluble in cold than in boiling water, yielding solutions of an alkaline reaction, but not precipitated by ordinary alkaloidal reagents nor by solutions of metallic salts. For further tests, see reference; also *P. J.*, vol. xviii, 171. The *poisonous honey* of Xenophon, derived from the flowers of *Rhododendron ponticum*, probably owed its toxic properties to andrometoxin. (See also *Ph. Z. R.*, 1883, xxii.) The oil of *Andromeda Leschenaultii*, of India, was found by J. Broughton to be methyl salicylate. (*P. J.*, Oct., 1871.)

Anemonin. (*Pulsatilla Camphor.*) $C_{10}H_8O_4$. —Yellowish-white crystals soluble in hot alcohol and insoluble in water. It is used as an antispasmodic, sedative and anodyne in *asthma* and pulmonary affections. *Dose*, one-fourth to three-fourth grain (0.015–0.05 Gm.), although as high as three grains (0.2 Gm.) has been administered.

Anesthesin. *N. N. R.* 1917. *Ethyl-ester of p-amido-benzoic acid. Ethyl aminobenzoate.* $COOC_2H_5[1].C_6H_4.NH_2[4]$.—This is a white, inodorous, crystalline powder, melting at 89.5° C. (193° F.), sparingly soluble in cold water, readily soluble in acetone, ether, petroleum benzin, chloroform, and in ethereal and fatty oils. The solutions do not alter even when exposed to light. Its oily solution may be boiled without decomposition, but prolonged boiling with water causes a breaking up of the compound. It is incompatible with acids and acid salts.

Anesthesin hydrochloride is soluble in 100 parts of water. This solution when injected, however, causes some unpleasant burning sensation and may be diluted to one-fourth. It is claimed for anesthesin that while not poisonous it is an active local anesthetic and may be freely injected in solution for surgical purposes. In the experiments of Binz colossal doses given to rabbits were found to produce only a transient methemoglobinemia. No renal irritation or methemoglobinuria were ever observed. Dunbar commends the following formula: Anesthesin hydrochloride, 0.25; sodium chloride, 0.15; morphine hydrochloride, 0.005 to 0.015; water, 100; the solution can be sterilized. As a local application in ulcerated conditions of the nose and throat, as *tuberculous laryngitis*, it may be applied in the form of insufflation or by lozenges (one-third to two-thirds grain, 0.02–0.04 Gm.). It is also externally useful to insensitize the surfaces of *wounds* and *ulcers*, as *burns*, etc. In the form of an ointment it may be used for *hemorrhoids*, *pruritus vulvæ*. Externally it may be used in the form of powder or ointment in 5 to 20 per cent. strengths. See also Merck's *Ann. Report*, 1913. Reiss (*Ther. Geg.*, 1905) highly recommends anesthesin for the relief of *vomiting* when due to gastric irritation. He has found that it counteracts the emetic properties of antimony, but not those of apomorphine, which goes to show that its antemetic action is not central. It is also useful in the same way to relieve the pains of *gastric ulcer*. Ordinarily the *dose* in these conditions is eight grains (0.5 Gm.), although, according to Reiss, if necessary it may safely be increased to as high as one hundred and twenty grains (8 Gm.). He finds it of no service in seasickness. Lozenges containing from three-tenths to six-tenths of a grain (0.019–0.038 Gm.) are stated to be effective in relieving irritation of the throat and palate. Anesthesin has been found very useful, in the form of suppositories containing from three to eight grains (0.2–0.5 Gm.), for the relief of painful *hemorrhoids;* it is also used in soluble bougies in the *vesical tenesmus* of women; in the form of an ointment (10 per cent.) in *pruritus vulvæ*, also in various *eczemas* about the genitalia. *Dose*, five to seven grains (0.3–0.45 Gm.).

Anesthol. *Anesthyle.*—This has a wide use abroad as a local anesthetic in dental surgery, and is composed of a solution of methyl chloride in ethyl chloride in unknown proportions. The same name * is also given to a general anesthetic combination of ether, chloroform and ethyl chloride.

Angelica.—Two species of this genus are used in medicine, the *Angelica Archangelica* L. (*Garden Angelica*), a native of Europe, and the *A. atropurpurea* (*Masterwort*), which grows throughout the eastern United States. *Garden angelica* has a long, thick, fleshy, biennial root, furnished with many rootlets, and sending up annually a hollow, jointed, round, channelled, smooth purplish stem, which rises five feet or more in height, and divides into numerous branches. The plant is a native of the north of Europe, and is found in the high mountainous regions in the southern section of that continent, as in Switzerland and among the Pyrenees. It is often cultivated. The whole plant is aromatic, but the root only is official in the Swiss, Austrian, and German Pharmacopœias, while the fruit is official in the N. F. IV. The root should be dug up in the autumn of the first year, as it is then least liable to become mouldy and worm eaten. It is spindle-shaped, 4 to 6 cm. thick at the crown, and beset with long descending rootlets. The fresh root has a yellowish-gray epidermis, a fleshy yellow parenchyma, and when wounded yields a honey-colored juice, having all the aromatic properties of the plant. The dried root is grayish-brown and much wrinkled externally, whitish and spongy within, and breaks with a starchy fracture, exhibiting shining resinous masses. It is very apt to be attacked by insects. The drug and the powder should be conserved by the addition of a few drops of chloroform or carbon tetrachloride. The odor is strong and fragrant, and the taste at first sweetish, afterwards warm, aromatic, bitterish, and somewhat musky. These properties are extracted by alcohol, and less perfectly by water. The constituents of the root are *angelic acid*, $C_5H_8O_2$, a monatomic acid of the acrylic series, valeric acid, $C_5H_{10}O_2$, resin, bitter principle, tannin, pectin, malic acid, sugar starch and a volatile oil consisting largely of phellandrene. For further information concerning the constituents of this drug, see *U. S. D.*, 19th ed., p. 1386. *Schim. Rep.*, 1902, 15; 1911, 21; 1913, 26.

Angelicæ Fructus, N. F. IV, *Angelica Seed*, is described by the N. F. as "the ripe fruit of *Angelica Archangelica* Linné (Fam. *Umbelliferæ*) and of other species of *Angelica*, without the presence of more than 3 per cent. of foreign matter. Cremocarps oval, externally of a pale yellowish-brown color, from 4 to 8 mm. in length, 3 to 6 mm. in breadth and from 1 to 2 mm. in thickness, the base faintly notched, the summit bearing five minute calyx-teeth and the remains of the style; the two mericarps joined by their broad faces, or separate; each mericarp nearly flat upon one surface, which bears a central longitudinal groove and has sharp, slightly upturned margins, convex upon the other surface which is traversed longitudi-

* Sometimes spelled *Anæsthol.*

nally upon the back by three strong ribs, separated from one another by narrow grooves and from the margin by much broader grooves; pericarp soft, rather tough and corky, and enclosing a single seed, showing on cross section six large oil-tubes. Odor characteristic and agreeable; taste aromatic, pungent, and sweetish. Angelica Fruit yields not more than 8 per cent. of ash."

Garden angelica is an aromatic tonic. The Laplanders, in whose country it flourishes, esteem it highly as a condiment and medicine. In Europe the stems are frequently made into a preserve. The *dose* of the root or seeds is from thirty grains to a drachm (2–3.9 Gm.).

The N. F. IV recognizes under the name of *Angelica Radix* (*Angelica Root*) "the rhizome and roots of *Angelica atropurpurea* Linné (Fam. *Umbelliferæ*) and of other species of *Angelica*, without the presence of more than 5 per cent. of stem bases and leaves or other foreign matter. Preserve Angelica Root in air-tight containers, adding a few drops of chloroform or carbon tetrachloride, from time to time, to prevent attack by insects. Rhizomes short and thick, from 5 to 10 cm. in length, sometimes split, frequently crowned with the bases of stem and leaves; the roots are numerous, from 10 to 20 cm. in length and from 5 to 7 mm. in thickness at the base and gradually tapering to about 1 mm.; frequently twisted or braided together, externally dark gray-brown to reddish- or purplish-brown and with conspicuous, rather deep furrows; when dry breaking with a smooth fracture. On cross section, the rhizome shows a distinct pith, which is absent in the root, and both exhibit a spongy bark nearly or quite as wide as the woody zone; in the bark are radial rows of brownish canals containing oleoresin. The wood rays are finely porous and narrower than the medullary rays. The bark is rich in starch. Odor strongly aromatic; taste sweetish, pungent, aromatic, and then bitter. The powdered drug is yellowish-brown and, when examined under the microscope, exhibits numerous, mostly simple, irregularly spherical starch grains, up to 0.008 mm. in diameter, sometimes with the cleft at the center and occasionally two- or more compound; tracheæ or fragments of tracheæ, with reticulate markings or large simple pores up to 0.075 mm. in width; brownish oil canals or fragments thereof, up to 0.25 mm. in diameter, sometimes with adjoining epithelial cells; fragments of parenchyma tissue with some of the cells filled with starch; fragments of large brownish cork cells; sclerenchymatous fibers with thin walls and often with oblique markings; yellowish oil globules. Angelica Root yields not more than 8 per cent. of ash." It has a strong odor and a warm aromatic taste. The juice of the recent root is acrid, and is said to be poisonous; but the acridity is dissipated by drying. The medicinal virtues of the plant are similar to those of the garden angelica of Europe, for which it has been proposed as a substitute. It is, however, inferior to the European angelica. Its uses are similar to those of the root.

Angrecum. *Angrecum fragans* Thouars.—This is an orchidaceous plant, indigenous to the Isle of Réunion and to Mauritius, where the leaves have been long used, under the name of *faham*, for the same purposes as tea leaves. For description, see *P. J.*, 1881, 913. They have a somewhat pungent aromatic taste, and a strong and highly agreeable odor, scenting the whole apartment with a delicious perfume. Given in infusion, they appear to have an effect on the system somewhat similar to that of Chinese tea, and they have been introduced into Paris as a rival of that popular beverage. The drink is made by putting the leaves and stalks, in the proportion of fifteen grains (1 Gm.) to a teacupful, into cold water, boiling for about ten minutes, and then pouring into a closed vessel, and sweetening it when used. (*A. J. P.*, 1866, 441.)

Anhalonium.—Under the name of *Pellote* are used in Mexico for narcotic purposes, certain cacti whose tops have entered commerce under the name *of Mescal Buttons*. These were formerly believed to belong to the genus *Anhalonium*, but at present are referred to species of *Mammalaria* and of the genus *Echinocactus*, which is characterized by a flexible epidermis, its freedom from spines and tubercles and its segments not assuming the form of a projecting or leaf-like organ. (See Schumann in Engler and Prantl's *Pflanzenfamilien*, and *Reports of Missouri Botanical Gardens*, 1898.) In a mass of such cactus tops sent to the Pharmaceutical Institute of Leipzig from Mexico as pellote, experts have recognized the products of *Mammalaria fissuratus*, *M. retusus*, *Echinocactus Williamsii* Lem., and *E. Lewinii* Henn. Moreover, from *A. jourdanianum* L., Lewin obtained traces of an alkaloid (*A. E. P. P.*, xxxiv). There is little doubt but that various allied species of cactus are represented in the commercial drug. The most important of these plants are *E. Lewinii* and *E. Williamsii*, which inhabit the valley of the Rio Grande in Mexico, and are furnished with stems reaching about half an inch above the surface of the ground, surmounted by a top composed mainly of the blunt leaves of the plant, bent around a tuft, of from half an inch to an inch in diameter, composed of short, yellow-white filaments or hairs. It is this top which constitutes the *mescal button*, which is from an inch to an inch and a half in diameter, one-fourth of an inch in thickness, with a convex under surface, a texture which is brittle and hard when dry, but becomes soft when moistened, a very bitter disagreeable taste, and an odor when moist which is peculiar and disagreeable, and is especially marked in the powdered drug. According to C. H. Thompson, the buttons of *E. Lewinii* and *E. Williamsii* are readily distinguished by the fact that the surface of *E. Lewinii* is traversed by thirteen shallow narrow furrows giving the appearance of there being as many irregular or much broken ribs or obtuse ridges, while in *E. Williamsii* the furrows and ridges are eight in number and regular.

In 1888, L. Lewin separated from *E. Lewinii* an alkaloid, *anhalonine*, which has the formula $C_{12}H_{15}NO_3$, and crystallizes in small white prisms, soluble in ether, alcohol, and chloroform. Subsequently, Heffter (*Ber. d. Chem. Ges.*, 1896) separated from *E. Lewinii*, besides *anhalonine*, three alkaloids: *mescaline*, $C_{17}H_{17}NO_3$, in white needles melting at 151° C. (303.8° F.); *anhalonidine*, $C_{12}H_{15}NO_3$, fusing at 160° C. (320° F.), and *lophophorine*, $C_{13}H_{17}NO_3$. (See also *A. E. P. P.*, 1898, xl.)

Kander (*A. Pharm.*, 1899, vol. ccxxxvii) has found that in commercial mescal buttons, besides the alkaloids already mentioned, are two other bases, *pellotine* and *anhalamine*, so that Merck has offered as commercial products the following salts:

Anhalininæ Hydrochloridum cryst., ***Anhalonidinæ Hydrochloridum*** cryst., ***Lophophorinæ Hydrochloridum*** cryst., ***Mescalinæ Sulphas*** cryst., ***Pellotinæ Hydrochloridum*** cryst. According to the researches of Heffter, pellotine, $C_{13}H_{19}NO_3$, is contained exclusively in *L. Williamsii*, but as this cactus is present in most, if not all, of the commercial buttons, it was naturally found by Kander in analyzing the commercial drug. However, the correctness of the conclusion of Heffter is challenged by Merck's chemists, who, in the analysis of *L. Williamsii*, found the same quantity of the same alkaloids as is present in the true mescal button. For a description of these alkaloids see *M. R.*, 1898 and 1900. E. White (*J. P.*, xxv) obtained *mescaline*, 1.16 per cent.; *anhalonidine*, 1.16 per cent.; *anhalonine*, 0.46 per cent.; *lophophorine*, 0.14 per cent. *Anhaline*, $C_{10}H_{17}NO$, is an alkaloid crystallizing in colorless stellate prisms, which has been extracted from *L. fissuratum*.

From time immemorial the Kiowa Indians of the Rio Grande have used the mescal buttons for the purpose of producing intoxication during their religious ceremonies. Attention was first called to the peculiar cerebral action of the drug by D. W. Prentiss and Francis P. Morgan (*T. G.*, 1895), who found that from two hundred and fifteen to two hundred and thirty grains (14–15 Gm.) (four to five buttons) will produce a peculiar cerebral excitement attended with an extraordinary visual disturbance, characterized by an incessant flow of visions of infinite beauty, grandeur, and variety, of both color and form, often followed after a time by the seeing of monsters, grotesque faces, and gruesome shapes. During the intoxication there are dilatation of the pupil, muscular relaxation, and some slowing of the pulse. Loss of sense of time, partial anesthesia, weakened heart's action, great muscular relaxation, wakefulness, and in some cases nausea and vomiting also have been noted, but no distinct alteration of the respiration. These results have been confirmed by several observers.

A. Mogilewa (*A. E. P. P.*, xlix, 137) found that mescaline, anhalonidine, anhalonine, lophophorine, and pellotine acted similarly in lessening the frequency and force of the isolated frog heart, varying simply in quantitative power. The most thorough research upon the anhalonium alkaloids is that of W. E. Dixon (*J. P.*, xxv) whose report is somewhat marred by the fact that he does not state in his experiments which one of the alkaloids was employed; he simply affirmed that anhalonine and anhalonidine are identical in physiological activity, that lophophorine differs only in being more toxic, and that mescaline has a physiological action almost indistinguishable from that of its associated alkaloids. He finds that "the alkaloid" is not locally anesthetic; that increased salivation is one of the most characteristic symptoms of its action; that in therapeutic doses, in man at least, it produces constipation, but that in toxic dose it causes diarrhea and bloody stools; that its main circulatory effect is upon the cardiac muscle and contained ganglia, causing slowing of the heart and a rise of arterial pressure; that it kills by action on the respiratory centers so that in man the most serious result of an overdose is rapid, shallow breathing, with a sense of suffocation; that upon the nervous system it acts most powerfully, producing in the frog, and to a lesser degree in the mammal, increasing loss of muscular power with heightened reflexes, believed to be due to spinal stimulation. The motor nerves appear to be depressed, since they are paralyzed when the drug is applied locally to them. In experiments upon two human subjects, there was wide dilatation of the pupils, with uncertainty of gait like that of alcoholic intoxication, tremors, and heightened reflexes, although sensation was distinctly blunted. The psychical symptoms caused by the largest doses resemble somewhat those from cannabis indica. The *dose* of the alkaloid used by Dixon was three and eight-tenths grains (0.25 Gm.).

In Heffter's experiments *pellotine* was found to be physiologically feeble, one-thirteenth grain (0.005 Gm.) causing only temporary stiffness in the legs of the frog, two-thirteenths grain (0.01 Gm.) producing stiffness, heightened reflexes, strychnine-like tetanus, lasting from three to four days, ending in recovery. In man, from seven-tenths to nine-tenths of a grain (0.045–0.058 Gm.) produced only temporary sleeplessness with sense of weariness. Pilcz (*W. K. W.*, ix, 1896) has used pellotine as a calmative in fifty-eight cases of *insanity* in *doses* of from one-third to one grain (0.021–0.065 Gm.). About half the cases were markedly affected, sleep coming on in from half an hour to an hour and a half after the hypodermic injection and continuing through the night. No disagreeable results and no collapse occurred, although Langstein is said to have seen collapse following the dose of seven-tenths of a grain (0.045 Gm.).

The value of mescal buttons as a remedial agent is doubtful; it has been employed to a slight extent in various forms of *neurasthenia* and *hysteria*, and is asserted by S. F. Landry (*T. G.*, 1888) to be especially valuable in cases of *asthma*. It has also been alleged to be useful in *neuralgic* and *rheumatic affections*. Prentiss and Morgan give the *dose* of the crude drug as from seven to fifteen grains (0.45–1.0 Gm.); of the fluidextract, from ten to fifteen minims (0.6–0.9 mils); of the 10 per cent. tincture, from one to two teaspoonfuls (3.75–7.5 mils).

Aniline. *Amidobenzene. Phenylamine.* $C_6H_5NH_2$.—This is an organic base obtained from coal tar or more immediately from nitrobenzene. It was first discovered by Unverdorben, in 1826, among the products of the dry distillation of indigo, and was named by him *Krystallin*. Fritzsche, who obtained it afterwards from indigo by another process, seems to have been the first to give it the name of aniline, from the Portuguese word *anil* (indigo). In 1837, Runge obtained three volatile principles from coal tar, which he named *kyanol*, *leucol*, and *pyrrhol*. Of these, kyanol was afterwards found by Hoffmann to be identical with aniline, and leucol has been ascertained to be the same as *quinoline* (*chinoline*). Zinn prepared it in 1840 by the reduction of nitrobenzene with hydrogen and called it *benzidam*. The identity of krystallin, aniline, kyanol and benzidam and the true composition of the substance was proved by Hoffmann in 1843. Aniline did not possess any commercial importance until the discovery in 1856, by Perkins, of the first of the so-called aniline colors, Perkins' purple or mauve, when the demand for aniline became so great that it became necessary to find a method for its preparation from one of the other coal tar fractions. (See coal tar colors, page 1324.) Nitrobenzene is now the source whence most of the aniline of commerce is de-

rived. Nitrobenzene, hydrochloric acid, and iron turnings, in equal weights, are introduced into a cast iron vessel, care being taken that the heat does not rise too high, when the following reactions take place:

$$C_6H_5NO_2 + H_6 = C_6H_5NH_2 + 2H_2O$$
$$C_6H_5NH_2 + HCl = C_6H_5NH_2HCl$$

The semi-solid mass which soon forms consists principally of ferrous chloride and aniline hydrochloride. This is distilled, after the addition of milk of lime, in a large cast iron cylinder, and the distillate redistilled, the portion coming over between 175° C. (347° F.) and 190° C. (374° F.) being collected, and considered sufficiently pure for manufacturing purposes.

Properties.—Pure aniline is a thin, colorless, highly refractive fluid, of an oily appearance; but as found in commerce it is generally more or less colored, and sometimes of a deep reddish-brown. It has a peculiar, not disagreeable odor, and a pungent, aromatic, burning taste; its sp. gr. is 1.024. It solidifies at −8° C. (17.6° F.) if pure, but if impure the freezing point may be below −20° C. (−4° F.). It boils at 183°–184° C. (361.4°–363.2° F.), and its vapors are condensed unchanged. It is slightly soluble in water, but dissolves in all proportions in ether, alcohol, methyl alcohol, acetone, carbon disulphide, and the oils, fixed and volatile. As a base it is weaker than ammonia in the cold but stronger when hot. Its aqueous solution does not react with litmus or turmeric. With the acids it forms soluble and readily crystallizable salts. It is inflammable, and absorbs oxygen from the air, becoming at first yellowish, afterwards reddish, and ultimately brown. A characteristic property is that it produces instantly a deep blue or purple color when brought into contact with chlorinated lime or other hypochlorite (whence the name kyanol, of Runge). (*P. J.*, Sept., 1862, 128.) It is a derived ammonia, having the group C_6H_5 in place of a hydrogen atom of the NH_3 molecule. It is hence often called *phenylamine*. The chief value of aniline is in the manufacture of numerous derivatives, some of which are used in medicine while others form one group of the numerous so-called coal tar colors of commerce. Beautiful reds, purples, yellows, blues, and various other tints are obtained from it.

Under the name of *aniline oil* a liquid is to be found in commerce which consists of a mixture of aniline, toluidine, xylidine, cumidine, and varying quantities of by-products found in the "tailings"; the boiling point ranges between 180° C. (356° F.) and 210° C. (410° F.), and the sp. gr. is also variable; it is used as a solvent for rubber, copal, etc. Certain of the aniline or coal tar dyes possess properties which have led to their employment in medicine. (See under their various names.)

Medicinal Properties.—The symptoms which are produced by the inhalation or ingestion of aniline are great prostration, heaviness in the head, giddiness, vomiting, violent neuralgic pains, and, if the dose has been large enough, cyanosis, coma with dilatation of the pupils, excessive perspiration, loss of reflexes and of voluntary movement, hurried weak pulse, rapid or irregular respiration, hemoglobinuria, a peculiar discoloration of the skin, and, if the patient survives sufficiently long, jaundice with great increase in the biliary pigment of the urine. At the autopsy reported by Müller (*A. J. P.*, 1887), in a woman killed by the swallowing of about a fluidounce (30 mils) of aniline, the blood was chocolate brown, and gave the spectrum of methemoglobin; the urine was free from sugar, albumin, or blood, but contained paramidophenol, and its distillates gave aniline reactions. The hemoglobinuria is evidently connected with an extraordinary destruction of the red blood corpuscles, for in the case reported by Dehio (*A. J. P.*, 1888), in a woman who had taken one hundred and fifty grains (9.8 Gm.) of aniline, the red blood corpuscles fell from normal, 5,000,000 per mil to 2,700,000 on the seventh, and 1,400,000 on the eleventh day.

The violent local effects which have been noticed as produced by some aniline dyes have probably been due to the presence of arsenic, which is used in their production and may remain as a contamination. A preferable designation for these colors of synthetic origin is *coal tar colors.* (See p. 1324.) The use of artificial coloring substances is now prohibited in some classes of materials and restricted in others to a limited few, which are known to be harmless and are required to be certified as to the absence of injurious constituents. (See *Chem. Ztg.*, 1910, No. 14; also LaWall, *Proc. Penna. Pharm. Assoc.*, 1904, 92, for methods of detection.) For list of colors permitted by the United States Government, see Food Inspection Decisions in the preliminary part of this work.

Aniline Blue. *Triphenyl-rosaniline, Toluidine Blue. Pure Blue. Water Blue.*—This dye-stuff is said to possess anti-malarial properties similar to those of methylene blue. The *dose* is five grains (0.3 Gm.) in capsules three times a day.

Aniline Sulphate, $(C_6H_5NH_2)_2H_2SO_4$, occurs in white crystals, soluble in water and alcohol. It is used as a nervine in *chorea* and *epilepsy. Dose,* three-quarters to one and one-half grains (0.05–0.1 Gm.) three times daily. Maximum *dose,* three grains (0.2 Gm.) with the daily maximum dose of six grains (0.4 Gm.).

Anilipyrine.—Gilbert and Yvon have given this name to a substance obtained by the melting together of one part of acetanilide and two parts of antipyrine. Anilipyrine is stated by Gilbert and Yvon to be extremely soluble in water and to be toxically very feeble. The fatal dose for the guinea-pig is 1.8 Gm. per kilo. Anilipyrine has been used by its introducers as an antipyretic and analgesic in *migraine, neuralgia, rheumatism,* etc. The *dose* is eight grains (0.5 Gm.) from two to four times a day.

Animal Charcoal. *Spodium. Ebur Ustum. Bone Black. Ivory Black. Charbon Animal Ordinaire,* Fr. Cod. *Noir Animal Pulvérisé, Noir d'os,* Fr. *Thierische Kohle, Knochenkohle, Beinschwarz, Thierkohle,* G. *Nero di ossa, Carbone animale,* It. *Carbon animal, Carbon de hueso,* Sp. "Charcoal prepared from bone." *U. S. VIII.*—Animal charcoal was not retained in the United States Pharmacopœia IX.

The animal charcoal employed in pharmacy and the arts is usually obtained from bones, by subjecting them to a red heat in close vessels. The residue of the ignition is a black matter, which when reduced to powder forms *bone black,* sometimes incorrectly called *ivory black.*

In manufacturing bone black, the bones, first treated with steam to separate the fat, are subjected to destructive distillation in iron cylinders connected with vessels which receive the ammoniacal liquor, called *bone spirit,* together with a dark tarry liquid (*bone oil*), this being a second-

ary product of the operation. When the distillate ceases to come over, the residue is charred bone, or bone black. Bone consists of animal matter with calcium phosphate and carbonate. In consequence of the decomposition of the animal matter involved in this destructive distillation, the nitrogen and hydrogen, united as ammonia, and a part of the charcoal, in the form of carbon dioxide, distil over, while the remainder of the charcoal is left in the cylinder, intermingled with the calcareous salts. Diess, of Paris, proposes carbon disulphide as a solvent for the fat of bones, as it furnishes a larger and better product of fat, and renders the bones fitter for producing a good bone black. This form of animal charcoal necessarily contains calcium phosphate and carbonate. Animal charcoal occurs in "dull black, granular fragments, or a dull black powder, odorless, nearly tasteless, and insoluble in water or alcohol. When ignited, it leaves a grayish or yellowish-white ash, amounting to about 85 per cent. of the original weight of the portion taken, which should have been previously dried at 120° to 125° C. (248°–257° F.) to a constant weight. The ash should be soluble in hydrochloric acid with the aid of heat, leaving not more than a trifling residue. If 1 Gm. of Animal Charcoal be boiled for several minutes with a mixture of 3 mils of potassium hydroxide T.S. and 5 mils of water the filtrate should be colorless or nearly so (evidence of *complete carbonization*)." *U. S. VIII.* It is more dense and less combustible than vegetable charcoal; from which, moreover, it may be distinguished by burning a small portion of it on a red hot iron, when it will leave a residue imperfectly acted on by sulphuric acid, whereas the ashes from vegetable charcoal readily dissolve in this acid, forming a bitterish solution.

Bone black consists of about 90 per cent. of calcium phosphate and carbonate, and 10 per cent. of carbon.

The decolorizing power of vegetable charcoal was first noticed by Lowitz, of St. Petersburg; and that of animal charcoal by Figuier, of Montpellier, in 1811. In 1822 the subject was ably investigated by Bussy, Payen, and Desfosses. The power is generally communicated to charcoal by igniting it in close vessels, but not always. The kind of charcoal, for example, obtained from substances which undergo fusion during carbonization scarcely possesses the property, even though it may be afterwards finely pulverized. The property in question is possessed to a certain extent by wood charcoal, but is developed in it in a much greater degree by burning it with some chemical substance, which may have the effect of reducing it to an extreme degree of fineness. The most powerful of all the charcoals for discharging colors are those obtained from certain animal matters, such as dried blood, hair, etc., by first carbonizing them in connection with potassium carbonate, and then washing the product with water. Charcoal thus prepared seems to be reduced to a state of extremely minute division, and is, therefore, very porous. The next most powerful decolorizing charcoal is *bone black*, in which the separation of the carbonaceous particles is effected by the calcium phosphate present in the bone.

Animal charcoal by no means invariably possesses the decolorizing property, as this depends upon its peculiar state of aggregation. If pure animal matter (soft tissues) is carbonized, it usually enters into fusion, and, from the gaseous matter which is extricated, becomes porous and cellular. The charcoal formed has generally a metallic luster, and a color resembling that of black lead. It has, however, little or no decolorizing power, even though finely pulverized.

In the manufacture of potassium ferrocyanide there is obtained a fine black sediment, which has a powerful decolorizing action; this is sometimes attributed to the organic nitrogenous character of the material from which it is made.

In order to determine the commercial value of animal charcoal, Corenwinder has proposed to ascertain its power of absorbing lime from a solution of calcium saccharate of determinate strength. The value is in proportion to the absorbing power of the charcoal. A given weight of the charcoal to be tested is left in contact, for an hour, with a given volume of the solution of the saccharate, taken in excess. The liquid is then filtered, and a small measure of it saturated with diluted sulphuric acid of known strength. The less the acid necessary for this purpose, the greater the amount of lime absorbed, and the better the animal charcoal. (*Chem. Gaz.*, 1854; *Scientific American*, April 22, 1876; *A. Pharm.*, 1887; *Proc. A. Ph. A.*, 1887.) See also Laval's investigations, *P. J.*, 1900, 214. Dupuy found that the addition of a few grains of animal charcoal to a few mils of cold fresh tincture of guaiacum immediately causes the development of a blue color, while wood charcoal does not give this reaction. (*P. J.*, 1897, 190.)

Spent animal charcoal, which has been used by the sugar refiners, may have its decolorizing power restored by calcination, which destroys the organic matters that have become fixed in it, and it is stated that it may be submitted to this process twenty times before becoming unfit for use, although this depends upon the amount of calcium salts it takes up from the raw sugars, beet sugars using up the black faster than sugars from the cane. According to Pelouze, the same object may be accomplished by subjecting it to a weak solution of potassium or sodium carbonate. In removing the coloring matter, the alkaline solution becomes yellow. After its action the animal charcoal must be carefully washed, first with boiling water, and afterwards with acidulated water. A process devised by Leplay and Cuisinier is probably more effectual. The charcoal, without being removed from the cylinders, is thoroughly washed, treated by steam to remove viscous substances, and then percolated successively, (1) by a weak alkaline solution, which removes salts and some coloring matter; (2) by weak hydrochloric acid, which, in removing a certain amount of salts of lime, liberates coloring matter; (3) again with a weak alkaline solution, to carry off the remaining coloring matter; and (4) lastly by a solution of calcium biphosphate, by which the decolorizing power of the charcoal is restored.

Animal charcoal is capable of taking the bitter principles from infusions and tinctures, and iodine from liquids which contain it in solution. Its power, however, of acting on solutions and chemical compounds is stated by Warington and Weppen to be more decided in its purified condition. (See *Carbo Animalis Purificatus*, page 1254; see also *Ephem.*, 1885, p. 721.) On the other hand, Carswell (*P. J.*, 1893, 615) believes that the purification of animal charcoal is based on erroneous conclusions, as charcoal possesses no inherent powers of decolorization but the latter depends partly on the aggregation of cellular spaces and chiefly on the mineral constituents.

Animal charcoal is used in pharmacy for de-

colorizing vegetable principles, such as gallic acid, quinine, morphine, veratrine, etc., and in the arts, principally for clarifying syrups in sugar refining, for depriving spirits distilled from grain of the penetrating impurity, called *fusel oil*, which imparts to them an unpleasant odor and taste, as first distilled, and for the filtration of petroleum residues in the manufacture of petrolatum and petroleum jellies. (See *Petrolatum*.) The manner in which it is used as a decolorizer is to mix it with the substance to be decolorized, and to allow the mixture to stand for some time. The charcoal unites with the coloring matter, and the solution by filtration is obtained white and transparent. Its use, however, in decolorizing the alkaloids and other vegetable principles, no doubt causes a loss by absorption, since it has been shown by the experiments of Lebourdais, mentioned under the head of purified animal charcoal, that several of these principles may be obtained by the sole action of charcoal. According to Guthe, a German chemist, bone charcoal, without purification, is to be preferred as a decolorizer in all cases in which the calcareous salts exert no injurious effect. Voilé uses animal charcoal as an absorbent in a pill excipient for making creosote and croton oil pills.

Because of its power in absorbing many toxic principles, animal charcoal has been recommended as an antidote in the treatment of various alkaloidal and mineral *poisonings* and, according to Secheyron (*Revue Internationale de Médicine*, 1909, p. 120), is especially to be recommended in *mushroom poisoning*. For this purpose a tablespoonful stirred up in water may be given at a dose. Because of its absorptive powers it has also been recommended by Adler (*W. K. W.*, 1912) in *enteritis* and by Pribran (*Pr. M. W.*, 1913) in *gastric flatulence*. For these latter conditions it may be administered in teaspoonful doses.

Animal Charcoal, Purified. *Carbo Animalis Purificatus. U. S. VIII. Charbon animal purifié*, Fr. Cod. *Gereinigte Knochenkhole*, G. *Carbone di ossa depurato*, It.—For a process of purifying animal charcoal see page 292, *U. S. D.*, 19th edition.

Animal charcoal, as it is made by charring bones, necessarily contains bone phosphate and calcium carbonate, the presence of which does no harm in some decolorizing operations; but in delicate chemical processes these salts may be dissolved or decomposed, and thus become a source of impurity. It is on this account that animal charcoal requires to be purified from its calcareous salts; and this is accomplished by diluted hydrochloric acid, which dissolves the phosphate and decomposes the carbonate. According to Stenhouse, aluminized vegetable charcoal is equally efficacious with purified animal charcoal as a decolorizer.

Properties.—Purified animal charcoal is "a dull black powder, odorless, tasteless, and insoluble in water, alcohol, or other solvents. If 2 Gm. of the powder be ignited at a red heat with free access of air in a broad, shallow porcelain or platinum dish, it should not leave a residue weighing more than 0.08 Gm., or 4 per cent. of the original weight (limit of *silicates* and *other fixed inorganic matter*). If 1 Gm. of the powder be boiled with a mixture of 3 mils of potassium hydroxide T.S. and 5 mils of water during three minutes, the filtrate should be colorless (evidence of *complete carbonization*)." *U. S. VIII.*

It has been shown by Robert Warington that bitter vegetable substances, including the organic alkalies, are removed from solution by passing through purified animal charcoal, especially when the action is assisted by heat. Weppen finds that it also removes resins from tinctures, tannic acid and bitter principles from infusions, and certain metallic salts from their solutions. Purified animal charcoal, thus employed, has been resorted to by Lebourdais as an agent for obtaining the active principles of plants. A decoction or infusion of the plant is either boiled with or filtered through the charcoal, which takes up, more or less completely, the bitter and coloring principles. The charcoal, after having been washed and dried, is treated with boiling alcohol, which dissolves the principles taken up. Finally, the alcohol is distilled off, and the principles are obtained in a separate state. In this way digitalin, ilicin, scillitin, columbin, colocynthin, arnicine, strychnine, quinine, and other principles have been obtained by Lebourdais. (*Chem. Gaz.*, Nov. 15, 1848.) (In relation to the method of Lebourdais, see a paper by J. S. Cobb, in *A. J. P.*, 1851.) A. B. Garrod proposed purified animal charcoal as an antidote to vegetable and animal poisons, with which it appears to combine. According to his experiments, common bone black has not one-fifth of the power possessed by the purified substance, and vegetable charcoal and lamp-black are nearly or quite useless. The amount of the antidote proposed by Garrod is half an ounce for each grain of a vegetable alkaloid. Alfred Taylor deemed the results of Garrod inconclusive. B. H. Rand made some interesting observations in relation to the antidotal powers of purified animal charcoal, and proved that poisonous doses of the strongest vegetable poisons may be swallowed with impunity if mixed with that substance.

In using animal charcoal for decolorizing active vegetable principles much loss is often incurred by the absorption of those principles by the charcoal.

Animé. *Gum Animé.*—The substance known at present by the name of animé is a resin supposed to be derived from the *Hymenæa courbaril* L., a leguminous tree of South America, although this origin was denied by Hayne. According to W. Hamilton, the resin exudes from wounds in the bark, and is found also underneath the surface of the ground, between the principal roots. It is in small, irregular pieces of a pale lemon-yellow color, sometimes inclining to reddish, more or less transparent, covered with a whitish powder, brittle and pulverizable, with a shining fracture, a weak but agreeable odor, and a mild, resinous taste. It softens in the mouth, adheres to the fingers when in powder, and readily melts with heat, diffusing its agreeable odor in an increased degree. It consists of two resins, one soluble, the other insoluble, in cold alcohol, and of a small proportion of volatile oil. There is a variety of a darker color, less transparent, and with small cavities in the interior, in other respects resembling the preceding. Another variety is the East Indian, supposed to be derived from *Vateria indica*, L. (Fam. *Dipterocarpaceæ*), but this never reaches American commerce. According to W. C. Ondaatje, the bark of this plant is in daily use by the natives of Ceylon to arrest the alcoholic fermentation of the juice of the Jaggery palm, *Caryota urens*, L., a favorite beverage. (*P. J.*, 1883, 818.) Animé formerly entered into the composition of various ointments and plasters; but it is now used only as incense, or in the preparation of varnishes. The Brazilians employ it internally in *diseases of the lungs*.

Anisic Acid. *Paramethoxybenzoic Acid. Dra-*

conic Acid. $C_6H_4.OCH_3.COOH$.—It is prepared from anisic aldehyde or by oxidization from *p-kresolmethyl ether.* It forms colorless crystals which are almost insoluble in cold water and slightly soluble in alcohol and ether. As an antiseptic it is alleged to have marked power and it is also used as an antirheumatic and antipyretic. *Dose,* five to fifteen grains (0.32–1.0 Gm.).

Anisodus. *Anisodus luridus* Link and Otto. (*Scopolia lurida* Dun.)—This is a Himalayan solanaceous plant in which Siebert has found *atropine* and *hyoscyamine.* (*A. Pharm.,* Feb., 1890; *P. J.,* March, 1890.)

Anisole.—This name has been applied to the *methyl ether of phenol* because of the fact that it was at one time manufactured from anisic acid. It has been found by Professor Fraenkel to be an active agent against *lice* and other body vermin.

Annatto. *Orleana. Annotta. Arnotta. Terre de la Nouvelle-Orléans,* Fr. *Orellana, Orlean,* G.—The coloring substance called *annatto, arnotta* or *roucou,* is the reddish pulp surrounding the seeds in the fruit of *Bixa orellana* L. (Fam. *Bixaceæ*), a middle-sized tree native to Northern South America, but widely cultivated in tropical Asia and Africa. The pulp is separated by bruising the fruit, mixing it with water, then straining through a sieve, and allowing the liquid to settle. The mass which remains is dried and formed into flat cakes or cylindrical rolls. Another mode is to bruise the seeds, mix them with water, and allow the mixture to ferment. The coloring matter is deposited during the fermentation, after which it is removed and dried. In commerce there are two kinds of annatto, the Spanish or Brazilian, and the French, the former coming in baskets from Brazil, the latter in casks from French Guiana. The French, which is also called *flag annatto,* has a disagreeable odor, probably from having been prepared by the fermenting process in which urine is sometimes used; but is superior, as a dye stuff, to the Spanish, which is without any disagreeable odor. Annatto is of a brownish-red color, usually rather soft, but hard and brittle when dry, of a dull fracture, of a sweetish peculiar odor, and a disagreeable, saline, bitterish taste. It is inflammable, but does not melt with heat. It softens in water, to which it imparts a yellow color, but does not dissolve. Alcohol, ether, the oils, and alkaline solutions dissolve the greater part of it. The South American Indians are said to produce directly from the annatto seeds, without fermentation, a color similar to and almost as brilliant as carmine. (*P. J.,* April, 1903.) For a proximate analysis of the leaves see *Ap. Ztg.,* 1899, p. 35. It contains a peculiar coloring principle, to which Preisser, its discoverer, gave the name of *bixin.* This has the formula $C_{28}H_{34}O_5$, and when pure is a dark, red, somewhat crystalline substance. According to Van Hasselt, bixin has the composition $C_{29}H_{34}O_5$, but Heiduschka and Riffart believe that the correct formula is $C_{28}H_{34}O_5$. (*A. Pharm.,* 1911, No. 1, 39.) It is accompanied by a yellow coloring matter, *orellin.* A coloring matter found in the root of *Escobedia scabrifolia,* a plant growing in tropical America, is used by the Mexicans in coloring fats and butter yellow. (*S. W. P.,* 1912, No. 18, 260.) The chief uses to which annatto is applied are for dyeing silk and cotton orange-yellow, and for coloring cheese and butter. The color, however, which it imparts to cloth is fugitive. It has been given internally as a medicine; but is not now used, and probably exercises little influence upon the system. In pharmacy it is employed to color ointments and plasters, and has occasionally been substituted for saffron. It is frequently adulterated with red ochre, powdered bricks, colcothar, farinaceous substances, chalk, calcium sulphate, turmeric, etc. The mineral substances, if present, will be left behind when the annatto is burned. *Tincture of annatto* is made by extracting 100 parts of annatto with 100 parts of water containing 1½ per cent. of potassium carbonate, and evaporating to 60 parts, mixing with 12 parts of alcohol and filtering.

Anona.—The seeds of *A. squamosa,* L., *Sugar Apple* or *Sweet Sop* of the West and East Indies, are said to be poisonous and to be used to kill lice, while the bark is a drastic cathartic. The seeds of *A. muricata,* L., *A. palustris,* L., and *A. spinescens,* Mart., are employed to poison fish and to exterminate destructive insects. (*Ph. Rev.,* Oct., 1896.)

Anthrakokali.—For an account of this preparation, which was introduced by Polya, see 16th ed. *U. S. D.,* p. 1711.

Anthrarobin. *Anthro-arobin. Leucoalizarin.*

$$C_6H_4\begin{cases}C(OH)\\ |\\ CH\end{cases}C_6H_2(OH)_2$$

—This substance, which is produced from commercial alizarin by reduction, was first described by Liebermann (*Ber. d. Chem. Ges.,* 1888), and proposed as a substitute for chrysarobin. It is a yellowish-white granular powder, almost insoluble in water and acidulated solutions, sparingly soluble in chloroform and ether, and readily soluble in alcohol and weak alkaline solutions. It mixes readily with fats to form ointments. It is a powerful reducing agent, which seems to be less toxic than chrysarobin, and probably equally effective in the treatment of *diseases of the skin,* it having been used by G. Behrend, E. B. Bronson, Köbner, and other clinicians, with asserted advantage in those diseases for which chrysarobin is employed. In alkaline solution anthrarobin readily absorbs oxygen and is reconverted into the blue alizarin. It is incompatible with hydrogen dioxide, potassium permanganate and other oxidizing agents. Behrend recommends the following. *Solution of anthrarobin:* anthrarobin, 10 parts; borax, 8 parts; water, 80 parts. *Glycerite of anthrarobin:* anthrarobin, 10 parts; glycerin, 80 parts. (*Th. M.,* 1888.) As a topical application, the ointment or the alcoholic solution (each 10 per cent.) may be used.

Anthrasol. *N. N. R.* 1916. *Colorless Coal Tar.*—Anthrasol is coal tar freed from bases such as pyridin and chinoline by acid treatment and from pitch by distillation. The distillate is purified to remove coloring principles and juniper tar is added to prevent separation of solid constituents. Oil of peppermint is added to correct the odor. It is a thin, mobile, light-yellow oil which stains neither skin nor fabric. Anthrasol is an antiseptic and parasiticide. Like ordinary coal tar it allays irritation of the skin but is said neither to obstruct the follicles nor to favor the development of *acne.* It is used in ointments in strengths varying from 5 to 30 per cent. A glycerin soap containing 20 per cent. of anthrasol is marketed under the trade name of *Anthrasolin.*

Anthriscus. *Anthriscus cerefolium* (L.) Hoffm. (*Chærophyllum sativum* Lam. *Scandix cerefolium,* L.), *Chervil.*—An annual European plant of the Fam. *Umbelliferæ,* cultivated in gardens as a pot-

herb, and naturalized in Eastern and Southern Pennsylvania. It has a strong agreeable odor, and a pungent, slightly bitterish taste. It contains a volatile oil of very feeble medicinal power, but it has been used as an emmenagogue and diuretic.

Antiaris.—Among the Asiatic arrow poisons one of the most important, which has long been used by the natives of Java and other East Indian islands under the name of *Upas antiar*, is a gum-resinous exudation obtained from the *Antiaris toxicaria* Lesch., a large tree belonging to the *Urticaceæ*, growing in Java, Celebes, and the neighboring islands. Like certain species of *Rhus*, this plant exhales a volatile poison which very unpleasantly affects some of those who approach it, causing eruptions upon the skin attended with much swelling; hence the fable of the *deadly upas tree*. The juice is mixed with various substances to give it due consistency. Whether taken internally or introduced into the system through a wound, upas acts with extreme violence, producing vomiting, great prostration, a feeble, irregular pulse, involuntary evacuations, and convulsive movements, which are soon followed by death.

Pelletier and Caventou obtained from it a glucoside, *antiarin*, crystallizable, soluble in water and alcohol, but scarcely so in ether, and of the formula $C_{14}H_{20}O_5$. According to Kiliani (*Ber. d. Chem. Ges.*, 1910, p. 3574), there are two glucosides, namely, *alpha- and beta-antiarin*. For the first of these he suggests the formula $C_{27}H_{42}O_{10} + 4H_2O$, while the formula for the second is uncertain, but may be $C_{22}H_{30}O_8$. Antiarin is a muscle poison, producing first strong fibrillary contractions of the voluntary muscles, followed by a rapid decrease in irritability and finally paralysis, the sarcolemma of the muscles and not the motor nerve endings being the part attacked. It also belongs to the digitalis group of cardiac stimulants, raising the blood pressure at first, and finally arresting the heart in systole. According to Stockman, antiarin diminishes the irritability of the peripheral vagi and stimulates the vasomotor centers. H. W. Bettink claims (*Ned. Tijdschr. v. Pharm.*) that besides antiarin there are present in *Upas antiar* two other active principles, *œpaïn* and *toxicarine*. Headborn (*A. E. P. P.*, 1901, xlv) states that *antiarigenin*, a derivative of antiarin, is more powerful than antiarin itself.

Antihydropin. *Pulvis Taracanæ.*—The powdered Russian *cockroaches* (*Blatta lapponica, Blatta orientalis*) are asserted, in the dose of from ten to fifteen grains (0.65–1.0 Gm.), to be actively diuretic and useful in *dropsy*. Bogomolow (*Ph. Cb.*, July, 1879) found in them a crystalline principle, *antihydropin*, or *taracanin*. L. Reuter (*A. Pharm.*, 1889, 868) affirms that the discredit into which cockroaches have fallen is due to the indifferent quality of the powdered insects in the market, and gives tests for their purity.

Antiluetin. — *Potassium-ammonium-antimonic bitartrate*, $SbO(C_4H_4O_6)_2K(NH_4)_2.H_2O$, has been used by Tsuzuki (*D. M. W.*, 1913, p. 825) in the treatment of *syphilis*. The beginning dose he used was two-fifths of a grain (0.025 Gm.) increased rapidly to three-fourths of a grain (0.05 Gm.).

Antimony Arsenate.—This is a heavy, snow-white powder, containing 80 per cent. antimonic oxide and 20 per cent. arsenic acid (Merck). *Antimony arsenite*, on the other hand, is said to contain equal parts of the two ingredients, arsenous acid and antimonic oxide. It is stated that antimony arsenate is used in Russia as an alterative in *doses* of one-fiftieth of a grain (0.0013 Gm.) four times a day. (*A. J. P.*, xliv, 301.)

Antimony Crocus. *Crocus of Antimony. Saffron of Antimony.*—This compound is formed during the deflagration of a mixture of equal weights of antimony trisulphide and potassium nitrate, to which one-twelfth of hydrochloric acid has been added. Fused crocus of antimony is in masses of a liver-brown color; the unfused is a saffron-brown insoluble powder, containing about four-fifths of trioxide, and one-fifth of trisulphide. It was formerly used in making tartar emetic.

Antimony, Diaphoretic. *Antimonium Diaphoreticum. Potassii Biantimonias. Antimoine diaphorétique lavé*, Fr.—This compound may be formed by deflagrating in a crucible, and keeping red hot for fifteen minutes, a mixture of pure antimony with three times its weight of potassium nitrate. The product, washed with water and dried, is *washed diaphoretic antimony*. For improved process, see 14th edition of *U. S. D.*, p. 1640. *Dose*, from one-half to two drachms (1.9–7.7 Gm.). This form of antimony is weak, variable, and rarely used.

Antimony Glass. *Vitrum Antimonii.*—This is prepared from antimony trisulphide by a partial roasting and subsequent fusion. Glass of antimony is an active antimonial; but, owing to its variable composition and unequal operation, it is very seldom used. For further information concerning this substance, see *U. S. D.*, 19th ed., p. 1391.

Antimony Aniline Tartrate. $SbO.C_6H_5NH_2.C_4H_4O_6$.—According to Loweran, this occurs in colorless, yellow crystals, soluble in water, containing 22 per cent. of antimony. Although antimony and potassium tartrate has been used both experimentally and clinically in the treatment of trypanosome infections, its high toxicity has discouraged the hope of its proving a useful therapeutic agent. The antimony and aniline tartrate, which was first prepared by C. S. Evans, was found by Loweran (*C. R. A. S.*, 1909, p. 546) to be much less toxic to the higher animals and to be an efficient trypanocide in guinea-pigs. Thiroux has used it clinically in the treatment of *sleeping sickness* and, although it is as yet too soon to say definitely concerning its value, his results are at least encouraging. He injected it intravenously in *doses* of one-fourth of a grain (0.15 Gm.).

Antimony Iodide. SbI_3. *Antimonii Iodidum. Antimony Triiodide* or *Teriodide.*—According to W. Copney, of London, this iodide may be conveniently prepared by gently heating, in a Florence flask, metallic antimony and iodine, in the proportion of one part to three. The elements combine with sudden heat and liquefaction, and, upon the withdrawal of the heat, the iodide formed solidifies, and is removed by breaking the flask. Antimony iodide, as thus prepared, forms a somewhat crystalline, foliated mass, which, when pulverized, yields a deep orange-red powder. By the action of water it is decomposed. It has been tried as an alterative in *doses* varying from one-fourth to one-half grain (0.016–0.03 Gm.), given in pill.

Antimony Sulphide. *Antimonium Nigrum*, Br. 1864. *Black Antimony. Japanese Antimony. Antimony needle. Prepared Sulphuret of Antimony, Stibium Sulfuratum Crudum et Lœvigatum, Antimonium Crudum, Sulfuretum Stibicum; Artificial Sulphuret of Antimony; Sulfure d'Antimoine du commerce*, Fr. Cod. *Antimoine sulfuré, Antimoine cru*, Fr. *Stibium sulfuratum nigrum*, P. G. *Schwefelantimon, Schwefelspiessglanz*, G. *Anti-*

moino crudo, Sp. *Antimonii Sulphidum*, U. S. 1890. *Antimony Trisulphide.* Sb_2S_3; 334.09.—"Native antimony sulphide, purified by fusion and as nearly free from arsenic as possible." *U. S.*, 1890.

Preparation.—The antimony sulphide which is found in commerce is obtained from the native sulphide, called *antimony ore*, by different processes of purification.

Much of the "Black Antimony" of commerce has been shown by Warder to contain no antimony whatever, but to be simply powdered coal and marble, and such can be easily distinguished by the fact that a dry, tared one-ounce bottle will hold, after shaking down, two and a quarter ounces of powdered black antimony, but only one and a quarter ounces of powdered coal. (*Proc. A. Ph. A.*, 1885, 479; see also S. W. McKeown, *Proc. Ohio State Pharm. Assoc.*, 1885.) Antimony sulphide should never be triturated with a strong oxidizing agent as an explosion is liable to occur. When exposed to the air it is partially converted into the oxide.

Properties.—Antimony sulphide is mostly prepared in France and Germany. It is called, in commerce, antimony, or *crude antimony*, and occurs in fused conical masses, denominated "loaves." "Steel-gray masses of a metallic luster and a striated crystalline fracture, forming a black or grayish-black, lusterless powder, without odor or taste, and permanent in the air. Insoluble in water or alcohol, but soluble in hydrochloric acid with the evolution of hydrogen sulphide." *U. S.*, 1890.

Uses.—This preparation is very uncertain in its operation, and ought not to be used in practical medicine. It has, however, been employed as a diaphoretic and alterative in *scrofula, glandular obstructions, cutaneous diseases*, and *chronic rheumatism*. It is used in the United States solely in veterinary practice. The *dose* for a horse or cow is from ten to thirty grains (0.65–2.0 Gm.), to be given in powder or bolus. For further information concerning antimony sulphide, see *U. S. D.*, 19th ed., p. 1391–1392.

Antimony Sulphide, Purified. *Antimonium Nigrum Purificatum*, Br. 1898. *Antimonious Sulphide. Antimonii Sulphidum Purificatum*, U. S. 1890. *Purified black Antimony. Sulfure d'Antimoine pur*, Fr. Cod. *Gereinigtes Schwefelantimon*, G. *Trisolfuro di antimonio depurato*, It.—"Native antimonious sulphide, Sb_2S_3, from which siliceous matter has been removed by fusion, reduced to fine powder, and, if any salt of arsenium be present, purified by digesting with half its weight of solution of ammonia for several days, washing and drying." *Br.* The process of the U. S. P., 1890, for its purification was as follows: "Antimony Sulphide, *one hundred grammes* [or 3 ounces av., 231 grains]; Ammonia Water, *fifty mils* [or 1 fluidounce, 5½ fluidrachms]; Water, *a sufficient quantity*. Reduce the antimony sulphide to a very fine powder. Separate the coarser particles by elutriation, and, when the finely-divided sulphide has been deposited, pour off the water, add the ammonia water, and macerate for five days in a well-closed vessel, agitating the mixture frequently. Then let the powder settle, pour off the ammonia water, and wash the residue by repeated affusion and decantation of water. Finally dry the product by the aid of a gentle heat."

These processes are intended to furnish a black antimony sulphide better fitted for the manufacture of the official preparations of antimony and for internal administration. Copper, a common impurity in the crude sulphide, is rendered soluble by the ammonia water, while the subsequent washing and decantation effectually remove all soluble impurities.

It is "a heavy, grayish-black, lusterless powder, without odor or taste, and permanent in the air. Insoluble in water or alcohol, but soluble in hydrochloric acid with the evolution of hydrogen sulphide. At a temperature below a red heat it fuses to a dark brown liquid." *U. S.*, 1890.

The official tests were as follows: "If 1 Gm. of the Sulphide be digested, and finally boiled, with 10 mils of hydrochloric acid, it should dissolve without leaving more than 1 per cent. of residue. This acid solution, completely deprived of hydrogen sulphide by boiling, yields, when added to water, a white precipitate, which is soluble in a solution of tartaric acid. After the separation of the precipitate by filtration, the filtrate yields an orange-red precipitate with hydrogen sulphide test-solution. If 2 Gm. of the Sulphide be mixed and cautiously ignited, in a porcelain crucible, with 8 Gm. of pure sodium nitrate, and, after cooling, the fused mass be boiled with 25 mils of water, there will remain a residue which should be white or nearly so, and not yellowish nor brownish (absence of *other metallic sulphides*). On boiling the filtrate separated from the last-mentioned residue with a slight excess of nitric acid, until no more nitrous vapors are evolved, then dissolving in it 0.1 Gm. of silver nitrate, filtering again if necessary, and cautiously pouring a few drops of ammonia water on top, not more than a white cloud, but no red or reddish precipitate, should appear at the line of contact of the two liquids (absence of more than about 0.1 per cent. of *arsenic*)." *U. S.*, 1890. "A grayish-black crystalline powder decomposed on boiling with *hydrochloric acid*, an almost clear solution being formed and hydrogen sulphide escaping. The solution affords the reactions characteristic of antimony. It should not yield more than slight characteristic reactions with the tests for arsenium." *Br.*, 1898. This preparation is not used in medical practice, but is used in the manufacture of sulphurated antimony (see p. 154).

Antimony Trichloride. *Butter of Antimony.* $SbCl_3$.—Prepared by subliming antimony sulphide with mercuric chloride, by the action of dry chlorine on the sulphide or metal, or by dissolving the sulphide in hydrochloric acid and concentrating the solution of the chloride; in the latter method the product is usually colored by contamination with iron, but by distillation the pure chloride will finally pass over, the distillate solidifying in a mass of fine white crystals. Antimony trichloride is a deliquescent, soft mass, known as butter of antimony, which melts at 72° C. (161.6° F.) and boils at 223° C. (433.4° F.). It is very hygroscopic and corrosive. The addition of water produces the oxychloride known, when dry, as *powder of Algaroth*. A solution was recognized in the Br. Ph., 1885, and is used in medicine as a caustic. McDonald and Hill have improved the formula for *solution of chloride of antimony* by dissolving 132 grains of antimonous chloride in 3 fluidrachms of hydrochloric acid and sufficient distilled water to make 1 fluidounce. If it is desirable to have a tinted solution, add 15 grains of ferric chloride to each fluidounce. (*P. J.*, 1908, 86.) It is extensively used to give a bronze surface to iron and steel ware.

Antinonnin. *Sodium ortho-di-nitro-cresolate.*—A yellowish, odorless, non-volatile paste said to be actively germicidal, odorless, and poisonous. On account of its being very effective and inexpensive, it has been highly recommended for spraying plants, etc., when attacked with mildew or other vegetable parasites: 1 to 2000 in soap solution may be used. It produces bright yellow stains upon fabrics, etc.

Antinosin. *Sodium tetra-iodophenolphthalein.* $(C_6H_2I_2ONa)_2C.O.C_6H_4O$.—A blue powder, soluble in water and employed as a succedaneum for iodoform as a surgical antiseptic in 5 to 10 per cent. wash. (See also *Nosophen.*)

Antipyrine Benzoate.—*Benzopyrine,* $C_{11}H_{12}N_2O.HC_6H_5O_2$, made by adding antipyrine to a boiling solution of benzoic acid. It is in the form of a yellow liquid, practically insoluble in hot and cold water, but soluble in alcohol and ether.

Antipyrine Tannate.—This is described as a yellow powder, insoluble in water, soluble in alcohol, and containing 37 per cent. of antipyrine. It is stated that it may be made by adding concentrated aqueous solutions of its constituents in the proportion of fifty parts of antipyrine to twenty-eight and a half parts of tannic acid. It has been specially recommended on account of its tastelessness, but is probably not an eligible preparation. Its incompatibilities are numerous, including those of both antipyrine and tannin.

Antisepsin. *Asepsin. Monobromacetanilide. Parabromacetanilide.* $C_6H_4Br.NH(C_2H_3O)$.—This substance has been used by Cattani as an antipyretic and analgesic (*G. M. P.*, 1890), but as such seems to be dangerous. Cattani affirms it to be a valuable antiseptic. *Dose,* from two to eight grains (0.12–0.5 Gm.).

Another compound, called antisepsin (or *antiseptin*), has been exploited as *iodoboro-thymolate of zinc,* which, according to Squibb, is a mixture of zinc sulphate, boric acid, zinc iodide, and thymol. (*Ph. Post,* 1893, 106.)

Antiseptol.—Under this name Yvon has recommended *cinchonine iodosulphate* as a substitute for iodoform. It contains 50 per cent. of iodine. For method of making this salt, see *U. S. D.*, 19th ed., p. 1392.

Antispasmin. $C_{23}H_{36}NO_8Na + 3C_6H_4(OH)COONa$.—In this compound 1 molecule of *narceine-sodium* is considered to have united with 3 molecules of sodium salicylate. This white, slightly hygroscopic powder contains about 50 per cent. of narceine, and is said to have the advantage over the other narceine preparations of readily forming with water a fairly permanent solution. According to Demme, it is a valuable hypnotic and analgesic, especially advantageous in painful *cramps.* It has also been recommended for *whooping cough. Dose,* from one-half to one grain (0.032–0.065 Gm.).

Antithermin. *Phenylhydrazin-lævulinic acid.* $C_6H_5.N_2O = C(CH_3).C_3H_5O_2$.—This substance, which is obtained by the action of phenylhydrazin upon *acetopropionic acid,* occurs in colorless crystals, insoluble in cold water, soluble in ether and hot alcohol, melting point 108° C. (226° F.). It was first proposed in 1887 by Nicot as an antipyretic, and it has been especially experimented with by Drobner (*W. M. P.*, 1892, 540), who finds it active in *doses* of from eight to ten grains (0.5–0.65 Gm.). It produces, however, pallor, cephalic distress, excessive sweating, and other evidences of vasomotor depression, which require great caution in its use, and not more than three grains (0.2 Gm.) should be given.

Antithyroidin Moebius. *N. N. R.* 1917. *Serum Antithyroideum, Thyrodectomized Serum.*—This is the blood serum of sheep from which the thyroid gland has been removed, at least six weeks before the blood is drawn, preserved with 0.5 per cent. of phenol. It is an amber-colored fluid, with the faint odor and taste of phenol. It is marketed in vials containing two and a half drachms (10 mils). With proper precautions it is said to keep indefinitely. It is employed in the treatment of *exophthalmic goitre.* It is administered either hypodermically or by the mouth in *doses* beginning with eight to fifteen minims (0.5–1.0 mil) three times a day, gradually increasing the dose.

Antituman. *Sodium Chondritin Sulphate.*—Oestreich (*B. K. W.*, 1910) having observed that in carcinoma the arterial walls and cartilaginous tissues were not affected, believed that this immunity of these tissues was due to some substance found in them. On this theory he has employed *sodium chondritin sulphate* in the treatment of *cancers.* According to his observations, the remedy lessens suffering and improves the general health of patients who are suffering with inoperable cancers. Because of the pain which follows the injection of the remedy, it is marketed in combination with eucaine. The beginning *dose* is one and a half grains (0.1 Gm.) once or twice a day subcutaneously, which may be gradually increased.

Antitussin.—*Di-fluor-di-phenyl,* $(C_6H_4F)_2$, occurs as colorless crystals melting at 87° C. (189° F.). It forms the active ingredient of antitussin, which has been strongly recommended by Max Heim (*B. K. W.*, Dec., 1899) in the treatment of *whooping cough.* It is used as an ointment consisting of five parts of di-fluor-di-phenyl, ten parts of vaselin and eighty-five parts of lanolin. For a child a year old, about one-half drachm (2 Gm.) is slowly rubbed into the skin daily on the back, chest, and abdomen, about a drachm (3.9 Gm.) being used for a child five years old. (See also *Merck's Annual Reports,* 1905, 22 and 1907.)

Antodyne. *Anodyne.*—This is asserted to be *phenoxypropanediol,* a condensation product of phenol and *epichlorhydrine.* It has been brought forward as an analgesic in *neuralgia, gonorrheal arthritis* and other painful conditions. The *dose* is eight to fifteen grains (0.5–1 Gm.).

Anusol.—A proprietary suppository, alleged to contain a bismuth compound of *iodo-resorcin-sulphonic acid,* but it is apparently a mixture of zinc oxide, resorcinol, bismuth oxyiodide, balsam of Peru, and cacao butter. (*West. Drug.*, 1898, 75; *J. A. M. A.*, 1911, lvi, 441.) It is used in the treatment of *hemorrhoids.*

Aperitol.—Under this name is marketed a palatable form of *iso-valeryl-acetyl phenolphthalein* formed by the combination of esters of isovalerianic acid and acetic acids, in equal proportions.

This substance, which has been introduced as a cathartic, appears to be without any toxic action upon the system, for Hammer and Veith (*Med. Klin.*, 1908, iv) fed fifteen grains (1 Gm.) to a dog daily for ten days without any apparent effect. The same authors report a case in which a man took by mistake twenty-four grains (1.6 Gm.) without any more serious symptom than catharsis. Those who have employed the remedy are almost unanimous in the statement that it causes catharsis without (except in very occasional cases) any

griping. According to Miklos (*K. T. W.*, 1909, p. 747), in *chronic constipation* the remedy has the advantage that after two or three doses have been administered the regular evacuations will continue for several days even if the cathartic is withdrawn. The drug has been used not only in the treatment of chronic constipation, but also as a substitute for castor oil in the treatment of *enteritis*. The *dose* for an adult is ordinarily about three grains (0.2 Gm.).

Aphloia theæformis Benn. (Fam. *Bixaceæ*).—This plant is a native of Madagascar and is claimed to possess marked alterative properties and beneficial effects upon hemoglobin. It is administered as an infusion of the leaves, 30 Gm. of the plant being used to make 1 liter of infusion.

Aphthisin.—Under this name a mixture of 9 parts of potassium guaiacol sulphate and petrosulphol ammonium, 1 part, is exploited as a remedial agent in lung and bronchial diseases. Being an extremely hygroscopic substance it is best administered as a 6 per cent. syrup or in gelatin capsules combined with an oil. *Dose*, a teaspoonful of the 6 per cent. syrup several times daily.

Apinol. *N. N. R.*, 1917.—This is a product obtained in the destructive distillation of the wood of *Pinus palustris* Will. (*Pinus australis*). It is stated to consist mainly of *lævo-menthone*, $C_{10}H_{18}O$. It is a clear amber-colored oil, with a pine odor and having a sp. gr. of 0.946. It is used locally as an antiseptic and anesthetic application for *wounds*. It is also employed as an expectorant in chronic catarrhal conditions of the respiratory tract in *doses* of five to ten minims (0.3–0.6 mil).

Apocynum. *N. F. IV* (*U. S. P. VIII*). *Canadian Hemp. Black Indian Hemp. Dogsbane. Chanvre du Canada*, Fr. *Canadische Hanfwurzel*, G.—"The dried rhizome and roots of *Apocynum cannabinum* Linné (Fam. *Apocynaceæ*), without the presence of more than 5 per cent. of stems or other foreign matter." *N. F. IV.* Although latterly apocynum has fallen into disuse, some physicians have insisted that the *A. cannabinum* is a valuable remedy and that its unfavorable reputation has arisen from the use of other species. The drug of commerce in recent years has consisted of several species of Apocynum. A number of physicians in the United States have come to the conclusion that the absorption of Apocynum in the gastro-intestinal tract is uncertain and irregular, which led to its being deleted from the Pharmacopœia. It has been admitted into the N. F.

There are several indigenous species of this genus of very similar general aspect, the rhizome and roots of two of them being collected, viz.: *Apocynum cannabinum*, L., and *A. androsæmifolium*, L. Both plants abound in a milky juice, and have a tough, fibrous bark, which, by maceration, affords a substitute for hemp; hence the common name. It is used by the Indians of California for making all manner of cordage and for weaving.

In *A. cannabinum* the stems and branches are upright or ascending, terminated by erect and close, many-flowered cymes, which are usually shorter than the nearly sessile leaves, and the corolla has nearly erect lobes, with the tube not longer than the lanceolate divisions of the calyx. In *A. androsæmifolium* the branches are divergently forked, the leaves are slender petioled, the cymes loose and spreading, the open bell-shaped corolla with revolute lobes and a tube much longer than the ovate-pointed divisions of the calyx. *A. cannabinum*, of which there are a number of well recognized varieties, grows in gravelly or sandy soil mostly near streams, while *A. androsæmifolium* grows in dry thickets and open woods. According to E. A. Manheimer, the root of the latter is distinguished from *A. cannabinum* by the thick-walled stone cells, which are arranged in an interrupted circle near the middle of the bark. (*A. J. P.*, Nov., 1881. See also *A. J. P.*, 1888.) Holm has contributed an article on the structure of *A. cannabinum*. (*Merck's Rep.*, 1910, p. 277.)

It is described in the N. F. as: "Cylindrical, somewhat branched, of varying length, from 3 to 10 mm. in thickness; externally reddish-brown to grayish-brown, longitudinally wrinkled and occasionally with transverse fissures having vertical sides extending through the bark; fracture short; internally, bark light brown, from 1.5 to 3 mm. in thickness, wood faintly radiate and with large tracheæ, a small pith occurring in pieces of the rhizome. Almost inodorous; taste starchy, afterwards becoming bitter and somewhat acrid. Under the microscope sections of Apocynum show numerous laticiferous vessels in both the bark and pith. The stems of Apocynum have a comparatively thin fibrous bark, a light brown porous wood and a large, hollow pith. The powder is light brown, starch grains numerous, from 0.003 to 0.015 mm. in diameter, spherical, ellipsoidal, ovate, pyriform, or more or less irregular, sometimes more or less altered, swollen, and with a hyaline central cleft; numerous fragments of strongly lignified wood fibers, associated with tracheæ mostly having bordered pores, occasionally with spiral thickenings; fragments of cork layer few, the walls being of a reddish-brown color; an occasional fragment with laticiferous tissues; stone cells few or absent (*Apocynum androsaemifolium* Linné). Apocynum yields not more than 5 per cent. of ash." *N. F. IV.* The fresh root, when wounded, emits a milky juice, which concretes into a substance resembling caoutchouc. The stems of Apocynum have a comparatively thin, fibrous bark, a light brown porous wood and a large, hollow pith. In the dried state, the rhizome and roots are brittle and readily pulverized, affording a powder which is light brown, containing numerous starch grains which are from 0.003 to 0.015 mm. in diameter, spherical, ellipsoidal, ovate, pyriform, or more or less irregular, sometimes more or less altered, swollen, and with a hyaline central cleft. It also contains numerous fragments of strongly lignified wood fibers which are associated with tracheæ having bordered pores or occasionally with spiral thickenings, a few fragments of cork, the walls being of a reddish-brown color, and an occasional fragment with laticiferous tissues. Stone cells are not present in *A. cannabinum*, but are common in *A. androsæmifolium*.

The nature of the active principle of apocynum is as yet somewhat uncertain. Finnemore, in 1908, obtained from the *A. cannabinum* a crystalline substance to which the name of *cynotoxin* was applied. The following year Moore (*J. Chem. Soc.*, 1909, xcv) separated from the *A. androsæmifolium* a glucoside having the formula $C_{14}H_{16}O_8$, to which he applied the name of *apocynamarin*. These two principles which appear to be identical, possess the characteristic physiological effects of the crude drug. Taub and Fickewirth (*A. G. P.*, cliii, p. 239) believe that neither of these principles is chemically pure and that the activity of the plant

is due to an intensely bitter principle which is not of glucosidal nature and to which they apply the name of *cymarin.* This latter substance has been studied pharmacologically by Impens and has also been used practically by Allard (*D. M. W.*, 1913, xxxix, p. 783) and others, and appears to exert the characteristic effects of the drug. Cymarin is given in oral single *dose* of one two-hundredth of a grain (0.003 Gm.); daily *dose,* one-sixtieth to one-thirtieth of a grain (0.001–0.002 Gm.) intravenous or intramuscular *dose,* one one-hundred and twenty-eighth to one sixty-fourth of a grain (0.0005–0.001 Gm.).

Von Oefele (*Journ. Pharm. Elsass-Lothr.*, 1891, 325) described *apocynteine,* an alkaloid obtained from *A. venetum;* it is said to be a cardiac sedative.

Apocynum belongs physiologically to the digitalis group of cardiac tonics. Like digitalis it slows the pulse by stimulating cardiac inhibition, increases the vigor and tone of the heart muscle, and in overdose causes systolic spasm of the frog's heart, increases vasomotor tone and the activity of the kidney. It differs from digitalis only in the relative degree of its different effects. It appears to be the most powerful of the whole group in its effect upon inhibition, the slowing of the pulse being so extreme that despite marked constriction of the blood vessels the pressure is often lowered instead of elevated. According to Dale and Laidlaw (*Proceedings of the Royal Society of Medicine,* Dec., 1909), its action upon the vasomotor system is also relatively strong. It appears to be more irritant to mucous membranes than either digitalis or strophanthus, and therefore is prone to cause nausea and catharsis. Perhaps this local stimulant effect is also the explanation of its very powerful diuretic action, although Dale and Laidlaw believe that the effect upon the kidneys is due chiefly to a relative dilatation of the renal arteries.

Apocynum is useful in medicine as a diuretic and as a cardiac tonic. For the former purpose it is especially of service in *dropsies* due to heart failure, but has been also highly recommended in the *ascites* of *hepatic cirrhosis;* indeed, so powerful are its hydragogue properties that it has been dubbed the "vegetable trocar." As a tonic to the heart it is useful in the same classes of chronic *heart disease* in which digitalis is of service. The N. F., however, adds the following caution: "It has been stated that the absorption of Apocynum in the gastro-intestinal tract is uncertain and irregular. To avoid an accumulation of the drug or toxic action, the physician should carefully guard the dosage and determine in each case the tolerance of the patient." Its irritant action upon the intestinal tract also militates strongly against its clinical usefulness; many patients are quite unable to take the drug because of the occurrence of emesis or purgation. *Dose,* five to fifteen grains (0.32–1.0 Gm.).

Aplopappus. *Aplopappus* (*Haplopappus*) *Baylahuen* Remy.—This composite herb is a native of Chili, where it is said to be relied upon as a stimulant in *flatulent dyspepsia* and *chronic inflammation* with *hemorrhage* of the lower bowels. It has been analyzed by H. H. Rusby (*A. J. P.*, 1890, 488), and later by H. Kahn (*A. J. P.*, 1891, 377). The former found a volatile oil, a fatty oil which had the specific odor of the plant, a brown acid resin of sharp taste, and tannin. The latter determined the percentage of volatile oil as 6.65, and of resin as 21.15. He also considers that this resin is a mixture of four different resins. G. Baille asserts (*B. G. T.*, Feb., 1889) that the remedy is valuable not only in *dysentery,* but in *genito-urinary catarrhs,* and also as a stimulating expectorant. *Dose,* one-half to one tablespoonful (7.5–15 mils) of a strong decoction, one part to five, may be given every two hours; or the fluid-extract, from five to twenty minims (0.3–1.3 mils). It has also been used in tincture form as an application to slowly healing *wounds* and *ulcers.*

Apocodeine Hydrochloride. $C_{18}H_{19}NO_2HCl$.—It is a greenish-yellow powder, soluble in water. Apocodeine has been investigated physiologically by W. E. Dixon (*B. M. J.*, 1902) who found that it lowered blood pressure by dilating the blood vessels, increased the intestinal peristalsis and produced a large secretion of saliva. Foy and Combemale (*R. T.*, 1907) have both employed it hypodermically as a laxative with pleasing results. Thirty minims (1.8 mils) of a 1 per cent. solution may be injected deeply into the muscles.

Apolysin. *Aconitylphenetidin. Monophenetidin Citrate.* $C_6H_4.OC_2H_5.NH(C_6H_7O_6)$.—A compound made by heating together citric acid and phenetidin with one molecule of water. It is a crystalline, yellowish-white powder of peculiar odor and taste. Its melting point is 72° C. (161.6° F.). It is soluble in cold water (1 in 25), alcohol, and glycerin, and in concentrated sulphuric acid without change of color. The solution in nitric acid turns a pale orange color. The aqueous solution is not clouded by silver nitrate, nor the acid solution by hydrogen sulphide. For tests of purity, see *Zeit. Oest. Apoth. Ver.*, 1910, 301. R. Seifert (*D. M. W.*, xxi, 1895) asserts that in *doses* of from eight to twenty-four grains (0.5–1.6 Gm.), three or four times a day, it is a valuable remedy as an antipyretic in various febrile diseases, and possessed of great power as an analgesic, similar in range of usefulness to acetphenetidin, but free from poisonous properties or disagreeable after effects.

Apomorphine-methylbromide. $C_{17}H_{17}NO_2CH_3Br$. *Apomorphine Bromomethylate. Euporphin.*—This occurs in colorless or yellowish crystals soluble in either water or alcohol. It is used as a nauseating expectorant in *acute bronchitis* and is asserted to have the advantage over apomorphine of being more stable and less liable to produce vomiting. The *dose* is from one-twentieth to one-twelfth of a grain (0.003–0.005 Gm.).

Aquilegia. *Aquilegia vulgaris,* L. *Columbine.*—A perennial herbaceous plant of the Fam. *Ranunculaceæ,* indigenous to Europe, but cultivated in our gardens. At one time considered diuretic and diaphoretic, columbine is not at present used in practical medicine. For further information concerning this drug, see *U. S. D.*, 19th ed., p. 1394.

Aralia. *N. F. IV. American Spikenard. Spignet.*—Aralia of the N. F. is "the dried rhizome and roots of *Aralia racemosa* Linné (Fam. *Araliaceæ*), without the presence of more than 5 per cent. of adhering stem bases, or other foreign matter. Rhizome of oblique growth, about 12 cm. in length and 5 cm. in thickness, somewhat flattened, tortuous, externally pale brown, somewhat annulately roughened, frequently cut longitudinally, whitish internally; nodes approximate, each with a prominent stem scar about 3 cm. in breadth; fracture fibrous; roots numerous, of varying length, from 5 to 25 mm. in thickness, usually cut longitudinally and furrowed, sometimes with transverse ridges and corky patches; light brown

or purplish-brown externally, whitish and spongy or porous internally; fracture of the cortex short, of the wood short and fibrous. Odor aromatic; taste mucilaginous, pungent and slightly acrid. A transverse section of the root shows a thick bark with several zones of secretion reservoirs containing oil, a well-developed cork with one or more hypodermal layers of lignified cells, and a more or less distinctly radiate wood. Examined microscopically, the powdered drug shows spherical or angular, single or two- or more compound starch grains, from 0.005 to 0.02 mm. in diameter, rosette aggregates of calcium oxalate from 0.03 to 0.07 mm. in diameter, tracheæ with scalariform or reticulate thickenings and simple or bordered pores, characteristic lignified cells from the hypodermis about 0.04 to 0.1 mm. in length and about one-half as broad, their walls showing simple pores (distinction from *Aralia nudicaulis*). Aralia yields not more than 10 per cent. of ash."

Aralia nudicaulis L. *False Sarsaparilla. Wild Sarsaparilla. Shotbush. Small Spikenard. Wild Licorice. Racine d'aralie nue, Petitnard,* Fr. *Nackte Aralienwurzel,* G.—This plant is an indigenous perennial. It grows from Canada to the Carolinas, inhabiting shady and rocky woods, being common in rich soil. The rhizome is horizontal, creeping, sometimes several feet in length, and 5 to 15 mm. in thickness, more or less twisted, of a yellowish-brown color externally, of a fragrant odor, and a warm, aromatic, sweetish taste. Alpers and Murray (*Proc. A. Ph. A.*, 1897, 182) found in it 3.05 per cent. of resin, 0.33 per cent. of oil, tannin, an acid, albumen, mucilage, and cellulose.

The roots of *Aralia racemosa* and *A. nudicaulis* have been used especially in domestic practice for their gently stimulant diaphoretic and alterative action, chiefly in *rheumatic, syphilitic,* and *cutaneous affections,* in the same manner and dose as genuine sarsaparilla. W. R. Monroe (*A. J. P.*, Oct., 1898) found in the rhizome of the *Aralia californica* S. Wats. a small amount of a pale yellow, very aromatic, volatile oil, but failed to detect saponin. Danzel found a glucoside *aralin* in the fresh leaves of *Aralia japonica.* (See *J. P. C.*, 1912, 530.)

Aralia spinosa, L. *Angelica-tree. Hercules club. Toothache-tree. Prickly Elder. Prickly Ash.*—The name "*prickly ash*" should be dropped, as it belongs properly to a species of *Xanthoxylum.* Angelica tree is an arborescent shrub which grows in Southeastern North America. The bark, root, and berries are used as alteratives.

Archidendron. *Archidendron Vaillantii.*—The bark and black beans of this leguminous plant of New South Wales are said to be an active paralyzant to the motor side of the spinal cord. (Bancroft, *Proc. Roy. Soc. N. S. W.*, 1886.)

Areca Nut. *Semen Arecæ. Betel Nut. Noix d'Areo,* Fr. *Arekanüse, Betelnüse,* G.—The *Areca Catechu,* L., is an East India palm. The fruit, which is ovoid and from 2 to 3 cm. in diameter, and of an orange-yellow color, contains the nut embedded in a fibrous, fleshy envelope, and invested with a brittle shell which adheres to the exterior flesh. The kernel, the betel nut of commerce, is of a roundish-conical shape, rather larger than a chestnut, externally of a deep brown, diversified with a fawn color, so as to present a reticulate appearance, internally brownish-red with whitish veins, very hard, of a feeble odor when broken, and of an astringent, somewhat acrid taste. It abounds in tannin, and contains also gallic acid, a fixed oil, gum, a little volatile oil, lignin and various saline substances. It yields its astringency to water, and in some parts of Hindustan an extract is prepared from it having the appearance and properties of catechu. A red coloring matter known as *Areca red* is extracted, probably resulting from the decomposition of a tannin. It is insoluble in cold water and ether, soluble in boiling water and alkaline liquids, out of which it is precipitated by acids. E. Jahns (*Ber. d. Chem. Ges.*, 1888, 3404) has found three alkaloids in areca nut: 1. *Arecoline,* $C_8H_{13}NO_2$, identical with the *arekane* of Bombalon. 2. *Arecaine,* $C_7H_{11}NO_2 + H_2O$, which occurs in permanent, colorless crystals, soluble in water, insoluble in absolute alcohol, ether, chloroform, and benzene. 3. An alkaloid which exists in such small quantities that sufficient was not obtainable for close examination. On heating arecoline with strong hydrochloric acid to 150° C. (302° F.) it is decomposed into methyl chloride, CH_3Cl, and *arecaidine,* $C_7H_{11}NO_2$. This latter base forms colorless plates, stable in the air, fusing at from 223° to 224° C. (433.4°–435.2° F.), easily soluble in water, difficultly soluble in strong alcohol, and insoluble in ether and chloroform. Arecaidine has been shown to be *methyltetrahydronicotinic acid,* and has been made synthetically from nicotinic acid. The third alkaloid of Jahns is probably *guvacine,* $C_6H_9NO_2$, of which the methyl derivative is the base arecaidine before mentioned.

Immense quantities of areca nut are consumed in the East, mixed with the leaves of the Betel pepper (*Piper Betle,* L., *Chavica Betle* (L.) Miq.) and with lime, forming the masticatory so well known by the name of *Betel.* The red color which this mixture imparts to the saliva and the excrements is owing to the areca nut, which is also powerfully astringent, and, by its internal use, tends to counteract the relaxation of bowels to which the heat of the climate so strongly predisposes. (See *N. R.*, 1876, 71.) Arecoline resembles pilocarpine in its effects on the system. (Pätz, *Z. E. P. T.*, 1910, vii.) According to Jahns (*B. G. T.*, 1889) arecaine is the active principle of the areca nut, and a powerful tænicide, and is an active poison with an action of the type of muscarine and pilocarpine. Locally applied, or when given internally, it contracts the pupils.

Arecoline hydrobromide, $C_8H_{13}NO_2HBr$, a commercial salt, according to the experiments of Fröhner, is more powerful as a stimulant to the salivary glands than pilocarpine, and more active as a laxative than eserine. It is commended by veterinarians in the *colic* of horses, given subcutaneously in the *dose* of from one to one and one-half grains (0.065–0.096 Gm.). In human medicine it has been used in the dose of from one-fifteenth to one-tenth grain (0.004–0.006 Gm.) against the *tape worm* and as a myotic. A one-half to one per cent. solution produces a myosis, which reaches its maximum in about ten minutes and begins to subside in half an hour. It is claimed by various ophthalmologists that although in *glaucoma* its action is very transient, it produces a more considerable reduction of the intraocular pressure than can be obtained either with pilocarpine or eserine. It may cause considerable irritation but does not injure the continuity of the epithelium.

In India the areca nut has long been used as a vermifuge, the dose being a teaspoonful of the freshly grated nut, and its value against the *tape worm* has been confirmed by various European and American practitioners. The usual *dose* is from

one to two drachms (3.9–7.7 Gm.). In this country the nut has also been used for the making of a hard charcoal, employed as a basis of tooth-powder.

Argemone. *Argemone mexicana*, L. *Prickly Poppy. Argémone*, Fr. *Stachelmohn*, G.—An annual plant, belonging to the *Papaveraceæ*, growing in our Southern and Western States, Mexico, the West Indies, Brazil and in many parts of Africa and Southern Asia. For an illustrated paper on the structure of the seed of this plant by Schlotterbeck and Eckler, see *Proc. A. Ph. A.*, 1906, 467. The whole plant abounds in a milky, acrid juice, which becomes yellow on exposure, and has been used as a local application in obstinate *cutaneous diseases*, especially that affection known in Upper India as *dhad*, and also in cases of *warts* and even *chancres*. The alleged presence of morphine in *Argemone mexicana* has been disproven by J. O. Schlotterbeck (*Proc. A. Ph. A.*, 1901, p. 247), who finds that the plant contains *berberine*, besides an alkaloid, *protopine* (*argemonine* of Peckoldt). The seeds of the plant have been used in *colic*, 8 grains (0.5 Gm.), given in emulsion, and repeated if necessary every half hour until three doses have been taken. (*P. J.*, xiii, 642.) For further information concerning this drug, see *U. S. D.*, 19th ed., p. 1395.

Argulan.—This preparation is stated by Kolle and Rothermundt (*Med. Klin.*, 1913, p. 835) to be an antipyrine-sulphamino-mercury, and to represent 46.8 per cent. of mercury. It is used in the treatment of *syphilis* in *doses* of five one-hundredths to two-tenths gramme (1–3 gr.).

Arheol. *N. N. R.* 1917. *Santalol* (see also *Oleum Santali*, p. 789).—Arheol is an alcohol of the formula $C_{15}H_{26}O$, obtained from oil of sandal wood and constituting from 60 to 90 per cent. of the latter. It is an oily liquid, and is marketed in three grain (0.2 Gm.) capsules, six to twelve of which are given per day. It is affirmed to have the same remedial action as oil of sandal wood, but to be free from the tendency to cause gastric disturbance. *Dose*, five to ten minims (0.3–0.6 mil).

Arhovin. *N. N. R.* 1917. $C_{10}H_{13}C_6H_4(COOC_2H_5)(C_6H_5)_2NH$.—This is asserted to be a mixture of *diphenylamine, thymolbenzoate* and *ethylbenzoate* in molecular proportion. It occurs as a yellowish aromatic liquid with a mentholic taste, and is readily soluble in alcohol, and the fatty oils. It has been used as a urinary antiseptic in *cystitis* and *urethritis* and also as a local application in *vaginitis* and *endometritis*. According to Burchard and Schlockow (*Med. Woch.*, 1903), the ingestion of twelve 4-minim capsules over a period of three days imparted to the urine a marked antiseptic power. Although there have been a large number of favorable reports concerning this preparation, Deutsch (*W. K. W.*, 1906) and others have not had successful results from it. The *dose* for internal administration is from four to eight minims (0.25–0.5 mil) repeated several times a day. For local application a 5 per cent. solution in olive oil may be employed.

Aristochin. *N. N. R.* 1917. *Aristoquin. Aristoquinine. Diquinine carbonic ester.* $CO(C_{20}H_{23}N_2O_2)_2$.—A white or pinkish amorphous powder, soluble in alcohol, ether, chloroform, glycerin, and dilute acids, but insoluble in water. It is incompatible with alkalies and acids, being decomposed with the liberation of quinine. It is said to contain 96 per cent. of quinine, and probably is an effective antiperiodic, but has been chiefly used in *whooping cough*. It has the advantage over quinine of being practically tasteless. The *dose* for infants is about one grain (0.06 Gm.); for adults eight to fifteen grains (0.5–1.0 Gm.).

Aristolochia.—There are several species of the genus *Aristolochia* which are found in the herbalists' stores of India but do not enter commerce. Of these *A. bracteata* Retz is employed as an emmenagogue. Aristolochia of the Br. Add. was the dried stem and root of *Aristolochia indica* L. As sold in commerce this drug consists chiefly of stems with attached roots and is employed for the cure of *snake bite* and to produce abortion. The possession by it of any distinct medicinal properties is very doubtful. Later investigation has shown *A. rotunda* L. to contain *aristolochine*, $C_{32}H_{22}N_2O_{13}$, which has been used in Europe as a general tonic in febrile debility. The Br. Add. recognized the *concentrated liquor* (1 in 2 of 20 per cent. alcohol) (*Liquor Aristolochiæ Concentratus*, Br. Add.), *dose*, one-half to two fluidrachms (1.8–7.5 mils); the *tincture* (1 in 5 of 70 per cent. alcohol) (*Tinctura Aristolochiæ*, Br. Add.), *dose*, one-half to one fluidrachm (1.8–3.75 mils). Among the other species of *Aristolochia* which have been used medicinally *A. Clematitis* L., *A. longa* L., *A. rotunda* L., are still retained in official catalogues of the continent of Europe, where they are indigenous. *A. Pistolochia* L. of Southern Europe appears to have been the aristolochia of Pliny and is still used under the name of *Pistolochia*. The rhizome of *A. Clematitis* is very long, cylindrical, about 5 mm. in diameter, as a goose-quill or thicker, variously contorted, beset with the remains of the stems and roots, of a grayish-brown color, a strong, peculiar odor, and an acrid, bitter taste; that of *A. longa* L. is spindle-shaped, from 5 cm. to 3 dm. in length, about 2 cm. in thickness, fleshy, very brittle, grayish externally, brownish-yellow within, bitter, and of a strong, disagreeable odor when fresh; that of *A. rotunda* L. is tuberous, roundish, heavy, fleshy, brownish on the exterior, grayish-yellow internally, and similar to the preceding in odor and taste; that of *A. Pistolochia* L. consists of numerous slender yellowish or brownish rootlets, attached to a common head, and possessed of an agreeable aromatic odor, with a taste bitter and somewhat acrid.

Many species of aristolochia, growing in the West Indies and Southern America, have been used medicinally. *A. cymbifera* Martius, known in Brazil as *milhommen, jarra, jarrinha*, and in Mexico as *guaco*, is said to have medicinal properties similar to those of the official species, but Butte affirms that it is depressant to the sensory nerve centers and is useful in *neuralgia* and *pruritus*. In the Argentine Republic the root of *A. argentina* is used as a diuretic and diaphoretic, especially in *rheumatism*. In the East Indies *A. indica* L. is employed for similar purposes with the European and American species, and the Arabians are said by Forskhal to use the leaves of *A. sempervirens* as a counter-poison. *A. fœtida* Kunth, of Mexico, or *Yerba del Indio*, is used as a local stimulant to foul ulcers. A number of species of aristolochia are employed as a remedy for *snake-bites* in various parts of the world, as *A. Serpentaria* L., in North America; *A. maxima* L. (the rhizome of which is called *Guaco* or *Contra Capitano*), in South America; *A. anguicida* L., in the Antilles; *A. brasiliensis* Mart. et Zucc.; *A. cymbifera* Mart. et Zucc.; *A. macroura* Gom.; *A. trilobata* L., etc. There is no sufficient reason for supposing that any one of them is effective.

Armeria. *Armeria vulgaris* Willd. (*Statice Armeria*, L.) *Maiden Pink.* (Fam. *Plumbaginaceæ*).—This plant, found in Europe, Asia, and Western North America, is said to be an active diuretic. (*Ph. Post*, May, 1890.)

Aromatic Wine. *Vinum Aromaticum. Vin aromatique*, Fr. *Aromatischewein*, G.—"Lavender, *one part* [or seventy-two grains]; Origanum, *one part* [or seventy-two grains]; Peppermint, *one part* [or seventy-two grains]; Rosemary, *one part* [or seventy-two grains]; Sage, *one part* [or seventy-two grains]; Wormwood, *one part* [or seventy-two grains]; Stronger White Wine, a *sufficient quantity*, to make *one hundred parts* [or one pint]. Mix the solid ingredients, and reduce them to a coarse (No. 20) powder. Moisten the powder with *four parts* [or six fluidrachms] of Stronger White Wine, pack it moderately in a conical glass percolator, and gradually pour enough Stronger White Wine upon it to make the filtered liquid weigh *one hundred parts* [or measure one pint]." *U. S.*, 1880.

This preparation of the U. S. Pharmacopœia of 1880 is practically identical with the *Vin aromatique* of the French Codex, which is made by macerating one hundred parts of aromatic species (a mixture of equal parts of the herbs used in our official aromatic wine, and in addition wild thyme and hyssop) with one hundred parts of *Teinture vulnéraire* (a tincture containing the same herbs, and ten more of similar properties) and one thousand parts of red wine. This wine is principally used as an astringent and stimulating lotion to *chancres, open buboes*, and other *indolent ulcers*. In many cases it should be diluted, but on occasion it may be employed of full strength. It is never given internally, and is rarely used in this country.

Arrow Poisons.—Up to the seventh century poisoned arrows were used in Europe in warfare, and they seem not to have disappeared from Spain until the sixteenth century, while poisoned daggers and poisoned swords were used even later for assassinations. The nature of the poisons employed is obscure, though it is stated that *Veratrum album*, L., and snake venom were used. The peregrinations of English and American travellers in Africa, and the various political changes and fomentations which have been the fruit of their discoveries—the war with Spain and the consequent bringing of attention to the Philippine Islands—have developed so much general interest in the wild natives of these various remote regions that we have thought it proper to prepare for our readers a general summary of what is known in regard to the poisons used by these various natives for the killing of game and the destruction of their enemies. In doing this we have thought that a geographical arrangement might well suffice. A number of arrow poisons in various parts of the world have been used to a greater or less extent as therapeutic agents, and are considered elsewhere in this work. Among these may be mentioned strophanthus, acocanthera, antiaris, and curare.

So far as our knowledge goes no poisonous arrows have ever been used in North America or in Northern Asia, unless, indeed, the statements made by Kracheninikow be correct. In the second volume of his *Voyage en Sibérie*, French edition, 1768, this traveller states that the roots of the plant known as *Zgate* are employed by several tribes living in the far north of Asia as an arrow poison, and it has been suggested, probably with insufficient reason, that the plant is an anemone. We have met with no recent author who has seen this poison.

The *Upas tieute*, which is used in the East Indies, is said to be obtained from a climbing woody plant growing exclusively in Java, the *Strychnos Tieute* of Leschenault. This author states that a decoction of the bark of the root is concentrated to the consistence of a thin syrup, then mixed with onions, garlic, pepper, etc., and allowed to stand until it becomes clear. The poisonous principles in both *Upas antiar* and *Upas ticute*, according to Pelletier and Caventou, is strychnine combined with igasuric acid. This poison produces death by violent convulsions, the heart stopping before respiration. (Hammond, *Am. J. M. S.*, 1860, p. 363.)

It is very probable that different extracts are employed by different tribes in the islands of the Malay Archipelago. Braidwood (*Ed. M. J.*, 1864) found the arrow poison known as *Dajaksh* to be a cardiac paralyzant. It is not clear whether this is the same as Borneo arrow poison examined by Leubuscher. (*Cb. I. M.*, Bd. xvii, 1896.)

The arrow poisons used by the natives of the Philippine Islands are, according to the researches of P. C. Plugge (*A. J. P.*, 1896, ii), obtained from the *Rabelaisia philippinensis* Planch. Plugge has found in it a non-nitrogenous glucoside, *rabelaisin*. This given in very large doses produced in animals some convulsive movements, followed by profound muscular relaxation, loss of reflexes, and general paralysis, ending in death from asphyxia. On the heart it acted as an energetic stimulant, belonging to the digitalin group. (See also I. Rosenthal, *Sitzungsb. f. Physk. u. Med. Soc.*, Erlangen, 1894.)

An arrow poison is used by the Malays, under the name of *Ipoh;* it is said to be obtained from *Derris* (*Pterocarpus*) *elliptica* (Fam. *Leguminosæ*), or the *tuba root*, which is much used in Java as a fish poison. It contains an active acid resin, to which the name of *derrid* has been given. Derrid appears to be one of the most powerful fish poisons known, as one five-millionth part stupefied gold fish in a few moments, and killed them within half an hour. (*P. J.*, 1890, xxi.) According to the researches of van Hasselt (*A. I. P. T.*, 1911, xxi, p. 242), closely allied, physiologically, to derrid are *pachyrhizid*, from the *Pachyrhizis angulatis*, and *nicoulin*, from the *nekoe* or *stink-wood*. These drugs are powerful poisons to the central nervous system, especially the respiratory center, and in larger doses cause slowing of the pulse by a direct action upon the heart muscle.

The natives of Perak, in the Straits Settlements, use an arrow poison stated to be a combination of aqueous extracts from the root bark of three trees, the individual extracts being known as *ipoh aker, aker lampong*, and *prual*. Ipoh aker and aker lampong are believed to be obtained from undescribed species of Strychnos; extracts were prepared from the root bark of these trees by Ralph Stockman (*Lab. Rep. Roy. Soc. Edinburgh*, vol. vi, 1897), and found to be of similar physiological power, each of them having a digitalis-like action and also a well marked curare-like action, causing arrest of the heart in systole and loss of power in the motor nerve endings. *Prual* is said to be made from the root bark of *Coptosapelta flavescens* Korth., now recognized as *C. macrophylla* (Roxb.) K. Sch. (Fam. *Rubiaceæ*); in the experiments of Stockman it was found to be a violent poison, very

rapidly killing the muscle at the point of inoculation, and soon involving in a fatal influence the whole muscular system, so that the animal after a large dose collapsed almost at once with diastolic cardiac arrest.

The *African arrow poisons* are quite numerous. *Exuja* or *Echugin* is a blackish-brown, crumbly, odorless, and intensely bitter arrow poison, used by the Ovambos of Southwest Africa. It is said to be yielded by an apocynaceous shrub, *Idaneum* (*Adenium*) *Boehmianum*. From it R. Böhm (*Cb. M. W.*, 1889) isolated the crystalline glucoside ($C_5H_8O_2$), *echugin*, and a resinous body, *echugon*. The glucoside crystallizes in small, colorless, satiny, rhombic plates, easily soluble in water and alcohol, and insoluble in ether. It is present to about 10 per cent. in the crude substance, and is said to very closely resemble strophanthin in its physiological properties.

The arrow poison used by the pygmies of Central Africa has been obtained by Surgeon Parke, and is described in the *P. J.*, April, 1891. It has been found to contain two active alkaloids, *erythrophlœine* and *strychnine*.

The Sakayes, the Somangs, and the Wa Kamba tribes in Eastern Africa produce arrow poisons whose relations with one another are still obscure. *Hippo*, according to Laborde, causes in the lower animals vomiting, followed by tetanic convulsions and an almost simultaneous arrest of the respiration and cardiac action. (*P. J.*, July, 1887.) *Vakamba* of Laborde (*Ibid.*) is probably the same as the *ukambin* which has been studied by H. Paschkis, who found its active principle to be a crystalline body belonging to the digitalis group, and causing in the lower animals elevated blood pressure, fibrillary contractions of the muscles, and systolic arrest of the heart. (*Cb. M. W.*, 1862.)

An exceedingly bitter arrow poison, used by the tribes who inhabit the country of Segon in the French Soudan, has been examined by Ferré and Busquet (*A. de P.*, 1895, vii), who find that its active principle is a crystalline glucoside which is a very powerful muscle poison, affecting directly the heart, and producing very rapidly general paralysis, with salivation, exophthalmia, disturbance of respiration and circulation. The first influence is to increase greatly the arterial pressure. The whole action of the poison is very similar to that of strophanthin. For an investigation of South African plants by Juritz, see *P. J.*, 1906, 87.

The Australian natives, according to Lewin, (*A. E. P. P.*, 1912, lxviii, p. 333), derive an arrow poison from the *Buphane disticha* Herb. (*Hœmanthus toxicarius* L.). He found in this an alkaloid to which he gave the name of *hœmanthine*. It somewhat resembled scopolamine in its action, being both a narcotic and mydriatic, and may be the same as that described by Tutin (*Tr. Chem. Soc.*, 1911, xcix) under the name of *buphanine*. Tutin also found several other alkaloids, one of which was identified as *narcissine*.

Animal Poisons.—The use of animal arrow poisons is uncommon, though the Choco Indians, in Colombia, South America, are said to prepare a very deadly extract by holding a tree-frog, the *Hyla choccensis*, on a stick near a fire, and scraping off the subsequent exudate from the skin. As it is asserted that an exudate can be obtained from the skin of the ordinary European toad which is a violent heart poison, the extract employed by the Choco Indians is probably a cardiac paralyzant. Again, according to Livingstone, confirmed by Baines, some of the Bushmen prepare a poison from a cream-colored grub or caterpillar, which they term *'Nga*, said to be the first stage of the beetle *Diamphidia locusta*. The grub is gradually squeezed between the forefinger and thumb, and the colorless exudate smeared over the arrowhead. Boehm and his pupil Starcke have found this poison to be similar in its action to the snake poisons, to be dependent for its activity upon a toxic albumose, and to be non-toxic when given by the mouth. As previously stated, it is also probable that snake venom is sometimes mixed with the various vegetable poisons used by barbarians.

Natives along the Amazon River obtain an arrow poison from the venom of a toad, the *Bufo agua*. This has been examined by Abel and Macht (*J. P. Ex. T.*, 1912, iii, p. 319) who found in it 5 per cent. of epinephrine, and a neutral principle to which they gave the name *bufagin*, and assigned the formula of $C_9H_{12}O_2$. It exercises a powerful digitalis-like effect, the fatal dose for the dog being seven-tenths of a milligramme per kilo.

Arsacetin. *N. N. R.* 1917.—Arsacetin is *Sodium Acetyl Arsanilate*, $C_6H_4(NH.CH_3CO)(AsO.OH.ONa) + 4H_2O$, a compound derived from sodium arsanilate by replacing a hydrogen atom of the amino group in sodium arsanilate, with an acetyl radical. It is a white, crystalline substance, odorless and tasteless, soluble to the extent of 10 per cent. in cold and 30 per cent. in warm water. It is free from arsenous or arsenic acid, and solutions are not affected by boiling. An hour's heating in the autoclave has no action on it. One part of arsacetin in ten of water and a few drops of silver nitrate solution added will produce a pure white precipitate. Its solution, clear and colorless, should show at most a faint acid reaction. Its capability of standing thorough sterilization gives it the advantage over compounds of the same nature—like sodium arsanilate, etc.

It has been used for the treatment of *syphilis*, and although some authors have reported favorably, the trend of opinion seems to be that it is inferior, in curative value, to mercury, and that there is danger of producing optic atrophy as is seen after atoxyl. It has also been used in the treatment of *trypanosomiasis* with more or less success, but is less efficient than atoxyl. Arsacetin has been used mostly in *doses* ranging from one-half up to one and a half grains (0.03–0.1 Gm.), although some authors have employed much larger quantities.

Arsenic Alginate.—This is the combination product of sodium alginate and arsenic chloride. It is a white powder, soluble in alkaline solutions. It is decomposed in the intestinal tract after passing through the stomach unaltered.

Arsenoferratin. *N. N. R.* 1917. (*Sodii arsenoferri albuminas.*)—This is an organic compound of albumen and arsenic with ferratin. A solution of a similar composition is on the market under the name of *arsenferratose*. The latter is a brownish liquid, contains 0.3 per cent. of iron and 0.003 per cent. of arsenic. The solid form of arsenoferratin is marketed in tablets of four grains (0.25 Gm.). They are used in the treatment of *anemias*. Of the solid form 3 to 6 tablets, each containing four grains (0.25 Gm.), may be given in twenty-four hours. Of the liquid arsenferratose the *dose* is one to two teaspoonfuls three times a day.

Arsenogen.—This preparation is a combination of iron, phosphorus and arsenic, with paranu-

cleinic acid. It is a yellowish powder and is used in the treatment of *anemia* and similar disorders.

Arsenophenyl Glycin.—This combination has been employed especially in the treatment of *sleeping sickness.* Zupitza and Raben (*B. K. W.*, 1910) report favorably upon it, but Scherschmidt (*D. M. W.*, 1911) finds it inferior to atoxyl; it appears to be equally dangerous. The *dose* is from eight to fifteen grains (0.5–1 Gm.) daily, for two or three consecutive days, by intramuscular injection.

Arsentriferrin is a tasteless, orange-colored powder furnished in tablets each containing five grains (0.32 Gm.). The *dose* is one tablet given in anemic conditions.

Arsentriferrol. *Elixir Arsen-triferrini.*—This is an elixir of arsentriferrin, containing in each fluidrachm (4 mils), about one grain (0.06 Gm.) or arsentriferrin. It is said to be useful in *anemia.* (See *Merck's Annual Report*, 1913.)

Arsoferrin.—This is said to be an organic combination containing iron, arsenic and glycerophosphoric acid. It is dispensed in the form of tablets and each tablet corresponds to one-third grain of iron oxide and one one-hundred and twelfth grain of arsenous acid. According to Gordon (*Med. Klin.*, 1909), this is a valuable remedy in the treatment of various forms of *anemia* and *debility* in which iron and arsenic would be indicated. The beginning *dose* is one tablet three times a day, which may be gradually increased up to three or four tablets three times a day.

Arsol.—This is a compound consisting of phosphorus and calcium arsenate. It is used as a nerve tonic.

Arsylin. *Arsen-protylin.*—This is an arsenic and phosphorus compound containing these two elements in combination with egg albumen. It is a yellowish-white, odorless powder insoluble in water, with a slightly acid taste. It is administered in *doses* of fifteen grains (1 Gm.) (equivalent to $^1/_{60}$ grain of arsenic).

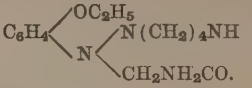
Artabotrys. *Artabotrys odoratissima* (Roxb.), R. Br. (Fam. *Anonaceæ*) and *Anona uncinata* Blanco. *Ilag-ilag de China*, Sp.-Fil. *Alag-ilag Sonson*, Tag.—A decoction of the leaves of these plants is used in the Philippine Islands in the treatment of *cholera;* the overdose is said to be capable of producing abortion.

Artar Root.—This is a drug coming from the west coast of Africa, possibly the product of *Fagara Xanthoxyloides* Lam. (Fam. *Rutaceæ*), the leaves of which have been found in commercial specimens. Two alkaloids have been discovered in it by Giacosa and Nionari, one of which is said to resemble somewhat in its action veratrine, but to be a stimulant to the heart. (*Ph. Centralh.*, 1887, No. xxv.)

Artemisia frigida Willd. *Sierra Salvia. Colorado Mountain Sage.* (Fam. *Compositæ.*)—This Rocky Mountain plant, which is found growing in immense quantities from the Saskatchewan to Western Texas, and westward, is said to be much used in that region as a diaphoretic, antiperiodic, and mild cathartic. F. A. Weiss (*A. J. P.*, 1890) found indications of a glucoside. One or two drachms (3.9 or 7.7 Gm.) of the powdered leaves, or one or two fluidrachms (3.75 or 7.5 mils) of the *fluidextract*, may be administered in hot infusion every half hour until perspiration has set in. The *Artemisia nana*, one of the North American sage brushes, is reported to yield a volatile oil, which is rich in camphor. (*P. J.*, 1910, xxxiv, 237.)

Arterenol.—*Aminoäthanolpyrocatechin* is a reduction product of aminoacetopyrocatechin. Its hydrochloride, $(OH)_2.C_6H_3.CHOH.CH_2.NH_2.HCl$, is crystalline and slightly soluble in water. Its therapeutic uses are analogous to those of epinephrine. It is incompatible with alkalies and with ferric chloride and should be kept away from light.

Arthritiicin.—A synthetic product used in the treatment of *gout* is a combination of diethylenamine and the nitrile of the ethyl kresol of amido acetic acid.



Arum.—The root or corm of *Arum maculatum* L. (Fam. *Araceæ*), is occasionally used as a medicine in Europe. Its properties closely resemble those of *Arisæma triphyllum.* Its constituents, according to Enz, are a neutral acrid volatile principle soluble in ether, starch, gum, mucilage, sugar, lignin, albumen, saponin, fixed oil, resin, and calcium phosphate, the fresh corm containing 58.4 per cent. of water, 5.2 of lignin, and 27.2 of starch. (*A. J. P.*, xxxi.)

Arisæma triphyllum (L.) Schott. *Gouet à trois feuilles*, Fr. *Dreiblättriger Aron*, G. (Fam. *Araceæ.*) *Dragon-root, Pepper Turnip, Indian Turnip, Jack-in-the-pulpit, Wake-robin.*—This plant is common in all parts of the United States, growing in moist shady places. The corm was formerly official. It is roundish, flattened, an inch or two in diameter, covered with a brown, loose, wrinkled epidermis, and internally white, fleshy, and solid. In the recent state it has a peculiar odor, and is violently acrid. It was found by D. S. Jones to contain, besides the acrid principle and from 10 to 17 per cent. of starch, albumen, gum, sugar, extractive, lignin, and salts of potassium and calcium. (*A. J. P.*, xv, 83.) The acridity has been ascribed to the raphides of calcium oxalate by R. A. Weber (*J. Am. C. S.*, 1891, p. 215). This has been denied, Schneegans proving that *A. maculatum* contains saponin and Spica and Biscaro ascribe the acridity to the same principle. (*Ph. Centralh.*, 1895, p. 731.) The Indian turnip may be preserved fresh for a year, if buried in sand.

From both *Arum maculatum*, L., and *Arum italicum*, Mill., Herbert and Heim (*P. J.*, July 31, 1897) separated a saponin, also a brownish, oily, liquid alkaloid closely resembling coniine in its properties, but less active. They also found a saponin in the arum tubers.

Both the European and American arum are, in their fresh state, violent irritants to the mucous membranes, producing when chewed insupportable burning in the mouth and throat. Taken internally, this plant causes violent gastro-enteritis, which may end in death. The fresh, partially dried root has been used internally as a stimulant to the secretions, especially in *asthma, whooping cough, chronic catarrh,* and *rheumatism. Dose,* ten grains (0.65 Gm.), two or three times a day, increased to half a drachm (2 Gm.). The perfectly fresh root should not be used, and the fully dried root is inactive.

The corm of the European arum contains much starch, and a farina is prepared from it, in small quantities, in the Isle of Portland, on the south coast of England, and called *Portland arrow root,* or *Portland sago.* The root of *A. esculentum*, L. (more correctly *Colocasia antiquorum* Schott.), which abounds in starch, is much used by the

natives of the Hawaiian and other islands of the Pacific as an article of food, having been previously deprived of its acridity by heat.

Asarabacca.—*Asarum europæum* L., is an acrid, herbaceous perennial plant, of the Fam. *Aristolochiaceæ*, growing in woods and shady places in Europe, Siberia and the Caucasus. The rhizome is from 2 to 3 inches in thickness, of a grayish color, quadrangular, knotted and twisted, and sometimes furnished with rootlets at each joint. It has an odor similar to that of pepper, and acrid taste, and affords a grayish powder. The leaves, which have long petioles, are kidney-shaped, entire, somewhat hairy, of a shining deep green color when fresh, nearly inodorous, with a taste slightly aromatic, bitter, acrid, and nauseous. According to Feneulle and Lassaigne, the *root* contains a concrete volatile oil (see *Asarum*), a very acrid fixed oil, a yellow substance analogous to *cystin*, starch, albumen, mucilage, citric acid, and saline matters. The root and leaves of asarabacca are powerfully emetic and cathartic, in *doses* of from thirty grains to a drachm (2.0–3.9 Gm.), but are used almost exclusively as an errhine in *headache*, and *rheumatic affections* of the face, mouth, and throat. One or two grains (0.065–0.13 Gm.), snuffed up the nostrils, produce much irritation, and a copious, persistent flow of mucus. For further information concerning this drug, see *U. S. D.*, 19th ed., p. 1400.

Asarum. *N. F. IV. Wild Ginger, Canada Snake-root. Asaret du Canada*, Fr. *Canadische Haselwurzel*, G.—"The dried rhizome and roots of *Asarum canadense* Linné (Fam. *Aristolochiaceæ*), with only an occasional leaf or flower present, and without the presence of more than 5 per cent. of other foreign matter." *N. F.* The plant has in all its parts an aromatic odor and an aromatic, slightly bitter taste, which it imparts to alcohol and hot water. "Of horizontal growth, occasionally branched, two-edged when young, quadrangular when older, finely striate, usually more or less twisted, from 5 to 17 cm. in length and from 2 to 4 mm. in thickness; nodes enlarged with irregular scars from petioles and remains of pedicels; internodes with annular scars from scales; dark purplish-brown externally; fracture short, internally whitish, starchy or resinous; attached roots few, from 5 to 7 cm. in length and not over 1 mm. in thickness, having from four to six radial fibro-vascular bundles. Odor aromatic, non-irritating upon heating; taste pungent and slightly bitter. In transverse section the rhizome shows a thick bark with numerous oil cells, a wood with about twelve fibro-vascular bundles and a large pith. Examined microscopically, the powdered drug shows simple and two- to four-compound starch grains, the individual grains being from 0.004 to 0.02 mm. in diameter, and tracheæ with scalariform or reticulate thickenings, a few spiral. Asarum yields not more than 12 per cent. of ash." *N. F.* The chief constituent is the volatile oil, at one time largely used in perfumery. According to Petersen, the oils of *Asarum Europæum* and *Asarum canadense* are composed in the main of one compound, which is identical with the *methyl ether of eugenol*, $C_6H_3(OCH_3)_2.C_3H_5$, a compound which has been made synthetically but not previously found in nature. Under the trade name *Asaron* a camphor derivative of *Asarum Europæum* is recommended as an antiseptic and tonic. It is given the formula $(CH_3)_3.C_6H_2(CH)_2CH_2CH_3$, and occurs as a whitish-yellow crystalline powder or fragments possessing a faint biting taste. According to the researches of Power and Lees (*Trans. Chem. Soc.*, 1902) the oil of *Asarum canadense* contains the following substances: a phenol, $C_9H_{12}O_2$; pinene, apparently a mixture of the d- and l- forms; d-linalool, l-borneol, l-terpineol, geraniol, eugenol-methyl-ether, a blue oil, of undetermined composition, consisting of oxygenated substances of alcoholic nature; a lactone, $C_{14}H_{20}O_2$, palmitic acid, acetic acid, and a mixture of fatty acids intermediate between acetic and palmitic acids. For formulas for fluidextract, syrup, and oleoresin, see *A. J. P.*, 1876, 155. F. P. Streeper (*A. J. P.*, 1888, 6) proved that strong alcohol was the proper menstruum for the fluidextract. The medicinal properties of this drug are those of a feeble aromatic. From a half to one drachm (2–3.9 Gm.) may be used. It is employed as an aromatic adjuvant to tonic mixtures and infusions. From *Asarum arifolium* Michx., E. R. Miller obtained from 7 to 10 per cent. of volatile oil having a sassafras odor, sp. gr. 1.0585 (*P. J.*, lxix); see also *Schim. Rep.*, 1902, p. 12; also *Proc. Alabama Pharm. Assoc.*, 1910, 56–58.

Asbestos.—This term is applied to several mineral substances which occur in long capillary crystals placed side by side, the whole producing a fibrous mass which possesses qualities that render asbestos very valuable in the arts. Asbestos is incombustible, insoluble, and a poor conductor of heat. It is either *hydrated magnesium silicate*, when it is known as *chrysotile*, or a compound of silicon, lime, and magnesium known as *amphibole* asbestos (for analysis, see *P. J.*, 1901, p. 575), and is found in Italy, in the Tyrol, Corsica, Savoy, in the Pyrenees, in Cornwall, Scotland, and elsewhere in Europe. It is largely mined in Canada, the production in 1915 having been 113,115 tons, valued at $3,491,450. For its general properties and uses, see *Ph. Rec.*, 1885, 232. In the laboratory it is used for filtering purposes, for which it is admirably adapted. It is also used as a non-conductor of heat in connection with various forms of apparatus. (See *A. J. P.*, 1883, 37; *Ph. Rund.*, 1885, 252.)

Asbolin.—Under this name Braconnot has introduced a brownish-yellow syrupy liquid, prepared from an aqueous infusion of lamp black. Béhal and Desvignes state that it consists mainly of pyrocatechin and homopyrocatechin. It has been used in the treatment of *tuberculosis*.

Asclepias. *N. F. IV. Butterfly weed. Pleurisy root.*—This is described in the N. F. as "the dried roots of *Asclepias tuberosa* Linné (Fam. *Asclepiadaceæ*), without the presence of more than 5 per cent. of foreign matter. Usually cut or broken pieces, of variable size, of an irregularly fusiform root, which, when entire is from 10 to 20 cm. in length and from 0.5 to 5 cm. in thickness; occasionally branched; externally pale orange-brown, becoming grayish-brown, annulate above, the surface roughened by numerous fine intersecting grooves; bark thin; fracture tough, the broken surface granular and white, with inconspicuous pale yellow wood bundles and large white medullary rays. Odor slight; taste bitterish and disagreeable, somewhat acrid. The powdered drug is yellowish-brown and, when examined with the microscope, shows numerous simple or two- to four-compound starch grains, the individual grains up to 0.015 mm. in diameter, somewhat spherical in shape, or truncate and often with a sleft at center; calcium oxalate crystals in rosette aggregates up to 0.04 mm. in diameter; strongly lignified thick-walled stone cells up to 0.075 mm.

in diameter and with simple or branching pores; tracheæ with reticulate markings, occasionally bordered pores; spindle-shaped sclerenchyma fibers few, lignified and mostly with simple pores. Asclepias yields not more than 9 per cent. of ash." *N. F.* It grows from Ontario to Minnesota, most abundantly southward and southwestward. It contains a glucosidal principle, *Asclepiadin*, which occurs as an amorphous body, is soluble in ether, alcohol and hot water. It also contains several resins and a trace of volatile oil. Besides the American species *Asclepias tuberosa*, *A. syriaca*, and *A. incarnata*, which were formerly recognized by the U. S. Pharmacopœia, various other species of the genus have been used medicinally.

To the root of the *A. tuberosa* have been ascribed diaphoretic, expectorant, and cathartic properties. In the Southern United States the drug has been given in *pulmonic catarrhs* in *doses* of from twenty grains to a drachm (1.3–3.9 Gm.) in a powder or in the form of a decoction; as a diaphoretic, a teacupful of the decoction (1 in 30) every hour until some effect is produced. For additional information concerning Asclepias species, see *U. S. D.*, 19th ed., p. 1400.

Aseptol. *Sozolic Acid. Orthophenol-sulphonic Acid.* $C_6H_4(OH)SO_3H[1.2]$.—A clear yellow to a yellowish-brown solution with a phenol-like odor. The marketed solution contains 33⅓ per cent. of the acid. It is very soluble in water, alcohol, etc., and is used as a disinfectant after the manner of phenol; claimed to be less toxic than phenol and more antiseptic.

Aseptolin. *Pilocarpinphenol. Pilocarpin carbolate.* $C_{11}H_{16}N_2O_2OH.C_6H_5$.—It is an oily fluid, soluble in both water and alcohol, and is used in a .02 per cent. aqueous solution with 2.75 per cent. solution of phenol added in the treatment of *malaria* and *tuberculosis*. Of this solution 4 mils is injected once daily or in 8 separate *doses* of 0.5 mil each.

Asferryl.—Asferryl is asserted to be a combination of an iron salt and arsenio-tartaric acid. It is a greenish-yellow powder, sparingly soluble in water and acids, readily soluble in dilute alkalies. It contains 18 per cent. of iron and 23 per cent. of arsenic. According to Bachem (*Ther. Rund.*, 1908), asferryl is thirty-five times less toxic than arsenous acid. Fries (*Ther. Geg.*, 1909), found that small doses were well tolerated by the stomach, but that larger quantities gave rise to loss of appetite, gastric pain and even vomiting. He used it with satisfactory results in various types of *anemia*. It is marketed in tablets containing two-thirds of a grain (0.04 Gm.) each. One-half to one tablet may be given two or three times a day.

Asimina. *Asimina triloba* (L.) Dunal. (Fam. *Anonaceæ.*)—J. U. and C. G. Lloyd have found in the common *pawpaw* an alkaloid, *asiminine*, besides a volatile oil. (*A. J. P.*, 1886.) T. M. Fletcher failed to find an alkaloid, but gives the principal constituents as fixed oil, 3.53 per cent.; resin, 343 per cent.; resin insoluble in ether, 9.5 per cent.; glucose and extractive, 8 per cent. (*A. J. P.*, 1891, 476.)

Asparagus. *Asparagus officinalis*, L. *Asperge*, Fr. *Spargel*, G. *Esparaguera*, Sp. (Fam. *Convallariaceæ.*)—This well-known garden vegetable is a native of Europe. It is perennial and herbaceous. The *root*, which is inodorous, and of a weak, sweetish taste, is used in France as a diuretic and aperient in the form of decoction, made in the proportion of one or two ounces of the root to a quart of water. Hayne asserts that, in the dried state, it is wholly inert. In the *berries* H. Reinsch has found a large proportion of glucose and a yellowish-red coloring matter, *spargin*. (*A. J. P.*, xlii, 371.) From the juice of the young shoots Robiquet and Vauquelin obtained a peculiar crystallizable principle, called *asparagin*, $C_4H_8N_2O_3$, which has since been found in a number of plants. (See *Althæa*, p. 120.)

There is at present no sufficient reason for believing that asparagus is of value in practical medicine. The peculiar heavy odor which it imparts to the urine has been the chief foundation for the belief in its diuretic properties; but Nencki (*Provincial Med. Journ.*, March, 1891) appears to have demonstrated that this odor is due to the presence in the urine of *methyl-mercaptan*, a gas which is frequently produced in minute quantities in the intestines by the decomposition of proteids. According to Justin D. Lyle (*N. Y. M. J.*, July, 1892), eating asparagus causes the urine to answer Trommer's, Fehling's, and Böttger's glycosuria tests, although sugar is not present. Tanret found two carbohydrates, *asparagose* and *pseudo-asparagose*, in the roots and green berries of asparagus. (*P. J. Tr.*, 1909, 205.) Certain physiologists have claimed that asparagin has an effect on metabolism, but this view is probably incorrect. (See *Z. B.*, 1892, x.) Asparagus may be administered internally in the form of the syrup produced from the fresh juice or from the tincture. For further information concerning Asparagus, see *U. S. D.*, 19th ed., p. 1401–1402.

Aspirophen. *Phenocoll Acetylsalicylate.*—Under this name has been introduced a mixture of thirty-seven parts of free salicylic acid with sixty-three parts monoacetylphenocoll. It is employed as an analgesic and antirheumatic. Fackelmann (*Th. M.*, July, 1907) asserts that it is less prone to produce cinchonism than other salicylates and is more potent in controlling pain and less likely to produce sweating than aspirin. The *dose* is from eight to fifteen grains (0.5–1 Gm.).

Asplenium. *Asplenium Filix-fœmina* (L.) Bern. *Female Fern.*—The rhizome of the female fern has been supposed to possess similar vermifuge properties to that of the male fern. At present, however, it is not used. The vulgar name of *female fern* is also given to the *Pteris aquilina*, or *common brake*, which is further said by some authors to have the property of destroying the *tape worm*. The leaves of two species of *Asplenium*, *A. Trichomanes*, L., or *common spleenwort*, and *A. Adiantum-nigrum*, L., or *black spleenwort*, are mucilaginous, and have been used as substitutes for *maidenhair* (*Adiantum Capillus-Veneris* L., and *A. pedatum* L.) as pectorals, though destitute of their aromatic flavor.

Aster. *Aster punicеus*, L. (Fam. *Compositæ.*)—The aromatic astringent rootlets of this indigenous plant have been employed as a stimulating diaphoretic in *rheumatic* and *catarrhal affections*.

Asteracantha. *Asteracantha longifolia* Nees. *Ik Kirit.* (Fam. *Acanthaceæ.*)—This Indian plant is said by A. Jayesingba to be an energetic hydragogue diuretic. (*Ph. Z. R.*, Sept., 1887.)

Asterol. *Mercury paraphenolsulphonate with ammonium tartrate.* $C_{12}H_{10}O_8S_2Hg.4(C_4H_4O_6[NH_4]_2) + 8H_2O$.—A micro-crystalline reddish-white powder soluble in warm water. This substance was brought forward as a local disinfectant by Steinmann (*B. K. W.*, 1899, p. 229) with the claims that it is as active as corrosive sublimate

in its antiseptic powers without having local corrosive properties, and also not losing its bactericidal action in albuminous media. Vertun (*B. K. W.*, 1899, No. 20), however, finds that these assertions are not warranted. It has also been employed by intramuscular injection in the treatment of *syphilis*. *Dose*, one-half to three grains (0.03–0.2 Gm.).

Astrolin. *Methyl-ethyl-glycolic antipyrin.* $C_5H_{10}O_3.C_{11}H_{12}ON_2$.—This is a colorless, crystalline powder, with pleasantly acidulous and faintly bitter taste, soluble in water or alcohol. It melts at 64°–65° C. (147.2°–149° F.) and represents 61.5 per cent. of antipyrin, for which drug it is proposed as a substitute: Winzheimer finds it without deleterious influence upon the lower animals. It is suggested for the treatment of *neuralgic headaches* in *doses* of fifteen grains (1 Gm.).

Asurol.—This is asserted to be a double salt of mercuric salicylate and amido-oxy-isobutyric sodium, containing 40.3 per cent. of mercury. It is readily soluble in water. This preparation has been recommended for the hypodermic injection of mercury, especially in the treatment of *syphilis*. According to Neisser (*Th. M.*, 1909, p. 627), however, while it is rapid in its effects, it is not of itself sufficient for the cure of syphilis and should therefore be used in conjunction with some other form of mercurial treatment. The solutions should always be made with boiled distilled water, as the drug is incompatible with both carbonic acid and sodium chloride. It should be freshly prepared because on long standing a turbidity occurs, probably through the action of the carbonic acid of the air. The beginning *dose* is sixteen minims (1 mil) of a 5 per cent. solution, which would represent one-third of a grain (0.02 Gm.) of mercury.

Atherosperma. *Atherosperma moschatum* Labill. *Australian Sassafras.* (Fam. *Monimiaceæ.*)—The bark of this tree, a native of Southern Australia, is said to have been long used by the aborigines, and later by the settlers, in *rheumatism* and in secondary *syphilis*, and has been highly commended by Greeves (*L. L.*, 1862) in acute *bronchitis*. It has been stated that both the bark and the volatile oil are powerful poisons, and Zeyer (*Vierteljahrschr. f. Pract. Pharm.*, x, 504) obtained from the drug an alkaloid, *atherospermine* ($C_{30}H_{20}NO_5$); see also Wittstein's *Organic Constituents of Plants*, 20. The abundant volatile oil is light yellow, and has a pleasant aromatic odor and taste, resembling those of oil of sassafras. Scott obtained from the leaves 1.7 to 2.65 per cent. of volatile oil. (*J. Chem. S.*, 101, 1912, 1612.) Ralph Stockman (*Lab. Rep. Royal Coll. Phys.*, vi, 1897) found it to resemble in its physiological action oil of sassafras and other allied volatile oils. He took repeatedly ten minims (0.6 mil) without any pronounced effect, and one fluidrachm (3.75 mils) given to a rabbit caused only temporary stupor, with slowing of the respiration, but not of the pulse. Three fluidrachms (11.25 mils) caused in the rabbit marked depression of the heart and of the respiration, coma, and death in twelve hours by asphyxia.

Atoxyl. *Sodium Arsanilate. N. N. R.* 1917. $C_6H_4NH_2.(AsO.OH.ONa) + 3H_2O$.—When atoxyl was first introduced into medicine it was supposed to be *metaarsenic anilide* ($C_6H_5NHAsO_2$), but more recent studies have shown it to be sodium arsanilate. It is a white powder soluble in cold water and still more so in warm water. It has a slightly saline taste. On standing the aqueous solution assumes a yellowish tint. It contains 26 per cent. of arsenic.

There is upon the market under the name of *soamin* a substance which appears to be of precisely the same composition as atoxyl, with the exception that it contains five molecules of water instead of three. It therefore contains only 22.8 per cent. of arsenic. The physiological and therapeutic properties of these two substances are the same.

While originally introduced as a means of producing the therapeutic action of arsenic without the toxic disadvantages of that drug, atoxyl owes its notoriety to the results achieved with it by Koch in the treatment of *sleeping sickness* (*D. M. W.*, 1907, p. 200). In this highly fatal disease Koch found that the use of the drug, even in fairly advanced stages, would cause the blood to become free from trypanosomes at least temporarily. Most of the cases, however, eventually relapsed and died of the disease. When the drug was used boldly in the milder cases of the infection, occasionally a permanent cure would result. From the beneficial effects which were produced in *trypanosomiasis*, several clinicians were led to test its efficacy against the biologically allied parasite which is regarded as the causative agent of *syphilis*. While the results in the latter infection were not altogether brilliant, the preparation showed itself to exercise a distinctly toxic action upon the spirochætæ. Blumenthal (*Med. Klin.*, 1907, p. 319) and others have reported more or less favorable results from the internal administration of the drug in *cancers*. It has also been employed against *relapsing fever, malaria, pellagra, leukemia* and *frambesia* with more or less evidence of good effects.

These striking results in some of the most hopeless diseases seemed to foretell for the remedy a most important place among our therapeutic agents. Unfortunately, however, wider experience with the drug showed that it was by no means the innocent remedy which had first been believed. Although the single dose is far less toxic than an equivalent amount of arsenic, when used over long periods of time it produces degenerative changes in various portions of the central nervous system in a large proportion of cases. Igersheimer (*D. M. W.*, 1909, xxv, p. 1142) reports forty-six cases of permanent blindness due to atrophy of the optic nerve following the use of atoxyl. He has also noted in the lower animals histological changes in the brain and in the spinal cord. Schlect (*M. M. W.*, 1909, lvi, p. 971) records fatal results from four injections given on alternate days of 0.6 Gm. each. After death there was found degeneration in the internal organs such as are commonly seen after arsenical poisoning. The number of cases of blindness and even death have been so large that it would seem that the therapeutic use of the drug is scarcely justifiable except in such hopeless infections as the *sleeping sickness*.

It has usually been administered hypodermically in *doses* of from one to three grains (0.06–0.2 Gm.), once every other day.

Atropine Salicylate.—This salt is alleged to have advantages over the sulphate, mainly because of its more rapid and efficient action, provided it be pure and perfectly neutral. It may be prepared by Frederici's process, which is to dissolve 23 parts of atropine in pure alcohol by a gentle heat, and to add enough salicylic acid (about 18 parts) to render the solution neutral, which is determined by the use of litmus paper.

The solution is carefully evaporated, and finally dried in a drying oven. It is deliquescent, and should be kept in securely stoppered vials. The *dose* is the same as that of the sulphate.

Atropine Santoninate, a compound of atropine and santonic acid, is described by Bombelon (*Ph. Ztg.*, April, 1886) as an amorphous non-hygroscopic powder, readily soluble in water, which presents advantages over other atropine salts in being non-irritating, and also in affording a solution which is stable if kept in yellow glass bottles to avoid the formation of photo-santonic acid. One drop of a solution of 0.01 Gm. in 20 mils of water is sufficient to dilate the pupil, the dilatation disappearing in from twelve to twenty-four hours. The powder should be kept in amber-colored vials to protect it from the light.

Atropine Sulphuric Acid.—This organic compound of atropine with sulphuric anhydride occurs in colorless crystals sparingly soluble in water, insoluble in most of the organic solvents, but dissolving readily in ammoniacal solutions. It has been recommended by Phillippstal (*B. K. W.*, 1913) in the treatment of *asthma* and *night sweats.* He claims that it has the advantage over atropine that it does not cause drying of the throat nor tachycardia. The *dose* he employed was one sixty-fourth of a grain (0.001 Gm.).

Azadirachta. *Azedarach, U. S.* 1880. *Pride of India. Pride of China. Ecorce d'Azédarach, Ecorce de Margousier,* Fr. *Zedrachrinde,* G.—The U. S. P. formerly recognized the bark of the root of *Melia Azedarach* L. (Fam. *Meliaceæ*), a beautiful tree, thirty or forty feet high, with a trunk fifteen or twenty inches in diameter. This species of *Melia* is a native of Syria, Persia, and the north of India, and is widely cultivated. It is abundant in our Southern States. North of Virginia it does not flourish. "The bark [root] is in curved pieces or quills of variable size and thickness; outer surface red-brown, with irregular, blackish, longitudinal ridges; inner surface whitish or brownish, longitudinally striate; fracture more or less fibrous; upon transverse section tangentially striate, with yellowish bast fibers; inodorous, sweetish, afterwards bitter and nauseous. If collected from old roots, the bark should be freed from the thick, rust-brown, nearly tasteless, corky layer." *U. S.*, 1880. The bark of the trunk is "externally of a rusty-gray color, internally yellowish, and much foliated; coarsely fibrous; inodorous, bitter and slightly astringent; structure and thickness varying according to age." *Br. Add.* (For a description of the leaves and root bark, see *Ph. Rev.*, 1896, p. 231.)

Oil of Azederach is found of two kinds in Eastern Asia where it is used. One is employed for burning, the other medicinally. The latter oil, according to Lewkowitch (*Oils, Fats, Waxes,* vol. ii, p. 426), is known as *Veepa Oil, Veppam Fat* and *Neem Oil,* and has a specific gravity of 0.914, a saponification value of 196.9, and iodine value of 69.6, a Reichert-Meissel value of 1.1 and a butyro-refractometer reading of 52° at 25° C. (77° F.).

Azadirachta indica Br. Add. *Neem Bark, Margosa Bark.* Under this name was recognized the bark of the stem of *Melia Azadirachta* L., or *Indian Lilac Tree.*—This contains, according to Broughton (*P. J.*, 1873, 992), a bitter amorphous resin, and a crystallizable principle, melting at 175° C. (347° F.). (See also *Ph. Rev.*, 1896, 231.) Cornish (*Ind. Ann. Med. Sci.*, 4, 104) had previously announced the presence of a bitter alkaloid, to which he gave the name *margosine.*

The decoction of azedarach is affirmed to be cathartic and emetic, and in large doses narcotic; but in a number of experiments made by H. C. Wood with extracts from the dried bark and fruit, it was found impossible to poison frogs or rabbits. Robins eating of the sweetish fruit, of which they are very fond, are often rendered so far insensible as to be picked up under the tree; though they usually recover in a few hours. Children are said to eat the fruit without inconvenience, and possibly the robins simply choke themselves with the large berries. The bark is considered, in the Southern States, an efficient anthelmintic. The form of decoction is usually preferred. A quart of water is boiled with four ounces of the fresh bark to a pint, of which the *dose* for a child is a tablespoonful every two or three hours, until it affects the stomach or bowels. Another plan is to give a dose morning and evening for several successive days, and then to administer an active cathartic. The *fresh* bark and the fruit are said to be superior as vermifuges. The Br. Add. recognized an *infusion* (*Infusum Azadirachtæ Indicæ,* Br. Add.), eighty-eight grains in a pint of cold water, *dose,* one-half to one fluidounce (15–30 mils); also a *tincture* (*Tinctura Azadirachtæ Indicæ,* Br. Add.), two ounces in a pint of 45 per cent. alcohol, *dose,* one-half to one fluidrachm (1.8–3.75 mils).

Baccharis. *Baccharis cordifolia* DC. *Mio Mio.*—This composite plant of Southeastern South America is notorious for its deadly effect upon sheep and cattle. Pedro N. Arata has isolated from it an alkaloid *baccharine.* (*P. J.*, x, 6.)

Bacillol is a kresol soap mixture similar to the compound solution of cresol. (See page 631.)

Bactoform.—This preparation consists of a neutral soap solution of formaldehyde and coal tar derivatives. It is used for rendering antiseptic the instruments and apparatus used in surgical operations. A 1 or 2 per cent. solution in water is used for this purpose. Under the name *bello-form* another preparation, identical with Bacto-form, is sometimes employed.

Balanites. *Agialida. Balanites Roxburghii* Planch. (Fam. *Zygophyllaceæ.*)—The fruit of this plant is used medicinally in India. It contains a principle closely resembling saponin. The ripe seed yield about 50 per cent. of a fixed oil (*zachun oil*), which is used for burning. (See *P. J.*, 1913, 905.) The unripe fruit is anthelmintic and purgative.

Balata. *Gum Chicle. Chicle. Tuno Gum. Leche de Popa,* Fr. *Zapota Gum.*—This is the dried milky juice of the *Bully Tree, Mimusops Balata* Gärtn. (*Sapota Muelleri* Linden) of the Fam. *Sapotaceæ,* a native of Northern South America from Mexico to Guiana. It is an oxidized hydrocarbon, both physically and chemically closely related to caoutchouc and gutta-percha, of a grayish-white color, with dark spots and veins; specific gravity 1.05; tasteless, but emitting an agreeable odor when warmed. It has the general properties of gutta-percha, differing, however, in being but slightly extensible, a property which specially fits it for the manufacture of transmission belts. Solid and somewhat crumbling at ordinary temperature, it softens at 49° C. (120.2° F.), and can be molded like gutta-percha. The chemical constituents of chicle have been investigated by Tschirch and Schereschewski who found so-called resins, two of them being crystallizable *a-balaban* and *b-balaban* and a yellow substance, *balafluavil.* (*A. Pharm.*, 243, No. 5, 1905, 358; see also Bosz and Cohen's investigations, *A. Pharm.*,

250, 1912, No. 1, 52; also *P. J. Tr.*, 1910, 609.) It is used as a substitute for gutta-percha, but more especially in the manufacture of chewing gum, for which purpose it is imported in large amounts from Mexico. It is sometimes adulterated with paraffin wax. It is not used in medicine.

Balm of Gilead. *Balsam of Gilead. Mecca Balsam. Balsamum Meccæ v. Judiacum. Balsamum Gileadense. Baume de la Mecque,* Fr.—The genuine balm of Gilead is the resinous juice of *Commiphora Opobalsamum* (L.) Engl. (Fam. *Burseraceæ*), a small evergreen tree, growing on the Asiatic and African shores of the Red Sea. It was in high repute with the ancients, and is still esteemed by the Eastern nations as a medicine and cosmetic. In Western Europe and in this country it is seldom found in a state of purity, and its use has been entirely abandoned. It is described as a turbid, whitish, thick, gray, odorous liquid, becoming solid by exposure. It possesses no medicinal properties not existing in other balsamic or terebinthinate juices. It was formerly known as *opobalsamum*, while the dried twigs of the tree were called *xylobalsamum*, and the dried fruit, *carpobalsamum*. In this country *Poplar buds* are often, incorrectly, called Balm of Gilead Buds.

Balsam of Cativo. *Cativo Balsam.*—This substance appeared in the London market in 1902 as a substitute for copaiba. It is a balsamic resin, opaque, of a dirty light brown color and slightly bitter taste, and having an extremely adhesive quality. According to Umney, it is not soluble in 90 per cent. alcohol, but is soluble in ether and consists chiefly of acid resins with the addition of an oily substance. According to Weigel's analysis it consists of 80 per cent. of resin acids and 2 per cent. of volatile oil. It is supposed to be a product of *Prioria copaifera* Gris. (Fam. *Leguminosæ*), a large tree indigenous to Panama and Jamaica. (See *P. J.*, vol. lxix; and *Ph. Centralh.*, March, 1903.)

Balsam of Cebur or Tagulaway.—*Cebur* or *Tagulaway Balsam* is prepared in the Philippine Islands by boiling the root and twigs of *Parameria vulneraria* Radl. (Fam. *Apocynaceæ*), in cocoanut oil, so as to form a yellowish-white, oily liquid, which is used with asserted excellent results for *skin diseases* and *wounds*. (*A. Pharm.*, Nov., 1885.)

Balsam of Lagam. *Lagam Balsam.*—A thick, yellowish, fluorescent liquid, of a peculiar aromatic odor, and bitterish, acrid taste, resembling copaiba. (*A. J. P.*, 1883, p. 368.)

Balsam of Riga. *Riga Balsam. Balsamum Carpaticum. Balsamum Libam.*—This is the product of *Pinus Cembra*, L. (Fam. *Pinaceæ*), a large tree growing in the mountainous regions and northern latitudes of Europe and Siberia. The juice exudes from the extremities of the young twigs, and is collected in flasks suspended from them. It is a thin, white fluid, having an odor analogous to that of the juniper, and possessing the ordinary terebinthinate properties. In this country it is very rare; but it is occasionally brought from Riga or Kronstadt in bottles. Keller, of Darmstadt, affirms that Riga Balsam is the product of the ordinary *Pinus palustris* Mill. A similar product, called *Hungarian balsam*, is obtained in the same manner from *Pinus Pumilio* Haenke, growing on the mountains of Switzerland, Austria and Hungary.

Balsam of St. Thome. *Pan Oleo. Belam Pu.* A balsam obtained from *Santiriopsis balsamifera* (Oliv.) Engl. (Fam. *Burseraceæ*). It is a resinous juice obtained by incisions in the trunk of the tree. It is used as a vulnerary and in diseases of the bladder and bronchi. (*Ap. Ztg.*, 1898.)

Balsam of Sulphur. *Oil of Linseed Sulphurated, Thiolinic Acid. Oleum lini sulfuratum. Oleum Sulphuratum.*—The old Edinburgh Pharmacopœia directed to boil *eight parts* of olive oil and *one part* of sublimed sulphur together, over a gentle fire, in a large iron pot, stirring them constantly until they united. As the vapors which rose were apt to take fire, a lid was to be at hand to cover the pot, and thus extinguish the flame if necessary. In this way the oil was partly decomposed, and the resulting preparation was an extremely fetid, acrid, viscid, reddish-brown fluid, which was formerly used in *pectoral complaints;* but inconvenience arose from its acrid properties, and its internal use was abandoned. It is sometimes applied as a stimulant to *foul ulcers. Haarlem Oil* is a mixture of oil of turpentine with balsam of sulphur. The *dose* is from five to thirty minims (0.3–1.8 mils).

Balsam Wood. *Palo Balsamo.*—This is a South American wood, derived from an unknown tree, which is believed to contain *guaiacin*, and which yields to distillation nearly six parts of a thick viscous aromatic oil. This contains as its chief constituent a crystalline solid of alcoholic character, melting at 91° C. (195.8° F.) and corresponding closely to the formula $C_{14}H_{24}O$. It has found employment in perfumery. (*Schim. Rep.*, April and Oct., 1892.)

Balsamorhiza. *Balsamorhiza terebinthinacea* Nutt. (Fam. *Compositæ.*)—The root of this plant, obtained from Idaho and Oregon, has a strong, terebinthinate odor, and is used medicinally in the Western States. It contains volatile oil, fixed oil, resin, organic acid, and sugar (Herman T. Kelly, *D. C.*, 1897, 32).

Baptisia. *N. F. IV. Wild Indigo. Indigo sauvage,* Fr. *Baptisie,* G.—"The dried roots of *Baptisia tinctoria* (Linné) R. Brown (Fam. *Leguminosæ*), without the presence of more than 10 per cent. of the crown and stem or other foreign matter." *N. F.* This is an indigenous perennial plant, abundant throughout the Eastern United States, in woods and dry barren uplands. The roots are "fleshy, from 0.5 to 4 cm. in thickness, usually cut into elongated cylindrical pieces; the crown from 5 to 8 cm. in thickness, more or less warty and marked by stem scars; outer surface dark-brown; usually longitudinally wrinkled, transversely warty, or the thicker pieces covered with a soft and friable corky layer, bearing few branching rootlets; fracture tough, the fractured surface whitish; bark section radially striate, wood-section inconspicuously radiate, porous. Nearly odorless; the bark bitter and acrid, the wood nearly tasteless. The powdered drug is light-grayish and, when examined with the microscope, shows numerous, rounded, simple, or two- to four-compound starch grains up to 0.016 mm. in diameter, the larger grains sometimes with a cleft through the center; tracheæ with bordered pores up to 0.085 mm. in diameter; numerous sclerenchyma cells, long, thick-walled, non-porous, more or less lignified and up to 0.024 mm. in width; fragments of medullary-ray tissue composed of cells with lignified walls and numerous simple pores; groups of parenchyma, many of the cells filled with starch; few epidermal and cork cells with brownish walls. Baptisia yields not more than 5 per cent. of ash." *N. F.* It contains a glucoside, *baptisin*, an alkaloid, *bapti-*

toxine, and a coloring principle which has been used as a substitute for indigo, but which is greatly inferior. It is not often used in medicine. For further information concerning this drug, see *U. S. D.*, 19th ed., p. 1406 and *A. Pharm.*, 245, 1907, No. 8, 561–572.

Barbados Nuts. *Purging Nuts. Physic Nuts. Semen Ricini Majoris. Pignon d'Inde (des Barbades), Semences du Médicinier*, Fr. *Purgirnuss, Schwarze Brechnuss*, G.—These are the seeds of *Jatropha Curcas*, L. (Fam. *Euphorbiaceæ*), growing in Brazil, the West Indies, and cultivated extensively in all tropical countries. The fruit is a three-locular capsule, containing one seed in each locule, and is about the size of a walnut. The seeds are blackish, oval, 1.5 to 2 cm. long, flat on one side, convex on the other, and the two sides present a slight longitudinal prominence. They yield a fixed oil, an acrid resin, sugar, gum, a fatty acid, glutin, a free acid, and salts. A. Siegel (*Bot. Centralb.*, xlvii, 120) found in the seeds a poisonous principle, *curcin*, which he states is analogous to *ricin*, and places in the class of toxalbumins. The oil, sometimes called *jatropha oil*, may be separated by hot expression, the yield being about 40 per cent. When fresh it is without odor or color, but becomes yellowish and slightly odorous by time. Alcohol does not readily dissolve it. It is colorless, odorless, of sp. gr. 0.91 at 19° C. (66.2° F.), solidifies to buttery consistence at −8° C. (17.6° F.). Bouis believed it to be the glyceride of a peculiar acid, *isocetic acid*, but it is now considered to be a mixture of palmitin and myristin. From three to five of the *seeds*, slightly roasted and deprived of their envelopes, operate actively as a cathartic, and not infrequently produce nausea and vomiting, with a sense of burning in the stomach. The *oil* purges in the *dose* of five to ten minims (0.3–0.6 mil), and is analogous in its action to croton oil, though less powerful. The cake left after the expression of the oil is an acrid emeto-cathartic, operating in the *dose* of a few grains. Either of these substances may produce serious consequences in overdoses. The leaves of the plants are rubefacient, and the juice is said to have been usefully employed as a local remedy in *piles*. (*A. J. P.*, 1893, 335.) The seeds of *Curcas multifidus* (L.) Endl. (*Jatropha multifida* Linn.) have similar properties, and yield a similar oil. This species also grows in Brazil and the West Indies. (See Peckoldt, *A. Pharm.*, 1887, 415.)

Jatropha gossypifolia Linn., of South America, is used as a local application in *leprosy* and to indolent *ulcers*, and probably has similar physiological influence to curcas. *Jatropha urens*, L., must be excessively poisonous, as accidental contact of the wrist of a gardener in Kew with a young plant produced such symptoms that for five minutes the man was thought to be dead. (*P. J.*, April, 1872, 863.)

The roots of the *Jatropha cardiophylla* Muell. Arg. are largely employed in Southern Arizona and Mexico for tanning purposes. According to the analysis of Josiah C. Peacock, they contain, when thoroughly dried, over 5 per cent. of tannic acid. (*A. J. P.*, 1900, 432.)

Barium. *Baryum*, Fr., G. Ba = 137.37.—This is the metal present in *baryta*. It was first obtained in 1808 by Sir H. Davy, who described it as a difficultly fusible metal, of a silvery-gray color, decomposing water readily, and considerably heavier than sulphuric acid. When exposed to the air, it instantly becomes covered with a crust of barium oxide. Barium chloride, barium dioxide, and barium carbonate were formerly official.

Barium Carbonate. $BaCO_3 = 197.37$.—It is the native carbonate, a rare mineral, discovered in 1783 by Withering, in honor of whom it is called *witherite*. It is found in Sweden and Scotland, but most abundantly in the lead mines of Northern England. It occurs usually in grayish, or pale yellowish-gray, fibrous masses, but sometimes crystallized. Its sp. gr. varies from 4.2 to 4.4. It is generally translucent, but sometimes opaque. It effervesces with acids, and, before the blow-pipe, melts into a white enamel without losing its carbon dioxide. It is distinguished from strontium carbonate, with which it is most liable to be confounded, by its greater specific gravity, and by its yielding a light greenish and not a reddish flame upon the burning of alcohol impregnated with its solution in hydrochloric acid. The presence of strontium is indicated by a reddish flame.

When pure, barium carbonate is entirely soluble in hydrochloric acid. Any barium sulphate present is left undissolved. If neither ammonia nor hydrogen sulphide produces discoloration or a precipitate in the hydrochloric acid solution, the absence of aluminum, iron, copper and lead is shown. Lime may be detected by adding an excess of sulphuric acid, which will throw down the baryta as a sulphate, and afterwards testing the clear liquid with sodium carbonate, which, if lime be present, will produce a precipitate of calcium carbonate. Barium carbonate acts as a poison on the animal economy. Its only pharmaceutical use is to prepare barium chloride.

Barium Chloride. *Barii Chloridum. U. S.* 1870. *Chlorure de Baryum*, Fr. *Chlorbarium, Chlorbaryum*, G. $BaCl_2.2H_2O$.—For the method of preparing this salt, see *U. S. D.*, 19th ed., p. 1407 (see also *Reagents*, Part III).

Barium chloride is a permanent white salt, possessing a bitter and disagreeable taste. It crystallizes in rhombic tables with bevelled edges. It dissolves in about two and a half times its weight of cold water, and in a little more than its own weight at 106° C. (222.8° F.), the boiling point of a saturated solution. It is scarcely soluble in absolute alcohol, but dissolves in rectified spirit. Alcohol impregnated with it burns with a greenish flame. When exposed to heat, it decrepitates and loses its water of crystallization, and at a red heat fuses. It is decomposed by the sulphates, oxalates and tartrates, and the alkaline phosphates, borates, and carbonates; also by silver nitrate, *mercurous* salts, and lead acetate. When pure it does not deliquesce. Its solution is not affected by ammonia, which proves the absence of aluminum and ferric oxide, or by hydrogen sulphide, which shows that neither copper nor lead is present. Tannic acid will precipitate the barium from a solution of its chloride, as tannate.

After the whole of the barium has been precipitated by an excess of sulphuric acid, the supernatant liquid is shown to be free from lime by the non-action of sodium carbonate. If strontium be present, an alcoholic solution of the salt will burn with a red flame.

Barium chloride is actively poisonous, causing when given in sufficient doses convulsions, dilatation of the pupil, and death from respiratory failure. According to Laborde (*B. A. M.*, July, 1891), after death the blood remains of a bright red color. In smaller doses it exercises a stimulant

effect upon various muscular tissues. Through its action upon the intestinal muscle it gives rise first to diarrhea and later to cramp-like spasm of both gastric and intestinal muscle. Upon the voluntary muscle it exercises an effect like that of veratrine, causing marked prolongation of the contraction; after death from barium poisoning, fibrillary contractions of the voluntary muscles may continue for a considerable period of time. It stimulates both the vascular and cardiac muscles and in sufficient dose throws the heart into permanent contraction like that produced by digitalis. In moderate dose the pulse rate is increased and the blood pressure greatly elevated. Because of its action upon the circulation it has been suggested as a cardiac stimulant in cases of *heart failure*. According to Lauder Brunton (*Practitioner*, June, 1889), the chloride is a rapidly acting heart stimulant steadying the rhythm and increasing the volume and force of the cardiac contractions. Filippi (*Lo Sperimentali*, 1907), however, asserts that the drug has such a profound influence upon metabolism that it is not suitable for medicinal purposes. It has also been used in veterinary medicine in the treatment of wind colic. A solution of barium chloride was formerly official (*Liquor Barii Chloridi, U. S.*, 1870) which contained 1 troy ounce of barium chloride in three fluidounces of water. The dose of this solution is three minims (0.2 mil). The *dose* of barium chloride is one-half to one and a half grains (0.03–0.1 Gm.).

Barium Dioxide. *Barii Dioxidum. U. S.* 1890. *Barium Peroxide.* $BaO_2 = 169.37$.—"Commercial, anhydrous barium dioxide. It should be kept in well-closed vessels." *U. S.*, 1890.

It is used chiefly for making hydrogen dioxide. Barium forms two oxides, BaO and BaO_2; the former is produced by the action of oxygen or dry air on barium. Barium dioxide, BaO_2, is made by heating barium oxide to about 450° C. (842° F.), when it takes up another atom of oxygen. It is "a heavy, grayish-white, or pale yellowish-white, amorphous, coarse powder, odorless and tasteless. When exposed to the air, it slowly attracts moisture and carbon dioxide, and is gradually decomposed. It is almost insoluble in cold water, with which, however, it forms a definite hydrate, and to which it imparts a decidedly alkaline reaction. Hydrochloric, phosphoric, and most other mineral acids decompose it, producing the corresponding barium salts, and hydrogen dioxide, which remains in solution for a considerable time, if the reaction has taken place in the cold, and an excess of the acid is present. When heated to a bright red heat, barium dioxide fuses, loses oxygen, and is reduced to barium oxide. Barium dioxide should be dissolved by diluted hydrochloric or phosphoric acid without leaving more than a trace of residue. It should contain at least 80 per cent. BaO_2. It is not used medicinally.

Barium Iodide. *Barii Iodidum. Iodure de Baryum*, Fr. *Jodbarium*, G. BaI_2.—This compound may be formed by double decomposition, by adding native barium carbonate in powder to a boiling solution of ferrous iodide. M. Henry, Jr., obtained it by decomposing a solution of barium sulphide by a concentrated alcoholic solution of iodine. Sulphur is precipitated, which is separated by filtration, and barium iodide formed in solution, from which it is obtained in the solid state by rapid evaporation to dryness. Barium iodide crystallizes in small, colorless needles, which deliquesce slightly, and are very soluble in water. The solution promptly undergoes decomposition on exposure to the air, barium carbonate being precipitated, and iodine set free, which colors the solution. It has been used by John and Lugol, as an alterative, in *scrofulous affections* and morbid growths. The *dose* is an eighth of a grain (0.008 Gm.) three times a day, gradually increased to three grains (0.2 Gm.).

Barium Oxide or *baryta* ($BaO = 153.37$) may be obtained from the native carbonate by intense ignition with carbonaceous matter, or from the native sulphate by ignition with charcoal, which converts it into barium sulphide, subsequent solution of the sulphide in nitric acid and strong ignition of the nitrate formed, to dissipate the acid. As thus obtained, it is an anhydrous solid, caustic, alkaline, difficultly fusible, and of a grayish-white color. Recently it has been obtained at Niagara Falls by a reaction in which, at the temperature of the electric arc, a small amount of the sulphide obtained by the reducing action of charcoal is made to react with an excess of unchanged sulphate,

$$3BaSO_4 + BaS = 4BaO + 4SO_2$$

Its sp. gr. is about 4. It acts on the animal economy as a poison. When sprinkled with water it slakes like lime, becomes hot, and is reduced to the state of a white pulverulent hydroxide. The same hydroxide is formed in mass when the anhydrous earth is made into a paste with water and exposed to a red heat in a platinum crucible. The excess of water is expelled, and the hydroxide undergoing fusion, may be poured out and allowed to congeal. Barium hydroxide dissolves in water, and forms the reagent called *baryta water*. A boiling saturated solution, as it cools, yields crystals of barium hydroxide containing eight molecules of water of crystallization.

Baryta consists of one atom of barium and one of oxygen. Its chemical formula, is, therefore, BaO. When barium oxide is heated in a current of oxygen or air, it takes up an atom of oxygen and is changed into barium dioxide, BaO_2. When this is heated somewhat higher, it gives off the extra atom of oxygen and becomes BaO again. This power of taking up oxygen from the air and giving it up at a somewhat higher heat is now utilized on a commercial scale in the Brin process for making oxygen, and it is found that this change from BaO to BaO_2 and back again can be effected at one and the same temperature by simply heating first under pressure and then by exhausting and reducing below the normal atmospheric pressure. Barium dioxide is also of growing importance as the material from which hydrogen dioxide, H_2O_2, is made.

Barium Sulphate. *Barii Sulphas.* $BaSO_4$. *Blancfixé. Permanent White.*—Barium sulphate is a heavy, lamellar, brittle mineral, varying in sp. gr. from 4.4 to 4.6. It is generally translucent, but sometimes transparent or opaque, and its usual color is white or pinkish. When crystallized, it is usually in very flat, rhombic prisms. Before the blowpipe it strongly decrepitates, and melts into a white enamel, which, in the course of ten or twelve hours, falls to powder. It is thus partially converted into barium sulphide, and, if applied to the tongue, will give a taste like that of putrid eggs, from the formation of hydrogen sulphide. Barium sulphate, on account of its great insolubility, is not poisonous. It is, however, soluble in a great excess of diluted hydrochloric acid. Ground to fine powder it is often mixed with white lead,

but impairs the quality of that pigment for some purposes; used alone as a pigment it possesses certain advantages over lead compounds. The artificial barium sulphate obtained as a by-product in many chemical manufactures, under the name of *permanent white, terra alba,* or *blanc fixé,* is much used in the arts as a water-color. It is made from both the native sulphate and carbonate. It forms a dazzling white color, unalterable by light, heat, air, or hydrogen sulphide. Barium sulphate is being used to coat the intestines for the purpose of making X-ray pictures (see Gunther, *D. M. W.*, 1911), replacing the more expensive bismuth subcarbonate and stated to be even more efficient.

Barium Sulphide. *Barium Sulphidum.*—An impure form of barium sulphide is found in commerce, containing about 50 per cent. BaS_2. It is used extensively in combination with starch, powdered orris root and other diluents in depilatory mixtures. As it is sometimes abbreviated "Bar. Sulph.," the same as is applied to Barium Sulphate used in X-ray work (which see), care must be taken in dispensing it, as it has on several occasions caused death when taken internally by mistake for barium sulphate.

Barringtonia. *Barringtonia speciosa.*—The large Indo-Malayan tree, *Barringtonia speciosa* Forst. (Fam. *Myrtaceæ*) contains, according to Maresuw, 3.3 per cent. of *barringtonin,* a colorless, amorphous glucoside, having the formula $C_{18}H_{28}O_{10}$, and belonging to the saponin group. It is said to be an active cardiac poison. (*S. W. P.*, xli, 1903, pp. 423, 435.)

Basicin. *Corticin.*—This preparation is a compound of quinine hydrochloride and caffeine. The two substances are dissolved in water. The solution is then heated to a high concentration and allowed to crystallize. It is employed intravenously for *malaria,* internally for *migraine, neuralgia, influenza* and similar ailments. The *dose* is three to eight grains (0.2–0.5 Gm.).

Bassia longfolia L. (Fam. *Sapotaceæ.*)—In this Indian plant, known as *mowrah* by the natives, there has been found a glucoside which was named *mowrin* by its discoverers, Moore, Baker, Young and Sawton. According to these investigators, mowrin has a digitalis-like action upon the heart and a saponin-like effect of destroying red blood cells.

Bassora Galls are cultivated in Persia and Asia Minor, and are exported by way of Smyrna for tanning purposes. They come into commerce ground and pressed into the form of bricks. They contain, on an average, 27 per cent. of tannin.

Bassora Gum. *Caramania Gum. Hog Gum. India Gum. False Tragacanth. Kutera Gum.*—This substance came into commerce originally from the neighborhood of Bassora, on the Gulf of Persia; but is often found mixed with gum brought from other countries, and is said to be the product of the almond and plum trees. It is in irregular pieces, about the same size as tragacanth, brown or yellow, intermediate in the degree of its transparency between gum arabic and tragacanth, inodorous, tasteless, and possessed of the property of yielding a slight sound when broken under the teeth. Only a small portion of it is soluble in water, whether hot or cold. The remainder swells up considerably, though less than tragacanth, and does not, like that substance, form a gelatinous mass, as it consists of independent granules which have little cohesion. The soluble portion is pure gum or *arabin,* and, according to Guérin, constitutes 11.2 per cent. The insoluble portion consists of *bassorin,* associated with a small proportion of saline substances, which yield, when the gum is burnt, 5.6 per cent. of ash. The gum is employed to adulterate tragacanth, and for this purpose is sometimes whitened by means of white lead, which can readily be detected, however. It is frequently used as a filler and thickener in the manufacture of certain food products, as cheap ice creams.

Batiator Root.—The root of the *Vernonia nigritiana* Oliver and Hiern. (Fam. *Compositæ*), a widely distributed plant of West Africa, is said to be largely used in Senegal as a febrifuge, emetic, and anti-dysenteric, resembling ipecac somewhat in its therapeutic application. The plant is a composite which climbs to the height of a foot and a half, and yields a root composed of numerous fibers from twenty to thirty centimeters long, slender and grayish-yellow externally, a number of which are united to form an irregular knotty rhizome, unequally spherical at the neck or crown, and covered at this point with silky hairs. The active constituent is a glucoside, *vernonin,* $C_{10}H_{24}O_7$. (Heckel and Schlagdenhauffen, *A. de P.*, Aug., 1888; see also *Zeit. An. Chem.*, 1893, p. 364.) This is a hygroscopic whitish powder, forming a pale yellow solution with water, and only slightly soluble in ether and in chloroform. By the absorption of 2 molecules of water it is split into a resinous body and glucose. Physiological experiments made upon frogs show vernonin to be a cardiac poison of the digitalis group; it is also said to act as a paralyzant to the motor nerve trunks. (*P. J.*, June 30, 1888.)

Baume Tranquille. *Balsamum Tranquillans. Huile de Jusquiame Composee. Oleum Hyoscyami Compositum.*—This preparation of the French Codex consists essentially of a fixed oil holding in solution the active matters of certain narcotic and aromatic plants. According to the Codex the fresh narcotic plants, belladonna, henbane, black nightshade, poppy and stramonium, are boiled with poppy seed in a copper kettle until all their water is driven off, and a gentle heat maintained until the oil acquires a fine green color; the oil is then expressed and the essential oils of lavender, peppermint, rosemary and thyme are added. The preparation is used externally by friction as an anodyne in local pains, but especially to relieve *earache,* a few drops being placed in the ear on a pledget of cotton. The National Formulary preparation is approximately the same as the above, although a little less complex. It is known as *Oleum Hyoscyami Compositum* and consists of a solution of oils of lavender, rosemary and thyme in infused oil of hyoscyamus. (See Part III.)

Baycuru Root.—This is the root of a Brazilian plant, probably the *Statice brasiliensis* Boiss. (Fam. *Plumbaginaceæ*), which is used by the natives as a discutient in glandular swellings and as an astringent gargle. F. A. Dalpe (*A. J. P.*, xiv, 361) believed that he has found in it an alkaloid, *baycurine,* besides volatile oil, gum glucose, etc. C. Symes found in it 12.5 per cent. of tannic acid. (*Newer Mat. Med.*, 51.)

Bdellium.—Under this name have been included various gum resins having little or nothing in common. The commercial Bdelliums are naturally divided into the Indian and the African, but E. M. Holmes, in an elaborate study (*P. J.*, lxi), recognizes five commercial varieties of African Bdellium—namely, 1. Perfumed Bdellium, which is be-

lieved to be collected in Northeastern Africa; 2. African Bdellium; 3. Opaque Bdellium; 4. Hotai Bdellium from the Somaliland, and 5. A non-aromatic acrid gum resin. *Perfumed Bdellium*, or *Habaghadi*, closely resembles in appearance *Somali myrrh*, but has a less bitter, more acrid and peculiar taste which distinguishes it at once from myrrh. *African Bdellium*, proper, occurs in hard, roundish pieces, of a pale to dark grayish-brown color with a resinous unstreaked fracture, dotted with glistening points. The odor is said to recall that of cedar wood; the taste is slightly acrid but not bitter. *Opaque Bdellium* is of a pale brown color and has a bitter, slightly acrid taste and cedar-like odor; it occurs in tough, roundish pieces about an inch to an inch and a half in diameter. *Hotai Resin* resembles opaque bdellium, but is distinguished by its lack of odor, its slightly soapy taste, and its brittleness. These four bdelliums of Holmes are for the most part collected in Somaliland. They are the product of different species of *Commiphora*, small trees or large shrubs which suggest in appearance the English hawthorn. The species are by Holmes divided into four groups. (See *P. J.*, lxxii.) According to A. Engler, the resin of *Commiphora roxburghiana* (Stocks) Engl. is the commercial *Gugul*, or *India Bdellium*, which is employed in the East Indies as a remedy for *leprosy*, *rheumatism*, and *syphilis*. Bdellium sometimes comes mixed with gum arabic and gum senegal. It is either in small roundish pieces, of a reddish color, semi-transparent, and brittle, with a wax-like fracture, or in large irreguliar lumps, of a dark brownish-red color, less transparent, somewhat tenacious, and adhering to the teeth when chewed. It has an odor and taste like that of myrrh, but weaker. It is infusible and inflammable, diffusing while it burns a balsamic odor. According to Pelletier, it consists of 59 per cent. of resin, 9.2 of gum, 30.6 of bassorin, and 1.2 of volatile oil, including loss. In medicinal properties it is analogous to myrrh, and was formerly used for the same purposes. In Europe it is still occasionally employed in plasters. The *dose* is from ten to forty grains (0.65–2.6 Gm.).

Bebeeru Bark.—*Nectandræ Cortex*, Br. 1885, is the dried bark of *Nectandra Rodiæi* Hook. (Fam. *Lauraceæ*). The *bebeeru*, *bibiru* or *sipiri*, as it has been variously named, is a tree sixty feet or more in height, growing in British Guiana and the neighboring regions of South America, and yielding the wood known as *greenheart*.

The bark occurs in large, flat, heavy pieces, from 30 to 60 cm. long, from 10 to 15 cm. broad, and about 6 mm. thick, with a short, granular fracture, of a grayish-brown color on its outer surface and a dark cinnamon color on the inner. It has an intensely bitter, somewhat astringent taste. On microscopical examination it is seen to be composed chiefly of very thick-walled parenchymatous cells. The inner bark contains peculiar short, sharp-pointed, undulate bast fibers. Within the cells dark brown masses (colored greenish-black by ferrous sulphate) may be seen. Analyzed by Maclagan, of Edinburgh, it was found to contain tannic acid of the kind that precipitates the salts of iron green, resin, gum, sugar, albumen, fibrin, various salts, and two peculiar alkaloids, named respectively *bebeerine*, $C_{19}H_{21}O_3N$, and *sipirine*, the former soluble and the latter insoluble in ether. In the seeds, besides the foregoing principles, Maclagan found 53 per cent. of starch, and a peculiar white, crystalline, volatile acid, which he named *bebeeric acid*. The alkaloids are extracted together from the bark, in the form of impure sulphate, by a process similar to that for preparing quinine sulphate. This preparation was formerly known as the *commercial bebeerine sulphate*. The sulphate, hydrochloride and alkaloid are all used in medicine, the *dose* of either being from one to two grains (0.065–0.13 Gm.). According to Flückiger (*P. J.*, xi, 193, 1869), pure bebeerine is a white, amorphous powder, whose concentrated aqueous solution is not precipitated by tartar emetic, but affords abundant white precipitates with sodium phosphate, potassium nitrate, iodide, or iodohydrargyrate, mercuric chloride, potassium platinocyanide, and nitric or iodic acid. Its acetate yields yellow amorphous precipitates with potassium ferrocyanide, potassium ferricyanide, potassium chromate, potassium dichromate, or platinum dichloride. D. B. Dott has confirmed the results of Flückiger's examination, although he found a larger percentage of alkaloids than the latter did. Owing to the difficulty of obtaining the alkaloids in crystals, it was almost impossible to ascertain the quantity present. (*Y. B. P.*, 1881, 442; 1885, 420.) Bebeerine was asserted by Walz, in 1860, to be identical with *buxine*, obtained from *Buxus sempervirens*. This statement was confirmed by Flückiger, who proved that *pelosine* was identical with both of the above principles. (*P. J.*, xi, 1870, 192.) (Palen gives $C_{19}H_{21}NO_3$ as the formula.)

By treating the mixed alkaloids obtained from the wood with chloroform, Douglas Maclagan and Arthur Gamgee have separated an alkaloid, *neotandrine*. It is a white powder, amorphous, and intensely bitter. It differs from bebeerine in being much less soluble in ether, and, when treated with strong sulphuric acid and manganese dioxide, in giving rise to a magnificent green, slowly passing into a beautiful violet, and, lastly, in having a higher molecular weight, its formula being $C_{20}H_{23}NO_4$. After separating nectandrine from the mixed bases, the authors succeeded in extracting another alkaloid, different from bebeerine, much more soluble in water than nectandrine, but insoluble in chloroform. (*A. J. P.*, 1869, 453.)

Nectandra is reputed to resemble cinchona in its virtues, although much inferior. It has generally been employed in the form of the impure bebeerine sulphate. In some cases of *intermittent* and *remittent fevers* it has apparently exercised a curative effect but it often fails, and cannot be relied on as a substitute for quinine. Bebeerine sulphate has been given in *dysmenorrhea*, *menorrhagia*, and *leucorrhea*. The *dose* is from two to five grains (0.13–0.32 Gm.). In *malaria* from ten to thirty grains (0.65–0.9 Gm.) may be given, in divided doses, between the paroxysms.

Bedeguar. *Fungus Rosarum.*—An excrescence upon the *sweetbrier* or *eglantine*, *Rosa rubiginosa*, and other species of *Rosa*, produced by the puncture of insects, especially by one or more species of *Cynips*. It is of irregular shape, usually roundish, about an inch in diameter, with numerous cells containing larvæ. It is nearly odorless, of slightly astringent taste, and was formerly considered a diuretic and anthelmintic. *Dose*, from ten to forty grains (0.65–2.6 Gm.).

Benzacetin. *Acet-amido-ethyl Salicylic Acid.*

$C_6H_3\begin{cases}OC_2H_5\\NH.COCH_3\\COOH\end{cases}$.—This occurs in colorless crys-

tals, melting at 205° C. (401° F.), sparingly soluble in water. It has been recommended by Frank as an analgesic in *migraine* and other forms of *neuralgia*, and as a sedative in nervous excitement. It has been used with alleged excellent results in conjunction with caffeine, ten parts to one. *Dose*, from eight to fifteen grains (0.5–1.0 Gm.) two or three times a day, or repeated in an hour for relief.

Benzanilid.—*Phenylbenzamide*, $C_6H_5NH(C_7H_5O)$, is closely related to acetanilid, containing the benzoyl radical C_7H_5O instead of the acetyl radical C_2H_3O. White to reddish, crystalline, odorless powder melting at 163° C. (325.4° F.), practically insoluble in water but soluble in alcohol. This substance has been recommended by Cahn as an antipyretic in diseases of children in *doses* of from one and a half to three grains (0.096–0.2 Gm.) for children one to three years of age; for adults the dose is ten to fifteen grains (0.65–0.9 Gm.). It has been little used.

Benzidine. (*Paradiaminodiphenyl.*) $(C_6H_4)_2(NH_2)_2$. *N. N. R.* 1917.—A grayish-yellow crystalline powder, difficultly soluble in cold water, more readily in boiling water. This substance, especially in the form of its hydrochloride, has attained a considerable use as the means of detecting the presence of occult blood. For ordinary purposes the benzidine paper is sufficiently accurate. The method of using this is to immerse the benzidine paper in the liquid suspected of containing blood and then drop upon it some hydrogen dioxide solution, and if blood be present there is produced within a minute a blue color. The blue color, however, will appear after a period of time even although no blood may be present. According to Einhorn, it may be assumed that if the blue color appears within a minute blood is present and if not that it is absent. A more satisfactory method of use is that which has been suggested by Ascarelli. (*D. M. W.*, 1908, p. 2307.) He uses a solution composed of 2 mils of a saturated alcohol solution of benzidine, 2 mils of 3 per cent. hydrogen dioxide solution and one or two drops of glacial acetic acid. This is mixed with the suspected substance and if blood be present there will immediately occur a blue color. The test appears to be much more delicate than the ordinary guaiac test. Walter (*D. M. W.*, 1909, p. 130), who employs sodium perborate instead of hydrogen dioxide, asserts that blood may be detected in a dilution of one in 100,000 parts; in fact, for the clinical detection of occult blood in the feces, the test is too delicate, for a sufficient amount of blood may occur in excreta to react to this test and yet have no pathologic significance. Schumm (*A. Pharm.*, 1909) says that the method is not absolutely reliable because other oxidizing agents, as salts of iron oxide and the sulpho-cyanides, will give a positive reaction with benzidine.

The pharmacological properties of benzidine have been investigated by Adler (*A. E. P. P.*, 1908, lviii, p. 167) who found that large doses exercised a paralytic effect upon the central nervous system and caused the appearance of glycosuria and degeneration of the red blood corpuscles. It was oxidized in the body and eliminated as diaminodioxyphenyl.

Benzoin. *Benzoin Æstivale* (L.) Nees. *Lindera Benzoin* Blume. (Fam. *Lauraceæ*.) *Spicewood. Spice-bush. Fever-bush. Benjamin Bush. Wild Allspice. Laurier Benzoin*, Fr. *Benzoelorbeer*, G.—An indigenous shrub, occurring in damp woods, throughout the Eastern and Central States, all parts of which have a spicy, agreeable flavor, strongest in the bark and berries. By warming and expression A. W. Miller obtained from the berries 50 per cent. of oily material, which, on distillation, yielded about 2 per cent. of volatile oil. The latter had a sp. gr. of 0.850, was thin, bright green, of a warm aromatic taste, and a fragrant odor. J. M. Jones found it to be of the cinnamyl series. (*Proc. A. Ph. A.*, xxvi, 772; also *A. J. P.*, xlv, 300; xlvii, 246.) The small branches are said to be employed in the form of infusion or decoction, by the country people, as a vermifuge, and an agreeable drink in *low fevers*, and the bark has been used in *intermittents*.

Benzo-Iodo-Hydrine. $C_3H_5ClC_7H_5O_2$.—Prepared by mixing *benzoyl iodide* and *epichlorhydrin*. It forms a brown, fatty mass, soluble in ether, alcohol, and petroleum oils, insoluble in glycerin. It is decomposed at 100° C. (212° F.), with separation of iodine. For dispensing, it is usually mixed with powdered sugar, so that the mixture contains 3¼ per cent. of benzo-iodo-hydrine, and a teaspoonful is about the equivalent of sixteen grains of potassium iodide. It is used as a substitute for potassium iodide, because of its freedom from irritating properties and from tendency to produce iodic poisoning.

Benzo-Naphthol. *N. N. R.* 1917. *Betanaphthol Benzoate. Benzoyl-Naphthol. β-Naphthyl Benzoate.* $C_6H_5COOC_{10}H_7$.—This compound is made by the action of benzoyl chloride upon β-naphthol. It is a whitish, crystalline powder, without taste or odor, melting at 110° C. (230° F.) and prone to darken with age. It occurs in microscopical crystals, almost odorless and tasteless, nearly insoluble in water at ordinary temperatures, more soluble in alcohol, with solubility rising rapidly with the temperature, but most soluble in chloroform. "A hot alcoholic solution should not give any cherry-red coloration when an equal volume of nitric acid and a few drops of mercuric nitrate solution are added, which would indicate the presence of free β-naphthol." This substance, which was proposed by Yvon and Berlioz (*Pract.*, Dec., 1891) as especially efficacious as an intestinal antiseptic, has been reported upon by Gilbert (*S. M.*, May, 1892), who affirms that it is of little value in *gastric fermentation*, but very valuable in *intestinal fermentation*. It is probably slowly broken up in the intestines into benzoic acid and naphthol, and the experiments made by Ewald (*B. K. W.*, 1892) indicate that it has a positive influence upon intestinal fermentation, a conclusion confirmed by various French clinicians. It appears to be free from irritant properties, and to be a very useful remedy in chronic *diarrhea*; also in *senile pruritus* dependent upon intestinal indigestion. It is best administered in small *doses* of from four to eight grains (0.26–0.5 Gm.), repeated frequently, in capsule; as much as seventy-five grains (5 Gm.) daily may be given to an adult. It is incompatible with antipyrine, camphor, phenol, ferric chloride, menthol, potassium permanganate or ethyl carbonate.

Benzo-Phenoneid. *Tetra-methyl-diapsido-benzo-phenoid.*—This substance, which is soluble in 100 parts of water, has been proposed by Galezowski as a non-irritant and efficient germicide, and as a local application in ulcerative diseases of mucous membranes or skin. (*L. L.*, Jan., 1891.)

Benzosalin. *N. N. R.* 1917. $C_6H_4\begin{cases}O.COC_6H_5\\COOCH_3\end{cases}$

Methyl-benzoyl Salicylate.—This compound is the methyl ester of benzoyl salicylic acid. It occurs as white, acicular crystals which melt at 85° C. (185° F.), insoluble in water, sparingly soluble in ether, but readily soluble in alcohol and chloroform. It is incompatible with acids or highly acid salts. This compound is asserted to pass through the stomach unchanged and be split up by the intestinal juices into its component parts, salicylic and benzoic acids, which exercise their characteristic antiseptic action upon the bowels, and after absorption their anodyne and antirheumatic properties. It has been employed with success in the treatment of *articular* and *muscular rheumatism* and in *neuritis, neuralgia* and similar conditions where the coal tar analgesics are of service. Freund (*D. M. W.*, 1907) believes that the benzoic acid lessens the excessive sweating as well as the local irritant action produced by salicylic acid. The *dose* is eight to fifteen grains (0.5–0.9 Gm.) three or four times a day.

Benzosol. *N. N. R.* 1917. *Benzoyl Guaiacol. Guaiacol Benzoate.*—A colorless, crystalline powder, almost free from odor and taste. It melts at 59° C. (138.2° F.). It is prepared from guaiacol, $C_6H_4\begin{cases}OCH_3,\\OH\end{cases}$ and benzoyl chloride, or benzoic acid, and has the formula $C_6H_4\begin{cases}OCH_3\,(1)\\OCO.C_6H_5\,(2)\end{cases}$ The compound is insoluble in water, soluble with difficulty in hot glacial acetic acid, readily so in chloroform, ether, and hot alcohol. In the digestive tract, it soon splits up into guaiacol and benzoic acid; this decomposition occurs partially in the stomach, but chiefly in the small intestine. It is said to appear in the urine as guaiacol and benzoic acid, and their derivatives. Benzosol is incompatible with alkali hydroxides.

Benzosol was first made by Bougartz, and highly commended by Walzer and Hughes (*D. M. W.*, 1891) as a substitute for creosote in *phthisis*, and has been used to a considerable extent by clinicians as an intestinal antiseptic in *intestinal indigestion, diarrhea*, and other conditions. It has also been used successfully in *cystitis*, and is affirmed by Piatokowski, J. Blake White, and others to be valuable in the treatment of *diabetes*. *Dose*, five to ten grains (0.3–0.6 Gm.) several times a day.

Benzoyl-acetyl-peroxide. *N. N. R.* 1917. *Benzozone. Acetozone. Acetyl Benzyl Peroxide.* $C_6H_5CO.O.O.CH_3CO$.—The pure peroxide forms a white, crystalline mass melting at 36.6° C. (98° F.). When gradually heated it slowly decomposes and evaporates; if suddenly heated it almost instantly decomposes and in a tightly-stoppered bottle an explosion will follow. Grinding, compressing, or pounding the undiluted substance will often bring about the same result. In crystalline form, the substance is soluble in oils to the extent of about 5 per cent., slightly soluble in alcohol, moderately soluble in ether, chloroform, and carbon tetrachloride, although gradually decomposed by all the solvents with the exception of neutral petroleum oils. It is decomposed by contact with alkaloids and organic matter of all kinds. It is slowly hydrolyzed and decomposed by water. Acetozone of the markets is benzoyl-acetyl-peroxide diluted with a neutral drying powder so that 50 per cent. of the pure article is represented. Benzoyl-acetyl-peroxide is moderately soluble in water so that fifteen grains of it may be dissolved in one-half gallon of boiled or distilled water; the solution should be used within thirty-six hours after it is made. If the commercial drug be employed, thirty grains may be used in the half gallon; the solution should be allowed to settle and be decanted without filtration. A mixture of acetyl-benzoyl-peroxide and chlorbutanol (chloretone) in liquid petrolatum is known as *acetozone inhalant*.

Benzoyl-acetyl-peroxide is a very active germicide. Experiments in the laboratories of the United States Government in the Philippines show that 1 part of the hydrolyzed substance to 177 of water, and containing only 0.05 per cent. of active oxygen, destroys all germs, including spores, almost instantly; even at a dilution of 1 in 3000, vegetating germs, as a rule, are killed within one minute, but the spores require an appreciable time. It was further shown that 1 part in 1000 absolutely destroys and that 1 in 30,000 distinctly inhibits the growth of the comma bacillus. In the experiments of Ferer and Novy (*Am. Chem. J.*, vol. xxvii, No. 3, March, 1902), one drachm (3.9 Gm.) of it a day, given for several weeks to a dog weighing eight kilos, produced no sensible effect. Charles L. Bliss has shown that acetozone is eliminated in the form of hippuric acid. In internal medicine benzoyl-acetyl-peroxide has been used in the United States hospitals with most excellent results in the treatment of *cholera*, given in double capsules in *doses* of from three to five grains (0.2–0.32 Gm.) every two to four hours. It was found that when the stomach was full at the time of administration vomiting frequently occurred, probably being due to the decomposition of the peroxide by the organic matter present, since no irritation was produced when the stomach was empty. Benzoyl-acetyl-peroxide has been employed by Wasdin, and subsequently by Harris and others (*T. G.*, 1902–1903), in *typhoid fever* with alleged most extraordinary results in the reduction of the local and general symptoms—one hundred and thirty to two hundred and ten grains (8.3–13.6 Gm.) being administered in the twenty-four hours. Acetozone has also been employed locally as a germicide in *gonorrhea, malignant edema, tinea tonsurans, infected ulcers*, and similar affections. In surgical cases acetozone may be applied directly to the wound. When used as an intestinal antiseptic in typhoid fever or in conditions similar to those resulting from this disease, a 1 in 1000 solution should be freshly prepared each day, and administered almost *ad libitum*.

Benzoyl Ecgonine. $C_{16}H_{19}O_4N + 4H_2O$.—This substance is made by heating cocaine in aqueous solution to decomposition. For details, see Paul, (*P. J.*, Oct. 17, 1885, March 27, 1886); (also Skraup, *Sitzungsb. Wiener Akad.*, 1885). The reaction consists in the substitution in cocaine [$C_{16}(CH_3)H_{18}O_4N$] of an atom of hydrogen (H) for the methyl group (CH_3). There results $C_{16}(H).H_{18}NO_4$ or $C_9H_{14}(C_7H_5O)O_3N$ = benzoyl ecgonine; while CH_3OH (methyl alcohol) is formed at the same time. M. R. Stockman (*J. A. P.*, vol. xxi) finds that it acts like caffeine, but less powerfully. It does not paralyze the sensory nerves.

Benzoyl-Eugenol.—*Benzeugenol*, $C_{10}H_{11}(C_7H_5O)O_2$, occurs in colorless prisms or crystals, melting at 70.5° C. (158.9° F.), soluble in alcohol, ether, and chloroform, insoluble in water. It is similar in its properties and medicinal uses to *cinnamyl-eugenol*, $C_{19}H_{18}O_3$. Both are used as antiseptics and in the treatment of *tuberculosis*.

Benzoyl Para Cresol. *Para kresol benzoate. Cresol Benzoate.*—This substance is prepared by the addition of para cresol to a solution of benzoyl

chloride previously rendered alkaline. It occurs in colorless crystals insoluble in water, soluble in alcohol and ether. As an intestinal antiseptic it is given in *doses* of four to five grains (0.25 Gm.).

Benzoyl Succinyl Peroxide—This occurs as a colorless, crystalline substance with an aromatic odor, and a warm taste, soluble in chloroform and in alcohol. In water it is decomposed, liberating benzoic and succinic acids. It has been brought forward as an antiseptic.

Benzoyl Superoxide. *Benzoyl peroxide. Lucidol.* $C_6H_5.CO.O.O.CO.C_6H_5$.—Sodium peroxide and benzoyl chloride are dissolved in water and heated. The resulting product is filtered and the crystals in the filter are washed with warm alcohol. The crystals of benzoyl superoxide are lustrous, white and prismatic, almost insoluble in water but a little more soluble in alcohol. According to Loevenhart (*Th. M.*, 1905, p. 426), it exercises a more powerful oxidizing effect than even hydrogen peroxide. When locally applied it is non-irritant. He recommends it as an antiseptic and analgesic application, either used pure in the form of a dusting powder, or in the form of a 10 per cent. ointment in *burns* and *skin diseases.*

Benzoyl Tropeine, $C_{15}H_{19}O_2N + 2H_2O$, is formed by heating tropine with benzoic and dilute hydrochloric acids to 100° C. (212° F.), when the benzoyl radical, C_7H_5O, derived from benzoic acid, $C_6H_5CO.OH$, replaces a hydrogen atom of the tropine, $C_8H_{15}NO$, and $C_8H_{14}(C_7H_5O)ON$ is produced. It forms silky needles, fusing at 58° C. (136.4° F.). When deprived of water, the anhydrous base fuses at from 41°–42° C. (105.8°–107.6° F.), and can be sublimed without decomposition. It has a strong basic reaction, and its salts are not very stable.

Filehne (*B. K. W.*, vii, 1887) has found that benzoyl tropeine is a powerful local anesthetic, also affecting the pupil and accommodation like other tropeines. He also found other benzoyl compounds to be local anesthetics, *benzoyl methyltriacetonalkamine* being the most powerful, *benzoyl quinine* next, *benzoyl morphine* the least.

Betaine.—This is an alkaloid of weak basic properties which Scheibler discovered in the juice of the sugar beet. (*A. J. P.*, xli, 559.) Husemann showed it to be identical with *lycine*, and to have the composition $C_5H_{11}NO_2$. (*A. J. P.*, 1875, 209.) Liebreich also obtained it by the oxidation of choline, and called it *oxyneurine*. (*Ber. d. Chem. Ges.*, iv, 735.) It has been made synthetically, and its relation to choline and similar compounds established. It is now known to be *trimethyl glycocoll*, $\begin{matrix} CH_2.N(CH_3)_3 \\ | \\ COO \end{matrix}$.

Waller and Plimmer (*P. J.*, lxxi, 517) find that betaine is feebly but distinctly toxic. In dose of 0.1 Gm. per kilo it produced in rabbits fall of blood pressure with final paralysis of the heart. They assert that pure betaine is less poisonous than the commercial. Boger and Josué (*S. M.*, 1898) believe that they have shown that betaine is capable of neutralizing tetanus toxin. Pelicaut (*Press. Med.*, 1904, p. 485) has recorded one case of recovery in which the alkaloid was used in *doses* of eight grains (0.5 Gm.) hypodermically twice a day. Since, however, both chloral and antitoxin were employed in this case, it is doubtful whether the favorable results were due to the betaine.

Betaine Hydrochloride. N. N. R. 1916. *Acidol. Lycine hydrochloride.* $C_5H_{11}NO_2HCl$.—It is prepared by the action of hydrochloric acid on betaine and consists of colorless crystals, freely soluble in water, and contains 23.8 per cent. absolute hydrochloric acid. When dissolved in water it gradually liberates the acid, and has been used by Flatow (*D. M. W.*, 1905) and others as a substitute for hydrochloric acid in *gastric indigestion. Dose*, eight grains (0.5 Gm.).

Beta-Naphtholsulphonic Acid. *Acidum Betanaphtholinsulphonicum.* $C_{10}H_6(OH).SO_3H$.—*Betanaphtholinsulphonic acid* occurs in white pearly scales, tinged with red. It is readily soluble in water and alcohol, and is of medical interest as a test for albumin in the urine. According to E. Riegler, the reaction is so delicate that it will make plainly visible the presence of one part of albumin in forty thousand of water. Albumoses and peptones are also thrown down, but such precipitates disappear on the application of heat, which does not occur with albumin. *Riegler's test* is best performed by adding from twenty to thirty drops of a 5 per cent. aqueous solution of the reagent to five or six milliliters of the urine.

Beta-Sulpho-pyrin. *Antipyrin Sulphanilate. Sulfopyrine.*—This combination of antipyrin with sulphanilic acid consists of a white powder fairly soluble in warm water and having a pronounced acid taste. It is asserted to be a specific in the treating of *iodism* and is also used in *asthma* and *influenza*, etc. *Dose*, fifteen grains (1 Gm.) three or four times daily.

Betol. *Naphthalol. N. N. R.* 1917. *Naphthosalol. Salinaphthol. Salicylic-naphthyl ester. Betanaphthyl Salicylate. Salicylic acid ester of β-naphthol.* $C_6H_4OH.CO.O.(C_{10}H_7)$.—Betol occurs in white, shining crystals, is odorless and tasteless, melts at 95° C. (203° F.), and is insoluble in cold or hot water, soluble in cold alcohol with difficulty, but readily dissolves in hot alcohol (1 in 3), in ether, and in benzene. It is not decomposed by acids or alkalies in the cold, but the alkaline pancreatic fluid has the power to decompose it into β-naphthol and salicylic acid.

Betol was proposed by Sahli as a substitute for salol, on the ground of its being less disagreeable and yielding in the intestines naphthol instead of the more poisonous phenol. It contains, however, 10 per cent. less salicylic acid than does salol, and, having a much higher melting point, splits up much less readily in the intestines; a fact which gains importance from the observation that frequently salicylic acid cannot be found in the urine after its ingestion. Sahli has given as much as one hundred and eighty grains (11.6 Gm.) in twenty-four hours. Betol may be used in *rheumatism*, and is especially commended by Kobert in ammoniacal *cystitis*. Butter of cacao will dissolve one-fourth of its weight of betol, so that suppositories or bougies are readily made. *Dose*, four to eight grains (0.26–0.5 Gm.).

The *salicylic ester of α-naphthol*, an isomer of betol, is known as *alphol*. It is also said to resemble salol in therapeutic effect. The *dose* is from eight to fifteen grains (0.5–1.0 Gm.).

Betonica. *Betonica officinalis*, L. *Wood Betony.*—A perennial European labiate herb, feebly aromatic and astringent. Its root has been considered emetic and purgative.

Betula. *Betula alba* L. *Paper, Canoe or European White Birch. Bouleau*, Fr. *Birke*, G. (Fam. *Betulaceæ.*)—Various parts of this tree have been applied to medicinal uses. The young shoots and leaves secrete a resinous substance, having acid properties, which, combined with alkalies,

is said to produce the effects of a tonic laxative. (*J. P. C.*, xxvi, 208.) The *inner bark*, which is bitterish and astringent, has been employed in *intermittent fever*. The epidermis is separable into thin layers, which may be employed as a substitute for oiled paper, and applied to various economical uses. The bark contains *betulin*, or *betula camphor*, which Hausemann (*Ann. Ch. Ph.*, 182, 368) has shown to be a diatomic alcohol, as it forms a diacetate. Its formula is $C_{36}H_{60}O_3$, fusing point 258° C. (496.4° F.). When oxidized it yields *betulinic acid*, $C_{36}H_{54}O_6$, and *betulinamaric acid*, $C_{36}H_{52}O_{16}$. When the bark is distilled, it yields an empyreumatic oil known variously as *dagget, oleum rusci, oleum betulinum, oleum muscoviticum, oleum fagi*, and *oil of birch tar*. This is a thick, brownish-black liquid, sp. gr. 0.955, having the odor of Russia leather, in the preparation of which it is employed. This oil has been found very useful as a local application in *chronic eczema* and other *skin diseases* in strengths varying between 1 and 20 per cent. Its medicinal properties closely resemble, if they be not identical with, those of oil of cade. (See *Oleum Cadini*, Part I.) Dutch and German *oil of birch* are quite different from the Russian oil. (See *P. J.*, xv, 769.) The National Formulary IV has introduced a rectified oil of birch. See *Oil of Birch Tar*. The *leaves* of birch, which have a peculiar, aromatic, agreeable odor, and a bitter taste, have been employed, in the form of infusion, in *gout, rheumatism*, and *dropsy*. Active diuretic properties are claimed for birch leaves and attributed to the *betulorentinic acid* in them. An alcoholic extract has been used in daily *doses* of from twenty-five to fifty grains (1.6–3.2 Gm.). When the stem of the tree is wounded a saccharine *juice* flows out which is considered useful in complaints of the kidneys and bladder, and is susceptible, with yeast, of the vinous fermentation. A beer, wine, spirit, and vinegar are prepared from it in some parts of Europe. *Tinctura Rusci* is made, according to Hager, as follows: Ol. Rusci 10, Alcohol, Æther, of each 15, Ol. Lavandulæ, Ol. Rosmarini, Ol. Rutæ, of each 0.4 part; filter. (*A. J. P.*, 1881.)

Bezoar.—This name has been given to concretions formed in the stomach or intestines of animals, which were formerly thought to possess extraordinary medicinal virtues. Many varieties have been noticed; but they were all arranged in two classes, the *oriental bezoar* (*lapis bezoar orientalis*), and the *western bezoar* (*lapis bezoar occidentalis*); the former was most esteemed. The bezoars are essentially impure calcium phosphate, except in the vegetable bezoars where the concretions are made up of plant hairs.

Bichetia. *Bichetia officinalis. Mureré Juice* is extracted in Brazil from the incised bark of this plant; it is a thick reddish liquid, sp. gr. 1.100, and is said to contain an alkaloid and to be useful in *rheumatism* and *syphilis*. The *dose* of the juice is one fluidrachm (3.75 mils) in water; in large doses it is drastic.

Bidens. *Bidens bipinnata*, L. *Spanish Needles.*—An indigenous composite plant, of which the root and seeds are popularly used as emmenagogues, and by the eclectics in *laryngeal* and *bronchial diseases*.

Biodal. *Monoiodo-dibismuth-methylene-dicresotinate.*—A pink, odorless, insoluble powder, suggested as a substitute for iodoform.

Bird-Lime. *Bird-glue. Vogelleim*, G.—A viscid substance, existing in various plants, particularly in the bark of *Viscum album* L. (mistletoe), and *Ilex Aquifolium* L., or *European holly*, from the latter of which it is usually procured. The process for preparing it consists in boiling the middle bark for some hours in water, then separating it from the liquid, and placing the latter in proper vessels in a cool situation, where it is allowed to remain till it thickens, when it is washed to separate impurities. Bird-lime thus prepared is greenish, tenacious, glutinous, bitterish, and of an odor analogous to that of flaxseed oil. Exposed to the air in thin layers it becomes dry, brown, and pulverizable, but reacquires its viscidity upon the addition of water. It is a complex body, but is thought to owe its characteristic properties to a proximate principle, which is called *glu* by the French chemists. This principle is without odor or taste, extremely adhesive, fusible by heat, inflammable, insoluble in water, nearly insoluble in alcohol, but dissolved freely by ether and oil of turpentine. According to Macaire, it is insoluble in the fixed oils, either hot or cold, a property which distinguishes it from the resins. Macaire proposed for it the name of *viscin*. (*J. P. C.*, xx, 18.) Its analysis corresponds to the formula $C_{20}H_{48}O_8$ (or possibly $C_{30}H_{32} + 8H_2O$). After the extraction of the viscin by ether, Reinsch found a substance soluble in oil of turpentine which he called *viscaoutchin*, because of its elastic caoutchouc-like character. He gives it the formula $C_8H_{16}O$. Bird-lime is so tenacious that it may be employed to catch small birds, which, when they alight on a stick thickly covered with it, are unable to escape.

Under the name of *viscum aucuparium verum*, or *viscin*, bird-lime has become a commercial substance which, when dissolved in benzene, gives a syrupy, intensely green solution capable of any degree of concentration, and possesses extraordinary adhesive powers, adapting it for use as the basis of plasters and also as a vehicle for various dermatological remedies. The ordinary base of *viscin plasters*, as proposed by Riehl, consists of a mixture of 1500 Gm. [or 52 oz. av., 399 grains] of solution of viscin, 100 Gm. [or 3 oz. av., 231 grains] of powdered orris, 400 Gm. [or 14 oz av., 48 grains] of starch, to which are added 280 Gm. [or 9 oz. av., 384 grains] of Venice turpentine, and 31 Gm. [or 1 oz av., 41 grains] of Dammar gum, the whole reduced to a paste by evaporation. In the preparation of salicylic viscin plasters the same formula is followed, excepting that the last two substances are replaced by 5 to 10 per cent. of salicylic acid. Various viscin plasters are made with mercury, iodoform, and other active substances. *Zincum viscosum* is a viscin solution of the consistency of linseed oil, containing 10 per cent. of zinc oxide. For medicinal properties of mistletoe, see *Viscum*.

Bismal. $4C_{15}H_{12}O_{10} + 3Bi(OH)_3$. *N. N. R.* 1916.—The bismuth salt of methylene-digallic acid. A grayish-brown powder, insoluble in water or the gastric juice, but soluble in alkaline solutions. It is used as an astringent in *diarrhea*, especially in prolonged cases that are not benefited by opium treatment. The color of this compound becomes darker with age and is found to vary from yellow to dark brown. *Dose*, from one and one-half to five grains (0.096–0.32 Gm.).

Bismon. *Colloidal Bismuth Oxide.* *N. N. R.* 1917.—A substance said to be produced by the reaction between bismuth salts and alkaline solutions of *sodium lysalbinate* or protalbinate. It occurs as a translucent amorphous mass, contain-

ing 22.3 per cent. of bismuth oxide; freely soluble in warm or cold water, the solution up to 25 per cent. being a reddish-yellow and slightly opalescent tasteless fluid; when stronger, syrupy or gelatinous. It has been highly recommended in the treatment of *gastro-intestinal catarrh*, especially in infants. It cannot be used hypodermically on account of its tendency to produce local disturbances and nephritis. Eighty minims (5 mils) of a 10 per cent. aqueous solution may be given three or four times a day to young children, and *doses* of fifteen grains (1 Gm.) are said to be borne without difficulty by older children; always given in solution and not in powder.

Bismutan. *Isutan.*—A yellow, odorless powder, consisting of bismuth, resorcinol, and tannin.

Bismuth Albuminate. *Bismuthi Albuminas. Bismuthum Albuminatum. Wismutalbuminat*, G. *Bismuthose.*—A compound of indefinite composition made by adding a solution of 75 parts of dried egg-albumin to 25 parts of bismuth and ammonium citrate dissolved in a small quantity of water and drying the product at a low temperature.

A pale gray or white powder, not wholly soluble in water, containing from 10 to 12 per cent. of bismuth. It is used in gastric and intestinal cramps in *doses* of from eight to fifteen grains (0.5–1.0 Gm.).

Bismuth Benzoate. $Bi(C_7H_5O_2)_3$. *Bismuthi Benzoas.*—It is a white powder, insoluble in water, and was originally proposed by P. Vigier as a substitute for the bismuth salicylate; it may be made by double decomposition between bismuth nitrate and sodium benzoate; like the salicylate, it is decomposed in the alimentary canal, benzoic acid being set free. It contains about 65 per cent. of bismuth, and may be given as an intestinal antiseptic in *diarrheas*, in *doses* of from eight to fifteen grains (0.5–1.0 Gm.) four to six times a day. It has been commended by Finger as a substitute for iodoform.

Bismuth Borate.—*Bismuthi Boras*, $BiBO_3$, is a grayish-white powder which has been used as an intestinal antiseptic in *doses* of from seven to fifteen grains (0.45–1.0 Gm.).

Bismuth Borophenate.—*Bismuthi Borophenas, Markasol*, has been recommended as a slightly astringent absorbent powder, to be used in the same way and for the same purposes as iodoform. It is free from odor, and is alleged to be locally antiseptic.

Bismuth-Cerium Salicylate is a reddish-white powder, insoluble in water and alcohol. This salt has been highly commended in *diarrhea, enteritis,* and *dysentery* by Salaya. *Dose*, ten grains (0.65 Gm.). With ferric salts it gives a violet color and is decomposed by acids and acid salts.

Bismuth Chrysophanate. *Bismuthi Chrysophanas. Dermol. Bismuthum Chrysophanicum.* $Bi(C_{15}H_9O_4)\,2Bi_2O_3$.—This is a yellow, amorphous, insoluble powder, which has been used in the treatment of various diseases of the skin.

Bismuth Citrate. *Bismuthi Citras. U. S. VIII. Bismuthi Citricum, Citrate de Bismuth*, Fr. *Wismut-citrat, Citronensaures Wismutoxyd*, G. $BiC_6H_5O_7$.—This salt which was formerly official may be prepared as follows: "Bismuth Subnitrate, *one hundred grammes* [or 3 ounces av., 231 grains]; Citric Acid, *seventy-five grammes* [or 2 ounces av., 282 grains]; Distilled Water, a *sufficient quantity*. Mix the Bismuth Subnitrate and the Citric Acid with *four hundred milliliters* [or 13½ fluidounces] of Distilled Water, and heat on a bath of boiling water, with frequent stirring, until a drop of the mixture yields a clear solution with ammonia water. Then add *five thousand milliliters* [about 11 pints] of Distilled Water, allow the suspended matter to deposit, wash the precipitate, first by decantation, and afterwards on a strainer, with Distilled Water, until the washings are tasteless, and dry the residue at a gentle heat." *U. S. VIII.* Bismuth citrate is formed; the completion of the process is known by the precipitate yielding a clear solution with ammonia water.

It is a white, amorphous or micro-crystalline powder, odorless and tasteless. Insoluble in water or alcohol, but soluble in ammonia water, and in solutions of alkali citrates. See *U. S. D.*, 19th ed., p. 237. A combination of bismuth citrate and ferric citrate (*Bismuthi et Ferri Citras*) corresponding to 21 per cent. bismuth and 9 per cent. of iron is marketed as *bismuth and iron citrate (soluble)* (*N. N. R.*, 1917). It occurs in yellowish-green scales and is readily soluble in water. It combines the therapeutic properties of its constituents and is intended for *dyspepsia* associated with *anemia*. *Dose*, five to ten grains (0.32–0.65 Gm.). The same manufacturers have also brought out a similar combination of lithium and bismuth citrate (*N. N. R.*, 1917) in soluble, colorless scales. It corresponds to 40 to 45 per cent. bismuth and 2.5 to 3 per cent. of lithium. It is incompatible with strongly alcoholic liquids, mineral acids and with some salts of heavy metals. It is recommended for *gouty dyspepsia* and *intestinal catarrh* in *doses* for adults of from five to fifteen grains (0.3–1.0 Gm.).

Bismuth Disalicylate.—Under the name of *gastrosan* appears in commerce a white powder insoluble in cold water and alcohol which is asserted to be a disalicylate of bismuth. In hot water one molecule of the salicylic acid is split off, leaving behind the ordinary bismuth subsalicylate. It is claimed for this preparation that it is superior in intestinal fermentation to other preparations of bismuth, because the second molecule of salicylic acid is liberated in the bowel and exercise a powerful antiseptic influence. Witthauer has employed it with beneficial effects in *diarrhea* and in *gastric disturbances*. (*Ph. Centralh.*, 1909, p. 716.) It is marketed in the form of lozenges each containing twelve grains (0.75 Gm.) of the salt and one or two lozenges may be given three times a day.

Bismuth Ditannate. *Bismuth Tannate, Bismuth Bi-tannate. N. N. R.* 1917.—Under the trade name of *Tannismuth* this salt has been introduced into medicine. It is a light yellow powder, insoluble in water, and represents from 17 per cent. to 21 per cent. of bismuth, one atom of bismuth being combined with two molecules of tannic acid. It has been used in the treatment of *intestinal catarrh*, and by some is believed to be more astringent than the other insoluble salts of bismuth on the supposition that one of the tannic acid molecules will be split off in the intestinal tract. The *dose* is five to thirty grains (0.3–2.0 Gm.).

Bismuth Dithiosalicylate. *Bismuthi Dithiosalicylas. Thioform.* $(S.C_6H_3(OH)COO.BiO_2 + Bi_2O_3 + 2H_2O$.—This is a yellowish-gray, odorless and tasteless powder, insoluble in water, alcohol, or ether, containing 72 per cent. bismuth oxide. It has been used externally as a dusting powder in *skin diseases* and in surgery, and probably acts precisely as does dermatol. It has been employed upon the eye to a considerable extent and is not irritant. Internally it has been given in *diarrhea* as an intestinal antiseptic in *doses* of five

grains (0.32 Gm.) three or four times a day in capsules.

Bismuth Formic Iodide.—This is a mixture of formaldehyde-gelatin, thymol iodide, and bismuth sub-iodide in the form of a yellowish powder and used as an antiseptic dusting powder applied to *ulcers* and *sores* that require stimulant action.

Bismuth Iodo-oxyquinoline-sulphonate. *Bismuthi Loretinas. Loretin Bismuth.*—This compound has been used in the *dose* of eight grains (0.5 Gm.) every four hours in the treatment of *tubercular* and other obstinate *diarrheas*, and as a local application in powder form to *epithelioma, syphilitic* and other forms of infected *ulcers*. The 10 per cent. ointment made with lanolin has been recommended in *eczema* and *psoriasis*.

Bismuth Lactate. *Bismuthi Lactas.* $C_3H_4O_3Bi$ $HC_3H_4O_3$.—This salt may be made as follows: Take of bismuth subnitrate, *sixty-one parts;* ammonia water, *fifty parts;* lactic acid, *fifty-five parts;* distilled water, a *sufficient quantity*. Mix the bismuth subnitrate, in a flask, with the ammonia water previously diluted with *seventy-five parts* of distilled water. Let the mixture stand for one hour, pour off the supernatant liquid, and wash the residue thoroughly with distilled water. To the moist residue add the lactic acid, and evaporate the mixture to dryness on the water bath. The product is a white powder, slightly soluble in water and insoluble in alcohol. It may be used in *diarrhea* in *doses* of one to two grains (0.065–0.13 Gm.).

Bismuth Metacresolate. *Bismuthi metacresolas.*—A pale gray or white powder, odorless and tasteless, insoluble in water and alcohol. It is used as an intestinal antiseptic and also as an antiseptic dusting-powder, to take the place of iodoform.

Bismuth Nucleinate.—*Bismuth paranucleinate* or *parabismuth* is a pale yellow, odorless, insoluble powder, containing about 50 per cent. of bismuth. It has been employed in the treatment of *enteritis* of both the acute and chronic types. *Dose*, fifteen to thirty grains (1–2 Gm.).

Bismuth Oleate. *Bismuthi Oleas.* $Bi(C_{17}H_{33}CO_2)_3$.—A compound resulting from the reaction between sodium oleate and bismuth trinitrate. It forms an insoluble powder or mass and is used as an emollient and astringent.

Bismuth Oxide. *Br.* 1898. *Bismuthi Oxidum. Bismuth Trioxide. Bismuthum Oxydatum, Oxydum Bismuthicum. Oxyde de Bismuth*, Fr. *Wismutoxyd*, G.—"Bismuth Oxide ($Bi_2O_3 = 464.00$), may be prepared by boiling bismuth oxynitrate with solution of sodium hydroxide." *Br.*, 1898. It is decomposed by solution of sodium hydroxide in this process, bismuth hydroxide being formed, which is precipitated, while sodium nitrate remains in solution.

$$2BiNO_4.H_2O + 2NaOH = Bi_2O(OH) \text{ (or } Bi_2O_3.3H_2O) + 2NaNO_3$$

At the temperature of 100° C. (212° F.) the bismuth hydroxide is decomposed, water is liberated, and the anhydrous oxide is left. Bismuth oxide is a powder of a dull lemon-yellow color, insoluble in water, but soluble without effervescence in nitric acid, mixed with half its volume of water. The British Pharmacopœia. 1898. describes it as "a slightly brownish-yellow powder. It should answer to the general characters and tests enumerated under 'Bismuth Oxycarbonate.' Each gramme should yield 1.1 grammes of bismuth sulphide. Heated to incipient redness it is scarcely diminished in weight (absence of bismuth oxycarbonate, bismuth oxynitrate, and moisture)." *Br.*, 1898. It resembles bismuth subnitrate in its medicinal properties, and may be administered in *doses* of from ten to thirty grains (0.65–2.0 Gm.).

Bismuth Oxybromide. *Bismuthi Oxybromidum. Wismutoxybromid*, G. BiOBr.—This is an impalpable yellow to a brown powder, used internally in gastric affections.

Bismuth Oxychloride. *Bismuthi Oxychloridum seu Subchloridum. Bismuth Subchloride. Bismuthyl Chloride. Oxychlorure de bismuth*, Fr. *Wismutoxychlorid*, G. BiOCl.—Made by slowly pouring a solution of bismuth trinitrate, in diluted nitric acid, into a solution of sodium chloride, collecting the white precipitate, washing and drying. It is sometimes known as *pearl white*, and in France as *blanc de fard*. Bismuth oxychloride is insoluble in water, soluble in acids. and is used for the same purposes as bismuth subnitrate and also for cosmetic purposes.

Bismuth Oxyiodide. *Bismuthi Oxyiodidum.* BiOI. *Bismuth Subiodide.*—For F. X. Moerk's process for the preparation of this salt, see *U. S. D.*, 19th ed., p. 1416. The oxyiodide has a light yellowish-red color, and contains no water of crystallization. (*A. J. P.*, 1887, 273.) In 1877 the bismuth oxyiodide was recommended as a local antiseptic and substitute for iodoform, by A. Sidney Reynolds. It has been used to a considerable extent with success in the Philadelphia Hospital, but its high price interferes with its general adoption. It has also been given internally in *gastric ulcer* and other gastric affections for which bismuth is usually employed. The *dose* is from five to ten grains (0.32–0.65 Gm.).

Bismuth Oxyiodogallate. *Bismuth Iodsubgallate. Airol. Airoform. N. N. R.* 1917. $C_6H_2(OH)_3COO(BiOHI)$.—This is a basic combination of bismuth, oxygen, iodine, and gallic acid, containing in 100 parts 44.6 parts of bismuth trioxide and 24.3 parts of iodine. It is prepared by heating molecular quantities of bismuth subgallate and hydriodic acid or bismuth oxyiodide and gallic acid in the presence of water until a grayish-green product results which is collected, washed and dried. It is a grayish-green odorless and tasteless powder insoluble in alcohol, ether, chloroform and olive oil, slightly soluble in glycerin. It is decomposed upon contact with water or aqueous solutions, slowly in the cold, more rapidly by heat. Airol is incompatible with water, diluted acids, dilute alkalies, etc., and it should be kept dry, as moist air causes liberation of iodine.

When airol is brought in contact with surgical secretions it becomes red from the liberation of iodine. According to the researches of Carl S. Haegler (Bruns, *B. k. Ch.*, xv, 1896), it is about as feeble an antiseptic as is iodoform, but as in the case of iodoform the substances liberated by its decomposition in wounds are actively germicidal. Von Herrenschwand (*Archiv. fur Ophthalm.*, 1913, lxxxii) finds, however, that one part of airol in a thousand is capable of killing gonococci and that one in ten thousand completely inhibits their growth. It has been largely used as a local remedy in all cases for which iodoform has been employed, having the superiority over that substance of being nearly free from odor. It does not irritate, but rapidly desiccates ulcerated surfaces. In the only case of poisoning by it which we have found recorded, symptoms of bismuth poisoning followed the injection into the

cavity of an abscess of nine and a half fluidrachms (35 mils) of its 10 per cent. glycerin solution (Nemmer).

Injected into the peritoneal cavities of the lower animals in the dose of from one to two grammes per kilo, airol causes colonic convulsions, with coma, nephritis, and fatty degeneration of the liver.

It may be used as a powder or as a 10 to 20 per cent. salve, which should be prepared with lard or vaseline free from water, since with water, airol undergoes rapid decomposition. Airol is used as an antiseptic dusting powder in the treatment of *wounds*. It has been found of service as a local remedy in various *catarrhs*, as *vaginitis* or *rhinitis*. Bernheimer has used airol successfully in the treatment of gonorrheal *ophthalmia*. The eye is first carefully cleansed and the everted lids are then dusted with the finely powdered drug. This procedure is to be repeated several times a day. A 10 per cent. glycerin emulsion has been recommended as an injection into *tubercular abscess* cavities.

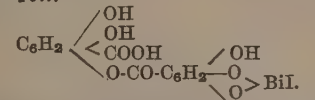
Bruns' Paste, which has been much used in various skin diseases and ulcerations, is made according to the following formula: Airol, *one part;* Mucilage, *two parts;* Glycerin, *two parts;* Argilla Alba (Kaolin), *sufficient to make a soft paste.* If the paste becomes too dry, use glycerin; if it be too soft, kaolin may be added. No metal instruments should be employed in preparing the paste, since many metals liberate iodine from airol. For the same reason, no water, only glycerin, should be used in the preparation. The paste is preserved in well-stoppered glass or porcelain jars, which are to be kept closed.

Bismuth Oxyiodo-methyl-gallol. *Bismuthi Oxyiodo-methylgallolum. Iodo-gallicin.* $C_6H_2COOCH_3(OH)_2O.BiOH.I$.—Made by acting upon gallicin (methyl gallate) with bismuth oxyiodide. It is in the form of a light, amorphous, dark gray powder, insoluble in ordinary solvents and containing 23.6 per cent. of iodine and 38.4 per cent. of bismuth.

It is used as a siccative and antiseptic powder to replace iodoform.

Bismuth Oxyiodo-pyrogallate. *Bismuthi Oxyiodo-pyrogallas.* $C_6H_2(OH)_2.O.Bi(OH)I$.—Made by digesting bismuth oxyiodide with pyrogallic acid or by precipitating a solution of potassium iodide and pyrogallic acid with bismuth nitrate in acetic acid. A fine, amorphous, yellowish-red powder, permanent in light and air. It is recommended as a surgical antiseptic powder.

Bismuth Oxyiodo-tannate. *Bismuthi Oxyiodotannas. Ibit.*



Bismuth oxyiodo-tannate is a greenish-gray, odorless, tasteless powder, becoming brownish on exposure, insoluble in water, and has been suggested as a surgical substitute for iodoform.

Bismuth Peptonate. *Bismuthi Peptonas.*—Prepared by adding a solution of 80 parts of dried peptone to 20 parts of bismuth and ammonium citrate, dissolved in a small quantity of water, and drying at a low temperature. A grayish-brown powder containing from 7 to 8 per cent. of bismuth. It is used in *dyspepsia* and *gastralgia* in *doses* of from fifteen to sixty grains (1.0–3.9 Gm.).

Bismuth Permanganate. $Bi(MnO_4)_3$.—A black bulky powder, soluble in dilute acids, used as an external antiseptic in the form of a dusting powder for *wounds* and *ulcers*, combining the properties of permanganates and bismuth compounds.

Bismuth Phenolate. *Bismuthi Phenolas. Bismuth Carbolate. Phenol-Wismut,* G. $C_6H_5O.Bi(OH)_2$.—Made by a reaction between solutions of bismuth trinitrate and sodium phenolate. A gray, insoluble, inodorous powder, used as an intestinal antiseptic, in *doses* of from eight to fifteen grains (0.5–1.0 Gm.), also as an antiseptic dusting-powder.

Bismuth Phosphate, Soluble. $BiPO_4$.—*Bismuthi Phosphas Solubilis,* which is prepared by the melting together of bismuth, sodium hydroxide, and phosphoric acid, is a white powder easily soluble in water, precipitated by alkalies, acids, or heat, and undergoing spontaneous decomposition when in concentrated solution. It contains 20 per cent. of bismuth, and has been used as an intestinal antiseptic in *choleraic* and other acute *diarrheas* in the *dose* of from three to eight grains (0.2–0.5 Gm.) three times a day.

Bismuth Pyrogallate. *Bismuthi Pyrogallas. Helcosol, Helsosal,* $C_6H_3(OH)_2OBiOH$.—It is a yellowish-green amorphous powder, insoluble in water and alcohol, soluble in acid and alkaline solutions and in the gastro-intestinal juices. According to von Heyden, it represents about 60 per cent. of bismuth oxide. It is said to be non-poisonous, and to be a valuable intestinal antiseptic; if, however, pyrogallic acid should be liberated in the alimentary canal, it might produce disagreeable effects, and the remedy seems to us dangerous. It is asserted that *acids* liberate pyrogallic acid from this combination, thus contradicting the previous statement. It is incompatible with strong alkalies and alkaline sulphur compounds.

Bismuth Resorcinate. *Bismuthi Resorcinas. Resorcin-Wismut,* G. $[(C_6H_4O_2)_3Bi_2]_3 + Bi_2O_3$.—Prepared by adding a solution of bismuth trinitrate to a solution of resorcinol in an excess of alkali. A yellowish-brown powder containing about 40 per cent. of Bi_2O_3. It is used in *chronic* and *acute catarrh* of the stomach. *Dose,* two to eight grains (0.12–0.5 Gm.).

Bismuth Subbenzoate, or *basic bismuth benzoate,* is official in the French Codex, $Bi(C_7H_5O_2)_3Bi(OH)_3$.—It is a white powder containing 60 to 70 per cent. of Bi_2O_3. It is insoluble in water and used externally as a dry dressing in *syphilitic ulcers.*

Bismuth Sulphite. *Bismuthi Sulphis,* $Bi_2(SO_3)_3$, is made by reacting on normal bismuth nitrate with sodium sulphite. It is used as an antiseptic and anthelmintic.

Bismuth Valerate. *Bismuthi Valeras. Valérianate de Bismuth,* Fr. *Wismutvalerianat,* G. $Bi(C_5H_9O_2)_32Bi(OH)_3$.—This salt is formed by double decomposition between solutions of bismuth trinitrate and sodium valerate. Bismuth valerate precipitates as a white powder, which is washed with water, and dried with a gentle heat. It has been recommended by Righini in *neuralgia,* and in *gastrodynia.* The *dose* is from half a grain to two grains (0.032–0.13 Gm.), repeated several times a day, and given in the form of pill.

Bismuthol. *Bismuthal.*—This substance, which is probably a mixture of the bismuth phosphate and sodium salicylate, is a white, crystalline, odorless powder, soluble in water. It has been commended by Radlauer as an antiseptic in the

treatment of *wounds* and inflammations of the mucous membrane. It has been especially recommended for excessive *sweating of the feet.*

Bismutose.—This substance is said to be an albuminous compound containing 22 per cent. of bismuth, and 66 per cent. of albumin. It is a tasteless, white powder which gradually acquires, under the influence of light, a slaty-gray color. It is insoluble in water and most other solvents; dilute acids partly dissolve it when warmed. With dilute alkaline solution it forms rapidly, especially when heated, an opalescent fluid from which it is precipitated by alcohol. It is affirmed to be non-poisonous. It has been highly praised by Laquer (*Ther. Geg.*, 1901) as a remedy, specially for children, in all those forms of *gastric* and *intestinal irritation* or *ulceration* for which bismuth has been employed. The *dose* for infants is fifteen to thirty grains (1–2 Gm.), for children a drachm (3.9 Gm.), and for adults larger quantities. It is also employed as a dusting powder in the treatment of *burns* and *intertrigo* as an absorbent.

Bistort. *Snakeweed. Bistorte, Couleuvrine,* Fr. *Weissenknöterich, Natterwurz,* G.—This is the rhizome of *Polygonum Bistorta,* L. (Fam. *Polygonaceæ*), a perennial herbaceous plant, growing in Europe and the north of Asia. The rhizome is cylindrical, somewhat flattened, about 1 to 2 cm. in thickness, marked with annular or transverse wrinkles, furnished with numerous rootlets, and folded or bent upon itself, so as to give it the tortuous appearance from which its name was derived. Externally it is dark purplish or blackish-brown. The fracture is nearly smooth, reddish or purple, the taste being astringent. It contains much tannin, some gallic acid and gum, and a large proportion of starch. H. K. Bowman found 21 per cent. of tannin in bistort root. (*A. J. P.*, 1869, 193.) Its medicinal properties are like those of kino, but it is less efficient. It may be employed in powder, decoction, or extract. The *dose* of the powder is twenty or thirty grains (1.3–2.0 Gm.).

Besides the bistort, some other plants belonging to the genus *Polygonum* have been used as medicines. Among these are *P. aviculare,* L., or *knot weed,* a mild astringent, formerly employed as a vulnerary and styptic; *P. Persicaria,* L., or *lady's thumb,* of a feebly astringent saline taste, and at one time considered antiseptic; and *P. Hydropiper,* L., common *smartweed,* or *water-pepper,* the leaves of which have a burning and biting taste, inflame the skin when rubbed upon it, and are esteemed diuretic, and have been used with asserted success in *amenorrhea* and other *uterine disorders.* Its irritant and also medicinal properties are due to an acid, *polygonic acid,* discovered by C. J. Rademaker. *Polygonum Hydropiper* has been used by Krawkoff (*Russki Vratch,* 1912) in the treatment of *internal hemorrhages,* especially of the uterus. He administered from thirty to forty drops of a fluidextract of the leaves. (*A. J. P.*, xliii, 490.) The *water-pepper* or *smartweed* of this country—*P. acre* H. B. K.—which grows abundantly in moist places, possesses properties similar to those of the European water-pepper, and is occasionally used as a detergent in chronic *ulcers,* and internally in *gravel.* B. Woodward found that the dried plant contains 18 per cent. of tannin, and used a saturated tincture with great advantage in *diarrhea* and *dysentery,* in *doses* of from twenty to sixty minims (1.3–3.75 mils). Aughey finds that *P. amphibium,* L., is readily cultivated, with a yield of from three to six tons to the acre, that the roots contain 21.75 per cent., the stems 17.1 per cent. of tannic acid, and urges the growth of it for tanning purposes. (*N. R.*, 1876, 75.)

Fagopyrum esculentum Moench is common *buckwheat.* The leaves of this plant have been found by Ed. Schunck to contain a crystallizable coloring principle, identical with the *rutin* or *rutic acid* previously discovered by Weiss in the leaves of the common rue, and probably, with the *ilixanthin* of Moldenhaus, existing in the leaves of *Ilex Aquifolium* L., or the common holly. Buckwheat leaves yielded to Schunck somewhat more than one part of rutin in a thousand. (*Chem. Gaz.*, No. 399, 201.)

From *P. cuspidatum* L. has been separated a glucoside, *polygonin,* and also *emodin.* (*P. J.*, Feb., 1896.) The bark of the rhizome has been recommended by Goris and Crète (*Bull. Sci. Pharmacol.*, 1907) as a laxative. The leaves of the *P. dumetorium* are, according to Tunmann (*Ph. Centralh.*, 1906), also practically useful as a laxative.

Various species of the genus *Polygonum* are used for the production of dye-stuffs; thus, indigo is obtained largely in China, Japan, and in some parts of Russia, from the leaves of *P. tinctorium* Ait., and is said also to be yielded by those of *P. aviculare* and *P. barbatum,* L.; while in India, China, and Japan the roots of the *P. cuspidatum* are employed for making a yellow dye. (*J. Chem. S.*, Dec., 1895.)

Bituminol. *Ammonium Sulpho-Bituminolate.*—This substance, manufactured by a German firm, is used as a substitute for ichthyol.

Blenal. *Santalol Carbonate.*—Blenal is the carbonic acid ester of santalol. It is a yellowish, oily fluid, soluble in alcohol and ether, but not in water. It is almost free from taste or odor, and represents 94 per cent. of santal oil. Blenal may be used for all the purposes for which santal is serviceable. It has, however, been employed chiefly as an internal remedy in the treatment of *gonorrhea.* The *dose* is fifteen drops three times a day, preferably given stirred up in milk, or it may be administered enclosed in capsules each of which may contain half of this quantity.

Blennostasine. *Cinchonidine dihydrobromide.*—This forms yellowish, deliquescent crystals and is freely soluble in water. W. F. Campbell (*N. Y. M. J.*, lxiv, 1896) asserted that it is a powerful sedative to the brain and spinal cord, and that in *doses* of from one to four grains (0.065–0.26 Gm.) every hour it is a valuable remedy in nasal and laryngeal hyperesthesia. It has been especially recommended to check excessive secretions in *acute coryza.*

Blepharis. *Blepharis capensis.* (Fam. *Acanthaceæ.*)—This plant is said to be physiologically very active and useful in the treatment of *anthrax.* (*P. J.*, lx, p. 140.)

Blood of Bullocks.—As long ago as 1852, Samuel Jackson, of Philadelphia, employed as a tonic the blood of bullocks carefully dried *in vacuo,* giving from five to ten grains (0.32–0.65 Gm.) of it as a *dose.* At one time it was used considerably in Europe, and even drinking fresh bullock's blood was at one time in fashion. *Bioferrin* is a liquid preparation of hemoglobin. It is prepared from carefully examined tubercle-free ox blood, by a process which renders it sterile and palatable. It is a brownish-red fluid with a peculiar, though not unpleasant taste and odor, and containing for its conservation 2.5 per cent. alcohol and 20 per cent. glycerin. It is used in the treatment of

anemic children. Under the name of *Sanguis Bovinus Exsiccatus*, F. E. Stewart introduced defibrinated dried bullock's blood, claiming for it that, by the simple addition of water, bullock's blood can be reproduced minus a small quantity of fibrin. There is no reason for believing that dried blood is more valuable than the more usual ferruginous tonics, if indeed it be of equal value.

Apparently by increasing the fibrinogen of the blood, foreign blood serum accelerates coagulation and has therefore been used in the treatment of *internal hemorrhages*. There are at least two derivatives of blood serum upon the market known respectively as *coagulose* and *coagulin*. Coagulose appears to be merely the desiccated sterilized serum of horse blood. It is marketed in sealed bulbs each containing one grain (0.65 Gm.) of the powder, which is equivalent to 10 mils of blood serum. It is administered by dissolving this powder in sterile water and injecting the resulting solution hypodermically. The injection may be repeated every two or three hours or less frequently as the case requires. There is, however, some objection to the use of horse serum on the possibility of anaphylactic reactions, and Curtis (*J. A. M. A.*, 1915, lxiv, p. 332) has found the hypodermic injection of whole human blood to be equally efficacious. He administered subcutaneously from ten to twenty mils. Coagulin was introduced by Kocher and Fonio (*Korrespondenzbl. f. Schweiz. Aerzte*, 1913) and is obtained by the action of the ferment thrombozyme on blood serum. It is used especially in the treatment of primary or secondary *hemorrhages* and of *wounds*.

Blue Flag. *N. F. IV.* (*U. S. P.* 1890.) *Iris Versicolor.*—"The dried rhizome of *Iris versicolor* Linné (Fam. *Iridaceæ*), without the presence of more than 5 per cent. of the roots and leaf bases." *N. F.* In all the species belonging to this genus, so far examined, the roots are more or less acrid, and possessed of cathartic and emetic properties. In Europe, *Iris fœtidissima* L., *I. florentina* L., *I. germanica* L., *I. pseudoacorus* L., and *I. tuberosa* L. have at various times been admitted into use, and the unpeeled roots of *I. germanica* are still sold in the Indian bazaars under the name of *Irisia*. *Iris versicolor* L., or blue flag, is found in all parts of the United States, flourishing in low wet places in meadows. The flowers afford a fine blue infusion, which serves as a test for acids and alkalies. The recent root is without odor, and has a nauseous, acrid taste, which is imparted to water by decoction, and still more perfectly to alcohol, the acrimony as well as medicinal activity is impaired by age. If cut, when fresh, into slices, dried at the temperature of about 37.8 ° C. (100° F.), then powdered and kept in bottles excluded from the air, the root retains its virtues unimpaired for a considerable time (Andrews). It is described as follows in the National Formulary IV:

"Rhizome frequently branched, up to 10 cm. in length and 2 cm. in thickness, usually cut into longitudinal pieces; outer surface grayish-brown to purplish-brown, somewhat annulate, the upper surface with markings of leaf bases, the lower with numerous root scars and remnants; fracture short, the broken surface pale purplish-brown and exhibiting a central stele with whitish fibro-vascular bundles distributed throughout, a distinct endodermis, and cortex. Odor slight, not distinctive; taste acrid, nauseous. The powder is light purplish-brown and, when examined under the microscope, exhibits numerous resin cells filled with yellow to brown resin; starch grains few, or, in some specimens, abundant, simple, or two- to four-compound, the simple grains being spherical or elliptical, up to 0.022 mm. in diameter; calcium oxalate in prisms, up to 0.35 mm. in length; tracheæ with spiral or reticulate markings or with bordered pores; sclerenchymatous fibers few, lignified and with oblique pores. Blue flag yields not more than 7 per cent. of ash." *N. F.*

D. W. Cressler found in this plant starch, gum, tannin, sugar, and acid resin, fixed oil, and indications of an alkaloid. (*A. J. P.*, 1881, p. 602.)

Blue flag is a cathartic and emetic, said to have been used by the Southern Indians, and may be given in *doses* of from ten to twenty grains (0.65–1.3 Gm.). *Iridin*, or *irisin*, of the eclectics, is an oleoresin obtained by precipitating a tincture of the root with water, and mixing the precipitate with an equal weight of some absorbent powder. Wm. E. Jenks (*A. J. P.*, 1881, p. 601) prepares the *oleoresin of iris* by exhausting the root with alcohol, sp. gr. 0.835, and distilling off the alcohol. (See also a paper on the constituents of the oleoresin by W. L. Cliffe, *A. J. P.*, 1884, p. 616.) The so-called irisin is undoubtedly purgative and is generally believed to have a very decided action upon the liver. Power and Salvay (*A. J. P.*, 1911, 14) isolated *isophthalic acid*, $C_6H_4(CO_2H)_2$. It may be given in pill in the *dose* of from three to four grains (0.20–0.26 Gm.).

The Pharmacopœia formerly recognized a solid *extract* (*Extractum Iridis*), made by the following process: "Iris, in No. 60 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, *a sufficient quantity*. Moisten the powder with *four hundred mils* [or 13 fluidounces, 252 minims] of Alcohol, and pack it firmly in a cylindrical percolator; then add enough Alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding Alcohol, until *three thousand mils* [or 101 fluidounces, 3½ fluidrachms] of tincture are obtained, or the Iris is exhausted. Distil off the Alcohol from the tincture by means of a water-bath, and evaporate the residue, on a water-bath, to a pilular consistence." *U. S.*, 1890. The *dose* of the extract of iris is one to two grains (0.065–0.13 Gm.).

A fluidextract is official in the N. F. (see Part III).

Blumea. *Blumea lacera* DC. (Fam. *Compositæ*.)—From this plant, which is used in India as an insect powder, Dymock has obtained a light yellow volatile oil. It has a sp. gr. of 0.9144 at 26.7° C. (80° F.), and an extraordinary rotating power, 1 mm. turning the ray 66° to the left.

Bocconia.—It is probable that various species of this papaveraceous genus have active medicinal properties. *B. arborea* Watson, of Mexico, has been found by Elliott to contain two alkaloids, one of which is probably *sanguinarine;* and the leaves of other species are used in South America as an abortifacient and purgative. (See Rusby, *Bull. Pharm.*, 1891.) Murrill and Schlotterbeck (*Proc. A. Ph. A.*, 1900, p. 128) examined all parts of *Bocconia cordata*, and isolated protopine, homochelidonine, chelerythrine and sanguinarine.

Boldo. *N. F. IV. Boldo Leaves.*—It is described by the N. F. as "the leaves of *Boldu Boldus* (Molina) Lyons (Fam. *Monimiaceæ*), without the presence of more than 2 per cent. of stems or other foreign matter. Broadly ovate or oval,

from 3 to 7 cm. in length and from 1 to 4 cm. in breadth, the base varying from rounded to very slightly indented, the summit rounded or slightly notched, the margin entire and sharply revolute; thick, coriaceous, rigid and brittle; from pale-green to brownish-green, papillose, roughened on both surfaces, the principal veins coarsely reticulate, impressed above, sharply prominent underneath; the petiole stout and rigid, from 1 to 5 mm. in length, reticulate. Odor peculiar; when crushed very strong, disagreeable, and somewhat like that of oil of chenopodium; taste bitter, warm and pungent, camphoraceous and slightly terebinthinate. Under the microscope a transverse section shows a well-marked hypodermis from which develop papilla-like excrescences, each crowned with a group of radiating, one-celled, thick-walled hairs; on the lower surface stomata numerous and hairs somewhat smaller, mesophyll with numerous oil secretion cells. Boldo yields not more than 10 per cent. of ash." This plant is an evergreen shrub, frequenting the meadows of the Andes in Chili, where its yellowish-green fruit is eaten, its bark used in tanning, and its wood is employed in charcoal making. The leaves contain an aromatic, volatile oil, of which they yield, on distillation, about 2 per cent. The oil boils between 175° and 250° C. (347° and 482° F.) and gives a green coloration with ferric chloride; it contains terpene and oxygenated bodies which have not as yet been investigated. For chemistry of the *Oil of Boldo*, see *Schim. Rep.*, Oct., 1907, p. 19. They have found that the oil is chemically related to the Oil of Chenopodium. A peculiar alkaloid, *boldine*, has been found in them by Bourgoin and Verne (*J. P. C.*, 4e sér., xvi, 191), and a glucoside, *boldoglucin*, $C_{30}H_{52}O_8$, a thick syrupy liquid, by P. Chapoteaut. (*C. R. A. S.*, xcviii, 1052.) According to Sigismond Pascaletti (*Terapia Moderna*, 1891), boldine when injected hypodermically paralyzes both the motor and sensory nerves, and also attacks the muscle fibers. When given internally in toxic dose it produces great excitement, with exaggeration of the reflexes and of the respiratory movements, increased diuresis, cramps, disorder of coördination, convulsions, and finally death from centric respiratory paralysis, the heart continuing to beat long after the arrest of respiration, finally stopping in diastole. Boldine has in recent years come into wide use in veterinary medicine as a remedy for *jaundice*. It has also been used in man in the treatment of hepatic affections, given in *doses* of one one-hundredth to one-twentieth of a grain (0.0006–0.003 Gm.) in conjunction with calomel. Boldoglucin is said to act on the lower animals as a narcotic, and has been given by Réne Juranviller in *doses* of one to three grains (0.06–0.2 Gm.) in diseases of the liver. Fifteen minims (0.9 mil) of the oil of boldo cause in man some warmth in the epigastrium; thirty minims (1.8 mils), much gastric irritation, with pain and vomiting, and passage of urine smelling strongly of the oil. Dujardin-Beaumetz finds the oil useful in *genito-urinary inflammations* in *doses* of five drops (0.25 mil) (*B. G. T.*, March, 1875), in diseases of which character the drug has long been employed in South America. (*Ibid.*, lxxxvi, 165.) In France boldo has been employed as a tonic in *chronic hepatic torpor* and in *hepatitis*, and Fedeli (*Il Policlinico*, 1907) reports favorable results in the treatment of *cholelithiasis*. Eight minims (0.5 mil) of a 20 per cent. tincture or four minims (0.25 mil) of the N. F. fluidextract may be considered as the commencing *dose*, increased *pro re nata*. Large doses are apt to vomit and purge.

According to A. T. De Rochebrune (*Toxicol. Africaine*, i, 1897), the tree *Monimia rotundifolia*, of Australia, contains an abundant volatile oil, an alkaloid, and a glucoside, which are very similar to, if they are not identical with, those obtained from the *Boldo*, and may be substituted for the latter in therapeutics.

Bole Armenian. *Bolus Armeniæ. Bolus Rubra. Argilla Ferruginea.*—The term *bolus* or *bole* was formerly applied to various forms of argillaceous earth, differing in color or in place of origin. Such were the *Armenian*, *Lemnian*, and *French boles*, and the *red* and *white boles*. Some of these substances were so highly valued as to be formed into small masses and impressed with a seal, and hence received the name of *terræ sigillatæ*. The only one at present kept in the shops is that called *bole Armenian*, from its resemblance to the substance originally brought from Armenia. It is prepared by trituration and elutriation, from certain native earths existing in different parts of Europe. It is in pieces of various sizes, reddish, soft, and unctuous, adhesive to the tongue, and capable of forming a paste with water. It consists chiefly of a hydrated aluminum silicate with ferric hydrate. The boles were formerly employed as absorbents and astringents in *acidity of the stomach* and in *relaxed bowels*. Bole Armenian is used chiefly as a coloring ingredient in tooth-powders.

Boliformin.—A condensation product of formalin with an aluminum salt is exploited under this name, as an antiseptic dusting powder, mainly used in veterinary practice.

Bonduc Seeds.—These are seeds derived from several species of the genus *Cæsalpinia* (Fam. *Leguminosæ*), which are used in India as febrifuges, tonics, and antiperiodics. Heckel and Schlagdenhauffen have discovered in them a bitter principle (*C. R. A. S.*, ciii, 89), probably identical with that previously isolated by Flückiger. (*Pharmacographia*, 2d ed., 212.)

Bone. *Os*, Lat., Fr. *Knochen-Asche*, G. *Ossa*, It. *Huesos*, Sp.—Under the name of *Os Ustum*, or *Bone ash*, the Br. Pharmacopœia formerly recognized "the residue of Bones, which have been burned to a white ash in contact with air. Bone ash consists principally of phosphate of calcium, mixed with about 10 per cent. of carbonate of calcium and a little calcium fluoride, silica, and magnesium phosphate." When bones are subjected to destructive distillation, in *closed* vessels, they are decomposed without alteration of shape, lose about three-sevenths of their weight, become brittle, and are converted into a black substance, containing the earthy salts of the bone, and constituting the species of animal charcoal called *bone black*. (See *Carbo Animalis*.) The portions which distil over consist of the usual ammoniacal products derived from animal matter, but are especially rich in nitrogenous bases of the pyridine and quinoline series. (See *Ammonii Chloridum*.)

When calcined in open vessels, bones are converted into a white friable substance consisting of the incombustible part, and commonly called *bone earth*, or *bone ash;* and a similar residue is obtained by calcining horns, and is termed *Cornu Ustum*. When bones are treated with boiling water, a small portion of the gelatinous matter is dissolved; but when acted on by water in a Papin's digester, the whole of it is taken up and the earthy salts, deprived of their cement, crumble

into powder, and become diffused through the solution. When acted on by diluted hydrochloric acid, the earthy salts are dissolved, and the bone softens without losing its shape and becomes semi-transparent and flexible. The portion remaining unattacked by the acid is the gelatinous tissue, which may be converted into gelatin by boiling with water. The hoof bones of the ox, boiled with water, furnish a peculiar oil, called *neat's-foot oil.*

The bones of different animals, and of the same animal at different ages, vary somewhat in composition. Dry ox bones consist of bone gelatin (cartilage of bone) 33.3, calcium bone phosphate with a little calcium fluoride 57.35, calcium carbonate 3.85, magnesium phosphate 2.05, and sodium hydroxide with a very little sodium chloride 3.45. Human bones differ somewhat in the proportions of their constituents, and in containing traces of iron and manganese. According to W. Heintz, however, bones exhausted by water, so as to remove the coloring matter of blood, do not contain a trace of iron. Marchand found 1 per cent. of calcium fluoride in human bone. *Calcium bone phosphate* consists of the tribasic phosphate, $Ca_3(PO_4)_2$.

Borago. *Borago officinalis,* L. *Borage. Bourrache,* Fr. *Borasch, Boretsch,* G. (Fam. *Boraginaceæ.*)—This European annual abounds in mucilage, and the stems and leaves contain potassium nitrate with other salts. To these constituents the plant owes its feeble medicinal properties. An infusion of the leaves and flowers is employed as a demulcent, refrigerant, and gently diaphoretic drink. The expressed juice of the stems and leaves is also given in the *dose* of from two to four fluidounces (60–120 mils).

Bornyval.—This isovaleric ester of borneol, $CH_3CH(CH_3).CH_2CO.O(C_{10}H_{17})$, $C_{10}H_{17}O.C_5H_9O$, is a limpid fluid with an aromatic odor, suggesting valerian; soluble in alcohol and ether, insoluble in water; boiling under ordinary pressure, at 255° to 260° C. (491°–500° F.); sp. gr. at 20° C. (68° F.) 0.951. Polariscopic rotation: $[\alpha]_D$ 20° = 27° 40′. Bornyval has been highly lauded by a number of physicians in the same class of cases in which valerian is commonly employed, such as *nervous headache, neurasthenia, dysmenorrhea,* and the like. It has also been recommended in the treatment of various forms of *sexual disturbances,* and even in *epilepsy.* The *dose* is four to eight minims (0.25–0.5 mil) several times a day.

Under the name of *Neo bornyval, N. N. R.* 1917, the iso-valeryl-glycolic ester has been introduced. This is supposed to have the advantage over the older bornyval in that it is less easily affected by the gastric juices and therefore less liable to give rise to disturbances of the stomach. It is used for the same purposes as bornyval and appears in commerce in the form of pearls, each of which contains 0.25 Gm. (3½ gr.). Of these one to three may be given at a *dose.*

Under the trade name *Gynoval* (*N. N. R.* 1917) $CH_3CH(CH_3)CH_2COOC_{10}H_{17}$, is marketed, being the isovaleric acid ester of isoborneol. It is similar in appearance and properties to Borynval. (See also *Brovalol,* p. 1290.)

Boro-Benzoic Acid is a colorless, crystalline product with the characteristic benzoic odor and a pungent taste. It is almost insoluble in cold water and slightly soluble in warm water and alcohol. It is employed as an internal antiseptic, in *doses* of ten to twenty grains (0.6–1.3 Gm.).

Boro-Citric Acid.—A combination of the two acids, forming a white, very soluble powder. It is used in *doses* of from five to twenty grains (0.32–1.3 Gm.) as a solvent for the urates and phosphates in *urinary calculi* and *gout.*

Borogen.—This is the ethyl ester of boric acid, $B(O.C_2H_5)_3$. It is a liquid, boiling at 120° C. (248° F.), which is decomposed by water into boric acid and alcohol. It is inflammable, burning with a green flame. This substance has been suggested as a local remedy in diseases of the nasal and respiratory mucous membrane, under the belief that it is decomposed into its constituents in the throat and lungs. Borogen is used by inhalation.

Boroglyceride. *Boroglycerinum. Glyceryl-borate.*—This substance has been largely employed as a convenient form of obtaining boric acid in a soluble condition. It is made by heating boric acid and glycerin together so as to effect a combination without discoloring the product by overheating. (See *Glyceritum Boroglycerini,* page 524.) James Kennedy (*Nat. Drug.,* 1887, 46) maintained that it is a chemical compound, and not a mere mechanical mixture, as has been supposed; he gave it the formula $C_3H_5BO_3$, and expressed the reaction in its formation thus:

$$C_3H_5(OH)_3 + H_3BO_3 = C_3H_5BO_3 + 3H_2O$$

The metallic boroglycerides, such as sodium and calcium boroglyceride, are not explained, however, in this case. Aqueous solutions of boroglyceride were formerly used for preserving milk, meat, fruit juices, etc., but are now prohibited by law. Boroglyceride has been largely sold in England under the name of *glacialin.*

Borol.—This is a compound possessing the structural formula $SO_2{<}^{BO}_{KO}$ or $SO_2{<}^{BO}_{ONa}$, or, as it may be written, $BKSO_4$ or $BNaSO_4$. It occurs in irregular, colorless, odorless, vitreous fragments, soluble in five times its weight of water. According to H. Jäger, it is three times as powerful as phenol as an antiseptic, the 2 per cent. solution rapidly destroying most pathogenetic germs. It has been used internally in various germ diseases and externally in *diphtheria, gonorrhea, ozena, psoriasis,* and other surgical affections. *Dose,* from thirty to fifty minims (1.8–3.1 mils) of a 20 per cent. solution well diluted. Locally a .1 to 2 per cent. solution has been used. (*Ther. Woch.,* iv.)

Boro-Phenol is a combination of borax and phenol. It has an agreeable odor, is completely soluble in water, and can be used for all the purposes for which carbolic acid disinfectants are used.

Boro-Salicylic Acid has been introduced by Cesaris and Carcano as an antiseptic; the solution contains 4 per cent. each of boric and salicylic acids.

Borsalicyl is made by Bernegau by triturating thirty-two parts of sodium salicylate with twenty-five parts of finely powdered boric acid with a little water; the hardened mass is dried and powdered. It is used as an antiseptic. (*Ap. Ztg.,* 1894, 876.)

Bowdichia. *Bowdichia virgiliodides* H. B. K. (Fam. *Leguminosæ.*)—Under the name of *Sucupira,* the hard, yellow, very bitter bark yielded by this tree is employed in Venezuela and Brazil in *fevers* and *rheumatism.* Petit has found it in a mydriatic alkaloid. (*P. J.,* June, 1885.)

Bragantia. *Bragantia Wallichii.* (Fam. *Aristolochiaceæ.*)—The roots of this shrub of India contain an alkaloid allied to *aristolochine,* a soft

resin, a resinous acid, and a substance related to dulcite. (*P. J.*, 1894, 231.)

Brassica.—In China the oil of *Brassica sinensis*, or *petsai*, is used for lighting, and is said also to be purgative, and useful in *skin diseases*, while the Japanese employ the yellow oil of *B. Campestris*, L., under the name of *aburana*, for culinary and lighting purposes. (*A. J. P.*, June, 1885.)

Brazil Nuts. *Cream Nuts. Butter Nuts* (not to be confused with the nuts similarly named and obtained from *Juglans cinera* L.). *Para Nuts. Chataigne du Brésil*, Fr. *Paranuss*, G.—These are edible nuts imported from Brazil, and sometimes employed in making cream syrups for giving flavor to carbonic acid water. In Brazil an expressed oil is obtained from them, which is said to be used for burning, making ointments, and adulterating copaiba. The nuts are the product of *Bertholletia excelsa* Humb. et Bpl. and *B. nobilis* Miers, a large and beautiful tree of the Fam. *Myrtaceæ*, growing over extensive regions in South America. Cornwinder has found in the kernel of the nut 65.60 per cent. of oil, and 15.31 per cent. of nitrogenous matter. (*P. J.*, Aug., 1873.) Hugo Kühl obtained from the seeds an average fat-content of 62.73 per cent., with 2.59 per cent. of nitrogen, corresponding to 16.20 per cent. of proteins. (*P. Zeit.*, 1909, No. 6, 58.)

Brazil Wood.—A red dye-wood, the product of different species of *Cæsalpinia*, growing in the West Indies and South America. Two varieties are known in commerce—1, the proper Brazil wood, said to be derived from *Cæsalpinia echinata* Lam., and sometimes called *Pernambuco* or *Fernambuco wood*, from the province of Brazil, where it is collected; 2, the *brasiletto*, produced by *C. brasilensis*, L., and *C. Crista*, L., which grow in Jamaica and other parts of the West Indies. The former is the most highly valued. The *Nicaragua* or *peach wood* is also analogous to the brasiletto, and is said by Bancroft to be derived from a species of Cæsalpinia. It is produced in the East Indies. Brazil wood is nearly inodorous, has a slightly sweetish taste, stains the saliva red, and imparts its coloring matter to water. It was formerly used in medicine, but has been abandoned as inert. In pharmacy it serves to color tinctures, etc., but its chief use is in dyeing. A red lake is prepared from it, and it is an ingredient in a red ink. Its dyeing properties are due to a crystallizable coloring principle, named *brazilin* or *brasilin*, $C_{16}H_{14}O_5$. This, as usually obtained, is of a sulphur-yellow color, which it preserves in the dark, but in the sunlight, to which it is remarkably sensitive, changes to a reddish hue after a few minutes' exposure, and also more slowly in diffused daylight. The principle should, therefore, be kept in perfectly opaque vessels. It is now stated that when absolutely pure it is colorless, and becomes red on exposure to the air. The change is due to the formation of *brasilein*, $C_{16}H_{12}O_5$, which can be prepared from the brasilin by a variety of methods, such as oxidation by nitrous acid, by alcoholic iodine solution, etc. Brasilin is sparingly soluble in water, yielding a sweet and almost colorless solution which is not changed by acids, but is deeply reddened by alkalies. In alcohol and ether it is somewhat more soluble than in water, giving a light yellow solution. Brasilin and hematoxylin (from logwood) are now recognized as related, each being derived from the pyrone nucleus $C_5H_4O_2$, from which the two groups, the xanthone group and the flavone group, are also taken. The coloring principles of most dye-woods are now referred to this source. (Kupe, *Die Chemie der natürlichen Farbstoffe*, Braunschweig, 1900.)

Brea Gum.—This substance, which has been proposed as a substitute for gum arabic, is believed to be derived from *Cæsalpinia præcox*, a Brazilian tree. It occurs in stalactitic pieces or oval reddish-yellow tears, isolated or agglomerated. It forms with water a viscous, pale reddish-yellow mucilage, of acid reaction, which may be partially decolorized by heating with a few drops of hydrochloric acid. It is said to contain 77 per cent. of arabin.

Bremen Blue or **Bremen Green.**—This substance, chemically, is *cupric hydroxide*, although sometimes *cupric carbonate* is sold under the same name. It is made by precipitating a copper salt with an alkali, and drying the precipitate below 40° C. (104° F.). When used as a water-color, it is blue, but when mixed with oil, a soap is formed which is of a green color.

Bromal. *Tribromacetaldehyde.* C_2HBr_3O.—This substance resembles chloral in its chemical properties, like it existing as an oily, colorless liquid, or, when united with water or alcohol, as a crystalline hydrate or alcoholate. It boils at about 172° C. (341.6° F.), and distils without decomposition. It is prepared by adding, little by little, from 3 to 4 parts of bromine to refrigerated alcohol. After fifteen hours of contact the mixture is distilled. The excess of bromine and the other volatile products come over first, and afterwards, at a temperature of from 160° C. (320° F.) to 180° C. (356° F.), the bromal, with an oily substance insoluble in water. Water being added, *bromal hydrate*, $C_2HBr_3O.H_2O$, is formed in rhombic scales fusing at 53.5° C. (128° F.). Much care should be exercised not to dispense bromal in combination with alkaloidal solutions and tinctures, due to the fact that bromal hydrate precipitates alkaloids from solution. Bromoform is formed when an alkali is added to a solution of bromal hydrate, and an alcoholate separates in a layer when an elixir or a tincture is added. According to S. Steinauer (*V. A. P. A.*, May 19, 1870), in frogs and mammals bromal produces at first great restlessness, followed by sleep of moderate intensity, accompanied by an almost complete analgesia. Dyspnea was usually very marked, and death sometimes occurred in convulsions. The cardiac ventricles after death were relaxed or tetanized, according as the dose had been large or small. Steinauer believes that the succession of symptoms is due to the first action being that of the bromal, and the subsequent, that of bromoform and nascent bromides generated in the blood from the bromal hydrate. Steinauer administered the drug to several patients, in *doses* of three grains (0.2 Gm.) at bedtime, with the effect of relieving pain or producing sleep. In *epilepsy* it seemed to avert the paroxysms.

Bromalbacid. *Albumen Bromate.*—This substance, whose therapeutic action is said to be identical with that of the bromides, is a *bromated egg albumen.* It is soluble in water and is administered in seven to ten (0.48–0.65 Gm.) grain *doses.*

Bromamide. *Tribromaniline Hydrobromide.* $C_6H_2Br_3NH_2HBr$.—This substance, which is said to contain 75 per cent. of bromine, and to be very stable, occurs in odorless, tasteless, colorless, needle-shaped crystals, insoluble in water, but soluble in sixteen parts of boiling alcohol, in chloroform, ether, and the fixed oils. It melts at

117.2° C. (243° F.), and volatilizes at 154.4° C. (310° F.) without change. It has been proposed by A. Caillé (*N. Y. M. J.*, 1892) as an antipyretic, antirheumatic, and analgesic. *Dose*, from ten to fifteen grains (0.65–1.0 Gm.).

Bromauric Acid. *N. F. IV. Acidum Bromauricum.*—The N. F. requires it to "contain HAu $Br_4 + 5H_2O$ (607.97) corresponding to not less than 32 per cent. of gold, Au. Preserve it in glass-stoppered, amber-colored bottles. It occurs as dark red-brown, flat, needle-shaped crystals, or as irregular, coarse granular masses; odorless, and having a metallic and acid taste. Permanent in the air when pure; when chloride is present the salt is deliquescent. Bromauric Acid melts at about 27° C. (80.6° F.). It is very soluble in water and in alcohol. Its aqueous solution is strongly acid to litmus, and yields with silver nitrate T.S. a yellowish-white precipitate, insoluble in nitric acid and but slightly soluble in ammonia water. Ignite 0.1 Gm. of Bromauric Acid, heat the resulting residue of gold with 5 mils of nitric acid, add 15 mils of distilled water and filter; no weighable residue remains on evaporating the filtrate and igniting. Dissolve 0.2 Gm. of Bromauric Acid in 10 mils of distilled water, add 16 mils of tenth-normal silver nitrate V.S. and 12 mils of ammonium carbonate T.S., digest the mixture for ten minutes on a water bath, then cool and filter. The filtrate, on super-saturating with nitric acid, does not become more than slightly opalescent (*chloride*). Bromauric Acid is decomposed on exposure to red heat and leaves a residue of metallic gold equivalent to not less than 32 per cent. of the weight taken."

It is used in the preparation of the N. F. solution of gold and arsenic bromide (see Part III). The *dose* is one-tenth grain (0.006 Gm.).

Brometone. *Tribrom Tertiary-Butyl Alcohol. Acetone Bromoform. N. N. R.* 1916. $CBr_3C(OH)(CH_3).CH_3$.—It is produced by the action of acetone on bromoform in a caustic alkali solution. It occurs in fine, white, prismatic crystals possessing a camphoraceous odor and taste. It is soluble in water and in almost all organic solvents. Brometone is said to have the sedative action of the bromides without the disadvantage of producing bromism. *Dose*, five grains (0.32 Gm.).

Bromile.—This is a combination of bromine with an unknown organic base. It occurs in large white scales, which are soluble in 8 parts of water, and, according to Filippi, represents 24 per cent. of bromine. It is used as a substitute for the bromides, especially in *epilepsy*, in *doses* of from thirty to sixty grains (2–4 Gm.).

Bromine. *N. F. IV* (*U. S. P. VIII*). *Bromum. Brominium. Brome*, Fr. Cod. *Bromum*, P. G.; *Brom*, G. *Bromo*, It., Sp.—Bromine was official in *U. S. VIII*, but it was dismissed and is now official in the National Formulary. "It contains not less than 98 per cent. of Br (79.92) and not more than 2 per cent. of Cl. Preserve Bromine in glass-stoppered bottles in a cool place, the bottle being enclosed in a larger vessel with the space between filled with some substance capable of absorbing and combining with any vapors which might escape." *N. F. IV.*

Bromine is an elementary body, possessing many analogies to chlorine and iodine. It was discovered in 1826 by Balard, of Montpellier, in the bittern of sea salt works, in which it exists as a magnesium bromide. Since then it has been found in the waters of the ocean, in certain marine animals and vegetables, in various aquatic plants, as the water cress, in numerous salt springs, and in the mineral kingdom. It has also been detected by Mène in the coal gas liquor of the Paris gas works. In the United States it was first obtained by Silliman, who found it in the bittern of the salt works at Salina, in the State of New York. It was discovered in the salt wells near Freeport, Pa., by David Alter, and is now obtained in largest amount from the brines of Ohio, Pennsylvania, Michigan, and West Virginia. The chief works are located at Parkersburg and Mason City, W. Va.; Pomeroy, Ohio, and Midland County, Mich. The annual production of bromine in the United States for the years 1914 and 1915 was as follows: 1914, 576,991 lbs., valued at $203,094, and in 1915, 855,857 lbs., valued at $856,307. The bromides contained in the mother liquors of the salt wells are oxidized by manganese dioxide in West Virginia and Ohio, while potassium chlorate is the favorite oxidizing agent in Michigan, because of the large proportion of calcium chloride in the liquor. Much is also produced in the latter state by electrolytic processes.

Preparation.—The original salt liquor or brine is pumped out of the ground at 9° B., evaporated to about 15° in large iron pans, then allowed to settle, and is further evaporated in wooden tanks heated by steam pipes to the point of crystallization of the salt. These tanks, five in number, are placed at different elevations, one above the other. Each day the liquor is run off from No. 1, the highest, to No. 2, next day to No. 3, and so on until it reaches No. 5, the crystallized salt being removed from each tank after draining off the liquor. The brine which reaches No. 5 is bittern, and consists chiefly of calcium magnesium, sodium, and some aluminum chlorides, with varying percentages of sodium and calcium bromides.

The bittern marking 30° to 38° B. is evaporated to about 45° B. By this further evaporation an additional percentage of impure salt is removed; the liquor is then run into stone stills, materials for generation of chlorine added, and heat applied by means of steam until the bromine has been all eliminated and vaporized. It is condensed and collected in cooled receivers. (*Proc. A. Ph. A.*, 1877, p. 448.) A bromine still is figured in *N. R.*, April, 1887; see also *N. R.*, 1883, 108; *Am. Drug.*, 1884, 121. The chief source of the bromine abroad is at Stassfurt in Germany, where the magnesium bromide remains as a residue in the working of the potassium salts. The bromine is extracted from the solution of bromide in a continuous process by the joint action of chlorine gas and steam.

Bromine has also been obtained from sea weeds by carbonizing them, lixiviating the carbonaceous residue, and then separating the ingredients, among which are iodine and bromine. For details, see *Chem. News*, July 6, 1866, p. 2. More than two-thirds of the bromine of commerce is used for the manufacture of bromides for medicinal use, and for photography; the remainder is used for aniline colors.

Properties.—The National Formulary IV gives the following description: "Bromine is a heavy, dark, brownish-red, mobile liquid, evolving, even at ordinary temperatures, reddish fumes, highly irritating to the eyes and lungs, and having a peculiar, suffocating odor, resembling that of chlorine. Specific gravity: about 3.016 at 25° C. (77° F.). Boiling point: about 63° C. (145.4° F.). One mil dissolves in about 90 mils of water; it is

freely soluble in alcohol, ether, chloroform, or carbon disulphide. On exposure to air it volatilizes. It destroys the color of solutions of litmus or indigo, and imparts a yellow color to starch T.S. Add 5 mils of Bromine to an excess of sodium hydroxide T.S.; it combines to form a permanently clear liquid, without the separation of oily drops (*organic bromine compounds*). Shake 10 mils of a saturated aqueous solution of Bromine with a slight excess of reduced iron until it becomes nearly colorless, filter the liquid and add 5 drops of ferric chloride T.S. and 5 drops of starch T.S.; it does not assume a blue color (*iodine*)."

Assay.—"Dissolve 10 Gm. of potassium iodide in 25 mils of distilled water, introduce the solution into a 100 mil measuring flask, stopper and determine accurately the weight of the flask and its contents. Add about 1 Gm. of Bromine to the contents of the flask, determine its exact weight and then fill the flask to the mark with distilled water and titrate 25 mils of this solution with tenth-normal sodium thiosulphate V.S., using starch T.S. as indicator. It shows not less than 98 per cent. of Br with not more than 2 per cent. of Cl. Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.007992 Gm. of Br. or 0.003546 Gm. of Cl. Each gramme of Bromine (containing not more than 2 per cent. of chlorine) corresponds to not more than 128.3 mils of tenth-normal sodium thiosulphate V.S." *N. F. IV.*

Bromine congeals at −7° C. (19.4° F.) and at −20° C. (−4° F.) becomes a hard, brittle, crystalline solid, having a dark leaden color, and a luster nearly metallic. It boils at about 63° C. (145.4° F.), forming a reddish vapor resembling that of nitrous acid, and of the sp. gr. 5.54. It evaporates readily, a single drop being sufficient to fill a large flask with its peculiar vapor.

Bromine is sparingly soluble in water to which it communicates an orange color, more soluble in alcohol, and still more so in ether, chloroform, and carbon disulphide. By the aid, however, of potassium bromide, it may be dissolved to any desirable extent in water. Its alcoholic and ethereal solutions lose their color in a few days and become acid from the generation of hydrobromic acid. It bleaches vegetable substances like chlorine, destroys the color of indigo sulphate, and decomposes organic matters. Its combination with starch has a yellow color. It corrodes the skin and gives it a deep yellow stain. Bromine is intermediate in its affinities between chlorine and iodine, since its combinations with metals are decomposed by chlorine, while, in its turn, it decomposes those of iodine. It forms acids which are analogous in properties and composition to the corresponding acids of chlorine and iodine.

Commercial bromine sometimes contains as much as 6 or 8 per cent. of *carbon tetrabromide*, as ascertained by Poselger. He discovered the impurity by submitting some bromine to distillation, during the progress of which the boiling point rose to 120° C. (248° F.). The residuary liquid at this temperature was colorless, and when freed from a little bromine, proved to be carbon bromine, as an oily, aromatic liquid. It is stated by T. L. Phipson that he has found in commercial bromine, accounted pure, a notable amount of cyanogen, and that it may be detected as follows. Take of iron filings and bromine, of each, half an ounce; add to the filings 2 or 2.5 ounces of water; introduce the bromine very gradually, stirring steadily; filter rapidly while warm from the reaction; and put the filtered liquid in a partially closed bottle. In the course of some hours a deposit of iron ferricyanide (Berlin blue) will have formed, and may be collected on a filter. In about two days the whole of the cyanogen will be deposited. In the samples of bromine thus examined he had found from 0.5 to 1 per cent. of cyanogen. (*Chem. News*, 1873, p. 51.) Chlorine and iodine are frequently found in bromine, the former being more common in American and the latter in German bromine.

In testing for bromine in mineral or saline waters, the water is evaporated in order to crystallize most of the salts. The solution, after having been filtered, is placed in a narrow tube, and a few drops of strong chlorine water are added. If this addition produces an orange color, bromine is present. The water examined, in order that the test may succeed, must be free from organic matter, and the chlorine not be added in excess. Bromine may be detected in marine vegetables by carbonizing them in a covered crucible, exhausting the charcoal, previously pulverized, with boiling water, precipitating any alkaline sulphide present in the solution by zinc sulphate, and then adding successively a few drops of nitric acid and a portion of ether, shaking the whole together. If bromine be present it will be set free and dissolve in the ether, to which it will communicate an orange color. (Dupasquier.) According to Reynoso, a more delicate test is furnished by hydrogen dioxide, which liberates bromine from its compounds without reacting on it when free. The mode of procedure is as follows: Put a piece of barium dioxide in a test tube, and add successively, distilled water, pure hydrochloric acid, and ether. The materials are here present for generating hydrogen dioxide; and as soon as bubbles are seen to rise to the surface, the substance suspected to contain bromine is added, and the whole shaken together. If a bromide be present, the hydrochloric acid will give rise to hydrobromic acid; and the hydrogen dioxide, acting on this, will set free the bromine, which will dissolve in the ether, and give it a yellow tint and the odor of Bromine.

Uses.—In concentrated solution Bromine is a powerful caustic and germicide. Its disinfectant properties appear to be somewhat inferior to those of chlorine; according to Koch, a 2 per cent. solution destroys the anthrax spores in twenty-four hours and Miquel gives the antiseptic limit as 1 in 1600. At one time it was employed internally in *scrofulous* and *syphilitic diseases*, but there is no reason to believe that it exercises any different effect upon the system from the salts of hydrobromic acid, and it has been entirely abandoned as an internal remedy. In dilute solution, from 10 to 40 minims to a pint of water, it is occasionally employed as a wash for *ulcers* but has no advantage over other disinfectants. It has been highly lauded by Goldsmith and others for its caustic and germicidal action in *hospital gangrene*. Applied pure it was found to destroy the diseased tissues more rapidly and thoroughly than did even strong nitric acid. Smith (*A. J. P.*, 1863, p. 202) suggested the following as a convenient formula for the application of Bromine in *hospital gangrene:* Dissolve 160 grains of potassium bromide in two fluidounces of water, add one troyounce of bromine, and, stirring diligently, pour in sufficient water to make the solution measure four fluidounces. The solution should be kept in tightly stoppered bottles. In overdoses it is a corrosive poison. About an ounce ingested caused

violent inflammation of the lips, mouth, tongue, and esophagus, with incessant burning pain, followed, in two hours and a half, by prostration, ending in death. (Snell, *N. Y. Journ. of Med.*, Sept., 1850.) In a vaporized state, it is one of the poison gases so frequently used in the trench warfare in France and Belgium in the European War. The best antidote, according to Alfred Smee, is ammonia, given largely diluted and mixed with sweet oil. Thiosulphates are also antidotes and an effective mask to prevent the inhalation of the fumes is provided by covering the mouth and nose with gauze which has been recently saturated with an aqueous solution of sodium thiosulphate.

Bromine Chloride. *Bromi Chloridum.* BrCl. —This chloride is prepared by passing chlorine gas through bromine, and condensing the vapors which form, by a freezing mixture. It is a reddish-yellow, very mobile and volatile liquid, emitting dark yellow fumes, which have a very powerful odor and cause a flow of tears. Its taste is hot and unpleasant. Lebeau doubts the existence of bromine chloride and states that it is a mixture of bromine and chlorine in which the chlorine is simply in solution in bromine. (*Chem. News*, 1906, 241.) Bromine chloride is used by Landolfi, of Naples, internally, in the treatment of *cancer* and as an ingredient in his caustic.

Bromipin. *N. N. R.* 1917.—*Brominized Sesame Oil* is probably a simple addition compound of bromine with the unsaturated oleins of sesame oil. The exact composition of this substance is not known, but it is asserted to be a stable combination of bromine and sesame oil. It is claimed for it that it has the sedative powers of potassium bromide and other alkaline bromides, but does not produce disturbances of the intestinal tract, skin, and general system which occur in bromism. Bromipin is used like the inorganic bromides in the treatment of *epilepsy, insomnia, neurasthenia*, and other conditions of chronic hyper-excitability of the nervous system. It appears to be more slowly absorbed than the ordinary bromides and therefore exercises a more evenly continuous effect. Although Bermann (*Th. M.*, 1910) has found that the larger part of the bromine appeared in the urine as an inorganic bromide, there is reason to believe that a larger proportion of the bromine of bromipin than of the inorganic bromides is taken up by the central nervous system, because of the fatty combination.

Bromipin is marketed in two forms, one of which contains 10 per cent. and the other 33⅓ per cent. of bromine. Of the weaker solution, which is the one generally preferred, 1 teaspoonful corresponds to about eleven grains (0.7 Gm.) of potassium bromide. The ordinary *dose* of the 10 per cent. bromipin is one-half to one fluidrachm (2–4 mils), which may be gradually increased to two or three fluidrachms (7.8–11.7 mils).

Bromochinal. *Bromoquinal Acid. Quinine dibromsalicylate.* $C_{20}H_{24}O_2N_2.2(C_6H_2Br_2.OH.COOH)_2$.—Bromochinal occurs in yellow crystals, sparingly soluble in water, alcohol, or ether. According to Von Noorden, in *doses* of nine to twelve grains (0.6–0.78 Gm.) given twice a day, it acts as a feeble antipyretic and is also soporific. (*Ther. Geg.*, v.)

Bromocoll. *Dibromtannin-gelatin.*—This is a yellow, tasteless, odorless powder, composed of 20 per cent. of bromine, 10 per cent. of water, 30 per cent. of gelatin, and 40 per cent. of tannic acid. According to the experiments of Brat (*Th. M.*, 1901, xv, 4), bromocoll is very resistant to gastric juice, but is readily dissolved with decomposition in the intestinal juices. It is claimed that it acts precisely like the bromides, but produces the disagreeable symptoms of bromism only in a very mild degree. Friedländer (*Th. M.*, 1901) determined by experimentation that it depresses the irritability of the psychomotor centers. Meier (*Med. Klin.*, 1906) has found that the subcutaneous injection of bromocoll is useful, at least in the lower animals in strychnine poisoning and in *tetanus*. The *dose* is thirty to seventy-five grains (2–5 Gm.) a day.

Bromol. *Tribromophenol. Tribromphenol.* $C_6H_2Br_3OH$.—Bromol is obtained as a white flocculent and gradually crystallizing sediment when bromine water is added to an aqueous solution of phenol. Pure tribromophenol occurs as a white, crystalline substance which melts at a temperature of 92° C. (197.6° F.), and is nearly insoluble in water, but readily so in alcohol, ether, chloroform, glycerin, and in fatty and ethereal oils; the odor is disagreeable, like that of bromine, but more penetrating; the taste is sweet and astringent. According to Grimm and Rademacher, tribromophenol is a powerful antiseptic and disinfectant, which, when in concentrated form, acts as a caustic, and is especially valuable in the treatment of *tuberculous ulcers* and *gangrene*. Grimm considered the remedy too caustic to be used upon the mucous membrane of the upper air-passages, but Rademacher has used it in the solution of olive oil (2 to 30) with asserted excellent results in *diphtheria*. It is said to be very slowly acted upon by the intestinal juices, and has been used as an intestinal disinfectant in *doses* of from three to eight grains (0.2–0.5 Gm.) a day. That it is absorbed in some form is shown by the fact of its excretion in the urine in the form of *tribromophenol-sulphonic acid*.

Bromolecithin. *Bromlecithin.*—This is asserted to be an additive product of bromine and lecithin containing from 25 to 30 per cent. of bromine, and is supposed to combine the tonic effect of lecithin with the sedative action of bromine. It is marketed in the form of tablets, each one of which represents three-quarters of a grain (0.05 Gm.) of the compound. From five to ten tablets may be given daily.

Bromolein is an addition product of bromine in which the unsaturated fatty oleins of the almond oil have taken up the bromine necessary for their saturation. This substance, introduced by Coronedi and Marchetti (*Settimana med.*, 1899, liii), is a yellow, clear, oily liquid, containing 20 per cent. of bromine combined with olein of the oil of sweet almonds. It is asserted that it may be used hypodermically or upon the skin, and affords an excellent means of using the bromides in nervous diseases, acting like the older bromides without causing bromism. It is said also not to be decomposed by the enzyme of the pancreas. The *dose* of bromolein is from one-half to one fluidrachm (1.9–3.9 mils).

Bromo-mangan is a ferro-mangan with the addition of 3 per cent. bromo-peptone which contains 11 per cent. bromine. It is a dark brown liquid of agreeable odor and taste, and is asserted to be a reconstructive tonic, especially efficient in the treatment of nervous conditions associated with anemia.

Bromophenol. *Phenol Monobromate. Orthomonobromphenol,* $C_6H_4Br.OH$, is obtained by the combination of bromine and phenol at a temperature of 150°–180° C. (302°–356° F.). It is a dark

yellow, oily, strong smelling fluid, soluble in alcohol and ether, slightly in water. It is used as a 2 per cent. ointment in the treatment of *erysipelas*, also to disinfect the sputum.

Bromophor.—This preparation, which is stated to be the *dibrom-ricinoleate*, is recommended as an external application in *pruritus* and *erysipelas*. According to Linke, however (*Ther. Neuheiten*, March, 1910), its use in *erysipelas* is not to be recommended because of its intense irritation of the skin.

Bromopyrin. *Monobromantipyrin.* $C_{11}H_{11}BrN_2O$.—This occurs in white, crystalline needles, almost insoluble in cold water, scarcely soluble in hot water, easily soluble in alcohol and chloroform. Its melting point is 114° C. (237.2° F.). Its influence upon the system seems not to have been investigated. A mixture of antipyrin, caffeine, and sodium bromide has also been sold as bromopyrin which must not be confused with the original compound.

Bromosin is a preparation similar to Bromalbacid (see p. 1286) containing 10 per cent. bromine.

Bromotan. *Bromotannin-methylene urea* is a light brown, odorless and tasteless powder, insoluble in water. It has been employed by Rockstroth (*Th. M.*, 1906) in the treatment of moist *eczema*. He finds it especially of service to control the itching. It may be mixed with four to five times its weight of talcum or zinc oxide and used as a dusting powder or as a 10 per cent. ointment.

Bromural. *N. N. R.* 1917. *Alpha-monobrom-isovaleryl urea.* $(CH_3)_2CH.CH.Br.CO.NH.CO.NH_2$.—This occurs as white, almost tasteless, needle-like crystals, soluble in hot water, ether, and alcohol, but only sparingly in cold water. Its melting point is 147°–149° C. (296.6°–300.2° F.). Bromural has been widely employed as a general nerve sedative and as a mild somnifacient. Eeckhout (*A. E. P. P.*, lvii, p. 338) administered to a rabbit 0.1 Gm. daily for two weeks with no apparent disturbance of the health. Sollmann and Hatcher (*J. A. M. A.*, 1908, li, p. 487), however, have found that in cats the relation of the sleep-producing to the fatal dose of bromural was practically the same as that of chloral, and that the effects of bromural come on even more quickly than those of chloral hydrate and last for a comparatively short time. According to Eeckhout, the action is similar to that of the bromides. Takeda (*A. I. P. T.*, 1911, xxi, p. 203) has, however, shown that only a small percentage of the molecule is decomposed in the body, and believes that the drug acts as bromural, not as its constituent parts.

While it is often of service in the milder types of *insomnia*, in severer cases bromural is an uncertain hypnotic. Its most important use is as a general nerve sedative, for which purpose it appears to combine the sedative actions of both the bromides and valerian. Like the bromides it has a certain amount of anodyne power in *neuralgic* pains and like valerian is useful to control the various *hysterical* manifestations. It appears, also, according to the experience of Ferrata and Golinelli (*Gaz. Internaz.*, 1908, No. 13), to exercise the motor sedative effect of the bromides in *epilepsy*. It has also been recommended as a sedative in *asthma*, in *whooping cough*, and for *sea-sickness*. The *dose* of bromural, as a sedative, is from five to ten grains (0.32–0.65 Gm.) several times a day, as may be required, as a hypnotic from ten to twenty grains (0.65–1.3 Gm.) should be administered immediately before retiring. It may be prescribed either in the form of a tablet or as a powder enclosed in a capsule.

Brovalol. *N. N. R.* 1917. *Brom-iso-valeric acid borneol ester. Bornyl brom-valerate. Valisan.* $CH_3CH(CH_3).CHBr.CO.O.(C_{10}H_{17})$.—A colorless, oily liquid, having a slightly aromatic odor, prepared by esterification of borneol with brom-isovaleric acid or its derivatives. It contains 25.2 per cent. bromine. Brovalol has been used as a nerve sedative in the same type of cases in which valerian is employed. It appears on the market in "pearls," each of which contains four grains (0.25 Gm.). The *dose* is one to three pearls, repeated as required.

Brunswick Green.—A color pigment, chemically either *copper oxycarbonate* or *oxychloride*.

Bryonia. *N. F. IV. Bryony.*—The N. F. describes it as "the dried root of *Bryonia alba* Linné or of *Bryonia dioica* Jacquin (Fam. *Cucurbitaceæ*), without the presence of more than 5 per cent. of foreign matter. Usually in circular or elliptical slices, obtained by cutting the root more or less transversely, from 1.5 to 10 cm. in breadth and from 3 to 15 mm. in thickness; the edges light gray or yellowish, rough and striate, the cut surface white or faintly yellow, showing a thin cortex and a wood with numerous projecting, collateral fibro-vascular bundles arranged in concentric zones; fracture short and mealy, whitish internally. Odor faint but distinct and characteristic; taste bitter and nauseous. The powdered drug is of a light yellow color and, when examined under the microscope, shows simple, rounded, or two- or more compound, starch grains from 0.004 to 0.024 mm. in diameter, frequently with a central cleft, tracheæ from 0.035 to 0.25 mm. in width, reticulate or with bordered pores, and large yellow cork cells. Add sulphuric acid to the powdered drug; it becomes reddish-brown and then brownish-purple. Bryonia yields not more than 8 per cent. of ash."

The peasants are said sometimes to hollow out the top of the root, and to employ the juice which collects in the cavity as a drastic purge. (Mérat and De Lens.) The berries are also purgative, and are used in dyeing. *B. americana* Lam. and *B. africana* Thumb. are respectively used in the West Indies and Africa as hydragogue cathartics in *dropsy*. The berries of the European *black bryony* (*Tamus communis* L.) are said to be an irritant poison, and Coutagne has found that their tincture causes in animals paralysis and convulsions. (See *Rép. de Pharm.*, Nov., 1884; also *P. J.*, Jan., 1903.)

Bryonia contains a glucoside, *bryonin*, $C_{48}H_{80}O_{19}$, and a peculiar resin called *bryoresin*. According to Power and Moore (*Tr. Chem. Soc.*, 1911, xciv), bryonin is a mixture of a glucoside and an alkaloid, neither of which is physiologically active. The activity of the plant resides in its resin. Bryonin occurs as a brownish-yellow amorphous powder of bitter taste, soluble in water and alcohol. It is used as a cathartic in hepatic congestion and in conditions following acute infectious diseases. *Dose*, one-sixtieth of a grain (0.001 Gm.) every two hours.

Bryonia is an active irritant hydragogue cathartic. In a number of cases it has produced serious or even fatal poisoning. Vomiting and purging have been commonly present, but in some cases there has been no diarrhea. Giddiness, delirium, and dilated pupils, coupled with fall of

the bodily temperature, imperceptible pulse, cold perspiration, and other manifestations of collapse, are the usual symptoms. Eighty minims (5 mils) of the homeopathic tincture caused very serious but not fatal poisoning. (For cases, see *P. J.*, 1858, p. 542; *L. L.*, May 9, 1868; *B. M. J.*, 1883, ii, 1067; *T. G.*, ii, 35; also *Woodman and Tidy.*) The fresh root is highly irritant, and is said, when bruised and applied to the skin, to be capable of producing vesication. The medicine was well known to the ancients, and has been employed as a hydragogue cathartic in *dropsy. Dose*, ten to thirty grains (0.65–2.0 Gm.). The tincture is official in the N. F. (see Part III).

Burgundy Pitch. *Pix Burgundica. Poix de Bourgogne, Poix des Vosges, Poix jaune*, Fr. Cod. *Poix blanche*, Fr. *Burgundisches Pech, Burgunder Harz. Wasserharz*, G. *Pece di Borgogna*, It. *Pez de Borgoña*, Sp.—Under the name of *Pix Burgundica* was formerly recognized both by the British (1898) and by the U. S. (1890) Pharmacopœias, "the resinous exudation obtained from the stem of the *Picea excelsa* Link., melted and strained." *Br.*, 1898.

Picea abies (L.) Karst. or *P. excelsa* Link. (Fam. *Pinaceæ*), commonly known as Norway spruce, is a lofty tree, rising sometimes one hundred and fifty feet in height, with a trunk from three to five feet in diameter. The leaves, standing thickly upon the branches, are short, obscurely four-cornered, often curved, of a dusky green color, and shining on the upper surface. The male aments are purple and axillary, the female of the same color, but usually terminal. The fruit is in pendent, purple, nearly cylindrical strobiles, the scales of which are oval, pointed, and ragged at the edges. This tree is a native of Europe and Northern Asia, and is cultivated in the United States as a shade tree. Commercially Burgundy pitch is derived not only from the Norway spruce, but also from the *Abies picea* or European silver fir tree. To obtain the *pitch*, portions of the bark are removed so as to lay bare the wood, or perpendicular grooved channels are cut, and the flakes of concrete resinous matter which form upon the surface of the wound, having been detached by iron instruments, are melted with water in large boilers, and then strained through coarse cloths. It is called Burgundy pitch from the province of that name in the east of France, although whether it was ever produced in that province is uncertain. It is chiefly collected in Finland, the Schwarzwald, Austria, and the Bernese Alps. A *factitious Burgundy pitch* is made by melting together common pitch, rosin, and turpentine, and agitating the mixture with water, which gives it the requisite yellow color. Its odor is different from that of the genuine. Hanbury gives as a test of true Burgundy pitch that it is almost entirely soluble in twice its weight of glacial acetic acid while the factitious article similarly treated forms a turbid mixture quickly separating into a thick oily liquid above and a bright solution below.

The resinous exudation from *Pinus sylvestris* is sometimes offered as Burgundy pitch, but Hirschsohn (*Ph. Z. R.*, xxiv) states that it is possible to distinguish the resin of *Picea excelsa* by its being only partially soluble in ether, chloroform, and solutions of salts of ammonium, sodium carbonate, and borax, which dissolve completely the resin of *Pinus sylvestris*. The resin of *Picea excelsa* is also precipitated by the addition of water from its sulphuric acid solution in red violet flakes, while *Pinus sylvestris* resin precipitates white.

As brought to this country, Burgundy pitch is generally mixed with impurities, which require that it should be melted and strained before being used. In its pure state, according to the U. S. P., 1890, it is "hard, yet gradually taking the form of the vessel in which it is kept; brittle, with a shining, conchoidal fracture, opaque or translucent, reddish-brown or yellowish-brown, odor agreeably terebinthinate; taste aromatic, sweetish, not bitter. It is almost entirely soluble in glacial acetic acid, or in boiling alcohol, and partly soluble in cold alcohol." *U. S.*, 1890. It is very fusible, and at the heat of the body softens and becomes adhesive. It differs from turpentine in containing a smaller proportion of volatile oil. Instead of the sylvic acid of ordinary rosin, it contains an isomeric acid, which has been called *pimaric acid*, melting at 148° to 149° C. (298.4°–300.2° F.), difficultly soluble in cold but readily soluble in boiling alcohol, and also soluble in ether. According to Perrenoud, its formula is $C_{30}H_{54}O_4$, but Vesterberg (*Ber. d. Chem. Ges.*, 1885, p. 3331) showed it to be a mixture, and has since (*Ibid.*, 1886, p. 2167, and 1887, p. 3248) prepared from it two isomeric crystalline acids, a *dextropimaric acid* and a *lævopimaric acid*, both of the formula $C_{20}H_{30}O_2$; with these is mixed a varying amount of an amorphous resin acid known as *pinic acid.*

Applied to the skin, in the shape of a plaster, Burgundy pitch acts as a gentle rubefacient, producing a slight inflammation without separating the cuticle. Sometimes it excites a papillary or vesicular eruption, and we have known it to act as a violent irritant, giving rise to severe pain, swelling, and redness, followed by vesication and even ulceration. It is used chiefly in chronic *rheumatic pains*, and in chronic affections of the chest or abdomen, which call for a gentle but long-continued revulsion of the skin.

Burra Gookeroo or *Burra Gokhroo.*—Under this name, in India, the fruit and sometimes the whole plant of the *Tribulus terrestris* L. (Fam. *Zygophyllaceæ*) is used as a diuretic and aphrodisiac. The carpels have been commended in London as a remedy in *nocturnal emissions; dose* of fluidextract, from twenty minims to one fluidrachm (1.3–3.75 mils).

Butylchloral-Antipyrine. *Butyl-hypnal.* $C_{11}H_{12}N_2O + C_4H_5Cl_3H_2O$.—This compound results when antipyrine and butylchloral hydrate, in the proportion of 188 parts of the former to 193.5 parts of the latter, are triturated together; the resulting oily liquid dissolved in hot water, and the solution set aside to crystallize. It is in the form of colorless, needle-like crystals, melting at 70° C. (158° F.), and soluble in about 30 parts of water. Its incompatibilities are the same as those of antipyrine, being also decomposed by alkalies. It liquefies when triturated with some of the synthetic drugs—urethane, exalgin, etc. *Dose*, of butylchloral-antipyrine, from five to twenty grains (0.32–1.3 Gm.) as an analgesic and hypnotic.

Butyl-iso-Phenate. $C_4H_9.C_6H_4OH$.—A colorless liquid, soluble in alcohol, ether and chloroform; specific gravity at 15° C. (59° F.) 0.935; it boils at 198° C. (388.4° F.). It is used as an external antiseptic, although it has also been proposed for internal administration.

Buxus. *Buxus sempervirens* L. *Evergreen Box.* (Fam. *Buxaceæ.*)—This evergreen shrub is too well known to require description. Though much cultivated in this country as an ornamental plant, it is a native of Europe and Western Asia.

The wood is considered diaphoretic in its native countries, and is used in decoction in *rheumatism, secondary syphilis,* etc. The leaves, which have a peculiar odor and a bitter and disagreeable taste, are said to be purgative in the *dose* of a drachm. A volatile oil distilled from the wood has been given in *epilepsy.* A tincture formerly enjoyed some reputation as an antiperiodic. (Mérat and De Lens.) The alkaloid *buxine,* which has been discovered in the leaves of this tree, is identical with the bebeerine of nectandra bark. (See p. 1274; also *P. J.,* Oct., 1869, 194.) Pavia obtained a second alkaloid from *Buxus sempervirens,* which was investigated by Pavesi and Rotondi. (*Jahresberichte,* 1874, 903.) They named it *parabuxine,* and ascribed to it the formula $C_{24}H_{43}N_2O$. Barbaglia (*A. J. P.,* 1885, 145) described still another alkaloid, *parabuxinidine.* It crystallizes in thin, colorless prisms, is insoluble in water, soluble in ether, freely soluble in alcohol, and colors turmeric paper deep red.

Cabbage-Tree Bark. *Ecorce de Geoffre,* Fr. *Kohlbaumrinde, Wurmrinde,* G.—The bark of *Vouacapoua inermis,* Swz. (*Andira inermis* H. B. K.) This is a leguminous tree, with a stem rising to a considerable height, branched towards the top, and covered with a smooth gray bark. The tree is a native of Jamaica, and other West India islands. The bark, which is the part used, is in long pieces, thick, fibrous, externally of a brownish-ash color, scaly, and covered with lichens, internally yellowish, of a resinous fracture, a disagreeable odor, and a sweetish, mucilaginous bitterish taste. Huttenschmidt obtained from it a crystallizable, bitter alkaloid and named it *jamaicine.* Two grains (0.13 Gm.) of it produced violent purging in pigeons.

On the continent of Europe the bark of *Vouacapoua retusa* Poir, which grows in Surinam, has also been used. It is considered more powerfully vermifuge and less liable to produce injurious effects. It has a grayish epidermis, beneath which it is reddish-brown, laminated, compact, and very tenacious, and, when cut transversely, exhibits a shining and variegated surface. In the dried state it is inodorous, but has an austere bitter taste. The powder is of a pale cinnamon color.

Cabbage-tree bark is cathartic, and, in large doses, prone to occasion vomiting, fever, and delirium. It is said that these effects are more liable to result if cold water be drunk during its operation, and may be relieved by the use of warm water, castor oil, or a vegetable acid. In the West Indies it is esteemed a powerful vermifuge, and is much employed for expelling *lumbrici;* but it is dangerous if incautiously administered, and instances of death from its use have occurred. It is almost unknown in this country. The usual form of administration is that of decoction, though the medicine is also given in powder, syrup, and extract. The *dose* of the powder is from twenty to thirty grains (1.3–2.0 Gm.); of the extract three grains (0.2 Gm.).

Theodore Peckoldt says of the wood of an allied species, *Vouacoupoua Anthelmia* (Vell.) O. Ktze, that the workmen engaged in sawing it are prone to be affected with inflammation of the eyes, constriction of the throat, excessive thirst, a bitter, burning taste, a troublesome itching over the body, and sometimes eruptions on the skin. By treating a concentrated decoction of the wood with calcium hydroxide, then filtering after forty-eight hours, evaporating to the consistence of syrup, and exhausting the residue with alcohol, Peckoldt obtained a yellowish-brown coloring matter which he called *andirin.* (This name has also been given to a glucoside said to have been found in *Vouacapoua inermis.* See *A. J. P.,* 1885, 558.) Peckoldt also obtained a peculiar resin by treating the wood with alcohol, filtering, distilling off most of the alcohol, and then precipitating by water. The resin is inodorous, of a bitter, acrid taste, soluble in alcohol, and but partially soluble in ether. This resin, and especially the portion soluble in ether, gives its irritating properties to the sawdust. (*Chem. Cb.,* Nov. 17, 1858.)

Cacodylic Acid. *Acidum Cacodylicum.* $AsO(CH_3)_2OH$.—Cacodylic Acid is a deliquescent, colorless, crystalline, and odorless solid, which is, however, chemically quite stable. It is very soluble in water with an acid reaction. Cacodylic Acid is *dimethyl-arsenic acid;* that is, arsenic acid in which two hydroxyl radicles have been replaced by two methyl radicles. In the metallic cacodylates the hydrogen in the remaining hydroxyl is replaced by the base; sodium cacodylate is, therefore, $As(CH_3)_2OONa$. The physiological and medicinal properties of Cacodylic Acid are the same as those of sodium cacodylate. (See Part I.) It is, however, rarely used except in the form of one of its salts.

The following preparations have been suggested:

Calcium Cacodylate. Calcii Cacodylas. $[(CH_3)_2AsO_2]_2Ca + aq$.—A white powder, soluble in water.

Guaiacol Cacodylate.—A reddish-white crystalline mass, which dissolves in alcohol and parts with cacodylic acid in the presence of water. Dissolved in oil it has been employed hypodermically in *tuberculosis.* From one to one and a half grains (0.065–0.096 Gm.) may be exhibited every other day.

Iron Cacodylate. Ferri Cacodylas. Ferricodil.—A grayish-yellow amorphous powder freely soluble in water, especially when heated, less soluble in alcohol. This salt has been specially recommended by Gilbert and Lereboullet (*R. T.,* 1900, No. 16) for hypodermic use in the treatment of *leukemia, lymphadenoma,* and other serious *anemias.* Montgomery (*J. A. M. A.,* 1916, lxvi, p. 491) calls attention to the fact that iron cacodylate even when given hypodermically may cause the disagreeable garlicky odor of the breath. It is too irritant to be used in concentrated solution, but as much as one grain (0.065 Gm.) dissolved in half a fluidrachm (1.8 mils) of water may be injected daily. The *dose* by mouth is one to two grains (0.6–0.12 Gm.) several times a day, hypodermically one-half to two grains (0.03–0.12 Gm.) may be given once a day.

Lithium Cacodylate. Lithii Cacodylas. $(CH_3)_2AsO_2Li + aq$.—A light, white powder, soluble in water. *Dose,* one-half to two grains (0.032–0.13 Gm.).

Magnesium Cacodylate. Magnesii Cacodylas. $[(CH_3)_2AsO_2]_2Mg + aq$.—A white powder, soluble in water. *Dose,* one-half to two grains (0.032–0.13 Gm.).

Mercury Cacodylate. Hydrargyri Cacodylas. $[(CH_3)_2AsO_2]_2Hg$.—White crystals freely dissolving in water, but sparingly soluble in alcohol. The solution of pure mercury cacodylate is unstable and locally irritant, and there has been introduced, under the same name, a double salt formed with sodium chloride. Mercury cacodylate is used in the treatment of *syphilis.* Its supposed advantage is in the belief that the cacodylic acid exercises some direct remedial action in syphilis, and will therefore enhance the effects of the

mercury. It is generally administered hypodermically in the form of a 5 per cent. solution of which eight to fifteen minims (0.5–0.9 mil) may be given daily, representing one-third to three-fourths of a grain (0.025–0.05 Gm.).

Potassium Cacodylate. Potassii Cacodylas. $(CH_3)_2AsO_2K$ + aq.—Small, white crystals, soluble in water, but sparingly soluble in alcohol and insoluble in ether.

Quinine Cacodylate. Quininæ Cacodylas. $C_{20}H_{24}N_2O_2(CH_3)_2AsOOH$.—A white powder, more freely soluble in cold than in hot water, but freely soluble in alcohol. *Dose*, one-half to two grains (0.032–0.13 Gm.).

Strychnine Cacodylate.—This salt occurs as a white, crystalline powder, soluble in 750 parts of water and 100 parts of warm alcohol. The aqueous solution is very unstable and should be dispensed only for immediate use. The dose is similar to that of other strychnine salts being given, however, in increasing *doses* commencing with one-sixtieth of a grain (0.001 Gm.). It is used in the treatment of *tuberculosis*.

Cactus Grandiflorus. *N. F. IV. Night Blooming Cereus.*—Cardiac stimulant properties have been attributed to two Cacti—namely, *Cereus Bonplandii* Parm. and *Cereus grandiflorus* Miller (*Cactus grandiflorus* L. *Night-blooming Cereus. Cierge à grandes fleurs*, Fr. *Königin der Nacht*, G.). Of these the latter only is now used in practical medicine. It is a native of tropical America, often cultivated in hot houses for the interest in its very fragrant night-opening white flowers. The N. F. drug is "the fresh succulent stems of the wild growing *Cactus grandiflorus* Linné (*Cereus grandiflorus* Miller) (Fam. *Cactaceæ*). As found in commerce, Cactus Grandiflorus is usually preserved in alcohol and the amount of alcohol present should be stated on the label. It occurs in pieces of varying length, from 1.5 to 4 cm. in diameter, and from five to seven angled. On the angles at intervals of about 2 cm. are tufts of from nine to twelve spines, each about 2 mm. in length, and three slender flexuous spines about 1 cm. in length; at irregular intervals are branched roots. It has a strong, herby odor; taste acidulous and mucilaginous. The transverse section shows a central cylinder about 3 mm. in diameter and a spongy parenchyma containing large crystals and raphides of calcium oxalate." *N. F. IV.* Due to the difficulty in obtaining this drug commercially the larger drug houses arrange for its collection and preservation for their own manufacturing. F. W. Sultan (*A. J. P.*, 1891, 424) believed that he had found in it an alkaloid, *cactine*, but the existence of this alkaloid is extremely doubtful.

It has long been used in tropical America in the treatment of *dropsy*. It was first brought into notice as a cardiac remedy by Rubini, of Naples. According to Myers (*N. Y. M. J.*, June, 1891), it elevates the arterial tension by increasing the muscular energy of the heart, and by contracting the arterioles through the vasomotor centers. Considerable clinical testimony has been given to the value of cactus as a cardiac regulator in functional disorders of the heart connected with *neurasthenia, Graves's disease, tobacco toxemia*, and allied affections. On the other hand, Hatcher and Bailey (*J. A. M. A.*, 1911, lvi, p. 26), experimenting with carefully identified specimens of the *Cactus grandiflorus*, as well as commercial preparations purporting to be of this drug, were unable to recognize any action upon the circulation, even when given in enormous doses.

Sharp could obtain from the drug only resins which were inactive, and concludes that it is inert. (*Pract.*, Sept., 1894.) The usual *dose* of the fluid extract is from five to ten minims (0.3–0.6 mil).

From *Cereus Cæspitosus* Engl. and A. Gray, Heyl separated an alkaloid, *pectenine*, which, according to Heffter (*A. Pharm.*, 1901, ccxxxix, s. 462), produced both in cold and warm blooded animals tetanic convulsions with heightened reflexes. According to the experiments of Mogilewa, the alkaloid acts upon the isolated frog's heart as a depressant.

From *Cereus pilocereus* (?), Heyl separated the alkaloid *pilocerëine*, which Hefftner found to produce in frogs central paralysis with great cardiac depression, and in warm blooded animals to kill by cardiac arrest.

Anthelmintic properties have been ascribed to *Cereus flagelliformis* Miller and to *C. divaricatus* (Lam.) DC.

Cacur.—This is a small gourd which, while still unripe, is used by the Kaffirs as an emetic, and which, according to Oliver, is yielded by the *Cucumis myriocarpus* Naud. (Fam. *Cucurbitaceæ*.) G. A. Atkinson (*A. J. P.*, 1887) obtained from it a neutral resinous body, *myriocarpin*, and found that twenty grains (1.3 Gm.) of the fresh pulp produced in man nausea and slight purgation. (*Ed. M. J.*, July, 1886.)

Cadmium. *Kadmium*, G.—This metal is associated with zinc in its ores, occurring principally as *greenockite* (CdS), a yellowish incrustation upon *zinc blende* (ZnS), and, being more volatile than that metal, comes over with the first portions of the zinc in the process for obtaining it. (See *Zincum.*) The cadmium is separated by dissolving the alloy metals in diluted sulphuric acid, precipitating the sulphate by hydrogen sulphide, treating the precipitates with hydrochloric acid, and again precipitating with ammonium carbonate. The cadmium carbonate thus obtained, after being washed and dried, is mixed with charcoal, and exposed to a dull red heat in an earthen retort, when the reduced metal distils over.

Properties.—Cadmium is a white metal, resembling tin, but somewhat heavier and more tenacious. Like that metal, it crackles when bent. Its sp. gr. is 8.7, melting point from 316° to 320° C. (600.8°–608° F.). It begins to volatilize at a temperature slightly above this, but under the boiling point of mercury, while it boils only at 770° C. (1418° F.). It is little affected by the air, but, when heated, combines with an atom of oxygen, forming a reddish-brown or orange-colored oxide, CdO, which combines with the acids to form salts. From its saline solutions the oxide is precipitated by the alkalies in the form of a white hydroxide. Cadmium also combines with chlorine, iodine, bromine, and sulphur. It is distinguished by forming a colorless solution with nitric acid, from which hydrogen sulphide or ammonium sulphide precipitates a lemon-yellow sulphide insoluble in an excess of the reagent or in solution of potassium hydroxide or ammonia water, and not volatilized at a red heat. Potassium hydroxide produces a white precipitate insoluble in an excess, and ammonia a similar precipitate soluble in an excess of the precipitant. Zinc precipitates Cadmium in the metallic state. The soluble Cadmium salts give white precipitates with hydroxides, carbonates or phosphates; and yellow precipitates with soluble sulphides or chromates.

Cadmium Iodide. Cadmii Iodidum. (CdI_2.) *Cadmium Iodatum. Iodidum Cadmicum. Iodure de Cadmium*, Fr. *Jodcadmium, Kadmiumjodür*,

G.—Cadmium Iodide may be prepared by mixing iodine and filings of cadmium in a moist state, or by dissolving the metal in hydriodic acid, or by double decomposition between potassium iodide and cadmium sulphate. It is soluble in water and alcohol, and may be crystallized from either solution, in large, white, transparent crystals, in the form of six-sided tables, of a pearly luster. These are permanent in the air, melt at 404° C. (759.2° F.), forming an amber-colored liquid, and give off violet vapors at a dull red heat. The salt is freely soluble in water and in alcohol, and the solution has an acid reaction.

Cadmium iodide was introduced by A. B. Garrod as an external remedy in the treatment of *scrofulous glands, nodes, chronic inflammation of joints,* and various *cutaneous diseases.* The ointment, which was formerly official in the British Pharmacopœia under the name of *Unguentum Cadmii Iodidi* (sixty-two grains to one ounce of simple ointment), is soft, white, and said to readily yield its iodine to absorption when applied by persistent gentle friction.

Cadmium Nitrate.—H. C. Dunning recommends a solution of this salt as an insecticide. (*Proc. Penna. Pharm. Assoc.,* 1909, 240.)

Cadmium Salicylate. Cadmii Salicylas. $Cd(C_7H_5O_3)_2 + H_2O$.—Prepared by acting on cadmium oxide with salicylic acid. It is colorless and crystalline, soluble in 24 parts of boiling water, and in alcohol, ether, and glycerin. It is used as an antiseptic.

Cadmium Sulphate. Cadmii Sulphas. Cadmium Sulfuricum. Sulfas Cadmicus. Sulfate de Cadmium, Fr. *Schwefelsaures Cadmiumoxyd, Kadmiumsulfat,* G. $CdSO_4.4H_2O$.—Cadmium Sulphate crystallizes in oblique prisms with rhomboidal bases, which are transparent and colorless, and resemble those of zinc sulphate. The ordinary crystals of cadmium sulphate have the formula $CdSO_4.8H_2O$, and, at very low temperature, $CdSO_4.7H_2O$. They have an astringent, slightly acidulous, and harsh taste, effloresce on exposure to the air, and are very soluble in water. The solution, even though acidulated, gives with hydrogen sulphide a yellow precipitate, becoming orange-yellow, of cadmium sulphide, which is dissolved by strong hydrochloric acid, but is insoluble in solutions of potassium hydroxide or ammonia, and is thus readily distinguished from arsenic sulphide. Zinc precipitates Cadmium in the metallic state from the solution. Cadmium suspended in a solution of copper sulphate precipitates that metal, leaving cadmium sulphate in solution, and this has been proposed as a method of obtaining the salt. For method of manufacture and tests of purity of cadmium sulphate, see *U. S. D.,* 19th ed., p. 1425.

Medicinal Uses of Cadmium.—It is probable that the insoluble preparations of Cadmium are not actively poisonous, but it is certain that the soluble preparations are corrosive poisons, causing in overdoses giddiness, vomiting, purging, slowing of the pulse and respiration, loss of consciousness, and spasm. In three cases in which the carbonate is said to have been inhaled, the chief symptoms were constriction of the throat, embarrassed respiration, vomiting and purging, giddiness, and painful spasms. (*Ann. Thér.,* 1859.) For a case of poisoning by the *bromide,* see *B. M. S. J.,* 1876.

It has been shown by Athanasius and Langlois (*C. R. S. B.,* 1895, ii) that the soluble salts of Cadmium arrest lactic fermentation. When given hypodermically they produce symptoms similar to those caused by zinc salts, than which, however, they are less powerful; the symptoms are rapid loss of voluntary motion with persistence of the reflexes and pronounced cardiac depression. In the higher animals there is destruction of the red blood corpuscles.

Cadmium Sulphate has been used as a local astringent and stimulant in *diseases of the eye* and in *gonorrhea.* It is employed either in solution, from half a grain to four grains to the fluidounce of distilled water, or in ointment, twelve grains to the ounce of simple ointment.

Cadogel.—This represents that portion of the oil of cade which distils over between 220° and 300° C. (428° and 572° F.). It is a yellowish-brown, oily liquid with a faint tar-like odor, turning brown on exposure to the air. It is employed in the treatment of *eczema* and other skin diseases either pure or diluted with alcohol up to ten parts. It is commonly employed in from strengths of 10 to 30 per cent.

Cæsium.—The physiological effect of cæsium chloride has been investigated by S. Botkin (*In. Dis.,* St. Petersburg, 1888.) He finds that it increases the blood pressure and retards the heart movements to a slight extent. Laufenauer (*Th. M.,* 1889, and *Pester Med. Chirurg. Presse,* 1889) asserts that cæsium bromide theoretically ought to, and practically does, control *epilepsy* better than do the ordinary bromides. The physiological and medicinal properties of *rubidium* have also been studied by these investigators and found to resemble those of cæsium. This investigation has led to the putting upon the market, by Merck, of the following preparations:

Cæsium and Ammonium Bromide ($CsBr + 3NH_4Br$).—A white, crystalline powder, readily soluble in water, given in *doses* of fifteen to forty-five grains (1–3 Gm.) in the treatment of *epilepsy.*

Cæsium Carbonate (Cs_2CO_3).—Crystals, white; melting at red heat; very hygroscopic; very soluble in water; soluble also in alcohol.

Cæsium Hydroxide (CsOH).—A crystalline, colorless or yellowish mass melting below red heat; rather deliquescent, behaving towards water or alcohol as potassium hydroxide does.

Cæsium Sulphate (Cs_2SO_4).—Anhydrous, colorless prisms, permanent in the atmosphere; extremely soluble in water; insoluble in alcohol.

The triple salt *Cæsium, Rubidium,* and *Ammonium Bromide* is also used.

Caffeine Arsenate.—A white powder soluble in hot water, used in *neuralgia* and as a cholagogue in certain forms of *jaundice. Dose,* one-sixtieth to one-thirtieth of a grain (0.001–0.002 Gm.) in single doses to a daily maximum dose of one-fourth of a grain (0.016 Gm.).

Caffeine Hydrobromide. *Caffeine Bromide. Caffeinæ Hydrobromidum. Caffeinum hydrobromicum. Koffeinhydrobromat, Bromwasserstoffsaures Koffein,* G. $C_8H_{10}O_2N_4.HBr + 2H_2O$.—In the form of transparent crystals, readily decomposed but more stable than the hydrochloride. When heated to 110° C. (230° F.) the hydrobromic acid is driven off. Its aqueous solution is very unstable. Used for nervous headaches and as a diuretic, injected subcutaneously.

Caffeine Hydrochloride. *Caffeinæ Hydrochloridum. Caffeinum Hydrochloricum. Koffein-hydrochlorat, Salzsaures Koffein,* G. $C_8H_{10}O_2N_4HCl + 2H_2O$.—Large, colorless, prismatic crystals, readily decomposed by washing with alcohol or water or by long exposure to the air, when water and chlorine are lost. If heated to 110° C. (230° F.) the chlorine is driven off. The normal salt contains about 73 per cent. of caffeine.

Caffeine Nitrate. *Caffeinæ Nitras. Caffeinum Nitricum. Koffeinnitrat, Salpetersaures Koffein,* G. $C_8H_{10}O_2N_4.HNO_3 + H_2O$.—In the form of yellowish crystals, quickly decomposed by water and alcohol. The salt contains about 70 per cent. of caffeine and all the nitric acid is driven off at a temperature of 100° C. (212° F.).

Caffeine Phenylate. *Caffeinæ Phenylas. Caffeinum Phenylicum. Caffeine Phenol. Koffeinphenol, Coffeo-phenol,* G. $C_8H_{10}O_2N_4.C_6H_6O + H_2O$.—Made by dissolving 22.6 parts of caffeine in 10 parts of fused phenol. It is in the form of a white or pinkish crystalline mass, soluble in water.

Caffeine Salicylate. $C_8H_{10}O_2N_4.C_7H_6O_3$.—White, crystalline masses, soluble in water and alcohol, its solutions, however, undergoing rapid decomposition. It is intended to produce the combined action of its constituents, but the proportion of salicylic acid is too small to exert any perceptible effect. The *dose* is two to four grains (0.12–0.25 Gm.).

Caffeine Sulphate. *Caffeine Sulphas. Caffeinum Sulfuricum. Koffeinsulphat, Schwefelsaures Koffein,* G. $C_8H_{10}O_2N_4.H_2SO_4$.—The sulphate may be made by dissolving caffeine in alcohol, containing more sulphuric acid than is needed to make the salt, and setting the solution aside to crystallize. It is decomposed by alcohol or water alone. The salt contains about 66 per cent. of caffeine. It is used for the same purposes and in the same doses as caffeine.

Caffeine Triiodide. *Diiodocaffeine.* $(C_8H_{10}O_2N_4.I_2HI)_2 + 3H_2O$.—This occurs in dark green, prismatic crystals soluble in alcohol and water with decomposition. It is used in place of potassium iodide, liberating iodine in the system and lacking the depressant effect of the potassium salt. The *dose* is from two to four grains (0.13–0.26 Gm.). It is incompatible with acids.

Cahinca. *David's Root. Radix Cainceæ. Cainça,* Fr. *Kainkawurzel,* G.—This medicine attracted at one time considerable attention. The name of *Cahinca* or *cainca* was adopted from the language of the Brazilian Indians. The Portuguese of Brazil call the medicine *raiz pretta,* or *black root.* When first noticed in Europe, it was supposed to be derived from the *Chiococca racemosa* (Fam. *Rubiaceæ*), which was known to botanists as an inhabitant of the West Indies. But Martius, in his work on *Materiæ Medicæ Brasiliensis,* describes two other species of *Chiococca, C. anguifuga* Mart. and *C. densifolia* Mart., both of which are now known as *C. brachiata* Ruiz and Pav., which afford roots having the properties of the root ascribed to *C. racemosa.* A. Richard, however, received from Brazil specimens of *C. racemosa* as the Cahinca plant.

A specimen brought to Philadelphia consisted of cylindrical pieces, from 1 to 2 cm. thick somewhat bent or contorted, slightly wrinkled longitudinally, and more or less roughened, internally ligneous, externally covered with a thin, brittle, reddish-brown bark, having a light brown or brownish ash-colored epidermis. The cortical portion, which was of a resinous character, had a bitter disagreeable, somewhat acrid and astringent taste; the ligneous part was quite tasteless. The virtues of the root reside almost exclusively in its bark. They are extracted by water and alcohol. Four distinct principles were discovered in it by Pelletier and Caventou—(1) a crystallizable, bitter substance, believed to be the active principle, and called *cahincic acid,* $C_{40}H_{64}O_{18}$ (also called *caïncic acid* and *caïncin*); (2) a green, fatty matter of a nauseous odor; (3) a yellow coloring matter; and (4) a colored viscid substance. Rochleder and Hlasiwetz found also caffetannic acid. Cahincic acid is white, without odor, of a taste at first scarcely perceptible, but afterwards extremely bitter and slightly astringent, slightly soluble in water, but readily soluble in alcohol, permanent in the air, and unaltered at 100° C. (212° F.). It reddens vegetable blues, and unites with the alkalies, but does not form crystallizable salts. It is thought to exist in the root as calcium subcahinate. When treated with diluted hydrochloric acid it is decomposed into glucose and other products, of which is obtained at first *chiococcaic acid,* $C_{28}H_{42}O_7$ (thought by some to be identical with *quinovic acid*), and later, by boiling with alcoholic hydrochloric acid, *caïncetin,* $C_{22}H_{34}O_3$.

Cahinca is tonic, diuretic, purgative, emetic, and is capable of producing serious gastro-intestinal irritation. In Brazil it has long been used by the natives as a remedy for the *bites of serpents,* also in *rheumatism* and in *dropsy. Dose,* of the powdered bark, from twenty grains to a drachm (1.3–3.9 Gm.); of the aqueous or spirituous extract, from ten to twenty grains (0.65–1.3 Gm.).

Calamine. *Calamina.*—Calamine is the old name of the native *zinc carbonate,* although in mineralogy the name *calamine* is now applied to *zinc silicate,* while the name *Smithsonite* is given to the carbonate. It is found in the United States, as well as in Belgium, Germany, and England. It occurs in compact or earthy masses, or concretions, of a dull appearance, readily scratched by the knife, and breaking with an earthy fracture, or it occurs crystallized in rhombic forms. Its color is very variable, being, in different specimens, grayish, grayish-yellow, reddish-yellow, and, when very impure, brown or brownish-yellow. Its sp. gr. varies from 3.4 to 4.4. Before the blow pipe it does not melt, but becomes yellow and sublimes. When of good quality, it is almost entirely soluble in the dilute mineral acids, and unless it has been previously calcined, emits bubbles of carbon dioxide.

Prepared Calamine. N. F. IV. Calamina Præparata. Lapis Calaminaris.—The N. F. describes it as "native zinc carbonate containing a varying amount of zinc silicate, calcined at a moderate temperature: or calcined zinc carbonate, containing a small amount of ferric oxide. Prepared Calamine is a pink powder readily passing through a number 100 sieve. It is insoluble in water, but mostly dissolved by hydrochloric acid. Digest 1 Gm. of Prepared Calamine for one hour on a water bath with 25 mils of diluted hydrochloric acid, adding distilled water to replace that lost through evaporation, filter the liquid and dilute the filtrate with distilled water to 100 mils. Portions of 10 mils each of this diluted filtrate conform to the following tests: no precipitate forms within ten minutes on adding potassium iodide T.S. (*lead*); boil a portion with a few drops of nitric acid, then with an excess of ammonia water and filter; it yields an abundant white precipitate with hydrogen sulphide T.S. (presence of *zinc*); an excess of hydrochloric acid added to another portion, followed by potassium ferrocyanide T.S., produces an abundant white or bluish-white precipitate (presence of *zinc*). Dilute a portion of the above solution with four parts of distilled water, slightly acidulate with acetic acid, and add ammonium oxalate T.S.; it shows not more than a slight turbidity (*calcium*); slightly acidulate a portion with hydrochloric acid, and add 2 mils of

potassium sulphate T.S.; not more than a slight turbidity shows at once (*soluble barium salts*). Fuse the residue, which remains after preparing the solution for the preceding tests, with sodium carbonate, treat the mass with hot distilled water, filter and wash. Then dissolve the residue in diluted hydrochloric acid and dilute to 20 mils. Ten mils of this solution does not become turbid upon the addition of 5 mils of potassium sulphate T.S. (*barium sulphate*)." *N. F. IV.* At the present time there is a revival of the use of calamine in dermatological practice and in consequence of an apparent scarcity of genuine calamine there has appeared upon the market a preparation known as *artificial calamine*, which consists mainly of zinc oxide colored with ferric oxide. It is used only externally as a mild astringent and desiccant in *excoriations* and *superficial ulcerations*, either as a dry powder dusted on the part, or as a cerate. It has no apparent advantages over zinc carbonate or zinc oxide, except that in the form of the ointment, as usually prescribed, it is more of a flesh tint in appearance and not so conspicuous when applied to the skin.

Calamus. *U. S. VIII. Sweet Flag. Radix Calami Aromatici. Radix Acori. Sweet Sedge (Cane, Rush, Root or Myrtle). Myrtle-flag (Grass* or *Sedge). Acore Vrai*, Fr. Cod. *Acore Odorant*, Fr. *Rhizoma Calami*, P. G. *Kalmus, Kalmuswurzel*, G. *Calamo aromatico*, It., Sp.—"The unpeeled, dried rhizome of *Acorus Calamus* Linné (Fam. *Araceæ*)." *U. S. VIII.* The sweet flag, or Calamus, has a perennial, horizontal, jointed, somewhat compressed rhizome, from half an inch to an inch thick, sometimes several feet in length, sending off numerous round and yellowish or whitish roots from its lower surface, and groups of brown fibers resembling coarse hair from its joints, internally white and spongy, externally whitish with a tinge of green, variegated with triangular leaf scars of light brown and rose color. The leaves are all radical, sheathing at the base, very long and sword-shaped. The scape or flower stem resembles the leaves, but is longer, and from one side, near the middle of its length, sends out a cylindrical spadix, tapering at each end, about two inches in length, and crowded with greenish-yellow flowers. The fruit is an oblong capsule, divided into three locules, and containing numerous oval seeds.

This plant grows abundantly in the wet places throughout the United States, Europe, Western and Southern Asia. The leaves as well as the rhizome have an aromatic odor; but the rhizome only is employed. It should be collected late in the autumn, or in the spring. After removal from the ground, the rhizomes are washed, freed from their roots, and dried with a moderate heat. Most of the commercial article has the outer portions of the cortex removed. By drying they lose nearly one-half their diameter, but are improved in odor and taste.

Calamus was officially described as follows: "Rhizome 1 to 2 cm. thick, usually in longitudinally split pieces of various lengths; when entire, cylindraceous and somewhat vertically flattened, externally reddish-brown, somewhat annulate from remnants of leaf-sheaths; upper surface with triangular leaf-scars, the lower surface with circular pitted scars of roots; fracture short, showing numerous oil cells and scattered fibro-vascular bundles, the latter crowded within the endodermis; odor aromatic; taste pungent and bitter." *U. S. VIII.*

The odor of Calamus is strong and fragrant; its taste warm, bitterish, pungent, and aromatic. Its active principles are taken up by boiling water. From 100 parts of the fresh root of the European plant, Trommsdorf obtained 0.1 of volatile oil. The volatile oil is contained in all portions of the plant, the leaves yielding to distillation, according to the analysis of Schimmel & Co., 0.2 per cent., the fresh root 1.5 to 3.5 per cent., the dried German root 0.8, and the Japan root as much as 5 per cent.

The oil is at first yellow, but ultimately becomes red, and has the odor and taste of Calamus. Kurbatow (*Ann. Ch. Ph.*, vol. 173, p. 4) examined oil of Calamus, and found that the portion boiling below 170° C. (338° F.) yielded, after treatment with sodium, a terpene, $C_{10}H_{16}$, having a sp. gr. .8793 at 0° C. (32° F.), and having a boiling point of 158° C. (316.4° F.). The extractive matter has an acrid and sweetish taste. H. Thomas (*A. Pharm.*, 1886, p. 465; *P. J.*, 1886, p. 1085) obtained from Calamus rhizomes a bitter glucoside, *acorin*, in the form of a clear, thick, yellow liquid, having a neutral reaction and having the formula $C_{36}H_{60}O_6$, splitting into oil of Calamus and sugar. By oxidation *acoretin*, a neutral resin, is formed, and from the extract remaining after the acorin is removed Thomas obtained an alkaloid which he named *calamine*. Calamus is sometimes attacked by worms, and deteriorates on keeping.

Uses.—Calamus is a feeble aromatic and as such is used, especially in domestic practice, in India and to some extent in other portions of the world. The volatile oil is largely used in perfumery, and the powdered root itself is esteemed in Ceylon and India as a vermifuge and an insecticide. *Dose*, in substance, fifteen to thirty grains (0.9–1.9 Gm.); of infusion (an ounce to one pint of boiling water), one to two wineglassfuls (60–120 mils).

The *fluidextract*, which was formerly official, *Fluidextractum Calami U. S. VIII*, was made as follows: "Calamus, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, Water, each *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix *seven hundred and fifty mils* [or 25 fluidounces, 173 minims] of alcohol with *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of water, and, having moistened the powder with *three hundred and fifty mils* [or 11 fluidounces, 401 minims] of the mixture, pack it firmly in a cylindrical percolator; then add enough menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close to the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding menstruum, using the same proportions of Alcohol and Water as before, until the Calamus is exhausted. Reserve the first *nine hundred mils* [or 30 fluidounces, 208 minims] of the percolate, and evaporate the remainder, at a temperature not exceeding 50° C. (122° F.), to a soft extract; dissolve this in the reserved portion, and add enough menstruum to make the fluidextract measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S. VIII. Dose*, from fifteen to thirty minims (0.9–1.9 mils).

Calcium Acetate. *Calcii Acetas. Acétate de Chaux*, Fr. *Essigsaurer Kalk*, G. $Ca(C_2H_3O_2)_2$.—Made by neutralizing acetic acid with precipitated calcium carbonate, evaporating and crystallizing. Colorless needle-like crystals, soluble in water, less so in alcohol.

Calcium Acetyl-Salicylate.—This has been introduced under the trade name of *kalmopyrin*. It is a white powder readily soluble in water, differing from the other salts of acetylsalicylic acid in that it is not hygroscopic and its aqueous solution not so rapidly decomposed. It is used as an antirheumatic and analgesic in *doses* of from eight to fifteen grains (0.5–1 Gm.).

Calcium Benzoate. *Calcii Benzoas.* $Ca(C_7H_5O_2)_2 + 3H_2O$.—This salt may be made by adding calcium carbonate to a hot aqueous solution of benzoic acid, filtering, and evaporating the solution, and collecting and drying the crystals, which usually form in beautiful radiating tufts. It is soluble in 18 parts of cold water and 6 parts of boiling water. *Calcium hippurate*, $Ca(C_9H_8NO_3)_2 + 3H_2O$, is made in a similar manner, and is identical in appearance and uses. Poulet recommends the latter highly in the *uric acid diathesis*, for *scrofula*, incipient *cirrhosis of the liver*, and in *struma*. *Dose*, ten grains (0.65 Gm.).

Calcium Borate. *Calcii Boras.* $Ca_3(BO_3)_2$.—Calcium Borate is prepared by mixing solutions of sodium borate and calcium chloride. It is a white, inodorous, tasteless powder. It is given internally in *diarrhea*, and used externally as a deodorant and antiseptic. *Dose*, ten to fifteen grains (0.65–1 Gm.).

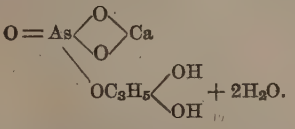
Calcium Bromoiodide.—A mixture of calcium iodide and bromide in molecular proportions. It forms a yellow powder, soluble in water and used as a sedative in *epilepsy* and *rachitis*. *Dose*, five to ten grains (0.32–0.65 Gm.).

Calcium Dithiocarbonate. *Dithio-Calcium Carbonate.* $CaCOS_2$.—An orange-red, crystalline, hygroscopic powder, slightly soluble in water, less so in alcohol. It has been especially employed by Tommasoli and Vicini (*Monatssch. f. Prakt. Dermatol.*, 1892) as a local application in *eczema, psoriasis, lupus, purulent syphilides* and other *skin diseases*, in the form of a 5 per cent. ointment or a somewhat stronger aqueous solution. A 20 per cent. solution produced distinct burning irritation and even pustulation. Sabbatini states that the 1 per cent. solution inhibits, but does not kill pyogenic micro-organisms. On exposure, its aqueous solution undergoes decomposition with the separation of sulphur and hydrogen sulphide.

Calcium Ferrophospholactate.—It occurs as a white powder, soluble in 5 parts of hot water. In *rhachitis* and *scrofula* it is given in three to five grain (0.2–0.32 Gm.) *doses* several times daily.

Calcium Fluoride. *Calcii Fluoridum.* CaF_2.—A white powder, which is insoluble in water, but becomes soluble in the presence of salts of ammonium. It has been recommended internally by Deninger (*Deutsche Zahnarztliche Wochens.*, 1907, p. 196), during pregnancy, to prevent the loosening of the teeth. It may be given in *doses* of from one-twelfth to one-sixth grain (0.005–0.01 Gm.) twice daily.

Calcium Glycero-arsenate. *Calcii Glycero-arsenas.*



A crumbling white powder which is insoluble in water and alcohol but freely dissolves in mineral and organic acids, especially in a dilute solution of citric acid. According to Schlagdenhauffen and Pagel, the lethal subcutaneous dose of this compound is, for guinea-pigs, 3.10 Gm. per kilo. The preparation is therefore only slightly poisonous and has been employed in daily *dose* of one-sixth grain (0.01 Gm.) internally in *phthisis* by Spillmann and in *diabetes* by Heinrich Stern, with alleged good results, in *doses* of 4 to 10 grains (0.26–0.65 Gm.) to be taken three or four times daily.

Calcium Iodate. *Calcii Iodas.* $Ca(IO_3)_2 + 6H_2O$.—This is a white, crystalline powder dissolving in about 400 parts of water. It contains 51 per cent. of iodine and 16 per cent. of available oxygen, which substances are liberated slowly in the presence of putrescent organic matters. It is stated further that in alkaline solution, while the organic matter is being oxidized by the oxygen set free from the decomposing iodate, the iodine slowly reforms iodates by the decomposition of water. The iodate so reformed, in contact with another portion of putrescible matter, yields further proportions of free oxygen and iodine to act as before, and so on. This salt was brought forward by E. Sonstadt as a valuable antiseptic, to be used in the preservation of food. (*Chem. News*, xxviii, 297; confirmed in *Provincial Med. Journ.*, March, 1890.) It is strongly recommended by W. Mackie (*L. L.*, 1900, No. 4035) as a substitute in surgery for iodoform and in internal medicine as a gastro-intestinal antiseptic. The internal *dose* is from three to five grains (0.2–0.32 Gm.) given in capsules after meals.

Calcium Iodide. *Calcii Iodidum. Calcium Iodatum. Iodure de Calcium*, Fr. *Jodcalcium, Calcium Jodid*, G. CaI_2.—According to Malem (*B. G. T.*, April 30, 1868), this salt is preferable to any other iodic compound in *phthisis*. Malem prepares it by treating a solution of ferrous iodide with milk of lime. This liquor thus obtained, being filtered and evaporated, yields crystals of calcium iodide. It may also be made by dissolving lime or calcium carbonate in hydriodic acid. Pure calcium iodide is white, and crystallizes in large plates of a pearly luster. It is deliquescent, and very soluble in water, and its solution is capable of dissolving iodine added to it. Calcium Iodide is much more unstable than potassium iodide. When taken into the stomach, it is rapidly decomposed into hydriodic acid and salts of lime, which are almost immediately absorbed. Most patients bear it very well. From one to three or four grains (0.065–0.2–0.26 Gm.) may be given after meals. It is incompatible with acids, soluble sulphates, carbonates and tartrates.

Eberbach (*P. J.*, 3d ser., i, 364) has proposed the following formula for a *Syrup of Calcium Iodide* (see also *Syrupus Calcii Iodidi*, N. F., Part III). Take of iodine 4 oz.; iron (in form of wire) 7½ dr.; distilled water q. s.; milk of lime (fresh) q. s.; sugar 28 oz.; simple syrup q. s.; mix 3 oz. of the iodine with the iron and 4 oz. of water, in a thin flask with long neck; shake occasionally until the reaction has ceased and the solution assumes a pale green color; filter the solution, and add the remainder of the iodine; heat to the boiling point, and add milk of lime until all of the iron is precipitated. Filter, and wash the precipitate with hot water until all the iodide is washed out, and then bring the whole to the measure of 20 fl. oz.; add the sugar, and dissolve by a gentle heat; to the solution add enough simple syrup to make it measure 40 fl. oz.; mix thoroughly, and fill into 2 oz. bottles, well corked. Williamson (*B. M. J.*, 1907, p. 909) has found calcium iodide to be

especially serviceable in various forms of *ulceration* and *diseases of the skin.* It is also a useful remedy in some cases of *asthma.* The *dose* is from five to ten grains (0.3–0.6 Gm.).

Calcium Lactophosphate. *N. F. IV. Calcii Lactophosphas.*—In the N. F. it is described as "a mixture in variable proportions of calcium lactate, calcium acid lactate, and calcium acid phosphate. Calcium Lactophosphate occurs in white granules or as a white powder, without odor. It is soluble in water, almost insoluble in alcohol. Its aqueous solution (1 in 20) is acid to litmus. The addition of ammonium oxalate T.S. to an aqueous solution of Calcium Lactophosphate produces a white precipitate insoluble in acetic acid but soluble in hydrochloric acid. Add 10 mils of diluted sulphuric acid and 5 mils of potassium permanganate T.S. to 5 mils of an aqueous solution of Calcium Lactophosphate (1 in 20) and gently warm the mixture; the odor of acetaldehyde is evolved. Add silver nitrate T.S. or ammonium molybdate T.S. to separate portions of an aqueous solution of Calcium Lactophosphate (1 in 20); a yellow precipitate is produced. Mix 0.5 Gm. of Calcium Lactophosphate with 5 mils of sulphuric acid; not more than a slight coloration results within one minute (*readily carbonizable impurities*). Ten mils of an aqueous solution of Calcium Lactophosphate (1 in 100), mixed with 1 mil of diluted hydrochloric acid, does not at once become turbid on the addition of a few drops of barium chloride T.S. (*sulphate*). Ten mils of an aqueous solution of Calcium Lactophosphate (1 in 100), when mixed with a few drops of nitric acid, yields not more than an opalescence on the addition of a few drops of silver nitrate T.S. (*chloride*). An aqueous solution of Calcium Lactophosphate does not respond to the Test for heavy metals (see *U. S. P.*, Test No. 3, Part III). Mix 0.2 Gm. of Calcium Lactophosphate with 1 Gm. of potassium nitrate, ignite the mixture cautiously in small portions at a time until the carbonaceous matter is all or nearly all burned off, then add to the residue 20 mils of diluted sulphuric acid and evaporate the mixture until fumes of sulphuric anhydride are evolved. The residue meets the requirements of the Test for arsenic (see *U. S. P.*, Test No. 1, Part III). Dissolve 1 Gm. of Calcium Lactophosphate and 2 Gm. of ammonium chloride in 75 mils of distilled water, heat the solution to boiling and add an excess of ammonium oxalate T.S. (about 20 mils). Allow the precipitate to subside completely, then filter and supersaturate the filtrate with ammonia water; not more than a slight turbidity is produced (*magnesium*)." *N. F.* This salt is a stomachic tonic, especially used for children. It is usually administered in the form of the official syrup, but the salt has now been recognized by the N. F. The *dose* is eight grains (0.5 Gm.).

Calcium Permanganate. *Calcii Permanganas. Acerdol.* $CaMn_2O_8$.—This salt probably has the same physiological and medicinal properties as the permanganate of potassium. It has been used in *gastro-enteritis* and *diarrhea* in *doses* of from one-half to one and a half grains (0.032–0.096 Gm.), but has been especially urged for the purification of water. For spring water twenty milligrammes, for river water forty milligrammes, per liter, are recommended. If the color of the water remains red for a short time the permanganate is in excess, as should be the case for effective purification. Calcium Permanganate has also been suggested by Stevens (*K. T. W.*, 1910, p. 166) for the treatment of *lead poisoning.*

Calcium Peroxide. *Calcii Peroxidum.* $CaO_2 + 4H_2O$. *N. N. R.* 1917.—"A mixture consisting essentially of calcium peroxide and calcium hydroxide and carbonate, containing not less than 60 per cent. of calcium peroxide, equivalent to 13.3 per cent. of available oxygen." A yellow, crystalline powder which dissolves but sparingly in water. The solution has an alkaline reaction and possesses a somewhat caustic and astringent taste. In the presence of water Calcium Peroxide splits up into calcium hydroxide and oxygen. It has been brought forward as a powerful oxidizing antizymotic and as an antidote to hydrocyanic acid. In Hornstein's experiments it failed as an antidote unless the cyanide was given in very small quantities and the antidote was administered immediately after the poison. Its germicidal powers appear to be feeble, and its proneness to decomposition is a practical difficulty in its use. It has, however, been highly recommended by Reszkowski (*Gazette Lekarska*, 1899) in the summer *diarrheas* of children, in *doses* of three to ten grains (0.2–0.65 Gm.), administered in milk. It is advised to keep it in parchment capsules in well-stoppered bottles. Under the name of *calcium superoxide* or *gorite* a probably identical oxide has been put on the market. The germicidal influence of gorite was determined by Hornstein (*A. J. P.*, 1901, viii) to be distinctly weaker than that of hydrogen dioxide. Tooth-powders purporting to contain calcium peroxide are upon the market, but in most of them the quantity of the salt present is too small to exercise any therapeutic effect. It is incompatible with acids or acid salts, with soluble phosphates, sulphates and carbonates.

Calcium Phenolsulphonate. *Calcii Sulphophenas. Calcium Sulphocarbolate. Calcium Phenolsulphonate. N. N. R.* 1917. *Karbolsulfosaures Calcium*, G. $[C_6H_4(OH)SO_3]_2Ca + H_2O$.—Made by neutralizing paraphenolsulphonic acid with precipitated calcium carbonate. In the form of a colorless, almost odorless powder, astringent and bitter, readily soluble in water and alcohol. It is incompatible with iron compounds, lead subacetate solution, and peroxides. A 1 per cent. solution is recommended as an intestinal antiseptic, and astringent in *doses* of a fluidrachm (3.75 mils) every three hours.

Calcium Saccharate.—Under the trade name of *Antacidin* this compound of calcium with cane sugar, $(C_{12}H_{22}O_{11})_3CaO$, has been recommended in the treatment of *dyspepsia* and *flatulency. Dose*, fifteen to sixty grains (1–4 Gm.).

Calcium Salicylate. *Calcii Salicylas.* $CaC_7H_5O_3 + H_2O$.—This compound is the basic calcium salt. It is a sandy, white powder, almost insoluble in water. The neutral salt is also known and is quite soluble in water. Calcium Salicylate has been used in Austria in *doses* of from seven to twenty grains (0.45–1.3 Gm.) for *diarrhea* and *gastro-enteritis.* For method of preparation, see *P. J.*, vol. xxii, 1891.

Calcium Santoninate. *Calcii Santoninas.* $Ca(C_{15}H_{19}O_4)_2$.—This is a white, tasteless, insoluble powder, obtained by saturating hot milk of lime with santonin, and has been brought forward by Bombelen as superior to santonin as a vermifuge on account of its tastelessness, and especially because of its insolubility, which causes it to be absorbed with great slowness. (*Ap. Ztg.*, March, 1899.) *Dose*, one grain (0.065 Gm.).

Calcium Sulph-Ichthyolate. *N. N. R.* 1916.—

This preparation, claimed to be more efficient than the ammonium ichthyolate, is made by submitting ammonium sulph-ichthyolate to the action of a solution of calcium chloride in calcium hydroxide solution.

Calcium Sulphate. *Calcii Sulphas Exsiccatus. U. S. VIII. Exsiccated Calcium Sulphate. Dried Calcium Sulphate. Calcii Sulphas,* Br. 1885. *Dried Gypsum. Plaster of Paris. Exsiccated Sulphate of Calcium. Calcis Sulphas. Sulphate of Lime. Gypsum. Calcium sulfuricum ustum,* P. G. *Gebrannter Gyps,* G.—"A powder containing about 95 per cent., by weight, of Calcium Sulphate [$CaSO_4 = 136.14$], and about 5 per cent. of water; prepared from the purer varieties of native gypsum [$CaSO_4 + 2H_2O = 172.17$], by carefully heating until about three-fourths of the water has been expelled. Exsiccated Calcium Sulphate should be kept in well-closed vessels, carefully protected from moisture." *U. S. VIII.* The native sulphate is best known as *gypsum,* and in its massive variety as *alabaster.* Gypsum is an abundant natural product, and the quantity mined in the United States has enormously increased in recent years. In 1913 the production amounted to 2,599,506 tons; in 1914, 2,476,465 tons, and in 1915, 2,447,611 tons, valued at $6,596,893. It was officially described as "a fine, white powder, without odor or taste. From moist air it attracts water, becomes granular, and then loses the property of hardening with water. When mixed with half its weight of water, exsiccated Calcium Sulphate forms a smooth, cohesive paste, which rapidly hardens. It is soluble in about 378 parts of water at 25° C. (77° F.), and in 451 parts at 100° C. (212° F.). In alcohol it is insoluble. It readily dissolves in diluted nitric or hydrochloric acid; also in saturated solutions of potassium nitrate, sodium thiosulphate, and of various ammonium salts. When heated above 204° C. (399.2° F.), exsiccated Calcium Sulphate becomes anhydrous and loses the property of forming with water a paste which hardens rapidly. Its saturated solution in water is neutral to litmus paper, and forms white precipitates with barium chloride T.S., with ammonium oxalate T.S., and with alcohol. No effervescence should occur on the addition of diluted acids to exsiccated Calcium Sulphate (absence of *carbonate*)." *U. S. VIII.*

The solubility of crystallized Calcium Sulphate, according to Poggiale, varies with the temperature; it is greatest at 35° C. (95° F.), and above or below that temperature gradually diminishes, so that at 100° C. (212° F.), or the boiling point of water, it is very nearly the same as at 5° C. (41° F.), not far from the freezing point. (*J. P. C.,* 4e sér., v, 86.) When deprived of its water by heat, and reduced to the state of a white powder, it rapidly absorbs water added to it, and, from the state of semi-liquid paste into which it is brought with that fluid, hardens without great change of bulk. It is this property which fits plaster of Paris so well for all kinds of molding; and to this also it owes its peculiar adaptability to the purpose of a splint. To prepare it for use, the gypsum must first be deprived of the greater part of its water by exposure to a heat of from 100° C. (212° F.), to 121.1° C. (250° F.). It loses both its molecules of water of crystallization at a temperature of about 170° C. (338° F.), and is then known as *burnt gypsum.* If heated above 204° C. (399.2° F.) it becomes *dead-burnt,* and does not take up water readily and does not harden. When dehydrated, it is reduced to fine powder, and kept in air tight vessels for use. As thus prepared, if mixed with two parts of water, it forms a semi-liquid cream-like mass, which becomes solid and hard in fifteen or twenty minutes, the temperature rising during the process, as in the slaking of lime. Plaster of Paris sets best when mixed with three-fifths of its weight of water. Colloids retard and crystalline substances hasten the setting; thus, 1 per cent. of salep increases the time of setting from 20 to 50 minutes, while 3 per cent. of alum reduces the time to about five minutes. The hydrated gypsum expands in solidifying, hence its advantages in preparing casts—the expansion causes it to fill accurately all interstices. Cloëz (*Chem. News,* 1903, 58) states that the "setting" of plaster of Paris is due to the succession of three phenomena: (1) Hydration. (2) Partial solution. (3) Solidification of a supersaturated solution.

Gypsum is used, in medicine, chiefly to provide mechanical support or to immobilize various parts of the body. Thus in *fractures* and *sprains* it frequently replaces various forms of splints. Plaster jackets are used to support the thorax in cases of tuberculous diseases of the spine. Ordinarily for surgical purposes it is applied by saturating bandages with the dry powder, these bandages being dipped in tepid water at the time of application. Usually muslin bandages are employed, but, according to T. E. Stark, a medical officer in the British army, flannel is the best material for bandages to be used with gypsum. It should be cut into strips an inch and a half broad and two or three yards long, which should first be spread on a table and rubbed well with the powdered gypsum on both sides, and always in the direction of the thread. The bandages should then be rolled up loosely, and kept for use in air tight cases. Thus prepared, the bandages, first thoroughly wetted, should be rolled round the limb, overlapping at the edges, so as to make a uniform covering. After application, it should be left to harden, which generally happens in fifteen or twenty minutes. A simpler method of using the gypsum for this purpose is, after the application of the bandages, to paint the whole thoroughly and carefully with the milk of gypsum, which will solidify, and enclose the part in a firm case. Dry Calcium Sulphate has also been recommended as an absorbent dressing in *wounds, foul ulcers* and similar conditions, for which its hygroscopic properties render it peculiarly valuable.

Calcium Thiosulphate. *Calcii Thiosulphas. Calcium Sulpho-sulphate. Calcium Hyposulphite.* CaS_2O_3.—The following mode of preparing this salt is recommended by J. Laneau, of Paris. Take 1000 parts of sulphur, 400 of lime, and 4000 of distilled water; slake the lime with sufficient of the water, add the sulphur and the residue of the water, and boil for an hour and a half, adding water to keep up the measure; when cool filter the liquid through linen covered with filtering paper, and wash the residue with 1000 parts of water. A solution is thus obtained of calcium polysulphide of the sp. gr. 1.141. Into this pass a current of washed sulphurous acid gas until the solution becomes colorless; separate the precipitated sulphur and evaporate the clear solution at a heat not exceeding 60° C. (140° F.), until it begins to crystallize, when it is to be set aside. The product is 700 parts of calcium thiosulphate. This is in six-sided crystals, which effloresce in a dry air. Laneau prepares a *syrup of calcium thiosulphate* by dissolving 10 parts of the crystallized salt in 20 parts of distilled water, and mix-

ing with the solution 170 parts of syrup of orange flowers. (See *A. J. P.*, 1863, 223.) This is used for similar purposes to sodium thiosulphate (see Part I). The *dose* of the salt is from ten to twenty grains (0.65–1.3 Gm.) three times a day, of the syrup from two to four fluidrachms (7.5–15.0 mils). It is incompatible with acids, with soluble carbonates, phosphates and tartrates.

Calendula. *N. F. IV.* (*U. S. VIII.*) *Marigold. Mary-bud. Holligold. Fleurs de Tous les mois, Souci*, Fr. *Ringelblume, Todtenblume. Goldblumen*, G. *Calendula*, Sp.—"The dried ligulate florets of *Calendula officinalis* Linné (Fam. *Compositæ*), without the presence of more than 2 per cent. of other parts of the plant or other foreign matter." *N. F.*

The N. F. drug is described as in "florets from 15 to 25 mm. in length, yellow- or orange-colored, one- to three-toothed, four- to five-veined, margin nearly entire, the short hairy tube occasionally enclosing the remnants of a filiform style and bifid stigma. Odor slight, somewhat heavy; taste slightly bitter, faintly saline. The powdered drug is light yellow to orange-yellow and, when examined under the microscope, exhibits a few characteristic, non-glandular hairs, consisting of a double row of thin-walled, more or less collapsed cells, with a one- or two-celled summit, and up to about 0.8 mm. in length; elongated epidermal cells with thin, somewhat wavy walls, a striated surface, and containing irregular chromoplasts and oil-like globules, the latter coalescing when mounted in hydrated chloral T.S.; pollen grains, more or less spherical, with numerous spinose projections, three pored, and up to 0.04 mm. in diameter; tracheæ about 0.009 mm. in width with spiral and annular markings; prisms or rosette aggregates of calcium oxalate from 0.002 to 0.004 mm. in diameter. Calendula yields not more than 11 per cent. of ash." *N. F.* The odor is much stronger in the fresh than in the dry flowers, and on exposure to light, the orange-red or yellow color fades. Among its constituents are a bitter principle, and an amorphous substance called *calendulin* (discovered by Geiger most abundantly in the flowers), considered by Berzelius as analogous to bassorin, though soluble in alcohol. *French* or *African Marigold*, so called, is very frequently substituted for the official drug. It is the *Tagetes patula* L., and *T. erecta* Linn., both of Mexico. The flowers are readily distinguished by the scales of the involucre being united to form a tube, and by the slender, flattish achenes being crowned with a few chaffy or awned scales. The broadly strap-shaped ray-florets are toothed, and of a light or deep orange color sometimes striped with red. Latour and Magnier de la Source isolated from African marigold a yellow crystalline substance, *quercetagetin*, which Perkin examined and gave the composition $C_{15}H_{10}O_8$. (*P. J.*, 1902, 294.)

In the days of therapeutic darkness *calendula* was thought to be medicinally active, but it has no virtues beyond that of a feeble aromatic. Both the leaves and the flowers were used; but the latter were preferred, and were usually administered in the recent state in the form of tea. *Dose*, from fifteen to sixty grains (0.9–3.9 Gm.) See *Tinctura Calendulæ, N. F.* (Part III).

Cali Nuts.—These nuts, which come from the west coast of Africa, are the seeds of a papilionaceous plant, either a species of *Mucuna* or *Dioclea*, and have a more circular shape than Calabar beans, but otherwise agree with the latter in essential external characters. They contain an alkaloid which is said to be chemically and physiologically closely allied to physostigmine. (Merck, *Chem. Cb.*, 1887.)

Callaquol.—*Callaquol* is an aromatic, milky fluid, which is claimed to be a suspension of the acid ester of *oxycarbtriallyl* in oil of thyme, the thyme oil being used to cover the disagreeable odor of the ester. It is used as an application in *pleuritis, cystitis*, etc.

Calliandrein.—A glucoside (probably a saponin) obtained from *Calliandra grandiflora* Benth. (Fam. *Leguminosæ*), a Mexican shrub. It is a white, odorless powder soluble in water, the solution forming a heavy froth on shaking. It possesses antipyretic properties, having been administered with asserted good results in *intermittent fever*. *Dose*, one grain (0.065 Gm.).

Calomelol. *N. N. R.* 1917.—*Calomelol* is a powder, almost without taste, insoluble in alcohol, forming with water a colloidal solution. It is prepared by acting on a solution of sodium chloride in the presence of a proteid with mercurous nitrate, and precipitating the calomel with alcohol. It is asserted to contain 80 per cent. of calomel in the colloidal state and 20 per cent. of albuminoids. It is recommended especially for inunction in the treatment of *syphilis*. The advantages over the ordinary inunction ointment claimed for it are, that it is better absorbed, less likely to cause irritation of the hair follicles, and is almost invisible on the skin. The *calomelol ointment* (*Unguentum Heyden*) contains 45 per cent. of calomelol. The amount applied at one time is ordinarily about ninety grains (5.8 Gm.). It should be guarded from the light and its solution is incompatible with alcohol or alcoholic tinctures and with acids.

Calotropis. *Br. Add. Mudar.*—The dried root-bark of *Calotropis procera* R. Brown (*Asclepias procera* L.) and of *Calotropis gigantea* R. Brown freed from the outer corky layer. These asclepiadaceous plants are natives of Hindostan, but have become widely naturalized in various parts of the East and West Indies. Their milky juice is a violent local irritant, which, when taken internally, acts as an emeto-cathartic and may produce a fatal gastro-enteritis. In India it has long been used not only for suicidal purposes but to kill newly-born female infants, and is also applied to the womb to cause abortion.

The root-bark occurs in short, more or less quilled pieces having a thickness of from one-tenth to one-fifth of an inch (two to five millimeters) and a width of not more than one and a half inches (thirty-seven millimeters). It is covered with a soft, grayish-buff, strongly furrowed and reticulated, easily separated periderm. The fracture is short and mealy; the taste bitter and acrid. According to C. J. H. Warden and L. A. Waddel, *calotropis* contains an acid resin, a crystalline, colorless substance, *madaralban*, an amber-colored viscid body, *madarfluavil*, and caoutchouc. (*P. J.*, 1885, 165.) Lewin (*A. E. P. P.*, 1913, lxxi, 142) has found a neutral principle (*calotropin*) which is a very active poison of the digitalis type.

Calotropis has been very largely used as a local remedy in Hindostan in *elephantiasis* and *leprosy*, and is asserted by John Morton (*Indian Medical Record*, viii, 1895) to act with extraordinary efficiency upon chronic *eczema*. It has also been

employed internally as a remedy in *diarrhea* and *dysentery;* also with less probability of usefulness in *syphilis* and *rheumatism. Dose,* of powder, from three to twelve grains (0.2–0.78 Gm.), three times a day, gradually increased until it affects the system.

Tincture of Calotropis. Tinctura Calotropis, Br. Add., two ounces to a pint (alcohol 6 per cent.), is given in *doses* of one-half to one fluidrachm (1.8–3.75 mils).

Calycanthus. *Calycanthus floridus* L.—This is a shrub of the fam. *Calycanthaceæ,* from six to eight feet high, which inhabits the low, shady woods along the mountains of Georgia and North Carolina, and also Tennessee, where it is known as *sweet shrub* or *Carolina allspice.* The whole plant is aromatic, having, when crushed, the odor of strawberries. According to R. G. Eccles, the seeds contain a fixed oil, and an alkaloid, *calycanthine.* H. W. Wiley (*A. J. P.,* 1890, 96) found in the seeds over 47 per cent. of oil and 4.25 per cent. of alkaloid. H. M. Gordin made an extensive investigation of calycanthine and its salts. (*Proc. A. Ph. A.,* 1905, 224.) According to Cushny (*A. I. P. T.,* 1905, xv, p. 487) calycanthine has the empiric formula of $C_{11}H_{14}N_2$. When injected into the lower animals it causes muscular weakness, by an action upon the peripheral motor nerves, associated with increased reflexes, and, in the higher mammals, with convulsions similar to those seen in picrotoxin poisoning. The alkaloid also exercises a powerfully depressant action upon the heart muscle. More recently, a second alkaloid, *isocalycanthine,* has been described by Gordin. (*Proc. A. Ph. A.,* 1908 and 1909, 889.) This alkaloid, according to the experiments of MacGuigan and Hess (*J. P. Ex. T.,* 1912, iii), is very similar in its physiological properties to calycanthine. It is asserted that the shrub is important as a source of poisoning to cattle and sheep. Calycanthus has been used as an antiperiodic. The *dose* of the fluidextract is thirty to sixty minims (1.9–3.75 mils).

Calystegia Solandella.—This plant—a member of the *Convolvulaceous* family—has lately come into vogue as a constipation remedy. A compound tincture of solandella has been used with some success, but whether this can be attributed to the calystegia or to other ingredients is not known.

Cam Wood.—A red dye-wood, procured from the *Baphia nitida* Lodd., a leguminous tree, growing on the western coast of Africa. The wood is usually kept in the shops in the ground state. It yields its coloring matter scarcely at all to cold water, slightly to boiling water, and readily to alcohol and alkaline solutions. The coloring matter is thought to be identical with *santalin,* $C_{15}H_{14}O_5$.

Camellin.—A glucoside obtained from the seeds of *Camellia japonica,* $C_{53}H_{84}O_{19}$. It occurs as a reddish-white, bitter powder, soluble in water. It is used as a cardiac stimulant in *endocarditis* and *pericarditis,* several foreign practitioners preferring it to digitalin.

Camphacollasis. *Camphacol.*—This is the *camphoric acid ester of methylene diguaiacol.* It occurs in crystals, and is used as an expectorant in *phthisis* and as an antiseptic in *cystitis. Dose,* five to twenty grains (0.32–1.3 Gm.).

Camphor Compounds.—A number of mixtures of camphor with organic acids have come into use, especially so on the continent. *Benzoated camphor, citrated camphor, phenolated camphor, salicylated camphor,* and *valerated camphor* are the combinations in general use. The therapeutic action of these compounds is essentially the same as the combined action of their constituents and the idea of marketing these as combinations seems unnecessary when they can be immediately compounded by the pharmacist.

Camphor Chlorated. Monochlorated Camphor. $C_{10}H_{15}ClO$.—A yellowish-white, crystalline powder, soluble in alcohol and ether. It is used as an antiseptic.

Camphor Dibromated. $C_{10}H_{14}Br_2O$.—A white to yellow, crystalline powder, soluble in alcohol and ether and used as an antiseptic. It has been used internally like the monobromated camphor, but in much smaller doses.

Camphoric Acid. *Acidum Camphoricum. U. S. VIII. Kamphorsaure, Kamphylsaure,* G. $H_2C_{10}H_{14}O_4 = 198.62$.—"A dibasic organic acid obtained by the oxidation of camphor." *U. S. VIII.* This acid is obtained by the oxidation of camphor by heating it with nitric acid, and purifying the crystals so obtained. On further oxidation it is changed into *camphoronic acid,* $C_9H_{14}O_6$. It has been made synthetically by Komppa. (*P. J.,* 1904, 77.)

It occurs in "colorless, odorless, monoclinic prismatic crystals or plates; melting at 187° C. (368.6° F.); at a higher temperature yielding an anhydride, and ultimately decomposing without leaving any weighable residue. Soluble in 125 parts of water at 25° C. (77° F.), and in 10 parts of boiling water; readily soluble in alcohol, less soluble in ether and chloroform; soluble in fatty oils. Camphoric Acid is dextro-rotatory, showing in 10 per cent. alcoholic solution, the value $[\alpha]_D = +47.8°$. The aqueous solution reddens blue litmus paper. If 2 Cc. of a saturated aqueous solution of Camphoric Acid be mixed with 2 Cc. of sulphuric acid in a test tube, and 1 Cc. of a solution made by dissolving 1 Gm. of ferrous sulphate in 2 Cc. of diluted sulphuric acid be poured carefully upon it, no dark-colored zone should develop at the line of contact (absence of *nitric acid*)." *U. S. VIII. Camphoric acid* was at one time used in the treatment of *night sweats* and to a lesser extent in *cystitis,* but both Tyrode (*A. I. P. T.,* 1908, x, p. 393) and Roth (*J. P. Ex. T.,* 1911, ii, p. 405) find that it has no effect on the secretion of either sweat or salivary glands. According to the latter, it is slightly stimulating to the central nervous system, but Tyrode finds that the neutral salts are entirely inert. The *dose* which has been used is from five to fifteen grains (0.3–1 Gm.).

Camphoroxol.—A compound of camphor with hydrogen dioxide. It forms a clear, colorless liquid with a fragrant odor of camphor.

Camphosal, $C_3H_{14}(CO_2C_{15}H_{23})_2$, is said to be neutral *camphoric ester of santalol* and to be a yellowish-brown oil, sp. gr. 0.987, soluble in alcohol and ether, having a faint aromatic odor and bitter taste. It has been used in *diseases of the prostate,* and *catarrh of the bladder, urethral fever. Dose,* four minims (0.26 mil) given preferably in capsules.

Camphosan.—This compound is a solution of 15 parts of neutral methyl-ester of camphoric acid in 85 parts santal oil. It is a clear, aromatic, bitter and oily fluid; sp. gr. 0.991. It has been recommended by Vollmer (*D. M. Ztg.,* 1908) as a urinary antiseptic in *cystitis* and *urethritis,* especially as a prophylactic against infection from frequent

catheterization. The *dose* is five minims (0.3 mil) three to five times a day.

Camphossil.—This is a crystalline, unctuous, deliquescent, tasteless mass, with a camphoraceous odor, insoluble in water. It is said to be a condensation product of camphor and salicylic acid, and as an antipyretic and antiseptic to be useful in *diarrheas* in *doses* of eight grains (0.5 Gm.).

Canada Pitch. *Pix Canadensis. U. S.* 1880. *Hemlock Pitch.*—The *Tsuga canadensis* (L.) Carr, *Hemlock* or *Hemlock Spruce* of the United States and Canada, when of full growth, is often seventy or eighty feet high, with a trunk of two or three feet in diameter, and of nearly uniform dimensions for two-thirds of its length. Its leaves are scattered, short, linear, obtuse, from 8 to 13 mm. in length, whitened beneath and appearing as two-ranked. The strobiles are ovate, little longer than the leaves, terminal and pendulous.

The tree is abundant in Canada, Nova Scotia, and the more northern parts of New England, and is found in the elevated and mountainous regions of the Middle States. Its bark is much used for tanning, an extract being made for the purpose. The tree contains much less juice than some other of the *Pinaceæ*, and very little flows from incisions made into its trunk. But in the trees which have attained their full growth, and are about to, or have begun to, decay, the juice exudes spontaneously, and hardens upon the bark, in consequence of the partial evaporation or oxidation of its volatile oil. The bark thus incrusted is stripped from the tree, broken into pieces, and boiled in water. The pitch melts, rises to the surface, is skimmed off, and is still further purified by a second boiling in water. Hemlock pitch is hard, brittle, quite opaque, of a dark reddish-brown color, becoming still darker by exposure to the air, of a weak peculiar odor, and scarcely any taste. It softens and becomes adhesive with a moderate heat, and even at ordinary temperatures takes the form of the vessel containing it, and melts at 92.2° C. (198° F.).

The constituents of this pitch are resin and a minute proportion of volatile oil. It is sometimes known by the incorrect name of *hemlock gum. Canada pitch* is a gentle rubefacient, closely analogous to Burgundy pitch in its properties, and employed for precisely the same purposes. It is, however, more readily softened by heat, and is sometimes almost too soft for convenient application at the temperature of the body. A volatile oil obtained from *Tsuga canadensis*, and called *oil of spruce* or *oil of hemlock*, has been employed to a considerable extent in veterinary liniments. It has also been used as an abortifacient, with the effect of endangering the life of the woman. (J. S. Paige, *N. Y. M. J.*, viii, 184.)

W. Zinn (*M. M. W.*, Oct., 1902) reports a case of stupor and involuntary evacuation of urine, and collapse with subsequent psychic disturbance, as produced by the inhalation for many hours of the emanations from branches of *Pseudotsuga taxifolia* (Lamb.) Britton (*P. Douglassi* Car.).

The U. S. Pharmacopœia of 1880 gave the following directions for preparing the *Hemlock* or *Canada Pitch Plaster* (*Emplastrum Picis Canadensis, U. S.*, 1880): "Canada Pitch, *ninety parts* [or nine ounces av.]; Yellow Wax, *ten parts* [or one ounce, av.], to make *one hundred parts* [or ten ounces av.]. Melt them together, strain the mixture, and stir constantly until it thickens on cooling." *U. S.*, 1880.

Canary Seed. *Fructus* (*Semen*) *Canariense. Semence de Canarie*, Fr. *Kanariensamen*, G.—The seeds of *Phalaris canariensis* L., an annual grass originally from the Canary Islands, but now growing wild in Europe and the United States. The seeds are ovate, somewhat compressed, about 5 mm. long, shining and of a light yellowish-gray color externally, and light within. Their chief constituent is starch, and they are used chiefly as bird seed.

Canchalagua.—This plant, *Erythræa venusta* A. Gray (Fam. *Gentianaceæ*), found on our Pacific coast, is a valuable bitter tonic and stomachic. (*Ph. Rec.*, 1887, 363.) *Erythræa australis* R. Br. is said to be similarly used in Australia. (*P. J.*, xix.)

Cancroin. (*Cancer Serum.*)—This so-called serum and its dilutions are designated by Heermann as phenol-neurin citrates. Cancroin I is prepared from neurin, 25 per cent. solution, 10 Gm.; phenol, 1.25 Gm.; acid citric, 1.82 Gm.; aqua. ster., *ad* 27 Gm. This Cancroin I diluted with equal weight of distilled water gives Cancroin II and with 3 times its weight of distilled water, Cancroin III. It enjoyed for a brief period a wide use in the treatment of *cancers*, but is probably of no value.

Canella. *N. F. IV.*—The N. F. describes it as "the dried inner bark of *Canella Winterana* (Linné) Gaertner (Fam. *Canellaceæ*). In quills usually from 1 to 3 dm. in length and from 1 to 4 cm. in thickness, occasionally two or three times this size, or in irregular fragments of quills, from 1.5 to 5 mm. in thickness and 2 to 3 cm. in width, the outer periderm mostly removed; outer surface light brownish-yellow or pale orange-brown, more or less scaly, with a very few shallow fissures, often more or less reticulate with slight ridges; inner surface paler, somewhat smooth, but showing coarse, longitudinal striæ; fracture short and sharp, pale yellow, with an irregular, slightly darker band just inside of the center. Odor slight unless the bark is heated, then aromatic, resembling that of cinnamon; taste aromatic, warm, somewhat bitter and mucilaginous. The powdered drug is light brown to brownish-red and, when examined under the microscope, exhibits numerous, isodiametric, thick-walled stone cells about 0.075 mm. in diameter, the walls with simple or branching pores; calcium oxalate in rosette aggregates up to 0.05 mm. in diameter; starch grains simple or two- to three-compound up to 0.02 mm. in diameter; oil cells with suberized walls numerous. Canella yields not more than 7 per cent. of ash." *N. F.* It was formerly recognized by the U. S. and Br. Pharmacopœias. The tree is a native of Florida and the Bahama and West India Islands. The bark of the branches, which is the part employed in medicine, is loosened and deprived of its epidermis by beating. After removal from the tree it is dried in the shade. It enters commerce solely from the Bahamas, where it is known as *cinnamon bark*, or as *white wood bark*. At first it was considered to be a variety of cinnamon bark and was at one time confused with Winter's bark. Boiling water extracts nearly one-fourth of its weight; but the infusion, though bitter, has comparatively little of the warmth and pungency of the bark. It yields all its virtues to alcohol, forming a bright yellow tincture, which is rendered milky by the addition of water. Canella bark yields from distillation from 0.75 to 1.25 per cent. of a volatile oil, having an odor

resembling that of a mixture of cajeput and clove. It contains benzoyl eugenol; l-pinene; cineol and caryophyllene. The bark yielded to Flückiger 0.74 per cent. of oil. According to John P. Frey, it contains volatile oil, 1.28 per cent.; resin, 8.2 per cent.; mannite, 8 per cent.; ash, 8.9 per cent.; also starch, bitter principle, albumen, and cellulose. (*A. J. P.*, 1884, 1.) Canella has been sometimes confounded with Winter's bark, from which, however, it differs widely. (See *Wintera.*) It is a mild, aromatic tonic, very acceptable to the stomach, and especially as an addition to tonic or purgative medicines. It is scarcely ever prescribed except in combination. Its best known compound is the famous *Pulvis Aloe et Canellæ* (see Part III), commonly known as *Hiera Picra*, literally "*Sacred Bitters,*" from the esteem in which it was once held. In the West Indies it is employed by the negroes as a condiment and as an antiscorbutic. *Dose*, ten to forty grains (0.65–2.6 Gm.).

Cangoura.—An evergreen creeper, *Bouea oblongifolia* (Fam. *Anacardiaceæ*), from the seeds of which the natives of Salvador are said to produce a paste which is a violent nerve poison, producing in some cases delirium lasting as long as eight days. (*Nouv. Rem.*, April, 1892.)

Caoutchouc, Artificial.—For many years attempts have been made to make rubber substitutes by the vulcanization of fatty oils with either sulphur or sulphur chloride. Linseed oil, cotton seed oil, and the fish oils have all been used for this purpose with varying success. Very successful results have been attained by the vulcanization of maize oil. These products, known in Germany as *Factis*, may be white or dark colored, the latter color being obtained by the prolonged action of the sulphur. Oxidized or blown oils and sulphonated oils are also used for the vulcanization. In 1894 Nobel patented solutions of nitrocellulose in heavy oil solvents as rubber substitutes for rubber varnishes and coatings. Much reclaimed rubber from old rubber articles is revulcanized and incorporated with pure rubber in the manufacture of new rubber articles. Synthetic caoutchouc, comparable in all respects, both chemically and physically with the natural product, has lately been produced by the polymerization of the hydrocarbon isoprene, C_5H_8, and its homologues. As isoprene is prepared from amyl alcohol or fusel oil its success commercially depends largely upon the cost of the amyl alcohol.

Capparis. *Capparis spinosa* L. *Caper-bush.* (Fam. *Capparidaceæ.*)—A low, trailing shrub, growing in the south of Europe and north of Africa. The buds of unexpanded flowers, treated with salt and vinegar, form a highly esteemed pickle, which has an acrid, burning taste, and is considered useful in *scurvy*. The dried bark of the root was formerly official. It is in pieces partially or wholly quilled, about one-third of an inch in mean diameter, transversely wrinkled, grayish externally, whitish within, inodorous, and of a bitterish, somewhat acrid, and aromatic taste. It contains *rutic acid* and a volatile substance of garlic-like odor. It is considered diuretic, and was formerly used in *amenorrhea* and *chronic rheumatism*.

Capsella. *Capsella Bursa-pastoris* (L.) Medic. *Shepherd's purse. Bourse à Pasteur, Molette*, Fr. *Hirtentäschlein*, G. (Fam. *Cruciferæ.*)—This very common weed in the United States, naturalized from Europe, is bitter and pungent, yields on distillation a volatile oil identical with oil of mustard, and, according to E. Bombelon, contains an alkaloid, *bursine*. (See *A. J. P.*, 1888; also *Provincial Med. Journ.*, 1858.) It has been used as an antiscorbutic, also in *hematuria* and in other *hemorrhages*, *amenorrhea* and *dropsy*. From two to four fluidounces (60–120 mils) of the fresh expressed juice may be given at a *dose;* or from one-fourth to one-half fluidrachm (0.9–1.8 mils) of the fluidextract of the dried plant.

Captol.—This proprietary preparation is said to be an impure condensation product of tannin and hydrated chloral. It is a brown hygroscopic powder, slightly soluble in cold water, very soluble in hot water and alcohol, not altered by acids but decomposed by alkalies, striking an olive-green color with ferric salts. According to Eichhoff, in *seborrhea capitis* washing the head morning and evening with a 1 to 2 per cent. alcoholic solution of captol is very successful.

Capulincullo.—This drug, derived from the *Rhamnus Humboldtianus* Roem. and Schult. (Fam. *Rhamnaceæ*) of Mexico, is said to be a violent poison, acting like curare. A non-toxic, non-drying fixed oil, tasteless and odorless, is obtained in considerable quantities from the fruit of the tree.

Caramel. *N. F. IV. Saccharum Ustum. Burnt Sugar Coloring.*—"A concentrated aqueous solution of the product obtained by heating sugar or glucose until the sweet taste is destroyed and a uniform dark brown mass results, a small amount of alkali or alkali carbonate being added while heating." *N. F. IV.*

Caramel is a complex mixture of a number of organic compounds produced by heating sugars to a temperature high enough to burn them dark brown without charring. At present it is produced almost exclusively from starch, syrup or glucose. The N. F. describes it as "a thick, dark brown liquid, having the characteristic odor of burnt sugar and a pleasant, bitter taste. Caramel mixes clear with water in all proportions, 1 part dissolved in 1000 parts of distilled water yielding a clear solution having a distinct sepia tint. The color of this solution is not changed and no precipitate is formed after exposure to sunlight for six hours. It is soluble in diluted alcohol, but is precipitated when the alcoholic content of the solution is increased to 80 per cent., by volume, or more. It is insoluble in ether, chloroform, acetone, benzene, petroleum benzin, or oil of turpentine. Specific gravity: not less than 1.35 at 25° C. (77° F.). Spread a thin layer of Caramel on a glass plate; it appears homogenous, reddish-brown and transparent. No precipitate is produced in 20 mils of an aqueous solution of Caramel (1 in 20) on the addition of 0.5 mil of phosphoric acid. Caramel swells when incinerated and forms a coke-like charcoal, which burns off only after prolonged heating at a high temperature, and yields not more than 8 per cent. of ash." *N. F.*

It contains several complex coloring substances, an odorous principle, some undecomposed sugar and a white hygroscopic substance known as *caramelan*. Sp. gr. of caramel, from 1.30 to 1.39. Beringer (*A. J. P.*, lxxxiv, p. 160) proposes, for the sake of uniformity (which is difficult to obtain in commercial caramels), a purified caramel made as follows: Caramel, 1000 Gm.; Alcohol, 3500 mils; Monohydrated Sodium Carbonate, 4 Gm.; Water, *a sufficient quantity*. Weigh the caramel into a capacious bottle or flask, add 250 mils of boiling water and thoroughly mix. Add

gradually 3000 mils of alcohol, shaking after each addition. Set aside for six hours. Decant the alcoholic solution and wash the precipitate on a filter with two portions of 250 mils each of alcohol. Allow the precipitate to drain free from alcohol, dissolve it in 1500 mils of warm water, add the monohydrated sodium carbonate, filter the solution, evaporate it to a thick syrup and spread it upon glass plates to dry. Remove from the plates when dry and place in a desiccator over sulphuric acid until it ceases to lose weight. This process yields about 40 per cent. of purified caramel which has a high coloring power and great uniformity. George A. Menge proposes to make a standard solution of caramel for adjusting the tinctorial power of caramel as follows: Make a sulphuric acid solution by adding 1 mil of pure concentrated sulphuric acid (sp. gr. 1.84) to 12 mils of water. Take 0.5 Gm. of sugar in a test-tube, add 5 mils of the acid solution described, and heat the mixture in a bath of boiling water, with the mixture continuously submerged and with constant agitation, for exactly five minutes. Immediately add a little cold water and then 35 mils of the U. S. P. test solution of potassium hydroxide; finally dilute to 100 mils. The whole procedure takes about fifteen minutes. (*A. J. P.*, 1911, 113.)

A very satisfactory test for the identification of caramel in flavoring extracts and other liquids where it may be used as a color, has been proposed by G. H. P. Lichthardt. (*J. Ind. and Eng. Chem.*, xi, p. 389.) The following solution is required: Tannic acid, 1 Gm.; Sulphuric Acid (sp. gr. 1.84), 0.75 Gm.; Distilled Water, q. s. to make 50 mils. Dissolve the tannic acid in about 30 mils of water, add the sulphuric acid (the precipitate at first forming will redissolve) and then the remainder of the water. Let it stand twenty-four hours and filter. Add 5 mils of this solution to 5 mils of the liquid to be tested, heat gently until the precipitate at first formed is nearly all dissolved, then set aside for twelve hours or over night; a brown precipitate adhering closely to the bottom of the tube will be found when caramel is present. A flocculent, non-adhering precipitate is to be ignored. With highly alcoholic liquids the alcohol should be removed by evaporation and the volume restored by the addition of water before applying the test.

F. Ehrlich (*Bull. Chim. Soc.*, 1909, 140) states that the coloring principle in cane sugar caramel is an amorphous, tasteless compound, not precipitated by lead acetate, and having the chemical formula, $C_{12}H_{22}O_{11} + 2H_2O$, and to which he gives the name *saccharane*. The yield from sucrose is about 20 per cent. Dextrose, fructose and starch produce no saccharane.

Pure grape sugar and pure cane sugar caramel, for experimental purposes, have been prepared by G. D. Beal and H. F. Greler, according to methods outlined in *J. A. P. A.*, 1914, p. 495. The resulting products are in the form of scales made by evaporating the solutions on glass plates. Sucrose produces a darker caramel than dextrose, when working under exactly the same conditions, in the ratio of about 10 to 1.

Carana. *Mararo. Gum Carana.*—A resinous substance, in pieces of a blackish-gray color, externally dark brown, internally somewhat shining and translucent, brittle and pulverizable when dry, but, in the recent state, soft and adhesive, like pitch, easily fusible, of an agreeable balsamic odor when heated, and a bitterish resinous taste. (Geiger.) It is said to be derived from *Urotium Carana* (Humb.) L. March (Fam. *Rutaceæ*), a tree growing in Mexico and South America. Geiger refers it also to *Bursera Simaruba* (L.) Sarg. (*Bursera gummifera* L.), of the West India Islands; but the resin of this tree is *résine de Gomari* or *résine de chibou* or *cachibou* of French writers, and is said to bear a close resemblance to the resin *tacamahac*. It is probable that in South America the name *carana* is applied to different products. (*A. J. P.*, xli, 233.)

Carbon Dioxide.—*Carbon dioxide* is used for several purposes in medicine. In solution, it is called carbonic acid, and its popular employment is to improve the taste of disagreeable medicines, especially certain salines, and as a refreshing beverage. *Aqua Acidi Carbonici* (*Carbonic Acid Water*, or *Soda Water* (so-called); *Acidum Carbonicum Solution*, *Eau gazeuse simple*, Fr.; *Kohlensaurewasser*, G.), which was formerly official in the U. S. Pharmacopœia, consists of water highly charged with carbon dioxide. It is also used as a mild counter-irritant to the skin in the form of effervescent baths. Certain spas in which there is a supply of naturally carbonated water, such as Nauheim, make these baths a prominent part of the treatment, especially in cases of circulatory weakness. A formula for preparing these baths is given under *Aqua* (see p. 165).

Another use for carbonic acid is as an escharotic. Its destructive action depends upon the intense degree of cold produced by the melting of the solidified gas commonly called *carbonic acid snow*. This is prepared by allowing the compressed gas to escape from a cylinder into a cone-shaped felt or woolen receptacle. The rapid expansion of the gas when freed from pressure causes it to solidify in the form of snow which is dished out of the cone with a spoon and pressed into molds of suitable shape. As its melting point is approximately −54° C. (−65.2° F.) when applied to the skin it absorbs an immense amount of heat and almost immediately freezes the area to which it has been applied. The depth and permanency of the results of this freezing depend upon the duration of the application. Superficial freezing of the skin causes complete cessation of all functions and therefore local anesthesia as well as arrest of blood flow. After thorough freezing, as is accomplished with carbonic acid snow, there is probably formed thrombi in the superficial capillaries which lead to a permanent obstruction of the circulation and consequent death of the part. Carbonic acid snow is used with great success for the destruction of various types of neoplasms, as *warts*, *hairy moles*, and *vascular nevi*. It is also of service in the treatment of *malignant ulcers of the skin* and *epitheliomata*. The duration of single applications is from thirty seconds to one or two minutes, according to the depth of action which is desired.

Carbon Tetrachloride. *Tetrachlor-methane. Carbonei Tetrachloridum. Carboneum Chloratum. Chlorocarbon. Tétrachlorure de Carbone, Formène Perchloré*, Fr. *Chlorkohlenstoff*, G. CCl_4.—This substance, though discovered by Regnault so early as 1839, did not come into general notice until December, 1865, when it was suggested as an anesthetic by Simpson, of Edinburgh. To procure it, dry chlorine is passed first through a bottle containing carbon disulphide, and then through a porcelain tube filled with pieces of porcelain and

kept at a bright red heat. The vapors are condensed in a well cooled receiver, forming a yellowish-red liquid, which is a mixture of *carbon tetrachloride* and sulphur chloride. The sulphur chloride is removed by slowly adding the liquid to an excess of potash lye or milk of lime, the mixture being set aside, and agitated from time to time until the sulphur compound is decomposed, and then distilled. Chloroform is made to yield it by the substitution of an atom of chlorine for one of hydrogen; thus $CHCl_3$ (chloroform) becomes CCl_4 (carbon tetrachloride), and conversely chloroform is now made on a large scale by the reduction of the tetrachloride by nascent hydrogen.

Carbon tetrachloride is a transparent, colorless liquid, of the sp. gr. 1.599 (Regnault), boiling at 77° C. (170.6° F.), with a vapor density of 5.33, and an agreeable aromatic flavor. At 30° C. (86° F.) it solidifies to a crystalline mass. It is extensively used as a solvent for fats and removing grease from garments, replacing petroleum benzin to advantage because of its non-inflammability (*carbona*). As a solvent for alkaloids in assay work and in manufacturing processes it takes the place of chloroform. Mixtures of 40 per cent. light petroleum benzin with 60 per cent. carbon tetrachloride, or 50 per cent. benzene with 50 per cent. carbon tetrachloride, are also non-inflammable. It is very valuable as a fire extinguisher, and under the name of *Pyrene* is so used. A solution containing 4 per cent. of caoutchouc and 0.4 per cent. of iodine in carbon tetrachloride has been used for the purpose of coating the hands of the surgeon with a sterile and impermeable covering. Carbon tetrachloride has been suggested as an agent for surgical anesthesia, but, although the inhalation of it will produce complete unconsciousness, Simpson (*M. T. G.*, 1865) found that it was more depressant to the heart than is chloroform. (See also *L. L.*, June, 1867.) Its vapor, applied to the eye by sprinkling a few drops on the hand, is asserted to be an effectual means of relieving some forms of *conjunctivitis, ulceration of the cornea, photophobia*, etc. Internally, Simpson tried it only in small doses in *gastrodynia*, in which it had the same effects as chloroform. Colman (*L. L.*, June 22, 1907) has reported poisoning from the use of carbon tetrachloride in dry shampoos.

Carbosant. *N. N. R.* 1917. *Santalolis carbonas.* $(C_{15}H_{23}).O.CO.O.(C_{15}H_{23})$.—This is produced by the chemical interaction of santalol with carbonyl chloride, $COCl_2$, and an alkali. It is an oily, yellow fluid, almost tasteless and odorless, insoluble in water and soluble in alcohol and ether. It contains 94 per cent. of santalol. The action of *carbosant* is identical with that of santol oil, diminishing the secretions of the mucous membrane of the urinary tract and relieving pains in the urinary organs. It is used in ten minim *doses* (0.6 mil) three or four times daily.

Cardamine. *Cardamine pratensis* L. *Cuckoo-flower.*—This is a perennial herbaceous plant, of the fam. *Cruciferæ*, with a simple, smooth, erect stem, about a foot in height. The plant grows in Northern Europe and to some extent in wet places and bogs from New Jersey northward to Labrador. Its bitterish and slightly pungent leaves are supposed to be antiscorbutic. The seeds are said to contain *myronic acid*, and to yield on decomposition by hydrolysis an oil analogous to oil of mustard. Feist investigated *C. amara* L. and its volatile oil and found *thio-urea.* Kuntze states that two kinds of crystals were isolated, both being forms of thio-urea. (*A. Pharm.*, 1907, 657.) In Europe they are sometimes added to salads. The flowers formerly possessed the reputation of being diuretic, and of being useful in *chorea* and *asthma.*

Carissin.—This is a glucoside which has been isolated from the bark of *Carissa ovata* R. Br. (Fam. *Apocynaceæ*), by J. H. Maiden and H. G. Smith. It is stated to be exceedingly bitter and very poisonous, and in its chemical relations to resemble strophanthin, from which it differs, however, in being precipitated by basic lead acetate and by tannic acid. Its most characteristic reaction is the production of a beautiful emerald-green color on the addition of a minute fragment of potassium dichromate to its solution in concentrated sulphuric acid. (*P. J.*, 1896.)

Carmine. *N. F. IV. Carminum.*—The N. F. describes it as "the aluminum lake of the coloring principle obtained from cochineal. Preserve it in well-stoppered, amber-colored bottles, protected from light. It occurs in irregular, angular, bright red fragments or as a powder, without odor or taste. When burned, Carmine emits an odor resembling that of burned feathers. Slightly soluble in water to which it imparts a red color; freely soluble in ammonia water and alkaline liquids, forming a dark purplish-red solution. The yield of ash does not exceed 12 per cent. Fuse the ash from 1 Gm. of Carmine with 1 Gm. of sodium cyanide, dissolve the fused mass in hydrochloric acid with the addition of a few drops of nitric acid, then dilute it with distilled water to 30 mils and filter the solution. Separate portions of 10 mils each of this solution yield no precipitate with hydrogen sulphide T.S. or with sulphuric acid (*tin, lead and soluble barium compounds*). Fuse the ash from 1 Gm. of Carmine with a mixture of 1 Gm. of sodium cyanide and 1 Gm. of potassium carbonate, extract the fused mass with boiling distilled water, filter, wash with hot distilled water and dissolve the residue in diluted hydrochloric acid; this solution does not become turbid on the addition of a few drops of sulphuric acid (*barium sulphate*)." *N. F.* It is used exclusively as a coloring agent for pharmaceutical preparations, confections, cakes, etc.

Carnallite.—This material, found in Stassfurt, Germany, is very extensively used in the preparation of potassium salts. It is a hydrous chloride of potassium and magnesium ($KMgCl_3 + 6H_2O$), associated with rock-salt. The amount of carnallite mined in 1911 was given by the Kali Syndicate as 4,441,664 tons.

Carnauba Root.—This root, the product of *Copernicia cerifera* (Ar.) Mart. (*Corypha cerifera*), the Brazilian wax palm, is several feet in length, about three-eighths of an inch thick, with a thick friable cortex of a mixed grayish and reddish-brown color. (*A. J. P.*, 1875, 349.) E. L. Cleaver found in it tannic acid, an acrid resinous body, a red coloring matter, and a minute portion of volatile oil and of an alkaloid (*P. J.*, 1875, 965.) It is said to act like sarsaparilla. *Carnauba Wax*, with which the young leaves of the palm are coated, is a dark colored, hard, brittle wax, melting at from 83° to 88° C. (181.4°–190.4° F.) and possessing an acid number of 4 to 8, a saponification value of 80 to 95, and an iodine number of 7 to 13. (See under *Cera*, p. 310.) It is used in church candles to prevent guttering, for the manufacture of phonograph records, in the

composition of sealing wax and for other purposes in the arts.

Carota. *U. S.* 1870. *Carotte,* Fr. *Mohre, Gelbe Rübe,* G. *Daucus Carota* L.—The *wild carrot* (Fam. *Umbelliferæ*) is widely distributed, growing along fences, and in neglected fields. It grows wild also in Europe. The well-known garden carrot is the same plant altered by cultivation. The fruits are very light, of a brownish color, an oval shape, flat on one side and convex on the other, and on their convex surface present four longitudinal ridges, which are beset with stiff, whitish hairs or bristles. They have an aromatic odor, and a warm, pungent, and bitterish taste. By distillation they yield a pale yellow volatile oil, upon which their virtues chiefly depend. Schimmel & Co. found the distilled brownish-yellow oil to possess the odor of carrots only to a slight extent and to yield 1.26 per cent. (*Schim. Rep.,* 1907, 31.) Pictet isolated from the leaves of carrots a liquid alkaloid. (*Chem. Ztg.,* 1905, No. 97.) Subsequently two volatile alkaloids, *pyrvolidine* and *daucine,* were reported to be present by Pictet and Court. Carrot *seeds* are slightly aromatic, moderately excitant and diuretic, and have been employed as a diuretic in chronic *renal diseases* and in *dropsy.* An ounce of them may be given in infusion, in a day. The flowers are sometimes substituted for the seeds, and the scraped root has been used as a local stimulant to sloughing or *indolent ulcers.* For additional information concerning this drug, see *U. S. D.,* 19th ed., p. 1432.

Carniferrin. *Iron Phospho-sarcolactate.*—A reddish-brown, tasteless powder, insoluble in water, but soluble in ether and in acid or alkaline solutions. It is considered to be an iron salt of the organic phospho acids of meat, and, consequently, readily assimilable. It is given in *chlorotic* conditions. *Dose,* eight grains (0.5 Gm.).

Carthamus. *Carthamus tinctorius* L. *Safflower.*—The *African, false, American,* or *dyers' saffron* is an annual composite, with a smooth, erect stem, somewhat branched at top, and a foot or two in height. The plant is a native of India, the Levant, and Egypt, and is cultivated in those countries, as well as in various parts of Europe and America. The fruit yields 25.82 per cent. of fixed oil, the separated kernels of the seeds, 50.37 per cent., according to Fendler. (*Ap. Ztg.,* 1904, 121.) The florets are brought to us chiefly from the ports of the Mediterranean. *Safflower* (*Flores Carthami; Fleurs de carthame, Safran bâtard,* Fr.; *Saflor,* G.; *Cartamo,* It., Sp.) in mass is of a red color, diversified by the yellow of the styles contained within the floret. It has a peculiar, slightly aromatic odor, and a scarcely perceptible bitterness. It contains a fixed oil; also two coloring substances—one red, insoluble in alkaline liquids, and called *carthamin* or *carthamic acid* by Döbereiner, who found it to possess weak acid properties; the other yellow, and soluble in water. Carthamin, $C_{14}H_{16}O_7$, exists to the amount of from 0.3 to 0.6 per cent. only in the safflower, while the safflower-yellow, to which Malin gives the formula $C_{24}H_{30}O_{15}$, is present to the amount of from 24 to 30 per cent. It is the former which renders safflower useful as a dye stuff. Kametaka and Perkins give the formula of carthamin as $C_{25}H_{24}O_{12}$. (*P. J.,* 1910, 299.) These flowers are sometimes fraudulently mixed with saffron, which they resemble in color, but from which they may be distinguished by their tubular form, and the yellowish style and filaments which they enclose. In large doses *carthamus* is said to be laxative, and, administered in warm infusion, diaphoretic. It is used in domestic practice, as a substitute for saffron, in *measles, scarlatina,* and other *exanthematous diseases,* to promote the eruption. An infusion, two drachms to a pint of boiling water, is usually employed *pro re nata.*

Caruba di Guiden.—Under this name are largely used, for the relief of *asthma,* certain gall-like bodies, formed on various species of *Pistacia,* especially *P. Terebinthus* L., as the result of the stings of a hemipterous insect. According to Ignaz Hoffman, they are used for smoking and fumigation. For this purpose they are coarsely pulverized and burned in the bowl of a pipe, or in a dish, using a small funnel attached to a rubber tube for inhaling the fumes. Preparations should be made beforehand, so that the smoke may be inhaled at the commencement of the attack. They appear to act by exciting free secretion, probably through the turpentine with which they are saturated. They are said to be useful in *chronic bronchitis.* (*S. Jb.,* Bd. clii.)

Carvacrol. *Isopropyl-o-cresol. Oxycymol.* $C_{10}H_{13}OH$.—A phenol-like body existing in the Trieste and Smyrna *Origanum* oil and some other labiate plants and made artificially from either carvone or camphor. It forms a thick, colorless oil which does not solidify at 25° C. (77° F.), and boils at from 233° to 235° C. (451.4°–455° F.). For an investigation of *Nitroso-carvacrol,* by Kremers and Brandel, see *Ph. Rev.,* 1904, 248. Cousin and Hérissey prepared from *carvacrol, dehydrodicarvacrol* or *dicarvacrol.* (*J. P. C.,* 1910, 2, 49.)

According to Martindale, carvacrol is almost as actively germicidal as its isomer, thymol. It has been used in medicine not only for its antibacterial properties, but also as a local anesthetic in *toothache,* cotton saturated with it being inserted into the carious cavity.

Carvacrol Iodide.—*Iodocrol,* $C_{10}H_{13}OI$, is a bulky, grayish-yellow or buff-colored amorphous powder having a faint aromatic odor. It is insoluble in water, slightly soluble in alcohol, soluble in ether, chloroform, petroleum, benzin, carbon disulphide, volatile and fixed oils. From its solution in ether and chloroform it is precipitated on the addition of alcohol, becoming paler in color. This purified product does not show signs of shrinkage until above 170° C. (338° F.), and at 200° C. (392° F.) becomes tarry and black. It is alleged that it combines the antiseptic properties of carvacrol with those of iodine, and possesses the advantage over iodoform in being odorless or nearly so, and in being five times as bulky. It has been used in surgical dressings in *eczema, pruritus, chancres,* and *chancroids.*

Carya. *Hicoria. Hickory.*—Several species of the genus *Carya* Nuttall (*Hicoria* Raf.) grow in the United States of which *Carya illinoensis* (Wang.) K. Koch bears the *pecan nut,* and grows in the Middle and Southwestern States; *C. ovata* (Mill.) K. Koch, a large and handsome tree known as *shell-bark* or *shag-bark hickory,* is the chief source of the hickory nuts of the market. There are six other common species of *carya* which are indigenous to the United States and Canada, and all yield edible fruits. The leaves of most if not all of these trees are somewhat aromatic and astringent, and the bark astringent and bitter. In the bark of *H. alba* F. R. Smith found a crys-

talline principle, *caryin*, which he believed to be *quercitrin*.

Cascara Amarga. *Honduras Bark.*—The bark of *Picramnia antidesma* Siv. (Fam. *Simarubaceæ*), a shrub growing in Jamaica, Mexico, Panama, and Columbia. It is a bitter tonic credited with specific alterative properties. For an elaborate discussion of the microscopic and chemical characters of the bark and its alkaloid *picramnine*, by Thompson, see *A. J. P.*, June, 1884.

Casearia. *Casearia esculenta* Roxb.—This Indian plant (fam. *Samydaceæ*) is said to be a valuable remedy in *hepatic torpor*, and to contain an organic acid allied to cathartic acid. (*P. J.*, xx.)

Casein.—This substance is one of the important constituents of milk and cheese. It is now made on a large scale in the United States from the "skim milk" obtained from creameries; this is conducted into tanks and heated by steam to 49° C. (120° F.), then coagulated by hydrochloric acid and thoroughly agitated; the *casein* separates into a mass, and the remaining liquid is used in the manufacture of sugar of milk. (See *Saccharum Lactis*, also a paper by C. H. LaWall in the *Alumni Report of the Philadelphia College of Pharmacy*, April, 1902, and one by J. W. England, *Proc. A. Ph. A.*, 1902, p. 357.) Commercial casein is used largely in the sizing of paper and in the manufacture of a glue substitute. The importation in 1915 amounted to 10,376,648 pounds. It has been proposed by Seger as an emulsifying agent in pharmacy. One gallon of milk is treated with two and a half fluidounces of water of ammonia for twenty-four hours, and, after removing the saponaceous matter from the surface of the mixture, the serum is precipitated with acetic acid. The magma of casein, strongly pressed, is treated with sodium bicarbonate, and with a sufficient quantity of sugar to make the dried product contain one-tenth of its weight of casein. The powdered substance dissolves easily in water, and, mixed with an equal weight of gum, may be used for almost all of the emulsions. Resinous matters and balsams previously dissolved in alcohol, essences, and oils, may be mixed with it in the bottle itself without using the mortar. The only defect in this casein saccharate is its slight odor. The casein of milk prepared by a somewhat similar process to the above is largely used in the preparation of many of the so-called "rolling" creams used for cosmetic purposes.

Pure casein has a sp. gr. of 1.259. It is readily soluble in 1 per cent. solutions of sodium fluoride, ammonium oxalate, and potassium oxalate, and 5 per cent. solutions of ammonium chloride or sulphate, as well as solutions of alkaline hydroxides, carbonates, borates, etc. Iodine compounds of casein are in use as follows: *periodocasein*, containing 17.89 per cent. iodine; *iodocasein*, containing 15.7 per cent. iodine; and *casein iodine*, containing 8.7 per cent. iodine. Bromine compounds are also known. Metallic casein compounds, as *silver caseinate*, are known and referred to under the appropriate heads. Compounds of casein with alkaloids are prepared by suspending casein in alcohol and adding an alcoholic solution of the alkaloid.

Casimiroa. *Casimiroa edulis* La. Llav. *Zapote blanco. Cochilsapote. White Sapota.*—This is a large tree belonging to the *Rutaceæ*, a native of Mexico, the leaves are employed in *diarrhea* and as an anthelmintic. The seeds are said to be narcotic. In them José Sanchez (*Breve estudio Zabote blanco, Thesis*, Mexico, 1893) has found a resin and a crystalline alkaloidal body. The glucoside *casimirose*, found in this plant by Altamirano, as well as the alkaloidal glucoside *casimirin*, isolated by Bikorn (*A. Pharm.*, ccxli, p. 166), have been found by Esch and Kochmann (*A. J. P. T.*, 1911, xxi, p. 353) to be inert. The extracts of the crude drug, however, have pronounced narcotic properties. They conclude that this drug has the extraordinary property of abolishing the sensation of pain without affecting consciousness or motility. Somewhat in contradiction to this conclusion, however, are the results of Robin and Cojon (*Press. Med.*, 1909, p. 454) who find that the fluidextract of *casimiroa* in *doses* of one to two teaspoonfuls has hypnotic properties.

Cassia. *Cassia marilandica* L. *Wild Senna. American Senna. Séné Américain*, Fr. *Amerikanische Senna*, G. (Fam. *Leguminosæ*.)—This is an indigenous perennial plant of vigorous growth, sending up annually numerous round, erect, nearly smooth stems, which are usually simple, and rise from three to six feet in height. The leaves are alternate, and composed of from eight to ten pairs of oblong-lanceolate, smooth, mucronate leaflets, green on their upper surface, pale beneath, and connected by short petioles with the common footstalk, which is compressed, channelled above, and furnished near its base with an ovate, stipitate gland. The *American senna* is common from New England to North Carolina. The leaves, which should be collected in August or the beginning of September, are sometimes brought into the market, compressed into oblong cakes, like those prepared by the Shakers from most herbaceous medicinal plants. The leaflets are from an inch and a half to two inches long, from one-fourth to half an inch in breadth, thin, pliable, and of a pale green color. They have a feeble odor, and a nauseous taste, somewhat analogous to that of senna. Water and alcohol extract their virtues. Hermann J. M. Schroeter (*A. J. P.*, 1888, 231) found in them *chrysophanic acid;* also an active principle corresponding in all respects with *cathartic acid*. For earlier analysis by Martin, see *A. J. P.*, i, 22. American senna is an efficient and safe cathartic, acting like senna but more feebly.

Cassia nictitans L., or *Wild Sensitive Plant*, was investigated by Gallaher (*A. J. P.*, 1888, 280), who failed to find any glucoside or alkaloid. The amount of volatile oil found was very small, and cathartic acid could not be prepared from it, although the powder produced griping. The leaves of *Cassia alta* L. are recommended by Conillebault in *ringworm;* they are moistened and the parts affected rubbed with them. (*A. J. P.*, 1887, 266.)

Under the names of *Cheshmat, Chashmizok, Schischen*, the seeds of *C. Absus* L. are said to be used in India and Africa in the treatment of inflammations of the eye, either in the form of a fine powder or an infusion made from the coarsely ground seeds to which several medicinal substances are added.

The root of the *Cassia bearensis* Miq. is said to be very useful in the so-called *black-water fever* of Africa. (See *P. J.*, vols. xlvii, xlviii.)

Castanea. *N. F. IV. Chestnut Leaves.*—"The dried leaves of *Castanea dentata* (Marshall) Borkhausen (Fam. *Fagaceæ*), collected in Septem-

ber or October while still green, and without the presence of more than 5 per cent. of twigs or other foreign matter." *N. F.* It was official in the U. S. P., 1890. Of the few species included in the genus *Castanea*, two are natives of North America. Of these *C. dentata* has been considered by many botanists as identical with *C. sativa* Mill. (*C. vesca* Gaertn.), of Europe, and was described by Michaux as a variety of that species under the name of *americana*. Botanists at present, however, generally consider the two species as distinct. "Petioles stout, about 12 mm. in length; blades entire or slightly broken and usually folded or matted together; about 15 to 25 cm. in length and about 5 cm. in breadth, oblong-lanceolate, apex attenuate, acute at the base, coarsely and sharply serrate with ascending, attenuate teeth, nearly smooth, coriaceous in texture, the upper surface dark green, the lower light green; distinctly pinnately veined, the veins of the first order diverging at an angle of about 60 degrees, each terminating in one of the teeth. Odor slight; taste astringent. The powdered drug, when examined under the microscope, shows a few non-glandular hairs from 0.1 to 0.5 mm. in length, nearly smooth, thick-walled, distinctly yellow, occasionally in groups of three to eight and spreading from the base; numerous calcium oxalate crystals in rosette aggregates or in monoclinic prisms, from 0.01 to 0.04 mm. in diameter; parenchyma cells containing irregular yellowish-brown tannin masses which are colored blue with ammonio-ferric alum T.S. Castanea yields not more than 5 per cent. of ash." *N. F.* It is almost impossible to exhaust the leaves by percolation. Their odor is feeble and their taste slightly astringent. They yield their virtues freely to water, and probably less so to alcohol. John B. Turner found in chestnut leaves chlorophyll, tannin, gallic acid, gum, and albumen. (*A. J. P.*, 1879, p. 542.) In addition to these constituents, L. J. Steltzer found potassium, calcium, magnesium, and iron carbonates, chlorides, and phosphates, and a trace of resin and fat. (*A. J. P.*, 1880, p. 294.)

There is a popular superstition that chestnut leaves are of value in *whooping cough*, but the possession by them of any physiological or medicinal power is extremely doubtful. They may be administered in the form of a *fluidextract* which is official in the N. F. (see Part III). *Dose*, one drachm (4 Gm.).

Castanea pumila (L.) Mill., *Chinquapin* of the Southern United States, is a bush or small tree usually eight or ten feet in height, but in the Gulf States reaches sometimes thirty feet. The oblong, acute, mucronately serrated leaves are readily distinguished from those of the ordinary chestnut by being whitish and downy underneath. The tree produces a small, edible nut. The bark has been used as an astringent tonic. (For analysis, see *A. J. P.*, 1899.)

Castela. *Castela Nicholsoni texana* Jorrey and Gray. (Fam. *Simarubaceæ*.)—This plant, which is known among the Mexicans as *Chaparro amargosa*, that is, *bitter bush*, has been highly recommended by Nixon (*J. A. M. A.*, 1916, lxvi, p. 946) in the treatment of amebic *dysentery*. He found that a detannated fluidextract in the proportion of one part in a million was sufficient to cause the *Entamœba histolytica* to become immobile and to assume a spherical shape, with sharp differentiations of ectoplasm and endoplasm. In ordinary diarrhea or in helminthiasis he found the drug of no value. Putegnat (*N. R.*, 1883, xii, p. 102) has separated a bitter principle, *amargosin*, which, however, is of doubtful importance. Nixon preferred a decoction of the drug, but the fluidextract is upon the market and may be given in *doses* of one to three fluidrachms (4.0–12.0 mils).

Castor. *Castoreum*, *Castoréum*, Fr. *Bibergeil*, G. *Castoro*, It. *Castoreo*, Sp.—In the beaver, *Castor fiber* L., between the anus and external genitals of both sexes, are two pairs of membranous follicles, of which the lower and larger are pear shaped, and contain an oily, viscid, highly odorous substance, secreted by glands which lie externally to the sac. After death, the follicles containing *castor* are removed, and dried either by smoke or in the sun.

This drug is derived either from the northern and northwestern parts of America, or from Russia, and is called in commerce, according to its source, Canadian or American and Russian castor. It is supposed by some that the American and Russian beavers are distinct species, the former being a building, the latter a burrowing animal, and additional ground for the supposition is afforded by the fact that the products of the two differ considerably. Of the Russian castor only a very small portion is imported into this country.

Castor comes to us in the form of solid unctuous masses, contained in sacs about two inches in length, larger at one end than at the other, much flattened and wrinkled, of a brown or blackish color externally, and united in pairs by the excretory ducts which connect them in the living animal. In each pair one sac is generally larger than the other. They are divided internally into numerous cells, containing the castor, which, when the sacs are cut or torn open, is exhibited of a brown or reddish-brown color, intermingled more or less with the whitish membrane forming the cells. Those brought from Russia are larger, fuller, heavier, and less tenacious than the American; and their contents, which are of a rusty or liver color, have a stronger taste and odor, and are considered more valuable as a medicine. A variety of Russian castor, described by Pereira under the name of *chalky Russian castor*, is in smaller and rounder sacs than the American, has a peculiar empyreumatic odor very different from that of the other varieties, breaks like starch under the teeth, and is characterized by effervescing with diluted hydrochloric acid. Müller found 40.646 per cent. of calcium carbonate. According to Kohli, Canadian castor, treated with distilled water and ammonia, affords an orange precipitate, while the precipitate thrown down from the Russian under similar treatment is white.

Good castor has a strong, fetid, peculiar odor; a bitter, acrid, and nauseous taste, and a color more or less tinged with red. It is of a softer or harder consistence according as it is more or less thoroughly dried. When perfectly desiccated, though still slightly unctuous, it is hard, brittle, and has a resinous fracture. Its chemical constituents, according to Brandes, are volatile oil, 2 per cent.; resinous matter, 14–50 per cent.; albumin; a substance resembling *osmazome;* mucus; salicin; cholesterin; calcium urate, carbonate, benzoate, phosphate, and sulphate; sodium acetate and chloride; potassium chloride, sulphate, and benzoate; ammonium carbonate; membranous matter, and a peculiar proximate principle discovered by Bizio, an Italian chemist, and called

by him *castorin*. For additional information concerning castor, see *U. S. D.*, 19th ed., p. 1435.

Castor was at one time much used as a stimulant antispasmodic, also as an emmenagogue, but has passed almost entirely out of vogue. It may be given in *hysterical affections* in *doses* of ten to thirty grains (0.65–2.0 Gm.), in capsules or emulsion.

A substance allied to castor is the secretion of the anal glands, used for the purpose of defence by the *Mephitis mephitica*, or *common skunk* of North America. According to T. B. Aldrich, this is a neutral, golden-colored liquid, having an extremely penetrating and disagreeable odor, containing mercaptan, allyl-sulphide, and traces of butyl-mercaptan. (*C. D.*, 1897.)

Catalpa. *Catalpa bignonioides* Walt. *Catalpa-tree*, or *Catawba-tree. Indian Bean.*—This is a beautiful indigenous, flowering tree, of the fam. *Bignoniaceæ*, the seeds of which have been employed in *asthma*. Eugene O. Rau obtained from them tannin and a bitter crystalline principle. (*A. J. P.*, xlii, 204.) F. K. Brown obtained from the seeds resin, fixed oil, tannin, sugar, and two crystalline bodies, their exact nature not being determined. (*A. J. P.*, 1887, 230.) I. Schneck states that large doses cause nausea, vomiting, and slow, weak, intermittent pulse. He gave two fluidrachms (7.5 mils) of the tincture (1 oz. troy to 1 pint) every one to three hours.

Cataplasms. *Cataplasmata. Poultices. Cataplasmes*, Fr. *Umschläge, Breiumschläge*, G.—*Cataplasms*, or poultices, are moist substances intended for external application, of such a consistence as to accommodate themselves accurately to the surface to which they are applied, without being so liquid as to spread over the neighboring parts, or so tenacious as to adhere firmly to the skin. As they are in this country seldom made by the pharmacist they were not deemed by the compilers of the U. S. Pharmacopœia proper objects for official direction. *Cataplasma Kaolini* was official in the U. S. VIII and was transferred to the National Formulary IV.

Catha. *Catha edulis.*—Under various Arabic names, such as *Kât, Khât, Chaat, Kus es Salahin, Tchaad, Tschut, Tohat, Tohai, Gât*, the leaves of *Catha edulis* Forsk. (fam. *Celastraceæ*) (*Abyssinian* or *African tea*) are very largely used as a stimulant in Northern Africa, the plant being extensively cultivated. According to Collin, from 1400 to 1500 camel loads are yearly sold in Aden. The plant is a shrub, reaching the height of 9 to 12 feet, with thin coriaceous leaves whose margins are bluntly serrate. The rounded grayish-green twigs are, for commercial purposes, dried with the leaves and tied together in bundles containing about forty twigs; the bundles are commonly from twelve to fourteen inches in length and three to four inches in diameter, but sometimes much smaller. The leaves are chewed both in the green and fresh condition, and are in some places made into a tea. The taste is sweetish and astringent, somewhat suggesting licorice. They are asserted to act as stimulants, overcoming the sense of fatigue in the same way as cocaine, or caffeine. Flückiger and Gerrock found in it an alkaloid, *katine*, $C_{10}H_{18}ON_2$, which has been studied by Chevalier (*B. G. T.*, 1911), who finds that it is a stimulant to the central nervous system. Stockman (*P. J.*, Nov. 30, 1912) found three alkaloids, *cathine, cathinine*, and *cathidine*, and also a fourth alkaloid in too small quantities for study. He found (*J. P. Ex. T.*, 1913, iv) that these alkaloids were stimulating to both the brain and spinal cord, and in large doses produced paralysis through a direct action upon the muscle.

Catnep. *N. F. IV. Cataria. Catmint. Catnip. Cataire*, Fr. *Katzenmünze*, G. *Cattara*, It. *Gatera*, Sp.—It is described in the N. F. as "the dried leaves and flowering tops of *Nepeta Cataria* Linné (Fam. *Labiatæ*). Tops, when whole, from 10 to 20 cm. in length, much branched, commonly crushed and broken; stems quadrangular, downy; leaves opposite, those of the stem petiolate, from 2 to 7 cm. in length, rounded heart-shaped at the base, oblong, pointed at the apex, pale gray-green, soft-hairy above, downy beneath, margin deeply crenate, floral leaves small, bract-like; flowers small, in dense, interrupted spikes; calyx hairy, tubular, curved obliquely and sub-equally five-toothed; corolla whitish, dotted with purple, throat dilated, limb bilabiate, the upper lip erect, two cleft, lower spreading, three cleft, the middle lobe largest, crenulate; stamens two pairs ascending under the upper lip, lower pair shorter. Odor faintly aromatic and mint-like; taste bitter, pungent and aromatic. Catnep yields not more than 16 per cent. of ash." *N. F.* Catnep is a perennial labiate plant which is common near dwellings in the United States, but is supposed to have been introduced from Europe. It is called *catnip* on account of the fondness which cats show for it either in the fresh or the dried condition. The active constituents are volatile oil, and tannin of the kind which produces a greenish color with the salts of iron. Therapeutically it is very feeble. *Dose*, one drachm (4 Gm.).

Caulophyllum. *N. F. IV. Pappoose Root. Squaw Root. Blue Cohosh.*—"The dried rhizome and roots of *Caulophyllum thalictroides* (Linné) Michaux (Fam. *Berberidaceæ*)." *N. F.* This is an indigenous, perennial, herbaceous plant, with matted, knotty rhizomes, from which rises a single smooth stem, about two feet high. "Rhizome of horizontal growth, from 7 to 25 cm. in length, and from 5 to 15 mm. in thickness, much branched, slightly compressed from above, bearing large, cup-shaped stem scars on the upper surface, underneath a tangled or matted mass of long, curved, thin, tough roots which frequently conceal the rhizome; both rhizome and roots of a grayish or yellowish-gray color; fracture tough and woody. Odorless but sternutatory; taste bitter-sweet and acrid. The powdered drug is light brown and, when examined under the microscope, it exhibits numerous starch grains, spherical in outline, mostly simple, up to 0.016 mm. in diameter; fragments of cork with cells about 0.05 mm. in diameter and having yellowish-brown walls; tracheæ with bordered pores, the cells being up to 0.05 mm. in width; wood fibers with heavily lignified walls; fragments of parenchyma tissue with many of the cells containing starch grains. Caulophyllum yields not more than 6 per cent. of ash." *N. F.*

Mayer found caulophyllum to contain a saponin and a colorless alkaloid. (*A. J. P.*, 1863, 99.) The *caulophyllin* of the eclectics is made by pouring a concentrated alcoholic tincture into water and collecting the precipitate, washing with ether, and drying. For an analysis of this substance by J. F. H. Gilbard, see *P. J.*, 1911, 101. J. U. Lloyd purified the substance which Ebert described as analogous to saponin, and for distinction terms it *leontin*. (See *Drugs and Medicines of North America*, vol. ii, 152.) He also obtained *caulophylline*, the alkaloid first announced by Mayer

in 1863. Lloyd describes it as colorless, odorless, possessed of little taste, and dissolving freely in water, alcohol, ether, and chloroform. It crystallizes with difficulty. The hydrochloride has been obtained, however, in crystals. It has not been tested physiologically. The fruit has been analyzed by Edith Stockton and C. G. Eldridge. (See *Chem. News*, 1908, 190.)

Caulophyllum has been used by eclectic and homœopathic practitioners. It is said to be sedative, antispasmodic, and oxytocic, and to have the power when *uterine inertia* occurs during labor to cause the contractions to become very severe, without altering their general character as does ergot. It is also alleged to be capable of arresting threatened *abortion*, to be very efficacious in *hysteria, amenorrhea, dysmenorrhea, menorrhagia, uterine subinvolution*, etc.; also to be capable of originating uterine contractions and of producing abortion. For a detailed description of the various contradictory powers ascribed to it, the reader is referred to Lloyd's *Drugs and Medicines of North America*, vol. ii, p. 155. It is given in decoction, infusion, or tincture, the first two being made in the proportion of an ounce to a pint of water, the last of four ounces to a pint of spirit. *Dose*, of decoction or infusion, one or two fluidounces (30 or 60 mils); of the fluidextract five to ten minims (0.3–0.6 mil). *Leontin* has been used in *doses* of six-tenths of a grain (0.04 Gm.) in a one per cent. solution.

Cayaponia. *Cayaponia globosa. Silva Manso.*—This is a cucurbitaceous plant of Brazil, from which Gubler has extracted the alkaloid *cayaponine*, said to purge without griping. *Dose*, one grain (0.065 Gm.). (*Rép. de Pharm.*, 1879, 193.)

Ceanothus. *Ceanothus americanus* L. *New Jersey Tea. Red-root. Céanothe*, Fr. *Seckelblumen-wurzel*, G.—A small indigenous shrub, of the fam. *Rhamnaceæ*, growing from western Ontario and Maine southward. The *root* is astringent, and imparts a red color to water. H. K. Bowman found in it 9.21 per cent. of tannin. (*A. J. P.*, 1869, 195.) F. C. Gerlach has again examined the root. (*A. J. P.*, 1891, 332.) He finds 6.48 per cent. of tannin and 0.52 per cent. of an alkaloid to which he gives the name *ceanothine*. J. H. M. Clinch has found in the leaves a resin and a volatile oil. (*A. J. P.*, xiv, 1884.) J. A. Buckner (*A. J. P.*, 1891, 428) found 9.45 per cent. of tannin in the leaves. *Ceanothus* is said to be useful in *syphilis*. Schoepf states that it is purgative. The leaves were used during the Revolutionary War as a substitute for tea. The Mexican *C. cæruleus* Lagasca (*C. azureus* Desf.) is used as a febrifuge.

Cearin.—An ointment vehicle capable of taking up a large proportion of water. Issleib makes it from a mixture of one part of carnauba wax and three parts of paraffin or ceresin (bleached by exposure to sunlight only); this is fused and mixed with four times its weight of liquid petrolatum and stirred until cold.

Cecropia Obtusa Trec. (Fam. *Urticaceæ*.)—An extract of these leaves is used as a diuretic, having an action similar to that of digitalis though less toxic than it. *Dose* of the liquid extract, thirty minims (1.8 mils).

Cedron.—The seeds of the *Simaba Cedron* Planch., a tree growing in Colombia and Central America, belonging to the *Simarubaceæ*. The fruit is a large solitary drupe, containing a single seed. *Cedron* seed is from 3 to 4.5 cm. long, and 1.5 to 2.5 cm. broad, elongated ovate, convex on one side, flat or slightly concave on the other, and presenting an oval scar near one extremity of the flat surface. It is often yellowish, hard and compact, but readily cut with a knife; is inodorous, but of a pure and intensely bitter taste, not unlike that of quassia. It yields its virtues to water and alcohol. Lowry (*J. P. C.*, xix, p. 365) separated from what he believed to be the seeds of *Simaba Cedron*, a crystalline substance which he named *cedrin*. Tanret, however, in attempting to confirm his work, was unable to obtain a crystalline substance from this plant, but he did from one closely allied to it, namely, the *S. waldivia*, and believed that Lowry was mistaken in the identity of his crude material. (See *P. J.*, 1908, lxxxi, p. 103.) Cedrin is now an article of commerce in the colorless crystals. It is bitter, slowly soluble in water, more readily so in alcohol or ether.

Cedron has been used in Central America as a remedy for snake bite and Purple has recommended it as an antiperiodic. The *dose* of the crude drug is from five to fifteen grains (0.3–0.9 Gm.). The bitter principle cedrin has been given hypodermically in *doses* of one-fifteenth of a grain (0.004 Gm.).

Celastrus.—Various species of the *Celastraceæ* have medicinal properties. In the East Indies the oil obtained from the seeds of *Celastrus paniculatus* Willd. is used as a powerful stimulant and diaphoretic in *rheumatism, gout*, and various *fevers*. The oil is said to be deep reddish-yellow, and to become thick and honey-like on keeping. It is sometimes known as *oleum nigrum*. In Abyssinia, according to Dragendorff, the leaves of *C. serratus* Hochst. (*C. obscurus* A. Rich.) are used as an antiperiodic under the name of *Add-add*. Dragendorff found in them tannic acid, a volatile oil, and a bitter principle, *celastrine*. (*A. J. P.*, xxvi.) In North America the bark of *Celastrus scandens* L. (*climbing staff tree, false bittersweet, fever twig*) has been used in chronic affections of the *liver* and in *secondary syphilis*, and is said to be emetic, diaphoretic, and alterative. C. H. Bernhard found in the bark acid and neutral resin, starch, glucose, gum, a caoutchouc-like body, coloring matter, and volatile oil. (*A. J. P.*, 1882, 1.) Wayne stated that he had isolated from *C. scandens* white minute crystals, to which he gave the name of *celastrine*. According to Ugolino Mosso (*Rivista Clinica*, 1891), celastrine arrests the frog's heart in systole; does not affect markedly the blood pressure in mammals, and influences the respiration only through its action on the vagus. The stimulant action is especially manifest on the brain and is not followed by a secondary depression. There is marked, persistent elevation of the temperature.

Celery Fruit. *Apii Fructus. N. F. IV. Celery Seed. March, Céleri*, Fr. *Sellerie, Eppich*, G.—"The ripe fruit of *Apium graveolens* Linné (Fam. *Umbelliferæ*), without the presence of more than 10 per cent. of foreign fruit or other foreign matter." *N. F.* The ordinary celery of our gardens is too well known to need description. The N. F. recognizes the fruits and describes them as follows: "The fruits consist of two mericarps which may be united or separate. Mericarps ovoid, slightly curved, from 1 to 2 mm. in length, rather more than half as broad and about half as thick, of a rather deep brown color; the inner surface flat, the outer convex, smooth except for five very slender light-colored ribs, two of which are mar-

ginal. Oil-tubes in the pericarp from 6 to 15. Odor characteristic, agreeable; taste aromatic, warm and somewhat pungent. Transverse sections, when examined under the microscope, exhibit nearly equilateral pentagonal mericarps, with somewhat convex surfaces; the carpophore consisting of two groups of strongly lignified sclerenchyma cells; each mericarp has from six to fifteen vittæ in the pericarp, the latter closely surrounding a somewhat pentagonal seed; the pericarp has an epidermal layer of cells elongated tangentially and with a thick cuticle; a few of the cells are developed into short, smooth, papillæ; a fibro-vascular bundle in each of the prominent ribs, composed of a few tracheæ and strongly lignified sclerenchyma fibers; the inner tissue of the pericarp consists of largely tangentially elongated parenchyma with brownish walls; the seed consists chiefly of endosperm; the seed coat is composed of several layers of yellowish more or less collapsed cells, the endosperm of thick-walled polygonal cells containing fixed oil and aleurone grains, the latter each containing a small rosette aggregate of calcium oxalate. The powdered drug is oily and has a brown color and, when examined under the microscope, exhibits fragments of the pericarp showing yellowish vittæ, brown secretion cells and few of the epidermal papillæ; tracheæ and sclerenchyma fibers; cells of the endosperm with aleurone grains containing rosette aggregates of calcium oxalate from 0.002 to 0.006 mm. in diameter. Celery Fruit yields not more than 8 per cent. of ash." *N. F.*

Oil of Celery Seed was investigated by Swenholt, who found that it consisted of two oils, one heavy, sp. gr. 0.877, at 20° C. (68° F.), the other light, sp. gr. 0.84. Celery seed contains apiol but in less quantity than parsley (see *Petroselinum*, Part I). Celery has by some been believed to act as a nerve sedative and is used in hysteroidal states, but with doubtful advantage. The *dose* is twenty to sixty grains (1.2–3.9 Gm.).

Apium nodiflorum (L.) B. et H. (*Sium nodiflorum* L.) *Water parsnip.*—This is a perennial, umbelliferous, aquatic, Eurogean plant, growing also in the southern section of the United States. It is commonly considered poisonous; but the fresh juice has been used by Withering and others, in the *dose* of three to four ounces every morning, for scrofulous *lymphadenitis* and obstinate *skin diseases.*

Celloidin. *N. N. R.* 1917.—Tough shreds consisting of a purified form of pyroxylin. It is supplied in shreds immersed in water.

Cellotropin. *Monobenzoyl Arbutin.* $C_6H_4.O.C_6H_5CO.O.C_6H_{11}O_5$.—This is prepared by acting upon arbutin with benzoyl chloride. It is a white, odorless and tasteless powder, practically insoluble in water or ether, but freely soluble in alcohol. To this substance Kapp (*Med. Rund.*, 1904) attributes the remarkable quality of being a specific curative in *pulmonary tuberculosis.* He asserts that it exercises direct action on the tubercle bacilli which he believes is probably due to an increase of the bodily enzymes. Its influence is generally manifest within a few weeks. It has also been used in *gastro-intestinal catarrh* and digestive disturbances of children. The *dose* for adults is put down as eight to fifteen grains (0.5–1.0 Gm.).

Celluloid. *Zylonite.*—This material, which has been manufactured into so many useful forms, furnishes an excellent substitute for ivory, tortoise shell, amber, and vulcanite. It is a nitro-cellulose, which is made capable of molding into any desired form by the admixture of a small amount of camphor. At the temperature at which the camphor melts, it acts as a solvent for the nitro-cellulose and forms a uniform plastic mass with it. This mass may be used directly in the manufacture of various articles, or it may be admixed with mineral coloring matters so as to imitate the various natural stones. The stratified appearance of ivory and the mottled appearance of tortoise shell and amber are obtained by passing between heated rolls plain and colored or clouded *celluloid* in alternating layers. The material is combustible when ignited, and in thin pieces burns rapidly with a bright light. For this reason it is a dangerous material from which to manufacture articles of wearing apparel, such as collars, combs, etc. Many of these articles are found on the market made of celluloid and some of these are falsely labeled rubber.

Within recent years so-called celluloid varnishes have come into extensive use for lacquering on metal; these are often nothing but pyroxylin solutions in which methyl alcohol, petroleum naphtha, and amyl acetate are used as a mixed solvent.

Centaurea. *Cnicus benedictus* L. (*Centaurea benedicta* L.) *Blessed Thistle. Chardon bénit,* Fr. *Herba Cardui Benedicti,* P. G. *Benedicten Distel,* G.—This is an annual herbaceous composite common in Europe and occasionally seen on roadsides and waste places in the United States. The leaves were formerly official. They should be gathered when the plant is in flower, quickly dried, and kept in a dry place. The herb has a feeble, unpleasant odor and an intensely bitter taste, more disagreeable in the fresh than in the dried plant.

Water and alcohol extract its virtues. The infusion with cold water is a grateful bitter; the decoction is nauseous, and offensive to the stomach. The active constituents are volatile oil and *cnicin.* This is crystallizable, inodorous, very bitter, neutral, scarcely soluble in cold water, more soluble in boiling water, and soluble in all proportions in alcohol. Its formula is $C_{42}H_{56}O_{15}$, and it is analogous to salicin in composition. It has been used as a bitter tonic, and is, in larger quantities, emetic. Tonic *dose,* from half a drachm to one drachm (2.0–3.9 Gm.) preferably given as an infusion.

Silybum Marianum Gaertn. (*Mariana Mariana* (L.) Hill, *Carduus Marianus* L.) was of old used for the same purpose as *C. benedictus.* Rademacher attributed great value to the seeds in *hemorrhages,* particularly when connected with diseased liver or spleen. Lobach found the decoction (two ounces to the pint of water), in *doses* of four fluidrachms (15 mils) every hour, useful in *amenorrhea* and *menorrhagia.* (*Am. J. M. S.*, April, 1859.)

Centaury. *N. F. IV. Centaurium. Common European Centaury. Herba Centaurii,* P. G. *Erythræa Centaurium* (L.) Pers. *Centaurium Centaurium* (L.) Wight. (Fam. *Gentianaceæ.*)—This is a small, annual herbaceous plant which grows wild in most parts of Europe. The dried flowering plant is found in commerce. It is described in the N. F. as "the dried flowering plant of *Erythraea Centaurium* (Linné) Persoon (Fam. *Gentianaceæ*). Glabrous, from 1.5 to 5 dm. in height, much branched from the base, but little branched, if at all, from above; stems slender, sharply angled or narrowly winged, sparsely leafy; leaves opposite, entire, mostly three-nerved, sessile,

those at the base obovate and obtuse, from 2 to 5 cm. in length, their base narrowed and petiole-like, those of above gradually changing to oval, then ovate or even lance-linear, acute; flowers in a terminal and at length compound cyme, rose-colored; calyx from 5 to 7 mm. in length, deeply five-parted, the tube short, sharply angled, lobes linear-attenuate with a sharp midrib; corolla tube nearly twice the length of the calyx, slender, the limb from 10 to 15 mm. in breadth, its lobes broadly oblong or oval; stamens five, exserted, bright-yellow, their anthers twisted when old; pistil two carpelled. Odor faint but characteristic; taste persistently bitter. Centaury yields not more than 5 per cent. of ash." *N. F.* The fresh, bitter, odorless herb yields an odorous, pungent distillate in which Méhu (*J. P. C.*, 1862, xliii, 38) has found valeric acid, also a peculiar, colorless, crystalline, non-nitrogenous substance, *erythrocentaurin*, $C_{27}H_{24}O_8$. Erythrocentaurin occurs in needle-shaped crystals, fusing at 136° C. (276.8° F.), and crystallizing easily on cooling again. They are strongly reddened by exposure to solar light, and reacquire their colorless character upon being again dissolved and crystallized, or by mere heating to 130° C. (266° F.). They are almost insoluble in cold water, more readily soluble in boiling water, alcohol, ether, and chloroform. Carbon disulphide, benzene, volatile and fatty oils dissolve them easily. J. F. Huneker believes that erythrocentaurin exists also in American centaury. (See *Sabbatia.*) Leuderich assigns to erythrocentaurin the formula $C_9H_{14}O_5$ and states that in its decomposition a dextrorotatory carbohydrate is produced, while R. Reis states that the formula of the crystals is $C_{10}H_{10}O_3$. (*Ap. Ztg.*, 1911, 148.) Hérissey and Bourdier isolated a glucoside from centaury, *erytaurin* (*J. P. C.*, 1908, No. 6), but later R. Reis could not detect a glucoside in it. (*Ap. Ztg.*, 1911, 148.) The common centaury of Europe has tonic properties very closely resembling those of gentian. The *dose* of centaury is from twenty to forty grains (1.2–2.3 Gm.).

A species of *Erythræa*, *E. chilensis* Pers., is employed to a considerable extent in Chili as a mild tonic. (For details, see *J. P. C.*, 3e sér., xxv, 434.) *E. acaulis*, which grows in great abundance in the territory of French Algiers bordering on the Sahara, yields a root which, under the name of *rejagnou*, is much employed by the natives for dyeing yellow. (*J. P. C.*, 1867, v, 87.)

Cephalanthus. *Cephalanthus occidentalis* L. *Button Bush. Button Wood. Crane Willow. Swamp Dogwood.* (Fam. *Rubiaceæ.*)—A common indigenous shrub which grows in moist places, as along streams or on the borders of swamps. Its bark is bitter, is said to be laxative as well as tonic, and has been given in periodical fevers, in decoction or infusion. (See *M. R.*, 1911, 216.) E. M. Hattan found in it a crystallizable fluorescent acid, a bitter uncrystallizable principle, a principle resembling saponin, tannin, two resins, fatty matter, gum, glucose, and starch. (*A. J. P.*, xlvi, 314.) According to Claassen (*Ph. Rund.*, Bd. vii, 1889), the fluorescent acid of Hattan is composed of two substances, *cephalin* and *cephaletin*. Carl Mohrberg has separated from the bark a substance which he knows as *cephalanthin*, and also a toxic saponin-like principle which, like its allied poisons, has the power of dissolving the blood corpuscles. Cephalanthin he finds to be a distinct poison to both cold and warm blooded animals, causing destruction of blood corpuscles with conversion of oxyhemoglobin into methemoglobin, violent vomiting, convulsions, and paralysis. (See *Kobert's Arbeiten*, viii, 1892.)

Ceratopetalum.—The New South Wales species of this genus, viz., *C. gummiferum* Sm. and *C. apetalum* Don., of the *Saxifragaceæ* yields considerable quantities of a kino-like gum. The barks contain coumarin. (See *P. J.*, xxi, 742.)

Cerberin.—The original substance described under this name was obtained from the seeds of the *Cerbera Odallam* Gärtn. (*Apocynaceæ*), but the name has been applied to principles from various allied plants. Under the name of *cerberid* there is upon the market a glucoside obtained from the *Thevetia Ycottli* DC. (*Cerbera Thevetia* L.). This is a yellowish, amorphous powder, with a bitter taste and soluble in water. According to Zotos (*In. Dis.*, Dorpat, 1892), it acts upon the heart like digitalis. Wagner (*Russki Vratch*, 1892, 1033) finds that it is too irritant to the intestinal tract to be clinically valuable. The *dose* is, hypodermically, one one-hundredth of a grain (0.0006 Gm.), by mouth, one-sixtieth to one-thirtieth of a grain (0.001–0.002 Gm.).

Cercis. *Cercis canadensis* L. *Judas Tree. Redbud.*—The bark of this beautiful leguminous tree, indigenous and well-known throughout the Eastern and Central United States on account of its brilliant red-purple flowers, which appear before the leaves, has been highly recommended by Wm. R. Smith as a mild but very active astringent in the treatment of *chronic diarrhea* and *dysentery*. *Dose*, of the fluidextract, from half to one fluidrachm (1.8–3.75 mils).

Ceresin. *Ozokerite. Earth-wax. Neft-gil.*—Under this name there has been introduced into commerce, as a substitute for wax, a substance which closely resembles white wax, but which is a natural mineral product. It is found most abundantly in Galacia, on the slopes of the Carpathian Mountains, and also on the Wallachian side of the range, in smaller deposits along the Caspian. A valuable deposit has also been discovered in Southern Utah. It consists of a mixture of solid paraffin with some oxygenated bodies. The crude ozokerite is melted to allow earthy impurities to settle out, is treated with sulphuric acid and alkali, as in the treatment of paraffin, and is clarified by bone black, or, better, the black from the manufacture of potassium ferrocyanide. The refined ozokerite or *ceresin* melts between 58° C. (136.4° F.) and 65° C. (149° F.), is quite odorless and colorless, and has the appearance of beeswax. It may be distinguished from the latter by its lower specific gravity (0.753 at 98° C. (208.4° F.) against 0.822) and its absolute resistance to alcoholic potassium hydroxide, no trace of saponifiable matter being present. F. Metz reports the finding of ceresin, colored with coal tar colors. (See *Ph. Ztg.*, 1904, 1031.) The production of Galician ozokerite in 1886 amounted to 13,925 tons, but had fallen in 1896 to 7925 tons. The production of Utah ozokerite in 1890 amounted to 350,000 pounds. The Galician product is worked chiefly in Vienna and in London, where ozokerite candles are manufactured. (See *A. J. P.*, xlv, 11.) In this country ceresin bottles have replaced the gutta-percha bottles formerly used to contain hydrofluoric acid.

Cetraria. *U. S.* 1890. *Iceland Moss. Iceland Lichen.*—Under this name the U. S. P. formerly recognized the dried plant of *Cetraria islandica* Acharius, *Lichen islandicus* L. This plant, although known as a moss, is not a moss, but a

lichen which grows in most northern latitudes and on elevated mountains further south, including the Northern United States.

The dried plant is of diversified color, grayish-white, brown, and red, in different parts, with less of the green tint than in the recent state. It was officially characterized as follows: "From 5 to 10 Cm. long, foliaceous, irregularly branched into fringed and channelled lobes, brownish above, whitish beneath, and marked with small, depressed spots; brittle and inodorous; when softened in water, cartilaginous, and having a slight odor; its taste is mucilaginous and bitter." *U. S.*, 1890. Macerated in water, it absorbs rather more than its own weight of the fluid, and, if the water be warm, renders it bitter. Boiling water extracts all its soluble principles. The decoction thickens upon cooling, and acquires a gelatinous consistence without viscidity. After some time the dissolved matter separates, and when dried forms semi-transparent masses, insoluble in cold water, alcohol, or ether, but soluble in boiling water, and in solution forming a blue compound with iodine. *Lichenin*, or *lichen starch*, $C_{12}H_{20}O_{10}$, resembles starch in its general characters, but differs from it in some respects. Lichenin has been found to consist of two distinct proximate principles, for one of which the name lichenin may be retained, while for the other no particular designation has been chosen, but which we may call *lichenoid*. According to Th. Berg (*Thèse de Dorpat*, 1872), *cetraria* yields 35.15 per cent. of the mixed principles, of which 20 per cent. is of lichenin, and 15.15 of the so-called lichenoid. To separate them, a decoction of the moss, concentrated to a small bulk, and still hot, is treated by alcohol. The lichenoid is deposited in flocculi, which gradually unite in a viscid mass. This, being washed by alcohol until it ceases to be bitter, and then dried, yields a light friable matter partly soluble in cold water, with which it forms a yellow, limpid solution. To deprive it of mineral and coloring substances, it is dissolved in a little water, and precipitated afresh by alcohol. Lichenin is insoluble in cold water, but swells up and easily dissolves in hot water. It is insoluble in alcohol and in ether. It is only tinged by iodine. Lichenoid is, on the contrary, colored blue by that reagent. It is, in part, dissolved in cold water, and the undissolved part is equally colored blue by iodine. It is, like lichenin, insoluble in alcohol and ether. Both substances have strong analogies with starch, yet are distinct. For a further account, see *J. P. C.*, 1873.

The name *cetrarin* has been conferred on the bitter principle. Herberger's process for extracting it may be found in the 18th ed., U. S. D. By it one pound of moss yielded to Herberger 133 grains of cetrarin. Schnedermann and Knop have ascertained that cetrarin consists of three distinct substances: (1) *cetraric acid*, $C_{18}H_{16}O_8$, which is the true bitter principle, crystallizable, and intensely bitter; (2) a substance resembling the fatty acids, called *lichen-stearic acid*, $C_{14}H_{34}O_3$, the crystals of which melt at 120° C. (248° F.); and, (3) a green coloring substance, which they name *thallochlor*. These principles are obtained perfectly pure with great difficulty. (*Ann. Ch. Ph.*, lv, 144.) Hilger and Buchner (*Ber. d. Chem. Ges.*, 1890, p. 461) give to lichen-stearic acid the formula $C_{43}H_{76}O_{13}$, and to cetraric acid the composition $C_{30}H_{30}O_{12}$, and both are shown to be dibasic acids.

The gum and starch contained in the moss render it sufficiently nutritive to serve as a food for the Lapps and Icelanders, who employ it powdered and made into bread, or boiled with milk, after having partially freed it from the bitter principle by repeated maceration in water. As suggested by Berzelius, the bitterness may be entirely extracted by macerating the powdered moss, for twenty-four hours, in twenty-four times its weight of a solution formed with 1 part of an alkaline carbonate and 375 parts of water, then decanting the liquid, and repeating the process with an equal quantity of the solution. The powder, being now dried, is perfectly sweet, and has been used to some extent in pharmacy as a substitute for acacia, although lacking in adhesiveness. (See also *Gelatina Lichenis Islandici Saccharata Sicca* (Germ. Unoff. Formulary), *Proc. A. Ph. A.*, 1892, 455.) This plan which has been proposed of first extracting the bitterness by maceration in water or a very weak solution of an alkaline carbonate, and afterwards preparing the decoction, has been criticised, as the peculiar virtues which distinguish the medicine from the ordinary demulcents are thus entirely lost. A pint (473 mils) of the decoction may be taken during the day.

Iceland Moss has been much used in chronic *catarrhs*, especially of the pulmonary mucous membrane and even in *phthisis*. It acts chiefly as a mucilaginous drink, but as Kobert has found that *cetrarin* is a stimulant to the gastro-intestinal mucous membrane and to peristalsis, cetraria probably is feebly tonic. A 20 per cent. tincture has been recommended in *doses* of twenty to thirty minims (1.2–2 mils) by Deying and Brice-Moret as an anti-emetic (*P. J.*, Oct. 30, 1897), which is confirmed by Gigon. (*R. T.*, 1905, p. 610.)

Cetrarin or *Cetraric acid*, $C_{30}H_{30}O_{12}$, a white, crystalline, bitter principle, soluble in solutions of alkalies and their carbonates, in hot water and slowly in cold water. It is administered in the treatment of *anemia*, *chlorosis* and *digestive disturbances*. *Dose*, one and a half to three grains (0.096–0.2 Gm.).

Decoctum Cetrariæ. U. S. 1890. *Decoction of Cetraria. Decoction of Iceland Moss.*

"Cetraria, *fifty grammes* [or 1 ounce av., 334 grains]; Water, *a sufficient quantity*, to make *one thousand cubic centimeters* [or 33 fluidounces, 6½ fluidrachms]. Cover the Cetraria, in a suitable vessel, with *four hundred cubic centimeters* [or 13 fluidounces, 252 minims] of cold Water, express after half an hour, and throw the liquid away. Then boil the Cetraria with *one thousand cubic centimeters* [or 33 fluidounces, 6½ fluidrachms] of Water for half an hour, strain, and add enough cold Water, through the strainer, to make the product, when cold, measure *one thousand cubic centimeters* [or 33 fluidounces, 6½ fluidrachms]." *U. S.*, 1890.

Saccharum Cetrariæ.—Cetraria 1, sugar 1, water 100. Wash the cetraria with water to remove bitterness, then boil with 100 mils of water, strain and express lightly, and in the strained liquid dissolve the sugar and evaporate upon a water bath. When sufficiently firm remove from the bath and dry in an oven to a scale or a powder.

The *Cetraria juniperina* (probably *Cetraria vulpina*) of Europe is said to be sometimes used as a poison for wolves and foxes, while the *wolf's moss* (*Ulfmossa*) of the north of Europe contains *vulpinic acid*, $C_{19}H_{14}O_5$, which has been found by Kobert to be an active protoplasmic poison; in

frogs it produces tetanus, convulsions, and paralysis of central origin; in mammals it causes dyspnea, vomiting, trembling, and a slowing of the pulse, with rise of the blood pressure due to stimulation of the respective nerve centers. After death the blood is not coagulable, and the secreting kidney cells are found covered with a crystalline or amorphous mass of a vulpinate. The acid is found also in species of *Calycium, Culveraria, Parmelia,* and *Cyphelium.* (Schmidt, *Ph. Chemie,* St. 1319.) No difference of action exists between vulpinic acid derived from wolf's moss and that synthetically produced. From *Cetraria pinastrin* Zopf has separated *pinastrinic acid,* which seems to be very closely allied to vulpinic acid. (*Sitzungsb. der Dorpat. Naturforsch.-Gesellschaft,* 1892.)

Cetyl Alcohol. *Alcohol Cetylicum.* $C_{16}H_{33}OH$.—*Cetylic alcohol, ethal, æthol, primary hexadecyl alcohol,* is a tasteless, odorless, waxy powder, which fuses at 49.5° C. (121° F.) and boils at 344° C. (651° F.). It is soluble in alcohol and ether. According to Grimm (*Derm. Zeit.,* 1899, vol. vi), *cetyl alcohol* is absorbed and obstinately retained by the epidermis, producing a peculiar velvety condition of the skin. It has been found useful in the treatment of *chapped hands,* weeping *eczema,* and *prurigo.* Mixtures of it with boric acid or the borates have been put upon the market as cosmetics under the name of *Borsyl.* Grimm especially recommends equal parts of cetyl alcohol with boric acid or one part with five of powdered talc.

Chamælirium. *Chamælirium luteum* (L.) A. Gray. (*C. carolinianum* Willd.) *Starwort. False Unicorn Root. Devil's Bit. Blazing Star.*—This plant is indigenous to the United States. The rhizome is the part employed in medicine. It is commonly known by the erroneous name *Helonias,* under which title it is recognized by the N. F. (for description, see *Helonias*). F. V. Greene obtained from it in 1878 a bitter principle, *chamælirin.* He states that it is a cardiac poison. *Helonin* is a term used by the eclectics to define the alcoholic extract found in commerce. Chamælirium is said to be diuretic, tonic, and anthelmintic. It is usually given in aqueous infusion, one in sixteen, in the *dose* of a wineglassful.

Champaca.—This is the *Michelia Champaca* L. (fam. *Magnoliaceæ*), a Javan tree which is famous for the sweet odor of its blossoms. From it Merck has obtained a camphor ($C_{17}H_{30}O$) to which the name *champacol* has been applied. For a study of the volatile *oil of champaca* flowers, see *Schim. Rep.,* Oct., 1907, p. 32.

Cheiranthus. *Cheiranthus Cheiri* L. *Wall flower.*—The flowers yield an oil which when highly diluted has the natural pleasant odor, but when concentrated the odor is disagreeable. (*Schim. Rep.,* 1911, 95; also *A. Pharm.,* 1912, 211.) From the leaves of this cruciferous European plant Moritz Reeb (*A. E. P. P.,* 1899, vol. xliii) has obtained a glucoside, belonging to the digitalis group, of such power that 0.0005 Gm. will produce systolic cardiac arrest in the frog; also a crystalline alkaloid, *cheirinine,* $C_{18}H_{35}O_{17}N_3$, which acts upon nerve centers and also upon muscles.

Chelidonium. *U. S.* 1890. *Chelidonium majus* L. (Fam. *Papaveraceæ.*) *Celandine. Tetterwort.* A perennial herbaceous plant growing wild in both Europe and America, recognized readily by its pinnate leaves, small peduncled yellow flowers and yellow opaque juice. The plant was formerly official and was described as follows: "Root several-headed, branching, reddish-brown; stem about 50 Cm. long, light green, hairy; leaves about 15 Cm. long, thin, petiolate, the upper ones smaller and sessile, light green, on the lower side glaucous, lyrate-pinnatifid, the pinnæ ovate-oblong, obtuse, coarsely crenate or incised and the terminal one often three-lobed; flowers in small, long-peduncled umbels with two sepals and four yellow petals; capsule linear, two-valved and many-seeded. The fresh plant contains a saffron-colored milk-juice, and has an unpleasant odor and acrid taste." *U. S.,* 1890.

Probst, of Heidelberg, found in it a peculiar acid denominated *chelidonic acid;* two alkaline principles, one of which forms neutral salts with the acids, and is called *chelerythrine* (see *Sanguinaria,* Part I), in consequence of the intense redness of its salts; the other unites with, but does not neutralize the acids, and is named *chelidonine,* $C_{20}H_{19}O_5N$; and lastly a neutral crystallizable, bitter principle, which from its yellow color he calls *chelidoxanthin.* Orlow believes, however, that the latter is an alkaloid, and gives a process for its preparation in *Ph. Z. R.,* 1893, No. 21. Chelerythrine appears to be an acrid narcotic poison. (*Ann. Ch. Ph.,* xxix, 113.) For an elaborate investigation of chelidonine, see a paper by Schlotterbeck and Knapp in *Proc. A. Ph. A.,* 1905, 217. For color tests for chelidonine, see *Proc. A. Ph. A.,* 1895, 922. *Chelidonine phosphate, chelidonine sulphate, chelidonine tannate,* and *chelidonine muriate* have been used medicinally. (See *Proc. A. Ph. A.,* 1897, 721.)

Although both Peronin and Meyer (*A. E. P. P.,* 1892, xxix, p. 397) asserted that chelidonine has distinct narcotic properties, the experiments of Hanzlik (*J. P. Ex. T.,* 1915, vii, p. 99) throw grave doubt on their conclusions. The latter investigator found that its only physiological action was a paralyzing effect on the unstriped muscle and suggested its use in *asthma* and *spasmodic colic.* Ribbing and Rumpf have used chelidonin clinically in *gastralgias* in *doses* of one and one-half to three grains (0.1–0.2 Gm.), but Peronin used from one-twentieth to one-third of a grain (0.003–0.02 Gm.). In 1902 J. O. Schlotterbeck showed that the *chelidoxanthine* of Probst is really *berberine.* Schlotterbeck has also established the identity of the most abundant of the alkaloids of sanguinaria with chelerythrine.

Celandine is an irritant purgative to which toxic properties have been ascribed with doubtful correctness; in the fatal case of poisoning reported in the *Zeitsch. f. Medizinalbeamte,* 1898, it was not the cause of death. The irritant juice has long been used locally upon *corns, warts, eczema,* and other diseases of the skin, and even in *cancer.* The *dose* of the dried root or herb is from thirty grains to a drachm (2.0–3.9 Gm.), that of the fresh root one or two drachms (3.9–7.7 Gm.), and the same quantity may be given in infusion. The *dose* of the aqueous *extract* is from five to ten grains (0.32–0.65 Gm.), of the expressed juice from ten to twenty minims (0.6–1.3 mils), to be gradually increased.

Chelone. *Chelone glabra* L. *Snake-head. Turtle-head. Balmony. Shellflower. Chelone,* Fr., G.—The leaves of this very common indigenous, perennial, herbaceous plant, of the fam. *Scrophulariaceæ,* have a bitter taste, and are said to be tonic and aperient, with a supposed peculiar action

on the liver. The decoction (two ounces of the fresh herb to the pint) may be given in the *dose* of one or two fluidounces (30–60 mils). *Chelonin*, an eclectic medicine prepared from *chelone*, is a brown, bitter powder administered as a tonic laxative in one and two grain *doses* (0.06–0.12 Gm.).

Cheltenham Salt, Artificial.—Several artificial mixtures have been prepared as imitations of the salts of the chalybeate Cheltenham water. One frequently used is equal parts of magnesium sulphate, sodium sulphate, and common salt; other formulas contain some iron. These combinations have the value of their ingredients.

Chemical Food. *Compound Syrup of Phosphate of Iron.*—For a formula for a compound syrup of phosphate of iron by Wiegand, made by introducing into it the phosphates of calcium, potassium, and sodium, and for remarks on the pharmacy of the phosphates by Procter, see *A. J. P.*, 1854 (pp. 111 and 112). A formula similar to Wiegand's, communicated by Edward Parrish as probably representing the process for a secret preparation considerably used in Philadelphia may be found in *A. J. P.*, 1857 (p. 573). These formulas are too complicated to have any therapeutic value. Nevertheless, as the preparations have had much vogue, under the name of *chemical food*, we give the formula of Parrish from the journal referred to. "Take of Sulphate of Iron, 600 gr.; Phosphate of Soda, 720 gr.; Phosphate of Lime, 720 gr.; Glacial Phosphoric Acid, 1200 gr.; Carbonate of Soda, 40 gr.; Carbonate of Potassa, 60 gr.; Hydrochloric Acid, Water of Ammonia, each, a sufficient quantity; Powdered Cochineal, 120 gr.; Water, a sufficient quantity, to make 20 fluidounces; Sugar, 36 troyounces; Oil of Orange, 10 minims. Dissolve the Sulphate of Iron in 2 fluidounces and the Phosphate of Soda in 4 fluidounces of boiling water. Mix the solutions, and wash the precipitated phosphate of iron till the washings are tasteless. Dissolve the Phosphate of Lime in 4 fluidounces of boiling Water with sufficient Hydrochloric Acid to make a clear solution, precipitate it with Water of Ammonia, and wash the precipitate. To the freshly precipitated phosphates add the Phosphoric Acid previously dissolved in Water. When clear, add the Carbonates of Soda and Potassa, and afterwards sufficient Hydrochloric Acid to dissolve the precipitate. Now add Cochineal mixed with the Sugar, apply heat, and, when the syrup is formed, strain and flavor it. Each teaspoonful contains about one grain of phosphate of iron and two and a half grains of phosphate of lime, with smaller quantities of the alkaline phosphates, all in perfect solution." The objection to such preparations as this is not that each of the ingredients may not be useful, but that they are so numerous that a morbid state of system in which they can all be indicated must be extremely rare, and every medicine is more or less noxious if given when it is not needed. The probability is that the therapeutic value of the preparation depends mainly on its ferruginous ingredient, and that, as a rule, its therapeutic effects may be equally well if not better obtained from a simple syrup of ferric phosphate. (See *P. J.*, 1893, 795, 797.) A simplified formula is official in the N. F. IV under the title *Compound Syrup of the Phosphates* (see Part III).

Chenopodium. *Chenopodium. American Wormseed.*—The fruit of *C. Ambrosioides* var. *anthelminticum* (L.) Gray (Fam. *Chenopodiaceæ*). This species of *Chenopodium*, known commonly by the names of *wormseed* and *Mexican Tea*, grows in almost all parts of the Eastern United States. The whole herb has a strong, peculiar, offensive, yet somewhat aromatic odor, which it retains when dry. All parts of the plant are occasionally employed, but the fruit alone was official in the U. S. P., 1890. This should be collected in October.

Wormseed, as found in commerce, is a small fruit, about 2 mm. in diameter, having a membranaceous pericarp, irregularly spherical, very light, of a dull greenish-yellow or brownish color, a bitterish, somewhat aromatic, pungent taste, and possessed in a high degree of the peculiar odor of the plant. These fruits, when deprived, by rubbing them in the hand, of the membranaceous covering which invests the proper seed, exhibit the shining, blackish surface of the obtusely-edged seed. They abound in a volatile oil, upon which their sensible properties and medicinal virtues depend and which is obtained by distillation. (See *Oleum Chenopodii*, Part I.) The same oil impregnates to a greater or less extent the whole plant.

Of the activity of the wormseed as an anthelmintic there can be no question, but it has been entirely displaced by the official oil. The *dose* of the crude drug is from twenty to forty grains (1.3–2.6 Gm.).

Chimaphila. *N. F. IV* (*U. S. P. VIII*). *Pipsissewa. Prince's Pine. Wintergreen. Bitter Wintergreen. King's Cure. Ground Holly. Love-in-winter. Rheumatism Weed. Herbe de Pyrole ombellée*, Fr. *Doldenbluthiges Harnkraut, Wintergrün*, G.—The name chimaphila is formed of two Greek words, *χεῖμα*, winter, and *φίλος*, to love. There are two American species, the official variety being described by the N. F. as "the dried leaves of *Chimaphila umbellata* (Linné) Barton (Fam. *Ericaceæ*), without the presence of more than 5 per cent. of stems or other foreign matter." *N. F.* It is a small evergreen plant, with a perennial, creeping, yellowish rhizome, which gives rise to several simple, erect or semiprocumbent stems, from four to eight inches in height, and ligneous at their base. The leaves are "oblanceolate, from 2.5 to 7 cm. in length and from 8 to 20 mm. in breadth, the upper portion coarsely and sharply serrate, acute or somewhat obtuse, the lower wedge-shaped and nearly entire; coriaceous, smooth and uniformly dark green on the upper surface, paler beneath, the veins prominent. Odor slight; taste astringent and bitter. The powdered drug is brownish-green and, when examined under the microscope, exhibits characteristic epidermal tissue composed of cells with unevenly thickened, porous, and wavy vertical walls; the fragments from the lower epidermis show numerous broadly elliptical stomata up to 0.04 mm. in length, the epidermal tissue in transverse view shows outer walls from 0.008 to 0.015 mm. in thickness; fragments of palisade and mesophyll tissue containing chloroplastids; tracheæ with spiral or annular markings; a few characteristic, elongated tracheal-like cells, about 0.014 mm. in width, thick-walled, slightly lignified and with minute, double-spiral bands or delicate reticulations; fragments of the epidermis from the stems and root-stocks, the cells containing a purplish coloring substance which is intensified when the powder is mounted in hydrated chloral T.S.; parenchyma cells containing a reddish-brown amorphous substance; calcium oxalate in rosette aggregates mostly about 0.035 mm. in diameter, occasionally up to 0.065 mm. in diameter; starch grains few, rounded, simple, up

to 0.016 mm. in diameter and sometimes with a central cleft or fissure, or two- to four-compound; trichomes absent. Chimaphila yields not more than 7 per cent. of ash." *N. F.*

The leaves are short petiolate, occurring in irregular whorls, of which there are usually two on the same stem. The flowers are disposed in a small terminal corymb, and stand upon nodding peduncles. It is found in the Northern latitudes of Europe and Asia, also in dry woods from Nova Scotia to Georgia and westward to the Pacific. The flowers appear in June and July.

C. maculata (L.) Pursh., or *spotted wintergreen*, though not official, probably possesses similar virtues. The character of the leaves of the two plants will serve to distinguish them. Those of *C. maculata* are lanceolate, rounded at the base, where they are broader than near the summit, and of a deep olive green, veined with greenish-white; the leaves of *C. umbellata* are broadest near the summit, gradually narrowing to the base, and of a uniform shining green color.

Pipsissewa, when fresh and bruised, exhales a peculiar odor. Boiling water extracts the active properties of the plant, which are also imparted to alcohol. Fairbank found in the leaves a peculiar substance which he calls *chimaphilin*.

Chimaphilin was obtained by extracting the tincture with chloroform, or by distilling the stems with water. It occurs in golden-yellow auricular crystals, odorless and tasteless, practically insoluble in water, but dissolving in alcohol, ether, chloroform, and the fixed oils. It is possessed of neither acid nor alkaline properties. Peacock (*A. J. P.*, 1892, p. 295) found that chimaphilin has the chemical composition $C_{24}H_{21}O_4$.

Ridenour (*A. J. P.*, 1895, 236) confirms the formula, $C_{24}H_{21}O_4$, given by Peacock. He finds the melting point of the purified chimaphilin to be 114° C. (237.2° F.). He also prepared another crystalline principle melting above 250° C. (482° F.), to which he gives the formula $C_{10}H_{19}O$, which agrees with Beshore's product. *Arbutin*, $C_{12}H_{16}O_7$, is also found in chimaphila.

This plant is stated to have been used internally by the North American Indians in *scrofula* and *rheumatism*, and was a popular remedy among the settlers of this country. It has no medicinal properties, however, beyond a feeble diuretic action and perhaps some antiseptic influence on the urine. It is occasionally prescribed for *cystitis*. The best preparation is the fluidextract, which may readily be made into a syrup. *Dose*, thirty to ninety grains (2–6 Gm.).

China Green.—This dye is asserted to have a specific antiseptic action on the *Bacillus coli* and to be useful as a means of distinguishing between that organism and the *B. typhosus*. For method of use, see Werbitzki, *Arch. f. Hyg.*, 1909, p. 191.

China Morada.—Under this name there appear to be used in Bolivia several barks. One of these has been ascertained by Arati and Canzoneri (*L'Orosi*, Feb., 1889) to be the product of a rubiaceous tree, *Pogonopus tubulosus* (Rich.) K. Sch., and to contain an alkaloid, *moradeine*, besides a fluorescent substance, *moradin*, allied to scolopetin. (See *P. J.*, xix.)

Chinaphenine. $CO\left\{\begin{matrix}NH.C_6H_4OC_2H_5\\OC_{20}H_{23}N_2O\end{matrix}\right.$. *Quinine Carbophenetidide. Phenetidin Quininecarbonate.*—*Chinaphenine* occurs as a white, tasteless powder, slightly soluble in water, easily in alcohol, ether, and chloroform and benzene, forming salts which are soluble in water. Chinaphenine has been recommended by von Noorden as a mild antipyretic, producing a fall of temperature which is at its lowest point four or five hours after the ingestion of the remedy; also as an analgesic in *diabetic* and other forms of *neuralgias;* also in *whooping cough*. The analgesic *dose* is twenty to thirty grains (1.3–2.0 Gm.) given in two portions. To children under a year old, von Noorden gave two to three grains (0.13–0.20 Gm.) and older children three to five grains (0.21–0.32 Gm.) three times a day. (*Ther. Geg.*, Jan., 1903.)

Chinaphthol. *Quinaphthol. Quinine-β-naphthol-α-mono-sulphonate.* $C_{30}H_{24}N_2O_2(C_{10}H_6OHSO_3H)_2$.—This substance is a yellow, crystalline powder fusing at 185° C. (365° F.), of a bitter taste, insoluble in cold water, moderately soluble in hot water and alcohol; it has been proposed by E. Riegler (*W. M. Bl.*, xix, 1896) as an antipyretic and intestinal antiseptic. He states that it is decomposed by the alkalies of the intestinal juices into its constituents—namely, quinine and β-naphthol sulphuric acid, and that he has used it up to forty-five grains (3 Gm.) a day with satisfaction in acute *rheumatism* as well as in *typhoid fever*. It contains about 42 per cent. of quinine.

Chineonal.—This is *quinine diethyl-barbiturate* and represents approximately 63.8 per cent. of quinine and 36.2 per cent. of veronal. It occurs as colorless bitter crystals, sparingly soluble in water, readily so in alcohol. The idea of combining the properties of quinine and diethyl-barbituric acid does not appear to us to be an extraordinarily happy one. Fraenkel and Hauptmann, however (*Med. Klin.*, 1912, p. 1871), believe that the drug is of special value in *whooping cough*. It has also been used as a general nerve sedative. The *dose* is five to ten grains (0.32–0.65 Gm.), preferably in the form of tablets.

Chinoform.—A product of the action of formaldehyde on an acidulated (hydrochloric acid) aqueous extract of cinchona bark is used as an internal astringent and antiseptic.

Chinoidinum. *U. S.* 1880. *Chinoidine. Quinoidine. Chinoidin. Quinoidin. Precipitated Extract of Bark. Amorphous Quinine. Quinine brute ou amorphe*, Fr.—The term chinoidine was first applied to all of the amorphous alkaloids existing naturally in cinchona bark, but it is now used to define a complex body consisting largely of alkaloidal products which are artificial and accidental, resulting from the application of heat. Upon the evaporation of the mother liquor left after the crystallization of the quinine sulphate in the preparation of that salt, a dark colored substance is obtained, having the appearance of an extract. Sertürner supposed that he had discovered a new alkaloidal principle in this product, but his conclusions were temporarily invalidated by the experiments of Henry and Delondre, which seemed to *prove* that the alkaline matter contained in it *consisted of quinine and cinchonine*, obscured by admixture with a yellowish substance that interfered with their crystallization. Nevertheless, under the name of *quinoidine* or *chinoidine*, given to the supposed new alkaloid by Sertürner, there was long employed in Europe a substance precipitated from the mother liquor of quinine sulphate by means of an alkaline carbonate, having a yellowish-white or brownish color, and when moderately heated, agglutinating into a mass of resinous

appearance. Later, by the conjoint labors of the chemists, Winckler, Liebig, and Pasteur, it was proved that ordinary quinoidine (chinoidine), or amorphous quinine, consisted of two alkaloids, derivatives from quinine and cinchonine, with which they are respectively isomeric, though differing in being uncrystallizable, and named, in view of their origin, *quinicine* and *cinchonicine*. The pure amorphous quinine of Liebig was the former of these alkaloids. (*A. J. P.*, xviii, 181.) The U. S. P. of 1880 described chinoidine as "a brownish-black or almost black solid, breaking, when cold, with a resinous, shining fracture, becoming plastic when warmed; odorless, having a bitter taste and an alkaline reaction. Almost insoluble in water, freely soluble in alcohol, chloroform, and diluted acids; partially soluble in ether and in benzol. The solutions have a very bitter taste. If Chinoidin be triturated with boiling water, the liquid, after filtration, should be clear and colorless, and should remain so on the addition of an alkali (abs. of alkaloidal salts). On ignition, Chinoidin should not leave more than 0.7 per cent. of ash." *U. S.*, 1880.

A simple method of purification consists in dissolving the chinoidine in diluted hydrochloric acid, adding water, filtering and precipitating with an alkali and washing and drying the precipitate.

Tinctura Chinoidini was formerly made, by the German Pharmacopœia, by simply dissolving 3 parts of chinoidine in one of hydrochloric acid and 17 of alcohol, sp. gr. 0.894.

Chinoidine hydrochloride is made by heating 1 part of the purified chinoidine with 4 parts of distilled water, adding sufficient diluted hydrochloric acid to complete the solution, filtering, evaporating, and powdering the residue. Zimmer furnished the German market with the purified hydrochloride, under the name of *Chininum amorphum muriaticum purum*. It has been largely used medicinally. For formulas for various salts of chinoidine, see *N. R.*, 1882, 11, or *Proc. A. Ph. A.*, 1882, 417.

As an antiperiodic, chinoidine is inferior to the cinchona alkaloids and more nauseating. From thirty grains to a drachm (2.0–3.9 Gm.) may be given, in divided doses, between the paroxysms of an *intermittent*, and its action closely watched.

Chinol. *Quinoline mono-hypochlorite.* $C_9H_6N.ClO$.—A white, crystalline powder, odorless, having a pungent but not disagreeable taste. It is almost insoluble in cold and hot water, but quite soluble in alcohol. This substance is said to be actively antipyretic and analgesic, useful for the purposes for which antipyrin is employed. *Dose*, from three to five grains (0.2–0.32 Gm.).

Chinosol. *Quinosol. N. N. R.* 1917. $(C_9O_7ON)_2H_2SO_4$. *Normal Oxyquinolin Sulphate.*—This is a neutral compound of oxyquinoline from which the latter is readily liberated in a nascent condition.

It is a crystalline, yellow powder, very soluble in water, insoluble in alcohol and ether, having a feeble saffron-like odor. Its aqueous solution when very dilute produces with ferric chloride a bright green color.

Chinosol does not precipitate albumin, is affirmed to be very slightly toxic, unirritating, and possessed of an extraordinary power of penetrating tissues. It is incompatible with alkalies, and with iron and mercury compounds. The early claims as to the germicidal powers of chinosol have been shown to be incorrect, and have been somewhat modified by the manufacturers of the product. In the report of the Council on Pharmacy and Chemistry of the American Medical Association (*J. A. M. A.*, 1910, liv, p. 1801), it was shown that the belief in its powerful germicidal properties was due to faulty technic. Chinosol is decidedly less efficient in its killing power on bacteria than is phenol; the 1 per cent. solution is not certainly fatal to the bacillus of typhoid fever even after ninety minutes exposure. On the other hand, its power of restraining development is far superior to that of phenol, and approaches that of corrosive sublimate. One part in ten thousand is sufficient to prevent development of the *Staphylococcus pyogenes* or the *Bacillus typhosus*, while 1 in 20,000 shows a marked inhibiting effect. Its toxicity is certainly very low; in the report of the Council on Pharmacy and Chemistry, guinea-pigs and rabbits frequently survive the administration of 3 Gm. by the mouth, or 1 Gm. hypodermically. In addition to its antiseptic action it is claimed for chinosol that while its own odor is comparatively little, it is a powerful deodorizer, and also energetic as a styptic.

Although it has been used in surgery for the disinfection of instruments and of the surgeons' hands, the use of chinosol for this purpose is not to be recommended, because of its low germicidal value. On the other hand, as an antiseptic in various conditions, as *vaginitis*, *rhinitis*, and similar *catarrhs*, there is much evidence of its value. It has also been used successfully as an intestinal disinfectant, and Lorch (*Deutsche Arzte Zeitung*, 1908, p. 406) has even obtained favorable results in the treatment of *Asiatic cholera*.

As a local application to mucous membranes, it may be used in strengths of from 1 to 500 to 1 to 2000. Internally, it has been given in *doses* of fifteen to twenty-five grains (1–1.6 Gm.).

Chinotoxine. *Dichinolindimethylsulphate Quinotoxin.*—This synthetic compound is said to possess properties similar to those of curare. This compound is reported to be formed at times in combinations of quinine and aspirin, giving to the resulting mixture toxic properties.

Chionanthus. *N. F. IV. Chionanthus virginica* L. *Fringe Tree Bark. Old Man's Beard.* It is described in the *N. F.* as "the dried bark of the root of *Chionanthus virginica* Linné (Fam. *Oleaceæ*), without the presence of more than 8 per cent. of other parts of the plant or other foreign matter. Usually in transversely curved pieces, occasionally in single quills from 1 to 10 cm. in length; bark from 2 to 10 mm. in thickness; heavy, some pieces of the whole drug sinking when thrown into water; outer surface usually reddish-brown, occasionally grayish-brown, with few transverse wrinkles, whitish cork patches and root-scars; inner surface yellowish-brown, more or less striate and undulate; fracture short, hard, and coarsely granular, due to projecting groups of stone cells; the broken surface of a light yellowish-white color. Odor characteristic; taste bitter. The powdered drug is light brown and, when examined under the microscope, exhibits somewhat rounded, simple or two- to four-compound starch grains, the individual grains mostly 0.003 to 0.025 mm. in diameter; numerous stones cells, in groups and isolated, the walls thick, strongly lignified and with simple and branching pores; brown resin masses; fragments consisting of light brown, thin-walled cork cells; parenchyma tissue with many of the cells filled with starch grains. Chionanthus yields not more than 5 per cent. of ash." *N. F.*

in the bark of this indigenous plant saponin was found by R. S. Justice (*A. J. P.*, xlvii, 195), but not by W. von Schulz, who, however (*Ph. Z. R.*, 1893, 579), detected a glucoside. The fluid-extract has been recommended in *doses* of from one-half to one fluidrachm (1.8–3.75 mils) two or three times a day, as an aperient and a diuretic.

Chione. *Chione glabra DC. Palo Blanco.*—The bark of this West Indian rubiaceous plant is said to be largely used as an aphrodisiac and tonic. According to B. H. Paul and A. J. Cownley, it yields 1.5 per cent. of a pale yellow volatile oil composed largely of phenols. (*P. J.*, vol. lx.)

Chloral Ammonium. $CCl_3.CH(NH_2)OH$. *Trichloramido-ethylic Alcohol.* This substance is said by W. B. Nesbit to act like hydrated chloral, but to be a stimulant to the circulation in *doses* of from five to twenty grains (0.32–1.3 Gm.). For method of preparation, see *T. G.*, 1888. The name *chloralamide* is correct as applied to this compound, but it is more frequently, although incorrectly, applied to the substance, Chloralformamide, which see.

Chloral Amylene Hydrate. *Amylene-chloral. Dormiol.* $CCl_3.CHOH.O(CH_3)_2C_2H_5$.—Made by mixing 10 parts of anhydrous chloral with 6 parts of amylene hydrate. It is a colorless, oily liquid having a pungent, mint- and camphor-like odor and a cooling pungent taste. It is not miscible with cold water and is decomposed by boiling water, but is freely soluble in alcohol, ether, acetone, and the fixed oils. While there is no doubt that dormiol is a powerful somnifacient, the experiments of Mayer (*Th. M.*, 1907, p. 250) indicate that its toxicity is practically the same as that of chloral hydrate. It is at present marketed in the form of a 50 per cent. solution, the *dose* of which is ten to thirty minims (0.6–1.8 mils).

Chloral Caffeine. $C_8H_{10}N_4O_2C_2Cl_3H_2O$.—Made by mixing 10 parts of caffeine and 7.8 parts of hydrated chloral, in a small amount of water or alcohol, and evaporating at a low temperature.

The resulting product is soluble in water and alcohol and is given in three to six grains (0.2–0.36 Gm.) *doses*.

Chloral Carbamide.—When 165.5 parts of trichloraldehyde hydrate are mixed in a porcelain mortar with 60 parts of carbamide (urea), the mixture liquefies. On dissolving this substance in three times its quantity of water warmed to 60° C. (140° F.) and then allowing the mixture to cool, a crystalline mass, *chloral carbamide*, is obtained. This substance dissolves readily in warm water and in alcohol, and less readily in warm alcohol. According to Kobert, it acts like hydrated chloral, but is too slow and uncertain to be of practical value.

Chloral Carbol. *Chloral Phenol. Carbolated Chloral.*—According to Boureiz, when hydrated chloral and phenol are rubbed up in the proportion of 10 parts of the former to 14 parts of the latter, a liquid is obtained which has the sp. gr. of about 1.5, and is soluble in all proportions in water, alcohol, and ether. Applied locally it is a counter-irritant and local anesthetic.

Chloral Cyanhydrate. *Chloral Hydrocyanate.* $CCl_3.CH(OH)Cn$.—This is a compound first prepared by Pinner and Bischoff, and recommended by Hermes (*Ph. Centralh.*, Aug., 1887) as a substitute for hydrocyanic acid, whose physiological action it is stated to share. *Chloral cyanhydrate* is represented by the formula $CCl_3—CH—\begin{cases} OH \\ CN \end{cases}$ and is described as a crystalline powder, consisting partly of colorless prisms and partly of rhombic tables, fusing at 61° C. (141.8° F.), easily soluble in water, alcohol, and ether. With the vapor of water it volatilizes in small quantity, and breaks up into its components, chloral and hydrocyanic acid. It contains 15.33 per cent. hydrocyanic acid. It is also decomposed by alkalies, with the formation of alkaline cyanides. Its aqueous solutions remain unaltered for a long time. Six and a half parts by weight of chloral cyanhydrate correspond with one part of anhydrous hydrocyanic acid.

Chloralformamide. *Chloralformamidum. U. S. VIII. Chloralamide. Chloralum formamidatum.* P. G. $CCl_3.CH(OH)NH.CO$. This compound of chloral and formamide which was formerly official is made by mixing 45 Gm. of formamide with 147 Gm. of anhydrous chloral, when combination ensues; the crystalline mass is purified by recrystallization. Chloralforamide occurs as in "colorless, lustrous crystals, without odor, and having a somewhat bitter taste. Soluble in about 18.7 parts of water, and in 1.3 parts of alcohol at 25° C. (77° F.). It is readily soluble in ether, glycerin, acetone, and acetic ether. When heated with water to 60° C. (140° F.), it is hydrolized, hydrated chloral and formamide being produced. When heated to from 114° to 115° C. (237.2° to 239° F.), it melts, but at a higher temperature it is decomposed. It is not affected by diluted acids, but it is decomposed on warming with alkali hydroxides, the solution becoming at first turbid, and then clear, while chloroform separates. If 0.2 Gm. be heated carefully in an open dish, it should not give off inflammable vapors, and should volatilize without leaving a weighable residue (absence of *inorganic impurities* and distinction from *chloral alcoholate* and *ethyl carbanate*). One Gm. of Chloralformamide dissolved in 10 mils of alcohol should yield a solution which does not redden moistened blue litmus paper (absence of *formic, hydrochloric,* or *other free acids*). If 1 Gm. of Chloralformamide be dissolved in 10 mils of alcohol, the addition of a few drops of silver nitrate T. S. should not at once produce turbidity (the absence of *decomposition products*)." *U. S. VIII.*

Chloralformamide is rapidly absorbed and after absorption gradually broken up in the system liberating chloral which exercises its characteristic narcotic effects. Apparently the formamide which is liberated at the same time antagonizes the depressant action of the chloral upon the nerve centres, for in the experiments of Wood and Cerna it was found that the action upon the circulation was feeble and the respirations more rapid than normal, which results are in accordance with those of Halasz (*W. M. W.*, 1889). On the other hand Langgaard (*Th. M.* 1889) maintains that both of these functions are depressed. Clinically the drug is much slower in its action than chloral hydrate and has the advantage of being less irritant to the stomach. It is, however, much less certain in its action and while often of service in the milder types of *insomnia* can not be relied upon for more obstinate cases. The *dose* is from fifteen to thirty grains (1 to 2 Gm.).

Chloralimide. $CCl_3.CH—NH$.—This compound should not be confounded with chloral*a*mide. Chloralimide is in colorless, inodorous, and insipid, long crystalline needles; melting at about 166° C. (330.8° F.); insoluble in water; readily soluble in alcohol, in ether, in chloroform, and in oils. Concerning its physiological action we have no certain knowledge; it is asserted to be hypnotic in doses of from fifteen to sixty grains (1 to 3.9 Gm.).

Chloral Menthol. *Mentholated Chloral.*—This is obtained by triturating equal weights of hydrated chloral and menthol, and heating gently in a water bath until liquefied. It is an oily, colorless liquid, with a distinct mint-like odor and warm taste, having a specific gravity of 1.1984. It is freely soluble in alcohol, chloroform, and petroleum benzin. (*A. J. P.*, 1886, 283.) *Chloral menthol* has been used as a counter-irritant and local anesthetic in facial and other *neuralgias.*

Chloral Urethane. *Uraline.—Uralium,* $CCl_3.CH\begin{cases}OH\\NHCO_2C_2H_5\end{cases}$, is a compound of chloral and urethane. It is insoluble in cold water, and is decomposed by boiling water; it is soluble in alcohol and ether, and melts at 103° C. (217.4° F.). This was brought forward as a hypnotic by Schmitt and Parisot (*R. M. Est*, Dec., 1890) found that it affected the heart like chloral, that it was very uncertain in its action, and was likely to disagree with the stomach, being on the whole inferior to hydrated chloral. *Dose,* ten to thirty grains (0.6–2 Gm.).

Chloralose. $C_8H_{11}Cl_3O_6$. *Anhydro-gluco-chloral.*—When equal parts of anhydrous chloral and glucose are heated together for an hour at the temperature at which chloral boils, two isomeric substances—*chloralose,* which is soluble, and *parachloralose,* which is insoluble—are formed. *Chloralose* occurs in small crystals having a very bitter and disagreeable but not acrid taste. It is freely soluble in alcohol and in hot water, slightly so in cold water, a little less than five grammes to the liter. Its melting point is 185° C. (365° F.). Chloralose was first brought forward as a remedial agent by Hanriot and Richet (*C. R. S. B.*, 1893), who state that five grammes of it will produce in a dog of ten kilogrammes' weight symptoms of intoxication, followed by a most profound sleep, in which all sensibility is lost, although the reflex activities are greater than normal. Upon the circulation the drug has but little power, the arterial pressure, even when there is profound anesthesia, being scarcely affected. During the anesthesia not only was the spinal motor side of the cord more active than normal, but the motor cerebral cortex was found to be excessively excitable, the animals experimented upon offering a strong contrast with chloralized dogs, in which the psychomotor cortex was almost devoid of responding power.

As a practical hypnotic, the action of chloralose is very variable and is often attended by disagreeable results, ten grains frequently failing to cause sleep, although the same amount has produced complete unconsciousness with alarming symptoms. Partial general paralysis, tremors, great slowing of the pulse, and marked evidences of enfeebled heart action have not rarely followed the use of the drug, while involuntary discharges of urine, delirious intoxication, excessive vomiting, and other disagreeable symptoms have been noted. The *dose* is from five to ten grains (0.32–0.65 Gm.), given in capsules.

M. H. Rendu (*B. Hôp. Par.*, xx, 1895) has reported violent collapse, excessively rapid feeble pulse, pronounced disturbance of respiration, epileptiform convulsions, and collapse as produced by four grains (0.26 Gm.) of chloralose.

Chloraloximes.—A series of compounds, whose strong physiological activities are asserted to be due to their splitting up in the system into hydrated chloral and their respective oximes. They are *chloralacetoxime* (melting point, 72° C., 161.6° F.); *chloralcamphoroxime* (melting point, 98° C., 208.4° F.); *chloralnitroso β-naphthol* (melting point, 100° C., 212° F.); *chloral acetaldoxime* (melting point, 74° C., 165.2° F.); *chloralbenzaldoxime* (melting point, 62° C., 143.6° F.). The compounds are easily soluble in alcohol and ether, and are readily recrystallized from petroleum benzin. Water dissolves them with difficulty, and when applied hot is likely to cause decomposition and the re-formation of hydrated chloral. (*Deut. Chem. Zeit.*, 1892.)

Chlorazene. *Sodium Para-Toluenesulphochloramine. N. N. R.* 1917. $CH_3.C_6H_4.SO_2Na : NCl + 3H_2O$.—"Sodium para-toluenesulphochloramine was first made by Chattaway (*Trans. Chem. Soc.*, 1905, lxxxvii, 153) by the action of sodium hydroxide on para-toluenesulphodichloramide. It may also be made by dissolving para-toluenesulphonamide (1 molecule) in a 5 per cent. cold alkaline solution of sodium hypochlorite (1.2 molecule), warming, if necessary, filtering and adding one and one-half volumes saturated sodium chloride solution. The crystals of sodium para-toluenesulphochloramine are collected, washed with sodium chloride solution and dried in the air." *N. N. R.* It is a white crystalline powder with a chlorine-like odor. Its range of incompatibilities is large, including the acids, alcohol, iodides, etc. It was introduced by Dakin (*B. M. J.*, Aug. 25, 1915, and January 29, 1916) as a surgical disinfectant. He originally proposed the name of *Chloramine,* but as this is also applied to the substance NH_2Cl, the title has been changed to chlorazene.

Chlorazene is a powerful germicide, especially suitable for the sterilization of *wounds* by virtue of the fact that it does not coagulate protein, that it is relatively non-irritant, and that it is much less injurious to the bodily cells than most of the other surgical disinfectants. It has been used with great success by French and English surgeons during the European war in badly infected wounds. It may also be employed as an antiseptic mouth wash and for irrrigation of the bladder, uterus, and other internal cavities. It is not suitable for a gastric antiseptic because it is decomposed by the secretions of the stomach. As a surgical disinfection it may be used in strengths of from 0.5 to 4 per cent. Under the name of *Dichloramine-T,* the paratoluenesulphodichloramide itself, from which chlorazene is prepared, has also been used as a disinfectant. This compound has the disadvantage of being insoluble in water; it is therefore used dissolved in a mixture of one part of eucalyptol and four parts liquid petrolatum, which are previously saturated with chlorine (see *J. A. M. A.*, 1917, lxix, 27). Solutions containing from 2 to 10 per cent. of dichloramine-T are sprayed into the wound. Dufresne (*J. Ex. M.*, 1917, xxvi, 91) recommends the use of a paste, made with sodium stearate, containing 0.5 to 1 per cent. of dichloramine-T.

Dichloramine-T occurs as a pale yellow, crystalline powder, with a chlorinous odor, having a melting point between 78° and 83° C. (172.4°–181.4° F.).

Dakin and Dunham (*B. M. J.*, May 20, 1917) have introduced also, under the name of *Halazone,* the para-sulphone dichloramide-benzoic acid, which is intended for the sterilization of drinking water.

Chlorcresols.—The combinations of chlorine with the cresols are all of them active germicides;

especially powerful is the *paracresol chloride*. According to Croner, a soapy solution containing 0.125 per cent. of this substance is more actively germicidal than a 0.5 per cent of solution of compound solution of cresol and in its action on spore-forming organisms was even more markedly superior to compound solution of cresol. The *chlorcresol* has the further advantage of being almost odorless.

The alcoholic solution of meta-chlorcresol has been highly recommended by Gottschalk (*D. M. W.*, 1911, p. 928) and others for the disinfection of the surgeon's hands. He used a proprietary preparation, *eusapyl*, which is an aqueous solution of chlorcresol in potassium ricinoleate. He used this solution in 1 per cent. strength in 70 per cent. alcohol. Another similar preparation is on the market under the name of *lysochlor*.

A compound of meta-chlorcresol with an alkali which is sold under the name of *grotan*, according to Schottelius, destroys all vegetative bacteria within five minutes if present in the strength of 0.5 per cent., and even the highly resistant anthrax spores are killed by a 1 per cent. solution in twenty minutes.

Chloretone. *Trichlorbutyl Alcohol. Acetone-chloroform. Chlorbutanol. N. N. R.* 1917. $CCl_3.(CH_3)_2.COH + \frac{1}{2}H_2O$.—It forms colorless crystals fusing at 80° to 81° C. (176°–177.8° F.), difficultly soluble in water, more readily soluble in alcohol and glycerin. It forms a mass or liquid when triturated with antipyrine, exalgine, menthol and phenol. *Chloretone*, in 1894, was introduced to the medical profession as an anesthetic and hypnotic by J. A. Abel. When given in proper doses it produces in the lower animals a profound sleep with complete anesthesia without the respiration or blood pressure being seriously affected, although the period of sleep may last some hours or even days. If the dose be sufficient, however, death occurs from asphyxia. Chloretone has no influence upon the blood, very little upon blood pressure, although when brought locally in contact with the heart it acts as a depressant. The bodily temperature is distinctly lowered during anesthesia. The results of Abel in regard to the toxicity of chloretone have been challenged by E. Impens, who finds that chloretone restricts the combustion of oxygen more than 50 per cent. and that it is more dangerous than hydrated chloral.

Chloretone, as a hypnotic and antispasmodic, has failed to achieve the confidence of the profession, possibly because of timidity in dosage. Hobbs (*B. M. J.*, Nov., 1910) finds it of service in the treatment of *tetanus;* he administered 36 grains (2.3 Gm.) per rectum two or three times in the course of a day. As a local remedy, chloretone is often of value because of its being both antiseptic and anesthetic, although its slight solubility in water interferes with its usefulness. A dusting powder containing 1 to 2 per cent. has been found a serviceable application in painful ulcerations. Fioca (*Press. Med.*, 1907, p. 460) has reported favorable results from the use of pure chloretone, finely powdered, in painful conditions of the mucous membranes, as in the dysphagia of *laryngeal tuberculosis*. It is also of service for the relief of *gastralgia* and *vomiting;* Wynter (*Lancet*, 1907) and others have reported good results in the treatment of *sea-sickness*. A 1 per cent. solution, with menthol and camphor, in liquid petrolatum, has been used as a spray in inflamed states of the nasal mucosa.

Chloretone is a very useful anesthetic in the physiological laboratory. For this purpose it is best dissolved in olive oil and administered by intraperitoneal injection. The *dose* should be from 0.1 to 0.2 Gm. (1.5–3 gr.) per kilogramme of body weight. The *dose* of chloretone for internal administration is ordinarily from five to fifteen grains (0.32–1 Gm.), but larger amounts may be given with safety.

Chloroiodolipol.—This is stated to be a chlorine substitution product of phenol, creosote, and guaiacol. It is used in chronic affections of the respiratory tract, by inhalation.

Chlorol.—A liquid disinfectant containing mercuric chloride, sodium chloride, hydrochloric acid and copper sulphate, dissolved in water. It should be used with caution.

Chlorolin.—This is a liquid disinfectant said to contain about twenty per cent. of monochlorphenol and trichlorphenol. It is applied to wounds in solutions varying in strength from one-half to three per cent. Pills containing one-thirtieth of a grain of *chlorphenol* have been used in the treatment of *tuberculosis*.

Chlorostigma. *Tasi.*—The *C. Stuckertianum* (*Asclepiadaceæ*), a South American plant, is asserted to contain an alkaloid, *chlorostigmine*, which has been used to stimulate the secretion of milk.

Chlorphenols.—By the action of chlorine upon phenol is produced a mixture of ortho- and para-chlorphenol ($C_6H_4Cl.OH$.) and by continued action trichlorphenol ($C_6H_2Cl_3.OH$.). *Orthochlorphenol* is a liquid boiling at 175° C. (347° F.) and solidifying at 7° C. (44.6° F.); the *parachlorphenol* forms crystals melting at 37° C. (98.6° F.) and boiling at 217° C. (422.6° F.). Both have an unpleasant, penetrating odor. *Trichlorphenol* (*omal*), which was discovered by Laurent, crystallizes in needles, which melt at 68° C. (154.4° F.) and boil at 244° C. (471.2° F.). It is easily soluble in alcohol and ether.

The introduction of one or more chlorine atoms into the phenol molecule increases very markedly the germicidal power and apparently in proportion to the number of chlorine atoms introduced. Unfortunately, however, the caustic and poisonous actions seem to be increased also. Karpow, working in the laboratory of Nencki, found that meta-chlorphenol is poisonous to the rabbit, the minimum fatal dose being 1.08 Gm. per kilogramme, and the chief symptom violent clonic convulsions. He experimentally demonstrated that both ortho-chlor- and parachlorphenol escape with the urine, in combination with sulphuric acid, and probably also with glycouronic acid, the urine becoming rapidly blackish on exposure to air, and confirmed the observations of Külz (*A. G. P.*, Bd. xxx) that the urine of dogs poisoned with the *chlorphenols* polarizes to the left. It would appear almost certain that the chlorphenols undergo at least partial decomposition in the organism, giving origin to hydroquinone, pyrocatechin, and other educts found after poisoning with phenol. The action of these chlorophenols upon the general system is probably practically that of phenol. According to Bechold and Ehrlich (*Z. P. C.*, 1906, xlvii, p. 173), trichlorphenol in the strength of 1 part in 10,000 prevents the growth of all bacteria and is equivalent to 1 in 800 of phenol. Nencki states that a 2 per cent. solution of monochlorphenol is superior to a 5 per cent. phenol solution.

Spengler (*Arch. des Sci. Biol.*, 1895, iv) states that the parachlorphenol is especially poisonous to the tubercle bacillus and recommends its 10 per

cent. solution in the treatment of *tubercular laryngitis*. In dilute solution the chlorphenols have also been used as general surgical disinfectants, but have failed to establish themselves clinically.

The *chlorsalols*, the *salicylic esters of chlorphenols*, were studied by Nencki and found to undergo decomposition in the intestines or system, the salicylic acid or its derivatives appearing in the urine. The antiseptic properties of these chlorsalols were found to be much greater than that of salol. Girard has used them in *doses* of from sixty to ninety grains (3.9–5.8 Gm.) a day in *cystitis* and *diarrhea* with excellent results. Passerini has employed them in *phthisis* and in *bronchitis* by means of an inhaling apparatus, in which fifteen minims (0.9 mil) are placed on a piece of cotton, the patient inhaling with slow and deep inhalations from five to ten minutes daily. Usually at first some pulmonic irritation, and even for a day or two temporary exacerbation, occur, but the final results are said to be remarkable.

Menthorol, so called, is a moderately thick liquid, with an agreeable taste and the odor of parachlorphenol, which is said to be a mixture of menthol and parachlorphenol. It may be used as a local remedy in a 5 to 15 per cent. solution in the treatment of *ulcerations of the throat and lungs*.

Cholesterin. *Cholestrin. Cholesterol.* $C_{27}H_{46}O$.—This is a monatomic alcohol and occurs in wool fat, bile, and cod liver oil. When pure it is in the form of white scales, unctuous to the touch, very sparingly soluble in water but readily so in ether or chloroform. It has the property of neutralizing many hemolytic poisons, such as snake venom, saponin, etc., as has been shown by Ranson (*D. M. W.*, 1901) and confirmed by Jahnson-Blohm. (*Z. P. C.*, 1913, lxxxv, p. 59.) Because of this property it has been used in medicine in the treatment of various dyscrasias of the blood; thus it has been employed in *malarial hematuria* and other forms of *hemoglobinuria*, in *purpura*, *chlorosis*, *pernicious anemia*, and other forms of *anemia*.

Pringsheim (*Med. Klin.*, 1913, p. 254) recommends that it be administered intramuscularly, using doses of eight grains (0.5 Gm.) daily in the form of an aqueous emulsion. Reicher (*B. K. W.*, 1908) administers it by mouth dissolved in olive oil. He gives a 3 per cent. solution in tablespoonful *doses*. Under the name of *choleol* there is upon the market an oily solution which is claimed to contain the palmitin and olein esters of cholesterin. Almangea and Mendes (*Il Morgagni*, March 30, 1907) assert that *cholesterin* has the power of fixing the toxin of tetanus, and report two cases of *tetanus* which were cured by daily injections of cholesterin.

Chroatol.—*Terpin-iodo-hydrate*, $C_{10}H_{16}.2HI$, occurs in greenish-yellow crystals, having an aromatic odor; it is insoluble in water, soluble in alcohol and glycerin, slightly soluble in ether and chloroform. It has been used externally in the treatment of *psoriasis* and other skin diseases as a dusting powder or 10 per cent. ointment.

Terpin hydro-iodide (Merck), a related compound $C_{10}H_{16}HI$, is a reddish liquid soluble in alcohol and ether.

Chrome Yellow. *Chromate of Lead. Lemon Yellow. Leipsic Yellow. Paris Yellow.* $PbCrO_4$.—This is the *neutral lead chromate* prepared by precipitating a solution of lead nitrate with potassium chromate. It is of a beautiful lemon-yellow color. The *basic lead chromate* ($PbO,PbCrO_4$) possesses a red color, and is sometimes used as a pigment. *Chrome green* is either *chromium sesquioxide* or a mixture of *chrome yellow* and Prussian blue. The chromates are often adulterated with lead sulphate. Duviller (*J. P. C.*, Août, 1873, 114) detects this by heating one part of the suspected pigment with a mixture of from two to three parts of nitric acid, sp. gr. 1.420, one to two parts of water, and one-fourth part of alcohol. The chromate is all dissolved, but any sulphate present remains unaffected. Lead chromate has been used by bakers in place of eggs for giving a rich yellow coloring to buns, and there can be no doubt of its having produced fatal poisoning in a number of cases. John Marshall has shown that its exhibition in animals is followed by an absorption, which takes place very slowly.

Chromium.—*Chromium* was discovered by Vauquelin in 1797. Its most common ore is *chrome iron*, consisting of ferrous oxide and chromium sesquioxide. This is not an abundant mineral, the principal source of supply being at present Asia Minor. Chromium is obtained by igniting its oxide in contact with charcoal with the aid of the electric arc; or by the more recent methods of reduction of its oxide by finely divided metallic aluminum (Goldschmidt), or by metallic silicon (Gren and Wahl). It is a brittle metal, of a grayish-white color like platinum, with some luster, and very hard, so that it scratches glass. Its sp. gr. is 6.5 to 6.8 at 15° C. (59° F.), atomic weight 51.7, and symbol Cr. It does not change by exposure to the air, and is with difficulty attacked by the acids. It forms with oxygen five compounds: (1) the monoxide (CrO), (2) the sesquioxide (Cr_2O_3), (3) the trioxide or chromic anhydride (CrO_3). (See *Chromii Trioxidum.*) Of the two others, one may be considered as a compound of the monoixde and sesquioxide ($CrO.Cr_2O_3$), and the other, called *perchromic oxide*, consists of two atoms of chromium and seven of oxygen (Cr_2O_7). Chromium combines with chlorine in two proportions, forming the *dichloride* and *sesquichloride*. The chief value of chromium in the arts is as the source of potassium dichromate and of pigments.

Chromium Sulphate.—This salt has been used by Kolipinski (*M. A.*, 1908) in a remarkably wide range of disorders. Thus, he has employed it with asserted success in *prostatic hypertrophy*, in *fibroid tumors* of the *uterus*, in *nervous vomiting*, for the relief of *menopausal symptoms*, but he especially recommends it in the treatment of *locomotor ataxia* and *exophthalmic goiter*. His results do not appear to have been confirmed.

Chrysarobin, Oxidized. *Chrysarobini Oxydatum.*—A brownish-black powder, obtained by boiling chrysarobin in water with sodium peroxide; its 5 to 10 per cent. ointment has been highly recommended by Unna in the treatment of facial, genital, and other forms of *eczema* for which chrysarobin is too irritating. It has no influence in dry eruptions.

Chrysoform.—*Dibromodiiodohexamethylenetetramine.*—A yellowish, very fine powder, having a faint iodine odor, and insoluble in water and alcohol. With properties resembling those of iodoform, it is used in a collodion emulsion for skin ailments and in a glycerin and water suspension or medicated gauze for antiseptic purposes.

Chrysoidin. (*Diamidoazobenzolhydrochloride.*) $C_6H_5N=N.C_6H_3(NH_2)_2HCl$.—This is a reddish-brown, crystalline powder, easily soluble in water. It is used in an aqueous solution as an antiseptic mouth wash or gargle.

Cichorium. *Cichorium Intybus L. Chicory. Succory. Blue Sailors.*—A perennial herbaceous composite plant, indigenous in Europe, but naturalized in the Northern United States and Canada, where it grows in fields, and in roads along the fences. The whole plant has a bitter taste, without acrimony or any very peculiar flavor. The taste is strongest in the root and weakest in the flowers. The leaves, when young and tender, are eaten as salad. Chicory is a feeble, non-irritating tonic.

The root is much used as a substitute for or adulterant of coffee. In preparing it, Dausse recommends that the dried root should be cut into rather large and equal pieces, which are to be roasted until they lose 140 out of 500 parts. The pieces are then easily ground in a mill, and afford a yellowish-brown powder. (*Ph. Cb.*, 1850, 688.) For methods of detection in ground coffee, see *P. J.*, 1867, 141; also Allen (*Com. Org. Anal.*, 2d ed., vol. iii, part 2, 540), and J. R. Leebody (*Chem. News*, 1874, 243); see also paper by LaWall and Forman (*A. J. P.*, 1913, 535). A glucoside has been obtained from the blossoms of *Cichorium Intybus* by Nietzki (*A. Pharm.*, (3) 8, 327), to which the formula $C_{32}H_{34}O_{19}$ is assigned. On boiling with dilute acids it yields glucose and a compound, $C_{20}H_{14}O_9$. This decomposition product seems to exist in the blossoms ready formed along with the glucoside. The garden *endive* is also a species of *cichorium, C. Endivia* L.

Cicuta. *Cicuta virosa* L. *Water Hemlock. Cowbane. Ciguë vireuse*, Fr. *Wasserschierling*, G.—A perennial, umbelliferous European plant, growing on the borders of pools and streams. It is very poisonous to most animals, though said to be eaten with impunity by goats and sheep. A number of the species of *cicuta* are intensely poisonous; indeed, the statement is made that *C. maculata* L. is the most poisonous plant native in the United States. The *C. vagans* (*Oregon water hemlock*), *C. occidentalis* Dougl. and *C. bulbifera* L., all of which are found in various parts of North America, are actively poisonous, as is also the European species *C. virosa*. From the last named, Van Ankum (*J. P. C.*, 1868) obtained a resinous body which was intensely poisonous, resembling picrotoxin in its physiological action, and to which he gave the name of *cicutoxin*. Böhm (*A. E. P. P.*, v, 281) has since obtained this principle pure, as a thick, tenacious, amorphous substance, of acid reaction, of slight odor but disagreeable taste. The dry root yielded about 3.5 per cent., the fresh 0.2 per cent. of cicutoxin. The presence of a volatile alkaloid resembling coniine, and termed *cicutine*, has been observed by Wittstein and Buignet. According to Jacobson (*J. Am. C. S.*, 1915, xxxvii, p. 916), cicutoxin is a complex derivative of pyrone and is fatal to lower animals in doses of 50 mgm. per kilo.

Cicuta maculata L., *American water hemlock, Musquash root, Beaver poison, Spotted cowbane.* This grows in meadows and on the borders of streams throughout the United States, and is closely analogous, in botanical character and in effects, to the European species. In several instances children have been fatally poisoned by eating its root. This consists of several oblong, fleshy tubers, sometimes as long as the finger, spreading out from the base of the stem, and having an odor and taste not unlike those of parsnip. For microscopic examination of plant, see *A. J. P.*, July, 1891, and Merck's Report, 1909, p. 35. Cicuta has been highly lauded as a specific in nervous and sick *headache* (*Proc. A. Ph. A.*, 1858, 253), but is rarely if ever used. J. E. Young found in the seeds an alkaloid supposed to be identical with coniine. (*A. J. P.*, xxvii, 294, confirmed by R. Glenk, *A. J. P.*, 1891, 328.)

Egdhal (*A. I. M.*, 1911, vii, p. 348) has collected the history of 46 cases of poisoning by cicuta, of which twenty-one were fatal. Nausea, vomiting, and convulsions occurred in practically all the cases. In most of them there was also bloody froth at the mouth and in many dilated pupils and unconsciousness. In his own case there was cyanosis apparently from interference with the respiration by the convulsions.

In cicuta poisoning there is generally violent vomiting, followed by vertigo, cold, clammy skin, slow, feeble pulse, general convulsions and later paralysis, unconsciousness and dilated pupils. Tannic acid has been suggested as an antidote, but its efficiency has not been proved. The treatment should be evacuation of the stomach, stimulants to combat the collapse, and the cautious use of morphine to control the vomiting and convulsions.

Cinchonidine Salicylate. *Cinchonidinæ Salicylas.* $C_{19}H_{22}ON_2.C_7H_6O_3$.—This salt occurs in needles soluble at 18° C. (64.4° F.) in 766 parts of water. It is capable of producing physiologically the action of the quinine salts, and no doubt is a powerful antiperiodic, inferior, however, to the ordinary preparations of that alkaloid. It has been recommended and considerably used as a specific in *chronic* and *subacute rheumatism*, in *doses* of from fifteen to twenty grains (1–1.3 Gm.) a day, best given in pill or capsule.

Cineraria Maritima L.—This composite plant, known popularly as *Dusty Miller*, is a native of the West Indies, and has been introduced as a house plant into this country. There is upon the market a proprietary preparation which professes to be the expressed juice of this plant, and is recommended in diseases of the eye, especially as an absorbent of *cataracts*. We do not know, however, of any sufficient scientific justification for a belief in this improbable property.

Cinnamic Acid. *Acidum Cinnamicum.* $C_6H_5CH{=}CH.COOH$.—This acid occurs naturally in Peru and Tolu balsams and from styrax, and is made synthetically by the reaction of acetyl chloride upon benzaldehyde, or by the action of a mixture of acetic anhydride and fused sodium acetate upon benzaldehyde. It forms colorless, lustrous plates, melting at 133° C. (271° F.), and is insoluble in cold water, but quite soluble in boiling water and in alcohol. Under the name of *hetol, sodium cinnamate* has been used to a considerable extent in the treatment of *tuberculosis*. For a volumetric method of assay of sodium cinnamate, see *P. J.*, 1910, 365. A. Landerer (*M. M. W.*, xxxv, Nos. 40, 41), the introducer of the treatment, put forward most remarkable claims, affirming that in the early stages of uncomplicated tuberculosis 85 per cent. of the cases can be cured. The heated controversy to which Landerer's paper gave rise has been well reviewed by W. J. Robinson (*M. A.*, 1902), with the conclusion that sodium cinnamate is not a direct curative agent in tuberculosis and is of no more value symptomatically than is creosote. Sodium cinnamate may be given by the mouth in *doses* of from two to three grains (0.13–0.2 Gm.). The initial intravenous *dose* of the intravenous treatment, recommended by Landerer, should not exceed one-fiftieth of a grain (0.0013 Gm.); the injection may be made every third day

and the amount increased until one-third of a grain (0.021 Gm.) has been reached. A 10 per cent. solution in glycerin affords an excellent method of administration. Sodium cinnamate has also been recommended for the treatment of *keratitis*. Pflüger (*Klin. Monatsbl. für Augenheilkunde*, 1901) instills into the eye a 1 per cent. solution to which is added 1 per cent. of cocaine.

Ciose. *N. N. R.* 1917.—A dry, completely soluble protein product of beef, containing from 83 to 85 per cent. protein. It is especially designed to augment the protein of any particular diet.

Citarin. *Goutine. Sodium Anhydromethylene-citrate.* $(NaO.COCH_2)_2.CO\begin{matrix}CH_2\\CO\end{matrix}>O$.—This is a white, granular, hygroscopic powder possessing a slightly acidulous taste. It is readily soluble in less than 2 parts of water. It readily liberates formaldehyde from its solutions, especially in the presence of alkalies. It is asserted to be a useful remedy in cases of *uric acid gravel*, and in *gout* and *chronic rheumatism*, in *doses* of thirty to forty-five grains (2–3 Gm.) four times a day.

Citrocoll.—This substance, though claimed to be a neutral citrate of amidoacetparaphenetedin $(C_6H_4.OC_2H_5.NH.CO.CH_2NH_2)_3\ C_6H_8O_7$, has also been stated to be a mixture of phenacetin and citric acid. It is soluble in water and is used as an antipyretic and analgesic remedy. *Dose*, ten to fifteen grains (0.6–1 Gm.).

Citrophen. $C_3H_4(OH)\ (CONH.C_6H_4OC_2H_5)_3.+3H_2O$.—This compound of citric acid and *p*-phenetidin is a white, crystalline powder, soluble in forty parts of water, with a faint acid taste; its melting point is 181° (358° F.) and its ready solubility in water adapts it for hypodermic use. It is used as an antipyretic, also in *migraine* and *neuralgia*. *Dose*, ten to fifteen grains (0.65–1.0 Gm.).

Citrullin.—A resinoid obtained from *Citrullus Colocynthis* L. It is a yellow, amorphous powder, soluble in alcohol and ether and employed per rectum as a purgative. *Dose*, one-sixth to one-third of a grain (0.01–0.021 Gm.) dissolved in alcohol and glycerin.

Civet. *Zibethum. Civette*, Fr. *Zibeth*, G.—This is an odorous substance, obtained from two animals of the genus *Viverra;* the *V. Civetta* or *civet* cat of Africa, and the *V. Zibetha*, which inhabits the East Indies. It is secreted in a cavity opening between the anus and external genitals, and is collected from animals confined for the purpose. It is semi-liquid, unctuous, yellowish, becoming brown and thicker by exposure to the air, of a very strong, peculiar odor, similar to that of musk, though less agreeable and less diffusible, and of a bitterish, subacrid, disagreeable fatty taste. When heated it becomes quite fluid and at a higher temperature takes fire and burns with a clear flame, leaving little residue. It is insoluble in water, and only slightly soluble in ether and cold alcohol, but heated alcohol dissolves it almost entirely, depositing it again upon cooling. It contains, among other ingredients, a volatile oil, fat, and free ammonia. E. Charabot and A. Hébert give the following tests for *civet* of normal quality: When dissolved in a mixture of alcohol and ether less than 6 per cent. residue should remain. The saponification number of civet should exceed 100, and the fatty acids which are separated from the saponfied civet after acidulation with sulphuric acid should exceed 50 per cent. (*Bull Soc. Chim.*, iv, 7, 1910, 687.) In medicine it was formerly employed in lieu of castor and musk; it is now used exclusively as a perfume. For analyses of commercial samples, see *P. J.*, 1897, 101.

Clematis. *Clematis recta* L. (*C. erecta L.*) *Upright Virgin's Bower. Clematite*, Fr. *Waldrebe*, G.—A perennial European plant. The leaves and flowers have an acrid, burning taste. When bruised in a mortar they irritate the eyes and throat, giving rise to a flow of tears and to coughing, and applied to the skin they produce inflammation and vesication; hence their old name of *Flammula Jovis*. The acridity is greatly diminished by drying. Störck found this *clematis* to be diuretic and diaphoretic, in *doses* of from one to two grains (0.065–0.13 Gm.) of the extract a day, or from thirty to forty grains (2–2.6 Gm.) of the leaves given in infusion three times a day, and to be useful, locally and internally, in *syphilitic, cancerous*, and other *foul ulcers*.

Other species of *clematis* have the same acrid properties; among these *C. flammula* L., or *sweet-scented virgin's bower*, which, though a native of Europe, is cultivated in our gardens, *C. vitalba* L., or *traveller's joy*, also a native of Europe, and several indigenous species, of which *C. virginiana* L., or *common virgin's bower*, *C. viorna* L., or *leather flower*, and *C. crispa* L. have been used as substitutes for *C. recta* L. All these are climbing plants. Rochebrune (*Toxical. Africaine.* i) affirms that he has found in *C. flammula* L. an alkaloid, *clematine*, two milligrammes of which will produce in the guinea-pig copious and frequent urination, general tremors, great disturbance of respiration, feebleness and intermittency of the heart beat, followed in seven minutes by convulsions ending in coma and death.

From the bruised roots and stems of *C. vitalba* L., boiled for a few moments in water to diminish their acridity, and then digested in sweet oil for a little while, is made a preparation used locally in Europe for the *itch*. Twelve or fifteen applications are said to be usually sufficient. Gaube has found in this species an alkaloid, also named clematine, which forms with sulphuric acid a salt crystallizable in six-sided needles; also an acrid volatile oil analogous to mezereon in its properties, tannic acid, mucilage, and earthy salts. (*J. P. C.*, Août, 1869.)

Clemens's Solution.—*Arsenic bromide* was introduced as a remedy in diabetes by Clemens. This preparation is recognized in the N. F. IV under the name *Liquor Arsenicalis Clemens* (see Part III). It was formerly called *Liquor Potasii Arsenitis et Bromidi* and contains one gramme of arsenic trioxide to the litre (in the form of a complex mixture with bromine and potassium). According to Clemens, the commencing dose of such a solution is one minim three times a day, increased gradually until the equivalent of one-fifth of a grain of the salt is daily exhibited. The clinical reports in regard to this remedy in *diabetes* seem to indicate that along with a restricted diet it is occasionally of distinct service, but in the majority of instances fails to accomplish good.

Clove Bark. *Cortex Caryophyllatus. Cassia Caryophyllata.*—Under these names two barks occur in the market. Of these the most abundant comes from the West Indies, and is derived from a tree, *Dicypellium caryophyllatum* Nees. (Fam. *Lauraceæ*.) It is usually in large compound quills, 1 to 2 mm. thick, composed of numerous separate pieces rolled around one another and having a

dark brown color, being more or less flaky on the outer surface and finely striate on the inner surface, a pungent taste, and an odor similar to that of cloves. The second variety of clove bark occurs in fragments, resembling the other form in odor and color but softer and lighter, and supposed to be derived from *Eugenia caryophyllœa* Wight (Fam. *Myrtaceæ*) which grows in Ceylon. This clove bark has aromatic properties not unlike those of the spice from which it derived its name, but it is much inferior and is not used in this country. Some authors have confounded with it a different bark, produced in the Moluccas and known by the Indian name of culilawan. (See *Culilawan.*) For description of a false clove bark, see *A. J. P.*, vol. xv.

Cnicus. *Cirsium arvense* (L.) Scop. (*Cnicus arvensis*, Hoffm.) *Canada Thistle.*—This European composite plant, to which have been attributed diaphoretic, emetic, and tonic properties, according to Herman J. Pierce (*A. J. P.*, lxviii, 1896), contains a volatile alkaloid, and also *Cnicin*, $C_{42}H_{56}O_{15}$, which is said to possess emetic and emmenagogue properties.

Coagulen Ciba. (*N. N. R.*, 1917). *Coagulin, Kocher-Fonio.*—An extract said to be prepared from blood platelets, and to contain *cytozym, thrombokinase*, and *thrombozym*, mixed with lactose. Each gramme represents 20 grammes of dried blood. It is used as a hemostatic intramuscularly or intravenously in 5 per cent. solution.

Coal Tar Colors.—Many colors used in dyeing and in coloring food-stuffs, beverages and medicines are synthesized from one or the other of the commercially valuable fractions of coal tar. Many of these were formerly known as *aniline colors*, because the earlier colors of coal tar origin came from the fraction known as aniline. As many of them are now commercially prepared from other fractions of coal tar, the term *coal tar colors* seems more appropriate. Most of these which have attained any therapeutic importance, are described under their appropriate titles. (See *Fuchsine, Methyl Violet, Scarlet Red, etc.*)

The use of coal tar colors for artificially imitating the natural color of any food-stuffs is now largely prohibited by law, with the exception of such instances where the color is used principally for æsthetic reasons, as in confectionery, or where proper notice is given to the consumer by plainly printing on the label of the package the words "Artificially colored." Even then such colors are sometimes prohibited, as in the legislation in Pennsylvania concerning fruit syrups (Act of 1905) where all coal tar colors are specifically prohibited in the act.

The feeling against the use of coal tar colors as such, which still largely obtains among the uneducated and less well informed, is undoubtedly due to the indiscriminate use of them in the early days and the fact that many of them were not freed from poisonous mineral constituents like arsenic or mercury, compounds of which were often used in their manufacture. Many of the coal tar colors in former use are now known to be harmful, such as *victora yellow* (*dinitrocresol*). A list of permissible colors has, therefore, been prepared by the U. S. Department of Agriculture, which may be used under such circumstances as permit the use of a harmless color and when not otherwise prohibited. (See *F. I. D.*, page 164.) This list has been adopted by a number of the States having food laws in harmony with the National legislation on this subject.

Cobalt. (Co=58.56.)—This not very abundant metal is usually found associated with arsenic, and is rarely used in its pure condition in medicine or pharmacy. It occurs as *smaltine* or *tin-white cobalt, cobalt glance*, or *sulpharsenide; cobalt bloom, erythrine*, or *arsenate; earthy cobalt* or *wad*, a mixture of cobaltous oxide and black manganese oxide, and *spiess cobalt*, (Co,Ni,Fe) As_2.

Spiess cobalt is frequently employed as the source of cobalt salts, and the substance called in commerce *zaffre* is an impure cobalt arsenate, made by simply roasting the crude cobalt ores or calcining them, with access of air, and is used to give a blue color to glass, enamels, and pottery glaze. The native ore is frequently found in commerce under the name of *flystone*, and is used for poisoning flies, by roughly grinding it and putting a small quantity in a saucer with sweetened water. *Smalt* is the common name used for glass colored by fusing with cobalt oxide, producing a blue pigment, for coloring glass, etc. The soluble salts of cobalt, particularly the *chloride* and *sulphocyanate*, have been used to impregnate paper, etc., giving it ordinarily a pink tint, indicative of the presence of moisture, while on elevation of temperature and drying the color changes to blue. Advantage has been taken of this fact to produce the so-called *barometer paper*.

A cobalt oxide, prepared by precipitating the chloride with potassium hydroxide, has been employed in *rheumatism*. It is emetic in the *dose* of 10 or 20 grains (0.65–1.3 Gm.). The salts of the metal are irritant poisons. The statement that the cobalt salts and hydrocyanic acid will form in the animal system a potassium or sodium-cobalt-cyanide and are antagonistic poisons and may be used as antidotes one for the other, is probably not correct. (See Hübner, *A. I. P.*, vol. ix.)

Cobalt Blue.—This beautiful pigment is a compound of cobalt oxide and aluminum oxide, obtained by precipitating the mixed solutions of a salt of aluminum and one of cobalt by means of an alkali, and washing, drying, and strongly calcining the precipitate. (Berzelius.) The *cobalt blue* of Thénard is made by heating together the hydrated cobalt subphosphate and aluminum hydroxide. It is used in painting.

Cobweb. *Spiders' Web. Tela Araneœ.*—Spiders' webs were formerly much used in *headache, hectic fever, asthmas, hysteria*, and *nervous irritation*, but probably acted solely through the imagination. *Dose*, from ten to twenty grains (0.65–1.3 Gm.) *pro re nata.* (See *L. L.*, 1867.) Spider's web was formerly used as a styptic, especially after extraction of teeth, the cavity being stuffed full of the web.

Cocaine Formate. $C_{17}H_{24}NO_4.H.COOH$. — A crystalline compound, melting point, 42° C. (107.6 F.), and soluble in water at 20° C. (68° F.). It is employed in the same manner and for the same purpose as the hydrochlorate of cocaine, having the slight advantage over the latter in possessing slight antiseptic qualities.

Cocculus Indicus. *N. F. IV. Fish Berry. Indian Berry. Coque du Levant*, Fr. *Kokkelskörner, Fischkörner, Tollkörner*, G. *Oriental Berries.*

It is described in the *N. F.* as "the dried fruit of *Anamirta Cocculus* (Linné) Wight et Arnott (Fam. *Menispermaceæ*)."

This is a climbing shrub, with a suberose or corky bark, and grows along the Malabar Coast, and in Eastern Insular and Continental India. By Roxburgh it was proved to be one source of

Cocculus, which is, however, probably derived also from other plants, notably from the *Cocculus Plukentii*, DC. (now *Pachygone ovata* Miers.), of Malabar, and *C. laconusus* DC. (now *Anamirta paniculate* Colebr.); of Celebes and the Moluccas. It was known to the Arabian physicians, and was imported into Europe from the Levant, from which circumstance it was called *Cocculus levanticus*. It is now brought exclusively from the East Indies.

The fruit bears some resemblance to the bay laurel berry, but is not quite so large, and may be distinguished by the fact that in the *Cocculus Indicus* the kernel never wholly fills the shell. When the fruit is kept long, the shell is sometimes almost empty. The Edinburgh College directed that "the kernels should fill at least two-thirds of the fruit." It is described by the N. F. as "reniform, about 10 mm. in length and 6 mm. in breadth and thickness, blackish-brown, wrinkled; hilum and micropyle close together, separated by a shallow sinus and connected by an obscure ridge running around the convex side. Seed urn-shaped, its longitudinal and transverse sections crescent-shaped. Taste slightly bitter; the seed whitish-yellow and intensely bitter. *Cocculus Indicus* yields not more than 5 per cent. of ash." *N. F.*

According to Merck its main constituents are *menispermine, paramenispermine, picrotoxin*, $C_{30}H_{34}O_{13}$, *picrotoxic acid* and *cocculin*.

A *tincture of Cocculus Indicus* is official in the *N. F.* (see Part III). For Procter's formula for preparing a fluidextract, see *U. S. D.*, 17th ed., or *A. J. P.*, 1863.

Cocculus Indicus is used in India to stupefy fishes. Both its poisonous properties and any therapeutic virtues it may contain depend upon picrotoxin (see p. 1550). It has been used in medicine for the purpose of destroying vermin in the hair, but it is an extremely dangerous drug. For cases of poisoning see Sozinsky (*M. News*, 1883, xliii, p. 485), Swift (*N. Y. M. J.*, 1897, lxvi, p. 664), and Haines (*P. M. T.*, 1884, xiv, p. 748). In spite of its highly toxic properties, *Merck's Index*, 1907, reports it as having nervine and sedative properties in *doses* of 1 to 3 grains (0.06–0.2 Gm.) *doses* of the powdered berries.

Coca. *Cocæ Folia. U. S. P. VIII. Br.* 1898. *Coca Leaves. Cuca. Feuilles de Coca*, Fr. *Cocablätter*, G. *Coca del Peru, Ipadu*, Sp.—"The dried leaves of *Erythroxylon Coca* Lamarck (Fam. *Erythroxylaceæ*), known commercially as Huanuco Coca, or of *E. Truxillense* Rusby, known commercially as Truxillo Coca, yielding when assayed by the process given below, not less than 0.5 per cent. of the ether-soluble alkaloids of Coca," *U. S. VIII.* "The dried leaves of *Erythroxylum Coca*, Lam., and its varieties." *Br.*, 1898.

The *coca* plants are shrubs or small trees, some of the species reaching the height of fifteen or twenty feet. It is conjectured that the original habitat was in the Peruvian mountains, from 7° South to 10° North, but either spontaneously or through cultivation the coca shrubs have spread until they are found in the whole Eastern curve of the Andes, from the Straits of Magellan to the borders of the Caribbean Sea, growing on the moist sides of the mountains at the elevation of 1500 to 6000 feet, the climatic requisites being moisture and equable temperature, with a mean of about 17.7° C. (64° F.) The wild coca shrub commonly reaches the height of 12 feet, and some are 18 feet, but the cultivated coca is usually kept down to about 6 feet. The leaves are gathered three times a year; the first harvest, or preliminary picking, is taken at the time of the trimming of the bushes, from the cut-off twigs. Then about the end of June, a scanty crop is gathered, while the last crop of the season is gathered in October or November. Harvesting must always take place in dry weather, so that the fresh leaves when spread out in layers two or three inches thick on the drying pavement can be collected in six or eight hours.

The coca plant, which is propagated from the seed in nurseries, begins to yield in eighteen months, and continues productive for half a century. The leaves, when mature, are carefully picked by hand so as to avoid breaking them or injuring the young buds, are slowly dried in the sun, and are then packed in bags (*cestos*) holding from twenty-five to one hundred and fifty pounds each. They were in general use among the natives of Peru at the time of the conquest, and have continued to be much employed to the present time. It is affirmed that nearly ten million dollars' worth, or forty million pounds, are annually produced, some plantations yielding three or four harvests a year. The importations into the United States have averaged for some years past about 1,000,000 pounds. For details as to method of cultivation, etc., see *T.G.*, Jan., 1886; also *C. D.*, 1897, 182. Two varieties of the coca leaf occur in the commerce of the United States, namely, the so-called Huanuco coca and the Truxillo coca, the Huanuco variety being produced in Bolivia, Huanuco, Brazil, Venezuela and Argentina, while the Truxillo coca is produced chiefly in Northern Peru. The great variation in the leaves and other portions of the coca plant, produced by its long-continued cultivation, has produced much doubt and discussion as to the specificity and characteristics of the plant; H. H. Rusby has made an elaborate study of the subject (*D. C.*, Nov., 1900).

Huanuco coca has been for a long time believed to be obtained from *Erythroxylon Coca;* this belief is confirmed by Rusby and has been accepted by the Pharmacopœial authorities. The plant was first described in 1786, in *Lamarck's Dictionary*, vol. ii, 393.

Truxillo coca is the product of the *E. Coca Spruceanum* of Burck; the name "spruceanum" had, however, been used elsewhere before it was suggested by Burck, and in obedience to the ordinary rules of botanical nomenclature it was changed by Rusby, who regards it as a distinct species, to *E. Truxillense*.

Coca is cultivated in the British East and West Indies, and in Java, and the product is said to appear, in the London markets, under the names of Truxillo coca and Java coca. This coca is entirely distinct from the Truxillo coca of the American market, and does not reach the United States. The coca shrubs of India and Ceylon are the offspring of plants originally sent out from Kew Gardens, which plants were derived from seeds obtained in Huanuco, and were considered by Morris as representing a variety of *E. Coca* to which he gave the name of *E. Nova-Garantense*. According to Rusby, however, this plant is a distinct species, and the same as that previously described by Jacquin, from Colombia, under the name of *E. carthagenense* (the name *E. carthagenense* not being, as it is held in the Kew Index, a synonym of *E. areolatum*).

The leaves of the different varieties of coca do not, on the whole, resemble one another at all closely, but are distinguished from most other

leaves by a slightly curved line on each side of the midrib, running from the base to the apex. This line has the appearance of a rib, but is really not of this character, having been produced during development by the peculiar folding of the leaf in the bud. The two commercial varieties were very well described in the *U. S. Pharmacopœia VIII* as follows:

"*Huanuco Coca.*—Greenish-brown to clear brown, smooth and slightly glossy, thickish and slightly coriaceous, stoutly and very shortly petioled; blade 2.5 to 7.5 Cm. long and nearly elliptical, with a very short and abruptly narrowed basal portion and a short point, the margin entire; midrib marked above by a slight ridge, very prominent underneath, the remaining venation rather obscure, especially above; underneath, a conspicuous line of collenchyma tissue runs longitudinally on either side of the midrib and about one-third of the distance between it and the margin, the enclosed areola being of a slightly different color from the adjacent surface; odor characteristic; taste bitterish, faintly aromatic, followed by a numbness of the tongue, lips, and fauces.

"*Truxillo Coca.*—Pale green, thin, brittle and usually much broken, smooth, but not shining, shortly and stoutly petioled; blade 1.6 to 5 Cm. long and one-third to one-half as broad, obovate to oblanceolate, narrowed from near the middle into the petiole, usually with a slight projecting point at the summit, the margin entire; underneath two irregular lines of collenchyma tissue, usually incomplete or obscure, and frequently wanting, run beside the midrib at about one-third the distance from it to the margin; odor more tea-like than that of Huanuco Coca; taste and numbing effect similar." *U. S. VIII.*[1] "The midrib itself is prolonged into a minute horny apiculus, which, however, is frequently broken off. Most of the epidermal cells of the under surface are seen in transverse section to project in the form of small papillæ." *Br.*, 1898.

Chemical Constitution.—In 1853, Wackenroder demonstrated the existence of tannic acid in coca leaves, and in 1859, Stanislaus Martin found in them a peculiar bitter principle, resin, tannin, an aromatic principle, extractive chlorophyll, a substance analogous to theine, and salts of lime. Previous to this (1855) Gardeke had isolated the crystalline alkaloid and given it the name of *erythroxyline.* Albert Niemann, of Goslar, made the first thorough investigation of the leaves, and gave to the alkaloid the name it now usually bears of *cocaine.* (See Part I, p. 359.)

Assay. U. S. VIII.—"Coca, in No. 60 powder, *ten grammes;* chloroform, ether, normal sulphuric acid V.S., ammonia water, distilled water, tenth-normal sulphuric acid V.S., fiftieth-normal potassium hydroxide V.S., cochineal or odeosin T.S., each, *a sufficient quantity.* Place the *Coca* in an Erlenmeyer flask, add 50 Cc. of a mixture of chloroform 1 volume and ether 4 volumes and insert the stopper securely. Allow the flask to stand ten minutes, then add 2 Cc. of ammonia water mixed with 3 Cc. of distilled water, and shake the flask well, at frequent intervals, during one hour. Then transfer as much as possible of the contents of the flask to a small percolator which has been provided with a pledget of cotton packed firmly in the neck, and inserted in a separator containing 6 Cc. of normal sulphuric acid V.S., diluted with 20 Cc. of distilled water. When the liquid has passed through the cotton, pack the Coca firmly in the percolator with the aid of a glass rod, and, having rinsed the flask with 10 Cc. of chloroform-ether mixture, transfer the remaining contents of the flask to the percolator by the aid of several small portions (5 Cc.) of a chloroform-ether mixture, using the same proportions as before, and continue the percolation with successive small portions of the same liquid (in all 50 Cc.). Next, shake the separator well for one minute, after securely inserting the stopper, and when the liquids have completely separated, draw off the acid liquor into another separator. Add to the chloroform-ether mixture 10 Cc. of a sulphuric acid mixture, using the same proportions as before, agitate well and again draw off the acid liquid. Repeat this operation once more, drawing off the acid solution as before into the second separator, introduce a small piece of red litmus paper, add ammonia water until the liquid is distinctly alkaline, and shake out with three successive portions of ether (25, 20, and 15 Cc.). Collect the ether-solutions in a beaker, place it on a water-bath filled with warm water, and allow the ether to evaporate entirely. Dissolve the residue in 3 Cc. of ether, and let this also evaporate completely. To the alkaloidal residue add 4 Cc. of tenth-normal sulphuric acid V.S. and 5 drops of cochineal or iodeosin T.S., then titrate the excess of acid with fiftieth-normal potassium hydroxide V.S. Divide the number of cubic centimeters of fiftieth-normal potassium hydroxide V.S. used, by 5, subtract this number from 4 (the 4 Cc. of tenth-normal sulphuric acid V.S. taken), and multiply the remainder by 0.03 and this product by 10, to obtain the percentage of ether-soluble alkaloids contained in the Coca." *U. S. VIII.* For methods of assaying coca leaves, see Lyons, *Ch. Ph.*, Sept., 1885; Squibb, *Ephem.*, 1887; Dohme, *Proc. A. Ph. A.*, 1893, 159; Prescott, *Organic Analysis; Proc. A. Ph. A.*, 1895, 268; *P. J.*, 1896, 1901, 222, 254; *Ph. Ztg.*, 1901, 965.

In South America many of the Indians habitually chew the leaf of the coca plant generally mixed with some alkali, as ashes or lime. It is stated on good authority that they will go for days performing hard physical labor without any other food. It is, however, clearly proven that these leaves do not take the place of nutriment, but simply put off the sense of fatigue and hunger. Eventually, however, this habit undermines the health and finally the inveterate excessive coca-chewer can be recognized by his uncertain step, general apathy, sunken eyes surrounded by deep purple aureoles, trembling lips, green and crusted teeth, and excessively fetid breath, with peculiar blackness about the corners of the mouth. An incurable insomnia is apt to be developed, emaciation becomes extreme, dropsy appears, and even death results from a condition of general marasmus. It has been believed that the effects of coca chewing are different from those produced by the alkaloid cocaine and hence it has been by some argued that the coca leaf contains other active principles, but there is no difference between the results

[1] In a series of measurements of the Bolivian and Truxillo leaves, H. G. Greenish found that the difference in thickness in the two varieties is more apparent than real, the same-sized leaves of the two varieties having the same thickness but the Huanuco leaves averaging much larger and therefore thicker than the others. The chief cause of the lesser fragility of the Huanuco leaf was found to be due to the thickening and lignification of cells in the parenchyma, the increased development of pericyclic fibers in the veinlets, and the increased development of sclereids in the neighborhood of the lines of the under surfaces of the leaf. Greenish affirms that the two leaves can be microscopically distinguished by the fact that the veinlets of the Bolivian leaf are connected with both the upper and the lower epidermis by a bridge of thick-walled lignified fibrous cells.

of the habit as practised by the South American Indian and the use of the alkaloid by depraved Caucasians, which cannot be readily explained on the ground of difference in the mode of taking the stimulant or racial variation. While there are other active substances present in the coca leaf, it is not manifest that they modify the action of the crude drug materially. For a study of the uses and effects of cocaine, see p. 362, and of tropacocaine, see p. 1649.

Coca has a slight bitter tonic effect as well as a stimulant action upon the central nervous system and has been used as a tonic in *neurasthenia* and other debilitated conditions. The danger of the formation of the habit, however, far outweighs any value the drug may possess, and the use of the crude preparation of coca seems to us hardly justifiable, except under the most extraordinary conditions. The *U. S. P., VIII,* recognized a fluidextract, the dose of which was from thirty to sixty minims (2–3.9 mils), and a wine the dose of which was two to eight fluidrachms (7.5 to 30 mils).

Cochlearia. *Cochlearia officinalis* L. *Common Scurvy-grass. Herbe au Scorbut,* Fr. *Herba Cochleariæ,* P. G. *Löffelkraut,* G. *Spoonwort.*—This annual or biennial cruciferous plant, is a native of northern and middle Europe and growing in Arctic America generally. The whole herb is active. It has, when fresh, a pungent, unpleasant odor if bruised, and a warm, acrid, bitter taste. These properties are lost by drying. They are imparted to water and alcohol by maceration, are retained by the expressed juice, and probably depend on a peculiar volatile oil, which is separable in very small quantity by distillation with water, and is probably produced by reaction between a fixed principle in the plant and water, under the influence of myrosin acting as a ferment. (*Chem. Cb.,* 1856, 124.) According to Hofmann, the oil is a sulphur-containing oil of the butylic series, having the formula $C_5H_9NS{=}C_4H_9CSN$.

Common scurvy-grass has been much used in *scurvy,* and even in *chronic rheumatism.* The fresh plant may be eaten as a salad, or used in infusion; the expressed juice has also been used.

Cocillana. *N. F. IV.*—It is described in the *N. F.* as "the dried bark of *Guarea Rusbyi* (Britton) Rusby (Fam. *Meliaceæ*). In flat or curved pieces of variable size and from 3 to 5 mm. in thickness; outer surface shallowly or deeply fissured, according to age and thickness, gray-brown, often ashy-gray from lichen growths, or of a deeper brown where the cork has been removed; inner surface of medium brown color, strongly and coarsely longitudinally striate, the striæ straight or wavy; inner bark usually much thicker than the outer, its fracture coarsely splintery-fibrous. Odor characteristic; taste slightly astringent, peculiar and slightly nauseous. Cocillana yields not more than 10 per cent. of ash." *N. F.* The bark of this large Bolivian tree, which was discovered by H. Rusby, is believed by him (*T. G.,* 1888) to contain an alkaloid; but by John W. Eckfeldt (*Med. Bull.,* 1891) its active principle is thought to be a glucoside. In *doses* of from twenty to fifty grains (1.3–3.2 Gm.) the bark causes vomiting, with prostration and some purging; also, it is said, much sneezing, dull frontal headache, and discharge from the nasal mucous membrane. The therapeutic action of the drug resembles that of ipecac, although as an expectorant it is somewhat more stimulant. (See *N. Y. M. J.,* Dec., 1889, and April, 1890). It has been used in various forms of *bronchitis* with asserted success. *Dose,* of the drug, fifteen grains (1 Gm.); of the fluidextract, from eight to twenty minims (0.5–1.3 mils) every three or four hours.

Codeonal.—Under this name a mixture which is asserted to contain 2 parts of *Codeine-diethyl-barbiturate* with 15 parts of *sodium-diethyl-barbiturate* has been introduced. The purpose of the combination is to obtain the sedative action of codeine and veronal in combination. It is used as a somnifacient, as a cough sedative, and as an analgesic. The *dose* recommended is from two to eight grains (0.13–0.5 Gm.).

Codeine Hydriodide. $C_{18}H_{21}O_3N.HI + 2H_2O$.—A crystalline powder, slightly soluble in cold and very soluble in warm water, is made by the action of hydriodic acid on codeine (alkaloid). It is used subcutaneously in lung affections and internally in *doses* of one-sixth to one-fourth grain (0.011–0.016 Gm.), several times daily.

Codeine Methyl Bromide. *Codeine Brom-methylate.* $C_{18}H_{21}NO_3$ $(Br.CH_3)$.—Under the trade name of *Eucodein,* this has been introduced as a cough sedative. The experiments of Jacoby (*Med. Klin.,* 1905, p. 208) indicate that it is a less powerful drug than codeine, but because of its more feeble convulsant effect can be used in larger doses. It has been used in *doses* of one or two grains (0.065–0.12 Gm.) three times a day.

Cœlocline. *Xylopia polycarpa* Oliver. (*Cœlocline polycarpa* D.C.) *Berberin Tree. Yellow-dye Tree of Soudan.*—This small tree, of the Fam. *Anonaceæ,* growing in Soudan, Sierra Leone, and certain parts of Western Africa, was described by William F. Daniell. (*P. J.,* Feb., 1857). When wounded, the tree exudes a juice which produces a yellow stain upon linen that cannot be washed out. The outer surface of the bark is greenish-gray interrupted by occasional blackish patches; the inner layers are of a golden yellow, and very fibrous, so that they can be separated in ribbon-like bands. The bark is moderately but disagreeably bitter, and stains the saliva yellow. Water extracts its color and bitterness. Stenhouse has ascertained that it contains *berberine.* The bark is much used in Africa for dyeing yellow. In Sierra Leone it is employed topically, in powder or decoction, for *obstinate ulcers.*

Coffee. *N. F. IV. Coffea Tosta. Roasted Coffee. Caffen. Semen Caffeæ. Café,* Fr. *Kaffee,* G. *Caffe,* It. *Cafe,* Sp. *Bun,* Ar. *Copi Cotta,* Cingalese. *Kaeva,* Malay.—The N. F. describes it as "the dried ripe seeds of *Coffea arabica* Linné or *Coffea liberica* Bulliard (Fam. *Rubiaceæ*), roasted until they develop a dark brown color and a characteristic aroma, and yielding not less than 1 per cent. of caffeine." *N. F.*

The *C. arabica* is a small evergreen tree from fifteen to thirty feet in height; native of Southern Arabia and Abyssinia, but cultivated in many parts of the world. The coffee berry is globular, umbilicate at top, at first green, then red, and ultimately dark purple. It is about as large as a cherry, and contains two seeds surrounded by a paper-like membrane, and enclosed in a yellowish-purple matter. These seeds, divested of their coverings, constitute coffee. The *Coffee* grains as seen in commerce are oval, having one side strongly convex, the other flat with a longitudinal groove upon the flat side and showing traces of the papery seed coat in the cleft. It has a characteristic aroma and a pleasantly bitter taste. About the year 1690 it was introduced by the Dutch into Java, and in 1718 into their colony of Surinam. Soon after this latter period the French succeeded in introducing it into their West India Islands, Cayenne, and the Isles of France and Bourbon.

The tree is raised from the seeds, which are sown in a soil properly prepared, and, germinating in less than a month, produce plants which, at the end of the year, are large enough to be transplanted. These are then set out in rows at suitable distances, and in three or four years begin to bear fruit. It is said that they continue productive for from thirty to forty years. Though almost always covered with flowers and fruit, they yield most largely at two seasons, and thus afford two harvests during the year. Various methods are employed for freeing the seeds from their coverings; but that considered the best is, by means of machinery, to remove the fleshy portion of the fruit, leaving the seeds surrounded only by their papyraceous envelope, from which they are separated by peeling and winnowing mills. They appear in commerce as "oval, of variable size, having one side strongly convex, the other flat with a longitudinal groove, and showing traces of the papery seed coat in the cleft. It has a characteristic aroma and a pleasantly bitter taste. Percolate 1 Gm. of powdered Coffee with ether until exhausted and evaporate the percolate to dryness; the residue weighs not less than 0.1 Gm. (presence of at least *10 per cent. of fat*). Boil 1 Gm. of powdered Coffee with 10 mils of distilled water, filter and acidify the filtrate with one mil of diluted sulphuric acid, and then decolorize it by the cautious addition of potassium permanganate T.S. This decolorized solution shows no blue coloration upon the addition of iodine T.S. (*starch*). Shake 1 Gm. of Coffee with 20 mils of water; the strained liquid shows no colored or heavy deposit. Shake 1 Gm. of Coffee with 20 mils of alcohol; the strained liquid shows no colored or heavy deposit, nor is any color imparted to the alcohol (*artificial colors or facings*). Powdered Coffee, when examined under the microscope, exhibits numerous fragments of the seed coat made up of parenchyma and irregular stone cells, the latter from 0.2 to 1 mm. in length and from 0.015 to 0.05 mm. in width with walls having simple pores; numerous brownish endosperm cells having porous walls about 0.01 mm. in thickness and containing oil and aleurone grains; starch grains few or absent. Coffee yields not less than 3 per cent. nor more than 5 per cent. of ash." *N. F.*

Assay.—"To 6 Gm. of Coffee, in No. 60 powder, contained in a small flask, add 50 mils of purified petroleum benzin and agitate the mixture occasionally during one hour. Then allow it to settle and decant the benzin solution. Add 50 mils more of the petroleum benzin, shake the mixture occasionally during fifteen minutes, then filter off the benzin and dry the drug. Now transfer the Coffee residue to a bottle having a capacity of about 250 mils and pour upon it 120 mils of chloroform and 6 mils of ammonia water. Stopper the bottle securely and shake it vigorously at intervals during six hours. Then allow it to stand one hour, and filter off 100 mils of the chloroform solution. Transfer this to a beaker and evaporate the chloroform at a gentle heat. Dissolve the alkaloidal residue in 10 mils of a mixture of 1 mil of diluted sulphuric acid and 9 mils of distilled water, by aid of a gentle heat, and filter the solution through a small filter, not exceeding 5 cm. in diameter, into a separator. Wash the beaker and filter with successive small portions of acidulated water, until a few drops of the filtrate give no test for caffeine when tested with iodine T.S. To the mixed acid washings, add a slight excess of ammonia water, and shake out the caffeine with successive portions of chloroform, collecting the chloroformic solutions in a tared flask or beaker. Evaporate or distil off the chloroform at a temperature not exceeding 75° C. (167° F.) and add to the residue 5 mils of ether. Evaporate off the ether cautiously, then dry the residue to constant weight at a temperature not exceeding 80° C. (176° F.) and add 0.0025 Gm. to the final weight of caffeine to replace that lost in the petroleum benzin washing. The weight represents the amount of caffeine in 5 Gm. of Coffee." *N. F.*

In recent years, because of the spread of a leaf disease, the cultivation of the more hardy *Coffea liberica* has been undertaken in the Island of Ceylon. This may be distinguished from the *C. arabica* by the fact that the corolla is nine-cleft in the Liberian and from four to five-cleft in the Arabian. The seeds of the Liberica plant are much larger than those of the Arabica; are not greenish and have the groove deeply wrinkled along its edges.

The annual production of coffee for the world is about one million tons, of which the American countries produce in the neighborhood of nine-tenths, Brazil giving to commerce three-fourths of the world's supply. After South America, the chief producer of coffee is Java, that island sending into commerce nearly twice as much as the remaining Asiatic countries. The amount of coffee entering commerce from Africa is small. The character of coffee varies greatly, not only with the climate in which it is grown but with the circumstances of its cultivation and the character of the stock which produces it. The most esteemed varieties are those which are known as *Mocha* and *Java*, but probably the bulk of the berry retailed as Mocha or Java is of South American origin. Coffee improves by age, losing a portion of its strength and acquiring a more agreeable flavor. It is said to be much better when allowed to ripen perfectly on the tree than as usually collected. The grains should be hard, and should readily sink in water. When soft, light, black or dark colored, or musty, they are inferior.

The composition is very complex. The principal constituents are (1) caffeine (identical with theine), (2) caffetannic acid, (3) fat, (4) carbohydrates, (5) albumenoids, (6) essential oil and aromatic substances. Parry (*Food and Drugs*, vol. I, 1911, p. 31) gives the following comparative figures for coffee before and after roasting:

	Raw (per cent.)	Roasted (per cent.)
Moisture ...	11.90 to 12.45	3.7 to 4.1
Ash	3.66 to 3.72	3.82 to 3.95
Cellulose ...	26.82 to 28.5	25.00 to 26.8
Caffeine	1.2 to 1.36	1.36 to 1.40
Sugar.	3.2 to 4.0	1.1 to 1.5

Among the adulterations of roasted coffee are the roasted or ground cereals; these are readily detected microscopically as well as by the positive reaction for starch in the decoction, which has been cautiously decolorized by the addition of potassium permanganate solution followed by diluted sulphuric acid. Coffee naturally contains no starch.

Chicory, dandelion and other similar roots used as adulterants may be detected microscopically, but a chemical method of detection has been proposed by LaWall and Forman (*A. J. P.*, lxxxv, p. 537 and *J. A. Ph. A.*, iii, p. 1669), which depends upon the determination of the ratio of reducing sugars to extractive matter in the aqueous decoction.

Mussaenda coffee, so called, is not a true coffee.

but the seeds of *Gaertnera vaginata* Lam. (Fam. *Loganiaceæ*). (*P. J.*, Nov., 1889.)

Coffee has a faint peculiar odor and a slightly sweetish, somewhat harsh taste. The sugar which is present is a reducing sugar, probably glucose, and is almost completely caramelized in the roasting process. *Caffetannic acid* has been ascertained by Hlasiwetz to be a glucoside with the formula $C_{14}H_8O_7$ and resolvable into glucose and a peculiar crystallizable acid, $C_8H_8O_4$, named by him *caffeic acid* (*J. P. C.*, 1867, 307), and which may be obtained from coffee by boiling a solution of the extract with potassium hydroxide, treating the resulting liquid with sulphuric acid in excess, and extracting the caffeic acid with ether, which yields it somewhat impure by evaporation. (*Ibid.*, January, 1868, 75.) Caffeic acid has the constitution of a dihydroxy-cinnamic acid, and on fusion with potassium hydroxide yields protocatechuic and acetic acids. The *coffee fat*, which ranges in different varieties from 14 to 21 per cent., is, when purified, white, without odor, of a buttery consistence, melting at 37.5° C. (100° F.), and becomes rancid on exposure. According to Rochleder (*Wien. Akad. Ber.*, xxiv, 40), it contains glycerides of palmitic acid and of an acid of the composition $C_{12}H_{24}O_2$.

The caffeine, according to Payen, is present partly free and partly as a *potassium and caffeine chlorogenate*, but H. Gorter (*Lieb. Annal.*, ccclix, 217, ccclxii, 237), in investigations made upon Liberian coffee, stated that caffeine does not exist free in coffee, but is all combined. The compound is given the following formula: $C_{32}H_{36}C_{19}K_2(C_8H_{10}O_{12}N_4)_2 + 2H_2O$. It decomposes at 225° C. (437° F.), without melting. The yield is 3.3 per cent. The salt is scarcely decomposed by dry chloroform, but is easily decomposed by the presence of water and then gives up its caffeine. This explains the fact observed by the manufacturers of decaffeinated coffees, that dry coffee yields only a small amount of its caffeine to chloroform, but that the extraction takes place readily and almost completely if the coffee is simultaneously treated with water or steam.

Chlorogenic acid is given the formula, $C_{32}H_{38}O_{19}$, and is a colorless, crystalline compound, melting at 206° C. (402.8° F.), and with a marked lævorotatory power. It is hydrolized by alkalies into caffeic and quinic acids. When strongly heated it emits an odor of roasted coffee and by some is believed to be the principle to which the flavor of the beverage is to be attributed. It is stated that when acted on by sulphuric acid and manganese dioxide it is converted into quinone, being in this respect analogous to quinic acid. Another acid was found which the author named *coffalic acid*. The coffee also contained citric acid, trigonelline, a pectin and an oxydase.

Julian E. Walter gives the following results of the analyses of several kinds of unroasted coffee: Java, 0.89 per cent. caffeine; Liberian Java, 1.08 per cent. caffeine; Costa Rica, 1.24 per cent. caffeine; Mocha, 0.54 per cent. caffeine; Pea-berry or Fenroll, 0.77 per cent. caffeine; Rio, 1.12 per cent. caffeine. (*Ph. Rec.*, May 5, 1890, 176.) Bertrand (*Bull. des Sci. Pharm.*, iv) gives the following results of studies of the percentage of caffeine in various coffee berries: In *Coffea arabica* the percentage varied from 0.69 to 1.60. Of species other than the *C. arabica*, *C. canephora* was found to be the richest in alkaloid, the berries yielding 1.97 per cent., while those of the *C. humboldtiana*, Baill., were remarkable by reason of their containing a bitter principle, *cafamarin*, but no caffeine at all, the berries of *C. mauritiana* contained only 0.07 per cent.

During the roasting process coffee swells to almost double its original volume, losing from 15 to 23 per cent. of its weight (*Ph. Cb.*, 1850, 687), and acquires a new, peculiar odor and a bitter taste. An active empyreumatic oil (*caffeol*, $C_8H_{10}O_2$) is developed during the process, probably at the expense of a portion of the caffeine. Much of the alkaloid, however, escapes change, and a portion of it is volatilized. The excellence of the flavor of roasted coffee depends much upon the manner in which the process is conducted, and the extent to which it is carried. It should be performed in a covered vessel, over a moderate fire, and the grains should be kept in constant motion. When they have acquired a chestnut-brown color, the process should cease. If too long continued, it renders the coffee bitter and acrid, or, by reducing it to charcoal, deprives it entirely of flavor. During a severe roasting the coffee loses a portion of caffeine, which sublimes, while in a slight roasting it loses none; yet ordinary coffee for drinking, prepared by percolation, contains rather more caffeine when prepared from strongly roasted than from slightly roasted coffee, because the caffeine is more easily extracted from the former. (Herman Aubert. See *A. J. P.*, 1873, 121.) Paul and Cownley found in preparing "low and medium roasted" coffee no perceptible loss of alkaloid, while in "over-roasted" coffee the loss amounted to one-third. The average of caffeine in roasted coffee they fix at 1.3 per cent. (*P. J.*, 1887, 822.) Seissir has devised a method for removing the caffeine from coffee. About 5 kilos of unroasted coffee berries are placed in a closed centrifugal drum which is surrounded by a hot-water jacket. After the addition of about 15 kilos of ethyl acetate, the drum is set in motion, so that the solvent and berries are thoroughly mixed, the temperature being maintained at 68° C. (154.4° F.). At the end of three hours the solvent is drawn off, and replaced by a further quantity of about 10 kilos, and the mixing and extraction are continued for a further two hours. The ethyl acetate is then run off, the berries are heated to 100° C. (212° F.) to remove the last traces of solvent, and finally dried at 40° to 46° C. (104°–114.9° F), the drum being rotated meanwhile. The ethyl acetate may be recovered by distillation, and the caffeine separated from the residue. The method is the subject of a French patent. (*Journ. Soc. Chem. Ind.*, 1909, 622.)

The *leaves* of the coffee plant possess properties analogous to those of the fruit, and are extensively used by the Malays. Stenhouse found them to contain caffeine in larger proportion than the coffee bean, and also caffeic acid. The leaves are prepared for use by drying over a clear fire and then powdering by rubbing in the hands. The powder is made into an infusion like common tea. The taste is like that of tea and coffee combined. (*P. J.*, xii, 443; xiii, 207 and 382, and xvi, 1067.)

The effects of coffee are due chiefly, if not solely, to the caffeine which it contains. Some writers, however, believe that the volatile oil, *caffeol* (*caffeone*) possesses stimulating properties. The evidence of this point, however, is so contradictory as to render conclusions impossible. (See Reichert, *M. News*, 1890, lvi; Erdmann, *A. E. P. P.*, 1902, xlviii; Geiser, *A. E. P. P.*, liii, p. 112.)

As a medicine coffee has been almost entirely

replaced by the alkaloid caffeine. The infusion is, however, sometimes administered by rectal injection in cases of narcotic poisoning. The disturbances of digestion which follow excessive coffee drinking are not considered by J. Burmann to be due to caffeine, but to a volatile toxic substance formed during roasting and only partly volatilized, named *cafeotoxin*, which can be eliminated by subjecting roasted coffee to successive treatments with steam under pressure of several atmospheres (*J. P. C.*, 1913, 8, 281.)

Syrup of coffee of the N. F. III was prepared by pouring 500 mils [or 16 fluidounces] of boiling water upon 250 Gm. [or 8 oz. troy] of roasted coffee, in moderately coarse powder, covering and boiling for five minutes, then straining and adding water through the strainer to make 500 mils [or 1 pint]. Then 800 Gm. [or 24 oz. troy] of sugar is dissolved in the strained liquid, by agitation without heat, and enough water added to make 1000 mils [or 2 pints]. Two tablespoonfuls of this syrup may be added to a cup of hot water or milk. It is also used with carbonic acid water.

Colalin. *N. N. R.* 1917.—A mixture of hyoglycocholic and hyotaurocholic acids obtained from bile, with a little magnesium carbonate to retain the pulverulent condition. *Dose*, one-fourth to one-half grain (0.016 to 0.032 Gm.).

Collinsonia. *Collinsonia canadensis* L. *Horse-weed. Horse-balm. Richweed. Heal-all. Stone-root. Knot-root. Knob-weed. Guérit-tout, Baume de Cheval*, Fr. *Collinsonie*, G.—A labiate plant, which grows in woods from Canada to the Carolinas. The whole plant has a strong disagreeable odor, and a warm pungent taste. C. N. Lochman (*A. J. P.*, 1885, 228) found in the root a resin, tannin, starch, mucilage, and wax; in the leaves resin, tannin, wax, and volatile oil. The alkaloid discovered by H. J. Lohmann in the root of the *Collinsonia canadensis* appears to have been a magnesium salt. (See *D. C.*, 1902.) Collinsonia is tonic, astringent, diaphoretic, and diuretic. It is said to be locally irritant. A decoction of the fresh root has been used in *catarrh of the bladder, leucorrhea, gravel*, and *dropsy*.

Colloids.—The studies of Thomas Graham in 1862 in connection with dialysis, in which he originated the terms "crystalloid" and "colloid," remained without any special industrial or therapeutic application for many years. Recently much work has been done upon this somewhat neglected subject and some wonderful results have been obtained. The *colloids* of Graham's time were mainly organic substances analogous to glue or gelatin, although some inorganic colloids were known, such as the colloidal form of ferric hydroxide formerly known as *dialyzed iron*. As the osmotic pressure observed in colloidal solutions is extremely small we may infer that the colloids possess large molecular weights. They do not form true solutions, but form pseudo-solutions known as *sols*, or *hydrosols* when they are placed in water. The substance separating from a sol or hydrosol is called a *gel* or *hydrogel*, and the phenomenon of separation is called gelatinization. In the case of suspension of a very fine solid in a liquid by means of colloids the sol is called a *suspensoid*, or if globules of liquid are suspended, it is called an *emulsoid*.

Hydrosols have all the external appearance of true solutions because they are homogeneous and may be filtered without leaving any solid residue on the filter and show no visible particles under ordinary microscopic observation. The small suspended particles of hydrosols may be seen clearly with the ultramicroscope (a microscope in which a luminous ray is concentrated by means of a lens and the illumination of the microscopic field produced by directing the ray at right angles to the direction of vision) as shown by the researches of Siedentopf and Zsigmondy in 1903. The particles thus observed are visible as luminous points which are in constant motion, called Brownian movements. The size of the particles varies from one ten-thousandth mm. to one two-hundred thousandth mm. A colloidal solution of gold containing 0.005 Gm. per mil contains about 1000 million particles of suspended gold per cu. mm., which is equivalent to an immense increase of exposed surface and which accounts for some of the marvellous effects of colloidal metal solutions, particularly as catalysts.

Colloidal metals, gold, silver, iron, etc., are all found in the market at the present time under various designations. They are prepared by either electrical or chemical methods. The electric method comprises the use of the electric arc which, passing between two pieces of a given metal under water, produces the microscopic pulverization of the metal, resulting in a colloidal solution (so called) or hydrosol of that particular metal. The chemical method consists in the application of a powerful chemical reducing agent to a solution of the salt of the desired element. Colloidal suspensoids of metallic salts, as calomel (see calomelol), or bismuth oxide (see bismon), are also coming into use.

In view of the increasing number and importance of colloidal silver preparations, the assay for silver content has been given considerable attention by various authorities (see *Merck's Rep.*, 1914, 69; *Arch. Pharm.*, 2529, 69 and 497).

The colloidal metals in some cases produce catalytic effects similar to those produced by certain enzymes, as, for instance, the inversion of cane sugar by colloidal platinum. The metallic hydrosols are therefore sometimes called metallic ferments.

The colloidal solutions of the metals usually exhibit dichroism to a certain degree, that is, they are clear by transmitted and turbid by reflected light. The coloration of the famed ruby glass is due to a colloidal state of the particles of metallic gold therein contained. The ripening of the silver bromide gelatin plates in photography and of certain clays in ceramics, which require several months' empiric treatment to produce the proper degree of elasticity, is now known to be due to the formation and action of colloids.

In 1905, Robin (*Nouv. Rem.*, 1905) reported the results of some observations of the effects of subcutaneous injection of hydrosols. He found that they produced an increased excretion of urea and uric acid and marked leucocytosis. He likewise reported favorable clinical results in *pneumonia* and *articular rheumatism* from their employment. His results were confirmed by Izar and Hergage, 1909, who also found that it was of no importance which metal was employed. While several have reported good results in various infectious diseases with these agents, Paderi (*Lo Sperimentale*, 1909) found that silver hydrosol was without bactericidal or antitoxic properties; and that infected animals died as promptly treated with the hydrosol as the control animal; and Caspeldi came to the conclusion that the hydrosols were useless in pneumonia. The metal solutions which have been employed contain very small quantities of metal,

not more than two parts in ten thousand. The amount of such a solution which has been ordinarily injected, is about 100 minims. The value of the colloids in medicine must be regarded as in the experimental stage Loeb (*Interstate Med. Journ.*, Dec., 1912, and Jan., 1913), Wolze and Pagenstecker (*M. M. W.*, 1913, 1036), have reported favorable results in *cancer* from colloidal copper.

For an account of colloidal silver, see p. 1609; of the suspensoid, calomelol, see p. 1300. Other colloidal metals which are on the market are:

Electrargol, a form of colloidal silver.
Electraurol, a form of colloidal gold.
Collaurum, another form of colloidal gold.
Electrocuprol, a form of colloidal copper.
Electroplatinol, a form of colloidal platinum.
Electropalladiol, a form of colloidal palladium.
Electrorhodiol, a form of colloidal rhodium.
Electromercurol, a form of colloidal mercury.
Electroselenium, a form of colloidal selenium.
Electromartiol, a form of colloidal iron.
Cuprase, a form of colloidal copper.

Cologne Water. *Spiritus Odoratus. N. F. IV. Perfumed Spirit. Eau de Cologne*, Fr. *Kölnerwasser*, G.—*Cologne water* is official in the N. F. IV (see Part III). A more fragrant spirit, and one more closely resembling the original, would be made if the quantity of oil of orange flowers or *neroli* were doubled.

Coltsfoot. *N. F. IV. Farfara. Coltsfoot Leaves. Tussilago Leaves. Folia Farfaræ*, P. G. *Tussilage, Pas d'âne*, Fr. *Huflattig, Rosshuf*, G. —"The dried leaves of *Tussilago Farfara* Linné (Fam. *Compositæ*), without the presence of more than 5 per cent. of other parts of the plant or other foreign matter." *N. F.* Coltsfoot is a low perennial herb, indigenous to Europe and growing in wet places from Quebec to Pennsylvania and westward to Minnesota. It possesses a horizontal rhizome from which, early in the spring, arise several leafless, erect, simple, unifloral scapes or flower-stems and bearing appressed scale-like bracts of a brownish-pink color. The flower, which stands singly at the end of the scape, is large, yellow, compound. The leaves do not make their appearance until after the flowers. The flowers have an agreeable odor, which they retain after desiccation. The dried root and leaves are inodorous, but have a rough, bitterish, mucilaginous taste.

The leaves are described as "petioles long, pubescent; blades very brittle, nearly orbicular or broadly ovate-reniform, from 8 to 15 cm. in length and nearly as broad, deeply cordate at the base, angulately lobed and dentate with red-brown teeth, palmately five- to nine-veined; young leaves white floccose all over, the older leaves with upper surfaces dark green and nearly smooth, the younger densely white floccose. Odor indistinct; taste mucilaginous, faintly herbaceous, bitter. The powder, when examined under the microscope, exhibits numerous multicellular, non-branching hairs, usually curved and twisted together, the lower cells about 0.035 mm. in width, the terminal cells much elongated, about 0.012 mm. in width and at times with spiral bands; broadly elliptical stomata about 0.05 mm. in length and associated with finely striated epidermal cells, the latter having wavy vertical walls; non-porous sclerenchymatous fibers few with walls from 0.006 to 0.01 mm. in thickness; parenchyma cells containing chloroplastids; tracheæ few, spiral, annular or with simple pores. Coltsfoot yields not more than 20 per cent. of ash." *N. F.* Boiling water extracts their virtues. C. S. Bondurant (*A. J. P.*, 1887, 340) examined coltsfoot chemically. He found evidences of a bitter glucoside. Klobb isolated two phytosterols from coltsfoot flowers. (*P. J.*, 1909, 999.) Coltsfoot exercises little sensible influence upon the human system. It is, however, demulcent, and is sometimes used in *chronic coughs, consumption* and other *affections of the lungs.* The expectorant properties which it was formerly thought to possess are not obvious. The leaves were smoked by the ancients in *pulmonary complaints*, and in Germany they are said to be substituted for tobacco. In the N. F. they are used in a pectoral tea (see *Species Pectorales*, Part III). Cullen used the fresh juice in *scrofula*, several ounces daily. *Dose*, of the dried leaves, one to two drachms (3.9–7.5 Gm.), which may be conveniently given in decoction.

Colubrina.—*Mabee bark*, yielded by the *Ceanothus reclinatus* L'Herit. (*Colubrina reclinata*, Brongn.) (Fam. *Rhamnaceæ*) of South America, has been analyzed by Elborne and Wilson, who find in it a glucoside. It is used in the West Indies as a stomachic. (See *P. J.*, April 11, 1885.)

Colutea. *Colutea arborescens* L. *Bladder Senna. Baguenaudier, Séné Indigène*, Fr. *Falsche Senna*, G.—A leguminous shrub growing spontaneously in the southern and eastern parts of Europe, and cultivated in gardens. The leaflets are purgative, and in some parts of Europe are used as a substitute for senna, which is said to be sometimes adulterated with them. Barbey (*P. J.*, 1895, 261) isolated *coluteic acid*, which occurs in white crystals, insoluble in water, soluble in alcohol, chloroform, and carbon disulphide. Bladder senna is comparatively very feeble. It is administered in infusion or decoction, of which the *dose* is about half a pint, containing the virtues of from one to three ounces of the leaves.

Combretum. *Jungle-weed.*—The roasted leaves and stalks of the *Combretum sundaicum* (Miquel) have been used in China in the treatment of the *opium habit.* Harrison (*P. J.*, lxxx, 52) was unable to find any alkaloid or glucoside in the plant, and Stanislaus (*J. A. Ph. A.*, 1912) confirmed the absence of active principle, but found a considerable proportion of tannic acid. The method of taking is as follows: Fifty Gm. of the dried herb is macerated with 4 liters of water, the filtrate evaporated to 1 liter. To one-half of this is added the accustomed daily dose of opium. Of this mixture the patient is given one fluidounce (30 mils) every three or four hours, the equivalent amount of *combretum* decoction being added after each dose is removed.

Heffner has reported favorably upon its use, but H. C. Wood, Jr., (*J. A. Ph. A.*, 1912), was unable to note any beneficial action from it which might not be justly ascribed to the tannic acid which it contains.

The *Combretum Raimbaultii* is a shrub native to West Africa, where it is known under the name of *Kinkelibah* and is used by the natives in the treatment of *black-water fever* and was introduced a number of years ago into Europe by a missionary, Father Raimbault. Dammermann has reported favorably on its value in this condition (*D. M. W.*, 1906, p. 921), but Heckel was unable to find any active constituent except a tannin. (*Jahresber, d. Pharm.*, 1891, p. 64.) Other species of the combretum appear also to have been used for the same purpose, notably the *C. Altum* Guill. et Perr. (*C. micranthum*, G. Don).

Commelina. *Day-flower.*—Under the name of

Yerba del Pollo, Commelina tuberosa L. is said to be very largely used in Mexico in the treatment of *internal hemorrhage*, especially from the womb. From thirty to sixty grains (2.0–3.9 Gm.) of the extract may be taken in the course of one day. (See *A. J. P.*, 1897, 290.) The North American species, *Commelina communis* L., has also had hemostatic properties attributed to it. For chemical and microscopical study, see *A. J. P.*, July, 1898.

Commiphora. *Commiphora Berryi* Engl. (Fam. *Burseraceæ.*) *Mulu Kilivary.*—This Indian thorn yields a gum resin in abundance. (*P. J.*, Aug., 1899.)

Comptonia. *Myrica asplenifolia.* (*Comptonia peregrina* L., Coulter). *Sweet Fern. Ferngale. Meadow-fern.* (Fam. *Myricaceæ.*)—A shrubby indigenous plant, named from the resemblance of its leaves to the spleenwort fern. It grows in sterile soil, from Nova Scotia to North Carolina and Michigan. All parts of it possess a resinous, spicy odor. R. T. Chiles has found in it tannic and gallic acids, volatile oil, extractive, gum, resin, and a substance resembling saponin. (*A. J. P.*, xlv, 306.) H. K. Bowman found it to contain 8.20 per cent. of tannin. (*A. J. P.*, 1869, 193.) It is said to be tonic and astringent; its decoction is used in *diarrhea.*

Condurango. *N. F. IV. Cundurango. Cortex Condurango, P. G.*—This drug some years ago attracted a great deal of attention as a reputed remedy in *cancerous disease*, but further experience has demonstrated its uselessness. It appears, however, to be used largely in South America as an alterative in *chronic syphilis*, has been recognized by the German Pharmacopœia, and so merits a brief notice here. According to an official investigation (*A Report on the Origin and Therapeutic Properties of Cundurango*, by Ruschenberger, Washington, 1873) made by Passed Assistant Surgeon Joseph G. Ayers, U. S. N., there are at least ten different plants known in the republic of Colombia as *condurango.* The variety which has been used in *cancer*, and which may be considered as genuine condurango, is the *condurango blanco*, the product of an asclepiadaceous vine from ten to thirty feet in length and from one to two inches in diameter. The plant is the *Marsdenia Condurango* of G. H. Reichenbach. The bark is prepared by pounding the stem with a mallet, to separate it, and then drying it in the sun. In the N. F. it is described as "the dried bark of *Marsdenia Condurango* (Triana) Reichenbach filius (Fam. *Asclepiadaceæ*). In quills or transversely curved pieces, usually from 4 to 13.5 cm. in length; bark 1 to 6 mm. in thickness; outer surface light grayish-brown to dark brown, nearly smooth and with numerous lenticels, or more or less scaly and considerably roughened; the scales soft, occasionally with brownish-black apothecia of a fungus; inner surface grayish-white or light brown, longitudinally striate; fracture short-fibrous and granular. Odor slightly aromatic, especially marked in the fresh drug; taste bitter and aromatic. Under the microscope, sections of Condurango show a corky layer consisting of several rows of thin-walled cells, frequently with yellowish-brown contents; a layer of phelloderm of eight to ten rows of cells, containing starch grains and membrane crystals of calcium oxalate, the latter in prisms, from 0.01 to 0.035 mm. in length; a primary cortex of collenchyma containing chloroplastids, starch grains, or rosette aggregates of calcium oxalate, from 0.015 to 0.04 mm. in diameter; a pericycle or pericambium of tangentially elongated parenchyma cells, with groups of bast fibers and laticiferous vessels in an interrupted circle; middle bark with large groups of stone cells varying from nearly isodiametric to elongated, sometimes very irregular in form; inner bark with medullary rays one or two cells in width, numerous laticiferous cells accompanied by small groups of sieve cells, parenchyma containing either starch grains or rosette aggregates of calcium oxalate, and an occasional isolated bast fiber or small group of stone cells. The powder is light yellowish-brown, consisting chiefly of groups of stone cells and parenchyma containing calcium oxalate crystals and starch grains; stone cells chiefly in large groups, the individual cells being more or less irregular in shape and with very thick porous walls, the lumina being usually filled with air; calcium oxalate chiefly in rosette aggregates, occasionally in single prisms, mostly from 0.015 to 0.02 mm. in diameter; starch grains mostly simple, frequently two- to four-compound, the individual grains being from 0.003 to 0.015 mm. in diameter; bast fibers non-lignified; very long and from 0.01 to 0.035 mm. in width; fragments of thin-walled latex tubes from 0.015 to 0.025 mm. in diameter and filled with a granular substance; fragments of cork grayish or light yellowish-brown. Macerate 1 Gm. of the powdered bark in 5 mils of cold water; filter and heat the filtrate in a test tube; it becomes cloudy, but on cooling assumes its original transparency. Condurango yields not more than 12 per cent. of ash." *N. F.* Thomas Antisell (*A. J. P.*, xliii, 289) found in it tannin, extractive matter, and a yellow resin, to which he attributes whatever of virtue the plant may possess. Vulpius (*P. J.*, 1885, 1066) found in it *condurangin*, a glucoside, very closely allied to *vincetoxin* of Tanret, and, like it, converted by warming when in concentrated solution into a tolerably stiff jelly. For Barthe's method of isolating it, see *A. J. P.*, 1892, 640. Merck gives the following constituents of condurango: *Alpha-condurangin*, $C_{20}H_{32}O_6$; *Beta-condurangin*, $C_{18}H_{28}O_7$; *Conduransterin*, $C_{30}H_{50}O_2$, and also a trace of an alkaloid resembling strychnine in action. Carrara (*A. J. P.*, 1892) obtained from the so-called condurangin of commerce two principles: One insoluble in water, soluble in benzene, a light, almost white, powder, melting at from 60°–61° C. (140°–141.8° F.), and of the composition $C_{20}H_{32}O_6$. Both compounds are decomposed by acids, yielding a brown pitchy substance, insoluble in water. Boehm (*M. M. W.*, lv, p. 1775) regards condurangin as a derivative of cinnamic acid. According to Firbas, condurangin in solution can be recognized by freeing from alcohol with gentle warmth, precipitating with a saturated solution of sodium chloride, dissolving the precipitate in chloroform, and adding a liquid composed of equal parts of sulphuric and hydrochloric acids and alcohol. On warming, the mixture assumes a green color, which turns a beautiful greenish-blue on the addition of a trace of ferric chloride. This *Lafon reaction* is given also by adonidin, oleandrin, sapotoxin and digitoxin. Brunton (*J. P.*, vol. v) reached the conclusion that *Condurango blanco* was inert, but Kobert found condurangin to be a violent poison, causing convulsions followed by paralysis; he believes it to be a mixture of several principles. (*S. Jb.*, 1889, No. 9.) H. Chiriboga states that three drachms of the bark taken by himself in the form of decoction produced considerable activity of the circulation, copious diaphoresis, increased secretion of urine, and even some vertigo and dis-

turbance of vision, Under the name of *Guayaquil condurango* a drug has appeared in the European markets composed of pieces of bark and fragments of woody branches, believed to be derived from an asclepiadaceous plant closely related to the genus *Gonolobus*. *Mexican condurango* is composed of split stems or thin adherent bark, and is thought to be yielded by an Aristolochia. For full description, see *Ph. Rund.*, May, 1888. Prof. P. E. Hommell recommends *Mistura condurango et ulmi* and *Fluidglycerate of condurango* for the internal administration of the drug. (See *Proc. N. Jersey Pharm. Assoc.*, 1913, 80; also *M. R.*, 1913, 231.) *Fluidextract of condurango* is official in the National Formulary. *Dose*, one fluidrachm (3.9 mils).

Condy's Fluid.—A solution made by dissolving 53 parts of potassium permanganate and 333 parts of crystallized aluminum sulphate in 777 parts of hot water.

The potassium alum, which crystallizes out when the liquid cools, is separated The liquid is therefore a solution of the permanganate of aluminum with some aluminum sulphate. It is used as a disinfectant.

Condy asserted that in this disinfecting solution all of the available oxygen in the permanganate is utilized, whereas only 60 per cent. of the oxygen is utilized in the simple alkaline permanganate.

Congluten.—A vegetable casein obtained from almonds, containing 18 per cent. nitrogen and 0.6 per cent. sulphur. It is a white powder, soluble in weak alkaline solutions, and used in the form of a 6 per cent. solution in endovenous nutrition.

Conium. *N. F. IV* (*U. S. P. VIII*). *Hemlock. Poison Hemlock. Spotted Hemlock* or *Parsley. Fool's Parsley. St. Bennett's Herb. Spotted Cowbane. Herba Cicutæ* (*Majoris*). *Ciguë officinale, ou Grande Ciguë* (Feuille), *Fr. Cod. Feuilles de grande Ciguë*, Fr. *Herba Conii*, P. G. *Schierlingskraut, Schierlingsblätter, Schierling, Gefleckter Schierling*, G. *Foglie di cicuta maggiore*, It. *Cicuta major*, Sp.—Formerly the fruit of the *Conium maculatum* was official in both the United States and British Pharmacopœias and the leaves in the British Pharmacopœia. The fruit has now been introduced into the National Formulary IV, where it is described as "the full grown, but unripe fruit of *Conium maculatum* Linné (Fam. *Umbelliferæ*), carefully dried and preserved, and yielding not less than 0.5 per cent. of coniine. After being kept for more than two years, Conium is unfit for use. Broadly ovoid, greenish-gray, the two mericarps of most of the fruits separated, each about 3 mm. in length and about 1.5 mm. in diameter, ovoid, somewhat curved, the inner, flattened side marked by a deep longitudinal groove, the outer, convex side with five, pale yellow, somewhat crenate ribs, the intervening surfaces wrinkled but otherwise smooth; pericarp without oil tubes. Odor slight, but when triturated with a solution of potassium hydroxide, strong, disagreeable, and mouse-like; taste characteristic, disagreeable, afterwards somewhat acrid. Transverse sections of the mericarp, when examined under the microscope, exhibit a pentangular outline, the angles projecting and forming the ribs, four of the sides being almost equal in length, the fifth or commissural side being about twice as long as one of the dorsal sides and usually concave near the middle; a distinct fibro-vascular bundle at each angle composed of thick-walled fibers about 0.013 mm. in diameter and a few tracheæ; epidermis consisting of one layer of cells which are sometimes slightly centrifugally developed, hairs are absent; pericarp thin, without vittæ, enclosing a single seed and extending inwardly on the commissural side for about one-third the diameter of the section; the inner epidermis of the pericarp composed of two layers of cells with yellowish-brown walls, the outer layer with cells from 0.06 mm. to 0.12 mm. in tangential length and with thickened radial and inner walls, the inner layer with thin-walled cells from 0.03 to 0.06 mm. in tangential length and about 0.03 mm. in radial diameter; the seed coat composed of small, thick-walled cells about 0.015 mm. in radial diameter; often obliterated; a large endosperm or central portion being somewhat pentangular-rounded in outline, with a deep channel on the commissural side and composed of polygonal parenchyma cells; the latter contain globules of fixed oil and aleurone grains with rosette aggregates of calcium oxalate. The powdered drug is greenish-gray and, when examined under the microscope, exhibits numerous angular or rounded, light colored fragments of endosperm tissue, composed of parenchyma cells containing fixed oil, aleurone grains and rosette aggregates of calcium oxalate, the latter from 0.002 to 0.006 mm. in diameter; a few more or less curved groups of lignified fibers; fragments of the seed coat with yellowish-brown walls; a few rounded starch grains about 0.005 mm. in diameter; spiral or annular tracheæ few; numerous oil globules on mounting the powder in hydrated chloral T.S. Conium yields not more than 8 per cent. of ash." *N. F. Conium fruit* (*Conii fructus*) is sometimes incorrectly called *conium seed*. The hemlock leaves (*Conii folia*) were described as "the fresh leaves and young branches of *Conium maculatum* Linn., collected when the fruit begins to form." *Br.*, 1898.

Conium maculatum is an umbelliferous plant, having a biennial spindle-shaped whitish root, and an herbaceous branching stem, from three to six feet high, round, hollow, smooth, shining, slightly striated, and marked with brownish-purple spots. The lower leaves are tripinnate, more than a foot in length, shining, and attached to the joints of the stem by sheathing petioles; the upper are smaller, bipinnate, and inserted at the division of the branches; both have channelled footstalks, and incised leaflets, which are deep green on their upper surface and paler beneath. The flowers are very small, white, and disposed in compound terminal umbels. The general involucre consists of from three to seven lanceolate, reflected leaflets, whitish at their edges; the partial involucre of three or four leaflets, oval, pointed, spreading, and on one side only. There are five petals, cordate, with their summits inflected, and nearly equal. The stamens are spreading, and about as long as the corolla; the styles diverging.

Conium is a native of Europe, and has become naturalized in America from Quebec to Pennsylvania, where it is also cultivated for medicinal purposes. The term *cicuta*, which has often been applied to this plant, belongs to a different genus. It grows usually in clusters along the roadsides or in waste grounds, and is found most abundantly near old settlements. It flowers in June and July. The whole plant, especially at this period, exhales a fetid odor, compared by some to that of mice, by others to that of the urine of cats, and narcotic effects result from breathing for a long time air loaded with the effluvia. The plant varies in narcotic power according to the weather and

climate, being most active in hot and dry seasons and in warm countries. The hemlock of Greece, Italy, and Spain is said to be much more energetic than that of the north of Europe. As a rule, those plants are most active which grow in a sunny exposure. The proper season for gathering the leaves is when the plant is in flower, and Fothergill asserts, from experiment, that they are most active about the time that the flowers begin to fade. The footstalks should be rejected, and the leaflets quickly dried, either in the hot sun, or on tin plates before a fire, or by a stove-heat not exceeding 48.8° C. (120° F.). They should be kept in boxes or tin cases, excluded from the air and light, by exposure to which they lose their fine green color and become deteriorated. The same end is answered by pulverizing them, and preserving the powder in opaque and well-stoppered bottles. But little reliance can be placed on the dried leaves, as, even when possessed of a strong odor and a fine green color, they may be destitute of the narcotic principle. When rubbed with potassium hydroxide they should exhale the odor of coniine. The fruit retains its activity much longer than the leaves. Commercial conium occasionally contains other umbelliferous plants, or it may be almost wholly composed of such plants, and even anise has been used as an adulterant to the fruit. (See *Anise.*)

The dried leaves of conium have a strong, heavy, narcotic odor, less disagreeable than that of the recent plant. Their taste is bitterish and nauseous; their color a dark green, which is retained in the powder. A slight degree of acridity possessed by the fresh leaves is said to be dissipated by drying. Water distilled from the fresh leaves has the odor of conium, and a nauseous taste, but does not produce narcotic effects. Upon destructive distillation, the leaves yield a very poisonous empyreumatic oil. Geiger first obtained the active principle in a separate state, the volatile alkaloid *coniine* or *conine.* As it exists in the plant in combination with an acid it is not readily volatilized, but it freely comes over with the distillate when an alkali has been previously added. The acid of conium, Peschier believed to be peculiar, and named *coniic acid,* but other observers assert that it is *malic acid.* For methods of isolating conium, see *U. S. D.,* 19th ed., p. 393. The seeds contain most of this principle; but even in these it exists in very small proportion. From six pounds of the fresh or nine of the dried seeds, Geiger obtained about an ounce of coniine, while from 100 pounds of the fresh herb only a drachm, and from the dried leaves none. Farr and Wright (*P. J.,* 1896, 273) confirm the views of Harley and Manlius Smith and affirm that green fruits are alone reliable. The volatility and tendency to undergo decomposition of coniine probably has its effect even in the dried unripe seed, otherwise it is difficult to explain the fact that in thirteen analyses of commercial conium fruit made by Farr and Wright, the average alkaloidal contents were 0.674; while the average of sixteen analyses of samples collected by themselves was 2.13. (*P. J.,* Feb., 1904.) For a method of assaying conium fruit, by Schwickerath, see *Ph. Rec.,* 1893, 282. The N. F. IV adopted the following assay process, requiring that conium should yield not less than 0.5 per cent. of coniine:

Assay.—"Place 15 Gm. of Conium, in No. 40 powder, in a 250 mil Erlenmeyer flask, add 150 mils of purified petroleum benzin and then 15 mils of solution of sodium hydroxide, insert the stopper securely, and shake the flask vigorously at frequent intervals during six hours. Allow the mixture to settle and decant 100 mils of the clear benzin solution (representing 10 Gm. of the drug) into a separator; extract the alkaloid by shaking with successive portions of weak hydrochloric acid until a few drops of the last washing gives no precipitate with iodine T.S. Collect the acid washings and concentrate by evaporation on a water bath to 10 mils, cool and transfer the liquid to a separator, then cautiously add sodium carbonate in excess. Extract the alkaloid by shaking out with successive portions of 15 mils each of purified petroleum benzin. Separate the benzin washings and filter into a beaker. Then add exactly 10 mils of tenth-normal sulphuric acid V.S. and stir thoroughly for two minutes so as to mix the acid and benzin solution. Evaporate the benzin layer in a current of warm air, at a temperature not exceeding 60° C. (140° F.), and as soon as the benzin has disappeared, cool, add five drops of cochineal T.S. or methyl red T.S. and titrate the acid solution with fiftieth-normal potassium hydroxide V.S. Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 0.0126 Gm. of coniine. Calculate the amount of coniine neutralized by the acid, and multiply the result by ten to obtain the percentage of coniine in the drug." *N. F.*

Harley has found in the root three proximate principles, one a very bitter resin, which he names *conamarine,* and the two others crystallizable bodies, named respectively *rhizoconin,* and *rhizoconolein.* They are all neutral, and, so far as known, medicinally inert. (See *P. J.,* Aug., 1867.)

Coniine, $C_8H_{17}N$, has been thoroughly studied by Hofmann (1881), who established the correct formula as given, instead of $C_8H_{15}N$, as it was formerly assumed, and Ladenburg (1886) effected its synthesis from *allyl pyridine* by reduction with sodium in alcoholic solution:

$$C_5H_4(C_3H_5)N+8H=C_5H_{10}(C_3H_7)N.$$

This reaction gives *a-normal propyl piperidine,* which is optically inactive, but by the crystallization of its tartrate splits into *coniine* (dextrorotatory) and a very similar lævorotatory coniine, just as racemic acid splits into dextrorotatory and lævorotatory tartaric acid.

Coniine is in the form of a yellowish oily liquid, of sp. gr. 0.862, of a very acrid taste, and a strong penetrating odor, compared to that of the urine of mice, and recalling the odor of fresh hemlock, though not identical with it. In volatility it resembles the essential oils, readily rising with the vapor of boiling water, but when unmixed requiring for ebullition a temperature of 166° C. (330.8° F.). It is freely soluble in alcohol, ether, and the fixed and volatile oils, and slightly so in water. It unites with about one-fourth of its weight of water to form a hydroxide. It reddens turmeric, and neutralizes the acids, forming with them soluble salts, some of which are crystallizable. With tannic acid it forms an insoluble compound. Like ammonia, it occasions a white cloud when approached by a rod moistened with hydrochloric acid; and the resulting hydrochloride is crystallizable, and not in the least deliquescent. The hydrochloride may also be obtained as a brilliant crystalline mass by dissolving coniine in anhydrous ether and passing dry hydrochloric acid gas through the solution. The salt is very soluble in water and alcohol, but insoluble in ether. It can be heated to 90° C. (194° F.) without decom-

position, and melts at 218° C. (424.4° F.). Coniine coagulates albumin, and precipitates the salts of aluminum, copper, zinc, manganese, and iron. It also precipitates silver nitrate, but in excess redissolves the precipitate. Most of its salts are decomposed by evaporation. When exposed to the air, it speedily assumes a deep brown color, and is ultimately converted into a resinous matter, and into ammonia, which escapes. Under the influence of heat this change takes place with much greater rapidity. The presence of coniine may be detected in an extract or other preparation of hemlock by rubbing it with potassium hydroxide, which instantly develops its peculiar odor. It is a most energetic poison.

In association with coniine in the hemlock are found also the following bases: *Ethyl-piperidine*, $C_7H_{15}N$ or $C_5H_{10}(C_2H_5)N$; *Methyl-coniine*, $C_9H_{19}N$ or $C_5H_9(C_3H_7)N(CH_3)$; *Conhydrine*, $C_8H_{17}NO$ or $C_5H_9(CHOH.CH_2CH_3)NH$; *Pseudo-conhydrine*, $C_8H_{17}NO$ or $C_5H_9(CH_3.CH_2OH.CH)NH$. Methyl-coniine, first obtained by Kekulé and von Planta in commercial coniine, is of minor importance.

Conhydrine is crystallizable, fusible below 100° C. (212° F.), and volatilizable at a higher temperature, diffusing an odor much like that of coniine. Water dissolves it considerably, ether and alcohol freely; and the solution has a strong alkaline reaction. Its formula is given as $C_8H_{17}NO$. By the action of P_2O_5 or fuming hydrochloric acid upon conhydrine, is obtained *coniceine*, $C_8H_{15}N$, and water. It may be separated from coniine by exposing the mixed alkaloids to a freezing mixture, expressing, and then repeatedly crystallizing from ether. (*Gmelin*, xiii, 169.) E. Merck obtained a small quantity of a new alkaloid from the high boiling portion of crude coniine. The isolation was accomplished by fractional distillation *in vacuo* and recrystallization. The alkaloid crystallizes in needles, is easily soluble in water, alcohol, ether, benzene, and chloroform, fuses at about 98° C. (208.4° F.), and boils at 230° to 232° C. (446°–449.6° F.). According to Ladenburg, the alkaloid is an isomer of conhydrine, having the formula $C_8H_{17}NO$, and for this reason the name *pseudo-conhydrine* was selected. (*Chem. Cb.*, 1891, 414; see also *P. J.*, 1891, 1170.)

Paraconiine.—Coniine was supposed to have been artificially produced by Hugo Schiff. From the reaction of *butyric aldehyde* with an alcoholic solution of ammonia, he obtained two bases, one of which, *dibutyraldine*, yielded, on distillation, first a neutral oily substance, and afterwards a strong alkaline base, which proved to have the physiological properties of natural coniine, but was optically inactive, while true coniine is dextrorotatory. Since the change in the formula of true coniine it will be seen that the base *paraconiine*, which is $C_8H_{15}N$, is not even isomeric with coniine.

Uses.—Hemlock or conium is supposed to be the narcotic used by the Athenians to destroy the life of condemned individuals, and by which Socrates and Phocion died. It was also used by the ancients as a medicine, but fell into entire neglect until Störck employed and extravagantly praised it. Though fatal to some animals, hemlock is eaten with impunity by others, as horses, goats, and sheep.

The alkaloids of conium all have the same physiological properties, although there is a difference in the degree of their power. Their most important effect is a paralysis of the peripheral endings of the motor nerves. In the account of the death of Socrates reference is made to loss of sensation as one of the prominent symptoms of his poisoning and there is evidence that the drug has an effect upon the sensory as well as upon the motor nerves, but the dominant action is certainly upon the motor system. Hayashi and Muto (*A. E. P. P.*, 1901, xlviii) have shown that the phrenic nerve is more susceptible to the drug than the other motor nerves of the body. It is evident, therefore, that if given in sufficient dose to control spasms, conium would stop the movements of the diaphragm and therefore cause death through asphyxia.

The drug has, however, been used in spasmodic disorders, such as *whooping cough*, *paralysis agitans*, and *acute mania* and by some with asserted good results. It was in the days of superstitious medicine believed to exercise an alterative effect in *scrofulous* and similar diatheses, but was long ago abandoned for this purpose.

Coniine acts precisely as does hemlock, and may be used for the same purposes. The *dose* is from one-fortieth to one-twelfth of a grain (0.0015–0.005 Gm.). Its solution has been used locally in the spasmodic contraction of the *orbicularis oculi* and *ophthalmia* with *photophobia* in scrofulous children. For these purposes from one-half to one per cent. may be employed.

Various salts, including the *hydrochloride* and the *benzoate* have been prepared, but the *hydrobromide* is the one most frequently used. This occurs in colorless prismatic needles, soluble in water and alcohol, less so in ether and chloroform, inodorous and almost tasteless, and are not deliquescent. It should be kept in the dark, otherwise it assumes a red tint. The salt has been used in the treatment of *whooping cough*. The usual dose of this salt is from one-sixtieth to one-twelfth of a grain, but in *tetanus* as high as one-sixth of a grain (0.01 Gm.) has been given. In *sciatica* it has been employed hypodermically in quantities of one-twelfth of a grain (0.005 Gm.) with good results. (*Répert. de Pharm.*, 1876, p. 369; *N. R.*, 1876, 1879, pp. 18, 178.) For an account of Harley's experiments to determine the relative value of different preparations of conium, see *U. S. D.*, 18th ed., p. 451. He concluded that the green fruit, as the basis of tinctures and extracts, is superior to any other part of the plant, and the spirituous extract of the green fruit should be substituted for the almost worthless extract of the former Br. Pharm. (*P. J.*, 1871, p. 585.)

Dose, of conium, three to five grains (0.2 to 0.32 Gm.).

Connarus. *Connarus guianensis* Lamb. *Seribéle.*—The seeds and root bark of this plant (Fam. *Connaraceæ*), from French Guinea, are used as tænifuges; two ounces of the seeds in decoction, without straining. (Maclaud, *P. J.*, 1896, 243.)

Contrayerva. *Contrayerba. Contrayerve*, Fr. *Bezoarwurzel, Giftwurzel*, G.—The root of *Dorstenia Contrajerva* L. (Fam. *Urticaceæ*), a native of Mexico, the West Indies, and Peru. The term *contrayerba*, in the language of the Spanish Americans, signifies *counterpoison* or *antidote*, and was applied to this root under the impression that it had the property counteracting all kinds of poison. The probability is that the root sold as contrayerva is derived from several species of Dorstenia, among which, besides *D. Contrajerva*, two others are mentioned by Houston, *D. Houstoni* L. and *D. Drakena* L., the former growing near Campeachy, the latter near Vera Cruz. According to Pereira and Martius, the *contrayerva* of the shops is the product of *D. brasiliensis* Lam., and is brought from Brazil.

The root, as found in commerce, is oblong, an inch or two in length, of varying thickness, very hard, rough, and solid, of a reddish-brown color externally, and pale within; and has numerous, long, slender, yellowish rootlets attached to its inferior part. The odor is aromatic; the taste warm, slightly bitterish, and pungent. The rootlets have less taste and odor than the tuberous portion. The sensible properties are extracted by alcohol and boiling water. The decoction is highly mucilaginous. The tincture reddens infusion of litmus, and precipitates on the addition of water. Mussi (*L'Orosi*, 1894, 259) investigated this plant and found two substances, which he called provisionally *cajapine* and *contrayerbine*. Contrayerva is a stimulant tonic and diaphoretic, and has been given in *low fevers, typhoid dysentery*, and *diarrhea*, and other diseases requiring gentle stimulation. *Dose*, of powdered root, half a drachm (2 Gm.). In the root of the *Gabbon ivy* (*Dorstenia klaineans?*) Heckel and Schlagdenhauffen have found a coumarin-like body, *pseudocoumarin*. (*Ph. Cb.*, xliii.)

Convallaria Flowers. *N. F. IV. Convallariæ Flores. Lily-of-the-Valley Flowers.*—It is described in the N. F. as "the dried inflorescence of *Convallaria majalis* Linné (Fam. *Liliaceæ*), without the presence of more than 5 per cent. of foreign matter. From 15 to 25 cm. in length, peduncle dull-green or suggesting purplish-green, and more or less angled; flowers white, when old drying to a brownish color, usually from ten to twenty in number, borne in a more or less secund raceme on recurved pedicels which are usually from a half longer than their flowers to twice their length, each pedicel subtended by a whitish, ovate, acute bract about half its length; flowers from 6 to 8 mm. in length and rather broader, bell-shaped, six-parted, the segments ovate, obtuse, and slighly recurved; stamens six, included, adnate to the base of the corolla; style columnar, three-grooved. Odor agreeable; taste sweetish, then somewhat acrid. The powdered drug is light yellowish-brown and, when examined under the microscope, exhibits ellipsoidal or nearly spherical pollen grains with a smooth exine layer and occasionally with a convex rupture through the walls; calcium oxalate in raphides up to 0.04 mm. in length; fragments of tissue from the corolla composed of nearly isodiametric parenchyma cells with broadly elliptical stomata up to 0.04 mm. in length; fragments from the anther lobes, many of the cells having reticulate walls; few fragments of the short filaments with cells containing calcium oxalate; fragments of the stigma, rough and warty, with adhering pollen grains; portions of the bracts composed of thin-walled elongated cells, a few vascular bundles and stomata; tissue of the peduncle and pedicel composed of fragments of the epidermis with cells tapering at each end about 0.20 mm. in length and 0.03 mm. in breadth with elliptical stomata between the ends; sub-epidermal cells with yellowish-green plastids; tracheæ about 0.021 mm. in width, spiral and with simple pores; sclerenchymatous fibers few, with lignified walls and simple pores. Convallaria Flowers yield not more than 12 per cent. of ash." *N. F.* For constituents and uses, see *Convallaria Root*.

Convallaria Root. *N. F. IV.* (*U. S. P. VIII.*) *Convallariæ Radix. Lily-of-the-Valley Root. Lilium Convallium. Muguet*, Fr. Cod. *Maiblumen*, G. *Convallaria, Mughetto*, It. *Convalaria, Lirio de los valles*, Sp.—It is described by the N. F. as "the dried rhizome and roots of *Convallaria majalis* Linné (Fam. *Liliaceæ*). Rhizome horizontal, elongated, usually branched, cylindrical, variable in length, from 1 to 3 mm. in diameter; externally yellowish-white or pale brown, with a few circular stem scars, and from the under and side portions at the nodes usually arise from three to five thin, tortuous, dark brown, branching roots; fracture short or fibrous; internally whitish. Odor faint; taste sweetish, becoming bitter and acrid. Under the microscope, transverse sections of the rhizome of Convallaria Root show an epidermal layer with a thick outer layer of cutin; a hypodermal layer of a single row of collenchyma; a cortex made up of about twenty rows of parenchyma cells, some of which contain starch and raphides of calcium oxalate; a prominent endodermis, the radial and inner walls of which are strongly thickened and lignified; inside the endodermis is an interrupted circle of collateral fibro-vascular bundles, the woody portion of which has in cross section the shape of the letter V; inside the circle of bundles is another interrupted circle of fibro-vascular bundles of the concentric type, the sieve tissue being surrounded by the xylem; the parenchyma cells of the pith separated by large intercellular spaces. Under the microscope, transverse sections of the root of Convallaria show a hairy epidermal layer, a hypodermis of a single row of cells; a cortex of about six rows of cells, some of which contain starch, raphides of calcium oxalate, and oil; the cells of the endodermal layer resemble those of the rhizome; fibro-vascular bundles mostly five. The powder is dark brown, tending to cake on standing, consisting chiefly of cellular fragments and a few starch grains and raphides of calcium oxalate; cells of endodermis with slightly oblique ends and considerably thickened, lignified porous walls; fragments of tracheæ with spiral and scalariform thickenings, or with porous walls; starch grains single or compound, mostly nearly spherical, and from 0.003 to 0.012 mm. in diameter; raphides of calcium oxalate few, from 0.02 to 0.045 mm. in length. Convallaria Root yields not more than 10 per cent. of ash." *N. F.*

The ordinary lily of the valley of the gardens is primarily a native of Europe, but may be found in America escaped from gardens, and a plant which grows wild in the higher Alleghenies from Central Virginia to South Carolina seems to be identical with it. G. F. Walz found in lily of the valley *convallarin* and *convallamarin*. (*A. J. P.*, 1859, p. 577.) Convallarin is in colorless, rectangular prisms, scarcely soluble in water, but sufficiently so as to render the solution acrid and to cause it when shaken to foam like soap and water. It is easily dissolved by alcohol. Its composition is represented by the formula $C_{34}H_{62}O_{11}$, and it is a glucoside, decomposed by long boiling with diluted acids into sugar and *convallaretin*. Convallamarin is a white powder, very bitter and afterwards sweetish, soluble in water and alcohol, but not in ether. This also is a glucoside. Its composition is $C_{23}H_{44}O_{12}$, and it is decomposed by heating with diluted sulphuric acid into sugar and *convallamaretin*, the formula of which is $C_{20}H_{36}O_8$. For preparing convallamarin, Tanret modifies Walz's method, as follows. An alcoholic tincture made from the whole plant is precipitated with lead subacetate and filtered; the excess of lead is removed with diluted sulphuric acid, avoiding the use of more than is necessary, and, after neutralizing, the tincture is distilled, the last portion of alcohol being driven off in the open air, then the cooled

and filtered liquor is treated with tannin, care being taken to keep the liquid neutral by cautiously adding a diluted solution of sodium carbonate. A compound of tannin and convallamarin is precipitated, which, after washing, is dissolved in 60° alcohol, the solution decolorized with charcoal, decomposed with zinc oxide, filtered, and evaporated to dryness. In this way convallamarin is obtained nearly white, and having the appearance of ordinary digitalin. To free it from the salts that are sometimes carried down by the tannin precipitate, it is a good plan to redissolve it in 90° alcohol, filter, and then evaporate. One kilogramme of the fresh plant collected in the first days of August yielded two grammes of convallamarin. (*P. J.*, 1882, p. 423.) Taken internally the flowers are said to be emetic and cathartic, and their extract purges actively in the *dose* of half a drachm. They were formerly used in *epilepsy* and against *worms*. The *root*, which is also bitter, has similar purgative properties, and in powder is said to be sternutatory. Hænsel obtained 0.058 per cent. of an aromatic volatile oil from the leaves of *Convallaria majalis*. (*Ph. Centralh.*, 1901, 495.)

Convallaria has long been used in Russia as a popular remedy for the relief of *dropsy*. While there is considerable divergence of statements as to the exact effects of this drug upon the circulation, it seems to be well established that it arrests the frog's heart in systole and produces the other phenomena characteristic of the digitalis group of drugs. *Dose*, of either the flowers or root, five to ten grains (0.32–0.65 Gm.).

Convallaria Polygonatum L. (*Polygonatum uniflorum* Gilib.; now *P. officinale* (L.) All.) *Sealwort. Solomon's Seal. Sceau de Salomon, Genouillet*, Fr. *Weisswurzel, Salomon's Siegel*, G. (Fam. *Liliaceæ*.)—A perennial, herbaceous European plant, whose root is inodorous. It is said to be emetic. In former times it was used externally in *bruises*, especially those about the eyes, in *tumors, wounds*, and *cutaneous eruptions*, and was highly esteemed as a cosmetic. At present it is not employed. The berries and flowers are said to be acrid and poisonous. *Polygonatum multiflorum* L. (All.) (*C. multiflora* L.), which grows in Europe and Asia, is analogous to the preceding in properties. (See John H. Rauch, *In. Dis.*, 1849.)

Convolvulus. *Convolvulus panduratus* L. (Now *Ipomœa fastigiata*, Sweet) *Wild Potato. Manroot. Man of the Earth. Wild Jalap.*—This native climber has a perennial root, which is very large, two or three feet in length, about three inches thick, branched at the basal portion, externally of a brownish-yellow color, and with numerous longitudinal fissures, internally whitish and milky, and of a somewhat acrid taste. It is feebly cathartic and diuretic (*N. Y. Journ. of Med.*, x, 375), and was formerly used in *strangury* and *calculous diseases*. Forty grains (2.6 Gm.) of the dried root are said to purge gently.

Copal.—The *copals* are a class of hard resins used principally in varnish manufacture. They are of various origins, both geographically and botanically. Their principal characteristics are their hardness, high melting point and comparative insolubility unless subjected to destructive distillation. There are three chief varieties: (1) *Fossil copal*, found in the ground in localities where the trees yielding it have entirely disappeared. (2) *Semi-fossil copal*, collected from the ground in the neighborhood of living copal trees. (3) *Fresh copal*, found on living trees, either as the result of natural exudation or from artificial incisions. The fresh copal is of least value and the fossil copal is most highly prized.

East African copals, known in commerce as *Animi gum* or *resin*, are fossil varieties coming from Zanzibar, Madagascar and along the East African Coast. American copals are collected in South America and probably originated from trees related to those which produced the East African copals, although the product is softer. *Kauri* or *cowrie copal* or *Kauri gum*, as it is often called, is found in New Zealand exclusively. M. Kahan has investigated *Accra copal* and *Benin copal* (*Arch. d. Pharm.*, 1910, ccxlviii, p. 443) and gives the percentages of the various constituents found.

A study of South American varieties of copal has been made by S. Machenbaum (*Arch. d. Pharm.*, 250, Nos. 1–6 and 13), in which the constituents are stated to be *copalic acid, copalolic acid, copaloresene, copalmic acid*, volatile oil and ash.

Fossil copal from Guiana has been studied by J. C. Essner (*Annal. Chim. Anal.*, xvii, p. 166), who gives the following constants: Sp. gr. 1.089; colorless portion, acid value 118, saponification value 127, iodine value 84.3; yellow portion, acid value 125, saponification value 151, iodine value 81.5.

Zanzibar copal is obtained from several species of *Trachylobium*. The trunk and limbs are covered with a clear resinous exudation, portions of which, after solidifying, drop to the ground and are collected, while other portions are broken from the tree. This kind of resin is always smooth, and is exported to India. Another variety, with an indented, goose-flesh surface, known in the English market as *animé*, is dug from the earth, and though the product of forests now extinct, originated probably from the same tree. (*P. J.*, 1869, 654.) It is in roundish, irregular, or flattish pieces, sometimes several pounds in weight, often rough over the surface, probably from the impression of sand in its soft state, colorless, or brownish-yellow, more or less transparent, very hard, with a shining, conchoidal fracture, inodorous and tasteless. By heat it melts and emits gases, loses from 15 to 20 per cent. of weight, and is altered so as to become more soluble in ether, alcohol, or oil of turpentine, and in this way copal varnishes are usually made. It is not a proximate principle, but consists of various resins united in different proportions. According to Unverdorben and Filhol, some five different resins can be obtained by the successive action of solvents. *Sierra Leone copal* comes from Western Africa. According to Daniell (*P. J.*, xvi, p. 369), this is derived from the *Copaifera Guibourtiana* Benth., a large tree growing preferably in mountainous regions. The drug is mostly collected, not from the tree itself, but from the beds and borders of streams, into which it is washed down, during the rains, from the hillsides, in the soil of which it had been deposited.

The Sierra Leone copal is described by Daniell as occurring "in small round tears, or irregular conical and smooth nodulated masses, seldom exceeding in size an ordinary duck egg. They are covered, to a greater or less extent, by a peculiar white efflorescence, which increases by age. Their color graduates from a pale green to a lemon or dull yellow."

Inhambane copal has been shown to be the product of *Copaifera Gorskiana* Benth. and seeds sent to Kew Gardens in 1886 germinated, and the plant has been widely introduced into both the East and West Indies, and into Australia. (*P. J.*, xix, 508.)

A variety of copal comes from the East Indies. This has been ascribed to *Vateria acuminata* Hayne (Fam. *Dipterocarpaceæ*), but is probably the product of a *Trachylobium;* at least a specimen of this resin was collected by Perottet from the *Trachylobium Hornemannianum* Hayne, which he found growing in the Isle of Bourbon. This tree is a native of Madagascar, and probably of the neighboring parts of Africa, and Perottet was informed that the copal of India is taken thither by the Arabs of Muscat, who obtain it from the east coast of Africa. (*J. P. C.*, 3e sér., i, 406.) It is described by Schindler as of a globular form, softer and more transparent than the other varieties, with a surface always clear, and having an agreeable odor when heated. It is readily and freely dissolved by the oils of turpentine and rosemary when pure, but not by these fluids when rendered resinous by age. It is more readily fusible than the others, and makes the best varnish.

The West India copal is in flat pieces, seldom weighing more than three ounces, rarely containing insects, very hard, of a rough appearance, of a yellowish color, and without odor or taste. It is much less readily dissolved by oil of turpentine than the East India variety, swells but does not dissolve in oil of rosemary and is slightly soluble in absolute alcohol. Another kind, probably also American, is in convex or concave pieces, about a pound in weight, often containing insects and other impurities. In solubility it resembles the last mentioned variety, in fusibility is intermediate between it and the East Indian, and is altogether inferior. (*P. J.*, 1850.) For an account of the present views on the nature of copal resins, see Tschirch, *Die Harze und die Harzbehälter*, Leipzig, 1900.

For descriptions of the so-called Manila copal and Kauri copal which are derived from the conifers, see p. 1417.

Copal lotion.—Under the trade name *Adhæsol* there appears on the market a lotion containing: Copal, 350 parts; benzoin, 30 parts; tolu, 30 parts; ol. thyme, 20 parts; alpha-naphthol, 3 parts; ether, q. s., 1000 parts. It is used as an antiseptic varnish in *diphtheritic affections* of the throat.

Copper Abietinate. $Cu(C_{19}H_{27}O_2)_2$.—This forms green scales, soluble in oils, imparting to the solutions a rich emerald color. It has been used as an anthelmintic and vermifuge in veterinary practice. It is also used technically for impregnating and preserving wood.

Copper Acetate. *Cupri Acetas. U. S.* 1880. $Cu(C_2H_3O_2)_2.H_2O$=198.14. *Crystallized verdigris. Crystals of Venus. Verdet, Cristaux de Vénus*, Fr. *Essigsaures Kupfer, Aerugo crystallisata, Crystallisirter Grünspan*, G.—This salt may be prepared by dissolving verdigris in acetic acid, or by precipitating a concentrated solution of lead acetate with copper sulphate. It is the normal cupric acetate, as distinguished from the basic salt. "Deep green, prismatic crystals, yielding a bright green powder, efflorescent on exposure to air, odorless, having a nauseating, metallic taste and an acid reaction. Soluble in 15 parts of water and in 135 parts of alcohol at 15° C. (59° F.), in 5 parts of boiling water and in 14 parts of boiling alcohol. When heated above 100° C. (212° F.), the salt loses its water of crystallization, and at a temperature above 200° C. (392° F.), it is gradually decomposed. The aqueous solution of the salt has a bluish-green color, which is rendered deep blue by an excess of ammonia. On heating the salt with sulphuric acid, acetous vapors are evolved. If the aqueous solution of the salt be treated with hydrogen sulphide until all the copper is precipitated, the filtrate should leave no residue on evaporation (alkalies, alkaline earths, and iron). If the aqueous solution be heated to boiling with solution of soda in excess, it will yield a filtrate which should not be clouded by hydrogen sulphide (absence of lead, zinc)." *U. S.*, 1880.

Verdigris. Impure Subacetate of Copper. U. S. 1870. *Copper Subacetate. Viride Æris, Ærugo*, Lat. *Acétate de Cuivre brut, Sous-acétate de Cuivre, Vert-de-gris, Acétate basique de Cuivre, Verdet gris*, Fr. *Grünspan, Spangrün, Basisches Essigsaures Kupfer, Kupferoxyd*, G. *Verde Rame*, It. *Cardenillo*, Sp.—This basic salt is prepared in the south of France, more particularly in the neighborhood of Montpelier. It is also manufactured in Great Britain and Sweden. In France the salt is prepared by exposing sheets of copper to the action of the residue of the grape (after the expression of the juice in making wine), which undergoes the acetous fermentation, and the acetic acid attacking the copper forms the subacetate. In England a purer verdigris is prepared by alternating copper plates with pieces of woollen cloth steeped in pyroligneous acid. Verdigris comes to this country exclusively from France, being imported principally from Bordeaux and Marseilles. It occurs in masses of a *pale green color*, and composed of a multitude of minute silky crystals. Sometimes, however, it occurs of a bright blue color. Its taste is coppery. It is insoluble in alcohol, and, by the action of water, a portion of it is resolved into the neutral acetate which dissolves, and the tribasic acetate which remains behind in the form of a dark green powder, gradually becoming black. It is hence evident that, when verdigris is prepared by levigation with water, it is altered in its nature. When verdigris is acted on by sulphuric acid, it is decomposed, vapors of acetic acid being evolved, easily recognizable by their vinegar-like odor. It is almost entirely soluble in ammonia, and dissolves in hydrochloric and diluted sulphuric acids with the exception of impurities, which should not exceed 5 per cent. When of good quality, it has a bright green color, is free from black or white spots, and is dry and difficult to break. The green rust, called in popular language verdigris (*vert-de-gris*), with which copper vessels are very frequently coated, when not kept clean, is a copper carbonate, and should not be confounded with true verdigris. Verdigris, apart from its impurities, is a variable mixture of the basic copper acetates.

The *blue variety* has approximately the composition $(C_2H_3O_2)_2Cu_3O$. When treated with water it is generally decomposed.

The *green variety* of verdigris has the composition $CuO.2Cu(C_2H_3O_2)_2$.

The local and general action of copper acetate upon the animal economy and the treatment of its poisoning are the same as those of copper sulphate. It is not used internally. Dr. G. Billard, *Presse Medicale*, 1909, uses the fine dust of copper subacetate by inhalation of minute quantities in the treatment of *tuberculosis;* he states that the cough is usually lessened and sometimes disappears completely.

Copper, Aluminated.—This copper compound in the form of a green powder or plates is a combination of copper and aluminum sulphates and potassium nitrate. It is soluble in water and is used solely as a mild caustic in *ophthalmology*.

Copper Ammonio-sulphate. *Cuprum Ammoniatum. U .S.* 1870. *Ammoniated Copper Sulphate. Cuprum Sulfuricum Ammoniatum. Sulfate de Cuivre ammoniacal, Cuivre ammoniacal,* Fr. *Schwefelsaures Kupferoxyd-Ammoniak, Ammoniakalisches Kupfersulfat,* G.—The character of the salt which results from the interaction between copper sulphate and ammonia varies according to the conditions under which the reaction takes place. The formerly official process was as follows: "Take of Copper Sulphate *half a troyounce;* Ammonium Carbonate *three hundred and sixty grains.* Rub them together in a glass mortar until effervescence ceases. Then wrap the Ammoniated Copper in bibulous paper, dry it with a gentle heat, and keep it in a well-stoppered glass bottle." *U. S.,* 1870. The salt which results from this process is probably the same as that which is made by adding copper sulphate to a solution of ammonia and has the composition $CuSO_4.4NH_3 + H_2O$. If this preparation be allowed to remain exposed to the air, it will lose ammonia and water, and be changed into a mixture of basic sulphates. Ammoniated copper sulphate loses two molecules of NH_3 and the one molecule of water at 150° C. (302° F.), and at 260° C. (500° F.) only anhydrous sulphate remains, which frequently, however, contains cuprous oxide.

This salt has a beautiful deep azure-blue color, a strong ammoniacal odor, and a styptic, metallic taste. It is soluble in water, and the solution has an alkaline reaction to vegetable colors; but, unless there is excess of ammonium sesquicarbonate, the solution deposits copper subsulphate if much diluted. When exposed to the air it parts with ammonia, and is said to be ultimately converted into ammonium sulphate and copper carbonate. This change is apt to occur, to a greater or less extent, while it is drying. It should not, therefore, be prepared in large quantities at a time, and should be kept in well-closed bottles. By heat the whole of it is dissipated, except the copper oxide. Arsenic trioxide precipitates a green copper arsenite from its solution. Solutions of potassium and sodium hydroxides, lime water, and the acids are incompatible with it. Ammoniated copper was at one time employed internally in various nervous diseases, especially *epilepsy,* as well as locally for its astringent action, but is at present very seldom exhibited. In overdoses it produces vomiting, and the poisonous effects which result from the other preparations of copper. *Dose,* in pill or solution, a quarter or half a grain (0.016–0.032 Gm.), twice a day, and gradually increased to four or five grains (0.26 or 0.32 Gm.).

Copper Arsenite. *Cupri Arsenis. Copper orthoarsenite.* $Cu_3(AsO_3)_2$. *Scheele's Green.*—This salt was brought forward for the purpose of treating *diarrhea* on the homeopathic principle, in the *Symptomen-Codex* of Jahn, in 1865, and has been greatly lauded by John Aulde and other regular practitioners in the treatment of *diarrhea, enterocolitis, cholera morbus,* and *dysentery.* It is to be given in doses of from one three-thousandth of a grain (0.000022 Gm.), at intervals of from ten to twenty minutes, until some effect is produced. It does not seem to be sustaining its first reputation. According to H. A. Hare, *copper arsenite* is a valuable remedy in *anemia.* The *dose* ordinarily is from one one-hundredth to one-twentieth grain (0.0006–0.003 Gm.).

Copper Citrate. *N. N. R.* 1917. $Cu_2C_6H_4O_7 + 2\frac{1}{2}H_2O$.—*Cupric citrate* contains from 34 to 36 per cent. of copper. It is a bluish-green, finely crystalline powder, without odor or taste. Very slightly soluble in cold water, soluble in acids and alkalies. Used for the same purposes and in the same doses as other salts of copper over which it possesses the advantage of its sparing solubility in water. Proprietary preparations of similar properties are known by the names of *cuprocitrol* and *cusylol.* Copper citrate has been used in the treatment of *conjunctivitis* and *trachoma* in aqueous solutions of from ½ to 5 per cent. An *ointment of copper citrate* in glycerite of boroglycerin has been proposed by Hoffman (*A. J. P.,* 1917, p. 298) for the treatment of *trachoma* and disturbances of the follicles of the ciliæ. It is prepared as follows: Copper citrate, 8 Gm.; glycerite of boroglycerin, 80 Gm.; wool fat, 2 Gm.; white petrolatum, 10 Gm. Heat the glycerite of boroglycerin to 125° C. (257° F.) and slowly add the copper citrate and continue the heat until it dissolves. Then remove the heat, and when it has cooled to 75° C. (167° F.) add the wool fat and white petrolatum and stir constantly until it has cooled to 50° C. (122° F.), and transfer to air-tight containers.

Copper Iodide. *Cupri Iodidum. Cuprous Iodide. Kupferjodür,* G. Cu_2I_2.—A white powder, insoluble in diluted acids and in water; soluble in ammonia water and solution of potassium iodide. Made by adding a solution of potassium iodide to a solution of copper and iron sulphates.

Copper Nitrate. *Cupri Nitras. Br.* 1885. *Cupric Nitrate.* $Cu(NO_3)_2,3H_2O$.—"May be obtained by dissolving copper in diluted nitric acid and evaporating the solution until crystallization takes place on cooling to a temperature not lower than 70° F. (21.1° C.)." *Br.,* 1885. This salt was introduced in the 1885 revision of the British Pharmacopœia, to be dropped in 1898. As obtained by the above process, the crystals are prismatic and of a deep blue color, and very deliquescent and corrosive. At a temperature below 21.1° C. (70° F.), with one-third of its weight of water, it forms tabular crystals which have the composition $Cu(NO_3)_2.6H_2O$. The addition of a very little more water causes the crystals to form a styptic and caustic fluid. The diluted aqueous solution should show only a faintly acid reaction to litmus paper. This salt has the physiological and medicinal properties of copper sulphate, and may be used in the same dose.

Copper Nucleinate. *Cuprol.*—This salt is a greenish powder and is said to contain 6 per cent. of the metal and to be readily soluble in hot water and not to be thrown out of its solution by alkalies and not to precipitate with albuminous liquids. It has been highly recommended in the treatment of *trachoma* and other conditions of the conjunctiva. The assertion is made that it has greater penetrating powers and produces less irritation than ordinary salts of copper. (Von Sicherer, *Die Ophthal. Kl.,* 1901.)

Copper Oleate. *Cupric oleate,* $Cu(C_{18}H_{33}O_2)_2$, with excess of oleic acid. A greenish-blue mass, consisting of 10 per cent. copper oxide dissolved in an excess of oleic acid. It is soluble in ether and is used for its antiseptic action as a 10 to 20 per cent. ointment in indolent *ulcers* and unhealthy *granulations.*

Copper Oxide, Black. *Cupri Oxidum Nigrum. Cuprum Oxydatum. Oxyde noir de Cuivre, Safran de Vénus,* Fr. *Kupferoxyd,* G.—*Cupric oxide,* CuO, is obtained most conveniently by heating the nitrate to redness. This oxide, in the form

of ointment, made by mixing four parts with thirty of lard, has been locally used twice a day to remove *chronic indurations of the glands.* (Hoppe, *Ann. Tér.*, 1855.) It is also asserted to be an active *tœnicide* of very feeble toxic power. It is given by Dörr in *doses* of one and a half grains (0.096 Gm.) four times a day for several days, the last dose followed by castor oil. (See *Ther. Geg.*, 1901.)

Copper Phenolsulphonate. *Cupri Phenolsulphonas. Copper Sulphocarbolate. Paraphenolsulfosaures Kupfer*, G. $(C_6H_4(OH)SO_3)_2Cu + 6H_2O$.—Green prismatic crystals soluble in water and alcohol. Made by reaction between copper sulphate and barium phenolsulphonate. A solution of from ½ to 1 per cent. is applied locally in *gonorrhea* and *blennorrhea*, and also as a styptic, hemostatic and antiseptic under the name of *cupriaseptol.*

Coptis. *N. F. IV. Goldthread. Coptide*, Fr. *Gelbe* (*Kleinste*) *Niesswurz*, G.—"The dried plant of the *Coptis trifolia* (Linné) Salisbury (Fam. *Ranunculaceæ*)." *N. F.* This plant inhabits the northern region of this continent and of Asia, and is found in Greenland and Iceland. It delights in the dark shady swamps and cold morasses of northern latitudes and alpine regions, and abounds in Canada and in the hilly districts of the Northern United States.

Dried goldthread, as brought into the market, is "in loose, matted masses consisting of long, much branched rhizomes and their small roots together with the leaves. Rhizomes orange or golden-yellow; leaves evergreen, long and slenderly petioled, trifoliate, the segments broadly obovate-cuneate, crenately lobed and toothed with sharp-pointed teeth, prominently veined, smooth, coriaceous, dark green and shining but often drying to a dull brownish hue; flowers, if present, small, solitary, terminating slender scapes, sepals five to seven, oblong, obtuse, deciduous; petals five to six, pale yellow, small club shaped; stamens numerous. Odor faint; taste purely bitter without astringency. The powdered drug is yellowish-green and, when examined under the microscope, exhibits numerous, mostly simple, starch grains, somewhat rounded, up to 0.007 mm. in diameter; fragments of leaf epidermis, composed of cells with wavy vertical walls and broadly elliptical stomata, the latter up to 0.024 mm. in length; fragments of the nerved scales from the nodes, composed of cells with yellow walls; leaf parenchyma cells containing chloroplastids; few, simple, thick-walled hairs from the midrib of the leaf, from 0.035 to 0.075 mm. in length; elongated, epidermal cells from the roots having yellow walls and filled with reddish contents; fragments of epidermal and sub-epidermal cells from the rhizome, similar to those from the root, but without reddish contents, often filled with a yellowish content; groups of elongated parenchyma cells about 0.06 mm. in length and about 0.01 mm. in width, many being filled with starch grains; tracheæ with bordered pores or spiral markings, about 0.02 mm. in width; narrow thin-walled, porous sclerenchyma fibers. Coptis yields not more than 8 per cent. of ash." *N. F.* It imparts a bitterness and yellow color to water and alcohol, but most perfectly to the latter, with which it forms a bright yellow tincture. The infusion is precipitated by silver nitrate and lead acetate. (Bigelow.) It affords no evidence of containing either resin, gum, or tannin. The plant undoubtedly contains *berberine*, which, according to F. F. Mayer (*A. J. P.*, 1863) and E. Z. Gross (*A. J. P.*, 1873), is associated with another alkaloid. Gross states that *coptine* differs from berberine in its colorless crystals, and by forming with mercuric potassium iodide (Mayer's reagent) a crystalline instead of flocculent precipitate. (See also John J. Schulz, *A. J. P.*, 1884, 261.)

Goldthread is a simple tonic bitter. In New England it is employed as a local application in *aphthous ulcerations* of the mouth, but it probably has no other virtues in this complaint than such as are common to the simple bitters. It may be given in substance, infusion, or tincture. The *dose* of the powder is from ten to thirty grains (0.65–2.0 Gm.); of a tincture made with an ounce of the root to a pint of diluted alcohol, one fluidrachm (3.75 mils), and of the N. F. fluidextract thirty minims (2 mils).

The *Coptis Teeta* of Wallich, which grows in the mountainous regions bordering on Assam, is much used as a tonic by the natives and by the Chinese. It is analogous in properties to *C. trifolia* Salisb., and is said to contain 8½ per cent. of berberine. It has been brought into use in British India. It is highly commended by Twining as a stomachic tonic. (*P. J.*, 1870, 161.) *Coptis anemonifolia* Sieb. and Zucc. also contains berberine, and has been used in Japan in *intestinal catarrh.* (*Sei-i-Kwai*, 1892.)

Coral. *Corail*, Fr. *Koralle*, G.—The solid mesodermal calcareous skeletons of the coral polyps, *anthozoa*, were formerly used in medicine, but have passed out of vogue. Their chief constituent is calcium carbonate, colored by ferric oxide, and united with more or less animal matter.

Corallin. *Pœonin. Aurine R.*—A coloring or dyeing material, derived from *rosolic acid* or *aurin* ($C_{19}H_{14}O_3$)—which is made by acting upon phenol with sulphuric and oxalic acids—by exposing together rosolic acid and alcoholic ammonia to a heat of 149° C. (300.2° F.), and is considered to be an intermediate product between pararosaniline and pararosolic acid. A solid substance is thus obtained, in scales of a peony redness, with reflected green or dull yellow rays, almost insoluble in water, soluble in alcohol and the fixed oils. Ambrose Tardieu (*J. P. C.*, 1859, p. 262), having met with some extraordinary cases of a severe vesicular eruption upon the feet, attended with violent inflammation and swelling, and with general febrile symptoms, attributed to the wearing of red socks, extracted from them a poisonous dye which he believed to be *corallin.* He also found that twenty centigrammes (about three grains) of corallin subcutaneously was sufficient to kill a dog, the symptoms being violent purgation, with intense fever and progressive prostration, and the leg of the side in which the injection had been made was very painful. After death the neighborhood of the wound was found suppurating, the stomach sound, and the intestines distended, with signs of violent inflammation of the mucous membrane; the liver presented evidences of fatty degeneration and the lungs appeared as if dyed by the scarlet coloring matter. Roussin succeeded in extracting a portion of the coloring matter from the lungs and liver, and dyeing with it a skein of silk. Hitherto the effects on the human subject have been confined to the painful cutaneous affection, which has been so satisfactorily traced to contact of the skin with the silk fabrics dyed with it; but even in these cases there were serious constitutional symptoms, as fever, headache, giddiness, and nausea. Some observers later than Tar-

dieu believe that pure corallin is not poisonous, and that the symptoms have been produced by arsenic or other contaminating substances. (See *M. T. G.*, 1869, 421; *P. J.*, 2d ser., xi, 360; also *N. Y. M. J.*, 1870, 599; *N. R.*, i, 228.)

Local poisoning may be caused by *aniline red* (see *Fuchsin*) as well as by corallin. The two colors may be distinguished in tissues. Aniline red disappears very rapidly by contact with ammonia; but the color reappears by the addition of an acid, or by the evaporation of the alkali. Corallin red is not dissolved by cold water, yields a slight color to boiling water, but rapidly disappears from the tissue under the action of boiling alcohol. Alkalies brighten the color without changing it; acids precipitate the coloring matter in yellow flakes.

Corallorhiza. *Corallorhiza odontorhiza* (Willd.) Nutt. *Coral-root.* (Fam. *Orchidaceæ.*)—This is a parasitic leafless herb, sending up from a coral-like rhizome a simple scape or flower stem, from six to sixteen inches high, furnished with sheaths instead of leaves, of a light brown or purplish color, and bearing small, greenish-brown flowers in a long spike. The plant grows throughout the United States east of the Mississippi. The rhizome is the part used. It is much branched and toothed, and of a brown color, and its resemblance to coral gave name to the plant. It has a strong peculiar odor, and an astringent bitterish taste. It is much valued by the eclectics as diaphoretic in *fevers; dose*, of powder, thirty grains (2 Gm.) every two hours.

Cordol. *Tribromsalol.* $C_6H_4.OHCOO.C_6H_2Br_3$.—A white, tasteless, and odorless powder, insoluble in water, ether, and alcohol, freely soluble in chloroform and glacial acetic acid. *Cordyl* or *acetyl tribromsalol* is insoluble in water, and occurs in the form of fine white needles. *Cordeine* or *methyl tribromsalol* occurs in small white crystals, which are insoluble in water, but soluble in alcohol and chloroform. Cordol, cordyl, and cordeine are used as intestinal antiseptics, easily decomposed, giving the combined actions of tribromphenol and salicylic acid when split up in the intestinal canal. The *dose* of either is from eight to fifteen grains (0.5–1.0 Gm.).

Coriaria. *Coriaria myrtifolia* L. *Currier's Sumach. Redoul, Sumach des Corroyeurs*, Fr. *Gerberstrauch*, G. (Fam. *Coriariaceæ*).—This is a shrub growing wild in Southern Europe, which is sometimes cultivated in gardens on account of its handsome foliage. The leaves, which are used for dyeing black, were at one time employed to a considerable extent in France in the adulteration of senna. They have recently been reported both in Europe and in America as an adulterant of sweet marjoram, the *coriaria* leaves being finely broken to facilitate admixture. The presence of coriaria in marjoram may be inferred by strewing a specimen of the broken up leaves upon the surface of a dilute ferric chloride solution, which does not affect the fragments of marjoram but which quickly stains the coriaria fragments a deep greenish-black, owing to their high tannin content. The fruit, resembling berries in form, are black, and about the size of a pea. Both these and the leaves are poisonous in large doses, and several instances of death are on record from eating the fruit. (Mérat and De Lens.) Riban (*J. P. C.*, 1864, p. 487) separated from the fruit a glucoside *coriamyrtin*. He obtained it by treating the juice with lead acetate, precipitating the lead with hydrogen sulphide, concentrating the lead with a filtrate to a syrupy consistency and extracting with ether. It occurs as extremely bitter, white crystals, fusing at 220° C. (428° F.), sparingly soluble in water but freely so in alcohol and other organic solvents. Its empirical formula is $C_{30}H_{36}O_{10}$. Marshall (*J. P. Ex. T.*, 1912, iv, p. 135) studied the substance supplied by Merck under the name of coriamyrtin which, however, he believed to be different from that described by Reban, because it was soluble in water. The lethal dose was 1 mgm. per kilo. He found that it was a stimulant to the medullary centers, increasing the blood-pressure and respiration and slowing the pulse; in large doses it caused cerebral convulsions. Coriamyrtin has been employed as a stimulant in *collapse* in doses of one-sixtieth of a grain (0.001 Gm.).

Tlolocopetale, a Mexican drug, is said to be the product of a Coriaria, probably *C. myrtifolia*, containing *coriarin* and *coriamyrtin*, and to be actively poisonous.

Toot-poison. Tu-tu.—In New Zealand a poisonous plant, known as the *toot-plant*, has proved very destructive to the domestic animals. W. Lauder Lindsay found it to resemble either *Coriaria ruscifolia* of Linnæus or *C. sarmentosa* Forst., and in its action on the system to be an irritant narcotic. For an elaborate account of the *toot-plant*, and its poisonous effects, see *Brit. and For. Med.-Chir. Rev.*, 1865, 153, and 1868, 465. From these it appears that more than one species of *Coriaria* inhabit New Zealand, *C. thymifolia* Humb. et Bonpl. and *C. angustissima* Hook. f., besides the *ruscifolia;* though Lindsay appears to think that the two former may be merely varieties of the third. It is not only cattle that are poisoned by the plant, but not infrequently also children, and occasionally even an adult. The cattle are probably, in general, poisoned by eating the young shoots. W. S. Key attributes poisonous qualities to an oil (*Chem. News*, 1890, xxii), but it has been shown by T. Hill Easterfield and B. C. Aston that the three New Zealand species of coriaria contain a glucoside, *tutin*, $C_{17}H_{20}O_7$, which is not identical with coriamyrtin, and which, according to Marshall, is toxic, especially to the medulla oblongata and the basal ganglia of the brain. (*Proc. Chem. Soc.*, xvi, 213.) It is affirmed by T. H. Hartwick (*P. J.*, vol. xv, 22) that goats are not poisoned by the tu-tu, and that they have even been used to eradicate the plant by browsing, also that the berries when ripe are not only not poisonous to man, but, if care is taken to reject the seeds, are a grateful and refreshing fruit. The prominent symptoms of the poisoning in man are giddiness, stupor, and coma, with or without delirium or convulsions. Occasionally the delirium resembles that of alcoholic intoxication, in other instances approaches that of acute mania, and is attended with violent muscular action. Loss of memory is a characteristic of the convalescence. The toxicity of tutin, which was demonstrated by Marshall, has been confirmed by Ford (*J. P. Ex. T.*, 1910, ii).

Cork. *Suber. Liége*, Fr. *Kork*, G.—The great use made of this substance in pharmacy and the arts justifies a brief notice of it. It is chiefly produced by *Quercus Suber* L. (Fam. *Cupuliferæ*), but is obtained also from the *Q. occidentalis* F. Gay. It consists of the exterior layers of the bark beneath the epidermis, which acquire in these species an extraordinary development, becoming thick, and of that peculiar spongy consistence which characterizes *cork*. The tree begins to yield cork when fifteen or sixteen years old, and every six or eight

years—the interval requisite for the renewal of the suberose layers by the living portions of the bark beneath—furnishes a fresh supply, even for a century and a half, before it perishes. There are four constituent layers of the bark: the epidermis, the cork, the cellular envelope, and the bast which lies upon the wood. Each of these increases year by year; but the cork thus naturally produced is not valued. The commercial product is the result of an artificial injury to the bark. The exterior layers are removed, and the bast exposed. In the interior of this, at a variable distance from the surface, a layer of the proper cork is now formed, apparently by a change in the substance of the bast, the outer portions of which perish, while annually a new layer is added to the cork already existing, until it acquires a thickness which will justify its removal. Incisions are made in such a way that the cork is removed in large concave plates, which are then flattened under pressure, and dried. At present cork comes into commerce from Portugal, Spain, France, Italy, Tunis, Algeria, and Morocco. About one million of quartels of it are said to be produced annually. The value of the cork imported into the United States in 1914 was $3,851,794, and in 1915 $2,761,895.

A cork has recently come into the United States commerce from Nicaragua. It has been found by E. F. D. Baker to be obtained from the roots of the *Anona*, a tree closely resembling in appearance the ordinary cottonwood of the United States.

In selecting cork for use, those parts should be preferred which are soft and of uniform consistence, and in the choice of the larger plates those should be selected which are thick, flexible, elastic, finely porous, and of a reddish color. Boiling hot alcohol extracts from rasped cork tissue some 10 per cent. of soluble principles. From the hot alcohol solution a substance crystallizes which was first noticed by Chevreul under the name of *cerin*. According to Kugler (*Dissertation on Suberin*, Halle, 1884), besides cellulose and lignocellulose, cork contains two constituents, *cerin*, to which he gives the formula $C_{30}H_{32}O$, and *suberin*, which is a fat, and contains stearic acid and *phellonic acid*, $C_{22}H_{42}O_3$. This constituent, suberin, prevents the penetration of liquid into the cork, and is only extracted by alcoholic alkali solutions. When treated with nitric acid, cork yields a peculiar acid, which has been denominated *suberic acid*. This is a dibasic acid homologous with oxalic acid, and has the formula $C_8H_{14}O_4$. It is formed by the oxidation of many other substances, such as the oils from linseed, castor bean, cocoa nut, almond, spermaceti, etc.

Stanislaus Martin has called attention in France to the use of refuse corks in Paris, where they are collected by the scavengers, and sold to persons whose business it is to revive them, recutting such as are of unsuitable shape, filling up the interstices with mastic, and covering them over with some powder which may give them a fresh appearance. Corks are sometimes bleached with sulphurous acid, and the odor of hydrogen sulphide has been noticed in prescriptions which have been compounded, when such corks have been used in the dispensing bottle. (*P. J.*, 1881, 1080.) Mohr has found that old corks may be regenerated by allowing them to soak for twenty-four hours in hot water, washing well several times, allowing to stand for a few hours in a mixture of one part of hydrochloric acid and fifteen parts of hot water, and finally washing well in pure water. (See also *A. J. P.*, 1875, 467.) It is easy to conceive that a cork at one time used to enclose arsenical or other deadly solution may become saturated with the poison, and afterwards impart enough of it to another liquid, if not to produce dangerous effects on the health, at least to give to tests evidence of its presence, and thus lead to serious suspicions. No cork, therefore, which has been used in a bottle containing a poisonous substance should be employed a second time.

Cornus. *N. F. IV. Dogwood Bark. Ecorce de Cornouiller à grandes fleurs*, Fr. *Grossblüthige Cornelrinde*, G.—This drug, which was at one time official in the U. S. P., is described by the N. F. as "the dried bark of the root of *Cornus florida* Linné (Fam. *Cornaceæ*). In irregular, chip-like pieces, or portions of quills, usually less than 5 cm. in length and from 1 to 4 mm. in thickness; externally of a dingy-brown color, lightly fissured and thinly scaly, or reddish where the corky layer has been removed; inner surface varying from pinkish-brown to red-purple, usually harsh to the touch from numerous short striæ; fracture short, the surface whitish with yellow striæ, except the inner layer, which is light purple. Odor slight; taste bitter and astringent. Cornus yields not more than 10 per cent. of ash." *N. F.*

The barks of two other indigenous dogwoods are sometimes substituted for that of *C. florida* L. Each of these is a shrub with opposite leaves, the flowers in flat spreading cymes, and the fruit globular and bright red. *C. circinata* L'Her. is further distinguished by its branches being greenish and warty; its leaves round-oval, abruptly pointed, and woolly underneath. *C. Amomum* Mill. (*C. sericea* L.), *Silky cornel* or *Swamp Dogwood*, is to be recognized by its purplish branches, and by the fact that the branchlets, stalks, and lower surface of the elliptical pointed leaves are silky and downy. (See also *Chem. News*, 1908, 191.)

These dogwoods are found in all portions of the United States east of the Mississippi.

Dogwood bark was used many years ago as an antiperiodic in *intermittent fever*, but it is only a feeble, astringent tonic. Formerly from one to two ounces of the powder were given in the interval between the paroxysms of intermittent fever. The N. F. IV also recognizes its fluidextract (see Part III). The *dose* of this fluidextract is from half a fluidrachm to a fluidrachm (1.8–3.75 mils).

Cornutine Citrate. *Cornutinæ Citras.—Cornutine citrate* of commerce is a blackish-brown powder. In the belief, now known to be erroneous, that cornutine was the active principle of ergot this salt was recommended as a uterine stimulant. *Dose*, from one-twelfth to one-sixth of a grain (0.005–0.01 Gm.).

Cornutol. *N. N. R.* 1917.—It is a proprietary preparation consisting of a biologically tested liquid extract of ergot containing the water-soluble, alcohol-insoluble constituents of ergot and about 10 per cent. of alcohol. *Dose*, ten to thirty minims (0.65 to 1.8 mils) hypodermically or double that amount by mouth.

Coronilla. *Coronilla scorpioides* Koch (Fam. *Leguminosæ*).—In 1886 Cardot, in a thesis (Nancy) announced that the *Coronilla scorpioides* (Medic.) Koch, a papilionaceous plant of Southern France, is an active cardiac poison. In 1889 Schlagdenhauffen and Reeb (*Rev. Gen. de Clin. et de Thérap.*, July, 1889) insolated a glucoside, *coronillin*, to which they assigned the formula $C_7H_{12}O_6$. It was a yellowish powder, soluble in water, acetone, and amyl alcohol; slightly soluble in chloroform and ether. Heated with diluted

hydrochloric acid an amorphous resin was separated, *coronillein*. This also occurs as a yellow powder, but is not bitter to taste. It is insoluble in water, but dissolves in alcohol, acetone, and chloroform. The physiological studies by Gley, by Schlagdenhauffen and Reeb, and by Maramaldi (*R. T.*, cxxxvi) have demonstrated that coronillin acts upon the heart in a manner similar to digitalis. In small doses it slows the pulse through stimulation of the inhibitory ganglia, and in larger quantity increases the tonicity and contractility of the heart, eventually leading to systolic spasm of the ventricle. This action upon the heart is accompanied by increase in the arterial pressure, followed after a time by lowering of the pressure, which apparently is the result of failure of diastole, causing the amount of blood forced out of the heart at each systole to be insufficient to fill the arteries. The drug also depresses the spinal cord, and lowers the respiratory movements by an action which is believed by Maramaldi to be partly centric and partly peripheral. Death is produced by cardiac arrest.

Locally, coronillin appears to be actively irritant. In Maramaldi's experiments it failed to assert its physiological action when administered to the dog by the mouth, a result believed by the investigator to be due to its decomposition by the acid in the stomach. As it has been found by various clinicians to be active in man when given by the mouth, it is probable that the comparative feebleness of human gastric juice permits of its absorption unchanged. The *dose* given by various clinicians has varied greatly, probably because of differences in purity of the various samples used; of the commercial coronillin the *dose* is commonly stated at present to be one and one-half grains (0.096 Gm.) from four to six times a day, but it must be noted that Schlagdenhauffen affirms that three-fourths of a grain (0.048 Gm.) is a toxic dose. *Coronilla varia* of Europe also probably contains coronillin. (V. Poulet, *B. G. T.*, 1891.)

Coryfin. *N. N. R.* 1917. *Menthyl ethyllycolate*, $C_{10}H_{19}O—CO—CH_2—O—C_2H_5$, is a colorless, inodorous fluid, slightly soluble in water and readily soluble in alcohol and ether. Alkalies immediately release the menthol. It is used as a local anesthetic and sedative to mucous membranes of the upper respiratory tract, especially in *catarrhal conditions* of the *nose*. It has the advantage over menthol in these conditions as being much less irritating. It is employed locally by means of a small swab in strengths of from 50 to 100 per cent. Inhalations of its vapors are also recommended in *laryngitis* and even in *bronchitis*.

Coryl is a mixture of methyl chloride and ethyl chloride. It has been used in dentistry and minor surgery as an anesthetic.

Corylus. *Corylus rostrata* Ait. *Beaked Hazel.*—This is a small indigenous shrub of the Fam. *Betulaceæ*, growing especially in mountainous districts. The nut is invested with a scaly involucre, projecting beyond it like a beak, and thickly covered with short spicules like those of *Mucuna pruriens* DC. (Fam. *Leguminosæ*.) These spicules have been employed by Huebener as an anthelmintic. They operate in the same way as cowhage, and may be administered in the same manner and dose. (See *A. J. P.*, xiv, 280.)

According to Baruttan and Davidsohn (*M. M. W.*, 1909, p. 2482), the *hazel-nut* contains an alcoholic soluble substance which acts as a stimulant to the uterine muscle. An alcoholic extract is placed upon the market under the name of *mensan* which these authors have found useful in the treatment of *uterine hemorrhages* due to chronic endometritis. The dose employed was a tablespoonful twice a day.

Cosaprin. *Sodium acetsulphanilate*, $C_6H_4 < \overset{SO_3Na\,(4)}{NH—CO.CH_3\,(1)}$, is the acetyl derivative of sodium parasulphanilate, and is obtained by the reaction of acetic anhydride upon the sodium salt of *parasulphanilic acid*. *Cosaprin* forms a greenish-white finely crystalline powder of a mild saline taste, freely soluble in water, difficultly soluble in alcohol, and almost insoluble in ether, forming a colorless solution with a weak acid reaction. It has been studied by V. Vámossy and Fenyvessy (*Th. M.*, 1897), who find that it resembles phenacetin very closely in its action, but is characterized by the promptness and shortness of its influence.

Corydalis. *N. F. IV. Turkey Corn. Squirrel Corn. Bicuculla.*—"The dried tubers of *Bicuculla canadensis* (Goldie) Millspaugh, usually somewhat mixed with the dried bulb-like portions of *Bicuculla Cucullaria* (Linné) Millspaugh (Fam. *Fumariaceæ*), and without the presence of more than 5 per cent. of other parts of the plants or other foreign matter." *N. F.* It is described in the N. F. as "the tubers are spheroidal and frequently vertically depressed, the flattened surface more or less concave, up to 15 mm. in diameter; usually single, rarely two or more in a cluster; externally, minutely pitted or nearly smooth; grayish-brown, grayish-black, or amber-colored and more or less translucent; one of the flattened surfaces with a triangular scar from detached roots, the other usually with remains of the slender rhizome; fracture, hard and horny, exhibiting a yellowish, waxy interior, or somewhat tough and granular, exhibiting a yellowish-white interior. The grains of the granulate bulb of *Bicuculla Cucullaria* are ovoid or triangular-ovoid and up to 12 mm. in length; the larger grains distinctly concave on one surface, with a scar at the apex from the detached petiole, and usually attached to the short root-stock in clusters of three; the smaller grains usually separated from the root-stock, with an acute apex, and a scar at the base; externally, yellowish- or grayish-brown, usually translucent; fracture hard and horny, exhibiting a grayish, waxy interior, or granular and tough, exhibiting a whitish interior. Nearly odorless; taste slightly bitter." *N. F.* It is said to yield its active properties to water and alcohol. It contains *corydaline*, *corycavine*, *bulbocapnine*, and *corydine*, all alkaloidal principles. Corydaline, $C_{22}H_{27}O_4N$, is a tertiary base; corycavine, $C_{33}H_{23}O_6N$, is a difficultly soluble base; bulbocapnine, $C_{19}H_{19}O_4N$, which is present in largest amount, was originally called corydaline; corydine is a strong base found in the mother liquors of bulbocapnine. The total amount of alkaloids in the dried bulbs is about 5 per cent. according to Gadarner, who found in addition to the foregoing crystalline alkaloids, corybulbine and several amorphous bases which were not named. The chemistry of these numerous bases is somewhat confused and needs further research work. It is used in the N. F. Compound Elixir of Corydalis, the Fluidextract of Corydalis, and the Compound Fluidextract of Stillingia.

"The powdered drug is light yellow or yellowish-gray and, when examined under the microscope, exhibits numerous oval, ovoid or oblong, simple starch grains, the broad end of the grain sometimes truncate, up to 0.06 mm. in length and fre-

quently with a cleft or horseshoe-shaped fissure in the small end of the grain; occasionally in two-compound grains; altered starch grains up to 0.09 mm. in length; numerous angular or rounded parenchyma cells isolated or in groups and containing more or less altered starch grains the outlines of which are indistinct; tracheæ few with reticulate, simple pores, annular or spiral markings; fragments of epidermal cells with thin brownish walls; sclerenchyma fibers very few or absent; few characteristic sclerotic cells from the rootstock of *Bicuculla Cucullaria*, irregular in outline, mostly elongated up to about 0.75 mm. in length and 0.1 mm. in width, walls heavily lignified and about 0.02 mm. in thickness and porous, occurring isolated or in groups of from two to four; very few sclerotic cells from the rhizome of *Bicuculla canadensis*, mostly isodiametric, uniformly smaller than in *Bicuculla Cucullaria* and with walls about 0.012 mm. in thickness, not distinctly irregular in outline; very few rosette aggregates of calcium oxalate, up to 0.02 mm. in diameter, from the portions of rhizome of *Bicuculla canadensis*. An infusion prepared by placing 5 Gm. of powdered Corydalis in 100 mils of hot distilled water, stirring occasionally during ten minutes and then filtering, is of a light amber color, and gives a precipitate with potassio-mercuric iodide T.S. and a dark blue color with iodine T.S. Corydalis yields not more than 8 per cent. of ash." *N. F.*

For further information concerning the composition of corydalis, see *U. S. D.*, 19th ed., p. 1414.

The tubers of bicuculla are asserted to be tonic, diuretic, and alterative, and are given in *syphilitic, scrofulous*, and *cutaneous affections*, in the *dose* of from ten to thirty grains (0.65–2.0 Gm.). They are also used in the form of tincture and decoction. *Corydalin* or *corydalia*, of the eclectics, is an impure resinous mixture. Fischer and Svell have found that the *Dicentra Cucularia* Torr., a plant closely resembling *B. canadensis*, but producing no tubers, contains three alkaloids, one of which is *protopine*. (*Ph. Archiv*, No. 7, 1903.)

Makoshi has found in *Corydalis ambigua*, which is employed as a medicine in China, a number of the same alkaloids as occur in the above species, and others closely allied to them. (*A. Pharm.*, 1908, ccxlvi, p. 387.) According to Heyl (*P. J.*, 1910, lxxxv, p. 325) the alkaloid protopine occurs in several species of corydalis, although it is not found in *C. cappa*.

Coscinium. *Br. Add.*—The dried stem of *Coscinium fenestratum* Colebr. The stem of this menispermaceous plant has long been used in Ceylon and Southern India as a yellow dye and bitter tonic, and has found its way into Europe under the names of *false columba* and *tree turmeric*. It almost certainly contains berberine and is an efficient stomachic. The Br. Add. recognized an *infusion* (*Infusum Coscinii*, Br. Add.), *dose*, one-half to one fluidounce (15–30 mils); a *concentrated solution* (*Liquor Coscinii Concentratus*, Br. Add.), *dose*, one-half to one fluidrachm (1.8–3.75 mils); and a *tincture* (*Tinctura Coscinii*, Br. Add.), *dose*, one-half to one fluidrachm (1.8–3.75 mils).

Coto Bark.—In the years 1873 and 1874 a bark bearing this name appeared in the London drug market, coming from Bolivia. Its botanical origin still remains unknown. Under the name of *coto-coto*, the bark of a rubiaceous plant (*Palicourea densiflora*) is employed in Brazil in *rheumatism*. Whether this be the Bolivian plant or not is uncertain. (See also *Paracoto*, p. 1536.)

Coto bark occurs in pieces 3 dm. or more long, from 3 to 6 cm. wide, and from 5 to 15 mm. thick. The outer surface is irregular, often looking as though it had been shaved or split off, and in other parts covered with a fine adherent corky layer free from lichens; the inner surface also is irregular, with numerous rather closely placed, longitudinal projecting bark bundles.

The general color approaches cinnamon-brown; upon fresh cross-section the bark is seen to be filled with yellowish spots, except in the outer portions. The odor is aromatic, and much more apparent if bruised; the taste hot, and somewhat aromatic; the powder is very pungent to the nostrils. The microscope shows the outer bark to be composed of thin-walled, colorless, parenchymatous cells, containing starch granules, with numerous yellowish sclerenchymatous cells joined into groups. The inner bark contains numerous yellow bark cells, mostly joined into bundles of from twenty to fifty. For microscopic structure, see *P. J.*, vi, 301, also *Ph. Era*, May, 1888. The coto bark which we have seen in the American market conforms with the original description, but other barks are said to pass under the name. The most important of these is the so-called *Paracoto bark*, which is stated to differ from the true coto bark chiefly in its having a less pungent but more agreeably spicy taste, and being marked with deep whitish furrows upon its surface. Wittstein found in coto bark a volatile alkaloid, a pungent aromatic volatile oil, yellowish-brown soft resin, brown hard resin, starch, gum, sugar, calcium oxalate, tannin, and formic, butyric, and acetic acids. (*A. Pharm.*, iii, 4, 219.) Jobst and Hesse obtained a crystallizable body, *cotoin*, from true coto bark, by making an ethereal extract from the powdered bark, treating this with warm petroleum benzin, and allowing the mixture to stand until clear. The clear liquid yields cotoin in crystals on spontaneous evaporation. The oily resinous residue contains considerable cotoin, which may be obtained by boiling with milk of lime and adding to the solution hydrochloric acid. After twenty-four hours the clear liquid will be found studded with large, glistening, laminated crystals of cotoin, of a pale yellow color. Cotoin (methyl-trioxy-benzophenone), $C_{14}H_{12}O_4$, is sparingly soluble in cold water, more soluble in hot water, insoluble in petroleum benzin, very soluble in alcohol, chloroform, benzol, acetone, and carbon disulphide. Nitric acid becomes blood-red in contact with cotoin, sulphuric acid is colored brownish-yellow, and ferric chloride blackens a dilute solution of cotoin. O. Hesse described a coto bark which did not contain cotoin but *cotellin*, $C_{20}H_{20}O_6$. (*Ph. Ztg.*, 1905, 845.)

Paracotoin, $C_{12}H_8O_4$, is extracted from paracoto bark, in which it exists associated with *hydrocotoin*, $C_{15}H_{14}O_4$, *protocotoin*, $C_{16}H_{14}O_6$, *methylhydrocotoin*, $C_{16}H_{16}O_4$, and *methylprotocotoin*, $C_{17}H_{16}O_6$. Paracotoin may be distinguished from cotoin by giving no reaction with ferric chloride. *Piperonylic* acid (*methyleneprotocatechuic* acid), $C_8H_6O_4$, is present in both barks.

Coto bark is decidedly irritating: its powder, rubbed upon the skin, is said to produce heat and redness, and, according to Burkart, fifteen grains (1.0 Gm.) taken into the stomach produce persistent burning pain, followed by repeated vomiting. The remedy was first introduced as serviceable in *diarrhea*, and seems to have established its reputation. Although observers are not explicit upon this point, it is evident that when there is a tendency

to acute inflammation it must be used with great caution. Inpens (*D. M. W.*, 1913, 1827) from his physiological studies concludes that it acts by lessening intestinal peristalsis. The *paracoto bark* is said to resemble it in its action, but to be much less powerful. The fluidextract and tincture are very eligible preparations, the former made with alcohol in the usual way, and the tincture 1 part in 10 of alcohol, which may be given in from five- to fifteen-minim (0.3–0.9 mil) *doses* every two or three hours.

The active principle, cotoin, is given by Dr. Burkart in *doses* of three-quarters of a grain (0.048 Gm.) every two or three hours. He states that he could detect it in the urine from four to six hours after the ingestion of the dose. Balz (Tokio, Japan) is said to have treated *cholera* successfully by hypodermic injections of three grains (0.2 Gm.) of paracotoin. The value of cotoin in the treatment of *diarrhea* has been confirmed by various clinicians. It has been used in *catarrhal diarrheas* and the *diarrheas* of *tubercular ulceration*, of *typhoid fever*, and of other conditions. (See *B. G. T.*, vol. xi, 167.) It does appear to have some special effect upon the alimentary canal, as, according to Pribram (*Prager Med. Wochens.*, 1880) and Albertoni (*A. E. P. P.*, xvii, 293), it markedly lessens the excretion of indican. Albertoni also believes that it actively dilates the abdominal vessels and thereby hastens absorption, and Bibrana, that it is an antiseptic. It is not probable that cotoin has any general action upon the system, and Jobst found that even fifteen grains (1.0 Gm.) injected hypodermically into the rabbit produced no other than local symptoms. *Dose*, of cotoin, from one to three grains (0.065–0.2 Gm.); of fluidextract of coto, from five to twenty minims (0.3–1.3 mils), four to six times a day.

Cotula. *U. S.* 1870. *Mayweed. Wild Chamomile. Dog Chamomile. Camomille puante, Maroute, Herbe de camomille puante, Herbe de maroute*, Fr. *Hunds-Kamille, Hunds-Kamillenkraut, Stinkende Kamille*, G. *Camomilla fetida, Cotula*, It. *Manzanilla loca*, Sp. *Herba Chamomillæ Fœtidæ. Anthemis Cotula* L.—Mayweed is an annual composite plant, which grows abundantly both in the United States and in Europe. In this country it is found in the vicinity of inhabited places, growing among rubbish, along the sides of roads, and in waste grounds. W. H. Warner found in the flowers volatile oil, oxalic, valeric, and tannic acids, coloring matter, acrid fatty matter, bitter extractive, and salts of potassium, calcium, magnesium, and iron. (*A. J. P.*, 1858, 390.) Pattone (1859) claimed to have found an alkaloid, *anthemidine*, and a crystallizable bitter acid, *anthemidic acid*, but his results have not been confirmed. The whole plant has a strong, disagreeable odor, and a warm, bitter taste, and imparts these properties to water.

The medicinal properties of this species of *Anthemis* are essentially the same as those of chamomile, for which it may be substituted, but its disagreeable odor is an obstacle to its general use. On the continent of Europe it has been given in *hysteria* as an antispasmodic. It has also been thought to be emmenagogue. It is said to have the property of vesicating, if applied to the surface fresh and bruised. The whole plant is active, but the flowers, being less disagreeable than the leaves, are preferred for internal use. The remedy is best administered in the state of infusion.

Cotyledon Umbilicus L. *Navelwort. Pennywort. Cotylet, Nombril de Vénus*, Fr. *Nabelkraut*, G.—This is a perennial, herbaceous, succulent plant, of the fam. *Crassulaceæ*. The plant is a native of England, where it grows upon old walls and rocks, and dry sandy banks.

According to Flétet, it contains trimethylamine, combined with an unknown acid. When the powder of the plant is exposed to the air, it attracts moisture, and exhales a disagreeable odor strikingly analogous to that of fish, and an extract treated with a fixed alkali disengages, even in the cold, an odor which, at first ammoniacal, soon acquires the fishy character referred to. The plant contains cellulose, starch, glucose, mucilage, chlorophyll, yellow coloring matter, a volatile oil of a sandarac-like odor, tannin, iron, and salts of potassium, sodium, calcium, and iron, with 0.9 per cent. of nitre, and 95 per cent. of water. (*Ann. Thér.*, 1865, 125.) It has been highly lauded in *epilepsy* (for references, see 16th edition *U. S. D.*), but it has very feeble and uncertain therapeutic properties. *Dose*, of fresh juice, from one-half to one fluidounce (15–30 mils), two or three times a day; of fluidextract, one fluidrachm (3.75 mils); of dry extract, five grains (0.32 Gm.); to be increased and given steadily for months.

Coumarin. *N. F. IV. Coumarinum.*—The N. F. describes it as "the anhydride [$C_6H_4(CH)_2OCO = 146.05$] of ortho-oxycinnamic acid, occurring naturally in Tonka, Melilot and other plants, or prepared synthetically." *N. F.* It is extracted from the plants by boiling alcohol (80 per cent.), the liquid concentrated, mixed with four volumes of water, filtered to remove fat, and set aside to crystallize. Synthetically it may be prepared by boiling a mixture of salicylic aldehyde, acetic anhydride, and anhydrous sodium acetate under a reflux condenser, distilling the oily liquid which separates, and crystallizing the distillate. "Coumarin occurs in colorless, prismatic crystals, having a characteristic, fragrant odor and a bitter, aromatic and burning taste. Sparingly soluble in cold water, more readily soluble in hot water, freely soluble in alcohol, ether, or chloroform; also soluble in fixed or volatile oils. When heated to between 67° and 68° C. (152.6°–154.4° F.) it melts, and at about 100° C. (212° F.) it commences to sublime; at from 290° to 291° C. (554°–555.8° F.) it boils without decomposition. Coumarin dissolves in solution of sodium, or potassium hydroxide, producing a yellow color and forming sodium or potassium coumarate, from which carbon dioxide precipitates the Coumarin. Coumarin is precipitated in colorless needles on the addition of hydrochloric acid to its hot concentrated sodium or potassium hydroxide solution. A saturated aqueous solution of Coumarin forms a precipitate upon the addition of iodine T.S. The precipitate is at first brown and flocculent and afterwards, on shaking, clots together, forming a dark green curdy mass and leaving the liquid clear (distinction from *vanillin*). Coumarin is not extracted from its solution in ether by ammonia water (distinction from *vanillin*). Warm 0.1 Gm. of Coumarin with 1 mil of an alcoholic solution of sodium hydroxide (1 in 4), add a few drops of chloroform and again warm; the mixture does not possess the disagreeable odor of phenyl-isocyanide (*acetanilid*)." *N. F.* It is employed in perfumery as a fixative and in the N. F. to flavor castor oil and also to disguise the odor of iodoform.

Cow Tree. *Palo de Vaca. Palo de Leche.*—The milky juice of the *Brosimum Galactodendron* D.

Don (fam. *Urticaceæ*) is much used in South America instead of cream in tea and coffee, etc. It is obtained by making incisions in the tree, is white and viscous, turns sour on exposure to the air, and deposits a caseous substance. According to the analysis of Boussingault, its composition varies very much, but it always contains a large percentage of fatty matters (32.2 per cent.), and much less casein, albumen, sugar, and phosphates. (*P. J.*, ix, 679.)

Crab Orchard Salt.—A mild, saline purgative, obtained by evaporating the waters of springs at Crab Orchard, Lincoln County, Kentucky. According to R. Peter, the composition of the dry salt is: magnesium sulphate, 63.19 per cent.; sodium chloride, 4.77; sodium sulphate, 4.20; potassium sulphate, 1.80; calcium sulphate, 2.54; calcium, magnesium, and iron carbonates, and silica, 0.89; water of crystallization and loss, 22.61; total, 100.00. *Dose*, from one to two teaspoonfuls. (See *A. J. P.*, 1874, 5.)

Crabs' Claws. *Chelæ Cancrorum.*—These, finely powdered, were formerly used in medicine. In 100 parts are 60 parts of calcium carbonate and 14 of calcium phosphate, with 26 of animal matter.

Crabstones. *Lapilli Cancrorum. Crabs' Eyes. Oculi (Calculi) Cancrorum. Yeux (Pierres) d'Ecrevisses*, Fr. *Krebsaugen, Krebssteine*, G.—Concretions found in the stomach, one on each side, of the European crawfish, at the time the animal is about to change its shell; chiefly procured in the province of Astrakhan, in European Russia. The crawfish are bruised with wooden mallets and laid up in heaps to putrefy. The animal remains are then washed away, and the stones picked out. They are inodorous, insipid bodies, somewhat hemispherical in shape, of a whitish or reddish color, hard and stony consistence, and laminated texture. They are very variable in size, weighing from one to twelve grains each. They effervesce with acids, and, without dissolving, become converted, owing to the animal matter which they contain, into a soft transparent mass, retaining the original shape of the stone. By this character they are distinguished from counterfeit stones, which are sometimes fabricated of chalk mixed with mucilaginous substances. They consist of calcium carbonate and phosphate, cemented together by animal matter. Crabstones have been used as an absorbent and antacid, given in the same dose as prepared chalk.

Cranberries. Fruit of *Vaccinium macrocarpon* Aiton. (Fam. *Ericaceæ.*)—These familiar berries, so well known as an article of diet, have come into notice as a source of citric acid. For method, see *J. P. C.*, 4e sér., xviii, 439. The leaves of the *Vaccinium Vitis-idæa* (L.) have been studied by Edo Claassen (*A. J. P.*, 1886) and A. M. Karger (*P. J.*, vol. lxx). They contain *arbutin, hydroquinone*, and *tannin. Benzoic acid* has also been recognized as normally present in small amounts. In the *cranberry*, Edo Claassen found an uncrystallizable glucoside, *oxycoccin*.

Crealbin.—Egg albumen in combination with creolin-Pearson, used for the internal administration of creolin, forms a brownish powder containing 50 per cent. creolin.

Creolin is said to be an emulsion of cresol, obtained by means of rosin soap. There are in the market at least two sets of preparations, the one of German the other of English origin. An analysis of creolin-Pearson, published by Pfrenger (*A. Pharm.*, 1890, 701), gives: phenols, 2.67; hydrocarbons, 44.94; organic bases, 2.76; sodium, 1.45; resin, 32.45; sulphur, 0.248; chlorine, 0.14; water (by difference), 5.34. The phenols consisted of ortho- and meta-cresol, with traces of phenol and the oxyleucols; the hydrocarbons, of the higher homologues of benzene, with naphthalene and anthracene; the bases belonged to the quinoline group. Creolin forms a milky emulsion or mixture with water; with chloroform, ether, and absolute alcohol it mixes in all proportions. It is sometimes called *cresoline* or *sanatol*.

The statements made concerning the germicidal powers of creolin have been extraordinarily at variance. Thus, Eisenberg asserted that a three per cent. solution of creolin destroyed anthrax spores in forty-eight hours, but Van Ermengen (*B. A. R. B.*, 1889, iii) failed to kill them by thirteen days' exposure to a 10 per cent. solution. Burgess reached the conclusion that a 20 per cent. solution of creolin was equivalent to a 2.5 per cent. of phenol while Schneyder finds that creolin is from two to four times as strong as pure phenol, according to the species of bacteria on which it is tested. The last conclusion seems to be as near to the truth as it is possible to decide in view of the contradictory reports and corresponds with the findings of the U. S. Hygienic Laboratory. It has been claimed that creolin is non-poisonous, but although its toxicity is certainly much less than that of phenol, it is not entirely innocuous. Mugdan (*V. A. P. A.*, 1890, cxv, p. 131) found that doses of from 5 to 10 Gm. of Pearson's creolin are fatal to rabbits when given by the mouth, and Korach (*D. M. W.*, 1895), Van Ackeren (*B. K. W.*, 1889) and Bitter (*B. M. J.*, 1890) reported serious, although not fatal, poisoning in adults. Fliesburg (*Northwestern Lancet*, 1891, xi, p. 417) reports death in a three-weeks-old baby from 30 drops of creolin. The symptoms of creolin poisoning have resembled those of carbolic acid; namely, nausea, vomiting, frequently convulsions or coma, with albuminous, bloody or smoky urine.

Internally, creolin is probably an useful remedy when it is desired to check fermentation in the alimentary canal. Locally applied, it has been largely used with success in the treatment of *scabies*, in the form of a 5 per cent. ointment with vaseline. Although creolin has been used for various surgical purposes, its most popular employment has been as a disinfectant douche for internal cavities. In *ammoniacal cystitis*, washing out the bladder with a ½ per cent. solution of creolin has yielded excellent results. In the treatment of *acute* and *chronic dysentery* large enemas of a ½ per cent. solution may be used; in the case of infants the strength should be about one-half of this. For washing out the uterus after *labor*, the strength of the creolin solution should be 1 per cent.

Creolin is recommended by Jaksch as a deodorant to iodoform; a mixture of from 1 to 2 per cent. of creolin with iodoform produces a compound *creolin-iodoform* of a faint aromatic odor, soluble in alcohol and ether, and believed to possess the therapeutic properties of iodoform. Water removes from it the creolin and leaves the iodoform.

Creosote Albuminate. *Creosotum Albuminatum. Nutrincreosote.*—A yellow-gray powder, which is said to contain 40 per cent. of pure creosote and to be free from irritant action.

Creosote Benzoate.—This is a yellowish liquid, soluble in alcohol and ether. It is used mainly for

its antiseptic action as a spray in the treatment of nose and throat diseases.

Creosote - calcium Chlorhydrophosphate.—A syrupy mass consisting of a mixture of calcium chlorhydrophosphate and creosote carbonate. It is used in *phthisis* and *scrofula* in *doses* of 5 to 8 grains (0.3–0.5 Gm.) twice or thrice daily in emulsion.

Creosote Iodide. *Creosotide.*—A product obtained by causing iodine to enter into combination with the cresol constituents of beechwood creosote. It contains approximately 25 per cent. of its weight of iodine. It is an amorphous brownish powder, practically insoluble in water and having a faint characteristic odor and taste. It is prescribed in incipient *tuberculosis* with alleged good results; also in *asthma* and as a gastric and intestinal antiseptic. *Dose*, one-fourth to one-half grain (0.016–0.032 Gm.) three or four times a day.

Creosote - phenyl - propionate. *Proposote.*—This is employed as a stimulating expectorant and is stated to have the advantage over creosote that it does not disturb the stomach as it is not affected by acid media, but passes into the intestine and is broken up by the duodenal juices with the liberation of creosote. It is administered in *doses* of five to ten minims (0.3 to 0.6 mil).

Creosote Phosphate. *Creosoti Phosphas. Phosote.* $PO_4(C_6H_7)_3$.—A combination of creosote and phosphoric acid, in the form of a syrupy, colorless liquid, with almost no odor or taste of creosote. It contains about 80 per cent. of creosote and 20 per cent. of phosphoric anhydride. The *dose* is fifteen to thirty minims (1–2 mils). *Creosote Phosphate* and *Creosote Tannophosphate* (*Tophosote*) have also been introduced as antiseptics.

Creosote Phosphite. *Phosphotal.*—This is a reddish-yellow, oily liquid with a faint creosote-like odor, dissolving readily in both water and alcohol. It represents over 90 per cent. of creosote. It is intended as a substitute for that remedy, especially in the treatment of *phthisis*. The *dose* is three to ten minims (0.2 to 0.6 Gm.).

Creosote Tannate. *Creosotum Tannicum. Creosal. Tannosal.*—The tannic acid ester of creosote. It is obtained by heating equal quantities of beechwood creosote and pure tannin to 80° C. (176° F.) and adding gradually phosphorous oxychloride and purifying the product. It is soluble in water, alcohol, glycerin, and acetone and occurs as a dark brown hygroscopic powder. It is astringent and antiseptic, and may be given in daily *doses* of fifteen grains (1 Gm.), representing 9 grains (0.6 Gm.) of creosote.

Creosote Valerate. *Creosotum Valeras.* (*Eosote.*)—A mixture of the valeric esters of the phenols contained in creosote. It forms a mobile oily liquid, boiling at about 240° C. (464° F.), and soluble in alcohol and ether. This substance as an internal medicine is practically identical in its properties with the creosote carbonate. *Dose*, three to ten minims (0.2–0.6 mil).

Cresatin. *N. N. R.* 1917. *Metacresylacetate.*—The acetic acid ester of metacresol, $CH_3C_6H_4OCH_3CO$. A colorless oily liquid, insoluble in water, soluble in immiscible solvents. Volatile with steam. Used as an external application, either pure or diluted, as an antiseptic and analgesic.

Crescentia. *Crescentia Cujete* L.—The fruit of this West Indian and South American plant (fam. *Bignoniaceæ*) has been found by Gustav Peckoldt to contain *crescentinic acid* and a blue coloring matter allied to indigo. (*Ph. Rund.*, Aug., 1884.)

Cresin. *Cresaprol.*—Made by dissolving 25 per cent. of cresol in 75 per cent. of a solution of sodium cresoxyl-acetate. A brown, clear liquid soluble in alcohol and water. It is said to be less toxic than phenol. *Cresin* is used in ½ to 1 per cent. solution as a disinfectant for wounds.

Cresol Iodide. *Iodocresol. Traumatol.* $C_6H_3I.(CH_3)OH$.—This is formed by the action of potassium iodide solution upon an emulsion of cresol and water. It contains but one atom of iodine, while losophan or cresol triiodide contains three atoms, and, consequently, a higher percentage of iodine. It is a violet-red, odorless, amorphous powder; insoluble in water, acids, and alcohol; dissolving with difficulty in ether, readily in alkaline solutions, and freely in chloroform. It contains 55 per cent. of iodine, and has been commended as powerfully antiseptic, non-irritant, and having local anesthetic properties. It is used locally in *syphilitic* and other *ulcers*, *eczema*, especially when attended with much discharge, *intertrigo*, and various other skin diseases. Also as a substitute for iodoform in surgery. In *herpes* a 10 per cent. traumatol collodium has been found very useful, and a 5 to 10 per cent. traumatol zinc ointment has been highly commended. Pure traumatol may also be used as a dusting powder.

Cresol Naphthol.—A brown, viscous, tar-like liquid, insoluble in, but emulsifying with, water. Guinard states that it is a very active germicide, and that it is impossible to produce poisoning in the lower animals by giving by the mouth, largely on account of its inducing vomiting at once. Its aqueous solution, like that of creolin, has the disadvantage of depositing in wounds.

Cresol Preparations.—The fact that cresol, which is only sparingly soluble in water, is readily dissolved in saponaceous solutions has led to the introduction of a number of proprietary disinfectants of this nature. There is no reason to believe that any of them has any real advantage over the official compound solution of cresol, but some of them are sufficiently used to justify a few words of description.

Several of these have been bacteriologically tested by the United States Hygienic Laboratory. We give below a table showing the phenol coefficient of these as published in this bulletin (see *Phenol*, Part I).

Preparation	*Phenol Coefficient* Without organic matter	With organic matter
Bacterol	1.58	1.34
Creolin-Pearson	3.25	2.52
Cresoleum	2.90	1.75
Germol	2.12	1.79
Kresolig	2.18	1.48
Kreso	3.92	2.32
Liq. Cresolis Comp. (U. S. P.)	3.00	1.87
Lysol	2.12	1.57
Saponified Cresol	1.03	0.57
Trikresol	2.62	2.50

Ethylenediaminetricresol or *kresamin* is a mixture of tricresol with ethylenediamine. It is a colorless, aqueous liquid, having a phenol-like odor, and after standing in the air becomes of a light yellow color without losing disinfecting power. According to H. Eckstein, it is an exceedingly powerful antiseptic, especially adapted to the preserving of specimens for microscopic use. As a local application the same author has found it very valuable in those cases of *eczema* in which

there was a pronounced secondary infection of the skin, and also in *sycosis* and similar parasitic diseases. Bandages of it wet with a solution of from 1: 4000 to 1: 400 were kept applied to the part. In *lupus* and some similar conditions local protracted baths of from three to twelve hours' duration, with a concentration of 1: 4000, were found efficacious. From 10 to 15 per cent. ointments of it were also employed.

Lysol was introduced by Gerlach (*Z. Hyg.*, 1891) and since then has been very widely used. Fox (*Penna. Health Bulletin*, 1910) has shown that lysol is inferior to the official Compound Solution of Cresol. As regards its toxicity, while it is probably less poisonous than phenol, it is an energetic poison. According to Blumenthal, there are about 100 cases annually of lysol poisoning in Berlin alone. Fries (*M. M. W.*, 1904), from a study of 38 cases of lysol poisoning, of which 17 were fatal, reaches the conclusion that the toxic dose for adults is from 10 to 12 mils. Cramer (*Cb. Gyn.*, 1898) has reported a death from its use as a vaginal douche.

Cresol Salicylates. *Cresalols. Cresol Salols.* $C_6H_4\begin{cases}OH\\COOC_6H_4CH_3\end{cases}$.—Salicylates may be prepared from ortho-, meta-, or para-cresol by a process similar to that used in the making of salol. They are insoluble in water, slightly soluble in cold alcohol, and are easily crystallized. The *meta-cresol salicylate* is the cresalol generally referred to by that name. It fuses at 74° C. (165.2° F.), and is easily soluble in alcohol and ether. Nencki states that the cresalols decompose in the alimentary canal, and are efficient substitutes for phenyl salicylate, and less poisonous. (*C. R. A. S.*, Feb., 1889.)

Cresol Triiodide. *Meta-cresol Tri-iodide.* (*Losophan.*) $C_6HI_3(CH_3)OH$.—A fine, yellowish powder, with a rather strong, but not disagreeable odor; insoluble in water, soluble in alcohol, ether, and chloroform, freely so in oil. Merck (*Jahresbericht*, 1892, 77) describes it as obtained in colorless needles, fusing at 121.5° C. (251° F.). It contains 78.39 per cent. of iodine. A specimen prepared by Friedrich Baeyer & Co. was found by Petersen (*M. M. W.*, July, 1891) to yield its iodine with difficulty, passing through the alimentary canal almost without absorption; applied to the mucous membrane of the nose in *acute inflammation*, it was found to act very well in checking secretion and lessening inflammatory action.

Cresosteril.—This is stated to be the oxalic acid ester of metacresol and represents seven parts of cresol and three parts acid. While it is claimed by its promoters to be a chemical union, when dissolved in water, it is split up into its constituents. Cresol, it is stated, is more active as a germicide when in the presence of acids, hence the asserted efficiency of this compound. Bierotte (*Hyg. Rund.*, 1910, xx) finds that a ¼ per cent. solution of *cresosteril* is approximately equivalent in germicidal power to a 2 per cent. solution of phenol.

Cresotinic Acid.—*Cresotic acid. Homosalicylic Acid. Oxytoluic Acid,* $C_6H_3\begin{cases}CH_3\\OH\\COOH\end{cases}$.—Although there are ten possible isomeric cresotinic acids, according to the location in the benzyl ring of the hydroxyl and the methyl radicals, the only ones which have been used in medicine are the three methyl derivatives of ortho-oxybenzoic (salicylic) acid. These may be made artificially from cresol by a reaction analogous to that used in making salicylic acid.

Although it was at one time believed that the small amounts of cresotinic acid which were formerly present in the synthetic salicylates had a toxic effect upon the system, the experiments of Demme (*Th. M.*, 1890) and of May (*B. M. J.*, 1909, ii, p. 791) and others show that they are only slightly more toxic than salicylic acid. May has also found that both the meta- and ortho-cresotinic acids were actively germicidal. In 1876 Buss suggested the use of sodium cresotinate—a mixture of the sodium salts of the three isomers—as a antipyretic. The value of cresotinic acid in *rheumatic fever* has been carefully investigated by Stockmann (*J. P. Ex. T.*, 1912, iv, p. 97) who comes to the conclusion that *sodium meta-cresotinate* is capable of entirely replacing the salicylates but has no advantage over it; that the ortho salt is an active antirheumatic but also depressant to the heart; that the para salt is much less efficient.

Crocus. *N. F. IV. Saffron. Stigmata Croci. Spanish Saffron. Safran,* Fr. Cod. *Crocus,* P. G. *Safran,* G. *Zafferano,* It. *Azafran,* Sp.—"The stigmas of *Crocus sativus*, Linné (Fam. *Iridaceæ*), without the presence of more than 10 per cent. of the yellow styles or other foreign matter." *N. F. IV.* "The dried stigmas and tops of the styles of *Crocus sativus*, Linn." *Br.*, 1898. *Crocus* was dropped at the 1914 revision of the British Pharmacopœia and the ninth U. S. P. revision. It has been recognized by the National Formulary IV.

Crocus sativus is a perennial plant, with a rounded and depressed bulb or corm, from which the flower rises a little above the ground, upon a long, slender, white, and succulent stem. The flower is large, of a beautiful lilac or bluish-purple color, and appears in September or October. The leaves are radical, linear, slightly revolute, dark green upon their upper surface, with a white longitudinal furrow in the center, paler underneath, with a prominent flattened midrib, and enclosed at their base, together with the tube of the corolla, in a membranous sheath, from which they emerge soon after the appearance of the flower. The style hangs out on one side between the two segments of the corolla, and terminates in three long convoluted stigmas, which are of a rich orange color, highly odorous, rolled in at the edges, and notched at the summit. The stigmas of the *Crocus orientalis* are used in the East.

C. sativus, or *autumnal crocus*, is believed to be a native of Greece and Asia Minor, where it has been cultivated from the earliest ages. There are three main varieties of it, the French, the Grecian, and the Chinese. The first of these is superior in color and flavor, the second in the amount of yield, while the third is said to unite these qualities. Saffron is also cultivated for medicinal use in Sicily, Spain, France, England, and other temperate countries of Europe. Large quantities of saffron are raised in Egypt, Persia. We cultivate the plant in this country chiefly as a garden flower, although some of the drug of very fine quality has been produced in Pennsylvania; the high cost of labor in America will probably prevent the possibility of its coming into commerce. Wild saffron is found growing in uncultivated fields in Southern Russia; Tichomirow believes that these are varieties of *C. sativus* and *C. speciosus* Marsh. Biebr., var. *β-Pallassii* (*C. Palassii* Marsh. Biebr.). He

further states that wild saffron from these sources is in no way inferior to the cultivated. (*A. Pharm.*, 1903, 656.)

In England the flowers appear in October, and the leaves continue green through the winter; but the plant does not ripen its seed, and is propagated by offsets from the bulb. The flowers are gathered soon after they show themselves, as the period of flowering is very short. The stigmas, or summits of the pistils, together with a portion of the style, are separated from the remainder of the flower, and carefully dried by artificial heat, or in the sun. During this process they are sometimes made to assume the form of a cake by pressure; but the finest saffron is that which has been dried loosely. The two forms are distinguished by the names of *cake saffron* and *hay saffron*. Five pounds of the fresh stigmas are said to yield one pound of the dried. The English saffron, formerly most highly esteemed in this country, has disappeared from our market; what may be sold under the name is probably derived from other sources. For an account of the cultivation in England, see *P. J.*, June, 1887. The Spanish saffron is generally considered the best in the United States, although most European writers on Materia Medica give the preference to the French saffron. The better grades of Spanish saffron are known as *Valencia* saffron, while *Alicante* saffron was said by Maisch to contain scarcely more than 50 per cent. of genuine saffron. According to Landerer, the stigmas of several other species besides those of *C. sativus* are gathered and sold as saffron in Greece and Turkey.[1]

Properties.—Saffron has a peculiar, sweetish, aromatic odor, a warm, pungent, bitter taste, and a rich deep orange color, which it imparts to the saliva when chewed. It is described in the N. F. as follows: "Stigmas 3, united or separate, attached to the summit of the style; usually about 25 mm. in length, cornucopia-shaped, of a dark, rich red color, the margin dentate or fimbriate; styles about 10 mm. in length, more or less cylindrical, solid, yellowish. Odor strong, peculiarly aromatic; taste bitterish, aromatic. When chewed it colors the saliva orange-yellow. Under the microscope, the upper end of the stigma shows numerous cylindrical papillæ about 0.15 mm. in length, among which occur a few spherical pollen grains, the latter being nearly smooth, and from 0.04 to 0.07 mm. in diameter; occasionally some of the pollen grains have germinated and show pollen tubes. When placed in sulphuric acid, the stigmas are immediately colored blue, gradually changing to violet, and finally become a deep wine-red color. Add 0.01 Gm. of finely powdered Crocus to 100 mils of cold water, allow it to macerate for several hours and filter; on adding 10 mils of this filtrate to 100 mils of water, it gives a distinctly yellow-colored solution. Macerate 0.01 Gm. of Crocus in 5 mils of methyl alcohol; a deep orange color is imparted to the liquid. Macerate 0.01 Gm. of Crocus in 5 mils of acetone, alcohol, or dehydrated alcohol; a distinct lemon-yellow color is produced. With corresponding quantities of Crocus and ether a very light lemon-yellow color is produced. With corresponding quantities of Crocus and chloroform a very slight, yellow tinge is imparted; and with corresponding portions of Crocus and xylene, benzene, carbon disulphide, or carbon tetrachloride, the solvents remain colorless. When Crocus is pressed between filter paper, the paper does not display transparent spots due to the absorption of oil. It loses not more than 14 per cent. of its weight when dried at 100° C. (212° F.). Crocus yields not more than 7.5 per cent. of ash and the ash is not fusible." *N. F.* The following tests were given in the Br., 1898: "Incinerated with free access of air, dried Saffron does not deflagrate (absence of nitrates), and yields about 7 per cent. of ash. It should not lose more than 12.5 per cent. of moisture when dried at 212° F. (100° C.)."

Analyzed by Vogel and Bouillon-Lagrange, saffron afforded 65 per cent. of a peculiar extractive matter, which they named *polychroïte*, but later researches have shown that it is a mixture of the glucoside crocin, sugar, and essential oil. (Planchon, *Drogues Simples*, vol. i, 210.) Kayser obtained (*Ber. d. Chem. Ges.*, 1884, 2228) pure *crocin*, having the formula $C_{44}H_{70}O_{28}$, as a yellow powder, easily soluble in water and diluted alcohol, only slightly soluble in absolute alcohol, and giving with concentrated sulphuric acid a deep blue color, which turns violet, then cherry-red, and finally brown. It is easily decomposed by lime or baryta water into *crocetin* and a dextro-rotatory sugar which Kayser calls *crocose*. The crocetin is a red powder, not soluble in water, but easily soluble in alcohol and ether. Its solution in alkalies shows an orange-yellow color, from which solution acids separate it again in orange-colored flecks. Its formula is $C_{34}H_{46}O_9$, or, according to Schmuck and Marchlewski, $C_{15}H_{20}O_4$. Kayser also found a colorless bitter principle, to which he gave the name *picro-crocin* or *saffron bitter*, and the formula $C_{38}H_{66}O_{17}$, which is also of glucoside character. Saffron contains, according to Henry, about 10 per cent. of essential oil. This has the formula $C_{10}H_{14}O$, boils at 208° to 210° C. (406.4°–410° F.), is yellow, of a hot, acrid, bitterish taste, and heavier than water.

The high price of this medicine gives rise to frequent adulterations. Water is said to be very often added in order to increase its weight. Oil or glycerin is also added for the same purpose, or to improve the appearance. In some specimens the dyed corolla of the crocus with the attached stamens is abundant. Sometimes the flowers of other plants, particularly *Carthamus tinctorius*, or safflower, *Calendula officinalis*, or marigold, and *arnica* are fraudulently mixed with the genuine stigmas. They may be known by their shape, which is rendered obvious by throwing a portion of the suspected mass into hot water, to expand them. (See *Carthamus.*) A specimen of this adulteration was at one time introduced into the American market, by the name of *African Saffron.* (Maisch, *A. J. P.*, March, 1872, p. 110.) Other adulterations are the fibers of dried beef, the stamens of the crocus, distinguishable by their yellow color, the stigmas previously exhausted in the preparation of the infusion or tincture, and various mineral substances, easily detected upon close examination. The flowers of a Brazilian plant named *Feminella*, or *Feminelle*, have, accord-

[1] At the International Exhibition in London in the year 1862, Geo. B. Wood noticed a specimen of saffron from the island of Ceylon, closely resembling that from *Crocus sativus*. It consisted of the stigmas of the *Crocus orientalis*. According to Charles A. Heinitsh (*A. J. P.*, 1867, p. 38), saffron was formerly cultivated to a considerable extent in Lancaster County, Pa. According to Heim, *Crocosma aurea* Pl., which is cultivated in Southern Africa as a dye-stuff, affords an excellent substitute for saffron, the dried petals giving, when treated with water, a brilliant yellow solution. The yellow coloring matter is more soluble in diluted alcohol and in alkaline solution than water, but is insoluble in absolute alcohol and in benzene. The partly dry aqueous extract gives with sulphuric acid a blue coloration, passing to violet, similar to that obtained from saffron.

ing to M. J. L. Soubeiran, been employed for the adulteration of saffron. They may be detected by shaking, gently but repeatedly, a large pinch of the suspected saffron over a piece of paper. The flowers of Feminella, being smaller and heavier, separate and fall, and may be seen to consist of very short fragments, with a color like that of saffron, but a rusty tint which the latter does not possess. (See *Ph. Rev.*, 1898, 258.) The name Feminelle is also applied in commerce to the dyed styles of crocus or ligulate flowers of Calendula. J. Müller recommends concentrated sulphuric acid as the most certain test of saffron. It instantly changes the color of pure saffron to indigo blue. (*Chem. Gaz.*, May, 1845.) An adulteration which has been largely practised appears to consist of yellow-colored chalk or barium sulphate, made into a thin paste, probably with honey, and attached to the stigmas, sometimes isolated, sometimes in groups of five or six, enveloping them almost completely. If this saffron be kept in a dry place, and often handled, the paste becomes partly broken up, and the colored powder spreads itself in the mass and the envelope. The chalk can at once be detected by shaking the suspected saffron with water, and treating the precipitated powder with hydrochloric acid, when effervescence will occur. A less than the ordinary brightness of color in the saffron should lead to suspicion of this adulteration. Much can be told as to the purity of saffron by agitating the suspected flowers in distilled water; if the drug be pure the liquid will remain clear, slowly assuming a fine pure yellow tint; the saffron also will retain its red color for hours. Another excellent plan is to scatter a pinch of the flowers upon the surface of warm water, when the stigmas should spread out and display their proper form. Minute fragments of red saunders, which are often added to saffron, may be separated by agitating with water. For an elaborate discussion of adulteration, see article by Kraemer, *A. J. P.*, 1898, p. 386. Adulterations of crocus may sometimes be detected by remembering that the pollen grains are spheroidal, nearly smooth, and from 0.040 to 0.075 mm. in diameter. In various European markets there has been offered a saffron largely adulterated with borates, chlorides, and other salts of sodium and potassium, and yet retaining the physical properties of saffron of high character. These and other adulterations with inorganic salts can be detected by the amount of ash left on burning, genuine saffron leaving from five to seven per cent. This saffron also yielded immediately to water an orange-yellow color. Further, some of it at least was hygroscopic, so that when rubbed up between the fingers into a ball it retained that form instead of being elastic as is true saffron.

Attention has been called to a product of the Cape of Good Hope, named *Cape saffron*, which has a remarkable resemblance to genuine saffron, having a similar odor, and yielding a similar color to water, though the flowers themselves are differently colored. It is the flower of a small plant very abundant at the Cape, belonging to the family of *Scrophulariaceæ*, and is said by Pappé of Cape Town, to possess medicinal virtues closely resembling those of true saffron. The flowers have been used successfully in the convulsions of children. (*P. J.*, vi, 462, 1865.)

Choice of Saffron.—Saffron should not be very moist, nor very dry, nor easily pulverized; nor should it emit an offensive odor when heated upon a porcelain dish. The freshest is the best, and that which is less than a year old should, if possible, be selected. It should possess in a high degree the characteristic properties of color, taste, and odor. When agitated with water it should color it bright yellow, and it should not effervesce in the presence of a diluted acid. If it does not color the fingers when rubbed between them, or if it has an oily feel, or a musty flavor, or a black, yellow, or whitish color, it should be rejected. In the purchase of this drug in cakes, those should be selected which are close, tough, and firm in tearing; and care should be taken to avoid *cakes made up of safflower.*

As its activity depends, partly at least, on a volatile ingredient, saffron should be kept in well-stoppered vessels. Some recommend that it should be enclosed in a bladder and introduced into a tin case.

Saffron was extensively used by the ancients and by medieval physicians, as a highly stimulant antispasmodic and even narcotic emmenagogue, and is still employed to some extent upon the Continent; but in Great Britain and the United States it has fallen into well deserved and almost complete desuetude. In domestic practice saffron tea is occasionally used in *exanthematous diseases*, to promote the eruption. At present it is chiefly used to impart color and flavor. Saffron should be preserved in tightly-closed containers protected from light.

A tincture of saffron is recognized in the N. F. and it is also an ingredient of several compound pills and tinctures.

Dose, from ten to thirty grains (0.65 to 2.0 Gm.).

Crotaline.—Under this name the *venom of the rattlesnake, Crotalus Adamanteus*, was recommended by Mays in the treatment of *phthisis, asthma, neuralgia*, and *epilepsy* several years ago. More recently, Spangler (*N. Y. M. J.*, September 9, 1911) revived this substance as an *antiepileptic*. He gave as a theoretic explanation of its use that the blood of epileptics coagulated with abnormal rapidity and that the venom delayed coagulation. Jenkins and Pendleton (*J. A. M. A.*, 1914, lxiii, p. 1749), in an extended study of 49 patients, found not only that the blood of epileptics was not more coagulable than normal, but that the number of convulsions after the use of crotallin was greater than without the drug. Thom (*B. M. S. J.*, 1915, clxxi), from a study of 203 cases, likewise reached the conclusion that the treatment was of no value. The danger of the injection is not merely from the injurious effects of the venom itself, but, as shown by Anderson (*J. A. M. A.*, 1914, lxii, p. 893), also from the fact that the commercial preparations are not sterile. The beginning *dose* recommended is one two-hundredth of a grain (0.0003 Gm.) hypodermically, which may gradually be increased as the patient forms a tolerance for the drug. The injections are generally followed by severe local irritation and should not be repeated for at least a week.

Crurin. *Quinoline-bismuth sulphocyanide.* ($C_9H_7NHSCN)_3Bi(SCN)_3$. *N. N. R.* 1917.—*Quinoline-bismuth rhodanate*, a reddish-yellow powder with weak odor of quinoline, insoluble in water, alcohol, and ether. *Crurin* of the markets is a preparation containing 25 per cent. of active ingredients with starch. According to the researches of Müller, it is bacteriologically active, and it has been especially recommended in the treatment of ulcers of the leg, by dusting them at intervals in

full strength or diluted, *pro re nata*. It has also been highly recommended by E. Jacobi in *gonorrhea*, according to the following formula: Rub fifteen grains (1.0 Gm.) of crurin with seventy-five minims (4.6 mils) each of distilled water and glycerin and gradually add sufficient distilled water to make six and one-half troyounces (201.5 Gm.).

Cryogenin. *Kryogenin. Metabenzamino carbazide.*—A white, crystalline, odorless and somewhat bitter substance. It is soluble in alcohol and ether and slightly soluble (about 1–40) in water. It has antipyretic properties and is employed in the treatment of *phthisis*.

Cryptocarya. *Cryptocarya australis* Bentham. (Fam. *Lauraceæ*.)—From the bark of this Queensland tree, T. L. Bancroft (*Austral. Journ. Pharm.*, March, 1887) has separated an alkaloid which is said to be a powerful respiratory poison.

Crystallin.—This is a solution of *pyroxylin* (1 part) in methyl alcohol (4 parts) and amyl acetate (15 parts). It is similar in appearance and properties to collodion and the film is, like the latter, capable of elasticity on the addition of castor oil and Canada balsam. It is said, however, to be a better vehicle for remedial agents like chrysarobin and iodoform, and this fact, coupled with its cheapness as compared with collodion, seems to give it a slight advantage over the latter, provided that its content of the harmful wood alcohol be considered as being too slight to cause any injurious effects.

Cucurbita. *Citrullus vulgaris* Schrad. *Watermelon.*—The seeds of the watermelon are employed, to a considerable extent, as a domestic remedy in *strangury* and other affections of the urinary passages. Power and Salway (*P. J.*, lxxxiv, 760) found in watermelon seeds a fixed oil very similar to that which is found in pumpkin seeds. The Russian peasants are said to employ watermelon in the treatment of *dropsy, urinogenital affections, chronic hepatic congestion*, and *chronic intestinal catarrh*. Manassein (*Vratch*, Nov., 1881), found that the melon honey acts upon the lower animals as a very powerful diuretic, and causes, when in sufficient dose, fall of the arterial pressure, rapid pulse, and death from cardiac paralysis. A resin, extracted in the amount of 0.3 per cent. from the press cake of watermelon seed, when administered to a dog in doses of 1 gramme exhibited no physiological activity. A chemical examination of this resin led, however, to some results of interest, inasmuch as it yielded, besides a little phytosterol, a new crystalline alcohol, $C_{24}H_{40}O_4$, which has been designated *cucurbitol*.

The pulp of the root of *Lagendaria vulgaris*, or *gourd*, is said by Chapin to be a powerful and even drastic purgative, and to be used by the natives of the Sandwich Islands successfully in the treatment of *dropsy*. (See *N. Y. Journal of Med.*, 1855, 203.)

Cudbear. *N. F. IV. Persio. Orseille de terre*, Fr.—"A purplish-red powder prepared from species of *Roccella* De Candolle, *Lecanora* Acharius, or other lichens." *N. F. IV.* Cudbear is described in N. F. IV as follows: "An aqueous or alcoholic preparation of Cudbear is of a deep red color which is rendered lighter in tint by the addition of acids and changed to purplish-red on the addition of alkalies. Agitate 2 Gm. of Cudbear occasionally with 200 mils of water during thirty minutes and then filter; the deep red-colored filtrate conforms to the following tests: Add to 5 mils of the filtrate 5 drops of glacial acetic acid and boil for one minute; then add 5 drops of stannous chloride T.S., and boil again for one minute; the liquid is only faintly pink (*brazilwood or logwood* which produce solutions of a deep red color); add 25 Gm. of kaolin to 100 mils of the filtrate in an Erlenmeyer flask, shake frequently during one hour and then filter; the filtrate is almost entirely decolorized in comparison with some of the original filtrate (*a number of coal tar colors*). Cudbear yields not more than 35 per cent. of ash, consisting mainly of sodium chloride." *N. F. IV.*

Cudbear was introduced into the National Formulary solely for coloring liquids. Two preparations were made official, *Tinctura Persionis*, N. F. IV (*Tincture of Cudbear*) and *Tinctura Persionis Composita* (*Compound Tincture of Cudbear*). Both tinctures are used to give a deep red color to syrups, tinctures, solutions, and elixirs of the National Formulary. George M. Beringer has given much attention to cudbear with a view of securing a uniform product. (See *Proc. New Jersey Pharm. Assoc.*, 1912, 56.) He declares that all of the ordinary methods, as color charts, colored yarns, threads, glass, etc., are unsatisfactory and inapplicable to pharmacy. He advocates the preliminary purification of cudbear by washing it with water to remove the sodium chloride so largely used as a diluent and the ammonium salts with their empyreumatic odor. He states that if the washing is properly done the cudbear loses scarcely any of its tinctorial power. He gives a table showing comparative values of eight tinctures prepared with various menstrua. He believes that the best results, however, would follow the preparation and use of a standard extract. Alexander Gardner gives the name *persionin* to an acetone extract of cudbear made as follows: The process consists in percolating commercial cudbear with purified benzin until free from wax, then drying the drug, repacking it in a percolator and percolating it with acetone to exhaustion—about 2500 mils being required for 1000 Gm. of cudbear. The acetone is recovered by distillation, the residual extract heated for thirty minutes to 98.8° C. (210° F.) in a porcelain capsule, then pulverized and placed in a sulphuric acid desiccator for three days, during which it loses about 25 per cent. of its weight. So obtained, "persionin" is a black, lustrous powder with an aromatic odor, soluble in alcohol, glycerin, chloroform, ether, and hydro-alcoholic liquids, but is only sparingly soluble in water. Five different lots of cudbear yielded, respectively, 6.5, 7, 6, 5, and 5.5 per cent. of persionin. Each sample of "persionin" was tested by dissolving 1 part in 100 parts of alcohol and 3 parts of glycerin. One mil of this was added to 99 mils of distilled water, and in each particular the color was the same. (*J. A. Ph. A.*, 1913, 51–52.) H. V. Arny (*J. A. Ph. A.*, 1913, 47) proposes to remove a brown pigment present in cudbear (which interferes with the tinctorial power) by macerating an alcoholic extract with chloroform and extracting the residue with acetone. The final product is then "scaled."

Because of the difficulty of completely extracting cudbear the liquid preparations are rarely uniform in color value. For this reason the N. F. uses powdered cudbear in several preparations, allowing it to macerate until all color is extracted. This plan results in more uniform coloring than if the tincture was directed. For the chemistry of cudbear, see under *Litmus*, p. 1472.

Culilawan. *Cortex Culilaban.*—An aromatic bark, produced by *Cinnamomum Culilawan*, Blume (*Laurus Culilawan* L.), (Fam. *Lauraceæ*), a tree of considerable size, growing in the Molucca Islands, Cochin-China, and other parts of the East. It is usually in flat or slightly quilled pieces, 5 to 10 cm. long, 2.5 to 3.5 cm. wide, and 2 to 4 mm. thick. Sometimes the bark is thinner and more quilled, bearing considerable resemblance to cinnamon. The periderm is for the most part removed, but when present is of a light brownish-gray color, soft to the touch, and somewhat spongy. The color of the bark itself is a dull, dark, cinnamon brown, the odor highly fragrant, the taste agreeable, aromatic, and not unlike that of cloves. The active constituent is a volatile oil, smelling like a mixture of the oils of cajuput and cloves. Culilawan has the medicinal properties of the aromatics, but is rarely used. (See *Cortex Caryophyllata.*)

Cumin. *Cyminum* Lond. *Cuminum* Ed. *Cumin*, Fr. *Kreuzkümmel, Mutterkümmel, Römischer* (*langer, scharfer*) *Kümmel*, G.—The so-called *cumin seeds* are the fruit of the *Cuminum Cyminum* L., an annual umbelliferous plant, which is a native of Egypt, but is cultivated for its fruit in Sicily, Malta, and other parts of Europe.

The cumin fruits (*seeds*) are elliptical, flat on one side, convex, furrowed, and rough on the other, from 5 to 6 mm. in length and about 1.5 mm. in thickness, and of a light brown color. Each has seven longitudinal ridges. Two mericarps are sometimes seen united. Their odor is peculiar, strong, and heavy; their taste warm, bitterish, aromatic, and disagreeable. They contain about 2.5 per cent. of an essential oil, which is lighter than water, yellowish, and has the sensible properties of the fruits. It consists of three distinct oils, one a hydrocarbon, *cymene*, $C_{10}H_{14}$, recognized now as *isopropyl-p-methyl-benzene*, another *cuminol*, $C_{10}H_{12}O$, which may be regarded as *cuminic aldehyde*, $C_{10}H_{11}OH$, and the third a terpene, $C_{10}H_{16}$. Dumas, a long time since, obtained a cymene identical with that of oil of cumin seeds, by dehydrating camphor, and Paternó prepared it in a similar way from oil of turpentine. (*J. P. C.*, 4e sér., xx, 409.) In his discovery Paternó seems, however, to have been preceded by seven chemists, C. R. A. Wright apparently having the priority. (*A. J. P.*, xlvi, 117; see especially *A. J. P.*, xliv, 452.) Cumin aldehyde has also, together with cymene, been obtained from the fruits of *Cicuta virosa* L. (Trapp, *Ann. Ch. Ph.*, cviii, 386; see also *Schim. Rept.*, 1909, 49.) In medicinal properties cumin fruits resemble the other aromatic umbelliferous fruits. *Dose*, fifteen to thirty grains (1–2 Gm.).

Cumol. *Cumene. Pseudocumol.* $C_6H_3(CH_3)_3$ (1 : 3 : 4).—An oily fluid derived from coal tar, boiling at 168° to 178° C. (334.4°–352.4° F.). Cumol has been especially recommended by Krönig (*Centralbl. f. Gyn.*, 1894) for the purpose of sterilizing catgut, which is placed in the cumol and slowly heated up to 160° C. (320° F.). After two hours it is removed and freed from the adhering cumol by petroleum benzin.

Cunila. *Cunila origanoides* (L.) Britt. (*C. Mariana* L.) (Fam. *Labiatæ*), *American or Common Dittany. Sweet Horsemint. Stonemint.*—A small indigenous perennial herb, growing on dry, shady hills, from New York to Georgia, and Illinois and Arkansas westward, and flowering in June and July. The whole herb has a warm, pungent taste and a fragrant odor, dependent on an essential oil. This, according to Philip Milleman, of Chicago, is of reddish-amber color, becoming light yellow by exposure to light, of a delicate, fragrant odor, very similar to that of oil of monarda, of a warm pungent taste, and of the sp. gr. 0.920. It is readily soluble in alcohol, ether, and chloroform. On spontaneous evaporation, it leaves a small crystalline residue. Iodine decomposes it, producing white vapors; by sulphuric acid it is reddened and decomposed, by nitric acid resinified, and by hydrochloric acid decolorized, though its color returns on exposure. It is slightly rubefacient; in the *dose* of five or ten minims (0.3–0.6 mil) it is carminative, and of from fifteen to twenty minims (0.9–1.3 mils) diaphoretic. The same author found in the dried herb tannic acid, a trace of glucose, gum, bitter extractive, resin, and salts of potassium, calcium, magnesium, and iron. (*A. J. P.*, Nov., 1866, 495.) American dittany is a gently stimulant aromatic, analogous to the mints.

Cuprargol.—*Cuprargol*, which is copper-silver albuminate, is a dull, grayish-white powder, which is slowly soluble in water, and has been used as an astringent in ophthalmology in 20 per cent. solutions.

Cupratin.—Is made by combining sodium albuminate with copper sulphate and subsequent purification of the copper albuminate. It is used as a germicide.

Curare. *Woorari. Woorara. Woorali. Urari.*—This powerful South American arrow poison was first brought to Europe by the celebrated traveller Waterton; it was in the form of a thick syrup, but as it now occurs in commerce it is a blackish extract, brittle, somewhat resinoid in appearance, encrusting the sides of gourds or little rude earthenware jars, into which it has been poured in a liquid state. The drug varies much in strength. It has been variously described. According to the researches of Planchon (*P. J.*, xi, 491), there are really four distinct varieties of *curare*. (1) That from the Upper Amazon, obtained from the *Strychnos Castelnœi* Wedd., and possibly from *S. Yapurensis* G. Planch. (2) That from the Upper Orinoco, extending towards the Rio Negro, yielded by *S. Gubleri* G. Planch.; this is the variety spoken of by Humboldt. (3) That of British Guiana, obtained from *S. toxifera*[1] Schomb., associated with *S. pedunculata* Benth. and *S. cogens* Benth. (4) That of French Guiana, made out of *S. Crevauxiana* Baill. (*S. Crevauxii* G. Planch.). These varieties are, however, commercially indistinguishable. The preparation of woorari has been witnessed by various travellers and variously described. (See *P. J.*, xvi, 502; *B. F. M. R.*, Oct., 1865; *P. J.*, x, 1881.)

The method followed in the Upper Amazon region is to make a decoction of the bark of *Strychnos castelnœi*, to which one-tenth of the stem of another liane is added. This is then concentrated by evaporation. To this concentrated juice then is added the leaves of *Petiveria alliacea*, the stems of *Dieffenbachia Seguine*, the root barks of two plants of the *Piperaceæ* and a species of *Marcgravia*. The fluid extract is then evaporated until it is in the condition of an extract, and poured into small vessels. Joubert asserts that the Tecuma Indians use, besides *S. Castelnœana* Weddell, *Cocculus toxi-*

[1] The bark of the *Strychnos toxifera* has been chemically examined by Villiers, who finds that its purified extract resembles in its chemical and physiological relations ordinary curarine. He was not able, however, to obtain the pure alkaloid. (*J. P. C.*, fifth series, vol. xi.)

ferus and an arum (*Taya*), which he found to be very poisonous. According to Kobert (*Ph. Ztg.*, June, 1885), *Malouetia nitida* Spruce (fam. *Apocynaceæ*), or *Guachamaca*, a plant which is abundant in the Orinoco and Rio Negro districts, enters largely into the composition of curare. The alkaloid, *guachamacine*, isolated by T. Schiffer in 1883, is very closely allied to, if it be not identical with, curarine, in both its chemical and its physiological activity. It is entirely possible that the varieties of woorari vary in their alkaloid and their physiological properties.

Allied, it may be, to the third variety of woorari are the arrow poisons brought by W. S. W. Ruschenberger from Colombia, and studied by W. A. Hammond and S. Weir Mitchell. (*Am. J. M. S.*, July, 1859.) *Corroval* was in dark brown lumps, having the appearance of a vegetable extract, and of an intensely bitter and persistent taste. They found its activity to depend upon the presence of a peculiar alkaloid, *corrovaline*. It resembles curare in that it produces general paralysis without previous spasm, but differs, in paralyzing also the heart. *Vao* or *Bao* appears to be a dilute and adulterated form of carroval. It would seem, therefore, that there is a variety of "woorari" used in South America which is more closely allied to strophanthus than to the true curares.

The term "curare" has no specific meaning, but according to Whiteford is simply the Indian word for poison, and it is evident that there are a considerable variety of arrow poisons used in South America under the same name.

In 1898 Boehm classified the curares of the markets as *Tubocurare*, originating from the Amazon, preserved in hollow bamboo canes, and said to contain about 9 to 11 per cent. of *tubocurarine* as its poisonous constituent; *Gourd curare*, derived from *Strychnos toxifera*, very rarely met with, and having curarine and a second alkaloid soluble in ether for its active principle; *Jor curare*, obtained from *Strychnos castelnœi*, also exceedingly rare in the European markets, containing three alkaloids—*protocurine*, having a feeble curare action; the non-poisonous *protocuridine;* and *protocurarine*, which is more actively poisonous than is curarine. (*Ph. Ztg.*, xlii, 41.)

R. Boehm has isolated the two bases, *curarine* (also called *tubocurarine* from its source in the curare packed in bamboo tubes), $C_{19}H_{26}ON_2$, and *curine*, $C_{18}H_{19}O_3N$. The free tubocurarine forms an amorphous brown-red mass. Boehm (*Ber. d. Chem. Ges.*, xx, 143) states that curine exists in many specimens of curare; it may also be obtained from the aqueous extract of curare. It is much less poisonous than the accompanying curarine. Curine is a crystalline powder fusing at 161° C. (321.8° F.), slightly soluble in cold water, freely soluble in alcohol, chloroform, and dilute acids. It forms a voluminous white precipitate with metaphosphoric acid.

Woorari is one of those poisons whose active principle passes through animal membranes with difficulty, and hence when given by the stomach or rectum it acts very slowly, and in some cases elimination may proceed so rapidly that no marked influence is exerted, because not enough of the alkaloid is in the blood at any one time. There is also reason for believing that the alkaloid is destroyed in the liver. When injected into a vein, or introduced by the hypodermic needle or the poisoned arrow into the cellular tissue, it acts with great promptness. The symptoms caused are progressive loss of muscular power, the animal growing weaker and weaker, the respirations becoming more and more feeble, until death by asphyxia results.

The action of curare is to paralyze the peripheral ends of the motor nerves, the muscles, when directly stimulated, retaining their irritability. In mammals, as a result of the paralysis of the phrenic nerves, there is failure of respiration, and consequent death from asphyxia. The heart usually continues beating after cessation of the breathing, only very large doses affecting the arterial pressure directly. If, however, the dose be sufficient, the drug paralyzes the peripheral ganglia, thereby causing a dilation of the blood vessels with consequent fall of pressure, increased rate of the pulse through lack of inhibitory control, loss of irritability in the secretory nerves, and other modifications of functions of less importance. Tillie (*A. E. P. P.*, xxvi) has brought forward evidence to show that there is a primary excitation of the spinal cord which, however, in ordinary poisoning, is masked by paralysis of the motor nerves. The sensory apparatus does not seem to be affected, unless by enormous doses. Glycosuria has been frequently noticed in animals as the result of curare poisoning. According to Morishima (*A. E. P. P.*, 1889, xlii), this is apparently independent of the amount of glycogen in the liver or muscles.

Voisin and Lionville describe two types of poisoning in human beings. In the milder type the pulse is increased in force and frequency, respirations somewhat rapid, the temperature a little elevated, and the urine contains sugar. After larger quantities symptoms begin with severe chill, tremors, small pulse, and early loss of power in the lower extremities, later the cold skin becomes hot, the pulse rapid and full, there is marked reduction of the body temperature, with redness of the skin, and frequently profuse sweating. In non-fatal cases, the paralysis of the extremities rarely lasts for an hour, but the fever may continue for several days.

In cases of poisoning from the injection of woorari, a ligature around the limb between the place of injection and the heart, the free exhibition of diluents and evacuants, and artificial respiration when required, are the measures recommended. (*Ed. M. J.*, 1867, 667.)

According to the experiments of Joseph Tillie, *curine* has no influence upon the motor nerves, but acts both in the frog and in the mammal upon the heart, belonging physiologically to the digitalis group. Boehm states that the presence of curine in curare can be recognized by the white precipitate made by metaphosphoric acid.

Although curare has in the past been used as an anti-convulsant in *tetanus* and *hydrophobia*, it is a remedy of no practical value, because the phrenic nerve is no less susceptible than the other motor nerves of the body, and if given in sufficient doses to control the spasm, will likely lead to fatal asphyxia. According to the elaborate experiments of Du Cazal (*A. G. M.*, Sept., 1869), from one-fourteenth to one-seventh of a grain (0.005–0.01 Gm.) daily were borne by a dog without inconvenience; at the dose of ten milligrammes the characteristic phenomena began to show themselves, but disappeared in a few hours; with fourteen milligrammes the animal perished. For man the *doses* administered by subcutaneous injection were from one-twelfth to one-third of a grain (0.005–0.02 Gm.) of the crude curare. According to Bernard, curarine is at least twenty times as strong as curare.

Curcuma. *U. S.* 1870. *Turmeric. Curcuma longa* L. (Fam. *Zingiberaceæ.*)—The rhizome of this plant is perennial, ovate or pear-shaped, and internally of a deep yellow or orange color. The plant is a native of Southern Asia, and is cultivated particularly in China, Bengal and Java, whence the root is exported to London, about 2,400,000 Kg. being shipped annually. The best is said to come from China.

The dried rhizome (*Safran des Indes, Souchet des Indes,* Fr.; *Kurkuma, Gelbwurzel,* G.; *Curcuma,* It., Sp.; *Zirsood,* Arab.; *Huldie,* Hindoo) is in cylindrical or oblong pieces (*Curcuma longa*), from 0.5 to 1.5 cm. in thickness, distinctly annulate, tuberculated, somewhat contorted, externally yellowish-brown or greenish-yellow, internally deep orange-yellow, hard, compact, breaking with a fracture like that of wax, and yielding a yellow or orange-yellow powder. Another variety, *Curcuma rotunda,* or *round turmeric* is ovate or pear-shaped, about the size of a pigeon's egg, and marked externally with numerous annular wrinkles. Sometimes it comes cut into two tranverse segments. The two varieties have a close resemblance in sensible properties, and are derived from the same plant, though formerly ascribed to different species. The odor of turmeric is peculiar; the taste warm, bitterish, and feebly aromatic. It tinges the saliva yellow. Analyzed by Pelletier and Vogel, it was found to contain lignin, starch, a peculiar yellow coloring matter called *curcumin,* a brown coloring matter, gum, an odorous and very acrid volatile oil, and a small quantity of calcium chloride. Curcumin was obtained, mixed with a little volatile oil (about 1 per cent.), by digesting the alcoholic extract of turmeric in ether, and evaporating the ethereal tincture. It has been obtained by F. A. Daube, in deep yellow crystals, of a high luster, by a process which may be found in the *A. J. P.* (1871, 308). C. L. Jackson and Menke have submitted turmeric root to a thorough examination, and give the following results: The turmeric oil was first removed from the ground root by treatment with ligroine, then the curcumin mixed with a large quantity of resin is extracted with ether, and finally purified by crystallization from alcohol. The oil extracted by ligroine was dark yellow, and amounted to 11 per cent. of the root. The purified curcumin amounted to 0.3 per cent., and melted at 178° C. (352.4° F.). Analyses of the pure curcumin, of several of its salts, and of derivatives, show its formula to be $C_{10}H_{10}O_3$. It is brown in mass, but yellow in the state of powder, without odor or taste, insoluble in benzin, scarcely soluble in water, but very soluble in alcohol, ether, and the oils. It is a diatomic monobasic acid. When treated with weak oxidizing agents it yields vanillin. The alkalies rapidly change its color to a reddish-brown, and paper tinged with tincture of turmeric is employed as a test of their presence. The paper is rendered brown also by boric acid, which it thus serves to detect. When treated with a mixture of sulphuric and boric acids it yields a product called *rosocyanin,* because it dissolves in alcohol with a fine red color, and is turned blue by alkalies. Its alcoholic solution produces colored precipitates with lead acetate, silver nitrate, and other salts. Turmeric is used for dyeing yellow, but the color is not permanent. James Cook has found in turmeric an alkaloid, which forms crystallizable salts with sulphuric and nitric acids, and, separated from these acids by ammonia, yields a semi-crystalline precipitate. He observed also indications of a second base. (*P. J.,* Nov., 1870.) Ivanow Gajewsky also states that there is an alkaloid in the root. (*Pharmacographia,* 641.)

This root is a stimulant aromatic, bearing some resemblance to ginger in its operation, and is much used in India as a condiment, the so-called *curry powder.* It is a constant ingredient in the curries so generally employed in the East. In former times it had some reputation in Europe as a remedy in *jaundice,* but its medicinal action was purely imaginary, based on the old doctrine of signatures, and at present it is employed only to impart color to ointments and other preparations.

Turmeric, when used as an adulterant, may be detected by means of a mixture of boric and sulphuric acids, but according to A. E. Bell, a much better test is afforded by the use of the reagent made by dissolving 1 gramme of diphenylamine in 20 mils of 90 per cent. alcohol, carefully adding 25 mils of pure sulphuric acid. To a little of the suspected powder, placed on a slide, a drop of the reagent is added with a glass rod. Spots of a fine purple color immediately develop, which may be readily recognized with the microscope.

Turmeric paper, used as a test, is prepared by the method described in the appendix of the U. S. P.

Curry Leaves. *Currie.*—The leaves of the *Murraya Kœnigii* Spreng. (fam. *Rubaceæ*), a tree of India, are very largely used in that country as an aromatic, stomachic stimulant; when powdered and mixed with spices and other substances it forms *curry powder,* which is much used for seasoning food, rice, cooked dishes, etc.; it is also employed in *dyspepsia, diarrhea,* and even *dysentery.* According to J. G. Prebble (*Pharmacographia Indica,* vol. i), curry leaves yield to distillation a small quantity of volatile oil, and also contain a greenish-black resin, and a glucoside, *kœnigin.* The clear oil extracted from the seeds is known as *simabolee oil.*

Cusparia Bark. *Cusparia Cortex. Br.* 1898. *Angustura, U. S.* 1870. *Angustura (Angostura) Bark. Carony Bark. Cortex Angusturæ. Angusture vraie,* Fr. Cod. *Angusture,* Fr. *Angusturarinde,* G. *Cortecoia dell' Angustura,* It. *Corteza de Angostura,* Sp.—"The dried bark of Cusparia febrifuga, *DC." Br.,* 1898. This bark was dropped from the U. S. Pharmacopœia at the revision of 1880 and from the British in 1914. The subject of Angostura bark in its botanical relations has been involved in some confusion. Humboldt and Bonpland were the first to throw light upon its true source. Unable to attach it to any known genus, they erected it into a new one with the title of *Cusparia,* a name of Indian origin, to which they added the specific appellation of *febrifuga.* On their authority, *Cusparia febrifuga* was generally believed to be the true source of the medicine, and was recognized as such by the London College. But it appears from the researches of Hancock, who resided for several months in the country of the Angustura bark tree, that it is doubtful whether the plant described by Humboldt and Monpland is that which yields the drug, and not another species of the same genus. Hancock proposed for the plant of the Orinoco the title of *Galipea officinalis,* which was adopted in the U. S. P., 1870. This name was afterward changed by Hancock to *Cusparia officinalis,* which is now generally accepted as the correct origin for true Angostura bark.

Cusparia febrifuga is a small tree, irregularly

branched, with an erect stem from three to five inches in diameter, and covered with a smooth gray bark. The leaves are alternate, petiolate, and composed of three leaflets, which are oblong and pointed at each extremity. They are very smooth and glossy, of a vivid green color, marked occasionally with small whitish round spots, and, when fresh, of a strong odor resembling that of tobacco. The flowers are numerous, white, arranged in axillary and terminal peduncled racemes, and of a peculiar unpleasant odor. The fruit consists of five two-valved capsules, of which two or three are commonly abortive. The seeds, two of which are contained in each capsule, one often abortive, are round, black, and of the size of a pea. The tree grows abundantly on the mountains of Carony, between the 7th and 8th degrees of N. latitude, at the height of from six hundred to one thousand feet above the level of the sea.

The bark is generally brought from the West Indies packed in casks; but, according to Brande, the original package as it comes from Angostura consists of the leaves of a species of palm, surrounded by a net-work of sticks.

Cusparia bark "occurs in flattened or curved pieces, or in quills, generally about 10 to 12 Cm. long, 2.5 Cm. wide, and 2 mm. thick. The outer layer usually consists of a gray or yellowish cork which is often soft and easily removed, disclosing a hard, dark brown inner layer; the inner surface is light brown and frequently laminated. The fracture is short and resinous; on the fractured surface many white points are visible. A transverse section exhibits numerous cells filled with acicular crystals of calcium oxalate and small oil glands, but seldom any sclerenchymatous tissue other than small isolated groups of bast fibers. Odor musty; taste bitter." *Br.*, 1898. Calcium oxalate raphides are abundant in the bark, but the most characteristic peculiarity is the presence of numerous cells a little larger than the other parenchymatous cells and completely filled with oil or a yellowish resin. The odor of Angustura bark is peculiar and disagreeable when fresh, becoming fainter with age; the taste is bitter and slightly aromatic, leaving a sense of pungency at the end of the tongue. According to Fischer, it contains volatile oil, bitter extractive, a hard and bitter resin, a soft resin, a substance analogous to caoutchouc, gum, lignin, and various salts. Oberlin and Schlagdenhauffen (1878) found in the bitter extractive an alkaloid, *angosturine*, $C_{10}H_{40}O_{14}N$, which melts at 85° C. (185° F.), is crystallizable, and is turned red by pure sulphuric acid, and green by sulphuric acid with admixture of nitric acid. The volatile oil, which may be obtained by distillation with water, is of a pale yellowish color, lighter than water, of an acrid taste, and with the odor of the bark. Beckurts and Froeger (Gildemeister and Hoffman, *Ætherische Oele*, p. 601) found as its essential ingredient a sesquiterpene alcohol, $C_{15}H_{26}O$, to which they give the name *galipol*. It $H_{17}O_3N$. Körner), melting at 89° C. (192.2° F.) and is optically inactive. *Cadinene*, $C_{15}H_{24}$, is also present and gives left rotatory character to the oil. A small quantity of an inactive sesquiterpene, *galipene*, is also present, as well as traces of a terpene which is probably *pinene*. The *cusparine* of Saladin has not been found by other investigators. Beckurts and Nehring (*A. J. P.*, 1892, 410) announced the discovery of four alkaloids in Angustura bark—viz., *galipine*, $C_{20}H_{21}O_3N$, melting at 115.5° C. (240° F.) and crystallizing in slender lustrous needles of white color; *galipidine*, $C_{19}H_{19}O_3N$, melting at 111° C. (231.8° F.) and crystallizing in silky lustrous plates of white color; *cusparine*, $C_{20}H_{19}O_3N$ ($C_{19}H_{17}O_3N$, Körner), melting at 90° C. (192.2° F.) and readily soluble in alcohol, ether, chloroform, acetone, and benzene, more sparingly in light petroleum; and *cuspardine*, $C_{19}H_{17}O_3N$, melting at 78° C. (172.4° F.) and crystallizing in minute slender white needles. Its salts are less soluble than those of galipine and galipidine, but more readily than those of cusparine. The four alkaloids are tertiary bases. (See also *A. Pharm.*, 233 (1895, No. 6), 410.) Beckurts and Nehring also extracted the essential oil, amounting to 1.5 per cent. It had a sp. gr. at 15° C. (59° F.) of 0.956. Distilled under a pressure of 35 mm. it commenced to boil at 153° C. (307.4° F.) and the greater part distilled between 200° and 220° C. (392°–428° F.) the last portions becoming solid when artificially chilled. (See also *A. Pharm.*, 1897, 518.) They found the bitter principle *angosturine*, which when purified was white and melted at 58° C. (136.4° F.). A glucoside was also found, the solution of which fluoresced; but it was not investigated. Troeger and Beck assert that angostura bark contains cusparine, $C_{19}H_{17}ON_3$ (thus confirming Körner's formula) *galapoidine*, $C_{19}H_{15}ON_4$, and a new alkaloid of the formula $C_{16}H_{13}O_2N$. (*A. Pharm.*, 1913, ccli, 246.) For a description of false Angustura barks, see *U. S. D.*, 19th ed., p. 417.

Angustura bark has long been used by the natives of South America and the West Indies as a stimulant tonic. In large doses it also evacuates the stomach and bowels, and is often employed for this purpose in South America. It is said to be peculiarly efficacious in bilious *diarrheas* and *dysenteries*, and has been recommended in *dyspepsia* and other diseases requiring a tonic treatment. The testimony, however, of practitioners in Europe and the United States, is not strongly in its favor.

The Br., 1898, *Infusion of Cusparia* was prepared as follows: "Cusparia Bark, in No. 20 powder, 1 *ounce* (Imperial) or 50 grammes; Distilled Water, boiling, 1 *pint* (Imp. meas.) or 1000 *mils*. Infuse in a covered vessel for fifteen minutes; strain." *Br.*, 1898. Under the name of *Infusum Angusturæ* this preparation was official in the U. S. Pharm., 1870, made in the proportion of half a troyounce of Angustura bark in a pint of water. *Dose*, two fluidounces (60 mils), repeated every two, three, or four hours.

It may be given in powder, infusion, tincture, fluidextract, or extract. *Dose*, of the extract, five to fifteen grains (0.32 to 1 Gm.), which, however, according to Hancock, is inferior to the powder or infusion. To obviate nausea, it is frequently combined with aromatics. *Dose*, in substance, ten to thirty grains (0.65 to 2.0 Gm.). In larger quantities it is apt to produce nausea. It is known best in the proprietary preparation called "Angustura Bitters."

Cuttlefish Bone. *Os Sepiæ, Os de Sèche* (*Seiche*), Fr. *Sepie, Weisses Fischbein*, G.—This is a calcareous body, situated underneath the skin, in the back of the *Sepia officinalis* L., or *cuttlefish*, of European seas. It is oblong-oval, from five to ten inches long, and from one and a half to three inches broad, somewhat convex on both sides, with thin edges, of a rather firm consistence upon the upper surface, very friable beneath, and composed of numerous layers, loosely connected, so as to give to the mass a porous con-

sistence. It is lighter than water, of a white color, a feeble sea odor, and a saline taste. It contains, according to John, from 80 to 85 per cent. of calcium carbonate, besides animal matter, a little common salt, and traces of magnesia. Its fine powder may be given as an antacid, and it is sometimes used as an ingredient of tooth-powders. Small pieces of it are often put into bird cages that the birds may rub their bills against them, and the powder is employed for polishing. Another product of the cuttlefish is a blackish-brown liquor, secreted by a small gland in an oval pouch, communicating externally near the rectum by a long excretory duct, through which the animal is said to have the power of ejecting it at will. This, when taken from the fish, is dried, and used in making the water-colors *sepia* and a writing fluid used by the inhabitants of China, India and Japan. It is not the India ink of commerce, which is made from a specially prepared lampblack.

Cyclamen. *Cyclamen europœum* L. *Pain de Porceau, Arthanite,* Fr. *Erdscheibe, Erdbrod, Schweinbrod,* G. *Sowbread.*—This is an herbaceous, perennial, stemless plant, of the subalpine mountainous regions of Europe. Some of the species of *Cyclamen* are among the most popular of winter plants on account of their beautiful foliage and exquisite flowers. The corm is globular, with many branched rootlets, almost black without, and white within, inodorous, and, when fresh, of a bitter, acrid, burning taste. By drying it loses much of its acridity, and is said to be rendered edible by roasting. Hogs are said to root it up from the ground and to eat it with impunity, and hence the common name "Sow Bread." The corm is a drastic cathartic, and is used to cause abortion, but has in such cases produced fatal gastro-enteritis. Its active principle appears to be *arthanitin* of Saladin, the *cyclamin* of S. De Luca. This is a poisonous glucoside, which, when boiled with diluted acids, splits into *cyclamiretin*, $C_{15}H_{22}O_2$, and glucose. It is white, amorphous, inodorous, and, when held a short time in the mouth, intensely acrid, extending its action even to the throat. With cold water it swells and becomes gelatinous, but is readily dissolved, and form a solution which froths like soap and water, and is coagulated by a heat of about 65.5° C. (150° F.). Alcohol dissolves it with difficulty when cold, but freely when hot; it is soluble in glycerin with the aid of heat; and is insoluble in ether, chloroform, carbon disulphide, and the essential oils. Its formula, according to an analysis by Klinger, is $C_{20}H_{34}O_{10}$, although Kobert (*Chem. Cb.*, 1893, i, 32) makes it one of the class of saponins, and gives it the formula $C_{30}H_{32}O_{10}$, which is the same as that of sarsaparilsaponin and smilacin. T. W. C. Martius recommends the following method of preparing it. The tubers, collected in the autumn, dried and powdered, are mixed with animal charcoal, and exhausted at a boiling heat by alcohol of 0.825; the tincture is filtered, concentrated, and set aside for six or eight weeks, when the cyclamin is deposited. This should be washed on a filter with alcohol till it passes colorless, and if the filtrate be concentrated, and set aside, it will deposit a further quantity in a few weeks. The whole is then mixed with animal charcoal and treated with boiling alcohol, which will slowly deposit the pure cyclamin on cooling. *Dose,* of powdered root, is said to be from twenty to forty grains (1.3–2.6 Gm.).

Cyclea Peltata H. and Th.—An East Indian drug, according to Sutterheim, contains an alkaloid, $C_{27}H_{31}O_4N_2$, which he named *cycleine;* it has the effect of a cardiac poison accompanied by action on the respiratory centers. (*Pharm. Weekbl.*, 1906, No. 32.)

Cycloform. *N. N. R.* 1917. *Isobutyl-para-amino-benzoate.* $C_6H_4(NH_2)COO.CH_2.CH(CH_3).CH_3$.—It occurs as white, crystalline scales, almost insoluble in water. Impens (*Ther. Geg.*, 1910, li, p. 348) asserts, however, that the saturated solution, which contains but 0.02 per cent., will produce complete anesthesia of the cornea of the eye and that even a solution of one-third this strength has a distinct anesthetic influence. He has also experimented with ethyl- and propyl-esters of amido-benzoic acid and finds they likewise possess anesthetic properties. According to this author, the salts of *cycloform* are more soluble, but dissociate in solution and are therefore locally irritant. Large doses produce in the lower animals drowsiness, general weakness and collapse with formation of methemaglobin.

Because of its sparing solubility cycloform has not been widely used for surgical purposes, but has received considerable commendation as a dusting powder in painful *ulcers,* especially after *burns,* and in *tuberculous laryngitis.* It appears not only to lessen the pain, but to stimulate the healing processes. Zeller (*Med. Klin.*, 1910) finds that the ointment is useful to relieve the itching of *chronic eczema* and other skin diseases as well as the pain of *anal fissure* and *hemorrhoids.* In making the ointment, Franke (*Aerzt. Rund.*, 1913) recommends that *cycloform* be dissolved in olive oil before it is incorporated with the ointment base. The dusting powder, which may be made with kaolin, should contain from 10 to 20 per cent. of cycloform. The ointment should contain from 5 to 20 per cent.

Cydonium. *U. S.* 1880. *Quince Seed. Semen Cydoniæ. Semeneces (Pépins) de Coing,* Fr. *Quittenkerne, Quittensamen,* G. *Semi di Cotogno,* It. *Simiente de Membrillo,* Sp.—*Cydonia vulgaris,* Pers. (Fam. *Rosaceæ*), or common quince tree, has been under cultivation since very remote times. It is supposed to be a native of Crete, but grows wild in Austria, on the banks of the Danube, and in Northern Africa, is extensively cultivated for its fruit. The fruit is yellow, downy, of an agreeable odor, and a rough, astringent, acidulous taste, and in each of its five cells contains from eight to fourteen seeds. Though not eaten raw, it forms a very pleasant confection, and a syrup prepared from it may be used as a grateful addition to drinks in sickness, especially in looseness of the bowels, which it is supposed to restrain by its astringency. The seeds, which were formerly official, are ovate, angled, reddish-brown externally, white within, inodorous, and nearly insipid, being slightly bitter when long chewed. Their coriaceous envelope abounds in mucilage, which is extracted by boiling water. They were officially described as follows: "About 6 mm. in length, oval, or oblong, triangularly compressed, brown, covered with a whitish, mucilaginous epithelium, causing the seeds of each cell to adhere. With water the seeds swell up, and form a mucilaginous mass. The unbroken seeds have an insipid taste." *U. S.*, 1880. The seeds which are still extensively imported and used in the preparation of *Bandoline* and cosmetic lotions are frequently adulterated with fragments of bark or other vegetable tissue of the same size and color as the seeds and only detected by a close examination of the drug. Two drachms of the seeds will render a pint of water thick and ropy. (*A. J. P.*, 1876, 35.) It has been proposed to evaporate the decoction to dryness,

and powder the residue. Three grains of this powder form a sufficiently consistent mucilage with an ounce of water. According to Garot, one part communicates to a thousand parts of water a semi-syrupy consistence. (*J. P. C.*, 3e sér., iii, 298.) Pereira considers the mucilage as peculiar, and proposes to call it *cydonin*. It differs from arabin in not yielding a precipitate with potassium silicate, and from bassorin and cerasin in being soluble in water both hot and cold. Tollens and Kirchner (*Ann. Ch. Phys.*, clxxv, 205–226) assign to it the formula $C_{18}H_{28}O_{14}$, regarding it as a compound of gum, $C_{12}H_{20}O_{10}$, and cellulose, $C_6H_{10}O_5$, less one molecule of water. Quince mucilage (*Mucilago Cydonii*, U. S., 1880) may be used for the same purposes as other mucilaginous liquids. The U. S. P., 1880, gave the following formula for its preparation. "Cydonium, *two parts* [or thirty-six grains]; Distilled Water, *one hundred parts* [or four fluidounces]. Macerate the Cydonium for half an hour, in a covered vessel, with Distilled Water, frequently agitating. Then drain the liquid through muslin, without pressure. This preparation should be freshly made, when required for use." *U. S.*, 1880.

Cynara. *Cynara. Scolymus* L. (*Artichoke*).—This is a composite plant, indigenous in the south of Europe, and cultivated as a culinary vegetable. The receptacle and the lower portion of the fleshy leaflets of the flower-heads are eaten. When young, the heads are cut up raw and eaten as salad; when older, they are boiled, and dressed variously. The flowers are said to curdle milk, and the plant to yield a good yellow dye. The leaves and their expressed juice are very bitter, and have been thought to be actively diuretic. *Cynara Cardunculus*, the cardoon of the garden, very much resembles the artichoke. The stalks of the leaves are used as a vegetable in France. Artichoke leaves have been used in *dropsies* and *rheumatic affections*.

Cynoglossum. *Cynoglossum officinale* L. *Hound's-tongue. Langue de Chien*, Fr. *Hundszunge*, G.—A biennial plant of the fam. *Boraginaceæ*, common both in Europe and in this country. The leaves and root have been employed, but the latter has been generally preferred. The fresh plant has a disagreeable narcotic odor, resembling that of mice, which is dissipated by drying. The taste is nauseous, bitterish, and mucilaginous. Although hound's-tongue has been believed by some to be nearly inert, there can be little doubt that it is a dangerous poison. The experiments of Diedülin (*M. S. Rep.*, 1868) many years ago demonstrated that the extract paralyzes motor nerves in vertebrate animals, and K. Greimer has found in it a poisonous alkaloid, *cynoglossine*, which acts upon the animal organism similarly to curare; also a toxic glucoside, *consolidin*, and a notable amount of *choline*. (*P. J.*, vol. lxv.) *Consolicin*, a derivative of consolidin, like consolidin, paralyzes the central nervous system. *Cynoglossum* has been used as a demulcent and sedative in *coughs, catarrh, spitting of blood, dysentery*, and *diarrhœa*. The *pilulæ de cynoglosso* owe their properties chiefly to opium.

Cypress Oil. *N. N. R.* 1917. *Oleum Cupressi.*—A volatile oil distilled from the leaves and young branches of *Cupressus sempervirens*. It has a specific gravity of 0.88 to 0.89 at 15° C. (59° F.) and an optical rotation of + 4° to + 18°. It contains furfural, d-pinene, d-camphene, cymene, d-sylvestrene, d-terpineol, and esters of the same, l-cadinene and cypress camphor. It is used as an inhalant in *whooping cough* by sprinkling on the pillow and coverlet of the patient. (See also p. 1519.)

Cypripedium. *N. F. IV* (*U. S. VIII*). *Lady Slipper. Rhizoma Cypripedii. Yellow Lady Slipper Root. Yellow Indian Shoe. Yellow Moccasin Flower. Yellow Noah's Ark. Venus' Shoe. Male Nervine. American Valerian. Racine de Cypripède jaune, Valériane américaine*, Fr. *Gelbfrauenschuhwurzel*, G.—"The dried rhizome and roots of *Cypripedium hirsutum* Miller, *Cypripedium pubescens* Wildenow, or of *Cypripedium parviflorum* Salisbury (Fam. *Orchidaceæ*), without the presence of more than 5 per cent. of other parts of the same plants or other foreign matter." *N. F. IV.*

Under the common name of *lady's slipper*, or *moccasin plant*, several species of *Cypripedium* inhabit the woods in different parts of the United States. They are small plants, with large, many-nerved, plaited leaves, sheathing at the base, and large, often beautiful flowers, of a shape not unlike the Indian moccasin, whence they derive one of their common names. Their generic name of *cypripedium* (Κύπρις *Venus*, and πόδιον, *sock*) had a similar origin. Several of them have been used by American physicians, the root being the part employed. R. P. Stevens of Ceres, Pennsylvania, says of them that he has found the *C. reginæ* Walt. (*C. spectabile* Salisb.), and *C. acaule* Ait., especially when growing in dark swamps, to be possessed of narcotic properties, and to be less safe than the *C. parviflorum* Salisb., which is gently stimulant with a tendency to the nervous system, and is quite equal to valerian. He has employed it advantageously in *hysteria*, and in the pains of the joints, following *scarlet fever*. (*N. Y. Journ. Med.*, iv, 359.) E. Ives considers *C. hirsutum* Mill. and *C. reginæ* Walt. identical in their effects, but *C. reginæ* more powerful. (*Trans. Am. Med. Assoc.*, iii, 312.) The roots of the two species, *C. hirsutum* and *C. parviflorum* are indiscriminately found in commerce and sold under the same name.

Cypripedium parviflorum var. *pubescens* or large *yellow lady's slipper*, has a simple, often flexuous, pubescent, leafy steam, from one to two feet high. The leaves are pubescent, ovate-lanceolate, acuminate, narrowing at the base, about four or five inches long by two in breadth, alternate, sessile, and sheathing. The flower is usually solitary and terminal, with four divisions of the perianth, the two outer cohering nearly to the apex, the inner longer, narrower, undulatory or twisted, and the lip an inch or two in length, swelling sac-like, and of a yellow color. The fruit is an oblong capsule, tapering at each end, recurved, pubescent, and peduncled. The plant is indigenous, growing abundantly in rich, moist woods throughout the United States.

Cypripedium parviflorum, Small-flowered Yellow Lady's Slipper, is a perennial plant with a leafy stem, a foot or two in height, and comparatively small yellowish-green flowers, appearing in May. The specific character of the flower, which is that also of the plant, is that the lobe of the style is triangular and acute; the outer petals are oblong-ovate and acuminate; the inner linear and contorted; the lips shorter than the petals, and compressed. This species grows extensively through the United States, south of the Potomac, east and west of the Alleghanies, and in several of the Northern States, particularly New York, Michigan, Connecticut and Vermont.

It is described by the N. F. IV as a "rhizome

of horizontal growth, curved, from 3 to 10 cm. in length, and from 2 to 6 mm. in thickness, orange-brown to dark-brown, the upper side showing numerous circular, cup-shaped scars, closely covered below with simple, wiry roots, varying from 3 to 15 cm. in length; fracture of rhizome short, white, that of roots somewhat fibrous. Odor distinct, heavy; taste sweetish, bitter, and somewhat pungent. The powdered drug is yellowish-brown and, when examined under the microscope, exhibits numerous rounded or somewhat angular, simple and compound starch grains up to 0.014 mm. in diameter; calcium oxalate in raphides up to 0.065 mm. in length and occurring isolated or in bundles, occasionally imbedded in a mucilage-like plasma; tracheæ spiral, scalariform, or with simple or bordered pores; a few tracheids; sclerenchyma fibers, long, thin-walled and lignified; a few non-lignified, thick-walled fibers; fragments of epidermal tissue composed of elongated cells with reddish-brown walls; groups of thick-walled parenchyma cells with numerous simple pores. Cypripedium yields not more than 12 per cent. of ash." *N. F.* Maisch gave a distinctive description of the roots of the two species. (*A. J. P.*, 1872, 297.) Poisonous properties have been attributed to *C. reginæ* Salisb. and *C. parviflorum* var. *pubescens* (see *Geol. Nat. Hist. Survey, Minnesota Bull.*, 9, part i), but it has been shown that the secretion from the glandular hairs simply exerts an irritant action.

Senega and hydrastis roots are sometimes found accidentally mixed with those of cypripedium, probably from the plants having a common habitat.

Cypripedium has a somewhat aromatic odor, which diminishes by time, and a bitter, sweetish, peculiar, and in the end somewhat pungent taste. Henry C. Blair found it to contain a volatile oil, a volatile acid, tannic and gallic acids, two resins, gum, glucose, starch, and lignin. (*A. J. P.*, 1866, p. 494.) The eclectic preparation *cypripedin* is said to be a resinoid, obtained by precipitating with water a concentrated tincture of the rhizome. The substance thus obtained is complex, and has no claim to the name given it, which ought to be reserved for the active principle when discovered. It is probable that the virtues of the rhizome reside in a volatile oil and a bitter principle.

Cypripedium appears to be a gentle nervous stimulant or antispasmodic, and has been used for the same purposes as valerian, though less powerful. E. Ives of New Haven, Conn., commends the remedy in *hypochondriasis* and *neuralgia*. It may be used in powder, infusion, or tincture.

Dose, of the powder, fifteen grains (1.0 Gm.), three times a day. The resinoid, obtained by precipitating the tincture, has been given in doses varying from half a grain to three grains (0.032 to 0.20 Gm.).

Cystopurin. $(CH_2)_6N_4.2CH_3COONa+6H_2O$.—A compound obtained by the interaction of formaldehyde, ammonia and sodium acetate. It forms nearly tasteless, colorless, lanciform crystals which are readily soluble in water. It is recommended for the treatment of *cystitis* and *gonorrhea* in *doses* of thirty grains (2 Gm.) dissolved in water. It is also used as a prophylactic.

Cytisus. *Cytisus Laburnum* L. (Fam. *Leguminosæ.*)—Laburnum is a small hardy tree, indigenous in the higher mountains of Europe and cultivated throughout the civilized world for its flowers, which appear early in the spring in rich pendant yellow clusters. All parts of the plants are probably poisonous. In fifty-eight boys poisoned simultaneously by the roots, the symptoms were intense sleepiness, vomiting, convulsive movements, coma, slight frothing at the mouth, and unequally dilated pupils. (*M. T. G.*, vol. ii, 875.) In some cases the diarrhea has been severe. The convulsions have at times been markedly tetanic; wide-spread anesthesia has been noted, and also excessive mydriasis, with loss of the pupillary reflex, elevation of temperature, delirium, and cyanosis. After death there have been found erosion of the colonic mucous membrane, extreme hyperemia of the brain, and nephritis. (*D. M. W.*, xxi, 1895.) For cases, see also previous editions of the *U. S. D.*; *Le Mouvement Méd.*, 1875, No. 28; *Dublin Q. J.*, 1863, 248; *M. T. G.*, Sept., 1862; *L. L.*, Aug., 1870.

Husemann and Marmé isolated in 1864 an alkaloid, *cytisine*, a white, crystalline solid, of a bitter, somewhat caustic taste, soluble in water and alcohol, but scarcely at all soluble in ether, chloroform, benzene, or carbon disulphide. The same alkaloid has been isolated from the seeds of several plants of the *Papilionaceous* group. A second alkaloid, *laburnine*, was also announced by them. (*Chem. News*, July 16, 1869, 36.) Partheil (*A. Pharm.*, 1892, 448) has since studied cytisine, and gives it the formula $C_{11}H_{14}ON_2$, which has been adopted by other authorities. Ferric chloride colors cytisine and its salts blood-red, which color, however, disappears on diluting with water or on addition of hydrogen dioxide. If after the addition of this latter reagent the mixture is heated gently in the water bath an intense blue color is developed. When cytisine is distilled with soda lime, pyrrol is obtained, besides a base, $C_9H_{13}N$, which is possibly a hydroquinoline. A. Rannerda purified crude cytisine, obtained from the seeds of *Cytisus Laburnum* L., by the well known shaking out process with chloroform, by distilling it in a partial vacuum. Under a pressure of 2 mm. and a temperature of 228° C. (442.4° F.), the alkaloid distils over as a colorless liquid and congeals in the receiver in the form of fine crystalline needles. It separates from absolute alcohol in the form of small transparent rhombic crystals, which have the sp. gr. 1.0046. (*Ap. Ztg.*, July, 1900, 486.)

According to the researches of P. C. Plugge (*A. Pharm.*, 1895), cytisine is a very widely distributed alkaloid. He has found it in eight species of the genus *Cytisus*, two of the genus *Genista*, two of the genus *Sophora*, two of the genus *Baptisia*, and in other plants. He asserts that *ulexine* of Gerrard, from *Ulex europœus* L., *sophorine* of H. C. Wood, from *Sophora secundiflora* (Cav.) DC. (*S. speciosa* Benth.), and *baptitoxine* of von Schroeder, from *Baptisia tinctoria* R. Br., are identical with cytisine. Plugge also believes that the alkaloid of *Euchestra Horsfieldii* Benn. (fam. *Leguminosæ*), a Javanese pea, whose seeds are used as a contra-poison by the natives, is identical with cytisine. Kobert and Radziwillowicz (*Arb. d. Pharm. Inst. Dorpat.*, 1888, ii) found that cytisine caused in lower animals, spinal convulsions, followed, if the dose were large enough, by paralysis, vomiting of central origin, primary stimulation, and secondary paralysis of respiration and a marked reduction in the ozonizing powers of the red corpuscles. The blood pressure was at first elevated and later depressed and there was a paralysis of the motor nerves similar to that produced by curare. Dale and Laidlaw (*J. P. Ex. T.*, 1912, iii) find that the rise and secondary fall of the blood pressure is due to effects upon

the sympathetic ganglia and that cytisine closely resembles nicotine in its physiological action. Gray (*J. P. C.*, 1862) found laburnum to produce in man narcotic effects, and commends it in *vomiting, bronchitis, whooping cough,* and *asthma.*

Of late years several salts of cytisine have made their appearance. The hydrochloride, hydrobromate and nitrate have all been used as diuretics and nervines in one-twentieth to one-tenth grain doses (0.003–0.006 Gm.).

Damiana. *N. F. IV. Turnera.*—"The leaves of *Turnera diffusa* Wildenow or of *Turnera aphrodisiaca* Ward (Fam. *Turneraceæ*), without the presence of more than 10 per cent. of stems and other parts of the same plants or other foreign matter." *N. F.* There are 57 species of *Turnera* which are mostly indigenous to tropical America. The 2 species which yield *damiana* are small shrubs indigenous to Southern California, Mexico and the Antilles. These leaves are "obovate to lanceolate, from 10 to 25 mm. in length and from 4 to 10 mm. in width, shortly petiolate, obtuse or acute at the apex, and with a short, cuneate base; sharply two- to ten-toothed on each side; the veins ascending, generally strong, straight and simple, and running to the sinuses of the teeth, but sometimes branched and sending the branches into the teeth; the upper surface smooth and pale green, the lower glabrous or with a few hairs on the ribs (*Turnera aphrodisiaca*) or densely tomentose over the entire surface (*Turnera diffusa*). Intermixed with the leaves are frequently found some reddish twigs, the young tips and buds of which are grayish with appressed pubescence (*Turnera aphrodisiaca*) or white floccose (*Turnera diffusa*), also flower buds, yellowish flowers, and globose pods. Odor aromatic; taste characteristic, aromatic and resinous. The powdered drug is light yellowish-green and, when examined under the microscope, exhibits numerous rough simple hairs, up to 0.8 mm. in length and 0.03 mm. in width at the base, with a narrow lumen usually distinct at the base only and with heavy, mostly non-lignified walls, often curved near the base so that the major portion of the hair lies nearly parallel to the surface of the stem or leaf; fragments of the epidermis from the stems composed of somewhat rectangular cells up to about 0.07 mm. in length and about one-half as broad, with square or somewhat pointed ends, with few broadly elliptical stomata about 0.03 mm. in length; sub-epidermal cells from the stem resembling those of the epidermis in shape but with lignified walls; tracheæ, spiral, up to 0.02 mm. in width, with bordered pores up to about 0.035 mm. in width; tracheids from stem few; strongly lignified, thick-walled sclerenchyma cells or fibers few; lignified pith-parenchyma with large simple pores; fragments of epidermal cells and mesophyll of leaf; the former with somewhat wavy, vertical walls and associated with stomata up to 0.024 mm. in length; numerous crystals of calcium oxalate in rosette aggregates up to 0.03 mm. in diameter and occasionally in prisms; starch grains few, simple, up to 0.005 mm. in diameter. Damiana yields not more than 10 per cent. of ash." *N. F.*

Parsons (*Arch. d. Pharm.*, 1881, p. 133) obtained 0.2 per cent. of a volatile oil; 8.06 of a soft resin, fixed oil and chlorophyll; 3.46 per cent. of tannin; 7.08 per cent. of a bitter principle; 6.39 per cent. of a hard brown resin; 10 per cent. of extractive; 13.5 per cent. of a gum; 6.15 per cent. of starch, etc.

The leaves of the composite plant *Aplopappus discoideus* DC. (*Bigelovia Veneta* Gray) were, formerly, also sold under the name of damiana.

Although damiana has achieved some repute in the treatment of sexual impotence, it is worthy of note that it is always given in conjunction with strychnine, phosphorus or some other stimulant; it is probably nothing more than a feeble tonic. *Dose,* one-half to one drachm (2–4 Gm.) of the leaves, either in the form of infusion or fluid-extract.

Danais. *Danais fragrans,* Commerc. (Fam. *Rubiaceæ.*)—In this Madagascar plant, the root of which is said to be tonic and antiperiodic, Heckel and Schlagdenhauffen found a glucoside, *danain.* (*A. J. P.*, 1886.)

Daphnandra.—The bark of *Daphnandra micrantha* (Tul.) Benth., an Australian tree (fam. *Monimiaceæ*), is asserted to be rich in poisonous alkaloid. (*P. J.*, Oct., 1887.) Bancroft states that the active alkaloid is soluble in water, and to some extent is antagonistic to strychnine.

Delpho-curarin.—Under this name an alkaloid obtained from the *Delphinium Scopulorum* A. Gray, has been placed upon the market as an amorphous white powder. It has been physiologically studied by Kahn (*A. I. P. T.*, 1909, p. 19) who found that it acts very similarly to curare, paralyzing the peripheral endings of the motor nerves. It has been introduced for use in the physiological laboratory as a substitute for curare, which is becoming somewhat difficult to obtain. According to Kahn, a dose of six milligrammes per kilo of body weight, given intravenously, is sufficient to completely paralyze the motor nerve of the dog. It should not be confounded with delphinine.

Dericin.—Under the names of *dericin* and *floricin* has been introduced a light colored viscous oil which is derived from castor oil. It remains fluid at −20° C. (−4° F.). It is used as a vehicle for menthol, oil of eucalyptus and similar water-insoluble substances.

It is claimed that this preparation has the power of absorbing considerable quantities of water, but unlike castor oil it is insoluble in alcohol.

Dermol. (*Bismuth Chrysophanate.*) $Bi(C_{15}H_9O_4)_2Bi_2O_3$.—This is a yellow, amorphous powder soluble in the inorganic acids but insoluble in the ordinary solvents. It is used as a drying agent in the treatment of various skin complaints, generally in the form of a 5 to 20 per cent. ointment.

Dextroform is a combination of formaldehyde and dextrin, soluble in water and glycerin, but insoluble in alcohol, ether or chloroform; it occurs as a white, almost odorless and tasteless powder; it should be used with caution. It affords, according to Bongartz, in from 10 to 20 per cent. solution, a useful injection in *gonorrhea* and other toxic diseases, or is used for irrigation in half strength.

Diagnostic Tests.—Besides the official diagnostic tests described in Part III the following serum tests are of importance:

Complement Fixation Reaction for Syphilis. Wassermann Reaction. Noguchi Reaction.—As mentioned in the article on Immune Serums (see p. 1603), animals which have been injected with disease-causing bacteria develop certain peculiar properties in their blood. Just so the blood serum of men who have been inoculated accidentally, that is, who have acquired an infectious disease, has similar specific attributes. One of these properties is the power of "binding" or "fixing" com-

plement in the presence of a suitable *antigen*. *Complement* is the substance present in all fresh serum, which is necessary to complete certain actions of immune serum, such as the bacteriolytic action (p. 998) of an antibacterial serum. In the same way, the serum of an animal which has been treated with red blood cells of an alien species, acting with the complement, acquires the property of destroying these corpuscles—just as if the blood cells had been bacteria—the coloring matter going out into the clear liquid. Now if the serum of a patient suffering with syphilis, for example, were brought in contact with a small amount of complement in the presence of a syphilitic antigen, the three would unite so that the complement would be no longer available for a second reaction, such as the hemolytic one. Thus we test for the presence of the syphilitic antibody by finding whether it will fix complement to itself, and we prove that the complement is fixed only by trying in vain to use it in destroying red blood cells. The antibody in the second part of the test—found in the serum of the animal which has been treated with red blood cells—is called the hemolytic amboceptor, or simply *amboceptor*. In the complement fixation test for syphilis, the rabbit is commonly used to produce amboceptor. The syphilitic antigen is usually not the microbe causing syphilis, but, strange to say, a heart extract whose only property in common with syphilitic material is in its chemical constitution, that is, it belongs to the class of lipoids.

To perform the test, the suspected blood serum is added to the antigen and a small amount of complement (fresh guinea-pig serum) and kept at 37° C. (98.6° F.) for an hour. The amboceptor and some red blood cells of the species used in preparing the amboceptor (usually sheep or man) are then mixed in and the five incubated together for a longer time. The tube containing the mixture is then examined and if the blood cells are still intact, forming a red opaque sediment, with colorless supernatant fluid, it signifies that the complement was fixed by the first incubation, therefore the patient has syphilitic antibodies in his blood. Other tests must be carried on at the same time to prove that the amboceptor will actually hemolyze the blood cells with the given amount of complement in the presence of a non-syphilitic serum with antigen, and in the presence of the patient's serum alone without antigen. A fourth tube should be arranged to ascertain that the complement will be fixed when a known syphilitic serum is used.

It is obvious that such a reaction requiring at least seven interacting bodies to prove the presence or absence of a characteristic in one of them, is so complicated that only by repeated practice and standardization of methods can reliable data be obtained. Any of the substances concerned may be so subject to change as to have a deleterious effect on the others and destroy the value of the reaction.

Agglutination Test for Typhoid Fever. Widal Test.—The blood of typhoid fever patients, in a great majority of cases, causes a clumping of typhoid bacilli. This reaction is made use of in the diagnosis of typhoid fever. To a suspension of typhoid bacilli there is added in various dilutions the serum of the patient; in the course of an hour, if the reaction is positive, the bacilli may be observed under the microscope to have lost their power of spontaneous motion and to have gathered in clumps with only very few outlying individual bacteria. To the naked eye their flocculation is also visible. If clumping takes place in one hour at room temperature in a dilution of 1 to 50, the reaction may be taken as positive. Positive reactions also occur after vaccination against typhoid fever, and may persist for some time. In the first few days of an attack of typhoid fever the reaction is less likely to be positive than later. A carefully killed suspension of typhoid bacilli, not overheated, may be used instead of a living culture in this test.

Tuberculins.—Tuberculins in the broadest sense are any products of tubercle bacilli used in the treatment, prevention, or diagnosis of tuberculosis. The product to which the name was first applied is now called *Old Tuberculin* (Koch) (*Tuberculin alt, Tuberculin O. T., Concentrated Tuberculin, Crude Tuberculin*), and is prepared by growing tubercle bacilli for weeks on glycerin broth, killing the culture by steaming it for 30 minutes, and evaporating the sterilized broth to one-tenth its volume over a hot bath. The dead bacilli are then filtered out through a bacteria-proof filter and the resulting brown fluid, viscous on account of its high glycerin content and with a characteristic odor, is the tuberculin. Koch's *New Tuberculin T. R.—Tuberkelbacillen Rest, Tuberculin Residue, Tuberkulin Rückstand*—is made by triturating living tubercle bacilli, thoroughly washing in water, and grinding the insoluble residue. By alternate suspension in water, centrifuging and grinding each sediment, a series of very fine suspensions are obtained and combined. Twenty per cent. glycerin solution is added in such amount that 1 mil of the final product represents the residue of 10 milligrammes of tubercle bacilli; this residue dried weighs about 2 milligrammes.

Tuberculin B. E. (*Bozillenemulsion* (Koch), *Bacilli Emulsion*) was Koch's final effort to find a specific for tuberculosis. This consists of ground tubercle bacilli in a 50 per cent. glycerin suspension. The coarser particles which settle in 24 hours are discarded. The dilution is such that 1 mil contains 5 milligrammes of bacillary substance.

Tuberculin B. F. (Denys) (*Bouillon Filtré, Bouillon Filtrate*) is the same product as old tuberculin prepared without heating or concentration. The glycerin broth culture is simply filtered free from bacteria. A similar preparation in Germany is called *T. O. A.* (*Tuberkulin Original, O. T.*), or if made from bovine tubercle bacilli instead of human, *P. T. O.* (*Perlsucht Tuberkulin Original*).

Numerous other preparations are to be found, some very closely allied to the four above mentioned, others more variant: *Tuberculol, Tuberculin A. F.* (albumose-free), *Vacuum Tuberculin, Tuberculosis Sero-Vaccine, Tuberculin-Rosenbach, Tuberculin-Beraneck, Tubercle Bacilli Extract* (Dixon), *Suspension of Dead Tubercle Bacilli* (Dixon), *Watery Extract of Tubercle Bacilli* (von Ruck), *Tulose, Oxytuberculin*, and others.

For diagnosis, old tuberculin is employed almost exclusively. It has been particularly useful in the diagnosis of tuberculosis in animals, by temperature reaction following subcutaneous injection. This method is also used in human medicine, but in any application of tuberculin, save the most external, extreme care must be used. The multitude of severe reactions and fatalities due to the use of tuberculin in the years immediately following its discovery are not to be forgotten; a dose easily borne by one individual may be highly

toxic to another. Careful two-hourly temperature records should be kept for two days preceding and two days following the injection. At first not more than 0.0002 mil may be given. A safer test is the application of the tuberculin to the skin; an abrasion is made through a drop of old tuberculin on the forearm, by means of a small drill twirled between the thumb and forefinger (*von Pirquet test*). A similar abrasion is made without the tuberculin. The appearance of a papule at the former site, but not at the latter, within twenty-four to forty-eight hours, indicates the presence of tuberculosis. By this delicate test, it is shown that nearly all adults have, at some time, contracted tuberculosis, even if not showing any clinical manifestations of the disease, so that the test is only applicable to children. A similar test (*Moro test*) is made by the use of a *tuberculin ointment*.

Calmette and Wolff-Eisner have devised a conjunctival test—the tuberculin, diluted 10 times or made up to a corresponding strength with glycerin-free dried tuberculin, is dropped in the conjunctival sac. Within 24 hours, if the reaction is positive, the conjunctiva so treated becomes red and often somewhat swollen. On account of reactions which have endangered the eyesight, this test has largely been given up.

In tuberculin treatment, also very great caution should be exercised. It is customary to begin a course of treatment with 0.00000001 to 0.0000001 mils hypodermically increasing gradually and not giving more than two injections per week.

Accurate record must be maintained of the patient's temperature and general condition, for only thus will the margin of safety in this dangerous product be observed. The success with any of the various tuberculin has not been remarkable, but it is asserted that in certain types of cases, some good may be accomplished.

Diamine. *Diamidogen.—Hydrazin,* $\left.\begin{matrix}H_2N\\H_2N\end{matrix}\right\}$, is a strong base crystallizing in white crystals at 1.4° C. (34.5° F.) and boiling at 113° C. (235.4° F.); it forms salts with the common acids. The free base mixes with water in all proportions and has a strong alkaline character and powerful reducing action. This substance has been proved by Julius Pohl to be actively poisonous. (*A. E. P. P.*, xli, 1898.)

Dianthus. *Dianthus Caryophyllus* L. *Clove Pink.* (Fam. *Caryophyllaceæ.*)—Of the ordinary garden pink those specimens should be selected for medicinal use which have the deepest red color and the most aromatic odor. The petals should not be collected until the flower is fully blown, and should be employed in the recent state. They have a fragrant odor, said to resemble that of the clove. Their taste is sweetish, slightly bitter, and somewhat astringent. Both water and alcohol extract their sensible properties, and they yield a fragrant essential oil by distillation. In Europe they are employed to impart color and flavor to a *syrup*, used as a vehicle. The Edinburgh Pharmacopœia directed this to be made by macerating one part of the flowers, without their claws, in four parts of boiling water for twelve hours, then filtering, and adding seven parts of sugar.

Diaphthol. *Quinaseptol. Ortho-oxyquinoline-metasulphonic Acid.* $C_9H_5N.OH.SO_3H$.—Occurs in yellowish-white crystals fusing at 295° C. (536° F.), slowly soluble in cold water. It is an antiferment said to be without toxicity and introduced by Guignard as a urinary disinfectant to replace salol.

Diaspirin. *Succinylsalicylic Acid. N. N. R.* 1916. $(CH_2.COO.C_6H_4.COOH)_2$.—A white, odorless powder, of a somewhat acid taste, readily soluble in alcohol, sparingly soluble in water. *Diaspirin* has been used with asserted benefit in the treatment of various *rheumatic* and *neuralgic* troubles. According to Kaminer (*B. K. W.*, 1909), its value is enhanced by the fact that when given in sufficiently large doses, passing unchanged through the stomach, it not only exercises the effect of the salicylic acid which is liberated in the intestinal tract, but that it also has a distinct diaphoretic action. Diaspirin is a dibasic acid and reacts with bases, either organic or inorganic, to form corresponding salts.

The *dose* is five to fifteen grains (0.3–1.0 Gm.) from three to six times a day.

Diastin.—A form of diastase introduced for use in certain forms of amylaceous *dyspepsia*. It is given in the *dose* of five grains (0.32 Gm.)

Diathesin. *Ortho-oxybenzylalcohol. Salicyl alcohol.* $C_6H_4(OH)CH_2OH$.—This phenol-alcohol may be prepared from salicin by the action of dilute acids or emulsin. It forms colorless crystals melting at 86° C. (186.8° F.) and soluble in fifteen parts of water at 22° C. (71.6° F.). It gives a blue color with ferric chloride. It has been proposed by L. Lederer (*M. M. W.*, No. 7, 1899) as an antirheumatic and antiseptic. It exists in salicin in combination with glucose, and it is believed by Lederer that the activity of salicin depends not upon the conversion of the ortho-oxybenzylalcohol into salicylic acid, but upon the direct influence of the *diathesin*. In *rheumatism* it may be given in seven-grain (0.45 Gm.) *doses* every two hours.

Diazyme, Essence and **Glycerole.** *N. N. R.* 1917.—These are proprietary preparations which are stated to contain the starch-converting enzyme of the pancreas without the protein-converting and fat-splitting enzymes.

Dicentra.—The *Dicentra pusilla* Sieb. et Zucc. is a Japanese plant belonging to the *Fumariaceæ* which is used in that country as a folk remedy in dysentery. Asahina (*A. Pharm.*, 1909, ccxlvii) has found it in an alkaloid, $C_{20}H_{21}NO_4$, which is isomeric with papaverine. It has been studied physiologically by K. Iwakawa (*A. E. P. P.*, 1911, lxiv), who finds that it produces in both cold and warm blooded animals a light narcosis, followed, if the dose be large, by convulsions. It also caused a fall in the blood pressure with slowing of the heart and depression of the respiratory center.

Dichloral Antipyrine. $C_{11}H_{12}N_2O.[CCl_3CH(OH)_2]_2$.—Made by triturating 94 parts of antipyrine with 165.5 parts of hydrated chloral and crystallizing from hot water. It differs from hypnal in containing one molecule more of the hydrated chloral. Its uses and *dose* are the same as hypnal, viz., from five to twenty grains (0.32 to 1.3 Gm.), as an analgesic and hypnotic.

Dichlorbenzol.—It occurs in colorless crystals and is used as an insecticide. It is said that the vapors are penetrating and kill insects, larvæ and eggs.

Dichondra Brevifolia.—An extract of this plant dissolved in glycerin is used as an application in the treatment of *diphtheritic ulcers*. It is applied direct to the mucous membrane and is claimed to possess specific action on the diphtheritic bacilli.

Didymium is now recognized generally as a mixture of *neodymium* and *praseodymium*, free as far as possible from lanthanum, the salts of the

neodymium being in general rose-colored, while those of the praseodymium are of a greenish-yellow. The by-products obtained in the manufacture of gas mantles and certain other chemical manufactures have been utilized in making the salts.

Didymium Chloride. Didymii Chloridum. $Di_2Cl_6+12H_2O$.—This salt has been used in the form of a rose-red, odorless and non-irritant solution containing 25 per cent. to 30 per cent. of the salts. It has been affirmed that the chloride is superior to phenol as a germicide, but the experiments of I. Schmidt and of Pflücker (*M. R.*, 1898, 1900) show that it is much inferior, a 5 per cent. solution being required to destroy ordinary germs.

Didymium Nitrate, Didymii Nitras, $Di_2(NO_3)_6.12H_2O$, occurs in rose-colored crystals soluble in water and alcohol. Antiseptic in solution of the strength of 1 in 2000. (*Cb. B.*, xxi.)

Didymium Salicylate. Dymal.—A very fine white powder free from odor. It has been specially recommended by Kopp, Roth, and others as an innocuous, non-irritant, desiccant, and antiseptic dusting powder in various skin diseases, especially in weeping *eczema,* and also *hidrosis,* and *burns* of the first and second degree. In *erysipelas* and drier forms of skin disease it failed to be of service. It is especially popular with the veterinarians because of its relatively low cost.

Didymium Sulphate. Didymii Sulphas. $Di_2(SO_4)_3+6H_2O$.—This salt has been marketed in the form of a pale rose-red powder to be used for disinfecting closets, etc.

Diervilla. *Diervilla Lonicera* Mill. (*D. trifida* Moench.) *Bush Honeysuckle.*—A low, erect, indigenous shrub, growing in dry woods and rocky places throughout the Eastern Northern States and Canada. L. E. Dawson (*Chem. News,* 1912) examined the fruit of *D. Florida,* the dark-red berries contain fructose, fixed oil, tartaric and citric acids and an alkaloid which he believes to be *narceine.* Charvaux found a glucoside identical with *fraxin* in *D. lutea.* (*J. P. C.*, 1911, 248.) The whole plant is supposed to be possessed of diuretic and astringent properties, and is given in infusion by the eclectics in diseases of the urinary passages.

Diethylketone.—*Propione,* $C_2H_5.CO.C_2H_5$, is obtained by the dry distillation of *calcium propionate* $(C_3H_5O_2)_2Ca$. A transparent liquid, soluble in twenty-four parts of water, mixing with water, alcohol, and ether, boiling at 101° C. (213.8° F.); recommended by Albanese and Barabini in 1892, as inducing sleep in animals. It has been used by Giovanni in the treatment of *maniacal* and *hysterical excitement* in *doses* of from eight to twenty grains (0.5–1.3 Gm.). It should be administered in dilute solution.

Diethyl-oxyacetyl-urea. *Hypnotal.*—This occurs as an oily liquid with a characteristic ethereal odor and taste, soluble in twenty parts of water and also in alcohol. Its sodium salt occurs in flaky crystals which are freely soluble. It has been suggested by Houghton (*J. A. M. A.*, December 23, 1905) as a somnifacient.

Difluorphenyl.—An organic fluorine compound, $C_6H_4FC_6H_4F$. A colorless, crystalline powder of an aromatic odor, insoluble in water, but easily soluble in alcohol, ether, chloroform, and in oils. It is used as an antiseptic both in the form of a dusting powder or a 10 per cent. talcum dilution or ointment.

Digalen.—Under the name of *digalen* there has been introduced into medicine a solution which is asserted to contain *soluble digitoxin.* There is no doubt that this preparation contains a principle which exercises a digitalis effect upon the heart, but that this principle is identical with digitoxin is improbable. The claim for the application of the term digitoxin is based upon the fact that it has the same empirical formula as this glucoside, but since it would appear that its molecular weight is only half of that of crystalline digitoxin it is more probable that it is a polymer of this body. According to Kiliani (*A. J. P.*, 1913, lxxxv, 224), it is identical with digitalein.

Digalen has been used to a large extent in the treatment of chronic cardiac conditions for precisely those cases in which digitalis is useful. It has been used by the mouth and by intramuscular and intravenous injections. Although it appears to be less irritant to the body tissues when injected intramuscularly than are most of the other digitalis preparations, this method of administration is not entirely painless. The *dose* of the remedy is from fifteen to twenty minims (0.9–1.3 Gm.).

Diiodacetylene, C_2I_2, is made simultaneously with *tetraiodoethylene,* C_2I_4, by the action of a solution of iodine in potassium iodide upon calcium carbide. The two are separated by reason of their different solubilities. It occurs in small crystalline needles, insoluble in water but dissolving in oil of sweet almond. It has been found by E. Mebert (*A. E. P. P.*, xli, 1898) to be very actively poisonous.

Diiodaniline. *Metadiiodoaniline.* $C_6H_3I_2NH_2$ [4:2:1].—Shining brown crystals, soluble in ether, chloroform, and used as an antiseptic for the skin, either in solution or ointment form.

Diiodoform. *Tetraiodoethylene. Ethylene Periodide.* C_2I_4.—Obtained by the action of iodine on a solution of acetylene iodide in carbon disulphide. In the form of bright yellow, odorless, needle-like crystals, insoluble in water, only slightly soluble in alcohol but readily soluble in chloroform. It contains 95.3 per cent. of iodine and is recommended in the place of iodoform. It is decomposed by exposure to light.

Diiodosalicylic Acid, $C_6H_2I_2.OH.COOH$, is a yellowish-white, crystalline powder, prepared by the combination of iodine, iodic and salicylic acids. It has a sweetish taste and is almost insoluble in water but very soluble in alcohol and ether. It is used as an antipyretic and analgesic, especially so in the treatment of *gout* and *rheumatism. Dose,* eight to twenty grains (0.5–1.2 Gm.).

Diiodosalol. *Phenyl Diiodosalicylate.* $C_6H_2I_2(OH)CO_2C_6H_5$.—Made by the condensation of diiodosalicylic acid with phenol. An odorless and tasteless crystalline powder melting at 135° C. (275° F.). Used as an antiseptic in the treatment of *skin diseases.*

Dimazon. *Diacetylaminoazotoluene.* $CH_3.C_6H_4.N:N.C_6H_3(CH_3)N(CH_3CO)_2$. *N. N. R.* 1917.—This is recommended for the purpose of stimulating epitheliazation over old *ulcers, wounds,* etc. It is asserted to have the advantage over similar preparations that it does not stain. It is used as a 2 per cent. ointment either made with petrolatum or a fatty oil or as a 5 per cent. dusting powder.

Dimethyl Acetal. *Ethylidenedimethyl Ether.* $CH_3.CH.(OCH_3)_2$.—It is a colorless liquid, boiling at about 60° C. (140° F.); sp. gr. 0.879. It is miscible with water, alcohol or chloroform. It is used as an anesthetic, employed alone or with equal proportions of chloroform.

Dimethyl Sulphate, $(CH_3)_2SO_4$, is a liquid boiling at 188° C. (370.4° F.), soluble in alcohol and ether. This substance has recently come into importance with toxicologists on account of the number of fatal cases of poisoning occurring from it, due to its extended use in chemical factories. It acts locally as a strong caustic and also influences the central nervous system, producing nystagmus, convulsions, and respiratory death during coma. (See S. Weber, *A. E. P. P.*, Bd. xlvii.)

Dinitrocresol. $C_6H_2(NO_2)_2\left\{\begin{matrix}CH_3\\OH\end{matrix}\right.$.—This is a coal tar dye, commercially called *Saffron Substitute* and is a mixture of the potassium salts of dinitro-ortho- and para-cresols. It is said to have been sold for saffron in Berlin, with fatal results. (*Ph. Rund.*, Prague, 1887.)

Dioform. *Acetylene Dichloride.* CHCl=CHCl.—This occurs as a colorless fluid with an odor somewhat like that of chloroform. Sp. gr. 1.29, melting point, 55° C. (131° F.). Reasoning from its chemical constitution that it should exercise a narcotic action, Villinger has carried out a series of experiments with it upon dogs. (*A. K. C.*, 1907.) He found that it produced a narcosis with abolition of reflexes without changes in the circulation or in the kidneys. He also employed it as an anesthetic for human beings in doses of from two hundred and fifty to three hundred and fifty grains (15–24 Gm.) and found that it produced a condition suitable for surgical operation in three to five minutes with very slight stage of excitation. It has not been used, however, sufficiently to justify any conclusions as to its value as a practical therapeutic.

Diogenal. *Dibrompropyl-diethylbarbituric Acid.*—This is a white, crystalline powder, almost insoluble in water, but soluble in alkaline solution and alcohol. It is used as a somnifacient and general nerve sedative. According to Heinz (*M. M. W.*, 1913, p. 2618), it is only about one-fourth as toxic as veronal. The *dose* is ten to thirty grains (0.65 to 2 Gm.).

Dioscorea. *N. F. IV. Wild Yam Root. Colic-root. Rheumatism-root.*—"The dried rhizome of *Dioscorea villosa* Linné (Fam. *Dioscoreaceæ*)." *N. F. IV.* An indigenous, perennial, twining plant, with long, knotty, matted, contorted, ligneous root stocks. It grows from Ontario to Wisconsin, and south to Florida and Texas. The rhizome is used by the eclectics, who consider the drugs efficacious in *bilious colic*, and by the Southern negroes in *rheumatism*. The rhizome is described by the N. F. as "knotted and woody, elongated, from 6 to 12 mm. in thickness, often compressed, bent and branched, bearing scattered nodular projections at the sides, slender, tough roots underneath and stem-scars on the upper surface; externally pale brown, surface more or less scaly from the partly detached, thin outer layer; fracture short but tough, the fractured surface whitish or pale-brown, with numerous small, scattered, yellowish wood bundles. Odorless; taste starchy, insipid, afterwards acrid. Dioscorea yields not more than 7 per cent. of ash." *N. F.*

W. C. Kalteyer found abundant saponin in the roots. (*A. J. P.*, 1888; see also *M. R.*, 1913, 311.) A substance, improperly called *dioscorein*, obtained by precipitating the tincture with water, is used in the *dose* of from one to four grains (0.0065–0.26 Gm.). *Dose*, one-half to one drachm (1.9–3.75 mils), which may be given either in the form of a decoction or a fluidextract.

Dioscorea hirsuta Bl. grows in the island of Java, where it is known as *Gadoeng*. In 1894 W. G. Boorsma (*Mededeelingen uit's Lands Plantentuin*, xiii) separated from it an alkaloid to which he gave the name of *dioscorine*. This alkaloid has been studied by Plugge and Schutte (*A. J. P.*, iv, 1897) who assigned to it the formula $C_{13}H_{19}NO_2$, and found it to be a convulsant poison, resembling closely in its action picrotoxin, but much more feeble. *Dioscorea bulbifera* L. grows in the Gaboon country of tropical Africa. Heckel and Schlagdenhauffen found in the tuber a glucoside, together with wax, chlorophyll, saccharose, and resin.

The root of *Dioscorea rhipogonoides* (?) Oliver, under the names of *Cunao*, *Shu-lang*, *faux gambier*, is exported in enormous quantities from Indo-China to Southern China for use as a dye-stuff.

Diospyros. *Persimmon. Date-plum. Fruits de Plaqueminier de Virginie*, Fr. *Persimmonfrüchte, Dattelpflaumen*, G.—The *Diospyros virginiana* L., or persimmon (fam. *Ebenaceæ*), is a small indigenous tree, occurring in woods and old fields from Connecticut, southward. The flowers appear in May or June, but the fruit is not ripe until the middle of autumn. The fruit is a globular berry, dark yellow when ripe, and containing numerous seeds in a soft yellow pulp. The seeds, dried, roasted, and ground, are used in some parts of Georgia as a substitute for coffee. (*M. S. Rep.*, 1873, 437.)

While green, the fruit is excessively astringent, and in this form was formerly included in the U. S. Secondary List; but, when perfectly mature, and after being touched by the frost, it is sweet and palatable. The unripe fruit, according to B. R. Smith of Philadelphia, contains tannic acid, pectin, sugar, malic acid, coloring matter, and lignin. (*A. J. P.*, xviii, 167.) The persimmon has been used by Mettauer in *diarrhea, chronic dysentery*, and *uterine hemorrhage*. The *dose* of the vinous tincture (an ounce of the fresh green fruit to two fluidounces of dilute alcohol) is half a fluidrachm (1.9 mils) or more for infants, and half a fluidounce (15 mils) or more for adults. The bark is astringent and very bitter. For further information concerning this drug, see *U. S. D.*, 19th ed., p. 1474.

Dioxynaphthalene, $C_{10}H_8O_2$, may exist in several modifications, the best known being the *α*- and *β-hydronaphthoquinones*. They are diatomic phenols in character. Lépine (*S. M.*, No. 31, 1887) finds that *dioxynaphthalene* produces in dogs and guinea-pigs violent convulsions, alteration in the color of the blood, due to the formation of methemoglobin, and blackening of the urine. He asserts that in asthenic persons *doses* of three grains (0.2 Gm.) a day increase power.

Diplosal. *N. N. R.* 1917. *Salicylic Ester of Salicylic Acid.* $OH.C_6H_4.COO.C_6H_4.COOH$.—On decomposition in the human organism, two molecules of salicylic acid are formed, water being taken up so that 107 parts of salicylic acid are formed from 100 parts of the ester. It is a white, crystalline powder, insoluble in water.

Diplosal owes its therapeutic virtues to its decomposition in the intestines and the liberation of salicylic acid. Its range of usefulness is precisely similar to that of the other salicylates over which, however, it has the advantage that because of its insolubility in dilute acids it is much less prone to disturb the stomach. It appears, however, to be decomposed in the intestines with comparative slowness, so that its action is less prompt than that of other salicylates and correspondingly

more persistent. It has been used by Strauch (*Th. M.*, 1909), Minkowski (*Ther. Geg.*, 1908) and others with success in the treatment of both *acute* and *chronic rheumatism*.

The *dose* is eight to ten grains (0.5–0.7 Gm.) repeated, if necessary, up to a daily maximum of ninety grains (6 Gm.).

Dipropæsin.—A condensation product of 2 molecules of propæsin, $CO.(NH.C_6H_4.COOC_3H_7)_2$. It is a white powder, insoluble in water, soluble in alcohol; melting point, 171°–172° C. (339.8°–341.6° F.). It is used as a local anesthetic. Kluger (*Th. M.*, 1909) suggested its employment as a local anesthetic in intestinal conditions, on the theory that its action is only made manifest in the presence of alkaline media and would, therefore, be limited when given by the mouth, to the intestinal tract. The clinical reports, however, are too scanty to justify any conclusion as to its value. The *dose* recommended is eight grains (0.5 Gm.).

Dirca. *Dirca palustris* L. *Leather Wood.* (Fam. *Thymelæaceæ.*)—A shrub growing widely in the Northeastern United States. The berries, which are small, ovoid, and of an orange or reddish color, are said to be narcotic and poisonous. The tough bark, in the fresh state, has a peculiar, rather nauseous odor, and an unpleasant acrid taste, and when chewed excites a flow of saliva. It yields its acridity completely to alcohol, but imperfectly to water even by decoction. Six or eight grains of the fresh bark produce violent vomiting, preceded by a sense of heat in the stomach, and often followed by purging. Applied to the skin it slowly excites redness and ultimately vesicates. It is analogous to mezereon in its medicinal as well as botanical characters.

Disaloin. *Desaloin.*—This preparation is a combination of egg albumen and chloroform—in reality it is a solid colloidal state of chloroform. It contains 25 per cent. of chloroform. It is used externally as a skin antiseptic and slight local anesthetic internally in stomachic *catarrh* in *doses* of four to ten grains (0.26–0.66 Gm.).

Dithio-Salicylic Acid. $\left.\begin{matrix} C_6H_3(OH)COOH.S \\ C_6H_3(OH)COOH.S \end{matrix}\right\rangle$. According to O. Z. (1889, 298) *dithio-salicylic acid*, a proposed substitute for salicylic acid, is made by heating equal molecules of *sulphur chloride* and salicylic acid to from 120° to 150° C. (248°–302° F.), dissolving the light yellow residue in sodium hydroxide, and precipitating the acid, by addition of HCl, as a resinous straw-colored mass, forming, after pulverization, a light yellow powder, easily soluble in alcohol, benzene, and glacial acetic acid. The sodium salt of the acid, *sodium dithio-salicylate*, called also *dithion*, is said by Lindenborn (*Rép. de Pharm.*, Sept., 1889) to be preferable in the treatment of *rheumatism* to salicylic acid, because more energetic and less apt to disturb the digestion. It is asserted that, as an antiseptic, it is fully equal to *sodium salicylate*. *Dose*, three grains (0.2 Gm.), repeated according to circumstances. Ten grains (0.65 Gm.) are said to produce nausea, tinnitus aurium, and sweating.

Dolomol. *N. N. R.* 1917.—A white insoluble powder, nearly inodorous and tasteless, consisting mainly of *magnesium stearate* with small amounts of magnesium oleate and palmitate. It is used as a dusting powder in affections of the skin, either alone or in combination with various other remedies.

Doundaké. *Dundaki. Quinquina Africaine. Kina du Rio Nunez.*—*Sarcocephalus esculentus* Afzel (fam. *Rubiaceæ*) of Africa yields a bark which is said to be an astringent and tonic febrifuge. For a description of the bark and its chemical characteristics, see *P. J.*, vol. xvi, 49. Heckel and Schlagdenhauffen do not believe that *doundaké* contains an alkaloid, but attribute its power to three distinct principles of a resinous nature, the first of which is of an orange-yellow color and very bitter, soluble in water, alcohol, and potassium hydroxide; the second light yellow in color, soluble in potassium hydroxide but not in water; the third soluble in potassium hydroxide, insoluble in water and in alcohol. (*J. Soc. Chem. Ind.*, 1886, 435.) The wood of the *Sarcocephalus Diderrichii* (?) (fam. *Rubiaceæ*), which is used for making shuttles, has been found by Gibson to contain an alkaloid, which is a cumulative cardiac poison. Workers in the wood frequently suffer and even die from cardiac disturbances. (*Bio-Chem. J.*, 1906, i, p. 39).

Dracontium. *Symplocarpus Fœtidus* (L.) Nutt. (*Spathyema fœtida* (L.) Raf. *Dracontium fœtidum* L. *Ictodes fœtidus* Bigelow.) *Skunk Cabbage. Skunk Weed. Polecat Weed. Racine de Pothos fétide*, Fr. *Stinkende Drachenwurzel*, G.—The plant of the Fam. *Araceæ* is abundant in wet places throughout the Northern and Middle United States. All parts of it have a fetid odor, dependent upon an extremely volatile principle, which is rapidly dissipated by heat. The rhizome should be collected in the autumn, or in the early spring.

The rhizome occurs either whole or in transverse slices. When entire, it is cylindrical or in the shape of a truncated cone, 5 to 10 cm. long and 2 to 4 cm. thick, externally dark brown and very rough from the insertion of the radicles, internally white and amylaceous. The rootlets are of various lengths, 2 to 4 mm. thick, coarse, simple, and very strong, very much flattened and wrinkled, white within, and covered by a yellowish or reddish-brown epidermis, considerably lighter colored than the body of the rhizome. The odor is fetid, the taste acrid; both are lessened by drying and progressively diminish with time, so that the dried rhizome should not be kept longer than a single season. This acridity is entirely absent in the decoction. The seeds are very acrid, and, though inodorous when whole, give out, when bruised, the peculiar odor of the plant.

The rhizome is affirmed to be antispasmodic and narcotic; occasioning nausea and vomiting, with headache, vertigo, and dimness of vision. It has been used with alleged success in *asthma, chronic catarrh, chronic rheumatism, chorea, hysteria*, and *dropsy*. *Dose*, of powder, from ten to twenty grains (0.65–1.3 Gm.), increased *pro re nata*.

Dragon's Blood. *Sanguis Draconis. Sangdragon*, Fr. *Drachenblut*, G. *Sangre de drago*, Sp.—*Dragon's blood*, of which there are several commercial varieties, is a resinous exudation obtained from the fruits of a number of palms. East Indian dragon's blood is obtained from a number of species of *Dæmonorops*, a genus which was previously ascribed to *Calamus*. Malay dragon's blood is obtained from *Dæmonorops didynophyllos, D. micranthus* and *D. propinquus;* Sumatra dragon's blood from *Dæmonorops Draco* Blume (*Calamus Draco* Willd.). In Borneo a dragon's blood is obtained from *Dæmonorops draconcellus* and other species of *Dæmonorops*. On the surface of the fruit, when ripe, is an exudation, which is separated by rubbing, or shaking in a bag, or by exposure to the vapor of boiling water, or finally by decoction. The finest resin is procured by the two

former methods. It comes in two forms: sometimes in small oval masses (*tear dragon's blood*) of a size varying from that of a hazelnut to that of a walnut, covered with the leaves of the plant, and connected in a row like beads in a necklace; sometimes in cylindrical sticks, eighteen inches long and from a quarter to half an inch in diameter, thickly covered with palm leaves, and bound round with slender strips of cane. See paper by E. M. Holmes in *P. J.*, 1905, 933.

Dragon's blood is inodorous and tasteless, insoluble in water, but soluble in alcohol, ether, and the volatile and fixed oils, with which it forms red solutions. According to Herberger, it consists of 90.7 parts of a red resin, which he calls *draconin*, 2.0 of fixed oil, 3.0 of benzoic acid, 1.6 of calcium oxalate, and 3.7 of calcium phosphate. Tschirch (*Harze und Harzbehälter*, 1900, p. 189) has made an elaborate study of dragon's blood, and finds 2.5 per cent. of *draco-alban*, $C_{20}H_4O_4$, a white substance melting with decomposition at about 200° C. (392° F.); 13.58 per cent. of *draco resen*, a yellow resinous substance of the formula $C_{26}H_{44}O_2$, and 56.86 per cent. of *draco resin*, a resin ester or mixture of esters, *benzoic dracoresinotannol ester* and *benzoylaceticdracoresinotannol ester*, and 18.4 per cent. of insoluble substances. It was formerly employed in medicine as an astringent, but is nearly or quite inert, and is now never given internally. It is sometimes used to impart color to plasters. For further information concerning this drug, see *U. S. D.*, 19th ed., p. 1475.

Drosera. *Sundew. N. F. IV. Herba Rorellæ. Rosollis. Rosée du Soleil*, Fr. *Sonnenthau*, G. —It is described by the N. F. as "the air-dried flowering plant of *Drosera rotundifolia* Linné (Fam. *Droseraceæ*), frequently mixed with the closely allied species *Drosera intermedia* Hayne and *Drosera longifolia* Linné, or at times wholly replaced by these. A delicate plant of a reddish color throughout, with few fibrous, blackish rootlets; leaves all in a basal rosette, blade orbicular, about 15 mm. in diameter, abruptly contracted into a slender, pubescent petiole, upper surface covered with prominent glandular hairs; scape filiform, smooth, from 10 to 20 cm. in length, bearing a few, five-parted, small, white fugacious flowers in a curved, one-sided raceme. *Drosera intermedia* is identified by its spatulate leaves with blades two or three times as long as they are wide and glabrous petioles. *Drosera longifolia* is identified by its elongated spatulate obovate leaves with blades six to eight times as long as they are wide, and its slender smooth petioles and scape, declinate at base. Odorless; taste faintly bitter and acidulous. Drosera yields not more than 30 per cent. of ash." *N. F.* Drosera has been employed in *phthisis*, but is probably of no value. (See *Proc. A. Ph. A.*, xxvii, 225.) Under the name of *droserin* an extract of various plants of this species has been recommended in *whooping cough*. It is marketed in the form of tablets of which there are two strengths; number one being intended for children, number two for adults. The *dose* of the crude drug is one drachm (4 Gm.).

Duboisia.—*D. myoporoides* R. Br. (fam. *Solanaceæ*) is a tall, glabrous shrub or small tree, which is a native of Australia, New South Wales, New Caledonia, and Queensland. The medicinal properties of this plant were made known by Baron von Mueller, who received the leaves from J. Bancroft. The alkaloid *duboisine* was discovered in the leaves by A. W. Gerrard. (*P. J.*, viii, 787). For his method, see 16th ed., *U. S. D.*; also, for an account of the chemical and medicinal properties of this alkaloid, and its relations to atropine, see *Belladonna*, p. 221.

According to the researches of Jos. Lanterer (*L. L.*, 1896), the old leaves and twigs of *Duboisia myoporoides*, contain hyoscyamine, the fresh young leaves scopolamine, the dried leaves being stronger than are belladonna leaves, and yielding 0.97 per cent. of alkaloid. *Duboisia Leichhardtii* F. v. Muell. is said to be still richer in alkaloid, which is chiefly amorphous scopolamine; while the leaves of *Datura arborea* L. (*Brugmansia arborea* Steud.) and of *D. cornigera* Hooker (*Brugmansia Knightii* Hort.), natives of South America, acclimatized in Queensland, contain a mixture of hyoscyamine and atropine.

D. Hopwoodii F. v. Muell., *pitury plant*, is the source of *pituri*, a narcotic stimulant largely used by the natives of Central Australia. The drug itself is a fine powder, composed of the leaves and twigs which are gathered during the month of August, while the flower is in bloom, and are put up in various forms of circular mats about 7.5 cm. in diameter. The natives smoke and chew pituri, and it is alleged to have a powerfully stimulating effect, assuaging hunger, and enabling those who are its devotees to perform much labor and go long journeys with but little food. Pituri yielded to A. W. Gerrard minute quantities of an alkaloid which he believed to be identical with nicotine, but Liversidge has shown that the liquid, acrid alkaloid, *piturine*, $C_{12}H_{16}N_2$, is distinct from nicotine. (*Proc. Roy. Soc. N. S. W.*, 1880.) Pituri contains from 1 to 2½ per cent. of the alkaloid.

Echinacea. *N. F. IV. Nigger-head. Sampson-root. Pale Purple Cone-flower.*—"The dried rhizome and roots of *Brauneria pallida* (Nuttall) Britton (*Echinacea angustifolia* De Candolle) (Fam. *Compositæ*)." *N. F. IV.* This composite plant, a native of the prairie region of America west of Ohio, has been introduced by the so-called eclectic physicians as a remedy in divers dissimilar diseases. The root is described by the N. F. as "nearly entire, cylindrical, very slightly tapering and sometimes slightly spirally twisted, from 10 to 20 cm. in length and from 4 to 13 mm. in diameter, externally grayish-brown, light brown or purplish-brown, slightly annulate in the upper portion, with occasional V-shaped stem scars, somewhat longitudinally wrinkled, or furrowed; fracture short, fibrous, bark less than 1 mm. in thickness, wood thick and composed of alternate light yellowish and black wedges; the rhizome with a circular pith. Odor faint, aromatic; taste sweetish, followed by a tingling sensation suggesting aconite, but lacking the persistent and benumbing effect produced by that drug. Under the microscope, sections show the presence of intercellular (schizogenous) oil and resin cavities or reservoirs in both the wood and bark, numerous stone cells distinguished by the presence of a blackish, resinous substance in the intercellular spaces between them and some of the adjoining parenchyma, the latter containing masses or aggregates of inulin. The walls of the tracheæ or vessels are marked with simple slit-like pores or annular and reticulate thickenings; bast fibers occur in the stem, and in some specimens true libriform or wood fibers are found. Echinacea yields not more than 6 per cent. of ash." *N. F.* Kraemer and Sollenberger (*A. J. P.*, 1911, p. 315) have described the physical characteristics of the drug. Lloyd (*Eclectic Med. Journ.*, 1897) obtained minute quantities of an inert alkaloid and believed that the active sub-

stance was a resin. Heyl and Hart (*J. Am. C. S.*, 1915, xxxvii, p. 1769) found the drug to contain inulin, 5.9 per cent.; inuloid, 6; sucrose, 7; vulose, 4; betaine, 0.1, and resins, 1.9 per cents.; the latter consisting of two isomeric phytosterols, phytosterolin, and the following fatty acids, oleic, linolic, cerotic and palmitic, but could find no physiologically active substance. Echinacea has been attributed with the property of increasing the resistance of the body to infection and is consequently used in *boils, septicemia, cancer,* and other infective conditions. It is also attributed with aphrodisiac and analgesic powers, but is probably without therapeutic value. The recommended *dose* of the fluidextract is from ten to thirty minims (0.6–1.8 mils). Hale (*Lancet Clinic,* March, 1901) injects an extract into the rectum in the treatment of *hemorrhoids.*

Brauneria purpurea D.C. Britton (*Rudbeckia purpurea* L., *Echinacea purpurea* Moench), *Black Sampson, Purple Cone-flower* (Virginia to Illinois and southward to Louisiana), has similar properties to *B. pallida,* and is similarly used.

Eggs. *Hen's Egg. N. F. IV. Ovum Gallinaccum.*—It is defined as "the recently laid egg of the hen, *Gallus domesticus* Temminck (Fam. *Phasianidæ*)." *N. F.* The egg of the ordinary hen consists of an exterior covering, the shell; a white, semi-opaque membrane; the white; and the yolk.

The *shell—testa ovi* or *putamen ovi*—consists, according to Vauquelin, chiefly of calcium carbonate, with animal matter, and a minute proportion of calcium phosphate, magnesium carbonate, ferric oxide, and sulphur. When exposed to a high degree of heat in the open air, the carbon dioxide is driven off, the animal matter consumed, and the lime left nearly pure. The membrane lining the shell appears to be of an albuminous nature. The *white—fresh egg albumen, N. F. IV, ovi albumen recens*—is defined as "the freshly separated liquid white, or albumen, of recently laid eggs of the hen, *Gallus domesticus* Temminck (Fam. *Phasianidæ*)." *N. F.* It is a glairy, viscid liquid, contained in very delicate membranes, without odor or taste, readily soluble in water, coagulable by the stronger acids, by alcohol, and by a heat of 56° C. (132.8° F.). Exposed in thin layers to a current of air, it becomes solid, retaining its transparency and solubility in water. By coagulation it is rendered white, opaque, and insoluble. At a temperature of 100° C. (212° F.), one part of it renders opaque one thousand parts of water in which it has been dissolved. It contains, according to Bostock, in 100 parts, 85 of water, 12 of pure albumin, 2.7 of mucus or uncoagulable matter, and 0.3 of salts, including sodium hydroxide and traces of sulphur. The white of eggs is precipitated by stannous chloride, gold chloride, lead subacetate, copper sulphate, corrosive sublimate, tannin, and numerous other chemicals. When kept in the fluid state it soon putrefies; but if carefully dried without coagulation it may be preserved unaltered a long time, and may be readily redissolved in water.

Fresh Egg Yolk, N. F. IV. Ovi Vitellum Recens. Vitellus, U. S. 1890.—It is defined as "the freshly separated yolk of recently laid eggs of the hen, *Gallus domesticus* Temminck (Fam. *Phasianidæ*)." *N. F.* The yolk is inodorous, of a bland oily taste, and forms an opaque emulsion when agitated with water. By heat it is coagulated into a granular solid, which yields a fixed oil by expression The researches by Gobley and others have established the constitution of the yolk about as follows: water, 51.8 per cent.; vitellin, 15.8 per cent.; nuclein, 1.5 per cent.; palmitin, stearin, and olein, 20.3 per cent.; cholesterin, 0.4 per cent.; phosphoglyceric acid, 1.2 per cent.; lecithin, 7.2 per cent.; cerebrin, 0.3 per cent.; coloring matter, 0.5 per cent.; salts, 1.0 per cent. (König, *Nahrungs- und Genussmittel,* 180.) Vitellin belongs to the class of globulins, and, while not precipitated from its solution by sodium chloride, is precipitated completely on saturation of its solution with ammonium sulphate. Chevreul states that there are two coloring principles, one reddish containing iron, the other yellow and similar to the coloring matter of bile. The former is more difficultly soluble in ether than the latter. (*N. R. Pharm.,* 1867, xvi, 697.) It is said that the yolk may be kept for a considerable time without observable change by adding to it 5 per cent. of sodium sulphate, in powder or concentrated solution. Granules have been found, with the aid of the microscope, in the yellow of the egg, which are rendered blue by iodine, and have all the other properties of the starch granules. (*J. P. C.,* Oct., 1868, 261.)

Under the name of *Glyconin* there has been employed in France for many years both for medicinal purposes and for those of the toilet, an emulsion made of glycerin and the yolk of egg. When these two substances are rubbed together, they unite to form a very intimate mixture, which does not separate. It has the consistence of honey, and forms an opaque emulsion with water. It may be preserved almost indefinitely. The usual proportions of the ingredients are four parts of the yolk of egg and five parts of pure glycerin. It has been repeatedly recommended as a basis for cod liver oil and other emulsions. (See also papers by Close in *Proc. A. Ph. A.,* 1884 and 1886.) It is itself not medicinal.

The Glycerite of Egg Yolk is recognized by the N. F. (see Part III).

The *white* of egg is used frequently for the clarification of liquids, which it effects by involving, during its coagulation, the undissolved particles, and rising with them to the surface, or subsiding. It is highly recommended as an antidote for corrosive sublimate, copper sulphate, and other caustic poisons, with which it forms insoluble and comparatively inert compounds. It is sometimes also used for the suspension of insoluble substances in water, but is inferior for this purpose to the yolk, and even to mucilage of gum arabic. Agitated briskly with a lump of alum, it coagulates, at the same time dissolving a portion of the alum, and thus forming the so-called *alum curd,* which is used between folds of gauze over the eye, in some states of *ophthalmia.* It is also used in the official pepsin valuation.

In pharmacy, the yolk is highly useful as an intermedium between water and insoluble substances, and is to be preferred to the white in preparing emulsions. It is employed in medicine for its food value and also to obtain the tonic effect of the lecithin it contains. See p. 1464.

Egols.—This name has been applied by E. Gautrelet (*C. R. A. S.,* 1899, 11) to a series of substances introduced by him. They are *o-nitroparasulphonates* of phenol, cresol, and thymol, in chemical combination with mercury and potassium. The *egols* are permanent compounds which crystallize with difficulty in rhombohedra, but which occur in commerce as reddish-brown powders, freely soluble in water, forming odorless and tasteless solutions, neutral in reaction, and free from

caustic or irritant character. In solutions of 0.4 per cent. they are said to be actively inhibitory to the growth of germs, and in stronger solutions powerfully bactericidal. It is claimed for them also that they are not poisonous to man, although when given in overdoses they sometimes act as an emetic.

Eigones.—This name has been given to certain albuminous compounds of iodine and bromine which, when taken into the alimentary canal or brought in contact with wounds or ulcerated surfaces, undergo decomposition with liberation of their active substances.

Bromeigone is a white, almost odorless, and tasteless powder, insoluble in water, and contains on an average 11 per cent. of bromine in organic combination.

Iodine eigones: *Alpha-eigone* is a compound of iodine and albumin and appears as a light brown powder without odor or taste; contains about 20 per cent. of iodine. *Alpha eigone-sodium* is a light colored, almost white, powder, containing about 15 per cent. of iodine. It is moderately soluble in cold and more readily in hot water. *Beta-eigone* is a *peptonized iodized iodoeigone*, readily soluble in water; eigone soap contains 5 per cent. of *iodoeigone*. Internally the iodine eigones have been used in *doses* of from six to nine grains (0.4–0.6 Gm.), best given in the form of pill, in *syphilis, rheumatism, bronchitis, asthma*, and other conditions in which potassium iodide is employed. They produce the ordinary symptoms of iodism when given in sufficient amount, but are said to have the great advantage over the older iodides of not irritating the stomach. As a local application they are employed in all forms of external infective wounds, in *nasal catarrh, tuberculosis, ulcers, abscesses*, and in the class of cases in which iodoform has been hitherto employed.

Peptoneigone is a peptonized bromine albumin compound which is comparatively readily soluble in water. It also contains about 11 per cent. of combined bromine. It is odorless and tasteless. Traces of hydrogen bromide are sometimes present as an impurity. The bromeigones are supplied commercially in the form of *bromeigone, brompeptone* or *peptonebromeigone*, and are odorless, tasteless powders. Bromeigone is insoluble, peptonebromeigone is soluble in water. The bromeigones have been given internally as substitutes for the bromides in various diseases. The *dose* of either of them is from ten to twenty grains (0.6–1.2 Gm.).

Eikonogen.—The sodium salt of amidobetanaphthalbetamonosulphonic acid, $NH_2C_{10}H_5(OH).SO_3Na+2\frac{1}{2}H_2O$. This is a white powder having a strong reducing action on silver salts. It is soluble in water and is used as a photographic developer. It has also been used in the treatment of *ivy poisoning*. It is decomposed by contact with fumes of ammonia.

Elarson. *N. N. R.* 1917.—Under this name *strontium-chlorarsenobehenolicate* has been introduced. It is a white, tasteless powder insoluble in water and sparingly soluble in alcohol or ether, and represents about 13 per cent. of arsenium. Its range of usefulness is precisely that of arsenous oxide. The beginning *dose* is about one one-hundredth of a grain (0.0006 Gm.) three times a day, which may gradually be increased up to one-twentieth of a grain (0.003 Gm.) three times a day or more.

Elastica. *U. S. VIII* (*Br.* 1898). *Rubber. Caoutchouc*, Br. *India-Rubber. Resina Elastica. Gummi Elasticum. Caoutchouc*, Fr. Cod. *Kautschuk. Federharz*, G. *Caucho, Cahuchu, Goma elastica*, Sp.—"The prepared milk-juice of several species of *Hevea* Aublet. (Fam. *Euphorbiaceæ*), known in commerce as Para Rubber." *U. S. VIII.* "The prepared milk-juice of Hevea brasiliensis, *Muell. Arg.*, and probably other species; known in commerce as pure Para rubber." *Br.*, 1898.

Rubber was made official in the U. S. P., 1890, because of its use in making mustard paper, and in the Eighth Revision it was used in the formula for belladonna plaster.

The importations into the United States of crude rubber for the year 1914, was 131,995,742 lbs., valued at $71,219,851; and for 1915, 172,068,428 lbs., valued at $83,030,269.

India-rubber or caoutchouc is a hydrocarbon obtained from the milky juice of certain tropical plants. This milky juice is contained chiefly in the so-called laticiferous vessels, situated in the internal zone of the bark, which are composed of isolated cells, so arranged as to form large vessels with many ramifications. A hydrocarbon is formed by the protoplasm of the cells which belong to the fundamental parenchymatous structure of the bark and not to the fibro-vascular bundles. That the hydrocarbon is a waste product, incapable of use in the economy of the plant, is believed by some naturalists; that it is necessary to the life of the plant, as believed by other naturalists, is not yet proved, the probabilities, however, are in favor of the latter view.

The latex as it first exudes from the wounded plant is said to have some resemblance to the milk of the goat, containing suspended microscopic granules which are affirmed by Adriani to have a diameter of not more than 0.002 mm. or two microns. In its best forms the yield of pure india-rubber from the latex, or milk juice, should be as much as 32 per cent.

Although various milky-juice plants of the temperate countries contain the hydrocarbon, commercially, india-rubber is a product only of the tropical and subtropical countries. It is said to be obtained for commercial purposes from at least 90 species of plants, representing five different botanical families, namely: the *Euphorbiaceæ, Artocarpaceæ, Moraceæ, Apocynaceæ*, and *Asclepiadaceæ*.

The india-rubber producing *Euphorbiaceæ* are chiefly South American trees, inhabiting the region from extreme Southern Brazil to Northern Venezuela. The most important of these belong to the genus *Hevea*. The *Hevea brasiliensis* (*Siphonia brasiliensis*) yields the most esteemed commercial rubber. The *Hevea guaianensis* has been acclimatized and is cultivated in Ceylon, British India, and other parts of Southern Asia. In the Gaboon Coasts, Congo, and Ceylon, the *Manihot Glaziovii* has been cultivated.

The india-rubber producing *Moraceæ* have a very wide distribution throughout tropical countries. Of the South American species the most important is the *Castilloa elastica*, a large tree which inhabits Mexico, Central America, Northern South America, and the West Indies, and formerly produced the bulk of the india-rubber of Mexico and Central America. In Asia and Africa the most important india-rubber *Moraceæ* belong to the genus *Ficus;* the chief species being the *Ficus indica* L., of Southern Asia and the Philippine Islands, familiarly known as the *Banyan tree;* and the *Ficus elastica* Roxb., of India and Java, the *india-rubber plant* of our hothouses.

Belonging to the *Apocynaceæ* are numerous *bind-weeds*, natives of Africa, Asia, and various parts of Oceania. The most important of these belong to the genus *Landolphia*, large woody bind-weeds, which grow over the trees of Liberia, Gaboon, Angola, Zanzibar, Madagascar, and other portions of Africa, reaching a length of 80 feet, and a trunkal diameter of 6 inches, covering large masses of ground and making forests almost impassible. From them comes the bulk of African rubber. The apocynaceous genus *Vahea* is represented in both South America, Eastern, Western and Central Africa; while the genus *Willoughbeia* grows in Southern Asia, and has been acclimatized in Australia.

The widespread destruction of the native rubber trees, especially in the valley of the Amazon, with other causes, slowly led to experiments in the cultivation of the plants. The first important trials were made in Assam in 1860, since which time, especially under the fostering care of the British Government, much has been accomplished. The attempts, however, to acclimatize the *Castilloa elastica* and the *Hevea brasiliensis* in Ceylon and India finally failed. More successful were the plantations of the *Manihot Glaziovii*, which has been found to thrive well at an altitude of about 6000 feet in Ceylon, and also in India, and which bids fair to be the great india-rubber tree of the future, especially in view of the fact that cultivation was stimulated by the rapid disappearance of the wild Landolphias in the French Congo; government experiments have proved that the Manihot grows well in that region.

In Brazil, india-rubber is procured from the trees by making vertical cuts with a narrow-bladed hatchet, in the bark, in the period between the end of August and the first of January, and collecting the latex as it falls, drop by drop, often to the amount of more than one fluidounce from each incision. Generally in Central and South America, as well as in Africa and Asia, the method of tapping the trees is similar, though the period of year at which the best yield of latex is obtained varies. The old method of obtaining rubber, by the cutting down of the tree, is probably no longer followed, except in Congo (Free) State. When collected the latex is caused to coagulate, usually by the use of heat, dry or moist, artificial or natural. The Para rubber owes its peculiar physical character to the fact that the coagulation of the latex is produced by smoking it. In Africa, and to some extent in America, coagulation is effected by the addition of certain chemicals, notably alum, sulphuric acid, common salt, soap, and citric acid.

Here is a barometer, of present and prospective, expansion in rubber supply:

	Plantation tons	Native tons	Total tons
1905	145	60,800	60,945
1907	1,000	68,000	69,000
1909	3,600	65,400	69,000
1911	14,100	61,900	76,000
1914	64,000	60,000	124,000
Estimated production after 1914.			
1917	147,000	34,500	181,500
1919	183,000	30,000	213,000
1921	209,000	30,000	239,000

The significant feature of the above is the enormously increased growth of cultivated rubber, on plantations.

Properties.—Rubber occurs in large flat pieces, or molded into various shapes. The latter are formed by applying successive layers of the juice upon molds of clay, which are broken and removed when the coating has attained a sufficient thickness and consistence. In the drying of these layers they are exposed to smoke, which gives to the concrete mass a blackish color. Rubber was officially described as "in flask-shaped or roundish masses, or in pieces of the same having sharply incised surfaces and exhibiting a laminated structure; floating on water; externally brownish to brownish-black; internally of a lighter tint, mottled; odor creosote-like; nearly tasteless. Pure Para rubber is insoluble in water, dilute acids, or dilute solutions of the alkalies; soluble in chloroform, carbon disulphide, oil of turpentine, petroleum benzin, and benzene; when heated to about 125° C. (257° F.) it melts, remaining soft and adhesive after cooling." *U. S. VIII.* "In elastic masses of varying thickness, brownish-black externally and mottled with a pale tint internally; insoluble in *water*, ethylic alcohol, alkaline solutions, or dilute acids, soluble in *chloroform, oil of turpentine, carbon bisulphide, benzol*, and *petroleum spirit*. When heated to about 257° F. (125° C.) it melts, remaining soft and adhesive after cooling. Odor characteristic, somewhat empyreumatic; nearly tasteless." *Br.*, 1898.

Chemical Constitution.—The juice of the rubber trees, when it concretes by exposure to the air, assumes on the outer surface a yellowish-brown color, while the mass remains white or yellowish-white within. It is said that a little alum facilitates the coagulation, while ammonia retards it, so that a little of the latter may be advantageously added, when it is desired to keep the milky juice in the liquid state. The recent juice contains, according to Faraday, 1.9 per cent. of vegetable albumen, traces of wax, 7.13 per cent. of a bitter nitrogenous substance soluble in water and alcohol, 2.9 of a substance soluble in water but insoluble in alcohol, 56.37 soluble in water with a little free acid, and only 31.7 of the pure elastic principle to which chemists have given the name of caoutchouc. Besides these principles, the concrete juice, as it reaches us, generally contains soot, derived from the smoke used in drying it. *Pure caoutchouc*, or rubber, is nearly colorless, and in thin layers transparent. It is highly elastic, lighter than water, without taste and odor, fusible at about 120° C. (248° F.), remaining unctuous and adhesive upon cooling, inflammable at a higher temperature, insoluble in water, alcohol, the weak acids, and alkaline solutions, soluble in ether when entirely freed from alcohol, soluble also in chloroform and most of the fixed and volatile oils, though, in the latter, at the expense of its elasticity. It is said, however, that the oils of lavender and sassafras, dissolve it without change, and that when precipitated by alcohol from its solution in oil of cajuput it is still elastic. But its best solvents, for practical purposes, are petroleum benzin, the empyreumatic oil obtained by distilling caoutchouc itself, carbon disulphide, and pure oil of turpentine. According to Bolley, the best method of effecting its solution, for the preparation of a varnish, is first to digest it, cut in small pieces, in carbon disulphide, which converts it into a jelly, and then to treat this jelly with petroleum benzin. A larger proportion is thus taken up than by any other method. Rubber is not immediately affected by atmospheric air, chlorine, hydrochloric or sulphurous acid gas, or ammonia. On prolonged expos-

ure to light and air, it slowly oxidizes and loses its elasticity.

Rubber chemically is composed of a mixture of polyterpenes. When destructively distilled, it yields *isoprene*, C_5H_8, and *dipentene*, $C_{10}H_{16}$. When isoprene is treated with concentrated hydrochloric acid, it is polymerized, and a substance obtained which resembles caoutchouc and is probably identical with it. When rubber is vulcanized, it may contain from 2 to 20 per cent. of sulphur, of which, however, not more than the lower amount is chemically combined, the rest being held mechanically, and capable of removal by treatment with caustic alkalies. Bouchardat succeeded in preparing from isoprene an artificial caoutchouc by acting upon the isoprene with saturated hydrochloric acid in sealed tubes. By the action of sulphur, rubber acquires properties which greatly increase its value in the arts. It either becomes pliable, soft, and tough, or if the amount of sulphur be increased, of a horny consistence, but preserves its elasticity under the influence of moderate heat or cold, is compressible with great difficulty, and resists the ordinary solvents, such as petroleum and oil of turpentine. In this state it is said to be vulcanized. The discovery of the process of *vulcanization* is ascribed to Charles Goodyear, of New York. (*Chem. Gaz.*, x, 193.) It consists in submitting rubber in thin sheets to the action of a mixture composed of 40 parts of carbon disulphide and 1 of sulphur chloride. For fuller details the reader is referred to the *J. P. C.* (3e sér., xvii, 205.) The same object may be effected by other methods. When thin layers of rubber are immersed for two or three hours in melted sulphur at the heat of 116° C. (240° F.), they are penetrated by the sulphur, but undergo no change of properties. If now heated in an inert medium to a temperature of from 135° C. (275° F.) to 160° C. (320° F.), a chemical reaction takes place, and the vulcanized product is obtained. The same result takes place if the rubber be first pounded with from 12 to 20 per cent. of finely powdered sulphur, and then heated to the temperature requisite for vulcanization. In either case a portion of uncombined sulphur remains mechanically mixed with the vulcanized rubber, from which it may be separated by various solvents, such as solutions of potassium or sodium hydroxide, carbon disulphide, oil of turpentine, anhydrous ether, etc. The *desulphurated* product thus obtained, while exempt from the disadvantages arising from the reaction of free sulphur, is more porous than before. For details of these two processes—viz., vulcanization by heat with sulphur or metallic sulphides, and cold vulcanization with solutions of sulphur chloride—see Sadtler's *Industrial Organic Chemistry*, p. 99–101.

Rubber is so insoluble that it cannot be absorbed in any form into the blood. It is used enormously in the arts for an infinite variety of purposes. In medicine it is used as the basis of various adhesive plasters as well as for numerous mechanical purposes.

Elaterium. Br. 1898. *Extractum Elaterii. Elaterium, Elaterion*, Fr. *Elaterium*, G. *Elaterio*, It., Sp.—"A sediment from the juice of the fruit of Ecballium Elaterium, *A. Richard.*" *Br.*, 1898. *Ecballium Elaterium* (L.) A. Rich., commonly known as the *wild* or *squirting cucumber*, is a perennial plant, with a large fleshy root, from which rise several round, thick, rough stems, branching and trailing like the common cucumber, but without tendrils. The leaves are petiolate, large, rough, irregularly cordate, and of a grayish-green color. The flowers are yellow and axillary. The fruit has the shape of a small oval cucumber, about an inch and a half long, an inch thick, of a greenish or grayish color, and covered with stiff hairs or prickles. When fully ripe, it separates from the peduncle, and throws out its juice and seeds with considerable force through an opening at the base, where it was attached to the footstalk. The name of squirting cucumber was derived from this circumstance, and the scientific and official title is supposed to have had a similar origin, though some authors maintain that the term *elaterium* was applied to the drug rather from the mode of its operation upon the bowels than from the projectile property of the fruit. It is derived from the Greek ἐλαύνω, *I drive*, or ἐλατήρ, *driver*. The word *elaterium* was used by Hippocrates to signify any active purge. Dioscorides applied it to the medicine of which we are treating. It is a native of the south of Europe, and is cultivated in Great Britain, where, however, it perishes in the winter. (For description of the culture in England, see *U. S. D.*, 19th ed., p. 432.)

Elaterium is the substance spontaneously deposited by the juice of the fruit, when separated and allowed to stand. Strong expression of the juice injures the product. When the fruit is sliced and placed upon a sieve, a perfectly limpid and colorless juice flows out, which soon becomes turbid, and in the course of a few hours begins to deposit a sediment. This, when collected and carefully dried, is very light and pulverulent, of a yellowish-white color, slightly tinged with green. It is the genuine elaterium, and was found by Clutterbuck to purge violently in the dose of one-eighth of a grain. But the quantity contained in the fruit is very small. Clutterbuck obtained only six grains from forty cucumbers. Commercial elatrium is often a weaker medicine, owing in part, perhaps, to adulteration, but much more to the fact that in order to increase the product, the juice of the fruit is often expressed with great force, and there is reason to believe that it is sometimes evaporated so as to form an extract, instead of being allowed to deposit the active matter. The French elaterium is prepared by expressing the juice, clarifying it by rest and filtration, and then evaporating to a suitable consistence. As the liquid remaining after the deposition of the sediment is comparatively inert, it will be perceived that the preparation of the French Codex must be relatively feeble. The following are the directions of the British Pharm. (1885): "Cut the fruit lengthwise, and lightly press out the juice. Strain it through a hair sieve, and set aside to deposit. Carefully pour off the supernatant liquor; pour the sediment on a linen filter, and dry it on porous tiles, in a warm place. The decanted fluid may deposit a second portion of sediment, which can be dried in the same way." The slight pressure directed is necessary for the separation of the juice from the somewhat immature fruit employed. The perfectly ripe fruit is not used, as, in consequence of its disposition to part with its contents, it cannot be carried to market.

The best elaterium is in thin flat or slightly curled cakes or fragments, often bearing the impression of the muslin upon which it was dried, of a greenish-gray color becoming yellowish by exposure, of a feeble odor, and a bitter, somewhat acrid taste. It is pulverulent and inflammable, and so light that it floats when thrown upon

water. When of inferior quality, it is sometimes dark-colored, much curled, and rather hard, breaking with difficulty, or presenting a resinous fracture. "In light, friable, flat or slightly curved, opaque cakes, about one-tenth of an inch (two and a half millimetres) thick; pale green, grayish-green, or yellowish-gray in color; fracture finely granular; odor faint, tea-like; taste bitter and acrid. It should not give the characteristic reactions with the tests for carbonates or for starch, and should yield half its weight to boiling *alcohol* (90 per cent.). When exhausted with *chloroform*, the solution evaporated, the residue washed with *ether*, and the process of solution, evaporation, and washing repeated, Elaterium should yield 25 per cent., or not less than 20 per cent., of Elaterin." *Br.* For an assay of elaterium by Jones and Ransom, see *U. S. Dispensatory*, 19th ed., p. 432. The *Maltese elaterium* is in larger pieces, of a pale color, sometimes without the least tinge of green, destitute of odor, soft, and friable, and not infrequently gives evidence of having been mixed with chalk or starch. It sinks in water, and usually contains so little elaterin that it should be employed only as a source of that principle. In the analyses of T. A. Elwood, the average yield of English elaterium was 21.5 per cent., of Maltese elaterium 15.3 per cent. (*P. J.*, Nov., 1891.)

Clutterbuck first observed that elaterium resided in the portion of it soluble in alcohol and not in water. The subsequent experiments of Hennell, of London, and Morries, of Edinburgh, which were nearly simultaneous, demonstrated the existence of a crystallizable matter in elaterium which is the active principle, and has been named *elaterin*. (See *Elaterinum*.) According to Hennell, 100 parts of elaterium contain 44 of elaterin, 17 of a green resin (*chlorophyll*); 6 of starch, 27 of lignin, and 6 of saline matters.

Uses.—Elaterium is a powerful hydragogue cathartic, and in a large dose generally excites nausea and vomiting. If too freely administered, it operates with great violence upon both the stomach and bowels, producing inflammation of these organs, which has in some instances eventuated fatally. It also increases the flow of urine. The fruit was employed by the ancients, and is recommended in the writings of Dioscorides as a remedy in *mania* and *melancholy*. It is at present employed only for its purgative effects. It is one of the most efficient hydragogue cathartics in the treatment of *dropsy*, especially valued when edema is due to disease of the kidney. It should be used with the greatest caution, or not at all, in the old or feeble or those prostrated by disease. Two-fifths of a grain (0.025 Gm.) of elaterium proved fatal by purging in an ill and feeble lady of 70 years. (*A. J. P.*, 1868, p. 373.) Because of its variability elaterium should never be employed, preference always being given to the official elaterin.

Elbon. *Cinnamoyl-para-oxyphenyl-urea.*—It occurs as white, tasteless crystals, very slightly soluble in water but readily dissolved by oils and alcohol. It is decomposed in the system and appears in the urine as a derivative of oxyphenyl-urea and hippuric acid. It is used as a stimulating expectorant, especially in *pulmonary tuberculosis*. According to Johannessohn (*B. K. W.*, 1913, p. 914), it also has an antipyretic action and increases the leucocytes. The *dose* is fifteen to forty-five grains (1–3 Gm.).

Elder Flowers. *Sambucus, N. F. IV. Elder. Sambuci Flores*, Br. 1898. *Sweet Elder, Black Elderberry. Sureau*, Fr. Cod. *Fleurs de Sureau, Hollunder, Fliederblumen*, G. *Sambuco*, It. *Sauco* (*Flor de*), Sp.—"The air-dried flowers of *Sambucus canadensis* Linné or of *Sambucus nigra* Linné (Fam. *Caprifoliaceæ*), separated from the peduncles and pedicels." *N. F.* The common elder, *Sambucus nigra*, of Europe, differs from the American most obviously in its size, the former approaching in height that of a small tree. The stem is much branched towards the top, and has a rough whitish bark. The leaves are narrower. The flowers are small, whitish and in five-parted cymes. The ovary consists of but three carpels, there being five cells in *S. canadensis* L. The berries are larger in the European elder, globular, and blackish-purple when ripe. A fungus growing on this plant, called *fungus sambuci*, has been used as a local application in *conjunctivitis*. According to Steckel, it is capable of taking up from 9 to 12 times its weight of water. (*N. R. Pharm.*, xiii, 476, 1864.) G. De Sanctis (*Gazz. Chim. Ital.*, 1895, xxv, 1, vol. xlix) obtained coniine from the leaves and stems of *Sambucus nigra*.

The indigenous *common elder, Sambucus canadensis*, is a shrub from six to ten feet high, with a branching stem, covered with a rough gray bark, and containing a large spongy pith. The small branches and leaf-stalks are very smooth. The leaves are opposite, pinnate, sometimes bipinnate, and composed usually of five to nine oblong-oval, acuminate, smooth, shining, deep-green leaflets; the veins of the under surface are somewhat pubescent. The flowers are small, white, and disposed in loose cymes; the cream-colored corolla is wheel-shaped, with five stamens on the tube. The berries are small, globular, and deep purple when ripe. The shrubs grow in low, moist grounds, along fences, and on the borders of small streams, throughout the United States, from Canada to the Carolinas, and westward as far as Arizona and Texas. It flowers from May to July, and ripens its fruit early in autumn. The flowers were official in the U. S. P., 1890, and Br. Pharm., 1898, and are now recognized by the N. F. IV. They have an aromatic though rather heavy odor. The berries as well as other parts of the plant are employed, in domestic practice, for the same purposes as the corresponding parts of the Euroean elder, to which this species bears a close affinity.

They are described by the N. F. as follows: "Small, from 2 to 3 mm. in breadth, shrivelled; calyx superior, five-lobed; corolla cream-colored to brownish-yellow, rotate, flat or slightly campanulate, regularly five-lobed; stamens five inserted at the base of the corolla, and alternating with its lobes, filaments slender, anthers oblong, yellow; pollen ellipsoidal or tetrahedral and rounded, covered with finely punctate markings and having three pores. Odor faintly sweet and aromatic; taste slightly bitter. Sambucus yields not more than 8 per cent. of ash." *N. F.*

The flowers yield their active properties to water by infusion, and when distilled give over a small proportion of volatile oil, which on cooling assumes a butyraceous consistence and contains an appreciable portion of ammonia. The *berries* are nearly inodorous, but have a sweetish, acidulous taste, dependent on the presence of saccharine matter and malic acid. Their expressed juice is susceptible of fermentation, and forms a vinous liquor used in Northern Europe. It is colored violet by alkalies, and bright red by acids, and the coloring matter is precipitated blue by lead acetate. The *inner bark* is without odor. Its

taste is at first sweetish, afterwards slightly bitter, acrid, and nauseous. Both water and alcohol extract its virtues, which are said to reside especially in the green layer between the liber and the epidermis. According to Simon, the active principle of the inner bark of the root is a soft resin, which may be obtained by exhausting the powdered bark with alcohol, filtering the tincture, evaporating to the consistence of syrup, then adding ether, which dissolves the active matter, and finally evaporating to the consistence of a thick extract. Of this, twenty grains produce brisk vomiting and purging. (*Ann. Ph. Ch.*, xxxi, 262.) The bark, analyzed by Kramer, yielded an acid called by him *viburnic acid* (which has proved to be identical with *valeric acid*), traces of volatile oil, albumen, resin, fat, wax, chlorophyll, tannic acid, grape sugar, gum, extractive, starch, pectin, and various alkaline and earthy salts. (*Chem. Gaz.*, May, 1846; from *A. Pharm.*) C. G. Traub found in the bark valeric acid, volatile oil, fat, resin, tannin, sugar, and coloring matter. (*A. J. P.*, 1881, p. 392.) J. B. Metzgar made a partial examination of the fruit and found sugar, gum, tannin, fat, and a resinous body. (*A. J. P.*, 1881, p. 553.) It was also examined by F. F. Lyons (*A. J. P.*, 1892, p. 1), who found 0.5 per cent. of a volatile oil, an amorphous yellow compound of a glucosidal character, and a tannin. The volatile oil of elder flowers was examined by W. J. Bush & Co. (*C. D.*, 1897, 53.) It has the sp. gr. 0.827, and is solid at ordinary temperatures like oil of rose. The liquid portion possesses the fragrance of fresh elder blossoms.

The flowers are gently excitant and sudorific, but are seldom used. The berries are diaphoretic and aperient, and their inspissated juice has been used as an alterative in *rheumatism* and *syphilis* in *doses* of from one to two drachms (3.9–7.7 Gm.); also as a laxative in *doses* of half an ounce (15.5 Gm.) or more. The inner bark is a hydragogue cathartic, and in large doses emetic. It has been employed in *dropsy*, *epilepsy*, and as an alterative in various *chronic diseases*. An ounce may be boiled with two pints of water to a pint, and four fluidounces (118 mils) given for a dose. It is also used in vinous infusion. The leaves are not without activity, and the young leaf-buds are said to be a violent and even unsafe purgative. The juice of the root has been highly recommended in *dropsy* as a hydragogue cathartic, sometimes acting as an emetic, in the dose of a tablespoonful, repeated *pro re nata*. The fruits of the California species *S. glauca* and *S. racemosa* are said to be used as food by the Indians. According to Combemale, confirmed by Lemoine, the aqueous solution of the European elder, *S. nigra*, is a very active diuretic, also causing in the lower animals, when given in sufficient amount, a pronounced fall of temperature, pulse, and respiration. It was found very useful in *cardiac* and *renal dropsies*. The drug itself sometimes caused vomiting and purging, but this effect never followed the use of the decoction. *Elder-flower water* was official in the Br., 1898, and was made by distilling one-fifth of the volume from a mixture of 10 pounds (Imperial) or 5000 Gm. of fresh elder flowers, and 5 gallons (Imp. meas.) or 25 liters of water. In the N. F. they are an ingredient in compound fluidextract of stillingia and laxative species. *Dose*, from one to two drachms (3.9–7.7 Gm.); as a laxative, half an ounce (15.5 Gm.) or more.

Elemi. *Gum Elemi. Elemi*, Fr.—This concrete resinous exudation is official in several of the European Pharmacopœias. The variety which is mostly used is known as *Manila* or *Philippine Elemi* and is derived from *Canarium commune* L. and probably also from *C. luzonicum* Gray (Fam. *Burseraceæ*). The name elemi is applied commercially to a large number of resins. The true elemi varieties contain from 20 to 25 per cent. of amyrin. These are further distinguished as "hard" or "soft" elemi, which are differentiated by the fact that the "soft" elemi contains from 20 to 25 per cent. of volatile oil. There are a number of other commercial varieties of elemi. The so-called carana-elemi is obtained from *Protium Carana* (Humb.) L. March., a tree growing in Venezula and Northern Brazil. Brazilian Almesseya-elemi is obtained from *Protium heptaphyllum* March., var. *Brasiliense* Engl. East African elemi is probably obtained from *Boswellia Frereana* Birdwood. Yucatan elemi is derived from *Amyris Plumieri* DC. All these plants belong to the *Burseraceæ*. The elemi is obtained by incisions into the trees, through which the juice flows and concretes upon the bark.

Carana-elemi occurs in masses of a greenish-yellow color, externally hard, internally soft, with a peculiar fennel-like aromatic odor. It is insoluble in water, soluble in sulphuric ether, chloroform, and benzene. According to Tschirch and Saal, carana-elemi contains 20 per cent. of exceedingly acrid resin. (*A. Pharm.*, Bd. 241, 1903.)

Elemi is in masses of various consistence, sometimes solid and heavy like wax, sometimes light and porous; unctuous to the touch; diaphanous; of diversified colors, generally greenish with intermingled points of white or yellow, sometimes greenish-white with brown stains, sometimes yellow like sulphur; fragile and friable when cold; softening by the heat of the hand; of a terebinthinate somewhat aromatic odor, diminishing with age, and resembling to some extent that of lemon and fennel; of a warm, slightly bitter, disagreeable taste; entirely soluble, with the exception of impurities, in boiling alcohol; and affording a volatile oil by distillation. "Moistened with rectified spirit, it breaks up into small particles, which, when examined by the microscope, are seen partly to consist of acicular crystals." *Br.*, 1885. Elemi is sometimes adulterated with rosin and turpentine.

According to Bacon (*Philippine Journal of Science*, 1909, iv, p. 93), the Manila elemi is derived from the *Canarium luzonicum* Miq. When first collected it is soft, but later becomes hard on exposure to the air and light, which has given rise to the belief that there were two varieties of the Manila gum. It is collected by incising the tree at the time when it is developing new leaves, the juice exuding through the bark and collecting in lumps at the point of the incision.

The two varieties of elemi that have been investigated chemically are the Manila, or soft elemi, and the Brazilian, or hard elemi. The Manila elemi contains 10 per cent. of an ethereal oil (made up of phellandrene and dipentene), *amyrin*, $C_{30}H_{50}O$, of which, according to Vesterberg, the isomeric varieties *α-* and *b-amyrin* are present, an amorphous *resin*, small amounts of *α-manelemic acid*, $C_{37}H_{56}O_4$, *β-manelemic acid*, $C_{44}H_{80}O_4$, *bryoidin*, $C_{20}H_{38}O_3$, and a bitter principle. The Brazilian elemi (*protium elemi*) contained *protomyrin*, 30 per cent.; *protolaminic acid*, 25 per cent.; and *protolaresine*, 37.5 per cent. The protomyrin has the same melting point and formula as the amyrin from Manila elemi.

Elemi has properties analogous to those of the turpentines, but is exclusively applied to external use. In the United States it is rarely employed even in this way, except as a constituent of plasters prepared upon the large scale. In the pharmacy of Europe it enters into the composition of numerous plasters and ointments. *Unguentum Elemi* (*Br. Ph.*, 1885) was of the strength of about 20 per cent.

Elixir of Iron, Quinine, and Strychnine Phosphates. (*U. S. P. VIII.*) *Elixir Ferri, Quininæ et Strychninæ Phosphatum. Elixir des Phosphates de Fer, de Quinine et de Strychnine*, Fr. *Elixir von phosphorsauren Eisen, Chinin und Strychnin*, G.—The U. S. P. VIII process was as follows: "Soluble Ferric Phosphate, *seventeen and one-half grammes* [or 270 grains]; Quinine, *eight and seventy-five hundredths grammes* [or 135 grains]; Strychnine, *two hundred and seventy-five milligrammes* [or 4¼ grains]; Phosphoric Acid, *two mils* [or 32 minims]; Ammonium Carbonate, in translucent pieces, *nine grammes* [or 139 grains]; Alcohol, *sixty mils* [or 2 fluidounces, 14 minims]; Acetic Acid, *twenty-eight and sixty-five hundredths grammes* [or 1 ounce av., 5 grains]; Ammonia Water, Distilled Water, Aromatic Elixir, each, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Dissolve the Quinine and Strychnine in the Alcohol, then add the Phosphoric Acid and *three hundred and fifty mils* [or 11 fluidounces, 401 minims] of Aromatic Elixir. Add the Acetic Acid to the Ammonium Carbonate, contained in a suitable vessel, and when solution is complete, neutralize with Ammonia Water and add enough Distilled Water to make the product measure *fifty mils* [or 1 fluidounce, 331 minims]. Mix the solution of Ammonium Acetate with the solution of the alkaloids, and add enough Aromatic Elixir to make the liquid measure *eight hundred and eighty mils* [or 29 fluidounces, 363 minims]. Dissolve the Ferric Phosphate in *thirty mils* [or 1 fluidounce, 7 minims] of Distilled Water, by the aid of a gentle heat, and if the solution be acid to litmus paper, neutralize exactly with Ammonia Water, and add enough Aromatic Elixir to make the product measure *one hundred and twenty mils* [or 4 fluidounces, 28 minims]. Finally, mix the two solutions and filter, if necessary." *U. S.*

This elixir was introduced into the U. S. P. VIII because it is largely used and deserved recognition, but because of the darkening of the elixir and frequent precipitation it was omitted from the U. S. P. IX. The difficulty is largely caused by the attempt to produce phosphates of the several ingredients and as this form possesses no special medicinal value it was believed that the use of the more permanent elixir of iron, quinine, and strychnine of the N. F. IV (see Part III) should be encouraged. The U. S. P. VIII process is essentially that recommended by Caspari, but as it did not prove satisfactory, Caspari has since recommended the following formula which is less likely to discolor or precipitate: Quinine (alkaloid), 8.75 Gm. [or 135 grains]; Strychnine (alkaloid), 0.275 Gm. [or 4¼ grains]; Ferric Phosphate (U. S. P.), 17.50 Gm. [or 270 grains]; Phosphoric Acid (U. S. P.), 2 mils [or 32 minims]; Alcohol, 60 mils [or 2 fluidounces, 14 minims]; Acetic Acid (U. S. P.), 16 Gm. [or 260 grains]; Ammonium Carbonate, 5.1 Gm. [or 83 grains]; Distilled Water, Aromatic Elixir, of each, *a sufficient quantity*, to make 1000 mils [or 33 fluidounces, 390 minims]. Add the ammonium carbonate, in firm translucent pieces, to the acetic acid contained in a beaker and when solution is complete, add 350 mils [or 11 fluidounces, 401 minims] of aromatic elixir and the phosphoric acid. Dissolve the quinine and strychnine alkaloids in 40 mils [or 1 fluidounce, 169 minims] of alcohol, add this solution to the acid mixture, and rinse the beaker or flask with 20 mils [or 325 minims] of alcohol, adding this also to the previous mixture; now add sufficient aromatic elixir to bring the volume of the mixture up to 880 mils [or 29 fluidounces, 363 minims]. Dissolve the ferric phosphate in 30 mils [or 1 fluidounce, 7 minims] of distilled water with the aid of heat, and when cool add sufficient aromatic elixir to bring the volume of the solution up to 120 mils [or 4 fluidounces, 28 minims]. (If the iron solution shows an acid reaction with litmus paper, it should be neutralized nearly, but not entirely, by the cautious addition of ammonia water.) Finally, mix the two solutions and keep the finished product in dark, amber-colored bottles. The ferric phosphate and the alkaloids are retained in solution in the elixir with the aid of an excess of phosphoric acid, but this makes the elixir unpleasantly acid to the taste; ammonium acetate is used to retain the ferric phosphate in solution with the other ingredients and to make a finished elixir which can be mixed with aqueous solutions without producing turbidity, and remain clear at low temperatures. This elixir should be preserved in amber-colored bottles protected from the light, otherwise the pale greenish color which it has when first made will disappear and be replaced by a brownish tint followed often by precipitation. *Dose*, one to two fluidrachms (3.75–7.5 mils).

Embarin.—This is a pale yellow fluid said to contain 6⅔ per cent. of *sodium-mercury-salicylsulphinate* and ½ per cent. of *dipara-anisylmonophenetyl guanidin hydrochlorate*. It is used as an injection in the treatment of *syphilis*. From eight to twenty minims (0.5–1.3 mils) are administered daily.

Emery. *Lapis Smiridis, s. Smiris. Emeri, Corindon granuleux ferrifère*, Fr. *Smirgel, Schmirgel*, G.—A very hard mineral, the powder of which is capable of wearing down all other substances except the diamond. It is an impure variety of *corundum*, which is *alumina* (Al_2O_3), containing oxide of iron. It was formerly derived almost solely from the island of Naxos, in the Grecian Archipelago. According to Landerer, it has been found in Asia Minor and the Morea, and it occurs in Chester, Hampden County, Mass. (See J. Lawrence Smith, *Am. J. Sci.*, 1866, xlii.) *Emery* is pulverized by grinding it in a steel mill, and the powder is kept in commerce of different degrees of fineness. It is used for polishing metals and hard stones. Compact corundum is now ground extensively for the manufacture of emery wheels, etc. Corundum is found abundantly in Northern Georgia, in North Carolina, and in Chester County, Pennsylvania. Both corundum and emery have been largely replaced in use by the product of the electric furnace, *carborundum*, which is *silicon carbide* (SiC).

Empyroform. *N. N. R.* 1917.—This is a condensation product of formic aldehyde and tar, forming a staple brown powder of a peculiar faint odor quite distinct from that of tar. Upon heating formic aldehyde is split off. It is insoluble in alcohol and water and soluble in acetone, caustic alkalies, and chloroform. It is used in inflammatory *skin diseases*, such as *acute* or *chronic*

eczema, in the form of ointment in strengths of from 5 to 15 per cent. Both antipruritic and disinfectant properties are claimed for it. It has the advantage over tar of being less irritant.

Enesol. *Mercury Salicylarsenite.*

$C_6H_4(OH)COO$
$C_6H_4(OH)COO$ > AsHg.—This is obtained by

reaction between one molecule each of methylarsenic acid and basic mercury salicylate. It is supplied in the form of a 3 per cent. solution of which 1 mil represents 0.0115 Gm. of mercury and 0.0043 Gm. of arsenic.

Enesol is recommended as a means of obtaining the effects of both mercury and arsenic in the treatment of *syphilis* and is intended especially for hypodermic administration. The *dose* is fifteen to thirty minims (1–2 mils) of the 3 per cent. solution, which may be administered every day or every alternate day, from 10 to 30 injections constituting the ordinary course of treatment, to be supplemented with the usual antisyphilitic treatment.

Energin.—An organic preparation of proteids and acids derived, it is claimed, from dried cod livers. It is a white, tasteless powder, soluble in water and recommended as a tissue reconstructor.

Enterorose.—A preparation of vegetable albumen impregnated with beef extract and diastase. It contains 18 per cent. albumen, 11 per cent. fat, 3.8 per cent. organic salts and 59.5 per cent. carbohydrates. In the treatment of *chronic constipation* it is claimed to show favorable results.

Endermol is a compound ointment vehicle containing hydrocarbons of the paraffin series and stearic acid amide. (Coblentz, *M. News*, Sept. 3, 1904.)

Eosin. *Bromeosin.* $C_{20}H_8Br_4O_5$.—A dye obtained by the action of phthalic anhydride upon phenols and introduction of bromine into the product. When phthalic anhydride acts upon resorcinol, $C_6H_4(OH)_2$, in the presence of a dehydrating agent like sulphuric acid or stannic chloride, at a temperature of 120° C. (248° F.), there is formed a compound *resorcinphthalein*, $C_{20}H_{12}O_5$, better known as *fluorescein*. By the action of bromine upon this is formed *tetrabromfluorescein* or *eosin*, $C_{20}H_8Br_4O_5$. Soluble *eosin* is the potassium salt of this compound, $C_{20}H_6Br_4O_5K_2$. It forms a bronze-colored crystalline powder having a strong green reflection. Its solution in water is a red liquid having a fine green fluorescence. On the addition of hydrochloric acid the fluorescence is destroyed, the liquid becoming yellow. Eosin is largely used at present as a dye; to make a brilliant *red ink*, dissolve 5 grains of eosin and 10 grains of gum arabic in a fluidounce of water. According to Mandach (*K. S. A.*, 1907), eosin affords a most sensitive reagent for the occurrence of bile pigment in the urine. For this purpose a stock solution of 0.1 per cent. is diluted until the yellowish-red color becomes a pale pink showing a slight green fluorescence. In the presence of bile this pinkish color is changed to a yellowish-brown, and later to a bottle-green. In normal urine no change of color is observed.

There is also sold under the name of *blue eosine* a *sodium iodeosine*, commercially known as *erythrosine*. It is a brown powder, soluble in water and used for dyeing wool, cotton and paper. It is also of use in histology as a stain for epithelial and muscular fibers and nuclei, etc.

Eosin Selenium is the name of a powder which has been used, experimentally, in investigations on the treatment of malignant tumors. The *dose* is one sixty-fourth of a grain (0.001 Gm.), to be increased if necessary.

Ephedra. *Ephedra vulgaris* Rich. (Fam. *Gnetaceæ*.)—Nagai has extracted from this Japanese plant an alkaloid, *ephedrine*, which, according to Kinnossuke, produces in the lower animals acceleration of the pulse, with lowering of the blood pressure, elevation of the rectal temperature, dilatation of the pupils, convulsions, and death by arrest of the heart and respiration. (*B. K. W.*, 1887.) Scriba found that a 10 per cent. solution dilates the pupil with certainty, in from forty to sixty minutes, without irritation, the dilatation not being complete, and the accommodation not at all or only slightly affected, and the pupils returning to normal in from five to twenty hours. An alkaloid has also been discovered in *Ephedra distachya* L., a shrub whose branches and root are used in Siberia as a remedy in *gout* and *syphilis*. According to Kobert, this alkaloid is essentially different from *ephedrine*, in not being mydriatic or poisonous. P. Spehr (*A. J. P.*, 1892, 234) considers that *E. vulgaris* contains two alkaloids, *ephedrine* and *pseudoephedrine*, isomeric and of the formula $C_{10}H_{15}ON$, while *E. monostachya* contains a crystalline base melting at 112° C. (233.6° F.) and having the formula $C_{13}H_{19}ON$. This latter, as stated by Kobert, is not mydriatic or poisonous. See paper by E. Schmidt, *A. Pharm.*, ccl, 1912, Nos. 2 and 3, 154, 161. According to Günsberg, pseudoephedrine is a powerful mydriatic, its 10 per cent. solution causing in fifteen minutes dilatation of the eye through excitement of the sympathetic nerve.

Ephedra nevadensis S. Wats and *E. antisyphilitica* C. A. Meyer, which grow abundantly in the extreme Western United States, are used under the names of *cayote*, *canutilo*, *whorehouse tea* as a remedy in *gonorrhea*. Loew thinks that their virtues reside in a peculiar tannin. *Dose*, of fluidextract, from one to two fluidrachms (3.75–7.5 mils). In Texas *E. trifurca* Torr. is similarly employed.

Epicarin. *N. N. R.* 1917.—A condensation product of creosotinic acid and naphthol which, according to Eichengrün, is *β-oxynaphthyl-o-oxy-meta-*

toluylic acid thus: $C_6H_3(COOH)(OH)(CH_2—C_{10}H_6OH)$. *Epicarin* forms slightly yellowish crystals or powder, with a faint odor, melting at 190°–195° C. (380°–389° F.), difficultly soluble in water but freely soluble in alcohol and ether as well as in soaps. It is said to be slightly poisonous, and was primarily introduced into veterinary medicine, especially for the treatment of *mange*, but has been used by Kaposi, Monti, and other dermatologists in *scabies*, *ringworm*, *prurigo*, and allied skin diseases as a substitute for naphthol. Its application is sometimes followed by irritation, which, though usually slight, may lead to papular and eczematous eruptions. It is claimed that the remedy is less poisonous than naphthol. In Kaposi's clinic no toxic symptoms followed covering the entire body of children with 10 per cent. ointment. Five to twenty per cent. ointment is used *pro re nata*.

Epichlorhydrin. *Chloropropylene oxide.* C_3H_5ClO.—A colorless liquid of specific gravity of 1.203 at 0° C. (32° F.) and miscible with alcohol and ether. It is used as a general solvent for resins, having a solvent action even on celluloid. It is

incompatible with alkaline hydroxides or carbonates, and it should be protected from exposure to air, which turns it red.

Epidermin.—A surgical dressing made by fusing 15 Gm. of white wax, and triturating in a warm mortar with 15 Gm. of powdered acacia until uniform, and adding a boiling mixture of 15 Gm. each of water and glycerin, and stirring until cold. Valentine and Schwartz have given the name *epidermin* to an ointment vehicle said to be composed of fluorxylol and difluordiphenyl.

Epigaea. *Epigaea repens* L. *Trailing Arbutus. Ground Laurel. Mayflower. Gravel Plant.*—This is a small prostrate or trailing ericaceous plant, having bristly woody stems; evergreen, entire, cordate-ovate leaves, and small, very fragrant dimorphic, subdioecious flowers, which appear early in the spring. It is found in the sandy woods or rocky soil, and grows on the sides of hills with a northern exposure. Darlington states that the plant has been supposed to be injurious to cattle, when eaten by them. (*Flora Cestrica*, 259.) Jefferson Oxley has found in this plant *arbutin*, $C_{12}H_{16}O_7$, *ursone*, $C_{20}H_{32}O_2$, *ericolin*, $C_{34}H_{56}O_{21}$ (the same constituents as are in uva ursi), tannic and formic acids, and a principle allied to gallic acid. (*A. J. P.*, xliv, 253.) Thal gives the simpler formula $C_{26}H_{30}O_3$ to ericolin. Eli Ives of New Haven, Connecticut, in 1849, highly commended epigaea as a substitute for uva ursi, and we now know that the two drugs contain the same active principles. The decoction of the leaves and stem may be used freely.

Epilobium. *Epilobium angustifolium* L. (*Chamænerion angustifolium* Scop.) *Willow-herb. Herbe de St. Antoine*, Fr. *Weidenröschen, Antonskraut*, G. (Fam. *Onagraceæ.*)—There are several indigenous species of *Epilobium*, which have the common name of willow-herb, from the resemblance of their leaves to the willow, all of which probably have nearly identical properties. The *E. angustifolium* is the largest of them. Its leaves and roots are said to be demulcent, tonic, and astringent, and yield their virtues to water and alcohol. They are used by the eclectics, generally and locally, in decoction, infusion, or cataplasm, as astringents. Oliver reports (*B. M. J.*, ii, 1897) violent poisoning with epileptiform convulsions caused by *E. hirsutum* L. Under the name of *Kaporie tea*, the leaves of *E. angustifolium* and of *E. hirsutum* are largely used in Russia as a beverage.

Epiosin, $C_{16}H_{12}N_2$, a derivative of oxamidophenanthrone, crystallizes in glassy prisms, melting at 195° C. (383° F.), readily soluble in alcohol and chloroform. It is a synthetic compound, produced by E. Vahlen, who claims for it the anodyne action of morphine without its objectionable after-results. Chemically it is a *methyl-diphenylen-amido-azol.* (*A. E. P. P.*, xlvii, 368.) *Dose*, one and one-half grains (0.096 Gm.).

Epithol.—*Epithol gold* and *epithol silver* are finely powdered copper and tin, which have been used in veterinary medicine by L. Hoffmann as a local application to *wounds.* (*B. Thier. W.*, 1902.)

Equisetum. *Equisetum hyemale* L. *Horsetail. Scouring Rush. Prêle*, Fr. *Schachtelhalm*, G. (Fam. *Equisetaceæ.*)—An indigenous plant, with slender annual stems from 3 to 9 dm. high, growing abundantly throughout the United States, and preferring wet places, as the banks of streams, etc. The plant derives its name of scouring rush from its use in scouring, for which it is fitted by the silicious character of the stems. Examined by F. J. Young (*A. J. P.*, 1886, 419), it yielded to petroleum benzin as a solvent 1.4 per cent. of a brownish-green, semi-liquid, fixed oil, which was readily saponified. It also contained a green semi-solid resin, sugar, and mucilage. The infusion of the whole plant is used sometimes in *dropsical* and *renal diseases*, but Cow (*A. E. P. P.*, 1912, lxx, p. 393) has shown that the diuretic action of *equisetum* is very feeble.

Erechthites. *Erechthites hieracifolia* (L.) Raf. *Fire-weed.*—An annual indigenous composite plant, growing in moist woods and recent clearings, and having a rank, somewhat aromatic odor. Its taste is bitterish, slightly acrid, and disagreeable. It yields its virtues to water. It has been especially recommended in *dysentery.* It is prone to infest the peppermint fields of Michigan, and its oil is said sometimes to deteriorate the oil of peppermint from that region. It has been shown however, that *Erigeron* (*Leptilon*) *canadensis* L. is far more injurious (see Erigeron).

Erepton. *N. N. R.* 1917.—This preparation, whose use is based upon the discoveries of Abderhalden that the system is capable of synthesizing albumin from the amino-acid, is prepared by digesting lean meat with pancreatic and intestinal secretions. It is a brown hygroscopic powder, readily soluble in water, containing 12 per cent. of nitrogen, and does not give the Biuret reaction. It has been recommended by Jacobsohn and Rawald (*Ther. Geg.*, 1911, p. 119) for rectal feeding. They administered 250 mils (8 fluidounces) of a 5 per cent. solution three to six times a day by enemata. They found that 85 per cent. of the nitrogen was absorbed.

Erigeron. *Fleabane. Scabious. Sweet Scabious. Daisy Fleabane. Herbe d'érigeron, Herbe de Vergerette*, Fr. *Berufkraut*, G.—Under this name the U. S. Pharmacopœia of 1870 recognized the herbal portions of *Erigeron annuus* (L.) Pers. and *E. philadelphicus* L. (Fam. *Compositæ.*)

The two species are abundant in the middle portions of the United States, grow in open fields, and are probably of identical medicinal value. They are popularly known as *fleabane.* The whole herb is used, and should be collected while the plants are in flower. It has a feebly aromatic odor and bitterish taste, and imparts its properties to boiling water.

The U. S. Pharmacopœia also formerly recognized, as *Erigeron canadensis* (*Leptilon canadense* (L.) Britt.), *Horseweed. Mare's tail. Fire-weed. Butter-weed. Colt's-tail.*

Canada fleabane is very common throughout the northern and middle sections of the United States, and has become naturalized over the world. It abounds in neglected fields, and is reported to be a very troublesome weed on the peppermint plantations of the West. It blooms in July and August. The plant, all parts of which are medicinal, should be collected while in flower. The leaves and flowers are said to be the most active parts. It has a characteristic odor, and a bitterish, acrid, somewhat astringent taste. Among its constituents, according to De Puy, are bitter extractive, tannin, gallic acid, and volatile oil. Both alcohol and water extract its virtues. Its acrimony is diminished by decoction, in consequence, probably, of the escape of the oil, upon which its virtues in part depend. All of the erigerons are reputed to be diuretic, tonic, and astringent: and useful in *dropsical complaints* and *diarrhea.* They have been given in substance (*dose*, a drachm, or 3.9 Gm.), infusion, tincture, or extract (*dose*, ten grains, or 0.65 Gm.), but the oil is the only proper preparation. The oil is of

value in *uterine, pulmonary,* and other *internal hemorrhages,* in *doses* of from five to fifteen minims (0.3–0.9 mil), every two hours. (See p. 1519.)

For further information concerning these drugs see *U. S. D.*, 19th ed., p. 1479.

Eriobotrya. *Eriobotrya japonica* Lindl. *Loquat. Japanese Medlar. Bibacier. Néflier du Japon. Nestole di Giappone.* (Fam. *Rosaceæ.*)—A small tree, indigenous to Japan and extensively cultivated. The fruit closely resembles the apricot and has a sweetish acid pulp. The seeds of this tree are said to contain amygdalin and emulsin, and to yield hydrocyanic acid in poisonous quantities. (*P. J.*, Aug., 1885.) Hérissey, in 1907, stated that Lehmann was incorrect in his conclusions that the glucoside was identical with *laurocerasin,* and states that the glucoside is *amygdalin.* (*A. Pharm.*, ccxlv, 1907.)

Erodium. *Erodium cicutarium* L. *Stork's-bill.*—An annual hairy plant belonging to the *Geraniaceæ.* It grows in Europe, Asia, Northern Africa and is widely cultivated, being found naturalized about cities in the United States. It is highly recommended by W. Abbots Smith in *dropsy.* (See *Am. J. M. S.*, 1865.)

Ervasin. *Acetyl-para-cresotic Acid.*—It occurs as white crystals, insoluble in water, but dissolving readily in alcohol. It is supposed to have the same properties as its homologue, acetyl salicylic acid, and is used as an anti-rheumatic, analgesic, and antipyretic. *Dose,* eight to fifteen grains (0.5 to 1 Gm.).

Eryngium. *Eryngium aquaticum* L. *Button Snakeroot. Corn Snakeroot. Rattlesnake's Master.*—The *button snakeroot* or *water eryngo* is an indigenous umbelliferous plant which grows in low wet places, from New Jersey as far south as Florida and Texas. The root, which is the medicinal portion, has a bitter, pungent aromatic taste, provoking, when chewed, a flow of saliva. It is said to be diaphoretic, expectorant, in large *doses* emetic, and the plant has been used as a substitute for senega.

Erythrina.—The bark of the Australian species of this genus, *Erythrina Broteroi,* is said to contain an alkaloid, *erythrinine,* while the Mexican species, *Erythrina coralloides* DC., bears poisonous seeds in which Altamirano has found *erythroidine,* a powerful paralyzant of the motor system, *erythroresin,* an emetic, *coralin* and *erythric acid.* The *extract* has been suggested as a substitute for curare. (*B. S. Ph. Br.*, 1900.) Langham obtained from the seeds of *E. zeyheri* (which have a scarlet pesta), *erythrine,* 15 per cent. (*C. D.*, 1911, 134.)

Erythrina lithosperma Blume. (*Hypaphorus subumbrans* Hassk.)—From the seeds of this beautiful leguminous tree, largely grown for shade in the coffee gardens of Java, P. C. Plugge has obtained *hypaphorine,* a tetanizing alkaloid. (*A. E. P. P.*, xxxii.)

Erythrol Tetranitrate. *N. N. R.* 1916. (*Tetranitrol. Butane tetrol.*) $C_4H_6(NO_3)_4$.—*Erythyrol tetranitrate* is solid and crystalline, and melts at 61° C. (142° F.). When pure it is colorless, and if kept in a dark and moderately cool place is fairly stable. If exposed to warmth, and especially sunlight, it rapidly undergoes decomposition, turning yellow and giving off nitrous fumes. It is also capable of rapid decomposition, and death has been caused by the explosion following its trituration in a mortar with glucose. (*B. M. J.*, i, 1896.) Its solubility in water is slight, but it dissolves readily in alcohol and in ether. It is a vaso-dilator, and belongs to the group of which glyceryl trinitrate (glonoin) or nitroglycerin is the representative. Blood pressure experiments show that the nitrates of erythrol and mannitol have a less marked and more prolonged action than those of glycerol and glycol. In man the effects of the remedy are said not to be apparent in less than half an hour and to last for two or three hours. It may be used in all cases for which glyceryl trinitrate is employed, and has been especially commended in *angina.* Its alcoholic solution is explosive, so that it should always be used in tablets, in preparing which great care is necessary. *Dose,* from a half to one grain (0.032–0.065 Gm.).

Erythronium. *Erythronium americanum* Ker. *Scrofula Root. Yellow Snowdrop. Rattlesnake Violet. Dogtooth Violet. Yellow Adder's Tongue.*—This is an indigenous, perennial, liliaceous plant, sometimes called, after the European species, *dog's-tooth violet.* It grows in rich woods from New Brunswick to Florida and west to Ontario and Arkansas. It flowers in the latter part of April or early in May. All parts of it are active. In the *dose* of twenty or thirty grains (1.3 or 2.0 Gm.) the recent bulb is emetic. The leaves are said to be more powerful. The activity of the plant is diminished by drying.

Eschscholtzia. *Eschscholtzia californica, Chamisso. California Poppy.*—Attention has been brought to this Californian member of the *Papaveraceæ,* as a powerful soporific and analgesic, which is free from the disadvantages of opium. The plant is extensively cultivated and there are now a number of garden varieties. Bardet and Adrain (*G. H. M. C.*, Nov., 1888) assert that they have obtained a glucoside, an alkaloid, and morphine in the proportion of from five to six grains in two pounds of the dried product. According to Fischer and Tweeden, there are seven alkaloids in *Eschscholtzia californica; protopine, β-* and *γ-homochelidonine,* "alkaloid *a,*" "alkaloid *b,*" *sanguinarine and chelerythrine.* As far as could be determined from the small quantities obtained, the alkaloids designated as *a* and *b* differ from any other alkaloids thus far known. (*Ph. Archiv.*, 1902, No. 7.) The narcotic power of the drug seems to be very weak, since, according to Bardet, three drachms were necessary to kill a rabbit. Ter-Zakariant (*G. M. P.*, Feb., 1889) states that the alcoholic extract acts as a respiratory depressant and narcotic, affecting in toxic dose also the spinal cord. Dujardin-Beaumetz has used the extract in commencing *doses* of twelve grains (0.78 Gm.), increasing to one hundred and eighty-five grains (12 Gm.) a day, and affirms that it is a harmless soporific and analgesic.

Escorcin. *Escorcinal, Aescorcin.* $C_9H_8O_4$.—This is prepared from *aesculetin* (a decomposition product of aesculin) by the action of sodium amalgam. It is a brown powder, soluble in alkalies, imparting to the solution a green color which quickly changes to red. It is used in discovering defects in the cornea and lesions in the conjunctival epithelium, the red color which it imparts to the lesions being much more distinct on the iris than the green color of fluorescin. *Dose,* one drop of a 10 to 20 per cent. aqueous solution.

Estoral. *Menthyl Borate,* $BO_3(C_{10}H_{19})_3$, is a white, crystalline, tasteless powder, possessing a slight menthol odor, permanent when dry, but splitting up into its component parts when moist or in contact with mucous membrane. It is soluble in ether and fatty oils, but separates from the latter on cooling. It has been recom-

mended by Feldt (*St. P. M. W.*, 1909) as a local application in various acute and chronic inflammations of the nose and throat. It may be applied as a snuff mixed with equal parts of milk sugar or in the form of an ointment. In the preparation of ointments the base, which may be preferably petrolatum, should be warmed and after the addition of the *estoral* the mixture stirred until cool.

Ethoxycaffeine, $C_{10}H_{14}N_4O_3$, is prepared by boiling 3 parts of bromcaffeine with 2 parts of potassium hydroxide and 10 parts of alcohol. It forms crystals fusing at 140° C. (284° F.); is difficultly soluble in water and ether, easily soluble in hot alcohol, insoluble in alkalies, soluble without decomposition in cold diluted hydrochloric acid; on warming it is decomposed. Filehne (*A. Phys.*, 1886) finds that *ethoxycaffeine* has upon frogs and rabbits a narcotic effect. From seven to ten grains of it produced in man vertigo, intellectual torpor, and sometimes pain in the head. Dujardin-Beaumetz (*B. G. T.*, March, 1886) finds that it acts in the guinea-pig as a narcotic and diuretic, and has given it for *headache* in *doses* of from three to fifteen grains (0.2–1.0 Gm.) a day, in capsules or dissolved in water by means of sodium salicylate. Cases of painful *zona, migraine,* and *nervous headaches* were relieved. The larger doses produced gastric irritation.

Ethyl Bromide. *N. N. R.* 1917. *Bromide of Ethyl. Hydrobromic Ether. Æther Bromatus,* G. P. *Bromure d'éthyle,* Fr. *Bromäthyl,* G. C_2H_5 Br.—This ether was discovered by Sérullas in 1827, who prepared it by acting on alcohol with bromine in the presence of phosphorus. (*Ann. Ch. Phys.*, xxxiv, 99.) Personne suggested the use of amorphous phosphorus, as less dangerous than ordinary phosphorus and more convenient to manipulate. (*C. R. A. S.*, iii, 468.) A process was also recommended by Remington, based upon Personne's suggestion. (*Proc. A. Ph. A.*, 1877.) De Vrij proposed to decompose potassium bromide with sulphuric acid in the presence of alcohol, and a modification of his method is now generally employed. (For description of methods of manufacture, see *U. S. D.*, 19th ed, p. 1480; *A. J. P.*, 1879 and 1880; *Ph. Centralh.*, 1887, xxviii.)

Ethyl bromide is a colorless, very volatile liquid, not inflammable, having an agreeable odor, and a hot, saccharine taste. Its sp. gr. is 1.453 to 1.457. It boils at from 38°–40° C. (100.4°–104° F.). It is very sparingly soluble in water, freely soluble in alcohol and ether. When a small portion is evaporated from a porcelain plate by causing it to flow to and fro over the surface, little or no foreign odor is yielded as the last portions pass off, and the plate is covered with a slight deposit of moisture.

The ethyl bromide prepared from alcohol and bromine in the presence of amorphous phosphorus should not be used in medicine because of the possible presence of organic compounds of sulphur and arsenic. Shaken with distilled water, ethyl bromide should not show any acid reaction from hydrobromic acid, nor should it cause any appreciable turbidity with silver nitrate. Shaken with an equal volume of pure concentrated sulphuric acid, no color should develop even after an hour's time; otherwise ethylene bromide may be present. Dropped slowly into potassium iodide solution, the drops of the ethyl bromide should settle to the bottom of the vessel without developing any appearance of violet color, which would indicate free bromine. Ethyl bromide should be kept in amber-colored glass bottles, completely filled and well stoppered. (Fischer, *Die Neueren Arzneimittel,* 6te Aufl., 74.)

Ethyl bromide was introduced some years ago as an anesthetic especially suitable for short operations. Its advantages were the rapidity of its action and the relative absence of nausea. H. C. Wood (*P. M. T.*, 1879 and 1880, x) found that it acted upon the system much like chloroform, but Hamœker (*International Clinics,* Dec. 20, 1891) affirms that in the lower animals death always occurred through arrest of the respiration. The further advantage for obstetric cases is claimed that it does not produce muscular relaxation. It has, however, been found to be a dangerous anesthetic; Gurlt (*A. K. C.*, lv) estimates the mortality at 1 in 5400. A serious practical objection to its use is the ease with which it undergoes decomposition on exposure to light. Its range of usefulness is similar to that of ethyl chloride, but it does not appear to possess any sufficient advantage over the latter to justify its employment. Its effects pass off so suddenly that there is danger of consciousness returning during an operation. On account of its loss by evaporation it is a very expensive anesthetic. Ethyl bromide has been especially recommended for use in *parturition,* it being stated that it suspends the pain of the uterine contractions without influencing their force, and it has been employed to a considerable extent in cases when a brief anesthetic is required. In using it, from two to four fluidrachms (7.5–15 mils) may be put upon an Allis inhaler or upon a napkin.

Ethyl Cyanide. *Hydrocyanic Ether. Propionitrile.* C_3H_5N, or C_2H_5CN.—This ether was discovered by Pelouze. It is formed by distilling a mixture of barium sulphovinate and potassium cyanide, or better, by the action of ethyl iodide on potassium cyanide in closed tubes at a temperature of 180° C. (356° F.). It is a colorless liquid, of an agreeable ethereal odor, soluble in alcohol, ether, and water, boiling at 98° C. (208.4° F.), and having the sp. gr. 0.78. *Ethyl cyanide* is very poisonous, but less so than hydrocyanic acid, with which it agrees in therapeutic action and dose.

Ethyldiiodo-salicylate. *N. N. R.* 1917. *Diiodosalicylic ether.* $C_6H_2I_2(OH).COOC_2H_5$.—White crystals, soluble in alcohol, fixed oils, and slowly soluble in water. Melting point, 132° C. (269.6° F.). It is used as a succedaneum for iodoform in surgery.

Ethyl Fluoride.—*Fluoride of Ethyl,* C_2H_5F, is said to cause in animals violent excitement, followed quickly by death. For properties and method of preparation, see *Chem. News,* Jan., 1889, also *B. A. M.*, March, 1890.

Ethyl Formate. *Formic Ether. Ethyl-formic Ester.* $CH(OC_2H_5)_3$.—A liquid with a peach-kernel odor, sp. gr. 0.937, soluble in ten parts of water. The inhalation of this compound is reputed to be useful in the treatment of infectious diseases of the respiratory organs. Internally it has been used as a hypnotic in *doses* of one to two fluidrachms (4–8 mils).

Ethyl Iodide. *Hydriodic Ether. Ethyl-hydriodic Ester. Iodure d'éthyle, Ether hydriodique,* Fr. *Jodäthyl, Jodwasserstoffäther,* G. C_2H_5I.—This liquid may be obtained by gradually and cautiously mixing five parts of alcohol, ten of iodine, and one of phosphorus, and distilling. The residue of the distillation, as ascertained by D. K. Tuttle, is *ethylphosphoric acid.* Personne (*C. R. A. S.*, 51, 468) proposed to use amorphous phosphorus instead of the ordinary kind, thus

avoiding danger. For description of his process see *U. S. D.*, 19th ed., p. 1481.

Ethyl iodide is a colorless non-inflammable liquid, insoluble in water, with a penetrating ethereal odor and pungent taste. Its density is 1.92, and boiling point from 71°–72° C. (159.8°–161.6° F.). Exposed to the air it becomes red from the liberation of iodine; the change in color is prevented by adding to the bottle containing it a globule of mercury.

Huette has proposed this ether, placed under a layer of water, as a medicine, to be used by inhalation. Fifteen or twenty inspirations suffice to impregnate the system with iodine. It acts as a powerful anesthetic, when inhaled for a sufficient time. It is said to increase the appetite, render the pulse fuller, and give vivacity to the feelings and activity to the intellect. (See *A. J. P.*, xxiii, 156.) James Turnbull, of Liverpool, and Henry Fisher, of New York, have used this ether by inhalation with satisfactory results in *chronic bronchitis* and *phthisis.* The *dose* is fifteen drops (0.75 mil) three or four times a day, inhaled from a handkerchief. Ethyl iodide often has an unpleasant odor from the presence of foreign substances which renders it offensive to patients. Phosphorus is a common and injurious impurity.

According to Linosier and Lannois (*S. M.*, 1897), ethyl iodide affords an excellent method of affecting the general system by external application. Absorption of the iodine is rapid; the liquid should be applied with a brush and then covered with paraffined paper; after applying two fluidrachms they recovered thirteen grains of iodine from the urine.

Ethyl Salicylate. $C_6H_4OHCO.O.(C_2H_5)$. *N. N. R.* 1917. *Sal Ethyl.*—This is the salicylic acid ester of ethyl alcohol and is analogous to methyl salicylate. It is a transparent, colorless, volatile liquid, possessing a pleasant characteristic odor and taste. Sp. gr. 1.132 at 20° C. (68° F.) and boiling point 231.5° C. (448° F.).

Ethyl salicylate was suggested by Houghton (*A. J. Phys.*, 1905, p. 331) as a substitute for methyl salicylate in the treatment of *rheumatism.* He asserts that it is only one-half as toxic as the methyl ester and that it is absorbed rapidly from the intestinal tract, although not through the skin. The *dose* is five to twenty minims (0.3 to 1.2 mils) several times daily.

Ethyl Valerate. $C_7H_{14}O_2$.—This compound is prepared by distilling sodium valerate with alcohol and an acid (HCl or H_2SO_4). It is a liquid having a strong odor with the characteristic valeric taste. It is used in *asthmatic* complaints as an antispasmodic and sedative. *Dose*, one to two drops during attacks.

Ethylene Bromide. *Brom-ethylene. Æthylenum Bromatum.* $C_2H_4Br_2$.—This is a colorless oily liquid smelling like chloroform, with a sweet burning taste. It boils at 131.6° C. (269° F.), and solidifies at 0° C. (32° F.) to a crystalline mass; sp. gr. at 20° C. (68° F.) 2.178. It is insoluble in water, miscible with alcohol in all proportions. In experiments made by Scherbatscheff (*A. E. P. P.*, 1902, xlvii) *ethylene bromide* was found not to act as a true anesthetic in the lower animals, but to produce serious symptoms, usually ending in death. The chief medicinal importance of this agent grows out of its liability to be confounded with the ethyl bromide, death in this way having been produced. Ten fluidrachms of it were inhaled without the production of anesthesia, followed by uncontrollable vomiting and complete suppression of urine. On account of its containing over 85 per cent. of bromine, Donath has used it in *epilepsy.* He gives it in an emulsion with oil, or mixed with almond oil in capsules. Children from eight to ten years begin with ten drops (0.5 mil) of a 5 per cent. solution; the adult *dose* is two to four minims (0.12–0.25 mil) of ethylene bromide, three times a day. (See also *P. J.*, xxi, 1068.)

Ethylene Diamine. *N. N. R.* 1917. (*Ethane diamine.*) $CH_2(NH_2).CH_2(NH_2)$.—It is a clean, colorless, thick liquid having the sp. gr. 0.87, boiling at 117° C. (242.6° F.), having a strong alkaline reaction, an ammoniacal odor and a caustic taste. It is said to be a non-corrosive solvent for false diphtheritic membranes, used in a diluted form. A solution in water of 25 per cent. of *ethylene diamine* and 25 per cent. of trikresol is sold under the proprietary name of *kresamine*, *N. N. R.*, 1917, to be used in dilutions of from 2 to 25 per cent. A silver preparation of ethylenediamine is known and used under the name of *Argentamin*, which see.

Ethylene Dichloride. *Bichloride of Ethylene. Dutch Liquid. Æthyleni Bichloridum. Æthylenum Chloratum. Elaylum Chloratum. Liquor Hollandicus. Æthylenchlorid, Elaylchlorid*, G. $C_2H_4Cl_2$.—By the mutual action of chlorine and olefiant gas an oily liquid is obtained, discovered by four associated Dutch chemists, and called *Dutch liquid.* Aran found that the monochlorinated Dutch liquid (*monochlorethylene chloride*, $CH_2Cl,CHCl_2$) had a useful anesthetic power, but its cost proved to be too high to allow of its general use at that time as a therapeutic agent. In consequence of this objection to the monochlorinated liquid, Mialhe and Flourens were induced to search for a substitute in the corresponding compound of a parallel series of ethers, formed by the action of successive portions of chlorine on hydrochloric ether, C_2H_5Cl; under these circumstances the hydrogen is replaced by the chlorine, atom for atom, and there are formed the five following compounds: $C_2H_4Cl_2$; $C_2H_3Cl_3$; $C_2H_2Cl_4$; C_2HCl_5; C_2Cl_6. Of this series, the first member is isomeric with Dutch liquid; the second, third, and fourth with the mono-, bi-, and trichlorinated Dutch liquid, and the fifth is a chloride of carbon, frequently called *carbon sesquichloride.* The first member, though identical with the Dutch liquid in elementary composition and having a vapor of the same density, has, nevertheless, a lower boiling point, *i.e.*, 60° to 64° C. (140°–147.2° F.), while the Dutch liquid boils at 84.9° C. (185° F.); it is also different in chemical properties. Thus, it is not decomposed by an alcoholic solution of potassium hydroxide, as the Dutch liquid is, and is not acted on by potassium, while the Dutch liquid is immediately attacked by it. The explanation of these facts is that the two compounds, while having the same empiric formula, are differently constituted molecularly. Thus, Dutch liquid is known chemically as *ethene dichloride*, CH_2Cl,CH_2Cl, while the chlorinated ethyl chloride is known as *ethylidene chloride*, CH_3CHCl_2. This difference of molecular structure, of course, runs all through their derivatives until the final product, C_2Cl_6, is reached in both cases, and here there is identity of product.

The conclusion arrived at by Mialhe and Flourens appears to be that the four chlorinated hydrochloric ethers all possess anesthetic properties; and, as it would be difficult to separate them, they propose the use of the mixed ethers, consisting principally of the tri- and quadrichlorinated compounds, as an anesthetic, under the indefinite name of *chlorinated muriatic ether.* Since the

time of Mialhe and Flourens's experiments, the matter has been taken up again, and Taube (*A. J. P.*, 1880, 603, and 1881, 119) proved the availability as anesthetics of monochlorethylidene chloride, CH_3CCl_3, and of monochlorethylene chloride, $CH_2Cl,CHCl_2$.

The precise action of the various esters upon the organism is unknown. The committee of the British Association found (*B. M. J.*, i, 1879) the *ethene dichloride* ("formerly named *ethylene dichloride*, or Dutch liquid, $C_2H_4Cl_2$") to cause convulsions in the lower animals, while E. T. Reichert (*P. M. T.*, xi, 518) found that "ethylene dichloride" produces anesthesia with the usual stages, and that, like chloroform, it depresses the heart and steadily lowers the arterial pressure. His experiments seem to show, however, that its action upon the heart is much less powerful than that of chloroform, and in all of its trials the animal died of centric respiratory paralysis while the heart was still maintaining some degree of circulation. He believes, therefore, that it is a much safer agent than chloroform, ranking it between the latter and ether. It is evident that Reichert was not using the same agent as the English committee were, but exactly what he did have is uncertain. Dr. A. W. Wallace found ethylene dichloride useful in dermatological practice. (*P. J.*, 1910, 787.)

Ethylidene Chloride, *Chlorinated hydrochloric ether, ethylene chloride* (CH_3CHCl_2), is a colorless, very mobile, neutral liquid, having an aromatic ethereal odor, and a hot, saccharine taste. It is sparingly soluble in water, but readily soluble in alcohol, ether, and most of the fixed and volatile oils. It is not inflammable, in which respect it agrees with chloroform. When purified it is a liquid somewhat resembling chloroform, of sp. gr. 1.174 at 17° C. (62.6° F.), boiling at 60° C. (140° F.), and not miscible with water. It can be distinguished from chloroform in that it combines with chlorine even in the dark, liberating hydrochloric acid. According to Flourens, its action is similar to that of chloroform. The British Association Committee (*B. M. J.*, 1879, i) believed it to be a valuable anesthetic, exerting little or no depressing effect upon the heart, but the work of the committee was not sufficiently thorough to be conclusive. Many years ago Snow used it on man, and gave judgment in its favor, and Binz has produced human anesthesia, and thinks it increases the force of the circulation (*M. T. G.*, 1879, i); but Reeve finds (*N. R.*, 1880, 334) that in animals it lowers the arterial pressure, but does not suddenly paralyze the heart, as does chloroform.

Eubornyl.—This is the borneol ester of a-bromisovaleric acid. It is a clear syrupy fluid with an aromatic odor and sweetish taste, insoluble in water, but readily miscible with alcohol or ether.

Eubornyl has been employed by Allina (*Ther. Geg.*, 1909) as a nerve sedative in *hysteria* and also as a depressant to the sexual organs, especially in cases of painful erections. *Dose*, 20 minims (1.3 mils) three times a day.

Eucaine Lactate. *Beta-eucaine Lactate* ($C_{15}H_{21}NO_2.CH_3.CH(OH).COOH$. *N. N. R.* 1917. A white, non-hygroscopic powder, melting at 155° C. (311° F.) and soluble in water and alcohol. Its solutions are non-irritating and are employed in dentistry and ophthalmology, 2 to 3 per cent. strength, for infiltration anesthesia, 0.12 per cent., and for the nose, throat or ear, 10–15 per cent.

Eucalyptus Manna. *Australian Manna.*—This substance exudes during the summer months from punctures made in the bark and leaves of the Australian tree *Eucalyptus viminalis* Labill. (fam. *Myrtaceæ*). It occurs in small round opaque masses, and is said medicinally to resemble ordinary manna. It contains melitrose. A similar manna is also formed on *Eucalyptus Gunnii* Hook. The "*blue-grass manna*" of Australia occurs on the stems of *Andropogon annulatus* Forsk. (fam. *Gramineæ*). The latter contains 75 per cent. of mannite.

Eucasin. *Ammonium Caseinate, Casein-ammonium.*—This compound is obtained by passing ammonia gas over casein. It is a grayish-white powder, having an odor somewhat like buttermilk, readily soluble in hot water. It has been brought forward by Salkowski as a very easily digested food. It may be given in broths or with cocoa, and, according to Feustell (*D. M. W.*, xxii, 1896), is a valuable food in cases of great failure of digestion. Thirty grains (2 Gm.) of *eucasin* correspond to twenty-four grains (1.6 Gm.) of albumin.

Eucerin.—This is a mixture of 5 parts of an oxy-cholesterin obtained from wool fat with 95 parts of paraffin. As put upon the market it is usually combined with equal parts of water. It is intended as an ointment base and is said to penetrate the skin with great readiness.

Eucodin. *N. N. R.* 1917. *Eucodine. Codeine Brom-methylate. Methyl-codeine Bromide.* $C_{18}H_{21}O_3N(BrCH_3)$.—A crystalline product, melting point 261° C. (501.8° F.) and soluble in slight proportions in water. *Eucodin* stimulates the respiratory center, allays bronchial irritation and acts as a general analgesic without narcotic action. Eucodin gives a bluish-green color when added to a solution of formin in sulphuric acid. It is employed in *phthisis* and *coughs* in *doses* of one grain (0.065 Gm.) several times a day.

Eucol. *Eucolo. Guaiacol Acetate. Guaiacol Ester of Acetic Acid.* $C_6H_4\begin{cases}OCH_3\\OCH_3CO\end{cases}$.—This product forms a colorless fluid with a specific gravity 1.138, and boiling at 238° C. (460.4° F.) with partial decomposition. It can be mixed in any proportion with ether or alcohol and may be dissolved to the extent of 20 per cent. in olive oil.

Eucol has the same range of usefulness as guaiacol.

Eudermol. *Nicotine Salicylate.*—This is recommended as an anti-parasitic in *scabies* and various other skin diseases. It is especially recommended in veterinary practice.

Eudrenine.—A local anesthetic in the form of capsules each containing one-twelfth of a grain of eucaine and one four-thousandth of a grain of adrenalin hydrochloride. Used especially in dentistry.

Eugenia Cheken Hook. et Arn. (*Myrtus Cheken* Spreng.) *Cheken. Chequen. Arrayan.* (Fam. *Myrtaceæ.*)—The leaves of this Chilian plant have entered commerce under the name of *Chekan leaves.* Weiss (*A. Pharm.*, 1888, p. 226) has found in them: (1) *chekenon*, $C_{40}H_{44}O_8$, a crystalline body; (2) *chekenin*, $C_{12}H_{11}O_3$, in yellowish rhombic tables; (3) *chekenetin*, $C_{11}H_7O_6 + H_2O$, in olive-colored crystals; (4) *cheken-bitter*, an amorphous, very soluble bitter substance. (See *P. J.*, 1889, 782, and Wein, *A. Pharm.*, 1888, 665.) The leaves are used in their native country as a remedy in *chronic respiratory catarrh*, and have been strongly recommended by Murrell and others in *chronic bronchitis.* Their virtues appear to reside in the

tannin, and especially in the volatile oil that they contain. The *dose* of the fluidextract is from one to three fluidrachms (3.9–11.6 mils).

Eugenia Jambolana Lam. (*Syzygium Jambolana* Lam.) *Jambul. Jambol. Rose Apple. Java Plum.*—This is a large tree belonging to the *Myrtaceæ*, growing in East India and also in Queensland; well known on account of its popular edible fruit. The bark and seeds are employed in medicine. *Jambul bark* is a dense, hard bark, about 1.5 cm. in thickness, of a pinkish-brown or reddish-brown color, with a whitish-gray mottled cork or thick bark, the inner surface is of a somewhat silky luster, frequently coarsely marked by waving lines or ridges; the fresh fracture varies from pinkish or purplish to fawn color, sometimes distinctly but shortly fibrous, more commonly absolutely abrupt. The taste is somewhat bitter, astringent, after a time distinctly pungent. The bark contains a resin, tannin, and gallic acid. *Jambul seeds* are grayish-black or blackish-gray, being abruptly truncated at the base, above rounded or dome-shaped. They are from 1 to 2.5 cm. long, and 8 to 12 mm. broad; so hard and dense that they cannot be chewed, and are almost tasteless. The analysis of the seeds by Thomas Christy yields the following results. Essential oil, a trace; chlorophyll and fat, 0.37; resin soluble in alcohol and ether, 0.30; gallic acid, 1.65; albumen, 1.25; colored extractive soluble in water, 2.70; moisture, 10.00; insoluble resin, 83.73. Power and Callan (*P. J.*, 1913, 245) found in these seeds a phenolic substance, *jambulol*, $C_{16}H_3O_4(OH)_5$, which is identical with *ellagic acid*.

In the experiments made by Thomas Christy of London (*P. J.*, 1888), it was found that when sufficient of diastasic matter was mixed with fifty grains of starch to convert 45 per cent. of the latter in fifty minutes into sugar, the addition of twenty-five grains of powdered jambul seeds reduced the conversion of the starch to 12 per cent. We have no knowledge of the effect of jambul or its active properties upon the general organization, but Binz (*Verhandl. der Kongr. für Innere Med.*, Wiesbaden, 1886) found that when dogs were made diabetic by the administration of phlorizin, according to the method of von Mering, the exhibition of jambul reduced the excretion of sugar from 50 to 90 per cent. without the production of any evidences of poisoning by the jambul. In India, jambul has long been used as a stomachic astringent and carminative in *diarrhea*, and also in the treatment of *diabetes*. The first therapeutic trials in Europe appear to have been made by Clacius, who found that the drug notably reduced the excretion of sugar in diabetic patients. The practice has been largely followed, and there would seem to be no doubt that in occasional cases of glycosuria jambul does good. No cases of poisoning or of disagreeable results from it have been reported.

Nevertheless jambul has failed to establish itself as a practical medicament. It may be that this has been due to the use of too small doses. The *dose* of the fluidextract usually recommended is ten minims (0.6 mil); but according to von Noorden (*Deutsche Praxis*, 1901) half a fluidounce (15 mils) of the fluidextract should be taken in eight fluidounces (240 mils) of hot water, one hour before breakfast and late in the evening.

Jamrosin is a proprietary preparation asserted to be the fluidextract of jambul. It is alleged to possess marked remedial qualities in the treatment of *diabetes*.

Eugenoform, *Eugenol carbinol sodium*, formed by the action of formaldehyde on phenol, forms colorless crystals fusing at 160° C. (320° F.), readily soluble in water, difficultly soluble in alcohol. Is used as an intestinal disinfectant in cases of *typhoid fever, cholera*, etc.

Eugenol Acetamide. $C_{10}H_{11}O_2.(CO.CH_2NH_2)$.—This substance occurs in shining scales or needles, soluble in alcohol and water, melting at 110° C. (230° F.). According to Merck, it is a local anesthetic and at the same time antiseptic.

Eugenol Benzoate. *Benzo-eugenol.* $C_6H_9(OCH_3)O.CO.C_6H_5$.—This is obtained by the combination of benzoyl chloride with sodium eugenol and forms white odorless crystals, soluble in alcohol, water, and ether. It is used in the treatment of *whooping-cough* and *phthisis*, in *doses* of eight to fifteen grains (0.5–1 Gm.).

Eugenol Iodide. *Iodo-eugenol.* $C_6H_2I(C_3H_5)(OCH_3)OH$.—A yellowish, inodorous, insoluble powder obtained by acting on eugenol-sodium with iodine. It is used as an antiseptic, and said to resemble aristol.

Euguform.—*Acetylized methylene diguaiacol* is obtained by the action of formaldehyde upon guaiacol and subsequent acetylization. It is a white, almost odorless, dust-like and amorphous powder, insoluble in water. It has been recommended by Ciesielski as a substitute for orthoform, as a dusting powder or in the form of a 2 to 10 per cent. ointment. A 50 per cent. solution of *euguform* in acetone is marketed as *neo-euguform*. (*Derm. Cb.*, 1901, No. 6; see also *M. R.*, 1912.)

Eukinase.—A powder obtained by desiccation of the pancreatic juice of swine, contains mostly trypsin, an active proteolytic ferment. The albumin digestive property of the pancreatic juice is said to be enhanced by the addition of *eukinase*. *Pancreatokinase* is a mixture in undetermined proportions of eukinase and pancreatin. These preparations should be administered in enteric capsules or pills.

Eulatin.—*Eulatin* is a mixture of amido-bromobenzoic acid and antipyrine. It is a white powder, almost odorless, of a slightly acid taste. It has been recommended by Fränkel (*B. K. W.*, 1909) in the treatment of *whooping cough*. He asserts that it not only acts as a sedative on the nervous system, but also renders more fluid the bronchial secretions, and has a stimulant influence upon the heart. It may be given at intervals of three or four hours in *doses* of one and a half to eight grains (0.1–0.5 Gm.) either in the form of a powder or of a mixture. Fränkel administers to children of four years, twelve tablets daily, each containing one-quarter gramme (4 grains).

Eumenol is a liquid preparation of the Chinese root *Tang-kui*, one of the *Araliaceæ*. It has been recommended for the relief of *dysmenorrhea* by Langes (*Th. M.*, 1901, 363) and others. *Eumenol* tablets have been placed upon the market by Merck.

Eupatorium. *N. F. IV* (*U. S. P. VIII*). *Boneset. Thorough-wort. Herba Eupatorii Perfoliati. Indian Sage. Thorough-stem. Cross-wort. Thoroughwax. Sweating Plant. Herbe d'Eupatoire perfoliée, Herbe à fièvre, Herbe parfaite*, Fr. *Durchwachsener Wasserhanf* or *Wasserdost*, G.—"The dried leaves and flowering tops of *Eupatorium perfoliatum* Linné (Fam. *Compositæ*)." *N. F.* This is an indigenous perennial plant, with numerous herbaceous stems, which are erect, round, hairy, from two to five feet high, simple below, and

trichotomously branched near the summit. The leaves serve to distinguish the species at the first glance. They may be considered either as perforated by the stem, *perfoliate*, or as consisting each of two leaves, joined at the base, *connate*. In the latter point of view, they are opposite and in pairs, which decussate each other at regular distances upon the stem; in other words, the direction of each pair is at right angles with that of the pair immediately above or beneath it. They are narrow in proportion to their length, broadest at the base where they coalesce, gradually tapering to a point, serrate, much wrinkled, paler on the under than on the upper surface, and beset with whitish hairs, which give them a grayish-green color. The uppermost pairs are sessile, not joined at the base. The flowers are white, numerous, supported on hairy peduncles, in dense corymbs, forming a flattened summit. The involucre, which is cylindrical and composed of imbricated, lanceolate, hairy scales, encloses from twelve to fifteen tubular florets, having their border divided into five spreading segments. The anthers are five, black, and united into a tube, through which the bifid filiform style projects.

This species of *Eupatorium* inhabits meadows, the banks of streams, and other moist places, growing generally in bunches, and abounding in almost all parts of the United States. It flowers from the middle of summer to the end of October. All parts of it are active, but the herb only is official. It has a faint odor, and a strongly bitter, somewhat peculiar taste. It is described as "usually more or less broken; leaves opposite, the pair united at the base, from 8 to 20 cm. in length and from 1.5 to 5 cm. in breadth, tapering regularly from near the base to an acute summit, crenate-serrate, rugosely veined, rough and bright green above, yellowish-gray-green, tomentose and resinous-dotted beneath; flower-heads small, numerous, corymbed, with a campanulate involucre of lance-linear, imbricated scales and with from ten to fifteen tubular, yellowish-white florets having a bristly pappus in a single row. Odor faintly aromatic; taste strongly bitter. Eupatorium yields not more than 10 per cent. of ash." *N. F.* The virtues of the plant are readily imparted to water and alcohol. W. Peterson found it to contain a peculiar bitter principle, chlorophyll, resin, a crystalline matter of undetermined character, gum, tannin, yellow coloring matter, extractive, lignin, and salts. (*A. J. P.*, xxiii, 210.) George Latin (*A. J. P.*, Aug., 1880) found a glucoside, *eupatorin*, and a crystallizable body of the nature of wax. O. F. Dana, Jr., obtained 3.80 per cent. of extract with petroleum benzin; 4.60 per cent. with ether; 33.80 per cent. with alcohol; 24.80 per cent. with water; 5.80 per cent. with alkali. (*A. J. P.*, 1887, p. 229.) Shamel (*Am. Chem. J.*, 1892, p. 224) published an analysis of the nitrate of the crystalline principle giving the formula $C_{20}H_{25}O_{36}HNO_3$.

Eupatorium is, in large doses, emetic and aperient. Because of its nauseating action, the warm infusion tends to increase perspiration and has been used to abort attacks of *muscular rheumatism* or *general cold*. H. S. Wilkins has found the infusion useful in the expulsion of *tapeworm*. (*A. J. P.*, 1874, p. 295.)

As an emetic and cathartic, a strong decoction, prepared by boiling an ounce with three half-pints of water to a pint, may be given in doses of from four fluidounces to a half-pint (120 to 240 mils), or more. (See *Fluidextractum Eupatorii*, N. F., Part III.)

Dose, twenty to thirty grains (1.3 to 2.0 Gm.).

Eupatorium purpureum L., *Joe-Pye Weed*, *Trumpet Weed*, or *Gravel Root*, is a perennial herbaceous plant, with a purple stem, five or six feet in height, and furnished with ovate-lanceolate, serrate, rugosely veined, slightly scabrous, petiolate leaves, placed four or five together in the form of whorls. The flowers are purple, and consist of numerous florets contained in an eight-leaved involucre. It grows in swamps and other low grounds, from Canada to Florida, and flowers in August and September. The root has, according to Bigelow, a bitter aromatic and astringent taste, and is said to be diuretic. Its vulgar name, *boneset*, indicates the popular estimation of its virtues. J. U. Lloyd found in it an apparently new, yellow, neutral, crystalline principle, *euparin*. (*A. J. P.*, 1890.) This euparin, with a number of derivatives, has been prepared by C. C. Mauger (*A. J. P.*, 1894, 120) and analyzed. The formula $C_{12}H_{11}O_3$ is assigned to it.

Eupatorium verbenæfolium Michx., commonly called *wild horehound*, is also an indigenous perennial, with an herbaceous stem, which is about two feet high, and supports sessile, distinct, ovate, acute, scabrous leaves, of which the lower are coarsely serrate at the base, the uppermost entire. The flower-heads are small, white, composed of five florets within each involucre, and arranged in the form of a corymb. The plant grows in low wet places from New England to Georgia, and abounds in the Southern States. It is in flower from August to November. The whole herb is used. In sensible properties it corresponds with *E. perfoliatum*, though less bitter and disagreeable, and has been used for similar purposes and in like manner. *E. incarnatum* and *E. aromaticum* are said to contain an aromatic principle similar to, if not identical with, coumarin, obtained by Guibourt from *Dipteryx odorata*, or Tonka bean. (See *P. J.*, Oct., 1874, 303.) The roots of *E. aromaticum* are said to be sold in the Western United States under the name of *white snake-root*. *E. cannabinum* of Europe, the root of which was formerly used as a purgative, and *E. triplinerve* Vahl (*E. Aya-pana* Vent.), of Brazil, the leaves of which at one time enjoyed a very high reputation, have fallen into neglect. The *Aya-pana* is an aromatic bitter, like *E. perfoliatum*, but weaker, and is said to be still occasionally met with in European commerce. (*A. J. P.*, 1887, 154; *Ph. Era*, 1898, 293.) *E. villosum* is used in Jamaica, under the name of *bitter-bush*, in the preparation of beer, as a tonic, and as a stimulant in low zymotic diseases. (*P. J.*, Oct., 1866; *A. J. P.*, 1887, 155.) *E. collinum* is included in the Mexican Pharmacopœia.

Euphorbia. *Wild Ipecac. Wild Hippo. Euphorbe*, Fr. *Wolfsmilch*, G.—The genus *Euphorbia* (Fam. *Euphorbiaceæ*) contains numerous species, having the common property of yielding a milky juice. They are herbaceous or shrubby, with or without leaves, and the leafless species, which are chiefly confined to the African deserts, have fleshy, naked, or spiny stems, like those of the cactus. They nearly all afford products which act powerfully as emetics and cathartics, and in overdoses occasion dangerous if not fatal prostration, with symptoms of inflammation of the gastro-intestinal mucous membrane. Their milky juice, which concretes on exposure, usually possesses these properties in a high degree, and, in addition, that of powerfully irritating the skin when applied to it. The U. S. Pharmacopœia

formerly recognized the indigenous species *E. corollata* L. and *E. Ipecacuanhæ* L. In a full dose the root of *E. corollata* L. acts as an emetic and cathartic and in smaller doses is a nauseating diaphoretic and expectorant. It is, however, too harsh and uncertain in its action for practical use, and has passed entirely out of vogue. The *dose* of the dried root as an emetic is from ten to twenty grains (0.65–1.3 Gm.), as a cathartic from three to ten grains (0.2–0.65 Gm.). The recent root, bruised and applied to the skin, produces vesication. C. Petzolt (*A. J. P.*, 1873) found in the root of *E. Ipecacuanhæ* fixed oil, resin, starch, glucose, and various salts. The resinous matter was a dark mass, of a taste slight at first but after a time nauseous and pungent, readily dissolved by alcohol, but insoluble in ether and petroleum benzin, and, when swallowed, producing in half grain (0.032 Gm.) doses watery stools, and in one and a half or two grain (0.096 or 0.13 Gm.) doses nausea and vomiting. It gave no evidence of the presence of an alkaloid. The medicinal properties of *E. Ipecacuanhæ* resemble those of *E. corollata*, though the former is said to be somewhat milder. The indigenous *E. Preslii* Guss. (*E. hypericifolia* A. Gray) and *E. maculata* L. are said by Zollickoffer to be a valuable remedy in *dysentery, diarrhea, menorrhagia,* and *leucorrhea.* (See 16th ed., *U. S. D.*, also *A. J. M. S.*, xi.) B. J. D. Irwin, U. S. A., states that, under the name of *gollindrinera*, the native Mexican uses the *Euphorbia prostrata* Ait. in New Mexico and Arizona as a remedy for *snakes bites.* (*Am. J. M. Sc.*, 1861.). In Chili the juice of *Euphorbia portulacoides* L. (*E. chilensis* C. Gay) is said to be used as a drastic purgative. (*A. J. P.*, 1966, 102.) The juice of *Euphorbia Drummondii* Boiss. is said in Australia to kill annually a great many sheep and cattle, and in 1886 John Reid (*Australasian Med. Gaz.*, No. 61) announced the discovery in it of a new anesthetic alkaloid, *drummine*, which he obtained in colorless crystals almost insoluble in ether, but freely soluble in chloroform and in water. The report of Alexander Ogsden (*B. M. J.*, Feb., 1887) throws, however, very grave doubts upon the anesthetic power of this new alkaloid. The *E. ocellata* Durand and Hilgard of the Pacific coast is used as an antidote for *snake bites*, and is said to contain 2.82 per cent. of resin, besides gallotannic acid, while *Euphorbia cremocarpus* Auct. of the same region is employed for the purpose of poisoning fish in still pools and streams, and is said to contain a volatile oil, besides acid and resins. (See *Proc. California Coll. Pharm.*, 1885.) The oil of *E. Lathyris* L. is stated to physiologically resemble croton oil. (*Proc. A. Ph. A.*, xxvi, 305.)

The *E. heterodoxa* Muell.-Arg., *alveloz* or *aveloz*, a Brazilian species, has been used with asserted extraordinary advantage against *cancerous* and *syphilitic ulcers.* It is a powerful irritant, and even mild caustic. The milky juice, preserved with salicylic acid, or a resin obtained by precipitating with water is employed. The ointment of the resin may be made 3 parts in 100 with vaseline. For further information concerning various euphorbia species which have been used in medicine, see *U. S. D.*, 19th ed., p. 1484.

Euphorbia Pilulifera. *N. F. IV. Pill Bearing Spurge.*—"The dried herb of *Euphorbia pilulifera* Linné (Fam. *Euphorbiaceæ*), collected while flowering and fruiting." *N. F.* This plant is a prostrate or ascending branched annual, found in almost all tropical countries; it is furnished with leaves which are opposite, shortly stalked, ovate to ovate-lanceolate or oblong, from 8 to 35 mm. long, denticulate, very oblique and narrow below, or with a semicordate base. Stipules minute and linear. The flower-heads are small, numerous, crowded in head-like cymes, globular, and are borne on a short stalk in one axil, only, of each pair of opposite leaves. The involucre is small, entire, and without petal-like appendages. According to De Candolle, the seeds are reddish, acutely oblong, four-sided, and transversely wrinkled, the ridges uniting irregularly. It is to be distinguished from *E. parviflora* (L.), which is sometimes substituted for it, by the flower-head of the latter having but few flowers, by the glands of the involucre being furnished with a white, obovate-orbicular appendage, and by the seeds being minutely papillose. The N. F. describes the drug as follows: "Roots usually present, small, branched, and reddish; stems slender, cylindrical, obliquely erect, dichotomously branched from near the base, branches recurved at apices; branches and stem only sparsely leafed at base, pale greenish-brown, rough or hairy; stems coarsely pilose with yellow hairs which are rather dense on the upper parts but sparse on the lower; pubescence consisting of short, nearly straight, unicellular hairs, becoming almost hispid at the flowering tops; leaves opposite, obliquely oblong, acute, serrulate, rusty pale green, pubescent, especially on the prominent veins on the lower surface, becoming brittle on drying and usually much broken in the drug; flowers small, numerous, in short peduncled axillary clusters; fruits about 1 mm. in diameter, three-celled capsules; seeds about 0.9 mm. in diameter, triangular ovoid, pale brown. Odor aromatic and characteristic; taste faintly bitter, aromatic and acrid. Euphorbia Pilulifera yields not more than 12 per cent. of ash." *N. F.* Levison found in it (*A. J. P.*, 1885, 147) several glucoside resins, wax, and volatile matter. Dr. F. B. Power (*C. D.*, 1913, 544) examined *E. pilulifera* from the Fiji Islands and found a monohydric alcohol, *euphosterol*, among other constituents, none of which seem to possess value therapeutically.

A physiological study of *Euphorbia pilulifera* led A. Marsset (*T. G.*, 1885) to the conclusion that the active principle acts directly upon the heart and respiration; that it is not an irritant to the skin, but in large dose it is to the gastric mucous membrane. It has been used by Dujardin-Beaumetz and a number of other clinicians with asserted excellent results in the treatment of *asthma* and *bronchitis.* The best preparation is the fluidextract (see *Fluidextractum Euphorbia Pilulifera. N. F. IV*), the *dose* of which is from a half to one fluidrachm (1.8–3.75 mils) three or four times a day.

Euphorbium. *Euphorbium*, P. G. *Euphorbe, Gomme-résine d'Euphorbe*, Fr. *Euphorbiumharz*, G.—The concrete resinous juice of *Euphorbia resinifera* Berg (Fam. *Euphorbiaceæ*). This is a fleshy cactus-like plant growing in Morocco. It is also said to be derived in part from another species of *Euphorbia.* These species, when wounded yield an acrid milky juice, which concretes on the surface, and constitutes the euphorbium of commerce. It occurs in the shape of tears, or in oblong or roundish masses, about the size of a pea or larger, often forked, and perforated with one or two small conical apertures, produced by the prickles of the plant, around which the juice has concreted, and which sometimes remain in the mass. The masses are occasionally large and

mixed with impurities. The surface is dull and smooth, bearing some resemblance to that of tragacanth; the consistence somewhat friable, the color light yellowish or reddish; the odor scarcely perceptible; the taste at first slight, but afterwards excessively acrid and burning. The color of the powder is yellowish. The sp. gr. of *euphorbium* is 1.124. Triturated with water it renders the liquid milky and is partially dissolved. Alcohol dissolves a larger portion, forming a yellowish tincture, which becomes milky on the addition of water. Its constituents, according to Pelletier, are resin, wax, calcium malate, potassium malate, lignin, bassorin, volatile oil, and water. It contains no soluble gum. The most abundant constituent is resin, and the remainder consists chiefly of wax and calcium malate. The resin is excessively acrid, is soluble in alcohol, and, when exposed to heat, melts, takes fire, and burns with a brilliant flame, diffusing an agreeable odor. Flückiger (*A. J. P.*, 1868) also found a substance analogous to lactucon, which he named *euphorbon*, $C_{15}H_{24}O$. Tschirch and Paul made an important investigation of euphorbium and found *euphorbic acid*, $C_{24}H_{30}O_6$, *euphorbin*, $C_{30}H_{48}O$, malic acid and a bitter, and also an acrid principle. (*A. Pharm.*, 1905, 249.)

Euphorbium taken internally is a very irritant emetic and cathartic, and in large doses acts as a violent gastro-intestinal irritant poison. In consequence of the severity of its action, its internal use has been entirely abandoned. Applied to the mucous membrane of the nostrils, it excites violent irritation, attended by incessant sneezing and sometimes bloody discharges. Persons who powder it are under the necessity of guarding their eyes, nostrils, and mouth against the fine dust which rises. Externally applied it inflames the skin, often producing vesication. It enters into some epispastic preparations, and is especially employed in veterinary practice as a vesicant.

Euphorin. *N. N. R.* 1917. (*Æthylis Phenylcarbamas—Phenyl Urethane, Phenylcarbamic Acid Ethyl Ester.*) $(C_6H_5NH)CO(OC_2H_5)$.—It is in the form of colorless needles or a white powder, melting at 50° to 51° C. (122°–123.8° F.), having a faint aromatic odor and taste. It is almost insoluble in water, readily soluble in diluted alcohol, alcohol, and ether. It is used as an anodyne and antipyretic in *doses* of eight to fifteen grains (0.5–1.0 Gm.); also externally in *skin diseases, ulcers*, etc., either as a dusting powder or in an ointment.

Euphrasia. *E. officinalis* L. *Eyebright. Eyewort. Euphraise*, Fr. *Augentrost*, G. (Fam. *Scrophulariaceæ.*)—A small annual plant, native of Europe, without odor, and of a bitterish, astringent taste. Enz (*Viertelj. f. Prakt. Pharm.*, viii, 175) obtained a little volatile oil, an acrid and bitter principle, mannite and glucose, and a tannic acid. The name "eyewort" so frequently ascribed to this drug, is derived from the practice of using it in eye affections in older medicine. It is used on the continent to-day as an astringent tonic in the treatment of *jaundice*. G. M. Garland (*A. J. P.*, 1890) states that ten minims (0.6 mil) of a concentrated tincture every two hours is a specific in acute *nasal catarrh*.

Euphthalmine Hydrochloride. $C_5H_6N(CH_2)_4(C_6H_5CHOH.COO).HCl$. *N. N. R.* 1917.—This is the mandelic acid derivative of Eucaine B, just as homatropine is the mandelic acid derivative of the base tropine. A permanent snow-white crystalline powder, very soluble in water and soluble in about two parts of boiling absolute alcohol, separating again on addition of ether, in crystalline aggregates. The salt is anhydrous; it melts at from 183° to 184° C. (361.4°–363.2° F.) and begins to run together at 181° C. (357.8° F.). The *salicylate*, $C_{17}H_{25}O_3N,C_6H_4(OH)COOH$, prepared by mixing ether solutions of the base and of salicylic acid, and recrystallizing from absolute alcohol and ether, melts at from 115° to 116° C. (239°–240.8° F.), and is very readily soluble in water. The *hydrochloride* is a colorless, crystalline powder, freely soluble in water.

When instilled into the eye in strengths of 2 to 5 per cent., euphthalmine hydrochloride causes a marked dilatation of the pupil, which begins in about fifteen minutes, reaches its maximum in about one hour, then slowly disappears and the eye completely recovers in about twenty-four hours. According to Jackson (*Ophthalmic Record*, July, 1899), there is a partial but not complete paralysis of accommodation from the 5 per cent. solution of the drug. It is relatively non-irritant to the conjunctiva, although its repeated use may produce conjunctivitis. It is not locally anesthetic. Its value in ophthalmology depends upon the comparatively short duration of the mydriasis and its relatively low toxicity. Mironescu (*Th. M.*, 1905) found that the lethal dose for the rabbit is about one gramme per kilo subcutaneously. The same author also asserts that it differs markedly from atropine in that it slows the pulse instead of accelerating it.

Eupicin.—*Eupicin* is asserted to be a condensation product obtained by the action of formaldehyde on coal tar, and occurs in the form of a light gray powder. It is employed in the treatment of *eczema, seborrhea, urticaria* and other skin diseases in the form of an ointment or lotion, in strengths of about 5 per cent.

Eupyrine. *N. N. R.* 1913. *Para-phenetidine-vanillin-ethyl-carbonate.*

$$C_6H_4\begin{cases}OC_2H_5\\ N{=}CH.C_6H_3\begin{cases}O.COOC_2H_5.\\ OCH_3\end{cases}\end{cases}$$

This substance occurs in pale yellow, tasteless needles, with a vanillin odor, melting at 87° to 88° C. (188.6°–190.4° F.), insoluble in water, sparingly so in cold alcohol, ether, and chloroform, but very soluble in these solvents when warmed. It forms salts by combination with a few acids, and is decomposed by a few other acids and by all alkalies. It has been brought forward by Overlach (*Cb. I. M.*, xxi, 1900) as an antipyretic, who found that half an ounce of it causes no serious symptoms in dogs. He claims that it produces a gradual but marked fall of the temperature, accompanied by a sense of euphoria rather than of depression. In neuralgia he found that it was without influence. Porges has confirmed the statements of Overlach. The remedy is stated to be of special value in the young and the aged. *Dose*, twenty to thirty grains (1.3–2.0 Gm.).

Euquinine. *N. N. R.* 1917. *Quinine Ethyl Carbonic Ether.* $CO\begin{cases}O.C_2H_5\\ O.C_{20}H_{23}N_2O\end{cases}$.—*Euquinine* is made by the action of chloro-carbonic ethyl-ether on quinine. It occurs in the form of fine needle-like white crystals, melts at 95° C. (203° F.), is scarcely soluble in water, but easily so in alcohol, ether, and chloroform. It forms crystalline salts. A solution in sulphuric or nitric acid fluoresces with a blue color like quinine. The thalleioquin reaction of euquinine is the same as that of quinine, but there is no herapathite reaction. The

euquinine hydrochloride dissolves readily in water, the sulphate much less easily, while the tannate is almost insoluble.

It has been alleged that it is possible by the use of euquinine to obtain the beneficial effects of quinine without unpleasant accompaniments of cerebral congestion and irritation, although tinnitus aurium is produced. It is absorbed rapidly, and according to Panegrosso and Gammarelli its elimination by the kidneys can be demonstrated within half an hour after its ingestion, and is completed in about forty-eight hours. It has been suggested, but not demonstrated, that within the body it is decomposed, quinine being re-formed from it. Euquinine has been employed with asserted satisfactory results by C. von Noorden (*Cb. I. M.*, 1896) in *pneumonia, pleurisy,* and various other acute diseases, as a substitute for quinine, and the results have been confirmed by Goliner (*Allge. Med. Central-Zeitung,* 1897) and by Overlach (*D. M. Ztg.*, 1897), while, following Panegrosso (*Gaz. degli ospedali,* Oct., 1897), numerous physicians have tried it in *malaria;* A. Celli and A. Mori, experimenting in the Pontine marshes and other malarial districts of Middle Italy, have found that in *doses* of ten grains (0.65 Gm.) a day it is very effective in preventing the contraction of disease. (*Cb. B.*, vol. xxix.) In *doses* of twenty to thirty grains (1.3–2.0 Gm.) it has been found effective in *intermittent fevers.* As a tonic Overlach found it useful in small doses in *chlorosis* and *anemia,* and this has been confirmed by other observers. Von Noorden, Castle, Niedermayer, and others commend it in *whooping cough.* It is so nearly tasteless that it may be administered in milk or syrup and is usually very well borne by the stomach, so that it is especially useful in the treatment of children. The necessary *doses* are larger than those of quinine; in ordinary acute diseases thirty grains (2 Gm.) may be given daily; in *malaria* forty grains (2.6 Gm.).

The salicylate of euquinine, a white, tasteless, crystalline powder, almost insoluble in water and melting at 195° C. (383° F.), exhibits the combined effects of salicylic acid and quinine, being particularly adapted to the treatment of children.

Euresol. *N. N. R.* 1917. (*Resorcin monoacetate, monoacetyl resorcinol.*) $C_6H_4(OH)OCOCH_3$.—A viscid honey-like liquid, boiling at 283° C. (541.4° F.). It is made by heating resorcinol with glacial acetic acid. It is used as a substitute for resorcinol in the treatment of *seborrhea, sycosis* and other diseases of the skin. According to Joseph and Vieth (*Derm. Cb.*, 1905), it has the advantage over resorcinol in exercising a deeper influence, and being less irritant. It may be employed in strengths of from 5 to 10 per cent.

Eurobin. *Chrysarobin Triacetate.*—This is a yellowish-red powder, *triacetyl chrysarobin,* used as a substitute for chrysarobin; it is soluble in chloroform, acetone, and ether, insoluble in water. It acts like chrysarobin on the skin, but is more powerful. Kromayer commends it applied as a paint, according to the following formula. Saligallol, 5 to 10 parts; eurobin, 1 to 20 parts; acetone, to make 100 parts. *Lenirobin,* the tetracetyl derivative, *chrysarobin tetra-acetate,* is less irritant than chrysarobin, and has the special advantage of not staining the linen.

Europhen. *N. N. R.* 1917. *Di-isobutyl-ortho-cresol - iodide.* $C_6H_3(C_4H_9)(CH_3)(OI)C_6H_2(CH_3):O(.C_4H_9)$.—This is a yellow amorphous powder, of a specific aromatic odor, which has been proposed as a substitute for iodoform. It is asserted that it is five times lighter than iodoform, and can be used in much larger bulk; that it is equally efficacious with iodoform; also that it is decomposed more slowly than iodoform, and is, therefore, less poisonous. (See *Ph. Ztg.*, July, 1891; also *Th. M.*, July, 1891.) *Europhen* is made by the action of iodine upon isobutylorthocresol in alkaline solution. It occurs as a fine, soft, amorphous powder, light yellow, tasteless, and having but a faint odor. It is soluble in ether, chloroform, collodion, alcohol, and fixed oils; insoluble in water and glycerin; melting at 110° C. (230° F.). Its solution undergoes decomposition when exposed to light or heat.

Europhen contains about 28.1 per cent. of iodine, which element is slowly liberated from its alcoholic and ethereal solutions. It is incompatible with metallic oxides and mercurial salts, and undergoes slight change in the presence of organic matter. Taken internally it is said to pass out in great part from the alimentary canal with the feces unchanged, though some absorption takes place. It is asserted that it is non-toxic, two or three drachms (7.7–11.6 Gm.) having been given to dogs and fifteen grains (1 Gm.) to human beings without effect. As an antibacterial it is affirmed to be about equivalent to iodoform. (*Revue Méd. de l'Est,* Feb., 1892.)

It has been used by a number of clinicians with asserted good results as a local application in *chancres, syphilitic ulcers, burns, psoriasis, eczema, lupus,* and various *skin diseases.* It may be applied either as a dusting powder or in an ointment varying in strength from 1 to 10 per cent. It has also been employed in *rhinitis, laryngeal tuberculosis,* and other inflammatory disorders of the preliminary air-passages. Internally it has been used, especially hypodermically, dissolved in oil, in *constitutional syphilis,* with not very encouraging results. *Dose,* one-half to one and one-half grains (0.032–0.096 Gm.).

Eurybin.—A glucoside obtained from a New Zealand plant, *Eurybia moschata.* (*Merck's Bericht,* 1893, 12.)

Euscopol. *N. N. R.* 1917. $C_{17}H_{21}O_4N.HBr$.—An optically inactive scopolamine hydrobromide. (See *Scopolamine,* p. 985.)

Eutannin. $C_{28}H_{20}O_{19}$.—Under this name is marketed a powder closely related to tannic acid. According to Thoms it is *chebulinic acid,* $C_{28}H_{20}O_{19}$, an acid which is also obtained from myrobalans. It is insoluble in the gastric juice and therefore passes undecomposed into the intestinal canal, where it exercises its function of antisepsis and astringency, after being split up by the intestinal juices into its component parts. It thus makes an effective curative agent in the treatment of *intestinal catarrh,* both acute and chronic. *Dose,* four to ten grains (0.25 to 0.65 Gm.) twice or thrice daily.

Evodia.—Several species of this rutaceous genus are stated to have medicinal properties. *Evodia febrifuga* St. Hil (*Esenbechia febrifuga* A. Juss.) of Brazil is astringent and tonic, *E. meliæfolia* Benth. of Japan contains berberine, while *E. longifolia* A. Rich. of the Fiji Islands is used to prevent abortion.

Exalgine. *Methylacetanilide.* $C_6H_5N(CH_3)COCH_3$ or $C_9H_{11}NO$.—This substance, which was discovered by Brigonnet, is one of the three isomeric methyl derivatives of acetanilide (*C. R. A. S.*, cviii, 571), and is made by warming together monomethylaniline and acetylchloride. It occurs

in needles, or in long tablet-like crystals, according as it is obtained by crystallization or from the mass after fusion. It is sparingly soluble in cold water, quite soluble in hot water, and readily soluble in very dilute alcohol, or in water to which a small amount of alcohol has been added; it fuses at 101° C. (213.8° F.) and boils between 240° and 250° C. (464°–482° F.) without decomposition. The hot aqueous solution is said by Upton to retain most of its exalgine on cooling.

According to Brigonnet, hypodermic injections of *exalgine* produce in the lower animals violent epileptiform convulsions, profuse salivation, cyanosis, disturbance of breathing, fall of temperature, and alteration of the blood, which becomes dark prune-colored and contains an abundance of methemoglobin. The muscles at the seat of the injection are said to be locally paralyzed, and although small doses increased slightly the blood pressure, after the toxic dose the pressure suddenly falls. The urine does not become albuminous or bloody. When given to man in full, non-poisonous doses, it produces some slight amblyopia, vertigo accompanied in some patients by vomiting, tinnitus aurium, headache, drowsiness, and vasomotor disturbances, such as sweating. After large doses, cyanosis is pronounced, but no eruption upon the surface of the skin seems as yet to have been noticed. After toxic doses, dyspnea, cyanosis, dilated pupils, paresis, heart weakness, and convulsions have been noted, but no fatal result has been recorded; in a boy fourteen years old two doses of three grains each produced most alarming symptoms.

Therapeutically, exalgine seems to be an antipyretic, but it has been used almost exclusively as an analgesic and antispasmodic. According to Moncorvo, it is very well borne in children; he has used it extensively in *chorea, polyuria,* and for the relief of *pain.* He believes that its analgesic effect is at least five times as strong as that of antipyrine; his dose, to a child five years old, is one and a half grains (0.096 Gm.). *Dose,* for an adult, three to five grains (0.2 to 0.32 Gm.), not more than twelve grains to be given in twenty-four hours.

Exodin.—This is stated to be a mixture of derivatives of *rufigallic acid.* It occurs as a yellow, odorless, tasteless powder, insoluble in water. It has been used with satisfactory results by a number of clinicians as a cathartic, especially in chronic constipation. It is claimed for it that it is non-irritant and does not produce after constipation. The *dose* is from fifteen to thirty grains (1 to 2 Gm.), usually given in the form of tablets.

Extract of Beef. *N. F. IV. Extractum Carnis. Beef Extract.*—It is defined by the N. F. as "the residue obtained from fresh beef broth by evaporation at a low temperature." *N. F.* In its preparation the sound fresh meat is usually cut into small pieces, the appropriate amount of water is added, and the mixture placed in a vessel which may be closed to prevent the escape of any aqueous vapor and permit the application of slight pressure. After digestion for several hours in this apparatus, with occasional stirring, the liquid portion is poured off, the solid material gently pressed to separate any remaining liquid, then cooled to remove fat, and afterward strained. The clear liquid is afterwards evaporated in vacuo to the consistence of a pasty mass. It is usually spoken of as the *Liebig type of beef extract.* The N. F. describes it as "a yellowish-brown to dark-brown, slightly acid, pasty mass having an agreeable meat-like odor and taste. Twenty-five Gm. of Extract of Beef, diluted to 250 mils with distilled water, yields a nearly clear solution, free from sediment. Separate portions of this solution respond to the following tests: Boil 10 mils of the solution for one minute with 1.5 Gm. of purified animal charcoal, add distilled water to replace that lost by evaporation and filter; the filtrate produces no blue coloration when one drop is added to three drops of a solution of diphenylamine (1 in 100) in concentrated sulphuric acid (*nitrate*). Distribute 10 mils of the solution over dry sand or asbestos and dry to constant weight in a flat-bottomed porcelain dish in an oven at a temperature of 105° C. (221° F.); it yields a residue of not less than 0.75 Gm., equivalent to 75 per cent. of solids in the original Extract. Incinerate the residue from 10 mils of the solution obtained in the preceding test; the ash does not exceed 30 per cent. of the residue, nor does the sodium chloride in the ash exceed 10 per cent. of the residue when determined as directed under the Assay for chlorides (see *U. S. P.,* Test No. 5, Part III). To 100 mils of the solution contained in a 500 mil Kjeldahl flask, add 5 Gm. of barium carbonate and 100 mils of distilled water and, using a connecting bulb, distil 100 mils into 10 mils of half-normal hydrochloric acid V.S. Titrate the excess of acid, using cochineal T.S. as indicator, and from the acid consumed by the distillate, calculate the percentage of nitrogen as ammonia. This does not exceed 0.35 per cent. of the total solids. Transfer 25 mils of the solution to a 100 mil Erlenmeyer flask, add 50 mils of alcohol and shake the mixture thoroughly When the precipitate has subsided, filter, collect the precipitate upon a 9 cm., counterpoised filter, wash the precipitate three times with a mixture of two volumes of alcohol and one volume of distilled water, and then dry it to constant weight at 105° C. The weight of this precipitate does not exceed 10 per cent. of the total solids. (Reserve the filtrate and washing for the following determination of nitrogen.) To an aliquot portion of the alcoholic filtrate from the preceding test corresponding to 1 Gm. of the alcohol soluble solids, add 4 mils of sulphuric acid and evaporate to dryness in a 500 mil Kjeldahl flask. Determine the nitrogen by the Gunning-Kjeldahl method. The amount of nitrogen thus found is not less than 0.06 Gm." *N. F.* Bones and tendons are not used as they introduce gelatin which is looked upon as an adulterant. The chief constituents present from the meat are *creatin, creatinin, xanthin, carnin,* and *carnic acid.* It is used as a nutritive and stimulant chiefly for invalids, but its nutritive value has been greatly exaggerated. Its chief value consists not in the amount of nutritive material which it contains, but the rapidity with which it is absorbed. In the N. F. it is used in the preparation of several wines in combination with iron (see Part III).

Fabiana. *Fabiana imbricata* Ruiz and Pavon. *Pichi.* (Fam. *Solanaceæ.*)—This is a small shrub growing in Bolivia, Peru, Chili and the Argentine Republic. The plant somewhat resembles a Juniper. The branches are brownish-gray and about 5 mm. in diameter; the wood is yellowish and tough; leaves scale-like, about 1 mm. in length, closely imbricated and bluish-green; the flowers are about 12 mm. in length and possess a white or purplish corolla; the fruit is a capsule containing a few sub-globular seeds. The odor of the drug is aromatic and the taste bitter and

terebinthinate. For microscopic structure, see *Ph. Ztschr. f. Russland*, 1891, No. 44; *Apoth. Zeit.*, 1892, p. 22.

A. B. Lyons obtained from it a fluorescent body resembling æsculin, a neutral crystalline principle, some volatile oil, resin, and apparently traces of an alkaloid. (*A. J. P.*, 1886, 65.) Henry Trimble and J. M. Schroeter (*A. J. P.*, 1889, 407) considered the crystalline principle to be a resin, and gave it the formula $(C_{18}H_{31}O_2)x$. H. Kunz-Krause (*A. J. P.*, 1900, p. 80) made a full study of pichi and found a tannin which he named *fabiana-tannoid*, a fluorescent substance proven to be *chrysatropic acid* (*β-methyl æsculetin*), $C_9H_5(CH_3)O_4$, while no alkaloids are present, the sole basic principle being choline. The volatile oil he names *fabianol* and gives it the formula $C_{54}H_{90}O_2$. The resin he calls *fabiana-resin* and gives to it the formula $(C_{18}H_{30}O_2)_3$. The resin appears in microscopical crystals, melting at 280° C. The tannin proved to be like caffetannic acid, which Kunz-Krause had previously shown to be *glycosyl-dioxycinnamic acid*. It contains volatile oil, a characteristic soft resin and tannin.

Pichi appears to be a terebinthinate diuretic, to which also are attributed tonic and cholagogue properties. It has been used to a considerable extent in the treatment of *acute* and *chronic vesical catarrh*, giving especially favorable results in cases in which the urinary irritation is kept up by *gravel*. It is said even to calm the irritability and aid in the expulsion of *renal*, *urethral*, or *cystic calculi*. It has been further recommended in the treatment of *jaundice* and *dyspepsia*, with lack of biliary secretion. It is somewhat irritating, and is usually said to be contra-indicated by the existence of organic disease of the kidneys; but cases have been reported in which *renal hemorrhage* connected with Bright's disease has been greatly benefited by the remedy. It has also been employed in *gonorrhea* and in *gonorrheal prostatitis*. The solid extract may be used in the *dose* of from two to ten grains (0.13–0.65 Gm.); the fluidextract, in the *dose* of from ten to forty minims (0.6–2.5 mils). It is probable that the resinoid precipitate, made from a strong tincture by means of water, would be the best preparation of the drug. The fluidextract does not mix with water unless the solution be made alkaline. It may be administered in capsules.

Fagacid.—This product, derived from beechwood tar, is an acid resin-like substance readily soluble in alkali solutions, giving water-soluble but not alcohol-soluble compounds. It is employed mostly as an antiseptic agent in the preparation of medicinal soaps, plasters, and dressings. (*Ph. Ztg.*, 1905, 870.)

Fanghi di Sclofani.—This is a light yellowish fine powder of volcanic origin, consisting chiefly of sulphur and small quantities of iron, manganese, calcium, etc., the sulphur being in an exceedingly fine powder. It is highly praised by Otto v. Fleischl as a remedy in *acne rosacea*. Two or three grains (0.13 or 0.2 Gm.) of the powder are mixed with a teaspoonful (4 mils) of water and the opaque mixture applied with the finger on going to bed and allowed to dry on the part.

Fenchyval.—Under this title has been introduced the iso-valeric ester of fennel oil. It is employed for the same purpose as the other valerates.

Fergon. Fergan.—Both of these preparations are organic compounds of iron and albumen. They are used as ferruginous tonics in *anemic conditions*.

Ferissol.—This is a substance said to be derived from cinnamic acid and guaiacol which occurs as a very soluble powder and has been used in *tuberculous diseases* intermuscularly in 10 per cent. solution, fifteen minims (0.9 mil) per *dose*, increased to forty-five minims (2.8 mils). The internal *dose* is fifteen grains (1 Gm.).

Fermentdiagnosticum. *N. N. R.* 1917. *Solution of Glycyltryptophan.*—This solution is used in determining the presence of a peptolytic ferment on account of its being split up by such ferments with the liberation of *tryptophan*, which may readily be detected.

Ferralbol. This is asserted to be a chemical combination of iron with eggs, containing not merely the albumin of the egg, but also the lecithin from the yolk. It is said to contain 3 per cent. of iron and 1 per cent. of lecithin.

Ferralbol is used in the treatment of *anemia*. The asserted advantages are that it has no harmful effect upon the teeth and does not disturb digestion.

Dose, eight grains (0.5 Gm.) three times a day.

Ferralbumose.—This is made by treating finely cut meat, freed from fat, with an artificial gastric juice, freeing the solution from albumin, neutralizing it with sodium carbonate, filtering and evaporating to dryness, *in vacuo*. A 10 per cent. solution of this *albumose* is precipitated by the addition of a 10 per cent. solution of ferric chloride and the precipitate dried, powdered and sifted.

Ferratin. *N. N. R.* 1917. *Sodii Ferrialbumas.*—This is a light brown powder containing from 6 to 8 per cent. of iron in a form soluble in alkaline liquids. It is an albuminous compound, originally prepared by Schmiedeberg from the liver of the hog, and believed to be the natural compound of iron as it exists in the system, and therefore of especial value in therapeutics. It is now made by the reaction of the albumin with a double tartrate of iron and an alkali. It is almost insoluble in water, soluble in alkalies, and contains 7 per cent. of iron in organic compounds. The iron is firmly united to the albumen molecule so that ammonium sulphide does not react at once. A solution of ferratin has also been put upon the market under the name of *ferratose*.

Ferratin may be given in *doses* of from three to five grains (0.2–0.32 Gm.) three times a day. It appears to be capable of acting as a chalybeate, but there is no sufficient reason for believing it to be superior to the older perparations of iron.

Ferratogen. *Ferri Nucleinas.*—This substance is obtained by the cultivation of yeast on a ferruginous nutritive medium and subsequently extracted. It occurs as a grayish-white or yellow powder, insoluble in water and gastric juice, but believed to be dissolved by pancreatic fluids. The content of iron is claimed to be slightly over 1 per cent. It has been recommended by Cloetta in *chlorosis* when the stomach is delicate. *Dose*, five to ten grains (0.32–0.65 Gm.).

Ferric Albuminate. *Ferri Albuminas.*—This preparation has come into some prominence, more particularly in Europe, on account of its asserted advantages over various other compounds of iron, Démarquay, Chrisnard, and others recommending its employment in *chlorosis* and *anemia*, as being very readily absorbed. Friese, Kobligk, Bernbeck, Biel, Holdermann, Nierck, Donitz, and Hager have each proposed methods for preparing either the solution or dry salt. C. L. Diehl, however, after a careful review of the processes of these investigators, offers the following: 4 troyounces of white of eggs are diluted with 8 fluidounces of water; 65 minims of official solution of ferric chloride diluted with 4 fluidounces of water are added, and the solution filtered. The filtrate

is now mixed with 10 fluidounces of a saturated solution of sodium chloride, the precipitate collected on a wet muslin strainer, washed with a mixture of one volume of the saturated solution of sodium chloride and 3 volumes of water, until the washings give but a faint reaction for iron. The washed ferric albuminate is, after draining, powerfully pressed to get it as dry as possible, and then exposed to a dry atmosphere, and finally powdered. This salt contains the equivalent of 5 per cent. of ferric oxide, or 10 per cent. of ferric chloride. (For other processes, see *A. J. P.*, 1880, 177.) As thus obtained, ferric albuminate is a cinnamon-brown powder, having a slight saline taste, soluble in water, particularly if slightly acidulated with hydrochloric acid. It is best administered in *doses* of from twenty to thirty grains (1.3–2.0 Gm.) in simple aqueous solution, which should be freshly prepared. It may also be given in the form of a pill, either alone or combined with strychnin, quinine, etc. See *Liquor Ferri Albuminati, N. F.* (Part III). For method of preparing *iron and potassium albuminate*, and *iron and sodium albuminate*, see 16th ed., *U. S. D.*

Ferric Alginate. *Alginoid Iron.*—Obtained from sodium alginate and ferric chloride. $C_{76}H_{77}N_2O_{22}Fe_3$. It is a brown, tasteless powder, containing about 11 per cent. of iron; insoluble in water, but soluble in ammonia. It is used for its hematinic properties and is stated to be decomposed in the intestinal canal. *Dose*, three to fifteen grains (0.2–1.0 Gm.).

Ferric Ammonium Sulphate. *Iron and Ammonium Sulphate. Ammonio-Ferric Sulphate. Ammonio-Ferric Alum. Iron Ammonium Alum. Ferri et Ammonii Sulphas. U. S. VIII. Ferrum Sulfuricum Oxydatum Ammoniatum. Ferrum Ammonio-Sulphuricum. Ferri Ammonio-Sulphas. Sulphas Ammonico-Ferricus. Alumen Ammoniacale ferricum. Iron Alum. Sulfate de Fer et d'Ammoniaque, Sulfate de Fer (ferrique) ammoniacal, Alun de Fer ammoniacal*, Fr. *Schwefelsaures Eisenoxyd-Ammonium, Ammoniakalischer Eisenalaun, Ferriammoniumsulfat*, G. $FeNH_4(SO_4)_2 + 12H_2O = 482.21$.—This is an ammonia iron-alum, in which the place of the aluminum oxide is occupied by ferric oxide. It is prepared by heating the solution of ferric tersulphate with ammonium sulphate until the latter salt is dissolved, and then allowing the solution to cool. The two salts unite to form iron and ammonium sulphate, which, being insoluble in the amount of liquid employed, crystallizes when it cools. The process is based on that of Wm. Hodgson (*A. J. P.*, 1856, p. 305). The *U. S.*, 1870, gave the following process for preparing this salt: "Take of Solution of Tersulphate of Iron *two pints;* Sulphate of Ammonium *four troyounces and a half.* Heat the Solution of Tersulphate of Iron to the boiling point, add the Sulphate of Ammonium, stirring until it is dissolved, and set the liquid aside to crystallize. Wash the crystals quickly with very cold water, wrap them in bibulous paper, and dry them in the open air." *U. S.*, 1870.

Ammonio-ferric alum is in "pale violet, octahedral crystals, without odor, and having an acid, styptic taste; efflorescent on exposure to the air. Soluble in 2.7 parts of water at 25° C. (77° F.), and in 0.8 part of boiling water; insoluble in alcohol. When strongly heated, the crystals fuse, lose their water of crystallization, expand, and finally leave a pale brown residue. The aqueous solution of the salt has an acid reaction upon blue litmus paper, and yields with potassium ferrocyanide T.S. a blue precipitate, and with barium chloride T.S. a white precipitate insoluble in hydrochloric acid. With potassium hydroxide T.S. Ferric Ammonium Sulphate yields a brownish-red precipitate, and if the mixture be heated, ammonia gas is evolved. If the iron be wholly precipitated from a solution of the salt by treating it with an excess of potassium hydroxide T.S., the resulting filtrate when neutralized with hydrochloric acid, and then mixed with ammonia water, should not yield a white, gelatinous precipitate (absence of *aluminum*). The addition of 3 Cc. of nitric acid to 30 Cc. of a solution of the salt (1 in 20), followed by a few drops of silver nitrate T.S., should not produce any turbidity (absence of *chlorides*). If 0.555 Gm. of the unefflorescd crystals of the salt be dissolved in 15 Cc. of water and 2 Cc. of hydrochloric acid, in a glass-stoppered flask having a capacity of about 100 Cc., and if, after the addition of 1 Gm. of potassium iodide, and securely closing the flask, the mixture be kept for half an hour at 40° C. (104° F.), and then cooled, it should require not less than 11.5 Cc. of tenth-normal sodium thiosulphate V.S. to discharge the color of the liquid (each Cc. of the tenth-normal sodium thiosulphate V.S. indicating 1 per cent. of metallic iron)." *U. S. VIII.* According to H. Rose, the pure salt is white, and gives a colored solution with water, in consequence of the formation of a basic ferruginous salt. This decomposition is prevented by dissolving it in diluted sulphuric acid, when the solution is colorless. Instead of ammonium sulphate, potassium sulphate may be employed with the solution of ferric tersulphate, in which case a potassium iron-alum is produced, called *potassio-ferric alum*, which has all the properties, physical and remedial, of the ammonio-ferric salt, and the two appear to have been indiscriminately used.

The iron-alum is an active astringent and is useful, as a local application in passive *leucorrheas*, and as a styptic.

Dose, from five to ten grains (0.32 to 0.65 Gm.), to be repeated twice or three times a day.

Ferric Arsenate. $Fe_3(AsO_4)_2 + 6H_2O$.—*Iron arsenate* is a green, amorphous powder, insoluble in water, but soluble in the presence of dilute mineral acids. It is used as an insecticide especially for agricultural purposes, and may be employed in strengths of from 0.1 to 0.2 per cent.

Ferric Arsenite. *Arsenite of Iron. Iron Arsenite.* $4Fe_2O_3As_2O_3 + 5H_2O$.—This is a brownish-yellow powder soluble in acids and insoluble in water, but the combination with ammonium nitrate is soluble and has been put upon the market under the name of ammoniated citro-arsenite of iron. This represents about 16 per cent. of iron and 1.4 per cent. of arsenous acid. It is used in the treatment of various forms of *anemia* but is especially commended in *pellagra.* It may be given either by the mouth or hypodermically. The *dose* for the latter purpose is from one-half to one grain (0.032 to 0.065 Gm.) every second or third day.

Ferric Arsenio-Citrate (Ammoniated).—This compound under the name of Ferr-Arseno-Citras Ammoniatus has been highly commended by Valvassori and Peroni (see *M. R.*, 1900) for the hypodermic treatment of *malaria*, especially in children. It is given in *doses* of three-fifths of a grain (0.036 Gm.) in sterilized water, injected at intervals of two or three days.

Ferric Benzoate. *Ferri Benzoas. Ferrum Benzoicum. Eisenbenzoat, Ferribenzoat*, G.—Fe_2

$(C_7H_5O_2)_6 + nH_2O$.—This is made by precipitating a solution of ammonium benzoate with a diluted solution of ferric chloride. The precipitate, after being washed, is dried at a temperature not above 30° C. (86° F.), protected from light. A brownish-red, odorless, tasteless, powder insoluble in water. When freshly prepared it is soluble in cod liver oil.

Ferric Bromide. *Iron tribromide.* Fe_2Br_6.—Dark red, deliquescent crystals, easily soluble in water, ether and alcohol and is used in *scrofula, phthisis,* and *gland enlargements,* and exhibits in a high degree the bromide action. *Dose,* one-third to one grain (0.021–0.065 Gm.) several times a day with a maximum daily dose of eight grains (0.5 Gm.).

Ferric Bromoiodide.—A deliquescent brown powder soluble in water with subsequent decomposition. It is employed for its alterative, tonic and chalybeate properties. *Dose,* one-half to three grains (0.032 to 0.2 Gm.).

Ferric Camphorate.—A yellowish-red, very bulky powder. It is insoluble in the usual solvents. It has been used in the treatment of *chlorosis. Dose,* one and one-half to three grains (0.096 to 0.2 Gm.) several times daily.

Ferric Citrate. *Ferri Citras. U. S. VIII. Citrate of Iron. Citras Ferricus. Citrate de Sesquioxide de Fer, Citrate ferrique,* Fr. *Ferrum Citricum Oxydatum,* P. G. *Ferricitrate, Citronensaures Eisenoxyd, Eisencitrat,* G. *Citrato di ferro,* It. *Citrato ferrico,* Sp.—"It should contain Ferric Citrate corresponding in amount to not less than 16 per cent. of metallic iron, and should be kept in well-stoppered bottles, protected from light." *U. S. VIII.* This preparation is made by evaporating a solution of ferric citrate. The latter was dropped from the U. S. P., but is now official in the National Formulary IV (see Part III).

Ferric Citrate is not a definite chemical salt, but a compound containing ferric citrate, to which the following formula has been assigned: $Fe_2(C_6H_5O_7)_2.6H_2O$. The U. S. P. required not less than 16 per cent. of metallic iron. It is important, in making it, that an excess of citric acid be avoided, and the ferric hydroxide be thoroughly washed to free it from sulphates, otherwise brilliant scales will not be formed.

Ferric citrate is in "thin, transparent, garnet-red scales, without odor, and having a slightly ferruginous taste. Slowly but completely soluble in water at 5° C. (77° F.), and readily soluble in hot water, but diminishing in solubility with age; insoluble in alcohol. When strongly heated, the salt chars, and finally leaves a residue of ferric oxide, which, when moistened with hot water, should not show an alkaline reaction upon red litmus paper (absence of *citrates* or *tartrates* of the *alkali metals*). An aqueous solution of the salt shows an acid reaction with blue litmus paper, and is not precipitated, but rendered darker in color, by ammonia water. With potassium ferrocyanide T.S. the aqueous solution yields a bluish-green color or precipitate, which is increased and rendered dark blue by the subsequent addition of hydrochloric acid (difference from *iron and ammonium citrate*). If Ferric Citrate be heated with potassium hydroxide T.S., it yields a brownish-red precipitate, without evolving ammonia. If an aqueous solution of the salt (1 in 10) be deprived of its iron by boiling with an excess of potassium hydroxide T.S., and the filtrate be slightly acidulated with acetic acid, a portion of the cooled liquid, when mixed with a little calcium chloride T.S., and again heated to boiling, will gradually afford a white crystalline precipitate. Another portion of the acidulated and cooled liquid, when allowed to stand for twenty-four hours, should not deposit a white crystalline precipitate (absence of *tartrate*). If 0.555 Gm. of Ferric Citrate be dissolved in 15 Cc. of water and 2 Cc. of hydrochloric acid, in a glass-stoppered flask having a capacity of about 100 Cc., with the aid of a gentle heat, and if, after the addition of 1 Gm. of potassium iodide, and securely closing the flask, the mixture be kept for half an hour at 40° C. (104° F.), and then cooled, it should require not less than 16 Cc. of tenth-normal sodium thiosulphate V.S. to discharge the color of the liquid, starch T.S. being used as indicator (each Cc. of the tenth-normal sodium thiosulphate V.S. indicating 1 per cent. of metallic iron)." *U. S. VIII.*

Ferric citrate was introduced to the notice of the profession in 1831 by Béral of Paris. It is an excellent chalybeate, nearly free from astringency and is preferably given in solution. Bullock (*J. A. M. A.*, 1911, lvii, p. 1428) has had most excellent results in the *anemia* of *tuberculosis* from the hypodermic use of this salt. He injected one grain (0.065 Gm.) directly into the muscle substance daily.

Dose, by mouth, three to ten grains (0.2 to 0.65 Gm.).

Ferric Glycerophosphate. *N. F. IV. Ferri Glycerophosphas. Ferrum Glycerinophosphoricum. Iron Glycerophosphate. Glycerinphosphorsaures Eisen,* G.—The N. F. standards are as follows: "It contains a variable quantity of $Fe_2(C_3H_7O_6P)_3$ (621.97) corresponding to not less than 14 per cent. nor more than 16 per cent. of Fe. Preserve it in well-closed containers, protected from light. Ferric Glycerophosphate occurs as yellowish-green, transparent, amorphous scales or as a greenish-yellow powder; odorless and nearly tasteless. One gramme dissolves slowly in about 2 mils of water at 25° C. (77° F.); insoluble in alcohol. An aqueous solution is acid to litmus and becomes turbid when heated. An aqueous solution of the salt (1 in 20) is colored dark blue by potassium ferrocyanide T.S.; on the subsequent addition of hydrochloric acid a dark blue precipitate is produced. Heat a powdered mixture of about 0.1 Gm. of the salt with about 0.5 Gm. of potassium bisulphate; the pungent vapors of acrolein are evolved. Incinerate 0.5 Gm. of the salt; it yields a red-brown residue, which is not alkaline to moistened litmus paper. Not more than a slight yellow turbidity is produced at once on mixing 5 mils of an aqueous solution of the salt (1 in 50) with 10 mils of ammonium molybdate T.S. (*phosphate*), but on standing or on warming, a yellow precipitate is formed. An aqueous solution of the salt (1 in 50), acidulated with hydrochloric acid, does not become more than slightly turbid on the addition of barium chloride T.S. (*sulphate*). Another portion of this aqueous solution, acidulated with nitric acid, does not become more than slightly turbid on the addition of silver nitrate T.S. (*chloride*)." *N. F.*

Assay.—"Dissolve about 0.5 Gm. of Ferric Glycerophosphate, accurately weighed, in 50 mils of distilled water, in a 100 mil grass-stoppered flask, add 5 mils of hydrochloric acid and about 3 Gm. of potassium iodide. Warm to 40° C. (104° F.), and allow the mixture to stand one-half hour at this temperature, in the stoppered flask, cool, and then titrate the liberated iodine with tenth-normal sodium thiosulphate V.S., using starch T.S.

as indicator. It shows not less than 14 per cent. nor more than 16 per cent. of Fe. Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.005584 Gm. of Fe. Each gramme of Ferric Glycerophosphate corresponds to not less than 25.07 mils nor more than 28.65 mils of tenth-normal sodium thiosulphate V.S." *N. F.* This is made by dissolving freshly precipitated ferric hydroxide in glycerophosphoric acid, evaporating the solution *in vacuo* and scaling it upon glass plates. It is in the form of yellow scales, soluble in water and diluted alcohol. The salt is used as a tonic and nervine in *doses* of from five to ten grains (0.32–0.65 Gm.).

Ferric Hydroxide. *Ferri Hydroxidum. Ferri Oxidum Hydratum. Ferric Hydrate. Hydrated Oxide of Iron.* $Fe(OH)_3 = 106.86$. *Ferri Peroxidum. Ferri Sesquioxidum. Ferri Oxidum Rubrum. Hydrous Peroxide of Iron. Ferric Oxyhydrate. Ferrugo. Hydrated Peroxide of Iron. Hydrated Sesquioxide of Iron. Moist Peroxide of Iron. Hydras Ferricus. Oxyde (sesquì) de fer Bihydraté,* Fr. Cod. *Sesquioxide (Péroxide) de Fer hydraté humide, Hydrate de Péroxyde de Fer gélatineux,* Fr. *Feuchtes Eisenoxydhydrat, Gegengift der Arsenigensaure,* G. *Ossido ferrico idrato,* It. *Hidrato ferrico gelatinoso,* Sp.—*Ferric hydroxide* was dismissed from the U. S. VIII but was made official in the N. F. IV under the name of *Magma Ferri Hydroxidi* (see Part III).

A change was made in this process in 1870; formerly the ammonia water was added to the iron solution and a basic clotty precipitate of uncertain composition resulted; by the present process, whereby the acid iron solution is added to the ammonia solution, this is prevented, but care should be used to avoid an excess of ammonia water which will dissolve some of the ferric hydroxide. As an antidote to arsenic poisoning, this preparation has been superseded by the official Ferric Hydroxide with magnesium oxide (PART I).

Ferric hydroxide is frequently used pharmaceutically as the basis for making scaled salts of iron.

Ferric hydroxide, as directed by the U. S. VIII formula, "is a brownish-red magma, wholly soluble in hydrochloric acid without effervescence." *U. S. VIII.*

As prepared by the Dublin process, in which it was heated to redness, it lost the second molecule of water, and became the anhydrous sesquioxide (Fe_2O_3), identical with the *colcothar* of commerce.

This is less easily soluble in acids, improper for medicinal use, and altogether without effect as an antidote. Kept for some time in the moist state, it loses half its combined water, and becomes less soluble in acids and less efficient as an antidote. Hirsch has given some useful details in making precipitated ferric oxide upon a comparatively large scale, in *Am. Drug.*, 1884, 66.

Ferric hydroxide is not an eligible ferruginous preparation for medicinal use. Its sole use in medicine is as an antidote in arsenical poisoning for which purpose it is inferior to the official *Ferri Hydroxidum cum Magnesii Oxido* (see p. 470).

The *monohydrated sesquioxide* is a reddish-brown, tasteless, insoluble powder, differing from colcothar in containing a molecule of water. Hence, "heated to dull redness in a test-tube it yields about 10 per cent. of moisture." *Br.*, 1885. It should not be deliquescent, and should dissolve entirely in hydrochloric acid without effervescence. Its solution in diluted hydrochloric acid yields a copious blue precipitate with potassium ferrocyanide, but none with the ferricyanide, showing that it contains ferric oxide but no ferrous oxide. If it contains copper, its hydrochloric solution will deposit this metal on a bright piece of iron. Dawies states that if the hydrated oxide recently prepared be kept for four days in boiling water it loses a large proportion of its water, containing at the end of that time only 5.77 per cent.; the larger portion of the oxide has, therefore, become dehydrated, and the same thing happens at a lower temperature, 41.1° C. (106° F.), as in two or three months it becomes of a brick-red color, and is but slightly soluble in nitric acid. (*J. P. C.*, 4e sér., iv, 400.) This oxide is not used as a medicine. It was employed in making iron plaster, *Emplastrum Ferri* (*U. S. P.*, 1890), troches of iron, *Trochisci Ferri* (*U. S. P.*, 1890), and reduced iron, for which purposes other forms of oxidized iron would answer as well. The former Dublin *rubigo ferri*, or *rust of iron*, formed by exposing moistened iron wire to the air until converted into rust, is essentially the sesquioxide, containing a little ferric carbonate, and does not differ materially from the iron subcarbonate formerly official.

Ferric Hypophosphite. *N. F. IV (U. S. P. VIII). Ferric Hypophosphis. Iron Hypophosphite. Hypophosphite of Iron. Ferrum Hypophosphorosum. Hypophosphis Ferricus. Hypophosphite de Fer,* Fr. *Unterphosphorigsaures Eisenoxyd, Ferrihypophosphit,* G.—According to the N. F. "it contains not less than 98 per cent. of $Fe(PH_2O_2)_3$ (251.01) corresponding to not less than 21.8 per cent. of Fe. Preserve it in well-closed containers." *N. F.* It may be made by the action of hypophosphorous acid on ferrous carbonate formed by precipitation from the sulphate; but as some difficulty has been found in obtaining this acid perfectly pure, C. H. Wood, of London, prefers the plan of double decomposition. He proposes that ferrous sulphate and calcium hypophosphite be made to react on each other in molecular proportions represented by 480 grains of crystallized ferrous sulphate and 326 grains of calcium hypophosphite: in the latter an allowance of 10 per cent. being made for impurities ordinarily found in that salt. These quantities will yield 320 grains of ferric hypophosphite, and the reaction will be represented by the following formula: $Ca(H_2PO_2)_2 + FeSO_4 = CaSO_4 + Fe(H_2PO_2)_2$. Calcium sulphate is precipitated, and ferrous hypophosphite is held in solution. (*P. J.*, 1868, p. 342.) In this condition the salt is a ferrous compound; but on evaporation the ferrous salt becomes ferric, and acquires the properties required of the official salt. Of this the following description and tests are given in the N. F. IV: "Ferric Hypophosphite occurs as a white, or grayish-white powder, odorless and nearly tasteless; permanent in the air. One gramme dissolves in 2300 mils of water at 25° C. (77° F.) and in 1200 mils of boiling water; more readily soluble in the presence of hypophosphorous acid or in a warm, concentrated solution of an alkali citrate, forming with the latter a green solution. When strongly heated in a dry test tube, the salt evolves spontaneously inflammable hydrogen phosphide gas, and finally leaves a residue of ferric pyrophosphate. Ferric Hypophosphite is readily oxidized by nitric acid or other oxidizing agents. Add 15 mils of acetic acid to 1 Gm. of the salt; no effervescence occurs (*carbonate*). Heat this mixture to boiling and filter; the filtrate responds to the

following tests: Add to a portion of the filtrate a few drops of silver nitrate T.S. and warm; a brown to black coloration or precipitate is produced. To another portion of the filtrate add, drop by drop, an excess of mercuric chloride T.S.; a white precipitate of mercurous chloride is formed upon gently heating. Another 5 mil portion of the filtrate shows no turbidity with ammonium oxalate T.S. (*calcium*). Dissolve 1 Gm. of the salt in 20 mils of diluted hydrochloric acid, with the aid of heat, and add 1 mil of barium chloride T.S.; not more than a slight turbidity is produced (*sulphate*). Boil 0.5 Gm. of the salt with 10 mils of sodium hydroxide T.S.; a reddish-brown precipitate is produced. Filter this mixture, slightly acidulate the filtrate with hydrochloric acid, add magnesia mixture T.S. and then an excess of ammonia water; no crystalline precipitate is produced (*phosphate*). Dissolve 1 Gm. of the salt in about 25 mils of boiling distilled water by the aid of sufficient hydrochloric acid, added drop by drop, then add 2 mils of nitric acid, boil and add a slight excess of ammonia water; the filtrate is colorless, and, after acidulating with hydrochloric acid, does not respond to the Test for heavy metals (see U. S. P., Test No. 3, Part III)." *N. F.*

Assay.—"To 1 Gm. of Ferric Hypophosphite accurately weighed, add 10 mils of nitrohydrochloric acid and evaporate to dryness on a water bath. Dissolve the residue in 25 mils of distilled water and 10 mils of hydrochloric acid, transfer the solution to a glass-stoppered flask, add 3 Gm. of potassium iodide, keep it at 40° C. (104° F.) for thirty minutes, cool and titrate the liberated iodine with tenth-normal sodium thiosulphate V.S., using starch T.S. as indicator. It shows not less than 21.8 per cent. of Fe. Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.005584 Gm. of Fe, and 0.025101 Gm. of Fe $(PH_2O_2)_3$. Each gramme of Ferric Hypophosphite requires not less than 39.04 mils of tenth-normal sodium thiosulphate V.S." *N. F.*

Syrup of ferrous hypophosphite may be prepared by simply adding syrup to the solution of the hypophosphite remaining after the separation of the calcium sulphate in the process of Wood above given. If two and a half ounces of water be used in the process, and the paste resulting from the precipitation of the calcium sulphate be pressed out, the remaining liquid, after filtration, will form with seven times its volume of syrup a liquid containing two grains of the hypophosphite in a fluidrachm. (*P. J.*, April, 1868.) But in this form, if the syrup be not thoroughly protected it quickly absorbs oxygen, and in a few hours begins to exhibit the formation of a precipitate, rendering it in a short time unfit for use. A little phosphoric or citric acid added to the syrup will obviate this result; but it is better perhaps at once to form a syrup from materials which will not be liable to this objection.

Wood employs the following process: "Take of granulated ferrous sulphate 480 gr., calcium hypophosphite 326 gr., diluted phosphoric acid 1 fl. oz., water 1½ fl. oz., syrup, a sufficient quantity. Dissolve, without heat, the ferrous sulphate in the phosphoric acid, previously mixed with the water. Rub the hypophosphite to fine powder, and pour on it the solution of the sulphate. Triturate together for two or three minutes, then pour the mixture on a piece of damp calico, and squeeze out the liquid with the hands. Filter this solution, and add to it seven times its volume of strong syrup. The resulting syrup will contain two grains of ferric hypophosphite in each fluidrachm." The dose may be from two to six fluidrachms (7.5 to 22.5 mils).

Ferric hypophosphite is a feeble chalybeate, but has no advantages over the official salts of iron. It enters into an N. F. elixir, solution, and syrup, and also into that therapeutic hodge-podge formerly official, the *Compound Syrup of Hypophosphites*, which is still in the N. F. (see Part III). It may be administered in the form of pill or powder, but the syrup is more elegant.

Dose, from five to ten grains (0.32 to 0.65 Gm.).

Ferric Iodate. *Ferri Iodas. Basic Ferric Iodate.* $Fe_2O_3.2I_2O_5+8H_2O$.—This has been proposed as a substitute for the iodide by Cameron. (*Dublin Q. J.*, 1869, 354.) It is prepared by precipitating five fluidrachms of the strong solution of iron perchloride (*B. Ph.*) in four fluidounces of water with a solution of one ounce of potassium iodate in ten ounces of water. It is said to be nearly tasteless, and not to injure the teeth. *Dose*, from two to five grains (0.13–0.32 Gm.).

Ferric Oxide, Magnetic. *Ferri Oxidum Magneticum. Magnetic Iron Oxide. Martial Ethiops. Ferrum Oxydatum Magneticum. Oxydum Ferroso-Ferricum. Black Iron Oxide. Oxyde de Fer noir* (*magnétique*), *Oxyde ferroso-ferrique*, Fr. *Magneteisen, Eisenoxyd-Oxydul*, G. $Fe_3O_3(OH)_2$.—"Take of Solution of Persulphate of Iron *five and a half fluid ounces* [Imperial measure]; Sulphate of Iron *two ounces* [avoirdupois]; Solution of Soda *four pints* [Imp. meas.]; Distilled Water *a sufficiency*. Dissolve the Sulphate of Iron in *two pints* [Imp. meas.] of the Water, and add to it the Solution of Persulphate of Iron, then mix this with the Solution of Soda, stirring them well together. Boil the mixture, let it stand for two hours, stirring it occasionally, then put it on a calico filter, and, when the liquid has drained away, wash the precipitate with Distilled Water, until what passes through the filter ceases to give a precipitate with chloride of barium. Lastly, dry the precipitate at a temperature not exceeding 120°." *Br.*, 1867.

Though the object of this formula is the same as that of the Br. Pharmacopœia of 1864, the proceeding is different. The point aimed at is to get an iron oxide containing one molecule of ferrous oxide and one of ferric oxide.

The artificial magnetic iron oxide is a brownish-black powder, without taste, and strongly magnetic. It dissolves without effervescence in hydrochloric acid diluted with half its bulk of water, and the solution gives a blue precipitate both with the potassium ferrocyanide and the potassium ferricyanide, showing the presence of ferrous and ferric oxide. *Dose*, from five to twenty grains (0.32–1.3 Gm.).

Scales of iron (*ferri squamæ*) were formerly official with the Dublin College under the name of black oxide. They were prepared from the scales found at the blacksmith's anvil, by washing them with water, separating them from impurities by means of a magnet, and reducing them to a fine powder. They are of variable composition, being mixtures of the two oxides of iron with metallic iron.

The magnetic iron stone has been introduced as a substitute for bismuth salts in röntgenological examination of the intestinal tract. Alexander (*D. M. W.*, 1909, p. 877) especially recommends a mixture of iron oxide with cocoa and milk sugar, known as *diaphanit*.

Ferric Pyrophosphate. *N. F. IV* (*U. S. P. VIII*). *Ferri Pyrophosphas. Soluble Ferric Pyrophosphate. Ferri Pyrophosphas Solubilis. U.*

S. P. VIII. Iron Pyrophosphate. Pyrophosphate of Iron. Ferri et Sodii Citro-pyrophospas. Ferrum Pyrophosphoricum cum Sodio Citrico. Pyrophosphate of Iron with Sodium Citrate. Sodio-ferric Citro-pyrophosphate. Pyrophosphate de Fer et de Soude, Fr. *Pyrophosphorsaures Eisenoxyd mit Citronensaurem Natron,* G.—"It contains Ferric Pyrophosphate corresponding to not less than 10 per cent. of Fe. Preserve it in well-closed containers, protected from light." *N. F.* The process formerly official for this salt was: "Ferric Citrate, *fifty grammes* [or 1 ounce av., 334 grains]; Sodium Pyrophosphate, unefflouresced, *fifty grammes* [or 1 ounce av., 334 grains]; Distilled Water, *one hunded mils* [or 3 fluidounces, 183 minims]. Dissolve the Ferric Citrate in the Distilled Water, by heating on a water-bath. To this solution add the Sodium Pyrophosphate, and stir constantly, until it is dissolved. Evaporate the solution, on a water-bath, at a temperature not exceeding 60° C. (140° F.), to the consistence of thick syrup, and spread it on plates of glass, so that, when dry, the salt may be obtained in scales. Keep the product in dark amber-colored, well-stoppered bottles." *U. S.,* 1890.

This formula is based upon a method proposed by M. E. Robiquet to the Academy of Medicine at Paris, in February, 1857, of preparing ferric pyrophosphate for use, by dissolving a gelatinous precipitate of the salt in a solution of ammonium citrate, and forming a syrup with the solution.

Ferric pyrophosphate consists probably of sodio-ferric pyrophosphate, sodio-ferric citrate, and free ferric citrate.

Sodio-ferric pyrophosphate, dried at 100° C., (212° F.), is considered by Flückiger (*Pharm. Chem.,* 2d ed., p. 607, 1888) to have the following composition: $Fe_4(P_2O_7)_3+3Na_4P_2O_7+14H_2O$. It is described in the N. F. as "thin, apple-green, transparent scales, without odor, and having an acidulous, slightly saline taste. The salt is permanent in dry air, when protected from light, but when unprotected soon becomes discolored. It is freely and completely soluble in water; insoluble in alcohol. An aqueous solution of the salt is slightly acid to litmus. Ferric Pyrophosphate, when boiled with sodium hydroxide T.S., produces a brownish-red precipitate without evolving ammonia. Fuse 0.1 Gm. of the salt with 0.1 Gm. each of potassium nitrate and sodium carbonate, boil the residue with 10 mils of distilled water and filter. The filtrate, after being rendered nearly, but not quite, neutral with highly dilute nitric acid, yields a yellow precipitate on the addition of silver nitrate T.S. Boil an aqueous solution of the salt (1 in 10) with an excess of sodium hydroxide T.S. until the iron is precipitated, filter, strongly acidulate the filtrate with hydrochloric acid and cool a portion of the liquid. This liquid, when mixed with an equal volume of magnesia mixture T.S., followed by a slight excess of ammonia water yields a finely divided white precipitate, which, after collecting on a filter and washing does not turn yellow when treated with a few drops of silver nitrate T.S. (*phosphate*)." *N. F.*

Assay.—"Dissolve about 1 Gm. of Ferric Pyrophosphate, accurately weighed, in 25 mils of distilled water and 15 mils of hydrochloric acid, in a glass-stoppered bottle, add 2 Gm. of potassium iodide, securely stopper the bottle, keep it at a temperature of 40° C. (104° F.) for thirty minutes, cool and then titrate the liberated iodine with tenth-normal sodium thiosulphate V.S., using starch T.S. as indicator. It shows not less than 10 per cent. of Fe. Each mil of tenth-normal sodium thiosulphate V.S. used corresponds to 0.005584 Gm. of Fe. Each gramme of Ferric Pyrophosphate corresponds to not less than 17.9 mils of tenth-normal sodium thiosulphate V.S." *N. F.*

Ridenour believed that the presence of orthophosphate in some samples of ferric pyrophosphate is due to the carelessness of the manufacturer and proposed a test for the presence of orthophosphate. (*A. J. P.,* 1900, 125.)

Iron pyrophosphate is a good chalybeate, without disagreeable taste or astringency, and, from its solubility, readily administered in any form that may be desirable, whether that of pill, simple solution in water or syrup.

Dose, two to ten grains (0.13 to 0.65 Gm.).

Ferric Saccharate. *Saccharate de Fer, Saccharure d'Oxyde de Fer soluble,* Fr. *Eisenzucker, Lösliches Eisenoxyd,* G.—The *Ferrum Oxydatum Saccharatum* of the German Pharmacopœia is of importance as an antidote to arsenic. The process is as follows: Dilute 30 parts of solution of ferric chloride with 150 parts of water; add to this, little by little, a solution of 26 parts of crystallized sodium carbonate in 150 parts of water; wash the precipitate thoroughly with distilled water on a muslin strainer and press out the excess of water; add 5 parts of sugar and 15 parts of solution of sodium hydroxide, U. S. P. *VIII;* heat on a water bath until a clear solution is obtained. This is evaporated to dryness and enough sugar added to make 100 parts. (See *Arseni Trioxidum,* p. 197; *A. J. P.,* xlvi, 559.)

Ferric Salicylate. *Ferri Salicylas. Ferrum Salicylicum. Ferrisalicylat,* G.—Made by adding sodium salicylate to a concentrated solution of ferric chloride. The violet colored precipitate, when washed and dried forms a brown mass or powder insoluble in water. It is sometimes used as a tonic and antirheumatic in *doses* of from three to ten grains (0.2 to 0.65 Gm.).

Ferric Subcarbonate. *Ferri Subcarbonas. U. S.* 1870. *Subcarbonate of Iron. Sesquioxide of Iron. Red Oxide of Iron. Precipitated Carbonate of Iron. Aperitive Saffron of Mars.*—"Take of Sulphate of Iron *eight troyounces;* Carbonate of Sodium *nine troyounces;* Water *eight pints.* Dissolve the salts separately, each in four pints of the Water; then mix the solutions thoroughly, and set aside the mixture until the precipitate has subsided. Then pour off the supernatant liquid, wash the precipitate with water until the washings pass nearly tasteless, and dry it on bibulous paper without heat." *U. S.,* 1870.

When the solutions of sodium carbonate and ferrous sulphate are mixed together, a hydrated ferrous carbonate, of a pale-blue color, is thrown down, and sodium sulphate remains in solution. The precipitate during the washing and drying absorbs oxygen and loses nearly all its carbon dioxide, whereby it is converted almost entirely into ferric oxide. The direction to dry the precipitate without heat is important, as even a moderate elevation of temperature has been shown by the experiments of J. A. Rex to modify the resulting product unfavorably, diminishing its solubility in hydrochloric acid in proportion to the heat employed. (*A. J. P.,* May, 1862, p. 193.)

Ferric carbonate is a reddish-brown powder, of a disagreeable, slightly styptic taste, insoluble in water, and not readily dissolved by any acid except hydrochloric, with which it effervesces slightly. When of a bright red color it should be rejected, as this color shows that it has been injured by exposure to heat. After precipitation from its hydrochloric solution by ammonia or potassium hydroxide, either of which throws down ferric

oxide, the supernatant liquor should give no indications of containing any metal in solution by the test of hydrogen sulphide or potassium ferrocyanide. It is incompatible with acids and acidulous salts. In composition it is a hydrated ferric oxide containing a little ferrous carbonate. By exposure to a red heat, it absorbs oxygen and loses water and carbon dioxide, being converted into the *astringent saffron of Mars* of the French Codex.

Ferric carbonate is a rather feeble ferruginous tonic, nearly free from astringency. It has been especially commended in *neuralgia* in doses of a teaspoonful. *Dose*, five grains (0.32 Gm.).

Ferric Succinate. *Ferri Succinas. Succinate of Iron.*—The precipitate obtained by adding ferric chloride to a solution of a succinate is a basic salt $(C_4H_4O_4)_2Fe_2(OH)_2$. This is yellowish in color, becoming darker on standing. Ferric succinate has been introduced as a remedy for *jaundice* resulting from obstruction of the biliary duct; also as a chalybeate. *Dose*, five grains (0.32 Gm.).

Ferric Tannate. *Ferri Tannas.* $Fe_2(C_{14}H_7O_9)(OH_3)$.—This salt is prepared by dissolving 44 parts of precipitated ferric subcarbonate, moderately dried, in a boiling solution of 9 parts of pure tannic acid, evaporating the solution at the temperature of 80° C. (176° F.), in a porcelain vessel, until it becomes thick, pouring it out on a glass or porcelain plate, and drying it with a gentle heat. As thus obtained, ferric tannate is in flat pieces, of a crimson color, without taste, and insoluble in water. It is not a definite chemical compound. It acts as an astringent and tonic, and may be given in *chlorosis*. *Ink* is an aqueous solution of the ferric gallotannate, and probably possesses similar medicinal properties. It is a popular application for *ring-worm*. *Dose*, of ferric tannate, from eight to thirty grains (0.5–2.0 Gm.), in the course of the day.

Ferric Valerate. *Ferri Valerianas. U. S.* 1890. *Ferric Valerianate.* $Fe_2(C_5H_9O_2)_2(OH)_4$.—This salt was at one time official in the U. S. Pharmacopœia, but was dismissed from the 8th revision. It may be prepared by precipitating a dilute solution of ferric sulphate with a solution of sodium valerate and collecting and washing the precipitate. When so made it forms a dark brick red powder of somewhat varying composition with the characteristic odor of the valerates. It is insoluble in water, but readily soluble in alcohol. It is decomposed by boiling water with the liberation of valeric acid and the formation of ferric hydrate.

Ferric valerate has been used as a chalybeate, especially in *nervous exhaustion* associated with *anemia*. It has also been alleged to have almost specific properties in *diabetes insipidus*. The *dose* is from two to five grains (0.13 to 0.32 Gm.).

Ferrichthyol. *N. N. R.* 1917.—This compound occurs as an amorphous, dry powder of brownish-black color devoid of taste and containing 3.5 per cent. of iron combined with Ichthyol. It is employed as a hematinic in daily *doses* of thirty grains (2 Gm.).

Ferripyrine. *Ferropyrine. Antipyrina cum Ferro. N. N. R.* 1917.—This compound is prepared by adding 5 parts of crystallized ferric chloride, dissolved in 10 parts of 96 per cent. alcohol, to a solution of 5 parts of antipyrine in 10 parts of alcohol and 50 parts of ether. It is in the form of a fine, orange-red powder, containing about 64 parts of antipyrine, 24 parts of chlorine and 12 parts of iron. Soluble in 5 parts of water at 15° C. (59° F.), less soluble (9 parts) in boiling water, very soluble in alcohol but insoluble in ether. Alkalies or alkaline carbonates added to an aqueous solution precipitate ferric hydroxide. It combines the properties of both antipyrine and ferric chloride and is given in *anemic conditions* accompanied by *headache*. It has been used in *chlorosis* as a chalybeate; is strongly astringent, and affirmed to be often useful in chronic *diarrheas*. In strong solution (1 to 5) it is said to be a powerful non-irritant styptic. *Dose*, from three to six grains (0.2 to 0.4 Gm.).

Ferromangan. *N. N. R.* 1916. *Liquor Ferro Mangani Peptonati*, "Dieterich." This is a proprietary solution containing 0.6 per cent. of iron, 0.1 per cent. of manganese and 1.5 per cent. of peptone. It is a clear liquid of a dark brown color and a pleasant odor and taste. It is used in *anemia, chlorosis* and as a general tonic in a *dose* of from one to four fluidrachms (3.75 to 15 mils).

Ferro-sajodin. *N. N. R.* 1917. *Basic ferric iodo behenate* (approximately $(C_{21}H_{43}COO)_2(OH)Fe$) representing at least 5 per cent. of iron and 24 per cent. of iodine. It exhibits the action of iodide and of iron and is claimed to be more stable and palatable than ferrous iodide. *Dose*, eight to fifteen grains (0.5–1 Gm.).

Ferro-silicon.—This is a mixture made by heating quartz, steel turnings and coal in an electric furnace and is used in the arts for increasing the tensile strength of steel. Its interest to medicine depends upon the fact that in the presence of moisture it evolves hydrogen phosphide and also hydrogen arsenide and has caused several deaths upon ships in which it was being transported. As a result of an investigation under the direction of the British Government, it was recommended that *ferro-silicon* should be exposed to the air for at least a month before being sold, that its carriage on passenger vessels should be forbidden and that when carried on cargo boats it should, if possible, be carried on the deck, or at least in well ventilated places, cut off by air-tight bulkheads from the quarters of the crew.

Ferrosol.—A solution of iron saccharate and sodium chloride. It is not affected by acids or alkalies—other salts or changes in temperature. It contains 0.77 per cent. of iron, and is employed in *anemia* and *chlorosis*. *Dose*, one tablespoonful.

Ferrostyptine. $(CH_2)_6H_4.HCl.FeCl_3$.—This is stated to be a double salt of hexamethylene-tetramine hydrochloride and ferric chloride, which occurs as yellow crystals melting at 111° C. (231.8° F.) and easily dissolved by water. It is used in dental practice as a combined styptic and antiseptic without being corrosive. Its solution is coagulated by heat.

According to Merck and other authorities, this seems to be a combination of *formaldehyde* and ferric chloride and not *formin* and ferric chloride.

Ferrous Arsenate. *Ferri Arsenas. Br.* 1898. *Iron Arsenate.* [*Arsenate of Iron, Br.* 1885.] *Ferrum Arsenicum. Arséniate Ferreux*, Fr. Cod. *Arséniate de Fer*, Fr. *Arsensaures Eisen, Arsensaures Eisenoxydul*, G. *Arseniato ferroso-ferrico*, It. *Arseniato de hierro*, Sp.—"Ferrous arsenate, $Fe_3(AsO_4)_2.6H_2O$, with ferric arsenate and some iron oxide." *Br.*, 1898. "Ferrous Sulphate, 20¾ *ounces* (Imperial) or 415 grammes; Sodium Arsenate, dried, 26½ *ounces* (Imp.) or 530 grammes; Sodium Bicarbonate, 4½ *ounces* (Imp.) or 90 grammes; Distilled Water, boiling, *a sufficient quantity*. Dissolve the Sodium Arsenate in about *five pints* (Imp. meas.) or two litres, and the Ferrous Sulphate in about *six pints* (Imp. meas.) or two thousand four hundred cubic centimetres of the Distilled Water; mix the solutions; add the

Sodium Bicarbonate dissolved in a little cold Distilled Water; stir thoroughly; collect the resulting precipitate on a calico filter; wash until free from sulphates; squeeze the washed precipitate between folds of strong linen in a screw-press; dry it on porous bricks in a warm air-chamber, the temperature of which does not exceed 100° F. (37.8° C.)." *Br.*, 1898.

This arsenic salt was deleted from the British Pharmacopœia (1914) but it is still employed to some extent. The washed precipitate described in the process is *ferrous arsenate*. A portion, however, remains dissolved in the solution. This is precipitated by the sodium bicarbonate, which also neutralizes the sulphuric acid liberated during the reaction, and carbon dioxide is evolved.

Ferrous arsenate is white when first formed, but quickly turns green on exposure to the air during the process of washing and drying, and finally becomes a ferroso-ferric arsenate of the probable composition $3Fe(FeO)AsO_4.16H_2O$. It is an amorphous powder, without odor or taste, insoluble in water, but readily dissolved by hydrochloric acid. The British Pharmacopœia gave the following characters of the salt: "A tasteless amorphous powder of a greenish color, insoluble in *water*, but readily dissolved by *hydrochloric acid*. It affords the reactions characteristic of ferrous and ferric salts and of arsenates. Each gramme dissolved in an excess of *sulphuric acid* diluted with *water* should not cease to give a blue precipitate with *solution of potassium ferricyanide* until at least 6.7 cubic centimeters of the *volumetric solution of potassium bichromate* have been added, corresponding to nearly 12½ per cent. of hydrous, or 10 per cent. of anhydrous, ferrous arsenate. It should yield no characteristic reaction with the tests for sulphates." The quantitative test proves that there is a due proportion of ferrous oxide present; for the potassium dichromate oxidizes the ferrous oxide, and until this is wholly converted into ferric oxide a blue precipitate continues to be produced, ceasing, however, when the conversion is complete. Thomas S. Barrie (*C. D.*, 1900, 484) found that iron arsenate is of variable composition and that the percentage of ferrous oxide affords no reliable indication of the amount of arsenic anhydride in the dried iron arsenate. For Nicholl's method of estimating the quantity of arsenic in iron arsenate see *Y. B. P.*, 1903, 572, 577.

Ferrous arsenate is said to unite the virtues of the two metals which enter into its composition, but the quantity of iron in any permissible dose is so small as to be nearly or quite insignificant, and the activity of the medicine is in fact due to the arsenic alone. The complaints in which it has been found efficient are those in which arsenic in other forms has proved to be a valuable remedy, and, judging from our own observation, there is no one of them in which the common solution of potassium arsenite will not produce all the effects that can be obtained from the arsenical preparations, with which this ought undoubtedly to be ranked rather than with the chalybeates. Should the coexistence of an anemic state of the system with any disease requiring the use of arsenic indicate the joint use of iron, it would be unsafe to depend on ferrous arsenate alone. This remedy is useful in chronic affections of the skin, especially those of a scaly character, as *lepra*, *psoriasis*, and the advanced stage of *eczema* and *impetigo*. It is useful also in *lupus*, and, mixed with twelve times its weight of simple cerate, may be employed externally in *cancerous ulcers*, though much caution is requisite.

Dose, from one-tenth to one-eighth of a grain (0.006 to 0.008 Gm.).

Ferrous Bromide. *Ferri Bromidum. Ferrum Bromatum. Bromure ferreux, Bromure de fer*, Fr. *Eisenbromid, Ferrobromid*, G. $FeBr_2$.—This bromide is obtained by heating gently, in thirty parts of water, two parts of bromine and one of iron filings. When the liquid has become greenish, it is filtered and evaporated to dryness in an iron vessel, and the dry mass, again dissolved and evaporated to dryness, furnishes the bromide. *Ferrous bromide* is a yellowish, deliquescent salt, very soluble, and extremely styptic. For medicinal employment it should be in aqueous solution, protected by sugar. Dillwyn Parrish has proposed the following formula. Take of bromine two hundred grains; iron filings eighty-five grains; distilled water four and a half fluidounces; sugar three ounces. Make a solution in the manner directed for preparing solution of ferrous iodide. (See *Ferrous Iodide*.) For other formulas, see *P. J.*, 3d ser., v. 67, 162. This solution has been used with alleged success as an alterative tonic in *chorea*, and in various *scrofulous* and *erysipelatous affections*. (See 16th ed., *U. S. D.*) The *dose* of ferrous bromide is from one to three grains (0.065–0.2 Gm.), three times a day, gradually increased until its affects are manifested.

Ferrous Fluoride. FeF_2.—A white powder or crystal, slowly soluble in water and used like ammonium fluoride in hepatic hypertrophy. *Dose*, one-twentieth to one-half grain (0.003 to 0.032 Gm.).

Ferrous Iodide. *Ferri Iodidum. Iodide of Iron. Iodure de Fer*, Fr. *Ferrum Jodatum. Eisenjodür, Jodeisen*, G. FeI_2+3H_2O.

"Take of Fine Iron Wire *one ounce and a half* [avoirdupois]; Iodine *three ounces* [avoir.]; Distilled Water *fifteen fluid ounces*. Put the Iodine, Iron, and twelve [fluid] ounces of the Water into a flask, and, having heated the mixture gently for about ten minutes, raise the heat and boil until the froth becomes white. Pass the solution as quickly as possible through a wetted calico filter into a dish of polished iron, washing the filter with the remainder of the Water, and boil down until a drop of the solution taken out on the end of an iron wire solidifies on cooling. The liquid should now be poured out on a porcelain dish, and, as soon as it has solidified, should be broken into fragments, and enclosed in a well-stoppered bottle." *Br.* 1867.

The solid ferrous iodide in its unprotected state is omitted in the present editions of the U. S. and Br. Pharmacopœias. The former directs it in pills and syrup prepared immediately from the materials. The iodide is extremely liable to spontaneous change.

Ferrous iodide is a crystalline substance, exceedingly deliquescent, of a greenish-black color, and styptic, chalybeate taste. Its solution, by evaporation with as little contact of air as possible, affords transparent, green, tabular crystals. When heated moderately it fuses, and, on cooling, becomes an opaque crystalline mass, having an iron-gray color and metallic luster. At a higher temperature it emits violet colored vapors, and the iron is left in the state of sesquioxide. It is very soluble both in water and in alcohol. When recently prepared it is wholly soluble in water, forming a pale green solution; but, if made for some time, it almost unavoidably contains some

ferric oxide, from a partial decomposition, and will not entirely dissolve. Lecocq, of Saint-Quentin, has proposed to preserve it in a wide-mouthed, ground-stoppered bottle, covered with a layer of reduced iron, which cannot decompose it, and protects it from the action of the air. When the iodide is wanted, the iron is removed with a bone spatula or a little brush. The aqueous solution is very liable to spontaneous decomposition, becoming at last orange-red from the generation of free iodine, and depositing ferric oxide. According to Richard Phillips, Jr., the first step in this change is the formation of ferrous oxide and hydriodic acid, from the decomposition of water. As the ferrous oxide immediately begins to be converted into ferric oxide by absorbing oxygen from the air, and in this state is precipitated, the hydriodic acid is set free, and hence is explained the acidity of the solution from the first moment the ferric oxide is deposited. Afterwards, the hydriodic acid is decomposed by the air, and iodine liberated. When the solution is prevented from generating free iodine, by placing in it a coil of iron wire, according to the plan of Squire, the iron acts by combining with the iodine of nascent hydriodic acid, and not with nascent iodine. (*P. J.*, iv, 19.) The plan of Squire does not prevent the deposition of ferric oxide, and has, therefore, been superseded by the use of saccharine matter, which affords a better protection to the solution. (See *Syrupus Ferri Iodidi.*) Ferrous iodide is incompatible with alkalies and their carbonates, with lime water, and with all other substances by which ferrous sulphate is decomposed. When crystallized, it has the composition $FeI_2.3H_2O$. *Tasteless Iron Iodide* (so called) is prepared in the following manner: 126.3 grains of iodine are combined with iron in the usual way to obtain the solution of ferrous iodide; this is filtered and 63 grains of iodine are dissolved in it; a solution of 201 grains of citric acid is exactly saturated with potassium hydroxide and then added to the first solution. When the green-apple odor has been developed, the solution is evaporated, with gentle stirring, to dryness, when cauliflower-like masses of acicular crystals will be obtained. These are stable except in direct sunlight.

Ferrous iodide was first employed in medicine by Pierquin in 1824. It was first used in the United States in 1832 by Samuel Jackson. For uses of this preparation, see *Syrupus Ferri Iodidi*, p. 1101. The *dose* is a grain (0.065 Gm.), gradually increased to eight grains (0.5 Gm.).

This salt, on account of its deliquescent property and proneness to decomposition, should not be given in pill, unless protected from change by saccharine matter by coating or other means. (See *Pilulæ Ferri Iodidi*, p. 864.) The most convenient form of exhibition is that of a syrup, but it has no advantage over the official syrup. For a process for making *Glycerite of Ferrous Iodide*, see *U. S. D.*, 19th ed., p. 1491. *Iron Iodates* have been used to some extent as therapeutic agents in Dublin. For formulas, see *P. J.*, i, 624.

Ferrous Lactate. *N. F. IV* (*U. S. P.* 1890). *Ferri Lactas. Iron Lactate. Ferrum Lacticum*, P. G. *Lactas Ferrosus. Lactate de Fer*, Fr. *Milchsaures Eisenoxydul, Eisenlactat*, G.—"It contains not less than 97 per cent. of $Fe(C_3H_5O_3)_2 + 3H_2O$ (287.98). Preserve it in well-closed containers." *N. F.* In the process of the U. S. P., 1870, the lactic acid unites with the iron, forming *ferrous lactate*, a part of which crystallizes when the solution cools, and the remainder is obtained by evaporation and crystallization. It may be more cheaply prepared, on the large scale, by digesting the impure acid first obtained in Louradour's process, with iron filings, or by reaction between ferrous sulphate and the calcium lactate prepared as a step in obtaining lactic acid.

Ferrous lactate is in "greenish-white, crystalline powder, or in crystalline masses, having a slight, characteristic odor and a mild, sweet, and ferruginous taste. One gramme dissolves slowly but almost completely in 40 mils of water at 25° C. (77° F.), and in 12 mils of boiling water; freely soluble in solutions of the alkali citrates yielding a green-colored solution; almost insoluble in alcohol. When strongly heated, the salt froths, gives out dense, white, acrid fumes, then chars and finally leaves a brownish-red residue. An aqueous solution of the salt is greenish-yellow, slightly acid to litmus, and separate portions give a deep blue precipitate with potassium ferricyanide T.S., and a light blue precipitate with potassium ferrocyanide T.S. Separate portions of an aqueous solution of the salt (1 in 20), acidulated with nitric acid, do not give more than a slight opalescence with barium chloride T.S. (*sulphate*), or with silver nitrate T.S. (*chloride*). Mix 25 mils of an aqueous solution of the salt (1 in 50) with 5 mils of diluted sulphuric acid, boil the mixture for a few minutes, then precipitate the iron by an excess of potassium or sodium hydroxide T.S., and filter; the filtrate, mixed with a few drops of alkaline cupric tartrate V.S. and heated to boiling, does not give a red precipitate (*sugar*). A portion of the salt triturated with sulphuric acid does not develop an offensive odor (*butyric acid*), nor is any gas evolved (*carbonate*); this mixture, after standing for five minutes, does not assume a brown color (*readily carbonizable impurities*). Ignite 1 Gm. of the salt; the residue is not alkaline to moistened litmus paper, and does not contain anything soluble in water." *N. F.*

Assay.—"Dissolve in a flask about 0.5 Gm. of Ferrous Lactate, accurately weighed, in 15 mils of solution of hydrogen dioxide and evaporate this solution on a water bath to 5 mils. Add 5 mils of sulphuric acid, boil the mixture for two minutes, cool to 40° C. (104° F.) and add 25 mils of distilled water and 0.5 Gm. of potassium iodide. Allow this mixture to stand for one-half hour at 40° C. (104° F.), cool, and then titrate the liberated iodine with tenth-normal sodium thiosulphate V.S., using starch T.S. as indicator. It shows not less than 97 per cent. of $Fe(C_3H_5O_3)_2 + 3H_2O$. Each mil of tenth-normal sodium thiosulphate V.S. corresponds to 0.0288 Gm. of $Fe(C_3H_5O_3)_2 + 3H_2O$. Each gramme of Ferrous Lactate requires not less than 33.7 mils of tenth-normal sodium thiosulphate V.S." *N. F.*

Ferrous lactate has the general medicinal properties of the ferruginous preparations, and has been especially used in *chlorosis*. As much as twelve or even twenty grains (0.78–1.3 Gm.) may be given in the course of a day. It may be administered in lozenge, pill, or syrup. The *lozenge* may be made of one grain (0.065 Gm.) of the lactate to twelve grains (0.78 Gm.) of sugar; the *pill*, of one grain (0.065 Gm.) of the salt, with an equal weight of some inert powder free from astringent matter, and sufficient honey.

The following is the formula for a *syrup* proposed by Cap: Take of ferrous lactate a drachm; white sugar twelve ounces and a half; boiling

distilled water six fluidounces and a half. Rub the salt to powder with half an ounce of the sugar, and dissolve the mixture quickly in the boiling water. Pour the solution into a flask placed on a sand bath, and add to it the rest of the sugar in small pieces. When the sugar is dissolved, filter the syrup, and, as soon as it is cold, transfer it to bottles, which must be well stoppered. This syrup has a very light amber color, and contains about four grains of the salt to the fluidounce. The *dose* is from two to four fluidrachms (7.5–15 mils). Bread, called *chalybeate bread*, containing ferrous lactate in the proportion of about a grain (0.065 Gm.) to the ounce (31 Gm.), has been used with advantage in cases of chlorotic patients in Paris. An elixir is official in the N. F. (see Part III).

Ferrous Malate. *Ferri Malas Crudus.*—This substance in an impure form has been long used and has been official in several European pharmacopœias under the name of *Extractum Ferri Pomatum (Ferrated Extract of Apples)*. It is made by digesting the juice of sour apples with iron filings until the reaction ceases, filtering and evaporating. Of a dark green color, containing varying amounts of iron. *Dose*, five to fifteen grains (0.32–1 Gm.).

Ferrous Oxalate. *Ferri Oxalas. U. S.* 1880. *Oxalate of Iron.* $FeC_2O_4H_2O$. *Ferrum Oxalicum. Oxalas Ferrosus. Oxalate de Fer*, Fr. *Oxalsaures Eisenoxydul*, G.—This salt was official in 1870 and 1880 and was properly dropped in 1890, as it is a very feeble, inefficient chalybeate. *Dose*, from two to three grains (0.13–0.20 Gm.).

Ferrozone.—A saccharated iron and vanadium combination used in tablet form, each containing three grains of the compound. It should not be confused with *Ferozon* which is a proprietary disinfecting agent.

Fersan is stated to be a preparation of the iron compound contained in the erythrocytes of the fresh blood of cattle, which is chemically a *ferruginous paranucleo-proteid*. It is soluble in water; the solution does not coagulate when boiled, and is not completely absorbed until it reaches the intestine. According to experiments made upon the lower animals, it remarkably increases the hemoglobin of the blood and it has been used by various clinicians in the treatment of *anemias*. *Dose*, a small teaspoonful after meals.

Fetron.—An ointment vehicle recommended by Liebrich. It is a mixture of 3 parts stearic acid and 97 parts of petrolatum.

Fig. *Ficus. N. F. IV (U. S. P. VIII). Caricæ. Ficus Passa, Fici, Fructus Caricæ. Figue*, Fr. Cod. *Feigen*, G. *Fichi*, It. *Higos*, Sp.—"The partially dried fruit of *Ficus Carica* Linné (Fam. *Moraceæ*)." *N. F.* "The dried fleshy receptacles of Ficus Carica, *Linn.*" *Br.*, 1898.

The genus *Ficus* yields a number of economic products. Many species possess a milky juice containing caoutchouc, as *F. elastica* Roxb., of Sumatra, etc. Some of the juices are employed externally as well as internally, as that of *F. indica* L. Some possess anthelmintic properties, as *F. anthelmintica* Mart. Some yield gum lac or shellac as a result of the puncture of an insect, as *F. religiosa* L., *F. laccifera* Roxb.; and some are esteemed for their fruits, as *F. Carica* L., *F. religiosa* L., etc.

Ficus Carica, or fig tree, though often not more than twelve feet high, sometimes rises in warm climates twenty-five or even thirty feet. Its trunk, which seldom exceeds seven inches in diameter, is divided into numerous spreading branches, covered with a brown or ash-colored bark. Its large, palmate leaves, usually divided into five obtuse lobes, are deep green and shining above, pale green and downy beneath, and stand alternately on strong, round foot-stalks. The flowers are situated within a common receptacle, placed upon a short peduncle in the axils of the upper leaves. This receptacle, the walls of which become thick and fleshy, constitutes what is commonly called the fruit; though this term is, strictly speaking, applicable to the small seed-like bodies found in great numbers on the internal surface of the receptacle, to which they are attached by fleshy pedicles. Cultivation has produced in the fig, as in the apple and peach, a great diversity in shape, size, color, and taste. It is usually, however, turbinate, or top-shaped, umbilicate at the large extremity, of the size of a small pear, of a whitish, yellowish, or reddish color, and of a mild, mucilaginous, saccharine taste. The dried figs can be partially restored to their original shape by soaking. The fig tree is supposed to have come originally from the Levant. It was introduced at a very early period into various parts of the south of Europe, and is now very common throughout the whole basin of the Mediterranean, particularly in Italy and France. Large numbers of Syrian fig trees were planted in the Pomona Valley, California, in 1890, and California figs are now commercial articles. To hasten the ripening of the fruit, it is customary to puncture it with a sharp pointed instrument covered with olive oil. *Caprification* consists in attaching branches of the wild fig tree to the cultivated plant. The fruit of the former contains great numbers of the eggs of insects of the genus *Cynips*, the larvæ of which, as soon as they are hatched, spread themselves over the cultivated fruit, and, by conveying the pollen or the male organs over which they pass to the female florets, hasten the impregnation of the latter, and cause to quickly come to perfection the fig which might otherwise ripen very slowly, or wither and drop off before maturity. In California the great difficulty in cultivating figs was found to be to get a Cynips which would flourish in the climate. According to Landerer, the unripe fig contains an irritant juice, which inflames the skin, and may even disorganize it. (See *A. J. P.*, xxxiii, 215.) The figs, when perfectly ripe, are dried by the heat of the sun, or in ovens. Those imported into this country come chiefly from Smyrna, packed in drums or boxes. They are more or less compressed, and are usually covered in cold weather with a whitish saccharine efflorescence, which softens in the middle of summer and renders them moist. The best are yellowish or brownish, somewhat translucent when held to the light, and filled with a sweet viscid pulp, in which are lodged numerous small yellow achenes. They are much more saccharine than is the fresh fruit. Their chief constituents are grape sugar, and gum or mucilage. An average of several analyses of dried figs as quoted by Königs (*Nahrungs und Genussmittel*, 3te Aufl., Bd. i, 781) gives —water, 31.20; nitrogenous material, 4.01; sugar, 49.79; ash, 2.86. Reckoned on the weight of absolutely dry material, the nitrogenous matter amounted to 5.75 per cent. and the sugar to 72.26 per cent. They are officially described as "usually compressed, of irregular rounded shapes, from 2.5 to 5 cm. in diameter, fleshy, light brown to yellow, frequently with an efflorescence of sugar; summit with a small, scaly orifice; base with a

scar or short stalk; internally hollow, with numerous small, brownish-yellow, glossy, and hard akenes. Odor distinctive, fruity; taste sweet, pleasant." *N. F.*

Figs are nutritious, laxative, and demulcent. In the fresh state they are considered, in the countries where they grow, a wholesome and agreeable ailment, and have been employed from time immemorial. They are prone, however, when eaten freely, to produce flatulence, pain in the bowels, and diarrhea. The latex of the fig has been used as an anthelmintic against intestinal parasites. Their chief medicinal use is as a laxative article of diet in constipation. They occasionally enter into demulcent decoctions, and, roasted or boiled, and split open, are sometimes applied as a cataplasm to inflamed gums.

Filicon.—A tænicide consisting of an extract of the rhizome of *Aspidium Spinulosum* (Filices) combined with an aromatized castor oil. The *dose* is stated to be one tablespoonful.

Filmogen. *Collosin. Liquor Adhesivus.*—A vehicle for the application of medicinal substances to the skin. It is said to be a solution of pyroxylin in acetone containing a trace of fixed oil. It forms an elastic coating impervious to water.

Flindersia. *Flindersia maculosa* (Lindl.) F. Muell. *Leopard Tree.*—This is a tree of New South Wales, belonging to the *Meliaceæ*. During the summer it yields large masses of a clear amber-colored gum, which has a pleasant taste and is eaten by the aborigines; it is used as a remedy for *diarrhea*. *Leopard tree gum* occurs in pieces as large as pigeons' eggs; dissolves rapidly in cold water, and has been found by J. H. Maiden to contain eighty per cent. of arabin but no metarabin. (*P. J.*, vol. xxi, 1890.)

Flour. *Farina tritici. Wheat flour.*—According to the official standards of the U. S. Department of Agriculture (see Circular 19, Bureau of Chemistry), "Flour is the clean, sound product made by bolting wheat meal and contains not more than 13.5 per cent. of moisture, not less than 1.25 per cent. of nitrogen, not more than 1 per cent. of ash, and not more than 0.5 per cent. of fiber." The same circular states that "Graham flour is unbolted wheat meal" and "Gluten flour is the clean, sound product made from flour by the removal of starch and contains not less than 5.6 per cent. of nitrogen and not more than 10 per cent. of moisture."

The farina or flour produced by grinding other grains is designated by the appropriate prefix in each case, as maize or corn meal, rice flour, oatmeal, rye flour, buckwheat flour, etc.

The highest grade of wheat flour is known as "patent"; other grades are known as "bakers' flour" or "low grade flour." A barrel of flour weighs 196 pounds and requires about 258 pounds of wheat for its manufacture.

There are many trade designations for grades of flour, such as "family," "blended," "gluten," etc., some of which (especially the last) are frequently misleading, if not actually illegal.

The nutritive value of flour depends upon a number of factors and the average composition of good flour is as follows: Moisture, 12.5 per cent.; proteids (N. x 5.70), 9.6 per cent.; dry gluten (including proteids), 10 per cent.; fat, 1.0 per cent.; ash, 0.5 per cent.; starch, 75 per cent.; crude fiber, 0.2 per cent.

The character of a wheat flour is measured largely by the quantity of gluten which it may contain. The separation of the gluten is accomplished by making a sticky, doughy mass with the flour by adding a small quantity of water, after which it may be washed with water accompanied with constant kneading until the gluten alone remains, which can be determined by the washings being no longer milky in appearance. The excess of moisture may then be removed from the gluten by squeezing and rolling it, after which it may be weighed as moist gluten (varying in amount from 25 to 35 per cent.), or dried to constant weight at 100° C. (212° F.) and calculated as dry gluten (which runs from 9 per cent. to 12 per cent. in ordinary flours).

As flour is usually valued in proportion to its whiteness it has been extensively bleached in the past by the use of ozone or of oxides of nitrogen. The question of the effect of bleaching upon the digestibility or harmlessness of bleached flour has never been satisfactorily settled, but owing to the numerous State laws prohibiting such treatment, it is fast disappearing from the American market.

Adulteration of flour, which was formerly very common, has not been practised to any extent for years in the United States. Occasionally samples are seen in which foreign seeds, smut, etc., have been ground with the grain, owing to insufficient cleaning of the grain preparatory to grinding. Such gross adulterants as terra alba or soapstone, which were formerly reported, are unheard of at the present time and even the practice of the addition of copper sulphate or alum in small proportions to flour, which was formerly made by bakers who were thus enabled to bake white bread from inferior grades of flour, seems to have been altogether abandoned. (For methods of testing flour see any modern work on food analysis.)

The proteids of wheat, usually included in the term "gluten," are several in number and, according to Osborne and Vorhees (*Am. Chem. J.*, xv, 392; xvi, 524) are as follows: Globulin, 0.6 to 0.7 per cent.; albumin, 0.3 to 0.4 per cent.; proteose, 0.3 per cent.; *gliadin*, 4.25 per cent.; *glutenin*, 4 to 4.5 per cent.

The last two are the only ones present in gluten as determined by the washing out process previously described, as the first three are soluble in water.

"*Gluten*" is a term popularly known in connection with the names "gluten flour" and "gluten bread," used and recommended especially in connection with the dietary of diabetics when starchy foods are to be administered in small amounts or altogether prohibited. These preparations are legion and in many instances are sold under claims which are as false and misleading as they are cruel in the hope which they hold out to the sufferer from the disease. For a complete discussion of these products with analyses of hundreds of commercial samples, see *Bull. Conn. Ag. Exp. Sta.*, 1913, on Diabetic Foods.

Pure Gluten prepared by the mechanical method described above for its estimation is sometimes used in combination with medicating agents, some of which, like certain salts of the metals, form insoluble and tasteless compounds with it.

It is scarcely necessary to state that *bread* is formed by making flour into a paste with water, with the addition of yeast, setting it aside to ferment, and then exposing it to the heat of an oven. The fermentation excited by the yeast is accompanied by the extrication of carbon dioxide, which,

being retained by the tenacity of the gluten, forms innumerable little cells or bubbles throughout the mass, and thus renders the bread light.

Wheat flour in its unaltered state is seldom used in medicine. It is sometimes sprinkled on the skin in *erysipelatous* inflammation, and in various itching or burning *eruptions*, particularly the *nettle-rash;* though rye flour is generally preferred for this purpose.

Bread is more employed; an infusion of toasted bread in water is a nutritive drink well adapted to febrile complaints. Boiled with milk, bread forms a good emollient poultice, which may be improved by the addition of a little perfectly fresh lard. Slices of it steeped in lead water, and the crumb mixed with the fluid and confined within gauze, afford a convenient mode of applying this preparation to local inflammations. The crumb (*mica panis*) is, moreover, frequently used to give bulk to minute doses of very active medicines administered in the form of pill. It should be recollected that it always contains common salt, which is incompatible with various substances.

Bran is sometimes used in decoction, as demulcent in catarrhal affections and complaints of the bowels. When taken in substance, it is laxative, and may be used with advantage to prevent *costiveness*. Bran bread, made from the unsifted flour, is an excellent laxative article of diet in some dyspeptic cases. The action of the bran is probably mechanical, consisting in the irritation produced upon the mucous membrane of the bowels by its coarse particles. Bran also forms an excellent demulcent bath.

Fluorescein. *N. N. R.* 1917. *Fluoresceinum. Resorcinolphthalein. Dioxyfluoran.* $O : (C_6H_3OH)_2 : C.C_6H_4.COO$.—This may be prepared by heating phthalic anhydride (5 parts) with resorcinol (7 parts) to 200° C. (392° F.). The mass is treated with water and the residue dissolved in solution of potassium hydroxide, after filtration the *fluorescein* is precipitated by an acid. It is a yellowish-red or dark red powder, soluble in alcohol with yellow-red color and green fluorescence. The sodium salt *uranin* (*sodio-fluorescein*), $C_{20}H_{10}O_5Na_2$, and the potassium salt (*potassio-fluorescein*) are marketed. They differ in that the first is a brownish-yellow and the second a yellowish-red powder; both of them yield aqueous solutions which are red by transmitted light and exhibit an intense yellow-green fluorescence.

An aqueous solution containing ten grains (0.65 Gm.) of fluorescein with fifteen grains (1 Gm.) of sodium bicarbonate to the ounce (30 mils) is used as a diagnostic agent in various ophthalmic conditions. In lesions of the cornea two per cent. solution is dropped into the eye, and those portions which are deprived of the epithelium will show a green discoloration, while the healthy parts of the cornea remain unaffected. The eye should be cocainized before applying the fluorescein. According to Hamburger (*All. M. C. Z.*, 1909, p. 368), if thirty to forty-five grains (2–3 Gm.) be given by the mouth, while the body becomes yellow as in jaundice, in the healthy eye there is no change of color. When there is intra-ocular disease, however, the aqueous humor assumes a bright green color. In diseases of the conjunctiva, the eye reacts as though healthy.

Fluorescein sodium has been recommended by Strauss (*B. K. W.*, 1913, p. 2226) as a test for renal function. He administers fourteen grains (1 Gm.) on an empty stomach. In healthy individuals the urine shows fluorescence within ten to twenty minutes and continues for thirty-five to forty hours; the continuation of the dye in the urine for a longer time in indicative of kidney disease.

It is also used as a test for death. It is stated that if 15 grains be injected into the human body the whites of the eyes will become a greenish color provided life remains, within one hour. After death there is no coloration. It is also used for the purpose of tracing the course of underground streams. One part in two billion can be recognized in water.

Owing to the close similarity in name between fluorescein and its derivative *fluorescin* much confusion has arisen, leading to the general belief that the two substances are identical. Fluorescin, however, is a reduction product of fluorescein, made by acting on the latter with sodium hydrate and zinc dust. It occurs as a yellow powder readily oxidizable to fluorescein. It is used like fluorescein as a diagnostic agent in ophthalmic practice. It has also been recommended by Fleig (*Press. Med. d'Egypte*, 1910, p. 281) as a test for the presence of blood in the urine. The test depends upon the fact that the non-fluorescent fluorescin-sodium shows an intense fluorescence in the presence of blood when treated with hydrogen peroxide.

Fluorides.—*Hydrofluoric acid* is a pungent, fuming, acid gas, very corrosive, attacking glass and porcelain and etching its surface. It is very soluble in water, the specific gravity of the solution rising to 1.25. The concentrated aqueous acid becomes weaker on boiling until, when boiling at 120° C. (248° F.), it attains a constant composition of from 36 to 38 per cent. of the anhydrous acid. Concentrated hydrofluoric acid is a powerful corrosive, having the peculiar property of hardening the skin or tissue with which it comes in contact and continuing its action underneath the hardened tissue, with an extraordinary amount and persistency of pain. For case, see *B. M. S. J.*, Jan., 1882; also *B. M. J.*, 1880, i. According to L. A. Waddell (*Indian Med. Gaz.*, 1883), the dilute 8 per cent. acid applied to the skin causes stinging sensation and pallor, followed by redness and desquamation. From 15 to 20 per cent. acid destroys the epithelium and produces severe burning and aching pain. The vapor of the acid is exceedingly irritant to the lungs, causing, even when very dilute, spasm of the glottis and other symptoms of irritation. According to Husemann, death has been produced by it. Nevertheless, L. Olivieri and F. Mergoni affirmed that in solution of 33 per cent. the daily inhalation of hydrofluoric acid from half an hour to an hour is a valuable adjuvant to quinine in chronic *malaria*.

Alkaline Fluorides.—According to the studies of Tappeiner (*A. E. P. P.*, xxvii), the fluorides are powerfully depressant to the blood pressure through an action upon the vasomotor centers and also produce lowering of the bodily temperature. Death occurred, amid symptoms of collapse, from respiratory failure. Waddell found in his studies a marked decrease in the number of red blood cells which he believed, but does not prove to be, the result of a direct action upon the spleen. Schwyzer (*Biochem. Zeit.*, 1914, lx, p. 932) finds that the continued intake of sodium fluoride in doses of 1 to 2 milligrammes per kilo causes increased coagulability of the blood and irritation of the bone marrow with a loss of chlorine and calcium. He believes that these symptoms are due to the affinity

of hydrofluoric acid for calcium with which it forms insoluble salts.

Sodium fluoride has been used by various authors in the treatment of *goiter, rheumatism, epilepsy,* and *phthisis.* Its value, however, is extremely questionable and it is certainly toxic. The *dose* which has been recommended is from one-sixth to one grain (0.01–0.065 Gm.).

The fluorides are active antibacterials. (*M. R.,* 1908.)

Ammonium Fluoride.—Under the name of *bifluoride of ammonium* a solution containing 20 per cent. of hydrogen-ammonium fluoride, and 10 per cent. of hydrofluoric acid has been used by Dr. Joseph Head in the treatment of *pyorrhea alveolaris.* This solution is actively germicidal, having a phenol coefficient of 5.82. According to Head it is not caustic to wet mucous membranes, although on dry it produces a burn like that of carbolic acid. It is applied by flowing it into the pus pockets; it should never be injected into the tissues and care should be taken to prevent it coming in contact with the mucous membranes in other parts of the mouth. Dr. Head claims for this solution that it aids in loosening the tartar as well as in destroying infective micro-organisms and that it is not injurious to the tooth.

A technical form of ammonium fluoride is used in cleaning granite and stonework and sometimes as an ingredient in roach preventives.

Silver Fluoride. AgF. *Tachiol.*—This salt, which occurs in deliquescent crystals acquiring a yellow color in the air and finally being converted into a black crystalline mass, making stable solutions in water, has been brought forward by Durante and Perez as a valuable antiseptic for surgical use. It is a feeble coagulant of albumin, and great penetrating power is claimed for its solution. It is employed in the proportion of one to a thousand; the one per cent. solution is said not to be distinctly irritant to the skin. It blackens linen and other organic substances. Zappuli has destroyed *malignant pustules* by injecting into them silver fluoride solution.

Organic Fluorides.—A number of organic fluoric compounds have been proposed and put upon the market. According to Tischer and Beddies (*Aerzt. Rund.,* 1898), they are antispasmodic, bactericidal, and are primarily stimulant, secondarily depressant to the motor nerve. *Antitussin* is a five per cent. ointment of *di-fluordiphenyl*, $\begin{matrix} C_6H_4\text{–}F \\ | \\ C_6H_4\text{–}F \end{matrix}$, which has been lauded as a local application to the throat and chest in the treatment of *whooping cough,* one to one and a half drachms (3.9–5.8 Gm.) being applied at a time. *Di-fluordiphenyl* itself, a white aromatic powder, insoluble in water, freely soluble in alcohol, ether, and chloroform, was originally recommended by J. Thimm as a local remedy in the treatment of *syphilitic ulcers* or *wounds,* applied either as a ten per cent. dusting powder or a ten per cent. ointment. (*Derm. Zeit.,* iv, No. 15.)

Fluorphenetol has been introduced, in the form of a five per cent. ointment, under the name of *fluor-rheumin,* as a local application in *sciatica* and other acute affections.

Fluor-pseudocumol.—Under the name of *neodermin,* the five per cent. ointment of this substance has been put upon the market. It is alleged to have local properties similar to those of difluordiphenyl and especially to give relief to painful ulcers.

Fluoroform. CHF_3.—This gas was originally suggested by Stepp (*M. M. W.,* 1899, No. 28) in *tuberculosis.* Afterwards studied by Binz (*Verhandl. des Kongresses inn. Med.,* Berlin, 1891, vol. ii, Sec. iv), who found it to have properties somewhat similar to those of chloroform. Under the name of *fluoroformol,* a two and eight-tenths per cent. aqueous solution has been introduced. It is almost odorless and tasteless, and is said to be non-toxic and non-irritant, so that four ounces a day may be given without the production of symptoms. Usually one fluidrachm (3.75 mils) has been administered in water four or five times a day. According to Stepp, it produces, when given internally, remarkable effects in *tuberculosis.* Gorl (*M. M. W.,* 1899, No. 50) found it, however, to be of very little value.

Fomitin.—This preparation is a fluidextract of the parasitic tree fungoids known as *Fomes Cinnamomens* and *Fomes Igniarius.* It is a brownish-red, transparent liquid, possessing a moldy, repulsive odor and an extremely bitter taste. It is used in one to two teaspoonful *doses* in the treatment of *dysmenorrhea* and *menorrhagia.*

Forgenin. *Tetra-methyl-ammonium Formite.* $HCOO.N(CH_3)_4$.—A neutral-hygroscopic crystalline salt which on the addition of sulphuric acid evolves carbon monoxide. Large doses act like curarin but small doses are stimulating and appetizing.

Formagen.—This preparation is a dental cement consisting of two parts—one a liquid containing creosote, phenol, olive oil, and alcoholic formalin—the other is a powder consisting of aluminum silicate, magnesium and zinc as carbonates, and lime free and partly as carbonate. The powder sets with water after the manner of a cement.

Formalbumin.—A condensation product of formaldehyde and casein is a yellowish, odorless powder, soluble in diluted acids. It is used as an external antiseptic.

Formaloin. $CH_2 : C_{17}H_{16}O_7$.—A condensation product of formaldehyde and aloin in the form of a yellow, amorphous, tasteless powder, soluble in alkalies, difficultly so in alcohol and totally insoluble in water. It possesses the therapeutic properties of aloin with the additional antiseptic action of the formalin.

Forman. *Chlormethylmenthyl-ether,* $C_{10}H_{19}$—$O.CH_2Cl$, a product formed by the action of formaldehyde upon menthol in the presence of hydrochloric acid. It is a colorless oil, emitting dense fumes and boiling at 160° to 162° C. (320°–323.6° F.) under a pressure of 16 mm. In the presence of water or merely moist air the ether splits up into its original constituents, formaldehyde, menthol, and hydrochloric acid, according to the equation:

$$C_{10}H_{19}—O.CH_2Cl + H_2O = CH_2O + C_{10}H_{19}OH + HCl$$

therefore it is possible that when it is locally applied *forman* may act as nascent menthol and formaldehyde. It has been used in the treatment of various conditions of the nasal and even bronchial mucous membrane. It is applied either by inserting tufts of cotton impregnated with the compound loosely into the nostrils so that air may be aspirated through the nose, or by having the patient breathe the vapor arising from four to six drops

of forman in warm water through a closed inhaler with nasal tips.

Formanilide. *Formanilidum. Phenylformamide.* $C_6H_5NH.COH$.—This substance, which is made by heating aniline with formic acid, or by distilling equal molecules of aniline and oxalic acid, occurs in long, colorless to yellowish, prismatic needles, melting at 46° C. (114.8° F.), soluble in water, alcohol, glycerin, and oil. It has been used as an antipyretic and analgesic, but is said frequently to produce cyanosis and cardiac depression. Externally, mixed with equal parts of chalk, it has been used in diseases especially of the nasal passages by Preisach, and in 2 per cent. solution by Meisel in *genito-urinary inflammations*. It is said to produce burning pain, lasting about a quarter of an hour, and followed by a mild analgesia continuing from eight to twelve hours. *Dose*, two to five grains (0.13–0.32 Gm.).

Formasal.—Under this name has been introduced a condensation product of formaldehyde and salicylic acid which is claimed to be a *methylene disalicylic acid*. Several salts of this acid are upon the market, including those of caffeine (*cafformasal*), bismuth (*bisformasal*) and sodium (*sodiformasal*).

It is claimed for *formasal* that it is decomposed in the system, liberating both salicylic acid and formaldehyde. Its sodium salt is used as an antirheumatic and anti-neuralgic in doses of five to fifteen grains (0.32–1.0 Gm.). The bismuth salt is used as an intestinal antiseptic. The dose is ten to twenty grains (0.65–1.3 Gm.). The caffeine salt is very soluble in water, and has been suggested as a means for the hypodermic administration of caffeine. It is used as a diuretic and in *rheumatism* in *doses* of five to fifteen grains (0.32–1.0 Gm.).

Formic Acid. *Acidum Formicum. N. F. IV. Ameisensaure*, G.—"An aqueous solution containing not less than 24 per cent. nor more than 26 per cent. of HCOOH (46.02)." *N. F.* This acid, although deriving its name from having first been obtained from the ant (*Formica rufa*), is remarkable for the number of sources of its production. It can be made from some species of caterpillars, from the blood, urine, fluid of the spleen, and perspiration of human beings; it is found in the products of decomposition of a number of vegetable substances, in common oil of turpentine, as a decomposition product of tartaric acid contained in various fruits and in the juice of the stinging nettle. It may be produced artificially in many ways: by the oxidation of methyl alcohol, the saponification of chloroform, and the hydrolysis of hydrocyanic acid; the following process yields good results: 50 Gm. of glycerine and 50 Gm. of crystallized oxalic acid are placed in a suitable retort attached to a condenser and the mixture carefully heated until the temperature rises to 105° C. (221° F.), it is then allowed to cool to about 50° C. (122° F.) and 50 Gm. more of oxalic acid are added and the mixture heated very slowly to 115° C. (239° F.). The condensed liquid may be drawn off and another addition of oxalic acid made and the distillation continued almost indefinitely. When oxalic acid and glycerin are distilled together, chemical reaction occurs, glyceryl formate being produced; this is saponified by the water which is separated, formic acid distils over and glycerin is reproduced. It is described by the N. F. as "a clear, colorless liquid, having a strongly acid reaction and a characteristic pungent odor. Specific gravity: about 1.058 at 25° C. (77° F.). It is miscible with water or alcohol. Formic Acid is volatilized on heating, and on evaporating 20 mils to dryness on a water bath, not more than 0.002 Gm. of residue remains. A white precipitate of mercurous chloride is formed on warming Formic Acid with mercuric chloride T.S. When Formic Acid is diluted with five times its volume of distilled water, separate portions yield no precipitate or turbidity on the addition of silver nitrate T.S. after adding nitric acid (*chloride*); or of barium chloride T.S. (*sulphate*); or of calcium chloride T.S. after supersaturating with ammonia water (*oxalic acid*). Formic Acid, when supersaturated with solution of sodium hydroxide, develops no pungent or empyreumatic odor (*acrolein, allyl formate*). Heat 1 mil of Formic Acid on a water bath with 1.5 Gm. of yellow mercuric oxide and 10 mils of distilled water for ten minutes and filter the liquid; the filtrate does not show an acid reaction (*acetic acid*). Add 1 drop of tenth-normal iodine V.S. to 10 mils of Formic Acid; the iodine color is not destroyed (*sulphurous acid*). Formic Acid does not respond to the Test for heavy metals (see *U. S. P.*, Test No. 3, Part III)." *N. F.*

Assay.—"Pour about 5 mils of Formic Acid into a weighing-bottle, stopper, weigh accurately, dilute with about 50 mils of distilled water and titrate with normal potassium hydroxide V.S., using phenolphthalein T.S. as indicator. It shows not less than 24 per cent. nor more than 26 per cent. of HCOOH. Each mil of normal potassium hydroxide V.S. used corresponds to 0.04602 Gm. of HCOOH. Each gramme of Formic Acid corresponds to not less than 5.2 mils nor more than 5.65 mils of normal potassium hydroxide T.S." *N. F.*

Spiritus Formicarum, P. G., *Spirit of Ants, Ameisengeist*, G., is made as follows: "Alcohol (90–91 per cent. vol.), *seventy parts;* Water, *twenty-six parts;* Formic Acid (24–25 per cent.), *four parts*. Mix them. A clear, colorless liquid of an acid reaction. Specific gravity from 0.894 to 0.898." *P. G.*

When formic acid is mixed with solution of lead subacetate, it throws down a white, crystalline precipitate. "When the Acid is mixed with five parts of water and saturated by yellow mercuric oxide, a clear solution results, which, on heating, evolves a gas and deposits a white precipitate, which rapidly turns gray and afterwards changes into shining, metallic, coalescing globules. When neutralized with solution of potassium hydroxide, it should have no pungent or empyreumatic odor. 10 Gm. of the Acid should neutralize 56 to 58 Cc. of volumetric solution of soda, corresponding to 24 to 25 per cent. of soluble Formic Acid. When diluted with five parts of water, the Acid should not be affected by silver nitrate, nor, after neutralization with ammonia, by chloride of calcium nor by hydrosulphuric acid. On diluting 1.5 Gm. of the Acid with 5 Gm. of water and heating on the water bath as long as gas is given off with 1 Gm. of yellow oxide of mercury, it should yield a neutral filtrate." *P. G.*

Formic acid was introduced into the N. F. chiefly for the preparation of the alkaline formates in the simple and compound elixirs of the formates (see Part III), but, diluted with an equal measure of water, is sometimes used to excite the circulation in paralyzed limbs. It is rarely used, internally. An aqueous solution of formic acid, usually the crude or unrefined product containing from 15 to 20

per cent. of absolute formic acid is used in the textile industries under the name of *scroop liquid*. Fabrics of certain composition when rinsed in this solution acquire what is known as scroop, which is the crisp crunching sound characteristic of silk when squeezed or twisted. Solutions of lactic acid and of tartaric acid are also employed for the same purpose.

The old folk lore that the sting of bees had a curative effect on *rheumatism*, led, at one time, to the therapeutic use of formic acid in this condition. The results, however, were not sufficiently satisfactory to win for the remedy a permanent place in therapeutics and the mode of the treatment became obsolete. More recently, however, the neutral salts of formic acid, notably *sodium formate*, have been employed in a large number of morbid conditions with some evidence of benefit. Fleig (*A. G. M.*, 1905) could obtain no physiological basis for the use of the formates except as stimulants to the gastric mucous membrane and to the kidney. As a diuretic it has been employed, either alone or in combination with theobromine. A mixture with the latter substance is marketed under the name of theophorin (see p. 1639). It has also been employed by Stern and others (*J. A. M. A.*, 1906) internally for the treatment of inoperable *cancers*, *diphtheria*, and *tuberculosis*. Berret (*K. T. W.*, 1906) reports good results from sodium formate in the treatment of muscular tremors, such as *paralysis agitans*, and senile or toxic tremors. The dose of sodium formate is from two to five grains (0.2–0.3 Gm.) three or four times a day.

Formic Ether.—The ethyl ester of formic acid has been especially recommended as a diuretic by Huchuard (*Anal. de pharmacie*, 1906) in doses of three grammes (45 grains) *per diem*. *Formic ether* occurs as a colorless fluid, miscible with both water and alcohol. A paper on the physiological action of this substance may be found in the *J. P. C.*, June, 1872, 453.

Formicin. *N. N. R.* 1917. (*Formaldehyde Acetamid.*) $CH_3.CO.NH.CH_2.OH$.—This product is prepared by a patented process involving the action of a formalin polymer on acetamid.

Because of its hygroscopic qualities, *formicin* is marketed only in concentrated solution. It is a colorless, syrupy liquid, specific gravity, 1.25, of a characteristic odor, miscible in all proportions of water, alcohol or chloroform. The addition of either acids or alkalies causes the liberation of formaldehyde. With Mayer's reagent it gives a reddish-violet color. According to Koch (*Ph. Ztg.*, 1905) this agent exercises at body temperatures a powerful bactericidal effect probably due to the liberation of formaldehyde. It has been used in strengths of from 2 to 5 per cent. for disinfecting internal cavities, as the bladder, and also as an injection in suppurative infection of the joints. Bartholdy (*D. M. W.*, 1906, p. 1601) has injected as high as 2 mils of the 5 per cent. solution daily into a child of eight years without causing any systemic symptoms. According to this author it has the great advantage over formaldehyde of causing practically no pain.

Formopyrine.—*Methylenediantipyrine*, $(C_{11}H_{11}N_2O)_2{=}CH_2$, is formed by heating five parts of antipyrine with four parts of formaldehyde solution for several hours to 120° C. (248° F.); crystals melting at 156° C. (312.8° F.), or when anhydrous at 176° to 177° C. (348.8°–350.6° F.); almost insoluble in water, readily soluble in alcohol. It unites the action of the two components.

Formyl-phenetidin. *Parathoxyformanilid.* $C_6H_4(OC_2H_5)NH.COH$.—This product is obtained by the action of a solution of sodium formate in formic acid on phenetidin hydrochloride. It forms colorless, odorless, and tasteless crystals, becoming yellow with age or constant exposure to the air. It is soluble in alcohol, ether and hot water, and has a melting point of 60° C. (140° F.). It is asserted to exert an antiseptic and analgesic action. *Dose*, three to six grains (0.2–0.4 Gm.).

Fortoin.—This is obtained by the action of formaldehyde upon *cotoin*, the active principle of the true coto-bark. Its composition is $CH_2\begin{matrix}C_{14}H_{11}O_4\\C_{14}H_{11}O_4\end{matrix}$ and it is therefore to be viewed in the light of a *methylenedicotoin*. *Fortoin* forms yellow needles or a yellow powder emitting a feeble cinnamon-like odor; it is freely soluble in chloroform, acetone, glacial acetic acid, and dilute alkalies, but dissolves sparingly in alcohol and ether, while in water it is absolutely insoluble; melting point, 211° to 213° C. (411.8°–415.4° F.). It is claimed for *fortoin* that it has the peculiar action of cotoin upon the intestinal mucous membrane, united with the antiseptic and disinfecting properties of formaldehyde. It is used in those cases of *chronic intestinal catarrh* in which there is no active inflammatory process. It has been also recommended by Overlach as a local application in badly *ulcerated sore throats* and in *gonorrhea*. In making local applications 10 per cent. of alcohol should be employed with water, and the strength may vary from one to six grains to the fluidounce. *Dose*, four to seven grains (0.26–0.45 Gm.) three to five times a day.

Frankenia. *Frankenia grandifolia* Cham. and Schlecht. *Yerba Reuma.* (Fam. *Frankeniaceæ*.)—This herb, which grows in California, Nevada, Arizona and Northern Mexico, contains about 6 per cent. of tannin and is employed as a topical remedy in *catarrhal affections*, especially of the nose and genito-urinary tract; also internally in *doses* of from ten to twenty minims (0.6 to 1.3 mils) of the fluidextract. For local application the fluidextract may be diluted with from two to five times its volume of water.

Frasera. *Radix Fraseræ. Radix Colombo Americanæ. Racine de Colombo de Mariette (d'Amérique)*, Fr. *Frazerawurzel, Amerikanische Colombowurzel*, G.—*American Columbo* is yielded by *Frasera carolinensis* Walt. (Fam. *Gentianaceæ*), a perennial herb which flourishes in rich dry soil from New York and Wisconsin southward. The period of flowering is from May to July; but the stems and flowers are produced only in the third year, the radical leaves being the only part of the plant which previously appears above ground. From this manner of growth, it is inferred that the roots, which were formerly included in the Secondary List U. S. P., should be collected in the autumn of the second or the spring of the third year. Before being dried, they should be cut into transverse slices.

As formerly in the market, frasera was in disc-like pieces resembling calumba, but are easily distinguishable by the greater uniformity of their internal structure, the absence of concentric and radiating lines, and their purer yellow color, without a greenish tinge. The root sliced longitudinally, so as to imitate gentian, has been offered in the market as *American gentian*. The taste of frasera is bitterish and sweetish. Water and diluted alcohol extract its virtues, and the

tincture precipitates upon the addition of water, but is not affected by tincture of galls. The hot infusion is not precipitated by solution of gelatin, and gives with iodine no signs of starch. These reactions afford additional means of distinguishing the root from calumba. It contains gum, pectin, glucose, wax, resin, fatty matter, yellow coloring matter, bitter extractive, and an acid which is probably peculiar. (*A. J. P.*, Jan., 1862, 23.)

Frasera is a feeble, simple bitter. *Dose*, of powder, one drachm (3.9 Gm.); of infusion (1 fl. oz. to 1 pint boiling water), two fluidounces (60 mils) a day. The fresh root is said to be emetic and cathartic.

Fruit Essences, Artificial.—Several of the esters of alkyl radicals with organic acid have been found to possess the odor and flavor of certain fruits, a property which has led to their employment as flavoring materials under the name of fruit essences. They are esters, which, according to the older nomenclature, were improperly called "ethers" or "compound ethers."

Ethyl Butyrate. Ethyl-butyric Ester. $C_3H_7COOC_2H_5$.—This ester is readily prepared by dissolving eight parts of normal butyric acid in five parts of ethyl alcohol and mixing this solution with ten parts of concentrated sulphuric acid. After warming the mixture for some time to about 80° C. (176° F.), and then allowing it to stand for some hours, it is poured into cold water, when the ether separates. It forms a layer on the surface, and may be purified by washing it with water and subjecting it to the action of calcium chloride. Butyric ether, as it is sometimes erroneously called, is sparingly soluble in water, but very soluble in alcohol, and boils at 121° C. (249.8° F.). It is said to be much used to communicate a pineapple flavor to rum. Dissolved in 8 to 10 parts of alcohol, it formerly was sold under the name of *pineapple essence. Butyric acid*, $C_4H_8O_2$, is formed during what is called the butyric fermentation, which usually consumes two or three months before it is completed, and which is preceded by the lactic fermentation. To prepare it, a solution of grape sugar is mixed with half its weight of chalk, and with about one-tenth of its weight of cheese to act as a ferment, and the whole is kept at the temperature of 32.2° C. (90° F.). The sugar is first transformed into a viscous substance, and afterwards into lactic acid, which is gradually converted into butyric acid, with the disengagement of hydrogen and carbon dioxide. At the end of the fermentation the liquid contains principally a mixture of calcium butyrate and lactate, from which the butyric acid may be obtained by precipitating the lime as a carbonate by sodium carbonate, aud decomposing the resulting sodium butyrate with sulphuric acid. Butyric acid is a colorless liquid, of disagreeable odor and rancid taste. It dissolves in all proportions in water and alcohol, boils at 163° C. (325.4° F.); density, 0.973.

Ethyl Pelargonate. Ethyl-pelargonic Ester. Œnanthic Ether. $C_8H_{17}COOC_2H_5$.—A preliminary step in forming this ether is to prepare the *pelargonic acid.* This is obtained, according to R. Wagner, by the action of nitric acid on oil of rue. Treat the oil with double its weight of very dilute nitric acid, and heat the mixture until it begins to boil. Two layers are formed in the liquid, the upper one being brownish, and the lower consisting of the products of the oxidation of the oil, with the excess of nitric acid. The lower layer, having been separated, is freed from the greater part of the nitric acid by evaporation in a zinc chloride bath, and then filtered. This filtrate is a solution of pelargonic acid, and may be converted into pelargonic ethyl ester by a prolonged digestion, at a gentle heat, with alcohol. The ether as thus prepared has the agreeable odor of quince, and when dissolved in alcohol in due proportion, was formerly sold as *quince essence.* It is also obtained from wine lees, by adding sulphuric acid and water, and distilling in a current of steam. Pure pelargonic ethyl ester (œnanthic ether) is a colorless liquid, having a peculiar, vinous, stupefying odor, and a taste at first slight but afterwards acrid. Its sp. gr. is 0.8635 at 17.5° C. (63.5° F.) and its boiling point from 227° to 228° C. (440.6°–442.4° F.). It is insoluble in water, but dissolves readily in alcohol and ether. It has been much used in the production of factitious or imitation brandy. Pelargonic acid, first obtained from *Pelargonium capitatum* (L.) Ait., or *rose geranium*, belongs to the fatty acid series and has the formula $C_8H_{17}COOH$. Delff's analysis of *œnanthic acid* gives it the same composition, and he considers the two acids identical. This ester is one of those naturally found in grape brandy and the artificial ester is much used in preparing artificial brandies.

Amyl Acetate. Amyl-acetic Ester. Pentyl Acetate. $CH_3COOC_5H_{11}$.—A cooled mixture of 100 parts of pure amyl alcohol and 130 parts of concentrated sulphuric acid is poured over 100 parts of anhydrous sodium acetate placed in a retort connected with condensing apparatus; after 12 hours' standing the ether is distilled off by the aid of a sand bath. The distilled liquid is purified from free acid by washing with a weak alkaline solution, and from water by distillation from calcium chloride. It is a colorless, limpid liquid, lighter than water, boiling at 137° C. (278.6° F.), insoluble in water, but soluble in alcohol. It is manufactured on a large scale as a solvent for lacquers and varnishes under the name of banana oil on account of the resemblance of the odor of the ester to that of ripe bananas. An alcoholic solution of this ether also has been sold under the name of *Jargonelle pear essence.* This ester is commercially sold under the name of "banana oil," and is the solvent used largely in lacquering, the film, as a rule, consisting of pyroxylin which is quite soluble in amyl acetate.

Amyl Valerate. $C_4H_9COOC_5H_{11}$. *Amyl Valerianate. Amyl-valeric Ester. Apple Oil.*—This is made by carefully mixing four parts of pure amyl alcohol (fusel oil) with four of sulphuric acid, and adding the mixture, when cold, to five parts of valeric acid. The whole is warmed for a few minutes in a water bath, and then mixed with a little water, which causes the ether to separate. Lastly, it is purified by washing it with water and a weak solution of sodium carbonate. It boils at 188° C. (370.4° F.), and has a sp. gr. of 0.879 at 0° C. (32° F.). An alcoholic solution of this ether, in the proportion of one part to six or eight of alcohol, has been used as a flavoring liquid under the name of *apple essence.* (See *Valeric Acid.*)

Besides the essences here described, there are found in commerce the strawberry, raspberry, apricot, greengage, mulberry, and black currant essences, all of which may be viewed as various

mixtures of the esters of the ethyl and amyl series, modified by the addition of pure nitrous ether, tincture of orris, vanilla, volatile oils, etc., to bring about a resemblance to the fruit the odor and taste of which it is the object to imitate.

The fruit essences have been extensively employed in the past for flavoring ices, jellies, lozenges, and drops, and for making fruit syrups and effervescent beverages. They are, however, vastly inferior to the concentrated juices and extracts from the real fruits, and their use is largely being abandoned on account of the necessity of labelling the products thus made as artificial or imitation under existing federal and state food laws.

Kletzinsky prepared a table giving the ingredients, and their proportions, of a large number of fruit essences. (See *U. S. D.*, 19th ed., p. 1497; also a paper by George R. Pancoast and Willard Graham, *Proc. Penn. Phar. Assoc.*, June, 1906.)

Fuchsine. *Magenta Red, Aniline Red, Azaleine, Solferino, Harmaline, Erythrol-benzin, Rosein, Rubin.*—This compound is now included among the U. S. P. reagents (see Part III). It is a mixture of salts of *rosaniline* and *pararosaniline*. One of the earliest coal-tar colors discovered, it has had an extended use for many years. The poisonous results which have been alleged to follow the use of fuchsine as a coloring for foods and as a dyestuff for fabrics, have been undoubtedly due to arsenical impurities remaining in the dye from its manufacture. There is still some doubt, however, as to its properties in this respect, and it is not included in the seven permitted colors under the ruling of the U. S. Dept. of Agriculture. (*F. I. D.*, 76.) It stains animal tissue directly violet-red, while vegetable fiber must first be mordanted. Reiss (*G. H. M. C.*, 1888) recommends fuchsine as a specific in *acute* and *chronic Bright's disease*. Fuchsine, according to Weber and Krause (*B. K. W.*, 1907, p. 192) surpasses trypan red in its destructive action upon trypanosomes. It does not appear, however, to have been as yet tried in human trypanomiasis. According to May (*J. A. M. A.*, 1912, lviii, and 1913, lx) it is a powerful germicide rivalling phenol in its efficiency, and like many of the other dye-stuffs stimulates granulation and epitheliazation. A number of other authors have reported favorable results in *varicose ulcers, burns,* and granulating *wounds* of various kinds. Triboulet also reports pleasing results in various *skin diseases,* especially *impetigo*. It is used generally in strengths of about 1 per cent. either as an ointment or as an aqueous solution.

Fuchsine and *safranine*, $C_{21}H_{20}N_4$, were formerly largely employed in France for coloring wines red. In the experiments of Cazeneuve and Lépine (*G. H. M. C.*, Nov., 1885) fuchsine was found to be free from toxic properties, but safranine proved itself a violent poison, causing marked dyspnea, acceleration of the heart's beat, violent diarrhea and albuminuria, and death from respiratory paralysis. *Dose* of rosaniline, one-tenth to one-sixth grain (0.006–0.010 Gm.).

Fucus. *N. F. IV. Bladderwrack. Sea-wrack. Kelp-ware. Black-tang. Cutweed. Querous Marina. Fucus* (*Varech*) *vésiculeux*, Fr. *Blasentang, Seetang, Meeriche*, G. (Fam. *Fucaceæ*.)—Fucus was retained in the National Formulary IV as "the dried thallus of *Fucus vesiculosis* Linné (Fam. *Fucaceæ*)." This is a common seaweed growing on the rocks in the North Atlantic Ocean. "Sometimes a meter in length, but usually in shorter pieces, from 1 to 4 cm. in width, dichotomously branched, brownish black, usually with a slight, whitish incrustation; flat, smooth, entire-margined, having a stout midrib throughout, along which are irregularly disposed pairs of air-vesicles which vary in diameter from 5 to 15 mm.; receptacles terminal, compressed, mostly ovate or elliptical and about 1 cm. in length, but varying from spherical and 5 mm. in diameter to linear-lanceolate and 5 cm. in length, forked, solitary, or in pairs. Odor strongly seaweed-like; taste saline and nauseous. Fucus yields not more than 20 per cent. of ash." *N. F.* The plant grows upon the shores of Europe and of this continent, attaching itself to the rocks by its expanded woody root. On the coasts of Scotland and France it is much used in the preparations of kelp. It is also employed as a manure, and is mixed with the fodder of cattle. It contains from 22 to 62 per cent. of mucilage and a peculiar cellulose, and about 0.1 per cent. of a volatile oil; the ash containing both iodine and bromine. Tollens and Rovoir state that 0.8 per cent. of a sugar named *fucose*, $C_6H_{12}O_6$, exists in dried seaweed. Votocek and Potmesil obtained from fucose an alcohol which they named fucitol. (*B. P. G.*, 1913, 3653.) Convoy has found in it 0.21 per cent. of iodine. (*P. J.*, x, 434.) These ingredients remain in its ashes, and in the charcoal resulting from its exposure to heat in close vessels. On the coast of France about a dozen species of seaweed have been used in making *kelp*. According to Eugene Marchand, *Fucus vesiculosus* is one of those poorest in iodine, the different species of *Laminaria* containing far larger amounts of iodine than this *Fucaceæ*. (See *P. J.*, 1884, 1011.) *Laminaria digitata* (L.) Lamx. and *L. stenophylla* contain ten times as much iodine as the *Fuci*, and are practically now the only kelps used in making iodine. (See *P. J.*, 1884, 1026.)

The charcoal derived from kelp was at one time used, under the name of *Æthiops vegetabilis* or *vegetable ethiops,* in the treatment of *goitre* and *scrofulous swellings*. The mucus contained in the vesicles was applied externally, with advantage, by Russell, as a resolvent in scrofulous tumors. Duchesne Duparc has obtained from it very good results in the treatment of morbid *obesity*. (*J. P. C.*, 1862, 65.) A. T. Carson affirms, however, that the *Fucus vesiculosus* is largely used in Ireland for fattening pigs, and it is doubtful whether its preparations are capable of reducing human obesity unless given in such doses as to interfere with digestion and injure the health. A possible explanation of the action of bladderwrack in obesity, if it exercise any, is found in the experiments of Hunt and Seidell (*J. P. Ex. T.*, 1910, ii, p. 15), who present evidence to show that the extract of this plant is a powerful stimulant to the thyroid gland. Dannecy prepares the extract from the plant, collected at the period of fructification and rapidly dried in the sun. The coarse powder he treats for three days, with four times its weight of alcohol of 86°, expresses at the end of this time, and subjects the residue twice successively to a similar treatment with alcohol of 54°. The tinctures are then mixed, the alcohol distilled off, and the remainder evaporated to the consistence of an extract. Of this extract, which is one-fifteenth of the plant, three pills, each containing 0.25 Gm. (3.75 grains), may be taken daily in the beginning, and increased gradually to twenty-four pills.

(*J. P. C.*, 1862, 434.) From the tincture a syrup may be prepared. *Fluidextractum Fuci*, N. F. IV is made with a menstrum of three volumes of alcohol and one volume of water from fucus in No. 30 powder.

Other species of *Fucus* are in all probability possessed of similar properties. Many of them contain a gelatinous matter and a sweet principle analogous to mannite, and some are used as food in times of scarcity. The varieties are classified by Fristedt as follows:

The *Ceylon moss* is a delicate fucus (*Fucus amylaceus*) growing on the coast of Ceylon. It abounds in starch and vegetable jelly, and is used like carrageen or Irish moss. (*P. J.*, xiii, 355.) *Sphærococcus Helminthochorton* (L.) Ag. (*Fucus Helminthochorton* L., *Gigartina Helminthochorton* Grev.) has some reputation in Europe as an anthelmintic and febrifuge. It is an ingredient in the mixture of marine plants sold in Europe under the name of *Corsican moss* or *helminthochorton*. This is used in decoction, from four to six drachms to the pint; *dose*, a wineglassful three times a day. Large quantities of a seaweed, *agar-agar*, are gathered on the rocky coasts of the East India islands, and sent to China, where it is valued for making jellies and as a size for stiffening silks. (See *Agar*, Part I.)

Attention has been called by Sloan of Ayr, Scotland, to *Laminaria digitata* (L.) Lamx., (*L. Cloustoni* Edmonst.), commonly called *sea-girdles* or *tangles*, of Scotland, as supplying an admirable material for bougies. The stem is from two to twelve feet long and an inch or more in breadth, is of great strength and tenacity, with the property of drying readily, and, in doing so, of shrinking much, and acquiring an elastic firmness, with a consistence, if the desiccation be arrested at the proper point, somewhat softer than horn. In this state the plant may be kept for years, and is capable of absorbing moisture at any time and swelling to the original size, so that it has been used for the making of dilating bougies and tents.

Fucol.—Under the trade name *fucol*, a cod liver oil substitute is marketed and stated to be prepared by extracting, under special precautions, roasted bladderwrack with a bland oil. It forms a clear green oil of an odor and taste resembling coffee.

Fucusin.—Tablets containing *fucusin* (alleged to be a principle of the *Fucus Vesiculosis*) are recommended as having antifat properties.

Fumaria. *Fumaria officinalis* L. *Fumitory. Beggary. Fumeterre*, Fr. *Erdrauch, Feldraute*, G. (Fam. *Fumariaceæ.*)—A small annual European plant, naturalized in this country, growing in waste places, and flowering from May to August. It was formerly considerably employed as a medicine, and is still used in Europe. The leaves are the official part. They are inodorous, have a bitter, saline taste, and are very succulent, yielding by expression a juice which has the sensible and medicinal properties of the plant. An extract, prepared by evaporating the expressed juice or a decoction of the leaves, throws out upon its surface a copious saline efflorescence. *Fumaric acid*, $C_4H_4O_4$, was early identified as present, and its isomerism with *maleic acid*, the acid obtained from malic acid by heat, was established later. The alkaloid *fumarine*, which was observed by Peschier, has been believed by some chemists to be identical with corydaline, but according to Reichwald (*P. J.*, xix, 990) its formula, $C_{21}H_{19}O_4N$, is different from that of corydaline, from which it further differs in producing immediately an intense violet with concentrated sulphuric acid and an intense golden color with strong nitric acid. It occurs in colorless, tasteless crystals, freely soluble in chloroform, less so in benzene, still less so in alcohol and ether, sparingly soluble in water. He obtained it by treating the pulp of the leaves with concentrated acetic acid, with the aid of heat, filtering, evaporating the liquid, treating the extract with boiling alcohol, filtering the alcoholic solution, and, finally, decolorizing, and evaporating so that crystals might form. The acetate thus procured was decomposed by the alkalies and yielded the fumarine. (See Adermann, *A. J. P.*, 1890, 396.) Fumitory has been considered gently tonic, alterative, and, in large doses, laxative and diuretic. Hannon has found fumarine, in the *dose* of about one-third or one-fourth of a grain (0.021–0.016 Gm.) to be moderately excitant; in that of three grains (0.2 Gm.) to be at first irritant and afterwards sedative. (*Ann. Thér.*, 1854, 78.) Both in ancient and modern times fumitory has been esteemed a valuable remedy in visceral obstructions, particularly those of the liver, in *scorbutic affections*, and in various troublesome eruptive diseases. Cullen gave two fluidounces (60 mils) of the expressed juice twice a day. Others have prescribed it in much larger quantities. The leaves, either fresh or dried, may be used in decoction or extract, in almost indefinite dose. The inspissated juice has also been employed.

Furfural. *α-Furol. Pyromucicaldehyde. Furfuraldehyde*, improperly called *furfurol. Artificial Oil of Ants.* $C_4H_3(CHO)O$.—A decomposition product of certain proteids, occurs in beer and brandy and is produced in the distillation of bran, pentoses, etc., with diluted sulphuric acid. It is a limpid, colorless liquid, soluble in 11 parts of water and freely in alcohol and ether.

According to Brunton and Tunnicliffe (*L. L.*, 4032), this toxic aldehyde is present in all raw spirits and is the cause of their toxic properties. The *dose* of one and a half grains (0.096 Gm.) of furfural produces in man a persistent headache. Ammonia is said to be antidotal to furfural, hence its value in "pick-me-ups." Furfurol occurs as a by-product in the inversion of sugar by acids, and its presence in commercial invert sugar makes it possible to detect that substance when used to adulterate honey. (See test for invert sugar under honey.)

Fustic.—A yellow dye-wood, obtained from *Chlorophora tinctoria* (L.) Gaud. (*Maclura tinctoria* D. Don.), a tree of the Fam. *Moraceæ*, growing in the West Indies and South America. It is not used in medicine or pharmacy. According to Bancroft, two different woods bear in England the name of fustic, one the product of the tree just mentioned, distinguished as *old fustic*, probably from the greater magnitude of the billets in which it is imported; the other derived from the *Rhus cotinus* L., or *Venice sumach*, and called *young fustic*, or sometimes *Hungarian fustic*. The wood of *C. tinctoria* owes its coloring properties to two principles, which have been isolated by R. Wagner; one denominated *morin*, or *morindon*, $C_{15}H_{10}O_5$, and the other *moritannic acid*, $C_{13}H_8O_6$, from its resemblance to tannin. The former, when distilled with zinc dust, yields methyl-anthracene, whence the conclusion has been drawn that it is a *trioxymethylanthraquinone*, $C_{15}H_7O_2(OH)_3$. (See *Chem. Gaz.*, ix, 1, 21, and 241.) From the fustic of *Rhus cotinus* L.

(fam. *Anacardiaceæ*), or Hungarian fustic, Chevreul extracted a yellow coloring matter, in small crystalline needles when pure, which he called *fisetin*. J. Schmidt (*Ber. d. Chem. Ges.*, 19, 1734–1749) has made a thorough study of fisetin, and prepared a number of derivatives of it. He states that it occurs in the wood as a tannic acid compound of the glucoside of fisetin, which he calls *fustin*. This latter body crystallizes from hot water in fine silvery needles, easily soluble in alcohol and dilute alkalies, sparingly in ether. It melts at from 218°–219° C. (424.4°–426.2° F.) with decomposition. By warming with dilute H_2SO_4 it is split up into fisetin and a glucose (probably *isodulcite*). The *fisetin* has the formula $C_{15}H_{10}O_6$, and as it contains four hydroxyl groups, it is probably a *tetroxymethylanthraquinone*, $C_{15}H_6O_2(OH)_4$. It is obtained by recrystallization from dilute alcohol or acetic acid; it forms fine yellow needles or yellow prisms. It is very slightly soluble in hot water, easily soluble in alcohol and acetic ether, sparingly in ether and benzene.

The recent importations have been: 1914, 7121 tons, valued at $100,501; and for 1915, 12,354 tons, valued at $179,959.

It has long been known in the Southwest that the wood of the *Osage orange tree, Maclura pomifera* (Raf.) Schneider, contains a dyestuff that would give a more or less fast yellow color. An examination of the wood from Texas by Kressmann showed that it not only contains *moric acid* and *morintannic acid*, the same as fustic wood, but also that the dyeing principles are present in amount to be commercially valuable. A comparative series of dyeing experiments made with fustic and Osage orange wood and extracts showed the latter to be of equal value with fustic in regard to depth of colors produced, the amount of extract, the character of the dyeing, and fastness to light, weather, washing, etc. (*Science*, 1914, 37.)

Gabianol is a substance prepared from a natural shale. It is described as a dark brown, oily liquid, with a greenish reflection, and is asserted to be of value in various diseases of the lungs and throat, administered in capsules, each containing 4 grains (0.26 Gm.).

Gadose.—This is made from cod liver oil, freed from fatty acids and ash-yielding substances. It is similar in composition to wool fat. *Gadose* forms a yellow unctuous mass, fusing at 34°–36° C. (93.2°–96.8° F.), soluble in ether and chloroform, slightly in alcohol. Its iodine number is 89.67 and saponification number 167. Commercially there is an "anhydrous gadose," "hydrated gadose," with 25 per cent. water and "glycerinated gadose" with 25 per cent. glycerin. The anhydrous gadose can take up two and a half times its weight of water and is particularly adapted for preparing mercurial ointment.

Galactochloral. *Galactochloralose.*—This is a combination of chloral and galactose, which is used as a somnifacient. It is soluble in alcohol but not in water or ether. The *dose* is five to fifteen grains (0.32 to 1 Gm.).

Galactose. $C_6H_{12}O_6$.—*Dextro-galastose* has been used by Bower as a test for functional activity of the liver. (*W. M. W.*, 1906.) He found that in healthy persons after the administration of six hundred and twenty grains (40 Gm.) of *galactose* none appeared in the urine, but that in cases of cirrhosis of the liver after the same quantity the presence of galactose could be recognized in the urine.

Galangal. *N. F. IV. Galanga. China Root. India Root. Galanga*, Fr. *East India Catarrh Root. Rhizoma Galangæ*, P. G. *Galgant*, G.—This is described in the National Formulary IV as "the dried rhizome of *Alpinia officinarum* Hance. (Fam. *Zingiberaceæ*.)" Two varieties are described by authors, the *Galanga major* and *Galanga minor*, or *large* and *small galangal*. They are probably the roots of different plants. The large galangal is derived from *Alpinia Galanga* Willd. (*Maranta Galanga* L., *Galanga officinalis* Salisb.). According to H. F. Hance of Canton, the smaller galangal is the product of a distinct but closely allied plant, *Alpinia officinarum* Hance. (*A. J. P.*, xliii, 408.) Both forms are brought from the East Indies. Galangal of the N. F. is described as "irregularly branched, from 2 to 10 cm. in length and from 1 to 2 cm. in thickness, the branches thinner toward the base; marked with the fine annuli of the leaf bases, which are from 3 to 10 mm. apart and of lighter color than the general surface; externally reddish- or rusty-brown; internally of a lighter orange-brown; cut ends of the branches circular, with recurved margin; fracture fibrous. Odor aromatic and agreeable; taste hot, spicy, resembling ginger. The powder is reddish-brown and, when examined under the microscope, exhibits numerous simple starch grains up to 0.06 mm. in diameter, the small grains few in number, the large grains narrow-ellipsoidal, broadened at one end, sometimes truncate, frequently curved, occasionally with a lateral development, lamellæ mostly indistinct, point of origin of growth circular or a cleft in the larger end of the grain, sometimes absent; numerous yellowish oil cells and reddish resin cells; fragments of tracheæ with reticulate thickenings or simple pores; thick-walled sclerenchymatous fibers with oblique pores. Galangal yields not more than 10 per cent. of ash." *N. F.* According to Morin, galangal contains a volatile oil, an acrid resin, *kaempferid*, $C_{16}H_{12}O_6$, *galangin*, $C_{15}H_{10}O_5$, *alpinin*, $C_{17}H_{12}O_6$, and galangol, with an unknown gummy substance and lignin. A. Vogel, Jr., found also starch and fixed oil. (*Ph. Cb.*, 1844, 158.) The active principles are the volatile oil and acrid resin. Galangal is a stimulant aromatic. It was known to the ancient Greeks and Arabians, and formerly entered into numerous compounds. (*A. J. P.*, xliii.) *Dose*, from fifteen to thirty grains (1.0–2.0 Gm.) in substance, and twice as much in infusion.

Galbanum. *Br.* 1898. *Gummi - Resina Galbanum. Galbanum*, Fr. Cod. *Galbanum*, P. G. *Galban, Mutterharz*, G. *Galbano*, It., Sp.—"A gum-resin obtained from Ferula galbaniflua, *Boiss. and Buhse*, and probably from other species." *Br.*, 1898. This gum resin was not admitted to the British Pharmacopœia, 1914. It was also formerly official in the U. S. Pharmacopœia, but was dropped in the 1890 revision. There has been some confusion as to the plant yielding *galbanum*. It is fairly well established now through the studies of the German traveller, F. A. Buhse, that it is a species of *Ferula*. He stated that in 1848 he met with the *galbanum* plant on the declivities of the Demavend, near the southern coast of the Caspian. He saw the gum-resin exuding spontaneously from the plant, and was informed by the natives that the drug was collected from it. The plant is the *F. galbaniflua* Bossier and Buhse. Buhse also

stated that the Persian galbanum is yielded by a second plant, which is doubtfully distant from *F. galbaniflua*, the *F. rubricaulis* Boissier. Schumann considers this identical with *F. galbaniflua*. Holmes is of the opinion (*P. J.*, 1891, 194) that "Levant" galbanum is yielded by *Ferula galbaniflua*, and its variety *β-Ancheri;* that solid "Persian" comes possibly from *F. Schair* Borscz, while the *liquid* "Persian," judging from the fruits found in it, derived from an undescribed species allied to *F. galbaniflua*. It would appear that all the varieties of galbanum of commerce come through Persia. Galbanum is said to be obtained by making incisions into the stem, or cutting it off a short distance above the root. A cream-colored juice exudes, which concretes upon exposure to the air. A portion of juice also exudes spontaneously from the joints, and hardens in the shape of tears.

Galbanum usually appears in the form of masses composed of whitish, reddish, or yellowish tears, from the size of a pin's head to that of a pea and larger, irregularly agglutinated by a darker colored yellowish-brown or greenish substance, more or less translucent, and generally mixed with pieces of stems, seeds, or other foreign matters. It is also found, though rarely, in our markets, in the state of distinct roundish tears, about as large as a pea, of a yellowish-white or pale brownish-yellow color, shining externally as if varnished, translucent, and often adhering together. Galbanum has in cool weather the consistence of firm wax, but softens in summer, and by the heat of the hand is rendered ductile and adhesive. At 100° C. (212° F.) it is sufficiently liquid to admit of straining, and it generally requires to be strained before it can be used. It is of a dark-brown or blackish color, and of a soft consistence. The absence of whitish grains, a deficiency in the characteristic odor and taste, and the intermixture of earthly impurities are signs of inferiority. According to Hirschsohm (*Ph. Z. R.*, 1893, 353), galbanum of commerce differs from that formerly found in the market; its consistence is now like that of white turpentine, although the odor is still that of Levant galbanum; the greatest difference is shown in the action of strong acids and solvents on it. (See *A. J. P.*, 1893, 384.)

The odor of galbanum is peculiar and disagreeable; its taste bitterish, warm, and acrid; its sp. gr. 1.212. Triturated with water, it forms an imperfect milky solution, which on standing deposits the greater portion of what was taken up. Wine and vinegar act upon it in a similar manner. Alcohol dissolves a considerable proportion, forming a yellow tincture, which has the odor and taste of galbanum, and becomes milky with water, but affords no precipitate. In diluted alcohol it is wholly soluble, with the exception of impurities. Ether dissolves the greater portion. "When moistened with alcohol, galbanum acquires a purple color on the addition of a little hydrochloric acid." *U. S.*, 1880. According to Conrady, the composition of galbanum is as follows: ethereal oil, 9.5 per cent.; resin, soluble in alcohol, 63.5 per cent.; gum and impurities, 27 per cent. The purified resin was found by Conrady to contain about 20 per cent. of combined *umbelliferone*, about 0.25 per cent. of free umbelliferone, and about 50 per cent. of *galbaresino-tannol*. This latter representative of the class of resino-tannols, first established by Tschirch, was proved to have the alcohol character by forming the acetyl and benzoyl derivatives. Conrady also considers that the umbelliferone is combined with this galbaresino-tannol in the form of an ester. The volatile oil which is obtained from galbanum to the extent of about 10 per cent. he found to consist essentially of a hydrocarbon of the formula $C_{10}H_{16}$, with small amounts of a sesquiterpene, $C_{15}H_{24}$. The terpene has been identified as *d-pinene* by the terpin hydrate formation, while the sesquiterpene, according to Wallach, is *cadinene*, identified by the formation of its chlorhydrate fusing at 117° to 118° C. (242.6° to 244.4° F.). (Gildemeister and Hoffman, *Aetherische Oele*, p. 753.) When the oil is extracted by solvents it is free from acid reaction, but when distilled with steam it acquires an acid reaction, and notable quantities of isovaleric acid are developed. These fatty acids are probably bound up as esters in the cold extracted oil. (*A. Pharm.*, ccxxxii (1894), 98.) The crude oil is dextrogyrate. The resin, constituting about 60 per cent., is very soft, and dissolves in ether or in alkaline liquids, even in milk of lime, but only partially in carbon disulphide. When heated with hydrochloric acid for some time, it yields *umbelliferone*, $C_9H_6O_3$, which may be dissolved from the acid liquid by means of ether or chloroform, and obtained on evaporation in colorless acicular crystals. The aqueous solution of umbelliferone exhibits, especially on addition of an alkali, a brilliant blue fluorescence, which is destroyed by an acid. If a small fragment of galbanum be immersed in water, a fluorescence will be produced by a drop of ammonia. Asafetida shows the same reaction, but ammoniac does not.

Galbanum submitted to dry distillation yields a thick oil of brilliant blue color. This oil on rectification yields a greenish portion, and then a superb blue oil. Kachler (*Ber. d. Chem. Ges.*, 1871, p. 36) found a colorless oil, $C_{10}H_{16}$, and a blue oil, $C_{10}H_{16}O$, boiling at 289° C. (552.2° F.). The blue oil, according to Kachler, after purification, agrees with the blue oil of the flowers of *Matricaria Chamomilla*. By fusing galbanum resin with potassium hydroxide, Hlasiwetz and Barth (*Ann. Ch. Ph.*, 130, p. 354) obtained resorcinol, together with acetic and volatile fatty acids.

According to Ludewig, a gum-resin, designated as *Persian galbanum*, is received in Russia by the way of Astrakhan or Orenburg, and is the kind used in that country. It comes enclosed in skins, and is in masses of a reddish-brown color with whitish streaks, of a disagreeable odor, somewhat like that of asafetida, and of an unpleasant bitter, resinous taste. It is so soft as to melt with a slight elevation of temperature. It differs from common galbanum in its odor, in its color, which is never greenish, and in the absence of tears, and is probably derived from a different plant. It abounds in impurities. This variety of galbanum is probably the same as that obtained by Aitchison in Afghanistan, which on chemical examination yielded—volatile oil, 3.108 per cent.; resin (ether extractive, 61.2, alcohol extractive, 7.576), 68.776; water extractive (gum), 17.028; insoluble matter, 1056. (*P. J.*, Dec. 11, 1886.)

Galbanum was known to the ancients. It is stimulant, expectorant, and antispasmodic, and is considered as intermediate in power between ammoniac and asafetida. It has chiefly been used in chronic affections of the bronchial mucous membrane, *amenorrhea*, and chronic *rheumatism*. It is occasionally applied externally as a plaster to *indolent swellings*, with the view of promoting resolution or suppuration.

Compound pills of galbanum were official in the British Pharmacopœia, 1898, under the name of *Pilula Galbani Composita*, the former name was *Pilula Asafœtida Composita* and the pills consisted of equal parts of galbanum, asafetida and myrrh, syrup of glucose being used as excipient.

Dose, from ten to twenty grains (0.65 to 1.3 Gm.), given in pill, or triturated with gum arabic, sugar and water, so as to form an emulsion.

Under the name of *Zalou root* there appears in the Bayrout markets the root of the *Ferula Hermonii* Boiss. This contains, according to Guiges (*P. J.*, 1906, p. 65) a resin which differs from Galbanum in that it gives with hydrochloric acid a green color, which disappears on heating. It is used by the people of that section as an aphrodisiac.

Galega. *N. F. IV. European Goat's Rue. Goat's Rue. Herba Rutæ Capratiæ. Rue de Chèvre*, Fr. *Geisraute, Pestilenzkraut*, G.—*Galega* was made official in National Formulary IV and thus defined: "The dried flowering tops of *Galega officinalis* Linné (Fam. *Leguminosæ*)." This is a perennial leguminous herb, growing in the south of Europe, and sometimes cultivated in gardens. It is without odor unless bruised, when it emits a disagreeable odor. The N. F. describes it as follows: "Stem smooth, erect, branched, when entire from 15 to 45 cm. in length, commonly cut and broken; leaves oddly-pinnate with from six to eight pairs of leaflets; stipules lanceolate, sagitate on one side; leaflets bright green, smooth or slightly hairy, short petioled, lanceolate or ovate-lanceolate, obtuse, slightly mucronate, from 2 to 5 cm. in length and from 2 to 6 mm. in breadth; flowers small, white to violet, in axillary racemes. Odor indistinct, taste mucilaginous, slightly bitter and astringent; it colors the saliva yellowish-green. Galega yields not more than 12 per cent. of ash." *N. F.* It contains a bitter principle and tannin. In former times it was much employed in *malignant fevers*, the *plague*, the *bites of serpents*, *worms*, etc. In 1873 Gillet-Damitte, in a communication to the French Academy, stated that this plant when fed to cows would increase the secretion of milk from 35 to 50 per cent.; since which time Cerisoli, Goubeaux, Masson d'Aury, Millbank, and Carron de la Carrière have affirmed that goat's rue is a powerful galactagogue. The best preparation appears to be an aqueous extract prepared from the fresh plant. This almost black extract has a pronounced odor, and may be given in *doses* of from eight to fifteen grains (0.5–1.0 Gm.), from three to five times a day.

Fluidextract of Galega is official in the National Formulary IV. It is made with a menstruum of diluted alcohol. *Dose*, sixty minims (3.75 mils). The root of the indigenous *Tephrosia virginiana* (L.) Pers. (*Galega virginiana* L.) is said to be diaphoretic and powerfully anthelmintic. It is given in decoction.

Galium. *Galium Aparine* L. *Cleavers. Goose-grass. Grateron, Rièble*, Fr. *Klebkraut*, G.—This is an annual, succulent, rubiaceous plant, common to Europe and the United States, growing along the seashore and much in shaded ground inland. It is inodorous, and has a bitterish, herbaceous, somewhat acrid taste. Analyzed by Schwartz, it was found, besides chlorophyll, starch, and other principles common to all plants, to contain three distinct acids—viz., a variety of tannic acid, which he names *galitannic acid*, citric acid, and a peculiar acid, previously discovered by Schwartz and Rochleder, and named *ribichloric acid*, $C_{14}H_8O_9$. (*P. J.*, xii, 190.) The expressed juice is said to be aperient, diuretic, and antiscorbutic, and has been used in *dropsy, congestion of the spleen, scrofula, scorbutic eruptions*, and *lepra*. Orwin (*T. G.*, vol. i, 767) commends it highly in *psoriasis*. Three ounces (90 mils) may be given twice a day.

Galium verum L. *Yellow Ladies' Bedstraw. Cheese Rennet. Caille-lait jaune*, Fr. *Megerkraut, Liebfrauenstroh*, G.—This European Galium (fam. *Rubiaceæ*) is inodorous, but has an astringent, acidulous, bitterish taste. The bruised plant is sometimes used to color cheese yellow, being introduced into milk before coagulation. It is also used for dyeing yellow. The roots of this and of most other species dye red, and the plant, eaten by animals, colors the bones like madder. Schwartz found the same principles in it as in *G. Aparine*. It was formerly highly esteemed as a remedy in *epilepsy* and *hysteria*, and was applied externally in *cutaneous eruptions*, in the form either of the recently expressed juice or of a decoction from the fresh plant. Of the American species, *G. tinctorium* L. is closely allied in properties to *G. verum*. It is said to be useful in *cutaneous diseases*, and the root is employed by the Indians for staining their feathers and other ornaments red. *G. triflorum* Michx. contains coumarin, as pointed out by L. von Cotzhausen. (*A. J. P.*, 1876, 405.)

Gallacetophenone. *Alizarine Yellow. C.*—$C_6H_2\begin{cases}(OH)_3\\CH_3CO\end{cases}$. This is a derivative of pyrogallol, containing an acetyl group replacing an H atom of the benzene nucleus. Forms a pale yellow powder, crystallizing from hot water, in which, as well as in alcohol and ether, it is readily soluble. It is also soluble in glycerin. This substance has been proposed as a substitute for pyrogallic acid in the local treatment of *psoriasis*, it being claimed that it does not stain, and is not so poisonous as the acid.

Gallicin. *Methyl Gallate. Methyl Ester of Gallic Acid.* $C_6H_2(OH)_3.COO.CH_3$.—This product is made by acting on a warm solution of tannin in methyl alcohol in the presence of hydrochloric acid gas. It forms rhombic prisms or fine needles melting at 202° C. (395.6° F.), soluble in hot water, ether and alcohol. It is a non-toxic antiseptic and is used in *conjunctivitis, keratitis*, and other ocular inflammations as an antiseptic dusting powder.

Gallinol. *Gallanol. Gallanilide.* $C_6H_2\begin{cases}CO.NH.C_6H_5\\(OH)_3\end{cases} + 2H_2O$.—This anilide of gallic acid is formed by boiling tannin with aniline, and was brought forward by Cazeneuve and Rollet as a local remedy to replace chrysarobin in the treatment of skin diseases. (*C. R. A. S.*, 1893.) It occurs in colorless crystals melting at 205° C. (401° F.), of a bitter taste, soluble in hot water, ether, and alcohol, insoluble in benzene and chloroform. It has been especially commended by Gonon, Bayet, Max Joseph, and others, not only in *psoriasis*, but also in chronic *eczema*, to be used in a 10 per cent. solution or ointment, or sometimes in very advanced cases as high as 20 per cent.; it is affirmed never to produce irritation. The removal of the hair is not necessary, provided the skin be thoroughly cleansed with alkaline soap solutions.

Gallobromol. *Dibromgallic Acid.* $C_6Br_2(OH)_3COOH$.—A light brown powder composed of

fine needles melting at 205° C. (401° F.); soluble with difficulty in cold water, easily soluble in hot water, alcohol, and ether, and having a strong acid reaction and a slightly bitter taste. It has been used by Lépine in *neurasthenia* and *epilepsy* to replace potassium bromide, but it would seem to be a somewhat dangerous remedy, as in Lépine's experiments a dog weighing 11 kilogrammes was killed in two hours by 11 Gm., death having been preceded by slowing of the heart's action, depression of respiration, rise of temperature, convulsions, and methemoglobinuria. According to Stein, it is to dogs more poisonous than the sodium bromide, less than the potassium bromide. In the dog small doses produce a primary moderate rise of the blood pressure, followed by fall of pressure, with cardiac arythmia. It is incompatible with alkalies or alkaline salts, and iron compounds. *Dose* (Lépine), as a sleeping potion, forty-five grains (3 Gm.); in *epilepsy*, from thirty to forty-five grains (2–3 Gm.) a day. (See *Cb. G. T.*, xiii, 1895.)

Galloformin. $C_6H_2(OH)_3COOH.(CH_2)_6H_4$.—A combination of gallic acid and formin. It is soluble in cold water, alcohol, ether, and glycerin, and insoluble in chloroform and olive oil. Solutions of galloformin should always be made in the cold. It is used internally in *hematuria*, *albuminuria*, and *cystitis*. It is also used externally in the treatment of skin diseases.

Gallogen. *N. N. R.* 1917. *Ellagic Acid.* $C_{14}H_6O_8$.—This is a yellowish powder devoid of odor and taste, insoluble in an acid or neutral fluid, but soluble in alkaline fluids. In solution it shows the characteristic tannic acid reactions. With nitric acid containing nitrous acid it gives a characteristic dark red color. It is employed as an intestinal astringent in all forms of *diarrhea*. *Dose*, adults fifteen grains (1 Gm.) several times a day; for children, five to eight grains (0.32–0.5 Gm.) several times a day.

Gallols.—E. Kromayer (*Monatshefte für Prakt. Dermatologie*, vii) has tested as remedies for diseases of the skin a number of chemical combinations of pyrogallol, chrysarobin, and resorcinol, with various acids. Of these a few give promise of therapeutic usefulness.

Lenigallol, pyrogallol triacetate, $(CH_3COO)_3C_6H_3$, is described as a white, insoluble powder, slowly soluble on warming with aqueous solutions of alkalies, with decomposition.

Eugallol, N. N. R. 1917, *pyrogallol monoacetate*, is a very thick, syrupy, transparent, dark yellow mass, readily soluble in water. Marketed only in a 66 per cent. solution in acetone.

These substances are stated not to be affected by contact with healthy skin, but to be slowly decomposed by the diseased skin with the liberation of pyrogallol. Strong ointments of lenigallol are to be employed in *psoriasis*, 1 or 2 parts of lenigallol to 200 parts of zinc paste in *eczemas*. Even the most acute eczemas, as well as those with impetiginous crusty exudations, are reached by the ointment.

Eugallol produces great local excitement, and is only to be employed in the most obstinate cases of *psoriasis*. Under such circumstances, however, the direct local application as a paint, daily or every other day, produces a marked inflammation, under which the most stubborn patches are said to disappear. Dusting the painted parts with zinc oxide before drying makes the action more vigorous. The value of eugallol has been strongly confirmed by Paul Gruneberg (*Derm. Zeit.*, vi, 1899), who uses in *lupus* a zinc paste with from 11 to 12 per cent. of eugallol continuously applied after free curetting, and in *psoriasis* he uses a 33½ per cent. acetone solution followed by zinc oxide dressing.

Gardenia. *Gardenia grandiflora* Lour. (Fam. *Rubiaceæ*.)—A Chinese tree, the fruit of which is employed in dyeing the yellow robes of the mandarins, and, according to Lorenz Mayer, contains *crocin*, which in powder is of a bright red color, and soluble in water and alcohol. According to the researches of Kayser (*Ber. d. Chem. Ges.*, 1884, 2228), its formula is $C_{44}H_{70}O_{28}$. When heated with diluted hydrochloric or sulphuric acid, it is decomposed into *crocetin*, $C_{34}H_{46}O_9$, and a dextrorotatory sugar called *crocose*. Alkalies bring about the same decomposition almost instantly. Concentrated sulphuric acid dissolves both the crocin and crocetin with deep blue color. The fruit of another species, *G. campanulata* Roxb., growing in the forests of Chittagong, in India, is said to be used by the natives as a cathartic and anthelmintic. (Lindley, *Flor. Med.*, 434.)

Garlic. *N. F. IV. Allium. English Garlic.*—The genus Allium includes a large number of species, of which nearly seventy are indigenous in this country. Many, and perhaps all, of these species contain volatile oil upon which their activity depends. The cultivated garlic, of which the bulbs are official in the N. F., is *Allium sativum* L., for which, according to Griffith, *A. canadense* L., has been substituted and found efficient.

Allium sativum, L., is a perennial plant with numerous bulbs which have a common membranous covering, from the base of which the fibers that constitute the proper root descend. The stem is simple, and rises about two feet. The leaves are long, flat, and grass-like, and sheathe the lower half of the stem. At the termination of the stem is a cluster of flowers and bulbs mingled together, and enclosed in a pointed spathe, which opens on one side and withers. The flowers are small and white, and make their appearance in July. This species of garlic grows wild in Sicily, Italy, and the south of France. The bulbs, or so-called cloves, are usually six or eight in number, oblong or wedge-shaped, and covered with dry membranous scales, with a pungent odor and a disagreeable and acrid taste.

The N. F. description is as follows: "The fresh bulb of *Allium sativum* Linné (Fam. *Liliaceæ*). Bulb subglobular, from 4 to 6 cm. in diameter, compound, consisting of from eight to fifteen bulbels and surrounded by one or two dry, whitish, membranaceous scales and attached to a flattened circular base from the lower portion of which arise numerous yellowish-white roots; bulbels more or less ovoid, in transverse section on three to four sided, the outer surface being convex, summit acute and narrowed into a thread-like fibrous portion, base truncate, each bulbel covered by one or two layers of whitish, membranaceous, scale-like leaves, beneath which is the light brown or pinkish, thin and coriaceous layer of epidermis, cohering but easily separable from the solid portion of the bulbel. Odor of broken or bruised bulbels powerfully alliaceous, taste intensely pungent and persistent. Under the microscope, transverse sections of the bulbel show three distinct portions: (a) the large fleshy scale consisting chiefly of parenchyma enclosing scattered vascular bundles, epidermis in both ventral and dorsal surfaces consisting of small tabular cells; (b) the middle layer nearly circular in outline, about 0.75

mm. in diameter, the tissues resembling those of the outer fleshy scale, but the cells containing numerous yellowish-brown plastids; (c) an innermost bright green layer consisting of a single leaf folded lengthwise along the midrib so that the ventral surfaces lie close together."

The *oil of garlic* is of a dark brownish-yellow color, heavier than water, and decomposed at its boiling temperature. It may be purified by repeated distillation in a salt water bath, and is then lighter than water, of a pale yellow color, and not decomposed by boiling. Semmler obtained from garlic bulbs 0.09 per cent. of the volatile oil, sp. gr. at 14.5° C. (58° F.) 1.0525; it was yellow, having an intense odor and optically inactive. By fractional distillation he obtained four products, $C_6H_{12}S_2$, $C_6H_{10}S_2$, $C_6H_{10}S_3$, and $C_6H_{10}S_4$, which decomposed during distillation, and hence could only be obtained by distillation *in vacuo*. The oil, according to Semmler, is free from allyl sulphide, the latter having the sp. gr. 0.8991. (*A. Pharm.*, 1892, p. 434.) The impure oil has an exceedingly pungent odor and a strong acrid taste, and, when applied to the skin, produces much irritation and sometimes even blisters. The pure oil combines with silver nitrate, forming a precipitate soluble in heated alcohol and afterwards separating in crystals. Besides this oil, fresh garlic, according to Cadet de Gassicourt, contains, in 1406 parts, 520 of mucilage, 37 of albumen, 48 of fibrous matter, and 801 of water. Bouillon-Legrange mentions among its constituents sulphur, a saccharine matter, and a small quantity of starch. The fresh bulbs yield upon pressure nearly a fourth part of juice, which is highly viscid, and so tenacious as to require dilution with water before it can be easily filtered. When dried, it serves as a lute for porcelain. It has the medicinal properties of the bulbs. Water, alcohol, and vinegar extract the virtues of garlic. Protracted boiling renders it inert. According to Semmler (*A. Pharm.*, 1887, p. 927), *Allium ursinum* contains a volatile oil which consists mainly of *vinyl-sulphide*, C_4H_6S or $(C_2H_3)_2S$.

Medicinal Properties and Uses.—The use of garlic as a medicine and as a condiment can be traced to earliest antiquity. When taken internally, and even when applied externally, the oil is absorbed and imparts its odor to the breath, urine, perspiration, etc. The oil of garlic has some influence upon the human system as a general mild stimulant. Its chief value in medicine is for its local action upon the stomach and as a stimulant expectorant. The garlic itself is sometimes employed as a rubefacient which, by yielding its volatile oil to absorption, stimulates the nervous system, especially in the case of young children. The oil may often be given with advantage in *chronic bronchitis* and in the advanced stages of *obstinate acute bronchitis*. It is especially valuable in the treatment of children when there is a distinct nervous element. In *catarrhal pneumonia* of young children the bruised garlic cloves are often applied as a poultice to the lungs, and similar applications were formerly used upon the feet for the *nervous restlessness* or even the *convulsions* of young children. Garlic clove may be swallowed either whole or cut into pieces of a convenient size, but the syrup has replaced most other methods of administration. The *dose* in substance is from half a drachm to two drachms (2–7.7 Gm.) of the fresh bulb. That of the juice is half a fluidrachm (1.8 mils). A syrup is official in the N. F. (see Part III).

Garrya Fremontii Torr. *California Fever Bush. Skunk Bush.*—The leaves of this bush (fam. *Cornaceæ*), indigenous to California and Oregon, have an intensely bitter taste, and are said to be largely used by Californians as a tonic and antiperiodic. D. W. Ross (*A. J. P.*, 1877) states that he found in them a new alkaloid, *garryine*. The *dose* of the fluidextract of the leaves is from ten to thirty minims (0.6–1.8 mils).

Galyl.—This arsenic compound is said to be *tetroxy-diphospho-amino-diarseno-benzene* with the gross formula $C_{24}H_{22}O_8N_4P_2As_4$. It is asserted to possess curative properties in *syphilis* similar to those of salvarsan (see Dudley, *L. L.*, July 8, 1916) and to be decidedly less toxic (Pearce and Brown, *J. Ex. M.*, 1915, p. 517). It is given in *doses* of from three to six grains (0.2–0.4 Gm.) injected intravenously or intramuscularly, at intervals of from three to seven days until a total of about thirty-two grains (2.0 Gm.) has been administered.

Gaultheria. *Wintergreen. Boxberry. Teaberry. Checker-berry. Feuilles de Gaulthérie couchée* (*de Paloninier*), *Thé du Canada, Thé de Terreneuve*, Fr. *Canadischer Thee, Bergthee*, G.—*Gaultheria procumbens* L. (Fam. *Ericaceæ*) is a small indigenous, shrubby, evergreen plant. The leaves, which were formerly official in the U. S. Pharmacopœia, are short-petiolate, obovate or oval, about 4 cm. in length and 2 cm. in breadth, acute, revolute, obscurely serrate at the edges, coriaceous, shining, bright green above, paler beneath, of unequal size, and supported irregularly on short red petioles.

The plant extends from Newfoundland to Georgia, growing in large beds in mountainous tracts, or in dry barrens and sandy plains, beneath the shade of shrubs and trees, particularly of other evergreens, as the *Kalmiæ* and *Rhododendra*. In different parts of the country it is variously called *checker-berry, tea-berry, aromatic wintergreen*, and *mountain-tea*. The flowers appear from July to August, and the fruit ripens at corresponding periods. To the very peculiar aromatic odor and taste which belong to the whole plant the leaves add a marked astringency. The aromatic and medicinal properties of wintergreen reside exclusively in an official volatile oil. (See *Methyl Salicylas*, page 695.)

Gelanth. *Gelanthum.*—*Gelanth* is a combination of equal weights of tragacanth and gelatin, prepared by Unna as a basis for various pastes for the skin. It is stated to be superior to the older pastes in drying more quickly and leaving a smoother coating upon the skin, as well as in holding more uniformly and in tighter suspense the drug used with it, and finally in not spoiling readily. It is made by allowing tragacanth to soften with twenty times its mass of water for four weeks, then warming the mass to fluidity with steam and pressing it through a mill. In the meanwhile gelatin has been softened in the water and then for some time exposed to a high pressure of steam in Unna's boiler, which exposure lessens its capability of gelatinization. The mixture of the two masses is allowed for two days to soften in the steam, then passed through a mill and mixed with 5 per cent. of glycerin, a little rosewater, and 2 per cent. of thymol. The finished gelanth contains about 2½ per cent. each of dry gelatin and tragacanth. In using it as a vehicle, fatty matters must first be emulsified and insoluble substances rubbed up with water to a soft paste before they are mixed with gelanth.

Genista. *Genista tinctoria* L. *Dyers' Broom. Dyers' Weed. Green Weed. Woad-Waxen. Genet des Teinturiers*, Fr. *Färberginster*, G. (Fam. *Legu-*

minosæ.)—A low shrub, growing wild in Europe, and established on sterile hills and roadsides from Maine to New York, cultivated in greenhouses in this country on account of its profusion of yellow leguminous flowers. The flowering tops of the plant are employed to dye yellow, whence its name was derived. Both these and the seeds have been used in medicine. They are said to be purgative and even emetic, especially the seeds, which were formerly given as cathartic in the *dose* of a drachm and a half (5.8 Gm.). By some authors they are said to be diuretic and to be useful in *dropsy.*

Genoform. *Methyleneglycol-salicylic-ester.*—This is stated to be a condensation product of acetyl-salicylic acid and formaldehyde. It occurs as a white powder having a slightly acid taste, which is sparingly soluble in cold water, but freely soluble in alcohol, ether and hot water. It is said to be split up in the intestines into salicylic acid, acetic acid, and formaldehyde. The *dose* is stated to be five to eight grains (0.32–0.5 Gm.).

Geranium. *N. F. IV* (*U. S. VIII*). *Cranesbill. Cranesbill Root. Spotted or Wild Cranesbill, or Storksbill. Alum Root. Racine de Bec-de-Grue tacheté, Racine de Pied-de-Corneille,* Fr. *Fleckstorchschnabelwurzel,* G.—"The dried rhizome of *Geranium maculatum* Linné (Fam. *Geraniaceæ*)." *N. F. Geranium* was deleted from the *U. S.* Pharmacopœia but is now official in the National Formulary IV. The stem is erect, round, dichotomously branched, from one to two feet high, of a grayish-green color, and thickly covered, in common with the petioles and peduncles, with reflexed hairs. The leaves are deeply divided into three, five, or seven lobes, which are variously incised at their extremities, hairy, and of a pale green color, mottled with still paler spots. Those which rise from the root are supported on foot-stalks eight or ten inches long; those of the stem are opposite, the lower petiolate, the upper nearly sessile, with lanceolate or linear stipules. The flowers are large, and usually of a rose-purple color. The peduncles spring from the forks of the stem, and severally support two flowers upon short pedicles. The calyx is composed of five oblong, ribbed, cuspidate leaves; the petals are five, obovate, and entire; the stamens ten, with oblong, deciduous anthers, the five alternate filaments being longer than the others, and having glands at their base; the ovary is ovate, supporting a straight style as long as the stamens, and surmounted by five stigmas. The fruit consists of five aggregate, one-seeded capsules, attached by a beak to the persistent style, curling up and scattering the seeds when ripe. The plant is indigenous, growing throughout the United States in moist woods, thickets, and hedges, and generally in low grounds. It flowers from May to July. The root should be collected in autumn.

Geranium is described as: "Rhizome cylindraceous, somewhat branched, bent, flattened and strongly tuberculated, from 2.5 to 10 cm. in length and from 3 to 15 mm. in diameter; surface marked with root scars and remnants of slender roots, longitudinally wrinkled; externally dark purple-brown; internally light purple-brown; fracture short, non-fibrous, the section shows a thin bark, a distinct cambium, irregular in outline, large central pith, wood indistinct, the fibro-vascular bundles few and at unequal distances. Odorless; taste strongly astringent. The powder is purplish-brown and, when examined under the microscope, exhibits tangentially elongated cork cells; parenchyma containing starch, scattered cells of pith and bark parenchyma containing tannin both in the content and walls of the cells and colored bluish-black by ammonio-ferric alum T.S.; tracheæ small, with scalariform markings; characteristic starch more or less abundant, grains smooth, mostly single, ovate, up to 0.035 mm. in length, hilum near the larger end, inner lamellæ concentric with hilum, the outer excentric. Geranium yields not more than 8 per cent. of ash." *N. F.* Water and alcohol extract the virtues of geranium. According to Edward Staples, it contains tannic and gallic acids, mucilage, red coloring matter, resin, and a crystallizable vegetable principle. (*A. J. P.*, 1829, p. 171.) Tilden found, besides tannic and gallic acids, gum, pectin, sugar, starch, albumen, resin soluble in alcohol, oleoresin soluble in ether only, coloring matter, chlorophyll, lignin, and various salts. (*P. J.*, 1863, p. 22.) Tannic and gallic acids are probably the sole active ingredients. Henry Trimble and J. C. Peacock (*A. J. P.*, 1891, p. 265) collected the plant at periods of the year ranging from January to October, and determined the percentage of tannin as calculated for the perfectly dry drug to vary from 9.72 to 27.85 per cent. They also determined that it belonged to the class of tannins analogous to gallo-tannic acid, yielding pyrogallol on heating. They decomposed the tannin by the action of hydrochloric acid, obtaining gallic acid, glucose, and geranium red as products.

Geranium is one of our best indigenous astringents, and may be employed for all the purposes to which these medicines are applicable. The absence of unpleasant taste and of other offensive qualities renders it peculiarly serviceable in the case of infants and of persons of very delicate stomach. *Diarrhea, chronic dysentery, cholera infantum* in the later stages, and the various hemorrhages, are the forms of disease in which it is most commonly used and with greatest advantage. As an application to *indolent ulcers,* an injection in *gleet* and *leucorrhea,* and a gargle in *relaxation of the uvula* and *aphthous ulcerations* of the throat, it answers the same purpose as kino, catechu, and other medicines of the same class. It is a popular domestic remedy in various parts of the United States, and is said to be employed by the Indians. It may be given in substance, decoction, tincture, or extract. (See *Fluidextractum Geranii, N. F. IV,* Part III.) *Dose,* fifteen to thirty grains (1–2 Gm.).

Geum. *Water Avens. Radix Caryophyllatæ Aquaticæ. Radix Benedictæ Sylvestris. Racine de Benoîte aquatique* (*de Benoîte des Ruisseaux*), Fr. *Sumpfnelkenwurzel, Wasser-Benedikten-Wurzel,* G.—Several species belonging to this genus have been medicinally employed, but three or four are deserving of particular notice—*Geum rivale* L., which once had a place in the U. S. Secondary List, *G. urbanum* L., formerly recognized by the Dublin College, *G. virginianum* L., an indigenous species, the root of which has been recommended in *dysentery* by W. A. Gibson (*Med. Rec.*, 1868), and *G. canadense* Jacq. (*G. album* Gmel.), recommended by W. A. Spurgeon in *gastric irritation* and *headache.* (*A. J. P.*, 1883.)

The rhizome and roots of *Geum urbanum* L., of Europe and Asia, are used in medicine. The rhizome is from 3 to 7 cm. in length and about 8 mm. in thickness. It is more or less branching, having on the upper surface the remains of the short stems and petiole-bases and on the lower surface numerous fibrous roots. Externally it varies from a brownish to a brownish-yellow. The

fracture is short and internally it is dark brown. When quite dry it is nearly inodorous, but in the recent state has an odor like that of cloves, whence it is sometimes called *radix caryophyllatæ*. The taste is bitterish and astringent. It imparts its virtues to water and alcohol, which it tinges red. Buchner obtained a yellow, amorphous, neutral, bitter-tasting mass, which he calls *geum-bitter*. Distilled with water it yields 0.04 per cent. of a thick, greenish-yellow volatile oil, consisting chiefly of eugenol, a tasteless resin, gum, bassorin, and starch. It has been much used in Europe as a tonic and astringent, in chronic and passive *hemorrhages, chronic dysentery* and *diarrhea, leucorrhea, intermittent fever*, etc. The *dose* is from thirty grains to a drachm (2.0–3.9 Gm.) of the powder three or four times a day, or an equivalent quantity in decoction.

Geum rivale L.—*Water* or *purple avens*, a plant growing in bogs and wet places in the northern United States, has a perennial, horizontal, jointed, scaly, tapering root, about 15 cm. long, of a reddish-brown color externally, white internally, and furnished with numerous descending yellowish fibers. The dried root is hard, brittle, easily pulverized, reddish or purplish, without odor, and of an astringent, bitterish taste. Boiling water extracts its virtues.

Water avens possesses similar therapeutic properties to avens, for which it is sometimes substituted, but is less esteemed. The *dose* of the powdered root is from twenty grains to a drachm (1.3–3.9 Gm.), to be repeated three times a day. *Dose* of the decoction (ounce to the pint), one or two fluidounces (30–60 mils). A weak decoction is sometimes used by invalids in New England as a substitute for tea and coffee.

Gillenia. *Bowman's Root. Indian Physic. American Ipecac. Racine de Gillénie*, Fr. *Gillenienwurzel*, G.—Under this name the U. S. P. formerly included in its Secondary List the roots of two species of *Gillenia*. (Fam. *Rosaceæ*.)

Gillenia trifoliata (L.) Moench. is an herbaceous plant with a perennial rhizome, having many long, slender, roots. It grows throughout the United States, east of the Allegheny ridge, and, in Pennsylvania, may also be found abundantly west of these mountains. The root should be gathered in September. (See *A. J. P.*, 1898, 501.)

G. stipulata (Muhl.) Trel. is herbaceous and perennial, though much taller and more bushy than the preceding. It grows as far north as the State of New York, and extends as far west as Kansas. Its root is precisely similar to that of the Eastern species, and is reputed to possess the same properties.

The roots of *G. stipulata* resemble those of Ipecac, the bark being thinner and enclosing in the inner layers numerous reddish resin cells. The roots of *G. trifoliata* are smaller and indistinctly annulate, exhibiting few or no distinct fissures. For microscopic characters, see G. L. Curry. (*Am. Pract. and News*, May, 1892.) The bark, which is easily separable, has a bitter, not disagreeable taste; the wood is nearly insipid and comparatively inert, and should be rejected. The powder is of a light brownish color, and possesses a feeble odor, which is scarcely perceptible in the root. The bitterness is extracted by boiling water, which acquires a red color. The root yields its bitterness also to alcohol. By various experimenters it has been shown to contain gum, starch, gallotannic acid, fatty matter, wax, resin, coloring matter, albumen, and lignin, besides salts. (*A. J. P.*, xxvi, 490.) *Gillenin* of W. B. Stanhope was a whitish substance, very bitter, slightly odorous, permanent in the air, soluble in water, alcohol, ether, and the dilute acids, and neutral to test paper. Nitric acid rendered it blood-red, chromic acid green. Tannic acid produced no effect. It gave white precipitates with potassium hydroxide, lead subacetate, and tartar emetic. Half a grain (0.032 Gm.) of it produced nausea and retching. (*A. J. P.*, xxviii, 202.) G. L. Curry (*A. J. P.*, 1892, 513) has found two glucosides: the first, *gillein*, obtained from the ethereal extract, formed white feathery crystals, was colored red by sulphuric acid, yellow by nitric acid, and deepened the color of chromic acid; the second, *gilléenin*, obtained from the aqueous infusion, was amorphous, of yellowish color, of faint taste at first but becoming very bitter, and giving no color reactions with the acids.

Gillenia is a mild and efficient emetic, and, like most substances belonging to the same class, occasionally acts upon the bowels. In very small doses it has been thought to be tonic, and has been used as a substitute for ipecacuanha, which it is said to resemble in its mode of operation. It was employed by the Indians, and became known as an emetic to the colonists at an early period. Linnæus was aware of its reputed virtues. *Dose* of the powdered root, as an emetic, from twenty to thirty grains (1.3–2.0 Gm.).

Ginseng. *Panax quinquefolius* L. *Panax. U. S.* 1870. *Ginseng*, Fr., G., Sp. *Ginsen*, It.—*American ginseng* grows in rich, cool woods, especially along the mountains from Quebec and Ontario, south to Georgia. The root is the part employed. This is collected to the extent of about 100,000 pounds annually in the United States and shipped largely to Shanghai. It is also cultivated. (*A. J. P.*, 1891; *Ph. Era*, 1895, 359.) It is not used in America, but is exported to China. While supplied with *ginseng* exclusively from their own country, which furnished the root only in small quantities, the Chinese entertained the most extravagant notions of its virtues, considering it a remedy for all diseases, and as possessing almost miraculous powers in preserving health, invigorating the system, and prolonging life. It is said to have been worth its weight in gold at Pekin, and the first shipment from North America to Canton yielded enormous profits. John Henry Wilson (*P. J.*, July, 1888) states that there are in the Chinese market five ginsengs, four of them of Asiatic origin, derived from *Panax Ginseng* C. A. Meyer, the fifth, the American ginseng, from *Panax quinquefolium*. According to E. M. Holmes, *T'ang-shên*, which is used by the poor of China as a substitute for the costly ginseng, is a root of a new campanulaceous plant, *Codonopsis Tangshen*, and is exported from Hankow and Oo-chang to the extent of five hundred tons annually. (*P. J.*, xxi.) For an account of the Chinese methods of using ginseng, see *P. J.*, vi, 86.

On account of the growing scarcity of the American ginseng plant, experiments have been made by the State of Pennsylvania to determine whether it can be grown profitably, resulting in the conclusion that in five years an acre of ground would yield a profit of fifteen hundred dollars, without allowance for rental, but, according to Jackson (*P. J.*, lxx, p. 785), many precautions are necessary for success. The cultivated roots were larger than those of the wild plant. For an account of the ginseng cultivation in Corea, see *P. J.*, 1885, 732; and of its collection in the United States, see *D. C.*, 1884, 33. (For details of culture and preparation, see *Bulletin 62, Pennsylvania*

State Agricultural Experiment Station; Bulletin No. 16, Division of Botany, U. S. Department of Agriculture; J. U. Lloyd's paper, *Proc. A. Ph. A.*, 1901, p. 90; *Ph. Era*, 1900, p. 581; 1903, p. 497; *P. J.*, 1904, p. 652.)

The root is fleshy, somewhat spindle-shaped, from 5 to 12 cm. long, and 1 to 2.5 cm. thick, and terminated by one or more stem scars. Frequently there are two portions, sometimes three or more, connected at their upper extremity, and bearing a supposed, though very remote, resemblance to the human figure, from which circumstance it is said that the Chinese name *ginseng* originated. When dried, the root is yellowish-white and wrinkled externally, and within consists usually of a hard central portion, surrounded by a soft whitish bark. It has a feeble odor, and a sweet, slightly aromatic taste, somewhat analogous to that of licorice root. It contains a glucosidal principle, *panaquilon*, besides *saponin*, a bitter principle, a volatile oil, resin, sugar, mucilage and starch. S. S. Garrigues prepared *panaquilon*, to which he gave the formula $C_{12}H_{25}O_9$, by heating a cold infusion so as to separate the albumen, filter, concentrate to a syrupy consistence, precipitate by a concentrated solution of sodium sulphate, wash the precipitate thoroughly with the saline solution, and then treat it with alcohol, which dissolves the principle in question, and yields it on evaporation. To purify it, he dissolved it in water, treated the solution with animal charcoal, again evaporated, and dissolved the residue in absolute alcohol, which is finally distilled off. Panaquilon is an amorphous, yellow powder, soluble in water and alcohol, but not in ether, of a sweet bitterish taste, and has the characteristic property that, when treated with strong acids, it is converted into a white substance, insoluble in water, with the escape of carbon dioxide and water. Garrigues proposed for this white substance the name of *panacon*, $C_{11}H_{19}O_4$. (*A. J. P.*, xxvi, 511.) Davydow (*A. J. P.*, 1890, 338) investigated these principles discovered by Garrigues, but adds nothing new to our information concerning them. The root is sometimes submitted, before being dried, to a process of clarification, which renders it translucent and horny, and enhances its value as an article of export. The extraordinary medicinal virtues formerly ascribed to ginseng had no other existence than in the imagination of the Chinese. It is little more than a demulcent, and in this country is rarely employed as a medicine. Some persons, however, are in the habit of chewing it, having acquired a relish for its taste, and it is sold chiefly to supply the wants of these.

Glaucium. *Glaucium flavum* Crantz. *Yellow Horned Poppy. Bruisewort. Pavot cornu*, Fr. *Hornmohn*, G. (Fam. *Papaveraceæ*.)—An annual or biennial plant indigenous to Europe and sparingly naturalized in waste places from New England to Virginia. It contains a saffron-colored, milky juice, clasping leaves and solitary yellow flowers. Two alkaloids have been separated from this plant, *sanguinarine* and *glaucine* (Merck). Maepmann and Helt recommended the plant in the treatment of *diabetes* (*Med. Neuigkeiten d. Pharm-Post.*, 1899, 346.)

Glechoma. *Nepeta hederacea* (L.) Trevisan (*N. Glechona* Benth.). *Herba Hederæ Terrestris. Lierre terrestre*, Fr. *Gundermann, Gundelrebe*, G. *Ground-ivy. Gill-over-the-ground.*—A small perennial, labiate herb, indigenous in Europe and widely naturalized in the United States, and growing in damp, shady, grassy places, as in orchards and along fences and hedges. The herb was formerly official, and still enjoys some credit as a domestic remedy. It has a peculiar, disagreeable odor, and a bitterish, somewhat aromatic taste, and imparts its properties to boiling water. It is very prone to have galls developed on it, and to be infested with certain fungi. (*J. P. C.*, 1875, 127.) It is said to be gently stimulant and tonic, diuretic, and aperient; used in chronic *pulmonary* and *urinary catarrhs*. From a half drachm to a drachm (2–3.9 Gm.) was usually given in infusion as a *dose*.

Gleditschine.—*Gleditschia triacanthos* L., or *Honey Locust*, and *G. Macracantha* Desf. (Fam. *Leguminosæ*), and are small, thorny trees having pinnate leases and forming elongated pods filled with a sweetish pulp. The trees grow in rich woods in the Eastern and Central United States and are common in cultivation. *G. Macracantha* is indigenous to China. These trees were chemically studied by B. F. Lautenbach (*P. M. T.*, 1878), who abstracted from them an alkaloid, which he found to produce in the frog stupor and loss of reflex activity, due to an action upon the spinal cord. To this alkaloid Lautenbach gave the name of *gleditschine*. In 1887 (*Med. Rec.*, 1887) Goodman, Seward, and Claiborne brought before the profession, as a local anesthetic, an alkaloid under the name of *stenocarpine* which was asserted to be obtained from the *Gleditschia triacanthos*. In November, 1888, however, F. W. Thompson, of Detroit (*Med. Age*), and T. G. Novy (*Ph. Rund.*) and John Marshall of the University of Pennsylvania (*Phila. Med. News*), published analyses of this solution, showing that it contained 6 per cent. of cocaine, besides some atropine or other mydriatic alkaloid. (See also *A. J. P.*, 1887, 589.)

Glidin.—*Glidin* is an albuminous preparation made from wheat flour and is asserted by Loeb (*Med. Klin.*, 1905–1906, p. 625) to represent 98 per cent. of albumin and 1 per cent. of lecithin. While it has been used to a slight extent as a nutrient, its greatest interest lies in the fact that it forms chemical combinations with various substances which are prone to irritate the stomach. An examination of *glidin* by Coblentz shows a composition of 30 per cent. albumen, 2 per cent. nutritive salts and 68 per cent. carbohydrates, varying greatly with Loeb's analysis.

Arsen-glidin (*Arsan*) is a yellowish-gray powder insoluble in water but dissolving with a yellow color in alkalies. Arsenious acid, of which it represents about 4 per cent., is easily split off even by the action of cold water and Loeb found that by the action of artificial digestants about half of the arsenic was free within an hour. In his experiments, the preparation seemed to be less toxic than would be an equivalent amount of arsenic. It is generally administered in the form of tablets, each of which represents one thirty-second of a grain (0.002 Gm.) of arsenic.

Bromo-glidin is a brownish, odorless, almost tasteless powder, sparingly soluble in water and is used in the same manner as the inorganic bromides. The *dose* is eight to fifteen grains (0.5–1.0 Gm.). Another of these compounds is *iodo-glidin* which is recommended in *doses* of fifteen to forty-five grains (1.0–3.0 Gm.) per diem in the various conditions in which iodine has been employed. It is a dark, yellow powder, said to contain 10 per cent. of iodine, and according to Boruttan (*D. M. W.*, 1907, p. 1490) it is much more slowly absorbed than the inorganic iodides. The combination with iron is known as *ferro-glidin*. It appears in the form of tablets, each equivalent to three-quarters of a grain (0.048 Gm.) of metallic iron.

Globularia. *Globularia Alypum* Delile. *Wild*

Senna of Europe. (Fam. *Globulariaceæ.*)—This is a small shrub, growing on the European shores of the Mediterranean, the leaves of which have been occasionally used as a cathartic since the Middle Ages. Heckel and Schlagdenhauffen obtained from the leaves *globularin*, $C_{15}H_{20}O_8$, an amorphous glucoside which splits by treatment with mineral acids into glucose and *globularetin*, C_9H_6O. *Globularia vulgaris* L. was found to contain the same substances. (*J. P. C.*, 1883, 361.) It is asserted that globularin is a vasomotor constrictor which acts especially upon the renal arteries. Jaksch (*R. T.*, 1910, p. 596) has observed diminution of the quantity of urine in *diabetes insipidus*, also of *diabetes mellitus* after the administration of the glucoside. The *dose* of globularin is one-half to one grain (0.03–0.065 Gm.) daily. It does not diminish the excretion of sugar. Globularetin, a brownish-yellow powder, has also been used in medicine as a diuretic and purgative, although no definite information can be found regarding either its efficiency or its manner of use. *Dose*, of globularia, according to Planchon, one ounce (31 Gm.), in decoction.

Gloriosa. *Gloriosa superba* L.—The roots, stalk, and leaves of this climbing liliaceous plant growing in the forests of tropical Africa and extending as far East as the East Indies, are said to be an acrid narcotic poison, and not infrequently used for suicidal purposes in India. C. J. H. Warden found in them two resins, and a very poisonous bitter principle, *superbine*. (*P. J.*, xi, 496.)

Glue.—An impure form of gelatin, obtained from various animal substances by boiling them in water, straining the solution, and evaporating it until upon cooling it assumes the consistence of jelly. The soft mass which results is then divided into thin slices, which are dried in the open air. Glue, when of good quality, is hard and brittle, of a color varying from light yellow to brown, and equally transparent throughout. It softens and swells very much in cold water, without dissolving, but is readily dissolved by hot water. It is soluble in large proportion of glycerin, and with heat forms with it in smaller proportion a jelly. It is employed chiefly for cementing wood.

An elastic and imputrescible preparation of glue may be made by dissolving glue in water by means of a water bath, concentrating the solution, then adding a weight of glycerin nearly equal to that of the glue employed, thoroughly mixing, evaporating the excess of the water, and finally pouring into molds, or on a marble slab. It is especially applicable to the preparation of artificial anatomical specimens. (*J. P. C.*, 1857, 23.) The various *hectograph compositions* introduced for copying purposes are similar mixtures. One of the best copying masses is made by dissolving one part of glue or gelatin in a mixture of two parts of water and four parts of glycerin, with a few drops of phenol, heating, straining, and adding three parts of sifted whiting or terra alba. (See *N. R.*, 1879, 338, 364.) A good *liquid glue* may be made by mixing two pints of distilled water, sixteen ounces of the best white glue and four ounces of dry white lead, heating upon a water bath until homogeneous, then adding four fluidounces of alcohol, and continuing the heat and the agitation for a few minutes. The mixture is to be poured into bottles while still hot. A liquid glue may also be prepared by mixing in a stoppered bottle 38 parts of glue, properly divided, and 100 parts of 36 per cent. acetic acid. On exposure the acid evaporates, leaving the glue unchanged. (*J. P. C.*, 3e sér., xlvi, 35.) Knaff prepares *strong liquid glue* by covering three parts of good glue, in small pieces, with eight parts of water, and, after it has stood for some hours, adding half a part of hydrochloric acid and three-fourths of a part of zinc sulphate, and exposing the whole for ten or twelve hours to a heat from 81.1° to 87.2° C. (178°–189° F.). This does not gelatinize, and keeps well. For a *water proof glue* add potassium dichromate to the solution of glue just before using, in the proportion of one part to fifty. (*A. J. P.*, xliii, 420.) *Chromatized gelatin*, obtained by the addition of one part of potassium dichromate to five parts of a solution (5 or 10 per cent.) of gelatin, forms an excellent cement for glass. The surfaces to be united, after being smeared with the cement, are placed upon each other and exposed to the sun. After a few hours the adhesion is perfect and almost invisible, and boiling water itself has no action on the cement. (*L. L.*, Nov. 11, 1876.) For other formulas for liquid glue, see *A. J. P.*, xliii, 421.

Glutannin.—This is a combination of tannic acid and glutin. It has been used by Deveaux (*M. M. W.*, 1911) in the treatment of various types of *diarrhea*. It is marketed in the form of tablets each of which contains five grains (0.32 Gm.). Two or three of these tablets may be given at a *dose*.

Glutaric Acid. *Acidum Glutaricum.* $COOH.CH_2.CH_2.COOH$.—*Glutaric acid*, also called normal *pyro-tartaric acid*, forms colorless crystals, soluble in water and alcohol. It melts at 97° C. (206.6° F.) and boils above 290° (554° F.) under decomposition.

Wilenko (*D. M. W.*, 1908) found that glutaric acid diminished or caused a complete disappearance of the glycosuria caused by phloridzin. In a later communication (*Ther. Geg.*, 1909, 277) he reaches the conclusion that this action is due to an effect upon the kidneys, for he found acute parenchymatous nephritis and does not believe that the substance has any effect upon the metabolism. The *dose* which was employed ranged from one-half to one grain (0.32–0.065 Gm.) per kilo, body weight.

Glutektone.—This preparation is a semisolid jelly marketed in pencil form and contains glycerin, alpha eigon, zinc oxide, salicylic acid and ichthyol. It is employed in *eczema* and other skin ailments, rubbing the diseased surface with the pencil after moistening that surface with water.

Glutin-peptone-sublimate hydrochloride. *Mercury Peptonate* (Paal).—This is a yellow liquid containing 1 per cent. of bichloride of mercury and consisting of a double salt of mercuric chloride and glutin-peptone hydrochloride. It is soluble in water and is adapted specially for hypodermatic injection in *syphilis*. Its solutions are not permanent. *Dose*, one mil of a solution (representing 0.01 Gm., $HgCl_2$) by injection. It is asserted that twenty injections are on an average required for successful treatment.

Glutoid Capsules.—Gelatin capsules which have been hardened by exposure to formaldehyde are recommended by Sahli in several grades, the weak capsule capable of withstanding the action of the gastric juices for from one and a half to seven hours, the strong for twelve hours. They appear to have great applicability for the purpose of conveying intestinal antiseptics, medicinal substances which are destroyed by the peptic secretions, and irritating drugs, through the stomach into the intestines. They have been used by Sahli (*D. A. K. M.*, lxi) for diagnostic purposes. By their means he asserts that he is able to deter-

mine the condition of the pancreatic secretion and the closure of the pancreatic duct, the varieties of jaundice, etc. (see also p. 511).

Glutol. *Glutol* Schleich. *Glutoform.*—This is made by the action of the solution of formaldehyde upon gelatin. It is a hard, clear, transparent mass, which may be pulverized. It is claimed to be a non-irritating and non-toxic antiseptic, exerting its action only when in contact with living cells in consequence of the liberation of nascent formaldehyde, employed in the undiluted form as a dusting powder, etc.

Glycerinophosphoric Acid. *Acidum Glycerino-Phosphoricum. Glycerophosphoric Acid.* $H_2C_3H_5(OH)_2PO_4$. This is an oily liquid whose salts have been commended as powerful nerve tonics in *neurasthenia* and allied conditions. The 25 per cent. sterilized solution of the sodium salt given hypodermically, in *dose* of fifteen minims (0.9 mil), increased to one fluidrachm (3.75 mils), has been especially used in *sciatica.* The iron salt has been used in *chlorosis.* (*K. T. W.*, 198.) Several of the salts are official, see *Calcii Glycerophosphas* and *Sodii Glycerophosphas* in Part I.

Glycogenal.—This substance, which is said to be closely allied to glycogen, is obtained from the animal system and occurs as a yellowish, tasteless, odorless powder, freely soluble in water, insoluble in alcohol and ether, and has been brought forward by Roerig as a specific remedy in *tuberculosis, puerperal fever, typhoid fever,* other infectious diseases, and also in *lupus,* and even in *cancer.* Applied hypodermically it is affirmed also to cure *Basedow's disease, migraine, catarrhs,* etc. It is said that although one and one-half ounces (46.5 Gm.) may be taken daily with safety, by the mouth one-third of a grain (0.021 Gm.) given hypodermically acts powerfully and is a sufficient *dose* if administered every three hours in *typhoid fever.* The substance has probably little value. (*M. R.*, 1900, 1901, and 1907.)

Glycosal. *Monosalicylic Glycerinester.* $C_6H_4OH.COO.C_3H_5(OH)_2$.—This substance, originally prepared by E. Tauber, is a white crystalline powder, soluble (one per cent.) in cold water and freely in hot water, very soluble in alcohol, decomposed by alkalies and alkali carbonates, and also, it is said, by the intestinal juices with the separation of salicylic acid. Under the name of *antirheumol* a 20 per cent. solution of the glycerin esters of salicylic acid in glycerin and alcohol is claimed to have marked remedial effects in the treatment of *rheumatism.* A concentrated solution, 50 per cent. strength, is also marketed as antirheumol concentrated. It is used externally with thorough friction.

Glycosal has been especially recommended as affording means of treating *rheumatism* by external application. Zeigan (*B. K. W.*, 1903) found that from 50 to 100 grammes of its twenty per cent. alcoholic solution, to which a little glycerin had been added, placed upon the rheumatic part and covered with waterproof wadding, was sufficient to produce in four or five hours strong sweating lasting from a half to two hours, and in from six to eight hours a notable elimination of salicylic acid with the urine with the relief of the local symptoms. Ratz, however, has been unable to secure absorption either by means of the alcoholic solution or yet by inunctions made with an indifferent fatty basis; although when ether, oil of turpentine, or chloroform was added in the proportion of fifteen per cent. to the ointment, a notable proportion of salicylic acid appears in the urine after the local application. R. Block (*Th. M.*, Sept., 1903) found that the best method of using glycosal is a twenty per cent. collodion, which he applied every two to four hours to swollen rheumatic joints with asserted most extraordinary results. He claimed that if no relief is afforded the inflammation may be positively considered not to be of rheumatic origin.

Glycosal is also used internally as an antirheumatic in *doses* of one hundred and fifty to one hundred and eighty grains (9.8–11.6 Gm.) a day, usually without the production of salicylism; eight to ten grains (0.5 to 0.65 Gm.) may be given every half to three hours until sweating is induced. The remedy is probably uncertain and feeble in its influence.

Glycotauro. *N. N. R.* 1917.—Under this name a proprietary preparation of bile salts freed from bile pigment and standardized to contain 50 per cent. of the natural mixture of sodium glycocholate and sodium taurocholate. Each gramme represents about 10 mils of fresh ox bile. (See *Extractum Fellis Bovis,* Part I.)

Glycozone.—A proprietary preparation claiming to possess antiseptic properties which has been found to consist essentially of 5 per cent. glyceric acid, 90 per cent. glycerin with a small proportion of water, and to contain no hydrogen or other peroxides or any ozones.

Gnaphalium. *Gnaphalium margaritaceum* L. (More correctly *Anaphalis margaritacea* (L.) Benth. and Hook.) *Cudweed. Life-everlasting. Pied de Chat, Immortelle,* Fr. *Katzenpfötchen, Immerschön,* G. (Fam. *Compositæ.*)—An indigenous herbaceous perennial, which with *G. obtusifolium* L. (*G. polycephalum* Michx.), or *sweet-scented life-everlasting,* is sometimes used in the form of tea in intestinal and pulmonary *catarrhs,* and, externally, in the way of fomentation, in *bruises,* but it probably possesses little medicinal virtue. In Europe different species of *Gnaphalium* are occasionally employed for similar purposes.

Gold.—The chief preparations of gold which have been employed in medicine are metallic gold in a finely divided state, the oxide (trioxide, incorrectly called *auric acid*), the chloride (trichloride), the iodide, the double gold and sodium chloride now official, the ammonium chloraurate (a compound of gold trichloride and ammonium chloride), and gold cyanide. Aqueous solutions of gold in the *colloidal* state have been prepared by Bredig by forming an electric arc under water with gold wires. The sparking between gold electrodes liberates finely divided gold which dissolves with bluish-red color. The addition of acids and certain salts coagulates this colloidal gold solution; the addition of gelatine prevents this coagulation. *Gold in powder* may be obtained by rubbing up gold leaf with ten or twelve times its weight of potassium sulphate until brilliant particles are no longer visible, and then dissolving away the sulphate with boiling water. The *chloride* is obtained by dissolving pure gold in three times its weight of nitrohydrochloric acid, with the aid of moderate heat. The solution is evaporated by a gentle heat nearly to dryness, being at the same time stirred with a glass rod. It is in the form of a crystalline mass of a deep red color. Its solution has a fine yellow tint. Being deliquescent, it requires to be kept in ground-stoppered bottles. (See *Auri et Sodii Chloridum.*) The *iodide* may be made by precipitating a solution of gold trichloride by one of potassium iodide, and washing the precipitate with alcohol to remove the excess of iodine. It is of a greenish-yellow color, and,

when heated in a porcelain crucible, is resolved into iodine vapors and a residue of pure gold. The *ammonium chloraurate* is formed by dissolving one part of the gold trichloride and two parts of ammonium chloride in distilled water, assisted by a few drops of nitrohydrochloric acid, and evaporating the solution to dryness by a gentle heat. The *cyanide* is best obtained, according to Oscar Figuier, as follows: Prepare the gold chloride as neutral as possible by repeated solutions and crystallizations; and to the solution of this salt add, very cautiously, avoiding any excess, a solution of *pure* potassium cyanide, so long as any precipitate falls. The precipitate, consisting of gold cyanide, is to be washed with pure water, and dried in the dark. According to Behring *gold and potassium cyanide* is an extraordinarily active antibacterial, one part in one million being sufficient to inhibit growth. Bruck and Glück (*M. M. W.*, 1913, p. 57) assert that sufficient of this salt may be introduced into the blood stream to exercise an antiseptic influence in the system and have used successfully intravenous injections in the treatment of *lupus*. They employed doses of from one-half to three-quarters of a grain (0.03 to 0.05 Gm.) two or three times a week. In a similar way it has also been used in *syphilis* and in *pulmonary tuberculosis*. Hauck (*M. M. W.*, 1913, p. 1824), however, reports a fatal case from the treatment which he attributed to gold poisoning.

The preparations of gold are decidedly poisonous, though in different degrees. The chloride is most virulent, and, according to Chrestien, is even more active than corrosive sublimate. In an overdose, it produces pain, inflammation, and even ulceration of the stomach and bowels and otherwise acts as a corrosive poison. It is said that these preparations, in moderate doses, produce increased fulness and frequency of the pulse, and augment the urine and insensible perspiration, without interfering with the appetite or the regular action of the bowels, but, if the dose be pushed too far, general irritation is apt to be produced, inflammation seizes upon some organ, according to the predisposition of the individual, and fever is developed.

Gold in powder, the oxide, chloride, and iodide are not as much used as the soluble gold and sodium chloride. The oxide may be given in the form of pill, containing the tenth of a grain (0.006 Gm.), in *scrofula* and *lymphatic swellings*, beginning with one pill daily, and afterwards gradually increasing to seven or eight in twenty-four hours. The chloride has been used with advantage as a caustic in *lupus*, and in *syphilitic tubercles* and *ulcers*, by Chavannes. The iodide may be given in the same cases with the other preparations. The *dose* is from one-fifteenth to one-tenth of a grain (0.004–0.006 Gm.).

In 1889 Goubert asserted before the French Academy that *gold bromide*, administered in a weak solution, is more efficacious and durable in its action in *epilepsy* than are any of the other bromides, and is also better tolerated. This statement led Shtcherbak to study the effect of the gold bromide upon the motor area of the cerebral cortex, according to the method of Albertoni. He found that in the dose of from one-half to three grains per kilogramme of weight it so depressed the cortical motor centers that even the strongest electric stimulation failed to bring about any epileptic seizures. It is further asserted that the gold bromide never causes in man general depression, languor, emaciation, or other pronounced symptoms of bromism. The amount of bromine in the bromide, 55 per cent. by weight, would seem too small to make it probable that the bromine is the active ingredient of the salt. The *dose* of the bromide for the adult is from one-eighth to one-fifth grain (0.008–0.012 Gm.); for children, one-twentieth to one-tenth grain (0.003–0.006 Gm.). As a substitute for this preparation, E. Merck has proposed *gold* and *potassium bromide* (*Aurum-Kalium bromatum*, $AuBr_3.KBr+2H_2O$), which has been tested by I. Jankura and Laufenauer (*Pest. M d. Chirurg. Presse*, 1892), and found to be a valuable anti-epileptic. It may be used hypodermically, by dissolving 2 parts of the salt in 100 parts of distilled water, and injecting of this eight minims (0.5 mil) and increasing the dose to thirty-two minims (2 mils). Solutions of gold pentabromide or pentachloride, recognized by their deep red color, are offered by several manufacturers under proprietary names, and advertised to produce remarkable effects in *anemia*, *diabetes*, and in various dyscrasias. *Solution of gold and arsenic bromide* is official in the National Formulary IV under the name of *Liquor Auri et Arseni Bromidi*, the dose is given as three minims (0.2 mil).

Ammonium chloraurate has been recommended by Bouchardat in *amenorrhea* and *dysmenorrhea* in debilitated subjects, in the *dose* of about the tenth of a grain (0.006 Gm.). A grain may be dissolved in five teaspoonfuls of alcohol and five of water, and a teaspoonful given morning and evening, mixed with sweetened water.

Gold cyanide is employed, like gold and sodium chloride, mixed with inert powders by friction, and in the form of pill. One-fifteenth of a grain (0.004 Gm.) may be rubbed into the gums daily for fifteen days, next, the fourteenth of a grain for fourteen days, and so on, increasing until the dose amounts to the ninth or eighth of a grain (0.0075 or 0.008 Gm.). The *dose* for internal exhibition is one-eighteenth of a grain, gradually increased to one-eighth (0.0038–0.008 Gm.). Gold cyanide has been found useful in the treatment of *syphilis* and *scrofula* by Pourché, and is said to be less irritating than the double chloride.

The different medicinal compounds of gold should not be prepared in pill, powder, or otherwise until they are wanted for use, as they are liable to undergo decomposition when kept. They should be carefully secluded from the light.

Gold salts of various alkaloids have been prepared by H. A. D. Jowett. (*Trans. Chem. Soc.*, 1897.)

Gomabrea.—This is an exudation from a Chilian tree, which has been offered in large quantities in France as a substitute for gum arabic, and is said to be of practical value.

Gratiola. *Gratiola officinalis* L. *Hedge-hyssop. Gratiole*, Fr. *Gnadenkraut, Gottesgnadenkraut*, G. (Fam. *Scrophulariaceæ*.)—This is a perennial herb, indigenous in the south of Europe, in meadows and other moist grounds. The whole herb is used. It is nearly inodorous, but has a bitter nauseous taste. The indigenous *G. virginiana* L. closely resembles the European plant and indeed was regarded by Michaux as identical with it. Both water and alcohol extract its active properties. F. G. Walz found in it the following constituents: 1, *gratiolin;* 2, *gratiosolin;* 3, *gratioloic acid;* 4, *gratiola fat; and* 5, a brown resin. For chemistry, see *P. J.*, lxix, 295, and lxx, 385. The gratiolin is decomposed on prolonged boiling with diluted H_2SO_4 into *gratioletin, gratiolaretin*, and sugar; the gratiosolin is similarly decomposed by dilute acids or alkalies into

gratiosoletin and sugar; the gratioloic acid is obtained in the form of pearly white scales of a fatty odor. Hedge-hyssop is a drastic cathartic and emetic, possessing also diuretic properties, and has been used in Europe for the relief of *dropsy, jaundice, worms, chronic hepatic affections,* and *scrofula.* The *dose* of the powdered herb is from fifteen to thirty grains (1.0–2.0 Gm.); of the infusion (half an ounce to the pint of boiling water), half a fluidounce (15 mils).

Ground Nuts. *Peanuts. Earth nuts. Goobernuts.*—The fruit of *Arachis hypogæa* L., a leguminous, annual plant, indigenous probably in Africa and South America and abundantly cultivated in our Southern States, China, etc. Recent government statistics show that about 16,000,000 bushels are produced annually in the United States, and about 29,000,000 bushels imported. There has, however, been a great increase in the domestic production in the last year or two, and the American crop will probably be much larger in the near future.

A remarkable property of the plant is that its fruit ripens under the surface of the ground, into which the pods penetrate after flowering, until the young fruit is completely buried under the soil in the progress of their growth. The kernels or seeds contain about 45 per cent. of a fixed oil. (See *Oleum Arachis,* Part I.)

Guaco.—This name is given in Central and South America and the West Indies to various plants belonging to the genera *Willughbœa* (better known under the newer name, *Mikania*) and *Aristolochia;* but it is in its application to the different species of the former genus that the drug is known in medicine. The species most used is *W. amara* (Willd.) O. Kze. (*Mikania amara* Willd.), and *M. Guaco,* genus Eupatorium, Humb. and Bonpl. Plants closely allied to the *M. Houstonis* (Willd.) O. Kze.—as *M. gonoclada* (DC.) O. Kze. (of the Fam. *Compositæ*); *Aristolochia fragrantissima* Ruiz., *A. grandiflora* Sw., *A. pentanara* Jacq. (of the Fam. *Aristolochiaceæ*); *Comocladia integrifolia* Jacq. (Fam. *Anacardiaceæ*)—are also known locally as guaco. *M. amara* is described as having twining stems, with round, sulcate, and hairy branches; ovate subacuminate, remotely dentate leaves, somewhat narrowed at the base, rough above and hairy beneath, and flowers in opposite axillary corymbs. The plant is a native of tropical America, and has been introduced into the West Indian Islands from the continent. The leaves are the part used. The result of a long and close investigation into the natural history of guaco by Guibourt is, that the guaco from this source, instead of possessing, as has been asserted, a strong, penetrating, and nauseous odor, is in fact inodorous, and destitute of all active properties, and that the strongly aromatic plants which have been employed under the name of guaco all belong to the genus *Aristolochia,* especially *A. cymbifera* Mart. and Zucc., growing in Brazil, after this *A. maxima* (DC.), and in less degree *A. maxima* Jacq. (*A. geminiflora* H. B. K.). (*J. P. C.,* 1867, 99.)

Although the guacos of South America seem to be entirely distinct drugs they appear to be indiscriminately used by the natives for the cure of the *bites of poisonous serpents.* The medicine is also used in South America as a febrifuge and anthelmintic, and has been considered antisyphilitic. A few years ago it attracted on the continent of Europe considerable attention on account of its alleged power in *epidemic cholera* and *chronic diarrhea.* The *Aristolochia cymbifera* Mart. and Zucc. has been the subject of a careful study by L. Butte. (*Annales de la Policlin, de Paris,* Sept., 1890.) The root of this plant as it occurs in commerce is cylindrical, from three to four centimeters in diameter, much broken up into long rootlets, yellowish, with a strong odor, especially in the bark. The plant itself is a vine, growing in great abundance in the province of Tabasco in Mexico. Butte was not able to find in it either an alkaloid or a glucoside, but he found a blackish resin which may be the active principle of the plant, though this does not seem probable, since Butte found the alcohol extract much less active than the aqueous extract, which would hardly be the case if the resin were really the active principle. In the physiological experiments made with the aqueous extract it was found that massive doses produced cries and excitement, followed after a time by sleep, with muscular relaxation and symptoms of gastro-intestinal irritation. There was also depression of the nerve center, both sensory and motor. If the dose were sufficient death was produced by an arrest of the respiration. The heart continued to beat after the cessation of respiration; nevertheless there was depression of the arterial pressure, apparently due to the action of the drug upon the heart. After death marked signs of irritation of the gastro-intestinal tract and kidneys were found. Butte believes that guaco has valuable therapeutic properties in the treatment of skin affections, especially *eczema* and *pruriginous maladies,* in which he used it both locally and internally. He gives the *dose* of the aqueous extract of guaco as three grains (0.2 Gm.) three times a day. In the external application the following formula was used. Guaco (bruised), 30 parts; sodium bicarbonate, 5 parts; water, 1000 parts; boil for a quarter of an hour, allow to macerate one hour, decant, and use the liquid as a lotion. Guaco is said to be largely used in South America as an antirheumatic and E. W. Pritchard (*P. J.,* 1861) affirms that in the *gouty paroxysms* it is especially effective given in the *dose* of a fluidrachm (3.75 mils) of the tincture every four hours, and applied locally.

Guaiacetin. *Sodium pyrocatechin monoacetate,* $C_6H_4.(OH).OCH_2.COONa$, has been used in the treatment of *tuberculosis* and *chronic bronchitis* and is especially recommended for children. It is marketed in the form of tablets, each containing eight grains (0.5 Gm.) of which one to three may be given to an adult at a *dose.*

Guaiacol Compounds and Derivatives.—A very large number of these compounds have been produced by pharmaceutical chemists and put upon the market as substitutes for and improvements on ordinary guaiacol. Few of them have any more are less effective. The advantages claimed for these compounds are lower toxicity, especially lack of irritant effects on the mucous membrane of the stomach. In regard to their manufacture we refer the reader to elaborate papers by F. G. Ehlert (*Ph. Rev.,* 1901 and 1902).

Guaiacol Albuminate. Histosan.—It is claimed for this compound that in the treatment of *tuberculosis* it not only acts as a stimulant expectorant, but improves the appetite and by preventing intestinal putrefaction leads to better digestion and assimilation. According to Huhs (*Ther. Geg.,* 1907, 313), while of service it is not superior to other creosote preparations.

The *dose* is eight to twelve grains (0.5–0.75 Gm.) three times a day.

Guacamphol. $C_8H_{14}.(COOC_6H_4O.CH_3)_2$.—This *camphoric ester of guaiacol* is a white, tasteless, insoluble powder, which is asserted to be broken up in the intestines into camphoric acid and guaiacol. It has been especially recommended as a remedy of great value in the treatment of the *night sweats of phthisis.* In some cases it is necessary to be administered for one or even two weeks for the desired effect. *Dose,* three to fifteen grains (0.2–1 Gm.) exhibited two hours before bed time.

Guaiacodeine. Codeine-ortho-guaiacol-sulphonate.—A preparation exhibiting mainly the action of codeine, as the proportion of guaiacol is too small to be of benefit. *Dose,* one-fourth to one grain (0.015–0.06 Gm.).

Guaiacol Benzyl Ester, Pyrocain, Brenzcain, $OCH_3.C_6H_4.OCH_2.C_6H_5$, occurs in colorless crystals, soluble in ether and melting at 62° C. (143.6° F.). It possesses the general therapeutic properties of guaiacol, but is less caustic. It is not to be confused with Benzosol (guaiacol benzoate). (See p. 1276.)

Guaiacol Biniodide, a reddish-brown powder, with something of the iodine odor, soluble in alcohol and fatty oils, has been proposed by Vicario as a local application in *tuberculosis.*

Guaiacodyl. Guaiacol Cacodylate. Cacodyliacol. $As(CH_3)_2O_2(C_6H_4OCH_3)$.—Reddish-white crystals soluble in water, alcohol or glycerin. It is used in the treatment of *phthisis* by subcutaneous injection in an oily mixture. *Dose,* one-half to one grain (0.03–0.065 Gm.)

Guaiacol Cinnamate or *Styracol, N. N. R.* 1917, $C_6H_5CH:CH.COO(C_6H_4OCH_3)$, the cinnamic acid ester of guaiacol, occurs in white, odorless, tasteless, stable needles, almost insoluble in water, readily soluble in alcohol, chloroform, acetone and benzene. They fuze at 130° C. (266° F.). It is said when taken internally to be broken up in the intestines into cinnamic acid and guaiacol and to be useful not only in *phthisis* but in various chronic *gastro-intestinal* and *genito-urinary catarrhs. Dose,* fifteen grains (1 Gm.), three or four times a day.

Guaiacol Ethyl, $C_6H_4OC_2H_5OH$, *Pyrocatechin Monoethyl Ether, Guethol, Thanatol, Guæthol* (Merck), is an oily liquid of an agreeable aromatic odor, soluble in water, which was brought forward as a remedy in *tuberculosis,* with the statement that it acts upon the human system like guaiacol, but more quickly and energetically. The researches of De Buck (*Belg. Méd.,* 1897) indicate, however, that it is not more effective than is guaiacol in tubercular diseases. It is affirmed, however, to be a pronounced analgesic, which when applied to the skin by means of a brush is rapidly absorbed, and in cases of *neuralgia* or *neuritis* produces great relief. It may also be used subcutaneously in 10 per cent. emulsions with sterilized glycerin, and has been so applied; the glycerin solution has also been used in *cystitis.*

Guaiacol Ethylene. Guaiacolum Aethylenatum $(CH_3O.C_6H_4O)C_2H_4(OC_6H_4.OCH_3)$.—Colorless crystals which dissolve in alcohol, but with difficulty in water, and melting at 138° to 139° C. (280.4°–282.2° F.). It is used like other guaiacol derivatives in the treatment of *phthisis. Dose,* eight to fifteen grains (0.5–1 Gm.).

Guaiacol Iodide.—The *para-iod-guaiacol* occurs as colorless crystals difficultly soluble in cold water but readily soluble in alcohol and the fixed oils. It is asserted that this preparation passes through the stomach unchanged and without irritation and in the intestinal juice is split up, liberating guaiacol and iodine. Beneficial results have been observed from it in *chronic arthritis* but in acute conditions it is of little value. It has also been employed in *pulmonary tuberculosis* but without decided benefit.

Guaiacol Iodoform is a reddish-brown syrupy liquid, which is really a solution of iodoform in guaiacol. It has been used, hypodermically injected into the supraspinal fossa, for *tuberculosis.* Fifty minims (3.1 mils) of a dilution of one part with sixteen parts of olive oil may be injected at a *dose.*

Guaiacol Methylglycolate. Monotal. N. N. R. 1917. *The Methyl-glycolic Acid Ester of Guaiacol.* $CH_2(OCH_3)COO(C_6H_4OCH_3)$.—A colorless, oily liquid, slightly aromatic, almost insoluble in water, soluble in alcohol and immiscible solvents. It is readily absorbed through the skin and is employed not only for its local anesthetic properties in various painful conditions, but to obtain the systemic effects of guaiacol through endermic administration. It is said to produce the effects of guaiacol without its toxic properties. Externally applied in *doses* of one-half to one fluidrachm (2–4 mils).

Guaiacol Phosphate. Phosphoric Guaiacol-ether. Biogaicol. $(C_6H_4O.CH_3O)_3PO$.—A white, crystalline powder has been shown by A. Gilbert (*S. M.,* 1897) to be split up in the intestines, with the liberation of its constituents, and to afford, therefore, a method of administering guaiacol, over which it has the advantage of being innocuous to the mucous membrane of the stomach. It would appear, however, much less active and much more uncertain in its influence than is guaiacol. *Dose,* one to three grains (0.06–0.2 Gm.).

Guaiacol Phosphite. Phoso-Guaiacol. $P(OC_6H_4OCH_3)_3$. *Phospho-guaiacol. Guaiacophosphal.*—*Phosphite of Guaiacyl-ether* is a white, crystalline powder, possessing a sharp taste and indifferent odor. It is soluble in water, dissolves very freely in alcohol, ether, chloroform, acetone, benzene, toluol, and the fatty oils, but it is sparingly soluble in oil of turpentine and in glycerin. Melting point 77.5° C. (171.5° F.). It contains 92.25 per cent. of guaiacol, and was introduced in 1897 by Ballard. (*Rép. de Pharm.,* 1897.) It is but slightly poisonous, and probably is capable of acting as do other preparations of guaiacol. *Dose,* three to fifteen grains (0.2–1.0 Gm.).

Guaiacol Salol. Guaiacol Salicylate. N. N. R. 1916. $C_6H_4OHCOO(C_6H_4OCH_3)$.—A compound closely related to phenyl salicylate (salol) which occurs in small odorless, tasteless, colorless crystals, readily soluble in alcohol, ether, chloroform or benzene, melting at 65° C. (149° F.). It is said to be split up into its constituents in the intestines and has been used in *phthisis* and as an *intestinal antiseptic. Dose,* ten to fifteen grains (0.65–1.0 Gm.).

Guaiacol Succinate. $(C_6H_4OCH_3)_2C_4H_4O_4$.—This drug occurs in fine, silky, white crystals insoluble in water, slightly so in alcohol and ether, very soluble in chloroform or acetone, and melting at 136° C. (276.8° F.). It is said to act medicinally like guaiacol.

Guaiacol Valerate. Geosote. $C_6H_4OCH_3O.COC_4H_9$.—This occurs as a pale yellow, oily, mobile liquid, insoluble in water, freely soluble in alcohol, ether, and benzene. Sp. gr. 1.038, boiling point variously given from 240° to 260° C. (464°–500° F.). Geosote is used in *phthisis* and as a gastro-intestinal antiseptic in fermentative *dyspepsia* and *diarrhea. Dose,* five to ten grains (0.32–0.65 Gm.).

Guaiaform. Geoform. Methylenediguaiacol. Pulmoform.—The drug is a tasteless yellow powder, odorless at first but acquiring a vanilla-like odor, soluble in alcohol or ether but insoluble in water. It is affirmed to contain 95.38 per cent. of guaiacol and to be non-irritating and non-toxic. *Dose,* five to fifteen grains (0.3–1 Gm.).

Guaiaconic Acid. *Acidum Guaiaconicum.* $C_{20}H_{24}O_5$.—This is a resinous acid obtained from guaiac resin; it is an amorphous, brown powder soluble in alcohol. This body has been shown by Hadelich and Schaer to be the agent which produces the well-known blue color in the guaiac test for blood. (*A. Pharm.*, 1898, 236). It has been used as a substitute for guaiac for this purpose. According to Doebner (*A. Pharm.*, 1896, 619), a solution of 0.1 Gm. in 40 Gm. of 50 per cent. alcohol may be used. This should always be freshly prepared.

Guaiacyl. *Gajacyl. Calcium Ortho-guaiacol Sulphonate.* $(C_6H_3(OH).(OCH_3)SO_3)_2.Ca$.—This is a powder of a bluish-gray color, soluble in water and in alcohol. The aqueous five per cent. solution has a violet-red color and may be used hypodermically in quantities of eight to twenty minims (0.5–1.3 mils). *Guaiacyl* has also been used as a local anesthetic in 5 to 10 per cent. solution.

Guaialin. *Methylene Diguaiacol Benzoic Ester.*—This substance occurs in an amorphous powder, of a pea-green color, said to contain 60 per cent. of guaiacol, 30 per cent. of benzoic acid, and 7 per cent. of formaldehyde. It is recommended as an antipyretic and alterative tonic in *tuberculosis.*

Guaiaperol. *Piperidin Guaiacolate.*—This salt occurs in colorless crystals, melting at 79°–80° C. (174.2°–176° F.), having a feeble creosote odor, soluble in water 1 to 30, freely soluble in alcohol, and has been used to a moderate extent. (*B. M. J.*, vol. ii, 1898.) In *doses* of from five to ten grains (0.32–0.65 Gm.) in capsules, three times a day, after meals, in *phthisis* it is said to lessen cough and cause general improvement.

Guaiaquin. *Quinine Guaiacol Bisulphonate.* $C_6H_4O_2CH_3HSO_3$ $C_{20}H_{24}N_2O_2$.—This substance occurs as a yellowish crystalline bitter powder, very soluble in water, alcohol and diluted acids. It represents about 45 per cent. of quinine and 34 per cent. of guaiacol. It has been used to some extent in internal medicine as a tonic, but especially as an antiperiodic in various *malarial diseases* with asserted good results. It is stated that the sterilized 10 per cent. solution may be given hypodermically with the production of little pain. This solution has also been used locally with alleged good results in *gonorrhea* and other infected conditions. *Dose,* three to ten grains (0.2–0.65 Gm.); sixty grains (3.9 Gm.) may be given in a day.

Guaiaquinol. $C_{20}H_{24}N_2O_2.2HBrC_6H_4OHOCH_3$. *Guaiakinol. Quinine Dibromoguaiacolate.*—This is a compound which combines the properties of quinine, guaiacol, and bromine. It is freely soluble in water and is used as an antipyretic and sedative in *tuberculosis. Dose,* eight to fifteen grains (0.5–1.0 Gm.).

Guaiasanol. *Gujasanol. Diethyl-glycocollguaiacol Hydrochloride.*

$$C_6H_4 < \begin{matrix} OCH_3 \\ O.CO.CH_2N.(C_2H_5)_2.HCl \end{matrix}$$

This substance occurs in very soluble white prisms fusing at 184° C. (363.2° F.), emitting an odor faintly suggestive of guaiacol and possessing an acrid taste. It was first produced by Einhorn and Hutz (*J. P. C.*, 1903, 174) through the union of aceticomonochlorguaiacol and diethylamine. In the presence of alkalies it breaks up, liberating guaiacol, which has been found in the urine of animals to which it had been given. Guaiasanol was introduced as a substitute for guaiacol, especially in the treatment of *pulmonary catarrhs.* Rahn (*M. M. W.*, 1905, p. 783) has also found the injection of a 2 to 4 per cent. solution a valuable treatment for *seat worms.* It has been given in *doses* of forty-five to one hundred and eighty-five grains (3–12 Gm.) daily.

Guajamar. *N. N. R.* 1917. *Guaiamar. Guaiacol-glyceryl Ester.*—This is a white crystalline powder,

$$C_6H_4 < \begin{matrix} OCH_3 \\ OC_3H_7O_2 \end{matrix}$$

, which possesses a bitter aromatic taste, melts at 75° C. (167° F.) and dissolves in alcohol, ether, glycerin or 20 parts of water at the ordinary temperature. According to G. Buttler, it splits up in the intestines into guaiacol and glycerin and affords an excellent method of intestinal antisepsis in *typhoid fever, diarrhea,* etc. Great relief has been obtained in *acute* and *articular rheumatism* by the local application of the remedy in the form of an ointment consisting of two parts of *guajamar* and one of lanolin. *Dose,* three to fifteen grains (0.2–1 Gm.).

Guano. *Bird-manure.*—A fertilizing excrement formerly found on many small islands in the southern ocean on the western coast of Africa and also near the Peruvian Coast of South America, but exhausted many years ago for agricultural purposes. These islands were the resorts of large flocks of sea birds and are largely composed of the excrement in a decomposed state. The beds of deposited excrement were sometimes 50 or 60 feet in depth. It constituted an excellent manure and was used for upward of a century for that purpose. It consisted of phosphates together with much ammonium urate and ammonium oxalate, and some peculiar nitrogenous bases. *Guano* is a powerful local irritant, which, when mixed with equal parts of potters' clay or other diluent, is capable of causing vesication. It has been used as a counter-irritant and also as a stimulant in certain *cutaneous diseases,* especially in *eczema, ecthyma,* and *tinea capitis.* For various preparations of guano, see 16th ed., *U. S. D.*

Guatannin.—*Guaiacol tanno-cinnamylate* is a fine powder, insoluble in water and most other solvents. It is soluble in alkalies giving an orange-colored solution, from which it can be reprecipitated with acids. It is employed in the treatment of *bronchial catarrh* in *doses* of three-fourths to one grain (0.048–0.065 Gm.).

Guayarsin.—A combination of guaiacol and arsenous oxide, usually administered in syrup form, ten grammes of which contain 0.005 arsenic and 0.2 Gm. guaiacol in combination with calcium chlorhydrophosphate and cinnamic acid.

Gum Cebil.—This gum is a product of the Brazilian leguminous tree *Piptadenia Cebil* Griseb. It occurs in reddish-yellow tears, or in dark-colored angular masses, and forms a reddish-yellow, odorless, viscous mucilage of acid reaction. It is said to contain 80.78 per cent. of arabin.

Gum, Cedar.—This, the product from *Cedrela Toona* Roxb. (*C. australis* F. Muell.), or *Red Cedar* of Queensland (Fam. *Meliaceæ*), is a very pale yellow or brownish gum, occurring in tears about 2.5 cm. long, having an astringent taste, swelling and, finally, almost dissolving in water. It contains about 68 per cent. of arabin, and 6 per cent. of metarabin, but no resin. (*P. J.*, vol. xx, 1890.)

Gum, Grass-tree. *Yellow Resin. Botany Bay Gum. Resina Acaroides. Yellow Acaroid Resin. Earth Shellac.*—An Australian product, occurring as an exudation upon the stems of *Xanthorrhœa hastilis* R. Br. (Fam. *Liliaceæ*.) It is of a resinous character, usually is found in the markets in the state of small fragments or coarse powder, resulting from the breaking up of the larger brittle masses in which it first occurs. It is of a deep reddish-yellow color in mass, but greenish-yellow in powder. It does not dissolve in the mouth when chewed, nor adhere to the teeth, but has a slightly astringent and aromatic flavor. It melts with heat, and at a higher temperature takes fire in the air, burning with a smoky flame, and emitting a fragrant odor not unlike that of balsam of Tolu. It yields picric acid largely under the action of nitric acid. The natives and early settlers employed it as a medicine in *diarrhea*. It is said to be used extensively, instead of shellac, as a resinous glaze for confectionery and also in cabinet work, but to be distinctly inferior. For much interesting information concerning it and other resinous products of the genus *Xanthorrhœa*, see paper by J. H. Maiden, *P. J.*, 1891, xxi. It is obtainable in inexhaustible quantities as the plants producing it are abundant throughout almost the whole of Australia. (*A. J. P.*, 1866, 465.) Three hundred tons of the resin of *X. hastilis* have been exported in one year, and at one time the price rose to £65 per ton for the best quality, but for ordinary quality it is from £7 to £10. (*A. J. P.*, 1885, 405.) (See article on *Xanthorrhœa Resins*.)

Gum Hogg. *Hog-Gum. Kuteera Gum.*—Under the name of *gum-hogg* a peculiar gum is much used in marbling paper. A full discussion of it may be found in the 14th edition of the U. S. D., but, as it appears to be only a variety of Bassora gum, and rarely found in commerce, we omit any further account of it.

Gum, Indian. *Ghatti Gum.*—Under the name of *Gummi Indicum* the Br. recognizes the gummy exudation from the wood of *Anogeissus latifolia*. (See p. 541.) The forests of India produce large quantities of other gums, a number of which have found their way into commerce and are used to a considerable extent as substitutes for gum arabic and gum tragacanth. *Indian gum* occurs in yellowish-white tears having a vitreous fracture. It is entirely soluble in water, forming a thick mucilage.

Of the other "so-called" Indian gums, that yielded by *Prosopis spicigera* L. (Fam. *Leguminosæ*) occurs in small, angular, yellowish fragments, or sometimes in large ovoid tears 5 cm. long, of an amber color, frosted externally with fissures. It forms with water a dark-colored tasteless mucilage and resembles in its behavior to reagents the *Mezquite gum*. The gum of *Feronia elephantum* Corr. (Fam. *Rutaceæ*) is in small, irregular tears varying from reddish-brown to pale yellow and forms a thick, tasteless, colorless mucilage which resembles gum arabic, but is precipitated by neutralized lead acetate and gelatinized by ferric chloride, although unaffected by borax. The most important of the Indian gums is that which is recognized in the Br. Pharmacopœia, and which in its solubility and relation to reagents closely resembles gum arabic. This is the product of *Anogeissus Latifolia* above referred to. It has double the viscosity of gum arabic and forms with water a colorless mucilage having a faint characteristic odor. It is well suited for pharmaceutical use, and is said to be specially valuable in the making of emulsions. It is insoluble in 90 per cent. alcohol. For further description of the properties of this gum see *Gummi Indicum*, p. 541.

The Br. Pharmacopœia allows of the substitution of Indian gum in official preparations in place of gum acacia, with the statement that one part of it should be substituted for two of the acacia. The *mucilage of Indian gum* (*Mucilago Gummi Indici*, Br., 1914) is made with two avoirdupois ounces of gum to six fluidounces of distilled water. See also *Gum Sterculia*, p. 1418.

Gum Kauri.—This is an amber-like substance, varying from a soft cream-white to an amber color, dug in large quantities from the soil of Australia and New Zealand. It is a resinous exudation from the Kauri Spruce, *Agathis australis* Salisb. (*Dammaris australis* Lamb.), of the Fam. *Coniferæ*, but, as it first exudes and is found on the surface of the ground, it is not esteemed. According to Tschirch and Niederstadt, it contains *kaurinic acid*, $C_{10}H_{16}O_2$, 1.5 per cent.; *α- and β-kaurolic acids*, $C_{12}H_{20}O_2$, 48 to 50 per cent.; *kaurinolic acid*, $C_{17}H_{34}O_2$, and *kauronolic acid*, $C_{12}H_{24}O_2$, together, 20 to 22 per cent. All these resin acids are soluble in solution of sodium hydroxide. *Baume Calédonien* consists of a solution of *kauri gum* in an equal weight of 90 per cent. alcohol. It has been used with alleged great success in the treatment of *wounds* and *ulcers*, of *eczema* and other skin affections, and as a substitute for collodion and the soluble sodium silicate. When applied to a well cleansed and dried wound it leaves a slight deposit of resin as a varnish, which is not affected by friction or contact with water.

The commercial product known as *Manila copal*, according to Tschirch and Koch, is derived from *Agathis Dammara* Rich. (*Dammara orientalis* Lamb.), a conifer. It consists chiefly of free amorphous resin acids, namely, *alpha-* and *beta-mancophalolic acid*, $C_{10}H_{18}O_2$ (about eighty per cent.), and contains besides about 12 per cent. of a resin, $C_{20}H_{32}O_2$, and about five per cent. of essential oil. The latter, when fresh, forms a liquid as clear as water, very mobile, having a pleasant odor, and the sp. gr. 0.840; it boils at from 165° to 170° C. (329°–338° F.), and mixes in all proportions with alcohol, ether, chloroform and fatty oils. See also the article on *Copal*.

Gum Mango.—This gum, which is obtained from the mango tree, *Mangifera indica* L. (Fam. *Anacardiaceæ*), occurs in the Indian bazars in amber-colored or reddish-yellow lumps, almost transparent, with a brilliant conchoidal fracture, 39.4 per cent. of which is soluble in water. (See *J. P. C.*, xix, 584.)

Gum Mesquite. *Mesquite Gum. Gum Mezquite.*—This is the product of *Prosopis juliflora* DC., and perhaps other species of the same genus. Mesquite is a small, thorny, acacia-like tree or shrub belonging to the Fam. *Leguminosæ*, and growing in New Mexico, Texas, and other neighboring regions, where it covers vast extents of country. The fruit is a long, compressed pod, filled with a sweet pulp, which is said to contain 30 per cent. of grape sugar, and to be used by the Indians as a food. A gum exudes from the stem and branches. It occurs in irregular, roundish pieces, of various sizes and usually of a dark amber-brown color, though sometimes, especially when gathered from young trees, it is nearly colorless. Procter found it to resemble gum arabic in its solubilities, but to differ essentially in not being precipitated by

lead subacetate, and in its strong solution not being coagulated by borax. (*A. J. P.*, xxvii, 224.) Campbell Morfit found in it a very little bassorin (0.206 per cent.), which did not exist in the specimens examined by Procter. (*Am. J. Sci.*, March, 1855, 264.) See also *A. J. P.*, 1855, 542, for a brief description of the gum and its character.

The saccharine pods of *Prosopis odorata* Torr. and Frem. (*P. pubescens* Benth.) are largely employed as food by the Indians, and those of all the species form valuable fodder for cattle.

Gum Sassa. *Sassa Gum.*—This name has been applied by Guibourt to a gum, occasionally brought into commerce from the East. It is produced by a tree growing in Abyssinia, *Albizzia Fastigiata* Oliv. (Fam. *Leguminosæ*). According to Guibourt's description, it is in mammillary masses, or in convoluted pieces resembling an ammonite, of a reddish color and somewhat shining surface, and more transparent than tragacanth. Its taste is like that of tragacanth, but slightly acrid. When introduced into water it becomes white, softens, and swells to four or five times its original bulk; but it preserves its shape, neither, like tragacanth, forming a mucilage, nor, like Bassora gum, separating into distinct flocculi. It is rendered blue by iodine.

Gum Sonora. *Sonora Gum.*—According to Krewson, the exudation from *Covillea tridentata* (DC.) Vaill. (*Larrea mexicana* Moric.) contains 17.27 per cent. of resin, and 11.71 per cent. of mucilage and allied substances. (For details, see *P. J.*, xvi, 128; also *A. J. P.*, May, 1898.) *Covillea tridentata* is also known in Southwestern United States and Mexico as "Creosote bush," because of the odor of the oleoresin which covers the herbage.

Gum Sterculia. *Sterculia Gum. Indian Gum Tragacanth. Indian Gum.*—A number of trees belonging to the genus *Sterculia* in India, particularly *Sterculia avens* and *Cochlospermum gossypium*, Africa, and Australia yield gums in considerable quantity, most of which resemble in their appearance tragacanth, some of which have remarkable adhesive properties and in some of which the adhesive power is lacking but the swelling power when moistened with water is enormous. These gums have been much used of recent years, frequently under the unqualified name of tragacanth. They are employed frequently as a filler in the manufacture of ice cream and even desserts where vegetable gums are found to be of service in preventing the product from losing its form as it melts. The difference between the sterculia gums and true tragacanth can be readily proved by a distillation test with water and the determination of the acidity which is due to acetic acid. (See *P. J.*, Nov., 1889; *A. J. P.*, Jan., 1900; 1912, pp. 155 and 393; *Drug. Circ.*, 1909, p. 116.)

Gutta-Percha. *N. F. IV. Gutta Pertscha. Gutta Gettania. Gutta Taban. Getah Pertscha. Getah Taban. Guetah* or *Gueutta-pertcha* Malay (meaning *gueutta*, gum; *pertcha*, rags or scraps). *Gummi plasticum.*—This is a hydrocarbon defined by the N. F. as "the purified, coagulated, milky exudate of various trees of the genus *Palaquium* Blanco (Fam. *Sapotaceæ*)." It is somewhat like India rubber, but less elastic, so that when changed in form by mechanical force it preserves its new shape. At a temperature of boiling water it becomes highly plastic and capable on cooling of preserving the shapes in which it has been molded, while India rubber, treated by heat, preserves its elasticity until the temperature becomes excessive, when it changes in its physical and chemical properties. Perhaps the most important difference between the two substances is in their reaction with sulphur, rubber readily vulcanizing, *gutta-percha* being practically incapable of so doing.

It is described as "in masses, sticks or sheets of irregular size and shape, tough, yellowish-white in color and usually with reddish, marbling streaks. Insoluble in water; partly soluble in chloroform, carbon disulphide, petroleum benzin, or oil of turpentine, leaving not more than 10 per cent. of undissolved residue. Slightly elastic at ordinary temperatures, becoming pliable at from 25° to 30° C. (77°–86° F.). It gradually softens on further heating, becoming quite plastic at 60° C. (140° F.). One Gm. of Gutta Percha when boiled for one hour with 20 mils of dehydrated alcohol in a flask, connected with a reflux condenser, leaves not less than 0.5 Gm. of undissolved residue. When exposed to air and sunlight, Gutta Percha absorbs oxygen and becomes brittle. Gutta Percha yields not more than 5 per cent. of ash." *N. F.*

The plants which are capable of yielding gutta-percha are quite numerous, but those yielding the commercial substance inhabit the limited region of South America between the third degree of south and the fifth degree of north latitude, and the limited portion of Asia between longitude 102° and 112°. It is probable that other equatorial or sub-equatorial regions do, however, produce gutta-percha.

Formerly the most important of the gutta-percha yielding trees was *Palaquium Gutta* Burck (Fam. *Sapotaceæ*). This furnished the article known commercially as *Gutta Taban* and *Getah Taban* Merah. At the present time most of the gutta-percha of commerce is obtained from *P. oblongifolium* Burck; *P. borneense* Burck; *P. Treubii* Burck and *Payena Leerii* Benth. et Hook. At the present time some of these species are being cultivated, viz., *P. Gutta* and *P. oblongifolium*. The latter is cultivated in Sumatra and is said to yield the best of all the gutta-perchas. Other saponaceous species of trees yield gutta-percha of inferior quality or in small quantities, and it is stated that *P. pustulatum* is cultivated in Ceylon and *Payena Leerii* is cultivated in its native Sumatra.

Gutta-percha is obtained in considerable quantities in the Philippine Islands, whence it is sent to Singapore. In obtaining gutta-percha, after the tree has been cut down, incisions are made through the bark into the latex, and the milk, after having been collected in gourds, is coagulated by heat, the resulting masses washed by kneading with water, increased in weight by additions of wood, dirt, pebbles, etc., and finally sent into trade worked into masses with a fair exterior.

It has been proven by the researches of Jungfleisch that the leaves of the gutta-percha trees contain, even after drying, nine per cent. of gutta-percha, as extracted by toluene. Hitherto the leaves have been simply lost in the forest. It is further stated that the year's product of leaves of the thirty year old tree will yield as much gutta-percha as does the tree when cut down, and efforts are being made to induce the Malays to collect the leaves instead of destroying the trees. Patents have been taken out for at least four different processes, in which carbon disulphide, toluene, rosin oil, and light petroleum are used as solvents.

In Singapore the gutta-perchas of various sources

are mixed, and three commercial articles are sold—viz., (1) first quality, (2) medium quality, (3) white gutta-percha.

Small quantities of commercial gutta-percha may be freed from impurities and obtained perfectly white by dissolving one part of gutta-percha in twenty of boiling benzene, shaking the solution frequently with calcium sulphate, which upon standing two or three days carries down with it the coloring matter, then decanting the clear liquid, and adding it, in small portions at a time, to alcohol, agitating continually. The deposited gutta-percha is then dried by exposure to the air.

Gutta-percha occurs in masses, sticks, or sheets of irregular size and shape, is of a dull white or yellowish-white color, usually with reddish-brown streaks, of a feeble odor, tasteless, at ordinary temperatures, hard and almost horny, somewhat flexible in thin pieces, having an unctuous feel under the fingers, and very tenacious. Its sp. gr. is 0.9791. (Soubeiran.) At about 49 ° C. (120.2° F.) it becomes softer and more flexible, but is still elastic, resisting, and tenacious. At from 66° to 71° C. (150.8°–159.8° F.) it is soft, very plastic, and capable of being welded and molded into any form; "plastic above 120° F. (48.8° C.)." *Br.*, 1885. It can be softened either by means of hot water or by dry heat. On cooling, it reassumes its former state, and retains any form which may have been given to it. In the softened state it is readily cut with a knife, though with some difficulty when cold. Exposed to a heat of 166° C. (330.8° F.), it loses a portion of water, and on hardening becomes translucent and gray; but it recovers its original characters if immersed in water. Subjected to destructive distillation, it yields volatile products resembling closely the volatile oil obtained from caoutchouc by the same process. Heated in an open vessel, it melts, foams up, and takes fire, burning with a brilliant flame and much smoke. A portion thus melted retains the state of a viscid fluid on cooling. Gutta-percha is a nonconductor of electricity. It is insoluble in water, alcohol, alkaline solutions, and the weak acids. Ether and the volatile oils soften it in the cold, and imperfectly dissolve it with the aid of heat. It is partly soluble in carbon disulphide, chloroform, petroleum benzin, and oil of turpentine, leaving not more than 10 per cent. of undissolved residue. It does not yield more than 3 per cent. of ash. It has an ultimate composition closely analogous to, if not identical with, that of caoutchouc. According to Bamhauer, pure gutta-percha, as it issues from the tree, is a hydrocarbon, with the formula $(C_{10}H_{16})_2$, which he calls *gutta*, and by the oxidation of which, in various degrees, the different bodies constituting gutta-percha are produced. This hydrocarbon can be separated by treating gutta-percha with diluted hydrochloric acid, and boiling the residue with ether, which deposits the gutta on cooling, but the ethereal treatment must be frequently repeated to obtain it quite pure. (*J. Pr. Chem.*, lxxviii, 279.) Arpe considers gutta-percha as a mixture of six different resins, which may have been formed from a hydrocarbon, $C_{10}H_{16}$. (See *Chem. Gaz.*, ix, 471.) Oudemans (*Jahresb.*, 1859, 517) finds two resinous products in gutta-percha: *fluavil*, fusing at 42° C. (107.6° F.), with the formula $C_{20}H_{32}O$, and soluble in cold alcohol, and *albane*, fusing at 140° C. (284° F.), with the formula $(C_{10}H_{16}O)_2$, and soluble in chloroform, carbon disulphide, and ether, from which last it crystallizes out on cooling. Payen has shown that three proximate principles exist in the natural gutta-percha—viz., *gutta* (insoluble in cold alcohol and in boiling alcohol), 78 to 82 per cent.; *fluavile* (insoluble in cold alcohol), 4 to 6 per cent.; *albane* (soluble in boiling alcohol), 14 to 16 per cent. Gutta-percha resists putrefaction strongly; but in certain situations, as when employed to protect underground telegraph wires passing near the roots of the oak, it has been observed to undergo speedy decomposition, in consequence, it is supposed, of the action of fungi. (*P. J.*, xvii, 193.)

The recent importations of gutta percha have been: 1914, 1,846,109 lbs., valued at $323,569; and for 1915, 1,618,214 lbs., valued at $230,750.

Gutta-percha is employed very largely in the arts for various purposes, especially as an insulating material. In medicine it is used simply for mechanical purposes, as in the formation of splints and the manufacture of surgical instruments. For details of its use the reader is referred to works on surgery.

Gymnema. *Gymnema silvestre* (Willd.) R. Br.—This is a woody climber, belonging to the *Asclepiadaceæ*, which grows in Australia, India and also in Africa. The root has for a long time been employed by the natives as a remedy in *snake bite*, and it is affirmed by T. Dyer (*Nature*, 1887) that directly after the eating of one or two leaves it is impossible to taste sugar, though other tastes are not obscured. Thus, pungency alone is detected in gingerbread, and a sweet orange tastes like a lime. The active principle, *gymnemic acid*, $C_{32}H_{55}O_{12}$, was discovered by Hooper, and has been used with considerable success as a remedy for *parageusia* and *hallucinations of taste*. The 1 per cent. aqueous solution is to be applied with a brush to the inside of the mouth, or a hot infusion (15 per cent.) of the crude drug may be used. (See *Th. M.*, ix.)

Gymnocladus. *Gymnocladus dioica* (L.) Koch. *Kentucky Coffee-tree. Kentucky Mahogany.* (Fam. *Leguminosæ.*)—A tall tree with pinnate leaves growing in the woods from New York southward and west as far as Oklahoma. The fruit is an oblong flattened pod containing several seeds in a fleshy pulp. The seeds are flattish and about 1 cm. in diameter. According to Bartholow, the aqueous extract of the seeds is toxic. (*Am. Drug.*, April, 1886.) Samuel S. Mell (*A. J. P.*, 1887, 230) obtained from them by petroleum benzin about 10 per cent. of fixed oil which is yellowish, saponifiable, and of sp. gr. 0.919. Ether extracted a little wax, fat, and resin. A little tannin and a small quantity of glucoside were also obtained. This latter had a peculiar odor and an acid burning taste. James H. Martin (*A. J. P.*, 1892, 558) obtained a yellow, saponifiable oil from the bean and the bark and a glucoside from the pulp.

Gynoval. *N. N. R.* 1917.—*Gynoval* is the isovaleric ester of iso-borneol, $(CH_3)_2CH.CH_2.COOC_{10}H_{17}$. It occurs as a colorless, neutral fluid with a peculiar aromatic odor and a slightly oily taste, very sparingly soluble in water, but readily soluble in alcohol and ether. Gynoval is asserted to have the advantage over other preparations of valeric acid that it does not irritate the stomach. It is employed in *hysteria* and the various functional neuroses for which valerian is commonly recommended. It is administered generally in capsules containing four minims (0.25 mil) of which one or two may be given at a *dose*.

Hageen. *Cremor Hydrargyri Saponatus.*—This is a mercurial ointment made with a soapy basis. It is claimed that it penetrates the skin more readily than the fatty ointments. It is said to contain the same quantity of mercury as the diluted

mercurial ointment and may be used in the same way.

Hectine. *Sodium-benzo-sulpho-paramino-phenyl-arsenate.* $C_6H_5SO_2NHC_6H_4N{<}^{O}_{ONa}{>}OH$.—It occurs as colorless needles, freely soluble in water, the solution not being decomposed by boiling. It has been brought forward as an organic arsenical, especially for the treatment of *syphilis*, and a number of writers have used it with good effects. Whether or not it will give rise to optic neuritis, as does atoxyl, is uncertain, but Ballet and Hirschmann (*Press. Med.*, 1911) have reported temporary disturbance of vision from its use. The *dose* recommended is from one and one-half to three grains (0.096–0.2 Gm.) daily, injected deeply into the muscle; by mouth, one grain (0.065 Gm.) several times a day. This treatment is kept up for two weeks and then discontinued for two weeks and this method is repeated as long as necessary.

Under the name of *hectargyre*, Balzer (*Press. Med.*, 1910) has brought forward a mixture containing 0.1 Gm. of hectine and 0.01 Gm. of mercuric oxycyanide in each mil. This dose is injected daily.

Hedeoma. *Pennyroyal. American or Mock Pennyroyal. Squawmint. Mosquito Plant. Herbe de Pouliot Américaine*, Fr. *Amerikanischer Polei*, G.—The U. S. VIII recognized "The dried leaves and flowering tops of *Hedeoma pulegioides* (Linné) Persoon (Fam. *Labiatæ*)." *U. S. VIII.*

This plant is entirely distinct from *Mentha Pulegium*, or European pennyroyal. It is probable that various other species of the genus are used in the localities in which they grow. Thus, *H. piperita* Bentham is said to be used in Mexico as a substitute for peppermint, and *H. thymoides* Gray, in Texas as an aromatic diaphoretic.

Hedeoma pulegioides (L.) Pers. (1807) [*Cunila pulegioides* L. (1762); *Melissa pulegioides* L. (1753)] is an indigenous annual plant, from nine to fifteen inches high, with a small, branching, fibrous, yellowish root, and a pubescent, quadrangular stem, which sends off numerous slender erect branches. The plant is common in the Eastern and Middle Western United States, preferring dry grounds. Hedeoma was officially described as "branchlets quadrangular, with numerous spreading hairs; leaves opposite, short-petioled, oblong, 15 to 35 Mm. long, thin, obtuse, obscurely serrate, glandular-hairy beneath; flowers in axillary fascicles, with a tubular-ovoid, bilabiate and 5-toothed calyx, and a pale blue, spotted, bilabiate corolla containing two sterile and two fertile, exserted stamens; odor strong, somewhat mint-like; taste aromatic and pungent." *U. S.* The activity of hedeoma depends upon a volatile oil. The oil of hedeoma (*Oleum Hedeomæ, U. S. VIII, Oil of Pennyroyal*), is "A pale yellow, limpid liquid, having a characteristic, pungent, mint-like odor and taste. Specific gravity: 0.920 to 0.935 at 25° C. (77° F.). It should form a clear solution with 2 volumes or more of 70 per cent. alcohol. It is dextrogyrate, the angle of rotation varying from about + 18° to + 22° in a 100 Mm. tube, at a temperature of 25° C. (77° F.)." *U. S. VIII.* Its chemical composition was investigated by E. Kremers (*A. J. P.*, 1887, p. 535) and F. W. Franz (*A. J. P.*, 1888, p. 161). Each of them found a body of the composition $C_{10}H_{18}O$, boiling at 217° to 218° C. (422.6°–424.4° F.) (constituting, according to Franz, about 33 per cent. of the oil). For this the name *hedeomol* was proposed. Franz also found a body of the composition $C_{10}H_{17}O$, boiling at 220° to 225° C. (428°–437° F.), and constituting 12 per cent. of the oil; likewise a body of the composition $C_6H_{12}O$, boiling at 165° to 170° C. (329°–338° F.), and constituting about 0.7 per cent. of the oil. Both investigators found *formic* and *acetic acids*, and Kremers considers *isoheptoic acid* also to be present. Beckmann and Pleissner (*Ann. Ch. Ph.*, cclxii, p. 1) found in American as well as in Spanish and Algerian pennyroyal oil a ketone, $C_{10}H_{16}O$, to which they gave the name of *pulegone*. This compound forms with hydroxylamine an oxime, $C_{10}H_{16}NOH.H_2O$, crystallizing in beautiful needles melting at 157° C. (314.6° F.), and with hydrogen bromide a crystalline compound melting at 40.5° C. (104.9° F.). The two compounds of the formula $C_{10}H_{18}O$, discovered by Kremers (*Ph. Rund.*, ix, p. 130), are also ketones and yield corresponding oximes.

American pennyroyal is a gently stimulant aromatic, and may be given in flatulent *colic* and *sick stomach*, or to qualify the action of other medicines. Like most of the aromatic herbs, it possesses the property, when administered in warm infusion, of promoting perspiration, and of exciting the menstrual flow when the system is predisposed to the effort. A large draught of the warm tea is in popular practice often given at bedtime, in recent cases of *suppression* of the *menses*, the feet having been previously bathed in warm water. The drug may be given in *doses* of two drachms (7.7 Gm.). The oil in *doses* of two to ten minims (0.12–0.6 mil).

Hediosit. $C_7H_{12}O_7$. *N. N. R.* 1917.—It is the lactone or inner anhydride of *alpha-glucoheptonic acid*, $CH_2OH.(CHOH)_5COOH$. It occurs as white crystalline powder without odor, but with a sweet taste, but inferior to that of saccharin. It is readily soluble in both water and alcohol, its solution reacting to litmus as an acid. It has been brought forward as a substitute for sugar in the management of *diabetes*. It is asserted that it has a food value equal to that of glucose, but does not increase the amount of sugar in the urine. According to the investigations of Lenel (*A. E. P. P.*, 1914, lxxvii, p. 335), only a very small proportion of the food value of *hediosit*, however, is utilized by the system. He found that from 25 to 75 per cent. might escape unchanged with the feces and of the remainder a very large proportion could be recovered unaltered in the urine.

Hedonal. *N. N. R.* 1917. *Methyl-propyl-carbinol-urethane.* $CH_3CH_2CH_2CH(CH_3)O.CO.NH_2$.—This is a white, crystalline powder of weak aromatic odor, fusing at 76° C. (168.8° F.), sparingly soluble in cold water, somewhat more so in boiling water, soluble in alcohol, ether, and other organic solvents. Decomposed by boiling with alkalies. It forms colorless crystals melting at 76° C. (168.8° F.). The solutions have a powerful menthol-like taste. Hedonal is believed to split up in the system into carbon dioxide, ammonia, and urea. Probably owing to the presence of the urea, it sometimes acts as a diuretic, but more usually it has no other effect than that of an hypnotic. It is claimed by de Moor that its diuretic action is much increased by its administration in solution. According to Dreser, in the dog it acts very feebly upon respiration and blood pressure. As an hypnotic it is mild in its action and but rarely produces disagreeable after-effects. In severe cases of *insomnia*, or when the patient is kept awake by pain, it is of little service. No cases of poisoning by it have been reported, and so far its prolonged use has not been followed by disagreeable symptoms. The *dose* is fifteen to forty-five grains

(1.0–3.0 Gm.), given preferably in capsules half an hour before the desired effect.

Hedera. *Hedera Helix* L. *Ivy.* (Fam. *Araliaceæ.*)—This well-known evergreen creeper is a native of Europe. The fresh *leaves* have a balsamic odor, especially when rubbed, and a bitterish, harsh, unpleasant taste. They are used for dressing issues, and, in the form of decoction, have been recommended in *sanious ulcers* and *cutaneous eruptions,* particularly *tetter* and the *itch.* The *berries,* which have an acidulous, resinous, somewhat pungent taste, are said to be purgative and even emetic. Vandamme and Chevallier discovered in ivy seeds a peculiar very bitter alkaline principle, *hederine.* It is obtained by treating the seeds with calcium hydroxide, dissolving the precipitated alkaloid in boiling alcohol, and evaporating the alcoholic solution. (*A. J. P.,* xiii, 172.) Posselt has discovered two acids in the seeds, one of which has their taste in a high degree, and was named by him *hederic acid,* the other he did not obtain quite pure. (See *Chem. Gaz.,* 1849, 93.) The seeds were also found to contain a variety of tannic acid, turning ferric salts dark green, to which Posslet gave the name of *hedera-tannic acid.* (*Ann. Ch. Ph.,* lxix, p. 62.) Moore (*J. P. Ex. T.,* 1913, iv) has separated a sapo-glucoside which he names *hederin.* This is not poisonous when taken by the mouth, but when injected intravenously causes death by respiratory paralysis. Davies and Hutchinson confirmed the existence of Posslet's hederic acid, and gave it the formula $C_{16}H_{26}O_4$. Kingzett believes that it is not an acid, but a glucoside. J. Vernet (*Ber. d. Chem. Ges.,* xiv, 685) obtained a glucoside, which separated from solution in boiling acetone, in silky needles, melting at 233° C. (451.4° F.), insoluble in water, chloroform, and ligroine, slightly soluble in cold acetone, benzene, and ether, more soluble in hot alcohol and hot alkalies. Its formula he gives as $C_{32}H_{54}O_{11}$, and states that it decomposes on heating with diluted sulphuric acid into a body, $C_{26}H_{44}O_6$, which fuses at from 278°–280° C. (532.4°–536° F.), and a non-fermentable sugar which reduces Fehling's solution. (*Y. B. P.,* 1877, 508.) Later, Van der Haar isolated two glucosides, *hederin,* $C_{42}H_{66}O_{11}$, and *hederagenin,* $C_{31}H_{50}O_4$. (*A. Pharm.,* 1912, 424.) From the trunks of old ivy plants, growing in the south of Europe and the north of Africa, a resinous substance exudes through incisions in the bark, which has been employed in medicine under the name of *ivy gum.* It is in pieces of various sizes, of a dark yellowish-brown color internally, of a vitreous fracture, pulverizable, yielding a lively orange-yellow powder, of a peculiar not disagreeable odor when heated or inflamed, and of a bitterish resinous taste. Its chief constituent is resin, though some pieces contain a considerable proportion of bassorin, and other large quantities of ligneous matter. It was formerly used as a stimulant and emmenagogue, but is now scarcely employed. Placed in the cavities of carious teeth, it is said to relieve *toothache.* The light and porous wood of the ivy is sometimes used for making *issue-peas.*

Hedychium. *Hedychium spicatum* Sm. (Fam. *Zingiberaceæ.*)—The root of this plant, which is used in perfumery in India has been found by J. C. Thresh to contain *ethylmethyl paracoumarate.* (*P. J.,* Nov. 8, 1884.)

Hegonon. *Silver Nitrate-ammonia-albumose.*—This is a light brown powder obtained by treating silver-ammonium-nitrate with albumose. It is readily soluble in water and contains approximately 7 per cent. of silver. It is used locally in the treatment of various forms of *gonorrhea* in concentrations of from 1 in 200 to 1 in 3000.

Helenium. *Helenium autumnale* L. *False Sunflower. Sneezewort. Sneezeweed.*—An indigenous perennial, bitter, somewhat acrid composite herb. The leaves and flowers snuffed up in the state of powder produce violent sneezing, and have been used as an errhine. F. J. Koch (*A. J. P.,* 1874, 221) found in the plant a bitter principle believed to be a glucoside, malic acid, traces of tannic acid, albumen, and volatile oil. Reeb found a crystalline bitter principle, *helenin,* with the formula $C_{20}H_{25}O_5$. This has been physiologically studied by Lamson (*J. P. Ex. T.,* 1913, iv) who found that it is an intense irritant to the mucous membranes, capable of causing a fatal gastro-enteritis, and that it acts as a paralysant to the heart and voluntary muscles. This principle must not be confounded with "helenin" from Inula, which see on page 1440. *Helenium nudiflorum* Nutt. has similar properties; *H. tenuifolium* Nutt., a common roadside weed of Mississippi and Louisiana, is stated by Galloway to produce in animals muscular twitchings, passing into violent convulsions, terminating in death. In four negroes *helenium* caused spasms with delirium and loss of consciousness. (*A. J. P.,* 1872, 309; DC., 1907, 459.)

Helianthemum. *N. F. IV. Rock-rose. Frostweed. Herbe de Hélianthème de Canada,* Fr. *Canadisches Sonnenröschen,* G. *Helianthemum canadense* (L.) Michx.—"The dried herb of *Helianthemum canadense* (Linné) Michaux (Fam. *Cistaceæ*)." *N. F. Frostwort* grows in all parts of the Eastern United States, preferring dry sandy soils. It is official in the National Formulary IV. The dried herb is employed in medicine and is described as follows: "Stems mostly less than 5 cm. in length, branched above, terete, frequently reddish, canescent, the slender branches mostly erect; leaves very short-petioled, from 1 to 3 cm. in length, and from 4 to 8 mm. in width, oblong to oblanceolate, with entire, revolute margins, green and somewhat rough on the upper surface, canescent underneath; flowers of two kinds, rarely present at the same time, the early ones mostly solitary, pedicelled, with bright yellow corolla, from 2 to 3 cm. in breadth, hairy calyx, about thirty stamens and a single three-carpelled pistil, producing an ovoid capsule, about 7 mm. in length; later flowers apetalous, clustered in the leaf-axils, nearly sessile, having but four stamens and producing a capsule about 4 mm. in length. Odor slightly aromatic; taste astringent and bitter." *N. F.* William Crutcher (*A. J. P.,* 1888, 390) found in it volatile oil, wax, fatty oil, tannin, and apparently a glucoside crystallizing in white needles. Fred J. Kruell found in *H. corymbosum* Michx., tannin in large proportion, resin, glucose, gum, extractive, chlorophyll, and inorganic salts. (*A. J. P.,* 1874, 358.) Frostwort has an astringent, slightly aromatic, and bitterish taste, and appears to possess tonic and astringent properties; it was formerly employed in *scrofulous diseases.* (See *U. S. D.,* 14th ed.) According to D. A. Tyler (*Pamphlet,* New Haven, 1846), *H. corymbosum* Michx. possesses similar properties, and may be indiscriminately employed with *H. canadense* in *scrofula, diarrhea,* and *secondary syphilis,* and locally as a gargle in *scarlatina,* and a wash in *prurigo.* Tyler, however, has known the strong decoction and the extract to produce vomiting. He considers two grains (0.13 Gm.) of the latter a full *dose* for an adult. The *Fluidextractum*

Helianthemi is recognized by the N. F. IV. (see Part III). The menstruum is diluted alcohol.

Helianthus. *Helianthus annuus* L. *Common Sunflower. Hélianthe, Grand Soleil,* Fr. *Sonnenblume,* G.—This very large composite is cultivated in this country, in Europe, and especially in China, chiefly for the sake of the fixed oil yielded by the seed. The oil has a sp. gr. of from 0.924 to 0.926, solidifies at −15° C. (5° F.), is colorless or yellowish, limpid, nearly tasteless and odorless, and dries slowly. It is said to make an excellent salad dressing, and to be one of the best burning oils known. The increase in cultivation is stated to be nearly a thousandfold, 275 pounds of oil being a fair yield per acre. For particulars as to cultivation, see *A. J. P.*, 1875, 460; also *N. R.*, 1876, 165. Ludwig and Kromayer (*A. Pharm.* (2), 99, 1 and 285) obtained a tannin which they called *helianthitannic acid,* and gave it the formula $C_{14}H_9O_8$. On boiling with moderately diluted hydrochloric acid they obtained a fermentable sugar and a violet coloring matter. E. Diek (*In. Dis.*, Göttingen, 1878) found only small quantities of inulin, large amounts of levulin, and a dextro-rotatory sugar. Chardon has obtained a peculiar oleoresin from sunflowers grown in Algeria. (*P. J.*, 1873, 323.) Buschmann obtained from the flowers of Russian helianthus, *betaine* and *choline,* he believed that their presence accounts for the observed activity of the extract. *Tincture of Helianthus* has been used in Russia. (*A. Pharm.*, 1911, 1; *M. R.*, 1908.) The stalk, when treated as is flax, yields a long, fine fiber, which is said to be used in China for the adulteration of silk. The sunflower also enjoys the reputation of protecting against marsh miasmata. (See *N. Y. M. R.*, 1868, 353.) Kazatchkoff states (*B. G. T.*, Oct., 1889) that in the Caucasus the inhabitants employ the sunflower in *malarial fevers.* The leaves are spread upon a bed covered with a cloth, moistened with warm milk, and then the patient is wrapped up in the spread. Perspiration is produced, and the patient is kept in this condition for an hour or two. The same process is repeated every day until the access of the fever has ceased. A tincture of the flowers and the leaves of the sunflower has been recommended by Beldau in combination with balsamics in the treatment of *bronchiectasis.* The Pah Ute Indians are said to use very freely as food the seeds of two indigenous sunflowers, *H. petiolaris* Nutt. and *H. lenticularis.* (*Proc. A. Ph. A.*, xxvii, 178.)

Helkomen.—A substitute for iodoform which is stated to be a bismuthdibromebetaoxy-naphtholate. It is a yellow, odorless, insoluble powder containing 73 per cent. of bismuth.

Helleborus. *Helleborus niger* L. *Black Hellebore. Hellébore noir,* Fr. *Schwarze Niesswurzel, Weihnachtswurzel, Winterrose,* G. *Elleboro nero,* It. *Eléboro negro,* Sp. (Fam. *Ranunculaceæ*).—*Hellebore* is a native of the mountainous regions of Southern and temperate Europe, and is sometimes cultivated on account of the early opening and beauty of its flowers, whose expansion in midwinter has given to the plant the name of *Christmas rose.* Black hellebore is sometimes called *melampodium,* in honor of Melampus, an ancient shepherd or physician, who is said to have cured the daughters of King Prætus by giving them the milk of goats fed on hellebore. For a history of the use of hellebore by the ancients, see 15th edition, *U. S. D.*

The formerly official rhizome is knotted, blackish on the outside, white within, and sends off numerous long, simple, depending fibers which are brownish-yellow when fresh, but become dark brown upon drying. The roots of various other plants, not belonging to the same genus, are said to be frequently substituted for the black hellebore. They may usually be readily distinguished by comparing them with the genuine root. The rhizomes of various plants which are sometimes substituted for true hellebore have been examined by Tschirch and Neuber, who state their results as follows: The rhizome of *H. niger* exhibits a small pith and comparatively large acutely wedge-shaped, radially-elongated wood-bundles. The odor of the rhizome and roots is slight but rather pleasant, especially in the fresh drug. The rhizome of *H. viridis* L. has a large pith and tangentially extended, bluntly wedge-shaped or almost square wood-bundles; older roots exhibit a wood with from five to seven-angular wedges. In both rhizome and root of *H. fœtidus* L., the wood is more strongly developed and radiate in appearance; it contains abundance of wood-fibers and encloses little or no pith. The rhizome of *Actœa spicata* L. is flattened and bears cushion-like protuberances, due to the remains of the aerial stems. The wood-bundles are thickened at either extremity and rounded by wood-fibers, so that in transverse section the wood-ring has a scalariform appearance. The root exhibits a regular three to five-rayed wood, the rays being broader toward the outside. (*S. W. P.*, xl, 410.)

The roots are the portion usually recommended. They are from 0.5 to 6 cm. long and 2 to 3 mm. thick, smooth, brittle, externally black or deep brown, internally white or yellowish-white, with little odor, and a bitterish, nauseous, acrid taste. In their recent state they are extremely acrid. This acridity is diminished by drying, and still further impaired by age. William Bastick discovered a crystalline principle, *helleborin,* $C_{36}H_{42}O_6$, of a bitter taste with a tingling effect on the tongue, not volatilizable, slightly soluble in water, more so in ether and alcohol, and more readily in these liquids hot than cold. (*P. J.*, xii, 274.) Marmé and Husemann obtained from black and green hellebore a glucoside, *helleboreïn,* $C_{37}H_{56}O_{18}$, by precipitating a solution of an extract of the root with solution of lead subacetate, freeing from lead by hydrogen sulphide, and again precipitating with phospho-molybdic acid; by boiling with acid it separated into glucose and *helleboretin,* $C_{14}H_{20}O_3$, a compound of a fine violet color. The helleboreïn exists both in the root and leaves. It has a taste at once sweet and bitter, is soluble in water and weak alcohol, much less so in ether and absolute alcohol, and is crystallizable in yellowish rhomboidal prisms. It is precipitable by tannic acid and mercurous acetate. (*J. P. C.*, 4e sér., ii, 258.) Husemann and Marmé (*Ann. Chem.*, cxxxv, 61) examined more thoroughly the *helleborin* of Bastick. They found that when boiled with diluted sulphuric acid, or, better, zinc chloride, it is converted into sugar and *helleboresin,* $C_{30}H_{38}O_4$. They obtain this glucoside by treating with hot water the green fatty matter which is dissolved out of the root by boiling alcohol. Though both helleborin and helleboreïn are poisonous, the products of their decomposition are said to be harmless. Neither of them is volatile.

Helleboreïn is strongly irritant to the mucous membranes, causing, when applied to the conjunctiva, redness, swelling, and increased secretion, with indirect enlargement of the pupil, and when applied to the nasal membrane, sneezing, though less than veratrine. Small doses produce little effect on the

stomach; but, repeated and accumulated, they cause anorexia, nausea even to vomiting, pain, increased secretion, and inflammation both of the stomach and bowels. The experiments of Van der Haide (*A. E. P. P.*, 1885, xix), Trendelenburg (*A. E. P. P.*, 1909, lxi, p. 262) and others demonstrate that physiologically helleboreïn belongs to the digitalis group of drugs. In small doses it diminishes the rate of the pulse, increases the force and out-put of the heart, and causes a rise in the blood pressure. In toxic doses, the pulse becomes rapid, and small in volume, and the heart is finally arrested in systole. According to Cushny, the action of helleboreïn on cardiac inhibition is less than most of the other members of the digitalis group. The *helleborin* of Marmé and Husemann is a more active poison, though less irritant to the mucous membrane. It acts on the tongue like aconite. Its influence appears to be directed especially to the nervous system. In the lower animals it causes quickened breathing, restlessness, tension and trembling of the muscles, uncertainty of movement; then retardation of the breathing and pulse, irritability of the peripheral nerves, dilatation of the pupil, loss of hearing, and finally almost complete anesthesia, with cerebral and spinal congestion, even to apoplexy.

Hellebore was formerly used as a drastic purge in *doses* of from ten to twenty grains (0.65–1.3 Gm.). This employment has, however, justly passed out of vogue. It was highly esteemed by the ancients in *mania, melancholy, amenorrhea, dropsy,* and *epilepsy. Bacher's pills,* celebrated for the cure of *dropsy,* consisted chiefly of black hellebore. The glucoside helleboreïn has been used internally as a cardiac tonic in *doses* of from one-sixth to one-third of a grain (0.010–0.021 Gm.) several times a day, but its irritant action on the stomach militates against its practical usefulness. Ischistowitsch (*Cb. M. W.*, 1887) has used an aqueous extract of hellebore with apparent benefit in *heart diseases.* Venturini and Gaspairini (*B. G. T.*, June, 1888) state that helleboreïn is a local anesthetic, which, in affections of the eye, is preferable to cocaine, because of the great permanency of the anesthesia, and because neither the pupil nor the intra-ocular pressure is affected. They use from three to four drops of a solution, each drop of which represents one one-hundred and sixty-fourth of a grain (0.0004 Gm.). In overdoses hellebore produces inflammation of the gastric and intestinal mucous membrane, with violent vomiting, hypercatharsis, vertigo, cramp, and convulsions, which sometimes end in death. The fresh root applied to the skin produces inflammation and even vesication. The *dose* of the powdered root is from ten to twenty grains (0.65–1.3 Gm.) as a drastic purge, two or three grains (0.13–0.2 Gm.) as an alterative. *Dose,* of the decoction (two drachms to a pint), a fluidounce (30 mils) every four hours till it operates.

Helonias. *N. F. IV. False Unicorn. Chamælirium luteum* (L.) A. Gray (*C. carolinianum* Willd., *Helonias dioica* Pursh.). *Starwort.*—"The dried rhizome and roots of *Chamælirium lutem* (Linné) A. Gray. (Fam. *Liliaceæ*)." *N. F.* It is described by the N. F. as follows: "Rhizome upright, or oblique, nearly cylindrical, from 0.5 to 3 cm. in length and about 1 cm. in diameter; externally grayish-brown, annulate from scars of bud-scales; upper portion with leaf bases enclosing a small bud; oblique rhizomes with a few stem scars about 0.5 mm. in diameter; lower portion with numerous whitish or pale yellowish, nearly straight or slightly curved wiry roots, from 5 to 8 cm. in length; fracture hard and horny; internally grayish-yellow, cortex from 3 to 4 mm. in thickness, central cylinder with three or four circles of small, nearly circular fibro-vascular bundles. Odor distinctive; taste bitter, slightly astringent. Sections of the rhizome, when examined under the microscope, show parenchyma cells with numerous spherical or ellipsoidal starch grains, varying from 0.002 to 0.015 mm. in diameter; numerous raphides varying from 0.025 to 0.035 mm. in length; the fibro-vascular bundles vary from 0.2 to 0.3 mm. in diameter, the tracheæ being at the periphery and the walls marked either with annular or reticulate thickenings or simple pores. In the root the cortex is always attached and there are usually six mestome strands. Helonias yields not more than 5 per cent. of ash." *N. F.* The rhizome and roots are used in medicine. They resemble those of Aletris but the rootlets of *helonias* are whitish or pale yellowish, nearly straight, grayish-yellow internally and of a bitter, slightly astringent taste. *Fluidextractum Helionatis* is official in the N. F. (see Part III).

Hemalbumin.—A dark brown powder soluble in water containing hematin, hemoglobulin, serum, albumen, paraglobulin and natural mineral salts. Employed in *tubercular* and *chronic coughs.*

Hemidesmus Root. *Br.* 1898. *Hemidesmi Radix. Indian Sarsaparilla. Nunnari. Racine de Hemidesmus,* Fr. *Hemidesmus-Wurzel,* G.—"The dried root of *Hemidesmus indicus* R. Br." *Br.*, 1898. *Hemidesmus indicus* (Fam. *Asclepiadaceæ*) is a climbing plant, with twining, woody, slender stems, and opposite, petiolate leaves, which are entire, smooth, shining, and of a firm consistence. The leaves vary much in size and shape, some being linear and acute, others broad-lanceolate, and others again oval or ovate. The flowers are small, green on the outside, purple within, and disposed in axillary racemes. The fruit consists of two long, slender, spreading follicles. This plant is common over the whole peninsula of Hindostan. The official portion was the root, which has long been used in India as a substitute for sarsaparilla. It is 30 cm. or more long and from 3 to 6 mm. thick, rigid, tortuous, cylindrical, and little branched, consisting of a ligneous center, and a brownish, corky bark, marked with longitudinal furrows and transverse fissures. The odor is aromatic, recalling that of tonqua bean, the taste is aromatic and sweetish. On one side of the root the cork is frequently separated from and raised above the cortex, and is transversely fissured. The transverse section exhibits numerous laticiferous cells in the cortex. For details of microscopic structure, see *P. J.*, 1872, 62. Garden obtained from hemidesmus a peculiar, volatilizable acid principle, which he named *smilasperic acid,* under the erroneous impression that the root was derived from *Smilax aspera.* Pereira proposed to call it *hemidesmic acid.* Scott also obtained a stearopten by distillation with water, presumably the same material. It has not been further investigated.

Hemidesmus root is said to be tonic, diuretic, and alterative. It was introduced into Great Britain from India, and was employed for some time under the name of *Smilax aspera.* It is used for the same purposes as sarsaparilla, and in some instances it is said to have proved successful in *syphilis* when that medicine had failed, but it cannot be relied upon. The native practitioners in India are said to employ it in nephritic com-

plaints, and in the sore mouth of children. It is used in the form of infusion or decoction, made in the proportion of two ounces of the root to a pint of water. A pint (500 mils) may be given in wineglassful doses in the course of the day. A *syrup* was official in the Br., 1898.

Hemoglobin. *Hæmoglobin.*—A constituent of venous blood, passing in the arterial blood into *oxyhemoglobin.* Its molecular formula is very complex. It is a conjugated protein, consisting of the protein, globin, in combination with the chromatogenic substance, hematin. It is readily obtained in a crystalline state and the crystals are said to vary in form according to the kind of animal from whose blood they are prepared. The principal property of hemoglobin is its power of combining with gases, especially oxygen and carbon monoxide. Whereas the oxygen compound readily dissociates with oxygen and hemoglobin, the carbon monoxide compound is very stable and cases of poisoning from illuminating gas where much carbon monoxide is present, as in the instances where it consists partly of water gas, are therefore generally fatal. Various preparations of *desiccated blood* containing hemoglobin have been put upon the market. Crystals of hemoglobin may be obtained from the blood of certain animals (guinea-pigs, rats, etc.) with ease by simply adding water to the blood. The hemoglobin dissolves in the water, the corpuscles separating, and the crystals form in a few minutes. Another method consists in adding to defibrinated blood 6 per cent. of its volume of ether, or a mixture of alcohol and ether; on shaking the mixture, the corpuscles dissolve, and a thick magma of crystals forms sooner or later; these may be purified by washing with 25 per cent. alcohol and by recrystallization. Freezing has been resorted to for the purpose of separating the crystals.

Ferrohemol is a brown, almost tasteless powder containing 3 per cent. of iron, which is made by the precipitation of blood by a dilute solution of iron and neutralization with soda. *Fer cremol* is a similar substance.

Hemol, N. N. R. 1917, and *Hemogallol, N. N. R.* 1917, are made, as suggested by Kobert, by the action of *reducing agents* upon the blood coloring matter. (See *E. Merck's Jahresber.*, 1891.) With the hemol, zinc dust is used as the reducing agent; with the hemogallol, pyrogallol is used. The former is a dark brown, the latter a reddish-brown, tasteless powder.

Either of these blood derivatives may be employed instead of the older preparations of iron. There is sufficient clinical evidence to show that they are effective ferruginous tonics which may be, as is claimed for them, less constipating and less disagreeable to the stomach than are the older preparations of iron; but there is no sufficient reason for believing that they have any real superiority. *Dose*, five to ten grains (0.32–0.65 Gm.).

A number of hemol preparations have also been recommended by Kobert and prepared by Merck & Co., such as *arsenhemol, bromhemol, iodohemol, iodomercuryhemol,* and *copperhemol.*

Heracleum. *Heracleum lanatum* Michx. *Masterwort. Cow-parsnip.*—This is one of our largest indigenous umbelliferous plants. The root, which is the part used, bears some resemblance to that of common parsley. It has a strong disagreeable odor and a very acrid taste. Both the leaves and root excite redness and inflammation when applied to the skin. Bigelow considers the plant poisonous. It appears to be somewhat stimulant and carminative, and has been used in *epilepsy.* (See 16th ed., *U. S. D.*)

Heretine.—An ether-soluble alkaloid obtained from *Heritiera javanica* (*Sterculiaceæ*), is said to be effective in the treatment of *epilepsy, chorea* and *migraine.*

Hermodactyls. *Hermodactyli.*—Under this name are sold in European commerce the roots or bulbs of an uncertain plant, growing in the countries about the eastern extremity of the Mediterranean. By some botanists the plant is thought to be a *Colchicum*, and *C. variegatum* L., a native of the south of Europe and the Levant, is particularly indicated by Fée, Geiger, and others, while by authors, no less eminent, the roots are confidently referred to *Iris tuberosa* L. They certainly bear a considerable resemblance to the corm of *Colchicum autumnale* L., being heart-shaped, channelled on one side, convex on the other, and from 12 to 25 mm. in length by nearly as much in breadth. As found in commerce, they are destitute of the outer coat, are of a dirty yellowish or brownish color externally, white and amylaceous within, inodorous and nearly tasteless, though sometimes slightly acrid. They are often worm-eaten. Their chief constituent is starch, and they contain no veratrine or colchicine. From this latter circumstance, and from their insipidity, it has been inferred that they are probably not derived from a species of Colchicum. They are in fact almost without action upon the system. It is doubted whether they are the *hermodactyli* of the ancients, which acted like colchicum and were useful in *gout* and *rheumatism.* Pereira describes a bitter variety of *hermodactyls*, which was brought from India by Royle. The bulbs are smaller and darker than the others, and have externally a striped or reticulated appearance.

Hermophenyl. *Sodio-mercuric Phenoldisulphonate. Mercurio-sodic Phenol-disulphonate.*—This substance, which contains 40 per cent. of metallic mercury, occurs as a white amorphous powder, freely dissolving in cold water (up to 22 per cent.). According to Lumiere and Chevrotier (*B. M.*, 1901, 690), it possesses very feeble toxic properties, while it is actively bactericidal. Its hypodermic injections are said to cause but little pain. Hermophenyl is used in the treatment of *syphilis.* It may be exhibited either by intramuscular injection or, in pill form, by the mouth. The *dose* is ordinarily from one-eighth to one-third of a grain (0.008 to 0.021 Gm.) which, when administered by the mouth is given several times a day, by injection, once a day. Bernard claims that it may be made into a 1 per cent. soap without decomposition, affording an excellent preparation for rendering the hands aseptic. The 2 per cent. aqueous solution may be used for surgical purposes.

Herniaria. *Herniaria glabra* L. (Fam. *Caryophyllaceæ.*)—This genus was formerly included in the family *Illecebraceæ*, but this is now segregated with the *Caryophyllaceæ.* Goblez has obtained from this plant a crystalline principle, *herniarine* (*J. P. C.*, 4e sér., xx, 270), which proved to be *methylumbelliferone*, $C_{10}H_8O_3$. Schneegans has also discovered an alkaloid, *paronychine.* (*A. J. P.*, 1890, 488.) This plant is recommended by Zeissl in *catarrh of the bladder.* Very active diuretic properties have been attributed to *herniaria* by Kuhn (*Med. Klin.*, 1908) and others, who have found that it was successful in the treatment of *dropsy,* whether of cardiac or nephritic origin.

Heteromeles. *Heteromeles arbutifolia* (Poir.) Roem. (Now ascribed to *Photinia arbutifolia*

Lindl. (Fam. *Rosaceæ*), D. D. Lustig has found in this Californian plant (*toyon* of the Indians) tannic, gallic, and hydrocyanic acids. (*A. J. P.*, April, 1882.)

Hetocresol. *Metacresol Cinnamate. Cinnamometacresol.* $C_6H_5CH=CH.COOC_6H_4CH_3$.—Forms crystals melting at 65° C. (149° F.), insoluble in water, but soluble in alcohol, ether, benzene, chloroform, and glacial acetic acid. It is claimed that this substance is especially valuable as a local remedy in external *tuberculosis*. In tuberculosis of the bladder Landerer uses, after cocainization, 1.4 per cent. solutions containing 0.7 per cent. of common salt. Fistulous tracts he injected with *hetocresol*, 1 part; iodoform, 2 parts; water, 1 to 8 parts. In *scrophuloderma*, after scraping, hetocresol has been found to be very useful.

Hetol Caffeine. *Caffeine Sodium Cinnamate.*—An amorphous odorless, bitter substance, soluble in water and alkaline in its reaction to litmus; is employed as a general stimulant. Administered subcutaneously. *Dose*, two to five grains (0.12–0.3 Gm.).

Heuchera. *Heuchera americana* L. *Racine d'Heuchère d'Amérique*, Fr. *Amerikanische Sanikelwurzel*, G.—The *alum-root* or *American sanicle* is a perennial, herbaceous plant, belonging to the *Saxifragaceæ*, which grows in shady, rocky situations from New England to Carolina and westward to eastern Kansas. The rhizome, which was formerly official, is horizontal, somewhat compressed, knotty, irregular, yellowish, and of a strongly styptic taste. Alum-root is powerfully astringent, and may be employed in similar cases with other medicines belonging to the same class. J. Peacock (*A. J. P.*, 1891, 174) found a percentage of tannin ranging from 9.33 to 19.66 reckoned on the dry drug, according to the season of the year when collected; also a percentage of starch, calculated the same way, ranging from 5.17 to 16.32. Frederick Stearns (*Proc. A. Ph. A.*, 1858, 263) speaks of two other indigenous species, *H. villosa* Michx. (*H. caulescens* Pursh.) and *H. pubescens* Pursh., as having similar properties; and F. W. Anderson reports (*Botan. Gaz.*, 1887, 65) that the roots of *H. hispida* Pursh., *H. cylindrica* Douglas, and *H. parvifolia* Nuttall are much used by hunters of Montana and others as astringents, particularly in *diarrhea* caused by the drinking of alkali water.

Hexamethylenamine Compounds. — There have been introduced an extraordinary number of combinations of hexamethylenamine. Some of the more important of these are considered below.

Hexamethylenamine Bromethylate. Bromalin. Bromethylformin. $(CH_2)_6N_4C_2H_5Br$.—Formed by the action of ethyl bromide upon hexamethylenetetramine. It occurs in colorless scales or white powder, melting at 200° C. (392° F.) with decomposition; nearly tasteless, readily soluble in water. Bromalin has been used by a number of neurologists as a substitute for the alkaline bromides in the treatment of *epilepsy*. It is asserted that it exercises all of the beneficial effects of the bromides in this disease, but does not give rise to symptoms of bromism. These statements, however, are hard to credit, as Bermann and Bilinski (*Th. M.*, 1910) have found that the compound is broken up in the body, and the entire content of bromine appears in the urine as an alkaline bromide. Bromaline represents 32 per cent. of bromine and is ordinarily administered in *doses* of thirty to sixty grains (2–4 Gm.).

Hexamethylenamine camphorate. Amphotropin. N. N. R. 1917. $((CH_2)_6N_4)_2.C_8H_{14}(COOH)_2$.—This is a white, crystalline powder easily soluble in both water and alcohol. It is used as a urinary disinfectant. *Dose*, eight to fifteen grains (0.5–1 Gm.).

Hexamethylenamine Di-iodide. Novoiodine.—This is a mixture of equal parts of hexamethylenamine di-iodide with powdered talc. It occurs as a brownish powder almost odorless and insoluble in all the ordinary solvents. It is intended as a dusting powder for suppurating wounds and ulcers. The advantage is claimed for it over other powders for similar purposes that it does not form crusts and that it has a marked deodorizing effect.

Hexamethylenamine Lithium Benzoate. Urystamine.—A mixture of formin and lithium benzoate administered in the treatment of gouty conditions and in promoting the elimination of uric acid. *Dose*, five to eight grains (0.32–0.5 Gm.).

Hexamethylenamine Lithium Citrate. Uresin.—A white powder freely soluble in water. It is intended as a uric acid solvent in *gouty conditions*. The *dose* is five to fifteen grains (0.3–1 Gm.).

Hexamethylenamine Methylene Citrate. Uropurgol. Helmitol. Citramine. N. N. R. 1917. $C_7H_6O_7.(CH_2)_6N_4$.—This substance is a white acidulous, odorless powder, soluble in water, but almost insoluble in alcohol, and is said to be a compound of anhydromethylene-citric acid and hexamethylene-tetramine, 2 Gm. representing 0.85 Gm. of the latter constituent. Theoretically, hexamethylene-tetramine should undergo decomposition in the human system with the formation and subsequent elimination of formaldehyde, and S. Goldschmidt (*Th. M.*, Jan., 1903) states that after the administration of helmitol formaldehyde is present in the urine when freshly voided. Helmitol has been highly recommended by P. Rosenthal (*Ther. Geg.*, Dec., 1902) in chronic *gonorrhea* and other infective diseases of the genito-urinary tract. Its value has been confirmed by S. Goldschmidt. It may be given in *doses* of fifteen to twenty-three grains (1.0–1.5 Gm.) up to forty-five to sixty grains (3–3.9 Gm.) a day.

Hexamethylenamine Oxymethyl-sulphonate. Thial.—This is a white, odorless powder which is freely soluble in water. It is used as an external disinfectant in strengths of from 0.5 to 2 per cent.

Hexamethylenamine Resorcinol. Hetralin. Dioxybenzenehexamethylenetetramine. $C_6H_6O_2C_6H_{12}N_4$.—Soluble in four parts of hot water and in fourteen of cold water. Contains 60 per cent. of *hexamethylenetetramine*. It has been used as a urinary antiseptic in precisely the same class of cases in which hexamethylenamine has been employed. Fries (*All. M. C. Z.*, 1906) asserts that it has an advantage over the latter, in that it exercises an antiseptic influence even in alkaline fluids. Birnbaum (*W. K. R.*, 1906) asserts that it is also a valuable remedy in *spermatorrhea* and allied complaints. The *dose* is from eight to fifteen grains (0.5 to 1.0 Gm.) three times a day.

Hexamethylenamine Salicylate. N. N. R. 1917. *Saliformin.* $C_8H_{12}N_4.C_6H_4OH.COOH$.—A white crystalline powder of a pleasant acidulous taste. Easily soluble in alcohol and water. It is employed as a uric acid solvent and genito-urinary antiseptic. *Dose*, eight to thirty grains (0.5–2.0 Gm.).

Hexamethylenamine Salicylsulphonic Acid. N. N. R. 1917. *Hexamethylenamine Sulphosalicylate. Hexalet Sulphosalicylate hexamethylenamine.* $(CH_2)_6N_4.SO_3H.C_6H_3(OH)COOH$, occurs

as white crystals soluble in water with a pleasant acid taste. It is claimed for it that it is broken up in the system, and that the sulphosalicylic acid exercises an astringent action upon the mucous membrane of the bladder as well as enhances the antiseptic action of the hexamethylenamine portion of the molecule. The *dose* is from ten to twenty grains (0.65–1.3 Gm.) three times a day.

Hexamethylenamine Sodium Acetate, Cystopurin is a double salt of hexamethylenamine and sodium acetate in the molecular proportion of 1:2, which according to Bergell (*Apoth. Zeit.*, xxii), has the following formula: $(CH_2)_6N_4 2CH_3COONa + 6H_2O$. This salt forms long, acicular crystals which are soluble in cold or warm water. This compound has been employed as a urinary antiseptic in *cystitis, pyelitis,* and similar conditions. It is asserted by one authority that its advantage over hexamethylenamine is that the formaldehyde is more slowly liberated and by another because the sodium acetate hastens the liberation of formaldehyde.

Hexamethylenamine Tannin. N. N. R. 1917. *Tannopin.*—A light brown, odorless and tasteless powder, insoluble in alcohol, water and ether, and soluble in alkalinated liquid. It contains 87 parts of tannic acid and 13 parts of hexamethylamine-tetramine. It is employed as an intestinal astringent and antiseptic. *Dose,* eight to fifteen grains (0.5–1 Gm.).

Hexamethylenamine Triborate. Borovertin. $(CH_2)_6N_4.3HBO_2$.—It is prepared by the direct combination of boric acid and formin. A white powder, slightly acid in its reaction, it is soluble in eleven parts of water and almost insoluble in alcohol and ether. On heating with acids formaldehyde is developed; on saturation with alkalies, ammonia.

It is asserted to have the advantage over hexamethylenamine that it of itself renders the urine acid and therefore leads to the splitting up of the hexamethylenamine molecule and the liberation of formaldehyde so that it is useful as an urinary antiseptic, when the urine is alkaline as well as when it is acid.

The *dose* is five to ten grains (0.32–0.65 Gm.) three or four times a day.

Hibiscus. *Hibiscus Abelmoschus* L. (*Abelmoschus moschatus* Möuch.) (Fam. *Malvaceæ.*)—An evergreen shrub, growing in Egypt, and in the East and West Indies, and yielding the seeds known under the names of *Semen Abelmoschi, grana moschata, Musk seed, Abelmosch, Semence on Graine d'Ambrette, Ambrettekörner, Bisornkörner, and Ambrakörner.* These are of about the same size as flaxseed, kidney-shaped, striated, of a grayish-brown color, of an odor like that of musk, and of a warm somewhat spicy taste. They were formerly considered stimulant and antispasmodic, but are now used only in perfumery. The Arabs flavor their coffee with them. They are said to be employed in the adulteration of musk. Another species, *Hibiscus esculentus* L., or *Abelmoschus esculentus* Moench., is cultivated under the name of *okra, bendee,* or *gombo* in various parts of the world, for the sake of its fruit, which abounds in mucilage (*gombine*), and is used for thickening soup. The leaves are sometimes employed for preparing emollient poultices. The roots, which are a foot or two long, are said also to abound in mucilage free from any unpleasant odor. Their powder is perfectly white, and superior to the marshmallow. The plant is largely cultivated near Constantinople, where it is much used as a demulcent. (*A. J. P.*, 1860, 224; *P. J.*, 1904, 892.) The bark is also used in making paper and cordage.

Hieracium. *Hieracium venosum* L. (Fam. *Compositæ.*) *Rattlesnake Weed. Poor Robin's Plantain. Epervière,* Fr. *Habichtskraut,* G.—The plant is common, growing in dry places and open woods from Maine to Georgia and westward. The leaves and roots are thought to possess medicinal virtues, and, being deemed astringent, have been used in *hemorrhagic diseases.* The juice is supposed by some to have the power of removing *warts. Dose* of infusion (two ounces to the pint), a wineglassful (60 mils).

Hippol. *Methylene Hippuric Acid.* $C_6H_5CO.N:(CH_2)_2COO$.—This is said to be not a true acid, but an ester of hippuric acid. It occurs as colorless, odorless and tasteless prismatic crystals, melting at 151° C. (303.8° F.), practically insoluble in water but soluble in chloroform and in hot alcohol. It has been brought forward by Nicolaiar (*Th. M.*, 1905) as a urinary antiseptic in *cystitis.* The recommended *dose* is twenty-five grains (1.66 Gm.) several times a day.

Hippuric Acid. $C_9H_9NO_3$. *Benzoylglycocoll,* $CH_2\begin{cases}NH.C_7H_5O\\COOH\end{cases}$.—This occurs in considerable amount in the urine of herbivorous animals, sometimes in that of man. Benzoic and cinnamic acids, toluol, and other aromatic substances, when taken internally, are eliminated as hippuric acid. It crystallizes in rhombic prisms, melting at 187° C. (368.6° F.), and at about 240° C. (464° F.) decomposes into benzoic acid, benzonitrile, and prussic acid. Boiling acids, alkalies, or high temperatures decompose it into benzoic acid and glycocoll. According to the experiments of Meissner and Shepard, hippuric acid injected into the blood of animals acts as a very decided poison, but the hippurates have been suggested by Garrod as a remedy in the *uric acid diathesis.* He affirms that if outside of the body the sodium hippurate be added to blood serum that shows the presence of a urate, the latter is soon removed. *Sodium hippurate* may be combined with lithium or potassium salts; the *dose* is ten grains (0.65 Gm.) three times a day.

Hirudin. *Hirudine.*—A principle obtained from the heads of leeches. It is said to prevent the coagulation of blood. It occurs as brownish scales easily soluble in water. One-sixtieth of a grain is said to permanently prevent two fluidrachms of blood from coagulating without changing its property in any other way. Its use in gynecology is based on this property. See *Hirudo,* Part I. Marshall (*J. P. Ex. T.*, 1915, vii, p. 157) finds that some commercial samples of *hirudin* are highly toxic. He believes that these effects are due to the presence of decomposition products.

Histamine. *N. N. R.* 1917. *Ergamine. Beta-iminazolylethylamine.* $\begin{matrix}CH{=}N\\ |\quad\quad\diagdown\\ NH{-}CH\end{matrix}\!\!>\!C.CH_2.CH_2NH_2$.—*Histamine* chemically is histidine minus one molecule of carbon dioxide. Histamine hydrochloride is used as a reagent for standardizing pituitary preparations. Histamine occurs in various putrefying proteins and also in ergot. The commercial supply, however, is obtained synthetically. It is a general stimulant to unstriped muscle, including the uterus, but through some action upon the blood vessels not clearly understood, it produces a fall of blood pressure. It also produces, in rodents, a spasm of the bronchial muscles, giving rise to symptoms very analogous to those of

the so-called anaphylactic shock. It has been suggested as a uterine stimulant in *postpartum hemorrhage.* The *dose* of histamine is one-sixtieth of a grain (0.001 Gm.).

Histogenol.—Monneyrat (*Prog. M.*, April, 1902), finding that *sodium methylarsenate* ($OAsCH_3O_2Na_2$) was not poisonous, has combined it with nucleinic acid to form this preparation, which he claims to be of great value in the treatment of *tuberculosis.*

Histosan is said to be a reaction product of egg albumen solution with an alkaline guaiacol solution. It is stated to be a triguaiacol albuminate compound and is accorded the following formula: $C_{72}H_{109}(C_6H_4OCH_3)_3N_{18}SO_{22}$. It is used in *tuberculosis. Dose,* four to eight grains (0.25–0.5 Gm.).

Hoang-Nan.—This is the bark of *Strychnos malaccensis* Benth. (Fam. *Loganiaceæ*), a climbing plant, which grows in Malacca and surrounding countries. Brucine and strychnine are stated to have been found in it, brucine being the more abundant of the two. It has been found to produce in animals general tetanic spasms similar to those caused by strychnine. It probably has the same range of medicinal application as has nux vomica, although special virtues have been claimed for it in the treatment of *chronic skin diseases. Dose* of powdered bark, three grains (0.2 Gm.).

Holadin. *N. N. R.* 1917. *Extractum Pancreaticum Integrum.*—A dried extract of the entire pancreas containing all the constituents of the glands and having power to digest starch and proteids, also aiding in the splitting up of fats. *Dose,* three to ten grains (0.2–0.6 Gm.).

Holigarna. *Holigarna longifolia* Roxb. Now *Senecarpus longifolia* Blume. (Fam. *Anacardiaceæ.*)—According to David Hooper (*P. J.*, xxv, 1895), the black juice of this tree, which is used in India as the basis of a varnish, is actively vesicant, and contains a body closely allied to, if not identical with, cardol.

Holocaine. *N. N. R.* 1917. *p-Diethoxyethenyl diphenylamidine. Phenetidyl-acetphenetidin,*

$$C_6H_4 \begin{cases} OC_2H_5 \\ NH.C(CH_3)=N.C_6H_4(OC_2H_5), \end{cases}$$

formed by the condensation of molecular amounts of phenacetin and paraphenetidine. The free base crystallizes well, is insoluble in water, and melts at 121° C. (249.8° F.). It is insoluble in fixed oil, a point which should be borne in mind, inasmuch as it is a frequent method of using holocain to prescribe it in a castor oil solution. The hydrochloride is, however, soluble in oils and should be dispensed when the other is called for. It should not be dispensed in alkaline solutions, being rapidly decomposed.

Holocaine Hydrochloride (*N. N. R.* 1913) forms colorless, lustrous, odorless crystals, melting at 189° C. (372.2° F.). It is soluble in 45 parts of water and readily in alcohol. It readily dissolves in boiling water, leaving on cooling a saturated solution containing about 2½ per cent. of the hydrochloride. This solution is slightly bitter, neutral in reaction, and keeps many months without change. In boiling, a porcelain vessel should always be used, as the solution at 212° C. (413.6° F.) is affected by the alkalinity of the glass.

It has been brought forward as a local anesthetic in the treatment of diseases of the eye. The anesthesia, which is said to develop in from fifteen seconds to a minute after the instillation of the solution, lasts from ten to fifteen minutes. The amount of burning produced is about the same as with cocaine. The advantages which are claimed for it over the latter alkaloid are that it does not change the pupil, the accommodation, or the intraocular pressure, and is antiseptic. It does not contract the blood vessels. The objections to it are that the instillation has to be renewed in from ten to fifteen minutes, and that it is about five times as toxic as is cocaine, so that it cannot be used hypodermically. According to the experiments of Heinz and Schlosser (*Klin. Monat. f. Augen.*, xxxv, 1897), the ½ of 1 per cent. solution affects bacteria, while the 1 per cent. solution is a powerful germicide, rapidly killing the lower organisms, including infusoria. Even in small doses it causes in frogs and in mammals violent convulsions which appear to be of cerebral origin, since after division of the spinal cord in the mouse the convulsions were confined to the anterior portion of the body. Holocaine is an active muscle poison, the 1 per cent. solution rapidly killing voluntary and cardiac muscles in the frog, and it exerts also a curare-like influence upon the motor nerves. According to Winselmann, its 1 per cent. solution exceeds in anesthetic power the 3 per cent. solution of cocaine.

Homorenone. *Ethylaminoacetopyrocatechin.* $C_6H_3(OH)_2CO.CH_2NH_2.C_2H_5$.—The hydrochloride occurs as bitter white crystals, readily soluble in water with a melting point of 260° C. (500° F.). It is asserted to resemble closely the physiological action of epinephrine except that it requires solutions of greater concentration to produce the same result. A 5 per cent. solution is asserted to be equivalent to one per mille of epinephrine. (See *P. J.*, 1908, lxxx, p. 784.)

Honthin.—This is a grayish-brown odorless and tasteless powder, insoluble in water but yielding a light-brown solution in alcohol and in aqueous alkali, in which it is partly soluble. It is said to be chemically a *keratinized albumin tannate.* It is given in *doses* of from ten to twenty grains (0.65–1.3 Gm.) three to five times daily, as an astringent, in all forms of *diarrhea* without great irritation.

Hoochinoo.—This is an alcoholic drink which is clandestinely distilled by the Alaskan Indians, and has been supposed, on account of the frenzy which it produces in them, to contain some poisonous substance other than alcohol. John Marshall found it, however, to be simply an alcoholic liquor of about the strength of sherry, *i.e.*, between 20 and 25 per cent.

Hordeine. *Hordenin, Para-oxyphenyl-dimethylethylamine.* $C_{10}H_{15}ON$.—It was isolated by Léger from malted barley and is isomeric with *ephedrine.* The sulphate, $(C_{10}H_{15}NO)_2H_2SO_4.H_2O$, crystallizes in prismatic needles giving a violet-blue color with ferric chloride.

Hordenine has been used by Sbrazes and Guerive (*C. R. A. S.*, 1908, cxlvii) and other authors, in the treatment of various forms of *diarrhea* and *dysentery* and in gastric hyper-secretion. According to the researches of Camus (*A. I. P. T.*, 1906, xvi), which are reported by the authors quoted, it would appear that it acts by paralyzing the peripheral ends of the secretory nerves, as does atropine. It appears to affect also the pneumogastric and motor nerves and is asserted to have a tonic action upon the heart. Jackson (*J. P. Ex. T.*, 1914, iv, p. 491) finds that hordenine has a powerful effect in overcoming bronchial spasm and suggests its use in asthma. We know, however, of no clinical trials of it in this condition.

The *dose* is three to eight grains (0.2–0.5 Gm.) three or four times a day.

Hordeum. *Barley Orge*, Fr. *Gerste*, G.—The grains of *Hordeum sativum* Jessen, and its cultivated varieties. The original country of the cultivated barley is unknown. The plant has been found growing wild in Sicily and in various parts of the interior of Asia.

Pillitz found (*Zeit. An. Chem.*, 1872) in the dry barley 14.3 per cent. of insoluble albuminoids, 2.1 per cent. of soluble albuminoids, 62.6 per cent. of starch, 1.9 per cent. of dextrin, 2.7 per cent. of sugar, 1.7 per cent. of extractive material, 3.1 per cent. of fat, 1.4 per cent. of soluble ash, 1.2 per cent. of insoluble ash, and 8.9 per cent. of lignin. The presence of sugar seems to have been shown by Kühnemann (*Ber. d. Chem. Ges.*, 1875 and 1876), who found a crystallized dextrogyrate sugar which did not reduce alkaline copper solution, and an amorphous lævogyrate mucilaginous substance called *sinistrin*. According to Kühnemann, barley does not contain dextrin.

Clifford Richardson (*Bulletin No. 9, Department of Agriculture*, 1886) gives the following as the average composition of American barley: water, 6.47 per cent.; ash, 2.87; oil, 2.67; sugar, etc., 7.02; dextrin and soluble starch, 3.55; starch, 62.09; albuminoids soluble in 80 per cent. alcohol, 3.66; albuminoids insoluble in 80 per cent. alcohol, 7.86; fiber, 3.81; total, 100.00. He finds, moreover, that on an average the grain makes up 84.78 per cent. and the hull 15.22 per cent. of the barley.

Barley contains *hordein*, a proteid substance somewhat related to *gliadin* which is derived from the kernels of wheat and rye. Hordein is soluble in alcohol. The name was formerly given to a pulverulent mixture obtained from barley which was believed to be a definite substance.

Hulled barley is merely the grain deprived of its husk, which, according to Einhoff, amounts to 18.75 parts in the hundred.

Barley meal is formed by grinding the seeds, previously deprived of their husk. It has a grayish-white color; the constituents are the same as described above for barley. It may be made into a coarse, heavy, hard bread, which in some countries is much used for food.

Pearl barley (*Hordeum decorticatum*, Br., 1885) is the seed deprived of all its investments and afterwards rounded and polished in a mill. It is in small round or oval grains, having the remains of the longitudinal furrow of the seeds, and of a pearly whiteness. It is wholly destitute of *hordein*, and abounds in starch, with some gluten, sugar, and gum. This is the proper form of barley for medicinal use.

Barley in the form of the decoction, popularly known as *barley water*, affords a mucilaginous drink much employed from the time of Hippocrates to the present. Pearl barley is the form usually preferred for the preparation of the decoction, made by pouring four pints of boiling water on two troyounces of pearl barley and boiling away to two pints, and straining. It is especially used in infant feeding, as it seems to prevent the formation of large milk curds.

Hormonal. *Peristaltic Hormone.*—It has recently been shown that certain substances are formed in the body which, being absorbed into the blood, act as stimulants to secretion in distant glands. The presence of these metabolic products, which are known to physiologists as *hormones*, is generally presumed to be essential for normal function. Zuelzer (*B. K. W.*, 1908) claimed to have demonstrated that there is formed in the cells of the mucous membrane of the stomach, a hormone which is an excitant to intestinal peristalsis, and that this hormone is stored in the spleen. He has accordingly brought forward as a remedy for *constipation*, under the name of *hormonal*, a preparation made from the spleen of an animal at the heighth of digestion, which is intended for intravenous injection. A number of authors have reported favorably on its effects, but there have been several cases of serious and even fatal collapse following its application. Zuelzer (*D. M. W.*, xxxviii) asserts that these mishaps have been due to errors in the manufacture by which the substance was contaminated with an albumose, and that since the discovery and correction of these there has been no further trouble. On the other hand, Dittler and Mohr (*Z. K. M.*, 1911, lxxv) from both laboratory and clinical observations, conclude that the remedy is of doubtful utility, and too dangerous for practical use.

Houttuynia. *Houttuynia californica* B. et H., now *Anemopsis californica* Hook. et Arn. *Yerba Mansa.*—The root of this piperaceous Californian plant is employed by the natives in *chronic malaria*, and also in *diarrhea* and *dysentery*, and has been used with asserted good results in *gonorrhea* and *rheumatism*. For elaborate histological study, see *D. C.*, May, 1897. *Dose* of the fluidextract, from fifteen to sixty minims (0.9–3.75 mils). A decoction of this root was used by the Indians as a local application in cuts and ulcers as well as internally in *diarrhea* and *dysentery*. It has also been recommended as a local application in nasal and pharyngeal *catarrhs*. The investigations of Lloyd (*A. J. P.*, 1879) showed a characteristic volatile oil and a tannin together with gum and a fixed oil.

Huamanripa.—This is a Chilian drug, the plant growing on the slope of the Cordilleras at considerable heights. Lapater found it to be stimulating, emetic, sialagogue, and diaphoretic. (*West. Drug.*, 1886, 410.)

Hura. *Hura crepitans* L. *Sandbox tree. Assacou. Sablier*, Fr. *Sandbüchsenbaum*, G.—This tree belonging to the family of *Euphorbiaceæ* is indigenous to tropical America and is extensively cultivated in the tropics. It is characterized by the tendency of its fruit when ripe to break with violence into several pieces, and thus scatter the seeds. It is an acrid emeto-cathartic; in large doses acting as a violent poison. The fresh juice, the seeds, and a decoction of the bark all have these properties; an oil expressed from the seeds is actively purgative. According to Richet, the toxicity is due to the presence of a toxalbumin to which he gave the name of *crepitin*. (*P. J.*, 1910, lxxxiv, p. 571.) The juice of *Hura crepitans*, which, according to J. J. Surie (*Nederl. Tijdscg. voor Pharm.*, 1900, 107), contains a volatile, colorless liquid, *hurin*, closely allied to cardol and is stated by Martius to be used to intoxicate fish, it has been employed to a considerable extent with alleged favorable results in the treatment of the *elephantiasis*, or *leprosy*, of Brazil. (For a method of using it, see *J. P. C.*, xiv, 424.) The juice is extremely acrid, producing on the skin, when applied to it, an erysipelatous redness and a pustular eruption; the natives are said to employ it in the preparation of a poison.

Hydracetin. *Pyrodine.*—The *hydracetin* of commerce is stated to be a varying compound, whose

active principle is *acetylphenylhydrazin* ($C_6H_5NH-NH.C_2H_3O$). It is soluble in alcohol and in water in proportion of 1 to 50. According to Guttmann (*Ph. Centralh.*, May 16, 1889, 311), hydracetin is a powerful antipyretic and antirheumatic remedy. It occurs as a white, odorless, almost tasteless crystalline powder, melting at from 128°–129° C. (262.4°–264.2° F.). It is stated that it cannot be continuously used without danger. Externally, hydracetin is used in place of chrysarobin in *psoriasis* and similar disorders, in an ointment of from 5 to 15 per cent. *Dose*, three-quarters of a grain (0.048 Gm.) two or three times a day.

Hydrangea. *N. F. IV. Seven Barks. Common Hydrangea.* (Fam. *Saxifragaceæ.*)—It is described by the N. F. as "the dried rhizome and roots of *Hydrangea arborescens* Linné. (Fam. *Saxifragaceæ.*) Rhizome cylindrical, usually cut into pieces from 3 to 10 cm. in length and from 3 to 20 mm. in diameter; externally light brown to yellowish-brown with a pinkish tinge, longitudinally wrinkled, marked by few elliptical lenticels and occasional prominent buds, short branches or stem scars; from the lower surface arise a few coarse fibrous roots; fracture tough, splintery; internally yellowish-white or light brown, bark thin, easily separable from the distinctly radiate wood which surrounds a prominent whitish pith. Roots attaining a length of 25 cm. and a thickness of 2 mm., irregularly bent and branching, otherwise resembling the rhizome with the exception of the pith being absent. Inodorous; taste sweetish, becoming slightly acrid. Under the microscope, sections of the rhizome of Hydrangea show a gray cork of a few rows of tabular cells, a cortex made up chiefly of parenchyma containing starch, large cells containing raphides and small isolated groups of stone cells or sclerenchymatous fibers; a woody cylinder composed of slender wedges made up of prominent tracheæ with reticulate thickenings and tracheids separated by medullary rays one to three cells wide, the cells of which are filled with small starch grains; pith of large polygonal cells with prominent simple pores. The powder is light yellowish-brown, containing irregular fragments consisting of strongly lignified tracheæ, tracheids and medullary ray cells; stone cells and sclerenchymatous fibers from 0.05 to 0.2 mm. in length, strongly lignified, the walls marked by simple and branching pores; raphides numerous, from 0.07 to 0.13 mm. in length; starch grains mostly single, more or less ellipsoidal, occasionally with a prominent central cleft and varying from 0.002 to 0.01 mm. in diameter. Hydrangea yields not more than 3 per cent. of ash." *N. F.*

Bondurant (*A. J. P.*, 1887, 122) isolated a characteristic glucoside, *hydrangin*, crystallizing in stellate clusters, melting at 235° C. (455° F.), and subliming without decomposition. It is decomposed by dilute acids into a resin-like body and glucose. Its aqueous solution fluoresces strongly on addition of an alkali, resembling æsculin, but distinctly different in several particulars. Bondurant also obtained a fixed oil and a volatile oil, the latter containing sulphur. Two resins seemed also to be present, together with saponin and sugar. He found no tannin, however. Y. Asahina has isolated two crystalline substances from the alcoholic extract of the flowers of *H. Hortensia; hydragenol* and *hydrangeaic acid*. The first occurs in white, odorless and tasteless crystals which are soluble in alkalies and dissolve in sulphuric acid without color; hydrangeaic acid forms yellowish, shining crystals, and its alcoholic solution when treated with ferric chloride yields a violet color. Its decoction is said to have been used with great advantage among the Cherokee Indians, and subsequently by settlers, in *calculous diseases*. (See *N. J. Med. Rep.*, 1850, 1854, and 1885.) In overdoses it occasions vertigo, oppression of the chest, etc. *Dose*, thirty grains (1.9 Gm.).

Hydrocotyle. *Hydrocotyle asiatica* L. *Thick-leaved Pennywort. Indian Pennywort. Bevilacqua*, Fr. *Wassernabel*, G.—This is a small umbelliferous plant growing in Southern Africa and in India, where it has long been used as an alterative; it is apparently indigenous also in the Southern United States. Jules Lépine discovered in it a peculiar oleaginous substance, *vellarin*, having a strong odor recalling that of the plant, and a bitter, pungent, and persistent taste. (*J. P. C.*, 1885, 49.) It is said to be diuretic, and has been given in *fever* and *bowel complaints;* also in *syphilitic* and *scrofulous affections*. (*P. J.*, 1860.)

C. Daruty de Grandpré (*Nouv. Rem.*, April 8, 1888) finds that in small doses it is an energetic stimulant, and that in large doses it is narcotic, producing stupor, headache, and in some persons vertigo with a tendency to coma.

Hydrogen Sulphide. *Hydrosulphuric Acid. Sulphuretted Hydrogen.* H_2S.—A colorless gas of unpleasant odor, soluble in water, to which it imparts an acid reaction. 3.23 volumes of gas are absorbed by one volume of water at 15° C. (59° F.). Also soluble in alcohol. Has been liquefied at ordinary temperatures under a pressure of 17 atmospheres, or at ordinary pressures by a cold of −74° C. (−101.2° F.), and at −85° C. (−121° F.) becomes an ice-like solid. *Liquefied hydrogen sulphide* is a colorless, transparent, very mobile fluid with strong solvent properties. (*Chem. Ztg.*, 1904, No. 70.)

The symptoms of poisoning by hydrogen sulphide vary with the amount taken. Its inhalation in a concentrated form is followed by giddiness, nausea, excessive weakness, and rapid or immediate loss of consciousness. The very diluted gas produces nausea, pain in the head, and great general weakness; followed, if sufficient be taken, by coma, or stupor with delirium, and in some cases by general convulsions. The blood becomes of a brownish-black color, and after death remains fluid. The general appearances at the autopsy are not to be distinguished from those produced by the absorption of carbon dioxide, but the diagnosis is readily made by the odor which pervades the whole corpse.

Bruère (*J. A. P.*, Oct., 1891) finds that bright red diluted blood under the influence of the sulphide becomes of an olive-green color, and that out of the oxyhemoglobin a new compound is formed, *sulphmethemoglobin* or *sulphemoglobin*, probably by a union of hydrogen sulphide with hematin. It has been shown by Paul Binet (*Rev. Méd. de la Suisse Rom.*, xvi, 1896) that this sulpho-methemoglobin is produced in the blood during life, especially when the gas is in very large amount. It is worthy of remark that Bruère found *hydrogen selenide* and *hydrogen telluride* to act the same as the hydrogen sulphide.

In 1886 Bergeon proposed to the French Academy a method of treating *tuberculosis* by injecting hydrogen sulphide, diluted with pure carbon dioxide, into the large intestine, the method being founded upon the supposed power of hydrogen sulphide to destroy the tubercle bacillus. The method of Bergeon had an extraordinary run, and then fell

rapidly into desuetude, but there can be no doubt that the hydrogen sulphide has a distinct influence upon mucous membrane. It is a useful remedy in *pulmonary catarrh,* chronic or acute, as well as in *chronic rheumatism* and in *gout.* It is for this reason that sulphur springs are so frequently resorted to. Water saturated with hydrogen sulphide and carbon dioxide is usually not objected to by patients after the first day or two of its taking, and does not disagree with the stomach. *Dose,* from two to four fluidounces (60–120 mils) three or four times a day.

Hydrohydrastinine Hydrochloride. $C_{11}H_{13}NO_2.HCl$.—A fine, white powder easily soluble in water and melting at 274° C. (525.2° F.). It is a vasoconstrictor, accelerating respiration and causing dyspnea, having no action on the heart and causing successive increase and decrease of blood pressure. It has heretofore been used in the treatment of *uterine hemorrhage. Dose,* one-third to one-half grain (0.021–0.032 Gm.) three times daily.

Hydronal. *Viferral.*—This is produced by the action of pyridine upon chloral. It is a white powder, having a disagreeable taste, soluble in cold water but decomposed by hot water. Used as a hypnotic. *Dose,* fifteen to thirty grains (1.0–2.0 Gm.).

Hydropyrine.—Under this name the *sodium acetyl salicylate,* or, as *hydropyrine* L., or *hydropyrine* Grifa., the *lithium acetyl salicylate,* have been introduced into medicine. The sodium salt has been found to be too unstable for practical use and the term *hydropyrine* is at present generally applied to the lithium salt. Even the latter is by no means permanent in the air, being decomposed into lithium salicylate and free acetic acid. It has been introduced as a substitute for acetyl salicylate acid in the treatment of *rheumatism* and *neuralgias.* It is, however, doubtful whether it has any advantage. The *dose* is from eight to fifteen grains (0.5–1 Gm.).

Hydroquinine. *Methyl-hydrocupreine.* $C_{20}H_{26}O_2N_2 + 2H_2O$.—This is a white, crystalline powder which is obtained from the mother liquor in the manufacture of quinine. Its chemical formula differs from that of quinine in that it contains two extra atoms of hydrogen in the molecule. It is sparingly soluble in water, readily soluble in alcohol, ether and chloroform, and gives the thalleiquin reaction. The hydrochloride, $C_{20}H_{26}O_2N_2HCl.2H_2O$, forms crystals which are readily soluble in water and alcohol. Morganroth and Halberstadter (*B. K. W.,* 1911) assert that this agent will cause a disappearance of trypanosomes from infected animals, which quinine will not do. Morganroth and Levi (*B. K. W.,* 1911) also assert that a closely allied compound, namely, *ethyl-hydrocupreine,* $C_{19}H_{22}ON_2H.OCH_5$, is a valuable agent both as a prophylactic and a curative in *pneumonia.* (See *Optochin.*) Giemsa and Werner (*Ob. G. T.,* 1912, p. 492) assert that *hydroquinine* is more efficacious in *malaria* than quinine. It has also been commended by Lenzmann (*M. M. W.,* 1912, p. 2193) as a local application in *whooping cough.* The *dose* used by Giemsa and Werner was three grains, three to four times a day.

Hydroquinone. *Hydrochinone. Quinol.* 1–4 $C_6H_4(OH)_2$.—This is one of the three isomeric diatomic phenols, of which resorcin is the *meta* variety, being *paradioxybenzene.* It was first prepared by the dry distillation of quinic acid, but is now made from quinone by reduction with sulphurous acid, the quinone being made by oxidizing aniline with dichromate mixture ($K_2Cr_2O_7 + H_2SO_4$). It is in shining white leaflets melting at 169° C. (336.2° F.), soluble in water, alcohol, and ether, and is used largely in photography as a developing agent. In 1877 Brieger found that *hydroquinone* produces in man giddiness, tinnitus aurium, and a lessening of the force and frequency of the pulse. The experiments of P. J. Martin have shown that in the frog hydroquinone causes violent convulsions, followed by paralysis. In the mammal small doses produce a rise in the arterial pressure, followed by a depression; both these phenomena are apparently the result of an action of the drug upon the arterial vasomotor system, although it is probable, from the experiments of Beyer, that the toxic dose of hydroquinone paralyzes both the heart muscle and the muscle fibers in the coat of the arterioles. The bodily temperature is lowered by large doses of hydroquinone, and, according to the experiments of Martin, this is chiefly due to an increase of heat dissipation, and is, therefore, probably the result of a vasomotor paralysis.

Hydroquinone is also anseptic, but inferior in power to phenol. The influence of hydroquinone upon the human being has been especially studied by Silvestrini and Picchini, and by Gaetano Traversa. (*France Méd.,* May, 1890.) According to these authorities, it is a prompt antipyretic, producing depression of temperature in *fever,* the reduction beginning in half an hour, and reaching its maximum in an hour and a half. Usually the antipyretic action is not accompanied by disagreeable symptoms, although after the larger dose excessive sweating chills, and some nervous disturbances have been noted. Hydroquinone has been used with asserted good results in *infectious fevers,* and in *acute articular rheumatism;* also as a gastro-intestinal disinfectant. *Dose,* three to eleven grains (0.2–0.71 Gm.).

Hydroxycaffeine. 1, 3, 7-*trimethyl Uric Acid.* $C_8H_{10}O_3N_4$.—It occurs as fine, white needles, melting at 345° C. (685° F.), with partial sublimation. It is readily soluble in hot water, in acids, alkaline carbonates and solution of sodium benzoate. It is soluble with difficulty in alcohol, ether and chloroform. Starkenstein (*A. E. P. P.,* 1907, lvii), as the result of a physiological study, reached the conclusion that this preparation possessed the diuretic power of caffeine and of other xanthine derivatives, but does not exert toxic action upon the muscles and nervous system.

Hydroxylamine Hydrochloride. $NH_2.OH.HCl$.—The free base is known only in solution, and is unstable. The crystalline hydrochloride forms colorless hygroscopic crystals similar to ammonium chloride in appearance, soluble in an equal weight of water, also in glycerin and in fifteen parts of alcohol. In 1888 Binz found that this substance caused in the lower animals stupor, convulsions, and a destruction of the red blood corpuscles, of such character that their hemoglobin was reduced to methemoglobin or even to hematin. In 1899 L. Lewin of Berlin, further investigated the subject, confirming in part the results obtained by Binz, and showing that the poison acts both upon the dead and living blood, and that its action upon the corpuscle is probably due to its decomposition, and the liberation of nitric or nitrous acid. In 1889 John Fabry (*Arch. de Derm. et de Sph.,* tome ii, 1889) found that a 10 per cent. solution is exceedingly irritating to most human skins, producing intense redness, violent burning, sweating, and not rarely vesication. Some skins will

not bear a 1 per cent. solution, so that it is not safe in any new case to use a solution stronger than this. The substance was employed by Fabry, and since then by other clinicians, as an agent to replace pyrogallol and chrysarobin in the treatment of skin diseases, offering at the same time the advantage of being colorless, and not staining the skin, linen, etc. It has been used in *chronic psoriasis*, in *scabies*, in *lupus*, *herpes tonsurans*, *parasitic sycosis*, etc., with asserted excellent results, though Groddeck condemns it as being too irritating and liable to produce constitutional symptoms, and inferior in its healing powers to chrysarobin and pyrogallol. The solution of *hydroxylamine hydrochloride* may be prepared with alcohol or water, but should always be rubbed up with prepared chalk to neutralize any excess of acid.

Hydroxylamine Sulphate. *Oxy-ammonium Sulphate.* $(NH_2OH).H_2SO_4$.—It has been suggested by Bang (*B. K. W.*, 1907, p. 216) for the quantitative estimation of sugar in the urine with Fehling's solution. The method consists in boiling definite quantities of the urine to be tested with an excess of the copper solution, and then determining the amount of hydroxylamine necessary to decolorize the copper. It is also used as a reducing agent in the quantitative determination of chlorates, bromates and iodates. (Schimpf, *Volumetric Analysis*, 5th edition.)

Hygrophila. *Br. Add.* 1900.—The dried herb including the root of *Hygrophila spinosa* T. And. (*Asteracantha longifolia* Nees). *Br. Add.* (Fam. *Acanthaceæ*.) This species of *hygrophila* has long been used in India as a diuretic in the treatment of *dropsies*, especially where there is hepatic obstruction, and also as a popular *aphrodisiac*. In Southern India the root is an article of commerce, but in Bombay the seeds are commonly employed. By means of petroleum benzin C. H. Warden obtained from the roots a crystalline principle (*Phg. Ind.*, vol. 3). The *decoction of hygrophila* (*Decoctum Hygrophilæ*, Br. Add., 1900), two ounces of the root with three pints of water boiled to a pint, is given in *doses* of one-half to two fluidounces (15–60 mils).

Hylopeia Aethiopica (?).—This plant is asserted to contain an alkaloid, *anonaceine*, which has been employed in combination with other reputed aphrodisiacs under the term of *aphrodisin* in the treatment of *impotence*.

Hypericum. *Hypericum perforatum* L. *St. John's Wort. Millepertuis, Casse-diable*, Fr. *Johanniskraut, Harthen*, G. (Fam. *Hypericaceæ*.)—A perennial herb, with a very acrid juice, naturalized from Europe and a pernicious weed in this country. It has a peculiar balsamic odor, which is rendered more sensible by rubbing or bruising the plant. Its taste is bitter, resinous, and somewhat astringent. It imparts a yellow color to cold water, and reddens alcohol and the fixed oils. Its chief constituents are volatile oil, a resinous substance, tannin, and coloring matter. This latter, known as *hypericum red*, is a reddish resin, smelling like the flowers, soluble in alcohol, ether, ethereal and hot fatty oils, coloring the solution from wine red to blood red. It is soluble in alkalies with green color, and gives yellow precipitates with the alkaline earths and metallic salts. As a medicine it was in high repute among the ancients and the earlier modern physicians. Among the complaints for which it was used were *hysteria, mania, intermittent fever, dysentery, gravel, hemorrhages, pectoral complaints, worms*, and *jaundice;* but it was, perhaps, most highly esteemed as a remedy in *wounds* and *bruises*, for which it was employed both internally and externally. It probably has somewhat analogous power to the turpentines. It formerly enjoyed great reputation for the cure of demoniacs, and the superstition still lingers among the vulgar in some countries. At present the plant is scarcely used except as a domestic remedy. The summits were given in the *dose* of two drachms or more. A preparation, *oleum hyperici* or *red oil*, made by macerating four ounces of the tops in a pint of olive oil, is still used in many families for bruises.

Hyperol. $CO(NH_2)_2.H_2O_2$.—This powder is asserted to be composed of two molecules of urea with one of hydrogen peroxide. It dissolves freely in water with the development of heat. It is decomposed by ether, the hydrogen peroxide going into solution. Keubat has found that it contains 34 per cent. of H_2O_2. It is suggested as a substitute for hydrogen peroxide for various analytical purposes.

Hypnal.—*Chloralhydrate antipyrine*, $C_{11}H_{12}N_2O.CCl_3.CH.(OH)_2$, results by rubbing together 188 parts of antipyrine and 165.5 parts of hydrated chloral and crystallizing out the product. It forms colorless crystals melting at 67° C. (152.6° F.). It is supposed to combine the somnifacient action of chloral with the anodyne effect of antipyrine, and is used not only in the treatment of *insomnias* of nervous origin, but also in those caused by pain. The *dose* is from fifteen to thirty grains (1.0–2.0 Gm.).

Hypnoacetin. *Acetophenonacetyl-p-amidophenol-ester.* $C_6H_4(OCH_2.CO.C_6H_5)(NH.CO.CH_3)$.—This compound forms glassy leaflets insoluble in water, soluble in alcohol and fusing at 160° C. (320° F.). It is used as an antiseptic and hypnotic in *doses* of three to four grains (0.2–0.26 Gm.).

Hypnone.—*Phenyl-methyl-ketone, Benzoylmethide, Acetophenone*, $C_6H_5.CO.CH_3$, is obtained by the dry distillation of a mixture of calcium acetate and calcium benzoate; colorless or yellow liquid of oily consistency, boiling at 198° C. (388.4° F.). It has a pleasant odor suggesting that of orange flowers. It has been used as a somnifacient. *Dose*, three to eight minims (0.2–0.5 mil).

Hypnopyrin.—This substance, which was brought forward by Bolognesi and Charpentier (*R. T.*, July, 1902), is said to be a derivative of quinine, although some French writers state that it is simply a mixture of undetermined quinine salts. It occurs in white, bitter needles, effervescing and turning yellow in the air, soluble in eight times its weight of cold water and very soluble in hot water and alcohol. In dose of thirty grains it is said to produce cinchonism. It is alleged that it is a rapid, efficient analgesic, and that as an antipyretic it produces a gradual fall of temperature without sweating; antirheumatic properties are attributed to it. It is said to be harmless. *Dose*, four to eight grains (0.26–0.5 Gm.), given hypodermically.

Hyraceum.—The dried excrement of *Hyrax capensis*, commonly referred to as "Klipdas" or "Dassy," a small rabbit-like animal of South Africa. It is rather hard, tenacious, of a blackish-brown color, and in taste and odor not unlike castor. Schrader has found in it stearin and gum-resin soluble in absolute alcohol. (See *A. J. P.*, 1879, 363; also Léon Soubeiran, *J. P. C.*, xxix, 378.) E. D. Cope states that a similar substance

is found in fissures of the rocks in New Mexico, and is probably a fecal and renal deposit of the wild rat, *Neotoma.*

Hyssopus. *Hyssopus officinalis* L. *Hyssop. Hysope,* Fr. *Isop, Ysop,* G.—This is a European labiate plant, found along roadsides in this country, whose flowering summits and leaves have been used in medicine. They have an agreeable aromatic odor, and a warm, pungent, bitterish taste, due to the presence of a volatile oil. This oil is colorless or greenish-yellow, of peculiar odor, sharp camphor-like taste, and neutral reaction. It has a sp. gr. from 0.88 to 0.98, distils between 142° and 162° C. (287.6°–323.6° F.), and is soluble in its own bulk of alcohol of 0.85 sp. gr. The acid found in the oil has been identified as *l-pinonic acid,* and the ketone *l-pinocamphene.* Hyssop is a warm, gently stimulant aromatic, applicable to the same cases as the other labiate plants.

Iatrevin.—This is a condensation product of menthol and isobutyl-phenol. It is a clear fluid of an aromatic odor, miscible with alcohol in all proportions. It has been used by Munter (*Med. Klin.,* 1906, p. 1097) as an internal antiseptic in the treatment of *pulmonary tuberculosis.* As, however, there is grave doubt of the possibility of exercising an anti-bacterial effect upon the tubercle bacilli in the system and as his conclusions, as far as we know, have not been confirmed the remedy cannot be conceded to have won a permanent place in our materia medica.

Iberis. *Iberis amara* L. *Bitter Candytuft.*—A small European herbaceous cruciferous plant. The leaves, stem, and root are said to possess medicinal properties, but the seeds are most efficacious. The plant appears to have been employed by the ancients in *rheumatism, gout,* and other diseases. In large doses it is said to produce giddiness, nausea, and diarrhea, and to be useful in *cardiac hypertrophy, asthma,* and *bronchitis,* in *doses* of from one to three grains (0.065–0.2 Gm.) of the seed.

Ibit. *Bismuth-oxyiodo Tannate.* $C_6H_2(OH)_2(COOH).O.CO.C_6H_3(OH).O_2BiI$.—Bearing a close relation to airol this preparation forms a greenish-gray powder, insoluble and inodorous. In contact with water or animal secretions it liberates iodine upon which property depends its antiseptic properties. It is used as a deodorant antiseptic in treating *wounds* and *burns.*

Ibogaine.—This alkaloid was separated by Dybouski and Landrim (*Nouv. Rem.,* 1905) from the roots of the *Tabernanthe Iboga,* a plant found in the Congo. In overdose it causes hallucination and generally paralysis, with death due to failure of the respiratory muscles. In *dose* of one-third to one-half grain it is said to act as a stimulant to the nervous system somewhat similar to caffeine.

Ichthermol. *Mercury Sulphichthyolate.*—A condensation product of sulphichthyol and metallic mercury. It contains nearly one-fourth its volume of mercury. It forms a dark, inodorous, insoluble powder which is used as an antiseptic in treating *wounds* and *burns* and also as an antisyphilitic.

Ichthoform. *N. N. R.* 1917.—This is said to be obtained by the action of formaldehyde upon the products of sulphonization of ichthyol hydrocarbons, and to be superior to iodoform as an antiseptic. Externally it has been used by Unna, and in skin diseases is superior to the ordinary formaldehyde preparations. He asserts that it softens rather than hardens the skin. It has also been employed as an intestinal antiseptic in *doses* of fifteen to thirty grains (1–2 Gm.) three to four times a day.

Ichthynat. *Ammonium Ichthynate.*—This is an oily substance which is obtained from bituminous slate. It is a thick, reddish-brown fluid, readily soluble in water, but only partially soluble in alcohol and ether. It resembles ichthyol in its physiological properties and is used for the same purposes as that drug. *Ichtammon* is another product similar to, and derived from the same source as, ichthynat.

Ichthyocolla. *U. S.* 1890. *Isinglass. Colla Piscium,* P. G. *Fish-glue. Ichthyocolle, Colle de Poisson,* Fr. *Hausenblase, Fischleim,* G. *Colla di Pesce,* It. *Colla de Pescado,* Sp.—Isinglass is a gelatinous substance prepared from the sounds or swimming bladders of many species of fish in various parts of the world. It is chiefly procured from the Volga and other streams of Southern Russia, our commercial supplies also being derived from the United States, Canada, Brazil, the East Indies, Manila, and the West Indies. It is prepared from the following species of Acipenser: the *Acipenser Huso,* or *beluga,* the *Acipenser ruthenus,* or *sterlet,* the *Acipenser Sturio,* or common *sturgeon,* and the *Acipenser stellatus,* or *starred sturgeon.* The air bags, having been split open, cleansed, and dried, are known in commerce by the name of *staple isinglass,* which is divided into the *long* and the *short staple.* Sometimes the membranes are dried in a flat state, or simply folded, and then receive the name of *leaf* or *book isinglass.* The scraps or fragments of these varieties, with various other parts of the fish, are boiled in water, which dissolves the gelatin, and upon evaporation leaves it in a solid state. This is called *cake isinglass,* from the shape which it is made to assume. It is sometimes, however, in globular masses. Of these varieties, the long staple and the finest book isinglass are the best. One hundred grains of this isinglass dissolve in ten ounces of water, forming a tremulous jelly when cold, and yield but two grains of an insoluble residue. That in cakes is brownish, of an unpleasant odor, and employed only in the arts. Inferior kinds, with the same commercial titles, are said to be prepared from the peritoneum and intestines of the fish. An inferior Russian product, known in English commerce by the name of *Samovey isinglass,* is procured, according to Pereira, from the *Silurius glanis.* It comes, like the better kind, in the shape of leaf, book, and the short staple. Isinglass, little inferior to the Russian, is made in Iceland from the sounds of the cod and ling. It is said also to be prepared by the fishermen of Newfoundland. We receive from Brazil the air-bladders of a large fish, prepared by drying them in their distended state. They are oblong, tapering, and pointed at one end, bifid with the remains of their pneumatic duct at the other, and of a firm consistence. The *Brazilian isinglass* is inferior to the Russian. Considerable quantities of isinglass are manufactured in New York and New England from the sounds of the *hake* (*Gadus merluccius*) and of the weak-fish (*Otolithus regalis*). This *American isinglass* is in thin ribbons 6 dm. in length, and from 2.5 to 6 cm. in width. It has a fishy taste and odor, which render it unfit for culinary or medicinal purposes. The sounds are dried whole, or merely split open, and vary much in size and texture, weighing from a drachm to an ounce. An article called *refined* or *transparent isinglass* is made by dissolving the New England isinglass in

hot water, and spreading the solution to dry on oiled muslin. It is in very thin, transparent plates, and is an excellent glue, but retains a strong fishy odor. In India and China the swimming bladders of various species of fish furnish the so-called Indian and Chinese isinglass. At the present writing the various forms of isinglass are comparatively little used, their place being supplied by various brands of gelatin produced from fresh bones. (See *Gelatinum*, p. 509.)

In its purest form it is "in separate sheets, sometimes rolled, of a horny or pearly appearance; whitish or yellowish, semitransparent, iridescent, inodorous, insipid; almost entirely soluble in boiling water and in boiling diluted alcohol. A solution of isinglass in 24 parts of boiling water forms, on cooling, a transparent jelly." *U. S.*, 1890. The inferior kinds are yellowish and more opaque. In cold water it softens, swells up, and becomes opalescent. Boiling water entirely dissolves it, with the exception of a minute proportion of impurities, amounting, according to Hatchet, to less than 2 per cent. The solution on cooling assumes the form of a jelly, which consists of pure gelatin and water. Isinglass is in fact the purest form of *gelatin* with which we are acquainted, and may be used whenever this principle is required as a test. It is insoluble in alcohol, but is dissolved readily by most of the diluted acids, and by alkaline solutions. It has a strong affinity for tannin, with which it forms an insoluble compound. Boiled with sulphuric acid, it is converted into a peculiar substance, called *glycocoll* or *sugar gelatin*, which is in reality *amidoacetic acid*, $CH_2.NH_2.COOH$. Its aqueous solution speedily putrefies. An ingenious adulteration has been practised by rolling a layer of gelatin between two layers of genuine isinglass. This may be detected by the disagreeable odor and taste of the adulterated drug, and the effects of water upon it. Genuine isinglass, cut into shreds and treated with water, becomes opalescent and more opaque than before; while the shreds, though they soften and swell, remain unbroken, and when examined by the microscope are seen to be decidedly fibrous. Gelatin, on the contrary, when similarly treated, becomes more transparent than before; the shreds are disintegrated, and the structure appears amorphous under the microscope. In the adulterated article both these characters are presented in layers more or less distinct. (*P. J.*, ix, 505.) Moreover, Redwood and Letheby observed that the ash of true isinglass does not exceed 0.9 per cent., while glue contains from 2 to 4 per cent. of ash. An adulterated isinglass would therefore yield more ash than the normal. A *false isinglass* has been imported into England from Para, in Brazil, consisting of the dried ovary of a large fish. It has somewhat the form of a bunch of grapes, consisting of ovoid or roundish masses attached by a footstalk to a central axis. It is not gelatinous, and is unfit for the purposes to which isinglass is applied. (*A. J. P.*, xxv, 144.) For table showing value of different kinds of European isinglass, see *P. J.*, 1884, p. 900.

Medicinal Properties and Uses.—Isinglass has no peculiar medicinal properties. It may be given internally, in the form of jelly, as a slightly nutritious article of diet, but it has no advantage over the jelly made from calves' feet. Three drachms impart sufficient consistency to a pint of water. It is employed for clarifying liquors, and imparting luster to various woven fabrics. Added in small quantities to vegetable jellies it gives them a tremulous appearance, which they lack when unmixed. As a test of tannin it is strongly recommended by Wm. T. Wenzell, who uses it instead of hide powder in the estimation of tannin. (*A. J. P.*, 1894, 447.)

Isinglass plaster or *court plaster* (*Emplastrum Ichthyocollæ*, U. S., 1890) was very properly dropped in the eighth decennial revision. The process of 1890 is as follows: Isinglass, *ten grammes* [or 154 grains]; Alcohol, *forty grammes* [or 1 ounce av., 180 grains]; Glycerin, *one gramme* [or 15½ grains]; Water, Tincture of Benzoin, each, *a sufficient quantity*. Dissolve the Isinglass in a sufficient quantity of hot Water to make the solution weigh *one hundred and twenty grammes* [or 4 ounces av., 102 grains]. Spread one-half of this, in successive layers, upon taffeta (stretched on a frame), by means of a brush, waiting after each application until the layer is dry. Mix the second half of the Isinglass solution with the Alcohol and Glycerin, and apply it in the same manner. Then reverse the taffeta, coat it on the back with Tincture of Benzoin, and allow it to become perfectly dry. Cut the plaster in pieces of suitable length, and preserve them in well-closed vessels. The above-directed quantities are sufficient to cover a piece of taffeta *thirty-eight centimeters* [or about 15 inches] square." *U. S.*, 1890.

Ichthyol. *N. N. R.* 1917. *Ammonium Ichthyol-Sulphonate.* $C_{28}H_{36}S_3O_6(NH_4)_2$.—The *ichthyol* preparations are obtained by the dry distillation of the bituminous shale of the Tyro. The ichthyol salts are the salts of *ichthyol-sulphonic acid*, $C_{28}H_{36}S_3O_6H_2$, which is obtained by the treatment of the raw ichthyol distillate with sulphuric acid, and subsequently neutralizing with sodium or ammonium carbonate. Under the name ichthyol is ordinarily understood the *ammonium ichthyol-sulphonate*, $C_{28}H_{36}S_3O_6(NH_4)_2$, but Merck calls ichthyol an indefinable chemical compound. This is a reddish-brown, syrupy liquid of a bituminous odor and taste, puffing up considerably and carbonizing when heated, and upon continued incineration volatilizing without residue. Water, or a mixture of equal volumes of alcohol and ether, dissolves it to form a clear red-brown liquid of a faintly acid reaction. Pure alcohol or ether dissolves it only partially; petroleum benzin takes up only a small quantity. Upon the addition of hydrochloric acid to the aqueous solution a dark resinous mass is precipitated, which when separated is soluble in ether and in water, but is again thrown out from the latter solution by hydrochloric acid or sodium chloride. Treated with potassium hydroxide solution, ichthyol develops an odor of ammonia, and the mixture dried and burnt yields an hepatic coal, which with hydrochloric acid gives off hydrogen sulphide. The ammonium ichthyolate loses upon drying in a water bath at least half its weight. The *sodium ichthyol* is a dark, tar-like substance of an alkaline reaction, perfectly soluble in water. Both preparations combine with fat and vaseline in all proportions and are very rich in sulphur, containing, it is said, 10 per cent. According to Baumann, they have a great affinity for oxygen, and are powerful reducing agents. The ichthyol sulphonates of lithium, zinc, mercury, sodium and calcium have also been prepared.

Odorless ichthyol has been made by treating ichthyol with hydrogen dioxide. It is questionable, however, whether the removal of the odorous constituents does not impair the therapeutic activity of the ichthyol.

A host of substances said to be similar to ichthyol

are upon the market. Among these may be mentioned *ichtammon, ichthium, ichtolithum, ichden, ichthynat, ichthyopon, isarol, petrosulpho, piscarol, pisciol, subitol,* and *tumenol.* Beckurts and Freerichs (*J. A. Ph. A.*, 1913, ii, p. 335) find that there is great difference in the chemical composition of these various preparations.

Ichthyol is used chiefly externally. Applied pure it is mildly irritant to the skin. According to Abel (*Cb. B.*, 1893, xiv, p. 413), it has feeble antibacterial properties. He finds that pure ichthyol will kill the staphylococci pyogenes in five minutes' exposure but will not destroy the typhoid bacillus after an hour; it is antiseptic against the streptococci in 1 to 2000, but against staphylococci it requires 5 per cent. to stop growth. Peculiar alterative properties have been attributed to it and also the power of penetrating through the skin so that it has been used with alleged extraordinary success as a local alterative and anodyne discutient in *chronic eczema, urticaria, acne, intertrigo, lupus,* and other skin diseases. It is especially prized in infections of the sub-cuticle as *cellulitis* or *furunculosis.* It has even been attributed with the power of influencing for good, *erysipelas* and *tuberculous lymphadenitis.* Probably because of its counter-irritant action it has been found of service in *frost-bites, sprains,* and subacute or chronic *gout* and *rheumatism.*

Internally it has been employed by Barnes (*N. Y. M. R.*, January 21, 1911) and others, in the treatment of *bronchitis* and *tuberculosis.* The investigations of Helmers (*V. A. P. A.*, 1894, cxxxv, p. 135), however, would indicate that it has very slight effect upon metabolism and indeed most of it is excreted unabsorbed with the feces. It may be exhibited either in pill form or in solution in *doses* of from one to five minims (0.06–0.3 mil) gradually increased to ten minims (0.6 mil) as the stomach becomes tolerant.

Ichthyol Albuminate. *N. N. R.* 1917. *Ichthalbin.*—This is a greenish-brown powder, insoluble in water and acid solutions, soluble in alkaline solutions, odorless, almost tasteless. It is prepared by precipitating *egg albumin* with ichthyol and prolonged washing of the precipitate until the ichthyol odor and taste are removed. It is stated to contain about 75 per cent. of ichthyol. It is not toxic, and when given internally, even in large doses, produces little or no irritation of the gastro-intestinal tract. It is affirmed that as an internal remedy it is practically the same as ichthyol, and as such is useful in various conditions connected with wide-spread vascular dilatation, in *syphilis,* in *struma,* and in other states of lowered nutrition. It has also been used in the treatment of various inflammatory conditions of the intestinal tract, especially in chronic *collitis* and *enteritis. Dose,* from fifteen to thirty grains (1–2 Gm.) three times a day, best taken in capsules; or in the case of young children it should be mixed with chocolate.

Igazol.—This substance, which is said to be a combination of formaldehyde or tri-oxy-methylene (paraformaldehyde) and iodine, has been employed to a considerable extent in the treatment of *tuberculosis.* According to Arends and Eichengruen this preparation consists of *paraform, terpin hydrate,* and *iodoform.* According to the method of Preisach the fumes of four grammes are daily liberated in a small room containing patients; the results are some diminution of cough and expectoration. (*Ungar. med. Presse,* vol. vi, 490.)

Ignatia. *N. F. IV* (*U. S. P.* 1880). *Saint Ignatius Bean. Ignatia Amara. Semen Ignatiæ, Faba Ignatii, Faba Sancti Ignatii,* Lat. *Fève igasurique, Fève de Saint Ignace,* Fr. *Ignatiusbohne, Bittere Fiebernuss, Ignazbohnen,* G. *Fava di Santo Ignazio,* It. *Haba de Santo Ignacio,* Sp.—"The dried ripe seeds of *Strychnos Ignatii* Bergius (Fam. *Loganiaceæ*), yielding not less than 2 per cent. of the alkaloids of Ignatia." *N. F. IV. Strychnos Ignatia* Berg. (*Ignatia amara* L. f.) is a large climbing shrub, a native of the Philippine Islands, and introduced into Cochin-China where the seeds were highly esteemed as a medicine, and, having attracted the attention of the Jesuits, were honored with the name of their founder. Flückiger and Arthur Meyer have found that the seed has a close structural analogy to nux vomica. (*P. J.*, 1881, 1.)

It is described by the N. F. as "heavy, hard, angularly ovate with obtuse angles, from 20 to 30 mm. in length and about 15 mm. in breadth and thickness; externally grayish or reddish-black, nearly smooth with few or no hairs; fracture granular and translucent in small fragments; a small irregular cavity in the center. Nearly inodorous and intensely bitter. The powder is grayish-brown and, when examined under the microscope, exhibits thin cells of the epidermis and the subjacent layer of the seed coat, polygonal cells with thickened, pitted walls; hairs characteristic, spreading and thickened at the base and having linear markings; endosperm tissue, the outer cells small, contents granular, the inner large, with thickened walls; lumen irregular in size and shape. Ignatia yields not more than 4 per cent. of ash." *N. F.*

Assay.—"Introduce 15 Gm. of Ignatia, in No. 40 powder, into a 250 mil flask and add 150 mils of a mixture of chloroform, 1 volume, and ether, 2 volumes. Stopper the flask, shake it well and allow it to stand ten minutes, then add 10 mils of ammonia water, shake the flask vigorously every ten minutes during two hours and allow it to stand for ten hours. Now add 25 mils of distilled water, again shake the flask well, and, when the drug has settled, decant 100 mils of the solution, representing 10 Gm. of Ignatia. Filter the solution through a pledget of purified cotton into a separator, and rinse the graduate and cotton with a little ether. Completely extract the alkaloids from the solution by shaking out repeatedly with weak sulphuric acid. Collect the acid washings in a separator, add ammonia water until the solution is decidedly alkaline to litmus, and completely extract the alkaloids by shaking out repeatedly with chloroform. Evaporate the combined chloroform washings to dryness, dissolve the alkaloids from the residue in exactly 10 mils of tenth-normal sulphuric acid V.S., and titrate the excess of acid with fiftieth-normal potassium hydroxide V.S., using cochineal T.S. or methyl red T.S. as indicator. Each mil of tenth-normal sulphuric acid V.S. consumed corresponds to 36.4 milligrammes of the alkaloids of Ignatia." *N. F.*

To Pelletier and Caventou Ignatia beans yielded the same constituents as nux vomica, and, among them, 1.2 per cent. of strychnine and 0.5 per cent. of brucine. J. M. Caldwell found strychnine and brucine, combined with igasuric acid, a volatile principle, extractive, gum, resin, coloring matter, fixed oil, and bassorin, but no starch or albumen. (*A. J. P.*, 1857, 298.) Flückiger, on the other hand, found 1.78 per cent. of nitrogen, corre-

sponding to about 10 per cent. of albuminoid matter. (*Pharmacographia*, 443.).

They have been used instead of nux vomica, in the preparation of that alkaloid, when their cost would permit of the substitution, but the nux vomica bean has been imported in such large quantities, and is now so low in price, that the ignatia bean is rarely used. The medicinal uses are those of nux vomica.

For process of making the *abstract* (*Abstractum Ignatiæ*, U. S., 1880), see *U. S. D.*, 19th ed., p. 1524. The *dose* of the abstract is from one-half to one and a half grains (0.032–0.096 Gm.). A tincture is recognized by the N. F. (see Part III).

Ilex. *Holly. Houx*, Fr. *Stechpalme Christdorn*, G.—Several species of *Ilex* (Fam. *Aquifoliaceæ*) are employed in different parts of the world. The *I. Aquifolium* L., or *European Holly*, is usually a shrub, but in some places attains the magnitude of a middling-sized tree. It is the most beautiful of all evergreens, but is unsuited to our climate, being too tender to withstand the winters in the Northern States and equally affected by the hot, dry summers in the Southern States. A viscid substance called *bird lime* is prepared from the inner bark (see p. 1278). The leaves, which are of a bitter, somewhat acrid taste, were formerly much esteemed as a diaphoretic, and in the form of infusion were employed in *catarrh, pleurisy, smallpox, gout*, etc. At one time they enjoyed a brief reputation in France as a cure for *intermittents*. They were used in powder, in the *dose* of a drachm two hours before the paroxysm, and this dose was sometimes repeated frequently during the apyrexia. Their febrifuge virtues are said to depend on a bitter principle, *ilicin*. Labourdais obtained this principle by boiling a filtered decoction of holly leaves with animal charcoal, allowing the charcoal to subside, washing it, then treating it with alcohol, filtering off the alcoholic solution, and evaporating it to a syrupy consistence. The liquid thus obtained was very bitter, and, on being allowed to evaporate spontaneously, yielded an amorphous substance, having the appearance of gelatin, which was the principle in question. (See *A. J. P.*, xxi, 89.) A yellow coloring substance called *ilexanthin*, and a peculiar acid called *ilicic acid*, were obtained by F. Moldenhauer. *Ilicic alcohol*, $C_{30}H_{50}O$, was separated by Personne from birdlime and found to be identical with α-amyrin. (*C. R. S. B.*, 1908, 862.) Ilexanthin is obtained in the following manner. The leaves are exhausted with alcohol, the alcohol is distilled off, and the residue set aside for several days. A sediment forms, which is separated from the mother liquor, treated with ether to remove the chlorophyll, and then purified by repeated solution in alcohol and crystallization. The composition of ilexanthin is $C_{17}H_{22}O_{11}$. It crystallizes in yellow needles, which change color at 185° C. (365° F.), melt at 198° C. (388° F.), and at 214° C. (417° F.) boil with decomposition, and are not sublimable. It is insoluble in ether, but soluble in alcohol. In cold water it is almost insoluble; but hot water dissolves it freely, and deposits it in crystals on cooling. The *berries* are about the size of a pea, red and bitter, and are said to be purgative, emetic, and diuretic. Ten or twelve of them will usually act on the bowels, and sometimes excite vomiting. Their expressed juice has been used in *jaundice*.

Ilex opaca Ait., or *American holly*, is a middling-sized evergreen tree, growing throughout the Atlantic section of the United States, and especially abundant in New Jersey. It is so similar to the European plant that it has been by some writers considered as the same species. The berries, examined by D. P. Pancoast, were found to contain tannin, pectin, two crystallizable organic principles, and salts of potassium, calcium, and magnesium. One of the crystallizable principles was inodorous and tasteless, the other inodorous but intensely bitter. The latter was obtained by evaporating a tincture to syrupy consistence, alkalizing with potassium carbonate and extracting with ether. The ether was allowed to evaporate spontaneously when crystals of the bitter principle were deposited. This is probably pure *ilicin*. (*A. J. P.*, xxviii, 314.) Walter A. Smith (*A. J. P.*, 1887, 1668) obtained a resin soluble in alcohol by the ether extraction, and in the portion of this soluble in water he obtained evidences of a glucoside. This species is said to possess the same medicinal properties as *I. aquifolium* L.

Ilex paraguariensis A. St. Hill (*I. Maté* St.-Hilaire) yields the celebrated *Paraguay tea*, or *Maté*, so extensively consumed as a beverage in the interior of South America. It is a small tree or shrub growing wild along the streams in Paraguay, and also cultivated for the sake of its leaves, which are the part used. These are stripped from each plant every two or three years. The period of their collection extends from December to August, sometimes beginning earlier but never continuing later. Companies are formed who penetrate far into the forest at a distance from the settlements, and devote a long time to the collection and preparation of the leaves. These are first dried by exposure to heat, and are then reduced to powder more or less fine, which is kept for several months protected from moisture, and then packed in sacks and delivered to commerce. (A. Demersay, *Ann. Thér.*, 1868, 72; see also *Pharm. Rec.*, May, 1891.) They have a balsamic odor and bitter taste, and are usually at first disagreeable to the palate. They have a pleasant and corroborant effect upon the stomach, but, when largely taken, cause purging and vomiting. They are used in the form of infusion, which is prepared from the entire leaves as we prepare tea; or, under the name of *cha maté*, a fine powder is put in a cup of hot water by the drinker, and after a moment's stirring, the fluid is sucked up by means of a tube expanded below, and pierced with fine holes, so as to strain out the powder. They contain, besides other substances, a peculiar tannin and the alkaloid caffeine in variable amount. Some fresh leaves of *Ilex Paraguariensis* grown in the Cambridge Botanical Gardens were found by A. H. Allen, after drying at 100° C. (212° F.), to contain: insoluble matter, 57.94 per cent.; tannin, by lead acetate method, 15.62; tannin, by cupric acetate method, 15.66; caffeine, 1.13; total ash, 6.14; soluble ash, 3.56. (*Com. Org. Anal.*, 2d ed., iii, Part II, 527.) Some elaborate proximate analyses of maté are also published by Theodore Peckolt. (*P. J.* (3), xiv, 121.) The consumption of *maté*, or *yerba*, in South America is enormous. Although largely produced in the Argentine Republic, tons are annually shipped to countries in South America. For an interesting account of the method of preparation, and an elaborate analysis, see *P. J.*, vol. xiv, 1017.

The *Ilex vomitoria* Ait. is a handsome evergreen shrub, growing in our Southern States, and especially abundant along the southern coast of Florida. Analysis of its leaves by Venable (*A. J. P.*, 1885, 390) gave 7.39 per cent. of tannic acid and 0.27 per cent. of caffeine. Smith (*A. J. P.*,

xliv, 217) found 0.011 per cent. of volatile oil and 0.122 per cent. of caffeine. It is the *cassena* of the North Carolina Indians, who formerly employed a decoction made from the toasted leaves, called *black drink*, or *Yaupon*, both as a medicine and as a drink of etiquette at their councils. It acts as an emetic. The leaves of the *Ilex Dahoon* L., or *Dahoon holly*, have similar properties, and are also said to have entered into the composition of the black drink.

Illicium. *U. S.* 1890. *Star-Anise.*—"The fruit of *Illicium verum* Hooker filius (Fam. *Magnoliaceæ*)." *U. S.*, 1890. Of the genus *Illicium*, seven species are recognized, of which two are found on the Atlantic coast of Southern North America, two in Hindostan, and three in China and Japan. Many of the species are possessed of aromatic properties.

The tree yielding star-anise is indigenous to Southeastern Asia and extensively cultivated in subtropical countries. The fruit is chiefly used in the manufacture of a volatile oil which resembles the official oil of anise. The fruit consists of usually 8 boat-shaped follicles or carpels arranged around a central axis. The carpels have an acute summit and taper to a nearly straight beak; externally, they are reddish-brown and somewhat wrinkled; the inner surface is smooth and shiny and encloses a single smooth seed. The odor and taste is aromatic, resembling anise, and this serves to distinguish them from the fruits of the Japanese star-anise which are also known as "*Shikimmi fruits*" or "*Skimmi fruits.*" The latter being obtained from *Illicium religiosum* Sieb. et Zucc., a tree which is extensively cultivated in the groves of the Buddhist Temples in Japan.

I. floridanum Ell., *poison bay, sweet laurel*, a small evergreen tree or shrub with oblong-lanceolate, acuminate leaves, which grows westward from Florida along the coast bounding the Gulf of Mexico, has its bark, leaves, and probably also seed vessels endowed with a spicy odor and taste, analogous to those of anise. Another species, *I. parviflorum* Vent. (*I. anisatum* Bartr., not L.), a shrub found by Michaux in the hilly regions of Georgia and Carolina, has a flavor closely resembling that of sassafras root. A decoction of the seeds is said to produce violent gastro-intestinal irritation, followed by motor and sensory paralysis, with convulsions and death if the dose has been sufficient. E. Barral (*Revue Gén. de Clin.*, Oct., 1889) states that he has obtained a poisonous glucoside from the kernel. H. C. C. Maisch (*A. J. P.*, 1885, 280) obtained from the leaves a crystalline alkaloid to which the bitter taste is due, tannin, and a resin. In the root bark and capsules he found volatile oil and a crystalline principle, melting at 100° C. (212° F.), insoluble in alcohol and ether, but soluble in chloroform, and neutral to test paper.

Star-anise was examined by C. E. Schlegel (*A. J. P.*, 1885, p. 426), who found a *saponin* in the aqueous extract; in the alcoholic extract, a crystalline principle of a strong musk-like odor, which did not show alkaloid or glucosidal reactions, and *oil of star-anise*.

I. religiosum Sieb., or *shikimi*, of India, is very poisonous, causing vomiting and epileptiform convulsions, with dilated pupil and exceedingly cyanosed countenance; in it has been found by J. F. Eykman (*P. J.*, xi, 1046) a crystalline principle, for which the name of *shikimine* or *sikimin* has been proposed.

Eykman (*P. J.*, 1885, p. 985) has shown that in the essential oil of the fruit of *Illicium religiosum*, safrol is found, accompanied by eugenol. On the other hand, the chief constituent of the oil of *I. verum* is anethol. The constituents of low boiling-point in star-anise oil, consisting of terpenes essentially, have been reported upon by the chemists of Schimmel & Co. (*Schim. Rep.*, April, 1893). They find *dextro-pinene*, boiling at 157° to 163° C. (314.6°–325.4° F.), and *lævophellandrene*, boiling at from 170° to 175° C. (338°–347° F.). The medicinal properties of the oil of star-anise are similar to those of oil of anise. Sikimin is not used in medicine. Sikimin is violently poisonous, belonging to the group of convulsants of which picrotoxin is the type. Plugge and Schutte associate in this group—*Dioscorine*, the alkaloid of *Dioscorea hirsuta; cicutoxin*, from *Cicuta virosa* L.; *coriamyrtin*, a glucoside of *Coriaria myrtifolia* L.; *digitalirésin* and *toxirésin*, prepared by Schmiedeberg from digitalin and digitoxin; *phytolaccatoxine*, the alkaloid of *Phytolacca acinosa; sikimin; œnanthotoxine*, the alkaloid obtained from the *Œnanthe crocata* L., by Pohl; *isonitroso-anilacétone*, an artificial substance prepared by Holleman. (See *A. I. P. T.*, iv, 1897.) See table by Eykman showing constituents of oil of *Illicium religiosum* compared with those from allied oils in *U. S. D.*, 19th ed., p. 1526.

Imiodid. *Imidiod.*—A substance obtained by heating para-ethoxy-phenyl-succinimid with a solution containing potassium iodide and iodine. It forms crystals which are black with reflected and red with transmitted light. It is claimed to be a powerful antiseptic.

Impatiens. *Impatiens biflora* Walt. and *I. pallida* Nutt. *Touch-me-not. Jewel-weed. Balsam-weed.*—These two species of *Impatiens* (Fam. *Balsaminaceæ*), the former of which is better known commonly as *Spotted Touch-me-not* and the latter as *Pale Touch-me-not*, are indigenous, annual, succulent plants growing in low, moist grounds, and flowering from July to September. They may be known by their tender, juicy, almost transparent stems; by their yellow flowers, which in *I. pallida* are pale and sparingly punctate, and in *I. biflora* are deeper colored and crowded with dark spots, and by their capsules, which burst elastically, and curl up with the slightest pressure. They probably possess properties similar to those of *I. nolitangere* L., of Europe and Asia, which has an acrid burning taste, and, when taken internally, acts as an emetic, cathartic, and diuretic, though considered dangerous, and therefore little used. Ruan of Philadelphia, employed with great advantage, in piles, an ointment made by boiling the American plants, in their recent state, in lard. The flowers may be used for dyeing yellow. The fresh juice is reputed to be efficacious in the treatment of rhus poisoning. The *I. Balsamina* L., or *balsam-weed, touch-me-not*, etc., of the gardens resembles the other species in its effects.

Imperatoria. *Imperatoria Ostruthium* (L.) Kch. *Masterwort. Rhizoma Imperatoriæ*, P. G. *Impératoire*, Fr. *Meisterwurz, Kaiserwurz*, G.—An umbelliferous plant, indigenous in Southern Europe. The root has a strong odor, similar to that of angelica, and a pungent, aromatic taste, attended by a flow of saliva, and followed by a growing warmth which remains long in the mouth. E. M. Holmes (*P. J.*, March 17, 1877) noticed this root mixed with aconite in the London market, but this probably arose from carelessness, as masterwort is worth twice as much as aconite. A

crystallizable, tasteless principle, called *imperatorin*, was extracted from the root by Wackenroder, and Gorup-Besanez found in the root another principle, to which he gave the name of *ostruthin*. Besides these two crystalline compounds, masterwort contains a volatile oil, composed of a hydrocarbon and an oxygenated compound, probably the aldehyde of angelic acid. (Wagner, *J. P. C.*, lxii, 283.) Jassoy (*Ap. Ztg.*, v, 150) has since investigated the substance ostruthin and gives it the formula $C_{18}H_{20}O_3$. He states that it does not contain a methoxyl group but a phenol-like hydroxyl. By fusion with potassium hydroxide, it yields along with a carbonaceous residue small amounts of resorcinol and acetic and butyric acids. By the action of bromine in chloroform solution it is changed in the presence of acid sodium carbonate into *tribromo-struthin*, $C_{18}H_{19}Br_3O_3$. (Schmidt, *Pharm. Chem.*, Bd. ii, 3te Auf., 1510.) Herzog subsequently examined the rhizomes and found a substance identical with *oxy peucedanin*. (*A. Pharm.*, 1908, 414.) The root of masterwort was formerly used in a wide circle of complaints with so much supposed success as to have gained for it the title of *divinum remedium*. It is, however, merely a stimulant aromatic, which in this country is unknown as a remedy. Its leaves are used as a potherb and to flavor cheese.

Incassa Poison.—This is an African ordeal bark, which has been studied by Liebreich, who found in it a very violent cardiac poison.

Indian Red.—A purplish-red pigment, brought from the island of Ormus in the Persian Gulf. It is *red ochre*, and owes its color to *ferric oxide*.

Indian Yellow.—This is a pigment manufactured from a yellow substance from India, called *purree*. Purree occurs in commerce in balls, from three to four ounces in weight, which are dark brown externally and deep orange within. It has a peculiar odor, closely resembling that of castor. This circumstance gave rise to the belief that it was of animal origin, but Stenhouse found it to consist of magnesia, united with a peculiar acid, which he names purreic (*euxanthic acid* of Erdmann), and which forms nearly one-half of the crude substance. *Purreic acid* is in small crystals of a light yellow color, dissolving sparingly in cold water, quite readily in boiling water, and abundantly in hot alcohol and ether. It has at first a sweetish and then a slightly bitter taste, and possesses, in appearance, considerable resemblance to berberine. When acted upon by boiling nitric acid, it is finally converted into trinitro resorcinol, $C_6H(NO_2)_3(OH)_2$. Heated with diluted sulphuric acid (3 per cent.) to 140° C. (284° F.), it decomposes into *euxanthon* and *glycuronic anhydride*. The euxanthon is recognized as *dioxydiphenylene-ketone oxide*, $CO\langle{}^{C_6H_3(OH)}_{C_6H_3(OH)}\rangle O$, and has been made synthetically. Purreic or euxanthic acid is monobasic, and has the formula $C_{19}H_{16}O_{10} + 3H_2O$. Stenhouse concludes that purree is probably the juice of some plant, saturated with magnesia, and boiled down to a solid consistence.

The term "Indian yellow" is sometimes applied to the *Cobalt and potassium nitrite* and to an aniline derivative, *Azoflavin-Z*, which is a mixture of nitrated diphenylamine orange and nitrodiphenylamine. These should not be confused with the foregoing drug.

Indigo. *Indicum. Pigmentum Indicum. Indigo*, Fr., G.—This well-known and highly important dye-stuff is obtained from various species of *Indigofera* (Fam. *Leguminosæ*), especially *I. tinctoria* L. and *I. Anil* L., and is accorded also by other plants, such as *Wrightia tinctoria* R. Br. (Fam. *Apocynaceæ*), *Polygonum tinctorium* Ait. (Fam. *Polygonaceæ*), *Tephrosia tinctoria* Pers., *Galega tinctoria* L., and *Tephrosia Apollinea* Link. (Fam. *Leguminosæ*), etc. For an interesting account of the manufacture in Manchuria of indigo from *Polygonum chinense*, see *Am. Drug.*, Aug., 1888. It does not exist ready formed, but is generated, during fermentation, from another principle existing in the plant. This principle appears to have been isolated from *Isatis tinctoria* L. (Fam. *Cruciferæ*), by Ed. Schunck, who has named it *indican*. Through the agency of the mineral acids, it is resolved into indigo and sugar, and perhaps the same result may take place in fermentation. Indican is yellow, amorphous, of a nauseous bitter taste, with an acid reaction, and readily soluble in water, alcohol, and ether. In the process of preparing indigo, the plant is macerated in water; fermentation takes place; the liquor becomes of a greenish color, and in due time is decanted; the coloring principle dissolved by the water absorbs oxygen from the air, and assumes a blue color, becoming at the same time insoluble; a gradual precipitation takes place, favored by the addition of lime water or an alkaline solution, and finally the precipitated matter, having been washed upon linen filters, is dried, shaped usually into cubical masses, and sent into market. It is of an intensely blue color, but assumes a coppery or bronze hue when rubbed by a smooth hard body, as the finger nail. Heated to 287.7° C. (550° F.), it emits a reddish-violet vapor, which condenses in minute crystals. It is insoluble in water or alcohol, but is readily dissolved by concentrated or fuming sulphuric acid, because of the formation of *monosulphindigotic* and *disulphindigotic* acids, of which the first is difficultly soluble in water and the second easily soluble. The sodium salt of this latter constitutes the *indigo-carmine* of commerce. Indigo is soluble in chloroform, aniline, oil of turpentine, paraffin, phenol, and benzene. By deoxidizing agents such as the acid sulphites, and in a less degree with sulphurous acid, it is deprived of its blue color, which it recovers by exposure to the air, in consequence of the absorption of oxygen. Certain volatile oils are said to have the reducing effect when boiled with tincture of indigo, as the oils of turpentine, peppermint, lavender, juniper, savine, or sage. (*J. P. C.*, 1859, 399.) The reduction and decolorization of indigo solutions by glucose is the basis of one of the most delicate tests we have for diabetic sugar in urine. Chlorine also destroys the blue color. For modes of testing the value of a specimen of indigo, see Sadtler's *Industrial Organic Chemistry*, 443. The most important of the methods for the determination of the indigo blue may be summarized under three heads,—viz., oxidation methods, reduction methods, and sublimation of the pure indigo blue from the commercial product. A table of analyses of commercial samples with results according to the several methods above referred to will be found in Allen, *Com. Org. Anal.*, 2d ed., iii, 311.

The artificial production of indigo has been the subject of much investigation and effort in recent years. The problem was successfully solved by A.

von Baeyer of Munich, who proposed several methods capable of commercial utilization.

One method is to start with *cinnamic acid*, $C_9H_8O_2$, made artificially from benzaldehyde, which is changed into *ortho-nitro-cinnamic acid*, $C_9H_7NO_4$, and this by the intervention of the di-bromine derivative into *ortho-nitro-phenylpropiolic acid*, $C_9H_5NO_4$, and this by the action of alkalies in the presence of reducing agents, like grape sugar or xanthogenates, is converted directly into *indigo blue* $(C_8H_5NO)_2$.

A second method was by the action of dilute alkalies upon a solution of *o-nitro-benzaldehyde* in acetone according to the reaction

$$2C_6H_4(NO_2)CHO + 2C_3H_6O = C_{16}H_{10}N_2O_2 + 2C_2H_4O_2 + 2H_2O.$$

A method of Heumann, also successfully carried out on a large scale, is to treat *phenylglycin*, $C_6H_5.NH.CH_2.COOH$, with alkalies, and then oxidize the resulting alkaline solution, when *indigotine*, $C_{16}H_{10}N_2O_2$, is formed. These methods were all too expensive, but it has finally been made commercially, and on a scale which is fast displacing natural indigo, by the following method:

Anthranilic acid, $C_6H_4(NH_2)COOH$, which can be prepared cheaply from naphthalene, combines with *monochloracetic acid* to form *phenyl-glycocollcarboxylic acid*, $C_6H_4\langle^{NH.CH_2COOH}_{COOH}$, and this on fusion with caustic soda yields *indoxyl*, $C_6H_4\langle^{NH}_{C(OH)}\rangle CH$, which, in alkaline solution, is converted by atmospheric oxidation into indigo.

Synthetically prepared indigotine is now produced at a price much cheaper than refined indigo. It has several advantages, as purity, fineness of division, and ease with which it is tested.

In former years the importation of indigo from India into the United States averaged about 2,000,000 pounds, representing over 50 per cent. of the imported dye colors, the ports of entry being New York and Boston. During the year 1902 the importation of the natural indigo from India amounted to 239,580 pounds during the first six months, and ceased entirely after the month of June. It is stated that the artificial indigotine can be sold at about one-fourth the price of the vegetable dye.

The importations of indigo (natural and synthetic) for the past two years were: 1914, 8,252,528 lbs., valued a $1,115,128; and 1915, 7,983,112 lbs., valued at $1,604,767.

Schunck first showed that all urines, whether pathological or not, contain an indigo-producing body in minute quantities. This body is commonly spoken of as *indican* in medical books. Its true chemical nature was first ascertained by Baumann, who showed that it was not a glucoside, like the indican of plants, but the potassium salt of a peculiar acid, *indoxylsulphonic acid*.

Indigo carmine, $C_{16}H_8N_2O_2(SO_3Na)_2$, has been used as a test of the functional power of the kidneys, especially in surgical affections of these organs. The method consists essentially of the injection of 4 mils of the 4 per cent. solution intravenously, the urine being collected separately from each kidney from 20 to 30 minutes after the injection. Healthy kidneys should excrete the drug within eight or twelve minutes, while if the kidneys are seriously affected the functional incapacity is shown by either the absence or the paleness of the urine.

Indigo was at one time considerably used in medicine, but at present is very rarely if ever employed. It is said to produce, when taken in sufficient quantity, nausea, vomiting, purging with bluish, dark stools, a dark violet or dark green color of the urine, and sometimes to cause a menstrual flux. It was formerly used in *epilepsy, infantile convulsions, chorea, hysteria,* and *amenorrhea. Dose,* from twenty grains to an ounce (1.3–31 Gm.) three times a day. For further details, see 16th ed., *U. S. D.*

Indium. In.=114.8.—A rare metal named from the indigo blue line given by the spectrum of the metal. It is a shining white ductile metal, softer than lead. Some of its salts have been prepared and are asserted to be of value as external antiseptics. They are the sulphate, $In_2(SO_4)_3+nH_2O$, and the trichloride, $InCl_3$, a yellow hygroscopic powder. Both of these salts are active poisons.

Indoform. *Salicylic Acid Methylene Acetate.*—Obtained by the action of formaldehyde on acetyl salicylic acid. It is a white powder of an acid astringent taste difficultly soluble in cold water, but more soluble in warm water. It liberates formaldehyde in the intestines and due to this property it is used in the treatment of *gout, rheumatism* and *sciatica. Dose,* eight to twenty-five grains (0.5 to 1.7 Gm.).

Insect Powder. *Camomille de Perse,* Fr. *Persische Bertramblumen,* G. *Pyrethri Flores.*—The unexpanded or partly expanded flower-heads of several species of *Chrysanthemum* (Fam. *Compositæ*). There are two principal commercial varieties: (1) the Dalmatian insect powder which is obtained from *Chrysanthemum cinerariifolium* (Trev.) Bocc., a perennial herb indigenous to Dalmatia and cultivated in the United States. (2) The Persian insect powder is obtained from the flowers of *C. roseum* Web. et Nohr and *C. Marschallii* Aschers, herbs growing in the Caucasus, Armenia and Northern Persia. The flowers are collected from plants that are from two to six years old, carefully dried and preserved. The most powerful insect powder is obtained from the closed or only partly expanded flowers providing they are properly dried and preserved.

Dalmatian Flowers.—The heads are hemispherical, about 12 mm. in diameter, and consist of a conical torus subtended by a straw-colored involucre and bearing upon the receptacle numerous yellow tubular flowers and a circle of cream-colored ray flowers. The latter are pistillate, the corolla being from 1 to 2 cm. in length, having about 15 delicately veined and 3 short, obtuse or rounded teeth.

Persian Flowers.—The heads are flattened top-shaped; the involucral scales are greenish-brown; the ray florets are reddish-brown or reddish-purple, attaining a length of 15 mm., being somewhat plicate and having 7 veins. The disc florets are tubular and yellow.

For details as to the special anatomical character of these flowers, see *P. J.*, lxvii, 474; also *J. P. C.*, 1902, xv, 409.

C. cinerariæfolium is now being cultivated on a large scale in California, and as more care is given to the preservation during drying of the color and of the volatile oil than in Dalmatia, the California product which is known by the name of *buhach* is said to be superior to the foreign drug. (*C. D.*, August, 1889; see also for method of cultivation, *Reports of the Fourth U. S. Entomological Commission,* 1885, and papers by Seidler, *Riedel's Berichte,* 1913, and Jüttner, *Ph. Ztg.*, 1912, 817.)

The insect powder of commerce varies in color from yellow, yellowish-brown, or brownish-yellow

to yellowish-green, the finer qualities verging towards brown and the poorer towards green. Brilliant yellow powder should be viewed with suspicion. On microscopical examination of an insect powder, it will be found to consist of fragments of involucral scales composed of sclerenchyma, perhaps bits of stems composed of collenchymatous cells, pollen grains, fragments of the corolla and of its epidermis and papillæ. The absence or scarcity of pollen in the powder shows the absence or scarcity of the flowers in the drug, while the proportion of collenchymatous tissue indicates the proportion of stems. As the activity of the insect powder resides in the flower, specimens containing little of the flowers or much of the stems should be rejected. The powder yielded by the Dalmatian plant can usually be distinguished from Persian insect powder by the following characters. The outer surface and edges of the scales of the Dalmatian flowers contain numerous hairs, consisting of a long cell with attenuated ends placed horizontally upon a one- to three-celled stalk. The Persian flowers are almost entirely glabrous, a white hoariness being found only at and near the base of the scales, and very few hairs near the apex; the hairs are of the same structure as the preceding, only the terminal cell being much longer. Sclerenchymatous cells are much more numerous in the Persian than in the Dalmatian. The so-called *Hungarian* or *Russian daisy*, probably a species of the subgenus *Leucanthemum*, was at one time used as an adulterant. The importance of the adulteration is increased by the fact that the Hungarian daisy appears to be entirely free from insecticidal properties. The Hungarian daisy is distinguished from the true *Pyrethrum* by the orange-yellow disk florets, by the depression of the involucre, by its prominent dark receptacle, and by the absence of pubescence and pappus. The odor is less pungent than that of the true insect flower, being more like that of matricaria. The difference in odor is more pronounced on infusing in warm water. The Hungarian daisy yields a powder somewhat darker in color than true insect powder. Microscopically, the Hungarian or Russian daisy differs only in the absence from the involucre and stems of the peculiar hairs seen on the scales of the true insect powder, and the presence in their place of certain hairs, consisting of from four to ten cells, and terminating with a much elongated, thin-walled, or inflated cell. There seems to be no recognizable difference between the pollen of the two plants which yield insect powder and of the Hungarian daisy. The presence of quassia, fustic, turmeric, and other adulterants may be made out by the aid of the microscope, and chrome yellow chemically, but the powder of Hungarian daisy cannot be detected microscopically. According to George R. Durrant, however, the Hungarian powder yields 10 per cent. of ash, whereas true insect powder yields but 6.5 per cent. F. Dietze, after careful study, found that the best method of valuation of insect powder is based on the amount, appearance and odor of the extract obtainable by the use of petroleum spirits boiling under 55° C. (131° F.). With such menstruum true insect powder affords a bright yellow percolate possessing the odor peculiar to the drug. (See *P. J.*, 1905, 902; also 1906, 891; *Ph. Ztg.*, 1905, 871.)

E. H. Gane, 1910, reports that insect powder is adulterated with ground stems and not ground from flowers only, at it should be. One sample from one of the largest pharmaceutical manufacturing houses was composed wholly of ground stems.

Insect powder does not appear to be actively poisonous to man, though it is said to cause some confusion of mind in those who sleep in close apartments where much of it is used. Upon the insects, however, which are apt to infest the person of man and animals, as well as bedding and sleeping apartments, it acts very destructively, first stupefying and then killing them. It is scattered over the person, upon the beds, about apartments, etc., and is even employed as a dressing for ulcers and wounds to prevent the formation of maggots. It also answers for preserving dried insects and plants in cabinet collections. The powder, exhausted by alcohol, is harmless to insects. The activity of insect powder is due to a toxic principle called *pyrethron*, and an amber-yellow syrupy substance which is the ester of certain unidentified species. The flowers also contain 0.5 per cent. of a volatile oil and from 4 to 7 per cent. of several resins. (Fujitani, *Arch. f. exper. Path. u. Pharmak*, 1909, 61, 47, and *Chem. Zentralblatt*, 1909, 80, ii, 1153.) The ash content varies from 5 per cent. to 8.3 per cent. In a series of experiments, Riley has found that the fumes of the burning powder are very poisonous to insects, and for certain purposes afford a ready mode of application, but that generally an aqueous infusion is the best and cheapest preparation. It is also used now in the form of cones made by making a mass with mucilage of gum arabic, with the addition of a small quantity of potassium nitrate. After drying these are ignited like a fumigating pastile. Twenty-five grains stirred up in two quarts of water were sufficient to kill young cotton worms. The infusion soon spoils. The tincture and the alcoholic extract are both efficient preparations. The tincture (one part to four) has been especially recommended, diluted with ten times its bulk of water, by F. Jager, to keep off vermin from the human body. According to Maisch (*A. J. P.*, 1869, 128), it is capable of causing a vesicular eruption like that produced by the poison ivy.

Insindiyandiya.—This substance, a remedy of the Kaffir doctors of South Africa, is a violent poison, and has been shown by E. M. Holmes to be derived from a *Bersama*, apparently identical with *B. abyssinica* Fresen. (*P. J.*, lxxiii, 893.)

Insipin. *Quinine Di-glycol Sulphate.* $O(CH_2.CO[C_{20}H_{23}O_2N_2])_2.H_2SO_4.3H_2O$.—This compound is very sparingly soluble in either water or alcohol, and is asserted to be practically tasteless. It was brought forward as a substitute for quinine. Werner (*D. M. W.*, 1911) has employed it in *malaria* in *doses* of from three to six grains (0.2–0.4 Gm.) given every three or four hours.

Inula. *N. F. IV* (*U. S. P.* 1890). *Inula Elecampane. Aunée*, Fr. *Alantwurzel*, G. *Enula Campana*, It., Sp. U. S. 1890.—"The dried rhizome and roots of *Inula Helenium* Linné (Fam. *Compositæ*), without the presence of more than 5 per cent. of its stem bases or other foreign matter." *N. F. IV.*

Inula Helenium is a stout, perennial herb naturalized from Europe and growing along roadsides and damp pastures from Nova Scotia to North Carolina and westward as far as Missouri. The rhizome and roots are used in medicine. The N. F. description is as follows: "Rhizome usually split into longitudinal or more or less oblique pieces to which may be attached one or more of the roots; up to 8 cm. in length and 4 cm. in diameter; externally grayish-brown to dark brown, longitudi-

nally wrinkled with occasional buds or stem scars and surmounted at the crown by a portion of the overground stem; inner or cut surface somewhat concave, the edges incurved with the overlapping bark, yellowish-brown to grayish-brown, longitudinally striate and more or less fibrous near the cambium zone; fracture short and horny; inner surface light brown and marked by numerous circular or elliptical oleoresinous canals; roots cylindrical and tapering, frequently curved or irregularly curled, up to 13 cm. in length and 1.5 cm. in diameter. Odor aromatic; taste acrid, bitter and pungent. Transverse sections under the microscope show a corky layer of from four to seven rows of broad tabular cells; a cortex of numerous parenchyma cells containing inulin in irregular or fan-shaped masses and a number of large, intercellular, oleoresinous reservoirs arranged in nearly radial rows and forming interrupted circles; woody portion consisting chiefly of parenchyma, a number of tracheæ with simple pores of reticulate thickenings and associated occasionally with a few, strongly lignified wood fibers, and oleoresinous reservoirs similar to those occurring in the bark; parenchyma cells in the pith of the rhizome large, containing less inulin than the cells of the wood and bark and separated by large intercellular spaces. The powder is light brown; consisting chiefly of fragments of parenchyma containing inulin and small, irregular, separated masses of inulin; tracheæ with simple pores and reticulate thickenings associated occasionally with strongly lignified wood fibers; occasional reddish-brown fragments of the walls of the oleoresinous canals. Inula yields not more than 10 per cent. of ash." *N. F.* A peculiar principle, resembling starch, was discovered in elecampane by Valentine Rose, of Berlin, in 1804, who named it *alantin;* but the title *inulin*, proposed by Thompson, has been generally adopted. It differs from starch in being deposited unchanged from its solution in boiling water when the liquor cools, and in giving a yellowish instead of a blue color with iodine. It has been found in the roots of several other plants. It may be obtained white and pure by precipitating a concentrated decoction with twice its volume of alcohol, dissolving the precipitate in a little distilled water, treating the solution with purified animal charcoal, and again precipitating with alcohol. (*A. J. P.*, xxxi, 69.) It readily dissolves in about three parts of boiling water; the levogyre solution is perfectly clear and fluid, not paste-like, but on cooling deposits nearly all the inulin. Its formula, according to Kiliani (Tollens, *Handbuch der Kohlenhydrate*, 1888, p. 202), is $3C_{12}H_{20}O_{10} + H_2O$. On prolonged heating with water, more rapidly under the influence of dilute acids, it is changed into *levulose* and reduces Fehling's solution. As in the case of starch, intermediate products can be obtained before it is completely changed into reducing sugar. Dragendorff obtained by heating with water for ten hours *metinulin*, and by heating for forty to fifty hours *levulin*, an optically inactive amorphous substance easily changing into *levulose*. Tanret, who has since investigated inulin (*J. P. C.*, 27, 449), confirms Kiliani's formula as given above. He finds associated with inulin two closely related principles: *pseudo-inulin* and *inulenin*. The first of these, to which the formula $(C_6H_{10}O_5)_{16}.H_2O$ is given, forms irregular granules, very soluble in water and weak alcohol while hot, but only slightly soluble in cold water, and insoluble in cold alcohol; the second is given the formula $(C_6H_{10}O_5)_{10}.2H_2O$, and forms microscopical needles slightly soluble in cold water and weak alcohol. The amount of inulin varies according to the season, but is most abundant in autumn. Dragendorff obtained from the root in October not less than 44 per cent., but in spring only 19 per cent. A crystallizable substance was long since noticed to collect in the head of the receiver when the elecampane root is submitted to distillation with water. Similar crystals may also be observed after carefully heating a thin slice of the root, and are even found as a natural efflorescence on the surface of a root that has been long kept. They can be extracted from the root by means of alcohol, and precipitated with water. Kallen (*Ber. d. Chem Ges.*, 1873, 1876) has found that these crystals consist chiefly of the anhydride, $C_{15}H_{20}O_2$, of *alantic acid*, melting at 66° C. (150.8° F.), and that what was formerly known as *helenin* was a mixture of these with a liquid, *alantol*, $C_{10}H_{16}O$, boiling at 200° C. (392° F.), the true *helenin* and *alant camphor*. The crystals of *helenin*, C_6H_8O, have a bitterish taste, but no odor, and melt at 110° C. (230° F.). The camphor melts at 64° C. (147.2° F.), and in taste and odor is suggestive of peppermint.

Korab (*L. L.*, vol. i, 1885, p. 672) states that helenin is a powerful antiseptic and bactericide, one part in ten thousand of urine being sufficient to arrest putrefaction, and a few drops of a solution of this strength immediately killing the ordinary bacterial organisms, including the tubercle bacillus. He lauds it as antiseptic in surgery and has given it with alleged success internally in *doses* of one-third to one grain (0.021–0.065 Gm.) in tubercular and catarrhal *diarrheas*. It is also stated by J. B. Obiol (*L. L.*, April, 1886) to be an efficient local remedy in the treatment of *diphtheria*. Every four hours the false membrane is to be dusted over with powdered camphor, and then painted with a two per cent. solution of helenin in oil of sweet almond. It is affirmed that when the treatment was commenced on the first day of the patches the cure followed in twenty-four hours. Bockenham (*Th. M.*, 1892, p. 145) asserts that helenin inhibits the growth of tubercle bacilli in the dilution of 1 in 10,000 and it has been employed by various writers in the treatment of *pulmonary tuberculosis* in *doses* of from one-sixth to five grains (0.01–0.32 Gm.). Helenin was also given internally. *Dose*, one and a half grains (0.096 Gm.) to children six years of age.

Elecampane is tonic and gently stimulant, and was employed by the ancients in *amenorrhea* and other diseases of women, also in *phthisis*, in *dropsies*, and in *skin affections*, in all of which diseases it was probably of no service. It has been given in powder, in the *dose* of twenty grains to one drachm (1.3–3.9 Gm.), or as a *decoction* (half ounce to the pint) in *doses* of one to two fluidounces (30–60 mils).

Iodacetone. *Iodoacetone. Mono-iodoacetone.* $CH_2I.CO.CH_3$.—This is a product of the action of iodine on acetone. It is employed freshly prepared as an application to incipient *carbuncles* and boils. Care should be exercised in applying it to a delicate skin, owing to its caustic action.

Iodal.—This substance, prepared by the action of iodine upon a mixture of alcohol and nitric acid, is decomposed by an alkali into iodoform and formic acid. Rabuteau found it to resemble hydrated chloral in its actions on animals. (*Ann. Thér.*, 1870, 98.) It is decomposed by moisture with the liberation of iodine.

Iodalbacid. *Albumen Iodate.*—An iodine-albumen compound which contains 10 per cent. of iodine in intramolecular combination. It is a cream-colored powder, inodorous, tasteless, and soluble in water. *Iodolbacid* is used in all cases where iodine is indicated, especially in *syphilis*, possessing the advantage of freedom from harmful action in the intestinal tract. It is especially recommended where protracted iodin action is desired. *Dose*, fifteen grains (1.0 Gm.) three to six times a day.

Iodalbin. *N. N. R.* 1917.—This is another iodine albumen product being soluble only in alkaline solutions. It is a reddish powder containing 21.5 iodine. It is used in preference to the alkali iodides due to its tastelessness, its freedom from harmful action on the stomach and to its ready assimilability. *Dose*, eight to fifteen grains (0.5–1.0 Gm.) several times daily.

Iodalgin.—A soluble inodorous substance containing 50 per cent. iodine is used as a succedaneum for iodoform.

Iodalia is a saccharated organic iodine compound containing tannin which affords an agreeable method of iodine administration to children, it being easily tolerated by infants. One teaspoonful contains one grain of iodine combined with tannin.

Iodamylene. *Valerylene Hydriodide.* C_5H_8HI.—A clear, colorless liquid soon darkening on exposure to light, is a reaction product of valerylene with fuming hydriodic acid. It is soluble in alcohol and boils at 140°–142° C. (284°–287.6° F.). Therapeutic data are lacking here, although several pharmaceutical houses list this drug.

Iodanisol. *Orthoiodanisol.* $C_6H_4.OCH_3.I.(1.2)$.—It occurs as a reddish, crystalline mass fusing at 47° C. (116.6° F.), and boiling at 240° C. (464° F.). It is an antiseptic and powerful local irritant.

Iodantifebrin. *Iodacetanilide.* $C_6H_4I.NH(C_2H_3O.)$—This occurs in rhombic flakes melting at 181.5° C. (358.7° F.), very slightly soluble in cold water, easily soluble in alcohol and in glacial acetic acid. In the experiments of E. Munz (*Pr. M. W.*, 1891) the physiological results following the administration of this remedy by the mouth were entirely negative, and neither iodine nor acetanilide could be recognized in the urine, the probable explanation of this being that the excessive insolubility of the drug prevents its absorption.

Iodeugenol.—This product, analogous to thymol iodide, is prepared by the action of iodine on an alkaline eugenol solution. It forms a yellowish powder having a faint eugenol odor, insoluble in water, soluble in ether and fats, and slightly so in alcohol. It fuses at 78° C. (172.4° F.). Used as a dusting powder and also in the form of salve.

Iodferratin. *Iodoferratin.*—This is an iodine compound of ferratin (which see), containing 6 per cent. each of iodine and iron. The iodine is in a ready available organic form of combination. It forms a stable red-brown neutral powder. *Dose*, four to ten grains (0.25–0.6 Gm.).

Iodgallicin. *Bismuth-oxyiodid-methyl-gallol.* $C_6H_2(COOCH_3).(OH)_2.OBi(OH)I$.—This is obtained through the action of bismuth oxyiodid on gallic acid methyl ester (gallicin). It forms a light, amorphous, dark gray powder, insoluble in the usual solvents but decomposed into its components by acids, alkalies and by prolonged boiling. *Iodgallicin* contains 23.6 per cent. of iodine and 38.4 per cent. of bismuth. It is used as a disinfectant and wound antiseptic.

Iodguaiacol. *Para-iod-guaiacol.*—This occurs as colorless crystals, difficultly soluble in water but readily so in alcohol, ether and fatty oils. It is asserted that it will pass through the stomach undecomposed and without irritation, that in the intestines it is broken up, yielding its compounds to absorption. It has been used in the treatment of *tuberculosis* of various types in *doses* of one grain (0.06 Gm.).

Iodic Acid and Its Salts. *Acidum Iodicum.* HIO_3.—*Iodic acid* occurs as a white, crystalline powder, soluble in its own weight of water. In concentrated solution it is caustic, and in solutions of 0.1 to 0.5 per cent. it is astringent and disinfectant. It has been employed as an astringent gargle and application to inflamed mucous membranes. In 1 to 3 per cent. solution it has been employed as a local application in *trachoma* and indolent *corneal ulcers*. Lutton (*Ann. Ther.*, 1874, 192) has proposed it as a remedy for *glandular enlargements* and in *goiter*. He injects 30 minims (2 mils) of the 2 per cent. solution. In *doses* of one to two grains (0.06–0.1 Gm.), well diluted, it has been used in *gastric hemorrhages*. Pencils made by adding iodic acid to powdered acacia have been used by Rudas in the treatment of *trachoma*.

The salts of iodic acid are actively disinfectant. According to Griffiths a 0.5 per cent. solution of potassium iodate is capable of destroying many forms of bacteria.

Sodium iodate, a white, odorless, crystalline substance, very soluble in water, has been recommended for internal use, but is much inferior to the iodides. As a local remedy it may be useful in tubercular and other inflammations of the nose and larynx, either pure or diluted. Ruhemann (*B. K. W.*, 1905) has employed sodium iodate in epidermic *cerebrospinal meningitis*. He administered four grains in water twice a day. Mackie (*L. L.*, 1905) recommends *zinc iodate* and *calcium iodate* as a local application in various suppurating *wounds, eczema, cystitis*, and similar conditions.

Iodine Trichloride. ICl_3.—This compound occurs in reddish-yellow crystals; very soluble in water and alcohol; rapidly decomposed with liberation of iodine and chlorine when brought in contact with organic matter. It has been especially recommended by Belfield (*B. M. J.*, Aug., 1892) as a powerful local antiseptic. A solution is prepared for medicinal use by suspending 5.5 Gm. of iodine in 22 Gm. of water, and passing in chlorine as long as it is absorbed by the well-cooled mixture. The solution contains 10 Gm. of *iodine trichloride*. The strength of the solution used is 1 to 5 per cent. Gauze sterilized by boiling and immersing in 1 to 10 per cent. solution and dried is said to retain iodine trichloride indefinitely. Iodine trichloride is a very powerful germicide, at least four or five times as active as phenol. According to Rideal five parts in a hundred thousand will kill the bacillus typhosus after half an hour's exposure. The five per cent. solution is fairly permanent if protected from the light, but dilute solutions rapidly deteriorate. It has been used locally in infectious conditions of the various mucous membranes in strengths of from 1 in 1000 to 1 in 2000. For disinfecting the hands a one per cent. solution is recommended. It has also been used internally as a gastro-intestinal disinfectant in *doses* of one and one-half grains (0.096 Gm.) a day.

Iodipin. *N. N. R.* 1917.—A yellow, oily fluid, of a purely oleaginous taste, said by Winternitz

(*D. M. W.*, xxiii) to be an iodine addition product of sesame oil, and to contain 10 per cent. of iodine in chemical combination. Similar preparations have been made from lard, cacao butter, and other fats. *Iodipin* has been introduced as a substitute for the alkaline iodides. There is much clinical evidence as to its value in all those conditions for which sodium iodide is useful, especially in the treatment of *asthma* and *arteriosclerosis*. It appears that when taken by the mouth it passes through the stomach unchanged and is partly broken up in the intestinal tract, liberating inorganic iodine, but a portion of it is unchanged and circulates in the blood as iodipin. How much of the substance which escapes the separation by the fat-splitting ferments of the intestines liberates its iodine in the body is uncertain, but it is probable that practically all the iodine is eventually liberated in the ionic state. The advantages claimed for iodipin are (1) when taken by the mouth it is less likely to disturb digestion than the inorganic iodine; (2) that it can be administered hypodermically; (3) that the iodine, being slowly liberated, there is obtained a more continuous effect with less danger of symptoms of iodism. For summary of the literature, see McLean, *A. In. M.*, 1912, x, p. 505.

There are two forms of iodipin, one a ten per cent. solution and the other a twenty-five per cent. solution intended especially for veterinary use. The *dose* of the ten per cent. preparation is ordinarily one drachm (4 mils) three or four times a day, although much larger quantities have been administered.

Under the name of *Iodipinum solidum*, tablets of an emulsified iodipin have been put upon the market. Each of these corresponds to five-sixths of a grain (0.05 Gm.) of iodine. Three or four tablets may be given at a *dose*, and repeated several times a day.

Iodized Oil.—The following is the original process of Personne. Five parts of iodine are mixed with a thousand parts of expressed oil of almond, and the mixture is subjected to a jet of steam, until decolorized. The same operation is repeated with five additional parts of iodine. The oil is then washed with a weak alkaline solution, to remove the hydriodic acid developed in the process. By this mode of proceeding it may be presumed that the iodine is intimately united with the oil, along with which it would find an easy entrance into the system, and that, while about half of the iodine is lost as hydriodic acid, the remainder takes the place of the hydrogen eliminated from the oil. Hugounenq objected to this or any process which requires the continued application of heat, as rendering the oil liable to become quickly rancid. His plan is to rub up the iodine, for five or six minutes, in a porcelain mortar, with a small portion of the oil, and then gradually to add the remainder. A red limpid liquor is obtained, which may be completely decolorized by exposure for fifteen minutes to the sun's rays. Iodized oil, thus prepared, has the odor and taste of almond oil, is not more liable to become rancid than the pure oil, and is free from hydriodic acid. (*J. P. C.*, March, 1856.)

Iodized Starch. *Amylum Iodatum. U. S.* 1880. (*Amyl Iodidum, Iodine of Starch; Iodure d'Amidon*, Fr. *Jodstärke*, G.).—"Starch, *ninety-five parts* [or four hundred and eighteen grains]; Iodine, *five parts* [or twenty-two grains]; Distilled Water, *a sufficient quantity*, to make *one hundred parts* [or one ounce av.]. Triturate the Iodine with a little Distilled Water; add the Starch gradually, and continue triturating until the compound assumes a uniform blue color, approaching black. Dry it at a temperature not exceeding 40° C. (104° F.), and rub it to a fine powder. Iodide of Starch should be preserved in glass-stoppered vials." *U. S.*, 1880. This preparation has been highly recommended as free from local irritant properties. Dalton, of New York, found that nearly all the animal fluids decompose starch iodide and destroy its blue color. (*Am. J. M. S.*, April, 1856, p. 327.) This result is owing, no doubt, to the alkaline nature of most of the animal fluids, especially those of the duodenum, alkaline iodides being formed at the expense of the starch. The *dose* is a heaped teaspoonful, given in water gruel, three times a day, and afterwards increased to a tablespoonful. No nicety is necessary in apportioning the dose. In some cases Buchanan has given half-ounce (15.5 Gm.) doses, increased to an ounce (31 Gm.).

Iodival. *Iodisovaleryl Urea. Monoiodoisovaleryl Urea.* $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!HC\text{–}CHI\text{–}CO\text{–}HN\text{–}NH_2$.—This is a white powder representing 47 per cent. of iodine. In cold water it is insoluble, but dissolves in alcohol and in hot water. It has been suggested as a substitute for the iodides in *syphilis, asthma, scrofula* and other conditions in which the iodides are employed. According to the investigations of Menne (*In. Dis.*, Bonn, 1909), it passes through the stomach unchanged but is dissolved and absorbed in the intestinal tract. Iodine appears in the urine in about an hour after its ingestion and the elimination is complete within two or three days. It is marketed in the form of tablets each containing five grains (0.32 Gm.). Of these tablets one may be taken from two to six times in the twenty-four hours.

Iodocaffeine. *Caffeine Sodium Iodide.*—A white powder containing 65 per cent. caffeine and soluble in water, but decomposed by hot water. It exhibits therapeutically the combined properties of the alkali iodides and caffeine increasing systolic energy, arterial pressure and diuresis, and used accordingly in mitral stenosis and other cardiac effects. *Dose*, five to eight grains (0.32–0.5 Gm.).

Iodocasein. *N. N. R.* 1917.—A compound of iodine and casein obtained by precipitation of sodium casein solution by means of a potassium iodide and iodine solution. It is a yellowish powder used for disinfecting *wounds*. *Dose*, five to twenty grains (0.32–1.3 Gm.).

Iodofan.—*Iodofan* is the subject of many contradictory statements as to its composition and properties. It has been given the formula $C_6H_3I(OH)_2HCHO$ or $C_6H_3I(OH)_2HCHO,2H_2O$. The product obtained in the market is amorphous, brownish-red, scarcely soluble in alcohol, ether or chloroform, insoluble in cold water. Auffrecht (*Ph. Ztg.*, 1906) found in it 36 per cent. of iodine, but Zernik (*Med. Klin.*, 1907) found only 4 per cent. Theoretically it should yield 42 per cent. It seems doubtful whether this substance has the composition claimed for it. Iodofan has been employed as a dusting powder for *wounds, burns* and moist *eczemas* and similar conditions. Piorkowski asserts that it has a high antiseptic power as well as considerable deodorant effect. (*B. K. W.*, 1907.)

Iodoformin. *Iodoformolin. Iodoform Hexamethylenamine.* $CHI_3(CH_2)_6N_4$.—*Iodoformin* is obtained through the action of an alcoholic iodoform solution on *hexamethylenamin*. It is a

white, crystalline powder of faint iodoform odor, fusing at 178° C. (352.4° F.) and insoluble in water. In boiling water or in wound secretions it is split up into its component parts yielding 75 per cent. iodoform. This compound not only is free from the odor but appears to have direct antibacterial properties far in excess of that of iodoform. It is asserted to have especial toxicity for the gonococcus. It is used in medicine as a dusting powder to *wounds* and also as a local application in *urethritis*. For the latter purpose bougies containing 10 to 20 per cent. of iodoformin have been recommended.

The *iodoformin-ethyl-iodide*, $C_6H_{12}NC_2H_6ICHI_3$, known as *iodoformal*, is stated to be still more actively antiseptic. This is obtained through the action of iodoformin on ethyl iodide. It forms yellow needle-like crystals or a heavy powder. It dissolves in boiling water and fuses at 128° C. 262.4° F.). It is used for the same purposes as iodoformin.

Iodoformogen. *N. N. R.* 1917.—According to K. Gaab (*Ph. Centralh.*, 1898, xi, 189), *iodoformogen* is a chemical combination of iodoform and albumin. It occurs as a fine, loose, dry, non-conglutinating powder, having a faint acidulo-ethereal odor, and being two and one-half times as voluminous as powdered iodoform. According to Kromayer (*B. K. W.*, xxxv, 1898) and to Aspegren (*Festschrift des Prof. Kaposi*, Vienna, 1901), iodoformogen is more slow and continuous and certain in its local action than is iodoform. It bears sterilization at 100° C. (212° F.) without change.

Iodol. *Iodolum. U. S. VIII.* $C_4I_4.NH$. *Tetraiodopyrrol. Pyrrol Tetraiodide. Jodol, Tetrajodpyrrol*, G. *Jodolo*, It. *Yodol*, Sp.—*Iodol* was discovered by Silber and Ciamician, and is made from the pyrrol obtained in Dippel's oil (bone oil), which, after purifying, is treated with a solution of iodine in potassium iodide, when the tetraiodide (iodol) precipitates. It is purified by redissolving in hot alcohol, and again precipitated by the addition of water. It contains nearly 89 per cent. of iodine. It should be protected from the light.

Iodol was official in the United States Pharmacopœia VIII. It was officially described as "a light grayish-brown, crystalline powder, without odor or taste. It is soluble in about 4900 parts of water, 9 parts of alcohol, 1.5 parts of ether, and 105 parts of chloroform at 25° C. (77° F.); soluble in fixed oils. It is soluble in concentrated sulphuric acid, producing a green solution gradually changing to brown. When heated to 100° C. (212° F.) it remains unchanged, but at a temperature of 140° to 150° C. (284° to 302° F.) it is decomposed with the liberation of violet iodine vapors. When ignited it should leave not more than 0.1 per cent. of residue (limit of *inorganic impurities*). If 0.5 Gm. of Iodol be shaken with 100 Cc. of water and filtered, the filtrate should not be made more than slightly opalescent by silver nitrate T.S. (absence of *hydriodic acid* or soluble metallic *iodides*). If 0.5 Gm. of Iodol be shaken with 100 Cc. of water and filtered, the filtrate should not communicate more than a light yellowish tinge to chloroform (absence of appreciable amount of *free iodine*)." *U. S. VIII.*

When given in sufficient dose to animals, iodol causes emaciation, albuminous urine, fall of temperature, general loss of muscular power, and finally death from fatty degeneration of the liver and kidneys and other tissues. That iodol applied externally is capable of producing constitutional symptoms is shown by C. Lauenstein (*T. G.*, 1887, 768), in a case in which the surgical use of the drug caused dizziness, marked rise in the temperature, vomiting, small irregular pulse of 136, albuminous urine, and apathy which did not subside for four days. Iodine was found in the urine for twelve days, but it is a less dangerous topical application than iodoform due to its slower absorption. Iodol may be employed for all purposes or which iodoform has been used. It has been found very valuable in the treatment of *tuberculous laryngitis*, and may be blown into the larynx directly upon the ulcers without causing irritation. It has been used with asserted great success in the treatment of blennorrhagic and simple *vaginitis*, in *chancres* and other *ulcers*, in suppurative *adenitis*, and as an antiseptic dressing to *wounds*. Mazzoni's solution was: iodol, one part; alcohol, sixteen parts; glycerin, thirty-four parts. One drachm of iodol forms with one ounce of ether a clear brown solution, which may be applied by the spray or brush to the nasal and other mucous membranes, on which it leaves a coating of iodol. Iodol pastilles are prepared by Wolfenden from one grain of iodol, one minim of glycerin, and eighteen grains of glyco-gelatin, and are by him strongly recommended for *laryngitis*. Iodol has also been used as an internal remedy in *tertiary syphilis* and in *scrofula*. Good effects have also been claimed for it in *diabetes*. Assaky and Reck have given thirty grains (1.9 Gm.) a day with asserted good results. *Dose*, two to four grains (0.13–0.26 Gm.).

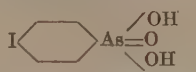
Iodolin. *Quinoline chlormethylate iodochlorid.* $C_9H_7NCH_3Cl.ICl$.—This is a yellow insoluble powder used as an iodoform succedaneum. It is the product of the action of a chloride on quinoline and methyl iodide.

Iodomenin.—This is an orange-yellow insoluble powder which is asserted to be a combination of iodine and bismuth with albumen. It is intended as a substitute for the iodides in the treatment of *syphilis*, *scleroses*, etc. Taege (*Med. Klin.*, 1910), however, asserts that the iodine is not chemically combined with the albumen, and that the remedy has no advantage over the alkaline iodides. It is marketed in the form of tablets each of which correspond to one grain (0.065 Gm.) of potassium iodide.

Iodonaphthol. *Naphthol Aristol.* $C_{10}H_6I_2O_2$. —This is obtained by treating a mixed solution of iodine with potassium iodide with a solution of sodium carbonate and hypochlorite. A yellowish-green powder, odorless, tasteless and decomposed by heat, giving off the violet fumes of iodine vapor. It is insoluble in water and slightly so in alcohol. It is used as an antiseptic after the manner of thymol iodide.

Iodophenacetin. *Iodophenine.* $C_{25}H_{23}I_3N_2O_4$. —To a solution of phenacetin in glacial acetic acid are added hydrochloric acid, water, and then a solution of iodine in potassium iodide. The product forms crystals resembling those of potassium permanganate, melting at from 130°–131° C. (266°–267.8° F.), with decomposition, and soluble in glacial acetic acid or alcohol. Decomposed by water, alkalies and other substances having an affinity for iodine. Scholvein (*O. Z.*, 1891) has found that this substance is a powerful germicide, and that it is locally very irritant, and when taken into the intestinal canal and is decomposed with the liberation of iodine, and liable to produce iodine poisoning. The drug probably has no practical value.

Iodo-phenyl-arsenic Acid.—By substituting iodine for the amido group in atoxyl a compound is obtained of the formula:



It occurs as needles of a pale pink color, which are soluble only in methyl alcohol and ethyl alcohol. The sodium salt of this acid, under the name of *iodo-atoxyl*, has been suggested as a substitute for that atoxyl, especially in the treatment of *syphilis*. As yet there seems to be no clinical information as to its usefulness.

Iodopyrine. $C_{11}H_{11}IN_2O$. *Antipyrine Iodide, Iodantipyrine.*—This substance contains 60 per cent. antipyrine and 40 per cent. of iodine. It forms colorless crystals melting at 160° C. (320° F.), and has been recommended as a substitute for the iodides in *muscular rheumatism* and in *asthma* and *syphilis*. It is capable of producing iodism. It has also been used as an analgesic in *neuralgia* and *herpes zoster* and as a local application in *syphilitic sores* and *psoriasis*. The *dose* given by Junkers was fifteen grains (1 Gm.) for adults every three or four hours. For children from 1 to 10 years old he gave one and a half to eight grains (0.096–0.5 Gm.). To those over 10 years he gave eight to twelve grains (0.5–0.78 Gm.). (*Th. M.*, vol. xiii, p. 604.)

Iodose.—This is a reddish powder stated to be a compound of iodine with a nucleo-proteid. It contains 10 per cent. of iodine and is soluble in the alkaline intestinal secretions, but insoluble in the gastric juice. Due to its being easily assimilated it is recommended especially in the treatment of *goiter* and *glandular enlargement*. *Dose*, five to thirty grains (0.32–2.0 Gm.).

Iodostarin.—This *tariinic acid di-iodide*, of the chemical formula $CH_3.(CH_2)_{10}CI=CI.(CH_2)_4CO\,OH$, melting at 49° C. (120.2° F.). It forms white, shining, crystalline scales, which are odorless and tasteless, containing 47.5 per cent. of iodine. It is insoluble in water, slightly soluble in cold alcohol, readily soluble in hot alcohol, in ether, chloroform and benzol. *Iodostarin* itself is not affected by light, but its solutions, after short exposure to light, turn brown with separation of iodine. According to the investigations of Bachem (*M. M. W.*, 1911) the iodine in this compound is much more slowly eliminated than from the alkaline iodides, and therefore a more continuous action is obtained. It is marketed in the form of tablets each containing four grains (0.26 Gm.).

Iodosyl. $C_6H_3I.OI.COOH$.—A bulky, amorphous powder of a deep red color, nearly odorless, and having only a faint taste suggestive of that of iodine. Insoluble in water and in oils and only sparingly soluble in chloroform and ether. Although resisting decomposition by acids, alkalies, and most chemical reagents, it seems to give up iodine when brought in contact with animal tissues and so has a pronounced alterative and antiseptic action. Its medicinal uses are those of iodoform, but it has the advantage that it is odorless and in an impalpable powder. It is used as a dressing for *wounds* and *ulcers* of every description, as a local application in *nasal catarrh* and *ozena*, in *ringworm* of the scalp, in various *cutaneous affections*, being especially recommended in the treatment of *corneal ulcers*. It is employed either as a dusting powder, in the form of an ointment, 2 to 10 per cent., or in that of a medicated gauze.

Iodoterpin. $C_{10}H_{16}I$.—This is prepared by gently warming on a water bath equal parts by weight of finely powdered iodine and terpin hydrate. Physically the product resembles ichthyol, in odor it resembles that of terpin hydrate, while the taste is aromatic. It is soluble in alcohol, chloroform, ether and benzine, and is miscible with water. The presence of 50 per cent. iodine and its ready absorbability recommend this product as a valuable and almost odorless iodoform succedaneum, used either in salve form or as a dusting powder when mixed with kaolin.

Iodothymoloform. *Iodothymoform.*—This product is obtained by iodizing thymoform. It forms a yellow, inodorous powder rich in iodine, soluble in all the volatile solvents and oils, insoluble in water and glycerin. It is used as an antiseptic dusting powder.

Iodylin. *Bismuth-iodo-salicylate.*—According to Israel (*Med. Wochens.*, 1902, p. 139), this substance is efficient as a substitute for iodoform.

Iodyloform.—This is a yellowish-brown insoluble powder, said to be a combination of iodine and gelatin, containing 5 per cent. of iodine, and has been used by Müller as a substitute for iodoform in *specific ulcerations*.

Iogen.—Iogen is produced by the action of iodine upon the anhydride of phthalic acid. It is a lustrous crystalline compound of dark green color, liberating 52 per cent. of iodine in the presence of moisture. It is claimed to be antiseptic and germicidal, and is used in about 4 per cent. strength in oil for the treatment of nose and throat affections, in ointment for application to the skin or to wounds, or as an antiseptic dusting powder.

Ionidium. *Ionidium Marucci.*—This name has been conferred by Bancroft upon a South American plant of the fam. *Violaceæ*, supposed to be the source of a medicine used with great asserted advantage, in Maracaibo and elsewhere, in *elephantiasis* and other cutaneous affections. A specimen, however, received from Bancroft, was reported by W. Hooker to be identical with the *Ionidium parviflorum* of Ventinat, which is now referred to *I. glutinosum* Vent. The medicine is called by the Indians *cuichunchulli*, and grows at the foot of Chimborazo. It is said to be diaphoretic, diuretic, occasionally sialagogue, and in large doses emetic and cathartic. The root is the part used. For further information, see *A. J. P.*, iii, 125.

Iothion. *N. N. R.* 1917. *Di-iodo-hydroxypropane.* $C_3H_5I_2(OH)$.—It is a thick, yellowish liquid, soluble in alcohol, ether, and the fixed oils, but almost insoluble in water. It contains about 80 per cent. of iodine.

Iothion is intended as a means of endermic administration of iodine. It is asserted that after its external application, iodine appears in the saliva within an hour, and that from 30 to 50 per cent. of the amount of the substance employed can be eventually recovered from the excretions. It has been used to a considerable extent in the treatment of *tertiary syphilis, asthma, chronic arthritis*, and other conditions in which iodine is indicated. (See Richter, *B. K. W.*, 1909.) It is applied generally in the form of an ointment containing from ten to fifty per cent. of iothion, of which a quantity equivalent to fifteen to thirty grains (1–2 Gm.) may be well rubbed into the skin once a day.

According to Herzfeld and Makler (*Med. Klin.*, 1912), a portion of the iodine is retained in the organism. It is used in the treatment of *syphilis* and other conditions in which a

continued iodine effect is desired. Herzfeld and Elin (*Med. Klin.*, 1912) found 50 per cent. of the iodine in the urine after application of a 10 per cent. iothion ointment.

Iridium. *Ir.*—This metal, discovered in 1804, and named after Iris the goddess of the rainbow, is a white lusterless, steel-like metal of the platinum group. It has a sp. gr. of 22.7 and is the heaviest of all metals. Several of its salts and compounds of its salts with other salts usually of the alkali group are prepared and marketed. Of these but one, the bromide, is used in medicine, and even this has failed to show any decided therapeutic value.

Iron and Ammonium Tartrate. *Ferri et Ammonii Tartras. U. S. VIII. Ferric Ammonium Tartrate. Ferrum Tartaricum Ammoniatum. Ferri Ammonio-Tartras. Ammonio-Tartrate of Iron. Tartrate Ferrico-ammonique,* Fr. Cod. *Tartrate de Fer et d'Ammoniaque. Tartrate ferrique ammoniacal,* Fr. *Weinsaures Eisenoxyd-Ammonium,* G.—This iron scale-salt was not admitted to the U. S. P. IX. It was officially described as follows: "It should contain Iron and Ammonium Tartrate corresponding in amount to not less than 13 per cent. of metallic iron, and should be kept in well-stoppered bottles, protected from light." *U. S. VIII.*

The process of the U. S. P., 1890, for preparing iron and ammonium tartrate was: "Solution of Ferric Sulphate, *one hundred mils* [or 3 fluidounces, 183 minims]; Tartaric Acid, *twenty-nine grammes* [or 1 ounce av., 10 grains]; Distilled Water, *two hundred mils* [or 6 fluidounces, 366 minims]; Ammonia Water, Water, each, *a sufficient quantity.* To *one hundred and ten mils* [or 3 fluidounces, 345 minims] of Ammonia Water, previously diluted with *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of cold Water, add, with constant stirring, the Solution of Ferric Sulphate, previously diluted with *thirteen hundred mils* [or 43 fluidounces, 460 minims] of cold Water. When the precipitate has subsided, draw off the clear, supernatant liquid by means of a siphon, then mix the precipitate intimately with about *fifteen hundred mils* [or 50 fluidounces, 346 minims] of cold Water, again draw off the clear liquid, and repeat the washing with Water in the same manner until the decanted liquid gives not more than a slight cloudiness with barium chloride test-solution. Then transfer the precipitate to a wet muslin strainer, allow it to drain, and express the water as completely as possible. Dissolve one-half of the Tartaric Acid in the Distilled Water, neutralize the solution exactly with Ammonia Water, then add the other half of the Tartaric Acid, and dissolve it by the application of a gentle heat. Now add the moist ferric hydrate, in successive portions, stirring constantly, and continue the heat, which should not exceed 60° C. (140° F.), until the hydrate is dissolved. Filter the solution while hot, evaporate it in a porcelain vessel, at or below the above-mentioned temperature, to the consistence of syrup, and spread it on plates of glass, so that, when dry, the salt may be obtained in scales. Keep the product in well-stoppered bottles, protected from light." *U. S.*, 1890.

Theoretically this process should yield a double salt consisting of one molecule of tartaric acid and two molecules of base, one of ammonia and the other of ferric oxide $2(FeO)NH_4.C_4H_4O_6.3H_2O$. It is hardly probable that the salt has exactly this chemical composition, as the scaled salts cannot be said to be definite compounds.

This compound is in "thin, transparent scales, varying in color from garnet-red to reddish-brown, without odor, and having a sweetish, slightly ferruginous taste; slightly deliquescent in the air. Very soluble in water; insoluble in alcohol. When strongly heated, the salt chars, emits fumes having the odor of burning sugar, and finally leaves a residue of ferric oxide, which, when moistened with hot water, should not show an alkaline reaction upon red litmus paper (absence of *citrates* or *tartrates* of the *alkali metals*). An aqueous solution of Iron and Ammonium Tartrate should be acid to litmus paper, and is not precipitated, but rendered darker in color, by ammonia water. With potassium ferrocyanide T.S. the solution does not yield a blue color or precipitate, unless it be acidulated with hydrochloric acid. If Iron and Ammonium Tartrate be heated with potassium hydroxide T.S., it yields a brownish-red precipitate, and ammonia is evolved. If an aqueous solution of the salt (1 in 10) be deprived of its iron by boiling with an excess of potassium hydroxide T.S., the filtrate, when slightly acidulated with acetic acid, will gradually deposit a white, crystalline precipitate. If 0.555 Gm. of the dry salt be dissolved in 15 Cc. of water and 2 Cc. of hydrochloric acid, in a glass-stoppered flask having a capacity of about 100 Cc., and if, after the addition of 1 Gm. of potassium iodide, and securely closing the flask, the mixture be kept for half an hour at 40° C. (104° F.), and then cooled, it should require not less than 13 Cc. of tenth-normal sodium thiosulphate V.S. to discharge the color of the liquid, starch T.S. being used as an indicator (each Cc. of the tenth-normal sodium thiosulphate V.S. indicating 1 percent. of metallic iron)." *U. S. VIII. Dose,* as a mild chalybeate, from five to ten grains (0.32–0.65 Gm.).

Iron and Magnesium Citrate. *Ferri et Magnesii Citras.*—This double salt, introduced by Van der Corput, is made by dissolving two ounces of freshly precipitated ferric hydroxide in a moderately heated solution of three ounces of citric acid, and saturating the liquor with magnesium carbonate. The solution, after filtration, is evaporated by means of a water bath to a syrupy consistence, and spread on glass to dry in scales. Three and a quarter ounces of ferrous sulphate will furnish by decomposition the necessary hydroxide for three ounces of the acid. (See formula for *Ferri Hydroxidum,* p. 505.) This salt is in transparent, greenish-yellow scales, having a slightly ferruginous, somewhat acid taste. It is very soluble in water, but insoluble in alcohol and ether. *Dose,* from five to ten grains (0.32–0.65 Gm.). (See *A. J. P.*, 1850, 315.)

Iron and Strychnine Citrate. *Ferri et Strychninæ Citras. U. S. VIII. Ferri et Strychniæ Citras,* U. S., 1870. *Citrate de Fer et de Strychnine,* Fr. *Citronensaures Eisen-Strychnin,* G.—Iron and strychnine citrate was dropped in the revision of U. S. P. IX. The U. S. P. VIII describes it as follows:

"It should contain not less than 0.9 nor more than 1 per cent. of strychnine, and ferric citrate corresponding in amount to not less than 16 per cent. of metallic iron. It should be kept in well-stoppered bottles, protected from light." *U. S. VIII.*

The U. S. P. VIII did not contain a process for this preparation; that of the U. S. P., 1890, is as follows: "Iron and Ammonium Citrate, *ninety-eight grammes* [or 3 ounces av., 200 grains]; Strychnine, *one gramme* [or 15.4 grains]; Citric Acid, *one gramme* [or 15.4 grains]; Distilled Water, *one hundred and twenty cubic centimeters*

[or 4 fluidounces, 27 minims], to make *one hundred grammes* [or 3 ounces av., 230 grains]. Dissolve the Iron and Ammonium Citrate in *one hundred cubic centimeters* [or 3 fluidounces, 181 minims] of Distilled Water, and the Strychnine, together with the Citric Acid, in *twenty cubic centimeters* [or 325 minims] of Distilled Water. Mix the two solutions, evaporate the mixture by means of a water-bath, at a temperature not exceeding 60° C. (140° F.), to the consistence of syrup, and spread it on plates of glass, so that, when dry, the salt may be obtained in scales. Keep the product in well-stoppered bottles, protected from light." *U. S.*, 1890.

This salt should never be prescribed in solution. E. R. Squibb has shown that a whitish deposit will begin to settle from the solution within two or three hours after it is made, and continue to increase for several days; the deposit was found to contain fifty per cent. of strychnine. When ammonia water or ammonium citrate was added, the precipitate was redissolved, but the solution could not be made permanent by the addition, as the precipitate reappeared. There might be dangerous or alarming symptoms if this solution were dispensed without shaking, and the last dose containing an undue proportion of the strychnine were administered. (*Ephem.*, June, 1888, p. 1128.)

It is officially described as in " thin, transparent scales, varying in color from garnet-red to yellowish-brown, without odor, and having a bitter, slightly ferruginous taste; deliquescent in moist air. Readily and completely soluble in water, partially soluble in alcohol. When strongly heated, the salt chars, and finally leaves a residue of ferric oxide, which, when moistened with hot water, should not show an alkaline reaction with red litmus paper (absence of *citrates or tartrates* of the *alkali metals*). The aqueous solution of Iron and Strychnine Citrate is slightly acid to litmus paper, and is not immediately precipitated, but rendered darker in color by ammonia water. With potassium ferrocyanide T.S. the aqueous solution does not yield a blue color or precipitate, unless it be acidulated with hydrochloric acid. On heating with potassium hydroxide T.S. the salt affords a brownish-red precipitate, evolving ammonia. If an aqueous solution of the salt (1 in 10) be deprived of its iron and strychnine by boiling with an excess of potassium hydroxide T.S., and the filtrate be slightly acidulated with acetic acid, a portion of the cooled liquid, when mixed with a little calcium chloride T.S., and again heated to boiling, will gradually deposit a white, crystalline precipitate. Another portion of the acidulated and cooled liquid, when allowed to stand for twenty-four hours, should not deposit a white crystalline precipitate (absence of *tartrate*)." *U. S. VIII.*

Assay for the Strychnine.—" Dissolve 4.44 Gm. of Iron and Strychnine Citrate, in a separator, in 15 Cc. of water, add 5 Cc. of ammonia water and 10 Cc. of chloroform, and shake the separator for one minute. Allow the liquids to separate, draw off the chloroformic layer, and shake the residuary liquid a second and a third time with portions of 10 Cc. each of chloroform. Allow the combined chloroformic liquids to evaporate spontaneously in a tared dish, and dry the residue at 100° C. (212° F.) to a constant weight. This residue should weigh not less than 0.04 (0.0399) Gm., nor more than 0.0444 Gm. (corresponding to not less than 0.9 nor more than 1 per cent. of strychnine), and should respond to the reaction and tests given under *Strychnina*."

Assay for the Iron.—" Heat the aqueous liquid, from which the strychnine has been removed in the manner just described, on a water-bath, until the odors of chloroform and of ammonia have disappeared, allow it to cool, and dilute it with water to the volume of 100 Cc. Transfer 25 Cc. of the liquid to a glass-stoppered flask having the capacity of about 100 Cc., add 4 Cc. of hydrochloric acid and 1 Gm. of potassium iodide, and, after securely closing the flask, allow the mixture to stand for half an hour at 40° C. (104° F.). After it has been allowed to cool, it should require not less than 32 Cc. of tenth-normal sodium thiosulphate V.S. to discharge the color of the liquid, starch T.S. being used as indicator (each Cc. of tenth-normal sodium thiosulphate V.S. indicating one-half per cent. of metallic iron)." *U. S. VIII.* It contains 1 per cent. of strychnine, there being in five grains one-twentieth of a grain of the alkaloid.

This combination has no advantages over the two active substances it contains when given conjointly in an uncombined state, and has the great disadvantage that the dose of one principle cannot be varied independently of that of the other.

Dose, from three to five grains (0.20 to 0.32 Gm.), in pill.

Iron, Ammoniated. *Ammoniated Iron. Ferrum Ammoniatum. Ammonio-chloride of Iron. Ammonii et Ferri Chloridum. Ammonium Chloratum Ferratum. Sel Ammoniac Martial*, Fr. *Eisensalmiak*, G.—This drug was formerly recognized both by the U. S. and London Pharmacopœias, which contained formulas for its preparation. (See *U. S. D.*, 15th edition, 1568.) There is no reason to believe that the ferric chloride and ammonium chloride are chemically combined in the preparation. According to Phillips, they are in the proportion of 15 parts of the iron to 85 of the ammonium salt.

Ammoniated iron is in crystalline grains, of a fine reddish-orange color, and a sharp, styptic, saline taste. It is entirely soluble in water and diluted alcohol, is deliquescent, and should be kept in well-stoppered bottles. As procured by sublimation (*Flores martiales, Ens martis*), it is of a yellow color and feeble odor. It unites aperient with chalybeate properties, and is said to have been used with advantage in *amenorrhea, epilepsy, scrofula, rickets*, etc.; but it is at best uncertain, and is now very seldom prescribed. *Dose*, from four to twelve grains (0.26–0.78 Gm.).

Iron Caseinate. *Ferri Caseinas. Ferrum Caseinatum. Ferrum nucleo-albuminatum.*—One part of freshly precipitated casein, thoroughly washed, and freed from fat by treatment with ether, is mixed with 1 part of calcium carbonate and 100 parts of water. The resulting solution, after being filtered, is precipitated by a slight excess of a 1 per cent., freshly prepared solution of ferrous lactate. The precipitated iron caseinate is washed and dried and is in the form of a flesh-colored, odorless, tasteless powder, insoluble in water but soluble in weak sodium carbonate and ammonia solutions. It is recommended as a form of iron which can be readily absorbed.

Iron Peptonate. *Ferri Peptonas. Ferrum Peptonatum. Peptonate de Fer*, Fr. *Eisen Peptonat*, G.—To a solution of 2 parts of dried peptone in 200 parts of water add a mixture of 24 parts of solution of dialyzed iron (*Liquor Ferri Oxychlorati*, P. G.) and 200 parts of water, in a thin stream and while stirring constantly. A solution of caustic soda (1.5 per cent.) is added until there is produced a very weak alkaline reaction. The

precipitated iron peptonate is washed rapidly with water until no reaction with silver nitrate is shown. The precipitate is drained on a wet strainer and dissolved in three parts of 25 per cent. hydrochloric acid. The solution is evaporated on a water bath and spread on plates to dry at a temperature not exceeding 50° to 60° C. (122°–140° F.). Iron peptonate, thus prepared, is in the form of shining brown scales, and contains from 24 to 25 per cent. of iron. It is slowly soluble in cold water, more quickly in hot water, and the solution is not clouded by boiling nor by the addition of alcohol. Iron peptonate, its solution, and a syrup prepared from it are used in preference to inorganic salts of iron because of the absence of injurious effects upon the teeth and mucous membrane and its deficiency in astringency. The *dose* is from three to ten grains (0.2–0.65 Gm.).

Liquor Ferri Peptonati.—Solution of iron peptonate is now included in the N. F. IV and is made by a process somewhat different from that given above (see Part III).

Iron-Wood. *Ostrya virginiana* (Mill.) Willd. (*O. virginica* Willd. *Carpinus virginiana* Mill.) (Fam. *Betulaceæ.*)—The wood of the *hop-hornbean* is said to be tonic, antiperiodic, and alterative, and the fluidextract has been used in *doses* of from a half to one fluidrachm (1.8–3.75 mils) in *ague.*

Irrigal.—This occurs in the form of tablets of a brownish-yellow color with a violet-like odor, and an alkaline reaction. It is obtained by the dry distillation of wood, and contains various phenol bodies. Moeller (*Th. M.*, 1909) found that a three per cent. solution kills all forms of the non-sporulating bacteria after thirty-minute exposures. It has been used as a vaginal douche in various types of inflammation of the female genitalia. One to two tablets are added to a quart of water.

Isarol. *Ichthyodin.*—This is a substance prepared by the action of sulphuric acid on impure ichthyol. It occurs as a brownish-red thick liquid, having an odor like that of ichthyol; containing about 9 per cent., or, when dried, 17 to 19 per cent., of sulphur. It makes a clear solution in water, and is also soluble in ten parts of 95 per cent. alcohol. It is said to be therapeutically equivalent to ichthyol, and has been recommended on account of superior cheapness to the refined ichthyol.

Isatis. *Isatis tinctoria* L. *Woad. Pastel.* (Fam. *Cruciferæ.*)—A biennial plant, indigenous to and cultivated in southern and central Europe to central Asia. The leaves have a fugitive, pungent odor, and an acrid, very persistent taste; they have been used in *scorbutic affections, jaundice,* and other complaints, but are of no value. They were formerly of importance as a source of indigo. (See *Indigo.*) The leaves are prepared by grinding them to a paste, which is made into balls, placed in heaps, and allowed to ferment. When the fermentation is at an end, the mass falls into a coarse powder, which is woad.

Isatophan. *Methoxy-atophan, 8-methoxy-2-phenyl-quinolin-4-carboxylic acid.* $CH_3O.C_7H_4N.C_6H_5.COOH$, 8 : 2 : 4.—It is a yellow, crystalline powder with a melting point of 216° C. (420.8° F.), insoluble in water, but soluble in alkalies and in alcohol. It is practically tasteless, and possesses but slight odor. It is employed in the treatment of *gouty* conditions in the same way as is atophan, over which it has the advantage of being tasteless (see *Acidum Phenylcinchoninicum*). The *dose* is five to ten grains (0.3–0.6 Gm.).

Isoform. *Para-iodoanisol.* $C_6H_4(OCH_3)IO_2$.—It is a white powder having an odor feebly suggestive of aniseed. It is sparingly soluble in cold water, but dissolves more freely in hot water. In alcohol and ether it is insoluble. When heated to about 225° C. (437° F.) it decomposed explosively.

Because of its explosive properties it is marketed only mixed with equal parts of calcium phosphate—if intended for a dusting powder—or as a paste, with equal parts of glycerin.

According to Winterberg (*Med. Klin.*, 1906), *isoform* in 1 per cent. strength has a distinct, and in 3 per cent. strength, a well marked antiseptic action. It has been used to a considerable extent as a surgical dressing, especially for suppurating *wounds.* It is applied either in the form of a dusting powder or by saturating gauze with it, or in paste or emulsion, as the conditions may indicate. It has also been employed as an antiseptic in purulent *otitis media,* various *skin diseases, urethritis,* and in tooth paste. Although Heile has stated that isoform is non-toxic, Hoffman (*B. K. W.*, 1905) has reported violent dermatitis from its use, and Urbantschitch (*W. K. R.*, 1907) asserts that it has a depressant action upon the central nervous system.

Isophysostigmine, $(C_{15}H_{21}O_2N_3)_3$.—This is an alkaloid—isomeric with *physostigmine*—extracted from the ether-soluble extract of the calabar bean. It is asserted to be superior to physostigmine in its peristaltic action on the intestines and to be more prompt in its myotic effects. It is recommended by Ogiu, who first discovered it, to be used in doses three-fourths those of physostigmine. The same care should be taken in compounding its solutions that must be exercised with the eserine. It should be kept in amber-colored bottles only. Merck recommends the addition of a little boric acid to its solution, thus aiding the permanency of the solutions. *Dose,* one-eightieth of a grain (0.0008 Gm.).

Isopral. *Trichlorisopropylalkohol,* $CCl_3.CHOH.CH_3$.—This substance, which has been proposed as a hypnotic, occurs in microscopic prisms, melting at 49° C. (120.2° F.), readily soluble in water, alcohol, or ether, readily subliming and having a camphor-like odor and aromatic taste. Heated with alkalies for a long time it loses chlorine without the formation of chloroform. According to Impens, it is readily absorbed through the skin, subcutaneous tissue, and the digestive tract, the impression, when taken internally, being manifested in from three to five minutes. It is said, also, that the inhalation of a stream of air directed over warmed *isopral* will produce marked narcosis in the lower animals in ten or twelve minutes. It is eliminated through the kidneys chiefly as a compound with glycuronic acid (*trichlorisopropylglycuronic acid*), although it is believed also to escape to some extent through the respiratory tract.

The experiments of Hatcher (*J. A. M. A.*, 1907) have shown that, although weight for weight it is somewhat more powerfully somnifacient than is chloral hydrate, it is correspondingly more toxic, so that in its therapeutic efficiency it is about the same. The *dose* is ten to twenty grains (0.65–1.3 Gm.).

Isopyrum. *Isopyrum thalictroides* L. (Fam. *Ranunculaceæ.*)—F. A. Harsten believes he has found two alkaloids, *isopyrine* and *pseudoisopyrine,* in the root of this plant, which grows in the forests of middle and southern Europe. (*A. J. P.*, xliv, 453.)

Isotachiol.—The composition of this substance, while not accurately known, is said to be almost identical with silver fluoride. It is an antiseptic and bactericide, being active in very dilute solutions. For the sterilization of water one part to 500,000 is asserted to be sufficient. This substance is non-toxic.

Issue Peas.—These were globular beads, of the size of a pea, made of woody substances of spongy structure, intended to be introduced into issues, abscesses, etc., for the purpose of promoting suppuration. They are not used by modern surgeons.

Istizine.—Under this name a synthetic dioxyanthraquinone has been introduced as a purgative. It occurs as an orange-yellow crystalline powder, difficultly soluble in water or the ordinary organic solvents, but an alkaline solution dissolves it with the formation of a cherry-red color. Ebstein (*Med. Klin.*, 1913) has used it as a laxative in *doses* of two to eight grains (0.13 to 0.5 Gm.).

Ivarancusa.—The roots of *Andropogon Ivarancusa* Boiss., now considered to be in large part *A. Schoenanthus* L. (Fam. *Gramineæ*), a native of Central India. It contains a volatile oil, resin, and a bitter substance, and is stated to be coming into wide vogue on the continent as a diaphoretic drug. It is also used in perfumery.

Jacaranda.—Several species of this genus (Fam. *Bignoniaceæ*) are employed in *syphilis* in Brazil and other portions of South America under the names of *caroba, carobinha*, etc. Peckolt (*A. J. P.*, 1882, 134) has found in them a crystalline substance, *carobin*, besides resins and acids, such as *carobic* and *steocarobic acids*, and *carobon, caroborelinic acid*, and *caroba balsam*. Hesse (*Ann. Chem.*, cclii, 150) found only an aromatic resin, but no alkaloid. The value of the remedy has been asserted in the *B. M. J.*, vol. i, 1885. For further information, consult *P. J.*, 3d series, vols. v, xii, and xiv, and also *A. J. P.*, 1882.

Jambosa Root.—This is the root of *Jambosa vulgaris* DC., of the Fam. *Myrtaceæ*, which is widely cultivated in the tropics under the name of the *rose-apple*. It has been found by A. W. Gerrard to contain an oleoresin, besides a crystalline principle, *jambosin*, $C_{10}H_{15}NO_3$. Lyons has also found in it minute quantities of an alkaloid. The decoction of the bark of the root is used as an astringent in *dysentery, gonorrhea*, and *leucorrhea*. (*P. J.*, March, 1884.)

Jambu Assu. *Piper Jaborandi.*—The root of *Piper Jaborandi* Vell. (Fam. *Piperaceæ*) is one of the *Pipers* of Brazil, which is used by the natives as a sudorific, a diuretic, and a febrifuge. It is said to contain an alkaloid and a pungent oleoresin. It has no botanical, and probably no medicinal, relation with *pilocarpus*.

Jatrevin.—This substance is a condensation product of menthol and isobutyl phenol. It is soluble in alcohol and slightly soluble in ether and water. It is a clear brilliant liquid with an aromatic peppermint-like odor, and is employed as a wash in chronic or acute *catarrh* and in *tuberculosis*.

Jatropha. *Jatropha macrorhiza* Benth. *Jicama.*—This is a euphorbiaceous plant which inhabits Northern Mexico and the adjoining United States. It is a purgative, acting excessively in overdose, and is believed by the Mexicans to be cholagogue. The *dose* of the fluidextract is stated to be from one-half to two fluidrachms (1.8–7.5 mils).

Jeffersonia. *Twinleaf. Rheumatism Root. Jeffersonia diphylla* (L.) Pers. *Twinleaf.* (Fam. *Berberidaceæ.*)—This herbaceous perennial is found in woods from New York to Wisconsin, extending southward. The rhizome, which, with the rootlets attached, is the part used, has a brownish-yellow color, and a bitter, acrid taste, which resides in its cortical part, the inner portion being nearly tasteless. E. S. Wayne of Cincinnati, found it to contain albumen, gum, tannic acid, starch, pectin, a fatty resin, hard resin, sugar, lignin, and a peculiar acrid principle having acid properties and resembling polygalic acid. The root is said to be emetic in large doses, tonic and expectorant in smaller doses and not unlike senega, as a substitute for which it is sometimes used. (*A. J. P.*, xxvii, 1.) According to Mayer, of New York, the rhizome of this plant contains a small quantity of berberine and a second white alkaloid. The pectin of Wayne he considers to be saponin. (*A. J. P.*, 1863, 99.) A. W. Flexor proved the absence of berberine from the root. (*Am. Drug.*, 1884.) Gordin has since confirmed this view (1902).

Jellies.—The form of jelly is sometimes a convenient method of administering medicines, especially the fixed oils, as cod liver oil, castor oil, resinous juices, etc. The following is a formula recommended by Parrish and William C. Bakes. "Take of the fixed oil or liquid resin a *troyounce;* honey, syrup, each, *half a troyounce;* gum arabic, in powder, *two drachms;* Russian isinglass, *forty grains;* orange-flower water, *six fluidrachms*. Dissolve the isinglass, with the aid of heat, in half a fluidounce of the orange-flower water, replacing the water as it evaporates. Triturate the other ingredients, with the remainder of the orange-flower water, into a homogeneous mass in a warmed mortar, then add the hot solution of isinglass, stir the mixture as it cools, and set it aside to gelatinize." (*A. J. P.*, 1861, 4.) Any other aromatic water may be substituted for that of the orange flower, and cinnamon water diluted with an equal measure of pure water would probably better cover the offensive taste. In reference to cod liver oil, the bitter-almond, or cherry-laurel water would be still more effectual, care, however, being taken, in this case, that the water be duly diluted, lest too large a dose of it be administered.

Juglans. *N. F. IV* (*U. S. P.* 1890). *Butternut Bark. Oil Nut. White Walnut. Ecorce de Noyer gris*, Fr. *Graue Wallnussrinde*, G.—"The dried inner bark of the roots of *Juglans cinerea* Linné (Fam. *Juglandaceæ*), collected in autumn." *N. F.*

J. cinerea is a tree extending in rich woods from New Brunswick to the mountains of Georgia. The fruit, when half grown, is sometimes made into pickles, and, when ripe, affords in its kernel a grateful article of food. The bark is used for dyeing wool a dark-brown color, though inferior for this purpose to that of the black walnut. It is said to be rubefacient when applied to the skin. The inner bark is the medicinal portion; that of the root, being considered most efficient, was directed by the U. S. P. It should be collected in May or June.

On the living tree, the inner bark, when first uncovered, is of a pure white, which immediately on exposure becomes a fine lemon color, and ultimately changes to deep brown. It has a fibrous texture, and under the title of *Juglans* is described as follows in the N. F. IV:

"In quills, curved strips, or in chips, from 3 to 10 mm. in thickness; of a deep brown color on both surfaces and throughout, except for the faint, intersecting, whitish, radial, and tangential lines shown in the transverse section; outer surface smooth, somewhat warty; inner surface smooth and striate, bearing fragments of thin stringy

fiber: fracture short, rather weak, somewhat fibrous. Odor faintly aromatic; taste bitter, astringent, somewhat acrid.

"The powdered drug is dark-brown and, when examined under the microscope, exhibits numerous rosette aggregate crystals of calcium oxalate, up to 0.050 mm. in diameter; simple rounded or occasionally 2- to 4-compound starch grains, the individual grains being up to 0.015 mm. in diameter, sometimes with a cleft through the center; stone cells, some with thick walls, with simple or branching pores, up to 0.10 mm. long and 0.05 mm. wide, sometimes with reddish contents; long thick-walled sclerenchymatous fibers up to 0.03 mm. in width, occasionally associated with crystal fibers, the latter containing prisms of calcium oxalate from 0.01 to 0.05 mm. in length; fragments of parenchyma containing brownish tannin masses and oil; fragments of epidermal tissue composed of polygonal cells having yellowish-brown walls, some with reddish-brown contents. Juglans yields not more than 8 per cent. of ash." *N. F.*

Its medicinal virtues are extracted by boiling water. Bigelow could detect no resin in the bark, and the presence of tannin was not evinced by the test of gelatin, though a brownish-black color was produced by ferrous sulphate. Charles O. Thiebaud found the bark to be destitute of tannic acid and of any vegetable alkaloid, but to contain bitter extractive, oily matter in large proportion, a volatilizable acid, *juglandic acid*, crystallizing in bright, orange-yellow crystals, and appearing to bear some analogy with chrysophanic acid, another acid crystallizing in tabular, colorless crystals, and a volatile acid. (*A. J. P.*, 1872, 253.) Maisch believes that the juglandic acid of Thiebaud is the *nucin* of A. Vogel, Jr., found in green walnut peel. (*A. J. P.*, April, 1874, 167.) E. D. Truman (*A. J. P.*, 1893, 426) made proximate analyses of the root bark and the trunk bark for comparison. In the trunk bark, instead of the crystallizable juglandic acid, he found an uncrystallizable acid and a crystalline resin. Tanret and Villers isolated from the leaves a carbohydrate, *nucite*, $C_6H_{12}O_6 + 2H_2O$, which fuses at 218° C. (424.4° F.), is not fermentable, and does not reduce Fehling's solution. It has since been shown to be identical with *inosite*. Tanret also (*Jahresb. f. Pharm.*, 1876, 198) thinks that he has obtained an alkaloid from walnut leaves, which he proposes to call *juglandine*. The European walnut bark yielded *glycyrrhizin* abundantly to Sestini. *Juglon*, $C_{10}H_6O_3$, the characteristic constituent of *Juglans regia*, has been prepared synthetically by Bernthsen and Semper, and is now recognized as *a-oxynaphthoquinone*, $C_{10}H_5(OH)O_2$, as it can be made from dioxynaphthalene by the action of chromic acid mixture. It is in brownish-red, crystalline needles having a faint odor of walnut hulls, and is sternutatory. (*Ber. d. Chem. Ges.*, 1887, 934.) The fluidextract is recognized by the N. F. (see Part III); the extract was official in the U. S. P., 1890.

Extractum Juglandis. U. S. 1890. *Extract of Juglans.* "Juglans, in No. 30 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Diluted Alcohol, a *sufficient quantity*. Moisten the powder with *four hundred mils* [or 13 fluidounces, 252 minims] of Diluted Alcohol, and pack it firmly in a cylindrical percolator; then add enough Diluted Alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed, gradually adding Diluted Alcohol, until *three thousand mils* [or 101 fluidounces, 212 minims] of tincture are obtained, or the Juglans is exhausted. Distil off the Alcohol from the tincture by means of a water-bath, and evaporate the residue, on a water-bath, to a pilular consistence." *U. S.*, 1890.

Butternut is a mild cathartic resembling rhubarb in its action, but less certain. It was much used during our Revolutionary war as an habitual laxative, and was especially esteemed by Rush in the treatment of *dysentery* and *hepatic congestions*. *Dose*, of the extract, from five to twenty grains (0.32–1.3 Gm.); of the fluidextract, thirty to sixty minims (1.9–3.9 mils).

Several products of *Juglans regia* L., or common European *walnut*, are used medicinally in Europe. The hull of the fruit has been employed as a vermifuge from the times of Hippocrates, and has been recommended in *syphilis* and for old *ulcers*. The expressed oil of the fruit has been deemed efficacious against the *tapeworm*, and is also used as a laxative injection. The leaves, long occasionally employed for various purposes in both regular and domestic practice, have been found by Négrier of Angers, in the highest degree efficacious in *scrofula*. He gave to children a teacupful of a fairly strong infusion, or six grains (0.4 Gm.) of the aqueous extract, or an equivalent dose of a syrup prepared from the extract, two, three, or four times a day, and at the same time applied a strong decoction to the ulcers, and as a collyrium when the eyes were diseased. No injury ever resulted from a long-continued use of the remedy. It appears to act as a moderately aromatic bitter and astringent. (*A. G. M.*, 3e sér., x, 399 and xi, 41.) They are said also to have proved useful as a topical application in *malignant pustule*. (*Ibid.*, 5e sér., x, 609.)

Nucitannic Acid.—In the walnut, between the kernel and the shell, is a thin membrane, which closely embraces the cotyledon, called the *episperm*, which consists of two layers, the inner very thin, colorless, translucent, and perfectly tasteless, the outer coarser, somewhat colored, and of a bitter, disagreeable taste. The latter, examined chemically by T. L. Phipson, was found to contain, among other principles, as gallic and ellagic acid, etc., a new variety of tannic acid, which he proposes to name *nucitannic acid* or *nucitannin*, to which the outer membrane chiefly owes its unpleasant taste. It is a glucoside, as when boiled for some hours with diluted hydrochloric acid it splits into glucose and a peculiar red acid substance, which he calls *rothic acid*, $C_{14}H_{12}O_7$, and the properties of which he has pretty thoroughly investigated. (*Chem. News*, Sept. 3, 1869, p. 116.) For an exhaustive chemical examination of black walnut leaves by Miss L. J. Martin, see *A. J. P.*, 1886, p. 468. The leaves of *J. nigra* L. (*black walnut*), and those of *J. cinerea*, probably possess the same properties.

Juniper Berries. *N. F. IV* (*U. S. P.* 1880). *Juniperus. Fructus Juniperi*, P. G. *Baccæ Juniperi. Genièvre, Baies de Genièvre*, Fr. *Gemeiner Wachholder, Wachholderbeeren*, G. *Ginepro*, It. *Enebro, Bayas de Enebro*, Sp.—"The carefully dried ripe fruit of *Juniperus communis* Linné (Fam. *Pinaceæ*). Preserve Juniper Berries in air-tight tin or glass containers, and reject old or insect-infected fruit." *N. F.*

Juniperus communis L. is an evergreen shrub, usually small, but sometimes twelve to fifteen

feet high, with numerous very close branches, and varying from an erect shrub to a decumbent or even trailing arborescent plant.

The common juniper is a native of Europe and the northern regions of Asia and North America. Northward it becomes a trailing shrub, seldom more than 2 to 4 dm. high, spreading in all directions, throwing out roots from its branches, and forming beds which are often many rods in circumference. The name of *J. depressa* has been proposed for this variety. The common juniper flowers in May, but does not ripen its fruit until late in the following year. All parts of the plant contain a volatile oil, which imparts to them a peculiar flavor. The wood has a slight aromatic odor, and was formerly used for fumigation. A terebinthinate juice exudes from the tree and hardens on the bark. This has been erroneously considered as identical with the gum known commercially as *sandarach*.

The berries, as the fruit is commonly called, were formerly occasionally brought to the Philadelphia market from New Jersey. But, though equal to the European in appearance, they are inferior in strength, and are not much used. The best come from the south of Europe, particularly from Trieste and the Italian ports. They are "nearly globular, about 8 mm. in diameter; externally smooth, shining, black-brown to purplish-black with a blue-gray bloom, at the apex a three-rayed furrow marks the cohesion of the three fleshy bracts forming the pericarp; internally loosely fleshy, greenish-brown, containing numerous large schizogenous cavities; seeds three, triangular ovate, hard, brown, with large uneven oil glands on the surface. Odor aromatic; taste sweet, pleasant, terebinthinate, slightly bitter.

"Sections, when examined under the microscope, exhibit a pericarp consisting of an epiderm of a single row of rounded polygonal cells filled with a brown granular substance, at the sutures of the bracts these become blunt papillæ; a hypodermis of two or three rows or brown-red, collenchymatous cells thickened at the angles; the fleshy portion (mesophyl) composed of loose, irregular parenchyma with large oval canals and traversed by fibro-vascular bundles with areolated fibers; a sclerenchymatous ring of six to eight rows of very thick cells with pitted walls, many enclosing prismatic crystals of calcium oxalate; the seed-testa shows a layer of two to ten rows of stone cells with radial markings on the walls and each enclosing a polygonal crystal of calcium oxalate; endosperm and embryo rich in fat and aleurone. Juniper Berries yield not more than 5 per cent. of ash." *N. F.*

These properties, as well as their medicinal virtues, they owe chiefly to a volatile oil. (See *Oleum Juniperi*, p. 766.) The other constituents, according to Trommsdorff, are resin, sugar, gum, wax, lignin, water, and various saline substances. The proportion of these constituents varies according to the greater or less maturity of the berries. The volatile oil is most abundant in those which have attained their full growth and are still green, or in those which are on the point of ripening. In the latter Trommsdorff found 1 per cent. of the oil. In those perfectly ripe it has been partly changed into resin, and in those quite black, completely so. The berries impart their virtues to water and alcohol. They are very largely consumed in the preparation of gin.

The tops of juniper were formerly directed by the Edinburgh and Dublin Colleges. Their odor is balsamic, their taste resinous and bitterish, and they possess similar virtues with the berries.

Juniper berries are gently stimulant and diuretic, imparting to the urine the odor of violets, and producing occasionally, when largely taken, disagreeable irritation in the urinary passages. They are chiefly used as an adjuvant to more powerful diuretics in dropsical complaints. The infusion is a good preparation. It is made by macerating an ounce of the bruised berries in a pint of boiling water, the whole of which may be taken in the course of twenty-four hours. The fluidextract is recognized by the N. F. (see Part III), but for most purposes the oil is preferable. (See *Oleum Juniperi*, p. 767.) Under the trade name of *junol* there appears on the market a hydroalcoholic extract of juniper berries recommended as a diuretic. Juniper berries are not administered in substance; the *dose* of the fluid extract is one fluidrachm (3.9 mils) (see Part III).

Juniperus Virginiana L. *Red Cedar. Cèdre de Virginie*, Fr. *Virginische Ceder, Rothe Ceder*, G.—The tops of this plant were formerly included in the Secondary List of the U. S. Pharmacopœia. The tree is an evergreen of slow growth, seldom very large, although sometimes attaining a height of 25 m.

It grows on dry hills or deep swamps from Maine westward to the Rocky Mountains, from Vermont to the Gulf of Mexico, is most abundant and vigorous in the southern section. The interior wood is of a reddish color, and highly valuable on account of its great durability. Small excrescences, which are sometimes found on the branches of the tree, are popularly known as *cedar apples* and used as an anthelmintic in the *dose* of from ten to twenty grains (0.65–1.3 Gm.) three times a day. The tops have a pleasant odor, and a strong, bitterish, somewhat pungent taste. These properties reside chiefly in a volatile oil, and are readily imparted to alcohol. The leaves, analyzed by Wm. J. Jenks, were found to contain volatile oil, gum, tannic acid, albumen, bitter extractive, resin, chlorophyll, fixed oil, lime, and lignin. (*A. J. P.*, xiv, 235.) They bear a close resemblance to the leaves of *Juniperus Sabina* L., an European shrub, from which they can be certainly distinguished only by the difference of odor. The *oil of red cedar* is now an article of commerce; it is used generally in perfumery, and was formerly one of the principal constituents of the popular extract of white rose. (*A. J. P.*, 1877, 186.) It possesses, in a marked degree, the well-known agreeable odor of the red cedar wood. Schimmel describes a volatile oil from Haitian cedar wood which differs from our domestic oil of cedar, only in having a higher specific gravity. (*Schim. Rep.*, 1905, 17.) I. W. Brandel obtained from the leaves of *J. Virginiana* 0.47 per cent. of volatile oil, sp. gr. 0.913 at 15° C. (59° F.). It had a very pleasant odor. (*Proc. A. Ph. A.*, 1906, 459.) *Cedrene camphor*, $C_{10}H_{26}O = C_{16}H_{24} + H_2O$, may be obtained by cooling the oil until coagulated, and separating the crystalline portion by expression; the expressed liquid is *cedrene*, $C_{15}H_{24}$, which, after rectification and distillation, has the sp. gr. 0.984 at 15° C. (59° F.), boiling at 237° C. (458.6° F.). Cedrene may also be prepared from the cedrene camphor by the dehydrating action of phosphoric anhydride, P_2O_5. The resemblance of red cedar to savin is said also to extend to its medicinal prop-

erties. It is, however, much less energetic, and has not acquired the confidence of the profession. Externally applied it acts as an irritant, and an ointment, prepared by boiling the fresh leaves for a short time in twice their weight of lard with the addition of a little wax, is employed as a substitute for savin cerate in maintaining a purulent discharge from blistered surfaces. Sometimes the dried leaves in powder are mixed with six times their weight of rosin cerate, and used for a similar purpose. But neither of these preparations is as effectual as the analogous preparation of savin.

The volatile oil, which resembles oil of savin in its medicinal properties, has been used for the purpose of producing abortion, and in some cases has caused death. The symptoms have been burning in the stomach, vomiting, convulsions, coma, and a slow pulse, with evidences of gastro-intestinal inflammation after death. (See S. C. Watt, *B. M. S. J.*, vol. xl.)

Under the name of *cedar* are known in commerce various trees, some of which do not belong to the genus *Juniperus*. The wood of *Juniperus bermudiana* L. is said to be largely used in making pencils. The cedar of Lebanon, *Cedrus Libani* Barrel, and its two varieties, the *African cedar*, *C. atlantica* Manetti, and the *Indian cedar* or *deodar*, *C. Deodara* Loud., are sometimes distilled for oil, and, under the name of *libanol*. An oil obtained from *Cedrus atlantica* Manetti, or *satin-wood*, has appeared in commerce and is said to be useful in the treatment of *blennorrhagia*, *phthisis*, *bronchitis*, and *eruptions* upon the skin, having properties very similar to those of the oil of santal. It may be given in capsules up to forty-five grains (3 Gm.) per day. In skin eruptions the 25 per cent. ointment made with vaseline has been used. Other trees known as cedars are the *white cedar*, *Cupressus thyoides* L.; the American white cedar, *Thuja occidentalis* Linn.; the Californian white cedar, *Libocedrus decurrens* Torr.; the New Zealand cedar, *Libocedrus Bidwillii* Hook. The Australian red cedar, *Cedrela Toona* Roxb., and the West India cedar, *Cedrela odorata* L., belong to an entirely different family, the *Meliaceæ* (*Cedrelaceæ*). The wood of the latter species is used in making cigar boxes, and, according to Schimmel, yields 3 per cent. of a volatile oil, which has a specific gravity of 0.915, boils between 265° and 270° C. (509°–518° F.), and has an optical rotation of 0.053° in a 100 mm. tube. It is said to be a powerful insecticide. (*P. J.*, Aug. 29, 1896, 179.)

Kairine. *Kairin*, G.—The hydrochloride of methyloxytetrahydroquinoline, ($C_{10}H_{13}ON.HCl + H_2O$), is the commercial kairine (kairine M). Quinoline is treated with sulphuric acid, forming quinoline-sulphonic acid, which, fused with caustic soda, yields oxyquinoline, which is then reduced with tin and hydrochloric acid, forming tetrahydroxyquinoline, and this, on treatment with methyl bromide, yields methyltetrahydroxyquinoline or kairine. *Kairine A* is the corresponding ethyl compound, and has similar properties. Kairine, as brought into commerce, is readily soluble in water and alcohol, and forms a grayish-white crystalline powder, with bitter, salty taste. Ferric chloride produces a dark brown color, which upon the addition of sulphuric acid turns purple.

Kairine belongs to the antipyretic remedies, and is without doubt capable of producing pronounced fall of temperature in *fever*, accompanied by copious sweating. It is, however, a cardiac depressant, which is said to act directly upon the cardiac muscles, and is very prone to produce cyanosis and collapse. The reports have been so unfavorable that, in the absence of advantage over antipyrine and antifebrine, kairine is no longer used in practical medicine. *Dose*, five to ten grains (0.32–0.65 Gm.).

Kairoline, M. or A. *Tetrahydromethylquinoline*, or *Tetrahydroethylquinoline*.—These bases differ from kairine in not containing oxygen. Their characters are similar. The sulphates are the commercial salts. For physiological action, see *Ber. d. Chem. Ges.*, xvi, 739.

Kalagua.—A study of this South American plant, which has been put upon the market as a specific for *tuberculosis*, made upon the lower animals by D. H. Bergey, shows that it has no specific influence upon the tubercle bacillus.

Kalmia. *Kalmia latifolia* L. *Laurel. Mountain Laurel. Broad-leafed Laurel. Calico-bush. Spoonwood. Kalmie*, Fr., G.—This well-known ericaceous evergreen shrub is found from New Brunswick to Florida and from Ohio to Louisiana, being especially abundant on the sides of hills and mountains. It is from 1 to 4 m. in height. The leaves, which are supposed to be possessed of poisonous, narcotic properties, have been found by Charles Bullock to contain gum, tannic acid, resin, chlorophyll, fatty matter, a substance resembling mannite, an acrid principle, wax, extractive, albumen, yellow coloring matter, lignin, and salts of potassium, calcium, and iron. (*A. J. P.*, xx, 264.) George W. Kennedy detected the glucoside arbutin in them. (*A. J. P.*, xlvii, 5.) Bourquelot and Fiehtenholz stated that the glucoside that they obtained from the leaves of *K. latifolia* is identical with the *asebotin* that Eykmann found in *Andromeda japonica;* both yield a red color with ferric chloride. The leaves are popularly believed to be poisonous to sheep and other small animals, but are said to be eaten with impunity by deer, goats, and grouse. It is also affirmed that severe and fatal poisoning has been produced by eating grouse that have fed upon these leaves. (See 16th ed., *U. S. D.*) Crawford (*Bulletin 121, Bureau of Plant Industry*, U. S. Dept. of Agriculture), in experimental investigations, found that laurel caused, either when fed to, or injected into, the lower animals, great salivation, lachrymation and emesis, convulsions, and later paralysis of the extremities, with greatly labored respiration. It is probable, although not proven, that the poisonous principle of this plant is *andromedotoxin*. (See page 1248.) The leaves have been used internally in *diarrhea* and in *syphilis*, and externally in skin diseases. (See 16th ed., *U. S. D.*)

It is probable that other species of *kalmia*, as *K. angustifolia* L., or *sheep-laurel*, and *K. glauca* Ait., or *swamp-laurel*, have properties identical with those of *K. latifolia*. A decoction of the leaves of *K. angustifolia* is used by the negroes as a wash for ulcerations between the toes.

Kamala. *U. S.* 1890. *Kamala. Glandulæ Rottleræ.*—The U. S. Pharmacopœia, under the name of *Rottlera*, U. S., 1870, *Kameela*, formerly recognized the glands and hairs from the capsules of *Mallotus philippinensis* (Lamarck) Muell.-Arg. (Fam. *Euphorbiaceæ*.) This tree grows in Abyssinia, Southern Arabia, Hindostan, the East India Islands, China, and Australia, reaching a height of from fifteen to twenty feet, and yielding a roundish, three-valved, three-locular capsule about the size of a small cherry, thickly covered with a

red powder, which is collected in Hindostan by rolling the berries about in large baskets until the freed powder sifts through the open wicker-work.

Kamala, as brought to our market, is a light, finely granular, very mobile powder, of a brownish-red or madder color, with little odor or taste, but producing a slight sense of acridity in the mouth, and feeling gritty under the teeth. (When the grittiness is excessive, the drug has probably been adulterated with earthy matters.) It is inflammable, and flashes almost like gunpowder when dropped into the flame of a candle. It is insoluble in cold and but very slightly soluble in boiling water; but alkaline solutions, alcohol, and ether dissolve a large proportion of it, forming a deep red solution, from which water precipitates resinous matter, "imparting a deep red color to alkaline liquids, alcohol, ether, or chloroform, and a pale yellow tinge to boiling water." *U. S.*, 1890. Under the microscope it consists of garnet-red, semi-transparent, roundish, glandular hairs from 0.040 to 0.100 mm. in diameter, and containing numerous red, club-shaped cells and admixed with minute stellate hairs, and the remains of stalks and leaves, the latter of which are easily removed by careful sifting. It has been examined chemically by Thomas Anderson, of Glasgow, and by G. Leube, in Germany. As given by the former, the constituents are, in 100 parts, 78.19 of resinous coloring matter, 7.34 of albumin, 7.14 of cellulose, etc., a trace of volatile oil and volatile coloring matters, 3.84 of ashes, and 3.49 of water. The amount of earthy impurities, chiefly sand, in commercial kamala, varies greatly, sometimes amounting to fifty or even sixty per cent. It can readily be estimated by heating the drug to redness and weighing the residue. The U. S. P., 1890, permitted the presence of "not more than 8 per cent. of ash." Any specimen of kamala containing more than the official percentage of impurity should be rejected. Rusby states that kamala often comes to this country adulterated. He found one shipment loaded with sand, one with olive stems, one olive stems and sand, and one ground bark. Two samples, 40.8 per cent. acid, 43.4 per cent. ash, were mostly sand. (See also *Ph. Rev.*, 1907, 129; *P. J.*, 1906, 258.) Of the resinous coloring substances, Anderson obtained one in a pure state by allowing a concentrated ethereal solution to stand for two days, draining and pressing in bibulous paper the resulting mass of granular crystals, and purifying them from adhering resin by repeated solution in ether and recrystallization. To this substance he gave the name of *rottlerin*. It is in the form of minute crystalline plates, of a yellow color and a satin-like luster, insoluble in water, sparingly soluble in cold but more so in boiling alcohol, and readily dissolved by ether, and by alkaline solutions, which assume a dark red color. Perkin (*Chem. Soc. Trans.*, lxiii, p. 975) shows rottlerin to consist of six distinct substances, *i.e.*, rottlerin, isorottlerin, wax, two resins and a coloring substance. The pure rottlerin has the chemical composition $C_{33}H_{30}O_9$. (See also *P. Ztg.*, 1906.) Crude rottlerin, sometimes known as *kamalin*, melts when heated moderately, and at a higher heat is decomposed, giving off pungent vapors. A. and W. Perkin (*Ber. d. Chem. Ges.*, xix, 3109) and Jawein (*Ibid.*, xx, 182) both stated that rottlerin can be extracted from kamala by the action of carbon disulphide. Jawein gave its fusing point as 200° C. (392° F.), and said that it was easily soluble in hot alcohol and acetic acid. In a later communication, A. G. Perkin (*P. J.*, 1893, 159, 236), stated that when he extracted it with ether, kamala yielded a dark brownish resinous product from which six distinct substances can be isolated; *rottlerin*, *iso-rottlerin*, a wax, and two resins, one of high and one of low melting point, form the principal constituents. There is also present a trace of a yellow crystalline coloring matter melting at from 192°–193° C. (377.6° 379.4° F.). Perkin also found in kamala a small quantity of a sugar soluble in water. Potassium permanganate oxidizes it to oxalic and benzoic acids; nitric acid of 1.5 sp. gr., on the other hand, oxidizes it to oxalic acid, ortho- and para-nitrocinnamic acids, and para-nitrobenzoic acid. The ashes were in the extraordinary proportion of 25.85 per cent., and of the ashes 83.8 per cent. consisted of insoluble silica. Silica probably enters essentially into the constitution of the minute granules, and its presence accounts for their grittiness under the teeth. The active constituent is supposed to be the resin.

Kamala is actively or even violently purgative in full doses, occasionally causing nausea, but seldom vomiting. Kamala has long been used in India against the *tape worm*, and was first made generally known by C. Mackinnon. (*Ind. Ann. Méd. Sci.*, 1854.) Semper (*A. E. P. P.*, 1910, lxiii, p. 10) has found that kamala has a paralyzing effect on motor nerves and muscles, to which action he believes it owes its tenifuge powers. It is given, without previous preparation of the patient, in the *dose* of from one to three drachms (3.9–11.6 Gm.), suspended in water, mucilage, or syrup. In the latter dose it sometimes acts violently. The worm is usually expelled at the third or fourth stool. If the first dose fails to operate on the bowels, it may be repeated in four hours, or followed by a dose of castor oil. The tincture (four ounces to eight fluidounces of diluted alcohol) is also said to be efficient in *doses* of from one to four fluidrachms (3.75–15 mils). As an external remedy, kamala is used by the people of India in various affections of the skin, particularly *scabies*. William Moore, of Dublin, has employed it successfully in *herpetic ringworm*. (*Dublin Hosp. Gaz.*, Nov. 15, 1857.) A tenifuge composed of kamala and koussin and known as *kamakosin*, is in use on the continent.

Kandol. *Canadol.*—This is a light fraction of petroleum of great volatility, which is said to afford a very cheap and efficient means of rapidly freezing the skin and subdermal tissues.

Kefaldol.—This seems to be a chemical compound of somewhat uncertain composition, which results from the interaction between phenetidin, quinine, citric acid and salicylic acid. It occurs as a yellowish powder with a slightly bitter taste, almost insoluble in water, but dissolved easily in alcohol. It has been used as an antipyretic and anti-rheumatic by Lill (*Med. Klin.*, 1910) and others. The *dose* is from eight to fifteen grains (0.5 to 1 Gm.).

Kefir. *Kephyr. N. N. R.* 1917. (See also *Lactic Acid Therapy.*)—From time immemorial the Tartars and the Balkan peoples have employed as a food and beverage one or another form of fermented milk. The Tartars prepared from mare's milk a drink known as *koumiss* or *kumys*. This is prepared by the action of a peculiar ferment known as *kephir* (*kepir*) and called also by the Mohammedans "*the prophet's millet.*" In Western Europe, mare's milk not being available, an imitation of kumys has been made from cow's milk, to

which the term "*kephir milk*" should be applied, limiting the word kumys to the genuine Tartar drink. The Armenians employed a fermented milk, *madzonn* or *matzoon*. *Giaourdi* is a fermented milk prepared in Greece from sheep and goat's milk with an enzyme obtained from fermented figs. The Bulgarians use a fermented milk known as *yoghourt* (*yaowite*). The Arabians have a fermented milk called *leben*.

The *kefir grains* (or seeds) are white, irregular, roundish bodies about the size of a walnut with a rough, ferruled surface, of gelatinous or, when dried, cartilaginous consistency. Despite considerable investigation, their composition is not yet definitely settled. They probably contain several micro-organisms as follows: (1) a yeast fungus which Spivak (*N. Y. M. J.*, 1896) believes identical with the ordinary yeast, *Saccharomyces cerevisiæ*, but which Beyerinck believes to be a distinct species, *S. Kefir*, (2) *Bacillus Dispora Caucasica* (Kern) or *Bacillus Kephir* (Sorokin), (3) *Bacillus acidi lactici*, (4) other bacteria which are probably of little importance to the process of fermentation.

There are a number of directions for preparing kephir milk, varying more or less in the details. The following is a simple one: About 120 grains of kephir grains are softened by soaking over night in a pint bottle full of water. The following morning the water is poured off and the bottle is three-quarters filled with unboiled milk and tightly stoppered. This is kept at a temperature of 20° C. (68° F.) for from one to three days. The milk is strained through cheese cloth immediately before use and the residue recovered may be used for fermenting other milk. For various other processes see Kobert (*Zeitsch. f. Krankenpflege*, 1904, p. 377; *Ph. Ztg.*, 1904, 819 and 1912, 277), Drasler (*Med. Klin.*, 1908), and Spivak (*N. Y. M. J.*, 1896). According to Spivak, the changes in milk during kephirization are as follows: 1. Fat, salts, and water remain unchanged. 2. The quantity of lactose is gradually lessened from 30–50 per mille to 16–30 per mille in the second-day kephir, and to 12–20 per mille in the third-day kephir. 3. Lactic acid is increased from 3.5–8.6 per mille in second-day kephir to 6.3–9.0 in third-day kephir. 4. Alcohol is produced from 5.3–8.0 mille in second-day kephir to 6.0–10.0 in third-day kephir. 5. Carbon dioxide is generated in quantities approximately 10 per cent. 6. A part of the casein—namely, about 10 per cent.—is transformed into acid albumin and peptone, 10 per cent. into hemialbumose, and the rest loses its lime, and therefore becomes more easily digestible.

There is largely sold, under the name of kumys, a spurious drink which is made by fermenting sweetened milk with ordinary yeast. It is a pleasant beverage, but differs in important regards from the true kephir milk. The following formula has been suggested by L. Wolff (*A. J. P.*, 1880, 291): "Grape sugar, half an ounce. Dissolve it in four ounces of water. Dissolve twenty grains of compressed yeast, or well-washed and pressed out brewer's yeast, in two ounces of milk. Mix the two solutions in a quart champagne bottle, which is to be filled with good cow's milk to within two inches of the top. Cork well, secure the cork with wire, and place in a cellar or ice chest, where a temperature of 10° C. (50° F.) or less can be maintained, and agitate three times a day. In three or four days the koumys is ready for use, and should not be kept longer than four or five days; it should be drawn only with a champagne tap." A beer bottle with patent stopper may be substituted for the champagne bottle.

The composition of true koumys, according to Stalberg, is given below; other analyses may be found in the *J. P. C.*, 1875, 62. *Koumys of June.* In 100 parts, alcohol 1.65, fat 2.05, sugar of milk 2.20, lactic acid 1.15, casein 1.12, salts 0.28, carbonic acid 0.75. *Koumys of September.* Carbonic acid 1.86, alcohol 3.23, fat 1.05, lactic acid 2.92, casein and salts 1.21. Stalbërg gives the following as the result of an analysis of Swiss koumys, made from cow's skimmed milk to which sugar had been added. Alcohol 3.622, lactic acid 0.256, sugar 2.376, albumin 2.099, butter 2.008, mineral salts 0.574, carbonic acid 1.997. Warnikiewicz found in koumys from cow's milk 6.32 per cent. of solid material, casein 3.08, butter 0.22, milk sugar 1.77, salts 0.33, lactic acid 0.62, alcohol 1.23 parts per hundred. (See also König's *Nahrungs- und Genussmittel*, 416–419.)

These fermented milks vary in composition with the milk they are prepared from. In the following analyses, the first three columns are taken from *A. J. P.*, 1887; the matzoon analysis is by Uffelmann.

	Cow's Milk	Koumys	Kephir	Matzoon
Albumin	48	11.2	38	31.2
Butter	38	20.5	20	16.0
Sugar of milk	41	22.0	20	16.2
Lactic acid	..	11.5	9	8.3
Alcohol	..	16.5	8	2.1
Water and salts ..	873	918.3	905	926.2

Gordon Sharp (*P. J.*, 1892, 512) stated that the composition of koumys is complex, and that the decomposition which its proteids undergo is closely allied to putrefaction.

Kephir milk is useful either as an accessory or sole food in various conditions of mal-nutrition. Not only does it offer the nutritive elements of milk in a partially digested form, but it is claimed that the living ferments which are contained in it have an influence in aiding digestion in the alimentary canal, and that it also stimulates the appetite. It first came into Europe as a remedy in *pulmonary tuberculosis*, but has also been recommended in various forms of *dyspepsia*, whether functional or organic, in *anemia* and *chlorosis*, in *rachitis*, *chronic rheumatism*, and other conditions of impaired nutrition. It has also been employed as an infants' food with asserted remarkable results. Its value in *phthisis* has been extraordinarily lauded by Uroganski. (*Wiener Med. Wochens.*, 1907.)

Keratin.—The outer skin surface, the material of horns, hoofs, tortoise shell, the finger nails, all show a similar chemical composition, the empirical formula of which is said to be $C_{41}H_{71}N_{12}SO_{14}$. The percentage of sulphur varies, however, considerably.

Gissmann boils the quills of feathers in glacial acetic acid for from twenty-four to thirty-six hours in a retort furnished with a return condenser. A thick yellow-brown liquid is thus obtained, which is filtered through glass wool, evaporated on a water bath to the consistence of an extract, and afterwards dried. Dietrich recommends that before the treatment with acetic acid the feathers be digested in water for ten hours and then for eight days macerated in a mixture

of equal weights of ether and alcohol, to eliminate fatty matters and cholesterin. The *keratin* obtained by the foregoing process is dissolved with the aid of a gentle heat either in acetic acid or ammonia, and the solution is allowed to clear by standing. Fischer recommends the employment of seven part of keratin with either one hundred parts of acetic acid, or a mixture of equal parts of ammonia and diluted alcohol.

According to Unna and Golodetz (*Monatshefte f. prakt. Dermatol.*, 1907, p. 109), when a horny material is treated with nitric acid, three sorts of keratin may be distinguished. Keratin A, not digested by either pepsin or hydrochloric acid, does not give xanthoproteic reaction, keratin B, not digested by pepsin nor hydrochloric acid but dissolved by nitric acid, gives a xanthoproteic reaction; keratin C, not affected by digestive mixture nor dissolved by nitric acid, gives the xanthoproteic reaction. The various horny substances may contain any one or two or these forms.

Keratin is insoluble in water, alcohol, ether, and diluted acetic acid, or acidulated pepsin solution. Diluted sulphuric acid on boiling changes it into leucin, tyrosin, and other products. It is soluble in concentrated acetic acid, alkalies, and ammonia.

Keratin is used sometimes for the purpose of coating pills, so as to enable them to pass through the acid juices of the stomach unchanged, and be dissolved in the alkaline intestinal fluids. While it has been suggested to protect in this manner the stomach against the effects of irritant drugs, the method is much more frequently used to protect drugs, such as the alkalies, bile, calcium sulphide, pancreatin, tannin, etc., whose activity would be injured by the gastric secretions.

For the preparation of a solution of keratin suitable for the coating of pills several formulas have been proposed in all of which either acetic acid or ammonia is used as a solvent. The acetic solution is suitable for coating pills containing salts of mercury, gold, or iron, arsenic, creosote, salicylic acid, tannin, alum, etc. On the other hand, an ammoniacal solution is preferred for pills containing pancreatin, trypsin, bile, alkalies, iron sulphide, etc. The pill mass must not contain water, for pills will shrink and fissures be produced in the keratin coating. It is, therefore, recommended to use in the making of such pills a mixture of yellow wax, one part, and suet or cacao butter ten parts. It is also necessary to avoid the use of vegetable powders as fillers and to employ in their place kaolin or charcoal powder.

When the pills are ready for coating they should first be dipped in cacao butter and rolled in charcoal powder. To coat with keratin, the pills, placed in a porcelain capsule, are moistened with a suitable quantity of keratin solution and then agitated in the presence of a current of air until the evaporation of the solvent takes place. This moistening and drying require to be repeated many times (sometimes ten) before the layer of keratin is sufficiently thick. The process employed for coating pills with gelatin, which consists in dipping into the solution the pill fixed on the point of a needle, is not suitable here, for it leaves a hole through the keratin coating that can never be completely closed.

In order to insure that the keratin used is insoluble in the stomach, Unna recommends that a preliminary experiment should be made with calcium sulphide pills coated with it. If in the course of some hours after such pills are taken eructations of hydrogen sulphide are observed, it would indicate that the pills have been dissolved in the stomach. When the keratin is of good quality nothing of the kind should occur. Finally, the pills when placed in water should not liquefy or crack. This method of producing what are commonly called *enteric pills* has been largely replaced by the simpler one of hardening a gelatin capsule or gelatin-coated pill by means of formaldehyde solution or vapor, or by coating with salol which gives the same result as regards insolubility in the stomach, but ease of solubility in the intestinal tract. (See *Glutoid*, p. 1411.)

Zypkin (*W. K. W.*, 1907, p. 727) believes that keratin has the property of inhibiting the growth of connective tissue and has used it with asserted benefit in the treatment of various sclerotic diseases, such as *locomotor ataxia* and *cirrhosis of the liver*. He gives from sixty to two hundred and forty grains (3.9–15.5 Gm.) by the mouth, or injects subcutaneously a solution containing 2 Gm. of keratin with 0.1 Gm. of sodium bicarbonate and 10 mils of water.

Kinkeliba. *Combretum album.* (Fam. *Combretaceæ.*)—This is the leaf growing in Western Africa which is affirmed to be of great value in the treatment of bilious *hematuric malarial fevers*. Heckel and Schlagdenhauffen found in the leaves nothing more active than tannin and potassium nitrate. (See Perrot and Lefevre, *Travaux du Laboratoire de Mat. Méd.*, p. 67.)

Kola. *N. F. IV. Cola. Kola Nuts. Semen (Nuces) Colæ. Noix de Cola, Noix de Gourou, Café du Soudan*, Fr. *Kolanuss*, G.—It is described by the N. F. as "the dried cotyledons of several species of *Cola* Schott and Endlicher (Fam. *Sterculiaceæ*), yielding not less than 1.5 per cent. of caffeine." *N. F.* The official drug is obtained chiefly from the large African tree *Cola Acuminata* R. Br., which is extensively cultivated in various portions of the tropical world for its seeds. The latter, under their Guinea name, or the Soudan name of *guru nuts*, are extensively employed as a caffeinic stimulant in Africa and other portions of the world. Six hundred tons of them are said to be sent yearly to Brazil for the use of the negroes, who, it is affirmed, also employ the seeds of *Sterculia Chica* A. St.-Hill. and *S. striata* A. St.-Hill. Three varieties of *kola nuts* are said to be the product of *Cola acuminata*. The most valuable, the kola of Sakhala, is the largest, and is of a white color. The kola of Kassi, of Siarra, and of Touté, is of medium size, red or white. The kola of Maninian is small and red. Of this white kola there are two varieties, one whitish, resembling the kola of Sakhala but smaller; the other more or less rose-colored and larger. The kola nut itself consists of the cotyledons which are "irregularly plano-convex, broadly oval, or approaching circular in outline, from 2.5 to 5 cm. in length, or triquetrous; heavy, hard and tough; brown with the outer surfaces slightly wrinkled, the inner surfaces lighter and smoother; edges slightly incurved and sharp. Odorless; taste slightly astringent. The powdered drug is reddish-brown and, when examined under the microscope, exhibits numerous starch grains, some of which show alteration, the normal grains up to 0.045 mm. in diameter, the smaller ellipsoidal or spherical, the larger ellipsoidal or irregularly oblong and occasionally with a protuberance on one side; many of the larger grains show lamellæ and a circular point of origin of growth or a fissure through the center,

and a distinct cross when examined with the polarizing microscope; parenchyma cells numerous, about 0.065 mm. in diameter, with reddish-brown walls."

Assay.—"Introduce 6 Gm. of Kola, in No. 60 powder, into a flask and add 120 mils of chloroform and 6 mils of ammonia water. Stopper the flask, shake it frequently for half an hour, then let it stand four hours. Again shake the flask vigorously and, when the drug has settled, filter the liquid rapidly through a pledget of purified cotton and collect 100 mils of the filtrate, representing 5 Gm. of Kola. Evaporate the clear filtrate to dryness and dissolve the residue in 5 mils of weak sulphuric acid with the aid of a gentle heat. When the liquid has cooled, filter it into a separator and wash the container and filter with several small portions of distilled water. Now add ammonia water until the liquid is distinctly alkaline to litmus and shake out the alkaloid with successive portions of chloroform until completely extracted, as shown by testing with iodine T.S. Evaporate the united chloroform solutions and dry the residue to constant weight at 80° C. (176° F.). The weight is the amount of caffeine from 5 Gm. of Kola. Kola yields not more than 3 per cent. of ash." *N. F.*

Daniell (*P. J.*, 1865) was the first to show that kola nuts contained caffeine. Subsequently an elaborate analysis yielded to Attfield 2⅓ per cent. of caffeine from the nut. Schuchardt summarizes the results of his chemical analyses as follows: 1, Martinique nuts contained 1.06 per cent. caffeine; 2, Ceylon, 1.39 per cent.; 3, Gaboon, 1.47 per cent.; 4, Tropical West African coast, Sierra Leone, 1.69 per cent.; 5, Tropical West Africa, interior, 1.61 per cent. The chemical studies of Parke, Davis & Co. show that as found in American commerce these nuts contain from 0.72 to 2.02 per cent. of caffeine. Heckel and Schlagdenhauffen (*A. J. P.*, 1884) give theobromine 0.023 per cent., caffeine 2.35 per cent., tannin 1.62 per cent., as the result of their analyses. The researches of Knebel (*A. J. P.*, 1892, 190), confirmed by Hilger (*Ibid.*, 568), show that fresh kola nuts probably contain no caffeine, but a glucoside, *kolanin*, which yields by its decomposition caffeine, glucose, and *kola-red* ($C_{14}H_{13}(OH)_5$). Betaine is also stated to be present. The glucoside is decomposed by a ferment present in the nuts, and therefore readily yields the caffeine as a decomposition product. Schweitzer (1895) confirmed the results of Knebel and Hilger, and proposed for kolanin the formula $C_{40}H_{56}N_4O_{21}$. Knox and Prescott (*Proc. A. Ph. A.*, 1896, 136), after an investigation, assert that the kola ferment does not assist in the liberation of caffeine, but attribute the presence of caffeine to the action of heat and moisture; they also give the name of *kolatannin* or *kolatannic acid* to the tannin of kola nuts, and propose a method of assay. (*Proc. A. Ph. A.*, 1897, 131.) For Carle's method of assay, see *P. J.*, 1896, 289. Goris (*P. J.*, 1906, lxxvi, p. 261) has separated from the kola nut a basic glucoside to which he gives the name of *kolatine*.

Travellers in Africa assert that the fresh kola nuts have a stimulant action which is not explicable on the ground of their caffeine content. But as they appear in European commerce their action is undistinguishable from that of the other caffeinic drugs. The experiments of Mosso (*A. I. B.*, xix) seem to demonstrate conclusively the inertness of kola-red.

Kola is about equivalent to guarana, tea, coffee, etc., and may be substituted for them. In *dose* of one hundred and fifty grains (9.8 Gm.) a day, A. Hudson (*T. G.*, ii) has found the nuts to act decisively in cardiac weakness.

The so-called *male kola* is essentially distinct from kola, being said to be the fruit of a small tree, *Garcinia Kola* (fam. *Guttiferæ* Heck.), and containing no caffeine. The fruit is oblong, about one and a half to three inches long and from three-quarters to one inch broad; it is trigonal in section, with a readily removable thin testa of a reddish-yellow to dark brown color, covered by markings which resemble those on the seed coat of the nutmeg. It is bitter and astringent. In the section the microscope reveals a number of resinous masses surrounded by cells rich in starch.

The seeds of *Lucuma mammosa* Griesbach (Fam. *Sapotaceæ*), sometimes mixed with kola nuts, are recognized at once by their strong odor of prussic acid. Heckel and Schlagdenhauffen have observed the seeds of *Heritiera litoralis* Dryand (fam. *Sterculiaceæ*) mixed with kola nuts. These *false kola nuts* contain no caffeine, and are nearly orbicular and flattened in shape, one of the fleshy, purplish-brown cotyledons being only half the size of the other. (*A. J. P.*, 1887, 446.)

Kosam Seeds. *Fructus Bruceæ*, Pharm. Nederland.—The seeds of the *Brucea sumatrana* Roxb. (Fam. *Simarubaceæ*) indigenous in China and Southern Asia. Schlagdenhauffen found in them saponin, and Physalis and Bertrand a glucoside, *kosamin*. They are asserted to be useful in *menorrhagia*, also in *dysentery* and *diarrhea*. (*P. J.*, lxiv, p. 463.) According to Power and Salway (*Year-book of Pharmacy*, 1907), the *B. antidysenterica* has similar properties and is largely used in Abyssinia.

Kossala.—An Abyssinian remedy against *tape worm*. (*Proc. A. Ph. A.*, xxvi.) It is said, however, to produce gastric irritation.

Kreosal. *Tannosal. Creosol.*—The tannic acid ester of creosote. This is a brown amorphous powder soluble in water, glycerin and alcohol, and containing 60 per cent. creosote. It passes through the gastric juice undecomposed but in the alkaline intestinal secretion it is split up into its components and acts as an antiseptic astringent of especial value in the treatment of *phthisical diarrhea*. *Dose*, fifteen to sixty grains (1–4 Gm.) daily.

Kryofine. *Cryofine. Methoxyacet-p-phenetidin. Methyl-glycollic Phenetidin.*

$$C_6H_4 \begin{cases} OC_2H_5 \\ NH.COCH_2OCH_3. \end{cases}$$

This phenetidin derivative or condensation product is made by heating paraphenetidin and methylacetic acid together; the acid replaces the acetic acid in the phenetidin derivative and is thus closely allied to acetphenetidin or phenacetin. *Kryofine* crystallizes from aqueous solutions in needles, with a melting point of from 98°–99° C. (208.4°–210.2° F.). These crystals are white, and in moderate doses tasteless. In doses exceeding fifteen grains (1.0 Gm.), they cause, after a few moments, the sensation of chewing willow bark. Kryofine is soluble in boiling water 1 in 52, in cold water 1 in 600, soluble also in alcohol, ether, chloroform, and the oils. The physiological action of kryofine has not been worked out, but in a medium-sized dog two hundred and one grains caused general paralysis and extreme slowing of respiration and pulse, ending fatally. Seventy-five grains (5 Gm.) given to man have produced no

more serious effect than cyanosis with some lessened frequency of respiration. Kryofine can be detected in the urine from fifteen to twenty minutes after taking, disappearing in from six to eight hours. (Ebstein.) In doses of from two and one-half to twenty-five grains it has been strongly commended by Ebstein, Eichhorst, Haas, Morrison, and other clinicians as an analgesic for *pains* of purely nervous origin and antipyretic in various *fevers*, as less dangerous, though acting more slowly, than other allied drugs.

The range of action of kryofine appears to be that of acetphenetidin. The assertion that it is less dangerous than that drug seems hardly to be sustained by the facts; depression and cyanosis have been produced by it in various cases. The usual *dose* is eight to fifteen grains (0.5–1 Gm.). In the feeble, great caution is necessary in its employment.

Kryogenin. *Meta-benzamino-semicarbazide.* $C_6H_4(CO.NH_2)(NH.NH.CO.NH_2)$.—This is a colorless, odorless, slightly bitter powder, soluble in forty parts of water. It is asserted by Lumiere (*Ph. Post*, 1903, 7) to be an antipyretic of value, especially used in *tuberculosis*, producing, it is said, a rapid fall of temperature without unpleasant symptoms. *Dose*, ten to twenty grains (0.6–1.2 Gm.) in capsules.

Labdanum. *Ladanum.*—A resinous substance, obtained from various species of *Cistus* (Fam. *Cistaceæ*), especially *C. creticus* L., *C. ladaniferus* L., *C. cyprius* Lam., and *C. laurifolius* L., small evergreen shrubs, inhabiting the islands of the Grecian Archipelago, and the different countries bordering on the Mediterranean. Upon the leaves and branches of these shrubs a juice exudes, which is collected by means of an instrument resembling a rake, with leather thongs instead of teeth, which is drawn over the plant. The juice adheres to the pieces of leather, and is afterwards separated. It is said that *labdanum* was formerly collected by combing the beards of goats which had been browsing upon the leaves of the cistus, and Landerer states that it is still gathered in Cyprus from sheep and goats whose fleeces become loaded with it while they are pasturing. (See *P. J.*, xi, 6; xv, 301; xvi, 386, 779.) It comes chiefly from the Grecian Islands. Two varieties exist in commerce. The purest labdanum is in masses of various sizes, sometimes weighing several pounds, enclosed in bladders, dark red, almost black externally, grayish internally when first broken, of the consistence of a plaster, softening in the hand and becoming adhesive, of an agreeable balsamic odor like that of amber, and of a bitter, balsamic, somewhat acrid taste. It is very inflammable, burning with a clear flame. On exposure it becomes dry, porous, and brittle. Little of this variety is found in the markets. Common labdanum is in contorted or spiral pieces, light, porous, blackish-gray, hard and brittle, not softening between the fingers, similar in odor and taste to the preceding variety, but less inflammable, and mixed with sand and other earthy matters, which are obvious to the sight. A specimen exhibited at the International Exhibition of 1862, at London, was in flattish pieces, an inch or more thick, with remains of leaves on one side, of a very dark greenish-brown color, and a granular, somewhat shining fracture. Guibourt found in 100 parts of the labdanum in masses, 86 parts of resin with a little volatile oil, 7 of wax, 1 of aqueous extract, and 6 of earthy substances and hair. In the contorted variety, Pelletier found 20 per cent. of resin, 3.6 of gum with calcium malate, 0.6 of malic acid, 1.9 of wax, 1.9 of volatile oil, including loss, and 72 of a ferruginous sand. Schimmel & Co. (*Schim. Rep.*, April, 1893) state that they obtained from labdanum resin 0.91 per cent. of a golden-colored essential oil having the penetrating odor of ambergris. Its sp. gr. is 1.011 at 15° C. (59° F.). Labdanum is a stimulant expectorant, formerly given in catarrh and dysentery and sometimes used in plasters.

Lac. *Lacca. Resina* (*Gummi*) *Lacca. Laque, Gomme lacque*, Fr. *Lack, Gummilack*, G.—A resinous substance obtained from several trees growing in the East Indies, particularly from *Croton laccifera* L. (Fam. *Euphorbiaceæ*); several species of *Ficus*, especially *F. religiosa* L. and *F. indica* L. (Fam. *Artocarpaceæ*), and, according to Valentine Ball, *Schleichera trijuga* Willd. (Fam. *Sapindaceæ*), *Butea frondosa* Roxb., of the Fam. *Leguminosæ*, and *Zizyphus jujuba* Lam. (Fam. *Rhamnaceæ*). Stillman states that *Acacia Greggii* A. Gray (Fam. *Leguminosæ*) and *Covillea tridentata* (DC.) Vail. (*Larrea mexicana* Moric.) (Fam. *Zygophyllaceæ*), plants growing in Arizona, Colorado, and the Western territories, furnish both *shellac* and *lac dye*. (*A. J. P.*, 1880, 409.) *Lac* is found in the form of a crust, surrounding the twigs or extreme branches, and is generally supposed to be an exudation from the bark, owing to the puncture of an insect belonging to the genus *Coccus*, and denominated *C. lacca*. By some it is thought to be an exudation from the bodies of the insects themselves, which collect in great numbers upon the twigs, and are embedded in the concreted juice, through which the young insects eat a passage and escape. Several varieties are known in commerce. The most common are *stick-lac*, *seed-lac*, and *shellac*.

Stick-lac is the resin as taken from the tree, still encrusting the small twigs around which it originally concreted. It is of a deep reddish-brown color, of a shining fracture, translucent at the edges, inodorous, and of an astringent, slightly bitterish taste. Its external surface is perforated with numerous minute pores, as if made by a needle, and when broken it exhibits many oblong cells, often containing the dead insect. When chewed it colors the saliva red, and when burnt, diffuses a strong, agreeable odor. It is in great measure soluble in alcohol.

Seed-lac consists of minute irregular fragments, broken from the twigs and partially exhausted by water. It is of a light or dark brown color, inclining to red or yellow, feebly shining, almost tasteless and capable of imparting to water less color than the stick-lac, sometimes scarcely coloring it at all. It is occasionally mixed with small fragments of the twigs.

Shellac is prepared by melting the *stick-lac* or *seed-lac*, previously deprived of its soluble coloring matter, straining it, and pouring it upon a flat smooth surface to harden, or pulling it out by hand into large thin sheets, which are broken up after cooling.

A variety of lac is mentioned by writers, in the form of cakes, called *cake-lac* or *lump-lac* (*lacca in placentis*); but this is at present rare in commerce.

According to John, lac consists of resin, coloring matter, a peculiar principle insoluble in alcohol, ether, or water, called *laccin*, a little wax, and various saline matters in small proportion.

The resin, according to Unverdorben, consists of several distinct resinous principles differing in their solubility in alcohol and ether. The laccin is nearly or quite wanting in shellac, which also contains scarcely any of the coloring principle. Hatchett found in stick-lac 68 per cent. of resin, and 10 of coloring matter; in seed-lac 88.5 per cent. of resin, and 2.5 of coloring matter; in shellac 90.9 per cent. of resin, and 0.5 of coloring matter. The other constituents, according to this chemist, are wax and gluten, besides foreign matters. R. E. Schmidt (*Ber. d. Chem. Ges.*, 1887, 1285–1303) has prepared the lac dye in a pure crystallized state. He gives it the formula $C_{16}H_{12}O_8$, and calls it *laccaic acid.* It was obtained crystallized from ethereal solution. Caustic alkalies dissolve it, giving a magenta color. Baryta water forms a violet lake. Laccaic acid shows some analogy to carminic acid, but the colors they give on wool and silk are different. Laccaic acid is decomposed on heating with concentrated hydrochloric acid to 180° C. (356° F.), as well as on fusing with caustic potash.

Japanese lac from *Rhus vernicifera* was examined by A. B. Stevens. (See *Proc. A. Ph. A.*, 1905, 311.)

The importations of gum shellac for the year 1914 was 16,824,130 lbs., valued at $2,686,480; and for 1915, 24,308,145 lbs., valued at $3,018,296.

Lac in its crude state is slightly astringent, and was formerly used in medicine, but at present it is not employed. Shellac is wholly inert. It is sometimes used in alcoholic solution as a glaze for confectionery. The use of such insoluble resinous glaze for a food product is prohibited in some states partly on account of its indigestibility *per se* and partly because in its preparation for varnish or pigment purposes arsenical compounds are used to heighten the color and many instances are on record where confectionery which had been coated with such glaze contained appreciable amounts of arsenic. A bleached form of arsenic-free lac has recently appeared in commerce, which would seem to be free from many of the objections previously urged against lac in coating confectionery. Stick-lac and seed-lac are used on account of the coloring principle which they contain. Shellac, as well as the other varieties, deprived of their coloring matter, is applied to numerous purposes in the arts. It is the chief constituent of *sealing wax.* The best *red sealing wax* is made by melting together, with a very gentle heat, 48 parts of shellac, 19 of Venice turpentine, and 1 of balsam of Peru, and mixing with the melted mass 32 parts of finely powdered cinnabar. But common rosin is often substituted in part for the lac, and a mixture of red lead and chalk for the cinnabar. For methods of detecting adulteration with rosin see *J. Soc. Chem. Ind.*, 24, 1905; also *Chem. Ztg.*, 1910, 991. The best *black sealing wax* consists of 60 parts of lac, 10 of turpentine, and 30 of levigated bone black; the best *yellow sealing wax*, of 60 parts of lac, 12 of turpentine, and 24 of lead chromate. (Berzelius.) Lac is also used as a varnish, and forms an excellent cement for broken porcelain and earthenware. It may be dissolved in alcohol, oil of turpentine, benzin, or naphtha. For a method of preparing a colorless varnish from lac the reader is referred to *P. J.*, 1864, 338. Lac has been highly recommended as an adhesive material for the dressing of *wounds, ulcers*, etc. It is prepared for use by dissolving, with the aid of a gentle heat, in alcohol contained in a bottle, sufficient lac to give it a gelatinous consistence, and then closing the bottle. It is used by spreading it on the bandages. For details of the preparation of shellac, see *U. S. D.*, 19th ed., p. 1543.

Lactagol.—Under this name has been introduced an extract from cotton seed. It occurs as a yellowish-white powder, which emulsifies when rubbed up with water.

Lactagol has been used for the purpose of increasing both the quantity and quality of milk in nursing women. According to Barlerin (*R. T.*, 1906, p. 393), it causes a marked increase in the percentage of fat and also of casein. Abramof (*Cb. G. T.*, 1906, p. 548) noted an increase in the quantity of milk with no change in its composition. Contrary to these experiences, Bruhn (*Ther. Neu.*, June, 1908, p. 161) was unable to notice any decided effect upon the lacteal glands.

Lactanin. *Bismuth Dilactomonotannate.*—This is a yellow, odorless, tasteless powder, insoluble in water, which has been used in *doses* of three to five grains (0.2–0.32 Gm.) in *tubercular* and other *chronic diarrheas* of young children.

Lactic Acid Therapy.—Lactic-acid producing bacteria occur frequently in nature and are responsible for the ordinary souring of milk. Common *buttermilk* is, however, an uncertain product; it may contain many varieties of organisms, some producing lactic acid, and others giving rise to various by-products which may be useless, distasteful, or even injurious. Cultures of lactic-acid producing bacteria are therefore supplied, in liquid or in tablet form. The purpose of such therapy is to render the lower intestine acid, by the growth of these organisms and consequent fermentation; the putrefactive bacteria, which are thought to cause undesirable consequences through their waste products, are unable to thrive in such an acid environment, and are reduced in numbers or disappear.

The organism chiefly used in lactic acid preparations is the *Bacillus bulgaricus* of Metchnikoff, originally isolated from the mixture of bacteria found in the starter used by the Bulgarians to produce their fermented milk, *Yahourth* or *Yoghurt* (see *Kephir*). If the starter from the previous lot is lost the Bulgarians commonly use a piece of mucous membrane from the alimentary canal of a calf instead. The *Bulgarian bacillus* is a non-spore-bearing, Gram-positive, long rod which grows in the presence of oxygen and carbohydrates, and produces a large amount of lactic acid from milk. Organisms of this group will withstand without inhibition a higher hydrogen-ion concentration or true acidity than any other ordinary bacteria.

The original Bulgarian bacillus acts best at a high temperature, 45° C. (113° F.). It also is said to attack the casein and the fat of the milk to some extent, as well as the milk sugar, and if allowed to act to its full extent, produces an undesirably high acidity with coagulation. For these reasons other organisms are at times added to preparations intended for the artificial souring of milk. *Bacillus paralacticus* acts at ordinary temperatures and produces a more palatable beverage than the Bulgarian bacillus. Alcohol formed by the presence of yeasts in addition to the lactic-acid producing bacilli are present in *kephir* and *koumiss.*

Cultures of these organisms are also prepared to be taken directly, in liquid or in tablet form. While it is claimed that in this way an acid condition of the alimentary tract can be established

and the putrefactive organisms overgrown, it must be remembered that study of the digestion in large numbers of infants, where the experimental conditions can be exactly regulated, has shown that it is the character of the intestinal contents, as determined by the food, which influences the bacterial flora of those contents; mere ingestion of bacterial bodies without a change in diet can have little influence on the large mass of bacterial life which has adjusted itself nicely to the acid or alkaline reaction and the food-supply present in the intestines. The cultures of lactic acid organisms should therefore be used in connection with the food itself or simultaneously with a dietary change to effect the desired alteration and the elimination of the putrefactive bacteria.

On account of their antagonism to tissue-destroying bacteria, lactic-acid bacteria have been suggested and used as application to diseased surfaces and membranes of the body.

Cultures of lactic acid bacteria should be kept cold and used when fresh. Many inert products of this class have been placed on the market, but by shortening the date of expiration and improving the medium in which they are suspended, the manufacturers have largely succeeded in eliminating this defect. Cultures may be tested for activity and relative purity by inoculating sterilized milk and incubating at 37° C. (98.6° F.) for 24 to 72 hours to determine whether acid is produced without putrefactive odors or taste; strict aseptic precautions should be used throughout.

Lactoiod (*proiodine*) is a compound of iodine and casein, representing about 8 per cent. of iodine. It is a yellowish powder, insoluble in water or dilute acids, but dissolving in the presence of alkalies or sodium phosphate.

It is used as a means of exhibiting iodine and is claimed to be less likely to disturb the digestion than the ordinary forms of iodine. According to Stanieck (*Ther. Geg.*, 1909, p. 134), it contains about 5 per cent. of iodine and may be given in *doses* of one to two drachms (4–8 Gm.) three times a day.

Lactol (*lactonaphthol*) is the lactic acid ester of β-naphthol, $CH_3.CHOH.COOC_{10}H_7$. It forms colorless crystals insoluble in water, but soluble in alcohol; used, as an intestinal antiseptic. *Dose*, from five to eight grains (0.2–0.5 Gm.).

Lactophenin. *Lactyl-p-phenetidin. N. N. R.* 1917. $C_6H_4\begin{cases}OC_2H_5\\NH.CO.CH.(OH).CH_3\end{cases}$.—A white crystalline powder, without odor, having a feeble, bitter taste, soluble in one part in five hundred of cold water, one in eight and a half parts of alcohol, and having a melting point of from 117.5° to 118° C. (243.5°–244.4° F.). It is produced by the action of lactic acid on phenetidin in the presence of dehydrating substances, the lactic acid radical replacing the acetic acid radical of acetphenetidin.

We have very little definite knowledge in regard to the physiological action of lactophenin, but it is improbable that it differs materially in its effects from acetphenetidin. Some assert, however, that it has a somnifacient effect and it is also affirmed to be valuable in *rheumatism*, having specific curative properties inferior to but resembling those of the salicylates.

The statements which have been made that its use is free from danger are, however, not correct. It sometimes produces an exanthematous eruption, which may be macular or diffuse. Wenzel (*Cb. I. M.*, xvii, 1896) reports a case in which, after the patient had been taking, for two weeks, fourteen grains of lactophenin a day, there was suddenly developed violent jaundice, with dark brown urine, without fever or slowing of the pulse, with colorless stools. Similar cases had been previously recorded by Franz Rield (*Zeitsch. f. Heilk.*, xvi, 1895). Kronig (*B. K. W.*, 1895) has reported a case of poisoning, with methemoglobin and cyanosis, followed by death. Lactophenin is eliminated, at least in part, by the urine as a paramidophenol.

Lactophenin may be given in *doses* of from five to twenty grains (0.32–1.3 Gm.), repeated in special cases up to a drachm and a half (5.8 Gm.) in a day.

Lakes.—These colors are compounds of vegetable or animal coloring principles with alumina or other metallic oxides, and are usually obtained by adding alum or stannic chloride to the solution of the coloring matter in water, and precipitating by means of an alkali. The alumina or stannic oxide unites with the phenolic bodies in coloring matter at the moment of separation, and forms an insoluble compound, usually of a very bright color. *Lakes* are obtained in this way, from cochineal, madder, Brazil wood, seed-lac, French berries, etc.

Lamium. *Lamium album* L. *White Dead Nettle.* (Fam. *Labiatæ.*)—A perennial herb introduced from Europe and found on roadsides and waste places in the United States. Hemostyptic properties were long since attributed by Lusitanus and by Florain to the flowers of this plant, and, according to the more recent researches by Kalabin (*Cb. G. T.*, xx, No. 12), their decoction produces a rise of the arterial pressure due to contraction of the peripheral vessels. The extract was found to cause firm, lasting contraction of the uterus, and the saturated tincture, in *doses* of twenty-five to forty minims (1.6–2.5 mils) every two or three hours, to be useful in *hemorrhagic metritis* and *metrorrhagia.* Its effects in puerperal hemorrhage were not pronounced.

Lantana. *Lantana brasiliensis* Link. *Yerba Sagrada.* (Fam. *Verbenaceæ.*)—This Brazilian plant contains, according to Negrete, an alkaloid, *lantanine*, which is actively antiperiodic in *doses* of from fifteen to thirty grains (1.0–2.0 Gm.) in the twenty-four hours, given directly after the paroxysm. It is also claimed to be an intestinal antiseptic. (*T. G.*, 1885.) *Lantana camara* L., known in the West Indies as *sage tree* or *wild sage*, contains an alkaloid, *lantanine*, said to resemble quinine in its action.

Lanthanum Nitrate.—*Lanthani Nitras*, $La_2(NO_3)_6.12H_2O$, occurs in large rose-colored prisms which are soluble in water and alcohol. This salt is employed as an antiseptic, preventing the growth of bacteria when used in solutions of the strength of 1 in 2000. (See *Cb. B.*, 1897, xxi.)

Lanthanum Oxide. La_2O_3.—The oxide of lanthanum is an almost white, amorphous compound easily soluble in diluted mineral acids and insoluble in water. It is used as a source of production for other lanthanum salts and technically instead of calcium in oxydrogen lights, being, it is said, superior to calcium in many respects.

Lappa. *N. F. IV* (*U. S. P. VIII*). *Burdock Root. Radix Bardanæ. Bazzies. Beggars' Buttons. Cuckoo Button. Harebur. Bardane*, Fr. Cod. *Glouteron*, Fr. *Klettenwurzel*, G. *Bardana*, It.—"The dried root of *Arctium Lappa* Linné, or of other species of *Arctium* (Fam. *Compositæ*), collected from plants of the first year's growth." *N. F.*

The stem of the burdock is succulent, pubescent, branching, and three or four feet in height, bearing very large, cordate, denticulate leaves, which are green on their upper surface, whitish and downy on the under, and stand on long footstalks. The flowers are purple, with heads globose, and in terminal panicles. The involucre consists of imbricated scales, with hooked extremities, by which they adhere to the clothing of man and the coats of animals. The achemes are oblong, somewhat compressed and three-angled, ribbed, truncate. Although a native of Europe, burdock is abundant in the United States, where it grows on the roadsides, among rubbish, and in cultivated grounds. There are three recognized species of *Arctium* in North America—viz., *A. tomentosum* (Lam.) Schk. (*Woolly* or *Cottony Burdock*); *A. Lappa* L. (*Burdock, Clotbur* or *Great Bur*); and *A. minus* Schk. (*Common Burdock*).

It is described by the N. F. as "nearly simple, fusiform, of variable length from 5 to 20 mm. in diameter near the crown; frequently split or in broken pieces; externally grayish-brown, longitudinally wrinkled, the crown somewhat annulate, sometimes surmounted by a woolly tuft of leaf remains; fracture somewhat horny; a dark cambium separating the thick brownish bark from the yellowish porous and radiate wood, centrally hollow or containing a white, pith-like tissue. Odor slight; taste mucilaginous, sweetish, and slightly bitter. The powder is light brown and, when examined under the microscope, exhibits parenchyma cells of the cortex; the medullary rays and wood containing amorphous masses or sphero-crystals of inulin; yellow resin cells occur in the cortical parenchyma of young roots; wood fibers few; no starch and no calcium oxalate. Lappa yields not more than 6 per cent. of ash." *N. F.*

Inulin has been found in it by Guibourt, and sugar by Fée, while F. E. Hendershott believes that it contains a glucoside, besides arabin and pectin and extractives. (*Proceedings of Mich. Pharm. Assoc.*, 1887.) Trimble also obtained from the root a bitter, crystalline glucoside. (*Ph. Era*, 1888, p. 133.) Thos. Donaldson (*A. J. P.*, 1890, p. 123) found 8.6 per cent. of yellow fixed oil and about 1 per cent. of white waxy matter. A small quantity of volatile oil (0.065 per cent.) has been found in burdock root according to *Haensel's Report*, Oct., 1902. The inulin usually exists in parenchymatous cells in a different state, but if sections of the green root be dehydrated by soaking in 95 per cent. alcohol, the inulin will be found in spheroidal form.

An interesting account of burdock and its use as an edible vegetable in Japan, by Inazo Nitobe, may be found in *A. J. P.*, 1897, 416.

Uses.—Burdock root has been employed as a diuretic and diaphoretic alterative, especially useful in the *gouty, scorbutic,* and *syphilitic* and *scrofulous diatheses;* also in various chronic skin diseases, especially in *psoriasis, prurigo,* and *acne.* (*M. S. Rep.*, 1868.) The fresh leaves have been employed both externally and internally in cutaneous eruptions and ulcerations. There is no sufficient reason, however, to believe it has any medicinal virtue. This fluidextract is recognized by the N. F. (see Part III).

Dose, thirty to ninety grains (2.0–5.8 Gm.).

Larch Bark. *Laricis Cortex. Br.* 1885. *Ecorce de Mélèze,* Fr. *Lärchenrinde,* G.—The bark of *Larix decidua* Mill. (*Larix europœa* DC.) (Fam. *Pinaceæ*) was found by Aldridge to contain gum, starch, resin, and tannic acid of the kind which precipitates the salts of iron olive-green. John Stenhouse has obtained from it a peculiar volatile acid, *larixinic acid* (*larixine*). For method of separation, see 16th edition, *U. S. D.* Larixinic acid occurs in beautiful white, lustrous crystals, often more than an inch long, of a peculiar somewhat empyreumatic odor, and a slightly bitter and astringent taste, inflammable, volatilizing at 93° C. (199.4° F.) and melting at 153° C. (307.4° F.), soluble in 87.88 parts of water at 13.3° C. (56° F.), very soluble in boiling water, soluble in cold but much more so in hot alcohol, and sparingly soluble in ether. It readily crystallizes from its solutions. A very singular and characteristic property is that of forming, when added, in strong solution, in excess, to baryta water, a bulky, transparent, gelatinous precipitate, occupying the whole measure of the liquids if concentrated. The probable formula of the acid is $C_{10}H_{10}O_5$. The inner *larch bark* possesses astringent and gently stimulant properties, and is supposed to have a special tendency to the mucous membranes. It has been found particularly efficacious in *purpura* and other *hemorrhagic affections,* especially *hemoptysis,* and has been given in *bronchitis* with copious expectoration, and in diseases of the urinary passages. It has been used also, mixed with soap and glycerin, as a local remedy in *psoriasis, chronic eczema,* and other cutaneous affections. Of the extract from three to five grains (0.20–0.32 Gm.), of the tincture from thirty minims to a fluidrachm (1.8–3.75 mils) or more may be given every three or four hours.

Lard Oil. *Oleum Adipis. U. S. VIII. Huile de Graisse,* Fr. *Schmalzöl, Specköl,* G.—"A fixed oil expressed from lard at a low temperature." *U. S. VIII.*

Lard oil is made in large quantities in this country by exposing lard to low temperatures and then subjecting it to very powerful pressure. In this way the stearin of the lard is separated from the olein, the latter oozing out from the presses in the form of a yellowish-white oil, while the stearin is found in the market in hard cakes, and is largely used in making soap. (See *Adeps.*)

Lard oil is "a colorless or pale yellow, oily liquid, having a peculiar odor and a bland taste. Specific gravity: 0.905 to 0.915 at 25° C. (77° F.). At a temperature a little below 10° C. (50° F.), it usually commences to deposit a white, granular fat, and at or near 0° C. (32° F.), it forms a solid white mass. Lard oil is almost insoluble in cold alcohol and only slightly soluble in boiling alcohol; easily soluble in ether, chloroform, benzene, and carbon disulphide. If 5 Cc. of the Oil be thoroughly shaken in a test-tube with 5 Cc. of an alcoholic solution of silver nitrate (made by dissolving 0.1 Gm. of silver nitrate in 10 Cc. of alcohol, and adding 2 drops of nitric acid), and the mixture heated for about five minutes on a water-bath, the Oil should remain nearly or quite colorless, not acquiring a reddish or brown color (absence of more than about 5 per cent. of *cotton seed oil*). The Oil should be completely saponifiable with alcoholic potassium hydroxide T.S. and the resulting soap should be completely soluble in water, without separation of an oily layer (absence of *mineral oils*). If 2 Cc. of Lard Oil be mixed in a test-tube with 2 Cc. of equal volumes of amyl alcohol and carbon disulphide containing 1 per cent. of sulphur in solution, and the test-tube be immersed to one-third or one-half its depth

in boiling salt water, no reddish color should develop in from ten to fifteen minutes (absence of *cotton seed oil* or of *certain other fats*)." *U. S. VIII.* Lard oil should show a saponification value of 195 to 197 and an iodine value between 56 and 74. It is not pure olein, but contains varying proportions of stearin, and is sometimes adulterated with paraffin oil. It was introduced into the U. S. P., 1880, for the purpose of rendering the ointment of mercuric nitrate softer and smoother in consistence, but it was not retained in the process of the U. S. P. IX, mainly owing to the difficulty of obtaining it of sufficient purity in commerce.

Largin. *Silver Protalbin.*—This is a grayish powder containing 11.1 per cent. of silver. It is soluble in 10 parts of water, giving a yellowish solution. Readily soluble in albumen solutions, insoluble in alcohol and ether. It possesses bactericidal and astringent qualities and is therefore employed in *gonorrhea* as an injection and also as a wash in eye diseases. For ophthalmic use from one to ten per cent. solutions are used, while for urethral injection 1 to 4 to 1 to 2 per cent. aqueous solutions are found suitable.

Larkspur Seed. *N. F. IV. Delphinium. Lark's claw. Knight's spur.*—It is described by the N. F. as "the dried seeds of *Delphinium Consolida* Linné or of *Delphinium Ajacis* Linné (Fam. *Ranunculaceæ*), without the presence of more than 5 per cent. of foreign matter. Irregularly tetrahedral, or by pressure somewhat triangulate, acute at one end, obtuse or rounded at the other, about 2 mm. in length and equally broad or slightly narrower, surface black or blackish-brown, deeply and narrowly furrowed, the furrows intersecting so as to give a sharply tuberculate appearance to the surface, with serrate edges; testa crustaceous; kernel whitish, fleshy; embryo small, in fleshy endosperm. Odor very faint; taste bitter, afterward biting and acrid. Larkspur Seed yields not more than 7 per cent. of ash." *N. F.* Thomas C. Hopkins, of Baltimore, found in the seeds of Larkspur, *delphinine*, $C_{22}H_{35}O_6N$, volatile oil, fixed oil, gum, resin, chlorophyll, gallic acid, and salts of potassium, calcium, and iron. (*A. J. P.*, xi.) Rochebrune (*Toxicol. Africaine*, i) has separated alkaloids believed by him to be identical with *delphinine* from *D. peregrinum* L. and *D. mauritanicum* Coss. From the expressed juice of the larkspur *aconitic acid* was obtained by W. Wicke. (*J. P. C.*, 1854.) Moreover, the seeds of the indigenous *D. exaltum* Ait. are stated to have a physiological action similar to that of the larkspur. Larkspur is a common weed in the Western States, where it occasions death among grazing cattle. It is said to lose its toxicity during the flowering period. It is a showy annual, which has been introduced from Europe into the United States, where it has become sparingly naturalized, growing in old grain fields and flowering in June and July. The flowers are bitter and acrid. The seeds are the only part of the plant which is official. In large doses the seeds produce violent vomiting and purging, and are said to be diuretic. A tincture is official in the N. F. and has been used in spasmodic *asthma* and *dropsy*, but is mainly employed as a parasiticide in a manner similar to the preparations of staphisagria. *Dose*, ten minims (0.6 mil), gradually increased. Brett has found that *D. peregrinum* L., when growing, is very effective in the destruction of grasshoppers. (*P. J.*, vol. xxi, 1891. See *Staphisagria* in Part I.)

Larosan. *N. N. R.* 1917.—A compound of casein and calcium containing 2.5 per cent. CaO. It is a fine, bulky, tasteless and odorless white powder, soluble in water with an alkaline reaction; used in disturbances of nutrition and diarrheas.

Lathyrus. *Lathyrus sativus* L. (Fam. *Leguminosæ.*) *Jarosse, Gesse, Kasari* (Ind.).—The *White* or *Chickling Vetch*, the seed of which is used in Europe as a food both by man and animals, under the name of "*mutters*," produces, when taken too freely, a condition known as *lathyrismus*. Horses which have been fed on the plant for a considerable period drop while performing the lightest work, in consequence of paralysis of the hind extremities, and in many cases death has followed from bilateral paralysis of the recurrent laryngeal nerves and consequent asphyxia. This laryngeal affection does not occur in the human subject, and death very rarely takes place. In man the muscles of the lower extremities below the knee are apt to be especially affected, the abductors more than the adductors. The muscles of the face, neck, and upper extremities are very rarely, if ever, attacked. The reflexes and the general sensibility are usually not influenced; but Giorgieri has seen the tendon reflexes increased. According to Cantani, the galvanic contractility of the paralyzed muscle is altered, and the transverse markings of the muscles are nearly obliterated by fat globules. In fatal cases the spinal cord has been found normal. Astier obtained from the seeds a poisonous alkaline volatile liquid. According to him, this, being volatile, is not present in preparations such as pressed cakes made at a high temperature, which are consequently not poisonous. If, however, such cakes have been prepared at low temperature, they exhibit toxic properties, owing to the retention of the toxic principle. This is in conformity with the experience of the peasants in some parts of Europe, who mix the ground white vetch seeds with wheat flour, and boil the mixture for food. E. M. Holmes states that these seeds should not be used in foods in any proportions, as they are poisonous. (*P. J.*, 1913, 795.)

Laurotetanine.—This alkaloid, $C_{19}H_{23}NO_5$, or $C_{16}H_{13}O_2(O.CH_3)_3NH$, has been found by Greshoff in *Litsea latifolia* Bl., and in other plants belonging to the *Lauraceæ*. It is said to be a powerful poison, acting like strychnine on the spinal cord. It gives with Froehde's reagent an indigo-blue color, which on the addition of water changes to yellow; with Erdmann's reagent, a transitory bright blue color, becoming brown, and with more nitric acid it gives immediately a bright red-brown, and with pure nitric acid a dirty brown. It is soluble in excess of alkali. (*P. J.*, vol. xxi, 1891.)

Laurus. *Laurus nobilis* L. *Sweet Bay. Laurier commun*, Fr. *Lorbeer*, G.—The *sweet bay* is an evergreen tree of the Fam. *Lauraceæ*, inhabiting the countries bordering on the Mediterranean. The leaves are alternate, on short petioles, oval-lanceolate or oblong, entire, pellucid-punctate, of a firm texture, smooth, shining, deep green upon their upper surface, paler beneath. They have a fragrant odor, especially when bruised, and a bitter, aromatic, somewhat astringent taste. They yield by distillation a greenish-yellow volatile oil. The volatile oil, of which the fruit yields 0.23 per cent., has a sp. gr. 0.88, and is solid at 0° C. (32° F.). It is largely composed of oxygenated compounds. The constituents thus far recognized are myrcene, phellandrene, methyl-chavicol, citral, methyl-eugenol, chavicol, and eugenol. (*Schim. Rep.*, April, 1897.) Water distilled from the

leaves has their peculiar odor. The *berries* when dried are black and wrinkled, and contain two oval fatty seeds within a thin, friable envelope; or they may be considered as drupes, with a kernel divisible into two lobes. They have the same aromatic odor and taste as the leaves, but are more pungent. Besides an essential oil, they contain a fixed oil, which, as obtained by expression from the fresh fruit, is of a greenish color, and aromatic odor from retained volatile oil. One of its chief constituents is the ether of *lauric acid*, the so-called *laurostearine*, $C_3H_5(C_{12}H_{23}O_2)_3$, which fuses at 45° C. (113° F.). The free acid may be obtained from this by saponification. It cannot be distilled without decomposition. Another constituent of the crude fat is *laurin*, $C_{22}H_{30}O_3$, which can be extracted by alcohol. It forms neutral, easily fusible prisms without odor or taste. Lard, impregnated with the odorous principle of the berries, and colored green by chlorophyll or sometimes by indigo and turmeric, is said to be often substituted for the genuine expressed oil. This may be detected by boiling alcohol, which dissolves the true oil. The leaves, berries, and oil are excitant and narcotic, but are rarely used internally as medicines, and in this country are scarcely employed in any manner. E. M. Holmes, however, states that the berries have been use in Europe to promote miscarriages. (*P. J.*, 1910, 52.) Their chief use is to communicate a pleasant odor to external remedies. The leaves are also used for culinary purposes in communicating their aromatic flavor to soups, stews, etc. They come into commerce frequently as the packing around stick licorice extract from Mediterranean countries.

Lavender Flowers. *Lavandula. U. S.* 1880. *Lavandula vera* DC. (*L. officinalis* Chaix, *L. spica* L.) *Lavender. Flores Lavandulæ*, P. G. *Lavande, Fleurs de Lavande*, Fr. *Lavandelblumen, Lavandelblüthen*, G. *Lavendola*, It. *Espliego, Alhucema*, Sp.—Lavender is a small labiate shrub. The plant is a native of Southern Europe, and covers vast tracts of dry and barren land in Spain, Italy, and the south of France. In England and America it is very largely cultivated. For method of culture and detailed descriptions of the various varieties that have been educed, see *B. M. S. J.*, Aug., 1873, 165. The cultivation of lavender has become an important industry and attempts are being made to cultivate the finer qualities of lavender in the United States.

For details of lavender culture, see *U. S. D.*, 19th ed., p. 1546.

Lavender flowers have a strong fragrant odor, and an aromatic, warm, bitterish taste. They retain their fragrance long after drying. Alcohol extracts their virtues, and a volatile oil upon which their odor depends rises with that liquid in distillation. Hager obtained from a pound of the fresh flowers from half a drachm to two drachms of the oil. The flowers are frequently sold for packing away with clothing as a moth preventive. Lavender is an aromatic stimulant and tonic, but is seldom given in its crude state. The products obtained by its distillation are much used in perfumery, and the volatile oil is official. (See *Oleum Lavandulæ*, p. 767.)

Lawsonia. *Lawsonia inermis* L. (*L. alba* Lam.) *Henna Plant. Mehndi.*—This is a shrub of the Fam. *Lythraceæ*, growing in the Levant, Egypt, Persia, and India, and well known as the source of a dyestuff denominated *henna*, much used throughout the Mohammedan countries of the East. It is largely cultivated in Egypt. The flowers have a strong, pungent odor, and a distilled water prepared from them is used as a cosmetic. The fruit is thought to have emmenagogue properties. The powdered leaves, under the name of *henna*, are used to stain golden yellow the feet and hair of women of the harem. Abd-el-Aziz of Cairo, Egypt, found in it a brown substance, of a resinoid fracture, having the chemical properties which characterize the tannins, and therefore named by him *hennotannic acid*. Henna has been employed both internally and locally, in *jaundice, leprosy*, and affections of the skin.

Lead Acetotartrate.—Colorless crystals soluble in water and possessing astringent and antiseptic properties. It is used in a similar manner to that of acetate of lead.

Lead Carbonate. *N. F. IV. Plumbi Carbonas.* (*U. S. P.* 1890.) *White Lead. Plumbum Carbonicum. Carbonas Plumbicus. Carbonate de Plomb. Céruse*, Fr. Cod. *Blanc de Plomb. Blanc de Céruse*, Fr. *Cerussa*, P. G. *Bleiweiss*, G. *Cerussa*, It. *Albayalde o cerusa*, Sp.—This is "a mixture of lead carbonate and hydroxide [approximately, $(PbCO_3)_2Pb(OH)_2 = 775.32$]." *N. F. IV.* Lead carbonate is prepared by several methods. By one method it is obtained by passing a stream of carbon dioxide through a solution of lead subacetate. The dioxide combines with the lead hydroxide of the basic salt, and precipitates as lead carbonate, while a neutral acetate remains in solution. This, by being boiled with a fresh portion of oxide, is again brought to the state of basic salt, when it is treated with carbon dioxide as before. In this way the same portion of acetate repeatedly serves the purpose of being converted into subacetate and of being decomposed by carbon dioxide. The carbonate obtained is washed, dried with a gentle heat, and thrown into commerce. This process, which produces white lead of the first quality, was invented by Thénard, about the year 1802, and is that which is usually pursued in France and Sweden, and known as the "Clichy process."

Another, called the "Dutch process" from its origin in Holland, consists in exposing lead to the vapor of vinegar, and is the one usually pursued in England and the United States—but in England with some modifications. In this country the lead is cast into thin sheets which are rolled up so as to form a cylinder five or six inches in diameter, and seven or eight high, which is placed in an earthen pot containing about half a pint of vinegar, and having within a few inches from the bottom three equidistant projecting knobs in the earthenware, on which the cylinder of lead is supported in order to keep it from contact with the vinegar. The pots thus prepared are placed side by side, in horizontal layers. The first layer is covered with boards, on which a stratum of tan-bark or of refuse straw from the stables is strewed, and fresh layers of pots, boards, and tan or straw are successively placed until the building is filled. The layers of pots are allowed to remain undisturbed for about six weeks, at the end of which time they are unpacked, and the cylinder of sheet lead in each pot, though still retaining its shape, is found almost entirely converted into a flaky, white, friable substance, which is the white lead. This is separated from the lead yet remaining in the metallic state, ground in water, and finally dried in long shallow reservoirs, heated by steam. Pelouze has succeeded in explaining these processes on one general principle. In Thénard's process it is admitted that the same

portion of lead acetate unites with oxide, and gives it up again to carbon dioxide to form the carbonate. In the Dutch process, Pelouze has rendered it almost certain that none of the oxygen or carbon dioxide of the carbonate is derived from the vinegar. In this process he supposed that the heat generated by the fermentation of the tan or straw volatilizes the vinegar, the acetic acid of which, with the assistance of the oxygen of the air, forms with the lead a small portion of subacetate. This, by reacting with the carbon dioxide resulting from the decomposition of the tan or straw, or derived from the atmosphere, forms lead carbonate, and is brought to the state of neutral acetate. The neutral acetate returns again to the state of subacetate, and, by alternately combining with and yielding up the oxide, causes the whole of the lead to be finally converted into carbonate.

The temperature of the stacks of pots in the Dutch process is about 45° C. (113° F.). If it falls below 35° C. (95° F.), a part of the lead escapes corrosion, and if it rises above 50° C. (122° F.), the product is yellow. The form of acetic acid usually employed in this process is vinegar, but the variable nature of that liquid as to strength and purity is an objection to its use, and, accordingly, other forms of the acid have been substituted with advantage, as, for example, the purified acetic acid from wood in a diluted state. The "German" or chamber process differs from the Dutch process only in that the vessels containing the lead are placed in chambers having a perforated floor, through the openings of which the fumes of acetic acid rise, acting upon the lead, while carbon dioxide from the burning of coke is passed in and through the chamber. This process is cheaper than the Dutch method, and is said to give an equally satisfactory product. In Carter's process, used in this country extensively, granulated metallic lead is moistened with acetic acid and submitted to the action of carbon dioxide gas in revolving barrels. A number of other methods have been suggested and used to a greater or less extent, but the Dutch process is the one most frequently employed.

The N. F. IV description is as follows: "A heavy, white, opaque powder, or as a pulverulent mass, without odor or taste; permanent in the air. Insoluble in water or alcohol, but dissolved by acetic acid or diluted nitric acid, with effervescence. When strongly heated it turns yellow without charring, and when heated in contact with charcoal it is reduced to metallic lead. Dissolve 2 Gm. of Lead Carbonate in a mixture of 2.5 mils of nitric acid and 40 mils of distilled water; not more than 0.01 Gm. of residue remains. Separate portions of this solution yield a black precipitate with hydrogen sulphide T.S.; a yellow precipitate with potassium iodide T.S.; and a white precipitate with diluted sulphuric acid. On completely precipitating 10 mils of this solution with hydrogen sulphide, the filtrate, on evaporation, leaves not more than 0.01 Gm. of residue. Ignite 1 Gm. of Lead Carbonate in a porcelain crucible; it leaves a residue of lead oxide weighing not less than 0.83 Gm." *N. F.* It is sometimes adulterated with barium, calcium, and lead sulphates, particularly the first. A mixture of equal parts of white lead and barium sulphate is known as *Venetian white*, while *Hamburg white* is a mixture of 1 part of white lead and 2 parts of barium sulphate, and *Dutch white* of 1 part to 3 of barium sulphate. Louyet has examined samples of French white lead containing considerably more than half their weight of barium sulphate. These sulphates, if present, are left undissolved by nitric acid. Chalk or whiting is another adulteration. This may be detected by adding to the nitric solution of the white lead an excess of potassium hydroxide which will redissolve the lead monoxide first thrown down but leave a white powder of lime.

Neutral lead carbonate consists of one atom of lead, one of carbon, and three of oxygen. The commercial white lead is a compound of lead carbonate and hydroxide containing, according to Baker (*Chem. News*, 1861, 74), variable proportions of the hydroxide from mere traces to the amount of one molecule to three molecules of the neutral carbonate.

White lead is largely used in the arts, especially in the preparation of paints. In medicine it has been employed externally as an astringent and protective application to *ulcers, excoriated surfaces, burns*, etc. Its free continued external use has produced lead poisoning and it has been, therefore, largely abandoned for less dangerous agents.

Lead Nitrate. *Plumbi Nitras. U. S. VIII. Nitrate of Lead. Plumbum Nitricum. Nitras (Azotas) Plumbicus. Azotate de Plomb, Nitrate de Plomb*, Fr. Cod. *Salpetersaures Bleioxyd, Bleisalpeter*, G. *Nitrato di piombo*, It. *Nitrato plumbico, Nitrato de plomo*, Sp. $Pb(NO_3)_2 = 331.12$.—"It should contain not less than 99.5 percent. of pure Lead Nitrate [$(NO_2.O)_2Pb$], and should be kept in well-closed vessels." *U. S. VIII.*

Lead nitrate occurs in "colorless, transparent, octahedral crystals, when obtained by the spontaneous evaporation of cold solutions, or white, nearly opaque crystals, when formed by the cooling of hot solutions; without odor, and having a sweetish, astringent, afterwards metallic, taste; permanent in the air. Soluble in 1.85 parts of water at 25° C. (77° F.), and in 0.75 part of boiling water; almost insoluble in alcohol. When strongly heated, the salt decrepitates, emits nitrous vapors, and finally leaves a residue of lead oxide. The aqueous solution of the salt has an acid reaction upon blue litmus paper, and yields a black precipitate with hydrogen sulphide T.S., a yellow one with potassium iodide T.S., and a white one with diluted sulphuric acid. The aqueous solution of the salt (1 in 10) should give, with potassium ferrocyanide T.S., a pure white precipitate (absence of *copper* and *iron*). If hydrochloric acid be added to the aqueous solution of the salt (1 in 10) until no further precipitate is produced, and the remainder of the lead be removed from the filtrate by hydrogen sulphide, a portion of the second filtrate should not yield more than a slight precipitate upon the addition of ammonia water (limit of *zinc* and *iron*). Another portion of this filtrate, when evaporated to dryness, should not leave more than a slight residue after gentle ignition (limit of *salts* of the *alkalies* and those of *magnesium, calcium, zinc*, and *iron*)." *U. S. VIII.* It is largely used in dyeing and calico printing, for the preparation of mordants, and of chrome yellow.

Lead nitrate possesses the astringent and antiseptic properties of the soluble lead salts, but has largely passed out of vogue. It is occasionally applied to excoriated surfaces, and a solution made in the proportion of ten grains to an ounce of water, and colored probably with alkanet, has been used on the continent of Europe as a secret remedy in *sore nipples, chapped hands, cracked lips*, etc. *Ledoyen's disinfecting fluid* is a solu-

tion of *lead nitrate* in the proportion of a drachm to an ounce. Moerlonge and Vanzette ascribe remarkable efficiency to lead nitrate in *onychia maligna*, and their statements have been confirmed by other practitioners. It is applied by sprinkling the powder on the surface, and, according to J. Scott, of Belfast, Ireland, a complete cure may be relied on in from fourteen to thirty days.

Dose, one-fourth to one-half grain (0.016–0.032 Gm.).

Lead Oxide, Red. *N. F. IV. Plumbi Oxidum Rubrum. Red Oxide of Lead. Red Lead. Minium*, P. G. *Deutoxide de Plomb, Oxide Rouge de Plomb, Minium*, Fr. *Mennige*, G. *Minio*, It., Sp. —"Lead orthoplumbate [$Pb_2PbO_4 = 685.3$] usually with some unconverted lead monoxide [PbO], corresponding to not less than 31 per cent. of lead dioxide [PbO_2]." *N. F.* Red lead is prepared on the large scale in a furnace, with the floor slightly concave and the roof arched, presenting a general resemblance to a baker's oven. The lead is placed on the floor, and gradually raised to a red heat, whereby it melts and becomes covered with a pellicle of monoxide, which is removed by means of a long iron scraper, and the pellicles, as they successively form, are scraped off until the whole of the metal has been converted into the monoxide. The product is subjected to further calcination, with occasional stirring, for some time, in order to oxidize any remaining particles of metallic lead; it is thus rendered yellow, and constitutes *lead monoxide*, or *massicot* (*litharge*).

This is taken out of the furnace, thrown upon a level pavement, and cooled by being sprinkled with water. It is next reduced to fine powder by trituration and levigation, and dried, and in this state is introduced into large, shallow, square tin boxes, which are placed in another furnace, closed from the air, and heated nearly to redness, the heat being allowed gradually to fall during a period of from twenty-four to thirty hours. At the end of that time the lead monoxide will have combined with an additional quantity of oxygen, and become the red oxide. This is taken out, and, after it has passed through a fine wire sieve, it is packed in barrels for the purposes of commerce.

The red lead of commerce may be considered as a mixture of what may be called the true red oxide and variable proportions of monoxide. That this is its nature is rendered probable by the action of cold diluted acetic acid, not used in excess, which takes up a variable quantity of monoxide, leaving a portion unchanged in color, which may be deemed the pure red oxide. This latter, when analyzed by nitric acid, has been proved, by the coincident results of Dalton, Dumas, and Phillips, to consist of three atoms of lead and four of oxygen, equal to $2PbO.PbO_2$ (Dumas), or $PbO.Pb_2O_3$ (Winckelblech). Mulder gives $Pb_4O_5 = 3PbO.PbO_2$, or $2PbO.Pb_2O_3$, as the usual composition of red lead.

Red lead enters into no official preparation. In the arts it is used chiefly as a paint, for protecting metal surfaces, in the manufacture of flint glass, and in cements for metal joints.

For further details concerning the manufacture and properties of red lead, see *U. S. D.*, 19th ed, p. 1547.

It is described in the N. F. as "a heavy, orange-red powder without odor or taste." On exposure to the air it slowly absorbs moisture and carbon dioxide. Almost insoluble in water, insoluble in alcohol, but dissolved by an excess of glacial acetic acid; also dissolved by lactic acid with the evolution of carbon dioxide and the odor of acetaldehyde. When heated in a porcelain crucible, Red Oxide of Lead at first changes color from red to a violet and then to a blackish tint, and regains its original color on cooling, but, when the heating is continued, it slowly decomposes, forming lead monoxide and oxygen. When heated in contact with charcoal, it is reduced to metallic lead. Treat 5 Gm. of Red Oxide of Lead with 50 mils of diluted nitric acid; little effervescence results (*carbonate*), and a brown, insoluble residue of lead dioxide (PbO_2) remains, which, upon the addition of solution of hydrogen dioxide, dissolves with the evolution of oxygen, forming a colorless solution. Boil this solution for fifteen minutes, cool, and filter; the undissolved residue weighs not more than 0.2 Gm. (*silicate or lead sulphate*). Separate portions of the solution obtained in the last test yield with hydrogen sulphide T.S., a black precipitate; with potassium iodide T.S., a yellow precipitate; and with diluted sulphuric acid, a white precipitate; the latter two precipitates being soluble in a solution of sodium hydroxide (1 in 4). From a solution of 0.5 Gm. of Red Oxide of Lead in diluted nitric acid, obtained by the aid of solution of hydrogen dioxide, precipitate the lead with sulphuric acid and filter the mixture. After the addition of an excess of ammonia water this filtrate does not develop more than a slight, bluish tint (*copper*), nor yield more than traces of a reddish-brown precipitate (*iron*). Heat a mixture of 1 Gm. of Red Oxide of Lead with 50 mils of distilled water to boiling, cool, and filter. The filtrate is colorless, is not more than faintly alkaline to litmus, and, when evaporated to dryness, leaves not more than 0.01 Gm. of residue (*soluble impurities*)." *N. F.*

Assay.—"Add about 1 Gm. of Red Oxide of Lead, accurately weighed, to a cool solution of 40 Gm. of crystallized sodium acetate and 2 Gm. of potassium iodide in 50 mils of 50 per cent. acetic acid, agitate the mixture until all of the Red Oxide of Lead has dissolved and then titrate the solution with tenth-normal sodium thiosulphate V.S. It shows not less than 31 per cent. of lead dioxide (PbO_2). Each mil of tenth-normal sodium thiosulphate V.S. corresponds to 0.01195 Gm. of lead dioxide (PbO_2). Each gramme of Red Oxide of Lead corresponds to not less than 25.9 mils of tenth-normal sodium thiosulphate V.S." *N. F.*

Lead Phenolsulphonate. *Lead Sulphocarbolate.* $Pb(C_6H_4OHSO_3)_2 + 5H_2O$.—White, lustrous needles, soluble in water and alcohol and possessing astringent and antiseptic properties. It is used externally in *skin diseases* and *ulcers* instead of, and as stated to be better than, zinc sulphocarbolate.

Lead Saccharate. *Plumbi Saccharas. Saccharate of Lead.—Lead saccharate* is made by saturating a solution of saccharic acid in water with freshly precipitated lead carbonate gradually added. As the acid becomes saturated, the lead saccharate falls in the form of a white powder, being insoluble in cold water, and but very sparingly soluble in that liquid boiling hot. From this E. Hoskins prepared his *lead nitro-saccharate*, by dissolving the saccharate in diluted nitric acid, containing only one part of the acid in twenty parts of the mixture, filtering the solution, and gradually evaporating. The nitro-saccharate is deposited in yellow crystals in the form of regular six-sided plates or prisms. By dissolving one grain of this salt, with five drops of pure saccharic acid, in a fluidounce of distilled water, a solution was obtained which, though slightly acid to test paper,

was perfectly bland. This solution has been used to dissolve urinary *calculi*.

Lead Tannate. *Plumbi Tannas.*—This is obtained by precipitating a solution of tannin with one of lead acetate, added drop by drop. It has been used locally in *chronic inflammations* of the *joints, ulcerations, bed sores,* and *sore nipples,* in 20 to 40 per cent. ointments. The preparation here described is a bitannate. Other lead tannates exist.

Lead Thiosulphate. *Lead Hyposulphite.* PbS_2O_3.—When freshly prepared this compound occurs as a white, amorphous powder turning black on exposure to air for some time, due to the formation of lead sulphide. It is soluble in solutions of the alkali thiosulphates and is used in this form in the external treatment of *rhus poisoning.* It is incompatible with acids or acid salts.

Lecin.—This is an elixir of iron albuminate. It is a permanent and non-gelatinizing preparation and asserted to be an extremely assimilable form of iron, containing 20 per cent. albumen and 0.6 per cent. iron.

Lecithin. $C_{42}H_{84}NPO_9$, or $C_{44}H_{90}NPO_9$.—*Lecithin* consists of the esters of oleic, stearic, palmitic, or other fatty acid, with glycerophosphoric acid combined with choline; occurring in combination with proteids in many animal and vegetable tissues, especially nerve tissue and the yolks of eggs. The class of lecithins is now known to be widely distributed in both animal and vegetable tissues, although most familiar in its occurrence in the nerve tissues and embryonic cells. It is a yellowish-brown, waxy solid, of a peculiar odor, soluble in an equal volume of cold absolute alcohol and readily soluble in chloroform, ether, and benzine. It is insoluble in water, but swells, however, and eventually decomposes. It is hygroscopic on exposure in the air and decomposes according to the extent of moisture absorbed. Lecithin is incompatible with alkalies and should be kept in glass-stoppered bottles away from the light.

The animal lecithin is *choline di-stearylglycerophosphate,* while the vegetable lecithin seems to be *betaine di-oleylglycerophosphate;* that is, the widely distributed vegetable base, *betaine* (*oxyneurine*), replaces the choline of egg lecithin and the oleic acid radical appears instead of that of stearic acid.

Vegi-lecithin has been studied chemically by C. Gordon Richardson. Besides the replacement of the choline by betaine and the difference in the fatty acids, it differs from *ovi-lecithin* (*vitellin*) in not being precipitated by acetone and being quite insoluble in alcohol, but soluble in all proportions in cold ether. Otherwise it is readily soluble in all the solvents of ovi-lecithin. It seems to resemble somewhat the *cephaline* of Thudichum, which was obtained from the brain tissue and which is now known as lecithin and asserted to be better borne than lecithin.

Choline is a substance with well marked physiological properties, and is closely allied chemically to the alkaloid *neurine,* a poison of considerable power, which was discovered by Strecker (*Ann. Ch. Ph.,* cxxiiix), and shown by Brieger (*Ueber Ptomaine,* Berlin, 1895) to occur in decomposing meat. These two substances are very similar in their effects upon the system. They are related physiologically to pilocarpine and muscarine in that they stimulate the peripheral ends of the autonomic nerves. Through this action on the nerve endings they cause an increase in various secretions, especially those of the salivary gland, slowing of the pulse, contraction of the pupil, and an increase in the peristaltic movements of the intestinal and probably other unstriped muscles. Besides these actions, they exercise a depressant influence upon the respiratory center, and in large doses also paralyze the peripheral motor nerves. Choline also lowers the blood pressure by dilating the blood-vessels. When injected into various organs choline produces, according to Hoffman (*W. K. W.,* 1905), destructive changes, similar to those caused by the X-ray. Exner and Sywek (*D. Z. Chir.,* 1906) confirmed these observations, and have had some encouraging results from injection of a 2 per cent. solution of choline in cases of inoperable *cancer.*

There are a large number of proprietary preparations of lecithin on the market. Concerning the liquid forms, attention may be again called to the fact that lecithin is insoluble in water or alcohol, so that any transparent liquid preparation of lecithin must be suspected as containing little of the drug.

When taken by the mouth lecithin is partially broken up by the fat-splitting ferments of the pancreas into its constituent parts, but appears also to be in part absorbed unchanged. The absorption of lecithin unchanged seems to be dependent upon the presence of bile in the intestines. Its presence in the intestinal tract, according to Usuki (*A. E. P. P.,* 1910, lxiii, p. 270) exercises a favorable influence upon the saponification and absorption of the neutral fats and perhaps accelerates the digestion of certain proteins. According to the researches of Maslow (*St. Petersburg M. W.,* 1913, xxxviii, p. 97), lecithin is capable of being built up into the bodily phosphates in a way that neither phosphoric nor glycerophosphoric acid can be utilized. Whether or not lecithin affects the excretion of nitrogen through the urine is at present a matter of difference of opinion, but the bulk of the evidence seems to indicate that it increases the nitrogenous output. On the other hand, it is almost universally conceded that although the output of phosphorus is greater the increase is not proportional to the excess of phosphorus ingested; that is, it causes a phosphorus retention.

Danilewski found that, in young animals, it caused an increase in the number of red corpuscles, and a gain in weight. Billon (*International Congress of Medicine,* 1904) has confirmed these findings, and also observed a marked increase in the number of white corpuscles. Serono, as a result of studies on human beings, reached the conclusion that the output of nitrogen was increased.

Lecithin was introduced into medicine with the idea that being a natural phosphorus, it would exercise the tonic effect of this element upon the system without the disadvantages of its toxic action, and there is considerable clinical evidence of its utility in *tuberculosis, neurasthenia, chlorosis, scrofula* and *rickets.* Lancereaux and Paulesco recommend it also in *diabetes,* but Erben (*S. M.,* 1909) observed no benefit from its use in this disease. Although a portion of the lecithin is decomposed in the intestinal tract by the fat-splitting ferments, Slowtzoff asserts that a part of it is absorbed unchanged. Whether or not pure lecithin has any advantage over the yolks of eggs may be questioned. The *dose* of lecithin is from one to three grains (0.065–0.2 Gm.) in pills or emulsion.

Lecithin, as has been shown by H. C. Wood, Jr. (*U. P. M. B.,* May, 1902), is not poisonous. The following are some of the more popular preparations:

Glyceritum Lecithini. Glycerol of Lecithin.—A 1.6 per cent. of lecithin in pure glycerin. *Dose,* one fluidrachm (4 mils).

Lecibrin.—A preparation of lecithin from the brain, containing 33⅓ per cent. of lecithin with nucleo-proteins. It is marketed only in the form of gelatin-coated pills, each containing three grains (0.2 Gm.) of *lecibrin.*

Lecipon.—This is stated to contain 10.5 per cent. of lecithin in soluble form.

Lecithan.—A trade name for lecithin.

Lecithcerebrin.—Lecithin prepared from the brain substance.

Lecithmedullan.—A lecithin prepared from bone marrow.

Lecithol.—An emulsion of brain lecithin representing 1.5 per cent. of lecithin. *Dose,* one to two fluidrachms (4–8 mils).

Neurolecithin.—A trade name for lecithin prepared from the brain and spinal cord of animals. *Dose,* one grain (0.065 Gm.).

Letalbin. (*Lecithin Albuminate.*)—This forms a yellowish, dry, stable powder of characteristic egg yolk taste. It contains 20 per cent. pure lecithin and is adapted as an addition to tablets, pastilles and infant foods.

Ledum. *Ledum palustre* L. *Marsh Tea. Rosmarinus Sylvestris. Marsh Cistus. Wild Rosemary. Lédon, Romarin sauvage,* Fr. *Porsch, Sumpfporsch, Wilder Rosmarin,* G.—A small evergreen ericaceous shrub, growing in swamps and other wet places in the northern parts of Europe, Asia, and America, and in the mountainous regions of more southern latitudes. The leaves have a balsamic odor, and an aromatic, camphorous, bitter taste, and contain, among other ingredients, volatile oil and tannin. For the properties of the volatile oil, see *J. P. C.,* 4e sér., xx, 244; also *Proc. A. Ph. A.,* xxv, 154. It contains *ledum camphor,* a stearopten, together with valeric and other volatile acids, and *ericinol,* $C_{10}H_{16}O$. The tannin has been named *leditannic acid,* $C_{15}H_{20}O_8$. On boiling with dilute mineral acids it is decomposed, and *ledixanthin,* $C_{30}H_{34}O_{13}$, separates as a yellowish or reddish powder. (Thal, *Ph. Z. R.,* 1883, 268.) Thal also extracted *ericolin,* $C_{34}H_{56}O_{21}$. This is a glucoside, which on heating with diluted sulphuric acid decomposes into sugar and *ericinol,* $C_{10}H_{16}O$, a colorless, peculiar-smelling oil, which turns brown in the air, owing to oxidation. The leaves are thought to be narcotic and diaphoretic, and have been employed in *dysentery* and in various cutaneous affections, particularly *leprosy* and *scabies.* In complaints of the skin they are used both internally and externally, in the form of decoction. In Germany they are sometimes substituted for hops in the preparation of beer. *Ledum grœnlandicum* Oeder (*L. latifolium* Ait.), or *Labrador tea,* which is a larger plant than the preceding, is a native of North America, growing in damp places in Canada and the northern part of the United States. The leaves have an agreeable odor and taste, and are esteemed pectoral and tonic. They are said to have been used as a substitute for tea during the war for independence.

Leek. *Porrum. Porreau,* Fr. *Lauch,* G.—The bulb of *Allium Porrum* Don. (Fam. *Liliaceæ.*) The *leek,* which is the national emblem of the Welsh, is a biennial bulbous plant, growing wild in Switzerland, and cultivated in the gardens of Europe and this country for culinary purposes. All parts of it have an offensive, pungent odor and an acrid taste, dependent on an essential oil, of which allyl sulphide, $(C_3H_5)_2S$, is the main ingredient. The bulb, which is the medicinal portion, consists of concentric layers, like the onion, which it resembles in medicinal properties, though somewhat milder. It is generally stimulant, with a direction to the kidneys. *Dose,* of expressed juice, a fluidrachm (3.75 mils).

Lenigallol. *N. N. R.* 1917. *Pyrogallol Triacetate.* $C_6H_3(CH_3CO_2)_3$.—This is a white powder, insoluble in water, and is used in paste form. This derivative of pyrogallic acid has been highly commended as a local remedy in acute and moist *eczema,* and in *pityriasis rosea.* It is said not to act well in the dry desquamating eczemas. It is generally applied in the form of a paste containing from 2 to 5 per cent. of *lenigallol.* In the strength of 30 to 50 per cent. it is also useful as a keratolytic.

Lentine. *Meta-diamido-benzene.* $C_6H_4(NH_2)_2$. 2HCl.—Under this name a meta-phenyleine-diamine-hydrochloride, previously used for technical purposes, has been introduced into medicine. It occurs as a colorless, crystalline powder changing to a reddish color in time, and soluble in both water and alcohol. It is used in the treatment of *diarrhea,* especially that accompanying *acute enteritis.* When administered the urine assumes a dark brown color. According to Duhem, its value is simply that of an intestinal antiseptic. While Boyé (*Cb. I. M.,* 1905) used it in *doses* of less than two grains (0.1 Gm.). Duhem recommends for adults five to eight grains (0.32–0.5 Gm.).

Leonotis. *Leonotis Leonurus* R. Br. *Wild Daggar.*—This handsome tropical labiate is said to possess purgative and emmenagogue properties. (See *P. J.,* May, 1885.) The leaves of this plant are smoked by the Hottentots like tobacco. It is asserted that in overdose it has a narcotic effect. It is used by the South African aborigines as a cathartic, and in the treatment of *snake bite.* A decoction is also employed externally for various skin eruptions. (*P. J.,* 1907, lxxix.)

Leonurus. *Leonurus Cardiaca* L. *Motherwort. Agripaume, Cardiaire,* Fr. *Herzespann, Wolfstrapp,* G.—An aromatic perennial labiate herb, growing wild in this country in waste places, around dwellings, etc., whose infusion of decoction is sometimes used in *amenorrhea* and sudden *suppression* of the *lochia.*

Lepargyræa. *Shepherdia argentea* Nutt. *Buffalo Berry. Bull Berry. Grains de Bœuf,* Fr.—The acidulous fruit of this plant, of the Fam. *Elœagnaceœ,* produced in great profusion in the region of the upper Missouri, is largely used as an article of food. According to Henry Trimble, it contains a little more acid than currants. (*A. J. P.,* Dec., 1888.)

Leptandra. *N. F. IV* (*U. S. P. VIII*). *Culver's Root. Culvers' Physic. Black Root. Racine de Leptandra, ou de Véronique de Virginie,* Fr. *Leptandra-Wurzel,* G.—"The dried rhizome and roots of *Veronica virginica* Linné (Fam. *Scrophulariaceœ*), without the presence of more than 5 per cent. of stems or other foreign matter." *N. F. Veronica virginica,* commonly called *Culver's root,* or *Culver's physic,* is an herbaceous perennial, with a simple, erect stem, three or four feet high, smooth or downy, furnished with leaves in whorls, and terminating in a long spike of white flowers. The leaves, of which there are from four to seven in each whorl, are lanceolate, pointed, and minutely serrate, and stand on short foot-stalks. A variety was seen by Pursh with purple flowers, which was described and figured as a distinct species by Rafinesque, under the name of *L. purpurea.* The plant flowers in July and August. It grows throughout the United States east of the

Mississippi, affecting mountain meadows in the South and rich woods in the North, and is not unfrequently cultivated. The National Formulary describes *leptandra* as follows "Rhizome usually of horizontal growth, nearly cylindrical, somewhat branched; branches readily separable from the main rhizome, from 4 to 10 cm. in length and from 4 to 13 mm. in diameter; externally grayish-brown to dark reddish-brown, annulate from circular scars of bud-scales, upper surface with short stem remnants, occasionally with buds, and numerous circular stem-scars; from the under and lateral portions arise numerous coarse roots; fracture very tough and woody; internally, bark rather thin, dark brown and resinous, wood about the same thickness as the bark, light brown and porous, pith large, more or less hollow, the color being similar to that of the bark. Roots from 1 to 10 cm. in length and from 1 to 2 mm. in diameter; externally dark brown to purplish-brown, smooth and faintly longitudinally wrinkled; fracture short; internally with a thick, brownish-black bark and small, light brown central cylinder. Nearly odorless; taste very bitter and acrid.

"The powder is brown to yellowish-brown; odor strong, penetrating; consisting of numerous irregular fragments, many of them being colored pink or violet upon the addition of hydrated chloral T.S.; starch grains numerous, mostly in the parenchymatous cells, the individual grains nearly spherical or more or less polygonal, and from 0.002 to 0.008 mm. in diameter; tracheæ with spiral thickenings or with simple or bordered pores; wood fibers with thick lignified walls, with simple pores or with bordered pores, resembling tracheids; fragments of parenchyma containing a light brown or brownish-black resin, the latter frequently closely coherent with the starch grains in the cells thus preventing the separation of the individual starch grains; mounted in hydrated chloral T.S., occasional elongated cells with a lemon yellow, oily substance are observed. Leptandra yields not more than 12 per cent. of ash." *N. F.* For a microscopical description of leptandra, by A. P. Breithaupt, see *A. J. P.*, 1897, 235.

Water and alcohol extract the virtues of the root. According to E. S. Wayne, of Cincinnati, it contains a peculiar crystalline principle, *leptandrin*, to which the virtues of the medicine may be ascribed. F. F. Mayer confirmed the presence of the crystalline principle, and classed it as a glucoside, but Power and Rogerson (*Tr. Chem. Soc.*, 1910, xcvi) were unable to find any such principle. The resinous matter obtained by making a tincture of the root and precipitating this with water has been improperly called *leptandrin*, and considered the active principle. Subsequently Wayne obtained from the root a saccharine principle having the properties of *mannite*. (*A. J. P.*, 1859, p. 557.) G. Steinmann (*A. J. P.*, 1887, p. 229) obtained pale lemon-yellow crystals of a peculiar agreeable odor and a very bitter taste. They were not precipitated from solution by Mayer's reagent or by tannin, and did not yield glucose on being boiled with diluted sulphuric acid.

The recent root is said to act violently as a cathartic, and sometimes as an emetic. In the dried state it is much milder, but less certain. The practitioners calling themselves eclectics consider it an excellent cholagogue, and use both the impure resin, which they call leptandrin, and the root itself as a substitute for mercurials. Rutherford, in his experiments upon dogs, found leptandrin to act rather feebly upon the liver. The powdered extract and fluidextract are recognized by the N. F. (see Part III). *Dose*, fifteen to sixty grains (1–3.9 Gm.); of the impure resin, two to four grains (0.13–0.26 Gm.).

Leucofermantin.—This is stated to be obtained from the blood serum of animals immunized against trypsin. It has been used in the treatment of various suppurative diseases, as *otitis media*, *tuberculous abscesses*, and *boils*. It is injected directly into the suppurating area in quantities ranging from 1 to 15 mils (8–25 minims) according to the size of the purulent tract.

Levisticum. *Radix Levistici*, P. G. *Livèche. Ache de Montagne*, Fr. *Liebstöckel*, G.—Several species of this umbelliferous genus are employed as domestic remedies. The stout perennial herb, *Levisticum officinale* (L.) Koch, or *lovage*, of the south of Europe, is extensively cultivated for its aromatic fruits. It is aromatic in all its parts, but only the roots and fruits are used. The fruits are small, ovate-oblong, somewhat flattened, curved, strongly ribbed and of a yellowish-brown color. Lovage is a stimulant aromatic, and has been employed as a carminative, diaphoretic, and emmenagogue. The best form for administration is that of infusion. The coloring principle has been isolated by M. J. Nicklés, who gives it the name of *ligulin*, and suggests an important application of it that may be made in testing drinking water. If a drop of its alcoholic or aqueous solution is allowed to fall into distilled water, it imparts to the liquid its own fine crimson-red color, which undergoes no change; but if limestone water be substituted, the red color disappears in a few seconds, and is followed by a beautiful blue, due to the alkalinity of the latter. (*J. P. C.*, 1859, 329.) The root of *Ligusticum sinense*, under the name of *kao-pên*, is largely used by the Chinese. In the Northwestern United States the large aromatic roots of *Ligusticum filicinum* S. Wats., *Osha Colorado cough-root*, are used to a considerable extent as stimulating expectorants. (See *A. J. P.*, 1890 and 1891.)

Lewisia. *Lewisia Rediviva* Pursh. *Spathum. Chita. Bitter Root.*—The roots of this plant, of the Fam. *Portulacaceæ*, abundant in the Northwestern United States, are very widely used by the Indians as an article of food. For analysis and description, see *A. J. P.*, 1889.

Liantral. *Lianthral.*—This substance is an extract of coal tar, obtained by treating with benzene, filtering from insoluble residue, and subsequently evaporating the benzene at a temperature not exceeding 80° C. (176° F.). It is a brownish-black viscous fluid which is insoluble in water, freely soluble in benzene, but dissolving only sparingly in fats, ethereal oils, alcohol, ether, acetone, petroleum benzin, and mixtures of these substances. *Liantral* has been commended by various clinicians as a substitute for coal and wood tars in the treatment of *eczema* and allied skin diseases. It is said to resemble wood tar in its action, but to be more energetic. It has been used in ten per cent. solution with olive oil, applied with a brush, or in the form of a dusting powder made by triturating to dryness with the aid of starch, or talc.

Liatris. *L. spicata* (L.) Willd. *Gay-feather. Devil's Bite. Colic Root. Button Snakeroot.*—An indigenous perennial composite plant growing in natural meadows and moist grounds from Southern Ontario and Minnesota, southward. It has a tuberous root, and an erect annual stem, which terminates in a spike of beautiful, purple, compound flowers, appearing in August. The root is said by Schoepf to have a terebinthinate odor,

and a warm, bitterish, terebinthinate taste; to be possessed of diuretic properties; and to be useful as a local application in *gonorrhea* and *sore throat*. The leaves of the allied *Trilisa odoratissima* (Walt.) Cass. (*Liatris odoratissimus* Willd.), or *Vanilla leaf*, are very largely employed in the Southern United States to flavor tobacco, and to preserve clothing, etc., from moths. As a preservative it is worthless. The agreeable odor is due to *coumarin*, $C_9H_6O_2$, which may be frequently noticed in crystals upon the surface of the smooth spatulate leaves. (*A. J. P.*, March, 1875; Sept., 1881; xlvii, 116; *N. R.*, 1882, 66.) The roots of *L. scariosa* Willd. (*Lacinaria scariosa* Hill) and *L. squarrosa* Willd. (*Lacinaria squarrosa* Hill) (*rattlesnake's master*) have been employed to cure the bite of the rattlesnake. According to Wm. P. C. Barton, all the tuberous-rooted species of *Liatris* are active diuretics.

Libanol.—This is an ethereal oil obtained from the wood of *Cedrus atlantica* Manetti (now *C. Libani* Barr) (Fam. *Pinaceæ*). It is a yellow liquid of pleasant odor and taste, soluble in alcohol and ether and insoluble in water. In diseases of the respiratory organs it is used as an antiseptic expectorant and also as an inhalation. It is claimed to be a valuable substitute for sandal wood oil in the treatment of *gonorrhea*. It has also been used externally in the form of an ointment in the treatment of *rheumatism*. *Dose*, fifteen to forty-five minims (0.9–2.8 mils) several times a day.

Lignol.—This is an oily or tarry substance which is said to be obtained by the dry distillation of a bituminous fossilized wood. *Lignol* is asserted to be in bactericidal power equal to the 5 per cent. solution of phenol, and is recommended in *eczema*, *acne*, *pruritus*, and other chronic skin diseases, and in *doses* of fifteen minims (0.9 mil) in pulmonary *tuberculosis*. Also, in chronic *irritation of the genito-urinary tract*.

Lignosulfit. *Lignosulfin.*—A by-product of the manufacture of cellulose. Its active ingredient appears to be sulphurous acid. It is employed by inhalation of vapors, in the treatment of pulmonary complaints, especially those conditions brought about by *tuberculosis*.

Ligroine. *Ligroïn.*—This name has been applied to a petroleum product which is chiefly used as a solvent. It boils between 100° C. and 120° C. (212°–248° F.) and has a specific gravity varying between 0.707 and 0.722 (64°–68° B.).

Ligustrum. *L. vulgare* L. *Troène*, Fr. *Rainweide, Hartriegel*, G. *Privet* or *Prim.*—A shrub of the Fam. *Oleaceæ*, from four to ten feet in height, growing wild both in Europe and the United States, usually in hedges and by the roadside. The leaves, which have an astringent, bitter taste, and the flowers, which are small, snow-white, and of an agreeable odor, have been used in the form of decoction in *sore throat* and *aphthous* and *scorbutic ulceration of the mouth*. The berries are black, have a sweetish bitter taste, and are said to possess purgative properties, and to color the urine brown. They are sometimes used for dyeing. Death in a child between two and three years old is recorded by James Cheese (*P. J.*, 2d ser., viii, 607), as due to the eating of privet berries. The bark was analyzed by M. G. Polex, who found a peculiar substance, which he denominated *ligustrin*, insoluble in ether and absolute alcohol, but soluble in water and diluted alcohol. Strong sulphuric acid gives with *ligustrin* a deep indigo-blue color. Kromayer (*A. Pharm.* (2), cxviii, 19) proved that Polex's ligustrin was only impure *syringin*, $C_{19}H_{28}O_{10} + H_2O$. The large white crystals become anhydrous at 115° C. (239° F.), and fuse at 212° C. (413.6° F.). He found in addition (see Kromayer, *A. Pharm.*, (2) ci, 281) mannite, sugar, muco-saccharine matter, starch, chlorophyll, bitter extractive, bitter resin, tannin, albumen, and salts. (*A. J. P.*, xii, 347.) Kromayer found besides the *syringin* a crystallized bitter principle, fusing at a little over 100° C. (212° F.), which he named *ligustron*.

Lilium. *Lilium canadidum* L. (Fam. *Liliaceæ*.) *Common White Lily.*—This well-known plant is a native of Southern Europe from Corsica to Asia Minor, but has been long cultivated in gardens. The bulb, which consists of imbricated fleshy scales, is without odor, but has a peculiar, disagreeable, somewhat bitter, and mucilaginous taste. It contains much mucilage, and a small proportion of an acrid principle. In the recent state it is said to have been employed with advantage in *dropsy*. Vomiting, purging, drowsiness, etc., are said to have been produced in a little girl by the pollen of the *tiger lily, L., tigrinum* Andr. (Jeffries Wyman, *Am. J. M. S.*, 1863.)

Lime Juice. *Succus Citri. N. F. IV.*—Under this name the National Formulary IV has very properly provided standards for a liquid which has been largely used and which is often adulterated. It enters into the N. F. preparation *Lime Juice and Pepsin*. It is defined as:

"The expressed juice of the ripe fruit of *Citrus medica acida* (Roxburgh) Bonavia (Fam. *Rutaceæ*), containing in each *one hundred mils* not less than 5 Gm. nor more than 10 Gm. of total acids, calculated as crystallized citric acid [$H_3C_6H_5O_7 + H_2O = 210.08$]." *N. F. IV.*

"Lime Juice is a clear or slightly turbid, pale yellow or yellowish-green liquid, having the characteristic odor and taste of limes. Specific gravity: 1.025 to 1.040 at 25° C. Add 20 mils of solution of sodium hydroxide to 5 mils of Lime Juice in a 100 mil flask and heat on a water bath for ten minutes, with 0.5 Gm. of granular aluminum or aluminum foil; no odor of ammonia is noticeable at any time during the heating (*nitrate*). Add 1 mil of barium chloride T.S. to 5 mils of clear, filtered Lime Juice; only a slight turbidity is produced after standing two minutes (*sulphate*). Add 1 mil of nitric acid, followed by 0.1 mil of silver nitrate T.S. to 5 mils of clear, filtered Lime Juice; only a slight opalescence is produced after standing two minutes (*chloride*). Warm a mixture of 5 mils each of sulphuric acid, alcohol, and Lime Juice; no odor of acetic ether is developed (*acetate*). Add 1 mil of an aqueous solution of potassium acetate (1 in 4) to 5 mils of filtered Lime Juice and then add 15 mils of alcohol to the mixture; a slight cloudiness may occur, but no crystalline precipitate is formed within fifteen minutes (*tartrate*). When evaporated and ignited until free from carbon, Lime Juice leaves not more than 0.5 per cent. of ash. The ash from 5 mils of Lime Juice, when dissolved in a few drops of nitric acid and diluted with distilled water, shows not more than traces of phosphate when tested with ammonium molybdate T.S. Transfer 10 mils of Lime Juice to a flask having a round bottom and a long neck, add 75 mils of distilled water, 5 mils of phosphoric acid and 1 Gm. of sodium bicarbonate and at once connect the flask with a condenser. Distil 50 mils, receiving the distillate under the surface of 25 mils of tenth-normal iodine V.S., acidulate the

distillate with 5 drops of diluted hydrochloric acid, add 1 mil of barium chloride T.S. and heat on a water bath until the liquid is nearly colorless. The precipitate of barium sulphate, if any, when filtered, washed, and ignited, weighs not more than 0.015 Gm., corresponding to not more than 0.04 Gm. of sulphur dioxide in 100 mils of Lime Juice, correction being made for any sulphate which may be present in the 25 mils of tenth-normal iodine V.S. To 200 mils of Lime Juice add an excess of calcium hydroxide and distil the liquid until the distillate measures 100 mils; the specific gravity of the distillate indicates not more than 2 per cent. of absolute alcohol, by volume, in the distillate, corresponding to 1 per cent. in the Lime Juice (limit of *alcohol*). Add to 10 mils of Lime Juice, 1 mil of diluted sulphuric acid, then shake it with 25 mils of ether, separate the ether and evaporate it to dryness; the residue is not crystalline, and, when dissolved in 3 mils of distilled water and carefully neutralized with ammonia water, produces neither a pink precipitate nor a purplish color on the addition of 1 drop of ferric chloride T.S. (*benzoic or salicylic acid*). Dilute 20 mils of Lime Juice with 100 mils of distilled water, filter, if necessary, and add 4 mils of diluted hydrochloric acid. Boil a piece of wool in a very dilute solution of potassium hydroxide T.S., wash with distilled water until free from alkali, then add the washed wool to the Lime Juice solution just prepared and boil for ten minutes. Remove the wool, wash thoroughly in distilled water, and boil in a very dilute solution of hydrochloric acid. After washing out the acid with distilled water, boil with about 200 mils of 2 per cent. solution of ammonium hydroxide until the color on the wool, if any, is dissolved. Remove the wool, add a slight excess of hydrochloric acid to the ammonia solution, and immerse in this solution another piece of wool which has been treated with potassium hydroxide solution in the manner described above. This second piece of wool should not be dyed (*artificial dyes*).

"*Assay.*—Measure accurately 25 mils of Lime Juice, dilute it with 50 mils of distilled water and titrate the solution with normal potassium hydroxide V.S., phenolphthalein T.S. being used as indicator. Not less than 17.8 mils nor more than 35.7 mils of normal potassium hydroxide V.S. is required, indicating the presence of not less than 5 Gm. nor more than 10 Gm. of crystallized citric acid in 100 mils of the Lime Juice.

"Each mil of normal potassium hydroxide V.S. corresponds to 0.07003 Gm. of citric acid ($C_6H_8O_7 + H_2O$). Each mil of Lime Juice requires not less than 0.713 mil nor more than 1.428 mils of normal potassium hydroxide V.S." *N. F. IV.*

Lime juice has the same medicinal virtues as lemon juice (see *Succus Limonis*, Part I), to most palates, however, its flavor is less agreeable.

Limonene.—This terpene, $C_{10}H_{16}$, which is found in many volatile oils, has an odor resembling that of Oil of Lemon. It has been suggested by Kobert as a substitute for Oil of Turpentine. Zickgraf (*M. M. W.*, 1910, lvii) has used it with good effects in fetid *bronchitis, bronchiectasis, gangrene of the lung,* and *pulmonary tuberculosis.* He asserts that it is not only much more pleasant to the patient than is oil of turpentine, but is more efficient and less irritant to the kidneys. It may be administered either by inhalation or internally. The *dose* is ten to twenty drops (0.6–1.3 mils) three times a day.

Linalyl Acetate Thiozonide. $C_{12}H_{20}O_2S_3$.—This compound has been used by Knorr as a local application in various gynecological conditions.

Linaria. *Linaria vulgaris* Hill. *Antirrhinum Linaria* L. *Common Toadflax. Butter and Eggs. Ramsted. Snapdragon. Linaire commune,* Fr. *Leinkraut, Flachskraut, Löwenmaul,* G.—This is a perennial herbaceous plant of the Fam. *Scrophulariaceæ* very common in America, Europe, and Asia. It should be collected when in flower, dried quickly, and kept excluded from the air. When fresh it has a peculiar, heavy, disagreeable odor, which is in a great measure dissipated by drying. The taste is herbaceous, weakly saline, bitter, and slightly acrid. Its constituents are stated to be two glucosides, *linarin* and *pectolinarin* (*P. J.*, lxxix, p. 316), with limarosnin, linaracrin, antirrhinic, tannic and citric acid. This plant is said to be diuretic and cathartic, and has been used in *dropsy, jaundice,* and *cutaneous eruptions.* It is most conveniently employed in infusion. The fresh plant is sometimes applied, in the shape of poultice or fomentation, to *hemorrhoids,* and an ointment of the flowers has been employed for the same purpose, and also locally in diseases of the skin. The flowers are used in Germany as a yellow dye.

Linden.—Boussingault calls attention (*J. P. C.*, 4e sér., xv) to a saccharine exudation which occurs upon the leaves of the European *Linden* (*Tilia europœa* L.), which he has found to have the same composition as manna of Mount Sinai.

Lint. *Linteum Carptum. Charpie,* Fr., G.—The term *lint* is applicable to a substance prepared from linen. It is in fact linen made soft and somewhat fleecy by various mechanical processes, so as to render it suitable for the dressing of wounds. The qualities required in good *lint* are—(1) perfect softness, to prevent mechanical irritation to the wound; (2) looseness of texture, to render it capable of absorbing the secretions from the surfaces to which it is applied; (3) a certain tenacity, so that it may receive unctuous dressings, yet with a facility of being torn in one direction; and (4) sufficient firmness of fiber to prevent small portions from being easily separated and remaining as foreign bodies in the wound. As formerly made for domestic purposes, from old linen scraped by means of a knife with the hand, it was unfit for general surgical use. A useable quality, however, was made from old linen thoroughly cleansed by machinery. This was first cleansed thoroughly by washing with soap and water, or by boiling with a weak lye of soda or pearlash. Sometimes, when colored, it was bleached before being washed. Thus prepared, it was operated on by a simple machine, in which the rag, wrapped round a cylinder, was submitted to the interrupted action of a knife made to descend upon it at intervals of one-eighth of an inch, so as to cut the thread in one direction. On being removed from the machine, the cut ends of the thread became untwisted and loose, giving a flossy character to the fabric. To render it smooth, it was passed through rollers, and its ragged edges were trimmed. Of course, it had different degrees of fineness, according to the character of the rags used, and this diversity rendered it fit for different purposes, the finer pieces being used merely as a dressing with unctuous matter to exclude the air, while the thicker were better adapted to the absorption of the liquid secretions.

In the progress of improvement, machines were invented and patented for manufacturing lint on the large scale. This so-called *patent lint* has almost completely displaced the older kind. It is generally prepared out of cloth manufactured for

the purpose, and therefore has whatever advantage may be derived from uniformity of shape and consistence. In other respects it is doubtful whether it has any superiority over the old-fashioned article; especially as, in consequence of competition, cotton, being the cheaper article, has frequently been in part or altogether substituted for linen. It is said that lint may be rapidly prepared by attaching a piece of linen to the toothed cylinder of the common carding machine, used in mills.

Cotton is in several respects inferior to linen for the preparation of lint, and, unless its presence in any manufactured article sold by this name be made known, it should be looked on as a fraudulent substitution. Its fiber is less soft and therefore more likely to irritate. it has much less absorbing power, and it conveys heat less rapidly. The following are methods by which it may be distinguished (Elsner): (1) A linen thread when held erect, and set on fire, appears, after the flame is extinguished, in a smooth continuous form, while cotton thread similarly treated has a tufted aspect. (2) Under a microscope which magnifies 300 diameters, the linen fiber appears to be a straight nearly solid cylinder, with a slender central canal; the cotton, flattened as a piece of tape, with a wide canal, and often twisted like a corkscrew. (3) The potassium test, proposed by Böttger, consists in exposing the doubtful substance to the action of a boiling concentrated solution of potassium hydroxide. If made of linen, it will in two minutes assume a deep yellow color; if of cotton, it will either remain colorless, or will become very faintly yellow, and if the texture be composed of both, it will exhibit a streaked or mottled aspect. The examination must be quickly made, as the yellow color of the potassium becomes faint with time. (4) Sulphuric acid dissolves the linen fiber, while it leaves that of cotton little changed. (5) Linen thoroughly oiled has the transparent appearance of oiled paper; cotton remains white and opaque. (6) Tinctures of the vegetable red dye-stuffs, as cochineal, madder, etc., will give a much deeper color to linen than to cotton, and cause a mottled appearance when the two are mixed.

Tow, and hemp in the state of *oakum*, have been employed for dressing wounds; but they are only applicable as exterior dressings to absorb the pus, when the discharge of this is very copious. L. A. Sayre prefers picked oakum to lint as more absorbent. (*B. M. S. J.*, lxvii, 84.) *Charpie*, so much used by French surgeons, generally consists of bundles of straight threads, each four or five inches long, made by unravelling old and rather coarse linen.

Linum catharticum L. *Purging Flax.*—Purging flax is an European annual of the Fam. *Linaceæ*, six to eight inches high. The whole plant is very bitter and somewhat acrid, and imparts its virtues to water, which acquires a yellow color. It appears to owe its activity to a peculiar drastic principle, which has received the name of *linin*, and which is afforded most largely by the plant after the flower has fallen. Schroeder (*N. R. Pharm.*, xi, 11) obtained it in lustrous, white, silky crystals, which are neutral in reaction and have a strong persistent bitter taste in alcoholic solution. Purging flax has enjoyed some reputation in Europe as a gentle cathartic, useful in *muscular rheumatism*, *catarrhal affections*, and *dropsy* with disease of the liver. *Dose*, of the extract, from four to eight grains (0.26–0.5 Gm.); of the powder, one drachm (3.9 Gm.).

Lipoiodine. *Di-iodo-brassidinic acid ethyl ester.* $C_{19}H_{39}CI$: CI : $ICCOOC_2H_5$.—This occurs as white needles, melting at 37° C. (98.6° F.), readily soluble in alcohol, ether, chloroform and fatty oils, but insoluble in water. Its solution undergoes slow decomposition with the liberation of iodine. It is said to represent 41 per cent. of iodine. Loeb and Velden (*Th. M.*, 1911) assert that this preparation is absorbed unchanged from the intestinal tract, but that after absorption it undergoes slow decomposition, and thereby exercises a continuous iodine effect. They recommend it as a substitute for the alkaline iodides in *doses* of from five to twenty-five grains (0.32–1.7 Gm.).

Lippia.—A number of the species of this genus (Fam. *Verbenaceæ*) contain aromatic oils, and several have been used in popular medicine. The *L. citriodora*, H. B. K., yield verbena oil, and is commonly known as *Lemon verbena*. From the *L. mexicana*, Podwissotzki (*Proc. A. Ph.* A., 1886) separated an essential oil somewhat resembling that of fennel, as well as a camphor-like substance which he named *lippioil*. According to Maisch (*A. J. P.*, xxlvii, p. 330), however, the plant used by Podwissotzki was probably the *Cedronella mexicana* (Benth.). Power and Tutin (*A. Pharm.*, 1907, ccxlv, p. 337) found in the *L. scaberrima* (Sonder), a native of South Africa, where it is popularly known as *Beukess boss*, an essential oil somewhat resembling lavender in its odor, a peculiar crystalline substance, which they named *lippianol*, having the qualities of a monohydric alcohol, and a number of other substances not peculiar to the plant.

Liquidambar. *Liquidambar Styraciflua* L. *Sweet Gum.*—An indigenous tree (Fam. *Hamamelidaceæ*), growing in different parts of the United States from Connecticut to Florida, and flourishing also in Mexico and Central America, where, as well as in our Southern States, it sometimes attains a great magnitude. In warm latitudes a balsamic juice flows from its trunk when wounded. This has attracted some attention in Europe, where it is known by the name of *liquidambar* or *copalm balsam*, and is sometimes, though erroneously, called *liquid storax*. It is not afforded by the trees which grow in the Middle Atlantic States, but is obtained in the Western States bordering on the Ohio, and southward as far as Central America. It is a liquid of the consistence of thin honey, more or less transparent, of a yellowish color, of a peculiar, agreeable, balsamic odor, and a bitter, warm, and acrid taste. By cold it becomes thicker and less transparent. It concretes also by time, assuming a darker color. It is sometimes collected in the form of tears, produced by the spontaneous concretion of the exuded juice. According to Bonastre, it contains a colorless volatile oil, a semi-concrete substance which rises in distillation and is separated from the water by ether, a minute proportion of benzoic acid, a yellow coloring substance, an oleoresin, and a peculiar principle, insoluble in water and cold alcohol, for which Bonastre proposed the name of *styracin*. The styracin of Bonastre has since been found to be *cinnamyl cinnamate*, $(C_9H_9)C_9H_7O_2$, which is found together with the ethyl, benzyl, and other esters of cinnamic acid. Examined by W. P. Creecy, of Mississippi, it was found to contain cinnamic acid as the prominent acid ingredient, besides a volatile, odorous principle melting at 65° C. (149° F.), and smelling of vanillin, and 30 per cent. of a hard resin (according to W. von Miller, *storesin*, $C_{36}H_{55}(OH)_3$). If the storesin be repeatedly extracted with diluted potassium hydroxide solution, it is separated into *a-storesin*,

which is amorphous and melts at from 160° to 168° C. (320°–334.4° F.), and *β-storesin*, which forms white flocks melting at from 140° to 145° C. (384°–393° F.). Of these, the β-resin is first extracted, while the residue is nearly pure α-resin. The volatile oil mentioned above contains a hydrocarbon, *styrol*, *styrene* or *cinnamene*, C_8H_8, which changes on heating into the polymeric *metastyrol*, a colorless, transparent solid. The results of W. L. Harrison, confirmed by Maisch (*A. J. P.*, xlvi, 160, 165), seem to prove that the American drug is identical with storax, except in containing no water mechanically mixed with it.

Another product is said to be obtained from the same tree by boiling the young branches in water, and skimming off the fluid which rises to the surface. It is of thicker consistence and darker color than the preceding, is nearly opaque, and abounds in impurities. This also has been confounded with liquid storax, which it resembles in properties, though derived from a different species of *Liquidambar*. It is said to be used in Texas in *coughs*. (Gammage, *N. O. M. S. J.*, xii, 636.) For an account of the collection of American storax, see *Ph. Rund.*, 1895, 57.

Liquidambar may be employed for the same purpose as storax, and is so used in the Southern United States, but it is almost unknown in the Northern States. The concrete juice is said to be chewed in the Western States in order to sweeten the breath. The bark of the tree is used with asserted great advantage in the Southern and Western States in *diarrhea* and *dysentery*, especially in children. It is taken in the form of syrup, which may be prepared from the bark in the same manner as the syrup of wild cherry bark, according to the U. S. Pharmacopœia. The *dose* is a fluidounce (30 mils) for an adult, repeated after each stool. (*Ann. J. M. S.*, N. S., xxxii, 126.)

Liquidambar Altingia (*Altingia excelsa*), a tree which inhabits a very wide region in Southern Asia, yields a storax-like substance varying in color from white to red. (See *P. J.*, viii, 243.) According to Tschirch and van Itallie, it differs from storax in the presence of benzoic and cinnamic aldehydes, the absence of ether and the small quantities of cinnamic acid in it. *Liquidambar storesin* is said also to be known in Eastern markets.

Liriodendron. *Liriodendron Tulipifera* L. *Tulip Tree. American Tulip-poplar Tree.* (Fam. *Magnoliaceæ*). *White Tulip Bark. Ecorce de Tulipier*, Fr. *Tulpenbaumrinde*, G.—The tulip poplar is a large tree which is abundant in rich soil in the forests from Southern Ontario to Wisconsin and extending into the Southern States, the timber being commonly known as Poplar or White Wood. Its formerly official bark was taken for use indiscriminately from the root, trunk, and branches, though that of the root is thought to be the most active. Deprived of the periderm, it is yellowish-white, the bark of the root being somewhat darker than that of the stem or branches. It is very light and brittle, of a feeble, rather disagreeable odor, strongest in the fresh bark, and of a bitter, pungent, and aromatic taste. These properties are weakened by age, and we have found specimens of the bark, long kept in the shops, almost insipid. Emmet believed the active principle to be the substance discovered by him and named *liriodendrin*. It is white, crystallizable, brittle, insoluble in water, soluble in alcohol and ether, fusible at 82.2° C. (180° F.), volatilizable and partly decomposed at 132.2° C. (270° F.), of a slightly aromatic odor, and a bitter, warm, pungent taste. It does not unite either with acids or alkalies, and the latter precipitate it from the infusion of the bark by combining with the matter which renders it soluble in water. Water precipitates it from its alcoholic solution. It is obtained by macerating the root in alcohol, boiling the tincture with magnesia until it assumes an olive-green color, then filtering, concentrating by distillation until the liquid becomes turbid, and finally precipitating the liriodendrin by the addition of cold water. (*A. J. P.*, iii, 5.) J. U. Lloyd believes that the active principle is the alkaloid *tulipiferine*, discovered by him in 1886, and this, according to Bartholow, appears to possess toxic properties. (*Ph. Rund.*, 1886, 169.) The virtues of the bark are extracted by water and alcohol, but are injured by long boiling.

Liriodendron is a stimulant tonic, with diaphoretic properties, and has been used in chronic *rheumatism* and *dyspepsia*. *Dose*, of bark in powder, from half a drachm to two drachms (2.0–7.7 Gm.); of saturated tincture, a fluidrachm (3.75 mils).

Lithio-mercuric Iodide. $3LiI + HgI_2$.—Under the name of *mercuricide*, a compound iodide of the above formula has been brought out as a germicide. It is soluble without decomposition in water, alcohol and ether, and crystallizes in lemon-yellow crystals which are deliquescent. It is alleged that it is as actively germicidal as corrosive sublimate, but is not corrosive, less poisonous and not precipitable by blood serum, albumins or alkalies.

Mercury and Lithium Iodide, or *Hydrargyrum-Lithium Iodatum* of Merck, is a red and granular crystalline powder of the formula $HgI_2.2LiI$. It is soluble in alcohol or ether, but wholly incompatible with water, forming a cloudy mixture which soon precipitates mercuric iodide. It has been used in Germany as an antisyphilitic, antilithic alterative, and especially in *gravel* complicated with *syphilis*.

Lithium Agaricinate.—A white powder of a slight saline taste easily soluble in water. It is used as an anhydrotic in the treatment of phthisical *night sweats*. *Dose*, one and one-half to three grains (0.096–0.21 Gm.).

Lithium Arsenate. $2Li_3AsO_4 + H_2O$.—A white powder soluble in water. It is employed for the same purposes as other arsenicals. *Dose*, one-sixtieth to one-fifteenth of a grain (0.001–0.004 Gm.).

Lithium Benzoate. *Lithii Benzoas. U. S. VIII. Lithium Benzoicum. Benzoate de Lithine*, Fr. Cod. *Benzoësaures Lithium, Lithiumbenzoat*, G. *Benzoato Litico*, Sp.—"It should contain not less than 98.5 per cent. of pure Lithium Benzoate [$C_6H_5.CO OLi$], and should be kept in well-stoppered bottles." *U. S. VIII.*

This salt of lithium is made by decomposing lithium carbonate with benzoic acid. E. B. Shuttleworth deviates from the usual method of first making a hot solution of benzoic acid and then adding carbonate until effervescence ceases, by reversing the order. One ounce (av.) of lithium carbonate is put into a dish with nine fluidounces of water, the mixture is heated, and three and a quarter ounces (av.) of benzoic acid in small portions added, until the carbonate is all decomposed and effervescence ceases; the solution is filtered and evaporated to dryness, or crystallized if desired. The yield is three and a half ounces. The advantage of this process is a saving in time and labor in evaporating:

$$Li_2CO_3 + 2HC_7H_5O_2 = 2LiC_7H_5O_2 + H_2O + CO_2$$

Properties.—It was officially described as a "light, white powder, or small, shining, crystalline scales; odorless, or of faint benzoin-like odor, and of a cooling, sweetish taste; permanent in the air. Soluble in 3 parts of water, and in 13 parts of alcohol, at 25° C. (77° F.); in 2.5 parts of boiling water, and in 10 parts of boiling alcohol. Its solubility in water is increased by the presence of sodium benzoate, but lessened when alcohol is in the solvent. When heated, the salt fuses; at a higher temperature it chars, emits inflammable vapors having a benzoin-like odor, and finally leaves a residue of lithium carbonate mixed with carbon. This residue imparts a crimson color to a non-luminous flame, and its aqueous solution has an alkaline reaction upon litmus paper. The aqueous solution (1 in 20) of Lithium Benzoate has an alkaline reaction upon litmus, but is neutral to phenolphthalein T.S. The addition of a few drops of ferric chloride T.S. to the above solution will produce a voluminous flesh-colored precipitate of ferric benzoate. If an excess of hydrochloric acid be added to a concentrated aqueous solution of 0.6 Gm. of Lithium Benzoate, a white precipitate of benzoic acid will be formed, which, after collecting upon a filter and thoroughly washing and drying, should respond to the tests of purity given under *Acidum Benzoicum*. If the filtrate and washings from this precipitate be evaporated almost to dryness on a water-bath, in a flat-bottomed flask of 50 Cc. capacity, and 10 Cc. of amyl alcohol (boiling point 132° C.) be added, and the mixture cautiously heated until the lower aqueous layer has evaporated, then, after the addition of 3 drops of hydrochloric acid and boiling for three minutes, the resulting insoluble residue should weigh not more than 0.004 Gm. (limit of *other alkalies*). The removal of the water from the amyl alcohol mixture is facilitated by passing a current of air through the hot solution. If 1 Gm. of the salt be dissolved in 20 Cc. of water, and the benzoic acid precipitated by the addition of a sufficient quantity of hydrochloric acid, the filtrate should respond to the following tests of purity: The addition of ammonia water until the solution has an alkaline reaction should produce neither turbidity nor precipitation, either before or after boiling (limit of *iron, aluminum*, etc.). Another portion of this solution should not respond to the Time-Limit Test for *heavy metals* (see Part III). If 0.5 Gm. of Lithium Benzoate be thoroughly mixed with about 1 Gm. of powdered anhydrous ammonium sulphate and cautiously ignited in a porcelain crucible, until of constant weight, the residue should weigh not less than 0.210 Gm., nor more than 0.216 Gm." *U. S. VIII.* Curtman stated that much of the *lithium benzoate* in the market contains not only sodium benzoate, but also hippurate, derived from urine-benzoic acid. This renders it much more soluble in water than the pure salt, and also more soluble in alcohol. The precipitated benzoic acid should melt at 121.4° C. (250.52° F.); hippuric acid, if pure, melts at 187.5° C. (369.5° F.). Hence a high melting point for the separated benzoic acid points to this source of contamination. Lithium benzoate possesses the therapeutic properties of sodium benzoate, over which, however, it has no advantage. *Dose*, from fifteen to thirty grains (1–2 Gm.).

Lithium Bitartrate. $LiC_4H_5O_6 + H_2O$.—White crystals soluble in water. It is used in the treatment of *gouty conditions* and *suppurative gingivitis*.

Lithium and Caffeine Sulphonate.—Under the trade name *symphorol* this compound was advanced as a diuretic. It is a white micro-crystalline powder of bitter taste and soluble in water. Its solution is not permanent. *Dose*, fifteen grains (1.0 Gm.) several times daily.

Lithium Dithiosalicylate. $LiC_7H_4O_3S$: $SC_7H_4O_3Li$.—A gray powder soluble in water and alcohol. It is used as an antirheumatic and antilithic. *Dose*, three to ten grains (0.2–0.65 Gm.).

Lithium Hippurate. $LiC_9H_8NO_3$.—A white powder slowly soluble in hot water and used in *uric acid diathesis*. *Dose*, five to twenty grains (0.32–1.3 Gm.).

Lithium Iodide (LiI = 133.86) may be prepared by taking of iodine 127 parts, iron, in filings, 35 parts, lithium carbonate 38 parts, distilled water 300 parts. Prepare a solution of ferrous iodide, using the whole of the distilled water, filter, add the lithinum carbonate to the still warm liquid, and heat gently to promote complete decomposition. The liquid must be slightly alkaline. Filter, wash the precipitated ferrous carbonate, add the washings to the filtrate, evaporate the latter, pour it out to cool and harden, and immediately transfer it into well-dried, glass-stoppered vials. It forms a white salt very soluble in water and alcohol. One gramme of it is entirely precipitated by 1.27 Gm. of silver nitrate.

Lithium Phenolsulphonate. *Lithium Sulphocarbolate.* $LiC_6H_5SO_4 + H_2O$.—A white crystalline powder soluble in water. It is used internally in *uric acid diathesis* and externally as an injection in *gonorrhea*.

Lithium Quinate. *Urosine.*—This is a mixture of lithium citrate and quinic acid containing 80 per cent. of the latter and 20 per cent. of the former. It is used in *uric acid diathesis* and as an antirheumatic.

Lithium Salicylate. *N. F. IV* (*U. S. P. VIII*). *Lithii Salicylas. Salicylate de Lithine*, Fr. Cod. *Lithium Salicylicum*, P. G. *Lithiumsalicylat*, G. *Salicilato de Litina*, Sp.—"It contains, when dried to constant weight at 120° C., not less than 98.5 per cent. of $LiC_7H_5O_3$ (143.98). Preserve it in well-closed containers, protected from heat and light." *N. F.*

No process is given in the N. F. for making this official salt. It may be prepared by adding to a mixture of eleven parts of salicylic acid and three parts of lithium carbonate twenty-five parts of water, and heating until effervescence ceases, filtering and evaporating. It may be obtained in crystals but is usually seen in the form of a granular powder.

"Lithium Salicylate occurs as a white or grayish-white powder; deliquescent in a moist atmosphere; odorless; taste sweetish. It is very soluble in water or alcohol. When heated, the salt is decomposed, emitting the odor of phenol, and finally leaving a residue of lithium carbonate and carbon. It imparts a crimson color to a non-luminous flame. An aqueous solution of the salt (1 in 20) is neutral or slightly acid to litmus, and when freshly made is colorless (*iron and organic coloring matter*); it does not effervesce upon the addition of diluted acids (*carbonate*). Copper sulphate T.S. added to an aqueous solution of the salt (1 in 20) produces a bright green color. Add a few drops of ferric chloride T.S. to an excess of an aqueous solution of the salt (1 in 4); a deep red color is produced. In a dilute solution of the salt (1 in 100) ferric chloride T.S. produces a deep violet-blue color. Hydrochloric acid added to an aqueous solution of the salt (1 in 20) produces a voluminous white

precipitate of salicylic acid. Dissolve 0.7 Gm. of the salt in 10 mils of distilled water, add an excess of hydrochloric acid and filter. Evaporate the filtrate almost to dryness on a water bath, in a 50 mil Erlenmeyer flask, and then add 10 mils of amyl alcohol and cautiously heat until the lower aqueous layer is evaporated; then add three drops of hydrochloric acid and boil the liquid for three minutes; the insoluble residue weighs not more than 0.005 Gm. (*other alkalies*). (The removal of the water from the amyl alcohol mixture is facilitated by passing a current of air through the hot solution.) Dissolve 1 Gm. of the salt in 50 mils of distilled water, precipitate the salicylic acid by the addition of a slight excess of hydrochloric acid and filter; the filtrate does not respond to the Test for heavy metals (see U. S. P. Test, No. 3, Part III)."

Assay.—"Incinerate in a porcelain crucible about 2 Gm. of Lithium Salicylate, previously dried to constant weight at 120° C. (248° F.) and accurately weighed, and proceed as directed under the Assay for alkali salts of organic acids (see U. S. P., Test No. 6, Part III). It shows in the dried salt, not less than 98.5 per cent. of $LiC_7H_5O_3$. Each mil of half-normal sulphuric acid V.S. used corresponds to 0.07199 Gm. of $LiC_7H_5O_3$. Each gramme of Lithium Salicylate, previously dried, at 120° C. (248° F.) corresponds to not less than 13.7 mils of half-normal sulphuric acid V.S." *N. F.*

The proportion of lithium in this salt is too small to sensibly modify the action of the salicylic acid. It may be used for the same purposes as the other salicylates.

Dose, ten to twenty grains (0.6–1.3 Gm.).

Lithium Salolo-phosphite. *Lithii Salolo-phosphis.* $C_6H_4\begin{cases}O.PO(OH)(OLi)\\COOC_6H_5\end{cases}$.—*Salvosal-Lithia*, the lithium salt of *salolorthophosphorous acid*, is a white crystalline compound, soluble in cold water but decomposed by boiling water with a phenol-like odor. This substance and the allied one known as *salvosal-potash* have been used in *doses* of four to five grains (0.26–0.32 Gm.) in *influenza* and *gouty conditions;* the half of one per cent. solution has been commended as a mouth wash.

Lithium Sozoiodolate.—This salt forms crystals or crystalline plates that are sparingly soluble in water. It is used as an antirheumatic in the place of the salicylates.

Lithium Valerate. *Lithium Valerianate.* $LiC_5H_9O_2$.—White crystals possessing the characteristic valerian odor. It is soluble in water and is used in the treatment of *rheumatism* accompanied *by nervousness. Dose*, five to fifteen grains (0.32–1.0 Gm.).

Lithospermum. *Lithospermum officinale* L. *Common Gromwell. Milium Solis.*—A European perennial, also found along roadsides and pastures of Canada and the northern United States, of the Fam. *Boraginaceæ*, the seeds of which are ovate, of a grayish-white or pearl color, shining, rather larger than millet seeds, and of a stony hardness, from which the generic name of the plant originated. They were formerly used as stimulant diuretics, but are nearly inert.

Lithræa. *Lithræa venenosa* Miers. (Fam. *Anacardiaceæ*).—The leaves of this Chilian plant are said to act upon the skin in a manner similar to *Rhus toxicodendron*, and to contain a resin and an ethereal oil. The tincture of the fresh leaves has been used as a counter-irritant.

Litmus. *Lacmus. Turnsole. Tournesol. Lacca Cœrulea. Lacca Musica. Laquebleu*, Fr. *Lackmus*, G.—Three purple or blue coloring substances are known in commerce, obtained from lichenous plants. They are called severally *litmus, orchil*, and *cudbear. Litmus* is yielded by numerous species of lichens which, under the French name of *orseille*, are brought into commerce from the coasts of Sweden and Norway; from the Alps, the Pyrenees, and other European mountains; from the European and African coasts of the Mediterranean; from the Canaries, Madeira, and various other rocky islands, especially from Mozambique, Madagascar, and Angola, and from California. The species of lichens concerned represent various genera; at present the two most important of the lichens are said to be the *Rocella Montagnei* of Mozambique and the *Dendrographa leucophœa* of California. In the north of Europe *Lecanora tartarea* Ach., or *Tartarean moss*, and on the Mediterranean coasts the *Roccella tinctoria* Ach., or *orchilla weed*, at one time furnished the great bulk of the orseille of commerce. The chromogenous ethers which constitute the coloring matter of the lichens may be readily detected *in situ* by reagents. (*P. J.*, Nov. 19, 1904.) In some of the lichens these coloring principles are chiefly situated in the cortex; in others they are especially abundant in the gonidial layer.

The principles in these plants upon which their valuable properties depend are themselves colorless, and yield coloring substances by the reaction of water, air, and ammonia. They are generally acids or acid anhydrides, and are named *lecanoric, orsellic, erythric*, etc., according to their origin. *Lecanoric* (*diorsellinic*) *acid*, $C_{16}H_{14}O_7$, the original constituent of most of these plants, when boiled with water or alkaline solutions, is changed into *orsellinic acid*, as follows:

$$C_{16}H_{14}O_7 + H_2O = (C_8H_8O_4)_2$$

Orsellinic acid, $C_6H_2\begin{cases}CH_3\\(OH)_2\\COOH\end{cases}$, fuses at 176° C. (348.8° F.), and decomposes into *orcin*, $C_6H_3(CH_3)(OH)_2$, and CO_2. The same decomposition is readily effected by distillation with milk of lime. Orcin combines with ammonia gas to form $C_8H_8O_2.NH_3$, the solution of which exposed to the air becomes colored reddish by the formation of *orcëin*, $C_7H_7NO_3$. This latter compound forms the basis of the commercial *orseille* extract (*orchil* or *archil*).

Kane described a deep red crystalline substance, *erythrolitmin*, and a brownish-red coloring principle, *azolitmin*, $C_7H_7NO_4$. This latter is considered as the distinctive coloring matter of the commercial litmus, and is now found in commerce under that name and is used as an indicator. It is nearly insoluble in cold water or benzene, but dissolves in alcohol with red, and in ether with yellow color. It appears to have the characters of a weak acid, the salts of which are blue and the potassium and calcium compounds of which exist in litmus.

To test the value of the plants as dye-stuffs, they may be macerated in a weak solution of ammonia, or a solution of calcium hypochlorite may be added to their alcoholic tincture. In the former case a rich violet-red color is produced; in the latter, a deep blood-red color appears, but soon fades.

Lacmus or *litmus* is prepared chiefly if not exclusively in Holland. The process consists in macerating the coarsely powdered lichens, in wooden

vessels under shelter, for several weeks, with occasional agitation, in a mixture of urine, lime and potash or soda. A fermentation ensues, and the mass, becoming first red and ultimately blue, is, after the last change, removed, mixed with calcareous or silicious matter to give it consistence, and with indigo to deepen the color, and then introduced into small molds, where it hardens. It is said that ammonia may be substituted for urine in the manufacture of litmus, but that the reactions necessary for the production of the coloring matter of the litmus are due to the action of the enzyme which is found in the lichens. Litmus occurs in rectangular cakes, from a quarter of an inch to an inch in length, light, friable, finely granular, of an indigo-blue or deep violet color. It has the combined odor of indigo and violets, tinges the saliva a deep blue, and is somewhat pungent and saline to the taste. From most vegetable blues it differs in not being rendered green by alkalies. It is reddened by acids, and restored to its original blue color by alkalies. For a method of purifying commercial litmus by Foerster, see *Nat. Drug.*, 1904, 460.

Its chief use in pharmacy is as an indicator. For this purpose it is employed either in infusion or in the form of litmus paper. The infusion, formerly called *tincture of litmus*, may be made in the proportion of one part of litmus to twenty of distilled water, and two parts of alcohol may be added to preserve it. *Litmus paper* is prepared by first forming a strong clear infusion with one part of litmus to four of water, and dipping slips of white unsized paper into it, or applying it by a brush to one surface only of the paper. The paper should then be carefully dried, and kept in well-stoppered vessels, from which the light is excluded. It should have a uniform blue or slightly purple color, neither very light nor very dark. As a test for alkalies the paper may be stained with an infusion of litmus previously reddened by an acid, care being taken to avoid all excess. By gas light it is said that the change of color cannot be determined by the eye exactly, as the blue of litmus becomes mauve; but this may be obviated by watching the process through a green glass, by which the faintest trace of blue becomes discernible. (*P. J.*, 2d ser., vi, 479.) For the official method of preparing litmus paper, see Tests, Test Solutions, etc., PART III.

Orchil, or *archil*, as prepared in England, is in the form of a thickish liquid, of a deep reddish-purple color, but varying in the tint, being in one variety redder than in another. The odor is ammoniacal. It is made by macerating lichens in a covered wooden vessel, with an ammoniacal liquor, either consisting of stale urine and lime, or prepared by distilling an impure salt of ammonia with lime and water. (Pereira.) For details as to the method of preparation, see *Chem. News*, 1874, 143. It is occasionally adulterated with the extracts of colored woods, as logwood, sappan-wood, etc. A mode of detecting these adulterations is given by F. Leeshing in the *Chem. Gaz.* of June 1, 1855, 219. A sulphonated derivative of orchil is much used in coloring foodstuffs under the name of "vegetable red."

Cudbear is a purplish-red powder procured in the same manner as orchil; but the mixture, after the development of the color, is dried and pulverized.

The point in which the preparation of these coloring substances differs from that of litmus appears to be, that potassium or sodium hydroxide is added, in the latter, to the ammoniacal liquid used. Orchil and cudbear are employed as dyestuffs and for coloring purposes, and sometimes, in like manner with litmus, as indicators (see *Cudbear*, p. 1351). For chemical constituents of lichens, see *A. J. P.*, 1898, 455.

Lobeline Sulphate.—This occurs as very deliquescent yellow friable pieces soluble in water and alcohol. It is asserted to be a very valuable antispasmodic drug, being of especial use in the treatment of *asthma*. Its incompatibilities are the same as those of alkaloids in general and it is a very active poison, emetics and tannin followed by systemic stimulants being the antidote. *Dose*, one-third to one-half grain (0.02–0.03 Gm.).

Loco Plants. *Crazy Weeds.*—These are plants growing in the far Western States, the eating of which by horses and cattle is believed to produce loss of flesh, disordered vision, delirium, convulsive movements, or stupor and death. The chief local plants are *Aragallus Lamberti*, commonly known as *rattle weed* or *white loco*, extending from Alaska southward. A plant of more limited range is the *purple loco*, *woolly loco* or *Texas loco* (*Astragalus mollissimus* Torr.). There are quite a number of other plants causing heavy losses to stock men of the West.

Isaac Ott found a plant, which he believed to be *A. mollissimus*, to act as a violent spinal poison and mydriatic (*N. R.*, Aug., 1882), and, according to Carl Ruedi, the decoction produces in the rabbit great hilarity, excitement, and even ferocity, and contains an alkaloid, *locoine*, and an acid. (*Tr. Col. State Med. Soc.*, 1895.) On the other hand, O'Brien, of the State Agricultural College of Colorado, was not able to obtain any active chemical substance from six U. S. species of the genus, including the two previously mentioned, while in a very careful study of a plant which was neither in flower nor in seed, but whose identification as *A. mollissimus* was clear, H. C. Wood found that it was not poisonous to rabbits or dogs, a result which has been confirmed by Ingersoll (*Proc. A. Ph. A.*, 1890) and O'Brien (*Bulletin 25, Agricultural Experiment Station of Colorado*) and others. It would appear that *A. mollissimus* is not a poisonous plant. Other species of the genus, especially *A. Hornii* A. Gray, *A. Bigelovii* A. Gray, and *A. caryocarpus* Ker., Gawl, have had poisonous properties attributed to them, and in the fruit of the last-mentioned species G. B. Frankforter believes he has demonstrated the presence of an alkaloid. In 1908 Crawford brought forward the interesting theory that the poisonous effects of the *loco weed* were due to barium, but Alsberg and Black (*Bull. 246, U. S. Bureau of Plant Industry*, 1912) have shown that many other plants in the same localities contain equal quantities of barium, but do not produce the characteristic symptoms, and that the barium is in such an insoluble form as to render improbable that it would be absorbed in the intestinal tract. There can be no doubt that domestic animals are destroyed in the West in very large numbers from an affection which is known as "loco," and hundreds of thousands of dollars have been spent in bounties by the State of Colorado for the extirpation of the supposed poisonous astragalus. It is probable that many of the deaths attributed to loco have been from other causes. Thus, Ingersoll of the Colorado State Agricultural College, found in a large number of locoed sheep masses of *Tœnia expansa*, which he believed to be the cause of death. It is a probable explanation that the

phenomena of loco disease are due to the fermentation of an astragalus or other plant in the intestines of the animals, and the production of one or more poisons which are absorbed and produce narcotic symptoms. If this be correct the loco disease is parallel in its etiology and nature to the lathyrismus of Europe. See *Lathyrus sativus;* also *N. Y. M. J.*, 1889, xlix. Similar effects are produced in horses by the pods of the mesquite (*Prosopis juliflora* DC.), when eaten too freely.

According to Haeckel (*Die naturlichen Pflanzen Familien*), the Russian grass *Stipa capillata* L. frequently kills sheep, not, however, by a direct poisonous action, but by its glumes working through the skin into the vital organs; and *Stipa Vaseyi*, which is said in some parts of New Mexico and Texas to be known by the name of "*sleepy grass,*" is believed by some ranchers to be the cause of loco disease. Lescohier (*M. R.*, 1911, xx, p. 273) finds that the sleepy grass is an active respiratory poison, and also has some depressant action upon the heart muscle. He suggests that the apparent narcosis produced by the injection of it into the lower animals, is due to partial asphyxiation. This explanation, however, seems improbable in light of the symptoms which are reported in animals which have eaten the grass. Gillespie (*B. M. J.*, 1908, ii, p. 1059) reports that the drug is not only a narcotic, but also a diuretic and sudorific.

Lodal. (6: 7-Dimethoxy-2-Methyl-3: 4-dihydro-*iso*quinolinium Chloride.)—Under this name has been introduced a derivative of papaverine. *Lodal* has been studied by Laidlaw (*Biochem. J.*, 1910, v, 243) who finds that it resembles hydrastinine in its physiological action, causing a rise in the blood pressure through a direct stimulating influence on the muscles of the heart and arteries. This stimulant influence on involuntary muscle is also shown most markedly in its effect upon the uterus in which it causes tonic contractions. It has been brought forward as a remedy for *menorrhagia* and *dysmenorrhea.* It is marketed in the form of tablets each containing one grain (0.065 Gm.).

Lolium. *Lolium temulentum* L. *Darnel. Bearded Darnel. Ivraie,* Fr. *Lolch, Taumelkorn,* G. —This grass, which has spread over the world wherever wheat is cultivated, is rarely found in the United States. It owes its importance to its growing especially with wheat, so that its ground seeds are eaten in the flour. From ancient times its seeds have been believed to produce an intoxication similar to that of alcohol; hence its specific Latin name and the French name, *Ivraie.* In the sweetish seeds, P. Antze (*A. J. P.*, 1891, 568) believed that he found a solid alkaloid, *temulentine,* and a volatile one, *loliine;* but Hofmeister (*A. J. P.*, 1892, 611) determined that the volatile alkaloid was an impure ammonia, while the temulentine was a mixture which contained a nitrogenous acid and an uncrystallizable alkaloid, *temuline,* of which the hydrochloride has the formula $C_7H_{12}N_2O.2HCl$.

It is alleged that *lolium* seeds produce vertigo, dizziness, headache, somnolence, and general intoxication in man, as well as in dogs, sheep and horses, while they are innocuous to hogs, cows, and poultry. Rivière and Maizière (*J. P. C.*, 1863, 280) have recorded death as occurring from the use of bread containing large amounts of darnel. P. Antze found that both *loliine* and *temulentine* are poisonous, causing violent gastro-intestinal irritation, dyspnea, and general depression. (*Ob. G. T.*, 1891.) M. P. Guerin believes the poisonous properties of darnel are due to the presence of a fungus. (*Morots Journ. de Bot.*, 1898.)

Lonchocarpus. *Lonchocarpus violaceus* (Jacq.) H. B. K. *Stinkwood.*—The wood of this papilionaceous tree is said to be used by the natives of Surinam as a fish poison. (*Ph. Cb.*, xxxix, 282.)

Lonicera. *Lonicera Caprifolium* L. *Honeysuckle. "American"* or *Italian Woodbine.* (Fam. *Caprifoliaceæ.*)—The flowers of the common honeysuckle are sometimes used in perfumery, and a syrup of the fruit has been commended in *asthma.* The fruit of all the species of *Lonicera* is said to be emetic and cathartic (Mérat and De Lens), and that of *L. xylosteum* L. to have caused serious poisoning. (*J. P. C.*, 4e sĕr., xviii, 65.)

Loretin. *Meta-iodo-ortho-oxyquinoline-ana-sulphonic Acid.* $C_9H_4IN.OH.SO_3H$.—This organic iodine compound, discovered by Claus of Freiburg, contains 36.2 per cent. of iodine and is a bright yellow, odorless, crystalline powder, insoluble in ether and oils, soluble in 500 to 1000 parts of cold water, and in 167 to 200 parts of boiling water; it forms neutral soluble salts with sodium, potassium, ammonium, and magnesium, yielding deep orange-yellow solutions. It is very stable for an iodine compound, not being affected by exposure to direct sunlight. It was found by Ammelburg to be much more powerful as a germicide than iodoform, with seven different pathogenetic germs essayed. Given hypodermically to guinea-pigs (5 mils of a 5 per cent. solution for long periods), it produced no poisoning, and no iodine could be detected in the urine. (*Deutsche Zeitsch. für Thier. Med. und Vergleich. Path.*, 1894.)

It has been especially commended as a substitute for iodoform by Schinsinger and by Snow. (*B. M. J.*, ii, 1895.) It may be used as a dusting powder alone or mixed with calcined magnesia or starch; as collodion, from 2 to 10 per cent.; as ointment, 5 to 10 per cent.; and in solution, 1 to 2 per cent. of the soluble sodium salt. The soluble calcium salt, *calcium loretin,* has been especially recommended for the manufacture of antiseptic gauze. Snow states that the pure powder may be used without danger of poisoning or of local irritation. A substance closely allied to loretin is known as *tryen* or *yatren.* Anselmino (*Ap. Ztg.*, 1914) believes that it is chemically identical with loretin, although there has been some difference of opinion on this point. Tryen appears to be an active germicide and has been used by Blun (*D. M. W.*, 1913) and others in the treatment of *gonorrheal infections,* and by Bischoff (*D. M. W.*, 1913) as an insufflation in *diphtheria.*

An isomer of loretin has also been advanced under the name of *lorenit,* and is used for the same purposes as loretin. It is *para-iodo-ana-oxyquinoline orthosulfonic acid.*

Under the trade name of *griserin* the *sodium loretinate* has been introduced for the purpose of combating various systemic infections, as *tuberculosis, typhoid fever,* etc. It has, however, been violently condemned by a number of authors as not beneficial, but even actually harmful.

Bismuth loretinate is used as a surgical dusting powder, also internally in *tuberculous enteritis* in doses of eight grains (0.5 Gm.) several times a day.

Losophan. *Tri-iodo-meta-cresol.* $C_6HI_3(OH).CH_3$.—*Losophan* forms colorless crystals insoluble in water, readily soluble in oils and warm fats and but sparingly soluble in alcohol. It contains

78 per cent. of iodine. It is employed externally as an antiseptic and astringent in *various skin diseases.* It is applied in a 2 per cent. solution or as a 10 per cent. ointment.

Lotus. *Lotus arabicus* L.—According to W. R. Dunstan and T. A. Henry, the leaves of this leguminous plant contain a yellow crystalline glucoside, *lotusin*, $C_{22}H_{19}NO_{10}$, and an enzyme, *lotase*, by which lotusin is converted into prussic acid and a yellow substance, *lotoflavin.* (*Proc. Roy. Soc.*, lxvii, 224.)

Lubraseptic. *N. N. R.* 1917. (Append.)—This is an irish moss (chondrus) jelly containing small amounts of formalin and boric acid. It appears on the market in collapsible tubes.

Lucuma.—This Brazilian genus of the fam. *Sapotaceæ* yields a number of species, which are used in Brazil as medicines or articles of diet. For an account of them, see *Ph. Rund.*, 1888. See also *Monesia.*

Luesan.—This is stated to be a combination of mercury and glidine and is used in the treatment of *syphilis.* It is marketed only in the form of tablets which are said to contain one-sixth of a grain of mercury. One or two of these tablets may be given at a *dose.*

Luffa. *Luffa cylindrica* (L.) Röm. *Vegetable Sponge. Wash-rag Sponge. Gourd Towel.*—A cucurbitaceous genus, indigenous to Arabia and Egypt, furnishing a gourd-like fruit, which presents upon the removal of the epidermis a durable skeleton of interwoven woody fibers, which are used in place of sponge. Reinhard J. Weber has furnished the following description of *Luffa cylindrica* as grown in this country: It is a large climbing vine, with a thin but very tough light green, succulent stem, attaining a length of from 10 to 30 feet. The leaves are alternate and palmately-lobed, of a light green color, and almost destitute of taste. The flowers are monœcious, petals five, united below into a bell-shaped corolla; anthers cohering in a mass; ovary two-celled, style slender, stigmas three. The fruit is elliptical-ovate, fleshy and dehiscent, with a green epidermis, longitudinally marked with black ridges, varying from ten to fifteen in number; under each of these ridges is found a tough, woody fiber. The seeds are numerous and almost flat, broadly-ovate, three-eighths of an inch long. (*A. J. P.*, 1884, 6.) The fruit of *L. echinata* Roxb., of India, is a violent irritant poison, from which C. J. H. Warden has separated a principle allied to, if not identical with, *colocynthitin.* (*P. J.*, June, 1890.)

Luminal. *N. N. R.* 1917. *Phenyl-ethyl-barbituric Acid.* $C_6H_5.C_2H_5.C.(CONH)_2.CO$.—This drug differs in its chemical composition from veronal in that one of the ethyl groups has been replaced by a phenyl group. It occurs as a white crystalline powder with a slightly bitter taste, almost insoluble in cold water, but dissolving readily in alkaline solutions. The sodium salt, *luminal sodium*, is also upon the market and differs in being freely soluble in water. It is a powerful somnifacient and in small doses is used as a sedative in *epilepsy, mania*, and other forms of nervous excitement. The sedative action after the oral administration of luminal appears in about half an hour, although the hypnotic effect may not be manifest for an hour. Like veronal its continued use has in a number of cases been followed by skin eruptions and other unpleasant symptoms. Farnell (*J. A. M. A.*, 1913, lxi) reports two cases in which only moderate doses of the drug gave rise to profound mental disturbance lasting for twenty-four hours.

As a somnifacient the *dose* of luminal by the mouth is from three to ten grains (0.2–0.65 Gm.). As a general sedative the quantity should be somewhat smaller. Luminal sodium is employed chiefly for hypodermic administration and may be given in doses of from five to nine grains (0.32–0.65 Gm.).

Lupetazin. *Dimethyl piperazin.* $(C_2H_3(CH_3)NH)_2$.—This is produced by the distillation of glycerin with ammonium chloride, yielding dimethyl-pyrazin and subsequently reducing the latter with alcoholic sodium solution. It forms a white crystalline compound analogous in its therapeutic action to piperazin, namely, that of being a uric acid solvent.

Lupinus. *Lupinus albus* L. *Lupin. Lupin*, Fr. *Feigbohne, Wolfsbohne*, G.—A plant belonging to the *Leguminosæ*, and a native of Europe and Western Asia, which is sometimes cultivated in our gardens. Other species are also met with—*L. hirsutus* L., *L. luteus* L., *L. polyphyllus* Lindl., *L. densiflorus* Benth. The last two are indigenous to the Pacific slope and the West. The bitter principle *lupinin*, $C_{29}H_{32}O_{16}$, is a glucoside, and its solution in alkalies is of a dark brownish-yellow color. On boiling with dilute acids it is decomposed into *lupigenin*, $C_{17}H_{12}O_6$, and a fermentable, dextro-rotatory glucose. The bruised seeds of white lupin, after soaking in water, are sometimes used as an external application to *ulcers*, etc., and internally are said to be anthelmintic, diuretic, and emmenagogue. An instance has been recorded where a decoction used as an injection in the rectum caused symptoms which suggested a poisonous character for the drug. An alkaloid, *lupanine*, $C_{15}H_{24}ON_2$, has also been discovered in *L. angustifolium.* It is a pale, yellow, syrupy fluid of an intensely bitter taste and showing a green fluorescence. Two alkaloids, *lupinine*, $C_{21}H_{40}O_2N_2$, and *lupinidine*, $C_8H_{15}O_2N$, have been isolated from the seeds of *Lupinus luteus* and *L. niger*, the former a crystalline powder and the latter a syrupy liquid. Steiger (*J. Soc. Chem. Ind.*, 1886, 385) has also studied a carbohydrate analogous to dextrin, which Baeyer and Eichborn discovered in *Lupinus luteus.* He finds that it is not changed by yeast, that nitric acid converts it into mucic acid, and that diluted sulphuric or hydrochloric acid converts it into galactose.

According to Schwartz (*W. K. R.*, 1906) the seeds of the *Lupinus arabicus* contain *calcium-anhydro-oxydiamine phosphate*, to which he has given the name of *magolan* and which is a useful remedy in *diabetes mellitus.* It occurs in crystals which yield a green precipitate with copper acetate. The *dose* of magolan is three grains (0.2 Gm.). several times daily.

Lupulin. *N. F. IV* (*U. S. VIII*). *Lupulinum. Lupulinic Glands. Lupulin*, Fr. Cod. *Lupulite*, Fr. *Glandulæ Lupuli, Hopfenmehl, Lupulin*, G. *Luppolino*, It. *Lupulino*, Sp.—"The glandular trichomes separated from the strobiles of *Humulus Lupulus* Linné (Fam. *Moraceæ*). Preserve it in tightly-closed containers, protected from light." *N. F.* Lupulin is obtained by rubbing or threshing and sifting the strobiles, of which it constitutes from one-sixth to one-tenth by weight. It is described by the N. F. as "a bright yellowish-brown, granular powder, having the characteristic odor and taste of hops; becoming darker in color, disagreeable and valerian-like in odor on aging, when it is unfit for use. Under the microscope, the glandular trichomes are somewhat globular or ellipsoidal, from 0.15 to 0.2 mm. in diameter, consisting of a single layer of secreting cells assum-

ing the form of a shallow cup, from the inner surface of which the cuticle has been separated by the secreted yellowish-brown oleoresin. Not less than 60 per cent. of Lupulin is soluble in ether. Lupulin yields not more than 16 per cent. of ash." *N. F.* It has the peculiar flavor of hops, and appeared to Lebaillif and Raspail, when examined by the microscope, to consist of glandular hairs filled with a yellow matter. They originate in a cell formed among those of the epidermis, and, when fully developed, secreting a resinous matter. (*J. P. C.*, 3e sér., xxvi.) It is inflammable, and when moderately heated becomes somewhat adhesive. The odor of lupulinic grains resides in the essential oil. This is obtained to the extent of 0.9 per cent. by distilling hops with water. When distilled from the fresh strobiles the oil has a greenish color, but a reddish brown when old hops have been employed. It is devoid of rotatory power, neutral to litmus paper, and gives no remarkable coloration with concentrated sulphuric acid. According to Chapman (*J. Chem. S.*, 1895, 54, 780) the essential oil consists of two terpenes, one $C_{10}H_{16}$, and the other $C_{10}H_{18}$, boiling between 160° and 171° C. (320° and 339.8° F.) and a sesquiterpene called *humulene*, boiling at 263° to 266° C. (505.4°–510.8° F.). This latter makes up almost two-thirds of the oil. There is also a small amount of an oxygenated constituent, probably $C_{10}H_{18}O$. The bitter principle, formerly called *lupulin* or *lupulite*, was first isolated by Lermer, who called it the *bitter acid of hops* (*Hopfenbittersaure*). It crystallizes in large brittle rhombic prisms, and possesses the peculiar bitter taste of beer. Its composition is $C_{32}H_{50}O_7$. The main contents of the hop gland consist of wax (*myricyl palmitate*, according to Lermer) and resins, one of which is crystalline and unites with bases. Besides the constituents of the glands, hops contain, according to Etti, *lupulo-tannic acid* and *phlobaphene*. The former is a whitish, amorphous mass, soluble in alcohol, hot water, or acetic ether, but not in ether. By heating the *humulo-tannic acid* to 130° C. (266° F.), or by boiling its aqueous or alcoholic solution, it gives off water and is transformed into phlobaphene, a dark-red amorphous substance,

$$2C_{25}H_{24}O_{13} - H_2O = C_{50}H_{46}O_{25}$$

The latter substance, on boiling it with diluted mineral acids, becomes hydrolized, and furnishes glucose and *hop-red*, according to the reaction:

$$C_{50}H_{46}O_{25} + 2H_2O = C_{38}H_{26}O_{15} + 2C_6H_{12}O_6$$

From raw phlobaphene, ether removes the bitter principles of hops, a colorless crystallizable and a brown amorphous resin, besides chlorophyll and essential oil. (*Pharmacographia*, 2d ed.) The existence of a peculiar alkaloid in hops, suggested by Lermer in 1863, and confirmed by Griessmayer, has been denied. A. Chaston Chapman (*P. J.*, 92, 878) found cultivated hops to contain from 1.7 to 4 per cent. of nitrogen which is a constituent of the following principles recognized by him in an investigation of the subject: *aspartic acid*, *l-asparagine*, *choline*, *betaine*, *adenine*, *histidine*, *hypoxanthine*, and *arginine* besides an unidentified base, no trace of a morphine like alkaloid could be detected, although this has been stated by some authorities to be present. Etti found arabic (pectic) acid, phosphates, nitrates, malates, citrates, and also sulphates, chiefly of potassium, to occur in hops. The amount of ash afforded by hops dried at 100° C. (212° F) would appear to be on an average about 6 to 7 per cent. (U. S. P. IX not more than 8 per cent.) H. Bungener has isolated from hops a bitter crystalline substance, $C_{25}H_{35}O_4$, which is insoluble in water, but soluble in alcohol and alkaline solutions. He believes it to be identical with Lermer's hop-bitter asid, to be feebly acid, and to possess the character of an aldehyde. (*P. J.*, 1884.)

Lupulin is supposed to possess the therapeutic properties of hops. (See p. 552.) It has been used in *gastro-intestinal affections*. J. S. Ward found, as the result of an examination, four samples of lupulin, which fairly represent the commercial article, to yield 54.24, 41.49, 40.4, and 39.41 per cent. of extractive, soluble in ether, and to yield 27.01, 29.10, 30.86, and 31.42 per cent. of ash. The samples were all gritty. (*P. J.*, 1886, 656.)

Dose, five to ten grains (0.32–0.65 Gm.).

A fluidextract is official in the N. F. (see Part III).

Lycetol. *N. N. R.* 1917. *Dimethylpiperazine Tartrate.* $NH(CH_2CHCH_3)_2NH + H_2C_4H_4O_6$.—This is the tartrate of a substitution product from piperazine, in which an atom of hydrogen in each of two CH_2 groups is replaced by the methyl group CH_3. *Lycetol* is a white powder melting at 250° C. (482° F.), readily soluble in water, having a taste which is described as pleasant and acidulous. Alkalies react on it, liberating from it the insoluble free base, and while anhydrous it is stated to be slightly hygroscopic. It is asserted that it is an active diuretic, exerting a powerful solvent influence upon uric acid, and causing no disturbance of digestion even when given continually in large doses. According to Hamonic, it acts very favorably in purulent *cystitis*, lessening suppuration and the tendency to decomposition of the urine. It has been used with asserted excellent results in *chronic* and *acute gout*, and in various other forms of *uric acid diathesis*, as well as for solution of *calculi*. *Dose*, of lycetol, from fifteen to thirty grains (1.0–2.0 Gm.) daily, administered in from one to two pints of water.

Lycium. *Lycium halimifolium* Mill. *Matrimony Vine.* (Fam. *Solanaceæ*.)—Different species have been used in various parts of the world for supposed medicinal virtues. *Lycium vulgare*, which is indigenous in the south of Europe and in Asia, is a thorny shrub, with long flexible branches, and is cultivated for hedges and arbors. Husemann and Marmé found in the leaves and stem an alkaloid, *lycine*, $C_5H_{11}O_2N$. (*A. J. P.*, 1864, 226.) It is very deliquescent, and is soluble in both water and alcohol, but nearly insoluble in ether. It is crystallizable, of a sharp but not bitter taste, and forms crystallizable salts with the acids. Husemann believes that lycine does not exist in the plant, but is formed during the process of extraction, and also that it is identical with *betaine*, $C_5H_{11}NO_2$, the alkaloid obtained from beet juice by Scheibler, and with the oxyneurine of Liebreich. (*A. J. P.*, xlvii, 209.) E. Schmidt found in *Lycium vulgare* traces of mydriatic alkaloids, resembling those of belladonna. (*Ap. Ztg.*, 1890, 511.) The young shoots of one of the species of *Lycium* are eaten in Spain as asparagus, and its leaves as salad, and the aborigines of Colombia used another species against *erysipelas*. The leaves of *L. vulgare*, as well as the fruit, are said to be used by the physicians of Japan. (**Mérat and De Lens.**)

Lycopodium Saururus Lam. *Piligan.*—In this Brazilian lycopod Adrian has found an actively poisonous alkaloid, *piliganine.* (*C. R. A. S.*, June, 1886; see also *B. G. T.*, cxi, 174.)

Lycopus. *U. S.* 1870. *Lycopus virginicus* L. *Lycope de Virginie*, Fr. *Virginischer Wolfsfuss*, G.—The *bugle-weed* is a labiate which grows throughout the greater part of the Eastern United States. The whole herb is used. Jos. L. Weil found 0.41 per cent. of fat melting at 50° C. (122° F.), 0.68 per cent. of a granular wax melting at 70° C. (158° F.), 0.43 per cent. of a crystallizable resin soluble in ether, a crystallizable glucoside, and a small quantity of gallic acid and tannin. (*A. J. P.*, 1890, 72.) It has a peculiar odor and a nauseous slightly bitter taste, which it imparts to boiling water.

Lycopus europœus L., a native of Europe, growing in waste places from Massachusetts to Virginia, is said to be frequently collected and sold for *L. virginicus.* The former may be distinguished by its acutely quadrangular stem, its narrow lanceolate leaves, of which the lower are somewhat pinnatifid, its more crowded flowers, and the acute segments of its calyx, armed with short spines. It has been employed in Europe as a substitute for quinine.

According to A. W. Ives, the bugle-weed is a mild narcotic and an astringent, useful in pulmonic and other *hemorrhages.* *Dose* of decoction (one ounce to one pint of boiling water), from one to four fluidounces (30–120 mils).

Lycoris. *Lycoris radiata* Herb. (Fam. *Amaryllidaceæ.*)—According to Morishima (*A. E. P. P.*, 40), this plant contains two alkaloids, *lycorine*, $C_{32}H_{32}N_2O_8$, which occurs in large colorless polyhedric crystals, and is physiologically very active, resembling emetine in its action, and *sekisanine*, $C_{34}H_{34}N_2O_9$, which occurs in colorless, anhydrous columns and is quite inactive physiologically.

Lygosine. *Sodium Lygosoinate. The Sodium Salt of Diorthocumarketone.* $CO(CH:CH.C_6H_4.ONa)_2 + 7H_2O$.—It occurs as shining, metallic, green crystals, forming a red solution in water. According to Aujezki, it is feebly bactericidal, also capable of lowering the temperature in fevered rabbits. It has been used by Stray (*D. M. Zeit.*, 1909, No. 7) successfully in the treatment of *gonorrhea*, especially in women. For this purpose it is employed in solutions containing from one to five per cent.

Quinine lygosinate is a vivid orange-yellow color, representing approximately 70 per cent. of quinine. It is odorless and almost insoluble in water, but soluble in alcohol. Filep asserts that quinine lygosinate is actively bactericidal, and it has been employed clinically by Fürth (*Pharmakologische und Therapeutische Rundschau*, 1905, No. 12, p. 89) as a dusting powder in *old ulcers*, and for other surgical purposes. It is also claimed for the substance that it possesses styptic properties.

Lyptol.—Oil of peppermint and oil of eucalyptus dissolved in alcohol with chinasol constitute this product which is used as an antiseptic and disinfectant.

Lysan.—This is a saponaceous alcoholic solution of a disinfectant which is the result of the action of formaldehyde on terpene. According to Aufrecht (*All. M. C. Z.*, 1907, p. 378), it is a powerful disinfectant, freely soluble in water, and without injurious effect upon the metal instruments, and comparatively non-toxic.

Lysargin.—A colloidal silver containing 60 per cent. of the metal. It forms steel blue lustrous scales, forming a brilliant brownish solution when dissolved in water. Solutions of *lysargin* are stable in the air, do not stain, are not affected by daylight, but are decomposed in direct sunlight. Possessing antiseptic value it is used as an injection in *gonorrhea* in 0.5 to 1 per cent. solution.

Lysidin. *N. N. R.* 1917. *Ethylenethenyldiaminehydrochloride. Methyl-glyoxalidin.* $C_4H_8N_2$ HCl.—The article sold as *lysidin* is a 50 per cent. solution of the base *methyl glyoxalidin.* The true base forms small colorless, extremely hygroscopic crystals, very soluble in water with an alkaline reaction, and giving the usual alkaloidal reactions. It is incompatible with acids and the salts of many metals and of the alkaloids. It is employed in the *uric acid diathesis*, thirty to one hundred and fifty grains (2–10 Gm.) being administered daily. The bitartrate forms the most stable salt. (*P. J.*, 1912, 371.)

Lysoform is an alcoholic potash soap containing formaldehyde. Its 5 per cent. solution is said to be effectively germicidal and non-irritant. *Lysoform* may be used as an antiseptic mouth or nose wash, one to three teaspoonfuls to a pint; as a vaginal or uterine douche, from four to six teaspoonfuls to a pint; for abscess cavities, suppurating sinuses, etc., six teaspoonfuls to the pint or stronger; for disinfecting the hands or instruments, six to twelve fluidrachms to the pint

Lysulfol.—A black, unguentous mass said to contain lysol with 10 per cent. of sulphur. It is entirely soluble in water and is highly commended by E. Rumpf in *pityriasis versicolor, scabies, acne, psoriasis* and *prurigo*, well rubbed in on the part in the evening and thoroughly washed off in the morning.

Lythrum. *L. Salicaria* L. *Spiked Loosestrife. Purple Willow-herb. Salicaire*, Fr. *Rother Weiderich*, G.—This is an elegant perennial plant of the fam. *Lythraceæ*, a native of Europe, but naturalized from Quebec to Delaware. The dried herb is inodorous, and has an herbaceous, somewhat astringent taste. It has been used as a demulcent astringent in *diarrhea* and chronic *dysentery.* The *dose* of the powdered herb is about a drachm two or three times a day. A decoction of the root, prepared by boiling an ounce in a pint of water, may be given in the *dose* of two fluidounces (60 mils).

Mace. *Macis. N. F. IV.*—"The arillode of the seed of *Myristica fragrans* Houttuyn (Fam. *Myristicaceæ*)." *N. F. IV.* *Mace* was official in the U. S. Pharmacopœia 1890, but was omitted in subsequent editions. It has very properly been admitted to the National Formulary IV. It is described as follows: "In narrow bands, 25 mm. or more in length, somewhat branched and lobed above, united into broader bands; yellowish to brownish-orange, and oily. Odor fragrant; taste warm and aromatic.

"The powder is orange-buff to orange-brown. Mounted in water and examined microscopically, the powder exhibits elongated epidermal cells; parenchyma containing very small amylodextrin granules, which are colored red-brown by iodine T.S.; large oil cells the contents of which are not greatly changed in color on the addition of alkali.

"Powdered false Mace or Bombay Mace is yellow-brown to deep-brown in color and deficient in odor and taste. When mounted in water and examined microscopically it exhibits flattened, thick-walled epidermal cells and oil cells much more numerous than in true Mace and containing

an orange-red resinous substance which is dissolved by alkalies forming a blood-red liquid.

"Moisten Mace with hydrochloric acid; no greenish color is produced (difference from and absence of the *arillode of Myristica malabarica* Lamarck or *Bombay Mace*).

"Add potassium chromate T.S. to an alcoholic extract of Mace (1 in 10); the precipitate formed is yellow and does not change to red on standing, nor does the solution develop a red coloration (difference from and absence of *Bombay Mace*).

"Saturate a piece of filter paper with an alcoholic tincture of Mace (1 in 10), and add one drop of potassium hydroxide T.S.; no blood-red coloration is produced (difference from and absence of *Bombay Mace*).

"Mace yields not less than 8 per cent. of volatile ether extract, and not less than 20 per cent. nor more than 30 per cent. of non-volatile ether extract.

"Mace yields not more than 3 per cent. of ash which is almost completely soluble in hydrochloric acid." *N. F. IV.* Mace is inferior when it is brittle, less than usually divided, whitish or pale yellow, or with little taste and odor. The presence of starch granules or other microscopic particles different from those spoken of in powdered mace is proof of adulteration. Mace contains from 7 to 9 per cent. of a volatile oil, the greater portion of which consists of *pinene*, along with which is some *myristicin*, $C_{12}H_{14}O_3$. Wallach separated two odorous fixed oils; one yellow, soluble in ether, insoluble in boiling alcohol; the other red, soluble in alcohol and ether in every proportion.

Mackay Bean.—This is the seed of *Entada scandens Benth.* (Fam. *Leguminosæ*), of Queensland, which has the reputation in the colony of being strongly poisonous, and in which John Moss found saponin. (*P. J.*, vol. xviii, 242.)

Maculanin. *Potassium Amylate.*—Ogata Osaka (*D. M. W.*, 1907) prepares a caustic in the following manner: Well washed rice grains are scattered on the bottom of a glass dish, the latter being filled with a ten per cent. solution of potassium hydroxide and allowed to stand for six or eight hours, after which time the water is poured off, and the transparent mass rubbed up in a mortar. This is applied like a paste to the diseased tissue which has been previously cleansed.

Magnesium Benzoate. *Magnesii Benzoas.* $Mg(C_7H_5O_2)_2$.—A white, crystalline powder, permanent in the air, soluble in 20 parts of water or alcohol. Used for *gout*, *urinary calculi*, and *tuberculosis*, in *doses* of from three to fifteen grains (0.2–1.0 Gm.).

Magnesium Borate. $Mg(BO_2)_2.2Mg(OH)_2 + 7H_2O$.—This magnesium salt was primarily introduced under the trade name *antifungin*. It forms colorless micro-crystals possessing decided antiseptic value. It is used almost exclusively as a preservative, although it has been given as an internal antiseptic in *doses* of five to fifteen grains (0.32–1.0 Gm.).

Magnesium Bromide. *Magnesii Bromidum.* $MgBr_2 + 6H_2O$.—Made by neutralizing hydrobromic acid with magnesium oxide, evaporating and crystallizing. In the form of colorless, very deliquescent crystals, used as a nervine, in *doses* of from five to thirty grains (0.32–2.0 Gm.).

Magnesium Chlorate. *Magnesii Chloras.* $Mg(ClO_3)_2 + 6H_2O$.—This salt in 20 per cent. ointment has been highly commended (*S. M.*, 1899) by Herscher and Gaucher in the treatment of *epithelioma*.

Magnesium Chloride. *N. F. IV. Magnesii Chloridum.* The N. F. description and tests are as follows: "It contains not less than 95 per cent. of $MgCl_2 + 6H_2O$ (203.34). Magnesium Chloride occurs as colorless, transparent crystals, or as white, translucent pieces; deliquescent in moist air. One gramme dissolves in about 0.6 mil of water; it is readily soluble in alcohol. The aqueous solution of the salt (1 in 20) is neutral to litmus paper. An aqueous solution of the salt, acidulated with nitric acid, yields a white precipitate upon the addition of silver nitrate T.S. A mixture of 10 mils of an aqueous solution of the salt (1 in 20) with 10 mils of ammonium chloride T.S., rendered slightly alkaline with ammonia water, yields a white precipitate on the addition of sodium phosphate T. S. One Gm. of the salt dissolves in 10 mils of alcohol, leaving not more than 1 per cent. of insoluble residue (*substances insoluble in alcohol*). Add 1 mil of potassium sulphate T.S. to 10 mils of an aqueous solution of the salt (1 in 20) slightly acidulated with hydrochloric acid; no turbidity results (*barium*). Ten mils of an aqueous solution of the salt (1 in 200), acidulated with hydrochloric acid, is not reddened by potassium sulphocyanate T.S. (*iron*). Warm 5 mils of an aqueous solution of the salt (1 in 10) with 10 mils of sodium hydroxide T.S.; the odor of ammonia is not evolved. A mixture of 10 mils of an aqueous solution of the salt (1 in 20), 10 mils of ammonium chloride T.S. and 5 mils of ammonia water, is not rendered more than slightly turbid upon the addition of ammonium oxalate T.S. (*calcium*). An aqueous solution of the salt does not respond to the Test for heavy metals (see U. S. P., Test No. 3, Part III). An aqueous solution of the salt meets the requirements of the Test for arsenic (see U. S. P., Test No. 1, Part III)."

Assay.—"Dissolve about 0.5 Gm. of Magnesium Chloride, previously dried and accurately weighed, in 50 mils of distilled water in a 200 mil measuring flask; add 3 mils of nitric acid, then add 50 mils of tenth-normal silver nitrate V.S. and sufficient distilled water to make the mixture measure 200 mils. Mix thoroughly, filter through a dry filter, reject the first 20 mils of filtrate, then collect 100 mils of filtrate, add 2 mils of ferric ammonium sulphate T.S. and titrate the excess of silver nitrate with tenth-normal potassium, sulphocyanate V. S. Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.010167 Gm. of $MgCl_2 + 6H_2O$. Each gramme of magnesium chloride corresponds to not less than 93.4 mils of tenth-normal silver nitrate V.S." *N. F.* Chilbret (*R. P.*, 1910, p. 646) has revived the use of this salt as a laxative, and believes it superior to either the sulphate or citrate. Being deliquescent, it is necessary to give it in solution. It may be given in small repeated *doses* of from four to sixty grains (0.26–3.9 Gm.), or single *doses* of from one to four drachms (3.75–15 Gm.) may be given.

Magnesium Copaivate.—A yellowish powder, slowly soluble in alcohol and asserted to be an antiseptic, diuretic and laxative. It is used in *gonorrhea*, *leucorrhea* and *dysentery*.

Magnesium Ergotate. *Magnesium Sclerotinate.*—A brown powder used as an emmenagogue and vasoconstrictor in *amenorrhea*, *uterine fibroids* and *epilepsy*. *Dose*, two-thirds to one grains (0.04–0.065 Gm.).

Magnesium Iodide. $MgI_2 + 8H_2O$.—A deliquescent, crystalline powder melting at 45° C. (113° F.), and rapidly decomposing in aqueous solution. It is used as an alterative and sialagogue in the treatment of *scrofula, syphilitic* and *chronic rheumatism. Dose,* three to eight grains (0.2–0.5 Gm.).

Magnesium Lactate. *Magnesii Lactas.* $Mg(C_3H_5O_3)_2 + 3H_2O$.—In white, granular crystals, soluble in about 30 parts of cold water and 6 parts of boiling water, insoluble in alcohol. Used as a mild laxative in *doses* of from fifteen to forty-five grains (1–3 Gm.). A combination of magnesium lactate and magnesium phosphate, known as *magnesium phospholactate,* is recommended as a tonic laxative. *Dose,* three to fifteen grains (0.2–1.0 Gm.).

Magnesium Malate. $MgC_4H_4O_5$.—A white, crystalline powder, soluble in water. It is stated to be a very mild laxative possessing also antilithic properties. *Dose,* thirty to one hundred and twenty grains (2–8 Gm.).

Magnesium Phenolsulphonate. *Magnesium Sulphocarbolate.* $Mg(C_6H_4.OH.SO_3)_2 + 7H_2O$.—This occurs as colorless crystals soluble in water. It is asserted to be efficient as a phenolsulphonate for internal administration combining with the antiseptic property of the latter the laxative effects of the magnesia. *Dose,* three to fifteen grains (0.2–1 Gm.).

Magnesium Salicylate. *Magnesii Salicylas.* $Mg(C_6H_4(OH)CO_2)_2.4H_2O$.—This salt has been used as an intestinal antiseptic by Boas (*B. K. W.,* 1910, p. 89) in *intestinal fermentation,* and by Huchard in *typhoid fever.* The *dose* is from fifteen to thirty grains (1–2 Gm.) three times a day.

Magnesium Silicate. *Hydrated Magnesium Silicate. Meerschaum.* $3MgSiO_3 + 5H_2O$.—Meerschaum is one of several hydrated silicates of magnesium, talc and serpentine being others of analogous formula. It is used for the manufacture of tobacco pipes. It was brought into notice as a medicine by Garraud, who used it successfully as a substitute for bismuth subnitrate in obstinate *diarrhea* and has the advantage of not darkening the feces. Trousseau employed it also with great success in numerous cases of *diarrhea.* It no doubt acts mechanically, either as an absorbent or a protective of the intestinal coats. (*J. P. C.,* 4e sér., iii, 385.) It should be reduced to a very fine powder, and given in *doses* of from one to four drachms (3.9–15.5 Gm.) a day. Asbestos, talc, and serpentine are all forms of more or less pure magnesium silicate in varying degrees of hydration.

Magnesium Sulphite. *Magnesii Sulphis. U. S.* 1880. $MgSO_3.6H_2O$.—This salt may be prepared by double decomposition between magnesium sulphate and neutral sodium sulphite. Owing to the almost universal presence of sulphate in the sodium sulphite, J. P. Remington proposes to prepare it by suspending eight parts of pure magnesia in sixteen parts of water, and then adding gradually, with stirring, official aqueous sulphurous acid in excess. The crystals which form are washed with very cold water, drained, and dried. (*A. J. P.,* xl, 97.) "A white, crystalline powder, gradually becoming oxidized on exposure to air, odorless, having a slightly bitter, somewhat sulphurous taste, and a neutral or slightly alkaline reaction. Soluble in twenty parts of water at 15° C. (59° F.), and in nineteen parts of boiling water; insoluble in alcohol. When heated to 200° C. (392° F.), the salt loses its water of crystallization (50.9 per cent.), and is converted into magnesium oxide and anhydrous magnesium sulphate. The aqueous solution of the salt, mixed with ammonium chloride, yields, with excess of test-solution of sodium phosphate and water of ammonia, a white, crystalline precipitate soluble in acids. When treated with four times its weight of diluted hydrochloric acid, the salt dissolves completely and emits the odor of burning sulphur, without becoming cloudy (difference from hyposulphite). A one per cent. aqueous solution, strongly acidulated with hydrochloric acid, should not afford more than a slight cloudiness with test solution of chloride of barium (limit of sulphate)." *U. S.* 1880. *Magnesium sulphite* shares the general medicinal properties of the sulphites, but is better fitted for internal administration on account of its less solubility and less disagreeable taste, etc. (See *Sodii Sulphis.*) The *dose* is from fifteen grains to half a drachm (1–2 Gm.).

Magnolia. *U. S.* 1880. *Magnolia Bark.*—Three species of *magnolia* were formerly official as follows: *Magnolia virginiana* L., *Small* or *Laurel Magnolia, M. acuminata* L. or *Cucumber-tree,* and *M. tripetala* L., commonly known as *Umbrella-tree* (Fam. *Magnoliaceæ*). In the latter Wallace Procter found in the fruit a neutral crystalline principle, *magnolin.* When pure, this is without odor and has at first little taste, in consequence of its insolubility in the liquids of the mouth, but after a time produces an irritant effect on the fauces. It is nearly insoluble in cold, but slightly soluble in hot water, very soluble in alcohol or ether. Procter considered it analogous to the liriodendrin obtained by Emmet, but quite distinct. It has been also found in other species. (See *A. J. P.,* 1872, 145; also Lloyd's paper in *Ph. Rund.,* 1866, 224.) W. F. Rawlins (*A. J. P.,* 1889, 7) obtained from the leaves of *M. glauca* a small quantity of a volatile oil of bright green color, with an odor resembling fennel or anise, but more pleasant. From the ethereal solution of this oil small crystals deposited. Indications were also obtained of a bitter glucosidal principle.

The bark and fruit of all the species of *Magnolia* are possessed of similar medicinal properties; but the bark only was official, and that of the root has been thought to be most efficient. "The bark from young wood is quilled or curved, thin, externally orange-brown and glossy, or light gray, with scattered warts and somewhat fissured, internally whitish or pale brownish and smooth; fracture short, in the inner layer somewhat fibrous; inodorous; taste somewhat astringent, pungent, and bitter. The bark of old wood, deprived of the cork, is whitish or brownish, fibrous, and less pungent." *U. S.,* 1880. The aromatic property, which resides in a volatile principle, is diminished by desiccation, and entirely lost when the bark is long kept. The bitterness, however, remains. The bark is destitute of astringency.

Magnolia is a gently stimulant aromatic tonic and diaphoretic. It has been used in *malaria* and in *rheumatism.* The *dose* of the recently dried bark in powder is from half a drachm to a drachm (2.0–3.9 Gm.), frequently repeated.

Malachite Green. *Tetra-methyl-diapara-amido-triphenyl-carbinol.*—The closely allied *brilliant green,* or *diamond green* G., while by some considered identical, appears to be the sulphate of a compound similar to that above with the exception that the methyl groups are replaced by a tetra-ethyl. *Malachite green* occurs as shining,

golden crystals forming a green solution in either water or alcohol.

There are several substances on the market known as malachite green, some of which are compounds containing zinc, and as investigators have not always stated closely which substance they were using it is difficult to determine the precise therapeutic value of this agent. It is probable, however, that all these closely allied compounds have similar properties. Malachite green is an active germicide but differs very greatly in its selective effect on certain organisms; thus Boer found that whereas one part in forty thousand was sufficient to destroy the anthrax bacillus in two hours' exposure, it required one part in three hundred to kill the typhoid bacillus in the same length of time. According to Loffler (*D. M. W.*, 1906, p. 269) it possesses such a marked influence over the *Bacillus coli communis* that it can be used as a means of separating this organism from the typhoid bacillus. Wendelstadt (*D. M. W.*, 1906, p. 863) has found it of service in the treatment of experimental trypanosomiasis, but we know of no clinical application of this result. Malachite and malachite green are the names applied to green copper carbonate formerly used largely as a pigment.

Malakin. *Salicyl-paraphenetidin.*

$C_6H_4 \begin{cases} OC_2H_5 \\ N : CH.C_6H_4(OH) \end{cases} + H_2O$.—This occurs in small, bright yellow, fine needles, melting at 92° C. (197.6° F.), insoluble in water, sparingly soluble in cold, but quite so in hot alcohol, insoluble in carbonates of the alkalies, but soluble with a yellow color in soda lye; weak mineral acids decompose it, forming salicylaldehyde and paraphenetidin.

Malakin contains about 50 per cent. of salicylaldehyde, and in 1893 Jacquet called attention to it as an anti-rheumatic remedy, stating that it is decomposed in the stomach, yielding salicylaldehyde to the blood, and offering, therefore, a method of giving salicylic acid. On the other hand, while a number of clinicians have reported favorably of its effect in *acute rheumatism*, Ottolenghi (*Ther. Woch.*, ii, 1895) has found that the decomposition and after-absorption of it is exceedingly slow and uncertain. The contention of Bauer, that it is distinctly inferior to the older salicylates, is in all probability correct. Ottolenghi suggests that malakin must act on intestinal parasites, and may therefore prove useful as an anthelmintic. *Dose*, fifteen to thirty grains (1–2 Gm.).

Malambo or Matias Bark.—A bark received from South America by Alex. Ure, under the name of *matias bark*, was found to have the characters of the *malambo bark*, which is held in high esteem in Colombia, where it is produced. According to H. Karsten, it is derived from a hitherto undescribed species of *Croton*, which he names *Croton Malambo* Karst. (Fam. *Euphorbiaceæ*). (See *Floræ Colombiæ Terrarumque adjacentium Specimina Selecta.*) This is a small tree or shrub, growing on the coast of Venezuela and Colombia. (*P. J.*, 1859, 321.) It has an aromatic odor and a bitter, pungent taste, and yields these properties to water and alcohol. Its active ingredients appear to be a volatile oil and a bitter extractive matter. According to Mackay, it has been used successfully in *intermittents*, convalescence from continued fevers, *hemicrania*, *dyspepsia*, and other cases in which tonic remedies are useful, and also as an adjuvant to diuretics. It is probably nothing more than an aromatic tonic. Ure has administered it with good effect as a substitute for Peruvian bark. (*P. J.*, iii, 169.)

Under the name of *Winter's bark*, a considerable quantity of malambo bark was at one time imported into the United States from South America.

Malarin. *Acetophenonephenetidine.* $C_6H_5C(CH_3).NC_6H_4OC_2H_5$.—This is a yellowish-white powder, insoluble in cold water, which is said to be a condensation product obtained by heating molecular equivalents of acetophenone and paramidophenetol. It has been suggested for use as an antipyretic in *doses* of six to ten grains (0.4–0.6 Gm.).

Mallow Leaves. *N. F. IV. Malvæ Folia. Malva sylvestris* L. *Common Mallow. Flores Malvæ Folia Malvæ*, P. G. *High Mallow.* Cheese *Cake Flower* or *Pancake Plant.*—It is described by the N. F. as the "the dried leaves of *Malva sylvestris* Linné and of *Malva rotundifolia* Linné (Fam. *Malvaceæ*). Reject leaves showing brown fungous growths of *Puccinia Malvacearum* Montagne." N. F. This is a perennial, herbaceous, European plant of the Fam. *Malvaceæ*. Almost all the species of the genus are possessed of the same properties. *M. rotundifolia* L., known as *cheeses*, one of the most common, as well as *M. sylvestris*, are both used in medicine. The leaves often show a fungus growth. "Leaves of *Malva sylvestris*, petiolate with petioles up to 10 cm. in length, orbicular or reniform, slightly truncate or cordate at the base, from 10 to 11 cm. in length, and from 15 to 20 cm. in width, with three to seven shallow, angular or rounded lobes, venation palmate, margins crenate-dentate, pubescent on both sides. Leaves of *Malva rotundifolia*, with petioles up to 20 cm. in length, obicular up to 8 cm. in width, base deeply cordate, five to seven shallow rounded lobes, venation palmate, margins with rounded blunt teeth, pubescence more scant than in *M. sylvestris*. Intermixed with the leaves are frequently found dark purple flowers and glabrous reticulated carpels (*M. sylvestris*) or pale bluish flowers and pubescent rounded carpels (*M. rotundifolia*). Inodorous; on chewing it becomes very mucilaginous, taste bland. When examined under the microscope, sections show an epidermis containing mucilage cells; numerous stomata, on both surfaces, each with three or four neighboring cells; trichomes of three distinct types, small, short-stalked glandular hairs, single, large, one-celled curved hairs with thick walls and compound or stellate hairs in groups of two- to six-cells (the latter especially numerous in *M. sylvestris*); palisade tissue of one or two rows of cells, the mesophyll of three or four rows; the parenchyma containing calcium oxalate in rosette crystals and numerous mucilage cells which are distributed in the tissue of the veins; veins with collateral bundles. The powder is light green and, when examined under the microscope, exhibits the characteristic hairs, mucilage cells, epidermis with stomata, and rosette crystals of calcium oxalate. Mallow Leaves yield not more than 16 per cent. of ash." *N. F.* The herb and flowers have a weak, herbaceous, slimy taste, without odor. They abound in mucilage, which they readily impart to water, and the solution is precipitated by lead acetate. The infusion and tincture of the flowers are blue, and have been used as indicators, being reddened by the acids and

rendered green by alkalies. The roots and seeds also are mucilaginous. Common mallow is emollient and demulcent. The infusion and decoction are sometimes employed in *catarrh, dysentery,* and *nephritis complaints,* and are applicable to all other cases which call for the use of mucilaginous liquids.

Malouetia. *Malouetia nitida* Spruce. *Gauchamacà.* (Fam. *Apocynaceæ.*)—This plant, of Venezuela, contains an alkaloid, *guachamacine,* which Kobert believes to be identical with *curarine.* (*A. J. P.,* 1885, 560.)

Manaca. *Vegetable Mercury.*—This is a portion of the root and stem of *Brumfelsia Hopeana* Benth. (*Franciscea uniflora* Pohl.), a Brazilian plant belonging to the Fam. *Solanaceæ.* It occurs in pieces from a few inches to one foot in length, and about one-half inch in diameter, very tough and woody, with a yellowish center and a dark, very thin outer bark. The stem portion has a very small yellowish pith. H. B. Parsons (*Am. Chem. J.,* vol. i, No. 6) came to the conclusion that it contains no alkaloid, but R. Lenardson (*In. Dis.,* Dorpat, 1884) asserts that he has found in it an alkaloid, *manacine,* besides a peculiar fluorescent substance supposed to be identical with *gelseminic acid.* Some investigators report failure to find any alkaloidal principles. E. P. Bruer (*T. G.,* 1882), as the result of experiments made upon the lower animals arrived at the conclusion that *manaca* acts upon the spinal cord, first stimulating, and then abolishing, the activity of the motor centers, the action being shared in by the respiratory centers. All the glands, especially the kidneys, were stimulated by it. In large doses he found it to produce in man lassitude, perspiration, and loose, greenish alvine discharges. Manaca has been very strongly recommended in the treatment of chronic or subacute *rheumatism* and *syphilis.* The *dose* of the fluidextract is from ten to thirty minims (0.6–1.8 mils) three times a day.

Mandragora. *Mandragora autumnalis* Bertol. *Mandrake. Mandragora.* (Fam. *Solanaceæ.*)—A perennial, European plant, with spindle-shaped root, which is often forked beneath, and is therefore compared, in shape, to the human figure. In former times this root was supposed to possess magical virtues, especially when collected at certain times, and was used as an amulet to promote fecundity, etc., and the superstition is still cherished in some parts of Europe. The plant is a poisonous narcotic, somewhat similar in its properties to belladonna, to which it is botanically allied. See a paper by Ekert for the history of this drug. (*S. W. P.,* 1913, 425.) Crouzel isolated an alkaloid, *mandragorine,* which he found similar in properties to atropine. (*P. J.,* 1885, 1067.) It has since been more thoroughly studied by F. B. Ahrens. (*Ber. d. Chem. Ges.,* 1889, 2159–2161.) *Mandragorine* is colorless, inodorous, deliquescent, melts at from 77° to 79° C. (170.6°–174.2° F.), and has the formula $C_{17}H_{23}NO_3$. It seems to be isomeric with atropine, but is not converted into it by alkalies. The sulphate and the hydrochloride are crystalline and deliquescent. A second alkaloid in much smaller amount was also extracted, of which the gold and platinum double chlorides were formed. Both alkaloids had a mydriatic action. It was much used by the ancients as a narcotic, and as an anesthetic agent before surgical operations. (*J. P. C.,* xv, 290.) *Morion* or *death-wine,* said to have been administered previous to the torture, was made from it. Its physiological action has been partially investigated by B. W. Richardson. (*B. F. M. R.,* 1874, 242.)

Manganese. *Manganum.* Mn.—This metal and its compounds with oxygen have been described. (See *Mangani Dioxidum Præcipitatum,* p. 680.) Several of its salts have been proposed as medicines, to be used as tonic and anti-anemic remedies. Small amounts of manganese have been detected in various solids and fluids of the body, but the metal is probably only an accidental constituent. It is stated, as an advantage of the preparations of manganese, that they may be prescribed in conjunction with tannic acid and the various astringent medicines, which are all incompatible with the preparation of iron. Of the manganous oxides, the *monoxide* only is strongly salifiable, and this is the oxide present in the ordinary salts of the metal. It may be obtained by precipitation, as a white hydrate, from any of the soluble manganous salts by the addition of a caustic alkali. This, according to Hannon, is a good medicinal preparation; but a strong objection to it is that it rapidly absorbs oxygen, and passes to the state of the brown hydrated manganic oxide.

Manganese Albuminate.—This preparation is made from potassium permanganate and egg albumen by a definite chemical process. The resulting product forms brown, almost tasteless scales, containing 3.3 per cent. manganese (as Mn_3O_4), which are readily soluble in warm water. The solutions of this substance are stable and very easily assimilable. Indicated in *anemia.*

Manganese Carbonate. *Mangani Carbonas. Manganous Carbonate.* $MnCO_3$.—This salt may be obtained by double decomposition between molecular proportions of manganous sulphate and sodium carbonate, using the same precautions to prevent oxidation that are employed in making the preparations of ferrous carbonate. It is given in the form of pills of four or five grains (0.26–0.32 Gm.) each.

Manganese Chloride. *Mangani Chloridum.* $MnCl_2 + 4H_2O$.—*Manganese chloride* is used locally as a stimulant to *syphilitic* and other *indolent ulcers.* For process of preparing, see *U. S. D.,* 19th ed., p. 1559.

Manganese Citrate, Soluble. *N. F. IV. Mangani Citras Solubilis. Manganese and Sodium Citrate.*—The N. F. description and Tests are as follows: "Manganous citrate rendered soluble by the aid of sodium citrate. It corresponds, when dried to constant weight at 120° C. (248° F.), to not less than 49 per cent. nor more than 51 per cent. of $Mn_3(C_6H_5O_7)_2$ (542.87). Preserve it in well-closed containers. Soluble Manganese Citrate occurs as a yellowish or pinkish-white powder, or as translucent scales; odorless, and having a slightly bitter and astringent taste. It is permanent in the air. One gramme dissolves slowly in about 4 mils of water; slightly more soluble in boiling water, nearly insoluble in alcohol. An aqueous solution of Soluble Manganese Citrate (1 in 20) is neutral or slightly alkaline to litmus, but does not redden phenolphthalein T.S. When strongly heated, it chars and finally leaves a residue which effervesces with acids and imparts an intensely yellow color to a non-luminous flame. An aqueous solution of Soluble Manganese Citrate (1 in 20) rendered alkaline with ammonia water, yields a solmon-colored precipitate on warming with ammonium sulphide T.S. Ten mils of an aqueous solution of Soluble Manganese Citrate (1 in 20), slightly acidulated with acetic acid and

mixed with 2 mils of calcium chloride T.S., remains clear while cold, but yields a white crystalline precipitate when heated to boiling. Separate portions of 10 mils each of an aqueous solution of Soluble Manganese Citrate (1 in 100), when acidulated with hydrochloric acid, are not more than slightly reddened by potassium sulphocyanate T.S. (*iron*); nor rendered turbid at once by barium chloride T.S. (*sulphate*); nor show more than an opalescence with silver nitrate T.S. when acidulated with nitric acid (*chloride*). Mix about 0.5 Gm. of Soluble Manganese Citrate with 5 mils of sulphuric acid in a porcelain dish previously rinsed with sulphuric acid, protect the mixture from dust, and heat it for fifteen minutes on a water bath; no color darker than yellow develops (*tartrates or other readily carbonizable substances*). An aqueous solution of Soluble Manganese Citrate does not respond to the Test for heavy metals (see U. S. P., Test No. 3, Part III)."

Assay.—"Dissolve about 0.5 Gm. of Soluble Manganese Citrate, previously dried to constant weight at 120° C. and accurately weighed, in 100 mils of distilled water, add 50 mils of solution of hydrogen dioxide, and 10 mils of ammonia water, and boil the mixture for several minutes. Collect the precipitate on a filter, wash it thoroughly with hot distilled water, dry and ignite to constant weight. The weight of the manganous-manganic oxide (Mn_3O_4) so obtained is not less than 20.65 per cent. nor more than 21.5 per cent. of the weight of the salt taken, corresponding to not less than 49 per cent. nor more than 51 per cent. of $Mn_3(C_6H_5O_7)_2$. Each gramme of manganous-manganic oxide is equivalent to 2.3728 Gm. of $Mn_3(C_6H_5O_7)_2$." *N. F.* It is used in the N. F. solution of iron peptonate and manganese. *Dose*, three grains (0.2 Gm.).

Manganese Glycerophosphate, Soluble. *N. F. IV. Mangani Glycerophosphas Solubilis. Soluble Manganous Glycerinophosphate.*—"Manganous Glycerophosphate rendered soluble by the aid of citric acid. It contains not less than 70 per cent. nor more than 75 per cent. of $MnC_3H_7PO_6$ (225.03). Preserve it in well-closed containers. Soluble Manganese Glycerophosphate occurs as a yellowish or pinkish-white powder, odorless, and having an acid taste. One gramme dissolves in 4 mils of water at 25° C. The aqueous solution is strongly acid to litmus and becomes turbid on heating. Alcohol dissolves the citric acid, leaving a residue which is nearly insoluble in water. Add an excess of ammonium sulphide T.S. to an aqueous solution of Soluble Manganese Glycerophosphate; on standing, it yields a salmon-colored precipitate soluble in acetic acid. No yellow turbidity is produced immediately on mixing 5 mils of an aqueous solution (1 in 20) with 10 mils of ammonium molybdate T.S. (*phosphate*), but on prolonged standing, or on heating, a yellow precipitate is formed. Heat a powdered mixture of about 0.1 Gm. of Soluble Manganese Glycerophosphate and about 0.5 Gm. of potassium bisulphate; pungent vapors of acrolein are evolved. Separate portions of 10 mils each of an aqueous solution of Soluble Manganese Glycerophosphate (1 in 20) are not rendered more than slightly turbid by barium chloride T.S. when mixed with a few drops of hydrochloric acid (*sulphate*); nor by silver nitrate T.S., after acidulation with nitric acid (*chloride*). Add a few drops of hydrochloric acid and 1 mil of chlorine T. S. to 10 mils of an aqueous solution of Soluble Manganese Glycerophosphate (1 in 200) and boil; no reddish color is produced in the liquid by potassium sulphocyanate T.S. after cooling (*iron*). An aqueous solution of Soluble Manganese Glycerophosphate does not respond to the Test for heavy metals (see U. S. P., Test No. 3, Part III)."

Assay.—"Dissolve about 0.5 Gm. of Soluble Manganese Glycerophosphate, accurately weighed, in 100 mils of distilled water, add 10 mils of ammonia water and 5 mils of ammonium sulphide T.S. and boil the mixture until the precipitate formed has become greenish. Allow the precipitate to settle, then transfer it to a filter, wash with hot distilled water containing a few drops of ammonium sulphide T.S., dry the filter and contents and incinerate them in an open crucible, first at a low temperature and then at strong red heat, until the weight is constant. The residue of manganous-manganic oxide (Mn_3O_4) so obtained is not less than 23.7 per cent. nor more than 25.4 per cent. of the weight taken, corresponding to not less than 70 per cent. nor more than 75 per cent. of $MnC_3H_7PO_6$. Each gramme of manganous-manganic oxide is equivalent to 2.95 Gm. of $MnC_3H_7PO_6$." *N. F.* It is stated to be a valuable remedy in the treatment of *phosphaturia, deficient nerve nutrition, neurasthenia*, etc. *Dose*, three to five grains (0.12–0.32 Gm.) several times daily.

Manganese Hypophosphite. *N. F. IV* (*U. S. P. VIII. Mangani Hypophosphis. Manganum Hypophosphorosum. Manganous Hypophosphite. Hypophosphite de Manganèse, Hypophosphite Manganeux*, Fr. *Unterphosphorigsaures Manganoxydul*, G.—"It contains not less than 97 per cent. of $Mn(PH_2O_2)_2 + H_2O$ (203.06). Preserve it in well-closed containers." *N. F. Manganese hypophosphite* may be prepared by the interaction of manganese sulphate and calcium hypophosphite by mixing a solution containing 1.31 parts of the former with a solution containing 1 part of the latter, filtering out the precipitated calcium sulphate, evaporating and crystallizing. This salt was introduced into the U. S. P. VIII solely for its use in making the Compound Syrup of Hypophosphites, which has now been transferred to the N. F. IV. (see Part III). "Manganese Hypophosphite is a pink, granular or crystalline powder; odorless and nearly tasteless; permanent in the air. It is freely soluble in water; insoluble in alcohol. An aqueous solution of the salt (1 in 20) is neutral or acid to litmus, and yields with ammonium sulphide T.S. a salmon-colored precipitate of manganese sulphide, soluble in acetic acid. When strongly heated in a dry test tube, the salt evolves spontaneously inflammable hydrogen phosphide and finally leaves a residue of manganous pyrophosphate. When an aqueous solution of the salt (1 in 20), acidulated with hydrochloric acid, is added, drop by drop with agitation, to an excess of mercuric chloride T.S., a white precipitate of mercurous chloride is formed, and, upon the further addition of the solution of Manganese Hypophosphite, the precipitate becomes gray from reduction to metallic mercury. Add about 0.5 Gm. of the salt to 5 mils of acetic acid; no effervescence is produced (*carbonate*). Boil 0.25 Gm. of the salt with 10 mils of sodium hydroxide T.S.; a white precipitate is formed which gradually acquires a brown color on exposure to the air. The filtrate from this mixture, after being slightly acidulated wtih hydrochloric acid, boiled for a minute, and then rendered alkaline with ammonia water, yields no precipitate upon the addition of magnesia mixture T.S. (*phosphate*). Dissolve 1

Gm. of the salt in 20 mils of diluted hydrochloric acid with the aid of heat, and then add 1 mil of barium chloride T.S.; not more than a slight turbidity is produced (*sulphate*). Dissolve 0.5 Gm. of Manganese Hypophosphite in 10 mils of hot distilled water, add 10 mils of solution of hydrogen dioxide and 10 mils of sodium hydroxide T. S., boil for one minute, then render slightly acid with acetic acid and again warm. Now cool, filter, and add 1 mil of ammonium oxalate T.S. to 10 mils of the filtrate; no turbidity is produced within five minutes (*calcium*). Pour 5 mils of an aqueous solution of the salt (1 in 30) into an evaporating dish containing 3 mils of nitric acid diluted with about 10 mils of distilled water, and evaporate to dryness on a water bath; the residue does not respond to the Test for arsenic (see U. S. P., Test No. 1, Part III)."

Assay.—" Dissolve about 1 Gm. of Manganese Hypophosphite, accurately weighed, in 30 mils of boiling distilled water in a 250 mil measuring flask. Add 25 mils of solution of hydrogen dioxide and 15 mils of sodium hydroxide T.S. and heat for ten minutes on a water bath with frequent agitation. Cool, add distilled water to make the volume exactly 250 mils, mix well and filter through a dry filter. Evaporate 25 mils of the clear filtrate to dryness with 10 mils of nitric acid, dissolve the residue in 10 mils of distilled water, transfer it to a 100 mil flask with the aid of a few mils of distilled water, add a drop of phenolphthalein T.S. and sufficient sodium hydroxide T.S. (free from chloride) to produce a pink color, then add 50 mils of tenth-normal silver nitrate V.S. and agitate the mixture well. Now gradually add zinc oxide (free from chloride) in small portions, agitating vigorously after each addition until the liquid is neutral to litmus. Then add distilled water to make 100 mils, agitate the mixture thoroughly, filter through a dry filter, collect 50 mils of the filtrate, add 2 mils of nitric acid and 2 mils of ferric ammonium sulphate T.S., and titrate with tenth-normal potassium sulphocyanate V.S. to the production of a permanent red color. It shows not less than 97 per cent. of $Mn(PH_2O_2)_2 + H_2O$. Each mil of tenth-normal silver nitrate V.S. used corresponds to 0.003384 Gm. of $Mn(PH_2O_2)_2 + H_2O$. Each gramme of Manganese Hypophosphite corresponds to not less than 286.6 mils of tenth-normal silver nitrate V.S." *N. F.* This salt probably possesses no medicinal virtues. *Dose*, three to five grains (0.2–0.32 Gm.).

Manganese Iodide. *Mangani Iodidum. Manganous Iodide.* MnI_2.—This very deliquescent salt may be prepared by adding manganese carbonate to aqueous hydriodic acid, filtering the solution, and granulating, carefully regulating the heat. This iodide may be administered in syrup or pill. For formula for these, see *U. S. D.*, 19th ed., p. 1559. According to Hannon, manganous iodide is particularly useful in the *anemia* attendant on *scrofula, phthisis*, and *cancer*, and in *syphilitica*. It is also affirmed that when given with cinchona it removes the enlargement of the spleen of malarial fevers. *Dose*, two to four grains (0.12–0.25 Gm.).

Manganese Phenolsulphonate. *Manganese Sulphocarbolate.* $Mn(C_6H_4OHSO_3)_2 + 7H_2O$.—This occurs as reddish crystals soluble in water and alcohol. It is used in the treatment of *intestinal derangement* with *anemia* or *chlorosis*. *Dose*, three to eight grains (0.2–0.5 Gm.).

Manganese Sulphate. *N. F. IV* (*U. S. P. VIII*). *Mangani Sulphas. Manganesii Sulphas. U. S.* 1870. *Manganum Sulphuricum. Sulfate de Manganèse*, Fr. Cod. *Schwefelsaures Manganoxydul. Manganosulfat*, G.—" It contains not more than 38 per cent. of water, and not less than 62 per cent. nor more than 68 per cent. of $MnSO_4$ (151.00)." *N. F.* This salt may be prepared by heating the native black oxide with concentrated sulphuric acid. Oxygen is thereby evolved, and the sulphate is formed. The product, when exhausted by water, furnishes a solution of the salt which must be heated nearly to the boiling point, and treated with manganese carbonate, added in small portions at a time, which will precipitate any iron present, and change the color of the liquid from a dark red to a pale rose tint. The liquid is then filtered, evaporated to the consistence of a thin syrup, and set aside to crystallize. For details of several methods of manufacture, see *U. S. D.*, 19th ed., p. 762. From its aqueous solution it crystallizes in rhombic prisms, which contain variable proportions of water of crystallization according to the temperature of the solution and other circumstances. " Manganese Sulphate occurs as pale rose-colored, translucent, tetrahedral prisms; slightly efflorescent when exposed to moist air. Odorless; taste slightly bitter and astringent. One gramme of the salt dissolves in about 1 mil of water at 25° C. (77° F.), and in about 0.6 mil of boiling water; insoluble in alcohol. An aqueous solution of the salt (1 in 20) is neutral or slightly acid to litmus. It yields with ammonium sulphide T.S. a salmon-colored precipitate soluble in dilute acids; and with barium chloride T.S. a white precipitate insoluble in hydrochloric acid. Mix a fragment of Manganese Sulphate with a small amount of sodium hydroxide and fuse the mixture; it yields a green mass which dissolves in water to form a green solution. Add a few drops each of hydrochloric acid and of chlorine water to 20 mils of an aqueous solution of the salt (1 in 100), boil until the excess of chlorine is removed, and then cool; it is not colored red by potassium sulphocyanate T.S. (*iron*). The addition of a few drops of silver nitrate T.S. to 10 mils of an aqueous solution of the salt (1 in 100), previously mixed with a few drops of nitric acid, does not at once produce more than an opalescence (*chloride*). Precipitate the manganese completely from a solution of 1 Gm. of the salt in 50 mils of distilled water by the addition of ammonium carbonate T.S. and filter; the filtrate evaporated and gently ignited leaves a residue weighing not more than 0.005 Gm. (*other salts or alkalies*). A solution of 1 Gm. of the salt and 1 Gm. of sodium acetate in 10 mils of distilled water, to which a few drops of acetic acid have been added, is not affected by hydrogen sulphide T.S. (*zinc*). Ignite 1 Gm. of the salt, in a porcelain crucible; it loses not more than 38 per cent. of its weight (distinction from *Manganese Sulphate containing a larger amount of water of crystallization*). An aqueous solution of the salt, slightly acidulated with hydrochloric acid, does not respond to the Test for heavy metals (see U. S. P., Test No. 3, Part III)."

Assay.—" Dissolve about 0.6 Gm. of Manganese Sulphate, accurately weighed, in 100 mils of distilled water, add 10 mils of ammonia water and 30 mils of solution of hydrogen dioxide and boil the mixture until precipitation is complete. Transfer the mixture to a filter and wash the precipitate with distilled water until barium chloride

T.S. ceases to produce a precipitate in the filtrate, then dry the filter and precipitate and incinerate these, first at a low heat and then at a strong red heat, until of constant weight. The weight of the residue of manganous-manganic oxide (Mn_3O_4) so obtained corresponds to not less than 31.3 per cent. nor more than 34.34 per cent. of the salt taken. Each gramme of manganous-manganic oxide is equivalent to 1.98 Gm. of $MnSO_4$." *N. F.* At one time manganese sulphate was said to be an active cholagogue and purgative, but it has failed to come into use as such. According to Thomas Thomson, of Glasgow, it resembles sodium sulphate both in taste and in effect, operating as a purgative in the dose of from one to two drachms (3.9–7.5 Gm.). A trial was made of it in *anemia*, as an adjuvant of the chalybeates, but the results have not been satisfactory and it is at present rarely given. *Dose*, as a tonic, from five to twenty grains (0.32–1.3 Gm.).

Manganese Tannate. *Mangani Tannas.*—Made by adding freshly precipitated manganese carbonate to a hot solution of tannic acid until it is neutralized, filtering and evaporating to dryness. Iron must be absent, and the solution must be protected from contact with iron or the solution and salt will acquire an inky color. It is soluble in water.

Manganous phosphate, tartrate, and malate have been proposed by Hannon as useful remedies. The phosphate is prepared by double decomposition between manganous sulphate and sodium phosphate. *Manganous lactate* has been given, associated with ferrous lactate, in *chlorosis*, in the *dose* of a grain (0.065 Gm.), which may be increased to five grains (0.32 Gm.).

Mangosteen.—The pericarp of the fruit of the *Garcinia Mangostana* L. (Fam. *Guttiferæ*). It is sometimes substituted for bael fruit (see *Belæ Fructus*, Br., Part I). It is an active astringent, and has been used as such locally in various *catarrhs*, and also in *diarrhea* and in *leucorrhea*. Ambrose has used the toasted and pulverized rind of *mangosteen* in the treatment of tropical *dysentery* with asserted benefit. He gives *doses* of one drachm (4 Gm.) every two hours. The activity of the drug appears to reside in the neutral principle *mangostin*. *Dose*, of fluidextract, from half to one fluidrachm (1.8–3.75 mils).

Manzanillo. *Manchineel. Hippomane Mancinella* L.—According to A. Betancourt, the milky juice of this euphorbiaceous tree, growing in the West Indies, is a violent irritant, acting as a vesicant when applied to the skin, and when taken internally in doses of twenty drops causing a fatal gastro-enteritis. In *doses* of two drops it acts as a powerful and very certain cathartic; it is also diuretic. In Cuba it has much repute in *tetanus*. (*L. M. R.*, Feb., 1889.)

Maranta. *Arrowroot. Arrowroot Starch.* (Fam. *Marantaceæ*.)—Under this name the U. S. Pharmacopœia, 1870, recognized the fecula or starch obtained from the rhizome of *M. arundinacea*, L.

The arrowroot plant is a native of the West Indies, where it is largely cultivated for the sake of its fleshy, irregularly cylindrical rhizomes whose cells are gorged with starch granules. It is cultivated also in the East Indies, Ceylon, Sierra Leone, and south of Africa, and formerly in our Southern States, especially Georgia and Florida. The plant is easily propagated by cuttings of the root. An analysis by Macdonald (*J. Soc. Chem. Ind.*, 1887, 336) gives the following as the composition of the St. Vincent root: Starch, 27.07 per cent.; fiber, 2.82; fat, 0.26; albumen, 1.56; sugar, gum, etc., 4.10; ash, 1.23; water, 62.96; total, 100.00. An analysis of the arrowroot starch from the same locality by Macdonald gave: Starch, 83.70 per cent.; fiber, 0.04; fat, 0.07; sugar, gum, etc., 0.18; ash and sand, 0.14; water, 15.87; total, 100.00. The fecula is prepared in the following manner. The rhizomes are dug up when a year old, washed, and then beaten into a pulp, which is thrown into water, and agitated so as to separate the amylaceous from the fibrous portion. The tissues are removed by the hand, and the starch remains suspended in the water, to which it gives a milky color. The milky fluid is strained through coarse linen, and allowed to stand that the starch may subside, which is then washed with a fresh portion of water, and afterwards dried in the sun.

The *Bermuda arrowroot* was formerly the most highly esteemed, but the production of it in the island has almost ceased. The Bermuda arrowroot of the American, and probably largely also of the English, markets, is of various sources, the name seemingly being applied to any superior product. For a list of other sources of arrowroot of commerce during different periods, see *U. S. D.*, 19th ed., p. 1561.

Attempts have been made to substitute finely prepared potato starch for arrowroot, and there is no doubt that in nutritive properties it is quite equal, but patients complain of an unpleasant taste of the potato which it is likely to retain. Arrowroot is in the form of a light, white powder, or of small pulverulent masses, without odor or taste. It is firm to the touch when pressed between the fingers, and produces a faint creaking sound when rubbed. It is a pure starch, corresponding in chemical properties with that of wheat and the potato. It is liable to become musty, and should then be rejected. The odor and taste are the best criteria of its quality. It should be perfectly free from odor and unpleasant flavor.

The microscope offers the best means of distinguishing the different varieties of fecula sold as arrowroot, or used for its adulteration. The granules of *Maranta arrowroot* are rarely oblong, somewhat ovate-oblong, or irregularly convex, from 10 to 70 microns in diameter, with very fine lamellæ, a circular hilum which is fissured in a linear or stellate manner. (Pereira.)

Arrowroot affords a light, very mild, and easily digested article of diet, well adapted for the sick and convalescent, and peculiarly suited, from its demulcent properties, to bowel complaints. It is prepared by dissolving it in hot water or hot milk, with either of which it forms a pearly, gelatinous solution, and, if in sufficient quantity, a jelly-like mass on cooling. A tablespoonful will communicate sufficient consistence to a pint of water. It should first be formed into a perfectly smooth paste with a little cold water or milk, and the boiling water then gradually added with brisk agitation. The preparation may be rendered more palatable by lemon juice and sugar, or by wine and spices.

Maretin. *Metatoxyl-hydrazine-carbaminate.* $C_6H_4.CH_3.NH.NH.CONH_2$.—This may be regarded as a methyl-acetanilid in which the acetyl group is replaced by the carbamic group $NH.CONH_2$. It occurs as white, tasteless crystals practically insoluble in water or ether but readily dissolved by chloroform or acetone. It is claimed for the compound that the urea nucleus is so firmly combined

that aniline is not liberated in the body; nevertheless, its effects are very similar to those of the other aniline derivatives. It has been used as an antipyretic and analgesic and is especially recommended in *acute articular rheumatism.* Heubner (*Th. M.*, 1911, xxv, p. 364, and 1913, p. 507) asserts that when used over long periods of time it causes destruction of the blood cells and may lead to a dangerous degree of anemia. The *dose* is from one and one-half to four grains (0.96–0.26 Gm.).

Margaron. $(C_{16}H_{33})_2O$.—This is a white, odorless, tasteless mass, used as a bland, easily absorbable, ointment base. It is obtained by distilling beef suet with lime.

Marrubium. *Hoarhound. Horehound. Herba Marrubii. Marrube Blanc,* Fr. Cod. *Andornkraut, Weisser Andorn,* G. *Marrubio,* It., Sp.—Under the title of *marrubium* the U. S. P. formerly recognized "The dried leaves and flowering tops of *Marrubium vulgare* Linné (Fam. *Labiatæ*)." *U. S. VIII. White hoarhound* has a perennial, fibrous root, and numerous annual stems, which are quadrangular, erect, very downy, and from twelve to eighteen inches high. The leaves are about 2.5 cm. long, roundish-ovate, dentate or deeply serrate, obtuse, wrinkled, veined, downy above, hoary on the under surface, and supported in pairs on strong foot-stalks. The flowers are white, and in crowded axillary woolly whorls. It contains a volatile oil, resin, tannin, lignin, and a bitter principle called *marrubiin* by Mein. This marrubiin is slightly soluble in cold water, crystallizes from alcohol in prismatic and from ether in tabular crystals, is not precipitated by tannin, and has a very bitter and somewhat acrid taste. The fusing point of the crystals is 160° C. (320° F.), according to Kromayer. Marrubiin was afterwards obtained by Harms (*A. Pharm.*, cxvi, 141), by Hertel (*A. J. P.*, June, 1890), and by Morrison (*A. J. P.*, July, 1890). It has also been studied by Matusow (*A. J. P.*, 1897, 201). He gives to it the formula $C_{30}H_{43}O_6$, and states the melting point of the purified substance to be from 154° to 155° C. (309.2°–311° F.). According to him, it is not a glucoside.

Hoarhound is tonic, and in large doses laxative. It was formerly considered a valuable deobstruent, and was recommended in *chronic hepatitis,* and various *cachetic affections,* but it exerts no specific influence over any of them, and has passed mainly from the hands of physicians into domestic use, where it is used in the form of a confection for *sore throat.* It is employed occasionally in *bronchitis* with copious expectoration. The infusion, made in the proportion of an ounce of the herb to a pint of boiling water, may be given in wineglassful doses. Geo. M. Beringer gives the following process for *Syrup of Hoarhound:* Hoarhound in No. 20 powder, 200 Gm.; sugar, 750 Gm.; glycerin, 125 mils; water, a sufficient quantity to make 1000 mils.

Mix the glycerin with 375 mils of water and moisten the drug thoroughly with sufficient of the mixture, then pack lightly in a percolator and add enough menstruum to saturate and leave a layer above the drug and macerate for twenty-four hours. Then percolate slowly, using the balance of the menstruum and then warm water till extracted. Reserve the first 500 mils of percolate and evaporate the remainder to 100 mils, then add the reserve and dissolve the sugar in the liquid, using a slight heat if necessary. When cold add sufficient water to make the preparation measure 1000 mils and strain. Syrup of hoarhound so made is clear, brown in color and possesses the characteristic bitter and aromatic taste of the drug and after keeping for more than six months has shown not the least tendency to change. (*Proc. N. J. Pharm. Assoc.*, 1909, 45–46.)

Dose, thirty grains to a drachm (2.0–3.9 Gm.).

Massoi Bark. *Lawang.*—In Eastern commerce certain aromatic barks occur under the name of massoi barks. Of these, three are believed by F. Hekmeyer to be the products respectively of *Cinnamomum xanthoneurum* Blume, *Cinnamomum Burmanni* Blume (*C. Kianis* Nees), and *Massoja aromatica* Becc. (*Sassafras gœsianum* Teijsm. and Binn.), all of the Fam. *Lauraceæ.* For a description of these barks, by E. M. Holmes, see *P. J.*, 1888, 465. The *massoi bark* which comes from New Guinea, and from which Messrs. Schimmel have distilled an oil resembling that of nutmeg and cloves, probably has a different origin from the true massoi bark which has a cocoanut-like odor. (*Y. B. P.*, 1912, 473.)

Mastic. *Mastiche. N. F. IV* (*U. S. VIII*). *Mastich. Mastix. Mastic,* Fr. *Resina Mastiche,* G. *Almaciga, Mastic,* Sp. *Sakes,* Turk. *Arak,* Arab. —"A concrete resinous exudation from *Pistacia Lentiscus* Linné (Fam. *Anacardiaceæ*)." *N. F. IV. Mastic* was deleted from the *U. S. P. VIII* because the official pill of aloes and mastic was dropped; the National Formulary IV has, however, admitted mastic and the pills containing it. The mastic tree, which is also called *lentisk* of *lentiscus,* is a shrub or small tree, seldom more than twelve feet in height, much branched towards the top, and furnished with petiolate, abruptly pinnate leaves. The flowers are dicœcious, and very small. The tree is a native of the countries bordering upon the Mediterranean. The fruit yields by expression a fixed oil, of a deep green color, and liquid at about 32.3° C. (90° F.), which the Arabs of North Africa use both as an article of diet and for light. A resinous exudation from the stem and branches is the official part, but it does not appear to be collected in all places where the tree flourishes. Under the name of *Bombay mastic* there occur in India masses of oleoresin said to be derived from the *Pistacia Terebinthus,* having the general appearance of true mastic with a deeper color, but lacking fragrance, and dissolving in hot alcohol. For an account of the collection of mastic from *P. Terebinthus* growing in the island of Cyprus, see *C. D.*, 1897, 273.

Mastic is obtained chiefly from the island of Scio, or Chios, in the Grecian Archipelago, where the tree is cultivated for this product. Incisions are made in the trunk and principal branches, from which the juice slowly exudes, and either hardens in tears upon the bark, or drops on the ground, where it is received upon cloths or the bare earth, and concretes in irregular masses. The tears are most esteemed, and are the only form recognized by the N. F. They are of various sizes, oval or roundish, often compressed, smooth, semi-transparent, of a pale-yellow color, of a shining fracture, friable, and usually covered with a whitish powder, occasioned by their friction against each other. They are brittle, but become plastic when chewed. The masses consist of yellowish agglutinated tears, with others of a darker color and less translucent, and often fragments of wood, bark, or earthy matter intermingled.

The N. F. describes it as "in subglobular, len-

ticular, elongated or pear-shaped tears, about 3 mm. in diameter, pale yellow or greenish-yellow, transparent, having a glass-like lustre, the surface sometimes very slightly dusty; brittle, becoming plastic when chewed; odor slight, balsamic; taste mild, terebinthinate. Mastic is completely soluble in ether and almost completely soluble in alcohol. The acid number, determined as directed by the U. S. P. (Test No. 10, Part III), is not less than 65." *N. F. IV.*

According to J. Léon Soubeiran the valuable tears are produced by spontaneous exudation from the branches. But the greater part of the resin comes from longitudinal incisions in the stem, made with a knife, close together, and extending from the root to the branches. In fifteen or twenty days the resin has concreted, and is collected in little panniers of white paper or cotton cloth. (*Proc. A. Ph. A.*, 1897, 563.)

Mastic is nearly inodorous, unless rubbed or heated, when it becomes fragrant. Its taste is weak, but agreeably terebinthinate, and, after long chewing, very slightly acrid. It is at first friable under the teeth, but soon becomes soft and ductile, and acquires a white, opaque appearance. Its sp. gr. is 1.074. It is fusible and inflammable by heat. Alcohol dissolves about 90 per cent. of it, leaving a viscid substance which becomes brittle when dried, and for which the name of *masticin* or *betaresin of mastiche* has been proposed. This substance, though not dissolved by alcohol, softens and swells up in it, as gluten does in water. Hlasiwetz gives $C_{20}H_{31}O$ as the formula of the resin. The portion dissolved by the alcohol is called by Johnston *alpha resin of mastiche* or *mastichic acid* because of its acid properties, and has the formula $C_{20}H_{32}O_2$. (*Handwörterbuch der Chemie*, iv, p. 280.) Mastic is wholly soluble in ether, chloroform, and oil of turpentine, scarcely soluble in the fixed oils, and insoluble in water. It consists chiefly of resin, with *masticin*, and a volatile oil. Flückiger, through Schimmel & Co., of Leipsic, ascertained that this volatile oil is present in mastic to the extent of 2 per cent. He found it to be a terpene of the composition $C_{10}H_{16}$. Schimmel & Co. (*Schim. Rep.*, April, 1897) state that mastic resin yields from 0.9 to 2.5 per cent. of a powerful balsamic essential oil of the same odor as the raw material, a sp. gr. of from 0.855 to 0.87 at 15° C. (59° F.), and an optical rotation (100-mm. tube) of from + 22° to +27°. Tschirch and Reutter (*A. Pharm.*, 1904, 104) examined mastic carefully; they found approximately 42 per cent. of free resin acids. These are: the isomeric *a*- and *β*-masticinic acids, $C_{23}H_{36}O_4$, masticolic acid, $C_{23}H_{36}O_4$ (slight amount), amorphous *a*-masticonic acid, $C_{32}H_{48}O_4$ (20 per cent.), and *β*-masticonic acid, $C_{32}H_{48}O_4$ (18 per cent.). Besides this, mastic contains 30 per cent. *a*-masticoresin, $C_{35}H_{36}O_4$, soluble in alcohol; 20 per cent. of *β*-masticoresin (masticin), insoluble in alcohol, and 2 per cent. of an ethereal oil, possessing a pale yellow color and a somewhat camphoraceous odor. Finally, there is also a bitter principle, which could not be isolated in pure form. For a chemical investigation of Egyptian mastic by Reutter, see *S. W. P.*, 1913, 537. Mastic is occasionally adulterated with olibanum, sandarach, and other resinous bodies, and, in seasons of scarcity, with sea salt.

Mastic was formerly thought to possess properties analogous to those of the turpentines, and was used in *debility of the stomach, hemoptysis* from ulcerations, *leucorrhea, chronic diarrhea*, etc.; but its virtues were overrated, and it is at present scarcely ever given internally. In the East, however, an aqueous infusion is said to be still used in *cholera infantum*, and the Greek employ cataplasms made by mixing it with bread and red wine, which they apply to the lower abdomen. (Landerer.) It is sometimes employed temporarily to fill the cavities of carious teeth, for which purpose it is well fitted by its softness. In Turkey it is habitually chewed by the women, under the impression that it sweetens the breath and preserves the gums and teeth. Dissolved in alcohol or oil of turpentine, it forms a brilliant varnish. A solution made by macerating half an ounce of mastic and fifteen grains of caoutchouc in two fluidounces of chloroform, and filtering in closed vessels, forms a valuable *varnish* for microscopic work. The following mode of applying it to carious teeth has been recommended. Dissolve four parts of mastic in one of ether, in a bottle well stoppered. With the solution thus formed, which is yellow and of an oily consistence, saturate a small piece of cotton of the size of the carious cavity, and, having well cleansed and dried the cavity, introduce the cotton, without painful pressure, so as to fill it exactly. The resin attaches itself to the diseased surface of the tooth, which it protects from the air, and from the food taken into the mouth. *Dose*, thirty grains (2 Gm.). It has been highly recommended by various surgeons as a dressing for wounds. Its use is chiefly for the purpose of preventing bacteria upon the surrounding skin getting into the wound. Voos (*M. M. W.*, 1911) paints the skin up to the edges of the wound without previous washing, with a solution of mastic in benzol and then cleanses the wound in the ordinary manner and applies an aseptic dressing. A special solution for this purpose is upon the market under the name of *mastisol*. Another formula for *mastic varnish* which has been used is 20 Gm. of mastic, 50 mils of chloroform, and 1 mil of linseed oil.

Matico. *N. F. IV* (*U. S. P. VIII*). *Matico Leaves. Feuilles de Matico*, Fr. Cod. *Maticoblätter*, G.—"The dried leaves of *Piper angustifolium* Ruiz et Pavon (Fam. *Piperaceæ*), without the presence of more than 5 per cent. of stems, flower spikes, or other foreign matter." *N. F. IV.* The genus *Piper*, according to Engler and Prantl, includes nearly six hundred species, which are distributed throughout the tropics of the Old and New World, being particularly numerous in tropical America and of relatively less number in Africa.

Piper angustifolium is a shrub with a jointed stem about twelve feet in height. The plant is a native of Peru, where the fruit, under the name of *thoho-thoho*, is employed in the same manner as cubeb. This species is also found in other parts of South America. The commercial drug matico is furnished, according to G. Dethan and R. Bertault (*J. P. C.*, 1897, 537), by two varieties of *Piper angustifolium*—viz., *a-cordulatum* (*Artanthe elongata* Miq.), and *β-ossanum*, which differ somewhat in the shape of the leaves. The former has the leaves larger, shorter, and broader, with an oblique cordate base. The midrib of *a-cordulatum* is much less convex below than in the other variety. In 1864 Bentley (*P. J.*, Jan., 1864) described a *false matico* from Central America believed to be yielded by the *Piper aduncum* L. It is distinguished by the want of the reticulations on the upper and the down

on the under surface which characterize true matico. (See also Thoms, *Arbeiten a. d. Pharm. Institut d. Universität*, Berlin, 1910, p. 70.)

The drug is described in the N. F. as: "Usually in compressed, matted masses with leaves more or less broken; leaves sub-sessile, lanceolate, from 10 to 20 cm. in length and from 2 to 5 cm. in breadth; summit tapering and acute; base slightly unequal, cordate; margin finely crenulate; upper surface dark green, tessellated; lower surface pale green, reticulate with prominent yellowish-brown midrib and veins forming small quadrangular meshes clothed with matted pubescence. Odor distinct, aromatic; taste pungent, pepper-like. Sections, when examined under the microscope, exhibit the epidermis of the upper side composed of regular polygonal cells and of the lower side of somewhat irregular and undulate cells, especially where covering the veins; numerous stomata with large neighboring cells on the lower side; the hypodermis of one row and palisade cells in two or three rows; mesophyll loose, spongy tissue; midrib in cross section oval, outer layer of thick-walled cork cells; secretion cells filled with yellow oil; upper surface with papillæ and few bristly hairs; hairs of the lower surface of two kinds, the one six to ten cells in length, pointed, bent and matted, having thick walls and astriate cuticle; the other bristle hairs of one stem cell and a head cell; calcium oxalate crystals few in parenchyma tissue of the venation, in the form of raphides or monoclinic prisms. The powder is greenish-yellow and, when examined under the microscope, exhibits the characteristic hairs, polygonal epidermal cells, and secretion cells of the leaf. Matico yields not more than 18 per cent. of ash."

Flückiger found it to contain 2.7 per cent. of the volatile oil, which was slightly dextrogyrate and boiling in large part at 180° to 200° C. (356°–392° F.). In the winter-time it deposited large crystals of a camphor, having the formula $C_{12}H_{20}O$, according to Kugler (*A. J. P.*, 1884, 477). Schimmel & Co. (*Schim. Rep.*, Oct., 1898, p. 37) and Thoms (*A. J. P.*, 1904, p. 584) state that the newer matico oils do not contain this camphor but contain *asarol* (propenyl-trimethyltrioxybenzene), $C_{12}H_{16}O_3$. Matico also affords, according to Marcotte, a crystallizable acid named *artanthic acid*, with some tannin. (*Pharmacographia*, 2d ed., p. 590.)

Matico is said to be employed in Peru in arresting *hemorrhages* and as a local application to *ulcers*, and has been used in European practice in the treatment of diseases of the genito-urinary organs, such as those for which cubeb is commonly prescribed. It has also been praised as a remedy in *dysentery* and *diarrhea* and especially as a local hemostatic, in which it probably acts in part mechanically in the same manner as does agaric. The powder is sometimes used, but the fluidextract (see Part III), is preferable for internal administration. *Dose*, forty-five to seventy-five grains (3–5 Gm.).

Medeola. *Medeola virginiana* L. (*Gyromia virginiana* L.) *Indian Cucumber.*—An indigenous perennial herb of the Fam. *Liliaceæ*, growing in all parts of the United States. The tuber, which in shape and flavor bears a strong resemblance to a small cucumber, is said by Pursh to be eaten by the Indians, and by Barton to be useful as a diuretic in *dropsies*.

Melaleuca (Cajuputi).—Under the names of *gomenol* and *Niaouli oil* there has been put upon the market a volatile oil obtained from the leaves of *Melaleuca Leucadendron* L. and the var. *minor* Smith, myrtaceous trees growing in upper India, the islands of the Indian Ocean and Australia. Its sp. gr. is 0.922, and its rotatory power plus 0.42°. Its odor and taste are said to resemble those of camphor and peppermint. The chief constituent of the oil (66 per cent.) is cineol, and in addition to this is a crystallized terpineol, $C_{10}H_{18}O$, and the valeric ester of the same. These together make up 30 per cent. additional. (Gildemeister and Hoffman, *Ätherische Oele*, p. 686.) It has been recommended in the *chronic catarrhs* of the pulmonary mucous membrane, and especially in *whooping cough*. It may be given by the mouth or exhibited in the form of intramuscular injections being diluted with from four to ten parts of a sterilized fixed oil to one part of volatile oil. The hypodermic *dose* of a 10 per cent. solution is two and one-half fluidrachms to one-half fluidounce (9.3–15 mils). The injections should be practised every other day. Gomenol has been used by Brimont (*Press Med.*, 1910, p. 800) as a vermifuge in *ankylostomiasis*, in *doses* of five minims (0.3 mil).

Melan.—Under the name of *melan*, there has been introduced a dark-brown, oily fluid which is stated to be a preparation of *Melilotus cœruleus*. It is used as a local application to *ulcers* and *burns*.

Melastoma. *Melastoma Ackermanni.*—This Colombian plant of the Fam. *Melastomaceæ* is used in South America as an anti-neuralgic. Its abundant essential oil resembles methyl salicylate, if indeed it be not identical with it. (See *N. R.*, Aug. and Sept., 1883.)

Meligrin.—This is a condensation product of dimethyloxyquinine and methylphenyl acetamid. It occurs as a white crystalline powder with a slightly burning, though not bitter taste. It is very soluble in water and is employed in the treatment of *migraine* and *neuralgia*.

Melilotus. *N. F. IV. Yellow Melilot. Yellow Sweet Clover. Herba Meliloti, Yellow Sweet Clover*, G.—'The dried leaves and flowering tops of *Melilotus officinalis* (Linné) Lamarck (Fam. *Leguminosæ*)." *N. F.* An annual or biennial plant of the Fam. *Leguminosæ*, indigenous in Europe, and growing also in this country. The plant, when in flower, has a peculiar sweet odor, which, by drying, becomes stronger and more agreeable, somewhat like that of the tonka bean. The N. F. describes it as follows: "Stems mostly less than 3 dm. in length, slender, straight, mostly simple, often leafy below, terminating in long slender racemes, the younger portions very finely pubescent; leaves glabrous or nearly so; petiolate, trifoliate, stipulate, the stipules subulate, entire, the leaflets from 1 to 3 cm. in length, varying from narrowly oblong to oval or occasionally broader above the middle, rounded, truncate, or slightly notched at the summit, sharply serrate; racemes 1 dm. or less in length, many flowered, the flowers yellow, from 5 to 6 mm. in length; calyx bell-shaped, the fine, nearly equal lobes shorter than the tube, corolla papilionaceous, the keel shorter than the other petals, which are about equal; legumes reflexed, from 2.5 to 3.5 mm. in length, obovate, wrinkled, one-seeded. Odor aromatic, tonka-like; taste sweetish, slightly pungent and bitter. Melilot yields not more than 10 per cent of ash." *N. F.* This similarity is accounted for by the fact that *coumarin*, $C_9H_6O_2$, the chief constituent of tonka beans, is present in melilot, combined with *melilotic acid*, $C_9H_{10}O_3$, and *coumaric acid*, $C_9H_8O_3$, of which latter acid *coumarin* is the anhydride. *M. alba* Desv. is a more robust

species, distinguished by its white flowers. Melilot is practically inert.

Melissa. *U. S.* 1890. *Melissa. Balm.*—Under this name were formerly recognized by the U. S. P. the leaves and tops of *Melissa officinalis* L. (Fam. *Labiatæ*), or the ordinary *balm* of Southern Europe, which has become naturalized in this country. Balm contains some tannic acid, and a yellowish, highly flavored essential oil which, however, is present in such small quantities that the plant has practically no remedial value. The allied *Satureja Calamintha* (L.) Scheele, var. *Sylvatica* Brig., is said to contain sufficient aromatic volatile oil to be of possible commercial interest.

Under the name of *oil of lemon balm* or *oil of balm* the essential *oil of melissa* has been used as a diaphoretic in doses of from one to three minims (0.06 to 0.2 mil). This oil is a yellow liquid with a specific gravity of 0.9 to 0.925. Its most important constituent is citral.

Melubrin. *N. N. R.* 1917. *Sodium Salt of phenyldimethylpyrazlon amidomethansulfonic* acid. $C_{11}H_{11}N_2ONHCH_2SO_3Na$.—This occurs as a white crystalline powder, readily soluble in water, with difficulty in alcohol, and is almost tasteless. It has been brought forward as an antipyretic, and antirheumatic and analgesic. According to Loening (*M. M. W.*, 1912), its effect in *acute rheumatic fever* is that of a specific. In its medical properties it seems to resemble antipyrine. The *dose* is fifteen to thirty grains (1–2 Gm.).

Menispermum. *U. S.* 1890. *Yellow Parilla. Canadian Moonseed. Texas Sarsaparilla.*—"The rhizome and roots of *Menispermum canadense* Linné (fam. *Menispermaceæ*)." *U. S.*, 1890.

M. canadense L.—This is a woody, climbing plant, which grows from Western Quebec and New England southward. It is specifically characterized by its peltate, three to seven-lobed leaves, its small clusters of greenish-yellow flowers, and its somewhat kidney-shaped, glaucous fruit, which is ripened in September. *Menispermum* was officially described as follows: "Rhizome 5 to 6 dm. long, 5 mm. thick, brown or yellowish-brown, somewhat knotty, finely wrinkled longitudinally and beset with numerous thin, rather brittle roots; fracture tough, woody; internally yellowish, the bark rather thick, the wood-rays broad, porous, and longest on the lower side; pith distinct. Nearly inodorous; taste bitter." *U. S.* 1890. Maisch proved the presence of a white alkaloid, and of a small quantity of berberine. The former reacts with the usual alkaloidal precipitants, is not very soluble in water, but soluble in alcohol and ether. H. L. Barber (*A. J. P.*, 1884, p. 401) obtained the white amorphous alkaloid above referred to, for which Maisch proposed the name *menispine*. Starch was also found in the root. (*A. J. P.*, 1863, p. 301.) H. M. Gordin states that berberine is not present in menispermum. (*Proc. A. Ph. A.*, 1909.) Menispermum has been used as a substitute for sarsaparilla but is probably inert. A *fluidextract* made with a menstruum of 2 parts of alcohol and one part of water was recognized by the U. S. P., 1890; *dose* one-half to one fluidrachm (1.8–3.75 mils).

Mensalin. *Diphenyldioxycarbonate of Dimethylpyrazolonhewahydrocymolvalerate.*—This forms a white, hygroscopic powder and is recommended as a nervine and in the treatment of *painful menstruation.*

Mentha Aquatica.—Under the name of *poco oil*, the volatile oil of this plant, which is a native of China, is used in the Island of Java as a popular remedy for *headache*, and also in *cholera.*

Mentha Pulegium L.—*European Pennyroyal. Pouliot commun*, Fr. *Polei*, G. *Pulegium vulgare* Mill.—This European labiate yields an oil which is known in England as the *oil of pennyroyal*, and must not be confounded with the American oil of the same name. The oil, which is also known as the *oil of poley*, has been examined by Beckmann and Pleissner (*Ann. Ch. Ph.*, 262, 1), who discovered as the most important constituent *pulegone*, $C_{10}H_{16}O$, an unsaturated ketone, which makes up 80 per cent. of the oil. It boils under a pressure of 60 mm. at from 54.5° to 55° C. (130°–131° F.), turns the plane of polarization to the right, and has a sp. gr. 0.9323 at 0° C. (32° F.). It forms crystalline compounds with hydroxylamine and with hydrogen bromide. When reduced by sodium in ethereal solution pulegone is changed into menthol. Pulegone is most abundant in the Spanish oil, and less abundant in American and Algerian oils. (See also Wallach, *Ann. Ch. Ph.*, 272, 122, and Semmler, *Ber. d. Chem. Ges.*, 25, 3515.) Schimmel states that the oil is sometimes adulterated with eucalyptus oil. (*Schim. Rep.*, 1908, 67.) It is stated (*B. M. J.*, March, 1890) that the oil is largely used for the purpose of producing abortion, and is popularly believed to be safer and more certain than the other volatile oils. Taylor denies, however, that the oil is an abortifacient and it appears to be demonstrated that it is capable of causing fatty degeneration. (See *S. Jb.*, cclxvii, p. 230.)

Menthiodol.—This substance has been recommended as a local application in neuralgia. It is prepared by carefully heating four parts of menthol in a capsule, adding one part of finely powdered iodol, and triturating into a homogeneous mass, which is made into cones or pencils of a suitable size. If the mass is too hard, it may be softened by remelting with a minute quantity of camphor.

Menthospirin. *Menthol Acetyl Salicylate.*—It is a yellowish thick fluid, insoluble in water but soluble in alcohol, ether, and the fixed oils. It is used internally by Loewenheim (*Med. Klin.*, 1913) in the treatment of *colds* and various *catarrhs*, both acute and subacute, of the upper respiratory tract. It has also been employed locally in *laryngeal tuberculosis.* The *dose* is from eight to twelve grains (0.5–0.78 Gm.) several times a day, usually in capsules or pearls.

Menthyl Camphorate.—The camphoric ester of menthol, which forms a white powder which is insoluble in water and chloroform but soluble in alcohol and the fatty oils. Hot water decomposes it with the liberation of menthol. It is used in *tuberculosis.*

Menyanthes. *N. F. IV. Buckbean. Marsh Trefoil. Bogebean. Water Shamrock. Folia Trifolii Fibrini.*—"The dried leaves of *Menyanthes trifoliata* Linné (Fam. *Gentianaceæ*)." It is an ingredient in *Vinum Aurantii Compositum*, N. F. IV. This gentianaceous plant is a native both of Europe and North America, from Greenland to Alaska and south to Pennsylvania, Minnesota, and California. All parts of menyanthes are efficacious, but only the leaves are official.

It is described by the N. F. as "glabrous; petioles from 10 to 15 cm. in length, stout but soft and weak, the base more or less sheathed with broad, thin, and membranaceous, somewhat translucent stipules; blade ash-green, trifoliate; leaflets, sessile or very short-petioled from 5 to 8 cm. in length and usually about two-thirds as broad, obovate, blunt, entire or ocasionally coarsely and unequally crenate. Odor slight but charac-

teristic; taste decidedly bitter. Menyanthes yields not more than 10 per cent. of ash." *N. F.* Its virtues depend on a bitter principle denominated *menyanthin*, which may be obtained sufficiently pure for use by treating the spirituous extract of the plant with hydrated lead oxide, removing the lead by hydrosulphuric acid, filtering and evaporating the liquor, exhausting the residue with alcohol, and again evaporating with a gentle heat. It has a bitter taste, is soluble in alcohol and water, but not in pure ether, and is chemically neutral. Kromayer (1865) assigned to it the formula $C_{30}H_{46}O_{14}$, and stated that it breaks up on heating with diluted sulphuric acid into a fermentable sugar and *menyanthol*, a colorless, difficultly volatilizable oil, with an odor like that of bitter almond. K. Leuderich (*A. Pharm.*, 1892, 38 and 48) has studied menyanthin, and gives it the formula $C_{33}H_{50}O_{14}$, and states that its decomposition products are a phenol-like body, menyanthol, $C_7H_{11}O_2$, a resinous product, and a left-rotatory sugar.

Vridevel (*P. J.*, 1910, lxxxv, p. 465) has separated a second glucoside from menyanthes, to which he gives the name of *meliatin*. It is a crystalline body, with a melting point of 217° C. (422.6° F.).

With the ordinary properties of the bitter tonics, menyanthes unites a cathartic power; in large doses it may cause vomiting. The *dose* of the powdered leaves or root as a tonic is from twenty to thirty grains (1.3–2.0 Gm.); of an infusion, prepared with half an ounce to a pint of boiling water, from one to two fluidounces (30–60 mils); and of the extract, ten or fifteen grains (0.65–1.0 Gm.), to be repeated three or four times a day. A drachm of the powder, or four fluidounces of the strong decoction, generally purges, and often occasions vomiting.

Mercuramine. *Mercury ethylenediamincitrate.*—This is a solution of 10 parts of mercury citrate and 4 parts of ethylenediamine in 86 parts of distilled water. Its 0.3 per cent. dilution is asserted to be equal in bactericidal value to a 1 in 1000 solution of mercuric chloride.

Mercurial Oil.—An unctuous mass containing 90 per cent. mercury in the form of aluminum magnesium amalgam, the vehicle being lanolin and almond oil. It can be used hypodermically in warmed anhydrous almond oil solution, three-quarters to three minims (0.045–0.20 mil) being injected every five days, employing altogether 6 to 10 injections. The mass must at all times be well protected from moisture.

Mercurialis. *Mercurialis annua* L. *Mercury Herb. French Mercury.*—An herbaceous European plant, of the Family of *Euphorbiaceæ* which has been employed from the most ancient times as a purgative, diuretic, and emmenagogue. When boiled, it loses its acridity, and in this condition has been used as an emollient. Another species, *M. perennis* L., or *dog's mercury*, also a native of Europe, is poisonous. (Mérat and De Lens.) Reichardt has discovered in *M. annua* a volatile alkaloid, which he named *mercurialine*. According to E. Schmidt (*P. J.*, vol. x, 29), *mercurialine* is identical with *methylamine*, CH_3NH_2, and is associated in the *mercurialis* with *trimethylamine*. It is a liquid of an oily appearance, narcotic odor, and alkaline reaction; boils at 140° C. (284° F.); forms salts with the acids; absorbs carbon dioxide; has a strong affinity for water; on exposure to the air it is changed into a resin of a buttery consistence, and is said to be poisonous to man; but Hugo Schulz (*A. E. P. P.*, April, 1886, 88) found that neither the fluidextract nor the herb given as food was capable of killing either the pig or the rabbit, and that four and a half grains (0.29 Gm.) of the mercurialine hypodermically injected had no effect. The urine is increased in quantity and colored reddish.

Mercuric Acetate. $(CH_3COO)_2Hg$.—Colorless, laminar crystals, soluble in 4 parts of water, also in alcohol and ether. Used internally as an antisyphilitic in *doses* of one-sixth to one grain (0.010–0.065 Gm.).

Mercuric Albuminate. *Hydrargyri Albuminas. Quecksilveralbuminat*, G.—This compound is not constant and is made by adding a 4 per cent. solution of mercuric chloride to a 1 in 8 solution of desiccated egg albumin and heating. The digestion is continued for forty-eight hours, during which time the albumin is kept in excess. The moist precipitate is then carefully dried and mixed with enough sugar of milk to make the amount of mercuric chloride present represent 0.4 per cent. It is used as an antiseptic surgical powder.

Mercuric Amidosuccinamate. *Mercury Asparaginate. Hydrargyri Amidosuccinamas. Asparagin Mercury.* $Hg(C_4H_7N_2O_3)_2$.—Made by dissolving mercuric oxide in a warm solution of amido-succinamic acid, or asparagin, and setting aside to crystallize. Colorless, needle-like crystals, insoluble in water, soluble in dilute acids. It is used hypodermically in the treatment of *syphilis* and is asserted to produce less irritation at the site of injection than other salts of mercury. The *dose* is one-twelfth to one-sixth of a grain (0.005–0.010 Gm.).

Mercuric Anilinate. *Hydrargyri Anilicum.* $Hg(C_4H_4.NH_2)_2$.—It is prepared by the action of a solution of bichloride of mercury on aniline and forms a white, micro-crystalline, odorless and tasteless powder containing 52.1 per cent. mercury. It is insoluble in water. Fedtscheutig has used this salt with success both hypodermically and by mouth in the treatment of *syphilis*. Hypodermically it may be given in a white oil suspension and by mouth, in a pill. It has also been used as an inunction with oleic acid and resorbin.

Dose, one-fourth of a grain (0.015 Gm.).

Mercuric Arsenate. $Hg_2H_2(AsO_4)_2$.—A yellow powder soluble in acids and insoluble in water. It is used in the treatment of *syphilis*. The *arsenite* of *mercury* (*mercurous arsenite*), Hg_3AsO_3, a brownish powder, soluble in acids and insoluble in water, is used in *syphilis*.

Mercuric Benzoate. *N. N. R.* 1917. *Hydrargyri Benzoas*, $Hg(C_6H_5COO)_2 + H_2O$, is obtained by double decomposition between an alkaline benzoate and a mercuric salt; it is a white crystalline, odorless, and tasteless powder, which is sparingly soluble in water, but easily in alcohol as well as in aqueous solutions of sodium chloride, the latter effect being due to its property of forming easily soluble double salts with the haloids. This salt is incompatible with acids, iron compounds and acid salts. It has been strongly recommended by Stukowenkow as a substitute for mercuric chloride, especially for hypodermic use and also locally in *gonorrhea*. For urethral injections the solution may be 1 to 1000 or 2000, with an equal quantity of sodium chloride. For subcutaneous injections it is employed in conjunction with cocaine, the following being the proportions: mercuric benzoate, 0.2 to 0.3; sodium chloride, 0.1; cocaine hydrochloride, 0.15; distilled water, 40.

Mercuric Betanaphtholate. *Hydrargyri Betanaphtholas.* $Hg(C_{10}H_7O)_2$.—This substance is made by the action of an alkalinated sodium

naphtholate solution on a mercuric acetate solution. It is a grayish-white, odorless powder, insoluble in water. It is administered internally in the treatment of *syphilis* in *doses* of one-sixth to one grain (0.010–0.065 Gm.).

Mercuric bromide ($HgBr_2$) (*Mercury Dibromide*) may be obtained by digesting *mercurous bromide* in water containing bromine. A. E. Ebert prepared it by reaction between potassium bromide and official solution of mercuric nitrate. For the particulars of the process, see a paper by Ebert in the *A. J. P.*, March, 1867, 107. It is in the form of colorless crystals, soluble in water and alcohol. Exposed to heat it melts and sublimes. This salt is used in the treatment of *syphilis*. *Dose*, one-fifteenth to one-eighth of a grain (0.004–0.008 Gm.).

Mercuric Cacodylate. *Hydrargyri Cacodylas. Mercuric Methyl Arsenate.* $[(CH_3)_2AsO_2]_2Hg$.—This occurs as a white crystalline powder soluble in water. It is used in the treatment of *syphilis* in intramuscular injections of half a grain (0.032 Gm.). Under the name of *mercuric iodocacodylate* there has been introduced a solution of this salt with cacodylic acid mixed with a solution of sodium iodide and the mixture neutralized with sodium hydroxide. It is recommended as an antisyphilitic and is used by intramuscular injection.

Mercuric Chloride-urea Solution. *Hydrargyri Chloridi Carbamidum. Hydrargyrum Bichloratum Carbamidatum Solution.*—As the solution quickly changes it should be prepared extemporaneously as follows: 1 Gm. of mercuric chloride is dissolved in 100 mils of water with the aid of heat, and, when cold, 0.5 Gm. of urea is added and the liquid filtered. The solution is given in doses amounting to 15 minims (0.9 mil) in twenty-four hours, equal to one-sixth grain (0.010 Gm.) of mercuric chloride. It is employed subcutaneously in *syphilis*.

Mercuric Cyanide. *N. N. R.* 1917. *Hydrargyri Cyanidum. U. S.* 1890. $Hg.(CN)_2 = 252.62$. *Hydrargyri Cyanuretum. U. S.* 1850. The process for the preparation of this substance, given in the U. S. P., 1850, is based upon the following: Hydrocyanic acid is generated by the action of sulphuric acid on potassium ferro-cyanide, and, being received in a vessel containing water and a portion of mercuric oxide, reacts with the oxide, according to the reaction

$$(HCN)_2 + HgO = Hg(CN)_2 + H_2O$$

generating, by double decomposition, water, and mercuric cyanide which is held in solution. Sufficient mercuric oxide is not used at first to saturate the whole of the hydrocyanic acid generated, because should there happen to be any excess of the oxide there would be produced an evaporation, instead of the substance wanted, a peculiar salt composed of cyanide and mercuric oxide, which would crystallize in small acicular crystals. Hence a portion of the water still containing uncombined hydrocyanic acid is set aside, to be added to the liquid in which the acid had been completely saturated by the addition of mercuric oxide, and thus at least neutralize any mercuric oxide that might be present in it in excess. A surplus of hydrocyanic acid would not be detrimental, except for the loss of material incurred, as it is evaporated in the subsequent concentration. Mercuric cyanide should be kept in well-stoppered, dark amber-colored bottles.

It occurs as colorless or white, prismatic crystals, odorless, and having a bitter, metallic taste (the salt is exceedingly poisonous), becoming dark-colored on exposure to light. Soluble, at 15° C. (59° F.), in 12.8 parts of water, and in 15 parts of alcohol in 3 parts of boiling water, in 6 parts of boiling alcohol; very sparingly soluble in ether. It is often contaminated with the oxycyanide. The presence of the latter may be shown by the production of a white precipitate by ammonia.

Mercuric cyanide has been brought forward as a substitute for corrosive sublimate especially for germicidal purposes. The experiments of various investigators show that these antibacterial properties are much inferior to those of the bichloride. According to Hüne (*Desinfektion*, 1912, v) it requires a 1 in 1000 solution of mercuric cyanide to kill the staphylococci in thirty minutes, which corrosive sublimate will do in 1 in 10,000 solution, and Harrington (*B. M. and S. J.*, January 14, 1904) found that a 1 in 500 solution was not certainly fatal to the pus-forming organisms in thirty minutes.

Prochorow gives from twenty-five to thirty-five drops of a 1 per cent. solution of hypodermically without causing local irritation, and with great asserted benefit, in chronic *syphilis*. Chaleix (*Journ. de Méd. de Paris*, March, 1900) reports death from the use of a vaginal injection containing fourteen grains of mercuric cyanide. *Dose*, internally, from one-sixteenth to one-eighth of a grain (0.004–0.008 Gm.).

Mercuric Formamide Solution. *Hydrargyri Formamidum. Hydrargyrum Formamidatum Solutum. Quecksilberformamidlösung*, G.—A solution made by dissolving freshly precipitated mercuric oxide, obtained from 10 Gm. of mercuric chloride, in a sufficient amount of formamide, and adding sufficient water to make 1000 mils. It is intended for hypodermic injection in *syphilis*, sixteen minims (1 mil) of the solution being given in twenty-four hours, corresponding to one-sixth grain (0.010 Gm.) of mercuric chloride.

Mercuric Gallate. *Hydrargyri Gallas. Mercurigallat*, G. $[C_6H_2(OH)_3CO_2]_2Hg$.—Made by rubbing together molecular proportions of gallic acid and moist precipitated mercuric oxide and drying the product. It forms a blackish or greenish powder, insoluble in most solvents. The compound is used in place of the tannate, which is less stable, as an antisyphilitic, in *doses* of from one-half to one grain (0.032–0.065 Gm.) daily.

Mercuric Guaiacol-sulphonate. *Mercuric orthoguaiacol-sulphonic acid*, $Hg(C_6H_3.OH.OCH_3.SO_3)_2$, occurs as brown crystals readily soluble in water. It has been used by Horand (*Lyon Med.*, 1911) by intramuscular injection in the treatment of *syphilis*. The beginning *dose* is one-half grain (0.032 Gm.) which may be gradually increased.

Mercuric Iodate. $Hg(IO_3)_2$.—A white amorphous powder, soluble in water containing sodium chloride or potassium iodide. It is used in the treatment of syphilis in *doses* of one-sixth to one-quarter of a grain (0.010–0.016 Gm.).

Mercuric Iodotannate. *Hydrargyri Iodotannas.*—This is prepared by dissolving one part of iodine in a solution of ten (10) parts of tannin in water, solution being effected by digestion until there is no longer a reaction with starch paper. Then a solution of mercuric acetate in warmed glucose and water is added to the iodine tannin solution and a gray-brown gelatinous precipitate results. This is then separated and purified. It is given in one- to two-grain (0.065–0.13 Gm.) *doses* three times daily in the treatment of *syphilis*.

Mercuric Lactate. *Hydrargyri Lacticum.* $(C_3H_5O_3)_2Hg$.—It forms a white crystalline powder, soluble in water. This preparation has been used

hypodermically in *dose* of one-sixth grain (0.010 Gm.) a day. Bouveyron (*S. M.*, 1905, p. 30) recommends that in cases of *syphilitic* lesions in the mouth, tablets of *mercury lactate* be allowed to dissolve slowly on the tongue.

Mercuric Oxycyanide. *N. N. R.* 1917. *Hydrargyri Oxycyanidum. Hydrargyri Oxycyanatum.* $HgO.Hg(CN)_2$.—This basic cyanide of mercury occurs as a white crystalline powder, soluble in 17 parts of water and turning litmus paper blue. The commercial preparations are frequently contaminated with the neutral cyanide of mercury. It has been brought forward as a substitute for mercuric chloride, both as a disinfectant and in the treatment of *syphilis*. The advantage is claimed for it as a germicide that it does not have an injurious effect upon steel instruments. Although Lehmann claimed that its germicidal power was equal to that of the bichloride, more recent experiments throw grave doubt upon this conclusion. Kruger, for example (*Desinfektion*, 1910, p. 456), reached the conclusion that its germicidal power was inferior to that of phenol. It is used in *syphilis* for hypodermic injection in the same doses as corrosive sublimate.

Mercuric Peptonate. *Peptonized Mercury.*—Two preparations are known under this name. One is a yellowish powder, representing 10 per cent. of mercuric chloride, the other a liquid representing 1 per cent. of the corrosive sublimate. Of the solution it is alleged that it may be used hypodermically without production of pain. Fifteen minims (0.9 mil) is said to be equivalent to one-sixth of a grain (0.010 Gm.) of mercuric chloride. As a substitute for this has been proposed *gluten-peptone sublimate.* This has been introduced as a white lustrous hygroscopic powder, or more commonly in 1 per cent. solution. It is said to contain 10 per cent. of corrosive sublimate, and to be an efficient, non-irritating preparation for hypodermic use.

Mercuric Phenylate.—*Hydrargyri Carbolas, Mercuric Carbolate, Mercuric Phenolate, Phenol Mercury,* $(C_6H_5O)_2Hg + H_2O$, occurs as colorless needles, insoluble in water and cold alcohol, but taken up by hot alcohol, by ether, or a mixture of alcohol and ether, and by glacial acetic acid. This substance has been used as an antisyphilitic in *doses* of from a third to a half grain (0.021–0.032 Gm.).

Mercuric Pyroborate.—*Hydrargyri Pyroboras,* HgB_4O_7, is an amorphous, brown, insoluble powder, which has been commended by V. Tokayer (*Ph. Post*, 1892) as a local application in the treatment of specific and other ulcerations.

Mercuric Salicylarsenate.—*Hydrargyri Salicylarsenas. Enesol.*—By the interaction of molecular quantities of basic mercuric salicylate on methyl arsenous acid, a white amorphous substance is formed which is difficultly soluble in water. The solution gives no reaction with hydrogen sulphide or with potassium iodide and may be sterilized without decomposition. The composition of the salt is mercury, 38.46 per cent., and arsenic, 14.4 per cent., with salicylic acid. It is asserted that its subcutaneous injection is painless. The *dose* of a 3 per cent. solution is given as fifteen to thirty minims (1–2 mils) when administered hypodermically.

Mercuric Sozoiodolate. *Hydrargyrum Sozojodolicum.* $HgC_6H_2I_2OSO_3$.—This compound is a lemon-yellow powder, scarcely soluble in water, but more so in solution of sodium chloride. This preparation, which is said to contain 31 per cent. of mercury and 38 per cent. of iodine, has been especially recommended by Witthauer (*M. M. W.*, Aug., 1892) in the treatment of *syphilitic ulcerations, enlarged glands,* and skin diseases, in the form of a 1 per cent. ointment. The 1 per cent. solution is also used by Genzmer, as an injection into diseased joints, etc.

Mercuric Subsulphate, Yellow. *Hydrargyri Subsulphas Flavus. U. S.* 1890. *Yellow Mercuric Subsulphate. Basic Mercuric Sulphate Turpeth Mineral.* $Hg(HgO)_2SO_4 = 729.87$. *Hydrargyri Sulphas Flava. U. S.* 1870. *Hydrargyri Subsulphas.*

When normal mercuric sulphate is thrown into boiling or even warm water it is instantly decomposed, and an insoluble salt is precipitated, which is yellow mercuric subsulphate. Its composition is $Hg(HgO)_2SO_4$.

Yellow mercuric sulphate is a heavy, lemon-yellow powder, odorless and almost tasteless; permanent in the air. Soluble in about 2000 parts of water at 15° C. (59° F.), and in 600 parts of boiling water; insoluble in alcohol; readily soluble in nitric or hydrochloric acid. When heated, the salt turns red, becoming yellow again on cooling. At a red heat it is volatilized, evolving vapors of mercury and of sulphur dioxide, and leaving no residue. It was originally called *turpeth mineral,* from its resemblance in color to the root of *Ipomœa Turpethum.*

Yellow mercuric subsulphate is capable of acting as a mercurial and producing ptyalism. It is, however, in full dose violently emetic, and has been chiefly used in true *croup.* It is a dangerous remedy, especially with young children, several cases having been reported in which, failing to cause vomiting, it has produced death preceded by symptoms similar to those of corrosive sublimate poisoning. (See *M. News,* xliii, 1883; also, *London Med. Gaz.,* 1847.) Emetic *dose* for a child two years old, two to three grains (0.13–0.2 Gm.); for adult, three to five grains (0.2–0.32 Gm.), repeated in fifteen minutes if it does not operate. Alterative *dose,* one-fourth to half a grain (0.016–0.032 Gm.).

Mercuric Succinimide. *Hydrargyri Succinimidum. Hydrargol. N. N. R.* 1917. *Mercury imidosuccinate.* $Hg[(CH_2.CO)_2N.]_2$.—This drug may be formed by heating together succinic acid, carbonic anhydride, and ammonia, which combine with mercuric oxide to form a compound which occurs as a white crystalline powder soluble in water. This solution remains quite unchanged when kept. According to Vollert, the solution of one and three-tenths grammes of this salt in one hundred of water is free from irritant properties, and when used hypodermically produces no disagreeable local or even secondary symptoms. (*Th. M.*, 1888.)

It was used by B. L. Wright with asserted extraordinary results in the treatment of *pulmonary tuberculosis.* Hartz (*J. A. M. A.*, 1911, lv, p. 915) and others were unable to see any beneficial effect from the drug in phthisical patients, except in those who were syphilitic. The *dose* employed was one-fifth of a grain (0.012 Gm.) injected intramuscularly every other day.

Mercuric Sulphate. *Hydrargyri Sulphas. Hydrargyrum Sulphuricum. Normal Mercuric Sulphate. Sulfate mercurique,* Fr. *Mercurisulfat,* G. $HgSO_4 = 296.67$.—Made by heating together 18 parts of mercury, 10 parts of concentrated sulphuric acid, 3 parts of water and 4 parts of 25 per cent. nitric acid, in a flask, on a sand bath, until reddish vapors cease to be given off, then drying with the aid of heat, in an open dish, constantly stirring. It is a heavy white crystalline powder, used in making turpeth mineral, and mercuric and

mercurous chlorides. It has no use in medicine.

Mercuric Sulphide. *U. S.* 1880. *Hydrargyri Sulphidum Rubrum. Red Sulphide of Mercury. Cinnabar.* HgS = 232.67.—This preparation, which was formerly official both in the United States and British Pharmacopœias, has been dropped from each. For process of making mercuric sulphide see *U. S. D.*, 19th ed., p. 1566.

Cinnabar is seldom prepared on a small scale, being made in large quantities for the purposes of the arts. Until within a few years it was nearly all manufactured in Europe, but it is now made to an enormous extent in this country. In Holland, where it is largely manufactured, the sulphur is melted in a cast iron vessel, and the mercury is added in a divided state, by causing it to pass through chamois leather. As soon as the combination has taken place, the iron vessel is surmounted by another, into which the cinnabar is sublimed. In the United States, Martin's method, consisting of the agitation together of quicksilver, sulphur, and an alkaline sulphide, appears to have the preference. Another process for its manufacture in the wet way very largely employed is Brunner's. (Wagner's *Chem. Tech.*, 13th ed., 1889, 552.)

Properties.—"Brilliant, dark red, crystalline masses, or a fine, bright scarlet powder, permanent in the air, odorless and tasteless, insoluble in water, alcohol, nitric or hydrochloric acid, or in dilute solutions of alkalies. It is dissolved by nitrohydrochloric acid with separation of sulphur. When heated, the salt becomes brown and then black, but, on cooling, it reassumes its red color. At a higher temperature it takes fire, burns with a bluish flame, emitting the odor of burning sulphur, and is finally volatilized without residue." *U. S.*, 1880. (For tests for purity, see *U. S. D.*, 19th ed., p. 1567.) In closed vessels at a red heat it sublimes without decomposition, and condenses in a mass, composed of a multitude of small needles. When duly levigated, it furnishes a brilliant red powder, which is the paint called *vermilion*. The same compound occurs native, being the sole ore—cinnabar—from which mercury is extracted. The preparation, if purchased in powder, should be carefully examined, as, in that state, it is sometimes adulterated with red lead, dragon's blood, or chalk. If red lead be present, acetic acid digested with it will yield a yellow precipitate (lead iodide) with potassium iodide. Dragon's blood may be detected by alcohol, which will take up the coloring matter of that substance, if present, and, if chalk be mixed with it, effervescence will be caused on the addition of an acid.

Cinnabar is employed in medicine by fumigation, as a rapid sialagogue, in *syphilitic affections*, when it is desired to obtain an immediate mercurial impression. Half a drachm may be thrown on a red-hot iron, in a close apartment, and fumes inhaled as they arise. These consist of sulphurous acid gas and mercurial vapor, the former of which must prove highly irritating to the patient's lungs. A better substance for mercurial fumigation is black mercurous oxide. It is also employed in the form of an ointment by Lassar (*Med. Klin.*, 1905, No. 3, 54), using red mercuric sulphide 1 Gm., sublimed sulphur 24 Gm., petrolatum 100 Gm., and oil of bergamot 30 drops. It is recommended in the treatment of *herpes tonsurans*.

Mercuric Thymolacetate. *Hydrargyri Thymolacetas. Thymolquecksilberacetat*, G. $Hg(CH_3COO)_2.Hg(CH_3COO.C_{10}H_{13}O)$.—Made by adding a warm alkaline thymol solution to a warm solution of mercuric acetate as long as the precipitate which forms redissolves on shaking. The crystals are afterwards purified by recrystallizing from dilute sodium hydroxide solution. In colorless crystals, not readily soluble in water or alcohol, very soluble in alkaline solution, from which it is precipitated by acids. It contains about 55 per cent. of mercury. Used by injection, in *syphilis*, suspended in liquid petrolatum, one and one-half grains (0.1 Gm.) being given once a week.

Mercuric Thymolate. *Hydrargyri Thymolas.* $HgC_{10}H_{13}OH$.—Made by precipitating a solution of mercuric nitrate with sodium thymolate. An unstable reddish-yellow powder.

Mercuric Thymolnitrate. *Hydrargyri Thymolnitras.*—This salt, $(C_{10}H_{13}O)Hg.HgNO_3$, and *mercuric thymolsulphate* $[(C_{10}H_{13}O)Hg.Hg]_2SO_4$, have been used with asserted benefit in *syphilis*, in hypodermic *doses* of from one-twelfth to one-sixth of a grain (0.005–0.010 Gm.). (See *Merck's Jahresbericht*, 1891, 1892; also *W. K. W.*, March, 1892.) Besides these preparations *mercuric naphtholate*, a lemon-yellow powder, containing 30.8 per cent. of mercury, has been put upon the market; also under the name of *hydrargyrol, mercury paraphenylthionate* $(C_6H_4.OH.SO_3)_2Hg$, has been suggested as an antiseptic, but in proportion to its cost is probably of no practical value.

Mercuric Tribromphenol Acetate. *Hydrargyri Tribromphenolacetas.*—A yellowish powder insoluble in water, containing 30 per cent. of mercury. It is employed as an antiseptic and antisyphilitic, best administered hypodermically in a white oil suspension containing about 25 per cent. of the salt. *Dose*, two grains (0.13 Gm.).

Mercuric and Zinc Cyanide.—*Hydrargyri et Zinci Cyanidum* is stated by Dunstan to be a true chemical compound, with the formula $Zn_4Hg(CN)_{10}$, but other authorities contradict this statement. It is a white powder, entirely insoluble in water. This substance has been very highly recommended by Lister as an antiseptic dressing, and is believed by him to be practically free from irritating or poisonous properties.

Mercurous Acetate. *Hydrargyri Acetas. Mercuroacetat.* $Hg_2(C_2H_3O_2)_2$.—White, scaly crystals, soluble in about 330 parts of water, insoluble in alcohol and ether. It should be kept dry and away from light as it is decomposed, by boiling water and exposure, into mercury and mercuric acetate. Used internally in *doses* of from one-fifth to one grain (0.012–0.065 Gm.) for *syphilis*.

Mercurous Bromide. *Hydrargyri Bromidum*, Hg_2Br_2, is formed by adding potassium bromide to mercurous nitrate. It falls as a white, curdy precipitate.

Mercurous Iodobenzolparasulphonate. *Anogon.*—It is a yellow, crystalline powder insoluble in all the ordinary solvents, representing 48.5 per cent. of mercury and 30.7 per cent. of iodine. It is used in suspension in olive oil, and as an intramuscular injection in the treatment of *syphilis*. The *dose* is fifteen minims (0.9 mil) of a 10 per cent. suspension.

Mercurous Sulphide. *Hydrargyri Sulphidum Nigrum. Black Sulphide of Mercury. Ethiops Mineral.* Hg_2S.—This now disused remedy was prepared as follows: "Take of Mercury, Sulphur, each, *a pound*. Rub them together till all the globules disappear." *U. S.*, 1850. For properties, see *U. S. D.*, 14th ed., 1259.

Mercuric Sulphocyanate. *Hydrargyri Sulphocyanas.* $Hg(CNS)_2$.—This substance, formerly

called *sulphocyanide of mercury*, is produced by mixing diluted solutions of mercurous nitrate and potassium sulphocyanate. The white precipitate which falls, after drying, swells up suddenly when ignited, giving off nitrogen, carbon disulphide, and poisonous vapor of mercury, leaving a voluminous gray residue, *mellon*, C_9H_{12}. The salt is used in the preparation of the toy, *Pharaoh's serpents*.

Mercurous Tannate. *Hydrargyri Tannas.* $Hg_3.3(C_{14}H_9O_9).OH$. *Hydrargotin.—Mercurous tannate*, which was first brought forward by Lustgarten (*N. Y. M. J.*, March, 1892), has received some favor at the hands of syphilographers, and is official in the Austrian Pharmacopœia (1906), under the name of *Hydrargyrum tannicum oxydulatum*. It is declared that it has the especial advantage of being unabsorbed in the stomach, but decomposed by the alkaline juices of the duodenum, in such a way as to yield very minute globules of metallic mercury. It may be prepared either by precipitating concentrated solution of tannic acid and mercurous nitrate or by rubbing together tannic acid and mercurous nitrate. According to Lustgarten, the first process yields the better preparation. It is asserted that it does not irritate the alimentary canal. In *syphilis*, three grains (0.2 Gm.) may be given to the adult daily, increasing to five grains (0.32 Gm.) or more.

Mercury Atoxylate. *Mercury Paraminophenylarsenate. Atoxyl Mercury. Aspirochyl. Asiphyl.* $C_{12}H_{14}O_6N_2As_2Hg$.—This occurs as a white powder insoluble in water, and represents 31.8 per cent. of mercury. It has been introduced as an antisyphilitic with the idea that it would combine the effects of its two constituents. Manteufel (*Med. Klin.*, 1908, p. 1651) found it to be actively destructive to *spirilli, spirochete* and *trypanosomes*, and obtained favorable clinical results in *syphilis*. Bergrath (*D. M. W.*, 1910), however, reached the conclusion that it had no advantage over other forms of mercury. It is administered by intramuscular injection in the form of a 10 per cent. emulsion in olive oil. Of this emulsion from eight to fifteen minims (0.5–1.0 mil) may be injected once or twice a week. It is also used in the form of an ointment (1 in 20).

Mercury Di-iodo Salicylate. $Hg(C_7H_3I_2O_3)_2$. —A yellow, amorphous powder containing 20.5 per cent. mercury and 52 per cent. iodine. It is soluble in alcohol but insoluble in water and is usually administered as a 10 per cent. suspension in liquid petrolatum by intramuscular injection.

Mercury Ethyl Chloride.—This is prepared by the interaction of mercuric chloride and mercuric ethide. It forms colorless, shiny scales of an unpleasant ethereal odor. It is slowly soluble in ether, water, and alcohol. It is used as an intramuscular injection, intended to replace mercuric chloride and bearing an advantage over the latter of being indifferent to albumen.

Mercury and Potassium Thiosulphate. *Hydrargyri Potassii Thiosulphatis.* $3Hg(S_2O_3)_2.5K_2S_2O_3$.—This substance, obtained by the action of an excess of potassium thiosulphate on mercuric oxide in aqueous suspension, forms small, water soluble crystals. It contains 31.4 per cent. of mercury. It is used in the form of a 2.5 per cent. subcutaneous injection in the treatment of *syphilis*.

Mercury Resorcinol Acetate. *Resorcinol Mercury Acetate.*—A yellow, crystalline powder containing 69 per cent. mercury. It is soluble in strongly alkaline solutions and in hydrochloric acid, but insoluble in alcohol and water. It is used as an antisyphilitic hypodermically in liquid paraffin and melted lanolin solution. Three minims (0.2 mil) of a solution of eighty-five grains (5.6 Gm.) of the salt in the same amount of paraffin oil and thirty grains (2.0 Gm.) of anhydrous lanolin is injected twice weekly, the mixture being warmed to 25° C. (77° F.) before being used.

Mergal. *N. N. R.* 1917.—Under this name there has been introduced into medicine a mixture which is asserted to contain one part of *mercuric cholate*, $Hg(C_{24}H_{39}O_5)_2$, with two parts of albumin tannate. It occurs as a yellowish-white powder, practically insoluble in water, but dissolving in alkaline solutions. *Mergal* has been highly lauded by a number of authors as a most highy satisfactory means of exhibiting mercury in the treatment of *syphilis*. According to Barges (*Fort. Med.*, 1907, No. 27) mercury appears in the urine within four hours after its exhibition by the mouth, and elimination—which is partially through the kidneys and partially through the intestinal glands—goes on with great regularity, so that the prolonged use of the remedy is less liable to lead to undesirable results than with the ordinary form of mercury. It contains approximately 4.4 per cent. of mercury and is dispensed in capsules, which contain 0.05 Gm. each (three-quarters of a grain) of mercuric cholate and one and a half grains (0.096 Gm.) of albumin tannate. Of these from five to ten may be given daily.

Mesembryanthemum. *Mesembryanthemum crystallinum* L. *Iceplant. Diamond Fig.*—A biennial plant of the Fam. *Aizoaceæ*, a native of the south of Europe, now distributed to the Canary Islands, Southern Africa, Australia and California. The stem and under surface of the leaves are covered with crystalline drops, which give the plant the appearance of being coated with ice. H. Mangon obtained as much as 43 per cent. of salts of potassium and sodium from the dried leaves. (*A. J. P.*, 1883, 370.) The herb is without odor, and has a saline, somewhat nauseous taste. It is considered demulcent, diuretic, and has been used in *inflammations* of the *pulmonic* and *genito-urinary* mucous membrane.

Mesenna. *Musenna. Bisenna. Muséna, Moucéna*, Fr. *Musennarinde*, G.—Under these different names has been brought into notice, as a powerful *tenifuge*, the bark of an Abyssinian tree, *Albizzia anthelmintica* Brongn. (Fam. *Leguminosæ*). The bark is in flat pieces from five to ten inches long, smooth, slightly fissured, of a rusty gray color exteriorly, and pale yellow and fibrous within. It consists of four layers, one of which contains very large cells, with thick coats, and is supposed to be the active part. E. Caventou and Legendre found in the bark no alkaloid, but a peculiar, acid, acrid, resinous substance. The *musennin* of Theil is probably the same, although not as yet in a pure state. The Abyssinians employ the powdered bark, in the *dose* of about two ounces, suspended in water or other liquid, or mixed with flour in the form of bread, or made into a confection with honey, butter, etc. It is taken in the morning, three or four hours before breakfast, and no other precautions are used. It produces no pain nor any disturbance of the functions, not even purging actively. Fragments of the worm are voided the same evening, and the greater portion of it the next day.

Mesotan. *Salicylic-acid Methyloxymethylester. Ericin. N. N. R.* 1917. $C_6H_4OHCOO(CH_2OCH_3)$. —This preparation is a yellow, clear fluid with a peculiar odor, miscible in all proportions with ordinary oils, sp. gr., 1.2, boiling point, 162° C. (323.6° F.). It has been brought forward as a

local application in all forms of *rheumatism*. In from half an hour to an hour after its local application the presence of salicylic acid can be demonstrated in the urine. When applied pure to the skin and confined by waxed paper or other appropriate dressing it produces redness and sometimes pronounced burning pains, so that it should be diluted with olive oil, castor oil, petrolatum, or liquid petrolatum. Even when diluted, *mesotan* may produce eczematous, urticarial, or other eruption upon the skin, requiring its removal or further dilution. From one and a half to two and a half fluidrachms (5.5–9.3 mils) of an oily solution, containing 20 to 50 per cent. of mesotan, may be applied daily to the affected part.

Mesothorium.—This is the name which has been applied to the first product of the disintegration of thorium. It appears to give off, like radium, three types of rays and an emanation. It has been used by Voigts (*M. M. W.*, 1913, lx, 1186) in *uterine hemorrhages*. It is probable that *mesothorium* has therapeutic properties very similar to those of radium. See also Emsmann (*B. K. W.*, 1911, p. 2108), and *P. J.*, 1913, 608. Mesothorium is obtained from the Monazite sand in Brazil.

Mespilus Germanica L. *Medlar.* (Fam. *Rosaceæ.*)—The fruit has been recommended by Mercier (*A. G. M.*, 1907) in the treatment of chronic *enteritis* and *colitis*. It may be either eaten fresh or preserved. The method he employed was to put the patient on a diet consisting of two quarts of milk and eight ounces of *medlar* daily, no other food being allowed.

Metaferrin.—This is an iron albumen combination representing 10 per cent. of iron. It is a brownish, odorless powder, insoluble in water and dilute acids, but soluble in alkalies. It is supposed to pass through the stomach unchanged, and be absorbed from the intestinal tract, and hence not to affect gastric digestion. It is used in *anemia*. The *dose* is four grains (0.26 Gm.) three times a day generally in tablet form. There is also a "liquid form of metaferrin," *metaferrose*, the *dose* of which is one tablespoonful.

Methacetin. *Para-acetanisidine. Para-oxymethylacetanilide.* $C_6H_4(OCH_3).NHC_2H_3O$.—This differs from acetanilide in having an atom of the nucleus replaced by the oxymethyl group (OCH_3) or from acetphenetidin by having oxymethyl instead of oxyethyl as a replacing group. It forms lustrous crystals free from color, odorless, melting at 127° C. (260.6° F.), and distilling at higher temperatures unchanged. It is scarcely soluble in cold water, readily soluble in hot water, soluble in alcohol, acetone, chloroform, glycerin, and fatty oils. When triturated with chloral, bromal or phenol it liquifies and with resorcin it forms a mass. Its color and identity reactions are similar to those of phenacetin from which substance it may be distinguished, however, by the fact that when it is heated with a quantity of water insufficient for solution it melts to an oily liquid, while phenacetin does not. According to F. Manhnert, when given in toxic dose to rabbits, it causes convulsions and death through its action on the central nervous system, and is germicidal in 1 per cent. solution. *Methacetin* appears to be a powerful antipyretic, producing in fever a very marked fall of temperature, with a slow afterrise; this effect being accompanied by a violent sweating, which especially in *phthisis* and allied diseases, greatly interferes with the practical use of the drug. It has also been much used in *acute rheumatism*, but is not as effective as the salicylates. As an analgesic, in *ataxic* and *neuralgic pains*, it appears to be distinctly inferior to phenacetin and antipyrine. No eruption from it has been noticed. During its administration the urine responds to Trommer's test, but does not contain sugar, nor is there hemoglobinuria. *Dose*, for adults, eight grains (0.5 Gm.).

Methonal. $(CH_3)_2C(SO_2CH_3)_2$. *Dimethylsulphonedimethylmethane.*—In the form of colorless crystals, made by a process similar to that for preparing sulphonal, excepting that methylmercaptan is used in place of ethylmercaptan. It is used as a hypnotic in *doses* of from twenty to forty grains (1.3–2.6 Gm.).

Methyl Acetylsalicylate. *Methyl Rhodin. Methyl Aspirin. Acetyl Salicylic Methylester.* $O.CO.CH_3.C_6H_4.COOCH_3$.—It occurs in colorless crystals, soluble in alcohol, ether, and fatty oils, but not in water. This has been used by Corsi (*K. T. W.*, 1905) and others in the treatment of *rheumatism* and *influenza*. It is stated that, not being affected by dilute acids, it passes through the stomach unchanged without irritation, and is therefore borne better than the salicylates. The *dose* is from eight to fifteen grains (0.5–1 Gm.).

Methyl Alcohol. *Methylic Alcohol. Methanol. Carbinol. Spiritus Pyroxylicus Rectificatus. Br.* 1864. *Pyroligneous Spirit. Pyroxylic Spirit. Wood Spirit. Wood Alcohol. Wood Naphtha. Alcool méthylique, Alcool formique, Alcool de Bois, Esprit de Bois, Esprit pyroligneux*, Fr. *Holzgeist, Methyl-alcohol*, G. CH_3OH.—*Methyl alcohol* was discovered in 1812 by Taylor. When wood is subjected to destructive distillation, there is formed, besides acetic acid, tar, and other products (see *Creosotum*, p. 386), about 1 per cent. of an inflammable volatile liquid, which, when separated and purified, constitutes methyl alcohol. The crude liquor, derived from the wood, separates on standing into two liquids; the heavier containing the tarry matters, and the lighter consisting of water, acetic acid, methyl alcohol, etc. The lighter liquid is saturated with lime, and subjected to distillation, whereby the impure methyl alcohol first comes over, mixed, however, with various compounds, among which are aldehyde and pyroacetic spirit (acetone). This, after having been redistilled and deprived of water by repeated rectifications from lime, forms the methyl alcohol of commerce. The commercial spirit may be purified by adding to it as much calcium chloride as it can dissolve, and allowing the mixture to stand for a few days. The methyl alcohol unites with the calcium chloride, and the compound formed is subjected to distillation to separate certain contaminating substances, which distil over. Finally, the methyl alcohol is separated from the calcium chloride by the addition of water and a new distillation, and from water by rectification from dry lime. Methyl alcohol, like the other monatomic alcohols, can also be formed synthetically in a variety of ways—from marsh gas, from formic acid, and from formaldehyde. Pure anhydrous methyl alcohol is a mobile, colorless liquid, possessing a hot, pungent taste, and a peculiar odor, recalling that of acetic ether. It mixes in all proportions with water, alcohol, and ether, without having its transparency disturbed. It burns like alcohol, but with a less luminous flame. Its sp. gr. as a liquid is 0.8021 at 15.5° C. (59.9° F.). Its vapor is irritating to the eyes. It boils at 66° C. (150.8° F.) (according to other authorities at 55° C. (131° F.), when absolutely anhydrous), and during ebullition its vapor causes concussions, which render its dis-

tillation difficult, but may be prevented by placing in the bottom of the vessel a layer of mercury. As a solvent it resembles alcohol, all bodies soluble in that menstruum being likewise soluble in it. Methyl alcohol is the first of a series of organic hydroxides known as *alcohols*. It may be considered as a molecule of water in which one hydrogen atom is replaced by the monad group CH_3 (methyl), derived from marsh gas (methane) by the withdrawal of one hydrogen atom. These organic hydroxides are basic, and form with both organic and inorganic acids salts called *esters*.

The pyroxylic spirit formerly official in the Br. Pharmacopœia was directed to have a sp. gr. from 0.841 to 0.846. From the density thus recognized, it might be implied that not the pure but the commercial pyroxylic spirit was contemplated, which has a straw-yellow color and a powerful odor of wood smoke. But the Pharmacopœia also directed that the spirit should be without action on litmus paper, free from smoky taste, and not rendered turbid by water. It therefore intended a purified spirit, and the greater density must be ascribed to the presence of the 10 per cent. of water allowed. According to Morson, of London, the impure commercial spirit, which is unfit for medicinal use, may be purified "by largely diluting it with water, when an oily substance separates, after the removal of which the spirit may be recovered by distillation." By passing the mixed liquids through animal charcoal the purification is rendered more complete. Pyroxylic spirit has been confounded with pyroacetic spirit. They may be distinguished, according to Scanlan, by calcium chloride, which is without action on the latter, but dissolves in the former. In applying the test, a drop or two of a *saturated* solution of calcium chloride is added to the doubtful liquid in a test tube. This solution is immiscible with pyroacetic spirit, separating after agitation, but dissolves instantly in pyroxylic spirit. The liquid examined must be so pure as not to separate into two layers, nor to become milky with water.

It is sometimes desirable to be able to distinguish the presence of methyl alcohol in ordinary alcohol, and in ether or nitrous ether which may have been prepared from the methylated instead of the pure spirit. For this purpose the official test is the best which has been proposed. See test for methyl alcohol under *Alcohol* (Part I); see also *Ph. Centralh.*, 1913, No. 29.

Columbian spirit is simply a brand of wood alcohol of a higher quality, free from empyreumatic odor and with only a slight trace of acetone as impurity. *Colonial spirit* is also a purified methyl alcohol.

Methylated spirit, much used in England, contains nine parts of ethyl alcohol to one part of methyl alcohol.

Denatured alcohol is now being produced in the United States in increasing amount. The production for 1914 was: Completely denatured 5,213,-129.56 wine gallons, especially denatured 5,191,-846.03 wine gallons; total 10,404,975.59 wine gallons, equivalent to 17,811,078.2 proof gallons; for 1915, 5,386,646.96 completely denatured and 8,599,-821.81 wine gallons; total 13,986,468.77 wine gallons, equivalent to 25,411,718.8 proof gallons.

Crude methyl alcohol is very largely used in the arts as a solvent, especially in the formation of varnish and other resinous solutions. It is also considerably employed as a source of heat, but the ordinary varieties of the spirit during burning give off an offensive odor.

Methyl alcohol is capable of producing an intoxication similar to that caused by ethyl alcohol, but distinct in the slowness of the onset and the extraordinary duration of the symptoms, which may last from three to four days after the comparatively moderate dose of the drug. The symptoms which have been observed in methyl alcohol poisoning are marked fall of the body temperature, convulsions, sometimes of a tetanic character, at others of a choreic type, vomiting, dilatation of the pupil, frequently nystagmus. The reflexes at first are increased, but after a period of a day or two loss of sensation and also of reflex power may occur. Quite characteristic of the poisoning is the loss of vision which begins generally within twenty-four hours and may progress to complete blindness. *Per se* methyl alcohol is less toxic than ethyl alcohol and the severity of the symptoms which it causes indicates that the effects must be due to some decomposition product. Krol (*A. E. P. P.*, 1913, lxxii) calls attention to the similarity of the symptoms of methyl alcohol poisoning and acidosis, and both Reid Hunt and Schmiedeberg have demonstrated that methyl alcohol is oxidized in the body to formic acid and it is probable that this is the chief cause of the symptoms. After death from poisoning from methyl alcohol there is found fatty degeneration of the liver and other organs. The cause of the amblyopia is a degeneration of the ganglion cells of the retina. It is worthy of note that methyl alcohol amblyopia has resulted from the use of essence of ginger or other aromatics in the preparation of which the wood alcohol has been used as a menstruum, from the inhalation of the vapors by workmen engaged in varnishing closed spaces, and there are one or two cases on record suggesting the possibility that it may be absorbed in sufficient quantities through the skin to cause poisoning. For review of the literature on this subject, see Holloway, *N. Y. M. J.*, 1911, xciii, p. 1030.

Methyl alcohol amblyopia may appear after a single debauch. It is accompanied with contraction of the field of vision, absolute, usually central, scotoma, and rapid failure of vision, and though temporary improvement may occur, in 90 per cent. of the cases it ends in permanent loss of useful vision.

Methyl alcohol has been used to some extent in practical medicine, but has no other remedial properties than those of ethyl alcohol, and is a so much more dangerous remedy that its use is unjustifiable and under no circumstance should it be employed by pharmacists as a menstruum. The treatment of *methyl alcohol poisoning* is very unsatisfactory. The best that can be done is to aid in the elimination of the alcohol, and of the products of its destruction within the body, by free sweating and by the administration of large quantities of alkalized (sodium bicarbonate) water.

Methyl Atropine.—Two salts are on the market, namely the bromide *methyl-atropine-bromide*, $C_{16}H_{20}O_3N(CH_3)_2Br$., and the nitrate (*methyl-atrophine-nitrate* or *Eumydrin*), $C_{16}H_{20}O_3N(CH_3)_2NO_3$.

Atropine Methylbromide occurs as white crystals with a melting point between 222° to 223° C. (431.6°–433.4° F.), freely soluble in either water or alcohol. *Atropine methyl nitrate* is a white, crystalline, odorless powder, soluble in both water and alcohol. Its solutions are permanent but have the incompatibilities of alkaloids in general.

Methyl-atropine closely resembles ordinary atropine in its effects on the system, but requires somewhat larger quantities to produce the same

effect. As a mydriatic it is employed in strengths of from 1 to 4 per cent. The dilatation of the pupil comes on more promptly than after atropine and is of less duration. Hudovernig (*B. K. W.*, 1906) asserts that it has a marked analgesic action and is a useful remedy in various types of *headaches* and *neuralgia*. It has been found useful for many of the purposes in which atropine is employed especially for the control of *night sweats* and in the treatment of *gastric ulcer*. A spray containing 0.3 per cent. of methyl atropine bromide with 1 per cent. of anasthesin has been recommended as an inhalation for the relief of *asthma*. The dose of either salt is from one-sixtieth to one-twentieth grain (0.001–0.003 Gm.).

Methyl Chloride. *N. N. R.* 1917.—*Monochlormethane*, CH_3Cl, is obtained by the action of hydrochloric acid gas upon methyl alcohol, best in the presence of a little zinc chloride. It is a colorless gas, condensing to a liquid at –23° C. (–11.5° F.), and is very soluble in alcohol, which dissolves thirty-five volumes of it, but is insoluble in water. On account of its extreme volatility, *methyl chloride*, when applied in the form of a spray, produces extreme cold and freezing of the part. It has been used in this way as a local anesthetic. At very low temperatures it forms with water a hydrate, $CH_3Cl.9H_2O$. According to Richet and Marcille (*S. M.*, 1902), methyl chloride acts upon the animal as an efficient anesthetic, which has practically no influence upon the circulation. Its usefulness seems to be limited by its failure to produce complete muscular relaxation. We know of no clinical reports upon its activity.

Methyl Iodide. *Iodomethane.* CH_3I. *Iodure de Methyl*, Fr. *Jodmethyl*, G.—This is a heavy, sweet-smelling liquid, boiling at 43° C. (109.4° F.), and has a sp. gr. of 2.23 at 15° C. (59° F.). In the cold it unites with water to form a crystalline hydrate, $CH_3I + H_2O$. It turns brown gradually on exposure to light. It is made by the action of dry hydrochloric acid gas upon a mixture of potassium iodide and anhydrous methyl alcohol.

R. Kirk (*L. L.*, Oct., 1885) commends *methyl iodide* as a vesicant, applied on lint under a watch glass, a drop or two of soda solution being added to neutralize the free iodine that may be present. It produces at once a tingling, burning, biting sensation, like pricking with a number of needle points. The maximum pain is reached in a few minutes, when the substance is to be removed. The blister produced is said to be as full of serum as that caused by cantharides.

Methyl Ether. $(CH_3)_2O$. *Methylic Ether. Methyl Oxide. Hydrate of Methylene. Ether méthylique, Oxyde de Méthyl*, Fr. *Methyläther, Holzäther, Formäther*, G.—This substance was discovered by Dumas and Péligot, but was first employed as an anesthetic by B. W. Richardson in 1867. He prepares it by mixing one part pure methyl alcohol with two of strong sulphuric acid, heating, collecting and washing repeatedly with potassium hydroxide solution the *methyl ether* which passes over. It is a gas even at low temperature. Richardson saturates absolute ethyl ether, at 0° C. (32° F.), with it, and at once closely bottles the compound under the name of *methyl-ethylic ether*. For a detailed description of the preparation of methyl ether and of its properties, see *J. P. C.*, 4e sér., xix, 438. According to Richardson, methyl ether is a very rapid and safe anesthetic, producing great muscular relaxation with extreme quickness. (*A. J. P.*, Sept., 1870; *Dublin Q. J.*, Aug., 1870; *L. L.*, March, 1870.)

Methyl Salol. $CH_3.C_6H_3(OH)COOC_6H_5$.—Phenyl ester of paracresotinic acid. It is used to relieve muscular pain. The *dose* is eight grains (0.5 Gm.) four times daily.

Methylal. *Methylene Dimethyl Ester. Formal.* $CH_2(OCH_3)_2$.—This is made by distilling methyl alcohol with sulphuric acid in the presence of manganese dioxide, or by abstracting one molecule of water from a mixture of one molecule of formaldehyde and two of methyl alcohol. It is a limpid colorless liquid, of sp. gr. 0.855 at 17° C. (62.6° F.), and boils at 42° C. (107.6° F.). It is soluble in water, alcohol, ether, and fatty and ethereal oils. It was originally proposed as an anesthetic and hypnotic by B. W. Richardson in 1868. Richardson, Motrokhin, and Personali are in general accord as to its physiological action. It produces in man a sleep closely resembling the normal sleep; or, if the dose has been large enough, a profound coma in which reflex actions are suspended. Recovery is rapid on account of its rapid elimination. The arterial pressure is reduced, as is also, according to Motrokhin, the irritability of the cerebral cortex. Both Personali and Motrokhin found that it arrests the tetanic spasms produced by small doses of strychnine, although in Motrokhin's experiments, when large doses of strychnine were given, methylal seemed to accelerate rather than put off death. It is employed as an hypnotic, and is said to be free from danger and unpleasant effects; but in most cases patients become so rapidly accustomed to it that its influence soon disappears, unless enormous doses are used. The *dose* is from one-half to one fluidrachm (1.9–3.75 mils), given in emulsion.

Methylene Dichloride. *Methylene Chloride. Dichloro-methane. Bichloride of Methylene.* CH_2Cl_2.—This was introduced by B. W. Richardson, of London. It may be prepared by exposing to sunshine, in a glass globe, pure chlorine and gaseous methyl chloride. *Methylene dichloride* is a colorless liquid, of an odor analogous to that of chloroform, of the sp. gr. 1.344, and the boiling point 40° C. (104° F.). The vapor of the dichloride is inflammable, burning with a brilliant flame, and yielding, as the result of combustion, carbon dioxide and hydrochloric acid. Methylene dichloride mixes readily with absolute ether, and, as the boiling points of the two approach nearly, they volatilize evenly and equably. It is neutral to test paper and an acid reaction in any specimen would be an evidence of the presence of hydrochloric acid, and should preclude its use as a respiratory anesthetic. To prevent the generation of the acid, the liquid should be kept carefully secluded from the sunlight, and the addition of a small quantity of absolute alcohol is recommended.

In his experiments upon the lower animals, Richardson found that methylene dichloride was a powerful and advantageous anesthetic, narcotism being produced more rapidly and continuing longer than when caused by other anesthetics, passing off, however, with great suddenness. (*M. T. G.*, 1867.) As the result of the paper of Richardson, the dichloride was used as an anesthetic by various English surgeons, also in Germany and America. The experiments of Geuther and Eichholz, and of Heymanns and Debuck (*A. I. P. T.*, i) show that the dichloride acts upon guinea-pigs and rabbits similarly to chloroform, but that chloroform is twice as poisonous to the heart.

Some years ago H. C. Wood had examined in

the chemical laboratories of the University of Pennsylvania methylene dichloride, supplied by one of the most reputable of the English manufacturing chemical firms, and sold as first quality. It contained, however, little or none of the methylene dicnloride, and was largely chloroform. Gutzart states, as the result of examination of German specimens of the drug, that they are mixtures of alcohol, methylene dichloride, and chloroform in varying proportions. It seems even probable that Richardson did not have the pure article. Merck states that methylene dichloride should not be confused with the Richardson product which is *methyl-bichloride* or in reality a mixture of one volume methyl alcohol with three volumes of chloroform. As yet methylene dichloride cannot be regarded as a safe anesthetic. Even the mixture of methylene dichloride and absolute ether, which Richardson introduced under the name of *methylene ether* (*M. T. G.*, ii, 1872; i, 1873), has caused death. (*P. M. T.*, iii, 718; *M. T. G.*, July, 1873.) The methylene dichloride may be given internally in the *dose* of from ten to thirty minims (0.6–1.8 mils), which may be dissolved in dilute spirit.

Methylethylcarbinol. $CH_3CH.OH.C_2H_5$.—There are two compounds known respectively as *methylethylcarbinol* and *trimethylcarbinol*. The former is a strong-smelling liquid, boiling at from 98° to 100° C. (208.4°–212° F.); the latter crystallizes in plates melting at 28° C. (82.4° F.), and boils at from 83° to 84° C. (181.4°–183.2° F.). These alcohols are said to be vasomotor depressants and antipyretics, the dimethylethyl compounds being the more powerful of the two. (*Ph. Post*, Jan., 1888.)

Methylphenacetin. $C_{11}H_{15}NO_2$.—This occurs as colorless crystals, soluble in alcohol and ether, but slowly so in water. It is said to give a quicker antipyretic action than phenacetin. *Dose*, five to fifteen grains (0.32–1 Gm.).

Methylphosphin.—Fürbringer (*Deutsch. Arch. f. klin. Med.*, lix, 1897) has found that this substance is a powerful convulsant poison, killing when in sufficient dose by respiratory paralysis, and having very little direct influence upon the circulation. The *di-methylphosphin* was found to be very slightly more poisonous than the *methylphosphin*, the fatal dose being about 0.5 gramme per kilo for the rabbit. Di-methylphosphin has been used in *malaria* by Julius Mannaberg, in the dose of nineteen grains (1.2 Gm.) per day, but is inferior to quinine. The urine becomes dark reddish-yellow and distinctly fluorescent, while numerous small yellow spots appear upon the skin.

Methylstrychnine. $CH_3.N:OC_{20}H_{22}(NH).CO.O + 4H_2O$. *Strychnine Methyl Ammonium Hydroxide.*—This is prepared by the interaction of strychnine and methyl iodide with subsequent removal of the iodine. It is a yellow powder, soluble in alcohol and water and used after the manner of curare.

The *methyl strychnine iodide*, $C_{21}H_{22}(CH_3)N_2O_2.I$, in the form of white, shining crystals slowly soluble in water.

Methylthebaine. $C_{20}H_{23}NO_3$.—This product from thebaine has been physiologically investigated by Crum Brown and Fraser, and by Stockman and Dott, and found to have an action similar to that of thebaine, but less powerful. (*B. M. J.*, Jan., 1891.)

Metol. *Monomethylpara-amido-meta cresol sulphate.* $(C_6H_3[OH]CH_3[NH]CH_3)2H_2SO_4$. — A white powder, soluble in water and extensively used as a developing agent in photography and in X-ray processes.

Michelia. *Michelia nilagirica* Zenker. (Fam. *Magnoliaceæ*.)—This tree, which is said to be abundant in the Neilgherry hills, India, yields an aromatic volatile oil, which has entered commerce. (*P. J.*, Jan., 1888.)

Micrampelis. *Micrampelis fabacea* (Naud.) Greene. (*Megarrhiza californica* Torr., *Echinocystis fabacea* Naud.) *Man Root. Big Root. Gerba marra.* (Fam. *Cucurbitaceæ*.)—J. P. Heaney has obtained a substance from this root of resinous character which he calls *megarrhizitin*, and another which he believes to be a glucoside and calls *megarrhizin*. It is said to be actively cathartic. (*A. J. P.*, 1876, 451.) A second glucoside was obtained by W. M. Young (*A. J. P.*, 1883, 195), to which the name of *megarrhin* was given. It resembles saponin, and possesses the property of dilating the pupil. Young also found two resins, one soluble in alcohol and the other soluble in ether.

Microcidin. *Betanaphthol Sodium.*—Under this name the varying compounds of *sodium naphtholate* with other naphtholates and phenates have been put upon the market, and used as surgical antiseptics in solution varying from three to five per cent. As a nasal or aural douche a 0.1 per cent. to 0.5 per cent. solution is recommended.

Micromeria. *Micromeria Chamissonis* (Benth.) Greene. *Yerba Buena.*—This sweet scented labiate, which is popularly known as *yerba buena* is a trailing perennial, indigenous to the Pacific Coast. Power and Salway have obtained besides 0.16 per cent. of a volatile oil with a mint-like odor, two new alcohols, which they named *micromol*, and *micromeritol*, and a phenol, *xanthomicrol*. (*J. Am. C. S.*, 1908, 251.) The fluidextract prepared from this plant has been used popularly as an emmenagogue. *Dose*, one-half to two fluidrachms (1.8–7.5 mils).

Midrol. *Iodomethylate of Phenylpyrazolon.*—*Midrol* forms white, bitter and water soluble crystals. One drop of a 10 per cent. solution introduced into the conjunctiva causes at first contraction, then dilation which lasts about two hours.

Milk, Cow's. *N. F. IV. Lac Vaccinum.*—"The fresh milk of the domestic cow, *Bos taurus* Linné (Fam. *Bovidæ*), without modification, and complying with the legal standards of the State or community in which it is sold." *N. F.* Milk, which is the secretion of the mammary gland of the mammalia provided for the nourishment of the young, is a natural emulsion containing proper proportions of nutritive constituents adapted for the particular species secreting it. Cows' milk is that most commonly used as food by man in civilized countries and is what is legally understood when the word "milk" is used unqualifiedly, but the milk of other animals is sometimes used. Among these may be mentioned the goat, sheep, llama, mare and reindeer.

The preference for cows' milk is a matter of custom determined largely by the fact that the hides and flesh of these animals are necessary to man, and by the naturally large volume of milk yielded which has been further augmented by selective breeding and scientific feeding.

Milk consists principally of water, casein and other proteins, fat, milk sugar, and mineral salts. Minute amounts of lecithin and nuclein, of enzymes and vitamines are also present and probably are of great value as nutritional factors. The following figures from Koenig give the compara-

tive average composition of the milk of the more important mammalian species:

	Water.	Casein.	Albumin.	Fat.	Sugar.	Ash.
Cow	87.17%	3.02%	0.53%	3.69%	4.88%	0.71%
Woman	87.41%	1.03%	1.26%	3.78%	6.21%	0.31%
Goat	85.71%	3.20%	1.09%	4.78%	4.46%	0.76%
Sheep	80.82%	4.97%	1.55%	6.86%	4.91%	0.89%
Mare	90.78%	1.24%	0.07%	1.21%	5.67%	0.35%

The physical properties and composition of cows' milk are subject to a certain amount of variation due to the species of cattle, character and amount of food, time of milking, etc. The reaction of cow's milk, when fresh, is amphoteric, that is, alkaline to red litmus paper and acid to blue litmus paper. The specific gravity averages about 1.0315, but varies with the percentage of butter fat which, being a more concentrated emulsion, rises to the surface of the milk as cream, leaving below it a liquid containing very little fat but almost all of the casein, sugar and salts, and known as skim milk. Gravity cream, or cream which separates on standing, has been largely replaced by separator cream in which centrifugal force is applied to a stream of milk entering the device known as a separator, which continuously separates it into cream and skim milk, the relative richness of the cream and freedom of the skim milk from butter fat being regulated by the speed of the centrifugal motion. During recent years there has come into use an apparatus known as a homogenizer, in which the milk is subjected to the influence of great pressure and is at the same time forced through diaphragms containing minute perforations. The normal size of the fat globules, which is from 0.0025–0.0035 millimetres, is much reduced and the physical properties of the cream or milk are modified to such an extent that the subsequent separation of cream takes place much more slowly and the supernatant cream layer is bulkier and less rich in butter fat. The milk therefore appears richer to the eye judging from the apparent amount of cream which separates. The use of the homogenizer gives to cream which is to be used for ice cream manufacturing, properties which make for smoothness and higher quality of the resulting product. The homogenizer can also be used to combine butter with skim milk to make products simulating either cream or milk, depending upon the proportions of the ingredients. It is said that fats normally foreign to milk, such as vegetable or animal oils, may be incorporated with skim milk by the use of this apparatus, and the resulting product used as a substitute for cream or milk.

The normal decomposition of milk upon standing is accompanied by the development of lactic acid (the acid of sour milk) which is formed by bacterial action from the lactose (see *Lactic* Acid). Under some circumstances milk undergoes the butyric fermentation with the development of butyric acid from the fats of the milk. The alcoholic fermentation of milk is discussed under *Kefir* (which see).

Condensed or *evaporated milk* is milk which has had part of its water removed by evaporation in a vacuum apparatus. The concentration is usually two-fold, but in some instances is higher. Sweetened condensed milk is milk which has been concentrated by evaporation and to which has been added either cane sugar or invert sugar. So-called "*evaporated cream*" is evaporated milk which has been concentrated to a higher degree than usual. There is no real evaporated cream produced. Milk may also be evaporated to the condition of a dry powder by the use of special forms of apparatus in which the effect of a vacuum is supplemented by distributing the milk in a very thin layer on a large metal cylinder or allowing it to escape into a very high vacuum or hot chamber in a very fine jet. *Powdered milk* may either be whole milk or skim milk. Both of these articles are now produced upon a very large scale for use in manufacturing confectionery, such as milk chocolate and for combining in concentrated food products. The U. S. minimum standards for these various forms of milk are as follows:

Milk, 3.5 per cent. fat, 8.5 per cent. solids not fat.
Cream, 18 per cent. fat.
Evaporated milk, 34.3 per cent. milk solids and 7.8 per. cent fat (sweetened or unsweetened).
Skim milk, 9.25 per cent. milk solids.

Some of the individual States have slightly different standards from the above U. S. standards, which apply only to milk shipped into interstate commerce.

The watering of milk is usually detected by the chemical analysis, a proportion of non-fatty solids less than 8.5 per cent., rendering the sample open to suspicion in this respect. The presence of added water is usually confirmed by taking the specific gravity of the milk serum or whey or by observing its refractive index by the use of an immersion refractometer.

The use of preservatives in milk is universally prohibited and instances of such adulterations are now rarely met with. Among the preservatives, which were in more or less widespread use at one time, were formaldehyde, borax, salicylic or benzoic acid, fluorides and hydrogen dioxide. The latter preservative disappears within 48 hours by reduction to H_2O. Its use may be inferred, however, by the disappearance of the characteristic enzymes of milk, which may be readily determined by appropriate tests. It is the presence of these enzymes together with the vitamines, which are undoubtedly responsible for much of the value of milk as a food, apart from the fat, protein and carbohydrates present. It is of interest to note that in modern methods of milk concentration these enzymes are usually unaffected and remain in the finished product. Artificial coloring, such as annatto or coal tar colors are sometimes used in milk to give a false appearance of richness. They are prohibited by law and are easily detected by appropriate tests. Such crude methods of milk adulteration as the addition of starch or chalk or similar thickeners, have entirely disappeared.

Modern methods of milk control are concerned with the production of clean milk as well as pure

milk. The bacterial count therefore plays an important part in judging of its quality. Standards vary in different localities, but the following is an example. In Chicago the milk, as it arrives in the city, is limited to 1,000,000 bacteria per Cc. from May 1 to September 1, and 500,000 per Cc. during the remainder of the year. Municipal requirements for pasteurization usually reduce this figure to 50,000 per Cc. when delivered to the consumer. *Certified milk* is required to be free from *B. tuberculosis* and to contain less than 10,000 bacteria per Cc. (Class A), and 100,000 bacteria per Cc. (Class B), without pasteurization.

As boiling milk is generally believed to lessen its digestibility as well as destroy its enzymes, the process known as *pasteurization* is employed to produce partial sterilization. For this purpose the milk is heated to a temperature of about 68° C. (154.4° F.) for from twenty to thirty minutes. This will destroy practically all the pathogenic bacteria likely to occur in milk without causing serious changes in its chemical composition.

Mikronal.—Stated to be menthol formalin combined with *tetrapyridin carbonate*, this substance is employed in the form of an inhalation containing 1 per cent. of *mikronal*, in the treatment of *catarrh* and *nasal affections*.

Mitchella. *Mitchella repens* L. *Squaw Vine. Partridge Berry. Checkerberry. Winter Clover.* (Fam. *Rubiaceæ*.)—This small, indigenous evergreen has been supposed to possess remedial properties, and is said to be employed, in decoction, by the Indian squaws, to facilitate parturition. It appears to be diuretic, tonic, and astringent, resembling in these respects the pipsissewa, for which it is often substituted. E. Breneiser (*A. J. P.*, 1887, 228) found it to contain some resin, wax, mucilage, dextrin, and what appeared to be saponin.

Mollin is a base for ointments that has attracted some dermatological notice in Germany. It is a soft soap, containing 17 per cent. of uncombined fat, and is stated to be prepared by saponifying without heat 100 parts of cocoa-nut oil or of fresh fat with 40 parts of solution of caustic potassium hydroxide, sp. gr. 1.145, mixing intimately with 30 parts of glycerin, and heating carefully. It is yellowish white, of a smooth and soft consistence, not readily altered by exposure, free from rancidity, and easily removed from the skin by warm or cold water.

Momordica. *Momordica Balsamina* L. *Balsam Apple. Balsamina.* (Fam. *Cucurbitaceæ*.)—An annual climbing East Indian plant, cultivated in our gardens for the sake of the ornamental fruit. The latter is ovate, attenuated towards each extremity, angular, warty, not unlike a cucumber in appearance, of a lively red or orange-yellow color, easily falling when touched, and spontaneously separating into several pieces. A liniment formed by infusing the fruit, deprived of its seeds, in olive or almond oil, is applied to *chapped hands, burns, piles, prolapsus ani*, etc.; and the mashed fruit is sometimes used as a poultice. According to Descourtilz, two or three drachms taken internally will kill a dog. An extract prepared from it is said to be useful in *dropsy*. *Dose*, six to fifteen grains (0.4–1.0 Gm.).

Monarda. *Monarda punctata* L. *Horsemint. Menthe de Cheval*, Fr. *Pferdeminze*, G.—This is an indigenous perennial or biennial labiate, growing in light gravelly or sandy soils from New York to Texas and west to Wisconsin. The whole herb is employed. It has an aromatic odor, and a warm, pungent, bitterish taste, and abounds in a volatile oil, which may be separated by distillation with water. Herman J. M. Schroeter (*A. J. P.*, 1888, 120) found the oil to consist of a hydrocarbon, $C_{10}H_{16}$ (56 per cent.), thymol, $C_{10}H_{14}O$ (25 per cent.), and higher oxygenated compounds, $C_{10}H_{18}O$. Kremers (*Ph. Rev.*, 1896, 223) examined the oil from authentic specimens and found it to yield from 56 to 61 per cent. of a phenol (thymol). Horsemint is stimulant and carminative, but is seldom used in regular practice. In the state of infusion it is occasionally employed in families as a remedy for flatulent *colic* and sick stomach, and for other purposes to which the aromatic herbs are applied. *Monarda fistulosa* L., *wild bergamot, Oswego tea*, an active diuretic (see *Proc. A. Ph. A.*, 1895, 256; 1896, 238), contains, according to J. W. Brandel and E. Kremers, *hydrothymoquinone, thymoquinone*, besides *cymene, carvacrol* and *limonene*. (*Ph. Rev.*, 19.) The oil of *Monarda citriodora* Cerv., or *prairie bergamot*, according to Brandel (*P. J.*, 53, 547), contains 65 per cent. of a phenol and 1.2 per cent. citral. See also *Midland Druggist*, 1910, 526, and a paper by Nellie Wakeman in the *Proc. A. Ph. A.*, 1910, 979. For the composition of monarda oils see *Ph. Archiv.*, 1899, 73.

Monesia.—A South American vegetable extract, which is believed to be derived from the bark of *Lucuma glycyphlœa* Mart. and Eichl. (Fam. *Sapotaceæ*), a tree of moderate size, growing in the forests near Rio Janeiro and elsewhere in Brazil. (*J. P. C.*, 3e sér., vi, 63.) The bark, which has also entered commerce, is in pieces, some of which are three or six mm. thick, is very compact and heavy, of a deep brown or chocolate color, contrasting strongly with the grayish color of the epidermis when this remains, and of smooth fracture. The extract is of a dark brown almost black color, very brittle, the fracture neither very dull nor very shining, and of a taste at first sweet, then astringent, and ultimately acrid, the acridity being very persistent, and especially felt in the fauces. It is entirely soluble in water. The bark contains, according to Peckolt (*A. J. P.*, 1884, 626), *monesiatannic acid*, which gives a black coloration with iron salts, gallic acid, *monesin*, an acrid, amorphous body, *lucumin*, a body crystallizing in silky needles, a bitter substance, glycyrrhizin, tartaric and citric acids, wax, etc. *Monesin*, which is considered as *identical with saponin*, $C_{32}H_{54}O_{18}$, was obtained by treating the bark or extract with alcohol, adding to the tincture an excess of calcium hydroxide in fine powder, filtering, evaporating the clear liquor to dryness, treating the residue with water and animal charcoal, filtering, and again evaporating to dryness. Thus procured it was in transparent, yellowish scales, which were easily pulverized, forming a white powder. It was uncrystallizable, readily soluble in alcohol and water, to the latter of which it gave the property of frothing, and insoluble in ether. It had no power to saturate acids, was without odor, but had a slightly bitterish taste, followed by a decided and permanent acrimony in the posterior mouth and fauces. Monesia owes its activity probably to this principle and to tannic acid.

Monesia is stomachic and feebly astringent, and has been used with asserted advantage in *diarrhea, hemoptysis, menorrhagia, scrofula, scurvy*, also as a local remedy in *leucorrhea, ulcerations of the mouth and fauces*, and *ulcers*. It is applied to ulcers either by being sprinkled in powder upon the surface or in the form of ointment made with one part of the extract and seven parts of simple ointment. The *dose* of the extract is from two to

ten grains (0.13–0.65 Gm.), repeated every one to three hours. Monesin has been given internally in the *dose* of about half a grain (0.032 Gm.), and has also been applied to ulcers. It is said to be a powerful oxytocic, but it is seldom used.

Mongumo Bark.—For analysis of this Madagascar bark, which is said by E. M. Holmes to resemble the bark of *Ochrosia borbonica* J. F. Gmel (Fam. *Apocynaceæ*), see *P. J.*, ix, 816. It was examined by Dragendorff, who found *mongumic acid*, resin, waxy substance, a glucoside soluble in water and alcohol, metarabic acid, fatty matter, calcium oxalate and a substance insoluble in alcohol and soluble in water.

Monotal. *N. N. R.* 1917. *Guaiacol methyl glycolate.* $CH_2(O.CH_3).CO.O.(C_6H_4OCH_3)$. *Ethyl Glycolic Acid Ester of Guaiacol.*—This is a colorless fluid, with a slightly aromatic odor. It is soluble in alcohol. *Monotal* is used for two distinct purposes, first, as a means of obtaining the general effects of guaiacol either in *tuberculosis* or as an anti-neuralgic through dermal obsorption and, secondly, as a local anesthetic. It is especially in the latter use, however, that it has attracted the most attention. When applied to the skin it is less irritant than guaiacol itself, but appears to be equally powerful as a local anesthetic. Hecht (*Heilk.*, 1907, No. 1) has found it to afford prompt relief in *neuralgia, neuritis, erysipelas*, etc., and also for various forms of *pruritus*. It may be painted on pure in *doses* of twenty-five to forty-five grains (1.7–3.0 Gm.), and covered with an impermeable dressing if absorption is desired. A number of authors have found it useful in *gouty* and *rheumatic* conditions.

Monsonia.—According to John Maberly (*L. L.*, Feb., 1897; July, 1898), certain South African plants belonging to the family of *Geraniaceæ*, having large fleshy roots, are valuable remedies in the treatment of both acute and chronic *dysentery;* such are especially *Monsonia ovata* Cav. and *M. Burkeana* Planch., also certain *Pelargoniums*. Under the name of *t'Namie*, the natives of Namaqualand are said to use the root of *Pelargonium antidysentericum* Kostel. Maberly believes that the *Pelargoniums* are especially valuable in ulceration of the stomach and upper portions of the intestinal tract, and the *Monsonias* when the disease is low down in the intestines. The *dose* of monsonia is given as half an ounce (15.5 Gm.). It is believed that the plants are not poisonous. *Dose*, of the saturated tincture, from one to two fluidrachms (3.75–7.5 mils) every three or four hours.

Morinda.—From the wood of the *Morinda tinctoria* Roxb. (Fam. *Rubiaceæ*), or *Indian Mulberry*, Anderson (*P. J.*, 1886) claimed to have obtained a glucoside *morindin*, which yielded on hydrolysis *trihydroxy-methyl-anthraquinone*. Oesterle (*A. Pharm.*, 1907, ccxlv), however, was unable to find this glucoside, but did obtain a monomethyl-ether-tri-oxymethyl-anthra-quinone, $C_{16}H_{12}O_5$. *M. umbellata* L., *M. citrifolia* L., and the *M. longiflora* G. Don., all yield anthraquinone derivatives. (See Barrowcliff and Tutin, *Trans. British Chem. Soc.*, 1907.) These plants are used by the African aborigines as remedial agents, but there is no reliable evidence of their therapeutic value.

Morphigenin.—This nitrogenated derivative of morphine, made by E. Vahlen, has been obtained by him only in solution in the form of morphigenin hydrochloride, $\begin{matrix} C_6H_4 = C.OH \\ | \\ C_6H_4 = C.NH_2HCl \end{matrix}$. It is said to possess distinct narcotic properties. (*A. E. P. P.*, xlvii, p. 368.)

Morphine Lactate ($C_{17}H_{19}O_3N,C_3H_6O_3$).—This salt crystallizes in four-sided prisms, one part being soluble in eight parts of water and ninety-three parts of alcohol. (*P. J.*, 1886, 958.)

Morphine Hydrocyanide.—J. M. Maisch noticed that when a soluble salt of morphine is added to a solution of soluble cyanide, crystals of morphine hydrocyanide form. This salt, although sparingly soluble in water, is freely dissolved by that liquid when acidulated. It is evident that potassium cyanide and morphine should not be prescribed together in solution, except in connection with free acid.

Morphine Hydrobromide, or *Morphine Bromide* ($C_{17}H_{19}O_3NHBr + 2H_2O$), is made by double decomposition between morphine sulphate and barium bromide. (*A. J. P.*, xliv, 447.)

Morphine Meconate. *Morphine Meconas. N. N. R.* 1917. $(C_{17}H_{19}O_3N)_2C_7H_4O_7 5H_2O$.—This is obtained by the interaction of morphine alkaloid and meconic acid. It occurs in minute, colorless crystals or a yellowish-white powder, slightly soluble in water but more so in alcohol. It contains 66.3 per cent. anhydrous morphine and is used after the manner of other morphine salts.

Morphine Methyl Bromide. *Morphosan.* $C_{17}H_{19}O_3NBrCH_3$.—This occurs in needle-like crystals soluble in 20 parts of water. It is asserted that it is free from any of the unpleasant secondary effects of morphine and it has been suggested as a substitute for the latter in the treatment of the morphine habit. The *dose* is one-twelfth to one-half of a grain (0.005–0.032 Gm.).

Morphine Phthalate is made by adding pure morphine to a hot solution of *absolutely pure* phthalic acid as long as it is dissolved, filtering, and evaporating. One part of the salt is soluble in five parts of water. The solutions are perfectly neutral, and have been especially recommended by E. Bombelon for hypodermic use. (See article in *Ph. Ztg.*, 1887, 488.)

Morphine Stearate. $C_{17}H_{19}O_3N.C_{17}H_{35}.COOH$.—This is made by the combination of morphine hydrochloride with sodium stearate. It forms a white, scaly product with a melting point of 85° C. (185° F.). A sweet almond oil solution (1 to 100) of this substance is known as *morphinol* and is used as an anodyne application.

Mountain Green or **Mineral Green.**—A pigment obtained by powdering green *malachite* or *copper oxycarbonate*, artificially prepared.

Moxa. *Moxa*, Fr. *Brenncylinder*, G.—These are small combustible masses used to produce an eschar by being burned in contact with the skin. In Japan and China they are made from the leaves or the downy hairs on the leaves and stems of one or more species of *Artemisia. A. chinensis* L. and *A. indica* Willd. (*A. vulgaris* L.) were indicated by the Dublin College; but Lindley states that it is the *A. moxa* of De Candolle which is employed. A similar *moxa* has been made in France, by a similar process, from the leaves of *A. vulgaris*. According to Percy, the dried stem of the ordinary sunflower may be used for moxa. Artificial moxas may be made by the following processes: One pound of cotton is introduced into a vessel containing two ounces of potassium nitrate dissolved in half a gallon of water, and a moderate heat applied till all the liquid is evaporated. The cotton, when perfectly dry, is formed into thin, narrow sheets, which are rolled round a central cord of linen, so as to form a cylinder from

half an inch to an inch in diameter, and several inches long. This is enclosed in a covering of silk or linen sewed firmly around it; and, when used, may be cut by a razor into transverse slices a few lines in thickness. By leaving a hole in the center of the cylinder, the combustion will be rendered more vigorous, and a deeper eschar produced.

Cauterization by fire has been used from time immemorial among savages, half-civilized, and intelligent communities, and is said to have been reintroduced into Europe by the early Portuguese navigators from the Far East. Though at one time much employed for the purposes of revulsion, this form of cauterization has fallen into complete desuetude. The details of its application are described in the 18th ed., *U. S. D.* The first sensation experienced is not disagreeable; but the operation becomes gradually more painful, and towards the close is for a short time very severe. The pain could probably be prevented by the use of cocaine.

Muawin Bark.—This is the bark of a Mozambique tree, which in Eastern Africa is used as an ordeal poison. In appearance and structure it closely resembles the erythrophlœum bark obtained from numerous species of *Erythrophlœum* (Fam. *Leguminosæ*). An alkaloid, *muawine*, was discovered in it by E. Merck, 1891. The hydrobromide, a yellowish powder soluble in water and alcohol. The characteristic test is said to be that with vanadinsulphuric acid, which gives with muawine first a pale green, passing into a pale blue. (H. Jacobsohn, *In. Dis.*, Dorpat, 1892; see also *Merck's Jahresbericht*, 1891.) According to Jacobsohn, the hydrobromide when injected subcutaneously does not cause any irritation, but produces in frogs symptoms similar to those caused by digitalin, and in warm-blooded animals slowing of the pulse, increase of the heart action, elevation of blood pressure, and contraction of the arterioles. The action of muawine is, therefore, like that of digitalin, but is distinguished by being very temporary.

Mucin.—This substance is a gluco-proteid found in bile, submaxillary gland, etc., being a mixture of serum, globulin and salts of true *Mucin* and bile. It forms a greenish-gray to yellow powder, insoluble in water and soluble in alkalies. It is used in the treatment of *gastric ulcers* in eight-grain (0.5 Gm.) *doses* mixed with sodium bicarbonate. It is also used as a 1 per cent. solution with small amounts of sodium bicarbonate and menthol as a spray in *rhinitis* and *pharyngitis*.

Mucuna. *Mucuna pruriens* De Cand. *Cowhage. Cowage. Setæ Siliquæ Hirsutæ. Pois velus, Pois à gratter*, Fr. *Kratzbohnen, Kuhkrätze*, G.—This is a leguminous climbing plant which grows in the West Indies and tropical countries of both hemispheres. The fruit is a coriaceous pod, shaped like the Italic letter *f*, about four inches long, and covered with brown bristly hairs, which easily separate, and when handled stick in the fingers, producing an intense itching sensation.

The spicula are said to be very destructive to the *round worm*, acting mechanically by penetrating their bodies. Neither the tincture nor the decoction is effective. Cowhage is efficient, but so disagreeable that it has passed out of vogue. The usual mode of preparing it is to dip the pods into syrup or molasses, and scrape off the hairs with the liquid, which is in a proper state for administration when it has attained the consistence of thick honey. The *dose* of this preparation is a tablespoonful (15 mils) for an adult, a teaspoonful (3.75 mils) for a child three or four years old, to be given every morning for three days, and then followed by a brisk cathartic.

Muira-Puama.—The wood of a Brazilian tree, believed to be from *Liriosma ovata* Miers (Fam. *Olacaceæ*), which, according to Th. Peckolt, contains an alkaloid, *muira-puamine*, and is used by the Brazilian aborigines as an aphrodisiac, also in the treatment of *dysentery*. In *impotence*, ten to twenty minims (0.6–1.3 mils) of the fluidextract may be taken three or four times a day. (See *M. R.*, 1902.)

Mukogen. *Dimethylphenylpara-ammoniumbeta-oxynaphthoxazime chloride.* $C_{18}H_{15}N_2O_2Cl$.—This occurs as a blue crystalline powder or medium-size crystals. It is soluble in alcohol and any alkaline liquids, but almost insoluble in water. It is used as a cathartic in *doses* of one and a half to five grains (0.096–0.32 Gm.).

Mulberry.—There are in the United States three species—the indigenous *Morus rubra* L., with dark purple fruit; *M. alba* L., introduced from Europe, and at one time extensively cultivated as a source of food for the silk worm, having a white fruit; and *M. nigra* L., a tree of middle size, supposed to have been brought originally from Persia into Italy and widely cultivated. The fruit of the last species has a sweet, mucilaginous, acidulous taste, and abounds in a deep red juice having the sp. gr. 1.060. (*Mori Succus*, Br., 1885.) For analysis of mulberries see *U. S. D.*, 19th ed., p. 1573. In amount of grape sugar the *mulberry* is surpassed only by the cherry, 10.79, and the grape, from 10.6 to 19.0. Mulberries are refreshing and laxative, and serve to prepare a grateful drink well adapted to febrile cases.

Murexide. *Acid Ammonium Purpurate.* $C_8H_4(NH_4)N_5O_6 + H_2O$.—A fine purple dye-stuff, made by the reaction of nitric acid on uric acid. As resulting from the action of nitric acid on urine, it was supposed by Prout to consist of purpuric acid and ammonia (which belief has been confirmed by further investigation), and hence was named *ammonium purpurate*. It was later made from guano. This was first treated with hydrochloric acid to remove foreign substances, and then with soda to dissolve the uric acid, which is separated by neutralizing the soda with hydrochloric acid. The uric acid is dissolved in nitric acid, the solution is heated, and after it cools ammonia or its carbonate is added, which develops the purple color. *Murexide* is obtained in crystals, which have a square form, and are a rich green color by reflected, but of a purple-red by transmitted, light. It is slightly soluble in cold water, more so in boiling water, and insoluble in alcohol and ether. With potassium hydroxide it forms a rich purple solution. It has been replaced as a dye by aniline colors.

Muscari. *Muscari comosum* (L.) Mill. (Fam. *Liliaceæ*.)—In the bulbs of this plant Curci (*Rép. de Pharm.*, March, 1889) has found *comosic acid*, which he believes to act physiologically like saponin.

Musculus. *Musculus venenosus.*—That certain mussels, or that mussels in certain condition, are actively poisonous is well ascertained. F. Crumpe (*Dublin Q. J.*, Oct., 1873) has reported collapse with complete paralysis of the voluntary muscles as produced by the mussel, and has also treated traumatic *tetanus* successfully with raw mussels. M. Breiger (*D. M. W.*) has isolated certain bases out of mussels. He thinks the most important is *mytilotoxine* ($C_6H_{15}O_2N$), which he has demonstrated to possess physiological properties closely

resembling those of curare. These poisonous principles are all probably ptomaines, and disappear when the mussel is boiled with sodium carbonate; so that boiling the mussel in an alkaline solution (three and a half grammes per liter of water) renders it harmless.

Musenna Abyssinica.—A substance known as *tæniol* which is claimed to be derived from the rind of the *Musenna abyssinica*, has been recommended as a vermifuge especially for the treatment of *anchylostoma*. According to Liermberger (*B. K. W.*, 1905, p. 390), it is an efficient and non-toxic anthelmintic. The only unpleasant symptom produced was slight giddiness. It is marketed only in the form of capsules of which 10 to 15 may be taken at intervals of ten minutes. After the sixth or seventh capsule there should be allowed an interval of an hour.

Mushrooms and Toadstools. (*Edible and Poisonous Fungi.*)—Notwithstanding the fact that it has been shown that edible fungi, when compared with other articles of food, do not possess a high food value, the interest in the study of the fungi, as well as the consumption of edible forms, is constantly increasing. The study of the fungi is one of the most highly specialized, as there have been up to the present time no less than 64,000 species described. From a food standpoint the differentiation of the edible from the poisonous is one of the most difficult that the novice can undertake, as it is almost impossible to lay down any invariable rules.

The fungi are divided into a number of classes, each of which is again subdivided into sub-classes, series, and families. The family of *Basidiosporeæ* include the largest and most conspicuous of the fungi and all of the mushrooms and toadstools. It is commonly believed that mushrooms are edible and that toadstools are poisonous; in reality, however, no such distinction should be made. The plants of the *Hymenomycetes* are characterized in general in that they arise from a mass of colorless threads, known as "mycelium" or "spawn," produced in the ground, bark of trees, etc. Their first appearance above ground is marked by the production of small solid balls (called buttons), which gradually enlarge, and at length shoot up into a stem or stipe bearing at its summit the umbrella top or "pileus," which is at first closed around the stalk like a closed umbrella and then expands more or less widely, according to the species. The under side of the pileus is the part which bears the spores, which correspond to the seeds of higher plants. In some cases the under surface consists of a series of gills resembling knife blades, which radiate from the top of the stalk to the circumference, like the spokes of a wheel, as in *Agaricaceæ;* in others it consists of a mass of small pores or tubes packed closely together, side by side, as in *Polyporaceæ;* in others of teeth, as in *Hydnaceæ;* in others only slightly wrinkled or undulated, as *Thelephoraceæ*, etc. The *Basidiosporeæ* include about 14,000 species which are included in nine orders and subdivided into twenty-five families. A few of the important are the following:

1.—*Agaricaceæ* (the mushrooms and toadstools proper) comprises about 4600 species, some of which are poisonous, as the *Amanitas* (Fly and Deadly Agarics) *Lactarius* (with a milky juice), whereas others are edible, as *Agaricus* (*Psalliata*) *campestris* L., the common mushroom, *Cantharellus cibarius*, Fr., etc.

2.—*Polyporaceæ* (pore-fungi) includes about 2000 species, many of which are parasites on trees and destructive to timber; some are edible, as *Boletus edulis* Bull., whereas others are poisonous, as *B. satana* Lenz.

3.—*Hydnaceæ* (teeth-bearing fungi): Most of the species are too small and woody to be eaten. *Hydnum repandum* forms "fairy rings" in woods.

4.—*Thelephoraceæ*: Most of the species are small, and the larger species are tough and leathery.

5.—*Clavariaceæ* (coral-shaped fungi) includes some large fungi; none are poisonous and some, as *Clavaria flava* Schaeff., are palatable.

Of these, the most important group are the *Agaricaceæ*, both from the point of view of the toxicologist and the epicure.

It is not possible in this limited space to even mention the various poisonous and edible fungi that experience has demonstrated as such. The number of species which have been eaten or experimented with, however, is small compared to the number recognized by botanists. Many students of fungi have formulated rules for distinguishing edible from poisonous fungi. "The different popular tests for distinguishing edible from poisonous fungi, such as, for instance, the blackening of a silver coin or spoon when placed in a mass of poisonous fungi while they are being cooked, are all absolutely worthless." The only safe rule is to use no mushroom which the collector is not absolutely sure from previous experience is edible.

The *common mushroom* (*Agaricus campestris* L.) is practically the only species cultivated in this country, and is the only fresh species sold in the northern markets during the winter months. It is found wild in open grassy fields and pastures in great abundance in August and September. It is not common on the mountains, never found in woods, and never grows on trees or fallen trunks. The color of the stalk and pileus varies from a whitish shade to drab, but the color of the gills, a point which should never be overlooked, is at first pinkish and then a brownish-purple. The stalk is cylindrical and solid, and has, rather more than half way up, a membranous collar called the ring; but there is no membrane or scales found at the base of the stalk, which appears to come directly out of the ground. "In specimens which are not fully expanded there is a thin membrane or veil which extends from the stalk to the margin of the pileus. When the veil is ruptured, exposing the gills behind, a part remains attached to the stalk, forming the ring already referred to. In older specimens the ring shrinks, but generally a mark remains showing where it has been attached."

Two of the most poisonous forms resembling the common mushroom, and which have been eaten in mistake for it, are the deadly agaric and fly agaric.

The *fly agaric* (*Amanita muscaria* (L.) Pers.), so called because decoctions have been used for killing flies, is in some localities much more abundant than the common mushroom. It is seldom found in the grassy pastures preferred by the common mushroom, but more generally in poor soil, especially in groves of coniferous trees. "It grows singly and not in groups and differs from the common mushroom in having gills which are always white, never pink or purple and in having a hollow stem, which is bulbous at the base and clothed with irregular fringy scales on all the lower part. The pileus varies in color from a brilliant yellow to orange and a deep red, the yellow and orange being more frequent than the red. The surface is polished, and has scattered over it a larger or smaller number of prominent, angular warty scales which can be easily scraped off. The gills and

stalks are white, and there is a large membranous collar which hangs down from the upper part of the stem."

The *deadly agaric* (*Amanita phalloides* (Pers.), Fr.), so named because it probably has been more frequently the cause of death than any other fungus, prefers a damper and less sandy soil than the fly agaric and is not pre-eminently an inhabitant of grassy pastures. "The pileus is often a shining white, but may be of any shade from a dull yellow to olive, and when wet is more slimy than the common mushroom or the fly agaric. It has no distinct scales and only occasionally a few membranous patches on the pileus. The gills and stalks are white, and the latter has a large ring like the fly agaric and is hollow, or when young, is loosely filled with cottony threads, which soon disappear. The base of the stalk differs from that of the fly agaric in being more bulbous and in having the upper part of the bulb bordered by a sac-like membrane called the volva. The volva is often of considerable size but more frequently it is reduced to a membranous rim."

The list of edible and poisonous fungi are relatively long, and while most belong to the *Hymenomycetes*, some are also yielded by the *Gasteromycetes*, as the puff-balls. The *giant puff-ball*, *Lycoperdon bovista* (*L. giganteum* Batsch), is found in the region of San Francisco Bay, not rarely forty inches in diameter.

We may conveniently consider the poisonous mushrooms in four groups following the divisions of Kobert. (*Ueber Pilzvergiftung*, 1891.)

In the first group is the genus *Lactarius* which owe their toxic properties to the presence of an irritant resin. Some of this genus, as *L. deliciosus*, are stated to be edible, but most of them produce severe or even fatal gastric enteritis.

The second group contains species belonging to the genus *Helvellæ*, whose juice contains *helvellaic acid*, isolated by Boehm. It is asserted that these fungi, when thoroughly dried are not poisonous, and that hot water also extracts from them the poisonous acid, so that boiling makes them edible. The chief physiological action of the acid seems to be to destroy the red blood corpuscles, and, probably by such action, to produce vomiting, hemoglobinuria, jaundice, irritation of the kidneys, etc.

The third and most important group are the *Amanitas*. They are the most common source of mushroom poisoning, not only because of their resemblance to many of the edible species, but also because of the virulence of their effects. The most important of this specie is the *A. phalloides*, or *skunk mushroom*. According to Ford (*J. P. Ex. T.*, 1910, l, p. 275), they contain two poisonous substances, one being hemolytic, and the other causing degenerative changes in the various internal organs, especially the liver, kidney, spleen and muscles. The *Amanita-hemolysin*, which is probably identical with the *Phallin* of Kobert, appears to be glucosidal, and because it is destroyed by heat, probably plays little part in human poisoning. The nature of *amanita-toxin* is not yet determined, but poisons of a similar nature appear to be widespread throughout the whole of the genus.

In the fourth group are included those which contain *muscarine*. This alkaloid was first obtained from the *Amanita muscaria*, but is also found in the *A. pantherina*, the *Russula emetica*, in *Boletus luridus*, *B. Satanus*, and, according to Ford (*J. P. Ex. T.*, 1911, ii, p. 549), occasionally also in the *Clitosybe dealbate*, which has by some been classed as an edible fungus. Decoctions of the *Amanita muscaria* are used to poison flies, whence the common name of the *fly agaric*. The inhabitants of the Caucasus also use this fungus as an intoxicant. The *A. pantherina* is used in Japan for like purposes.

Muscarine was first obtained in a state of purity by Schmiedeberg and Koppe. (*Das Muscarin*, Leipzig, 1869.) The alkaloid may be produced artificially by gently heating choline platino-chloride with strong nitric acid. Potassium chloride is used to decompose the muscarine platino-chloride and produce muscarine hydrochloride; treatment with moist silver oxide yields the muscarine as a hydrate ($C_5H_{15}O_3NH_2O$). Muscarine resembles pilocarpine in its physiological action, and is antagonistic to atropine. It increases the secretions of the sweat, salivary and lachrymal glands, contracts the pupil, slows the pulse, and causes motor weakness. The reduction in the pulse rate is due to stimulation of the pneumogastric nerve, and after very large doses diastolic arrest occurs. If atropine be given so as to paralyze inhibition the cardiac movements reoccur. The vasomotor nerves are said to be paralyzed. There is a stimulation of the muscles of the intestines, bladder and spleen. Thus the intestines are transformed into hard, white cords, or afterwards, becoming somewhat relaxed, exhibit a tumultuous peristalsis. The abdominal secretions are greatly increased.

The symptoms of mushroom poisoning will vary greatly according to the special fungus which has been ingested. In the case of the deadly agaric (*Amanita phalloides*) which is the most common source of toadstool poisoning, the symptoms usually do not appear for several hours after the fungus has been eaten. They consist of great prostration and collapse, cold sweats, stupor, sometimes preceded by delirium, convulsions, frequently cyanosis and not rarely icterus. There is usually, also distinct fever and either hemoglobinuria or methemoglobinuria, and evidence of irritation of the kidney is shown by the presence of albumen, or partial suppression of the urine. When the poisoning is produced by fly agaric, to these symptoms will be added those of muscarine poisoning, namely, profuse salivation, contracted pupils and slowing of the pulse. In the poisoning by the lactarii the symptoms are those simply of violent inflammation of the alimentary tract, vomiting, purging and collapse. In poisoning by the *Helvellæ* the symptoms resemble those produced by the *Amanitas*.

Little can be done to save the patient. Our utmost efforts should be directed to preventing absorption. A promptly acting emetic, such as apomorphine, should be administered to produce vomiting. Secheyon (*P. J.*, 1910, liiv, p. 492) highly recommends animal charcoal for the purpose of absorbing the poison, and thus preventing its entrance into the system. At least a tablespoonful, stirred up in water, should be administered, and repeated libitum. It is also advisable to administer atropine hypodermically in one-sixtieth-grain doses (1 mgm.), as it is the physiological antagonistic to muscarine, and may prove a life-saving remedy in poisoning by fly agaric, and by its general stimulant effect will also exercise a feeble influence in combating the collapse even although due to other forms of poisoning. A rapidly acting cathartic should also be administered to cleanse the intestinal tract. Aside from these measures, the treatment is purely symptomatic—the use of opium if necessary to check the diarrhea

and vomiting, and various stimulants to maintain the circulation and respiration.

B. W. Richardson, having noticed that the smoke of the *Lycoperdon Proteus* or *puff-ball* was used for stupefying bees, found that the inhalation of the fumes caused various animals to become insensible. He has himself inhaled the fumes clarified by passing them through water, and experienced symptoms of intoxication and drowsiness. (*M. T. G.*, 1853, 610.) Thornton Herapath, however, maintains, as the result of his experiments, that these anesthetic effects are in reality not owing to any narcotic principle present in the fungus, but to the carbon dioxide gas generated during their combustion. (*Philos. Mag.*, July, 1855.)

Musk, Artificial. *Moschus Factitius.*—An artificial musk introduced as a patented preparation, called "*Musk Baur*," from the name of the discoverer, A. Baur, is *trinitrometabutyltoluene*, $C(CH_3)_3.C_6H(NO_2)_2CH_3$. It is prepared by adding tertiary metabutyltoluene slowly in the cold to five times its weight of a mixture of concentrated nitric and sulphuric acids, and afterwards heating the mixture for from eight to nine hours on a water bath. There are several closely related compounds, all derived from butyltoluene, which are commercially known as "artificial musk." They melt at temperature ranging from 89° C. to 96° C. (192.2°–204.8° F.). They are insoluble in water but soluble in alcohol, ether, benzene, chloroform, and petroleum benzin.

Artificial musk is an antispasmodic and nervine, which has been highly commended in *spasm of the glottis* of children. *Dose*, ten grains (0.65 Gm.); for a child two years old, from half a grain to a grain (0.032 0.065 Gm.), every two or three hours.

Mussanin.—An extract obtained from *Albizzia anthelmintica* (Fam. *Leguminosæ*). It is used as a vermifuge. *Dose*, one to two ounces (30–60 Gm.) in infusion.

Mutisia. *Mutisia viciæfolia* Cav.—This composite, a native of Chile, is stated to be a valuable anti-spasmodic, useful in *hysteria* and *croup;* it is also a cardiac tonic.

Mydrol. *Iodo-methyl-phenyl-pyrazolon.* — A colorless, inodorous powder of bitter taste, easily soluble in water and alcohol. It is used as a mydriatic in 5 and 10 per cent. solutions.

Myrica. *N. F. IV. Myrica cerifera* L. *Wax Myrtle. Bayberry. Candle Berry. Arbre à suif*, F. *Wachsbaum, Wachsgagel*, G.—"The dried bark of the root of *Myrica cerifera* Linné (Fam. *Myricaceæ*), without the presence of more than 5 per cent. of adhering wood." *N. F. IV.*

This is an indigenous myrtaceous shrub growing in great abundance in the sandy soil along the seashore, and even on the shores of our northern lakes. The leaves of the wax myrtle have resinous dots on both sides, and are very fragrant when rubbed. The fruit is covered with a coating of white wax, and sometimes continues on the plant for two years or more. The coating of wax upon the surface is collected, and known in commerce as *myrtle wax*. (See *Vegetable Wax*.)

For a study of the *Myricaceæ* of the Eastern United States, see Youngken. (*A. J. P.*, 1915, p. 391.) The bark of the stem and root is supposed to possess valuable remedial properties, and has been employed to a considerable extent. It yields its virtues to water and alcohol. George M. Hambright found in it volatile oil, starch, lignin, gum, albumen, extractive, a red coloring substance, tannic and gallic acids, an acrid resin soluble in alcohol and ether, an astringent resin soluble in alcohol and not in ether, and a peculiar acrid principle having acid properties. (*A. J. P.*, 1863, 193.) Myrtle wax consists of the glycerides of stearic, palmitic, and myristic acids and a small quantity of oleic acid. (Lewkowitsch, *Oils, Fats, and Waxes*, p. 542.)

The National Formulary IV describes the bark as: "In quills or quilled pieces or strips, of variable length and up to 20 mm. in breadth, the bark rarely exceeding 2 mm. in thickness; outer surface varying from dark-brown to gray-brown, occasionally slightly silvery, somewhat lustrous, at least in patches, bearing occasional warts or slight transverse ridges, the periderm frequently much wrinkled; inner surface deep rusty-brown, finely short-striated and somewhat roughened; fracture short and weak, light brown in the outer layer, yellowish-brown in the inner layer. Odor characteristic, rather disagreeable; taste astringent, mildly bitter and slightly acrid." *N. F. IV.*

The bark appears to be moderately tonic and astringent, and in large doses emetic. It has been considerably used by the eclectics in *diarrhea, jaundice, scrofula*, etc. Externally the powdered bark is used as a stimulant to indolent *ulcers*, and the decoction as a gargle and injection in chronic *inflammation of the throat, leucorrhea*, etc. *Dose* of the powder, twenty to thirty grains (1.3–2.0 Gm.), of a decoction (one ounce to one pint), one or two fluidounces (30–60 mils). An alcoholic extract, very inappropriately named *myricin*, is given in the *dose* of about five grains (0.32 Gm.).

From the bark of *Myrica Nagi* Thunb., the yellow coloring matter of which is known as *myricetin*, A. G. Perkin has separated a glucoside, *myricetrin*, closely resembling *quercitrin*. (See *Proc. Chem. Soc.*, xviii, 11.) For analysis of the rhizome, *Myrica asplenifolia* L., see *A. J. P.*, 1892, 303.

The leaves of the *Myrica Gale* L. (*sweet gale*) or *Dutch myrtle* have been used in France as an emmenagogue and abortifacient, and were formerly official in that country under the name of *Herba Myrti Rabantini*. They contain a poisonous volatile oil.

Myrtus. *Myrtus communis* L. *Myrtle.* (Fam. *Myrtaceæ.*)—From the leaves of this plant is distilled a volatile oil which, under the name of *myrtol* is employed in medicine. This oil contains pinene, cineol and a characteristic alcohol, *myrtenol*. The mixture usually known as *myrtol* is collected between 160° and 180° C. (320°–356° F.). Myrtol has been recommended as an antiseptic and a powerful stimulant to the pulmonic and genito-urinary mucous membranes, and useful in chronic *bronchitis, cystitis*, or *pyelitis*. *Dose*, from one to two minims (0.06–0.13 mil), given in capsules, from four to eight times a day. A. de Vevey (*R. T.*, lxiii, 1896) has used the 10 per cent. solution in sterilized olive oil hypodermically in doses of eighty to one hundred and sixty minims (5–10 mils) once or twice in twenty-four hours.

Nabalus. *Prenanthes alba* L. *Rattlesnake Root. White Lettuce. Cancer Weed. Gall of the Earth. Lion's Foot.* (Fam. *Compositæ.*)—In certain portions of Virginia and North Carolina, where this perennial herb grows, great value is attached to it in *rattlesnake bite*. The milky juice is taken freely internally, and its leaves steeped in water which is locally applied and frequently changed. The plant is also used in *dysentery*, and N. B. Williams has found tannin in the rhizome. (*A. J. P.*, 1887.)

Nance Bark.—This bark is believed to be obtained from the *Malpighia glabra* L. (Fam.

Malpighiaceæ.) It is much used in Mexico for tanning, and, according to F. Holberg, contains 26.2 per cent. of tannin. (*A. J. P.*, xvi, 239.)

Naphthalan. *Naftalan.*—This is a greenish-black soft mass, prepared by the fractional distillation of naphtha obtained from the Armenian highlands, having a slightly empyreumatic odor, a neutral reaction, and a specific gravity of 0.89. It melts at 70° C. (158° F.), is insoluble in water and glycerin, but mixes readily with fats and oils, and is soluble in ether and petroleum benzin. It has been recommended by Rosenbaum and others as very efficacious in the treatment of *pruritus* and *burns*, as well as in *chronic eczema*, *sycosis*, and other parasitic skin affections, and as having a range of usefulness closely parallel to that of the oil of cade. It is necessary to apply it in the form of a thick coat to the affected skin and envelop it so as to exclude the air. Stains produced by it on the clothing can be removed by petroleum or benzene. Applied as a paste, 50 per cent. naftalan, 25 per cent. each of zinc oxide and of starch, with or without 2 to 5 per cent. of menthol. (See *Praktitchesky Vratch*, vol. i, No. 31.)

Kupzis recommends a naftalan which is a combination of the higher boiling portions of Caucasus naphtha from the naphtha residues, having a sp. gr. 0.94–0.97, and deprived of odor by vacuum distillation, by dissolving from 6 to 8 per cent. of perfectly neutral stearine soap in it. The product is not distinguishable from the commercial naftalan. (*Ph. Ztg.*, 1905, 499.)

Naphthalene. *Naphthalenum. U. S. VIII. Naphtalin. Naphthalin. Tar Camphor.* $C_{10}H_8 = 128.06$.—"A hydrocarbon obtained from coal-tar, and purified by crystallization. It should be kept in well-stoppered, amber-colored bottles." *U. S. VIII.*

This may be obtained by subjecting coal-tar to distillation, when it passes over in the middle oil and heavy oil; in the fractions of the latter it often constitutes the main constituent, causing it to become almost solid on cooling. It is frequently produced during the dry distillation of organic bodies. For a method of preparing it on a large scale for commercial purposes, see a paper by Vohl, in the *J. P. C.*, 1868, 399; from *Polytech. Journ.*; see also Lunge's *Coal-tar and Ammonia*, London, 1887. It is made very extensively and cheaply at present, the sublimed commercial product being nearly pure. It is a white, shining, crystalline substance, fusible at 80° C. (176° F.), and boiling at 218° C. (424.4° F.), but volatilizing with vapor of water. According to Kopp, its sp. gr. in the liquid state is 0.9774; according to Alluard, at 98.8° C. (210° F.), 0.9628.

It was officially described as in "colorless, shining, transparent laminæ, having a strong, characteristic odor resembling that of coal-tar, and a burning, aromatic taste; slowly volatilized on exposure to air; by exposure to light acquiring a brownish color. Insoluble in water, but when boiled with it, the water acquires a faint odor and taste; soluble in 13 parts of alcohol at 25° C. (77° F.), and very soluble in boiling alcohol; also very soluble in ether, chloroform, carbon disulphide, and fixed or volatile oils. Naphthalene volatilizes slowly at ordinary temperatures, but rapidly when heated. It also volatilizes with the vapors of water or alcohol. At 80° C. (176° F.) it melts, and at 218° C. (424.4° F.) it boils. Its vapor is inflammable, burning with a luminous but smoky flame. When ignited, it is consumed, leaving no residue. Naphthalene is neutral to litmus paper moistened with alcohol. On shaking a small portion of naphthalene with concentrated sulphuric acid, the acid should remain colorless, and should not acquire more than a pale reddish tint if the mixture be heated for five minutes on a water-bath (absence of *impurities derived from coal-tar*)." *U. S. VIII.*

The importation of naphthalene for the year 1914 amounted to 3,880,108 lbs., valued at $70,428. The production of napthalene in the United States for 1915 was: From coal gas plants 223,000 lbs.; from by-product plants 465,865 lbs.

Naphthalene has acquired in recent years a new industrial utilization, in that it is the starting point in the manufacture of artificial indigo, which has already become an extensive industry. (See *Indigo.*) Napthalene is possessed of antiseptic properties, and is poisonous to most fungi and probably to most insects. Under the name of "*tar camphor*," it has largely supplanted true camphor as a means of preventing the deposition by moths of eggs in woollen clothing, and of preventing the destruction by insects in natural history museums. In internal medicine it was some years ago brought forward by Dupasquier as an expectorant especially valuable in *chronic bronchitis* accompanied with a large amount of secretion. It has also been used with asserted excellent results as a tenicide, and as a vermifuge in cases of *seat worms*, when it should be given by injection, from fifteen grains to half a drachm in two to three ounces of olive oil. First employed by Rossbach of Jena, in *intestinal catarrh*, it has been largely used in all forms of *intestinal inflammation* and in *typhoid fever*. There seems to be no doubt that in some cases it acts very happily, but the reports concerning it vary, and it has been superseded by naphthol. Eighty grains are said to have been given in a day without deleterious effects, but J. A. Otte (*Chinese Med. Missionary Journ.*, xi, 1897) violently poisoned himself by eight grains of naphthalene. The symptoms were excessive vomiting and purging and great abdominal pain, followed by nephritis. Moreover, employees in gutta-percha works, where it is largely used, are said to be occasionally thrown into a peculiar condition of delirious intoxication. Seventy-seven grains caused in a man a cataract requiring extraction of the lens. (*S. J.*, 1902.) Napthalene has been used externally as an antiseptic dressing, and also in the treatment of various skin diseases. When given internally, it should always be in the form of powder, and is best administered in capsules.

Dose, one to five grains (0.065–0.3 Gm.).

Naphthylaminsulfonic Acid. *Acidum Naphthylaminsulfonicum. Naphthionic Acid. Sulphonaphthylaminic acid* ($C_{10}H_6(NH_2)HSO_3$) is a white powder, soluble in about four thousand parts of cold water, exhibiting a deep reddish-blue fluorescence, which has been proposed by E. Riegler on chemical grounds as an antidote for poisoning by the nitrites and in severe *iodism*. It is eliminated through the kidneys, causing acidity of the urine, and has been recommended in the treatment of chronic *cystitis*. The *dose* is eight grains (0.5 Gm.), taken with starch in a capsule every three or four hours.

Naples Yellow.—A yellow pigment prepared by calcining a mixture of lead, antimony sulphide, dried alum, and ammonium chloride, or a mixture of lead carbonate, diaphoretic antimony, dried alum, and ammonium chloride.

Narcissus. *Narcissus Pseudonarcissus* L. *Daffodil. Narcisse des prés, Porillon,* Fr. *Gelbe Narcisse,* G. (Fam. *Amaryllidaceæ.*)—Both the bulb and the bright yellow flowers of this common garden plant have been used in medicine. The flowers have a feeble peculiar odor, and both have a bitter mucilaginous taste. They are an uncertain emetic. It is probable that the flowers of the wild European plant are more powerful than those of the cultivated. A. W. Gerrard examined the bulbs of daffodil, and obtained a crystalline neutral principle and an amorphous alkaloid, which he calls *pseudonarcissine.* According to Ruiger, the alkaloid obtained by Gerrard from the bulb of the flowering plant dries the mouth, checks perspiration, dilates the pupil, especially when applied locally, quickens the pulse, and acts on the heart of the frog antagonistically to muscarine and pilocarpine, while the alkaloid taken from the bulb after flowering causes salivation and perspiration, internally taken contracts the pupil, and topically applied dilates it slightly. (*J. P.,* i, 436.) In France, narcissus flowers have been used as an antispasmodic. The *dose* of the powder, to produce an emetic effect, varies, according to the statements of different physicians, from twenty grains to two drachms (1.3–7.7 Gm.); while the extract is said to cause vomiting in the *dose* of two or three grains (0.13–0.20 Gm.). The bulb is most powerful in the recent state.

Narcophin. $C_{22}H_{23}O_7N.C_{17}H_{19}O_3N.C_7H_4O_7 + 4H_2O$.—This is a double salt containing one molecule of morphine and one of narcotine united to meconic acid. Although it corresponds to only 38 per cent. of morphine hydrochloride, according to Straub (*Biochem. Zeit.,* 1912, xlii, p. 316), it equals the latter salt in narcotic power. On the other hand Zehbe (*M. M. W.,* 1912) finds that it is somewhat weaker in equal dose than morphine, but the dose may be safely increased without the production of the common secondary effects of morphine. It is given in *doses* of from one-sixth to one-half grain (0.010–0.032 Gm.).

Narcyl. *Ethyl-narceine-hydrochloride.* $C_{25}H_{31}O_9N.HCl$.—It is sparingly soluble in cold water, readily soluble in alcohol; its solubility in water is greatly increased by the presence of organic acids. The various alkaloidal reagents precipitate it and the addition of chlorine water followed by ammonia will show a cherry-red color with a fresh solution of this compound. The precipitate formed by the addition of sodium hydroxide redissolves in an excess of the precipitant (distinction from narceine). According to Pouchet and Chevalier (*B. G. T.,* 1904, p. 779), its physiological action is very similar to that of codeine. It has been used as a cough sedative in *phthisis, bronchitis,* and *whooping cough. Dose,* half to one and a half grains (0.032–0.096 Gm.).

Nard. *Spikenard.*—Several aromatic roots were known to the ancients under the name of *nardus,* distinguished, according to their origin or place of growth, by the names of *Nardus indica, Nardus celtica, Nardus montana, etc.* They are supposed to have been derived from different valerianaceous plants. Thus, the *Nardus indica* is referred to *Nardostachys, Jatamansi* (Roxb.) DC. (*Valeriana Jatamansi* Roxb.), of Bengal, the *Nardus Celtica* to *V. celtica* L., inhabiting the Alps, Apennines, etc., and the *Nardus montana* to *V. tuberosa,* which grows in the mountains of the south of Europe. The *Indian nard,* or spikenard, sometimes also called *Syrian nard,* is still occasionally to be found in commerce. It is a small delicate root, from one to three inches long, beset with a tuft of soft, light brown, slender fibers, of an agreeable odor, and a bitter aromatic taste. It was formerly very highly esteemed as a medicine, but is now almost out of use. Its properties are analogous to those of valerian.

Naregamia, or **Goanese Ipecacuanha.**—The root of *Naregamia alata* Wight and Arn. (Fam. *Meliaceæ*), of Western India, has been much employed as an emetic, as an hepatic stimulant in *dysentery,* and in small doses as an expectorant in *bronchitis.* Drasche of Vienna, confirms the value of the drug. (*Cb. G. T.,* 1890.) In it Hooker has found an alkaloid, *naregamine,* an oxidizable fixed oil, and a wax. (See *P. J.,* vol. xv, 1887.) The *dose* of a concentrated tincture (1 to 4) is from five to ten minims (0.3–0.6 mil); as an emetic, from fifteen to thirty minims (0.9–1.8 mils).

Nasrol. $C_8H_9N_4O_2SO_3Na$. *Sodium Sulphocaffeate. Sodium Caffeine Sulphonate.—Symphoral-sodium* is an intensely bitter powder recommended as a diuretic in *dropsy. Dose,* one grain (0.065 Gm.) given in capsules.

Nastin.—This substance which was originally prepared by Deycke and Reschad (*D. M. W.,* 1907, p. 89) from a culture of the bacilli of leprosy is stated by the discoverers to be a peculiar paraffin-like substance, of fruity odor and composed of a glycerin ester and *nastinic acid* (a fatty acid of high molecular weight). It was at one time thought to be characteristic of these bacteria, but has been found in the bodies of other bacteria. It is claimed that the injection of this substance causes the death of the leprosy germs and hence arrests the disease. It is not claimed for it that it will cure the lesions which are already present, but simply that it prevents further progress of the disease. It is employed in the form of a 1 per cent. solution in warm sterile olive oil of which at first eight minims (0.5 mil) and later 1 mil is injected weekly. Kupffer (*Cb. G. T.,* 1909, p. 311) has also obtained favorable results from its employment.

Nasturtium. *Watercress. Cresson de fontaine,* Fr. *Brunnenkresse,* G. *Radicula Nasturtium aquaticum* (L.) Britten et Rendle. (Fam. *Cruciferæ.*)—In sensible and medicinal properties watercress bears some resemblance to scurvy grass, though milder, and on this account is preferred for the table. It is thought to be useful in *scorbutic affections* and *visceral obstructions.* It contains a volatile oil, which, according to A. W. Hofman, contains as its chief constituent a body boiling at 253° C. (487.4° F.), which he considers to be the nitrile of *phenyl-propionic acid,* $C_9H_{10}O_2$, and therefore has the formula $C_9H_{10}N$. The expressed juice is sometimes given in the *dose* of one or two fluidounces (30–60 mils); but the herb is more frequently used in the form of a salad.

Other species of *Radicula* grow in similar situations with the *R. Nasturtium,* and act similarly.

Neoform. *Bismuth-oxytri-iodo-phenate.* $C_6H_2I_3O.BiO_2H_2$.—It occurs as a yellowish insoluble powder, with but very slight taste. It is suggested as a dusting powder to *ulcers* and *wounds.*

Neopyrin. *Valeryl-amido-antipyrine.*—This is in the form of odorless crystals, of very bitter taste, and a melting point of 203° C. (397.4° F.). It is sparingly soluble in water, more so in alcohol, and freely so in chloroform.

Bachem (*Th. M.,* 1909, p. 588) has experimented upon the lower animals with valeryl-amido-antipyrine and also with its bromine derivative. The latter, however, he finds is too toxic to give promise of therapeutic usefulness, although it exercises a marked antipyretic action. He finds

neopyrine is less poisonous than antipyrine and believes that it may prove a useful antipyretic. We are not acquainted, however, with any practical trials of the drug.

Dose, five to ten grains (0.32–0.65 Gm.).

Neosalvarsan. *N. N. R.* 1917.—In this preparation the basis of salvarsan (3-diamino-4-dihydroxy-1-arseno-benzene) is not combined with hydrochloric acid to form the hydrochloride, but with the radical of sodium formaldehydsulphoxylate or sodium methanalsulphoxylate (CH_2O)OSNa, to yield the compound present in neosalvarsan. Approximately 3 parts of this modified salvarsan (sodium - 3 - diamino-4-dihydroxy-1-arseno-benzene-methanalsulphoxylate, $NH_2.OH.C_6H_3.As:As.C_6H_3OH.NH(CH_2O)OSNa$ is equivalent to two of salvarsan. (See p. 1594.) It has been introduced to replace the widely used salvarsan as requiring less complicated methods for its injection. It occurs as an orange-yellow powder, which is very unstable in the air. It differs from the older salvarsan in that it immediately dissolves in water, forming a neutral solution which deposits a brown precipitate on standing. It appears to be less efficacious than the older form. It contains about two-thirds the amount of arsenic as salvarsan, and consequently is given in somewhat larger doses. The *dose* is from ten to fourteen grains (0.65–0.9 Gm.) given either intramuscularly or intravenously.

Neosiode. $(C_{15}H_{14}O_6,3H_2O)_8I$.—This is said to be an organic iodine compound, probably iodocatechin, and is asserted to be an efficient method of iodine administration, either internally or externally, due to the easy assimilation of this substance. It is a yellow amorphous powder soluble in ordinary solvents. *Dose*, two to five grains (0.13–0.32 Gm.).

Nerium. *Nerium Oleander* L. *Laurier Rose, Laurose*, Fr. *Oleander, Rosenlorbeer*, G. (Fam. *Apocynaceæ*.)—The common ornamental shrub known as *oleander* is affirmed to have been used from time immemorial in portions of Southern Europe for destroying rats, and a number of cases of poisoning by it have been reported. (For collection, see *T. G.*, July, 1888.) The symptoms have been vomiting, abdominal pain with frequent cries, dilatation of the pupil, vertigo, convulsive movements, insensibility, small, very slow pulse, and in fatal cases epileptiform convulsions with coma ending in death. The action on the heart has in some cases in which death has not ensued, been very pronounced, the pulse for five days remaining as low as forty per minute. The infusion made from four ounces of the root is affirmed to have taken life.

Two supposed alkaloids have been discovered in oleander by Leukowsky (*J. P. C.* (3), 46, 397), one named *pseudocurarine*, the other named *oleandrine*. Both neutralize acids; the former dissolves in water and alcohol, but not in ether, and is neither volatile nor poisonous; the latter is yellow, amorphous, very bitter, very slightly soluble in water but more freely in alcohol and ether, and poisonous in its action on the system. H. G. Greenish isolated two substances, *neriodorin* and *neriodorein*, which are probably not pure proximate principles. (*A. J. P.*, 1881, 350.) B. C. L. Bose (*P. J.*, 1901, 553) obtained a resinous substance, *karabin*, $C_{21}H_{42}O_6$, which he states is one of the active constituents of this plant. Haemel (*Ph. Ztg.*, 1901, 58) obtained a semi-concrete oil to the amount of 0.025 per cent. from the leaves of *N. Oleander*. Dubigadoux and Durieu affirm that they have obtained strophanthin from the oleander of Algeria.

Schmiedeberg (*A. E. P. P.*, 1883, Bd. xvi, 145) finds two active substances in the oleander leaf—*nerin* and *oleandrin*. Schmiedeberg shows that the latter, which had been previously described by Leukowsky as an alkaloid, is a glucoside, and on boiling with very dilute acids breaks up into sugar and a yellow resinous substance like digitaliresin. With concentrated acids it also decomposes, yielding an inactive resin. Schmiedeberg also obtained from African leaves a glucoside, *nerianthin*, which he surmises to be an educt from oleandrin. He found oleandrin to be a powerful cardiac poison, but nerianthin not to have the power of arresting the frog's heart, although it exerts some influence upon it, possibly, as Schmiedeberg surmises, through contaminating oleandrin. Pieszczek obtained from oleander bark a principle which he named *rosaginin*, which was very poisonous, resembling strychnine in its action. (*A. Pharm.*, ccxxviii, 352.) (See also *M. R.*, 1911, and *J. P. C.*, 1912, 108.)

Leulier found in oleander bark a glucoside which seems to be identical with the lævo-strophanthin of Thoms. (*P. J.*, lxxxvii, p. 407.)

Pouloux (*B. G. T.*, May 15, 1888) having confirmed the earlier conclusions of Pelikau (*C. R. A. S.*, 1866, 239) that oleander acts upon the heart like digitalis, used it successfully in a few cases of valvular *heart disease*. In seventy-five cases under the care of Freiherr (*Aerzt. Rund.*, 1892) it acted promptly as a heart stimulant and tonic. Its diuretic action is said to be very marked, and not rarely it acts as a cathartic. Any irritation of the alimentary canal contra-indicates its use. Under its influence the pulse rapidly becomes regular and slow, and dyspnea and edema disappear. Freiherr asserts that it is safer than digitalis in atheromatous diseases. Freiherr used it in infusion or tincture, representing as the daily dose from three-quarters to one and a half grains (0.048–0.096 Gm.) of the dried oleander bark, one and a half to three grains (0.096–0.2 Gm.) of the fresh bark, one and a quarter to three and a half grains (0.08–0.23 Gm.) of the dried fruit. Pouloux's dose of the extract was three-quarters of a grain (0.048 Gm.). Orfele has used the dried flowers—dose, three grains (0.2 Gm.) in substance, or from ten to twenty minims (0.5–1.0 mil) of a 10 per cent. tincture—with success.

Nervocidine.—This is a yellow, amorphous, hygroscopic powder, readily soluble in water, which is affirmed to be an alkaloid, obtained from the East Indian plant, *Gasu Basu*, and to be a powerful local anesthetic, its 1 per cent. solution producing marked anesthesia of the cornea. It is stated to be so irritant that its 2 per cent. solution will cause in dogs and rabbits an ulcerative keratitis along with an anesthesia which lasts for days. It is affirmed, further, to be a paralyzing poison, causing such symptoms as to almost invalidate its usefulness and render it unsafe. (*L. L.*, 1902, 1.)

Neuraltein. *Neraltein. Sodium p-ethoxyphenyl-amino-methane-sulphonate.* $C_2H_5O.C_6H_4NH.CH_2SO_3Na + H_2O$.—This is in the form of white crystals which are soluble in 10 parts of water, and very soluble in boiling water.

It is claimed that it has the advantage over other derivatives of paramido-phenol of being much less toxic. Astalfoni (*W. K. W.*, 1909, p. 119) has found that it causes an increase in the blood pressure with slowing of the pulse. The

primary phase of hypertension lasts about an hour and is not followed by depression. Gottlieb (*Cb. I. M.*, 1909, xxx, p. 1049) has employed it in a number of febrile conditions. He finds that it exercises in many cases a distinct antipyretic effect but that its analgesic action is much inferior to that of other coal-tar antipyretics. Skutetzki (*M. M. W.*, 1909, p. 2314) on the other hand has obtained a marked relief of pain in *rheumatic fever* and believes that it is of value rather as an analgesic than an antipyretic. It may be given in *doses* of eight grains (0.5 Gm.) three to six times a day.

Neurodin. *Acetyl-p-oxy-phenyl-urethane.* $C_6H_4(OCOCH_3)NH.COOC_2H_5$.—Forms colorless, odorless crystals, fusing at 87° C. (188.6° F.), soluble in 1400 parts of cold water. It is used as an anodyne in *neuralgia* in *doses* of from fifteen to twenty grains (1–1.3 Gm.).

Neurolæna. *Neurolæna lobata* R. Br.—From the leaves of this composite plant, used in the Windward Islands as a substitute for quinine, and in *dysentery*, B. H. Paul and A. J. Cownley obtained an uncrystallizable alkaloid. (*P. J.*, ix.)

Neuronal. *Diethylbromacetamid.* $Br(C_2H_5)_2CO.NH_2$.—A crystalline substance slightly soluble in cold water, but is decomposed in hot water. It possesses a camphoraceous odor and a bitter cooling taste. Melting point 66° to 67° C. (150.2°–152.6° F.). It has been used as a somnifacient by a number of clinicians with more or less satisfactory results. While apparently a useful drug in the treatment of the milder forms of *insomnias*, it does not seem to possess sufficient power in the severer cases. Heineicke (*Med. Clin.*, 1906, 572) observed that when used repeatedly, the remedy is liable to lose its power. The *dose* is from fifteen to thirty grains (1–2 Gm.).

Neusidonal.—This preparation is asserted by its promoters to be the inner anhydride of quinic acid, but analysis has proved it to be irregular proportions of quinine, $C_7H_{10}O_4$, and quinic acid, $C_7H_{12}O_5.H_2O$, usually containing 75 per cent. of the former and 25 per cent. of the latter. It is administered in the treatment of *gout*, one hundred and fifty grains (9.8 Gm.) being given daily in divided *doses*.

Neutral Red.—*Dimethyldiamidotoluphenazine Hydrochloride.—Toluylene red* has been employed by Schlaepfer (*M. M. W.*, 1908, No. 36) as a means of testing the motor function of the stomach. Nine mils of a one-half per cent. solution of the dye is mixed with a meal and the passage of the gastric contents through the pylorus is indicated by the coloration of the urine. The remainder of the contents of the stomach are then syphoned out and the activity of the digestion may also be approximately ascertained by a degree of change in the color of from red to yellow which is caused by the gastric secretions.

Nickel. *Niccolum.*—T. P. A. Stewart (*A. E. P. P.*, Bd. xviii, 154) finds that in frogs soluble preparations of nickel produce palsy with convulsive movements which are due to an action upon the nerve centers, the muscles remaining intact, the heart also being affected, as it is believed, by an action upon its motor ganglia. In mammals the chief symptoms produced by nickel are paralysis, with motor disturbance bearing some resemblance to chorea, with convulsions and great irritation of the gastro-intestinal tract, and a marked fall of the blood pressure, due to paralysis of the vasomotor center. Large doses of *nickel* seem, however, to be necessary for a toxic influence, and the use of nickel in culinary instruments appears to be entirely safe. Riché (*B. A. M.*, 1888), as the result of experiments made upon dogs and guinea-pigs, reaches the conclusion that nickel is not more poisonous than iron. Thus, a dog absorbed over five drachms of it in sixty days, and increased in weight. The results obtained by Riché have been confirmed in Germany by von Hamel Roos and by Schulz. (*P. J.*, Dec., 1887.)

Nickel Bromide, *nickelous bromide*, $NiBr_2$, is a greenish-yellow powder, of a sharp, almost burning taste, freely soluble in water, and making a grass-green solution. It is made by the action of bromine vapor upon the finely divided metal, either by heating the nickel in the vapor, or by the action of the two in the presence of water. It was first brought forward by J. M. Da Costa as a remedy for *epilepsy* and kindred disorders, and its value has been confirmed by R. Leaman. (*Med. Gaz.*, April 18, 1885.) He affirms that ten grains of the nickel salt are equal to thirty grains of potassium bromide; and that it is best used in effervescing form. It has been physiologically investigated by H. A. Hare, who finds (*T. G.*, vol. ii, 297) that it is a powerful paralyzant to the spinal cord, the motor and sensory nerve trunks, and also to the voluntary muscle. In sufficient dose it causes immediate diastolic cardiac arrest. In smaller doses it lessens the arterial pressure by depressing the heart and the vasomotor center.

Dose, five to ten grains (0.3–0.6 Gm.).

Nickel Carbonate. *Nickelous Carbonate. Niccoli Carbonas. Carbonate Niccolique*, Fr. *Nickelkarbonat*, G. $NiCO_3 + Ni(OH)_2$.—Made by precipitating the solution of a nickel salt with potassium carbonate. It is from pale green to dark green, of variable composition and is little used, though at one time it was employed in *anemia* in *doses* of two grains (0.13 Gm.).

Nickel Carbonyl. *Carbonic Oxide Nickel. Nickel-Kohlenoxyd*, G. $Ni(CO)_4$.—This substance was first investigated by Mond, Lang, and Quincke, who reported to the Société de Biologie, 1890, that it is difficult to handle because its vapors produce excruciating headache, and that it is a violent poison, evidently destroying the hemoglobin of the blood. A. Mittasch (*A. E. P. P.*, xlix, 367; *L. L.*, 1903, i) found that the vapors produced febrile reaction with violent disturbances of respiration, followed by great and very persistent malaise and weakness. Langlois (*C. R. S. B.*, 1891), also McKendrick and Snodgrass (*B. M. J.*, June, 1891), have shown that it acts by being broken up in the body and yielding carbon dioxide to the hemoglobin. It produces prolonged fall of temperature, but it is not probable that it will prove of any practical value in medicine. For physical properties and methods of preparation, see authors quoted.

Nickel Chloride. *Niccoli Chloridum. Chlorure de Nickel*, Fr. *Nickelchlorür*, G. *Nickelous Chloride.* $NiCl_2 + 6H_2O$.—A green, very deliquescent salt. The anhydrous chloride is yellow and sublimes in yellow scales, without melting.

Nickel Sulphate.—*Niccoli Sulphas*, $NiSO_4.7H_2O$, is formed by dissolving *nickel carbonate* in diluted sulphuric acid, concentrating the solution, and setting it aside to crystallize.

It is in the form of emerald-green crystals efflorescent in the air, soluble in three parts of water, but insoluble in alcohol and ether. It has a sweet, astringent taste. Simpson found this salt to act as a gentle tonic, useful in *migraine* in *doses* of from half a grain to one grain (0.032–0.065 Gm.) three times a day. In large doses it

is liable to produce nausea and vomiting, especially when the stomach is empty. (See *Braithwaite's Retrospect*, xxvii, 446.) Kolipinski (*J. A. M. A.*, 1911, lvii) states that *nickel sulphate* has a strong parasiticidal effect, that in solutions from one to two per cent. it is a useful application in *impetigo contagiosa*, *tinea*, and other parasitic skin disease.

Nicotine Salicylate. *Nicotinæ Salicylas.* $C_6H_4(OH)COOH.C_{10}H_{14}N_2$.—This substance occurs in colorless crystals, soluble in water and alcohol, fusing at 118° C. (244.4° F.). Under the name of *eudermol* a substance composed chiefly of lanolin, containing 0.1 per cent. *nicotine salicylate*, has been put upon the market and highly commended for the treatment of *scabies* and other parasitic diseases of the skin, also of *itching eczema*. Ointments containing a larger per cent. are said to be dangerous. (*Th. M.*, 1898.) The application of the ointment should be followed after some hours by a soap bath. L. C. Fettich has used the 1 per cent. lanolin ointment of nicotine salicylate in cases of *mange* of dogs. When the mange is of the acaridic variety the treatment should be assisted by baths containing 2-to 4 per cent. of potassium sulphide.

Nierenbergia Hippomanica. *Chus-chu.*—This solanaceous plant is the not infrequent source of poisoning to cattle in Argentine, where it is a native. Laveuir and Sanchez (*J. P. C.*, 1907, xxvi) have isolated a poisonous alkaloid to which they give the name *nierenbergine*. Apparently this alkaloid resembles saponin in some of its properties. They were not able to find the glucoside *hippomanin* which had previously been reported.

Nigella. *Nigella sativa* L. *Nutmeg-flower. Small Fennel-flower. Faux Cumin*, Fr. *Schwarzkümmel*, G. (Fam. *Ranunculaceæ.*)—A small, annual plant, growing wild in Syria and the south of Europe, and cultivated in various parts of the world. The seeds, *semen nigellæ*, are ovate, somewhat compressed, from 2.5 to 3.5 mm. in length and less than 2 mm. in thickness, usually three-cornered, with two sides flat and one convex, black or brown externally, white and oleaginous within, of a strong, agreeable, aromatic odor, like that of nutmegs, and a spicy, pungent taste. (*P. J.*, 1882, 681.) Their chief constituents are a volatile and a fixed oil (1.5 per cent. of the former and 35 per cent. of the latter), and an amorphous glucoside, *melanthin*, which is decomposed by diluted hydrochloric acid into *melanthigenin* and sugar. The *nigellin* of Reinsch does not seem to have been a pure substance. Rochebrune has found a powerful paralyzing alkaloid, to which he gives the name of *nigelline*. (*Toxicol. Africaine*, vol. i.) Melanthin, according to W. von Schulz, exhibits the typical physiological action of the most poisonous saponins. In India the seeds are considered as stimulant, diaphoretic, and emmenagogue, and are believed to increase the secretion of milk. They are also used as a condiment, and as a corrigent or adjuvant of purgative and tonic medicines. In the seeds of the *Nigella Damascena* Schneider (*Ph. Centralh.*, 1890, xxxi, p. 173) found an alkaloid which he called *damascenine*, whose construction was studied by Pommerehne and Keller. (*A. Pharm.*, 1904, ccxlii, p. 295.) It has been made synthetically. They were unable to find any alkaloid in *N. sativa*. (See also *A. Pharm.*, 1908.)

Nigrosine. *Aniline Black. Coupier's Blue.*—A series of blue to black dyes prepared by oxidizing various proportions of nitrobenzene, aniline and toluidine. The process is purely empirical and admits of great variation in the resulting product. It is used as a black dye and in the manufacture of aniline inks.

Ninhydrin. *N. N. R.* 1917. *Triketohydrindenhydrate.*—This occurs in the form of colorless, water-soluble crystals. It is not employed therapeutically, being used solely as a reagent to demonstrate the presence of albumen, peptone, polypeptid, and amino acids, especially in the diagnosis of pregnancy after Aberhalden's method.

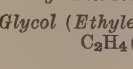
Nirvanin.—The *hydrochloride of diethylglycocoll-p-amido-o-oxybenzoic-methylester.* It occurs in colorless prismatic crystals, with a melting point of 185° C. (365° F.), affording a violet reaction with ferric chloride, and soluble in water.

Nirvanin has been brought forward as a local anesthetic, with a claim that it is only about one-tenth as toxic as cocaine, and is as effective as a local anesthetic. It is also alleged to be actively antiseptic, the 1 per cent. solution effectively preventing the growth of bacteria. The 5 per cent. solution placed in the eye produces a temporary irritation followed by lasting anesthesia. It has been used to a considerable extent as a substitute for cocaine in infiltration anesthesia, the strength of the solution used varying from one-tenth to one-third of 1 per cent. Nirvanin has also been used to a considerable extent in dentistry; eight grains (0.5 Gm.) are stated to have been given to an adult, hypodermically, without the production of toxic symptoms. (Elsberg, *Ther. Prog.*, April, 1900.)

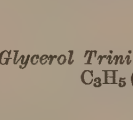
Nitrated Alcohols.—The following substances of the possible series of nitrated alcohols have been studied by J. B. Bradbury (*B. M. J.*, 1895, ii):

Methyl Nitrate, (CH_3NO_3).

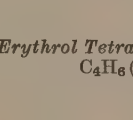
Glycol (Ethylene) Dinitrate $C_2H_4(NO_3)_2$



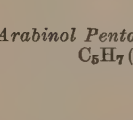
Glycerol Trinitrate (Nitroglycerin) $C_3H_5(NO_3)_3$



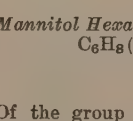
Erythrol Tetranitrate $C_4H_6(NO_3)_4$



Arabinol Pentanitrate $C_5H_7(NO_3)_5$



Mannitol Hexanitrate $C_6H_8(NO_3)_6$



Of the group the first three are liquid. The others are crystalline, colorless solids, stable in the dark at a moderately low temperature, turning yellow and exploding when heated above 150° C. (302° F.), or percussed. Of slight solubility in water, soluble in alcohol and ether, responding when heated to the meta-phenylene diamine test.

Bradbury has shown that all these substances have similar physiological action, differing among themselves and from amyl nitrite simply in the rapidity and fugaciousness of influence. Glycol dinitrate in one-hundredth-grain (0.0006 Gm.) *doses* markedly influences arterial tension in the

human being, but its effect is not maintained longer than sixteen minutes. Erythrol and mannitol nitrates were found to be slow in action but of remarkable permanence and influence, their effect on the lower animals lasting more than four or five hours. Methyl nitrate was feeble and fugacious in its influence.

Both erythrol and mannitol nitrates have been used by Bradbury and others in *angina, aneurism, Raynaud's disease, asthma, headache,* and various other affections for which nitroglycerin has been employed. Erythrol nitrate, as more soluble, appears to be preferable to mannitol nitrate. It is less easily exploded than nitroglycerin, but great care must be practised in any attempt at powdering, as a very serious explosion has occurred from rubbing it in a mortar with sugar of milk. It is usually administered in tablet form in *doses* of one-half to two grains (0.03–0.12 Gm.). The *dose* of the 1 per cent. alcoholic solution of mannitol nitrate is one and a half fluidrachms (5.5 mils).

Nitrobenzene. *Nitrobenzole. Oil of Mirbane.* $C_6H_5NO_2$.—*Nitrobenzene* is formed by the action of strong fuming nitric acid upon benzene,

$$C_6H_6 + HNO_3 = C_6H_5NO_2 + H_2O.$$

The product, after having been washed with water, is an oily, yellowish, intensely sweet liquid, with an odor like that of oil of bitter almond. Its sp. gr. is 1.186, and boiling point 209° C. (408.2 F.). It has become of commercial importance, being produced as an intermediate product in the manufacture of aniline oil, and, under the name of *artificial oil of bitter almonds,* or *oil of mirbane,* being employed for scenting soaps and pomades. Its use in articles of food and for flavoring, as a substitute for bitter almond oil, is properly forbidden under pure food regulation. For method of detecting nitrobenzene in oil of bitter almond, see *Oleum Amygdalæ* (Part I). It is of commercial importance, as being used in the manufacture of aniline.

In manufactories where nitrobenzene is made, headaches, with sleepiness, are not infrequently produced by inhalation of the fumes; much more serious poisoning is liable to occur, and there have been a number of deaths produced by nitrobenzene. The symptoms may come on almost immediately, or they may be delayed for some hours. According to Filehne (*A. E. P. P.,* Bd. ix), the slowness of action is chiefly dependent on the fact that nitrobenzene, when mixed with the contents of the stomach and intestines, is absorbed with very great slowness; for if the drug be injected directly into the blood of the rabbit, it produces death in convulsions in less than a minute. The first symptoms of poisoning are headache, with muscular weakness, and a peculiar bluish color of the face, and disturbance of consciousness. In the fully developed poisoning the whole surface of the body is a deep bluish color, and the mucous membranes a bluish-gray; the pupils are dilated; the muscular relaxation is complete, except that sometimes the jaw is rigidly set; consciousness is lost; respiration rapid, but shallow and irregular; pulse rapid and thready, or entirely absent. The urine contains urobilin, indican, and acetone. Recovery may occur, as in a case reported by Stevenson (*Guy's H. R.,* vol. xxi, 1876), after many hours of unconsciousness, the bluishness of the skin and the headache remaining for several hours longer. After death, the blood is of a deep chocolate brown, and, according to Filehne, has lost the power of absorbing oxygen. Lewin has seen the blood so changed that, after five weeks' standing, the oxyhemoglobin lines could still be made out, and its spectrum is altered. (See *A. Phys.,* 1879.)

In poisoning of the lower animals convulsions are frequent phenomena, and, according to Letheby (*P. J.,* Sept., 1863), after small doses, the animal sometimes for days will have more or less unconsciousness, with epileptic attacks, and at length die of exhaustion, or gradually recover. In the guinea-pig, but not in the dog, Ewald has found nitrobenzene to produce glycosuria. (*P. M. T.,* vol. iv, 312.)

The cause of death appears to be paralysis of the motor nervous centers. Letheby states that nitrobenzene is partly converted in the body into aniline, but this is denied by Filehne, who asserts that the aniline was produced by the processes used by Letheby. According to Caspar, death from prussic acid and nitrobenzene may be distinguished by the fact that when the body is left open for some hours, the odor of prussic acid leaves, while that of nitrobenzene persists. The minimum fatal dose is not known; according to Taylor, fifteen drops (0.75 mil), taken by the mouth, have proved fatal, and in Stevenson's case, twenty-three minims (1.42 mils), taken in seven doses, in forty-eight hours produced unconsciousness and respiratory arrest, so that death would probably have occurred if treatment had not been instant.

The proper treatment would appear to be emetics, the early use of artificial respiration, maintenance of the bodily temperature, and the stimulation of the respiration and circulation by hypodermic injections of atropine, strychnine, and digitalis. In a case reported by Werner (*B. K. W.,* 1884, xxi), life was apparently saved by bleeding sixteen fluidounces (480 mils) and transfusing twelve fluidounces (360 mils) of defibrinated blood.

Dinitrobenzene. Dinitrobenzol. 1–3 $C_6H_4(NO_2)_2$.—On boiling benzene with fuming nitric acid, there is formed chiefly *metadinitrobenzene,* fusing at 90° C. (194° F.), with small amounts of the ortho and para compounds. By crystallizing out of alcohol, the meta compound can be obtained pure. Dinitrobenzene has attracted considerable attention on account of the number of cases of poisoning by it occurring among the workmen in aniline works. The symptoms are said to be jaundice, enlargement with tenderness of the liver, diarrhea with colorless stools, and dark brown urine in which dinitrobenzene can be located by the phenylene-diamine test. The toxicology has been especially studied by Strassmann and Strecker (*Friedreich's Blätt. f. Gerich. Med. u. Sanitätspolizei,* Heft iv, 1896), who add to the symptoms already given, headache, a peculiar bluish discoloration of the face and general surface, a tendency to fainting, with excessive sweating, vomiting, fall of temperature, great muscular weakness, and finally collapse. It is noted also that in animals experimentally poisoned there has been destruction of the red blood corpuscles with consequent hemoglobinuria and wide-spread fatty degeneration. According to White and Hay (*L. L.,* ii, 1901) pure dinitrobenzene is much less poisonous to the workers than is the commercial dark colored substance which contains *mononitrobenzene.* Mononitrobenzene is, however, according to the same authority, scarcely poisonous, the reason that the commercial mixture is more poisonous than the pure dinitrobenzene being that the mononitrobenzene is a powerful solvent of dinitrobenzene, making an oily mass which adheres to the skin and yields to absorption the dinitrobenzene. The fact that the dinitrobenzene is absorbed through the skin of the workmen

is so generally recognized that in most commercial laboratories the workmen are required to wear specially close fitting clothing over the body and head, and to practise absolute cleanliness.

Nitro-Propiol. *Ortho - nitro - phenyl - propiolic acid*, when heated with grape sugar in the presence of soda, forms indigo, according to the following equation:

$$2C_6H_4(NO_2).C{\equiv}C{-}COOH + 4H = C_{16}H_{10}N_2O_2 + 2CO_2 + 2H_2O$$

The formation of indigo is rendered evident by a blue coloration of the fluid. The compound therefore serves as a qualitative test for the glucose in urine. Von Gerhardt recommends the following method for carrying out the test: Place 10 to 15 drops of the urine under examination in a test tube, add one hundred and sixty minims (10 mils) distilled water and a *nitro-propiol tablet*, and carefully heat the mixture for two to four minutes. In the presence of sugar the fluid first becomes green and subsequently intensely blue. This reaction is sufficiently sensitive to indicate with certainty 0.3 per cent. of sugar and possesses the advantage that it only takes place if grape sugar is actually present in the urine.

Nizin. *N. N. R.* 1917. *Zinc Sulphanilate.* $Zn[C_6H_4(NH_2)SO_3]_2 + 4H_2O$.—It is intended as an astringent and antiseptic injection in the treatment of chronic gonorrheal *urethritis*. It is recommended to be employed in about one-half per cent. aqueous solution.

Njimo Wood.—The wood of *Sarcocephalus esculentus* Afzel. (Fam. *Rubiaceæ*), known as *Njimo*, was introduced into Germany from the Cameroons with the statement that it had digestive properties similar to those of pepsin. It is a stem wood, often with pieces of root, of a yellow color, musk-like odor, and bitter taste. Schulz (*Ph. Ztg.*, June 12, 1886) finds that it is not a digestive, and that it yields a resinous extract not poisonous to frogs. The alcoholic extract of the drug is yellow by transmitted light, but exhibits a green fluorescence resembling uranium glass. The bark of this same plant called "Dundaki," according to Heckel and Schlagdenhauffen (*Compt. Rend.*, 1885, 69) contains an alkaloid, *Dundakine*.

Nosophen. *Tetraiodophenolphthalein. Iodophen.* $C_{20}H_{10}I_4O_4$.—*Nosophen* is obtained by the action of iodine on solutions of phenolphthalein. It is an impalpable, yellowish-gray, odorless, tasteless powder, containing 61.7 per cent. of iodine in combination. It may be heated up to 220° C. (428° F.) without decomposition. It is insoluble in water and acids, soluble with difficulty in alcohol, glacial acetic acid, ether, and chloroform, but readily soluble in alkalies, with the last of which it forms salts from which it is easily freed at low temperature by carbon dioxide. In the presence of heat it liberates carbon dioxide from its alkaline salts. By virtue of its two hydroxyl groups, nosophen is an acid, readily soluble in alkalies with replacement of the hydrogen atoms of both hydroxyl groups by a metal. Three of the salts of nosophen have been put upon the market—the sodium salt (antinosine), the bismuth salt (eudoxine), and the mercury salt (apallagin).

Antinosine has the following formula:

$$(C_6H_2I_2ONa)_2C.O.C_6H_4O.$$

It is a dark blue, amorphous powder which is readily soluble in water and alcohol.

Eudoxine, $(C_6H_2I_2OBi_2)_3C.OC_6H_4O$, is a red-dish-yellow, tasteless, odorless powder, insoluble in water, which is decomposed by alkalies into bismuth oxide and a soluble salt of tetra-iodo-phenol-phthalein. It contains 52.9 per cent. of iodine and 14.5 per cent. of bismuth.

Apallagin. Mercury Tetra-iodo-phenol-phthalein.—A gray powder which is recommended as a powerful antiseptic.

Medicinal Properties and Uses.—It is stated that in nosophen and its two salts the iodine is so firmly combined that it is not liberated in the human system, either when applied locally or administered internally, and that the preparations are therefore incapable of producing toxic effects. It is further affirmed that nosophen is in itself germicidal and locally an alterative, and that, being free from toxic properties, it is superior to iodoform. It is not irritant, and may be used freely as a local application in powdered form in all those cases to which iodoform is applicable, and has been especially recommended in nasal and laryngeal diseases. It has been administered internally as an intestinal antiseptic in *doses* of from five to eight grains (0.32–0.5 Gm.).

It is affirmed that antinosine has the same general properties as a germicide as nosophen, and that being soluble in water it affords a valuable application in many cases to which the nosophen as a dusting powder is scarcely applicable. The strength of the local application varies: from 2 to 3 per cent. in diseases of the nose, mouth, and throat, from 1 to 2 per cent. in *gonorrhea*, from ½ to 1 per cent. for irrigation of the bladder and in *cystitis*, from 1 to 500 to 1 to 1000 for washing out of the stomach in *gastric catarrh, cancer*, etc.

Its 2 per cent. solution is said by W. F. Coleman to act most favorably in all forms of external inflammation about the eye, in purulent *otitis media*, etc. Owing to its solubility in water and its freedom from odor and taste, it is coming into vogue as a mouth wash; for this purpose its glycerin solution is preferable, aromatics being added to taste. A teaspoonful (3.75 mils) of the 1 per cent. solution in a tumblerful of water is the strength commonly employed, but when there is a severe *stomatitis* a 2 per cent. or even stronger solution may be used without dilution.

Its intravenous use has been suggested, but, according to Binz and Zantz (*Fort. Med.*, xiii, 1895), it is decomposed in the blood when so given and nosophen precipitated.

Eudoxine is believed to be slowly decomposed by the alkaline juices of the intestines, with liberation of nosophen and bismuth. It has been given in *doses* of from five to eight grains (0.32–0.5 Gm.) three times a day, with alleged most excellent results, in *diarrheas, gastric* and *intestinal indigestions*, and even *gastric cancer*.

Novargan. *N. N. R.* 1917. *Silver Proteinate.*—This occurs as a yellow, amorphous powder, freely soluble in water, yielding a neutral solution. It is asserted that the silver from this solution is not precipitated either by chlorides, sulphides, alkalies, or by any of the substances that ordinarily precipitate silver or its salts from solutions. The compound represents 10 per cent. of silver.

Novargan has been employed as a germicide for the local treatment of *gonorrhea*. It may be used in acute cases in strengths of from 0.2 to 0.75 per cent. According to Von Hoessle and Grater (*D. M. Ztg.*, 1905, p. 92) it is less irritating to the mucous membranes than protargol and has also the advantage of a deeper penetration. Regenspurger (*Med. Klin.*, 1908, No. 8) has used it for the abortion of *gonorrhea* in the following man-

ner. After washing out the urethra he injects 8 to 12 mils of a solution containing five parts of novargan and ten parts of glycerin and water to make one hundred which is allowed to remain in the urethra for from five to fifteen minutes. If no inflammatory reaction follows this twenty-four hours later he injects a 10 per cent. solution. He claims that a very considerable number of cases with this treatment are cured within a period of eight days.

Novaspirin. *Methylene-citric-acid-ester of Salicylic Acid. N. N. R.* 1917.—This is a white, crystalline powder representing 62 per cent. of salicylic acid. It is almost insoluble in water, but dissolves readily in alkaline solutions or alcohol. Its melting point is 150° to 152° C. (302°–305.6° F.). This substance is used for those various conditions in which aspirin has been found of service, such as acute and chronic *rheumatism, neuralgia,* etc. It is stated that it is better borne by the stomach than aspirin and less likely to produce excessive sweating and the other undesirable sequelæ sometimes seen after the older remedy. Lehmann (*D. M. W.*, 1907, No. 10) has found, however, that it is less powerful in its effects than aspirin, especially in acute *rheumatic fever.* Gresic (*K. T. W.*, 1908, No. 4) has found it also of service in the treatment of *asthma,* both to prevent and to relieve the paroxysms. It is incompatible with iron compounds and with acids or strongly acid salts. The *dose* of novaspirin is from ten to thirty grains (0.65–2 Gm.) three or four times a day or oftener if needed.

Novatophan. *N. N. R.* 1917. *Ethyl Ester of Paratophan. Ethyl-6-methyl-2-phenylquinoline-4-Carboxylate.* $CH_3.C_9H_4N.C_6H_5COOC_2H_5$. — The uses and dosage of this are the same as those of atophan (see *Acidum Phenylcinchoninicum,* Part I), over which the advantage is claimed of being less disagreeable to the palate.

Paratophan is *methylatophan.* It occurs as a yellow, crystalline powder, insoluble in water, but soluble in the presence of alkalies, also in alcohol, ether, or chloroform.

Noviform. *Tetrabrom-pyrocatechin-bismuth.*—This is a yellow, insoluble powder. It is used as a surgical dressing in much the same way that iodoform has been employed.

Novocaine. *N. N. R.* 1917. *Novocain. P-amino-benzoyl-diethyl-amino-ethanol Hydrochloride.* $CH_2(C_6H_4.NH_2.COO).CH_3[N(C_2H_5)_2].HCl$. — *Novocaine* occurs as colorless, needle-like crystals, soluble in equal parts of water and in thirty parts of alcohol. Its melting point is from 150° to 156° C. (302°–312.8° F.). The solutions of novocaine will withstand boiling. The nitrate of the same base is also obtainable. All alkaloidal precipitants react on its solutions and it is incompatible with alkalies and their carbonates.

Novocaine appears to be the least toxic of all the local anesthetics thus far introduced, with the possible exception of eucaine. Biberfeld (*Med. Klin.*, 1905, p. 1218) has found that the fatal dose of novocaine is about four times that of cocaine and twice that of stovaine. LeBrocq (*B. M. J.*, March 27, 1909) has also shown that its toxic powers and very low, and claims that it has the added advantage over eucaine and other local anesthetics of being much less irritant to the tissues and, therefore, less likely to produce unpleasant local reactions. When introduced into the blood stream its general action is very feeble, neither circulation nor respiration showing any changes from an ordinary dose. It further differs from cocaine in that it causes neither contraction of the pupil nor local vasomotor spasm and that it is not decomposed by boiling and may, therefore, be usually sterilized. Novocaine has been used with success by a number of physicians both to produce local anesthesia at the point of application and also for injection into the subarachnoid space in the so-called spinal anesthesia. According to Schley (*N. Y. State Journ. of Med.*, Dec., 1907) for mucous membranes its action is not entirely satisfactory, but when injected into the tissues its local anesthetic action is marked. When it is desired to produce a localized anesthesia by injecting into a tissue it is well to combine it with epinephrine, since the latter drug, by causing spasm of the blood-vessels, prevents its being carried away, and hence prolongs the anesthetic action. Schley finds that secondary hemorrhage is less likely to occur after this injection than after cocaine or cocaine-epinephrine injections. Hoppe (*Aerztliche Praxis,* 1906, No. 16), who employed novocaine in ophthalmological work, found that even 5 per cent. solutions did not produce complete anesthesia, and that it was surpassed both in depth and rapidity of action by cocaine, which conclusion agrees with that of other observers. For spinal anesthesia from one to one and a half grains (0.065–0.096 Gm.) may be injected into the subarachnoid space. Gabbett (*In. Med. Gazette,* Feb., 1911) has reported a death from the intraspinal injection of novocaine and strychnine.

Nuclein. *N. N. R.* 1917. *Nucleinum. Nucleol.* $C_{29}H_{49}N_9P_9O_{22}$.—The term *nuclein* is applied to a group of substances containing proteins which possess a *nucleinic acid* group in their structure, $C_{40}H_{54}N_{14}O_{27}P_4$. These proteins are derived from tissues rich in cell nuclein. The nuclein, however, probably does not exist as such in the cell but is produced by decomposition of the nucleo-proteids. It may be separated by digesting the cells with artificial gastric juice by which means the investing protoplasm is dissolved leaving the nuclein unaffected. The term *pseudonucleins* or *paranucleins* is applied to a group of bodies somewhat resembling the real nucleins, which are produced by the peptic digestion of proteins containing phosphorus but not nucleinic acid. *Nucleinic,* or *nucleic acid,* may be obtained from nuclein by the action of alkalies or by tryptic digestion. It occurs as an amorphous, white powder, strongly acid in reaction, sparingly soluble in water, but readily soluble in alkalies, and insoluble in alcohol or ether.

When nuclein-containing foods are taken, the nuclein is partly separated but not destroyed by the gastric digestive juices. In the intestines, however, the nuclein is broken up and nucleic acid liberated. Some of this may be further destroyed in the intestines but the larger part is absorbed. The nuclein absorbed is partially eliminated as purin bodies—allantoin, uric acid, etc.—and probably in part broken up into urea. As an almost constant accompaniment of the introduction of nucleic acid into the system, whether from the ingestion of food rich in nuclein or from the parenteral absorption of nucleinic acid or its salts, there is a great increase in the number of white blood corpuscles. Renner (*Mitt. Grenz. M. C.*, 1905, xv, p. 89) has reported as high an increase in the number of leucocytes as 452 per cent., and several authors have noted more than double the number of normal. This leucocytosis is usually preceded by a hypoleucocytosis of six or eight hours' duration.

Nucleinic acid has a distinct bactericidal effect; according to Kossel 0.5 per cent. of nucleinic

acid kills streptococci *in vitro* in two hours and staphylococci after six hours. As has been shown by Vaughan and confirmed by Parlavecchio (*A. K. C.*, 1909, xc) and others, nucleinic acid also possesses bacteriolytic properties and even precipitates bacterial toxalbumins and in the body increases the formation of agglutinins and alexins. Chantemesse (*B. A. M.*, 1907, lvii) and others have noted an increase in the opsonic index.

These effects of nuclein should tend to increase the bodily resistance to bacterial infections and the drug has consequently been largely used in the treatment of *septicemia, furunculosis, tuberculosis, diphtheria,* and other diseases of bacterial origin. While the clinical reports have not been uniformly flattering they have been sufficiently encouraging to justify the further trial of this remedy in infectious conditions. In addition to this it has been used to a lesser extent for its influence upon metabolism in *anemia, neurasthenia,* and similar diseases. Donath (*M. M. W.*, 1912) asserts that it is a useful drug in parasyphilitic diseases, such as *general paresis.* He injects from eight to fifteen grains (0.5–1.0 Gm.) of *sodium nucleinate,* in the form of a 10 per cent. solution, gradually increasing the *dose* to sixty to seventy-five grains (3.9–5.0 Gm.), or until there is a febrile reaction.

Nuclein is frequently used in the crude form as found in various foods, such as yeast (see p. 1668). There are, however, a considerable number of proprietary preparations more or less purified. Some of these are as follows:

Sodium tritico-nucleinate, a sodium nucleinate derived from wheat. It is a grayish-white powder, readily soluble in water.

Nuclein from yeast, a grayish-white, amorphous powder, sparingly soluble in water, but soluble in alkaline solutions. *Dose,* eight grains (0.5 Gm.) four to six times a day.

Protonuclein.—This is stated by the manufacturers to be prepared from the lymphoid structures and glandular organs of the body. *Dose,* three to ten grains (0.2–0.65 Gm.).

Nucleol.—This is stated to be pure nuclein. It occurs as a white powder, readily soluble in water.

Nucleinic acid from yeast, a white or grayish-white powder obtained from yeast nuclein; it is sparingly soluble in water, but is readily soluble in alkalies. *Rhomnol* is a trade name for *nucleinic acid.*

Animal Nucleinic Acid.—A yellowish powder prepared from the thymus gland and other similar animal glands containing nuclein: it has almost the same solubility as nucleinic acid from yeast.

Sodium Nucleinate.—A yellowish-white powder prepared from nucleinic acid from yeast. It is readily soluble in water and contains approximately 4.5 per cent. of sodium.

Quinine Nucleinate.—A yellowish-white powder, slightly soluble in water, rather more soluble in alcohol (50 per cent.) and in dilute glycerin. It contains 40 per cent. of quinine.

Copper Nucleinate. Cuprol.—Cuprol occurs as a greenish powder, soluble in water, containing about 6 per cent. of metal. It is used as an astringent application in all those cases in which the older copper salts have been employed. In *conjunctivitis* a 5 to 10 per cent. solution has been recommended.

Ferric Nucleinate. Ferrinol.—Ferrinol is a brown powder, freely soluble in water, containing about 6 per cent. of iron.

Mercury Nucleinate. Mercury Nucleide.—Two forms of this compound are known to medicine, the one a direct combination of mercury with nucleinic acid known as *mercurol,* and the other known as *levurargyre,* made by acting upon yeast with mercuric chloride.

Mercurol is a colorless or brownish-white powder, containing 10 per cent. of mercury, soluble in water with a weak alkaline reaction, and has been used both internally and locally as a substitute for corrosive sublimate, over which it has the advantage of not coagulating albumin. In *syphilis* from half to one grain (0.032–0.065 Gm.) of *mercurol* may be given hypodermically. Two grains (0.13 Gm.) are said to have produced salivation. Another preparation similar to mercurol is called *Rhomnogyre.*

Levurargyre. Nuclein mercurate is a grayish-white powder, soluble in water, and unaffected in solution by hydrogen sulphide. It is given in the treatment of *syphilis,* usually hypodermically, in *doses* of one-sixth to one-half grain (0.010–0.032 Gm.).

Argentic Nucleinate. Nargol. Silver Nucleinate.—This is a light, brownish-white powder, readily soluble in water, contains 10 per cent. of silver. It has been recommended as a local application in those conditions for which silver nitrate has been used. It may be used in solution up to 25 per cent. on most mucous membranes. The solution should be recently made, as it undergoes change after a few weeks.

Nutrose. *N. N. R.* 1917. *Casein Sodium. Sodii Caseinas.*—The acid sodium salt of casein. This product forms a white, inodorous and tasteless powder, slightly soluble in cold and very soluble in warm water. It is given in water or milk in large doses in the treatment of convalescent and anemic patients.

Nymphea.—The seed of *Nuphar luteum* Smith (*Nymphæa lutea* Linné), *European Yellow Pond Lily* (Fam. *Nymphæaceæ*), according to W. Grüning, contains *nuphar-tannic acid,* $C_{56}H_{56}O_{37}$, in considerable quantity. (*A. J. P.*, 1883, 96.) Goris and Crété state that the *nupharine* of Grüning has the composition $C_{18}H_{24}O_2N_2$. They obtained it from the fresh rhizome of *N. luteum.* (*J. Chem. S.*, 1910.) The name *Nymphæa* has been incorrectly applied also to the American white pond lily, which belongs to the genus *Castalia, Castalia odorata* (Ait.) Woodv. and Wood. (*Nymphæa odorata* (Ait.)), *Sweet-scented Water Lily.* The root of this well-known American plant is very astringent and bitter, and, according to Bigelow, contains much tannin and gallic acid. The root of *Castalia alba* Presl. (*Nymphæa alba* L.), or European *white water lily,* was esteemed anaphrodisiac by the ancients and the tannic acid contained in it has been named *nymphæ-tannic acid,* and the formula $C_{56}H_{58}O_{38}$ given it. (*A. J. P.*, 1883, 96.)

Nyssa. *Nyssa aquatica* L. *Tupela Gum. Sour Gum. Swamp Tupelo.* (Fam. *Cornaceæ.*)—A large tree growing in deep swamps in the Southern United States. The root, known as *Tupelo root,* has been recommended for surgical tents. (*A. J. P.*, 1883.)

Oatmeal. *Avenæ Farina. Farine d'Avoine,* Fr. *Hafermehl,* G. *Farina dell' Avena,* It. *Harina de Avena,* Sp.—*Avena sativa* L., or the common oat (Fam. *Gramineæ*), is so well known that a minute description would be superfluous. It is specifically distinguished by its "loose panicle, its two-seeded plumes, and its smooth seeds, one of which is awned." It was known to the ancients, and is now cultivated in all civilized countries; but its original locality has not been satisfactorily ascertained. It grows wild in Sicily, and is said to

have been seen by Anson in the island of Juan Fernandez, off the coast of Chili. The seeds deprived of their husks are sometimes known as *groats*. As a human food coarsely ground oatmeal is usually preferred to the fine meal, and the grain grown in a northern climate is superior to that produced farther south. Hence Canada and Irish and Scotch oatmeals are better than the meals produced in the middle of the United States, the product of which country is chiefly consumed by horses. Diuretic properties have been attributed to the oatmeal, but probably incorrectly. *Tinctura Avenæ Sativæ* may be made by permeating 4 troyounces of the ground oatmeal with 1 pint of diluted alcohol, reserving the first 5½ fluidounces, and evaporating the remainder down to half a fluidounce and adding to the reserved portion. (H. E. Heinitsh, *A. J. P.*, 1886, 86.)

A very elaborate report on the composition of American cereals by Clifford Richardson (*Department of Agriculture, Bulletin* No. 9) gives as the average ratio in oats from all parts of the country 70 per cent. of kernel to 30 per cent. of husk. According to the same authority, the composition of the kernel (average of 179 analyses) is as follows: Water, 6.93 per cent.; ash, 2.15; oil, 8.14; carbohydrates, 67.09; fiber, 1.38; albuminoids, 14.31; corresponding to nitrogen per cent. 2.28. The nitrogenous principle has been called *avenin*, and resembles legumin somewhat. Ritthausen (*Die Eiweisskörper*, Bonn, 1872, 135) considers Nortin's avenin to have been a mixture of legumin or vegetable casein and a vegetable gluten containing sulphur, to which he gives the name *gliadin*, the legumin, however, predominating.

Gruel made with fine oatmeal affords a nutritious, bland aliment, which, from its somewhat laxative tendency, is often preferable to other amylaceous preparations. *Oatmeal gruel* may be prepared by boiling an ounce of the meal with three pints of water, to a quart, straining the decoction, allowing it to stand until it cools, and then pouring off the clear liquor from the sediment. Sugar, lemon juice, or wine may be added to improve its flavor.

Ochres.—These are native mixtures of argillaceous or calcareous earth and iron and manganese oxides, employed in painting. They are prepared for use by elutriation. The color of the *ochres* varies with the state of oxidation of the iron, and with the proportion which the iron bears to the other ingredients, and is sometimes artificially modified by the agency of heat. Several varieties are known in commerce under different names, according to their color or place of origin. Such are *brown ochre, yellow ochre, red ochre, Roman ochre,* which is of a brownish-yellow color, changing by heat to a purple-red, *Oxford ochre,* of a brownish-yellow color less deep than the Roman, and *French ochre,* which is yellow. The *Indian red,* from the Persian Gulf, and *Spanish brown* and *Venetian red* may also be ranked in this class of pigments. Sometimes ochres come in powder, and sometimes in hard masses known as *stone ochres.*

Ocimum. *Ocimum Basilicum* L. *Basil. Sweet Basil. Grand Basilic,* Fr. *Basilienkraut,* G. (Fam. *Labiatæ.*)—An annual, aromatic plant, a native of India and Persia, and cultivated in Europe and in this country in gardens. It yields by distillation from 0.02 to 0.04 per cent. of a yellowish, volatile oil. The French and German oil have a penetrating odor resembling estragon, the Reunion has a camphor-like odor, a higher specific gravity and is dextrogyrate. Basil has the ordinary properties of the aromatic plants, and is used as a condiment. The seeds are said by Ainslie to be used in India in *gonorrhea.*

Œnanthe. *Œ. crocata* L. *Water Hemlock. Water Dropwort. Dead Tongue.*—A perennial, umbelliferous, aquatic, European plant, exceedingly poisonous both to man and inferior animals. The root, which has a sweetish not unpleasant taste, is sometimes eaten by mistake for other roots, often with fatal results. The symptoms produced are those of irritation of the stomach, besides failure of circulation, and great cerebral disturbance, indicated by giddiness, convulsions, and coma. (See *P. J.*, 1874, 202.) Externally applied, the root produces redness and irritation of the skin, with an eruption. It is said to be sometimes used empirically as a local remedy in *piles.* Other species of *Œnanthe* are poisonous, and the whole genus should be suspected. We have two or three indigenous species. In cases of poisoning, the stomach should be at once evacuated, and symptoms met as they arise. A peculiar resinoid principle, denominated *œnanthin,* has been found by Gerding in *Œnanthe fistulosa* L., the common water hemlock of Europe, of which half a grain (0.032 Gm.), given to an adult, produced long-continued irritation of the fauces, and a grain (0.065 Gm.), occasional vomiting. (See *A. J. P.*, xxi, 68.) Poehl (*A. E. P. P.*, 1895, xxxiv, p. 258) claimed to have isolated a toxic principle, to which he gave the name of *œnanthotoxin,* and assigned a formula of $C_{17}H_{22}O_5$. Tutin, however (*P. J.*, Aug. 26, 1911), asserts that this body is not a pure principle but a mixture of neutral resins of unknown nature. He confirms the conclusions that the resin is an active poison. He also examined the tuberous roots of *O. crocata* and found *triacontane,* $C_{30}H_{62}$, and *hentriacontane,* $C_{31}H_{64}$. In the *P. J.*, vol. xvi, 357, is a paper by Henry William Jones upon the recognition of *Œ. crocata* in cases of suspected cattle poisoning; he found that the starch granules possessed characters which enabled him to distinguish the tubers from all others.

Œnanthe aquatica Lam. (*Œnanthe Phellandrium* Lam., *Phellandrium aquaticum* L.) *Fine-leaved Water Hemlock. Water Fennel. Fructus Phellandrii. Wasserfenchel,* G. *Phellandrie aquatique, Fenouil d'Eau,* Fr.—A biennial or perennial, umbelliferous, European water plant, the fresh leaves of which are said to be injurious to cattle, producing a kind of paralysis when eaten. By drying, they lose their deleterious properties. The *seeds* are from 4 to 5 mm. in length (about 2 mm. broad), ovate-oblong, narrow above, somewhat compressed, marked with ten delicate ribs, and crowned with the remains of the calyx, and with the erect or reverted styles. Their color is yellowish-brown; their odor peculiar, strong, and disagreeable; their taste acrid and aromatic. Among their constituents is a volatile oil, upon which their aromatic flavor depends. By C. Fronefield it has been rendered probable that they contain a volatile alkaloid, analogous to coniine, if it be not *coniine* itself, for if the powdered seeds are rubbed with solution of potassium hydroxide, the peculiar mouse-like odor of that alkaloid is exhaled. The powder was submitted to distillation with potassium hydroxide, the alkaline liquid obtained was neutralized with sulphuric acid and evaporated to a syrupy consistence, alcohol was added to precipitate the ammonium sulphate, the liquid was then filtered, treated with potassium hydroxide, and again distilled. On the surface of the distillate a yellow oily fluid floated, which was only

slightly soluble in water but readily so in ether and alcohol, evinced an alkaline reaction with turmeric paper, and neutralized the acids. (*A. J. P.*, May, 1860, 211.) The ethereal oil of water fennel which is present to the extent of 1 to 2½ per cent. is a yellow liquid of strong, pleasant characteristic odor and burning taste. It has a sp. gr. of 0.85–0.89 and is dextrorotatory. It contains about 80 per cent. of the terpene *phellandrene*, $C_{10}H_{16}$. In overdoses the seeds produce vertigo, intoxication, and other narcotic effects. They have been used in chronic pectoral affections, such as *bronchitis*, *pulmonary consumption*, and *asthma;* also in *dyspepsia*, *intermittent fever*, obstinate *ulcers*, etc. The *dose* of the seeds, to commence with, is five or six grains (0.32–0.4 Gm.), so repeated as to amount to a drachm (3.9 Gm.) in twenty-four hours. They should be given in powder. *Dose*, of the alcoholic extract, three grains (0.2 Gm.). (*P. J.*, xii, 591.)

Œnothera. *Œnothera biennis* L. *Tree Primrose. Evening Primrose. Onagre*, Fr. *Nachtkerze*, G. (Fam. *Onagraceæ.*)—The fleshy root of this plant, before the introduction of the potato, was used as a table vegetable. Many years ago R. E. Griffith commended very highly a strong decoction of the plant frequently applied to eruptive skin diseases. More recently the drug has been commended in *whooping cough* and spasmodic *asthma*, and the ointment has been used in *prurigo* and other cutaneous affections of infants, and as an application to *ulcers*. *Dose*, of fluidextract, from a half to one fluidrachm (1.8–3.75 mils). The ointment may be made by incorporating four ounces of the fluidextract in a pound of vaseline or lard.

Oil of Akee.—This is a yellow, non-drying, butter-like fat obtained from the *Blighia sapida* Kon. (Fam. *Sapindaceæ*), native of Guinea, but cultivated in Jamaica. (*P. J.*, 65, p. 691.)

Oil of Aleurites Triloba.—The *Aleurites triloba* Forst. is a small tree belonging to the *Euphorbiaceæ*. It is widely diffused throughout the tropics. The fruit is a nut nearly as large as a walnut, consisting of a thick shell enclosing a kernel containing much protein and rich in oil, of which it is said to yield nearly one-half its weight by expression. The nuts strung together on the fibers of the palm leaf were formerly used in many Pacific islands as a substitute for candles. The oil has been long known in the various countries inhabited by the plant, being called in Jamaica *Spanish walnut oil*, in India *Belgaum walnut oil*, in Ceylon *kekune oil*, and in the Hawaiian Islands *kukui oil*. It is very fluid, of an amber color, without odor, of a nutty, pleasant taste, congealing at 0° C. (32° F.), insoluble in alcohol, readily saponifiable, "and very strongly drying." It is said to be a mild cathartic, acting like castor oil, but more promptly and without griping effects. (*J. P. C.*, 3e sér., xxiv, 228.) The *dose* is from one-half to one fluidounce (15–30 mils), the smaller quantity generally answering. The cake left after the expression of the oil, given to a dog in the *dose* of about half an ounce (15 Gm.), produced no vomiting, but acted strongly as a purgative.

The oil of the *Tung Tree, Aleurites cordata* (Thunb.) Müll.-Arg., is used to a large extent in the arts in China, under the name of *Chinese wood oil* or *tung oil*. (This must not be confounded with the Indian oil of wood, see p. 1522.) It is prepared in China by a crude process of expression. It occurs in two forms, *white oil*, a moderately thick, yellowish, transparent liquid, and the *black oil*, which is thick, black, and opaque. Wood oil is used in China and Japan either as a direct application to wood or mixed with various substances, as lacquer varnish, or paint. Its most remarkable characteristic is its extraordinary drying property, which is said to exceed that of any known oil. When applied to wood it forms a resinous layer which is affirmed to be impermeable by water and ordinary solvents. Wood oil is also exported to Europe, where it is used in the making of varnishes. This oil is obtained from the seeds of the tung tree, which contains about 53 per cent. of fixed oil. According to R. H. Davies, its sp. gr. at 15.5° C. (60° F.) is 0.94015; it remains liquid at −13.3° C. (8° F.). 100 Gm. of the oil require 0.39 Gm. potassium hydroxide for neutralization, and 21.1 Gm. for complete saponification. (*P. J.*, 1885, 636.) E. M. Holmes believes that the dark colored oil is made by boiling the kernels previous to expression, the cold drawn oil being colorless, inodorous, and nearly tasteless. The latter, according to Cloëz (*C. R. A. S.*, 1875, vol. lxxxi, 469), has the sp. gr. 0.9362, congeals at −18° C. (−0.4° F.) to a transparent mass, solidifies rapidly when exposed to light in a closed vessel, and is the most drying oil known. (*C. D.*, May, 1902.) (See also *Proc. A. Ph. A.* 1897, 677; and *Chem. News*, 1912, 14.) Over 60,000 kilogrammes are said to be sent yearly from Hankow, on the Yang-tse-kiang, to the various Chinese seaports. It has been used in *ulcerations* and *skin diseases*. The seeds of the tung tree are used in China for killing rats, and are also affirmed to have emetic properties.

Oil of Anda.—A fixed oil procured by expression from the seeds of *Johannesia princeps* Vell. (Fam. *Euphorbiaceæ.*) The bark of *J. princeps*, growing in the maritime provinces of Brazil, yields on being wounded a milky juice, which is said to be poisonous, and to be used for stupefying fish. The fruit, which is about as large as an apple, ash-colored, with two larger and two smaller ridges, encloses a two-celled nut, containing two seeds, about the size of a chestnut. Like the seeds of other euphorbiaceous plants, these are actively purgative, one seed, according to Martius, being the *dose* for a man. By expression these seeds yield a pale yellow, transparent oil, with little odor or taste, which is said to be used in Brazil for burning and painting. It has a sp. gr. 0.927, and in properties belongs to the class of semi-drying oils. (*P. J.*, 1905, 910.) Mello Olliveria has found in it an alkaloid, *johannesine*, which Couty affirms to be inert. (*N. R.*, 1881, 260.) Norris, who tried the oil at the Pennsylvania Hospital, found it to operate on the bowels moderately in the *dose* of fifty drops (2.5 mils), and copiously when more largely given. Manoel de Castro and other Brazilian physicians assert that in *doses* of from one to two teaspoonfuls (3.75–7.5 mils) it acts in a manner very similar to castor oil, over which it has the great advantage of not being nauseous to the taste.

Oil of Anise Bark.—There has appeared in the European markets a bark, closely resembling Massoi bark, and is supposed to be derived from a species of *Illicium*, probably *I. parviflorum* Michaux, growing in Madagascar, which yields fully three and a half per cent. of a light, yellow oil, the odor of which slightly resembles safrol. It has a spicy taste, but is only slightly sweet. Its specific gravity is 0.969 at 15° C. (59° F.). Optical rotation −0° 46′ in a 100-mm. tube. Refractive index at 16° 1.52510. It contains a small quantity of ordinary anethol, but consists principally of the isomeric fluid anethol, the *methyl-*

chavicol of Eykman, $CH_3O.C_6H_4.CH_2.CH : CH_2$.

Oil of Ben. *Behen Oil.*—This is a fixed oil extracted from the seeds of *Moringa arabica* Pers. (Fam. *Moringaceæ*), and from *M. pterygosperma* Gaertn. (*M. Oleifera* Lam.). It should not be confounded with oil of benne from *Sesamum indicum* L. (Fam. *Pedaliaceæ*). These are trees of the Fam. *Moringaceæ*, inhabiting different parts of India, Arabia, Syria, etc., and introduced into the West Indies. The leaves and other parts have an acrid property, which has probably given the name of *horseradish tree* to *M. pterygosperma*. According to Henry Schachan (*Nouv. Rem.*, 1890), the tincture of the root is very actively diuretic and useful in cardiac *dropsy*. The oil of the seeds has long been known, though used in the arts rather than in medicine. It is prepared in Europe from the seeds brought from Egypt; and it would appear, from the statements of Macfadyen, that the idea generally prevailing that it is also extracted in the West Indies is incorrect. The oil has a sp. gr. of from 0.912 to 0.917; it solidifies at about 0° C. (32° F.); indeed at 7° C. (44.6° F.) it begins to deposit the solid fats. It is inodorous, clear, and nearly colorless, and keeps long without becoming rancid. It resembles olive oil, and is used for similar purposes. Mérat and De Lens say that it is purgative; but most of the fixed oils are so in sufficient doses. According to Völcker, the oil contains palmitin, olein, and a peculiar fatty matter yielding an acid by saponification, which he names *benic* (or *behenic*) *acid*. (*J. P. C.*, xvi, 77.) Heintz considered benic acid as simply a mixture of palmitic and myristic acids. (*Pogg. Ann.*, xcii, 601.) It is, however, now recognized as one of the normal fatty acid series, possessing the formula $C_{22}H_{44}O_2$.

Oil of Bergamot. *N. F. IV* (*U. S.* 1890). *Oleum Bergamottæ. Oleum Bergamii. U. S.* 1880. —"A volatile oil obtained by expression from the rind of the fresh fruit of *Citrus Aurantium Bergamia* (Risso et Poiteau) Wight et Arnott (Fam. *Rutaceæ*), and containing not less than 36 per cent. of ester, calculated as linalyl acetate. Preserve it in small, amber-colored, well-stoppered bottles in a cool place, protected from light." *N. F.*

The bergamot tree has oblong-ovate, dentate, acute, or obtuse leaves, somewhat paler on the under than on the upper surface, and with footstalks more or less winged or margined. The flowers are white, and usually small; the fruit is pyriform or roundish, about three inches in diameter, terminated by the remains of the short style, with concave receptacle of oil in the rind. The pulp of the fruit is sourish, somewhat aromatic, and not disagreeable. The rind is shining, and of a pale-yellow color, and abounds in a very grateful volatile oil. This may be obtained by expression or distillation. In the former case it preserves the agreeable flavor of the rind, but is somewhat turbid; in the latter it is limpid but less sweet. The mode of procuring it by expression is exactly the same as that used for oil of lemon. (See *Oleum Limonis.*) It is brought from Italy, the south of France, and Portugal.

"Oil of Bergamot is a green or greenish-yellow liquid, neutral or only faintly acid, having a characteristic fragrant odor and an aromatic bitter taste.

"Two volumes of the Oil, when mixed with 1 volume of alcohol, give a clear solution and this does not become turbid on the further addition of alcohol. It is soluble in 2 volumes of 80 per cent. alcohol with not more than a slight cloudiness, and no separation of oil globules. Also soluble in all proportions in glacial acetic acid.

"Specific gravity: 0.875 to 0.880 at 25° C. (77° F.).

"It is dextrorotatory, the angle of rotation varying from + 8° to + 24°, in a 100 mm. tube, at 25° C. (77° F.).

"Evaporate in a tared dish on a water bath about 2 Gm. of the Oil, accurately weighed, until the odor has completely disappeared; a soft green residue remains, corresponding to not more than 6 per cent. of the Oil (*fixed oils*).

"To 2 Gm. of Oil of Bergamot add 10 mils of alcoholic potassium hydroxide V.S., free from chloride, evaporate to dryness and incinerate. Extract the ash with distilled water and acidify with diluted nitric acid; no cloudiness is produced on the addition of silver nitrate T.S. (*chlorinated compounds*).

"*Assay.*—To 2 Gm. of the Oil add 20 mils of half-normal alcoholic potassium hydroxide V.S. and heat the mixture in a flask on a water bath, under a reflux condenser, for a half hour. Cool the mixture, add 100 mils of distilled water and titrate with half-normal sulphuric acid V.S., using phenolphthalein T.S. as indicator. Not more than 12.6 mils of half-normal sulphuric acid V.S. is required, corresponding to not less than 36 per cent. of ester, calculated as linalyl acetate, in the Oil.

"Each mil of half-normal potassium hydroxide V.S. consumed corresponds to 0.09808 Gm. of ester, calculated as linalyl acetate." *N. F.*

The oil of bergamot, often called *essence of bergamot*, has a sweet, very agreeable odor, a bitter, aromatic, pungent taste, a pale greenish-yellow color, and a slightly acid reaction.

It contains limonene, dipentene, linalool, a solid greasy compound called *bergaptene*, or *bergamot camphor*, and *linalool acetate*, $C_{10}H_{17}.C_2H_3O_2$, which latter makes up about 40 per cent. of the expressed oil, but is decomposed in large part by the process of steam distillation. Bergaptene has been very fully studied by Pomeranz. (*M. Chem.*, 1891, 379.) It melts at 188° C. (370.4° F.), and has the composition $C_{12}H_8O_4$, being the lactone or inner anhydride of *bergaptenic acid*, $C_{12}H_{10}O_5$. By fusion with potassium hydroxide, bergaptene yields *phloroglucin*. (See *Schim. Rep.*, April, 1893, and 1895, 24; also *Proc. A. Ph. A.*, 1897, 630.) The oil is distinguished from lemon and orange oils by readily dissolving in solution of potassium hydroxide and forming with it a clear solution. (Zeller.) Though possessed of the stimulant properties of the volatile oils in general, it is employed chiefly as a perfume.

According to Galewsky (*Ph. Ztg.*, 1915, lx, p. 55) the oil of bergamot is an extraordinarily active insecticide and useful to protect the body against lice and other vermin.

It is often adulterated. (See *C. D.*, 1908, 383; also 1910, 52.)

Oil of Birch Tar, Rectified. *Oleum Betulæ Empyreumaticum Rectifactum. N. F. IV. Rectified Oil of Birch Tar. Rectified Empyroligneous Oil of Birch. Oleum Rusci Rectificatum.*—"The pyroligneous oil obtained by the dry distillation of the bark and wood of *Betula alba* Linné (Fam. *Betulaceæ*), rectified by steam distillation." *N. F.*

Under this name the National Formulary IV

has introduced this oil of tar from the birch. It is, however, not certain whether the rectification has removed some of the valuable constituents. (See *Betula*, p. 1277.)

It is described as follows:

"Rectified Oil of Birch Tar is a limpid, dark brown liquid having a penetrating, empyreumatic odor resembling that of Russian leather.

"It yields clear solution with 3 volumes of dehydrated alcohol, and with ether, chloroform, glacial acetic acid, amyl alcohol, oil of turpentine, benzene, or carbon disulphide. When mixed with 3 volumes of alcohol or purified petroleum benzin, the solution is not more than slightly turbid but a decided turbidity is produced when mixed with the same volume of methyl alcohol.

"Specific gravity: 0.886 to 0.950 at 25° C. (77° F.).

"Warm 2 mils of the Oil with 10 mils of distilled water, agitate and allow the mixture to cool; separate and filter the aqueous liquid. The filtrate is colorless, has a strong, empyreumatic odor and an acid reaction. Add two drops of potassium dichromate T.S. to 4 mils of the same aqueous filtrate; it produces a bright yellow solution which soon becomes darker and turbid. Add one drop of dilute ferric chloride solution (1 in 100) to 4 mils of the filtrate; it produces a green coloration which changes to brown and becomes turbid (distinction from *oil of cade*)." *N. F.*

Oil of Callitris.—The pine trees of Australia belong to the genus *Callitris*, of which only one or two species are found outside of Australasia and New Zealand. The wood of these trees is of great value as building timber because of the fact that it is not attacked by white ants. According to Baker and Smith ("Research on the Pine Trees of Australia," 1910) this protection is due to the presence of a phenol-like body, to which they give the name *callitrol*. The constitution of this substance which they have obtained from the wood of *C. glauca* they have not as yet determined. Several of the Australian species yield a resin with the same properties as those of Sandarac (see p. 1595), but at present they have not been employed commercially as sources of this resin. The term *cypress pine* is applied in Australia to a number of these trees.

Oil of Cardamom. *N. F. IV. Oleum Cardamomi.*—"A volatile oil distilled from the seeds of *Elettaria Cardamomum* White et Meton (Fam. *Zingiberaceæ*). Preserve it in small, well-stoppered, amber-colored bottles, in a cool place, protected from light." *N. F.*

This oil has been introduced into the National Formulary IV. It is used in the preparation of *compound spirit of cardamom*, which is an ingredient in *compound elixir of cardamom*. It is also used as a flavor in other elixirs. It is to be regretted that cardamom seeds were not used instead of this oil which is largely adulterated. In fact *oil of cardamom* has been found in the market made from oils which contain no oil of cardamom whatsoever. The high price of cardamom seeds and the small percentage of volatile oil found in them offers an extraordinary inducement to adulterators. Care must therefore be used to employ only the oil which complies strictly with the requirements of the National Formulary IV. It is described as follows:

"Oil of Cardamom is a colorless or very pale yellow liquid having the characteristic, aromatic, penetrating and somewhat camphoraceous odor of cardamom, and a persistent, pungent, and strongly aromatic taste.

"It is very soluble in alcohol and readily soluble in four volumes of 70 per cent. alcohol, forming a clear solution.

"Specific gravity: 0.924 to 0.947 at 25° C. (77° F.).

"It is dextrorotatory, the angle of rotation varying from +22° to +44°, in a 100 mm. tube, at 25° C." (77° F.) *N. F.* (See *A. J. P.*, 1910, 167.)

Oil of cardamom is not used medicinally but solely for pharmaceutical purposes.

Oil of Chione.—The bark of this West Indian tree, *Chione glabra* (Fam. *Rubiaceæ*) yields on distillation 1.5 per cent. of a light yellow volatile oil, consisting chiefly of *o-oxyacetophenone*, $C_6H_4.OH.CO.CH_3$. A compound obtained synthetically from *o-nitrocinnamic acid* proved to be identical with that isolated from the oil. (See *J. Chem. S.*, vol. lxxv, 1899.)

Oil of Citronella.—There are a group of closely allied grasses which yield sweet scented volatile oils. Of these volatile oils, which are sometimes spoken of collectively as *Indian Grass Oils*, there are at least five commercial varieties, namely, *Oils of Citronella, Lemon Grass, Palmarosa, Ginger Grass*, and of *Vetiver*. The botany of the sweet-scented grasses from which perfumery oils are obtained, has been somewhat confused. Stapf (see *Schim. Rep.*, April, 1907, p. 20) divides them into three groups, the *Cymbopogon, Andropogon* and *Vetiveria*.

Andropogon nardus L. (Fam. *Gramineæ*) yields citronella oil. It grows in Ceylon, the Malaccan Peninsula, India and to some extent in tropical East Africa. There are two principal varieties, the one, *Lana Batu*, grows widely in Ceylon and yields an oil relatively poor in geraniol and is the principal source of the oil of commerce. The second variety, known as *Maha pangiri*, is generally cultivated in the Straits Settlements and in Java. This latter oil has a lower specific gravity, a lighter color and is claimed to be superior in quality.

Oil of citronella is produced in Ceylon, the Straits Settlements, close to Malabar, the Malay Peninsula and Java, the last named being the most highly esteemed. The exports of citronella oil from Ceylon amounted in the year 1909 to 1,512,084 pounds. Oil of citronella is of a yellowish-green color, having a characteristic odor and pungent taste. Its sp. gr. is, according to Gildemeister and Hoffmann, 0.886–0.900. It mixes with alcohol in all proportions, and the test for purity given by Schimmel and Co. is based upon its behavior towards alcohol of 80 per cent: "One volume of the oil must form an absolutely clear solution with two, or at least two and a half, volumes of 80 per cent. alcohol at a temperature not below 20° C. (68° F.). A cloudy mixture indicates the presence of turpentine, certain fixed oils, and other essential oils which are sometimes used to adulterate it." The most important ingredients in this oil are *geraniol* and *citronellal* which together may make up as much as 93 per cent. of the oil. It is not used in medicine, but is largely used in the arts, for perfuming cheap soaps, especially so-called honey soap. An ointment containing 25 per cent. of the oil of citronella affords an excellent protection against the bities of mosquitoes and other insects.

Oil of lemon grass is official in the British Pharmacopœia (1914). (See *Oleum Graminis Citrati*, Part I.)

The *Palmarosa oil* is produced chiefly in India, and is the product of the *Cymbopogon martini* (*Andropogon schœnanthus* Flück. and Hanb. not

L.). Its most important ingredient is geraniol, of which it may contain as high as 94 per cent. It is largely employed in the perfumery arts, and also as an adulterant to the oil of rose and the oil of geranium.

Ginger grass oil resembles palmarosa oil in its properties but contains a much smaller percentage of geraniol.

From the roots of the *vetiver* or *cus-cus grass*, *Vetiveria zizanoides* Stapf. (*A. muraticus* Retz), which grows in the island of Reunion and in the Philippine Islands, is distilled a volatile oil. The odoriferous principle of this oil is at present unsettled. It has been attributed by Genivesse and Landlois to a peculiar alcohol which they named *vetivenol*, but this has been denied by Bacon. (*Philippine Journal of Science*, 1909, iv, p. 118.)

Various other allied grasses, such as the *Cymbopogon polyneuros* or *Delft Grass*, and the *C. Coloratus*, etc., yield sweet-scented oils which have, however, not become commercially important.

Oil of Coconut. *Cocoanut Oil. Cocoanut Butter. Oleum Cocos*, P. G. *Oleum Cocois. Beurre de Coco*, Fr. *Kokosnussöl*, G.—This must not be confounded with the fixed oil of the chocolate nut, which is often called *cocoa butter*. (See *Oleum Theobromatis*, p. 797.) The substance here considered is the fixed oil of the coconut, which is the fruit of a species of palm, *Cocos nucifera* L., universally known as the *coconut tree*, or *cocoanut tree*. The oil is obtained either by expression or decoction, often by *insolation—i.e.*, exposing the rasped nuts to the heat of the tropical sun. It is of a fine white color, of the consistence of lard at ordinary temperatures, becoming solid, like suet, between 4.4° C. (40° F.) and 10° C. (50° F.), and liquid at about 26.7° C. (80° F.), of a bland taste, and a peculiar, not disagreeable odor. It is readily dissolved by alcohol. It contains large quantities of the glycerides of myristic and lauric acids, with smaller quantities of the glycerides of palmitic and oleic acids. It has also been found to contain several volatile acids, as caproic, caprylic, and capric acids. (Lewkowitsch, *Chemical Analyses of Oils, Fats, and Waxes*, 2d ed., 1898, 538.)

The oil has been used for various purposes in medicine and pharmacy. It has been employed as a substitute for cod liver oil, especially in the form of a proprietary preparation, *coco-olein*. In Germany it has been used in pharmacy, to a considerable extent, as a substitute for lard, to which, according to Pettenkofer, it is preferable on account of its lesser tendency to rancidity, its more ready absorption when rubbed on the surface of the body, and its lesser liability to produce chemical changes in the substances with which it is associated. Thus, the ointment of potassium iodide, when it is made with lard, becomes yellow in a few days, while, if made with coconut oil, it remains unchanged for two months or more. Vegetable substances also keep better in ointments prepared with this oil than with lard. Besides, it takes up one-third more water, which is a useful quality when it is desirable to apply saline solutions externally. To prepare it for use, nothing more is ordinarily necessary than to melt it at a moderate heat, and strain it through linen. If colored, it may be digested with powdered animal charcoal, and subsequently filtered through paper. (*A. J. P.*, xxix, 331.) When chilled and pressed, a solid residue, which is *coco-stearin*, is obtained. This is extensively used as a substitute and adulterant of the genuine cocoa butter in the confectionery trade. Coconut oil is employed in the manufacture of soap, particularly of the transparent varieties, and the so-called "*marine soaps*" and *filled soaps;* it is also largely used for giving firmness and lathering qualities to the ordinary soap; this property also permits of the addition of a large quantity of water to the soap. Unfortunately, coconut oil soap is very apt to contain free caprylic acid; and the persistent rancid odor, resembling that of infants' vomit, left upon the skin after washing with its soap is an effectual bar to its very extended use. The exportations of coconut oil from Ceylon amount to 15,000 tons annually, from British India to 4000 to 6000 tons, and from the Dutch Indies to 1300 tons per annum. Besides the oil itself, the dried pulp of the coconut is sent to European markets in large amounts under the name of *copra*. The export of copra from Ceylon amounts to 5000 tons annually, from Tahiti to 4000 tons, from Samoa to 3000 tons, and from Singapore to 4000 tons.

The importations of coconut oil into the United States for 1914 amounted to 74,386,213 pounds, valued at $6,703,942, and for 1915, 63,135,428 pounds, valued at $3,430,581.

According to Parisi, the endocarp or meat of the coconut is a powerful tenicide. The patient should drink the milk and then eat the flesh of the nut. The coconut is said to be largely used in India as a vermifuge, and the matter appears to have practical importance.

Powdered coconut shells have been largely used in America as an adulterant for spices. Their débris is readily recognized by the microscope. (See *A. J. P.*, 1901.)

E. Millian describes the following test to determine the purity of coconut oil: 4 mils of the clean, water-free fat is introduced into a test tube with 2 mils of ethereal solution of phloroglucin and mixed by circular agitation; 2 mils of benzene solution of resorcin is then added and the whole again mixed. The tube is then immersed for a few minutes in ice-water, to bring the temperature to 10° C. (50° F.); 4 mils of nitric acid, sp. gr. 1.35, free from nitrous fumes, is then added, and the tube being closed with a rubber cork previously washed with the same acid, the whole is well shaken for five seconds. Pure coconut oil remains perfectly unaltered, negligible traces of impurities may impart a scarcely perceptible rose tint to the mixture; but the presence of any seed oil, such as cotton, sesame, arachis, etc., will at once be indicated by a distinct currant-red color if 5 per cent. of the adulterant be present. The color reactions which occur later, when the temperature of the mixtures rises to 40° C. (104° F.) are disregarded. It is important that the reagents and solvents employed should be absolutely pure, and that the temperature of the reagents and the oil should be between 10° C. (50° F.) and 12° C. (53.6° F.). (*C. R. A. S.*, 1905, cxl, 1702.)

Oil of Colza.—An oil expressed from the seed of *Brassica campestris* L., or *field cabbage*, a cruciferous plant which grows wild throughout the greater part of Europe, and is largely cultivated in France and Germany for the sake of this oil. *Colza oil* is used in Europe as a burning oil, as a lubricating oil, and, after purification by heating with starch, as a table oil. The raw oil has a sp. gr. of 0.915, and the refined oil 0.9136. Chilled to −4° C. (24.8° F.), stearin separates out, and at −6° C. (21.2° F.), it becomes a yellowish buttery mass. The oil contains the glycerides of stearic, *erucic* (or *brassic*) *acid*, $C_{22}H_{42}O_2$, and an acid isomeric with, but differing in some respects from, ordinary oleic acid. A similar oil is derived from

rape-seed (*Brassica napus*). The total consumption of rape and colza oil in Europe is estimated at from 280,000 to 300,000 tons per annum. For analysis of commercial samples, see *C. D.*, 1894, 140.

Oil of Cypress.—An oil derived from *Cupressus sempervirens* L. (Fam. *Pinaceæ*) has been strongly recommended by Bravo in *whooping cough;* it is used by sprinkling the oil upon the clothes, bed, etc., of the patient.

Winterseel (*In. Dis.*, Bonne, 1908) has studied *cypress oil* physiologically and finds that its action is similar to the other essential oils, but is of relatively low toxicity. When the reflexes are excited by spinal stimulants it acts as a depressant to the spinal cord. He confirms the favorable results of its inhalation in cases of *whooping cough.*

Oil of Dœgling. *Oleum Chœnoceti. Dœgling Oil. Dœgling Thran. Huile de Rorqual Rostré*, Fr.—The oil derived from the Norwegian whale, *Balæna rostrata*, is said by Gustave Guldberg to possess a lower specific gravity than any other animal oil (0.876 at 15° C. (59° F.)), and also remarkable penetrative properties. It is affirmed that if mixed in equal quantities with chloroform it carries the latter agent through the skin, and enables it to act as a local anesthetic in *pruritus, neuralgia,* etc. Mixed with wax, it is highly recommended as a basis for ointments by the same authority.

Oil of Egg Yolk.—A fatty oil obtained by expression from the yolks of fresh eggs. It has been used in lotions and as a popular remedy on the continent in the treatment of *corneal opacities.*

Thorpe's Dictionary gives the following composition and properties of egg oil: Specific gravity, 0.9144; solidification point, 8°–10° C. (46.4°–50° F.); melting point, 22°–25° C. (71.6°–77° F.); acid value 1.2; saponification value 184.4–190.2; iodine value 68.5–81.6; insoluble fatty acids and unsaponifiable matter 95.16 per cent.

Benedikt states that the refractive index of egg oil is 1.4655 and that it gives the elaidin reaction. It is also stated that the oil obtained by expression differs from that extracted by solvents in that the latter contains *cholesterol* and *lecithin.*

Oil of Erigeron. *Oil of Fleabane. Oleum Erigerontis. U. S. VIII. Oil of Canada Fleabane. Essence d'Erigeron*, Fr.—"A volatile oil distilled from the fresh, flowering herb of *Erigeron canadensis* Linné (Fam. *Compositæ*)." *U. S. VIII.*

Oil of erigeron is limpid, of a light straw color, a peculiar, aromatic, persistent odor, and a characteristic taste. By exposure it becomes darker and thicker. Its reaction is neutral. Its sp. gr. is about 0.850, increasing with age (0.855 to 0.890, *Schim. Rep.*). It consists chiefly of dextrogyrate *limonene*, together with some *terpineol.* (*A. J. P.*, 1893, 420.) It was officially described as "a pale yellow, limpid liquid, rapidly becoming darker and thicker by age and exposure to the air, having a peculiar, aromatic, persistent odor, and an aromatic, slightly pungent taste. Specific gravity, 0.845 to 0.865 at 25° C. (77° F.). Soluble in an equal volume of alcohol (distinction from *oil of fireweed* derived from *Erechthites hieracifolia* Rafinesque (fam. *Compositæ*) and from *oil of turpentine*). It is dextrogyrate, the angle of rotation being not below +45° in 100 mm. tube, at a temperature of 25° C. (77° F.)." *U. S.* When distilled without water, it comes over colorless, and a little resinous matter is left behind, probably resulting from the oxidation of one or both of the constituent oils. It is slowly reddened by potassium hydroxide, combines with iodine without explosion, is instantly decomposed by sulphuric acid, and is acted on by strong nitric acid, slowly at ordinary temperatures, but with heat explosively. (Procter, *A. J. P.*, xxvi, 502.) The plant yields 0.2 to 0.4 per cent. of oil. When exposed to the air, the oil darkens and rapidly resinifies. For an account of the difference in properties between this oil and that from *Erechthites hieracifolia*, see a paper by Albert M. Todd, *A. J. P.*, 1887, p. 302; also one by Frank Rabak, *Ph. Rev.*, 1905, 81, and also *Ph. Rev.*, 1906, 326.

It was first brought into notice by the so-called eclectic physicians, who use it in *diarrhea, dysentery,* and the *hemorrhages,* and apparently it is a valuable remedy in *hemoptysis* when there is no fever or other marked evidence of constitutional irritation. J. W. Moorman speaks of it most highly, in *diarrhea of debility,* in *dysentery* after sufficient evacuation of the stomach and bowels, and especially in *hemorrhage from the bowels during typhoid fever.* (*Am. J. M. S.*, Oct., 1865, p. 393.) It probably acts like the oil of turpentine as a hemostatic, but is much less irritant and stimulating.

Dose, ten minims to half a fluidrachm (0.6–1.8 mils), repeated every hour or two.

Oil of Eulachon.—The fish known by the North Pacific Indians under the name of *Eulachon* or *Oulachon*, and by the English as *Hoolakins* or *Candle fish*, the *Thaleichthys pacificus* of scientists, yields a great abundance of an oil which has been proposed as a substitute for cod liver oil. According to the editor of *N. R.* (1881, 356), this oil first begins to congeal and become opaque at −7° C. (19.4° F.), although authorities state that at ordinary temperatures it grows solid and lard-like. Specific gravity at 15.5° C. (60° F.), 0.907; mixed with one-half its volume of nitric acid, specific gravity 1.37, it develops a beautiful pink color which fades slowly to amber, and after standing fifteen hours it is considerably thickened and its color is changed to a deep amber of a reddish cast. It contains about 20 per cent. of palmitic and stearic acids, and 60 per cent. of oleic acid and 13 per cent. of an unsaponifiable substance, which resembles the similar constituent of sperm oil. (*T. G.*, Sept. 15, 1884.)

Oil of Euphorbia.—A fixed oil, obtained from the seeds of *Euphorbia Lathyris* L. (Fam. *Euphorbiaceæ*), a biennial plant somewhat naturalized in this country, though believed to have been introduced from Europe. It is often found near gardens and in cultivated fields, and is generally called *mole plant*, under the impression that moles avoid the ground where it grows. (Pursh.) It is the *caper plant* of England. Like the other species of *Euphorbiaceæ*, it contains a milky juice, which is extremely acrid, and the whole plant possesses the properties of a drastic purge; but the oil of the seeds is the only part used in medicine. This may be extracted by expression, or by the agency of alcohol or ether. In the first case, the bruised seeds are pressed in a canvas or linen bag, and the oil which escapes is purified by decanting it from the whitish flocculent matter which it deposits upon standing, and by subsequent filtration. By the other process, the bruised seeds are digested in alcohol, or macerated in ether, and the oil is obtained by filtering and evaporating the solution. According to Soubeiran, however, the oils obtained by these different processes are not identical. That procured by expression is probably the purest.

Oil of euphorbia is colorless, inodorous, and, when recent, nearly insipid; but it speedily be-

comes rancid, and acquires a dangerous acridity. Soubeiran has ascertained that it has a complex composition, containing, besides the pure oil, four distinct proximate principles. (*J. P. C.*, xxi, 259.) From 40 to 44 parts are obtained by expression from 100 of the seed. It is a powerful purge, but in *doses* of from five to ten drops is stated by Continental physicians to act kindly upon the bowels. In this country, however, it has been found very uncertain in its effects, and very liable to cause vomiting. (*A. J. P.*, iv, 124.)

Oil of Jasmine.—This oil is obtained from the flowers of the common *white jasmine* (*Jasminum grandiflorum* L.). Alternate layers of the fresh flowers, and of cotton saturated with the oil of ben or other fixed oil, are exposed in a covered vessel to the warmth of the sun, the flowers being renewed until the oil becomes impregnated, when it is separated from the cotton by pressure. This method is necessary, as the flowers do not yield their aroma by distillation. According to Gildemeister and Hoffmann, jasmine oil contains 65 per cent. of *benzyl acetate*, and in addition *linalyl acetate, benzyl alcohol*, and *linalool*. The oil is used only as a perfume. W. H. Hall records (*M. S. Rep.*, Jan., 1861) the case of a child poisoned by the fruit of a jasmine, probably the common white species. The symptoms were coma, widely dilated pupil, and snoring respiration, with a cold pale surface, and slow and feeble pulse, followed by violent convulsions, with rigidity of the muscles about the head and throat.

Oil of Kuromoji.—Under this name there have entered commerce two fragrant Japanese oils—one, *Kouro motsi*, said to be obtained from the *Lindera sericea* Bl., and one, *Kuro matsi*, yielded by *Lindera umbellata* (Fam. *Lauraceæ*). (See *Schimmel's Bericht*, 1904.)

Oil of Linaloe.—This volatile oil which is produced in Mexico, according to Seyffert (*Schim. Rep.*, Oct., 1907), is obtained from the wood of two species of *Bursera*, one of which is known in the Spanish as *Linaloe*, and the other as *Copal limon*. The latter tree is probably the *B. aloexylon* Engl. Better grades of this oil have a pleasant odor resembling a mixture of lemon and jasmine, while the poorer grades have a caraway-like odor. It is important in perfumery as the source of *linalyl acetate*, and is used as a substitute for oil of bergamot.

Oil of Maize.—Our American maize or Indian corn yields a bright golden-yellow oil, of peculiar pleasant odor and taste. It is moderately thick, and has a sp. gr. at 15° C. (59° F.) of 0.916 to 0.924. It consists of olein and palmitin, and solidifies at −10° C. (14° F.). The oil is contained in the germs of the seed alone. Reckoned on the whole weight of the seeds the oil constitutes about 5 per cent., reckoned on the weight of the germ itself, after separation from the starchy body of the seed, the oil amounts to nearly 50 per cent. It is now being extensively produced in connection with the working of starch and glucose factories. It is used as a lubricant and for soap making, and as a substitute for cotton seed oil. In 1914 the amount of corn oil exported was 18,281,576 lbs., and in 1915, 17,789,635 lbs.

Oil of Myrcia. *N. F. IV. Oleum Myrciæ. Oil of Myrcia. Oil of Bay.*—"A volatile oil distilled from the leaves of *Pimenta acris* Wight (not *Myrcia acris* DC.) (Fam. *Myrtaceæ*)." This oil, formerly official in U. S., 1890, is now official in the National Formulary IV.

"A volatile oil distilled from the leaves of *Pimenta acris* (Swartz) Wight (Fam. *Myrtaceæ*). Preserve it in small, well-stoppered, amber-colored bottles, in a cool place, protected from light." *N. F.*

The commercial oil of bay is a mixture of both heavy and light oils, as G. M. Beringer found the specific gravity of two samples of undoubted purity to be 0.975 and 0.994. (*A. J. P.*, 1887, 286.) Mittmann (*A. Pharm.*, 1889, 529) reported the following constituents: 1, pinene; 2, possibly *dipentene;* 3, a polyterpene, probably *diterpene* (insoluble in alcohol); these three in small quantity only; 4, eugenol, the chief constituent; and, 5, methyl-eugenol, in smaller quantity. It has since been examined (March, 1895) by Power and Kleber, who state that it contains from 60 to 65 per cent. of phenols, of which two were identified: *eugenol*, $C_{10}H_{12}O_2$, and chavicol, $C_9H_{10}O$; two phenol esters, methyl-eugenol, $C_{11}H_{14}O_2$, and methyl-chavicol, $C_{10}H_{12}O$; phellandrene and a newly discovered terpene which they named myrcene, $C_{10}H_{16}$, and *citral*, $C_{10}H_{16}O$. (*Ph. Rund.*, 1895, 60.) The oil is officially described as "a yellow or brownish-yellow liquid having a pleasant, aromatic odor and a pungent, spicy taste.

"With an equal volume of alcohol, glacial acetic acid, or carbon disulphide, it yields slightly turbid solutions. An alcoholic solution is slightly acid to litmus paper.

"Specific gravity: 0.962 to 0.990 at 25° C. (77° F.).

"It is lævorotatory, the angle of rotation not exceeding −3°, in a 100 mm. tube, at 25° C. (77° F.).

"When mixed with an equal volume of a concentrated solution of sodium hydroxide it forms a semi-solid mass.

"Dissolve 2 drops of the Oil in 4 mils of alcohol, and add a drop of ferric chloride T.S.; a light green color is produced; if the same test is made with a drop of dilute ferric chloride T.S., prepared by diluting the test solution with 4 times its volume of distilled water, a light bluish coloration is produced, which soon disappears.

"To 3 drops of the Oil contained in a small test tube, add 3 drops of sulphuric acid, cork the test tube and allow the mixture to stand for half an hour; a resinous mass is obtained. Add 4 mils of diluted alcohol to this mass, vigorously shake the mixture, and gradually heat on a water bath to the boiling point; the liquid remains nearly colorless, and does not acquire a red or purplish-red color (distinction from *oil of pimenta or oil of clove*).

"Shake 1 mil of the Oil with 20 mils of hot distilled water and filter; the filtered aqueous solution does not give more than a scarcely perceptible acid reaction with litmus paper and on adding a drop of ferric chloride T.S. it yields only a transient, grayish-green but not a blue or violet color (*phenol*)." *N. F.*

Oil of bay is not used internally, but solely for making *bay rum*. (See *Spiritus Myrciæ Compositus*, Part III.) For a paper describing the manufacture of bay rum and oil of bay, see W. C. Fishlock, *C. D.*, 1912, 714.

For an English formula for bay rum, see *P. J.*, 1896, 468.

The oil of bay is an active antiseptic, 1 part in 1000, according to Peck (*J. A. M. A.* 1899, xxxii, p. 6) being sufficient to prevent the growth of bacteria.

Bay rum is used chiefly as a refreshing perfume in cases of *nervous headache, faintness* and other *nervous disorders*, either held to the nostrils, or applied on soft linen to the head and forehead. According to Berger (*Th. M.*, 1907, xxi, p. 221) it

is a valuable local application in various diseased conditions of the skin, especially in *seborrhea* of the scalp. It is also grateful to the feeble and convalescent patient, by being sprinkled on the bed covering or otherwise made to impregnate the air of the chamber. The oil of bay is often adulterated, and is frequently sold by smugglers.

Oil of Neat's-foot. *Oleum Bubulum. Oleum Pedum Tauri. Axungia Pedum Tauri. Huile (Graisse) des Pieds du gros Bétail,* Fr. *Klauenöl, Ochsen Klauenfett,* G.—This formerly official oil is obtained by boiling for a long time the feet of the ox, previously deprived of hoofs. The fat and oil which rise to the surface are removed and introduced into a fresh portion of water, heated nearly to the boiling point. The impurities having subsided, the oil is drawn off, and, if required to be very pure, is again introduced into water, which is kept for twenty-four hours sufficiently warm to enable the fat which is mixed with the oil to separate from it. The liquid being then allowed to cool, the fat solidifies and the oil is removed and strained, or filtered through layers of small fragments of charcoal free from powder. The oil is clear and yellowish in color, of sp. gr. 0.916 at 15° C. (59° F.), and, when properly prepared, inodorous and of a bland taste. It thickens or congeals with great difficulty, and is, therefore, very useful for greasing machinery. It is also used for softening leather and in grinding metals. It has been given as a substitute for cod liver oil in scrofulous diseases. It is apt to be laxative, and in certain cases proves useful in this way. It is given in the same dose as cod liver oil. (See *Am. J. M. S.*, N. S., xxiv, 498.) It is at present difficult to obtain pure neat's-foot oil in commerce.

Oil of Orange Flowers. *N. F. IV* (*U. S. P.* 1890). *Oleum Aurantii Florum. Oil of Neroli. Oleum Naphæ,* G.—"A volatile oil distilled from the fresh flowers of the Bitter Orange, *Citrus aurantium amara* Linné (*Citrus vulgaris* Risso, *Citrus Bigaradia* Risso). (Fam. *Rutaceæ*). It should be kept in well-stoppered bottles, in a cool place, protected from light." *U. S.*, 1890. *N. F.*

This oil, official in the U. S. P., 1890, is employed for its odor and taste, and is largely used as an ingredient in cologne water, perfumes, etc. The best quality of *oil of neroli,* as it is universally called in commerce, comes from Nice, and is derived from the flowers of the *Citrus Aurantium sinensis* L., or *sweet orange,* by distillation with water; this is called *néroli pétale.* The next quality is obtained in the same way, but by using the blossoms of the *Citrus Bigaradia* Risso, or bitter orange: this is called *néroli bigarade;* while an inferior sort, *essence de petit grain,* is made by distilling the leaves and unripe fruit. This should not be classed with neroli, as it is unworthy of the name. *Oil of petit grain citronnier* is a fragrant oil, distilled from the leaves and twigs of the lemon tree; it closely resembles the essence de petit grain which is made from the orange leaves and fruit. (*C. D.*, 1897, 53.)

It is officially described as follows:

"Oil of Orange Flowers is a pale yellow, slightly fluorescent, neutral liquid, having a distinctive fragrant odor similar to that of orange blossoms and an aromatic, at first sweet then somewhat bitter, taste.

"It is soluble in an equal volume of alcohol, the solution having a violet fluorescence and a neutral reaction to litmus paper. Also soluble in two volumes of 80 per cent. alcohol, the solution becoming cloudy on the further addition of alcohol of the same percentage.

"Specific gravity: 0.868 to 0.880 at 25° C. (77° F.).

"It is dextrorotatory, the angle of rotation varying from +1° 30′ to +5°, in a 100 mm. tube, at 25° C. (77° F.).

"When agitated with a concentrated solution of sodium bisulphate it assumes a permanent purple-red color." *N. F.*

The greater part of the oil is a hydrocarbon, distilling at from 185° to 195° C. (365°–383° F.), with which is a small amount of the crystalline solid called *neroli camphor.* According to Flückiger, this is a neutral inodorous, tasteless substance, fusing at 55° C. (131° F.). According to Semmler (*Ber. d. Chem. Ges.*, 26, 2711), the oil contains about 20 per cent. of limonene, 30 per cent. of linalool, $C_{10}H_{18}O$; 40 per cent. of linaloyl acetate, and 3 per cent. of geraniol. *Schim. Rep.*, April, 1897, mentions a small amount of a paraffin as also present. Noel distinguishes the different volatile oils of the orange tribe by shaking five drops of the oil with one mil of pure concentrated hydrochloric acid. After one minute seven or eight mils of 90 per cent. alcohol are added, whereby the color is changed, and increased or decreased according to the extent of the adulteration. It is obvious that to use effectually such a test requires special education. (See *Proc. A. Ph. A.*, 1887.)

Under the name of *nerolin* an artificial product has been placed upon the market in the form of a white crystalline powder, soluble in alcohol and fixed oils and almost insoluble in water. It is used by soap makers as a substitute for oil of neroli, and is said to be ten times as strong. This compound is said to be the *ethyl ether of β-naphthol.* (*Ber. d. Chem. Ges.*, 1893, 2706.) It is also used in the manufacture of eau-de-Cologne with advantage instead of neroli oil. (*Schim. Rep.*, April, 1893.) Oil of neroli of excellent quality is now produced artificially; Schimmel & Co. state that it contains pinene, camphene, dipentene, terpineol, phenyl, acetic acid, benzoic acid, decylic aldehyde, and linalool.

Oil of Palm. *Palm Oil. Huile (Beurre) de Palme,* Fr. *Palmöl, Palmbutter,* G.—This highly valuable fixed oil is the product of *Elœis guineensis* Jacq., a palm growing on the western coast of Africa, and cultivated in the West Indies and South America. It is among the handsomest trees of its graceful family which flourish in the tropical regions of Africa. The oil is obtained by expression from the fruit. It is brought to this country chiefly from Liberia and other places on the African coast, although prepared also in the West Indies, Cayenne, and Brazil. It is not improbable that various species of *Palmaceæ* contribute to the supply of this article of commerce. At present the chief ports for its shipment are Cape Palmas and Lagos, prima and secunda Lagos being the choicest varieties. The annual export from the African coast is about 50,000 tons, of which the bulk goes to England. The importation into the United States amounted in 1914 to 61,753,482 lbs., valued at $4,118,077, and in 1915 to 31,482,292 lbs., valued at $2,024,827.

Palm oil has the consistence of butter, a rich, orange-yellow color, a sweetish taste, and an agreeable odor, compared by some to that of violets, by others to that of the Florentine orris. By age and exposure it becomes rancid and of a pale yellow or nearly white color. It melts with the heat of the hand, and when perfectly fluid

passes readily through blotting paper. Highly rectified alcohol dissolves it at common temperatures, and in ether it is soluble in all proportions. Its constituents are *tripalmitin* and *triolein*, $C_3H_5(C_{16}H_{31}O_2)_3$ and $C_3H_5(C_{18}H_{33}O_2)_3$. The tripalmitin is converted into *palmitic acid* by superheated steam, with liberation of glycerin. It appears also that a considerable proportion of this acid, together with some glycerin, exists uncombined in the oil, as ascertained by Pelouze and Boudet; so that the changes which are effected in oils, through the agency of alkalies, in the process of saponification, take place, to a certain extent, spontaneously in palm oil. (*J. P. C.*, xxiv, 389.) Hence it is more easily saponified than any other fixed oil. Preparatory to saponification, it may be bleached rapidly, according to J. J. Pohl, by heating it quickly to 240° C. (464° F.) and keeping it for ten minutes at that temperature. It loses for a time its peculiar odor by the process, acquiring an empyreumatic one; but this after a while ceases to be perceived, and the characteristic odor returns. (See *A. J. P.*, xxvii, 346.) Englehart bleaches it in the following manner: 1000 lbs. of the oil are heated in a boiler to 62.2° C. (144° F.) and kept at that temperature until the next day, when it is decanted into a clean vessel, and cooled to a point between 36.6° C. (98° F.) and 40° C. (104° F.). In another vessel 15 lbs. of potassium dichromate are dissolved in 45 lbs. of boiling water, and, when the solution is partially cooled, 60 lbs. of hydrochloric acid are added. This solution is then mixed with the oil, and briskly agitated. In five minutes the color changes to green, through the reduction of the chromic acid, and, with a continuation of the agitation, the chromium oxide separates, and then nothing more is necessary than washing with water to get the oil colorless. (*A. J. P.*, 1868, 333.) Palm oil is said to be frequently imitated by a mixture of lard and suet, colored with turmeric, and scented with Florentine orris. It is much employed in the manufacture of toilet soap, which retains its pleasant odor. Palm oil is emollient, and has sometimes been employed in friction or embrocation, though not superior for this purpose to many other oleaginous substances. It is sometimes used to impart a yellow color to mixtures of fats or manufactured products, such as oleomargarine. In the latter case it is considered as an artificial coloring matter which necessitates the payment of ten cents per lb. additional tax. It is detected in the presence of other fats by a color reaction developed when sulphuric acid is added to a mixture of the suspected oil and an equal volume of acetic anhydride. This is known as Crampton-Simons test for palm oil, but it has been attacked by A. G. Gill (*J. I. & E. C.*, 1917, p. 136) as being fallacious, due not to a specific substance present in palm oil only, but to the presence of *carotin*, which is present in butter and some other constituents likely to be normally present in oleomargarine, to which this test is usually applied for the purpose of detecting the palm oil as an added coloring matter. The test as carried out is as follows: *Preparation of Sample:* The sample should be kept in a cool dark place until tested, as exposure to light and air or the presence of water, alcohol, ether or similar reagents, interferes with the tests. Immediately before testing, the sample is filtered as quickly as possible at a temperature not exceeding 70° C. (158° F.). *First Method:* Dissolve 100 mils of the fat in 300 mils of petroleum ether and shake out with 50 mils of a 0.5 per cent. potassium hydroxide solution. Draw off the aqueous layer, make distinctly acid with hydrochloric acid and shake out with 10 mils of pure carbon tetrachloride. Separate the carbon tetrachloride solution, transfer a portion to a porcelain crucible, add 2 mils of a mixture of one part colorless, crystallized phenol and two parts of carbon tetrachloride, then 5 drops of hydrobromic acid (sp. gr. 1.19) and mix by gentle agitation. The almost immediate development of a bluish-green color is indicative of palm oil.

Second Method (usually preferred): Shake out 10 mils of the melted and filtered fat with an equal volume of colorless, chemically pure, acetic anhydride, add 1 drop of sulphuric acid (sp. gr. 1.53) and shake the mixture for a few seconds longer.

If palm oil is present the lower layer, on settling, will be found to be colored blue with a tint of green. The color in this as well as in the preceding test is transient. *Leach*, p. 541–543.

Oil of Patchouli.—The genuine oil is obtained from *Pogostemon Patchouli* Pellet, a plant cultivated in the Straits Settlements and in Penang. The plant has also been cultivated in the West Indies and in Paraguay. A small amount of oil is also obtained from *Microtæna cymosa* Prain, a plant cultivated in the mountainous districts of Assam. The patchouli herb is sometimes dried and sent into commerce. It is not infrequently adulterated with a number of other plants, the latter being present to the extent of 80 per cent. It is believed by Arabs, Chinese, and Japanese to possess prophylactic powers. The oil as found in commerce is of two kinds. The best is that distilled in the East in the neighborhood of the patchouli plantations, from selected fresh leaves; the other kind is distilled in Europe from imported leaves; the latter often arrive in a more or less damaged condition, and are frequently adulterated. *Oil of patchouli* is a thick, brownish-yellow oil with a green tint, and was shown by Gladstone to contain *cœrulein*, an intensely blue compound found in oils of absinthium, calamus aromaticus, matricaria, achillea, etc. The oil has the sp. gr. 0.970–0.990 at 15° C. (59° F.), and is lævorotatory. Rodie states that the odor improves by age and hence perfumers prefer the older oils. It deposits a solid, *patchouli alcohol*, $C_{15}H_{26}O$, which crystallizes in hexagonal prisms, melts at 56° C. (132.8° F.), and boils at 206° C. (402.8° F.), while *cadinene*, $C_{15}H_{24}$, remains; oil of cedar and oil of cubeb are frequently used to adulterate the oil. They may be detected by fractional distillation. Oil of patchouli is used in perfumery mainly for its valuable property of conferring upon other odors lasting qualities; its characteristic and persistent odor when uncombined is usually not popular among Caucasians.

Oil of Turtle. *Turtle Oil.*—In South America an oil is prepared from the eggs of turtles, and in the Seychelle Islands and in Jamaica from the fat of the turtle itself. These oils are said to be of equal value with cod liver oil for strumous persons and others in whom the nutritive processes are defective. (See *P. J.*, vol. xv, 573.) C. E. Sage examined *turtle oil* as sold in London drug auctions and found the sp. gr. 0.919 at 25° C. (77° F.). The oil was yellow and semi-solid, having an odor of beef-drippings. (*C. D.*, 1906, 691.) It is stated that 50,000 gallons are sent to Para yearly from the Orinoco, the Amazon, and the Rio Negro, and that 60,000 gallons are consumed by the tribes who prepare the oil. The Seychelles Islands are said to produce 6000 gallons of oil yearly.

Oil of Wood. *Wood Oil. Gurjun Balsam.*—In the *P. J.* for August, 1854 (p. 65), appeared an

account by Charles Lowe of Manchester, of a "new variety of balsam of copaiba," derived from the East Indies. In a subsequent communication to the same journal (1856, 321) from Daniel Hanbury, it appears that this product, though offered for sale in the London market as *balsam of copaiba*, is known in India under the names of *wood oil* and *gurjun balsam*. Considerable quantities had been imported from Moulmein, in Burma, specimens of a similar drug had been received from Canara and Tenasserim, and it appears to be widely diffused in the Indian markets. This must not be confounded with the *Chinese* wood oil, which is used as a varnish. (See *Oil of Aleurites*, p. 1515.)

This liquid is obtained from *Dipterocarpus turbinatus* Gaertn. f., and several other species of *Dipterocarpus* growing in East India (Fam. *Dipterocarpaceæ*), a very large tree which forms forests in Pegu and other parts of Farther India. A large notch is cut in the trunk of the tree, between two and three feet from the ground, and a fire made so as to char the wound. The juice then begins to flow, and is received in suitable vessels. Every three or four weeks the charred surface is cut off and burned anew. A single tree sometimes yields forty gallons in a season. *D. tuberculatus* Roxb. yields a liquid known in Burma as *in oil*, which is sometimes sold as gurjun balsam. (*Proc. A. Ph. A.*, 1913, 223.) It is at first turbid, but may be clarified either by filtration or deposition. After filtration, wood oil is a clear, dark brown liquid, of the sp. gr. 0.964 (Hanbury), and, in consistence, odor, and taste, bears a close resemblance to copaiba. It is soluble in two parts of alcohol of the sp. gr. 0796, with the exception of a very small proportion of darkish flocculent matter, which subsides on standing. According to Lowe, it contains 65 per cent. of volatile oil, 34 of resin, and 1 of acetic acid and water. A characteristic property noticed by Lowe, by which it may be distinguished from copaiba, is that, when heated in a closed vial to 266° F. (230° F., Lowe), it becomes slightly turbid and coagulates, so that the vial may be inverted without changing the position of its contents, and this consistence is retained when the liquid cools. By a gentle heat with agitation the fluidity returns; but the liquid again coagulates if heated to 266° F. According to D. Brandis, this property of coagulation is characteristic of the wood oil from *D. alatus* Roxb. (*P. J.*, xxv), a wood oil which is further to be distinguished by the greenish opalescence of its surface.

Guibourt states that wood oil does not solidify, like copaiba, with one-sixteenth of magnesia, and the two separate on standing. (*J. P. C.*, xxx, 192.) De Vrij of Rotterdam, proposes the reaction of benzene with wood oil and copaiba respectively as a test to distinguish them. With an equal volume of the wood oil, benzene forms a turbid mixture, from which, after a long time, a resinous matter is deposited in flocculi; with copaiba it forms a transparent solution. (*P. J.*, 1857, 374.) The volatile oil from gurjun balsam is a yellow, somewhat thick liquid, of sp. gr. 0.915 to 0.930, and has at times a high optical rotation—viz., −35° to −130°. The oil boils in larger part at 255° to 256° C. (491°–492.8° F.) and consists of a sesquiterpene, $C_{15}H_{24}$. With hydrochloric acid it yields a deep blue color. The resin left after distilling off the volatile oil is essentially *gurjunic acid*, $C_{22}H_{34}O_4$. This when purified dissolves readily in ether and strong alcohol, and slowly in benzene. It melts at 220° C. (428° F.) and congeals again at 180° C. (356° F.). Flückiger has also described a neutral resin from gurjun balsam, which is insoluble in caustic potash, fuses at 126° C. (258.8° F.), and is of the composition $C_{28}H_{46}O_2$. Flückiger (*A. Pharm.*, 1876, 420) noticed that wood oil may be recognized by the violet color it assumes if dissolved in twenty parts of carbon disulphide and mixed with a drop of a cold mixture of equal parts of concentrated sulphuric and nitric acids.

According to O'Shaughnessy, the oil of dipterocarpus is little inferior to copaiba in the diseases for which that medicine is employed. T. B. Henderson has found it very useful in *gonorrhœa*, given in the *dose* of a teaspoonful two or three times a day, uncombined. (*M. T. G.*, 1865, 571.) It probably has a remedial influence on diseased mucous membranes similar to the different turpentines, which it appears to resemble in composition. The juice may be given in emulsion, in *doses* of from fifteen to forty minims (0.9–2.5 mils); the volatile oil from ten to thirty minims (0.6–1.8 mils).

Oil of Ylang Ylang. *Cananga Oil. Oleum Anonæ. Oleum Unonæ.*—This is a volatile oil obtained from the flowers of *Cananga odorata* Hook. f. and Thoms (Fam. *Anonaceæ*), a large tree inhabiting most parts of Southern Asia; the oil from the Philippine Islands is especially esteemed. According to Schimmel & Co. (*Schim. Rep.*, April, 1897), it contains pinene, linalool, geraniol, esters of acetic and benzoic acids, cadinene, and paracresol-methyl ester. It is used only as a perfume. (See *N. R.*, April, 1881.) The so-called *Macassar hair oil* is said to be a solution of it in coconut oil. (See *A. J. P.*, 1881, 123; also *A. J. P.*, 1893, 529.)

Ointment of Casein. *Unguentum Caseini. Unna. Caseinsalbe*, G.—Prof. Francis Hemm quotes Dr. Unna's formula for casein ointment as follows: Take milk from which the cream or fat has been entirely removed and curdle it by the addition of rennet at a temperature of 30° to 40° C. (86°–104° F.). Collect the coagulum and wash freely with cold water until the washings are no longer acid. Dry carefully and reduce to powder. Dissolve 34.5 parts of caustic potassium hydroxide and 8.5 parts of caustic sodium hydroxide in 5000 parts of water and dissolve 1400 parts of casein in this solution. Now add 700 parts of glycerin and 50 parts of phenol, and when dissolved incorporate 2100 parts of white petrolatum and 50 parts of zinc oxide and finally enough water to make 10,000 parts. (*M. B. D.*, 1906, 192.) It has the consistence of thick cream, is incompatible with acids and acid salts, but mercury, tar, balsam of Peru, zinc oxide, resorcinol, pyrogallol, and ichthyol may be incorporated with it. Certain forms of casein creams are known as rolling creams because when rubbed over the surface of the skin they take the dirt out of the pores by rolling up into small particles which can be brushed off. They are extensively used as cosmetics.

Ointment of Cucumber. *Cucumber Ointment.*—An emollient ointment, prepared from the common cucumber (fruit of *Cucumis sativus* L., Fam. *Cucurbitaceæ*), has been considerably employed in *irritated states of the skin*. The following is the mode of preparing it, recommended by Procter. Take of green cucumbers 7 pounds avoirdupois, pure lard 24 ounces, veal suet 15 ounces. Grate the washed cucumbers to a pulp, express, and strain the juice. Cut the suet into small pieces, heat it over a water bath till the fat is melted out from the membrane; then add the lard, and, when melted, strain through muslin into an earthen vessel capable of holding a gallon, and stir until

thickening commences, when one-third of the juice is to be added, and the whole beaten with a spatula till the odor has been almost wholly extracted. The portion which separates is to be decanted, and the remaining two-thirds of the juice is to be consecutively incorporated and decanted in the same manner. The jar is then closely covered and placed in a water bath, until the fatty matter entirely separates from the juice. The green coagulum floating on the surface is now removed, and the jar put in a cool place that the ointment may solidify. The crude ointment is then separated from the aqueous liquid on which it floats, melted and strained, and placed in glass jars, which must be kept closely sealed. A layer of rose water upon its surface will favor its preservation. A portion may be triturated with a little rose water until white and creamy, and put into a separate jar for present use. (*A. J. P.*, xxv, 409.)

Emile Mouchon prepares the ointment by obtaining the juice mixed with a little alcohol, and incorporating this with benzoinated lard and stearin. He directs 16 parts of the cucumber to be rendered to a pulp, 1 part of alcohol of 36° B. (87 per cent. vol.) to be added, and the mixture to be placed on the diaphragm of a percolator. Twenty-four hours afterwards 10 parts of the liquid are obtained of 19° B. Of this liquid 6 parts are to be incorporated with 37.5 parts of benzoinated lard and 12.5 of stearin; the fatty matters having been previously melted together by means of a water bath, and beaten vigorously on cooling. The liquid is to be added before the completion of the beating, which should then be continued until the whole becomes as light and white as possible. The benzoin and alcohol enable the ointment to keep a long time. (*J. P. C.*, Juillet, 1854, 41.) We prefer to make this ointment by incorporating one part of distilled *spirit of cucumbers* with seven parts of benzoinated ointment. The spirit is made by distilling a mixture of one part of grated cucumbers with three parts of diluted alcohol, retaining the first two parts or distillate which come over. This spirit is permanent, and ointment or cream made from it keeps well, and cucumber cream can be made extemporaneously.

The most frequently used preparation of cucumber at the present time is the cosmetic preparation known as cucumber jelly, which is used as a soothing application in roughness of the skin, etc. It consists of a jelly of tragacanth, quince seed, or some similar mucilaginous drug made up with cucumber juice which imparts to the preparation a characteristic odor.

Oleates.—W. A. H. Naylor communicates the following working formulas for unofficial oleates which he has found in practice to yield satisfactory products. The soap used is a genuine olive oil soap of high quality, and contains 15 per cent. of water.

Oleate of Aluminum. Aluminum Oleate.—Dissolve 1 oz. av. pure potassium alum in 6 fl. oz. of boiling water and pour the solution, while stirring, into a solution of 2 oz. av. of soap in 10 fl. oz. of boiling water. The clotty precipitate is washed with boiling water by decantation, until free from sulphate, and dried over a water bath. The oleate is adhesive, of yellowish-gray color, opaque, and weighs about 2¼ ounces, av. On ignition it yields about 6 per cent. of aluminum oxide (= 3 per cent. Al). This oleate is used in treating various skin diseases.

Oleate of Bismuth. Bismuth Oleate.—Dissolve 1 oz. av. of bismuth subnitrate, by the aid of heat, in 5½ fl. drachms of nitric acid, diluted with its own volume of distilled water; then dilute the solution with three times its volume of distilled water, and pour it, hot and while stirring, into a hot solution of 3 oz. av. of soap and 24 fl. oz. of water. The precipitate is washed with hot water by decantation, and dried over a water bath. The yield of dry oleate is about 3 oz. av. It has a light citron color and yields on ignition 22 per cent. of bismuth oxide (= 20 pr cent. Bi).

Oleate of Copper. Cupri Oleas.—It is made by adding sodium oleate to a saturated solution of copper sulphate, then washing the precipitate. It is a handsome dark green, waxy solid, and is used chiefly in the treatment of ringworm.

Oleate of Ferrous Iron. Ferrous Oleate.—In spite of all precautions this oleate undergoes considerable oxidation during the process of its preparation, which must therefore be as expeditious as possible. Dissolve 1 oz. av. of pure ferrous sulphate in 5 fl. oz. of distilled water and pour the solution while stirring into a solution of 2 oz. av. of soap in 16 fl. oz. of water. When the precipitate produced has been sufficiently washed, it should at once be strongly expressed and dried (in the unbroken state of press-cake), at a temperature not exceeding 50° C. (122° F.).

Oleate of Ferric Iron. Ferric Oleate, on the other hand, is easily and quickly made, by pouring 4 fl. oz. of solution of iron acetate, B. P. 1898, into a solution of 2½ oz. av. of soap in 16 fl. oz. of boiling water. The washed precipitate, dried on the water bath, is of a deep red color, weighs a little over 2 oz. av., and yields 8 per cent. Fe_2O_3 (= 5.6 per cent. Fe), on ignition. It is readily soluble in fixed oils.

Oleocreosote. *Creosote Oleic Ester. Creosote Oleate.*—This product is a yellowish, oily liquid, specific gravity 0.950, and is insoluble in water. It is used as an antiseptic in catarrhal conditions of the respiratory organs in the treatment of *scrofula* and *phthisis*. *Dose*, thirty-five minims to two and one-half drachms (2.32–9.3 mils) a day emulsionized or in oil.

Oleoguaiacol. *Guaiacol Oleate. Oleic Acid Guaiacol Ester.*—This substance is used for the same purposes and in the same doses as oleocreosote.

Olibanum. *Thus. Oliban, Encens*, Fr. *Weihrauch*, G.—*Olibanum*, the *frankincense* of the ancients, was erroneously ascribed by Linnæus to *Juniperus phœnicea* L. (*J. lycia* L.). There are two varieties of olibanum, one coming to Europe from the Mediterranean, and the other directly from Calcutta. These varieties were formerly considered distinct, but recent researches indicate their common origin. In 1843 Captain Kempthorne, of the East India Company's navy, saw the olibanum tree growing upon the mountains, on the African coast, between Bunder Maryah and Cape Guardafui. According to his statement, it grows on the bare marble rocks composing the hills of that region, with very brittle soil or the slightest fissure to support it, adhering by means of a substance thrown out from the base of the stem. This rises forty feet, and sends forth near the summit short branches, covered with a bright green, singular foliage. The juice, which exudes through incisions made into the inner bark, has at first the color and consistence of milk, but hardens on exposure. (*P. J.*, iv, 37.) Sir William J. Hooker says that the African olibanum is derived from *Boswellia papyrifera* Hochst., one of the *Burseraceæ;* but thinks it highly probable that it is furnished by more than one species which has

since proven to be the case. (P.-J., 1859, 217.) Birdwood asserts (*Tr. Linn. Soc.*, xxvii) that no olibanum is obtained in India, all coming from a coast district of Arabia (the same district as that described by Theophrastus), and being the product of a new species of *Boswellia, B. Carterii* Birdwood. It is very likely that several species of Boswellia furnish the olibanum of commerce—viz., *B. Carterii* Birdw. (furnishes what is known as *Luban Bedowi* or *Luban Sheheri*), and *B. Frereana* Birdw. (furnishes *Luban Meyeti* or *Luban Matti*). It appears that the resin of *B. papyrifera* Hochst. is not gathered at all. The product of *B. serrata* Roxb. (known as *Salaigugul*) is not sent into general commerce, but is employed medicinally only in India.

The Arabian or African frankincense is in the form of yellowish tears, and irregular, reddish lumps or fragments. The tears are generally small, oblong or roundish, not very brittle, with a dull and waxy fracture, softening in the mouth, and bearing much resemblance to mastic, from which, however, they differ in their want of transparency. The reddish masses soften in the hand, have a stronger taste and odor than the tears, and are often mixed with fragments of bark and small crystals of calcium carbonate which are visible under the microscope.

The Indian frankincense, or olibanum, consists chiefly of yellowish, somewhat translucent, roundish tears, larger than those of the African, and generally covered with a whitish powder produced by friction. It has a balsamic resinous odor, and an acrid, bitterish, somewhat aromatic taste. When chewed it softens in the mouth, adheres to the teeth, and partially dissolves in the saliva, which it renders milky. It burns with a brilliant flame and a fragrant odor. Triturated with water, it forms a milky, imperfect solution. Alcohol dissolves nearly three-fourths of it, and the tincture is transparent. Tschirch (*Harze und Harzbehälter*, 1900, p. 253) has made a thorough study of olibanum and determined all of its constituents with care. Alcohol extracts 72 per cent., consisting of resins 65 per cent. and volatile oil 6 per cent.; water soluble gum, 20 per cent.; bassorin, 6–8 per cent.; plant residue, 2–4 per cent. The resins were composed of *boswellic acid*, $C_{32}H_{52}O_4$, a resin acid of which well crystallized salts were obtained, and *olibanoresin*, $C_{14}H_{22}O$, a neutral resin.

In the essential oil Wallach identified l-pinene and dipentene, while the chemists of Schimmel & Co. found in addition phellandrene.

W. F. Daniell has described an odorous product, used as *frankincense* in Sierra Leone, and obtained from a large tree, growing in the mountainous districts of that region. The tree has been described by J. J. Bennett in *P. J.*, 1854, 251, as *Daniella thurifera* (Fam. *Leguminosæ*). According to Daniell, the juice exudes through openings made by an insect, and, concreting in connection with the woody particles resulting from the boring of the insect, falls at length to the ground, where it is collected by the negroes. (See *A. J. P.*, xxvii, 338.)

Olibanum is stimulant like the other gum-resins, but is now very seldom used internally. According to Delioux, of Toulon, however, it affords a cheap, efficient substitute for the balsams of Tolu and Peru. It appears to act more favorably when combined with a little soap. Delioux has also obtained advantage from the inhalation of its fumes, when heated, in chronic *bronchitis* and *laryngitis*. (*B. G. T.*, Fév. 28, 1861.) It is chiefly employed for fumigation and in unofficial plasters. *Dose*, fifteen grains (1.0 Gm.), which may be increased to a drachm (3.9 Gm.) or more.

Canadian olibanum is reported by Karl Dieterich to be an American substitute for olibanum, which comes into the drug market from Hamburg. Its melting point is 77–78° C. (170.6°–172.4° F.). Thus occupies a place about midway between Canadian olibanum or gum thus. It is a valuable American pine resin, which, however, contains no gum and therefore is not a gum resin. (*Ph. Zhalle*, 1912, 652–654.)

Omorol.—A compound of albumin and silver. It is a yellow powder, said to represent 10 per cent. of silver. It is insoluble in water, but soluble in physiological saline solution, and in the various body fluids. This silver compound is used as an antiseptic in the treatment of *catarrhs* of various mucous membranes, such as *pharyngitis, conjunctivitis*, etc., and also for its antiseptic influence on infected *wounds* and old *ulcers*. It is claimed that it is non-irritating and because of its relative insolubility the powerfully antiseptic effect is much more persistent than the ordinary preparations of silver. Viett (*Med. Klin.*, 1906, p. 436) has found it useful in the treatment of *diphtheria;* he dusts a finely powdered preparation on the infected area for one or two hours after previous cleansing of the throat with a gargle.

Omphalea.—According to Calmody, the government chemist in Trinidad, the seeds of the *Omphalea megacarpa* (?), Fam. *Euphorbiaceæ*, yield an oil which acts as a brisk cathartic in about three hours after taking, without pain or much continuance. (*P. J.*, Feb., 1898.) Cash (*J. P.*, 1911, xxxvi, p. 488) obtained from the *Omphalea triandra* seed, 56 per cent. of a pale yellow oil, with a specific gravity of 0.924, which, in doses of 0.5 Gm. exercised a cathartic and diuretic action. From the *O. diandra* (*Megacarpa*) he obtained an oil somewhat darker in color than the preceding which had a specific gravity of 0.922 and a saponification value of 190.3, and an iodine value of 119.7. This oil was also a cathartic and diuretic, although somewhat larger doses were required than in the oil from the *O. triandra*. From the allied plant, *Garcia nutans*, he also obtained a cathartic oil.

Onion. *Cepa.*—The bulk of *Allium Cepa* L. (Fam. *Liliaceæ*.) Fourcroy and Vauquelin obtained from the ordinary onion a white, acrid, volatile oil containing sulphur; also albumen, much uncrystallizable sugar and mucilage, phosphoric acid, both free and combined with lime, acetic acid, calcium citrate, and lignin. The expressed juice is susceptible of the vinous fermentation. The oil is essentially the same in chemical composition as the oil of *Allium sativum* L., and consists largely of allyl sulphide, $(C_3H_5)_2S$. (See *A. Pharm.*, 1892, 434.) Perkin and Hummel found *quercetin* in the outer skin of onion bulbs, and the skins have been used in dyeing.

By virtue of its volatile oil the onion taken in moderate quantities is a stimulant to the stomach and promotes digestion, but in large quantities is apt to cause gastric uneasiness. It is slightly rubefacient, said to be diuretic, and belongs among those expectorants to be employed in the advanced stages of subacute *bronchitis* or in chronic *bronchitis*. Although the onion has been asserted to exercise a marked influence on nitrogenous metabolism it can scarcely be doubted that any apparent influence which it may exert in the direction spoken of is secondary to its action upon digestion.

Onion poultices are somewhat effective as a

counter-irritant and nerve stimulant in cases of *bronchitis* or *pneumonia* in young children, with nervous symptoms. According to M. V. Pogorelsky, a decoction made with the outer reddish skin of the bulb is widely used in Russia for the production of abortion. He attributes the ecbolic effect to the presence of allyl sulphide. One or two tumblerfuls of the concentrated dark brown or dark red infusion are taken at a *dose*.

Ononis. *Rest Harrow. Ononis spinosa* L.—The roots are official in several European Pharmacopœias under the title of "*Radix Ononidis*." The plant is common throughout Europe. The root is more or less flattened, twisted and slightly branched; from 10 to 60 cm. in length and 1 to 2 cm. in thickness; externally it is grayish-brown, deeply wrinkled; the odor resembles that of licorice, the taste being sweetish, mucilaginous, afterward bitter. Reinsch obtained from this plant *ononin*, $C_{25}H_{26}O_{11}$, a glucoside. *Onocerin*, a disecondary alcohol, $C_{26}H_{42}(OH)_2$, was isolated by Thoms, who proposed to change its name to *onocol*. (*A. Pharm.*, 1897, 28.) Cow (*A. E. P. P.*, 1912, lxix, p. 393) has found that in the dog, the aqueous extract of *ononis* exercises a diuretic effect approaching in power that of juniper, which conclusion has been clinically confirmed by Breitenstein. It also contains tannin.

Ophioxylon. *Radix mustelæ. Rauwolfia serpentina* Benth. (*Ophioxylon serpentinum* L.) (Fam. *Apocynaceæ*.)—In the root of this plant, which is used in East India as a purge and anthelmintic, Wefers-Bettink found a yellow crystalline principle, *ophioxylin*, melting at 72° C. (161.6° F.), and possessing the formula $C_{16}H_{12}O_6$; also a volatile oil. (*A. J. P.*, 1890.) It is widely used in India as an antidote against bites of serpents, stings of insects, etc.

Opopanax.—A concrete juice or oleo-gum-resin of *Opopanax chironium* Koch. (*Pastinaca Opopanax L.*, Fam. *Umbelliferæ*). This species of *parsnip* has a thick, yellow, fleshy, perennial root, which sends up annually a strong branching stem, rough near the base, about 2 cm. in thickness, and from 1 to 3 m. in height. The leaves are variously pinnate, with long sheathing petioles, and large, oblong, serrate leaflets, of which the terminal one is cordate, others are deficient at their base upon the upper side and the whole are hairy on their under surface. The flowers are small, yellow, and form large flat umbels at the termination of the branches. The plant is a native of the Levant, and grows wild in the south of France, Italy and Greece. When the base of the stem is wounded, a juice exudes, which, when dried in the sun, constitutes the *opopanax* of commerce. Some authors state that it is obtained from the root. A warm climate appears necessary for the perfection of the juice, as that which has been collected from the plant in France, though similar to opopanax, is of inferior quality. The drug is brought from Turkey. It is said to come also from the East Indies; but Ainslie states that he never met with it in any Indian medicine bazaar. The method of its production is not known with any certainty.

It is sometimes in tears, but usually in irregular lumps or fragments, of a reddish-yellow color, speckled with white on the outside, paler within, and, when broken, exhibiting white pieces intermingled with the mass. Its odor is strong, peculiar, and unpleasant, its taste bitter and acrid. Its sp. gr. is 1.622. It is inflammable, burning with a bright flame. It is a gum-resin, with an admixture of other ingredients in small proportion. Pelletier found in it gum, starch, wax, malic acid, lignin, a volatile oil, and traces of caoutchouc. Subsequently, Tschirch found opopanax to consist of resin, 19 per cent., ethereal oil, 6.5 per cent.; gum and plant tissues, 70 per cent.; water and loss, 4.5 per cent. (*A. Pharm.*, 1895, 209.) Schimmel states that the oil consists of an alcohol with a sesquiterpene as the chief constituent. (*Schim. Rep.*, 1904, 67.) Water by trituration dissolves about one-half of the gum-resin, forming an opaque milky emulsion, which deposits resinous matter on standing, and becomes yellowish. Both alcohol and water distilled from it retain its flavor; but only a very minute proportion of oil can be obtained in a separate state. Opopanax was formerly employed, as an antispasmodic and deobstruent, in *hypochondriasis, hysteria, asthma*, and chronic visceral affections, and as an emmenagogue; but it is now scarcely ever used. *Dose*, ten to thirty grains (0.65–2.0 Gm.).

Optochin. *Ethylhydrocupreine.*—This is a proprietary salt. *Cupreine* is found in some of the cinchona barks, especially the *Remijia Cuprea*. Quinine is methyl-cinchonine, cupreine is hydroxy-cinchonine. *Optochin* was originally introduced by Morgenroth (*B. K. W.*, 1910 and 1911), who found that it had a beneficial effect in experimental *trypanosomiasis* and also a specific action against the pneumococcus. Schiemann and Ischaivara (*Z. Hyg.*, 1914, lxxvii, p. 49) showed that a concentration of 1 to 400,000 would destroy pneumococci even in the presence of blood serum. A number of authors, as Fraenkel (*Ther. Geg.*, Jan., 1915, p. 1) and others, have reported favorable results from its use in *pneumonia*, but Waetzold (*Ther. Geg.*, 1915, lvi, p. 262) and others find it of limited value. Waetzold says that it is not capable of destroying pneumococci in the system of the patient, but that it may possibly exert a restraining influence upon the growth of the organism if administered early in the disease. The *dose* recommended in pneumonia is from 4 to 5 grains (0.25–0.3 Gm.) repeated four times a day, but not more than for a few days because of the danger of amaurosis. Smith and Fantus (*J. P. Ex. T.*, 1916, viii, p. 53) report a study of its physiological action with a review of the literature. They find that it is decidedly more toxic to infusoria than corresponding solutions of quinine. It is also somewhat more poisonous to animals, its toxicity for white mice as compared to quinine being as 7 to 5. As an antipyretic it is less efficient than quinine. When given to frogs in large doses it causes first exaggerated reflexes followed by paralysis of the peripheral nerves. They state that quinine produces the same symptoms. In mammals it causes motor weakness with exaggeration of reflexes and death from respiratory failure. In large quantities it depresses the heart but has less effect on the circulation than quinine. In solutions of more than 1 per cent. optochin is irritant to the conjunctiva, and later anesthetic. Recently it has been found by Liefmann (*Th. M.*, 1915, xxix, p. 260) to cure *malaria* which had resisted quinine.

Opuntia. *Opuntia vulgaris* (Mill.). (Fam. *Cactaceæ*.) *Prickly Pear. Figue de Barbarie*, Fr. *Indische Feige*, G.—A common cactus composed of flattened, prickly or spinose jointed stems, and occurring in sandy soil from Nantucket to South Carolina. For analyses of fruit of this cactus, see *A. J. P.*, 1884, 3, and 1896, 170.

Orange Red. *Orange Mineral. Sandix.*—Red lead oxide, prepared by calcining lead carbonate.

It is of a lighter color than *minium*, and is used as a pigment.

Orcin. *Dihydroxytoluene. Dihydroxymethyl benzene. Orcinol.* $C_6H_3(CH_3)(OH)_2[1:3:5]$.—This is a white, stable powder, of a peculiar sweetish taste and aromatic odor, crystallizing with one molecule of water. It is easily soluble in water, alcohol, and ether, and has a sweet taste. It is used as a reagent and is described in Part III. It melts at 58°–60° C. (136.4°–140° F.) when it contains water, but, deprived of this, melts at 107° C. (224.6° F.). It boils at 290° C. (554° F.). It is said to resemble resorcinol in its local action and to be useful in the same class of skin diseases. A coloring matter obtained from *orcin* by the action of ammonia is known as *orcein*, $C_{28}H_{24}N_2O_7$. It is used in microscopic staining. According to J. Andeer (*Med. Chron.*, Dec., 1885), orcin is distinctly antiseptic, and in poisonous doses produces death by a direct action upon the heart muscle.

Oreodaphne. *Umbellularia californica* (Hook et Arnott) Nutt. (Fam. *Lauraceæ.*)—The *California Bay Laurel* is an evergreen tree of considerable size, rather abundant throughout the State. Its wood is much prized on account of the beauty of its grain and its immunity from the attacks of insects. The leaves yield about 4 per cent. of a neutral, straw-colored, limpid, volatile oil, which has a warm camphoraceous taste and a pungent aromatic odor, resembling somewhat that of a mixture of oils of nutmeg and cardamom. It is soluble in 1000 parts of water, and in alcohol and ether in all proportions. It is said, when inhaled, to cause dizziness and headache. Its chemical characters have been studied by John P. Heamy. (*A. J. P.*, 1875, 105.) He finds it to consist of a pure hydrocarbon, sp. gr. 0.894, boiling at 175° C. (347° F.), and an oxygenated, pungent portion, which boils at 210° C. (410° F.). This he calls *oreodaphnol. Oreodaphene* was obtained by distilling oreodaphnol with glacial phosphoric acid. For the reactions, see Heamy's paper.

Orexin. *Phenzoline. Cedrarine. Phenyldihydroquinazoline Hydrochloride.* $C_{14}H_{12}N_2.(C_{14}H_{10}O_9)$.—A complex derivative of quinoline. It forms colorless, odorless, lustrous crystals with bitter, pungent taste, freely soluble in hot water. *Orexin* was first brought forward by F. Penzolt as a stomachic. It appears to be practically free from toxic properties, two grains of it per pound not being sufficient to kill a rabbit. It appears to be a very active remedy in those cases of failure of appetite in which simple bitters are indicated, and to be contra-indicated by hyperacidity of the stomach, gastric catarrh and gastric ulcer.

The *tannate* is affirmed to be more efficient than the hydrochloride, which salt it has practically replaced in the market. The tannate is a yellowish powder, tasteless, odorless, insoluble in water, freely soluble in acid solutions. It is very highly praised in all forms of *atonic dyspepsia, loss of appetite* in convalescence, and similar conditions. It is affirmed also to be very useful in the treatment of *vomiting*, following the use of narcotics, such as opium, chloroform, etc. It is chemically incompatible with iron salts. It is best administered in the form of powder, five to ten grains (0.3–0.7 Gm.) given in capsules, one to two hours before meals.

Organotherapeutic Extracts.—The use of the extracts of various organs as medicinal agents is one of the oldest known therapeutic measures. Thus, Pliny mentions the use of the brains of animals in the treatment of *jaundice*, and it is probable that this drug was used also by the ancient Egyptians. The modern use of organic extracts may be dated from the investigations of Brown-Sequard. (*A. de P.*, 1889, p. 51.) Since this time extracts of nearly every portion of the body have been tested therapeutically. From many of these extracts there is no reason to expect any beneficial influence in diseased conditions. On the other hand, it is impossible to deny that many of the glandular organs of the body deliver their secretions directly into the blood stream, and that these secretions are essential for the maintenance of health and it is *a priori* not unreasonable to expect that the artificial administration of these secretions will have a beneficial influence in certain diseased conditions. It is among the last group of drugs that *opotherapy* finds a justification for its existence. Three of these organs of internal secretion have achieved so fixed a place in medicine as to have received official recognition, namely, the hypophysis, the suprarenal capsule, and the thyroid gland. Although the pancreas probably also delivers an internal secretion, the pancreatin of the Pharmacopœia represents an external and not an internal secretion of the pancreatic gland. There are some which have firmly established their claims, although not yet included in the U. S. P., but the great mass of them are still in the experimental stage.

Cerebrin. Cerebrum Siccum.—The dried *brain* substance has been used by Babes and others (*K. T. W.*, 1900) in the treatment of *neurasthenia, insanity* and *epilepsy*. The treatment, however, has no scientific foundation. Wassermann (*B. K. W.*, 1898, p. 4) has shown that an emulsion of the brain is capable of neutralizing the tetanus toxin. It has subsequently been shown also that this holds true for strychnine and morphine. On this evidence an emulsion of the dried brain substance has been used in the treatment of *tetanus* and *rabies*. (Kowalski, *K. T. W.*, 1900, No. 5.) The *dose* of the dried brain substance is 30 to 60 grains (2–4 Gm.).

Bronchial Gland. Glandula Bronchialis Siccum.—The dried bronchial gland has been used in the treatment of *tuberculosis* and *chronic bronchitis*, but with no very encouraging results. The *dose* is 1 to 3 grains (0.06–0.18 Gm.).

Ciliary Body. Corpus Ciliaræ.—The extract of the ciliary body, as well as the *vitreous body* has been used in sympathetic *ophthalmia* by Dor and by Wecker. (*Annals d'Oculistique*, August, 1902.) *Oculin* is a name applied to a glycerin extract of the ciliary body and vitreous humor.

Kidneys. Renes Siccum.—There is considerable evidence that the kidneys supply an internal secretion, but that failure of this internal secretion is the cause of uremia, as claimed by some, has certainly not been established. Although a number of authors have claimed beneficial results from the administration of the kidney substance in *nephritis* and *uremia*, it is probable that the treatment is useless. The *dose* recommended is from four to fifteen grains (0.26–1.0 Gm.) several times daily. *Nephritin* is a proprietary extract of this class.

Lungs. Pulmones Sicci.—The dried substance of the lung has been used by Brunet (*Press. Med.*, 1898, p. 22) in *tuberculosis, emphysema*, and *asthma*. The *dose* is seventy-five grains (5 Gm.) a day.

Liver. Hepar Siccum.—Gilbert and Karno (*S. M.*, 1897, p. 184) believe that there is some substance in the liver which leads to a retention of the glycogen out of the blood in the liver, and that the administration of this substance is of benefit

in the treatment of *diabetes.* Gyr asserts that the extract of the liver is also useful in *hepatic cirrhosis* (*R. M. S. R.*, June 20, 1908), and in *hemeralopia* by Roncagliolo (*Med. Klin.*, 1905, p. 909). The *dose* of the dried liver is one-half to one ounce (15–31 Gm.) per day.

Mammary Gland. Mammæ Siccatæ.—On the theory that there is some relation between the uterus and the mammary gland, the latter has been used by Shober (*Phila. M. J.*, Nov., 1899) and others, in the treatment of *menorrhagia, fibromata, dysmenorrhea,* etc. The *dose* of the dried gland is five to ten grains (0.32–0.65 Gm.) three times a day.

Ovaries.—That the ovaries deliver an internal secretion which if not essential to life, certainly modifies in some way metabolism, is almost universally accepted. One of the strongest proofs of this is seen in the symptoms which occur at the menopause or after double oöphorectomy. The *corpus luteum,* according to Ott and Scott (*Proc. of the Soc. of Exper. Biol. and Med.*, 1910, viii, p. 49), has a marked stimulating effect upon the mammary gland, but the ovarian substance when deprived of this was without such action. There is strong clinical evidence that the administration of the ovarian substance will at least temporarily relieve the symptoms seen at the menopause, whether the latter is natural or artificial. Richter (*D. M. W.*, 1899) has found that there is a marked increase in the fatty metabolism under the feeding of the ovarian substance. These investigations have been confirmed by Thumim. (*Ther. Geg.*, 1900, p. 451.)

The ovarian substance has also been used in the treatment of *neurasthenia* by Vidal (*Press. Med.*, 1900, p. 173) as well as in a host of other diseases in which there was much less likelihood of benefit following its administration. (For review of the literature, see Offergeld, *D. M. W.*, 1911, p. 1172.)

The *corpus luteum* has been used for various disturbances of *pregnancy* on the ground that these were due to the natural intermission in this function. The dried ovarian substance is marketed in various strengths. *Ovarin* represents eight times its weight in fresh bovine ovarian substance; the *dose* is three to six grains (0.2–0.4 Gm.). *Ovaraden* represents two parts of the gland and may be given in *doses* of fifteen to thirty grains (1–2 Gm.). Other proprietary preparations of the ovarian substance are *glandnovin, ovadin, ovarial, ovarigen, oophorin, ovaron,* and *lutein.* The dried corpora lutea is given in *doses* of one to five grains (0.065–0.32 Gm.) two or three times a day.

Parotid Gland. Parotis Siccum. Glandula Parotidis.—Believing that there is some connection between the parotid and the sexual organs, Bell (*Ther. Woch.*, 1896, p. 659) has employed the parotid gland in the treatment of *dysmenorrhea, ovarian neuralgias,* and other disorders of the pelvic organs. The dried substance is usually administered in tablet form in *doses* of from one to three grains (0.065–0.2 Gm.) three times a day.

Parathyroids. Glandula Parathyroidea.—These are four small bodies growing near the lateral lobes of the thyroid gland. Because of their anatomical proximity it was at one time believed that their function in the body was similar to that of the thyroid body, but it is now known that these two organs are in no way physiologically connected. The parathyroid bodies, however, are among those organs whose removal is fatal. The most prominent symptom caused by parathyroidectomy are tetanic convulsions. Ott and Scott (*Amer. Med.*, 1910) have found that the parathyroid extract has a powerful diuretic influence. The dried parathyroid gland has been used in the treatment of *tetany.* (Loewenthal, *Med. Klin.*, 1907, p. 1012.) It has also been used by Meyer (*Ther. Geg.*, 1913, 354) and Berkley (*N. Y. M. J.*, Nov. 23, 1907) in treatment of *paralysis agitans.* The *dose* is one-tenth of a grain (0.006 Gm.) two or three times a day.

Prostate. Glandula Prostatæ Siccæ.—This substance has been used, without any reasonable justification, in the treatment of prostatic enlargement, and in *prostatorrhea.* The *dose* of the dried substance is two grains (0.125 Gm.).

Spleen. Lien Siccus.—It can hardly be considered definitely established that the spleen furnishes any internal secretion. According to Danilewsky and Salensky (*A. G. P.*, 1895, p. 264), however, the subcutaneous injection of the splenic extract produces an increase in the percentage of hemoglobin, and in the number of red blood cells. It is also asserted that there is an increase in the number of the white corpuscles. It is possible that these effects are not due to any substance peculiar to the spleen, but to the nucleinic acid which it contains. Accordingly, the splenic extract has been used in the treatment of *anemias,* with more or less beneficial results. Carpenter (*D. M. Ztg.*, 1907, p. 571) asserts that it has a specific action in *malaria.* H. C. Wood (*A. J. M. S.*, 1897, p. 511) has found it useful in *Graves's disease.* It has also been recommended in various forms of *insanity.* One of the difficulties in the use of this drug is to obtain a preparation which is active and yet will be borne by the stomach. The dried powder is given in *doses* of four to fifteen grains (0.26–1 Gm.) three times a day. It is doubtful, however, how far it entirely represents the drug. Under the name of *eurythrol,* an aqueous extract has been marketed. The *dose* of this is one to two teaspoonfuls, given generally in soup. *Lienaden* and *opo-lieninum* are proprietary preparations of spleen.

Testicles. Testes Sicci.—The basis of the famous elixir of Brown-Sequard, *Liquor spermaticus,* was the fluid contained in the testicles. The persistent use of the various imitations and modifications of the *Brown-Sequard Elixir* would argue that it must possess some therapeutic virtue. It is claimed by those who use it that it has a powerful tonic effect, not merely improving the strength, but also exercising a beneficial influence upon the metabolism, so as to lead to a permanent augmentation of power. It has been recommended for *neurasthenia, diabetes, locomotor ataxia, arteriosclerosis,* and a large number of other chronic complaints.

The dried testicular substance is given in *doses* of from ten to thirty grains (0.65–2 Gm.), but it is generally recommended as a liquid preparation, and that it should be given hypodermically. Among the preparations which contain testicular fluid as their important ingredient are the *Siccus e Testibus Paratus, orchidin, Hawley lymph, testaden, testidin* and *teston.*

Mesentery Gland. Coeliacin.—The dried mesentery gland has been used by Schwerdt (*M. M. W.*, 1907, p. 1230) in the treatment of *scleroderma.* The *dose* he employed was five grains (0.3 Gm.) twice a day.

Thymus Gland. Glandula Thymi Sicca.—This body, which is the ordinary *sweet-bread,* is found only in young animals, disappearing as adult life comes on. Physiologists are not agreed as to its exact importance or function. It appears to have

some connection with the growth of bone and also of the formation of the white corpuscles of the blood. It has been used in medicine chiefly for two purposes, namely, in the treatment of *exophthalmic goiter*, and for the purpose of stimulating bony growth in *rickets* and *ununited fracture*. It should be remarked that thymus contains a larger percentage of nuclein than any common food stuffs, and for this reason its use is generally forbidden to gouty patients. The *dose* of the fresh gland is from one drachm to half an ounce (2–15 Gm.); of the dried gland five to forty-five grains (0.32–3 Gm.).

Bone Marrow. Medulla Ossium.—This has been used by Gullan (*Lancet*, 1907, p. 520), and others, in the treatment of *pernicious anemia*. Gullan administered it by spreading the fresh red bone marrow on bread, which is taken at meal times. It is very prone to produce nausea. The *dose* of the fresh marrow is one to three ounces (31–93 Gm.); of the dried marrow two to five drachms (7.7–20 Gm.). *Opo-osslin* and *ossagen* are proprietary preparations made from bone-marrow.

Spermin.—A salt solution of the hydrochloride of the amine spermin ($C_5H_{14}N_2$), a normal constituent of the spermatic fluid. It is used as a nerve tonic and stimulant in all diseases due to auto-intoxication, as *typhus, syphilis*, etc. *Dose*, subcutaneously, sixteen minims (1 mil) of a two per cent. solution; by mouth, ten to thirty drops (0.6–1.8 mils) of a four per cent. solution.

Origanum. *Wild Marjoram. Marjolaine sauvage*, Fr. *Wilder Majoran* (*Meiran*), G.—Two species of *Origanum* (Fam. *Labiatæ*) have been used in medicine. *O. majorana* L., or *sweet marjoram*, and *O. vulgare* L., or common marjoram. The former grows wild in Portugal and Andalusia, and is cultivated as a garden herb in other parts of Europe and in the United States. Some authors, however, consider *O. majoranoides* Willd., which is a native of Barbary, and closely allied to *O. majorana*, as the type of the sweet marjoram of our gardens. This is by others considered to be simply a form of *O. vulgare* L. *Sweet marjoram* has a pleasant odor, and a warm, aromatic, bitterish taste, which it imparts to water and alcohol. By distillation with water it yields a volatile oil. It is tonic and gently excitant, but is used more as a condiment than as a medicine. In domestic practice its infusion is employed to hasten the tardy eruption in *measles* and other exanthematous diseases.

The plant is a native of Europe and America. In this country it grows along the roadsides, and in dry, stony fields and woods, from Pennsylvania to Virginia, and is in flower from June to October; but is not very abundant, and is seldom collected for use.

Sweet marjoram imported during recent years from Europe is alleged to be adulterated by mixing with it broken fragments of leaflets of the poisonous *coriaria myrtifolia*.

Two kinds of *oil of origanum* are now known commercially: the Trieste oil, of dark color and high specific gravity, and the Smyrna oil, of lighter color, lower specific gravity, and milder taste. The former contains from 60 to 85 per cent. of *carvacrol*, $C_{10}H_{14}O$, a trace of another phenol, and *cymene*, $C_{10}H_{14}$. The latter contains from 25 to 60 per cent. of *carvacrol* and, in addition, *linalool* and *cymene*. The specific gravity of the Trieste oil ranges from 0.94 to 0.98, while that of the Smyrna oil is from 0.915 to 0.945. (Gildemeister and Hoffmann, *Aetherische Oele*, pp. 813, 814; see also *Schim. Rep.*, 1913, 76.)

The French oil of marjoram is said to be distilled from *Clinopodium Nepeta* (L.) Kze. (*Calamintha Nepeta* Link. and Hoffm.). It is colorless, but gradually turns yellow on exposure. It is neutral in reaction, sp. gr. 0.904 at 16° C. (60.8° F.), and optical rotation $[a]_D = +18° 39'$ in chloroform solution. On fractionating, three constituents were isolated, *lævo-pinene, calaminthone*, and *pulegone*. *Calaminthone* is a new ketone, $C_{10}H_{16}O$. (See *P. J.*, March, 1903.)

Origanum floribundum, of Algeria, yields largely of a volatile oil containing 25 per cent. of thymol. (*P. J.*, Feb., 1903.)

Orobanche. *Epifagus virginiana* (L.) Bart. (Fam. *Orobanchaceæ*.) *Beech-drops. Cancer Root. Orobanche de Virginie*, Fr. *Krebswurz*, G.—This is a parasitic, fleshy plant, found in Northeastern America, growing upon the roots of the beech tree. The plant has a bitter, nauseous, astringent taste, which is said to be diminished by drying. It has been given internally in bowel affections; but its credit depends mainly upon the idea that it is useful in obstinate *ulcers* of a cancerous character, to which it was directly applied. Other species of *orobanche*, growing in America and Europe, have been employed. They are all parasitic, fleshy plants, without verdure, and of a bitter, nauseous taste. In Europe they are called *broom rape*. C. Charaux believes that *Chlorogenic acid* which can be easily converted into *caffeic acid* exists in plants of the fam. *Orobanchaceæ* and other families. The allied plants, *Conopholis americana* (L. f.) Wallr. (*Orobanche americana* L. f.) and *Orobanche uniflora* L., growing throughout the United States, are used for the same purposes as the species above noticed, and, like it, are called *cancer root*.

Oroxylon. *Oroxylon indicum* Vent. (Fam. *Bignoniaceæ*.)—This East India bark is said to be not only a tonic and astringent, useful in *diarrhea*, but also a powerful sudorific. A yellow crystalline substance, *oroxylin*, has been separated from the bark by Naylor and Chapman (*P. J.*, Sept., 1890), and from the seeds by Hooper (*P. J.*, vol. lxi). The seeds have been used in veterinary medicine.

Orpiment. *King's Yellow.* As_2S_3.—A native arsenic trisulphide. It is in masses of a brilliant lemon-yellow color, composed of flexible laminæ, and slightly translucent. It exists in various parts of the world, but is obtained for use from Persia and China. (Guibourt.) It is sometimes mixed with realgar, which gives it a reddish or orange hue. A similar sulphide may be made artificially by passing hydrogen sulphide through a solution of arsenic trioxide in hydrochloric acid.

Artificial orpiment is prepared for use by fusing together equal parts of arsenic trioxide and sulphur. (Turner.) In Germany, according to Guibourt, it is prepared by subliming a mixture of these two substances. In this case, however, it retains a large portion of the acid undecomposed, and is therefore highly poisonous. Guibourt found a specimen which he examined to contain 94 per cent. of arsenic trioxide and only 6 per cent. of the trisulphide.

Orpiment is an ingredient of certain depilatories. *Atkinson's depilatory* is said to consist of one part of orpiment and six parts of quicklime, with some flour and a yellow coloring matter. (*Ann. Ch. Ph.*, xxxiii, 348.) But this arsenical sulphide is chiefly used in fireworks and as a pigment.

Orris. *N. F. IV. Iris. Orris Root. Rhizoma Iridis*, P. G. *Radix Iridis Florentinæ, Radix Ireos.*

Iris de Florence, Fr. *Florentinische Violenwurzel, Veilchenwurzel*, G. *Ireos*, It. *Lirio Florentino*, Sp.—The National Formulary IV description is as follows: "The rhizome of *Iris florentina* Linné, *Iris germanica* Linné or *Iris pallida* Lamarack (Fam. *Iridaceæ*), freed from the roots and peeled and dried." *N. F.* The rhizomes when taken from the soil are horizontal, fleshy, fibrous, and covered with a brown epidermis. This plant is a native of Italy and other parts of the south of Europe, where it is also cultivated. The rhizome is dug in spring, and prepared for the market by the removal of its outer layers and roots. It is cultivated for commerce chiefly in the neighborhood of Florence, and is exported from Leghorn in large casks.

"In pieces of various forms and sizes, usually jointed and branched, from 5 to 10 cm. in length and from 1.5 to 3 cm. in width, rounded or flattened, with knotty enlargements; under surface shows numerous root scars, the upper with leaf scars; externally yellowish-white; internally light yellow; fracture hard, rough and at times mealy, showing a narrow cortex, a distinct, endodermis and a large stele with numerous fibro-vascular bundles, especially near the endodermis. Odor fragrant, resembling that of violet flowers; taste slightly aromatic, bitterish, somewhat irritating. The powder is light yellow, and when examined under the microscope, exhibits parenchyma cells of the cortex and the stele filled with characteristic starch grains, oval, rounded at one end and flattened at the other, some curved or with irregular protuberances, mostly single, from 0.02 to 0.05 mm. in diameter; cortical parenchyma cells irregularly polygonal, with thickened and porous walls and large intercellular spaces; endodermal cells tangentially elongated; elements of fibro-vascular bundles with tracheæ showing spiral markings and from 0.01 to 0.025 mm. in width; calcium oxalate in large prisms, up to 0.5 mm. in length and 0.03 mm. in width, in intercellular spaces and in parenchyma with suberized walls. Cork cells, sclerenchyma cells and fibers absent. Orris yields not less than 2 per cent. nor more than 5 per cent. of ash." *N. F.*

Vogel obtained from Florentine orris, gum, a brown extractive, fecula, a bitter and acrid fixed oil or soft resin, a volatile crystallizable oil, and vegetable fiber. According to Landerer, the acrid principle is volatile, separating in the form of a stearopten from water distilled from the root. (*A. Pharm.*, lxv, 302.) The solid oil which is prepared in Europe from orris root by distillation has been examined by Flückiger. By repeated crystallization from alcohol and treatment with animal charcoal, inodorous crystals were obtained, having the composition $C_{14}H_{28}O_2$ and the properties of myristic acid, while the odorous principle remained in the mother liquor, so that *oil of orris* must be regarded as myristic acid impregnated with volatile oil. The acid does not pre-exist in orris root, and is probably liberated from a fat by the influence of steam. (*A. J. P.*, 1876, 411; also 1885, 133.) According to Hager, the commercial oil has the following properties. At the ordinary temperature it is a pea-yellow acid, resembling basilicon ointment (*P. G.*) in color and consistence. It is lighter than water, fuses at from 38° to 40° C. (100.4°–104° F.) to a transparent liquid, and commences to congeal at about 28° C. (82.4° F.). One part of orris oil yields, with from three thousand to four thousand parts of weaker alcohol, a solution of which a few drops put upon a handkerchief develop a persistent odor of violets. (*A. J. P.*, 1877, 302.) In order to preserve the root from the attacks of insects, it is recommended to put a little chloroform in the bottle in which it may be kept. (*A. J. P.*, 1858, 310.) The odoriferous principle of orris root was found by Tiemann to be *irone*, $C_{13}H_{20}O$. In endeavoring to effect its synthesis Tiemann was led to the discovery of an isomeric body, *pseudoionone*, by the condensation of acetone and citral. While pseudoionone does not possess the violet odor it can be changed into *ionone*, which has the true violet odor and is now largely manufactured for the perfumery trade in making toilet waters and handkerchief extracts.

Orris root is cathartic, and in large doses emetic, and was formerly employed to a considerable extent on the continent of Europe. It is said also to be diuretic, and to have proved useful in *dropsies*. At present it is valued chiefly for its agreeable odor. It is occasionally chewed to conceal an offensive breath, and enters into the composition of tooth powders. In the form of small, round balls, about the size of a pea, it is used by the French for maintaining the discharge from issues, a purpose to which it is adapted by its odor, by the slight acrimony which it retains in its dried state, and by the property of swelling very much by the absorption of moisture.

Orsudan. *Sodium 3-methyl-4-acetylaminophenylarsenate.*—This is soluble in three times its weight of water, and contains 25.4 per cent. of arsenic.

Orsudan has been brought forward as a means of obtaining the anti-syphilitic action of the organic compounds of arsenic. Although favorable results have been reported, the experience of Lane (*B. M. J.*, 1910, ii, p. 599), who reports a case of permanent total blindness following its use, would make one hesitate greatly before employing it. The *dose* ordinarily administered is ten grains (0.65 Gm.) deeply injected into the muscles on alternate days until ten doses have been given.

Orthin. $C_6H_3\begin{cases}OH\\COOH\\HN.NH_2\end{cases}$. *Orthohydrazin-para-oxybenzoic acid* is very unstable, but unites with hydrochloric acid, forming *orthin hydrochloride*, which is stable. This substance was proposed by Kobert (*D. M. W.*, 1890) as an antipyretic; but in the experiments conducted by Unverricht, which have been confirmed by Kaufmann, it was found to have comparatively feeble antipyretic action, and to produce in a great many cases sweating and collapse.

Orthoamidosalicylic Acid. *Acidum Orthoamidosalicylicum.* $C_6H_3(NH_2)(OH)COOH$.—This is a grayish, amorphous, almost odorless, slightly sweetish powder, insoluble in water, alcohol, and ether, which has been used by R. Neisser (*In. Dis.*, Bern, 1892) in subacute *rheumatism*, with alleged good results.

Orthoform. *N. N. R.* 1917. *Methyl Para-amido-metaoxybenzoate.* $C_6H_3\begin{cases}COOCH_3\,(1)\\NH_2\quad(4).—\\OH\quad(3)\end{cases}$

This compound forms a white, odorless and tasteless powder, difficultly soluble in water, easily soluble in alcohol, melting at 118° to 120° C. (244.4°–248° F.). This kind of *orthoform* has disappeared from the market, being replaced by the isomeric *methyl metamido-paraoxybenzoate*, C_6H_3.

$NH_2.OH.CO.O.(CH_3)$, which is sometimes called *orthoform-new*, to distinguish it. It has similar physical properties to the older form but melts at 142° C. (287.6° F.).

Orthoform was introduced into practical medicine by Einhorn and Heinz (*M. M. W.*, 1897). Its chloride is soluble in water, but is so acid in its reactions as to interfere with its use.

The physiological action of orthoform is only so far made out as to show that, probably on account of its insolubility, it has very little influence upon the system whether given by the stomach or hypodermically, Heinz having found that ninety grains produce no distinct symptoms in the lower animals, and seven hundred grains have been applied to a facial ulcer in a week without injurious effect (*L. L.*, 1897); also, according to Neumayer (*M. M. W.*, xliv, 1897), sixty grains taken by a man in the course of a day produced no symptoms whatever, not even evidences of gastro-intestinal irritation.

Locally orthoform has been believed to be actively antiseptic, but Lichtwitz and Sabrazes (*B. M.*, xi, 1897) found that bouillon saturated with it was still capable of serving as a culture medium. The antiseptic influence of orthoform is probably due to its decomposition by ulcerated surfaces. Brought in contact with sound skin or mucous membrane orthoform has no perceptible anesthetic influence, but in any variety of *ulceration, abscess*, etc., where it would be brought in contact with the exposed sensitive nerve endings, its influence is decided and prolonged on account of its slow solution and consequent non-absorption for many hours. Externally, orthoform may be used either as a dusting powder, ointment or solution.

According to Yonge (*B. M. J.*, i, 1898), for many purposes the saturated solution of orthoform in collodion is most effective. In diseases of the larynx the parts may be sprayed with a solution of five grains of orthoform and fifty minims each of alcohol and water, which soon coats the diseased surface. In *keratitis* with ulceration, Boisseau commends an ointment made with one drachm each of lard and lanolin and twenty-four grains of orthoform. In many cases orthoform may also be added with advantage, on account of its anesthetic properties, to ointments containing medicinal substances. According to Neumayer, its local analgesic action is not accompanied by abolition of the sense of touch.

Internally, orthoform in *doses* of eight grains (0.5 Gm.) has been used with asserted good results in *cancerous* and other *ulcerations of the stomach* and has been found useful in the treatment of *gastralgia*. Gustav Spiess found that insufflations into the posterior part of the pharynx may greatly alleviate the paroxysms of *whooping cough*. It may be used by insufflation in *tuberculous laryngitis*.

Occasionally orthoform produces marked irritation and even violent inflammation at the seat of its application, and several cases have been reported in which it has produced sloughing, which has been compared to that caused by pure phenol. According to the majority of clinical reports, orthoform is of little value except as a local remedy, though relief has been claimed from it in the treatment of *syphilitic headaches*. In the treatment of *sciatica, locomotor ataxia*, and other nervous affections, it seems to be of little use.

Doses of five to ten grains (0.32–0.65 Gm.) may be given three to four times a day.

Orthosiphon. *Orthosiphon stamineus* Benth. *Java Tea.* (Fam. *Labiatæ.*)—This drug occurs in commerce in the form of small, oval, finely toothed, green leaves, rolled up like tea. Van Itallie has discovered in it a volatile oil and a crystalline glucoside, *orthosiphonin*, and potassium salts. (*Ph. Ztg.*, Sept., 1886; see also *Répertoire de Pharm.*, 1887, 191.) It is said to be a powerful diuretic, and is highly recommended in *nephritic colic, gravel, uric acid diathesis*, and even *ascites*. The *dose* is from fifteen to thirty grains (1.0–2.0 Gm.) a day.

Ortizon. *Perhydrate.*—Under these names has been introduced a combination of hydrogen dioxide and urea containing about 34 per cent. of hydrogen dioxide. This occurs as a white crystalline powder without odor, permanent in dry air and soluble in 2.5 parts of water, the hydrogen dioxide being split off by solution. It is intended as a convenient method of carrying hydrogen dioxide for the preparation of solutions. Bactericidal properties of the solutions prepared from this compound have been used by Ungermann. (*Hyg. R.*, 1913, p. 1137.)

Osha Root.—This is the root of *Ligusticum filicinum* Wats. (Fam. *Umbelliferæ*), a perennial herb indigenous in Utah and neighboring States and known as *Colorado cough root*. It is highly prized as an expectorant. H. Haupt found in it an acid, *oshaic acid*, closely resembling angelic acid. (*A. J. P.*, 1867, 1868, 1873.)

Osmic Acid. *Osmium Tetroxide. Osmic Anhydride. N. N. R.* 1917. OsO_4.—A volatile, odorous, crystalline compound, produced by the action of nitrochloric acid on osmium or either of its lower oxides. Its vapor is very pungent and poisonous, attacking the eyes and respiratory organs. Claus recommends as an antidote to its action cautious inhalation of hydrogen sulphide. *Osmic acid* melts to a colorless liquid at 90° C. (194° F.), softening at a temperature of 35° C. (95° F.). It is slowly soluble in water; soluble in alcohol and ether; but these solutions are unstable, depositing black *osmic hydroxide*, $Os(OH)_4$. *Potassium osmate*, $K_2OsO_4 + 2H_2O$, is made by adding potassium hydroxide to an alcoholic solution of osmium tetroxide, and separating the crystals by careful evaporation. In the form of deep, garnet-red crystals, readily soluble in water, but decomposing when in solution or moist air; permanent in dry air. It is incompatible with organic substances, phosphorus, ferrous sulphate and iodides.

Osmic acid is used largely as a histological stain. We have no definite knowledge as to its influence upon the animal system when given in small doses. It has, however, been used internally especially in the form of potassium osmate in *rheumatic affections*, such as *sciatica*, and in *epilepsy*. The *dose* is one-sixtieth of a grain (0.0011 Gm.) at short intervals up to a daily dose of one-quarter of a grain (0.016 Gm.). In 1887 Stekoulis (*L. L.*, Aug. 13, 1887) suggested the injection along the course of the nerve trunks for the relief of *sciatica*. The method has been extended to include other painful diseases of the peripheral nerves, such as *tic douloureux*. According to Hammerschlag (*A. K. C.*, 1906, lxxix), while it generally gives temporary relief it rarely causes permanent cure. From five to fifteen minims (0.32 to 1 mil) of a 1 to 2 per cent. solution are injected immediately into the nerve trunk. Auerbach (*Journ. of Laryngology and Rhinology*, June, 1891) recommends osmic acid for the destruction of morbid growths.

Ossalin. *Adeps Ossium.*—A fat prepared from

ox-bone marrow claimed to be capable of holding 200 per cent. water. It is neutral in reaction, and free from all irritating action on the skin. *Ossalin* is of a gray-white color and is somewhat similar in its odor to tallow.

Ovogal. *N. N. R.* 1917.—This is a product obtained by the combination of bile acids with egg albumen. Alkalies dissolve *ovogal* with recomposition into its primal constituents. Ovogal is a yellowish-green powder, insoluble in water and acid solutions, but in the presence of alkalies it dissolves with decomposition. It therefore should not be prescribed in combination with alkalies.

It has long been well known that the salts of the bile are the most potent stimulants to hepatic secretion that we possess and this combination of cholic acid with albumin has been shown by Worner (*Med. Klin.*, 1906, p. 547) to increase the secretion of bile. The favorable results obtained by him in *intestinal dyspepsia, atonic constipation, acute* and *chronic catarrh of the biliary passages* has been confirmed by a number of authors. From ten to fifteen grains (0.65–1.0 Gm.) may be given four or five times a day. Rahn (*M. M. W.*, 1907, No. 10) proved the harmlessness of the drug by taking himself one and one-half teaspoonfuls without any evil result. It may be administered either as a dry powder or enclosed in capsules.

Oxalic Acid. *U. S.* Reagent (see Part III). *Acidum Oxalicum. Acide oxalique ou carboneux*, Fr. *Oxalsaure, Kleesaure*, G. $H_2C_2O_4.2H_2O$ = 126.05.

This acid is found both in animals and vegetables. It is generated occasionally in disease. and it may be deposited in the bladder as calcium oxalate, forming the *mulberry calculus*. In vegetables, it occurs in a free state in the bristles of the chick pea (*Cicer arietinum* L., Fam. *Leguminosæ*), as an acid potassium oxalate in *Rumex Acetosa* L. (Fam. *Polygonaceæ*),[1] or common sorrel, in *Oxalis Acetosella* L. (Fam. *Oxalidaceæ*), or wood sorrel, in *Chenopodium Quinoa* Willd. (Fam. *Chenopodiaceæ*), *Amaranthus caudatus* L. (Fam. *Amaranthaceæ*), *Mesembryanthemum crystallinum* L. (Fam. *Aizoidaceæ*), and in many other plants. It is said to be formed in the leaves. (*J. Chem. S.*, 1886.) United with lime as raphides, it is abundant in almost every portion of the vegetable kingdom.

Preparation.—According to W. Zopf, a certain *Saccharomyces* (*S. Hausenii*) has the property of producing a fermentation which forms oxalic acid out of sugar. It was formerly prepared from sugar, through the action of nitric acid but the process has been replaced in practice by the "sawdust process."

Many substances, besides sugar, yield oxalic acid by the action of nitric acid, as molasses, rice, potato starch, gum, wool, hair, silk, and many vegetable acids. When the acid is obtained from potato starch, this is first converted into starch sugar by the action of sulphuric acid. For details of this process, see 15th edition *U. S. D.*, p. 90. The yield of oxalic acid from a given quantity of material has been much misunderstood. If properly treated with nitric acid, 100 lbs. of good sugar will yield from 125 to 130 lbs. of oxalic acid, and the same weight of molasses from 105 to 110 lbs.

The oxalic acid of commerce is obtained by heating sawdust or wood shavings with a mixture of sodium hydroxide and potassium hydroxide. Sodium hydroxide alone will not generate the acid, and potassium hydroxide is too costly to be used by itself for the purpose; but Dale ascertained that, by mixing the two in the proportion of two molecules of sodium hydroxide to one of potassium hydroxide, the same or an even better result was obtained than from the latter alone. The mixture of caustic alkalies and sawdust is made into a thick paste and then heated for several hours to a temperature which is gradually brought to 240° C. (464° F.). The gray mass is then washed with sodium carbonate, whereby the potassium is removed as carbonate, the less soluble sodium oxalate remaining. This is converted into calcium oxalate by milk of lime, and the calcium salt then decomposed with sulphuric acid and the resulting crude oxalic acid purified by recrystallization.

Properties.—Oxalic acid is a colorless crystallized solid, possessing considerable volatility, and a strong, sour taste. Its crystals have the shape of slender, flattened, four- or six-sided prisms, with two-sided summits, and, when exposed to a very dry atmosphere, undergo a slight efflorescence. It is soluble in 4.5 parts of dehydrated alcohol, in 2.5 parts of alcohol, and almost insoluble in ether, chloroform, benzene, and petroleum benzin. The crystals should dissolve in ten parts of water at 25° C. (77° F.) (greater solubility indicating contamination with adherent nitric acid); soluble in 3 parts of boiling water.

It fuses in its water of hydration at 98° C. (208.4° F.), although continued exposure to a heat of from 60° C. (140° F.) to 70° C. (158° F.) will render it perfectly anhydrous. Solutions of oxalic acid at 100° C. (212° F.) lose acid by sublimation, and at 157° C. (314.6° F.) the anhydrous acid itself sublimes rapidly. If the heat rise to 160° C. (320° F.), much loss of acid occurs. (Allen, *Com. Org. Anal.*, 1879, 233.) (See also *Oxalic Acid* under Reagents, Part III.)

It combines with salifiable bases, and forms oxalates. The most interesting of these are the three *potassium oxalates*, severally called *oxalate*, $K_2C_2O_4 + H_2O$, *binoxalate*, $KHC_2O_4 + H_2O$, and *quadroxalate*, $KHC_2O_4.H_2C_2O_4 + 2H_2O$, and *calcium oxalate*. Potassium binoxalate and quadroxalate, both popularly called *salt of sorrel* or *essential salt of lemons*, are employed for removing iron mold from linen, and act by their excess of acid, which forms a soluble salt with the ferric oxide constituting the stain. Salt of sorrel is also used extensively in the bleaching of straw goods and other vegetable fibers. Oxalic acid is used for removing ink stains and iron mold, for cleaning the leather of boot tops, and for discharging colors in calico printing. Prussian blue dissolves in aqueous oxalic acid to a clear blue liquid which is often employed as a *blue ink*.

This acid has a very strong affinity for lime, and makes with it an insoluble precipitate consisting of *calcium oxalate*, whenever the acid and the earth are brought into contact in solution. An aqueous solution forms with solution of lime a white precipitate, insoluble in an excess of oxalic or acetic acid, but dissolved by diluted hydrochloric acid. It is even capable of decomposing calcium fluoride, evolving hydrofluoric acid. (J. W. Slater.) Oxalic acid and its soluble combinations are the best tests for lime, and, conversely, a soluble salt of lime for oxalic acid. In weak solution the acid is said to absorb oxygen and to be converted into carbonic acid; but a strong solution is quite permanent. (*A. J. P.*, 1870, 317.)

Oxalic acid is distinguished from all other common acids by the form of its crystals, and by its

[1] For fatal poisoning by *Rumex Acetosa*, see *Hospital Gazette*, June, 1886.

solution yielding a precipitate with lime water, insoluble in an excess of the acid or of acetic acid. It is incompatible with iron and all its salts, with calcium salts, alkalies and arsenates.

Oxalic acid is a dibasic acid. When crystallized, two molecules of water must be added, making the molecular weight of the crystals 126.05. These two molecules of water may be driven off by a regulated heat, by which the acid is made to effloresce. As oxalic acid is the final oxidation product of the diatomic alcohol *glycol*, to which the formula $\begin{matrix}CH_2.OH\\|\\CH_2.OH\end{matrix}$ is given, we may conclude that its structural formula is $\begin{matrix}CO.OH\\|\\CO.OH\end{matrix}$ which explains the readiness with which sulphuric acid splits it up into carbon dioxide, CO_2, and carbon monoxide, CO, by withdrawing H_2O from its formula, and with which oxidizing agents like manganese and lead dioxide change it into carbonic acid. Anhydrous oxalic acid may be obtained by dissolving the ordinary crystals in ten times their weight of sulphuric acid or concentrated nitric acid and cooling the solution.

Uses and Toxicology.—Oxalic acid has been strongly recommended by F. Poulet and by A. W. Marsh (*T. G.*, 1891) in *amenorrhea*. Marsh has also found it serviceable in *cystitis*. It is a very active germicide, and its solution is used in conjunction with potassium permanganate for the disinfection of the surgeon's hands. *Dose*, half a grain (0.032 Gm.) from three to five times a day.

Attention was first called to it as a poison by Royston in 1814, and the certainty and rapidity of its action have caused it to be largely used for suicidal purposes. Death has been produced by it in ten minutes. (Case, *Chem. News*, April 24, 1868.) The minimum fatal *dose* recorded is one drachm (3.9 Gm.). From the general resemblance which the crystallized oxalic acid bears to Epsom salt, fatal mistakes have occurred in consequence of its being sold for that saline purgative. It is, however, at once distinguished by its sour taste.

Oxalic acid acts on the economy in two principal ways, according as its solution is concentrated or dilute. When concentrated it causes great pain, followed by violent retching, then sudden dulness, languor, and great debility, and finally death without a struggle. When dissolved in twenty times its weight of water, it possesses no corrosive and hardly any irritating power, but causes death by acting on the brain, spinal marrow, and heart. It should be noted, however, that the acid, even in weak solution, always exercises a corroding or softening power on the animal tissues.

After death from oxalic acid the mucous membranes of the alimentary canal are either soft and pultaceous or entirely destroyed.

The stomach usually contains a dark fluid, resembling coffee grounds, consisting chiefly of altered blood. In a few cases no morbid appearances have been discovered.

In 1879 Kobert and Kürsner announced that in animals oxalic acid may produce glycosuria; this has since been confirmed, and Sarganeck has noted the symptom in human poisoning, so that it is probably a constant phenomenon.

In the treatment of poisoning by oxalic acid, the remedial measures must be employed with great promptitude. Vomiting may be encouraged and the stomach tube used, but unless the antidote be at hand death will rarely be averted. The proper antidote is chalk or magnesia, mixed with water, and as soon as either can be procured, it must be administered in large and repeated doses. In many cases whitewash or some other preparation of lime can be obtained sooner than chalk, and should be at once administered; tooth powder can usually be obtained quickly, and generally (not always) consists chiefly of calcium carbonate. These substances act by forming with the poison an insoluble, inert calcium or magnesium oxalate. The soluble salts of oxalic acid, as ammonium oxalate and potassium oxalate, are equally poisonous, and the antidotes for them are lime water or solutions of magnesium salts.

Oxalis. *O. Acetosella* L. *Wood Sorrel. Acetosella. Alléluia, Surelle, Pain de Coucou,* **Fr.** *Sauerklee, Hasenklee,* G.—Wood sorrel is a small, creeping plant having radical leaves and scapes from 5 to 15 cm. high. (fam. *Oxalidaceæ*). It is a native of Europe and naturalized in the Northern United States. Other indigenous species of *oxalis* possess similar properties to *O. Acetosella*. The whole herbaceous portion may be used.

Wood sorrel is without odor, and has an agreeable sour taste. It owes its acidity to *acid potassium oxalate* or *potassium binoxalate* (HKC_2O_4).

The fresh plant, eaten raw, is useful in *scurvy*.

Oxalis crassicaulis Zucc., a Peruvian species, yields edible tubers and, by expression from its leaves, a very sour and astringent juice, which is employed, in the form of syrup, in *hemorrhages, chronic catarrh,* and *gonorrhea*, with asserted advantage.

Oxycamphor. $C_8H_{14}\begin{matrix}CHOH\\|\\CO\end{matrix}$. This oxidation product of camphor is a white crystalline powder, melting at from 203° to 205° C. (397.4°–401° F.) and volatile in a current of steam. Soluble to a slight degree in cold water; more soluble in hot water. It is decomposed by prolonged exposure to the air.

It is stated that oxycamphor acts as a stimulant to the cardiac muscle and also to the centric and peripheral vasomotor nervous system, and as a calmative to the respiratory centers. It has been used with asserted good results for the relief of both cardiac and pulmonic *dyspnea*. *Dose*, from eight to fifteen grains (0.5–1.0 Gm.). A fifty per cent. solution of *oxycamphor* in alcohol is sold under the trade name of *oxaphor*. (*N. N. R.*, 1917.)

Oxychinaseptol. *Diaphtherin.* $C_6H_4(SO_2)\begin{cases}O—NH.C_9H_6(OH)\\O—NH.C_9H_6(OH)\end{cases}$. This substance is made by uniting two molecules of oxyquinoline, $C_9H_6N(OH)$, with one molecule of phenol-sulphonic acid, $C_6H_5(HOS_3)OH$. It occurs in yellowish hexagonal crystals, melting at 85° C. (185° F.), very soluble in water and diluted alcohol. Its solution is decomposed by alkalies. According to the researches of Emmerich (*M. M. W.*, 1892), it is much more powerful as an antiseptic than phenol; two-tenths of one per cent. solution is sufficient to kill the comma or diphtheria bacilli in ten minutes, and three-tenths of one per cent. solution destroys the pus organisms in thirty minutes. It is also asserted that it is practically innocuous to higher animals, the subcutaneous injection of five cubic centimeters of a 5 per cent. solution producing no serious effects upon guinea-pigs. It has been used in practical surgery, especially by Kronacher, who has employed from ½ to 1 per cent. solution with great satisfaction for the general

purposes of the antiseptic treatment of wounds. Such solution produces no irritation except in some cases a momentary burning. Rohrer (*Corresp. f. Schweiz. Aerz.*, Nov., 1892) commends the remedy as a local application in disease of the nasal mucous membrane. The solution does not stain the hands, but forms on steel instruments a black deposit which is readily washed off.

Oxydendrum. *Oxydendrum arboreum* (L.), DC. *Sour Wood. Elk Tree. Sorrel Tree.* (Fam. *Ericaceæ.*)—The leaves of this indigenous tree possess an acrid taste, whence the common names of the tree, and are said by eclectic physicians to be a powerful diuretic, useful in *dropsy*. A semi-solid extract may be made, one part representing five of the drug; *dose*, from five to fifteen grains (0.32–1.0 Gm.). Of the fluidextract the *dose* is from a half to two fluidrachms (1.8–7.5 mils).

Oxynaphthoic Acid. *Alpha-naphthol-carboxylic acid,* $C_{10}H_6 \begin{cases} COOH \\ OH \end{cases}$.—This is the counterpart among the naphthalene derivatives of salicylic acid among the benzene derivatives, and is made in an analogous way by the action of carbon dioxide and sodium upon *α-naphthol*. It forms a white, inodorous, micro-crystalline powder, fusing at from 185° to 186° C. (365°–366.8° F.), and is soluble in 30,000 parts of cold water, more readily soluble in alcohol, chloroform, benzene, and oils, both fixed and volatile, also in aqueous solutions of ammonium bicarbonate, which form salts. It is sternutatory antizymotic, disinfectant, and recommended against phylloxera. Its antizymotic action is said to exceed that of salicylic acid as five to one, and a 5 per cent. ointment has been lauded in *scabies*.

Oxyntin.—This is a compound of protein and hydrochloric acid containing 5 per cent. of the absolute acid in unstable combination. It is a dry granular powder readily miscible with water, to which it imparts a slightly acid taste. *Dose*, five to fifteen grains (0.32–1.0 Gm.).

Oxypropylenediisoamylamine.—Louise affirms that this colorless liquid, which is soluble in alcohol, ether, and oils and insoluble in water, resembles atropine in its action upon the heart, and that it causes great rise of the arterial pressure and of the temperature of the body. (*L. L.*, 1887.)

Oxyspartein. $C_{15}H_{24}N_2O$.—This is an oxidation product of sparteine. It forms white soluble crystals fusing between 48° and 50° C. (118.4°–122° F.). *Oxyspartein* is employed in the treatment of certain types of *heart diseases* in *doses* of three-quarters to one and one-half grains (0.048–0.096 Gm.). Both the hydrochloride and the sulphate are in use.

Ozokerite.—This substance, which is found in Galicia, in Austria, and from near the Caspian Sea, as well as in Southern Utah, is in its crude state, a solid, varying in color from a dirty green to nearly black. When purified by treatment with sulphuric acid and alkali and subsequent filtration while melted through bone black or other filtering medium, it is a hard, white, spermaceti-like substance, and is extensively used in England as well as in Austria in the manufacture of candles. (See *Ceresin.*) It is a mixture of natural paraffins. It is said to resemble tar in its therapeutic properties, and, mixed with glycerin or linseed oil, has been employed in *skin diseases* by Purdon as a substitute for that remedy. (*B. F. M. R.*, 1872, 535; see also *A. G. M.*, April, 1873, and *Am. Drug.*, 1892, 40.)

Ozone (O_3) is recognized as an active modification of the element oxygen. It is considered to differ from the common form in being more condensed and at the same time more active. It has a peculiar odor, somewhat resembling that of diluted chlorine. *Ozone* changes gradually at the ordinary temperature into common oxygen, and at 237° C. (458.6° F.) the change in instantaneous. It is one of the most powerful oxidizing agents known, attacking and at once destroying organic substances, such as caoutchouc, paper, cork, etc. It also decolorizes most organic pigments. Ozone is somewhat soluble in water, imparting to water its peculiar odor, as well as its oxidizing power. According to Carius, 1000 volumes of water dissolve 4.5 volumes of ozone, and it is much more soluble in certain ethereal oils. The power of these latter as carriers of oxygen and deodorants is thus explained. At one time ozone was thought to be peroxide of hydrogen, but Marignac and De la Rive demonstrated its true nature. Hautefeuille and Chappius (*C. R. A. S.*, xciv, 1249) succeeded in producing "liquid ozone" by applying a pressure of 125 atmospheres to richly ozonized oxygen at −100° C. (−148° F.). It is stated to be of a dark indigo color.

Ozone has not been obtained free from oxygen; indeed, it is probable that 1 per cent. of ozone is the highest concentration reached in its production. It is prepared by the decomposition of water by the battery, by the passage of the silent electric discharge through air or oxygen, by the slow oxidation of phosphorus in moist air and in other cases of slow combustion, and, lastly, by the action of sulphuric acid upon barium dioxide and potassium permanganate.

The presence of ozone in the air or in gases is indicated by its action on paper moistened with potassium iodide and starch solution. This is turned blue, and if reddened litmus paper is moistened with potassium iodide, this is also blued. Another test is found in the use of paper moistened with an alcoholic solution of guaiacum, which is changed to light blue.

Its presence in the air is now fully established, although in thickly inhabited districts it is almost always absent, as it is reduced to ordinary oxygen by the organic emanations constantly sent out into the air. In the air of the country, and especially in sea air, the presence of ozone can often be recognized by its peculiar odor. The probable cause of the formation of ozone in the air has been pointed out by Gorup-Besanez, as he has shown that ozone is invariably formed when water evaporates, and it is to this source, rather than to the electrical discharges, that the production of ozone must be traced.

Contrary to the common superstition ozone has neither deodorant nor disinfectant virtues. There is no evidence that it has any more therapeutic use than ordinary oxygen.

Pæonia. *Pœonia officinalis* L. *Peony. Pivoine,* Fr. *Gichtrose, Pfingstrose,* G. (Fam. *Ranunculaceæ.*)—The root of the garden peony consists of a thick rhizome which sends off in all directions spindle-shaped roots, which gradually taper into thread-like fibers, by which they hang together. It has a strong, peculiar, disagreeable odor, and a nauseous taste, which is at first sweetish, and afterwards bitter and somewhat acrid. The odor is lost, or much diminished, by drying. Peony root was in very great repute among the ancients as a charm and as a medicine in *epilepsy*. In modern times it has been used as an antispasmodic. According to Rochebrune (*Toxicolog. Africaine,* i), it contains an active alkaloid,

pœonine. The expressed juice is milky, of a strong odor and very disagreeable taste. The *seeds* are roundish-oval, about as large as a pea, externally smooth, shining, and nearly black, internally whitish, inodorous when dry, and of a mild oleaginous taste. By some authors they are said to be emetic and purgative, by others antispasmodic. The *dose* of the fresh root or seeds is from two drachms to an ounce (7.7–31.0 Gm.), boiled in a pint of water down to half a pint, which should be taken daily. It is said to be less active when dried. *Dose,* of the expressed juice of the root, one fluidounce (30 mils).

W. Will obtained from an aqueous distillate of the root of the Japanese *Pœonia Moutan* Simson, an aromatic ketone in colorless crystals. (*Ber. d. Chem. Ges.,* xix, 1777.) According to Nagae, this substance has the formula $C_9H_{10}O_3$. (*Ibid.,* xxiv.) It has been prepared by Schimmel & Co., under the name of *peonol.* It has a pleasant aromatic odor, and crystallizes in large needles. No essential oil was found in the root. (*Schim. Rep.,* Oct., 1890.) Dragendorff has found in the seed of *P. peregrina* Mill., a fixed oil, an alkaloid, and *pœonic acid.* (*Jahresb.,* 1879.)

Palicourea. *Palicourea rigida* H. B. K. (Fam. *Rubiaceæ.*)—The leaves of this tree are used in Brazil as a diuretic and diaphoretic. In 1866 Peckholdt found in them an alkaloid and three organic acids. One of these acids, consisting of a yellow, oily liquid with an overpowering odor, was found to be distinctly poisonous, one drop injected into a pigeon being enough to cause death. This was called *myotonic acid.* A crystalline *palicouric acid,* an amorphous tannin, and another amorphous non-toxic bitter principle were also isolated. Santesson has confirmed the presence of an alkaloid. (*A. Pharm.,* 235.)

Palladious Chloride. *Palladous Chloride. Palladii Chloridum.* $PdCl_2$.—This is a blackish-brown mass, soluble in water, which has been recommended as a reagent for determining the malic acid in wine. It has been used to some extent in medicine as a local germicide, and has been recommended in the treatment of *phthisis* in *doses* of one-fourth to one-third of a grain (0.016–0.021 Gm.) three or four times a day.

Under the name of *leptynol* an emulsion of *palladium hydroxide,* $PdOH_2$, has been employed as an injection for the treatment of *obesity* by Kauffmann. (*M. M. W.,* 1913, p. 1260.) Two mils of this preparation, containing 50 mgm., are injected once a week into the abdominal fat.

Palmiacol. *Cetiacol. Pyrocatechinmethylether.*—This liquid is insoluble in ordinary menstrua. It is intended as a substitute for guaiacol in the treatment of *bronchitis* and *pulmonary tuberculosis.* The *dose* is three to ten minims (0.2–0.6 mil).

Panase. *N. N. R.* 1917.—This is a combination of the digestive enzymes of the pancreas, derived from the pancreatic glands of the pig. It is a light, yellowish-white powder, having a slight animal odor and a somewhat mucilaginous taste. It is not entirely soluble in water or in glycerin, due to a small amount of proteid present. This can, however, be filtered out without impairing the digestive quality of the solution. *Panase* is incompatible with strong alcohol acids, alkalies and other substances which destroy the activity of ferments. It is used for the same purposes as pancreatin. *Dose,* two grains (0.13 Gm.).

Panbotano Bark.—The root of the Mexican leguminous tree, *Calliandra Houstoni* Benth., has been highly recommended by Valude as an antiperiodic, although Villejean was not able to find in it either an alkaloid or a glucoside. (*Journ. de Sci. Méd. de Lille,* 1890.) Pouchet (*Nouv. Rem.,* 1896), however, states that he has found in panbotano, besides saponin, an alkaloid which produces death by systolic arrest of the heart. Both Dinau (*Thèse de Paris,* 1896) and Crespin confirm its antiperiodic value. (*B. G. T.,* Aug., 1895.) A tincture representing two ounces of the root is taken in four *doses* during twenty-four hours.

Pancreon (*pankreon*) (*N. N. R.* 1917) is a preparation obtained by the action of tannic acid on pancreatin, containing 8 per cent. of the former in combination. It is a grayish, odorless powder soluble in water and acidulated liquids and is affirmed to have strongly trypsilytic, amylolytic, and emulsifying properties. It is further claimed to be superior to pancreatin in not losing its activity in the stomach. *Dose,* eight to fifteen grains (0.5–1.0 Gm.).

Pangium. *Pangium edule* Reinw. (Fam. *Bixaceæ.*)—This East Indian tree, which is said to possess anthelmintic and narcotic properties, and to be capable of causing death, according to Blume, contains an alkaloid resembling *menispermine.*

Pantopon. *Omnopon.*—Sahli introduced, in 1908, this combination of the alkaloids of opium as being more actively narcotic in proportion to its poisonous properties than morphine and having the advantage over crude opium that it was fitted for hypodermic administration. Both Straub (*Biochem. Zeit.,* 1912, xli, p. 419) and Macht (*J. P. Ex. T.,* 1915, vii, p. 339) have shown that narcotine is stimulating to the respiratory center and therefore antagonistic to morphine and codeine. There are, therefore, scientific grounds for this combination and the conclusions of Sahli have received considerable clinical confirmation. The *dose* of *pantopon* should be about double that of morphine. From one-sixth to one-third of a grain (0.010–0.021 Gm.) may be given by mouth.

Pao-Pereira Bark. *Pereiro Bark.*—Under this name a bark is employed in Brazil as a febrifuge. It is supposed to be the product of *Geissospermum lævе* (Vell.) Baill. (Fam. *Apocynaceæ*). O. Hesse has found an alkaloid, *geissospermine,* $C_{19}H_{24}N_2O_2 + H_2O$, in it (see *P. J.,* viii, 648), but he seems to have been preceded in this discovery by Santos. (*A. J. P.,* 1878, 184.) Peretti has discovered in the root a second alkaloid, *pereirine,* $C_{19}H_{24}N_2O$, which, according to Guimaraes (*B. M. J.,* vol. i, 1887), in sufficient doses causes paralysis with elevation of temperature, ending in death. It has been given to man as an antiperiodic in *doses* of thirty grains (2.0 Gm.) a day. (See also *A. J. P.,* 1886, 278.) Later a third alkaloid, *vellosine,* $C_{23}H_{28}N_2O_4$, was found. This forms colorless, crystals, melting at 189° C. (372.2° F.), insoluble in water, easily soluble in alcohol and ether. In concentrated nitric acid it dissolves with a purplish-red color, which is very stable.

Papaya. *Melon Tree. Papaw.*—The *Carica Papaya* L. (Fam. *Caricaceæ*) is a shrub, everywhere cultivated in tropical countries for the sake of its fruit. The ovoid fruit sometimes attains a length of 30 cm. and weight 4 or 5 K. According to Peckholdt (*P. J.,* Nov., 1879), the milky juice is contained in all parts of the tree, but in such small quantity, save in the unripe fruit, that it is always procured from the latter. One fruit will yield about 33 Gm., which is ob-

tained by scratching through the skin in various places; the process does not interfere with the ripening of the fruit, but it is said that the seeds will not germinate. The milk has an acid reaction, an astringent bitterish taste, and a sp. gr. of 1.023. Upon standing for a few minutes it separates into two parts, an aqueous liquid and a white, somewhat coagulated pulpy mass. In the aqueous portion is an albuminous substance, possessed of enzymic properties, to which the names of *papaïn* and *papayotin* have been given. According to the researches of S. H. C. Martin, papaw juice contains besides papaïn, a milk-curdling ferment and globulin, albumin, and two phytalbumoses. No peptones occur in the juice, but leucine and tyrosine are present. (*J. Chem. S.*, 1886, 642; see also *P. J.*, 1885, 129.) In a representative preparation the ferment action seems to be most marked when all the proteids are associated together in the natural form. In its action upon albumin the enzyme of the papaw produces products which have a close relation to those produced by tryptic and peptic digestion. In the action of the papaw ferments on milk there is first curdling, in which the casein is separated into a soft flocculent precipitate, and afterwards a digestion of the proteids, during which process they are converted into soluble and diffusible products. The amount of starch-converting ferment is not large, but sufficient in the fresh latex to promptly act upon starch paste, thinning it, and converting a portion at least into soluble starch and dextrin. The import of the rennet ferment and the pectase probably present require further investigation.

According to Wurtz, fibrin is dissolved whether the solvent solution be alkaline or acid. Brunton and Wyatt and also Martin affirm, however, that one-half per cent. of hydrochloric acid will prevent digestion, but Albrecht reasserts that hydrochloric acid hastens the action of the ferment, and states that the official preparation in use in Paris hospitals is an acid one. In order entirely to convert fibrin into pure peptone so that nitric acid will produce no precipitate, the proportion of the ferment should be as great as 3 per cent., and digestion must continue for forty-eight hours at 50° C. (122° F.).

Papaya juice has a tendency to spoil by undergoing a butyric fermentation, but Wurtz found that the addition to it of glycerin preserved it without interfering with its digestive power. Imported in this form, it was a thick, milky liquid. As it now occurs in commerce, papaïn is a grayish, fine powder, which in appearance, odor, and taste strongly suggests pepsin.

The seeds of the papaw tree contain a glucoside, *caricin*, which resembles *sinigrin*. These seeds also contain the ferment, *myrosin*, and by the reaction of the two a volatile pungent body is produced, suggestive of oil of mustard in odor. An alkaloid, *carpaine*, $C_{14}H_{25}O_2N$, has been obtained from the leaves. Physiologically, this alkaloid has the effect of a heart stimulant, quite similar to that of digitalis. (*A. J. P.*, July and August, 1901, 336–48 and 383.)

Under the name of *papayotin*, *papaïn*, or *papoid*, the dried juice of the *Carica Papaya* is put upon the market. It is frequently adulterated with starch, which is not naturally present in the fruit. Its digestive power is far below the claims formerly made for it. It is asserted for it that, when the stomach is acid, it is much superior to pancreatin, because its action is not markedly affected by contact with the acid. In experiments made by H. C. Wood with a papoid from one of the most renowned manufacturers no digestion occurred, and it is probable that much of the article of commerce is inert. It has been used as an internal medicine in *dyspepsia* and *gastric catarrh*, and as a local application for the destruction of false membranes, *warts*, *tubercles*, walls of old sinuses, and even of *epithelioma*. (See Branch, *B. M. J.*, 1907.) It is not caustic nor astringent, but destroys the part by virtue of its power of dissolving not only muscular but connective tissue. Jacobi affirms (*T. G.*, vol. ii) that diphtheritic membranes are dissolved in a few hours by the hourly application of a mixture of one part of papaïn with two parts each of water and of glycerin. It is stated that from time immemorial the fresh leaves of the papaya plant have been used by the Indians to wrap meat in to make it tender, and as a dressing to *foul wounds*. Peckoldt says that, taken internally, the juice is reputed to cause intestinal inflammation. No recent observers have noted such influence. According to Brunton, the *dose* is from five to ten grains (0.32–0.65 Gm.). Injected into the venous circulation it acts as a powerful poison, of which a single grain is sufficient to kill a rabbit.

Paracoto. *N. F. IV. Paracoto.*—"The dried bark of an unidentified tree indigenous to Northern Bolivia." *N. F.*

This drug was introduced into the National Formulary IV. It is not official in the U. S. or Br. Pharmacopœia. A tincture and fluidextract are official in the N. F. (see Part III). Paracoto is described as follows:

"In quills, or fragments of quills, of indefinite length, usually from 3 to 6 cm. in breadth, from 5 to 15 mm. in thickness; of a deep-brown color throughout, the outer surface nearly smooth, lightly, transversely fissured, and often very thinly scaly, the inner surface very coarsely striate; hard and heavy, but splitting and breaking readily, the fracture mealy in the outer layer, with an irregular resinous band, coarse splintery in the inner layer with large, yellowish-brown bast fibers and stone cells and darker resin tissue. Odor strong and characteristic, nutmeg-like; taste strongly aromatic and pungent. Paracoto yields not more than 3 per cent. of ash." *N. F.*

Paracotoin, $C_{12}H_8O_4$, is extracted from paracoto bark, in which it exists associated with *hydrocotoin*, $C_{15}H_{14}O_4$, *protocotoin*, $C_{16}H_{14}O_6$, *methylhydrocotoin*, $C_{16}H_{16}O_4$, and *methylprotocotoin*, $C_{17}H_{16}O_6$. Paracotoin may be distinguished from cotoin by giving no reaction with ferric chloride.

Paracotoin forms yellowish crystals soluble in alcohol and water and fusing at 149° to 151° C. (300.2°–303.8° F.). For a special reason its manufacturers have warned against its use in intestinal hyperemia. *Piperonylic* (methylene protocatechuic) *acid*, $C_8H_6O_4$, is also present. Paracoto bark has been used in various types of *dysentery* and *diarrhea*, especially in *tuberculous enteritis*. Balz (of Tokio) has employed paracotoin hypodermically in the treatment of *cholera* in doses of three grains (0.2 Gm.). This principle has also been recommended for *night sweats*.

The *dose* of paracoto bark is five grains (0.3 Gm.). (For uses see *Coto Bark*, p. 1344.)

Paralysol. *Solid Cresol.* $C_6H_4.CH_3OK.3C_6H_4CH_3.OH$.—Under this name has been introduced a combination of cresol and potassium which occurs as colorless crystals with a melting point of 146° C. (294.8° F.) and a faint phenylic odor. It is

stated that a one-half per cent. solution is fatal to non-sporulating bacteria in three minutes. (See *P. J.*, 1908, p. 9.)

Parameria. *Parameria vulneraria* Radlkofer. (Fam. *Apocynaceæ.*)—This tree yields the *Balsamo de Taguloway* of the Malays. (See *A. Pharm.*, Nov., 1885.)

Paramidoacetophenone. $C_6H_4.NH_2.CO.CH_3$.—This substance occurs in crystals soluble in boiling water, alcohol, and ether, and melting at 106° C. (222.8° F.). It has been used in the practical application of Ehrlich's *diazo test.* Two solutions are used for this purpose, as follows:

Solution 1.—*Paramidoacetophenone,* 0.5 Gm.; hydrochloric acid, 50 Gm.; water, 1000 Gm. Solution 2.—Sodium nitrite, 0.5 Gm.; distilled water, 100 Gm. Both solutions must be kept in dark bottles, and when required for use 2 mils of Solution 2 should be added to 100 mils of Solution 1. In testing, fill one-fourth of the test glass with the urine, add an equal quantity of the diazo reagent and mix both fluids; then add at one pouring a quantity of ammonia equal to about one-seventh or one-eighth of their combined bulk and shake vigorously. The reaction is regarded as positive if the fluid acquires a distinctly red color, while the foam produced by shaking should be wine-colored.

Paraphenetidin Acid Tartrate.—A white, crystalline powder, soluble in cold water but decomposed by hot water, used as an antipyretic in *doses* of eight to fifteen grains (0.5–1.0 Gm.). It is known by the proprietary name of *Vinopyrin.*

Paratoxin.—This is asserted to be an extract of the gall substance with subsequent distillation with benzin. It is soluble in alcohol and slightly soluble in fats and oils. It is used in the treatment of *tuberculous diseases.*

Paraxin. *Dimethyl-amino-para-xanthin.*—This substance forms white crystals slightly soluble in cold and readily soluble in hot water. Slightly alkalinated or acidulated water also rapidly dissolves the crystals. *Paraxin* fuses at 226° C. (438.8° F.) under sublimation. It has been used by Forschbach and Weber (*A. E. P. P.*, 1907, lvi, p. 186) as a diuretic. It resembles theophylline in its action, but is somewhat less certain. They employed it in *doses* of from thirty to forty grains (2–2.6 Gm.) per diem.

Pareira. *N. F. IV* (*U. S. P. VIII, Br.* 1898). *Pareira Brava, Pareiræ Radix,* Br. *Pareira Root.*—"The dried roots of *Chondrodendron tomentosum* Ruiz and Pavon (Fam. *Menispermaceæ*) without the presence of more than 5 per cent. of stems or other foreign matter." *N. F.*

Chondrodendron tomentosum is a climbing, woody vine, which attains often a considerable height, and is remarkable for the size of its leaves. These are about a foot long, broadly ovate or rounded, slightly cordate, with a smooth upper surface, and on the under surface, between the veins, covered with a fine close wool of an ashy hue. The racemose fruits are of the size of large grapes, oval and black. This plant inhabits both Brazil and Peru.

Pareira was formerly official in the U. S. VIII and Br. Pharmacopœias, but is now official in the N. F. IV, where it is described as follows: "Nearly cylindrical, more or less tortuous, of variable length and from 1 to 6 cm. in diameter. Externally brownish-black or blackish-brown with transverse ridges on knot-like projections, occasionally fissured and longitudinally wrinkled or even furrowed. Hard, heavy and tough; when freshly cut having a waxy luster; the transverse surfaces exhibiting several successive eccentric and distinctly radiate concentric zones of projecting, secondary fibro-vascular bundles, each from 2 to 4 mm. in width, and separated by distinct concentric zones of parenchyma and stone cells. Stem deeply furrowed, grayish in color, usually covered with foliaceous patches of lichens bearing their blackish apothecia; internally grayish-yellow, with a prominent development of wood with a tendency to separate fibro-vascular bundles and without a waxy luster. Odor slight, taste very bitter.

The powder is dark brown, containing numerous starch grains and a few woody fragments; starch grains mostly simple, occasionally unequally two- to four-compound, the individual grains ellipsoidal or oblong, 0.005 to 0.02 mm. in diameter and occasionally with central clefts or irregular markings; fragments with large, wide tracheæ, the walls with numerous slit-like pores and associated with long, thick-walled, strongly lignified, porous wood fibers; stone cells in small groups, with thick porous walls and in form resembling those of the fruits and seeds; fragments of starch-bearing parenchyma; the cells of the root being thick-walled, strongly lignified and with large, longitudinal, elliptical pores; occasional fragments of blackish-brown cork. Pareira yields not more than 5 per cent. of ash." *N. F.*

For account of commercial history, see *U. S. D.*, 18th ed., 1916.

The root imparts its virtues readily in water. Feneuille found in it a soft resin, a yellow bitter principle, a brown substance, a nitrogenous substance, fecula, acid calcium malate, potassium nitrate, and various other salts. He considers the yellow bitter substance as the active principle. It is soluble in water and alcohol, and precipitated from its solution by tincture of galls. Wiggers announced in 1838 the existence in pareira brava of an alkaloid, for which he proposed the name of *pelosine* or *cissampeline.* Peretti of Rome, and Pelletier afterwards, separated from the root an alkaloid characterized by assuming a beautiful purple color upon contact with strong nitric acid. (*J. P. C.*, xxvi, 162.) It is stated to be uncrystallizable, insoluble in water, soluble in ether, alcohol, and the acids, and of an intensely bitter and sweetish taste. Flückiger (*P. J.*, 1870, p. 192) found an alkaloid in pareira, and, having thoroughly determined its origin, investigated its properties, and fixed its composition at $C_{18}H_{21}NO_3$, showed its identity with the *bebeerine* of nectandra and the *buxine* of *Buxus sempervirens* obtained by Walz. Ringer and Brooke (*A. J. P.*, 1892, 255) proved that the true chondrodendron root contained a larger quantity of chemical and extractive principles than do the substitutes. (See also Dohme's paper, *D. C.*, 1896, 296.)

Pareira is supposed to have a diuretic effect and to act as an antiseptic in the bladder. It is chiefly employed for the relief of *chronic inflammations of the urinary passages.* In Brazil it is used in the cure of the *bites of poisonous serpents,*—a vinous infusion of the root being taken internally, while the bruised leaves of the plant are applied to the wound. The dose of pareira in substance is from thirty grains to a drachm (2.0–3.9 Gm.). The infusion (1 oz. in 1 pint of boiling water) is useful. The aqueous extract may be given in the dose of from ten to thirty grains (0.65–2.0 Gm.). There is an official fluidextract made with diluted alcohol in the N. F. IV (see Part III).

For preparations of pareira see *U. S. D.*, 19th ed., p. 917.

Dose, thirty to sixty grains (2.0–3.9 Gm.).

Parietaria. *Parietaria officinalis* L. *Wall Pellitory. Pariétaire, Perce-muraille*, Fr. *Glaskraut*, G. (Fam. *Urticaceæ.*)—A perennial European herb, growing on old walls and heaps of rubbish. It is diuretic and refrigerant, and was formerly used in urinary complaints and *dropsy*, in the form of decoction or of the expressed juice.

Paris Green. *Schweinfurt Green. Aceto-Arsenite of Copper.* $Cu(C_2H_3O_2)_2.3Cu(AsO_2)_2$.—This substance, which was originally made for a pigment, is now used to an enormous extent for dusting on potato vines to destroy the so-called *potato bug*, or *Colorado beetle, Doryphora decemlineata.* It is made by mixing five parts of verdigris with sufficient water to form a thin paste, and adding to this a boiling solution of four parts of arsenic trioxide in fifty parts of water, keeping the mixture at the boiling temperature, and adding a little acetic acid to cause it to retain a brilliant color. It is rarely found pure in commerce. Numerous cases of poisoning have occurred through carelessness in its use as an insecticide. The treatment would be the same as that for poisoning by arsenic. *Lead arsenate* (*Chem. News*, 1896, 17) has been largely superseded by *Paris green* as an insecticide.

Parkia. *Parkia biglandulosa* W. and A. (*P. africana* R. Br.). *African Locust. Nitta* or *Nutta Tree. Doura. Houllé. Neretou.*—This is an African leguminous tree, from the dried seeds of which a farinaceous food is prepared by the natives. According to De Rochebrune (*Toxicolog. Africaine*, 1898), it contains a peculiar crystalline alkaloid, *parkine*, which resembles in its physiological activity physostigmine.

Parnassia Palustris.—An infusion of the bark of this tree has been used in the treatment of *epileptics*, administered in teaspoonful *doses* three times daily.

Parsley Root. *N. F. IV. Petroselini Radix. Petrosel Rad.* It is described by the N. F. as "The root of *Petroselinum sativum* Hoffmann (Fam. *Umbelliferæ*). The entire fusiform root, measuring up to 20 cm. in length and up to 2.5 cm. in thickness at the crown, or broken or cut into pieces; usually cut lengthwise into two or four sections; externally light yellowish, wrinkled longitudinally, somewhat annulate, root scars distinct and corky; fracture tough when damp, brittle when dry; internally, cortex whitish and characterized by numerous, reddish-brown oleoresin cells, cambium zone distinct and brownish; wood about the same thickness as the cortex, slightly radiate and light yellow. Odor aromatic; taste sweetish and pungent. The powdered drug, when examined under the microscope, shows numerous truncate or somewhat angular starch grains up to 0.03 mm. in diameter, reticulate tracheæ up to 0.06 mm. in width and thin-walled, lignified fibers with simple pores. Parsley Root yields not more than 6 per cent. of ash." *Dose*, thirty grains (2 Gm.). (See *Petroselinum*, Part I).

Parthenium. *Chrysanthemum Parthenium* (L.) Bernh. *Feverfew. Matricaire*, Fr. *Mutterkraut*, G. (Fam. *Compositæ.*)—A tall, perennial, branching herbaceous plant, with bipinnately divided leaves, the divisions being ovate, and compound flowers in a corymb. It is a native of Europe, but cultivated in our gardens and naturalized in some places. The whole herbaceous part is used. The plant has an odor and taste analogous to those of chamomile, which it resembles also in the appearance of its flowers and in its medicinal virtues. It yields a greenish volatile oil which boils between 165° and 220° C. (329° and 428° F.), and separates on standing, *pyrethrum camphor*, $C_{10}H_{16}O$. (Dessaignes and Chautard, *J. P. C.* (3), xiii, 241.)

The flowers of this and of a closely resembling species, *Matricaria Anthemis parthenoides* Desf., are said to be used in France, to a considerable extent, indiscriminately with those of the true chamomile plant, *Anthemis nobilis*, which they closely resemble, especially when double. They may, however, be distinguished, in this state, by their peculiar odor, their small receptacle, which is, moreover, rounded and flattened above, instead of being conical and somewhat pointed as in the *Anthemis*, and by the tubular five-toothed central florets, which in the chamomile are small, few, and scarcely visible, but in the two former species are large, very numerous, and very long.

Parthenium Hysterophorus L.—José Torar has found *parthenine* and four other alkaloids besides *parthenic acid*, in this Cuban plant which is used by the natives as a febrifuge and antiperiodic. Of the alkaloids, *parthenine* is crystallizable and is apparently the active principle. It has been extracted and studied again by H. Vin Arny (*A. J. P.*, 1890, 121), who believes it to be a bitter glucoside and not an alkaloid. In doses of three grains (0.2 Gm.) it is said to quicken the heart, and in doses of fifteen grains (1.0 Gm.) to slow cardiac action, while fifty grains (3.2 Gm.) not only lessen the arterial pressure and respiratory frequency but reduce the bodily temperature. In *doses* of from seven to ten grains (0.45–0.65 Gm.) it is affirmed to be useful in *neuralgia.* (See *Journ. de Méd. de Paris*, March, 1887; *J. P. C.*, xii, 1885; *A. J. P.*, 1897, 169.)

Parthenium integrifolium L., *American Feverfew, Wild Quinine* (Fam. *Compositæ*), is an herbaceous perennial, growing abundantly in the prairies of the Southwestern States, which has been used as a tonic and antiperiodic; two ounces (62 Gm.) of the flowering tops may be given in infusion.

Passion Flower. *N. F. IV. Passiflora. Passion Vine.* "The dried herbage of *Passiflora incarnata* Linné (Fam. *Passifloraceæ*), collected after some of the berries have matured." *N. F.*

It is described in the N. F. as follows: "Stems glabrous or slightly pubescent above, striate, from 6 to 8 mm. in diameter, of variable length, woody, hollow, the cavity about one-half the diameter; bark very thin, greenish or purplish; wood very porous and bordered on the inner side by a thin layer of pith; fracture of the wood uneven, of the stem smooth, of the bark coarsely fibrous. Leaves more or less broken in drying, rather thick, glabrous or often pubescent, when entire nearly orbicular in outline, base cordate, deeply three- to five-lobed, lobes ovate, acute, finely serrate, petioles from 1 to 5 cm. in length, with two glands near the summit. Tendrils numerous and closely coiled. Flowers solitary, axillary, peduncles as long as the petioles, usually three bracted; calyx cup-shaped, four to five lobes; lobes linear, imbricated, cuspidate, corona of the fresh flowers purplish; petals four to five, yellow; ovary oblong, stalked; stamens monadelphus in a tube about the stalk of the ovary, separated above, anthers narrow, versatile. Fruit from 4 to 5 cm. in length, an ovoid, many-seeded berry; externally green or yellow, shriveled and wrinkled; seeds flat, ovate, yellowish

to brown arilled. Taste and odor slight. Passion Flowers yield not more than 12 per cent. of ash." *N. F.*

This indigenous plant has been supposed to possess narcotic properties and used in *neuralgias, sleeplessness, dysmenorrhea,* as well as in *diarrhea* and *dysentery.* I. Ott (*Medical Bulletin,* Dec., 1898) finds that it is a depressant to the motor side of the spinal cord, but increases the rate of the respiration, and that it has very little effect upon the circulation, only temporarily reducing the arterial pressure. *Dose,* three to ten grains (0.2–0.65 Gm.).

Patent Yellow. *Mineral Yellow.*—A pigment, consisting of lead chloride combined with lead monoxide. It is prepared by mixing common salt and litharge with a sufficient quantity of water, allowing the mixture to stand for some time, then washing out the liberated soda, and exposing the white residue to heat.

Paulowilhelmia. *Paulowilhelmia speciosa* Hochst.—This acanthaceous plant is used by the Aquapine tribe on the Gold Coast, as a fish poison, under the name of *adubiri.* (*P. J.*, xx, 1890.)

Peach Leaves. *Leaves of Prunus Persica* (L.) Sieb. et Zucc. (Fam. *Rosaceæ.*) *Pechier,* Fr. *Pfirsich,* G.—The peach tree is supposed to have been originally brought from Persia, but flourishes everywhere in the warm temperate zone. Peaches are among the most grateful and wholesome of our summer fruits. They abound in saccharine matter, which renders their juices susceptible of the vinous fermentation, and a distilled liquor prepared from them has been much used, in some parts of the country, under the name of *peach brandy.* The kernels of the fruit resemble, physically and chemically, bitter almonds, for which they are frequently, and without inconvenience, substituted in commerce. The flowers, leaves, and bark also have the peculiar odor and taste of bitter almonds, and yield hydrocyanic acid. The leaves afford a volatile oil by distillation. The distilled water prepared from them was found in one instance to contain 1.407 parts of hydrocyanic acid in 1000, and in another only 0.437 parts in the same quantity. From some experiments it is inferred that the proportion of acid is greatest where there is least fruit. (*A. J. P.*, xxiv, 72.)

Peach kernel oil made by expression has found its way into Western Europe from the Levant, and is used in Italy and Southern France largely as an adulterant of almond oil. It is described as of a light yellow color, having the taste and odor of almond oil. It thickens at −9° C. or −10° C. (15.8° F. or 14° F.), and solidifies at −18° C. (−0.4° F.). The sp. gr. at 15° C. (59° F.) is 0.915. It gives with strong nitric acid a dark brown color, with sulphuric acid a dark brown becoming lighter, with solution of zinc chloride a purplish-brown; forming with the elaidin test in two hours a mass of butter-like color and consistence. Peach kernel oil has a saponification value of 189–192 and an iodine figure of 93.5. (See *Oleum Amygdalæ Expressum,* PART I.)

The leaves of the peach are said to be laxative, and have also been used with asserted advantage in *whooping cough, irritability of the bladder,* etc. The dried leaves may be employed (an ounce to a pint of hot water) in infusion. The flowers of the peach are affirmed to be laxative and vermicidal, in half-fluid-ounce (15 mils) doses when fresh, given in the form of syrup. Cases of fatal poisoning in children from their use are on record. The peach kernels are distinctly active, and when rubbed up with cold water form an emulsion which may be used in place of cherry-laurel water or other preparations of hydrocyanic acid.

Peganum. *Peganum Harmala* L. *Wild Rue.* (Fam. *Rutaceæ.*)—A tall herbaceous plant growing in the Mediterranean region of Europe and Africa and extending into Thibet. In the seeds of this plant Goebel (1837) found the alkaloid *harmaline,* and Fritzsche (1847) a second alkaloid, *harmine,* which have been re-studied by Fischer and Täuber. (*A. J. P.*, 1886, 89.)

The seeds of *peganum* were used by the ancient Greeks in the treatment of *eye diseases.* In modern times it has been used as an emmenagogue, anthelmintic and sedative.

Harmaline or *harmine dihydride,* $C_{13}H_{14}N_2O$, is in the form of trimetric, octahedral crystals. It is soluble in alcohol and ether and slowly so in water. It melts at about 238° C. (460.4° F.) with decomposition. Flury (*A. E. P. P.*, 1911, lxiv, p. 105) finds that harmaline in moderate doses produced symptoms in the dog similar to those produced by cannabis and in toxic quantities it caused salivation. Its anthelmintic effect he attributes to a paralytic action upon the muscular tissues of the worm.

Pegnin. *N. N. R.* 1917. *Milk-sugar Rennet.*—Under this name is marketed the milk curdling enzyme of calf's rennet diluted with milk sugar and a little sodium chloride. It is a fine, white powder, having a sweet saline taste, readily soluble in water, forming a solution that rapidly coagulates the casein of milk. It is used mainly in the extemporaneous preparation of infant food and in stomachic disturbances, such as *hyperacidity* and *flatulence.*

Pelargonium. *Pelargonium odoratissimum* Willd. *Rose Geranium.* (Fam. *Geraniaceæ.*)—The *Pelargoniums,* commonly referred to as *geraniums,* are indigenous to South Africa and largely cultivated as decorative plants. Some of the species are cultivated for the distillation of the volatile oil, in France, Spain, Algiers, and the Island of Reunion. According to Guibourt, several species of *Pelargonium* yield a volatile oil by distillation, closely analogous in odor to that of the rose: the species above named, *P. capitatum* Ait., and *P. roseum* Willd., the last being regarded as a variety of *P. radula* Ait. (*Hist. Nat. des Drogues,* 4e ed., iii, 52.) The oil is obtained from the leaves. Recluz obtained from thirty-five ounces of *P. odoratissimum* W., two drachms of a volatile, crystallizable oil. (Mérat and De Lens, *Dict. de Mat. Méd.*, iii, 368.) According to Septimus Piesse, one cwt. yields about two ounces. (See *A. J. P.*, xxvi, 368.) The oil which occurs in commerce, purporting to be the oil of *P. odoratissimum,* is fluid at ordinary temperatures, of a pale brownish-yellow color, and the characteristic odor of the plant, merely recalling that of the rose. This oil is now much used in perfumery. Piesse states that, as this oil is used to adulterate that of roses, so is it in its turn adulterated with the cheaper oils of species of *Andropogon.* (See p. 1517.) (*A. J. P.*, xxvi, 368.) It appears, however, that the oil known as *oil of palmarosa* (see *Oil of Citronella,* p. 1517), distilled in India, is the one which is used most largely to adulterate oil of rose and oil of rose geranium. According to Baur, the oil is shipped in large copper flasks from Bombay to the Red Sea, and thence to Constantinople and Kizanlik. For Burtell's description of the method of distilling palmarosa oil see *Schim. Rep.*, 1909, 88. Jallard

states that the true oil of rose geranium from *P. roseum* is freely soluble in 70 per cent. alcohol. The oils likely to be used to adulterate it are insoluble in this liquid. If, therefore, six drops of the suspected oil be mixed with 5 mils of 70 per cent. alcohol, there should be no separation. (*A. J. P.*, 1878, 260; from *J. P. C.*) F. W. Semmler (*Ber. d. Chem. Ges.*, xxiii, 1098) has shown that the chief ingredient in the various geranium oils is an alcohol, *geraniol*, $C_{10}H_{16}O$, which boils at from 231° to 232° C. (447.8°–449.6° F.), and has a sp. gr. 0.884 at 15° C. (59° F.). When oxidized by chromium trioxide mixtures, it is changed into *citral*, $C_{10}H_{16}O$, an aldehyde found in many of the essential oils, and this when oxidized by silver oxide yields *geranic acid*, $C_{10}H_{16}O_2$. The geraniol is both free and combined as *tiglic acid ester*. The oil also contains citronellol. (*Schim. Rep.*, April, 1897.) Geranium oil is sometimes adulterated with dimethyl sulphide, $(CH_3)_2S$. (*Schim. Rep.*, 1909, 55; see also *Am. Perf.*, Jan., 1913.)

Pengawar Djambi. *Paku Kidang. Golden Moss.*—This is composed of silky, long, yellow or brownish hairs, very soft, which are obtained in Sumatra from the base of the shrub of various ferns, especially *Cibotium* Link. (Fam. *Cyatheaceæ*), a peculiar fern related to Dicksonia. (See also *S. W. P.*, 1910, No. 43, 661.) It has the power of causing rapid coagulation of blood, and, when properly used, of mechanically arresting hemorrhages from capillaries. It has been much used in the physiological laboratories of Europe and this country, and was employed in human medicine during the Middle Ages under the name of *Agnus Scythicus*. The medieval drug was composed of pieces of the rhizome with the attached scales and petioles so cut as to resemble animals. Interest in the *pengawar djambi* was revived on account of the assertions of Junker of its usefulness during the Franco-German war. (*L. M. R.*, Dec., 1887.) It is undoubtedly a very efficient styptic.

Pental. *Tri-methyl-ethylene. Isoamylene.* C_5H_{10} or $(CH_3)_2C{:}CH.CH_3$.—A hydrocarbon prepared by distilling amyl alcohol with zinc chloride and treating the distillate with sulphuric acid. A colorless liquid, sp. gr. 0.6783, boiling at 38° C. (100.4° F.), insoluble in water, and miscible with alcohol, ether, and chloroform. It was proposed as an anesthetic, but is probably of very little value in medicine.

Penthaclethra. *Penthacelthra macrophylla* Benth. (Fam. *Leguminosæ.*) *Owalá Grains.*—The seeds of this plant, which grows in the Congo States, are said to contain an alkaloid, *paucine*, crystallizing in yellow foliaceous crystals, melting at 126° C. (258.8° F.), insoluble in ether and chloroform, having the formula $C_{27}H_{38}O_5N_5$. (*P. J.*, lix.) *Paucine hydrochloride*, $C_{27}H_{39}O_5N_5\ 2HCl + 6H_2O$, is marketed by Merck and Co., and is stated to be physiologically inactive.

Peptones.—The general name of a class of albuminoids into which the nitrogenous elements of food (such as albumin, fibrin, casein, etc.), are converted by the action of the gastric or pancreatic juices. This conversion is caused by the ferment pepsin, and also by trypsin present in the pancreatic juice.

Peptones are not precipitated by potassium ferrocyanide in the presence of acetic acid like other proteids, and are not coagulated by heat. They are readily assimilated by the intestinal mucous membrane and peptonized meats are used as nutrient. Most of the material known as "peptone" is not a true peptone, but hemialbumose. The vinous solutions of so-called "predigested foods" have deceived many persons. Their nutritive value is generally less than that of milk and even this is due in large part to their alcohol content.

Perezia Root.—This root is obtained from several Mexican plants, *Perezia Wrightii* A. Gray, *P. Nana* A. Gray, and *P. Dugesii* A. Gray. (Fam. *Compositæ.*) It contains *pipitzahoic acid*, a substance which crystallizes in beautiful golden-yellow needles. R. Anschütz and J. W. Leather obtained from the dried roots of *P. adnata* A. Gray (*Trixis Pipitzahoac* Schaffner), an average of 3.6 per cent. of this acid, which melts at from 103° to 104° C. (217.4°–219.2° F.), sublimes readily, and is easily soluble in alcohol, ether, chloroform, benzene, and glacial acetic acid. The authors confirm the formula given to the acid in 1855—viz., $C_{15}H_{20}O_3$. It is a quinone, and bears great resemblance, when recrystallized from diluted alcohol, to *oxythymoquinone*, which, recrystallized from the same liquid, is scarcely distinguishable from it. (*A. J. P.*, 1884, 185, and *Ph. Rund.*, 1883, 245; *A. Pharm.*, 1887, 183.)

Under the name of *perezol* the 0.5 per cent. alcoholic solution of *pipitzahoic acid* has been recommended by Duyk as an alkalimetrical indicator. By acids it is at once decolorized; with alkalies it becomes reddish. Boric, and perhaps other acids, and acetates, borates, bicarbonates, and carbonates act with respect to the solution like alkalies. For a paper on pipitzahoic acid by Altamirans, see *Analen del Instituto Mex.*, Nat. 7, p. 21, or *P. J.*, 1905, 553.

Periploca. *Periploca græca* L.—From the bark of this asclepiadaceous shrub, growing in the neighborhood of the Black Sea, has been separated by Lehmann (*A. Pharm.*, 1897, p. 157) a colorless glucoside, *periplocin*, $C_{30}H_{48}O_{12}$, soluble in 125 parts of water, freely soluble in alcohol. According to the experiments of Burschinski (*St. P. M. W.*, 1897), it is an active cardiac poison belonging to the digitalis group. It has been used as a cardiac tonic by Cholewa (*Th. M.*, 1904, p. 292), Silberberg (*In. Dis., Odessa*, 1909), and others, as a practical remedy in the treatment of *heart disease*. Silberberg asserts that it is better suited for intravenous injection than strophanthin. The *dose* is from one one-hundred-and-twentieth to one-sixtieth of a grain (0.0005–0.0011 Gm.).

Peronine. *Benzyl-morphine Hydrochloride.* $C_{17}H_{18}NO_2.O.C_6H_5CH_2HCl$.—This is the hydrochloride of morphine benzyl-ester, produced by replacing the hydrogen of the hydroxyl group in morphine, which is analogous to the hydroxyl group of phenols, with the alcohol radical ($C_6H_5CH_2$). *Peronine* occurs as a bitter, odorless, white powder, consisting of prismatic crystals. At 65.5° C. (150° F.) it dissolves in water in the proportion of 7.5 to 1000, but dissolves readily in 10 parts of boiling water, the aqueous solutions having a bitter taste and being neutral to litmus. It is soluble in 218 parts of 95 per cent. alcohol. Although precipitated from its solutions by the general alkaloidal reagents, peronine differs both in its solubilities, and also in its behavior towards special reagents, from morphine and codeine.

Peronine was first therapeutically investigated by Schröder (*Th. M.*, 1897), and the conclusion reached that in its medicinal activities it is intermediate between morphine and codeine. The physiological action of the drug has been partially studied by Mayor (*Revue Méd. de la Suisse Ro-*

mande, 1898), who finds that it produces in guinea-pigs and rabbits exaggerated reflexes, ending, if the dose have been large enough, in convulsions and death by asphyxia. The lethal dose for rabbits, according to Mayor, is 2.5 Gm. per kilo, or little less than one-third that of codeine. On the other hand, Pierart affirms, as the result of his experiments, that peronine is more poisonous than morphine. Clinically, peronine has been used to some extent as a substitute for morphine, having analgesic and hypnotic powers inferior to those of that alkaloid, but being of distinct value in the treatment of *phthisis, chronic bronchitis*, and other pulmonary diseases. The *dose* is from one-third of a grain to one grain (0.021–0.065 Gm.).

According to Bufalini, confirmed by Gevaert, the 1 to 2 per cent. solution of peronine placed in the conjunctival sac produces a complete anesthesia which lasts for many hours. The drug, however, has not been used for this purpose on account of its causing pain, edematous swelling, and even serous chemosis of the conjunctiva.

Peroxides.—There has recently been introduced into medicine a series of superoxygenated compounds with various inorganic bases. The theoretical basis for the introduction of these compounds into medicine is that in the presence of water they part with an atom of their oxygen, which unites with the elements of the water to form hydrogen peroxide, as in the following reaction:

$$MgO_2 + H_2O = MgO + H_2O_2$$

and that the hydrogen peroxide which is formed under these circumstances will exercise the well-known disinfectant properties of that substance. It is to be remembered, however, that hydrogen dioxide is very unstable in the presence of an alkali, and since, in the above reaction, an alkaline salt is left behind, there will be a rapid decomposition of the hydrogen dioxide, with the liberation of free oxygen. The more highly alkaline the oxide which is left after the splitting off of one atom of oxygen, the more rapidly will the resulting hydrogen dioxide be broken up. Of this group of salts, the sodium perborate has received official approbation, and the following are of sufficient importance to deserve mention.

Magnesium Peroxide. Magnesii Peroxidum. N. N. R. 1917.—Theoretically, *magnesium peroxide* should form about 28 per cent. of its weight of hydrogen dioxide. Commercial samples of magnesium peroxide, however, often contain only from 15 per cent. to 25 per cent. of the salt; a 15 per cent. preparation will evidently form only 4.2 per cent. of its weight of hydrogen dioxide, therefore a drachm of magnesium peroxide will represent about the same amount of hydrogen dioxide as a drachm and a half of the official solution of hydrogen dioxide.

Magnesium peroxide is an odorless, white powder, practically insoluble in all the ordinary solvents. It has been used as an antiseptic with asserted good results in the treatment of gastric and intestinal disorders, but it does not seem probable that whatever benefit may have followed this treatment can be laid to the disinfectant properties of the drug. It will, in these cases, evidently act as an antacid and laxative as does the ordinary magnesium oxide. It has also been used internally as a substitute for the ordinary oxide in the treatment of *rheumatism, gout* and *hyperacidity of the stomach*, and also, with less reason, in the treatment of *diabetes*.

Although the germicidal power of magnesium peroxide has not been as yet satisfactorily determined, the experiments of Park indicate that it is a germicide of considerable power. Croner states that the addition of 0.7 Gm. of magnesium peroxide per liter drinking water exercised a bactericidal effect, but did not produce complete sterility of the water. It has been used locally as a dusting powder in infectious conditions of the throat, such as *acute tonsillitis*, but chiefly as an ingredient of dentifrices. Magnesium peroxide is also known under various brand names, such as *Magnesium Perhydrol, Biogen, Novozone*, and *Magnodat*. The *dose* for internal administration is from five to twenty grains (0.32-1.2 Gm.).

Sodium Peroxide. Bioxydum Natri, Sp.—This occurs as a white or yellowish powder which dissolves in water with the development of heat and the evolution of oxygen. It should contain at least 95 per cent. of absolute sodium dioxide, Na_2O_2. It is largely used as a bleaching agent in the arts and is also used by dentists for bleaching teeth. Unna recommends a sodium peroxide soap made of 3 parts of liquid petrolatum, 7 of dried soap, and from 2½ to 7 per cent. of sodium peroxide. It is said to impart to a pale and excessively cornified facial skin pitted with comedones, a healthy, rosy color and a softened surface. It has also been used in *rosacea pustulosa*. A proprietary preparation of fused sodium peroxide, containing also some catalytic agent is sold under the name of *oxone*.

Calcium Peroxide. N. N. R. 1917.—*Calcium peroxidatum* or *gorit*, CaO_2, occurs as a cream colored, odorless and tasteless powder, which is practically insoluble in water. The standard of the N. N. R. requires 60 per cent. of absolute calcium peroxide. It is chiefly used as an addition to dentifrices, but often in such small quantities as to be absolutely incapable of any antiseptic action in the mouth. It has also been used as an antacid and disinfectant in gastric and intestinal disorders in *doses* of five to fifteen grains (0.32–1.0 Gm.).

Strontium Peroxide. N. N. R. 1917. SrO_2.—This is a white, odorless and tasteless powder, almost insoluble in water. It is rarely employed in medicine.

Zinc Peroxide. N. N. R. 1917. ZnO_2.—This occurs as a white or yellowish insoluble powder, representing from 40 per cent. to 50 per cent. of absolute *zinc peroxide*. It is used in medicine as an antiseptic in various ulcerated conditions, such as *burns*, old *leg ulcers*, and the like. It has been recommended as a local application in various *skin diseases*. It may be used either mixed with talc as a dusting powder, or in the form of an ointment in strengths of 5 to 25 per cent. *Ektogan* is the name of a proprietary form of zinc peroxide.

Persulphates.—*Persulphates* are obtained by the electrolysis of solutions of sulphates. Sulphuric acid is decomposed into H_2 and SO_4, and the SO_4 ion unites with a molecule of the normal sulphate, as:

$$Na_2SO_4 + SO_4 = Na_2S_2O_8.$$

They have been brought forward for use in medicine and dentistry on account of their yielding oxygen when heated and their germicidal properties. According to Friedländer (*Th. M.*, Feb., 1899), the half per cent. aqueous solution checks the growth of pathogenic bacteria, and the 5 per cent. solution kills them. They are said to be actively poisonous, 0.5 gramme per kilo rapidly causing

death in the rabbit, and to be violently irritant to mucous membranes; one and one-half to five per cent. solutions have been used to some extent in the dressing of *wounds*.

The important persulphates are *ammonium persulphate*, $(NH_4)_2S_2O_8$, which occurs in colorless crystals, making a turbid solution with water; *potassium persulphate*, $K_2S_2O_8$, which occurs in colorless crystals, very slightly soluble in water; and *sodium persulphate*, $Na_2S_2O_8$, a colorless crystalline powder, sparingly soluble in water.

Sodium persulphate has been recommended internally as an aperitive stimulant to digestion, in *hypochondria*, *chlorosis*, and *neurasthenia*. Lumière (*Lyon Chirurgical*, October, 1915) has found sodium persulphate useful in the treatment of *tetanus*. From experiments in the test tube as well as in the lower animals he concludes that its effect is due to the destruction of the toxin. It has been used in various intestinal conditions as a stimulant and antiseptic. Cannaday (*Press. Med.*, 1905, p. 286) reports favorably upon its action in *typhoid fever*. The *dose* in a day is three grains (0.2 Gm.).

Persodine is the one and three-tenths aqueous solution which has been supplied commercially in France.

Ammonium persulphate has been strongly recommended by Strzyzowski (*Schweizer Wochen. f. Chemie u. Pharmacie*, 1898, No. 48) as a urinary reagent; if its ten per cent. solution is allowed to fall into a test tube containing urine the presence of albumin will be revealed by a whitish-gray zone at the juncture of the two liquids. The development of a green tint indicates the presence of biliary pigments. Its therapeutic energy depends upon the production of free sulphuric acid and oxygen. The salt is readily soluble in water, and its solutions keep unchanged for weeks unless they be heated or in contact with easily oxidizable bodies. (*Th. M.*, 1899, 99.)

Perugen.—A synthetic imitation of Peru balsam obtained through solution of aromatic gum resins and balsams in aromatic esters. It behaves similarly to the true balsam in its action towards solvents, etc., but can be distinguished by the difference in its lower saponification number and iodine number, that of *perugen* being 206 and 33.7, respectively.

Peruol.—This is a twenty-five per cent. solution in castor oil of *peruscabine*, the active principle of Peruvian balsam, which has been produced synthetically by Erdmann. Peruscabine itself is pure *benzoic benzyl-ester* and is a colorless oil, boiling at 173° C. (343.4° F.). It has been used in skin diseases and is said to be especially valuable in *scabies* and in *mange*. The whole or a part of the body should be freely anointed with some friction three or four times in thirty-six hours, and after a day or more a soap bath given.

Petroleum. *Rock Oil. Oleum Petræ. Huile minéral*, Fr. *Bergöl*, G.—*Petroleum* is a native mixture of hydrocarbons with very small amounts of oxidation or alteration products admixed. The hydrocarbons may be gaseous, liquid, or solid, and in crude oil, fresh from the wells, all three classes are present. The hydrocarbons belong to several of the homologous series known to organic chemistry. The researches of Pelouze and Cahours, of Warren, and more especially of Schorlemmer, have established the presence of the paraffin series, C_nH_{2n+2}, beginning at methane and continuing through the liquid members, which constitute the bulk of the oil, to the solid hydrocarbons known commercially as "paraffine"; of the olein series, C_nH_{2n}; of the benzene series, C_nH_{2n-6}. After the oil has been heated, as in distillation, pyrogenic products form, so that in the residues of petroleum distillation, naphthalene, anthracene, and other higher hydrocarbons have been detected. In Caucasian petroleum, Beilstein and Kurbatow (*A. J. P.*, 1880, 612) have also found another homologous series of hydrocarbons, *hexahydrobenzene*, C_6H_{12}, and its homologues known as the *naphtenes*. These same hydrocarbons under the name of *polymethylenes* have been shown by Richardson to make up California petroleums and to be present in other asphalt base oils.

Pennsylvania petroleum consists, however, chiefly of paraffins, and the individual hydrocarbon making the bulk of illuminating oil is *heptane*, C_7H_{16}. The oxidation products accompanying petroleum constitute only a small fraction of 1 per cent. usually, and have not been very fully studied. It is known, however, that these alteration products are largely acid in character. Prolonged atmospheric exposure may, however, cause a petroleum to thicken, at least superficially. In this way the semi-solid deposits of California are explained, as well as Rangoon tar and Trinidad pitch or bitumen. When the bitumen is in the solid state it is called *asphaltum*. This is black and sometimes dry, friable, and is insoluble in water or alcohol. Not infrequently asphaltum exists in nature mixed with more or less of the liquid substance, and this semi-solid mixture is distinguished by the name of *maltha* or *mineral tar*.

Petroleum has been known from the earliest historical period. Within the limits of the United States it has long been known to exist in a few localities. On the borders of Seneca Lake in the State of New York small quantities of it were collected, and to some extent used in medicine under the name of *Seneca oil*. In Western Pennsylvania, on Duck Creek in Ohio, near Scottsville in Kentucky, and on the Kanawha in Virginia, it attracted local attention, and a certain locality in Western Canada had acquired some notoriety by its burning spring. But little attention was paid to it until the year 1859, when, the preparation of oil for burning, distilled from bituminous shales, having proved very profitable, and a strong resemblance having been shown to exist between this and petroleum, enterprise was directed towards some of the known resources of the latter liquid, and, being greatly stimulated by success, soon led to further and astonishing discoveries. At first the most productive locality of petroleum was in Western Pennsylvania; but it is now obtained in many States. After the Pennsylvania field, in order of development, is that of Ohio; but most of the oil produced in this State is from a different geological horizon—viz., the Trenton limestone—and contains a persistent sulphur impurity. This renders the Ohio oil (popularly known also as *Lima oil*, from the town of Lima, Ohio) more difficult and expensive to refine. It is hence very largely used in the crude state as *fuel oil*, and as such has been of the greatest industrial value, being shipped by pipe line or tank cars to great distances. Within recent years large quantities of petroleum have been found in California, Texas, Louisiana, Kentucky, and Kansas, but in the main it is of a grade much inferior to that known as Pennsylvania oil, being largely used as fuel oil.

In the early days of the petroleum discovery the oil was gathered as it floated on the surface of the water in springs or small streams. In 1859 the first oil well, the Drake well, was sunk

near Titusville, Pa., and the oil-bearing strata were reached at a depth of seventy-one feet, with the result of some eight barrels per day. In 1861 and 1862 the first large flowing wells were struck in drilling for oil. The explanation of these flowing wells is simply that in new territory the gaseous hydrocarbons have accumulated with the liquid oil in such amount that they exert an enormous pressure, causing a flow of oil at the rate of two, three, and in one case as high as eight thousand barrels per day. Often, however, the pent up gas escapes with enormous force without any accompanying oil. These *gas wells*, as they are termed, are well known throughout the oil regions, and they have been utilized on a large scale as sources of gaseous fuel for manufacturing and domestic purposes. The statistics show that the value of the coal displaced by natural gas as fuel in 1903 was $35,815,360, and in 1904, $38,496,760. Of this amount nearly one-half was obtained in Pennsylvania, while Indiana, West Virginia, and Ohio followed in the order named. (*Mineral Resources of the U. S.*, Washington, 1904.) Sadtler has analyzed numerous samples of this natural gas, and finds it to consist chiefly of methane and its homologues, with traces of the olefines and of carbon monoxide. In one case free hydrogen was present. (*Proc. Amer. Philos. Soc.*, xvi, 585, 1877.) After a well has flowed oil for a time, it will continue to yield on pumping. Indeed, many smaller wells never have flowed, and have to be pumped from the start. In some districts "torpedoing" with nitroglycerin has been largely resorted to after a well has begun to decline in power, in order to increase the flow. The explosion effects this by shattering the sandstone and pebble conglomerate which holds the oil, so that new channels are opened.

Oil wells are of various depths. The first or Drake well, as stated, was only seventy-one feet deep, while in Butler County the fourth sand rock was reached only at a depth of from 1500 to 1800 feet, and in Washington County and other localities in the southwestern part of Pennsylvania the oil was obtained from a depth of 2000 feet.

There are two theories as to the origin of petroleum. According to one, it is simply a product of distillation from the bituminous shales which underlie almost the whole of this oil producing country. The gas and the liquid oil are equally products of this distillation. According to the other, it represents the decomposition of marine plants and animal life which accumulated in these sand rock formations. These decomposition products may have also been in part subjected to distillation.

Studies by Engler (*Ber. d. Chem. Ges.*, 1888, 1816) on the distillation under pressure (ten atmospheres) of fish oils and of olein and other fats show that large amounts of light oils, composed of pentane, hexane, heptane, octane, and nonane, can be obtained, thus making the second theory very probable.

S. P. Sadtler (*Proc. Amer. Phil. Soc.*) has shown that linseed oil, distilled under pressure, may be made to yield hydrocarbons of the paraffin series, and has obtained products of all gravities from light benzin to solid scale paraffin. Thus, Engler's theory must be broadened sufficiently to allow of the vegetable seed oils being taken as original sources of petroleum production as well as animal oils.

Crude petroleum is occasionally of a clear color when taken from the earth, but is generally of a greenish color, appearing claret-red by transmitted light. The green color may, however, become so dark as to be almost black. In gravity it varies from 0.865 to 0.777, or from 32.5° to 52° Baumé.

The enormous production of crude petroleum in the last twenty-five years has had the effect of developing a variety of new industries connected with the working or shipping of it. The whole producing area of Western Pennsylvania and adjacent States is now covered with a net work of wrought iron pipes, for the conveyance of the oil; and these "pipe lines" now extend to Cleveland, Buffalo, Pittsburgh, New York, Philadelphia, and Baltimore, so that crude oil is pumped from the vicinity of the wells to the seaboard cities, to be refined there or to be exported in bulk. The refining of crude oil, and the working up of the several liquid and solid products that are known commercially, are also immense industries. The production of crude petroleum for the year 1915 amounted to 426,892,673 barrels, of which the United States produced 281,104,104 barrels, the next largest producers being Russia with 68,548,062 barrels and Mexico with 32,910,508 barrels. The exports of crude and refined petroleum for the year 1916 were: crude petroleum, 163,734,200 gals.; naphtha and light distillates, 294,793,357 gals.; illuminating oils, 823,164,882 gals.; lubricating oils and paraffin, 87,459,482 gals.; gas oil and fuel oil 897,853,433 gals.; residuum, 13,539,443 gals.; total of all grades, 2,443,478,080 gals.

After American petroleum the next in importance is Russian or Caucasian. The wells here, although only a few hundred feet in depth, are wonderfully prolific and are veritable "oil fountains." Two of them, the Droobja well and Nobel's No. 9, each yielded for a time nearly 48,000 barrels of crude oil every twenty-four hours.

The method of purifying petroleum is analogous to that already described for purifying coal tar. The crude oil is put into large retorts of wrought iron and exposed to a heat rising gradually to between 315.5° C. (600° F.) and 426.6° C. (800° F.), by which all the volatile ingredients are distilled, leaving from five to ten per cent. of solid residue, constituting a sort of coke. The liquids thus obtained are comparatively colorless, though still retaining the strong odor of the crude oil. The several fractions are collected separately and show very varying gravity and volatility, and are applied to different uses. An average result of a normal distillation may be stated as follows: gasoline 1½ per cent., refined naphtha 10 per cent., benzin 4 per cent., refined petroleum or kerosene (sometimes called coal oil), 55 per cent., lubricating oil 17½ per cent., paraffin 2 per cent., loss, gas, and coke 10 per cent. As the greater demand for illuminating oil makes it desirable to get the maximum quantity of this fraction, the distillation is generally so conducted that by the process of "cracking" the yield of burning oil is increased at the expense of the lubricating oil and heavy naphtha. Many distilleries obtain, therefore, from 75 to 80 per cent. of illuminating oil from the crude material. A crude distillate, however, would not be adapted for the purposes of an illuminating oil, so the distillate must be treated with acid. It is placed in the treating tank or "agitator" and 1 or 2 per cent. of strong sulphuric acid is added, when, by the aid of an air blast introduced below, the whole is violently agitated. The acid combines with the impurities of the oil and forms a tarry substance, called "*sludge acid*," which settles to the bottom, and after the whole has subsided is removed. The oil is then washed with water and again agitated, the process being re-

peated once or twice. It is then treated with caustic soda solution and again washed. The oil is now clear and almost colorless. It is then placed in large settling tanks to allow the water to separate. If it does not have the desired fire test, it is "steam stilled" and the lighter vapors taken out until the desired test is obtained. In most States of the Union the legal fire test for illuminating oil is 43.3° C. (110° F.); that is, it must not evolve inflammable vapors below the temperature of 43.3° C. (110° F.). Many special brands of illuminating oil have a much higher fire test, as high even as 148.8° C. (300° F.).

Lubricating oils, on the other hand, are valued according to their "cold test"; that is, they must not congeal except at very low temperatures. A lubricating oil, therefore, consists of the heavy liquid hydrocarbons of the paraffin and olefin series, but is free from the solid paraffin.

Medicinal Properties and Uses.—Petroleum has been deemed a stimulating antispasmodic, expectorant, and diaphoretic. In large quantities it may prove poisonous, as shown by a case recorded in the *J. P. C.* (March, 1869, 227), in which, after swallowing by mistake a quantity of rectified petroleum, a workman was seized almost immediately with violent inflammation of the throat, with colicky pain, and a desire to vomit, followed in an instant by a fearful tetanic seizure, and a general rigidity, attended by the most frightful cries. After a relaxation of ten minutes the symptoms returned with still greater violence; and life was probably saved only through the prompt action of the powerful emeto-cathartic medicines administered. Petroleum is used as a folk remedy in the treatment of acute *bronchitis*, but probably with no beneficial action in this condition save by virtue of its nauseating effect. The inhalation of asphalt vapors have been recommended by Floer (*Ther. Geg.*, 1909, p. 405) in the treatment of *pulmonary tuberculosis*. It is stated that the influence of these fumes is not merely upon the bronchial mucous membranes, but that there is a marked improvement in the appetite and in the digestive power. In Germany it has been used successfully as a remedy against the *tape worm*. Schwartz's formula in such cases is a mixture of one part of petroleum with one and a half parts of tincture of asafetida, of which forty drops were given three times a day. Externally, petroleum is employed in *chilblains*, *chronic rheumatism*, affections of the joints, *paralysis*, and diseases of the skin, and is said to be very effectual in *psora* and *prurigo*. (See also *Petrolatum* and *Petrolatum Liquidum*.) It is an ingredient in the popular remedy called *British Oil*. It is affirmed that many cases of *asthma* are much benefited by inhaling petroleum vapors.

The lighter fractions of petroleum are capable of absorption and are highly toxic substances. There have been a number of cases of serious and even fatal poisoning reported both from the swallowing and inhalation of various products of this nature. The symptoms have been dizziness, cyanosis, rapid small pulse, respiration slow and labored. If the dose is large enough the patient becomes stuporous and occasionally delirious. When taken by the mouth to these symptoms are added gastro-intestinal irritation. H. C. Wood, Jr. (*Phila. Medical Journal*, 1899), has shown that the mixture known as benzine is a direct depressant to the heart and vasomotor system. Various of these substances are used by depraved humanity as intoxicants.

Extraordinary claims have been made for various commercial emulsions containing some form of petroleum, but there is no certain substantiation of these claims. The *dose* of petroleum is from thirty to sixty minims (2–4 mils).

A water and alcohol soluble combination of petroleum oil has been originated by Max Doenhardt (*Ph. Ztg.*, 1913, p. 266), who discovered that when petroleum is mixed with *terpineol* and the solution treated with *triolein* and potassium hydroxide solution, the mixture develops heat spontaneously, a product resulting in a short time which forms a perfectly clear solution with alcohol, which in turn may be diluted with water to produce a permanently clear solution. The proportions of the ingredients depend upon the amount of petroleum, an excess of alkali always being necessary. The author has patented a product called "*Terpipetrol*" made by the above process.

Petrosapol.—This is a brown ointment-like compound of soap and the by-products of petroleum; especially used as a vehicle for ointments. It does not melt below 90° C. (194° F.), and does not, therefore, liquefy on the skin.

Petrosulfol.—This is said to be an ichthyol-like compound useful as a local remedy in *eczema* and allied diseases.

Peucedanum. *Chucklusa. Hog Fennel. Sulphurwort.*—This is the root of *Peucedanum officinale* (Fam. *Umbelliferæ*), originally an European plant but now growing in North America. The active constituent of the root is *peucedanin*, $C_{16}H_{16}O_4$, stated to be diuretic and emmenagogue.

Peucedanum palustre Mnch. *Marsh Parsley. Marsh Smallage. Persil de Marais*, Fr. *Radix Olsnitii. Sumpfsilge, Elsenich*, G.—The root of this European umbellifer is, when dried, of a brown color externally, having a strong aromatic odor, and an acrid, pungent, aromatic taste. Peschier found it to contain a volatile oil, a fixed oil, and a peculiar acid which he calls *selinic*. It has been used for *epilepsy* in Russia. *Dose*, from twenty to thirty grains (1.3–2.0 Gm.) thrice daily, rapidly increased to four times the amount. (*J. P. C.*, 1859.)

Pharbitis.—A genus constituted by Choisy, 1833, its species referable to *Ipomœa* or *Convolvulus*. *Ipomœa hederacea* (L.) Jacq. (*Pharbitis Nil* Choisy).—The seeds of this Japanese plant have been chemically examined by K. Hirano and also by Y. Inoko, who find that they contain a large proportion of a resinous substance, seemingly identical with *convolvulin*, and acting as a cathartic in *doses* of from seven to ten grains (0.45–0.65 Gm.). (*Sei-i-kwai*, 1891.)

Phaselin.—This substance is represented as the active constituent of the bean of *Dilkas Mexicano*, a South American plant. It is used similarly to papain as a digestive in *doses* of eight to fifteen grains (0.5–1.0 Gm.).

Phaseolus. *Phaseolus vulgaris* L. *Common Kidney* or *String Bean.* (Fam. *Leguminosæ*.)—Of this species there are some 70 cultivated varieties. Soltsien found an alkaloid, *phaseoline*, in the legumes of the common bean. He, during a toxicological analysis, traced the source of the alkaloid which might, under other circumstances, have been mistaken for a ptomaine, to the beans found in the stomach under examination. The new substanee is not crystallizable in the free state, but it crystallizes as a hydrochloride. (*A. Pharm.*, 1884.)

Phecine.—Two substances have been introduced under this name, one being sulfometadihydroxybenzene, recommended as a dermal antiseptic, and the other a mixture of 8.15 parts resorcinol

and 18.5 parts zinc sulfocarbolate, also used for the same purpose.

Phenegol. $C_6H_5(O.NO_2.SO_3K) : Hg : (KSO_3.NO_2.O)C_6H_5$.—Nitrated derivatives of paraphenolsulfonic acid unite readily with mercury, forming compounds known as *egols*. According to the phenol selected these products are called *phenegol, cresegol* (from cresol), *thymegol* (from thymol). *Phenegol* is the mercuric potassium salt of nitro-p-phenol sulfonic acid and forms a red-brown, soluble, tasteless powder, containing one-third mercury. It is asserted to be free from irritating action, does not coagulate albumen, precipitates toxins and is rapidly eliminated from the system. A 0.4 per cent. solution sterilizes all bacterial cultures.

Phenetidin Camphorate.—The camphorate of phenetidin, or phenacetin in which the acetic radical is replaced by camphoric acid. It forms a crystalline substance insoluble in water and having a pronounced camphoraceous odor and characteristic taste. It is used as an antihydrotic and febrifuge in eight to fifteen grain (0.5–1 Gm.) *doses*.

Phenoco. *N. N. R.* 1917.—This compound is said to be a mixture of coal tar creosote and higher phenol homologues suspended in a soap solution. It contains 8 per cent. phenol homologues. With water it forms a milky, white emulsion of a high antiseptic value. The phenol coefficient test showed a germicidal value over 15 times that of phenol. (*U. S. Hygeine Bull.*, vol. viii, No. 1, 1911.) It is used in dilutions of 1 to 5 per cent.

Phenocoll. *Amido-aceto-para-phenetidin. Glycocoll-para-phenetidin. Phenamine.*

$$C_6H_4\begin{cases}OC_2H_5\\NH.COCH_2NH_2H_2O.\end{cases}$$

—This is formed by the action of glycocoll (amidoacetic acid) upon phenetidin. It is a white, finely crystalline powder, soluble at 17° C. (62.6° F.) in sixteen parts of water; also soluble in warm alcohol. The hydrochloride of *phenocoll* has almost entirely displaced the base as a therapeutic agent. Ammonia, alkalies, and alkaline carbonates throw down the pure base phenocoll from the solution of the hydrochloride, in the form of white needles with one molecule of water of crystallization.

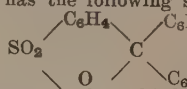
Phenocoll closely resembles the other phenetidin compounds in its physiological action. In moderate quantities it causes practically no alteration in the functions of the body, but in large doses is depressant to the spinal cord, and respiratory center, and according to Ott, also to the circulation. Hertel and Herzog (*D. M. W.*, 1891) find that its antipyretic action is prompt, and that the sweating which is a common accompaniment may be readily controlled with small doses of atropine. Antiperiodic powers have also been attributed to it, but without any convincing evidence. The *dose* of the hydrochloride is from eight to fifteen grains (0.5–1.0 Gm.). The salicylate of phenocoll is also used, conjoining the action of salicylic acid and phenocoll. *Dose*, eight to fifteen grains (0.5–1.0 Gm.).

Phenocoll Salicylate, Salocoll, N. N. R. 1917, $C_6H_4\begin{cases}OC_2H_5\\NH.COCH_2.NH_2.C_6H_4(OH)COOH\end{cases}$, has been put upon the market as an antirheumatic. It may be used in the *doses* of ten to thirty grains (0.65–1.9 Gm.).

Phenol-Bismuth. *Bismuth Carbonate.* $Bi(OH)_2(C_6H_5O)$.—A white, non-irritant and non-toxic powder, almost odorless and tasteless, which, according to its manufacturer, contains 80 per cent. of bismuth in chemical combination with 19 per cent. of phenol. It is stated by M. F. A. Jasenski to be decomposed in the gastro-intestinal tract, with absorption of the phenol and escape of the bismuth, in great part with the feces. It is also asserted by Jasenski that even the largest doses (seventy-five grains) of it produce no evidences of phenol poisoning, and the probabilities are that but a small portion of the compound suffers decomposition in the intestinal tract. It has been used in all forms of gastro-intestinal *catarrhs*, fermentative *dyspepsias*, and similar complaints, as an antiseptic; also to some extent locally in various mucous inflammations. *Dose*, eight to thirty grains (0.5–2 Gm.).

Phenol Sodium Sulphoricinate.—It is used as a local application to various ulcerative and catarrhal conditions. Baumgarten (*K. T. W.*, 1905, 793) finds it especially useful in *atrophic rhinitis*. He uses a 30 per cent. solution applied by inunction.

Phenolsulphonephthalein. *N. N. R.*—This product of the reaction of phenol and sulphobenzoic acid anhydride differs from phenolphthalein in containing an SO_2 group in place of the CO group. It has the following structural formula:



This substance was brought forward by Geraghty and Rowntree in 1910 (*J. P. Ex. T.*, 1910, i, 579; *J. A. M. A.*, 1911, lvii, 811) as a test for the functional capacity of the kidney. The determination is carried out as follows: Half an hour after having drunk a glass of water the patient is catheterized and the catheter left in place. One-eighth of a grain (0.008 Gm.) of *phenolsulphonephthalein* dissolved in fifteen minims (1.0 mil) of water is then injected intramuscularly. The urine is allowed to drain through the catheter into a vessel containing a drop of a 25 per cent. solution of sodium hydroxide until the appearance of a pinkish tint. This time is noted and the catheter withdrawn. Subsequently the urine is collected at one hour and two hours after the ingestion, and after this it is saved for twenty-four hours. The quantity of the dye in the urine is determined by alkalizing with sodium hydroxide, diluting accurately up to one liter and comparing the depth of color with a standard solution of phenolsulphonephthalein. Various instruments to facilitate this part of the test are on the market. In health the dye appears in the urine within five or ten minutes, about one-half of the dose is eliminated in the first hour and 75 or 80 per cent. in two hours. In cases of *nephritis* the elimination is more or less delayed according to the character of the lesion.

Phenopyrine. *Antipyrine Carbolate. Antipyrine Phenate.*—This is a colorless, oily liquid, without odor, insoluble in water, but soluble in ether and chloroform. According to Arends, Merck, and Coblentz, it is a mixture of antipyrin and crystalline phenol. It is used externally as an analgesic in *rheumatic* and *neuralgic* affections, and occasionally internally as an antipyretic in *doses* of three to ten grains (0.2–0.6 Gm.).

Phenosal. *Phenetidin Salicylate.*

$C_6H_4\begin{cases}OC_2H_5\\NH.CO.CH_2.OC_6H_4.COOH\end{cases}$. It forms colorless crystals of acidulous taste, difficultly soluble in water. *Phenosal* is said to contain 57 per cent. of phenetidin and 43 per cent. of salicylic acid;

to be decomposed into its constituents in the alimentary canal, and to be a useful remedy in the treatment of *rheumatism*, and also of *tabetic* and other *nerve pains*. *Dose*, eight grains (0.5 Gm.).

Phenostal. *Diphenyloxalic Ester.*—This is asserted to be a combination of oxalic acid with phenol. It has long been known that phenol and the allied germicides are more active in the presence of acids than in neutral medium. *Phenostal* is asserted to have the advantage of appearing not only in solid form, but of being more actively germicidal than simple phenol. According to Hailer (*Arb. a. d. k. Gesundtsamte*, 1901, 500) the combination of phenol with oxalic acid is stronger than with either sulphuric or acetic acids. Phenostal has been used as a wound and hand disinfectant in strengths of from one-fourth to one per cent.

Phenoxycaffeine. $C_8H_9(OC_6H_5)N_4O_2$.—This product forms a white, crystalline powder, fusing at 142° C. (287.6° F.). It is used as an analgesic in neuralgias in *doses* of four to five grains (0.26–0.32 Gm.).

Phenoxy-proprandiol. *Glycerine-monophenyl-ether.* $C_6H_5OCH_2CHOH.CH_2OH$.—This occurs as white crystals, freely soluble in both water and alcohol, and melting at 69° to 70° C. (156.2°–158° F.). Under the name of *antodyne* it has been introduced as an analgesic. It appears to differ from other coal-tar anodynes in that it is not antipyretic. The *dose* is from eight to fifteen grains (0.5–1.0 Gm.).

Phenyform is a condensation product of phenol and formaldehyde, and occurs as a grayish, odorless powder, insoluble in water, but dissolving in alkaline solutions, or alcohol. It is asserted by Schuftan (*Th. M.*, 1906, 249) that *phenyform* is completely non-toxic. Brenning (*All. W. M. Z.*, 1906, 182) has used it as a dusting powder in various suppurating processes and states that it not only checks the formation of pus, but also acts as a deodorizer and favors the formation of healthy granulations. It has also been employed in *urethritis*, a finely powdered preparation being blown into the urethra, under which circumstances it is asserted that it adheres firmly to the mucous membranes.

Phenylchinaldine. *Phenylquinaldine.—Methylquinol*, $C_{10}H_8(C_6H_5)N$, is prepared by the action of hydrochloric acid on a mixture of aniline, acetophenone, and aldehyde. The hydrochloride occurs in colorless crystals, which are readily soluble in water; the sulphate easily soluble in water, with a feebly acid reaction. Leo Fürbringer (*D. A. K. M.*, lix, 1897) finds that it produces in the lower animals tremors, violent cramps, fall of temperature, and death (if the dose has been large enough) from failure of respiration. The fatal dose to the rabbit is about fifteen grains (1 Gm.). It has been used in *malarial fever* in the *dose* of eight grains (0.5 Gm.) three times a day, but found to be much inferior to quinine.

Phenylchinoline. *Phenylquinoline.* $C_9H_6(C_6H_5)N$.—According to Tappeiner (*D. A. K. M.*, lvi, 1896), the action of this substance on the lower organisms is almost identical with that of quinine and about equal to it in strength.

Phenylenediamine. $C_6H_4(NH_2)_2[1:4]$.—*Para-phenylenediamine* and *meta-phenylenediamine* have been physiologically studied by Dubois and Vignon (*C. R. A. S.*, cvii, 533), who find that in *doses* of 0.01 Gm. per kilogramme it causes in the dog vomiting, diarrhea, and fatal coma, with peculiar symptoms.

Under the name of *ursol* paraphenylenediamine has been used as a dye for furs, and also as a hair dye. Its use on the human head, however, has given rise to violent dermatitis and it is entirely unsuitable for the purpose. Colman and Loewy (*D. M. W.*, 1911), however, have found that by combining it with reducing substances, the toxic properties of paraphenylenediamine were reduced. They recommend as a hair dye a solution of *paratoluylenediamine* with neutral sulphites, which is put upon the market under the name of *primal*.

Phenylhydrazine. $C_6H_5NH.NH_2$.—This is prepared from diazobenzene hydrochloride (resulting from the action of sodium nitrite upon aniline hydrochloride) by reduction with stannous chloride or sodium sulphite. The various compound derivatives of this substance have been tested by Heinz (*B. K. W.*, 1890) and others, and found to be too toxic for use in practical medicine. Phenylhydrazine is a colorless, slightly yellowish, highly refractive liquid, while the hydrochloride is a white crystalline powder, melting at about 200° C. (392° F.). (See under Reagents, Part III.) *Phenylhydrazine hydrochloride* has been employed in the following manner as a test for sugar in the urine. (*Fischer's Test.*) "To 8 mils (120 min.) of the urine, add 1 mil of normal solution of barium chloride with a few drops of solution of potassium hydroxide; filter, add 0.2 Gm. (3 grains) of sodium carbonate, heat to boiling and filter. To the filtrate add 2 mils (30 minims) of acetic acid (36 per cent.), and about 0.1 Gm. (1½ grains) of phenylhydrazine hydrochoride, evaporate the solution on the water-bath to one-half its volume." An amorphous precipitate will be formed if only a small quantity of sugar be present, but if the sugar be present in considerable quantity a precipitate of minute yellow needles will be deposited. This test was discovered by Emil Fischer, and is founded on the property of glucose in the urine forming with phenylhydrazine, crystals of *phenylglucosazone*.

Phenylhydrazine is an active irritant and toxic agent, producing in warm-blooded animals violent disturbances of breathing, with gastro-enteritis. It is remarkable for the changes which it produces in the blood, causing that fluid to become of a distinct green color when seen in thin sheets. The coloring matter appears not to be due to a derivative of phenylhydrazine, but to have at least spectroscopic relations to acid hematoporphyrin and to chlorophyll. (See *Z. B.*, N. F., xxiv, 1901.)

Phenylhydroxylamine. $C_6H_5.NH.OH$.—This substance has no known application to the treatment of disease, but requires notice on account of the occasional poisoning by it of those who are engaged in the manufacture of certain chemicals. For cases, see Hirsch and Edel (*B. K. W.*, xxxii, 1895), L. Lewin (*A. E. P. P.*, Bd. xxxv). The symptoms, which have developed with great suddenness, have consisted of coma, cyanosis, pulselessness, abolition of corneal and pupillary reflexes, chocolate-colored blood, methemoglobinuria, grayish-blue lips, and intense blue-red surface of limbs. The treatment of these cases should consist in active artificial respiration, together with hypodermic injections of strychnine and of digitalis. For the action of *phenylhydroxylamine* upon the blood, see L. Lewin (*A. E. P. P.*, Bd. xxxv).

Phenylo-boric Acid. *Acidum Phenylo-boricum.* $C_6H_5.B(OH)_2$.—A white powder, soluble with difficulty in cold water, which was found by G. Molinari (*Chem. Cb.*, 1892, ii, 224) to be a powerful ger-

micide, checking putrefaction in 0.75 per cent. solution, and being very poisonous to the *cholera* and other pathogenic bacilli. It is said to act especially well locally upon *venereal ulcers*, and to be less poisonous than phenol. The fatal *dose* for the rabbit is fixed at twenty-three grains (1.5 Gm.).

Phenylo-salicylic Acid. *Acidum Phenylo-salicylicum. Oxydiphenylcarbonic Acid. Ortho-oxydiphenyl-carboxylic Acid.* $C_6H_3(OH)(C_6H_5)COOH$. —A whitish powder, soluble in water with difficulty, easily soluble in alcohol, ether, and glycerin; which, according to F. Bock (*In. Dis.*, Berlin, 1892), is about equivalent in germicidal properties to salicylic acid. Its salts are said to be less poisonous than are those of salicylic acid. It is made by subjecting a mixture of calcium benzoate and salicylate to dry distillation and fusing the product with potassium hydroxide. It is used as an antiseptic dusting powder.

Phenylurethane. *Euphorin. Ethyl Phenylcarbamate. Carbamilic Ether.* $C_9O_2H_{11}N$, or $CO\begin{cases}OC_2H_5\\NH(C_6H_5)\end{cases}$.—This is a white, crystalline substance, having an aromatic odor and clove-like taste, and is made by the action of ethyl chloroformate (or ethylic ether) on aniline. It is almost insoluble in cold water, very soluble in boiling water, alcohol, and ether, and melts at 51° C. (123.8° F.). It has been physiologically investigated by Giacoasa, who finds that its 2 per cent. solution very distinctly hinders or altogether arrests the growth of bacteria and bacilli; that in the frog it produces a general paralysis due to an action upon the nerve centers; that in the rabbit it causes somnolence, hebetude, albuminuria, gastritis, etc.; but very large doses are required to have any effect, over three hundred grains having been given to a dog without producing inconvenience. It does not form methemoglobin in the blood. After its ingestion about 8 per cent. of it was found in the urine in the form of *oxyphenylurethane* in combination with sulphuric acid. It has been used by Sansonia (*Th. M.*, 1892, p. 452) as an antiseptic in obstinate *ulcers*, and in chronic *ophthalmia*, and by others in the treatment of *rheumatism*, but it has failed to establish its value in these conditions. More recently Stroll (*M. M. W.*, 1907, p. 2262) has asserted that it is an extraordinarily powerful local anesthetic, and of great service in painful *ulcers* of the foot.

The similarity of names has led to euphorin being confused with europhen. *Dose*, eight to fifteen grains (0.5–1.0 Gm.).

Phesin. *Acet-p-phenetidine-sodium Sulphonate.* $C_6H_3\begin{cases}O—C_2H_5\\SO_3Na\\NH—CO—CH_3\end{cases}$.—*Phesin* is a sulphonic derivative of phenacetin, and occurs as a pale, reddish-brown, amorphous, tasteless powder, having a slightly irritant salt taste, very soluble in water, affording a brown solution of acid reaction. It has been studied by Von Vámossy and Fenyvessy (*Th. M.*, 1897), who find that it resembles phenacetin very closely in its action, but is characterized by the promptness and shortness of its influence. *Dose*, eight to fifteen grains (0.5–1 Gm.).

Phlorizin. *Phloridizin. Phlorrhizin. N. N. R.* 1917. $C_{21}H_{24}O_{10} + 2H_2O$.—This is a bitter principle, discovered by De Koninck, of Germany, in the bark of the apple, pear, cherry, and plum trees. It is most abundant in the bark of the root, and derived its name from this circumstance (from two Greek words, φλοιός, bark, and ῥίζα, a root). It is light, white, crystallizable in silky needles, of a sweet, afterwards bitter taste, soluble in about 1000 parts of cold and in all proportions in boiling water, very soluble in alcohol and methyl alcohol, scarcely soluble in ether, cold or hot, dissolved without change by solutions of the alkalies, deprived of its water of crystallization at 100° C. (212° F.), and fusible at a somewhat higher temperature. The ammoniacal solution becomes red on exposure to the air on account of the formation of *phlorizein*, $C_{21}H_{30}N_2O_{13}$. *Phlorizin* is a glucoside. When heated with diluted hydrochloric or sulphuric acid, it is converted into sugar and a peculiar substance called *phloretin*, $C_{15}H_{14}O_5$. (See *Chem. Gaz.*, viii, 392.) To obtain phlorizin, the fresh bark of the root of the apple tree should be selected, as the dried bark is said to contain it in much smaller proportion. It is obtained by extracting the bark with boiling water and allowing the glucoside to crystallize out by cooling; the crude substance later being purified with animal charcoal. Rochleder states that the leaves contain a principle, *isophlorizin*, isomeric with phlorizin.

When given to the lower animals in very large doses (from seven to ten grains to the pound), phlorizin produces polyuria, glycosuria, emaciation, and other symptoms of diabetes, with chronic nephritis. (See Coolen, *Archiv. de Pharmacod.*, vol. ii, 1896; also Kossa, *Z. B.*, xl, 1900.) Although at one time recommended as an *antiperiodic* in doses of from ten to fifteen grains (0.65–1.0 Gm.), it is of no use in practical medicine except as a test for renal insufficiency. In the *phlorizin test*, five to ten milligrammes of phlorizin are added to a sterilized solution containing an equal quantity of sodium carbonate, and given subcutaneously, the bladder having been emptied just before administration. If the kidney be normal, sugar should appear in the urine half an hour later; if there be no excretion, or if the excretion of sugar be delayed, the renal function is considered to be insufficient. (*Boston City Hospital Report*, 1902; see also *M. R.*, 1911.)

Phosphine. *Diamidophenylacridine Binitrate.* —This is a reddish powder, a solution of which in alkaline fluid is phosphorescent. Notwithstanding its commercial name, it contains no phosphorus and should not be confounded with the definite chemical substance, phosphine, PH_3. It has been asserted to be a valuable analgesic, but Dujardin-Beaumetz finds *phosphine* too irritant to the stomach for practical use. (*G. H. M. C.*, June, 1888.)

Phosphorescent Powder or **Paint.**—Made by mixing calcined oyster shells, 100 parts; caustic lime, 100 parts; calcined sodium chloride, 25 parts; then incorporate about 55 parts of sulphur and from 8 to 18 parts of calcium, barium, strontium or magnesium sulphide. It may be used as a paint by mixing it with varnish. If the substance has been exposed to sunlight, it becomes luminous in the dark. *Radio-active substances* are now used for this purpose as they do not require exposure to sunlight to render them luminous and are said to retain this property indefinitely. *Canton's phosphorus* consists of 2 parts of oyster shells and 1 part of sulphur.

Photoxylon.—This is a nitro-cellulose, which is said to be entirely soluble in a mixture of equal parts of concentrated ether and alcohol. According to Beringer, a 3 per cent. solution leaves on evaporation a very tough collodion-like film. *Pho-*

toxylon is made from wood pulp, by methods of nitration similar to those given under pyroxylin, which is its chemical counterpart.

Phyllanthus. *Phyllanthus Niruri* L.—Ottow isolated from this widely distributed euphorbiaceous plant *phyllanthin*, $C_{30}H_{37}O_8$, which crystallizes in colorless needles, is intensely bitter, insoluble in water, but soluble in alcohol, petroleum benzin, chloroform, and ether.

Physalis. *Physalis Alkekengi* L. *Alkekengi. Common Winter Cherry. Alkékenge, Coqueret*, Fr. *Judenkirsche, Schlutte*, G.—A perennial herbaceous plant, belonging to the *Solanaceæ*, growing wild in the south of Europe, cultivated in our gardens and said to be escaping locally. The fruit is a round red berry, about as large as a cherry, enclosed in the inflated calyx, and containing numerous flat kidney-shaped seeds. All parts of the plant are bitter, especially the leaves and the capsules enveloping the fruit. The berries are very juicy, and have an acidulous, bitterish taste. By drying they shrink, and become a brownish-red color. A bitter principle, *physalin*, has been isolated by Dessaignes and Chautard by extracting an infusion of the plant with chloroform. It is a yellowish, bitter powder, very slightly soluble in cold water and freely soluble in alcohol and chloroform, especially with the aid of heat. Its composition is $C_{14}H_{16}O_5$. (*J. P. C.*, 3e sér., xxi, 24.) The berries are said to be aperient and diuretic, and have been recommended in *suppression of urine, gravel*, and other diseases of the urinary passages. Gendron recommends them very highly as a febrifuge. (*A. G. M.*, xxiii, 536.) They also have been highly commended in *gout*. An extract of alkekengi berries to which lithium salt has been added is sold under the name of *lithal*. From six to twelve berries, or half an ounce of the expressed juice, may be taken for a *dose;* and much larger quantities are not injurious. They are consumed to a considerable extent in some parts of Europe as food.

The berries of *Physalis viscosa* L., of this country, are said by Clayton to be diuretic.

Physostigmine Borate. *Eserine Borate.*—This eserine salt is advanced by Merck as possessing the advantage over the sulphate or salicylate of forming permanent aqueous solutions that do not become irritant. Its uses are the same as those of other eserine salts. (See PART I.)

Physostigmine Sulphite. *Eserine Sulphite.* $(C_{15}H_{21}N_3O_2)_2H_2SO_3$.—This salt of physostigmine has been brought forward as being more permanent than either the sulphate or salicylate. Its uses are precisely the same as those of the official salt. (See PART I.)

Physostol.—A sterile solution consisting of 1 per cent. of an eserine salt in a perfectly water-free olive oil. It is used in the treatment of certain *eye diseases* (*glaucoma*, etc.) and also as a myotic.

Phytelephas.—*Phytelephas macrocarpa* Ruiz. and Pav., or *negrito-palm*, of Eucador, yields the *Tagud nut*, from which is derived the hard white substance, *vegetable ivory* or *corajo*. The nuts contain a fixed oil which is said to enter commerce. (*J. P. C.*, xvi.) The ground nuts have been recently used as an adulterant in cattle powders.

Phytin. *Calcium-magnesium Salt of Anhydro-oxymethylene-diphosphoric Acid.* $(C_2H_6O_9P_2)_2Mg\,Ca$.—It is a white powder, slowly soluble in water, of a somewhat acid taste. *Phytin*, which was discovered in 1900 by Posternak (*C. R. S. B.*, lv, p. 1190), who has obtained it from the seeds of the hemp, sun-flower, sesame, peas, beans, and other plants. So universal is its distribution that he believes it an ingredient in all seeds, bulbs, and roots, and that it represents 70 to 90 per cent. of the entire phosphorus content of the plant seeds. It contains 22.8 per cent. of phosphorus. It is a heavy white powder, which when rubbed up with water forms a milky emulsion which is almost without taste.

Phytin was introduced into medicine on the supposition that being an organic form of phosphorus it would be more readily assimilated by the system, but the experiments of Mendel and Underhill (*A. J. Phys.*, 1906, xvii, 75), who find that it is eliminated as an inorganic phosphate, throw grave doubt on this supposition.

The preparation has been employed in *rickets, anemia, tuberculosis, neurasthenia* and other conditions in which phosphorus is useful. It is doubtful, however, whether this preparation possesses any very valuable therapeutic properties. The beginning *dose* is fifteen grains (0.1 Gm.) a day, given in divided doses.

Phytolacca. *N. F. IV* (*U. S. P. VIII*). *Poke Root. Phytolaccæ Radix. Phytolacca Root. Racine de Phytolaque*, Fr. *Kermesbeerenwurzel*, G.—"The dried root of *Phytolacca decandra* Linné (Fam. *Phytolaccaceæ*), collected in the autumn." *N. F.*

The U. S. P. has in the past recognized both the root and the berries of the *Phytolacca decandra* L. This is an indigenous plant, with a large, branching, perennial root, often 20 to 25 cm. in diameter, which is fleshy, fibrous, whitish within, and covered with a thin brownish cork. The stems, which are annual, frequently grow to the height of 6 to 15 dm., and divide into numerous spreading branches, which are green when young, but becoming purple especially in the upper portions after the berries have ripened. The leaves are alternate, ovate-oblong, entire, pointed, smooth ribbed beneath, and on short foot-stalks. The flowers are small and in long racemes. The raceme of flowers becomes a cluster of dark purple, almost black, shining berries flattened above and below, and divided into ten loculi, each containing one seed.

Poke is abundant in all parts of the United States, flourishing along fences, by the borders of woods, in newly cleared fields, and especially in the muck thrown up from the ditches or swamps. It also grows spontaneously in Northern Africa and Southern Europe, where, however, it is supposed to have been introduced from America. Its flowers begin to appear in July, and the fruit ripens in autumn. The magnitude of the poke weed, its large rich leaves, and its beautiful clusters of purple berries, often mingled upon the same branch with the green unripe fruit and the flowers still in bloom, render it one of the most striking of our native plants. The young shoots are much used as food early in the spring, boiled in the manner of asparagus. The ashes of the stems and leaves yield, according to Braconnot, not less than 4.2 per cent. of potassium hydroxide. In the plant the potassium is combined with an acid resembling malic acid. The leaves, berries, and root are used in medicine, but the latter is the most active. It should be dug up late in November, cut into thin transverse slices, and dried with a moderate heat. As its virtues are diminished by keeping, a new supply should be procured every year. The berries should be collected when per-

fectly ripe, and the leaves about the middle of the summer, when the foot-stalks begin to redden.

The berries (*Phytolaccæ Fructus*, U. S., 1890, *Phytolaccæ Baccæ, U. S.*, 1880, *Poke Berry*) contain a succulent pulp, and yield upon pressure a large quantity of fine purplish, red juice. They have a sweet, nauseous, slightly acrid taste, with little odor.

The dried root is "cylindrical, somewhat tapering, sparingly branched, from 3 to 7 cm. in thickness, mostly in transverse or longitudinal slices; externally yellowish-brown, finely longitudinally or spirally wrinkled and thickly annulate with lighter colored, low ridges; fracture fibrous, characterized by alternating layers of fibro-vascular tissue and parenchyma, the layers of the latter being much retracted. Odor slight; taste sweetish, afterwards highly acrid. Phytolacca yields not more than 14 per cent. of ash." *N. F.*

From the analysis of Edward Donnelly, the root appears to contain tannic acid, starch, gum, sugar, resin, fixed oil and lignin, besides various inorganic substances. (*A. J. P.*, xv, 169.) Claussen (*Pharm.*, 1879, p. 466) prepared from the seeds of *Phytolacca decandra*, by extraction with alcohol, evaporation to dryness, and taking up with chloroform or ether, after washing the residue with petroleum benzin, a neutral principle in silky lustrous crystals, insoluble in water, soluble in alcohol, ether, and chloroform, which he named *phytolaccin*. A. Tereil (*C. R. A. S.*, 91, 856) obtained from the berries an acid (*phytolaccic acid*) as an uncrystallizable yellowish-brown mass of gummy consistency. It was soluble in water and alcohol, slightly soluble in ether, of acid reaction, and gelatinizing with hydrochloric and sulphuric acids. W. F. Wagner (*A. J. P.*, 1887, p. 69) found tannin in the berries, but not in the root. W. A. Partee (*A. J. P.*, 1888, p. 123) made a proximate examination of poke root and found crystals deposited from a solution of an alcoholic extract in absolute alcohol; he also discovered traces of tannin, glucose, and indications which pointed to the presence of a glucosidal principle. Frankforter and Ramaley (*A. J. P.*, 1897, 281) have again analyzed the root with care. They find nearly 10 per cent. of a non-reducing sugar, free acid, identified as formic acid, but no certain proof of either alkaloid or glucoside. The very bitter resin amounted to 1 per cent.; *phytolaccine*, an alkaloid, has been said to exist in minute quantities in the root.

Uses.—Phytolacca is emetic, purgative and somewhat narcotic. As an emetic it is very slow in its operation, frequently not beginning to cause vomiting in less than one or two hours after it has been taken, and then continuing to act for a long time upon both the stomach and the bowels. The vomiting produced by it is said not to be attended with much pain or spasm, but narcotic effects have been observed by some physicians, such as drowsiness, vertigo, and dimness of vision. In overdoses it produces excessive vomiting and purging, attended with great prostration of strength, and sometimes with convulsions, and has, in several instances, proven fatal. According to Robert Bartholow, phytolacca causes in the lower animals convulsions and death from paralysis of respiration. It is not fit for use as an emetic, but has been employed as an alterative in *chronic rheumatism, granular conjunctivitis*, and even in *cancer*. Locally it has been used in the form of ointment (a drachm to the ounce) in the treatment of *psora, tinea capitis, sycosis*, and *favus*. It occasions at first a sense of smarting and heat in the parts to which it is applied. Alcohol, diluted alcohol, and water, extract the virtues of the poke root. A fluidextract is included in the National Formulary.

Dose, emetic, ten to thirty grains (0.65–2.0 Gm.), alterative, one to five grains (0.065–0.32 Gm.).

Phytolacca Acinosa Roxb. (Fam. *Phytolaccaceæ.*)—This plant has long been used in Japan as a diuretic, and is said to be violently poisonous. C. Nagai has separated from it an amorphous resin, *phytolaccotoxin*, which appears to be a spinal convulsant, and at the same time stimulant to the circulation, probably through the vasomotor centers. (*Sei-i-kwai. Med. Journ.*, April, 1891.)

Pichurim Beans. *Semen Pichurim. Sassafras Nuts. Fèves Pichurim, Noix de Sassafras*, Fr. *Pichurimbohnen, Sassafrasnüsse*, G.—The seeds of *Nectandra Puchury-major* Nees v. E., and *N. Puchury-minor* Nees (*Ocotea Puchury-minor* Mart.) (Fam. *Lauraceæ*), yielding respectively "*Fabæ Pichurim majores*," or larger pichurim seeds, and "*Fabæ Pichurim minores*," smaller pichurim seeds. The two species are closely allied and both have been known to botanists as *Ocotea Pichurim* H. B. K. (*Laurus Pichurim* Willd.). The trees grow in Brazil, Guiana, Venezuela, and other parts of South America, and are sometimes spoken of as *Brazilian* or *South American Sassafras*. Carson, of the University of Pennsylvania, had specimens of the fruit and other parts of the trees sent him, sufficient to verify the ascription of the *pichurim beans* to this source. (*A. J. P.*, xxvii, 385.) The seeds of commerce usually consist of the separated cotyledons. They are plano-convex, from 3 to 5 cm. in length and nearly 2 cm. in width. Externally they are smooth and blackish-brown, being internally light brown. They have an aromatic odor combining that of nutmegs and sassafras, and a spicy pungent taste.

Pichurim beans contain a concrete volatile oil, a fatty matter of the consistency of butter, besides resin, fecula, gum, sugar, and lignin. The fatty matter, which is known as *pichurim fat*, amounts to about 30 per cent. and contains *laurostearin*, $C_3H_5(C_{12}H_{23}O_2)_3$, and *pichurim camphor* which appears to be identical with *laurel camphor*. A liquid product brought from South America and known as the *native oil of laurel* or *sassafras*, or *aceite de sassafras*, is obtained by incising the trunk of the *Nectandra puchury*. This, as described by Procter (*A. J. P.*, 1851, p. 1) is a reddish oleoresin with a specific gravity of 0.898, a characteristic odor, and an aromatic somewhat camphoraceous taste. It is believed to be the same as that with which the copaiba from Maracaibo is adulterated. It may be distinguished from copaiba by its ready solubility in alcohol of 0.838 and by the fact that its volatile oil is acted on by potassium.

Müller, by distilling the oil in contact with sulphuric acid, obtained a greenish-yellow oil possessing the peculiar odor of the beans. By fractional distillation he separated—1, a colorless oil, boiling at 150° C. (302° F.); 2, a colorless oil, boiling between 165° C. (329° F.) and 170° C. (338° F.); both of these oils consisting principally of hydrocarbons, $C_{10}H_{16}$; 3, a greenish-yellow viscid oil, boiling between 235° C. (455° F.) and 240° C. (464° F.), and having the composition $C_{38}H_{56}O_2$; 4, a deep blue oil, having a faint odor, boiling between 260° C. (500° F.) and 265° C. (509° F.).

In medicinal properties the pichurim beans

resemble the common aromatics, and may be employed for the same purposes. In South America they are said to be used as a substitute for nutmeg, and have even been called by that name. They are rare in this country. The oil obtained from the tree is said to impart its odor to the perspiration and urine, and to be useful in *rheumatism, gout,* etc. The bark is sometimes employed as a tonic and febrifuge.

Picoline. *Alphamethylpyridine. Alphapicoline.* $C_5H_4.N(CH_3)$.—This is obtained by the dry distillation of bones or coal. It is a colorless liquid having a specific gravity of 0.952, and is miscible with both water and alcohol. It has been used as a nerve sedative and to lessen heart action when diseased.

Picrasma. *Picrasma quassioides* (Ham.) Benn. (Fam. *Simarubaceæ.*)—The wood of this tree, which grows in the subtropical Himalayas, and resembles closely the *Ailanthus* in its appearance, has an intensely bitter taste, and has been proposed as a substitute for quassia. W. Dymock and C. J. H. Warden have found in it a crystalline principle which they believe to be quassin, and to exist in the probable proportion of from 0.02 to 0.03 per cent. The same investigators believe that the drug has in it a peculiar alkaloid. (*P. J.*, xx, 1889.) A principle analogous to quassin was isolated by Shimoyamo from the bark of *P. ailantoides.* (*Ap. Ztg.*, 1892, 439.)

Picrol. *Di-iodo-resorcin-potassium-monosulphonate.* $C_6HI_2(OH)_2SO_3K$.—This antiseptic contains about 53 per cent. of iodine. It occurs in colorless and odorless crystals having a very bitter taste, soluble in water, glycerin, and ether. It is used as a substitute for iodoform and corrosive sublimate.

Picrotoxin. *Br.* 1898. *Picrotoxinum.*—"A neutral principle obtained from the fruits of Anamirta paniculata, *Colebr.*" *Br.* 1898. Picrotoxin has not been official in the U. S. P. since 1890. This substance is obtained from *Cocculus indicus* (*Anamirta paniculata*), which see (Part II). The formula $C_{15}H_{16}O_6 + H_2O$ which was fomerly given for picrotoxin belongs, according to Paterno and Oglialoro (*Gazz. Chim.*, ii, 41), to *picrotoxinin,* which with *picrotin,* $C_{15}H_{18}O_7$, is a decomposition product of the original picrotoxin, $C_{30}H_{34}O_{13}$.

Picrotoxin was thus described in the U. S. 1890: "Colorless, flexible, shining, prismatic crystals, or a micro-crystalline powder, odorless, and having a very bitter taste; permanent in the air. Soluble, at 15° C. (59°F.), in 240 parts of water, and in 9 parts of alcohol; in 25 parts of boiling water, and in 3 parts of boiling alcohol; also soluble in solutions of the alkalies, and in acids. Very slightly soluble in ether or chloroform. Picrotoxin is neutal to litmus paper. When heated to 200° C. (392° F.), picrotoxin melts, forming a yellow liquid, and upon ignition it is consumed, leaving no residue. Concentrated sulphuric acid dissolves Picrotoxin with a golden-yellow color, very gradually changing to reddish-brown, and showing a brown fluorescence. On mixing about 0.2 Gm. of powdered sodium nitrate with 3 or 4 drops of sulphuric acid, in a small, flat-bottomed capsule, sprinkling a minute quantity of Picrotoxin over it, and then adding, from a pipette, concentrated solution (1 in 4) of sodium hydrate, drop by drop, until it is in excess, the particles of Picrotoxin will acquire a brick-red to deep red color which fades after some hours. On diluting 2 mils of alkaline cupric tartrate volumetric solution with 10 mils of water, and adding a small portion of Picrotoxin, red cuprous oxide will be separated within half an hour at ordinary temperatures, and much more rapidly upon the application of heat. The aqueous solution of Picrotoxin should remain unaffected by mercuric or platinic chloride test-solution, tannic acid test-solution, mercuric potassium iodide test-solution, or other reagents for alkaloids (absence of *alkaloids*)." *U. S.*, 1890. The Br. 1898 described it as follows: "It melts at 378° F. (192.2 C.). It is soluble in 330 parts of cold or 35 of boiling *water,* and in 13 of cold or 3 of boiling *alcohol* (90 per cent.). It is soluble in 10 parts of *solution of potassium hydroxide,* and the resulting liquid, on boiling, immediately reduces *Fehling's solution.* Heated on platinum foil, the crystals melt, forming a yellowish liquid, which on further heating, becomes charred, and is at length completely dissipated. It dissolves in *sulphuric acid* with a saffron-yellow color. Its aqueous solution is not precipitated by *test-solution of mercuric chloride, solution of platinic chloride,* or *solution of tannic acid* (distinction from alkaloids)." *Br.* 1898. E. Schmidt and Löwenhardt, who made a study of picrotoxin (*Ber. d. Chem. Ges.*, xiv 812), found with it several principles. They identified the easily soluble body *picrotoxinin,* $C_{15}H_{16}O_6$, fusing point from 200° to 201° C. (392° –393.08° F.), and the difficultly soluble anhydrous *picrotin,* $C_{15}H_{18}O_7$, fusing point from 240° to 245° C. (464°–473° F.). Picrotoxinin shows a brick-red color, when tested with the Langley reaction, while picrotin is indifferent in this case. See a paper by Meyer and Bruger, *Ap. Ztg.*, 1899, 67. In Europe, picrotoxin is said to be added to malt liquors in order to give them bitterness and intoxicating properties,—although the practice is forbidden by law, in England, under heavy penalties. Gunckel proposes the following mode of detecting and separating picrotoxin from liquids containing it, founded on the facts that it is soluble in dilute acids though not combining with them, and that ether extracts it from its acid solutions, but not from those in water or alcohol, even in the presence of potassium hydroxide. The substance suspected to contain it, having been brought to the consistence of paste, is to be digested with alcohol and a little tartaric acid, the liquid separated, the alcohol vaporated, the residue diluted with a little water and then treated with ether, and, finally, the ethereal solution submitted to evaporation in a watch glass. Picrotoxin, if present, is deposited, recognizable by its feathery crystallization, its bitter taste, and the property of reducing the tartrate of copper and potassium. If strychnine, which perhaps resembles it most closely in its effects, is present, it will be left behind in the acidulated solution. (*J. P. C.*, 1858, p. 78; from *A. Pharm.*, xciv. 14.) In the instance of adulterated malt liquor, in consequence of the resin of hops it contains, it might be expedient first to evaporate the liquor to dryness, and prepare an aqueous extract of the residue, and then to proceed as stated. J. W. Langley proposes, as a means of detection, the oxidation of picrotoxin. When to a little of this substance, mixed with potassium nitrate in a watch glass, a drop of sulphuric acid is added, no observable reaction takes place; but, if a very strong solution of potassium or sodium hydroxide be now added, a bright reddish-yellow color will be produced, which will be highly characteristic. A very minute quantity may thus be detected. Langley, however, thinks it probable that this phenomenon is owing to a minute quantity of some nitrogenous principle, for

if picrotoxin be purified by combining it in solution with potassium hydroxide, and then precipitating it with an acid, it does not answer the test. (*Am. J. Sci.*, 1862.) To procure picrotoxin, the aqueous extract of the seeds is triturated with pure magnesia, and then treated with hot alcohol, which dissolves the picrotoxin, and yields it upon evaporation. In this state, however, it is impure. To obtain it colorless it must be again dissolved in alcohol, and treated with animal charcoal. After filtration and due evaporation, it is deposited in the crystalline form. Accompanying the picrotoxin in the seeds is *anamirtin*, $C_{10}H_{26}O_{10}$. Possibly identical with this is the *cocculin* of Löwenhardt, to which, however, the formula $C_{19}H_{26}O_{10}$ is given by its discoverer. It does not give any color with the Langley reaction. Besides picrotoxin, *Cocculus indicus* contains a large proportion of fixed oil, and other substances of less interest. In the shell Pelletier and Couërbe discovered two distinct principles,—one alkaline and named *menispermine*, $C_{18}H_{24}O_2N_2$, the other identical with it in composition, but distinguishable by its want of alkalinity, its volatility, and its solubility and crystalline form, and denominated *paramenispermine*. They found also in the shell a new acid, which they called *hypopicrotoxic*. The picrotoxin of Boullay they believed to possess acid properties, and proposed for it the name of *picrotoxic acid*. (*J. P. C.*, xx, 122.) Picrotoxin is a violent poison to all classes of vertebrates, producing when in sufficient dose, violent convulsive attacks with periodic arrest of respiration, slowing of the heart beat, and finally death. An almost characteristic phenomenon is the alternation of clonic and tonic convulsions with a peculiar, almost purposive, movement in the clonic attacks; the motions of swimming, walking, rotation, etc., are usually some or all of them present. In mammals the pupils are usually contracted although later dilated, there is salivation, frequently vomiting, and stupor deepening into coma. The precise mechanism of the convulsive attacks is not known but there appears to be an intense stimulation of the whole central nervous system, including the cerebrum, medulla and spinal cord. The exciting effect upon the medullary centers is shown by the rise in blood pressure due to an action upon the vasomotor center, by the slowing of the pulse from stimulation of the cardio-inhibitory center, by the rapid respirations, and by the emesis. There is salivation, contraction of the pupil, and sweating, also due to an action upon the nerve centers. According to Hayashi (*A. E. P. P.* 1903, l, p. 247) the drug has a marked antipyretic effect even in doses too small to cause convulsions. Koppen (*A. E. P. P.*, 1892, xxix) has found that it is a physiological antagonist to poisons of the chloral group but according to Kóssa (*Ungar. Arch. f. Med.*, 1892, i) it increases the toxicity of morphine. In man picrotoxin acts as it does in the lower animals and a number of cases of serious and even fatal poisoning have been produced by it or the plants in which it is found.

Picrotoxin has been used in various nervous diseases such as *epilepsy*, *hystero-epilepsy* and *chorea*. It has also been used in the treatment of *night sweats;* such effect as it may have in this condition is due to its stimulant action upon the circulation and respiration. Paterson (*S. M.*, 1907) recommends it for the prevention of post-anesthetic *vomiting*. *Dose*, from one-hundredth to one-thirtieth of a grain (0.0006 to 0.002 Gm.).

Pilocarpine Phenate. $C_{11}H_{16}N_2O_2OHC_6H_5$.—This is an oily liquid soluble in alcohol and water. It is used in the treatment of *malaria* and *tuberculosis*. The following *dosage* is recommended for hypodermic use: 1 drachm (4 mils) of a 0.02 per cent. aqueous solution to which 2.5 per cent. phenol is added, injected once daily, and the quantity is increased by 8 minims (0.5 mil) daily until a maximum *dose* of two drachms (8 mils) is reached.

Pimenta. *N. F. IV* (*U. S. VIII*). *Allspice. Pimento. Semen Amomi. Piper Jamaicense. Pimento. Allspice. Jamaica Pepper. Piment de la Jamaïque, Toutepice, Poivre de la Jamaïque,* Fr. *Englisches Gewürz, Neugewürz, Nelkenpfeffer,* G. *Pimenti,* It. *Pimienta de la Jamaica, Sp.*—"The dried, nearly ripe fruit of *Pimenta officinalis* Lindley (Fam. *Myrtaceæ*), without the presence of more than 5 per cent. of stems or other foreign matter." *N. F.*

Pimenta was dropped from the U. S. and Br. Pharmacopœias but admitted to the National Formulary IV.

The tree yielding pimenta is a native of the West Indies, Mexico, and South America, and is abundant in Jamaica, whence its fruit received the name of *Jamaica pepper*. The allspice plant is cultivated in Central America and the surrounding countries, but more than half the supply to the United States comes from Jamaica, where the tree is so abundant as to form in the mountainous districts whole forests, and to require no further cultivation than the clearing out of the underbrush. The berries are gathered after having attained their full size, but while yet green, and are carefully dried in the sun. When sufficiently dry, they are put into bags and casks for exportation. The fruits of four other species of the genus *Pimenta*, found in Venezuela, Guiana, and the West Indies, are employed in their native countries as spices.

It is described by the *N. F.* as: "Sub-globular, from 4 to 7 mm. in diameter, summits with four calyx teeth forming a minute ring; externally dark brown, somewhat rough and glandular-punctate; pericarp brittle, about 1 mm. in thickness; two-celled and two-seeded; dissepiments thin; seeds plano-convex, slightly reniform, externally reddish-brown, smooth, somewhat wrinkled and shiny. Odor and taste, particularly of the pericarp, aromatic and distinctive. The powder is reddish-brown or dark brown and, when examined under the microscope, shows irregular fragments and numerous starch grains, the latter being either simple or compound, the individual grains spherical, from 0.003 to 0.015 mm. in diameter, plano-convex or polygonal, and frequently with a central circular marking or cleft; stone cells numerous, of tabular, pyriform or variable shape and with thick, porous, and strongly lignified walls, the lumina frequently filled with a yellowish- or reddish-brown amorphous substance, fragments with oil secretion reservoirs containing globules of a yellowish-brown oil; parenchyma cells with reddish-brown tannin masses. Stem fragments very few, and characterized by more or less curved, thick-walled, non-glandular hairs, rosette aggregates of calcium oxalate, from 0.006 to 0.017 mm. in diameter, tracheid-like tissues of the wood and long narrow bast fibers. The yield of crude fiber does not exceed 25 per cent. when estimated as directed in the U. S. Pharmacopœia (see U. S. P., Test No. 11, Part III). Pimenta yields not more than 6 per cent. of ash." *N. F.*

The odor of Pimenta berries is thought to re-

semble that of a mixture of cinnamon, cloves, and nutmeg. Hence the name of *allspice*, by which they are best known in this country. They impart their flavor to water, and all their virtues to alcohol. The infusion is of a brown color, and reddens litmus paper.

Pimenta yields a volatile oil by distillation having the sp. gr. of from 1.04 to 1.05 at 15° C. (59° F.). (See *Oleum Pimentæ.*) Bonastre obtained from them a volatile oil, a green fixed oil, a fatty substance in yellowish flakes, tannin, gum, resin, uncrystallizable sugar, coloring matter, malic and gallic acids, saline matters, moisture, and lignin. The green oil has the burning aromatic taste of pimenta, and is supposed to be the acrid principle. Upon this, therefore, together with the volatile oil, the medicinal properties of the berries depend, and, as these two principles exist most largely in the shell or cortical portion, this part is most efficient. According to Bonastre, the shell contains 10 per cent. of the volatile and 8 of the fixed oil, the seeds only 5 per cent. of the former and 2.5 of the latter. Berzelius considered the green fixed oil of Bonastre as a mixture of volatile oil, resin, fixed oil, and perhaps a little chlorophyll. Dragendorff, in 1871, announced the existence of an alkaloid in allspice. It is present in exceedingly small quantity, and has somewhat the odor of coniine. W. W. Abell obtained from 448 Gm. of pimenta leaves one-half of one per cent. of volatile oil resembling oil of bay; he also found tannic acid. (*A. J. P.*, 1886, 163.) A convention of hygienists at Vienna decided that ground allspice should not yield more than 6 per cent. of ash, of which not more than 0.5 per cent. should be soluble in hydrochloric acid.

Pimenta is sometimes adulterated by the larger and less aromatic berries of the Mexican *Myrtus Tobasco* Mocino.

Uses.—Pimenta is an aromatic spice, used in medicine chiefly as an adjuvant to tonics and purgatives. It is particularly useful in cases attended with much *flatulence*. It is, however, much more largely employed as a condiment than as a medicine.

It is one of the ingredients in compound tincture of guaiac of the National Formulary IV. *Aqua Pimentæ* Br., 1898, was formerly official—it was a distilled water.

Dose, ten to forty grains (0.65–2.6 Gm.).

Pimento Water (*Aqua Pimentæ*). *Eau de piment de la Jamaïque*, Fr.; *Nelkenpfefferwasser*, G.—It was prepared by the Br. 1898 as follows: "Pimento, bruised, 8 ounces (Imperial) or 250 grammes; water, 2 gallons (Imp. meas.) or 10 litres. Distil one-half." *Br.*, 1898. Pimento water is an agreeable aromatic water, used as a vehicle.

Pimpinella. *N. F. IV. Pimpernel Root. Pimpinella Saxifraga* L. *Small Burnet Saxifrage. Saxifraga. Radix Pimpinellæ*, P. G. *Grand Boucage*, Fr. *Pimpinell, Bibernell*, G.—"The dried rhizome and roots of *Pimpinella Saxifraga* Linné, or *Pimpinella magna* Linné (Fam. *Umbelliferæ*)." *N. F.*

This is a perennial umbelliferous European plant growing on sunny hills, and in dry meadows and pastures. It is also naturalized, growing along roadsides and in waste places in the northern United States and Canada. The root has a strong, aromatic, yet unpleasant odor, and a sweetish, pungent, biting, aromatic, bitterish taste. Pimpinella is described by the N. F. as "cylindrical or slightly tapering, from 10 to 20 cm. in length and from 1 to 1.5 cm. in diameter at the crown, frequently branching, sometimes split longitudinally or broken into pieces; the upper or rhizome portion annulate, with undeveloped stem buds and a few attached stem remains which should not be over 5 cm. in length; roots longitudinally wrinkled, slightly annulate, cortex thin, easily detached; fracture short when dry, tough and flexuous when damp; externally light yellowish-brown; internally porous; cortex broad and whitish with numerous groups of projecting radial bast fibers and reddish-brown oleoresin cells; wood yellowish, usually with a few indistinct fibers, medullary rays interrupted, cambium zone distinct. Odor aromatic; taste sweetish, pungent and acrid.

"The powdered drug, when examined under the microscope, shows numerous simple or two- to four-compound starch grains, the individual grains being from 0.004 to 0.01 mm. in diameter; secretion canals from 0.05 to 0.06 mm. in diameter; tracheæ reticulate or scalariform, from 0.035 to 0.07 mm. in breadth; fibers, thin-walled numerous, thick-walled with simple pores few (*P. magna*).

"Pimpinella yields not more than 5 per cent. of ash." *N. F.*

Its active constituents are volatile oil and an acrid resin. The yellow volatile oil has an odor recalling parsley, and a biting taste. Buchheim obtained from the alcoholic extract a crystalline principle, which he called *pimpinellin*, $C_{13}H_{10}O_5$. It is insoluble in water and petroleum ether, but soluble in alcohol. It is considered diaphoretic, diuretic, and stomachic, and has been used in *chronic catarrh, asthma, dropsy, amenorrhea*, etc. The *dose* in substance is about half a drachm (2.0 Gm.), and in infusion two drachms (7.7 Gm.). The root is used also as a local stimulant in toothache, etc.

Pinckneya. *Pinckneya pubens* Rich. *Fever Tree.* (Fam. *Rubiaceæ.*)—A large shrub or small tree, growing in South Carolina, Georgia, and Florida, in low and moist places along the seacoast. It is botanically allied to the *Cinchonas*. The bark is bitter and has been used with alleged advantage in *intermittent fever*. E. H. Naudain (*A. J. P.*, April, 1885) found in it a glucoside, *pinckneyin*, but no alkaloid.

Pineapple. *Ananas sativa* Schult. f. (Fam. *Bromeliaceæ.*)—Some years ago V. Marcano discovered that the juice of the ordinary *pineapple* has the power of digesting proteid vegetable and animal substances. R. H. Chittenden (*Trans. Connecticut Academy*, vol. viii, 1891) found that the fresh pineapple juice is a very constant and powerful digestant of albuminous matters; that the ferment is decidedly active in the presence of either acids or alkaline carbonates, but is most energetic in neutral solution; that the ferment is most active between 50° and 60° C. (122° and 140° F.); still digests at 30° C. (86° F.), but is destroyed at a temperature of 70° C. (158° F.); that the digestion takes place with rapidity; that the ferment, to which the name *bromelin* has been given, is more nearly related to trypsin than to pepsin, forming during its action not only proteoses and peptone, but also leucine and tyrosine.

E. V. Flack subjected pineapples grown in Cape Colony to analysis. He found in the fresh fruit: Crude fat 1.11 per cent., proteins 0.49 per cent., crude fiber 0.33 per cent., nitrogen-free extract 13.51 per cent., ash 0.70 per cent., silica 0.069 per cent., lime 0.047 per cent., potash 0.358 per cent., phosphoric oxide 0.024 per cent., and moisture 83.86 per cent. (*Chem. News*, 1912, 99.)

Pinguicula Vulgaris and **Pinguicula Alpina** L. (Fam. *Lentibuliariaceæ.*)—These perennials of the

northern United States and Canada are used as a folk medicine in the treatment of wounds and as a purgative. It has been asserted that *P. vulgaris* contains a proteolytic ferment; this has been used in combination with the extract of thyme in the treatment of whooping-cough under the name of "*diatussin.*" The *dose* of diatussin for a child of five years is one to three drops twice a day.

Pini-Pini. *Arra Diabo.*—This is the bark of *Jatropha urens* (Fam. *Euphorbiaceæ*).—This Brazilian plant has been long used by the natives of Southern America as a blistering agent. Very little is known of its constituents and it is but lately that it has come into notice as a caustic and blistering medium.

Pinosal.—This is a distillate from tar which occurs as a brownish-yellow liquid about the consistency of honey. It is insoluble in water but dissolves in strong alcohol and the various organic solvents. It is used as a local application in much the same way that tar is in various *skin diseases* in strengths of from 5 to 20 per cent.

Piper Novæ-Hollandiæ Miq. (Fam. *Piperaceæ.*)—The berries of this Australian pepper contain a volatile oil, and are said to be useful in *gonorrhea* and allied diseases.

Piper Ovatum Vahl.—From the leaves of this plant, found growing in Trinidad, Dunstan and Carr (*Chem. News*, 1895, 278) extracted a crystalline principle, *piperovatine*, $C_{16}H_{21}NO_2$. It is insoluble in water, but soluble in alcohol. It is said to act as a depressant of both motor and sensory nerves, and as a stimulant to the spinal cord.

Piperazine. *N. N. R.* 1917. *Arthriticine. Diethylenediamine. Piperazidine.* $N_2\left\{\begin{matrix}H_2+6H_2O\\(C_2H_4)_2\end{matrix}\right.$.—This is formed by the action of ammonia upon ethylene bromide or chloride. A mixture of bases from this reaction is fractionated, and from the fraction boiling between 130° and 180° C. (266°–356° F.), the diethylenediamine separates on cooling. It forms glassy lustrous tables, melting at from 104° to 107° C. (219.2°–224.6° F.), and boils at 145° C. (293° F.). Both the free base and the hydrochloride are very soluble in water. The latter crystallizes in silky, lustrous, lanceolate forms. *Piperazine* has an alkaline taste and reaction and a weak but characteristic odor. It is very soluble in water and slightly less so in alcohol. Exposure to air is said to cause its eventual decomposition, due to the fact that it absorbs carbon dioxide from the air. It is strongly alkaline and combines with acids to form salts, and is incompatible with alkaloids; almost all oxidizing agents decompose it. Iron salts or compounds precipitate it from solution and when triturated dry with acetanilid, phenacetin or antipyrine it forms a liquid compound. In experiments made by Bock upon rabbits, no evidences of stimulating properties could be obtained. The blood pressure was never increased, but if the dose were large enough was temporarily depressed. In a cold aqueous solution it is said to dissolve twelve times as much uric acid as will lithium carbonate, and one part of uric acid and piperazine dissolves in fifty parts of water, while lithium urate requires three hundred and sixty-eight times its own weight to dissolve it.

Piperazine was introduced into medicine because its power of dissolving uric acid in the test tube led to the hope that it would exercise a similar solvent action in the system, and prove a valuable remedy, not only in the treatment of uric acid *gravel* and *calculi*, but also in *gout*. While it enjoyed for a period a wide popularity in the treatment of uric acid diathesis, the light of time has thrown much doubt as to its real value in these conditions. When taken by the mouth only a portion of it appears in the urine unchanged, so that the oral administration is not likely to prove useful in cases of the deposit of uric acid in the bladder. Nor has it manifested very great activity in dissolving power upon the deposits of uric acid in the joints. As far as its general effects upon the system are concerned, it has but slight action. Van der Klip has found that in lower animals, in sufficient dose, it produces vomiting, irregular breathing, general muscular weakness, and relaxation; that it also decreases the coagulability of the blood, and has power in checking the action of peptonizing ferments. He further states that it decreases the evolution of oxygen by oxyhemoglobin. Umpfenbach found it to be a powerful diuretic and even recommends it in dropsies. In *stone*, injections of piperazine into the bladder are worthy of trial. During the taking of piperazine the urine usually is reddish-brown, and the drug can be readily obtained from the urine by methods which are detailed in *N. R.*, 1892. Piperazine may be given hypodermically in a 2 per cent. solution, which is said to produce some pain but no abscesses; or, better, fifteen grains (1.0 Gm.) of it may be administered during the day in a quart of plain or carbonated water. It is so hygroscopic that it cannot well be given in pill or powder.

Under the name of *ichthyolidin* the ichthyolate of piperazine has been proposed as a more effective method of administering this drug.

Piperazine Quinate. *Sidonal. N. N. R.* 1917. This is introduced with the idea of combining the powers of quinic acid, which hastens uric acid elimination, with the solvent properties of piperazine. It is a white crystalline powder with a faintly acid reaction, readily soluble in water. It is used in *gout* and in *neurasthenia* in *doses* of from ten to twenty grains (0.65–1.9 Gm.).

Piperine. *Piperina. U. S. VIII. Piperin, Piperinum. Pharm.* 1890. *Pipérine*, Fr. *Piperin*, G. $C_{17}H_{19}O_3N = 285.16$.—"A feebly basic substance [$CH_2O_2.C_6H_3.CH:CH.CH:CH.CON.C_5H_{10}$] obtained from Pepper and other plants of the *Piperaceæ.*" *U. S. VIII.*

It will be observed that the official title of this principle was changed in the U. S. P. VIII to "Piperinia," thus restoring it to the class of alkaloids. It has never been claimed by chemists that piperine had all the properties of the alkaloids as a class; it was described as a "principle of feebly alkaloidal power" in the U. S. P., 1880, and this view has been retained in the U. S. P. VIII.

Piperine was discovered by Œrsted of Copenhagen, who considered it to be the active principle of pepper. Pelletier, however, denied its medicinal activity, and ascribed all the effects supposed to have been obtained from it to a portion of the acrid concrete oil with which it is mixed when not very carefully prepared. It is obtained by treating pepper with alcohol, evaporating the tincture to the consistence of an extract, submitting the extract to the action of an alkaline solution by which the oleaginous matter is converted into soap, washing the undissolved portion with cold water, separating the liquid by filtration, treating the matter left on the filter with alcohol, and allowing the solution thus obtained to evaporate spontaneously or by a gentle heat. Crystals of piperine

are deposited, and may be purified by alternate solution in alcohol or ether, and crystallization. Piperine may be regarded as a *piperidine*, $C_5H_{11}N$, in which one H is replaced by the radical of *piperic acid*, thus: $C_5H_{10}N.C_{12}H_9O_3$. Piperine does not yield salts with acids. (*Buchner's Neues Rep.; A. J. P.*, Oct., 1876.) Rügheimer (*A. J. P.*, Aug., 1882, 397) has regenerated piperine by the union of piperidine and the chloride of the radical of piperic acid, thus making piperine artificially. The properties of this artificial principle are identical with those of the natural piperine.

Piperidine is a powerful volatile alkaloid, soluble in all proportions in water and alcohol, and forming crystalline salts with acids. It is one of the decomposition products of piperine and is of great chemical interest as being a simple derivative of pyridine, C_5H_5N, which seems to underlie the molecular structure of so many alkaloids. Piperidine is *hexahydropyridine*, $C_5H_{11}N$, and can be easily obtained from pyridine by the action of tin and hydrochloric acid, or when sodium acts upon the alcoholic solution. Conversely, piperidine can be changed into pyridine when sulphuric acid at 300° C. (572° F.) or gentle oxidizing agents act upon it. Coniine, it will be remembered (see *Conium*), has been shown synthetically to be a normal propyl-piperidine.

Properties.—When perfectly pure, piperine is in colorless transparent crystals, without taste, with no perceptible action on litmus paper, and fusible at 128° to 129.5° C. (262.4°–265° F.) (Rügheimer, *A. J. P.*, Aug., 1882, p. 397), capable of being sublimed under favorable circumstances in perfect crystals (Waddington, *P. J.*, March, 1868, p. 415), insoluble in cold water, slightly soluble in boiling water which deposits it upon cooling, soluble in alcohol, ether, and acetic acid, and still more readily in chloroform, benzene, and petroleum benzin, decomposed by the concentrated mineral acids, with sulphuric becoming of a blood-red color, with nitric first of a greenish-yellow, then orange, and ultimately red. As ordinarily procured, the crystals are yellow. Piperine is generally believed to be a weak alkaloid of the formula $C_{17}H_{19}O_3N$. When boiled with strong solution of potassium hydroxide or heated with soda-lime it is converted into *piperic* (*piperinic*) *acid*, $C_{12}H_{10}O_4$, and *piperidine*, $C_5H_{11}N$.

It was officially described as "colorless or pale yellowish, glistening, monoclinic crystals, odorless, permanent in the air, and containing no water of crystallization. When put into the mouth, it is at first tasteless, but on prolonged contact it develops a sharp, biting taste. It is optically inactive. Insoluble in water; soluble in 15 parts of alcohol, 36 parts of ether, and in 1.7 parts of chloroform at 25° C. (77° F.); soluble in 4.4 parts of alcohol at 60° C. (140° F.). It melts at 130° C. (266° F.). Upon ignition, it emits alkaline vapors, and is completely consumed. Its alcoholic solution is neutral to litmus paper. Sulphuric acid dissolves Piperine with the formation of a blood-red color, which disappears on dilution with water. On heating Piperine with alcoholic potassium hydroxide, it is converted into piperinic acid and piperidine, the latter recognizable by its alkaline, pepper-like odor, and the former by its melting point, 215° C. (419° F.). On adding a crystal of Piperine to sulphuric acid containing about half its volume of solution of formaldehyde, a permanently green liquid is formed. On adding a crystal of Piperine to sulphuric acid containing a fragment of potassium dichromate, it at once acquires a purple color, and, on stirring, dissolves, forming a reddish-brown solution, which becomes greenish on adding water to it. On adding a crystal of Piperine to sulphuric acid containing a trace of selenous acid, it turns brown, changing at once to violet, and dissolves, forming a brown solution changing to green. When heated with nitric acid, Piperine is colored at first orange, then red, and the acid acquires a yellow color, deepening to reddish as the crystals dissolve. On adding to this solution an excess of potassium hydroxide T.S., the color is at first yellow, but upon boiling, it become blood-red." *U. S. VIII.* (See *Piper*, p. 867.)

Piperine appears to possess some feeble antiperiodic powers, but is rarely employed, unless in conjunction with more potent remedies.

Dose, three to five grains (0.2–0.32 Gm.).

Pipi Root.—The root of the *Petiveria alliacea* L. (Fam. *Phytolaccaceæ*), which more than sixty years ago attracted notice in Europe, is said to have re-entered commerce. It is described as consisting of irregularly bent pieces, 3 to 6 mm. thick, externally grayish-brown, upon transverse section showing a brownish bark with white dots, and a lighter colored radiating ligneous wood. The cork layer consists of 3 or 4 rows of cells, the thick primary bark encloses crystals of calcium oxalate; the woody cord contains tracheids with narrow dotted tracheæ, two-rowed medullary rays and in the center a thin pith. The genus *Petiveria* grows in tropical America, extending into Mexico and Texas. The shrubby plants are mostly acrid and have an alliaceous odor. It is reported to be a stimulant, expectorant and diaphoretic. (*A. J. P.*, Aug., 1887.)

Piscidia. *Piscidia Erythrina* L. *Jamaica Dogwood. Dogwood Bark. Ecorce du Bois de chién. Écorce de Piscidie. Mulungu. Murungu.*—This is a leguminous tree growing throughout the West Indies and the neighboring countries, being found in Florida, Texas, Mexico, and the northern portion of South America, and yielding to commerce a very valuable wood. From time immemorial the bark has been used for catching fish. The leaves, twigs, and root bark are collected, macerated with the residue from the distillation of rum or with lime water, then transferred into baskets, and the latter dragged up and down the water until the fish are stupefied.

In 1844 William Hamilton called the attention of the profession to the plant (*P. J.*, Aug., 1844) as a powerful narcotic and analgesic. The bark of commerce is in pieces of 5 to 10 cm. in length and about 8 cm. in width, having a thickness of 1.5 cm. The outer surface of some of the pieces is of a dark gray-brown, while others are of a yellow-brown, with no shade of gray present. The bark is frequently studded with flattened protuberances of a lighter color than the surrounding cork. The central part of the bark is much lighter colored, and, when wet or freshly broken, is of a peculiar blue-green color. The inner part of the bark is of a dark brown color and very fibrous. It has a strong odor resembling opium when broken into pieces. It is acrimonious, and produces a burning sensation in the mouth and pharynx.

E. Hart obtained a neutral principle, $C_{29}H_{24}O_8$, to which he gave the name *piscidin*. (*A. J. P.*, 1883, 369; see also *Ibid.*, Sept., 1898.) Paul C. Freer and A. M. Clover have examined Hart's piscidin and found it to consist of two distinct chemical compounds. The first of these forms colorless, highly refracting rectangular prisms, melting at 201° C. (393.8° F.); composition

$C_{23}H_{20}O_7$. The second separates from alcohol in fine yellow needles, melting at 216° C. (420.8° F.); composition $C_{22}H_{18}O_6$. The authors found also in the aqueous extract of the bark *piscidic acid*, soluble in water; insoluble in chloroform, benzene or ligroin. It forms acicular crystals, which melt at 182° to 185° C. (359.6°–365° F.); composition $H_2.C_{11}H_{10}O_7$. (*A. Pharm.*, Feb., 1901.)

The action of the drug upon the lower animals has been studied by J. Ott and A. C. Nagle with similar results. (*Jamaica Dogwood*, Parke, Davis & Co., 1881.) The conclusions reached are, 1. It is narcotic to frogs, rabbits, and men. 2. It does not affect the irritability of the motor nerves. 3. It does not attack the peripheral ends of the sensory nerves. 4. It reduces reflex action by a stimulant action on the centers of Setschenow. 5. It produces a tetanoid state by a stimulant action on the spinal cord, and not by a paralysis of Setschenow's centers. 6. It dilates the pupil, which dilatation passes into a state of contraction upon the supervention of asphyxia. 7. It is a salivator. 8. It increases the secretion of the skin. 9. It reduces the frequency of the pulse. 10. It increases arterial tension by stimulation of the vasomotor center. 11. This increase of pressure is soon succeeded by a fall, due to a weakening of the heart itself.

The exact practical value of the drug has not been determined, nor are the results produced in man, by doses approaching toxic, known. Hamilton took a drachm, when suffering with severe toothache, on going to bed. He first felt a violent sensation of heat internally, which gradually extended to the surface, and was followed by profuse perspiration, with profound sleep for twelve hours. On awaking, he was quite free from pain, and without the unpleasant sensations which follow a dose of opium. Various practitioners have reported good results from its use as an anodyne in *neuralgia, nervous insomnia, whooping cough*, etc., but in other hands it has failed to do good. H. C. Wood found it in one case of neuralgia to produce great nausea and gastric distress without evincing the slightest narcotic effect. (For formula for fluidextract by Lemberger, see *U. S. D.*, 19th ed., p. 1616; also *D. C.*, 1881, 179.) The *dose* of the fluidextract is a fluidrachm (3.75 mils), to be carefully increased.

Pithecolobium.—*Pithecolobium Saman* Benth. (Fam. *Leguminosæ*.)—A shade-tree, growing from Mexico to Brazil, and planted for shade in Japanese coffee plantations, which yields a poisonous alkaloid, *pithecolobine-saponin*, whose physiological action is analogous to that of sapotoxin.

Pittylen.—*Pittylen* is a mixture of pine tar with formaldehyde. It occurs as a brownish-yellow powder with an odor somewhat suggesting that of tar, and soluble in 9 parts of strong alcohol, and also in dilute alkalies, soap solution, acetone, and collodion.

This product has been used by Hadtke (*D. M. W.*, 1909) in the treatment of various *skin diseases*, such as *pityriasis, eczema, scabies, acne* and *pruritus*. It may be applied either in the form of a paste containing 5 to 10 per cent. of pittylen or the agent may be dissolved in acetone and painted over the diseased area.

Pixol is a form of wood tar, soluble in water, made by warming three parts of wood tar and one part of green soap together and gradually adding three parts of a 10 per cent. solution of potassium hydroxide with stirring. It is a clear dark brown syrupy liquid. The disinfecting power of a 5 per cent. solution is said to be not less than that of a 5 per cent. solution of phenol.

Plantain. *Plantago major* L. *Rib Grass. Ribwort. Ripple Grass. Plantain*, Fr. *Wegerich*, G. (Fam. *Plantaginaceæ*).—The leaves are saline, bitterish, and acrid to the taste; the root is saline and sweetish. The common plantain weed was formerly considered refrigerant, diuretic, deobstruent, and somewhat astringent. The ancients esteemed it highly, but it is at present never used, except externally in domestic practice as a stimulant application to sores. The leaves are applied whole or bruised in the form of a poultice. *Plantago media* L., or *hoary plantain*, and *P. lanceolata* L., or *rib grass*, which are also naturalized in America, possess properties similar to those of *P. major*, and may be used for the same purposes.

For results of examination of the leaves of *P. major*, see Rosenbaum (*A. J. P.*, 1886, 418.) J. F. Strawinski found in the rhizome a substance which he believes to be either phlobaphene or protocatechuic acid. (*A. J. P.*, 1898, 189.)

Bourdier (*A. Pharm.*, ccxlvi) has found in a number of species of *plantago*, including the *P. major*, a glucoside *aucubin*, which was isolated from the *Aucuba japonica*.

Semen psyllii is the name given to the seeds of several species of European *Plantago*. The best are those of *Plantago Psyllium* L., or *fleawort*, which grows in the south of Europe and in Northern Africa. They are ovoid, about 3 mm. in length, and 1 to 1.5 mm. in width, convex on one side, concave on the other, dark-brown and on flat side reddish-brown, shining, inodorous, and nearly tasteless, but mucilaginous when chewed. They are demulcent and emollient, and may be used internally and externally in the same manner as flaxseed, which they closely resemble in medicinal properties. *Spogel seed*, used in India as a demulcent in intestinal irritation, is derived from *P. Isphagula* Roxb., probably a variety of *P. ovata* Forsk. (See *Journ. Méd. de Paris*, Sept., 1887.)

Plasmon.—The freshly precipitated casein of skimmed milk, after mixing with a slight amount of sodium bicarbonate is kneaded and dried at a temperature of 70° C. (158° F.), in an atmosphere of carbonic acid gas. It contains a large amount of proteids and is asserted to be a highly nutritious and palatable food for convalescents and invalids.

Platinum. *Platine, Orblanc*, Fr. *Platin*, G.—*Platinum* and its salts are of much importance for various chemical manipulations. The *platinum sponge* is an active catalyzing agent, and is used for various oxidation processes. *Colloidal platinum*, formed by the action of an electric arc between platinum wires under water, forms in water a deep black liquid, which has a strong catalytic effect, resembling in many respects the action of organic ferments. Under the name of *platinum chloride* there is used to a wide extent as a precipitant for alkaloids, and for various other chemical purposes, *chloroplatinic acid*, $H_2PtCl_6.6H_2O$. This is made by dissolving the metal in nitro-hydrochloric acid, and evaporating with hydrochloric acid until all the nitric acid is removed. *Platinum tetrachloride*, $PtCl_4.5H_2O$, may be obtained by mixing an aqueous solution of chloroplatinic acid with a solution of silver nitrate; a precipitate containing the silver, combined with some platinum and chlorine, separates, and the yellowish-red solution yields on evaporation fine, large, red crystals of platinum chloride. Under the name of *bichloride of platinum*, the double *chloride of platinum and*

sodium was formerly used in medicine to a small extent in the treatment of *syphilis*, but has been abandoned. When injected into the circulation in *doses* of fifteen to thirty grains, the soluble salts of platinum cause in the lower animals a primary stage of motor excitement, followed by paralysis of the central nervous system and later of the muscles themselves. The *dose* of platinum and sodium chloride is from one-half to two grains (0.032–0.13 Gm.) two or three times a day, generally in pill form.

Pleiapyrin.—This antipyretic drug is the condensation product of benzamide and phenyldimethyl pyrazolon. It is a white, odorless, very soluble powder possessing a bitter taste; melting point 75° C. (167° F.). It is used as an antipyretic or analgesic in *doses* of fifteen grains (1.0 Gm.) several times daily.

Plevacol.—This is a mixture of tri-cresol, formalin and *amido-benzoyl-eugenol*, which is employed in dentistry for the purpose of filling roots and capping amputated pulp. It forms yellowish-white, or colorless crystals, melting at 155° to 156° C. (311°–312.8° F.), soluble in acetone, benzol, alcohol, and in glacial acetic acid on warming.

Plumbago Europea L. *Leadwort. Dentellaria.* (Fam. *Plumbaginaceæ.*)—A perennial, herbaceous plant, growing in the south of Europe. It has an acrid taste, and, when chewed, excites a flow of saliva. This is particularly the case with the root, which has been long used to relieve toothache; hence its French name *dentelaire*. A decoction of the root in olive oil has been highly recommended for *itch*. A crystallizable, acrid principle, called *plumbagin*, has been extracted from the root by Dulong. (*J. P. C.* (2), xiv, 441.) *Plumbago zeylanica* is said to be a very powerful diaphoretic.

Plumiera. *Pagoda Tree.*—The bark of *Plumiera sucuuba Spruce* (Fam. *Apocynaceæ*), a plant growing in South America which the natives of Brazil have long used in the treatment of fevers. It is asserted also to be an anthelmintic and emmenagogue. Plumier, the French botanist, first brought this plant to the attention of the medical profession. The important constituents of the plant are *Plumierin* (*agoniadin*), $C_{21}H_{26}O_{12} + H_2O$, and *plumieric acid*, $C_{20}H_{24}O_{12}$. The *P. acutifolia*, said to contain an alkaloid, $C_{57}H_{72}N_{33}$, has been used in the treatment of *gonorrhea*.

Pneumin. *Methylene Creosote.*—This is a yellowish, odorless, tasteless powder obtained by the action of formaldehyde upon creosote, freely soluble in alcohol and ether; insoluble in water. It is supposed to be a mixture of the methylenic compounds of phenols of beech tar and their ethers, and has been recommended by Jacobson in the treatment of *tuberculosis* and in *pulmonary catarrh*. According to Eschbaum (*M. M. W.*, 1909, p. 239) it exercises no influence upon the cough or expectoration, but is valuable because of its increasing the appetite. The *dose* is from eight to fifteen grains (0.5–1.0 Gm.) three times a day.

Pollantin (Fall). *Dunbar's Serum.*—A hay fever serum prepared by introducing the pollen of golden rod and other plants into the blood of animals. After a certain period of time, blood is drawn and from this the serum is prepared. While the claims made for this product by its manufacturers are no doubt exaggerated, yet clinical evidence has proven it to be of value in some cases. It is used by instillation in the eye and nostrils, and not intended for hypodermic use. This serum may also be obtained in powder form, which is merely the evaporated serum powdered and diluted with milk sugar. The *dose* is the same as that of the liquid.

Polygala. *Polygala polygama* Walt. (*P. rubella* Muhl.) (Fam. *Polygalaceæ.*) *Bitter Milkwort. American Bitter Polygala. Polygale, Laitier*, Fr. *Kreutzblume, Milchwurz*, G.—Bitter *polygala* is an indigenous, perennial plant, which was formerly official. It has a strong and permanent bitter taste, which it yields to water and alcohol. In small doses bitter polygala is tonic, in larger, laxative and diaphoretic. It appears to be closely analogous in medicinal virtues to *Polygala amara* L., of Europe, which is used for a similar purpose. From the seeds of the *P. butyracea* Heck. and Schlag., an African plant, the natives prepare an edible fat. (See *P. J.*, xx, Aug., 1889.)

Polymnia. *Polymnia uvedalia* L. *Bear's Foot.* (Fam. *Compositæ.*)—A tall, branching plant, growing in rich soil from New York to Missouri and southward. Great virtues as a remedy in *malarial splenic enlargements* have been attributed to this plant.

Polypodium. *Polypody. Fern Root.*—Various species of this genus of ferns are asserted to have medicinal properties. *Polypodium vulgare* L., very common both in Europe and America, was believed by the ancients to be an active cholagogue purgative, and has been used in modern times as an expectorant in chronic *catarrh* and *asthma*. *Dose*, from one to eight drachms (3.9–31 Gm.), usually given with a cathartic. The rhizome, as it usually occurs in commerce, is from 2 to 12 cm. in length and 3 to 8 mm. in thickness, somewhat contorted, covered with brown, easily separable scales, which should be removed before being used. Its color is reddish-brown, with a tinge of yellow, its odor disagreeably oleaginous, its taste peculiar, sweetish, somewhat bitter, and nauseous. *P. adiantiforme*, of Porto Rico, is believed by the natives to be a powerful antisyphilitic. It must be used freely for several months in the advanced stages of the disease. *P. friederichsthalianum*, of Central America, has had similar properties attributed to it.

Polytrichum. *Polytrichum juniperinum* Hedw. (Fam. *Polytrichaceæ.*) *Herba Adianti Aurei. Rock-brake Herb. Female Fern Herb. Perce Mousse. Frauenhaar. Jung Fernhaar. Widertot. Wolfgerste. Hair Cap Moss. Robin's Rye. Golden Maidenhair.*—This indigenous moss is stated by William Wood to be a powerful diuretic, and, when given indefinitely in infusion, very useful in *dropsy*. (*Am. J. M. S.*, N. S., xxvii, 267.) Ariel Hunter confirms these statements. (*N. J. Med. Rep.*, ix, 417.)

Pongamia. *Pongamia glabra* Vent. (Fam. *Leguminosæ.*)—*Pongamia* or *kurung oil* is expressed from the seeds of an East Indian tree. It is deep yellow to reddish-brown, fluid at 15.6° C. (60° F.), but below that it is solid with sp. gr. of 0.9352 (*P. J.*, 72, p. 492). It is especially commended in *pityriasis versicolor* and other parasitic skin diseases. (*P. J.*, February, 1883.)

Poplar Buds. *N. F. IV. Populi Gemmæ. Balsam Poplar Buds. Balm of Gilead Buds.*—"The *air-dried*, closed winter leaf-buds of *Populus nigra* Linné or *Populus balsamifera* Linné (Fam. *Salicaceæ*), collected early in the spring. Preserve the buds in tightly-closed containers of glass or tin." *N. F.*

In most trees of the genus Populus, the leaf-buds are covered with a resinous exudation, which

has a peculiar, agreeable, balsamic odor, and a bitterish, balsamic, somewhat pungent taste. It is abundant in the buds of *Populus nigra* L., or the *black poplar* of Europe, which are official in some parts of that continent. They contain resin and a peculiar volatile oil. The buds of *P. balsamifera* L., the *Balsam Poplar* or *Tacamahac*, growing in the northern parts of North America and Siberia, are also highly balsamic; and a resin is said to be furnished by the tree. The buds are obtained from *P. canadicans* Ait and are often called Balm of Gilead buds. Poplar buds are described in the N. F. IV as "conical, pointed, up to 2 cm. in length and from 2 to 5 mm. in thickness, consisting of closely imbricated scales, externally brown and glossy, glutinous with fragrant resin. Odor pleasant, balsamic; taste aromatic and bitter." The virtues of the *poplar buds* are probably analogous to those of the turpentines and balsams. They have been used in pectoral, nephritic, and rheumatic complaints, in the form of a tincture, and a liniment, made by macerating them in oil, has been applied externally in local *rheumatism*. The *unguentum populeum*, *Pommade de Bourgeons de Peuplier*, is made, according to the directions of the French Codex, from 100 Gm. each of the dried contused leaves of white poppy, belladonna, henbane, and black nightshade, and 800 Gm. of dried poplar buds. The leaves are moistened with 400 Gm. of alcohol and allowed to stand twenty-four hours in a closed vessel; 4000 Gm. of lard is now added and the mixture heated gently during three hours, stirring frequently, the crushed poplar buds are then added and allowed to digest for ten hours at a gentle heat, and the whole strained and cooled slowly. This is an anodyne ointment, employed in Europe in painful local affections. It has been ascertained that poplar buds are capable of imparting a principle to ointments which obviates their tendency to rancidity. Poplar buds are an ingredient of *Syrupus Pini Strobi Compositus*, N. F. and of *Syrupus Pini Strobi Compositus cum Morphina*, N. F.

The bark of *P. tremuloides* Michx., or *American aspen*, and of *P. tremula* L., or *European aspen*, is possessed of tonic properties, and has been used in *intermittent fever*. In the bark of the latter Braconnot found *salicin*, $C_{13}H_{18}O_7$ (see p. 965), and another crystallizable principle which he named *populin*, $C_{20}H_{22}O_8 + 2H_2O$. It is in these, probably, that the febrifuge properties of the bark reside. They may be obtained by precipitating a saturated decoction of the bark with solution of lead subacetate, filtering, precipitating the excess of lead by sulphuric acid, again filtering, evaporating, adding animal charcoal towards the end of the evaporation, and filtering the liquor while hot. Salicin gradually separates, upon the cooling of the liquor, in the form of crystals. If, when this principle has ceased to crystallize, the excess of sulphuric acid in the liquid be saturated by a concentrated solution of potassium carbonate, the populin will be precipitated. If this be pressed between folds of blotting paper, and redissolved in boiling water, it will be deposited, upon the cooling of the liquid, in the crystalline state. The leaves of *P. tremula* are also said to yield more populin than does the bark. It is probable that both principles exist in the bark of *P. tremuloides* and other species. Schaak (*A. J. P.*, 1892, 226) found a bitter principle in the bark of *P. alba* L., which was most likely populin. Populin is very light and white, of a bitter, sweetish taste, analogous to that of licorice. It is soluble in 1896 parts of cold and about 70 parts of boiling water, and is more soluble in boiling alcohol. It loses its two molecules of water of crystallization at 100° C. (212° F.), and at 180° C. (356° F.) it fuses to a colorless liquid, from which at a higher temperature benzoic acid may be sublimed. Acetic acid and the diluted mineral acids dissolve it, and, upon the addition of an alkali, let it fall unchanged. Piria first showed it to be *benzoyl salicin*, $C_{13}H_{17}(C_7H_5O)O_7 + 2H_2O$. He then decomposed it and prepared salicin from it. Populin has been prepared synthetically by Schiff and by Dobbin and White. (*P. J.*, 73, p. 233.) When populin is boiled with baryta water or milk of lime, the benzoic acid precipitated by ferric chloride, the excess of iron removed by lime, and the excess of lime by carbon dioxide, the remaining liquid yields salicin on evaporation. The same conversion may be effected by heating populin with an alcoholic solution of ammonia to 100° C. (212° F.). Piria obtained from populin 28.9 per cent. of benzoic acid. (*P. J.*, xv, 378.) T. L. Phipson, basing his experiments upon the results of Piria, has succeeded in preparing populin artificially by combining salicin and benzoic acid. Nothing more is necessary than to dissolve the two substances in alcohol, and to concentrate the solution. Crystals are formed having all the characters of populin, and consisting of salicin and benzoic acid combined in the proportion of their equivalents. (*Chem. News*, Dec. 6, 1862, 278.) Dobbin and White make populin from salicin and benzoyl chloride. (*Y. B. P.*, 1904, 506.) The flower-buds of *P. tremuloides* yielded a bitter resin to R. Glenk. It was of yellowish-brown color, strong, hop-like odor, and had a melting point of 51° C. (123.8° F.). (*A. J. P.*, 1889, 240.)

Poppy Capsules. *N. F. IV. Papaveris Fructus. Papaveris Capsulæ.* Br., 1898. *Papaver*, U. S., 1870; *Capsules de Pavot blanc ou Pavot officinal*, Fr. Cod.,; *Fructus Papaveris immaturi*, P. G.; *Unreife Mohnköpfe, Kapseln des Weissen Mohns, Mohnkapseln, Mohnköpfe*, G.; *Papavero*, It.; *Cabezas de amapola*, Sp.—"The dried, fully grown, unripe fruit of *Papaver somniferum* Linné (Fam. *Papaveraceæ*). Separate and reject the seeds before using the fruit in pharmaceutical preparations." *N. F.*

Poppy capsules were official in the Br. Pharmacopœia, 1898; they have been admitted to the N. F. IV. In England the poppy has been largely cultivated for its capsules, which are gathered as they ripen, and taken to market enclosed in bags. The N. F. directs them to be collected before they are quite ripe, as they then contain more of the active milky juice. When ready for collecting they are a yellowish-green color. They are occasionally imported, but, as no effect is produced by them which cannot be as well obtained from opium, they are little employed.

Dried *poppy capsules* vary in size from the dimensions of a small egg to those of the fist. They differ also in shape according to the variety of the poppy from which they are procured. On the Continent two sub-varieties of the white poppy are recognized, the *long*, and the *round* or *depressed*. Of these, according to Aubegier, the long are richest in morphine, and his conclusions are confirmed by Meurein, who also found the largest capsules most efficient. Those commonly found in commerce are spheroidal, flattened below, and surmounted by a crown-like expansion—the persistent stigma—which is marked by numerous diverging rays that rise somewhat above the upper surface and appear to be prolongations of partial septa,

or partitions, proceeding along the interior circumference of the capsule from the top to the bottom. In the recent state, the seeds, which are very numerous, adhere to these septa, but in the dried capsule they are loose in its cavity, and the N. F. directs that they should be separated before the capsule is used. They are described in the N. F. as "globular or ovoid, usually from 3 to 3.5 cm. in diameter, but varying in size, more or less sunken or depressed on the sides, contracted at the base into a sort of neck immediately above a tumid ring at the point of attachment with the stalk; crowned at the summit with the seven- to fifteen-rayed stigma disk; outer wall of pericarp smooth, hard, grayish-yellow to brownish-yellow, often marked with black spots; interior surface rugose, finely striated transversely, and bearing thin, brittle, membranous placentæ which extend from the sutures toward the center, and bear on their faces and edges numerous, minute, conspicuously reticulated, reniform white seeds. Odorless; taste slightly bitter.

"Macerate 1 Gm. of the powdered Capsules for two hours with 10 mils of water containing 1 per cent. of hydrochloric acid, and filter; the filtrate yields distinct precipitates with iodine T.S. and with potassio-mercuric iodide T.S.

"The powdered drug is grayish-yellow, and, when examined under the microscope, exhibits fragments of the epicarp composed of thick-walled polygonal cells, the cells of the outer layer non-porous, up to 0.05 mm. in diameter and with occasional stomata, the latter up to 0.035 mm. in length; the cells of the inner layer of the epicarp often with numerous simple pores; portions of the soft, spongy sarcocarp consisting of isodiametric or irregular parenchyma and branching milk ducts, the latter up to 0.06 mm. in width, of variable length and with thin, non-porous walls; fragments of the inner wall of the pericarp and the outer wall of the placental tissue composed of polygonal or somewhat elongated cells with porous walls, up to 0.06 mm. in width and up to 0.3 mm. in length, the walls of the latter cells often slightly lignified; spiral and annular tracheæ up to 0.035 mm. in width and reticulate tracheæ up to 0.06 mm. in width; sclerenchyma cells few with simple or oblique pores; starch grains few, small, somewhat rounded; fragments of the reticulately pitted seed-coat very few or absent. Poppy Capsules yield not more than 10 per cent. of ash." *N. F. IV.*

On the continent of Europe, the poppy is cultivated largely for its seeds, which yield about fifty per cent. of an excellent fixed oil on expression. *Poppy seed oil* is of a pale golden color, liquid at 5.5° C. (42° F.), easily dried, inodorous, and of a pleasant flavor. It is bleached by exposure in thin layers to the sun. (*P. J.*, March, 1874, p. 731.) It belongs to the class of drying oils, ranking after linseed and hemp seed oils in power. For chemical composition the reader is referred to *Opium*, page 803.

Dried poppy heads, though analogous to opium in medicinal properties, are exceedingly feeble. They are nevertheless asserted to have proved fatal, in the form of decoction, to a child. The case, reported by F. L. Winckler, was that of a babe, in the stomach of which he found a little morphine, but no meconic acid. (*N. R. Pharm.*, 1867, xvi, 38.) They are sometimes employed in decoction, as an external emollient and anodyne application, and, in emulsion, syrup, or extract, are used internally, in Europe, to calm irritation, promote rest, and produce generally the narcotic effects of opium. The *dose* is from ten to twenty grains (0.65–1.3 Gm.).

Portulaca. *Portulaca oleracea* L. *Garden* or *Common Purslane.* (Fam. *Portulacaceæ.*)—This fleshy annual, common in cultivated and waste grounds, has been considered a cooling diuretic, and recommended in *scurvy* and urinary affections. The seeds have been considered anthelmintic, but are inert.

Potassio-Mercuric Iodide. $HgI_2 2KI = 786.48$. *Mercuric Potassium Iodide. Iodohydrargyrate of Potassium. Mayer's Reagent.*—A mercuric iodide, HgI_2, unites with metallic iodides, forming a series of double salts, sometimes called *iodohydrargyrates.* These have been particularly studied by Boullay (*Ann. Ch. Phys.* [2], 34, 345), who finds that a concentrated solution of potassium iodide will dissolve mercuric iodide in the ratio of three molecules of the mercuric salt for every two of the potassium salt. When the solution is cooled, one molecule of red mercuric iodide crystallizes out, and then from the mother liquor deposits yellow prisms. It occurs in commerce in yellow, crystalline pieces, deliquescent in moist air. Under the name of *Mercuric potassium iodide test solution* this liquid is official in the U. S. P. IX. (See Part III.) Clayton suggests the practical method of simply evaporating *Nessler's solution* and collecting the crystals. (*Chem. News*, 1894, 102.)

This is an active preparation, which may be given in the same dose and for the same purposes as corrosive sublimate. It is formed when its components are prescribed together extemporaneously. It is not decomposed by the compound syrup of sarsaparilla, which is frequently used as a vehicle for it. Potassio-mercuric iodide was suggested by F. L. Winckler as a qualitative test of the organic alkaloids. F. F. Mayer subsequently employed, for volumetric analysis, a solution made with 13.546 grammes of corrosive sublimate, 49.8 grammes of potassium iodide, and a liter of distilled water. (See *Mercuric Potassium Iodide Test Solution, U. S. D.*, PART III.) For further observations, see *A. J. P.*, 1886, 579, and 1887, 1.

Potassio-mercuric Thiosulphate. *Mercury and Potassium Thiosulphate.* $3Hg(S_2O_3)_2 + 5K_2S_2O_3$. —This is obtained through solution of yellow mercuric oxide in potassium thiosulphate solution. It forms white crystals soluble in water. It is used subcutaneously once daily in the treatment of *syphilis. Dose*, one-sixth to one-half grain (0.010–0.032 Gm.).

Potassium Bisulphate. *Potassii Bisulphas. Acid Sulphate of Potassium.* $KHSO_4 = 136.18$.—This is a by-product in various chemical operations, being left as residue when potassium salts are decomposed by sulphuric acid in excess. It is a white salt, the crystals having the form of right rhombic prisms so flattened as to be tabular. The salt has a bitter and extremely acid taste. It is soluble in twice its weight of cold and in less than its weight of boiling water. Alcohol does not dissolve it, but when added to an aqueous solution, precipitates the neutral sulphate. Exposed to the air, it effloresces slightly on the surface, and when moderately heated readily melts, and runs like oil. At a red heat it loses water and the excess of acid, and is reduced to a neutral sulphate. Owing to its excess of acid, it acts as an acid on the carbonates, causing them to effervesce. It is incompatible with alkalies, alkaline earths, and their carbonates, with many of the metals, and with most oxides. This salt was formerly called *sal enixum.* It is aperient. It answers, according to Barker, for preparing a cheap aperient effervesc-

ing draught. Equal weights—a drachm, for instance—of the bisulphate and of sodium carbonate may be dissolved separately, each in two fluidounces of water, then mixed, and taken in the state of effervescence. *Dose*, one or two drachms (3.9–7.7 Gm.).

Potassium Bromate. $KBrO_3 = 167.02$. *Potassii Bromas. Bromate de potase*, Fr. *Kaliumbromat, Bromsaures Kali*, G.—This salt is formed in the process employed for making the bromide and may be separated by crystallization. Colorless, cubical or tabular crystals, soluble in 15 parts of cold and 2 parts of hot water. Like potassium chlorate it oxidizes matter like sugar and sulphur and must be mixed with great caution, with readily oxidizable substances. It is an ingredient in *Koppeschaar's solution*, which is employed in titrating phenol. (See *Tenth-normal Bromine Volumetric Solution*, Part III.)

Potassium Bromsalicylate. *Potassium Brom-ortho-oxybenzoate.* $KC_7H_4BrO_3$.—A white, crystalline powder soluble in water and used as an antirheumatic and hypnotic in five to ten grain (0.32–0.65 Gm.) *doses*.

Potassium Camphorate. $K_2C_{10}H_{14}O_4$.—White, deliquescent crystals soluble in water and used mainly as an antiseptic. It should be kept in stoppered bottles well protected from moisture and air. It is employed for the same purposes as camphoric acid. *Dose*, ten to thirty grains (0.65–2.0 Gm.).

Potassium Chloride. *Potassii Chloridum. N. F. IV. Kalium chloridum (chloratum). Sal digestivum Sylvii. Sel digestif*, Fr. KCl.—"It contains, when dried to constant weight at 100° C., not less than 99 per cent. of KCl (74.56). Preserve it in well-closed containers." *N. F. IV. Potassium chloride* was made official in the National Formulary as an ingredient in *Liquor Hydrastini Compositus* or *Compound Solution of Hydrastini; Sal Kissingense Factitium* or *Artificial Kissingen Salt;* and *Sal Kissingense Factitium Effervescens* or *Effervescent Artificial Kissingen Salt.* It is described as follows: "Potassium Chloride occurs in colorless, elongated, prismatic, or cubical crystals, or as a white, granular powder; permanent in dry air. Odorless; taste saline. One gramme dissolves in 2.8 mils of water at 25° C., slightly more soluble in boiling water; insoluble in alcohol. An aqueous solution of the salt (1 in 10) is clear and neutral to litmus. When heated, the dry salt decrepitates. To a non-luminous flame it imparts a violet color unmasked by yellow. An aqueous solution of the salt yields with silver nitrate T.S. a white, curdy precipitate insoluble in nitric acid but soluble in an excess of ammonia water. Boil 5 mils of an aqueous solution of the salt (1 in 10) in a test tube, then add an equal volume of barium hydroxide T.S. and stopper the tube; the solution is not rendered cloudy within fifteen minutes (*calcium or magnesium*). Dissolve 2 Gm. of the salt in 6 mils of distilled water, add 1 mil of chloroform, and then add, drop by drop, with constant agitation, 5 mils of half-strength chlorine water; the chloroform does not acquire a transient violet or permanent orange color (*iodide or bromide*). An aqueous solution of the salt meets the requirements of the Test for arsenic (see page 356). An aqueous solution of the salt does not respond to the Test for heavy metals (see page 357).

"*Assay.*—Dissolve about 0.25 Gm. of Potassium Chloride, previously dried to constant weight at 100° C. and accurately weighed, in 25 mils of distilled water in a 200 mil measuring flask. Add 50 mils of tenth-normal silver nitrate V.S. to the solution, then 5 mils of nitric acid, afterward sufficient distilled water to make 200 mils and mix thoroughly. Filter the mixture through a dry filter, reject the first 20 mils of the filtrate, collect the following 100 mils of filtrate, add to this 2 mils of ferric ammonium sulphate T.S. and titrate with tenth-normal potassium sulphocyanate V.S., until the supernatant liquid remains reddish after it is well shaken. It shows, in the dried salt, not less than 99 per cent. of Potassium Chloride. Each mil of tenth-normal silver nitrate V.S. corresponds to 0.007456 Gm. of KCl. Each gramme of Potassium Chloride, dried to constant weight, corresponds to not less than 132.8 mils of tenth-normal silver nitrate V.S."

Potassium Chloro-Platinite. *Potassium Platinochloride.* $PtCl_2.2KCl$.—Eight grains (0.5 Gm.) of this salt, which is used as a toning agent in photography, caused death in an infant of two months, preceded by violent gastro-enteritis and collapse. (*B. M. J.*, i, 1896.)

Potassium Cobalti-Nitrite. $CO_2(NO_2)_{12}K_6 + 2H_2O = 934.32$.—When potassium nitrite is added to a cobalt salt solution acidified with acetic acid, nitrogen is set free, and in course of time the double cobaltic and potassium nitrite separates as a yellowish crystalline powder, almost totally insoluble in acid solution. Wolcott Gibbs having suggested that this nitrite might be less fugacious than other nitrites, on account of its stability and relative insolubility, J. W. Roosevelt tried it in doses of from one-quarter to one-half grain (0.016–0.032 Gm.), every two hours, in kidney cases with high arterial tension and dyspnea, in *asthma*, and also in *cardiac valvular diseases*. He stated that the effects of the drug are similar to those of the nitrites, beginning in fifteen minutes and lasting from two to four hours.

Potassium Creosote-ortho-sulphonate.—This preparation appears on the market in two distinct forms, one a powder, grayish-brown in color and having a creosote odor, the other a brown, pulpy mass. The true ortho salt is a powder, hence the mass is a mixture of the ortho and para compounds. The powder dissolves readily in water, yielding a brown solution which is strongly alkaline in reaction. When acidified this solution turns yellow. Ferric chloride produces an intense violet color when added to an aqueous solution of this substance.

Potassium Cyanide. *Potassii Cyanidum. U. S. VIII. Cyanide of Potassium. Potassii Cyanuretum. U. S.* 1850. *Cyanuret of Potassium. Cyanure de Potassium*, Fr. Cod. *Kalium Cyanatum, Cyanuretum Potassicum, s. Kalicum. Kaliumcyanid, Cyankalium*, G. *Cianuro potasico*, Sp. $KCN = 65.11$.—*Potassium cyanide* was deleted from the U. S. P. IX, sodium cyanide replacing it because the sodium salt is more stable, and cheaper to produce. (See *Sodii Cyanidum*, PART I.) For processes of manufacture, see *U. S. D.*, 19th edition, p. 996. Potassium cyanide is in "white, opaque, amorphous pieces, or a white, granular powder, odorless when perfectly dry; deliquescent in the air and exhaling the odor of hydrocyanic acid. *Great caution should be used in tasting and handling this salt.* Soluble in about 2 parts of water at 25° C. (77° F.). Boiling water dissolves its own weight of the salt, but rapidly decomposes it. In alcohol it is but sparingly soluble. At a low red heat the salt fuses. Its aqueous solution (1 in 20) has a strongly alkaline reaction upon red litmus paper, and emits the odor of hydro-

cyanic acid. With an equal volume of sodium bitartrate T.S. the solution yields a white, crystalline precipitate. With sodium cobaltic nitrite T.S. a copious yellow precipitate is produced. A few drops of a solution of the salt (1 in 20) yields with silver nitrate T.S. a white precipitate, which is soluble in an excess of the solution of Potassium Cyanide, also in ammonia water, and in concentrated nitric acid. If 5 Cc. of a solution of the salt (1 in 20) be shaken with a few drops of ferrous sulphate T.S. and of ferric chloride T.S. and a slight excess of hydrochloric acid then added, a blue precipitate (Prussian blue) will be produced.

"The addition of diluted hydrochloric acid to the aqueous solution of the salt (1 in 20) should produce not more than a slight effervescence (limit of *carbonate*). After the diluted hydrochloric acid has been added in slight excess, a drop of ferric chloride T.S. should produce neither a blue color (absence of *ferrocyanide*) nor a red color (absence of *sulphocyanate*). If 1 Gm. of Potassium Cyanide be dissolved in sufficient distilled water to measure 100 Cc., then 64.7 Cc. of this solution mixed with 5 Cc. of ammonia water and 3 drops of potassium iodide T.S. should require not less than 47.5 Cc. of tenth-normal silver nitrate V.S. before the appearance of a permanent precipitate (each Cc. of the tenth-normal silver nitrate V.S. indicating 2 per cent. of pure Potassium Cyanide)." *U. S. VIII.* If yellow, it contains iron. Its solution effervesces with acids. The salt and its solutions, when exposed to the air, exhale the odor of hydrocyanic acid, and become weaker; but the change takes place slowly. Orfila found that the salt, after fourteen days' exposure, by which it was almost entirely liquefied, still possessed energetic poisonous properties; he thinks, therefore, that the bad effects of opening the containing bottle, in dispensing the medicine, have been exaggerated. Unfortunately, the salt varies in quality independently of the effects of time and exposure. Besides water, the usual impurities are potassium hydroxide, carbonate, cyanate, and formate. They sometimes amount to half the weight of the cyanide, consisting principally of the carbonate. From the extensive use at present made of potassium cyanide in electrometallurgy and photography, it is of importance to have a reliable test of its purity. Such a test has been discovered by Fordos and Gélis, founded on the fact that one molecule of iodine rapidly reacts with one of the cyanide, so as to form a colorless compound, consisting of one molecule of potassium iodide and one of cyanogen iodide:

$$KCN + I_2 = KI + CNI$$

Besides the very extensive use of potassium cyanide and sodium cyanide in preparing electroplating solutions for gilding and silvering by electro-deposition, and in photography, large quantities are now consumed in the extraction of gold and silver from the fine residues or "tailings" where amalgamation fails to take up the precious metals. From such solutions of gold in potassium cyanide the metal is thrown out by the action of metallic zinc.

Potassium cyanide acts precisely like hydrocyanic acid as a poison and as a medicine. (See *Acidum Hydrocyanicum Dilutum.*) Five grains of it have repeatedly taken life, and hydrocyanic acid has been detected in the blood of a person who had been fatally poisoned by the cyanide. (Venghauss, *A. Pharm.*, clii, 138.) Potassium cyanide has the power of dissolving silver oxide and may be used for the removal of silver nitrate stains from clothing. According to Guthrie a solution of three grains (0.2 Gm.) to the ounce (30 mils), dropped in the eye every other day, will remove olive colored stains from the conjunctiva caused by silver nitrate. Owing to the large use of potassium cyanide for the recovery of gold, numerous accidental cases of poisoning occur in the reduction works. For the treatment of poisoning, see under *Acidum Hydrocyanicum Dilutum*, p. 40.

Potassium Ferricyanide. *Ferricyanide of Potassium. Red Potassium Prussiate.* $K_3Fe(CN)_6$.—This is formed by passing a current of chlorine through a solution of potassium ferrocyanide, until the liquid ceases to form a precipitate with a solution of ferric chloride, a proof that the whole of the ferrocyanide has been converted into the ferricyanide. The solution, by due evaporation, yields the compound in question. It may also be prepared, in the dry way, by agitating finely powdered ferrocyanide with chlorine as long as it is absorbed. The theory of the formation of this compound is that two atoms of chlorine withdraw from two molecules of the ferrocyanide two atoms of potassium, forming potassium chloride, which remains in the mother water, while the two atoms of iron, having assumed the ferric condition, together with the remaining potassium, saturate the cyanogen. The reaction is explained by the following equation:

$$2K_4Fe(CN)_6 + Cl_2 = 2K_3Fe(CN)_6 + 2KCl$$

The radical ferricyanogen is supposed to be formed by the coalescence of two molecules of ferrocyanogen, and is sometimes represented by the symbol Cfdy. This salt, discovered by Gumelin, is in beautiful, deep, hyacinth-red, anhydrous crystals, which are soluble in four parts of water. Its solution forms a delicate test for ferrous salts, with which it produces a blue precipitate; but with ferric salts it only strikes a green or brown color. It is used in dyeing and calico printing. (See *Test Solutions*, PART III.)

Potassium Ferrocyanide. $K_4Fe(CN)_6 + 3H_2O = 422.35$. *Potassii Ferrocyanidum. U. S. VIII. Potassæ Prussias Flava. Ferrocyanide of Potassium. Yellow Prussiate of Potash. Cyanuretum Ferroso-potassicum. Ferrocyanuret of Potassium, Ferroprussiate of Potassa. Prussiate of Potassa. Ferrocyanure de Potassium*, Fr. Cod. *Protocyanure jaune de Fer et de Potassium, Prussiate jaune de Potasse*, Fr. *Kalium Ferrocyanatum, Kalium Borussicum, Cyaneisenkalium, Ferrocyankalium, Gelbes Blutlaugensalz*, G.—"It should contain not less than 99 percent. of pure Potassium Ferrocyanide, and should be kept in well-stoppered bottles." *U. S. VIII. Potassium ferrocyanide* was formerly prepared on the large scale by heating animal matters, such as dried blood, hoofs, chips of horn, woollen rags, old leather, the refuse of tallow chandlers called *greaves*, and other substances rich in nitrogen, with the pearlash of commerce and scrap iron.

Some years ago this salt was manufactured by a process which dispensed with the use of animal matter, the necessary nitrogen being obtained by a current of atmospheric air. Fragments of charcoal, impregnated with 30 per cent. of potassium carbonate, were heated to a white heat in a cylinder through which a current of air was drawn by a suction-pump. This process is understood to have succeeded in a chemical sense, but failed on the score of economy, chiefly from the circumstance that the necessary fire-clay tubes could not be made

to resist the combined action of the alkali and heat. In recent years almost all potassium ferrocyanide is prepared from the spent oxide which is obtained in abundance during the purification of coal gas and consists of a mixture of sawdust, lime, iron oxide, and sulphur, together with ferrocyanides and sulphocyanides. This mass is first lixiviated with water in order to separate ammonia and soluble salts. It is then dried, the sulphur extracted with carbon disulphide and the residue mixed with powdered lime. The whole is then heated with steam from 40° to 100° C. (104°–212° F.) in closed pans so that the ammonia which distils may be utilized, and calcium ferrocyanide is thus obtained in strong aqueous solution. On adding a boiling solution of potassium chloride to this, the almost insoluble double ferrocyanide of calcium and potassium separates, and on heating this with a solution of potassium carbonate, a solution of potassium ferrocyanide is formed together with insoluble calcium carbonate.

Potassium ferrocyanide is in "large, soft, transparent, yellow, four-sided, monoclinic, tabular crystals or prisms; odorless, and having a mild, saline taste. Slightly effiorescent on exposure to the air. Soluble in about 4 parts of water at 25° C. (77° F.), and in 2 parts of boiling water; insoluble in alcohol. When heated to 60° C. (140° F.), the salt begins to turn white from loss of water of crystallization, and when heated at 100° C. (212° F.), it is rendered anhydrous. The aqueous solution is neutral to litmus paper. With sodium bitartrate T.S. the concentrated aqueous solution yields a white crystalline precipitate. The color of the pricipitate produced by the addition of ferric chloride T.S. to the diluted aqueous solution of the salt is dark blue; that produced by copper sulphate T.S. is reddish-brown; lead acetate T.S. or silver nitrate T.S. causes a white precipitate. No effervescence should be caused by the addition of diluted sulphuric acid to a concentrated solution of the salt (absence of *carbonate*). The precipitate produced by silver nitrate T.S. in the aqueous solution, acidulated with nitric acid, should be of a white color, without a tinge of red (absence of *ferricyanide*)." *U. S. VIII.* (See also under U. S. reagents, Part III.) It acts but slightly, if at all, on turmeric paper. The alkaline reaction, when it exists, is probably owing to the presence of a little potassium hydroxide. When ignited, the insoluble residue amounts to 18.7 per cent. of ferric oxide, resulting from the oxidation of the iron of the salt. It is characterized by striking a deep-blue color with ferric salts, a deep-brown one with the salts of copper, a white one with those of zinc, the several precipitates formed being ferrocyanides of the respective metals. Heated with eight or ten times its weight of concentrated sulphuric acid, it evolves carbon dioxide. Half an ounce of the salt yields about 250 cubic inches of the gas. (C. Grimm and G. Ramdohr.) When boiled with diluted sulphuric acid, it emits the easily recognized odor of hydrocyanic acid. The non-toxic green coloring compounds known as *ferrocyanide green* and *ferricyanide green* have been produced from potassium ferrocyanide and ferricyanide. (*P. J.*, 1908, 258.)

Potassium ferrocyanide consists of six groups of the monad radical cyanogen (CN), saturated by four potassium atoms and one atom of the dyad iron. The potassium is more readily displaced than the iron, so that it is considered as the potassium salt of an acid called *hydroferrocyanic*. This acid in the free state would be $H_4Fe(CN)_6$. The salt is remarkably pure as it occurs in commerce.

Uses.—Pure potassium ferrocyanide is almost non-toxic. Thus, Combemale and Dubiquet proved that in *doses* of twelve grains to the pound of bodily weight it is not poisonous to the lower animals, while Callies, as quoted by Pereira, found the commercial salt slightly poisonous, but the pure salt unproductive of harm in the *dose* of several ounces. Westrumb and Hering proved that it passed with rapidity into the blood and urine.

This salt is manufactured on a large scale, chiefly for the use of dyers and calico printers. In pharmacy it is employed to prepare diluted hydrocyanic acid, Prussian blue, and potassium and silver cyanides. Its only medicinal value is as an antidote in *copper sulphate poisoning*. *Dose*, five to ten grains (0.32–0.65 Gm.).

Potassium Glycerophosphate. *Potassii Glycerophosphas.* $C_3H_7O_3.PO_3K_2$.—The salt is very hygroscopic and has an alkaline reaction. This salt appears in commerce to-day as a colorless to yellowish liquid, miscible with water in all proportions, and containing 50–75 or 100 per cent. of the salt. It is used for the same purposes as sodium glycerophosphate in *doses* of from three to six minims (0.2–0.4 mil).

Potassium Iodate. *Potassii Iodas. Iodate de Potasse*, Fr. *Kaliumjodat, Jodsaures Kali*, G. KIO_3.—Demarquay and Custin propose the following mode of preparation, which was followed by the Br. Pharm. (1885) in making its test solution. Take of iodine and potassium chlorate, each, one part, and mix them with five or six parts of water, previously acidulated with a few drops of nitric acid, and heated to ebullition. As soon as chlorine ceases to escape, treat the liquid with a concentrated solution of barium chloride. Wash with distilled water, and decompose the barium iodate precipitated with diluted sulphuric acid; filter to separate the barium sulphate, and slowly evaporate the solution. Wash with distilled water the crystals of iodic acid that are formed, dissolve them in boiling distilled water, and saturate with potassium bicarbonate. On cooling the iodate is deposited in small crystals. Stas prepares it by moderately heating equal molecular weights of potassium iodide and chlorate, dissolving out the chloride formed with cold water, and repeatedly crystallizing the iodate from hot water. (*A. J. P.*, 1870, 217.) Egidio Pollacci has found that phosphorus affords a very delicate test for the iodate, as does also the iodate for phosphorus, free iodine being liberated. (*J. P. C.*, 4e sér., xx, 104.) Demarquay and Custin assert that potassium iodate is superior to potassium chlorate as a local remedy in ulcerative and gangrenous *stomatitis*, *ptyalism*, *diphtheria*, and other diseases of the pharyngeal and buccal mucous membrane. *Dose*, from four to eight grains (0.26–0.5 Gm.). (*Dorvault's Rev. Pharm.*, 1858.)

Potassium Nitrite. *Potassii Nitris.—Nitrite of potassium* ($KNO_2 = 85.11$) is most readily obtained by fusing saltpeter with lead, which withdraws one atom of oxygen from the former, and forming thereby litharge. It is a white, fusible, and uncrystallizable mass, usually cast into sticks like the hydroxide. It is very deliquescent, and absorbs carbon dioxide from the air. It shares the activities of the nitrites, producing in animals their physiological effects, and being capable of replacing them in the treatment of disease. Its influence is comparatively slow and permanent. Five grains (0.32 Gm.) have produced mild poisoning. *Dose*, one to three grains (0.065–0.2 Gm.).

Potassium Percarbonate, $K_2C_2O_6 + H_2O$, is a

colorless powder which slowly decomposes under the action of water, as follows:

$$K_2C_2O_6 + H_2O = 2KHCO_3 + O$$

In the presence of sulphuric acid, potassium percarbonate decomposes and forms hydrogen peroxide.

$$K_2C_2O_6 + 2H_2SO_4 = 2KHSO_4 + 2CO_2 + H_2O_2$$

This substance has not as yet been used in practical medicine, but is believed to be the material known as *antihypo*, much used in photography, and which has been recommended by Müller for the purposes of decolorizing and counterstaining tubercular bacilli. He washes the preparations for this purpose in 50 to 70 per cent. alcohol and places them for fifteen minutes in a 5 to 10 per cent. solution of potassium percarbonate, and after differentiating rinses in water and counterstains with methylene blue.

Potassium Perchlorate. *Potassii Perchloras. Hyperchlorate of Potassium.* $KClO_4 = 138.56$.—This salt is prepared by fusing potassium chlorate until it begins to assume a pasty condition. The cooled mass consists of *potassium perchlorate* and chloride. The absence of undecomposed chlorate may be known by a sample failing to communicate a yellow color to hydrochloric acid. The mass must be dissolved in the smallest possible quantity of boiling water, when perchlorate crystallizes out. It is sparingly soluble in water, and insoluble in alcohol. Its effects are wholly different from those of potassium chlorate, and it has been commended in *intermittents*. (*Ann. Thér.*, 1869, 141.) *Dose*, five to fifteen grains (0.3–1.0 Gm.).

Potassium Perosmate. *Potassium Osmate.* $K_2OSO_4 + 2H_2O$.—Violet crystals used for their alterative and sedative properties in the treatment of *epilepsy, goiter* and *neuralgia*. *Dose*, one-fifteenth to one-quarter grain (0.004–0.016 Gm.).

Potassium Persulphate. *Potassii Persulphas. Kaliumpersulfat*, G. *Anthion.*—Obtained by electrolyzing a solution of potassium bisulphate. It forms colorless crystals, soluble in about 50 parts of water. Used in photography, owing to its oxidizing of sodium thiosulphate to sulphate.

Potassium Phenolsulphonate. *Potassium Sulphocarbolate.* $C_6H_4(OH)SO_3K + H_2O$. — This forms white crystals soluble in water and alcohol, and melting at 400° C. (784° F.). Therapeutically it is very little used, but it has some use as an antiphylloxerin in checking the ravages of the grape vine parasite.

Potassium Phosphate. *Potassii Phosphas. Phosphate of Potassium.* $K_2HPO_4 = 174.25$.—The *potassium phosphate* which has come into use as a medicine is the *dipotassic orthophosphate*, having a composition precisely analogous to that of the medicinal sodium and ammonium phosphates. It may be formed precisely as sodium phosphate is prepared; or by nearly saturating, by means of potassium carbonate, common or orthophosphoric acid, H_3PO_4. The medicinal potassium phosphate is a white, amorphous, deliquescent salt, crystallizing with difficulty. It has been given as an alterative in *scrofula* and *phthisis* with supposed advantage. The *dose* is from ten to thirty grains (0.65–2.0 Gm.), three times a day, dissolved in a teaspoonful of water.

Potassium Picrate. *Potassium Trinitrophenate. Potassii Picras. Kaliumpikrat, Pikrinsaures Kalium*, G. $C_6H_2(NO_2)_3OK$.—This salt may be made by neutralizing a hot solution of 20 parts of picric acid with 7 parts of potassium carbonate and crystallizing in a cool place. Small, yellow crystals, or a yellow powder of a bitter taste, soluble in 230 parts of cold water and 15 parts of hot water; nearly insoluble in alcohol. It must be handled with care, as it explodes by a blow or when heated.

Potassium Salicylite. *Potassium Salicylaldehyde. Potassium Ulmarate.* $C_6H_4.OK.COH$.—A yellow, deliquescent powder, soluble in water and alcohol and used as an antirheumatic, alleged by some as being superior to, and quicker in, its action than the salicylates. *Dose*, three to fifteen grains (0.2–1.0 Gm.).

Potassium Silicate. *Potassii Silicas.—Silicate of potassium*, K_2SiO_3, also known as *soluble glass*, is prepared in the same way as the sodium salt. It has been used in *rheumatism* and *gout*, but is probably of no service. It may be used as a substitute for plaster of Paris in the preparation of immovable surgical dressings. The solution is applied of a syrupy consistence, by means of a brush, to the bandages, upon which it rapidly hardens, requiring only five or six hours for this result. The facility of removing the bandages by means of hot water is the advantage which *potassium silicate* possesses over most other dressings.

Potassium Sozoiodolate. *Potassium Diodoparaphenolsulphonate.* $C_6H_2I_2.OH.SO_3K$.—A colorless, inodorous, crystalline powder, soluble in 50 parts of water. It is used as a 10 per cent. dusting powder or ointment in the treatment of *herpes* and *eczema*, etc., and as a 25 per cent. ointment in *laryngitis, adenitis*, etc.

Potassium Sulphite. *U. S.* 1880. *Potassii Sulphis.* $K_2SO_3.2H_2O = 194.30$. *Kali Sulfurosum, Sulfis Potassicus. S. Kalicus. Sulfite de Potasse*, Fr. *Schwefligsaures Kali, G.*—Potassium sulphite is prepared by causing sulphurous acid to pass through a strong solution of potassium carbonate until decidedly acid; an equal weight of potassium carbonate is now added. The sulphite crystallizes out upon standing. "White, opaque, obliquely-rhombic, octahedral crystals, or a crystalline powder, somewhat deliquescent, odorless, having a bitter, saline, and sulphurous taste, and a neutral or feebly alkaline reaction. Soluble in 4 parts of water at 15° C. (59° F.) and in 5 parts of boiling water; only sparingly soluble in alcohol. When gently heated, the salt loses its water of crystallization (18.5 per cent.); at a red heat it is decomposed and leaves a residue of an alkaline reaction. The aqueous solution of the salt yields a white, crystalline precipitate on the addition of a saturated solution of bitartrate of sodium. Addition of diluted hydrochloric acid to the aqueous solution gives rise to the odor of burning sulphur, and the solution does not become cloudy (difference from *hyposulphite*)." *U. S.*, 1880. It decrepitates when heated. In the air it effloresces, absorbing oxygen, and being partially converted into the sulphate.

The medicinal uses of this salt are essentially those of the other sulphites. It acts as a slight laxative and diuretic. It escapes from the system with the urine, and may be found for some hours unchanged; at the end of twenty-four hours potassium sulphate is found in the urine instead of the sulphite, proving that the salt undergoes oxidation in the body. It is used for the same purposes as sodium sulphite, over which, however, it has no advantages. *Dose*, from fifteen grains to a drachm (1.0–3.9 Gm.), repeated so as to amount to from a fourth of an ounce to an ounce in twenty-four hours.

Potassium Sulphocyanate. *Potassii Sulpho-*

cyanas. Potassium Thiocyanate. Potassium Thiocyanide. KSCN = 97.18. *Sulfocyanure de Potassium*, Fr. *Kalium Sulfocyanat, Rhodankalium*, G.—Potassium sulphocyanate, formerly called *potassium sulphocyanide*, is prepared by fusing in an iron vessel, at a low red heat, a mixture of two parts of dried potassium ferrocyanide and one part of sublimed sulphur. The mass, when cold, is dissolved in boiling water, and to decompose some ferric sulphocyanate, the solution is treated with potassium carbonate, which throws down the iron as a carbonate, and gives rise to the formation of a fresh portion of potassium sulphocyanate. The whole is then boiled for a quarter of an hour, filtered to separate the precipitated iron, and evaporated that crystals may form. These are purified from potassium carbonate by being dissolved in alcohol, which takes up the sulphocyanate and leaves the carbonate. The alcoholic solution is then allowed to crystallize. Potassium sulphocyanate is in long, striated, anhydrous prisms, deliquescent in a moist atmosphere, very soluble in alcohol, and having a cooling, somewhat biting taste. It has been proposed by Sömmering as a substitute for hydrocyanic acid and potassium cyanide, on the ground that it possesses the same therapeutic properties without their inconveniences.

Potentilla.—*Potentilla reptans* L., the *creeping cinquefoil* of Europe, growing in waste places from Massachusetts to Ohio, and *Potentilla canadensis* L., one of the common cinquefoils of America (Fam. *Rosaceæ*), have each been used as astringents in *diarrhea, chronic catarrhs, night sweats*, etc. According to J. C. Peacock (*A. J. P.*, 433, 1900), dried *P. norvegica* L. contains four, and *P. canadensis* thirteen, per cent. of tannic acid. (See *P. J.*, 1911, 350.)

Powder of Algaroth. *Pulvis Algarothi. Oxychloride of Antimony. Nitro-muriatic Oxide of Antimony.*—A powder rarely used now. For a description of its uses, properties, etc., see 14th edition, *U. S. D.*

Primula.—The leaves of the various species of this genus produce irritation when handled, due to a secretion in the glandular hairs. For a study of primula dermatitis, see Forster, *J. A. M. A.*, 1910, lv, p. 642. From the roots of *Primula grandiflora*, Bongault and Alland have separated a crystalline polyatomic alcohol, *primulite*, which is said to be identical with the hepatomic alcohol, *volemite*. (*C. R. A. S.*, 135, 796.) Two glucosides, *primverin and primulaverin*, and an enzyme, *primverase*, were isolated by Goris and Mascnè. (*Chem. Cb.*, 1910, No. 3.)

Prinos. *Black Alder. Winterberry. Feverbush. Prinos*, Fr., G.—The U. S. P. formerly recognized under this name the bark of *Ilex verticillata* (L.) A. Gray (*Prinos verticullatus* L.) (Fam. *Aquifoliaceæ*). This shrub, of which there are 3 well recognized varieties, grows in the United States from Canada to Florida, and west to Missouri and Wisconsin, frequenting low, wet places. The berries, which have a bitter, sweetish, somewhat acrid taste, are sometimes used medicinally for the same purposes as the bark. The dried bark occurs in "thin, slender fragments, about 1 Mm. thick, fragile, outer surface brownish ash-colored, with whitish patches and blackish dots and lines, the corky layer easily separating from the green tissue; inner surface pale greenish or yellowish; fracture short, tangentially striate; nearly inodorous, bitter, slightly astringent." *U. S.*, 1880. It has no odor, but a bitter and slightly astringent taste. Boiling water extracts its virtues. William J. Lerch failed to find berberine in it. (*A. J. P.*, 1873, 251.)

Black alder has been considered tonic and astringent, and has been used in *diarrhea* and as a substitute for Peruvian bark, but has no antiperiodic properties. In cases of flabby or ill-conditioned *ulcers* it is popularly used both locally and internally in decoction (two ounces in three pints of water boiled to a quart); *dose*, from two to three fluidounces (60–90 mils).

Prioria. *Prioria Copaifera* Griseb. (Fam. *Leguminosæ.*)—The *oil tree* is a native of the West Indies. The seeds are edible and in Panama are sold under the names of *Cativa* or *Amanza muger*. The tree yields an exudate which is known as the *gum of the oil tree*. This is a thick, adhesive liquid, resembling copaiba, usually turbid on account of a greenish substance, which, however, finally subsides, leaving a clear, brownish-yellow liquid. For chemical study, see *A. J. P.*, Jan., 1898.

Propaesin. *N. N. R.* 1917. *Prophylis Aminobenzoas. Propylamine Benzoate. Paramido-benzoic Acid Propyl Ester.*—It occurs as a white, crystalline powder, very sparingly soluble in water, but freely soluble in both alcohol and ether. Perl (*Med. Klin.*, 1909, v, p. 1892) has found it useful to relieve the pain of *sore throat*, and, internally, to quiet *vomiting* and the pain of *gastric ulcer*. The internal *dose* is approximately one to four grains (0.065–0.25 Gm.), although Cluger asserts (*Th. M.*, 1909, p. 77) that fifteen grains (1 Gm.) may be given without harmful symptoms.

Propione. *Di-ethyl-ketone.* $C_2H_5.CO.C_2H_5$. (Corresponding to acetone or di-methyl-ketone.) A mobile, easily soluble liquid, boiling at 101° C. (213.8° F.). *Dose*, as an hypnotic, from eight to forty-five minims (0.5–3.0 mils).

Propionyl-Salicylic Acid. $C_6H_4(O)CH_2.CH_3.CO.COOH$.—This product forms white, glossy scales, insoluble in water, readily in the volatile solvents, and fusing at 95° C. (203° F.). When boiled with water or when treated with alkalies it splits up into its component parts. This has been proposed as a rheumatism remedy.

Proponal. *Propal. Dipropyl Barbituric Acid.* $(C_3H_7)_2C(CONH)_2CO$.—It occurs as colorless crystals which melt at 145° C. (293° F.), sparingly soluble in cold, but more so in boiling water and easily soluble in dilute alkalies. This hypnotic appears to be closely allied in its range of therapeutic usefulness, as it is in its chemical structure, to veronal. According to Bumke (*Med. Klin.*, 1906) it is one-half again as powerful a somnifacient as veronal, but Ziehen (*D. M. W.*, 1908, p. 583) found that although it was more rapid in its action it was not so certain. It appears also to be less liable to be followed by unpleasant consequences, especially by post-nocturnal drowsiness. The *dose* is from two to eight grains (0.13–0.5 Gm.).

Propyl Alcohol (normal propyl alcohol, $C_2H_5.CH_2OH$) is formed in the fermentation of certain sugar and wine residues, as from the marc of grapes, and is separated from the fusel oil of this fermentation. It is a colorless, pleasant-smelling liquid, boiling at 96° C. (204.8° F.).

Propylamine. *Mono-propylamine.* $CH_3.CH_2.CH_2.NH_2$.—For many years this compound was considered to be identical with trimethylamine, but at the present time it is known to be an entirely different product, although isomeric, and to possess distinctive properties. The boiling point of

propylamine is 49° C. (120.2° F.), trimethylamine 93° C. (199.4° F.). Pure propylamine is a clear, highly refractive fluid, pure trimethylamine is a gas. It is generally prepared by heating propyl nitrate with a 10 per cent. alcoholic ammonia solution and is a clear alkaline fluid with a powerful ammoniacal, fishy odor, and soluble in both water and alcohol. In 1854 it was brought forward by Awenarius, of St. Petersburg, as an antirheumatic, but it is rarely used to-day for this purpose. It is used as a sedative in *chorea* and *hysteria*, the *dose* ranging from thirty to one hundred and fifty grains (2–10 Gm.), depending on the acuteness of the attack. In *rheumatism* the *dose* is two to five grains (0.13 to 0.32 Gm.) several times daily. In *acute pneumonia* fifteen to forty-five grains (1.0–3.0 Gm.) have been administered.

Propylamine Hydrochloride. $CH_3.CH_2.CH_2.NH_2.HCl$.—Deliquescent colorless crystals, easily soluble in water. Uses and properties same as preceding. The *sulphate of propylamine*, $(CH_3CH_2CH_2NH_2)_2H_2SO_4$, well formed crystals, has also been used.

Protargol. *N. N. R.* 1917. *Protargolum. Protein Silver Salt.*—A combination of silver and albumin, containing about 8 per cent. of metallic silver. A yellow powder, soluble in 1 part of water, the solution not being affected by heat, albumin, hydrochloric acid, weak sodium chloride solution or sodium hydroxide solution. The dry salt as well as the solution should be protected from light.

Protargol is the representative of a widely used class of compounds, in which an attempt has been made to obtain the anti-bacterial properties of silver nitrate without the local irritation of the inorganic salts, by combining the metal with some form of albumen. It is hardly to be expected that any of these substances will equal silver nitrate in germicidal power because, as is well known, albuminates do not ionize readily, and the disinfectant power of silver salts appears to be in ratio to the amount of ionizable silver, and not with the amount of total silver. According to the experiments of Kelly (*B. M. J.*, 1907, ii, p. 1475), silver nitrate is nearly 300 times as powerful a germicide as protargol, and in the experiments of Post and Nicoll (*J. A. M. A.*, 1910, lv, p. 1635) a ten per cent. solution of protargol was inferior to a one-tenth per cent. solution of silver nitrate. On the other hand, Derby (*B. M. S. J.*, cxlv, p. 341) found that *Staphylococcus aureus* was killed by a two to four per cent. solution of protargol in three to five minutes. It is evident that in germicidal power, protargol is far inferior to silver nitrate. It is claimed, however, that it has greater penetrating power, and that it can be used much stronger, because of its relative slight irritant properties. As to the first of these claims, Derby has shown that the presence of blood serum interferes with the activity of protargol, as well as all other preparations of silver, and both Kelly and Marshall and Neave (*B. M. J.*, 1906, ii, p. 350) assert that the penetrating power of silver nitrate into agar-agar is not greatly inferior to the protein compound of silver. As to the second claim that protargol is less irritant in proportion to its germicidal power, the data concerning its anti-bacterial properties are so contradictory that it is impossible to state categorically whether, in strengths of similar irritation, silver nitrate or protargol is the more efficient germicide.

Protargol has been used very extensively, especially in *gonococcus infections* either of the urethra or conjunctiva. In *acute urethritis* it may be used in strengths of from 0.5 to 2 per cent. for injections, and has been used in 10 per cent. strength for the so-called abortive treatment. In *ophthalmia neonatorum*, Speiro (*M. M. W.*, 1909) drops a 10 per cent. protargol solution into the conjunctival sac, once or twice daily, while, according to Cogwill (*D. M. Ztg.*, 1904) the strength may at times be increased to as high as 30 per cent. in this condition. Protargol has also been used as a germicide for various other conditions. Berliner (*M. M. W.*, 1908, has found it useful in the treatment of *acute tonsillitis*, and it has also been employed as a surgical antiseptic in suppurating *ulcers*, *carbuncles* and the like.

Protea. *Protea mellifera* Thunb. (Fam. *Proteaceæ*.) *Sugar Bush.*—A plant growing in South Africa, from the leaves of which Merring Beck in 1886 obtained *proteacin*. Merck and Hesse subsequently named the principle *leucodrin*. Hesse found the leaves to yield from 2 to 5 per cent. of *hydroquinone* associated with *proteacic acid*. (*P. J.*, 1896, 426.)

Protiode. *Iodo-ethyl-glycin.*—It contains approximately 52 per cent. of iodine. It is a colorless crystalline inodorous substance which is readily soluble in water and is non-toxic. It is used as an iodide and in the same doses as the iodides.

Protosal.—The *salicylic glycerin-formalester*, $CH_2O.OC.C_6H_4OH.CHO.CH_2O.CH_2$, occurs as a colorless oily fluid with a specific gravity of 1.344. It is insoluble in water or glycerin, but dissolves freely in alcohol, ether, chloroform and fatty oils.

This ester is used as a means for the endermic administration of salicylic acid in the treatment of various *rheumatic affections* in the same manner as mesotan. Friedlander (*Th. M.*, 1905, p. 637) uses it diluted with equal parts of olive oil.

Protylin.—A preparation containing phosphorus in combination with egg albumin, forming a cream-colored, almost tasteless and odorless powder which is insoluble in water. It contains 13 per cent. nitrogen and 2.7 per cent. of phosphorus. *Protylin* is digested by the pancreatic secretions. It is used in place of lecithin in *rachitis*, *neurasthenia*, etc. *Dose*, fifteen to forty-five grains (0.9–2.9 Gm.) in food. Bromated and ferrated protylin containing 4 per cent. and 2.3 per cent. are also offered.

Prune. *Prunum. N. F. IV. Prunes. Pruneau noir*, Fr. Cod. *Pflaume, Zwetsche*, G.—"The partly dried ripe fruit of *Prunus domestica* Linné (Fam. *Rosaceæ*)." *N. F. IV. U. S. VIII.* "The dried ripe fruits of Prunus domestica *Linn., var.* Juliana, DC." *Br.*

Prunus domestica or the cultivated *prune* or plum tree is so well known as to render a minute description unnecessary. The varieties of the tree produced by cultivation are very numerous. Nearly one hundred are to be found in the British gardens. Though at present growing wild in various parts of Europe, it is thought to have been brought originally from Asia Minor and Syria. It is the partly dried ripe fruits only that are official in the N. F. IV. They are officially described as "oblong, ellipsoidal, more or less compressed, 3 to 4 cm. long; externally brownish-black, shrivelled; the sarcocarp sweet and acidulous; putamen hard, smooth or irregularly ridged; the seed, shaped like that of the almond but smaller and of a bitter-almond taste." *N. F. IV.* The prunes brought to our market come chiefly from the south of France, the best from Bordeaux. They are derived from the variety of the tree named *Juliana* by Linnæus. The fresh fruit, called *Prune de Saint-Julien* by

the French, is of an oval shape, nearly an inch in length, and of a deep violet color. It is prepared by drying in the sun, after having been exposed to the heat of an oven. The finest prunes, used on the tables of France, are prepared from the larger kind of plums, such as the *Saint Catharine*, and *Reine Claude* or *greengage*. An inferior sort is brought from Germany.

Prunes have a feeble odor, and a sweet mucilaginous taste, which is generally also somewhat acid. They contain uncrystallizable sugar, malic acid, and mucilaginous matter. The following is given as the average of nine analyses of dried prunes. Water 29.30 per cent., nitrogenous material 2.35 per cent., fat 0.53 per cent., free acid 2.72 per cent., sugar 44.35 per cent., other nitrogen-free material 17.89 per cent., woody fiber (not including the stone) 1.48 per cent., ash 1.38 per cent. (König, *Nahrungsmittel*, ii, 397, 1880.) In Hungary a kind of brandy (*Zwetschenbranntwein*), containing about 40 per cent. of alcohol, is obtained from them, which in some districts is largely consumed. Bonneberg, a German chemist, has extracted from prunes crystallizable sugar equal to that of the cane.

Prunes are laxative and nutritious, and, stewed with water, form an excellent diet in *costiveness*. Imparting their laxative properties to boiling water, they serve as a pleasant and useful addition to purgative decoctions. Their pulp is used in the preparation of laxative confections. Too largely taken, they are apt to occasion flatulence, griping, and indigestion. Prunes were dropped from the former U. S. Pharmacopœia, but admitted to the National Formulary IV because confection of senna, which was the only preparation in which prunes entered, was not admitted to the U. S. P. IX, but confection of senna is now official in N. F. IV.

Prunella. *Prunella vulgaris* L. *Self-heal. Heal-all. Carpenter Weed. Brunella vulgaris. Paquerette*, Fr. *Braunelle, Braunheil*, G.—A small perennial labiate herb, which is common both in Europe and the United States. It was formerly used in *hemorrhages* and *diarrhea*, and as a gargle in *sore throat*.

Prussian Blue. *Ferri Ferrocyanidum. U. S.* 1870. *Ferri Ferrocyanuretum. U. S.* 1850. *Ferrocyanide of Iron. Ferrocyanuret of Iron.* $Fe_4Fe_3(CN_6)_3$.—"Take of Ferrocyanide of Potassium *nine troyounces;* Solution of Tersulphate of Iron *a pint;* Water *three pints.* Dissolve the Ferrocyanide of Potassium in two pints of the Water, and add the solution gradually to the Solution of Tersulphate of Iron, previously diluted with the remainder of the Water, stirring the mixture during the addition. Then filter the liquid, and wash the precipitate on the filter with boiling water until the washings pass nearly tasteless. Lastly, dry it, and rub it into a powder." *U. S.*, 1870.

In the above process the salt is decomposed by the gradual addition of the solution of potassium ferrocyanide. Three molecules of ferrocyanide and two of ferric sulphate are mutually decomposed, with the result of forming one molecule of *Prussian blue*, or the 3–4 ferric ferrocyanide, which precipitates, and six molecules of potassium sulphate, which remain in solution.

Prussian blue at one time was manufactured on a large scale by the action of fused alkali and iron salts on nitrogenous organic matter, as dried blood, but it is now prepared from calcium ferrocyanide, formed in gas purifiers, by decomposing it with ferrous sulphate. Gas free from tar is brought into intimate contact with a saturated solution of ferrous sulphate, when *cyanogen mud* is produced. This is heated to boiling and the residue, filtered from the mixture, contains about 30 per cent. of Prussian blue.

A preparation under the name of *Soluble Prussian Blue* has been introduced into use for injecting anatomical preparations by Schroeder van der Kolk, and is said to be much esteemed for this purpose. To obtain it there must be a great excess of the potassium ferrocyanide in concentrated solution. The iron should be in a state of sesquichloride, in the proportion of not more than one-eighth or one-tenth of the ferrocyanide employed. After their mixture, the precipitate is washed with water till it begins to become blue, when it is expressed and dried in the air. On the small scale it may be economically obtained in the following manner: Take solutions of the ferrocyanide containing 217 grammes to the liter of water, and of the sesquichloride containing one part of the solid salt in 10 parts of water. Then, taking equal volumes of the two solutions, add to each one twice its volume of a cold concentrated solution of sodium sulphate, and mix the solutions. Pour on a filter, and treat as directed above. The product dried in the air is perfectly soluble, and admirably adapted for injection. (*J. P. C.*, 4e sér., iv, 238.) For other formulæ for soluble Prussian blue, see *Ibid.*, 4e sér., xix, 227.

Properties.—Pure Prussian blue is a tasteless powder, insoluble in water and alcohol, and having a rich deep blue color. It is insoluble in dilute acids, decomposed by fuming nitric acid, and dissolved without decomposition by strong sulphuric acid, forming a white mass of the consistence of paste, from which the Prussian blue may be precipitated unchanged by water. Concentrated hydrochloric acid decomposes it, dissolving ferric oxide, and liberating hydroferrocyanic acid. When boiled with mercuric oxide, it generates mercuric cyanide. (See *Hydrargyri Cyanidum.*) By the contact of a red-hot body it takes fire and burns slowly, leaving a residue of ferric oxide. When it is heated in closed vessels, water, hydrocyanic acid, and ammonium carbonate are evolved, and iron carbide is left. Its composition has been given above. The Prussian blue of commerce was discovered by accident, in 1710, by Diesbach, a preparer of colors at Berlin. It has the same general properties as the pure substance. It occurs in small rectangular masses, which are heavier than water and have a fracture presenting a bronzed appearance. Besides the constituents of pure Prussian blue, it always contains uncombined ferric oxide, and a portion of alumina, derived from the alum employed in its manufacture, whch serves to give it body as a pigment. These substances may be detected by boiling the pigment with diluted hydrochloric acid and precipitating the filtered solution with ammonia. Pure Prussian blue treated in this manner yields no precipitate.

Uses.—Prussian blue has been deemed tonic, febrifuge, and alterative, but is at present very rarely used, and is probably of no medicinal value. It is sometimes employed as an application to ill-conditioned *ulcers*, mixed with simple ointment in the proportion of a drachm to the ounce. The *dose* is from three to five grains (0.20 to 0.32 Gm.), repeated several times a day, and gradually increased until some effect is produced.

Psidium. *Psidium Guayava* L. *P. pomiferum* L. *P. pyriferum* L., and other species of *Psidium*. (Fam. *Myrtaceæ*.) *Guava.*—Hartwich has exam-

ined the root, bark, and leaves of these plants from India. (See *Ph. Rev.*, 1896, 257.)

Psoralea.—Of this genus (Fam. *Leguminosæ*) various species are useful. The tubers of *P. esculenta* L. are employed by the Indians of the Northwestern United States, and by the settlers, as articles of food, being the *prairie turnip* or *prairie potato*, the *tipsinah* and *taahgu* of the Indians. C. Richardson found in it nearly 70 per cent. of starch, and 5 per cent. of a new, rapidly crystallizing sugar, which has not been further investigated. *P. glandulosa* L., *culen, yolochiahitl*, of the Mexican Pharmacopœia, yields a leaf which is used as a tonic or anthelmintic, and an emetic root. *P. bituminosa* L., of Europe, and *P. physodes* Dougl., of California, are popularly considered tonic and emmenagogue, the former being presented under the name of *Herba Trifolii Bituminosi*. *P. pedunculata* (Mill.) Vail. (*P. melilotoides* Michx.) (*Congo root, Bob's root, Samson's snakeroot*), of Virginia, has been recommended as an aromatic bitter tonic, especially useful in *chronic diarrhea*. The part employed is the root, from which MacNair obtained about 2 per cent. of a volatile oil, having the specific gravity 0.93, a pungent and bitter taste, and a neutral reaction; also a bitter principle, but not tannin. For further description, see *A. J. P.*, July, 1889; also 14th and 16th editions of *U. S. D.* *P. corylifolia* L., of India, yields an oleoresin which is used in the treatment of *leucoderma* and other skin diseases. (*P. J.*, Sept., 1881.) Mann and Griffiths obtained from the seeds of *P. coryfolia* 13.7 per cent. of a thick brownish oil and 37.2 per cent. of an alcoholic extract which yielded by purification 9.2 per cent. of a resinoid. (*P. J.*, 1912, 260.)

Ptelea. *Ptelea trifoliata* L. and the variety *Mollis* T. and G. *Wafer Ash. Wing Seed. Shrubby Trefoil. Hop Tree. Orme à trois feuilles*, Fr. *Hopfenbaum, Kleebaum*, G. (Fam. *Rutaceæ*.)—This is a shrub with 3-foliate leaves growing in rocky places from Long Island to Minnesota and southward. The root bark has a peculiar somewhat aromatic odor, and a bitter, persistently pungent, and slightly acrid, yet not disagreeable taste. Steer obtained from it an oleoresin of an acrid and bitter taste and the alkaloid *berberine*. An alkaloid, *arginine*, $C_6H_{14}O_2N_4$, is stated also to be present in the root. (*A. J. P.*, 1867, 337.) It was formerly employed among the physicians of the Western States in the treatment of *dyspepsia*, and generally in diseases requiring a mild, non-irritating, bitter tonic.

Ptomaines.—Within recent years a class of very interesting compounds have been described and are known under this name. They are alkaloid-like bases obtained from animal tissue after decomposition has commenced, hence sometimes called *cadaveric alkaloids*. Bence Jones and Dupré (*Ph. Centralh.*, xvi, No. 10) first published a notice of the finding of an alkaloid-like base from a decomposing human liver. Its sulphate solution fluoresced, and in other ways resembled quinine, yielding precipitates also with the usual alkaloidal reagents, potassio-mercuric iodide, phosphomolybdic acid, and gold and platinic chlorides. It appears, however, that Marquardt had isolated such bases even previous to this. The chief investigators of this class of alkaloids have been Selmi, who first systematically studied them and gave them the name *ptomaines*, and Brieger, who since 1882 has published a series of elaborate studies and has classified their reactions.

Brieger's researches established the fact that ptomaines are formed during the earlier stages of decay, and that they are in general of a non-benzenoid character, but that as putrefaction continues they gradually disappear and give place to well-known benzenoid compounds, phenol, cresol, indol, etc. Brieger studied the ptomaines from (*a*) putrid horse flesh, beef, and human muscular tissue; (*b*) from putrid fish; (*c*) from putrid cheese; (*d*) from putrid glue; and (*e*) from putrid yeast. The bases obtained are of two classes. At first are obtained oxygenated bases, like *choline*, $C_5H_{15}NO_2$, *muscarine*, $C_5H_{15}NO_3$, *neurine*, $C_5H_{13}NO$, *gadinine*, $C_7H_{18}NO_2$, and *tetanine*, $C_{13}H_{20}N_2O_4$. These seem later to disappear, and amines seem to be almost the only products. Among those mentioned, the simplest are *dimethylamine*, $(CH_3)_2NH$, *trimethylamine*, $(CH_3)_3N$, and *triethylamine*, $(C_2H_5)_3N$. A number of the others seem to be diamines, like *putrescine*, $C_4H_{12}N_2$, *cadaverine*, $C_5H_{14}N_2$, *saprine*, $C_5H_{16}N_2$, *neuridine*, $C_5H_{14}N_2$, all four discovered by Brieger in the cadaver, *collidine*, $C_8H_{11}N$, *hydrocollidine*, $C_{11}H_{13}N$, *parvoline*, $C_9H_{13}N$, and *tyrotoxicon* (*diazobenzene*), $C_6H_5N_2$, discovered by Vaughan in poisonous cheese and in ice cream which had been allowed to become stale.

Barger and Walpole (*J. P.*, 1909, xxxvi) separated from putrescent horse meat *parahydroxyphenylethylamine* which is formed by the decomposition of tyrosine. This base also occurs in ergot. Dale and Dixon (*J. P.*, xxxix) have shown that this base as well as *isoamylamine*, which also occurs in putrescent meat, acts upon the system like adrenalin, causing marked rise in the blood pressure.

The formation of these volatile and frequently actively poisonous bases in the cadaver would seem to make the task of the toxicologist very difficult when the search for poisonous bases has been delayed until decomposition has set in. Any reagent or reagents, therefore, which will enable the chemist to decide between vegetable bases and these ptomaines becomes very important. Brouardel and Bontury (*C. R. A. S.*, xcii, 1056) state that they have found such a decisive reagent in potassium ferricyanide. This compound when treated with a solution of a pure vegetable alkaloid is unacted upon by it; while, under the same conditions, it is instantly reduced to the state of ferrocyanide by a ptomaine, and thus becomes capable of forming Prussian blue with a ferric salt. Up to the present but two exceptions to this rule have been found—morphine, which readily reduces potassium ferricyanide, and veratrine, which gives traces of such reduction. It is possible, however, that in this last case the reducing action is due to certain impurities which the investigators were unable to remove completely from the veratrine employed by them.

Ptomaines are probably devoid of medicinal properties, but are of great interest to the toxicologist, not only from a chemical standpoint, but also from the fact that they are excessively fatal in their effects upon the animal economy. The well-known action of putrescent flesh, the curious poisonings sometimes produced by lobsters and other animals which feed upon carrion, are in all probability caused by them. In regard to treatment of poisoning by putrid animal matters, our present knowledge only justifies the immediate evacuation of the stomach and bowels and the meeting of the various indications as they arise. For fuller information as to the formation of ptomaines, their detection, separation, and clin-

ical features, see *Ptomaines and Other Animal Alkaloids*, by A. C. Farquharson, M.D., Bristol, Eng.: John Wright & Co., 1892.

Pulmoform. *Methylene-diguaiacol.*

$CH_2 \begin{matrix} C_6H_3(OCH_3)(OH) \\ C_6H_3(OCH_3)(OH) \end{matrix}$. This is a yellow tasteless powder obtained by the action of formaldehyde upon guaiacol. It is used as a substitute for creosote, especially in the treatment of *chronic bronchitis* and *tuberculosis*. The *dose* is eight grains (0.5 Gm.).

Pulmonaria. *Pulmonaria officinalis* L. *Lungwort. Pulmonaire*, Fr. *Lungenkraut*, G. (Fam. *Boraginaceæ*.)—An herbaceous perennial, European plant, sometimes cultivated. The leaves have been employed in *catarrh, hemoptysis*, and *consumption*, but their virtues are doubtful.

Pulsatilla. *N. F. IV. Pasque Flower. Meadow Anemone.*—"The dried herb of *Anemone Pulsatilla* Linné, *Anemone pratensis* Linné, or of *Anemone Ludoviciana* (Nuttall) Heller (Fam. *Ranunculaceæ*), without the presence of more than 5 per cent. of foreign matter." *N. F.*

The plants are common throughout Europe and should be employed in the fresh condition. The drug is collected at the time of flowering of the plants which extend from March to May. The drug is frequently sold in the dry condition and should be carefully preserved.

The genus *Anemone* is composed of small herbal plants growing in almost all the temperate countries of the world, and probably possessed very generally of the acrid rubefacient properties of the *Ranunculaceæ*.

Pulsatilla was official in the U. S. P. 1890 and has been admitted to the N. F. IV. It has been introduced to make the tincture of pulsatilla of the strength of 10 per cent., with a menstruum of 3 volumes of alcohol with 1 volume of water. It is described by the N. F. as follows:

"Leaves and flowering scapes matted, silky-villous; basal leaves with petioles up to 30 cm. in length, the latter hollow, often purplish in color, the blades twice or thrice deeply three- or four-parted or pinnately cleft, the lobes linear and acute, the base of the petiole more hairy than above and frequently attached to the short rootstock; flowering scapes up to 30 cm. in length, solid in the lower portion and hollow in the upper part, with sessile, involucral dissected leaves near the flower, occasionally with remains of the dull purple hairy sepals and the dense-woolly, plumose-tailed akenes. Nearly odorless; taste very acrid.

"The powder, when examined under the microscope, shows numerous simple, thick-walled hairs up to 2.5 mm. in length and up to 0.02 mm. in thickness; tracheæ up to 0.03 mm. in breadth with spiral markings or with simple or bordered pores; fragments of epidermal tissue with stoma, the latter being broadly elliptical and up to 0.05 mm. in length; some epidermal cells with wavy vertical walls; calcium oxalate crystals and starch grains few or absent. Pulsatilla yields not more than 10 per cent. of ash." *N. F.*

The *A. ludoviciana* Nutt. (*Pulsatilla ludoviciana* (Nutt.) Heller, *A. nuttalliana* Gray), an American species, growing in Minnesota and other parts beyond the Mississippi, has been employed with supposed advantage by W. H. Miller of St. Paul, in *chronic diseases of the eyes*, in *cutaneous eruptions*, and in *syphilitic affections*. A. W. Miller found *anemonin* in it. (*A. J. P.*, 1862, p. 300; see also *A. J. P.*, xlv, 299.) *A. nemorosa* L., which is common in Europe, is said to act as a poison to cattle, producing bloody urine and convulsions. It is stated also to have proved, when applied to the head, a speedy cure for *tinea capitis*. It is probable that the American *A. quinquefolia* L., at first described as a variety of *A. nemorosa*, has similar properties. The American *Pasque Flower* (*A. patens* L., var. *Wolfgangiam* (Bess.) Koch), formerly known as *A. patens* L. var. *Nuttaliana* Gray, was recognized as a source of pulsatilla. This plant is also designated as *Pulsatilla hirsutissima* (Pursh.) Britt.

Beckurts obtained from pulsatilla *anemone camphor* by treating in each case the aqueous distillate of *A. nemorosa*, *A. pratensis*, and *A. pulsatilla* with chloroform. It is unstable, splitting easily into anemonin and anemonic acid, the latter, when treated with alkalies, yielding *anemoninic acid*, $C_{10}H_{12}O_6$. (*P. J.*, 1885, 365.) The formula of anemonin is $C_{10}H_8O_4$. It is decomposed at temperatures above 152° C. (305.6° F.), and dissolves in alkalies with yellow color, changing at the same time into *anemonic acid*, $C_{10}H_{10}O_5$. When treated with nascent hydrogen in an acid solution, anemonin yields *hydroanemonin*, $C_{10}H_{12}O_4$, which crystallizes from boiling petroleum in large colorless laminæ which contain 1 molecule of H_2O, melt at 78° C. (172.4° F.), and distil without decomposition at from 210° to 212° C. (410°–414° F.) under a pressure of 10 mm. Hydroanemonin is much more stable than anemonin.

Medicinal Properties and Uses.—Pulsatilla is a violent irritant, producing when taken in sufficient amount excessive vomiting and purging, with pain, hematuria, tremors, dyspnea, and collapse. The statements of the physiological action of anemonin vary so much that there can be little doubt that different experimenters have used different substances under the same name. Noel and Lambert (*A. J. P.*, 1897) affirm that it has no action upon the heart but affects powerfully the central nervous system, producing in the lower animals progressive paralysis of spinal origin. On the other hand, Bronevski (*Med. Press*, Aug., 1886) affirms that anemonin affects very powerfully not only the nerve centers but the heart itself. The strength of commercial anemonin is variable. Broudgeest gives the fatal dose for the rabbit as 200 mgm. per kilo, while in Noel and Lambert's experiments 0.16 gramme per kilo was required to kill a guinea-pig. Authors place the *dose* for man at from five-sixths to one and one-half grains (0.05–0.096 Gm.) a day, in divided amounts.

It has been claimed for pulsatilla that it acts powerfully upon the genitalia in men and women, and is useful in *dysmenorrhea* and *ovarian irritation;* also *epididymitis* and *orchitis*. Our own experience with it is in accord with that of many practitioners—that unless given in infinitesimal dose, with much ceremony, it fails to achieve any good in these various cases, so that the effect which sometimes follows its use in hysterical women is of psychical origin. Noel and Lambert especially commend a fluidextract made from the fresh herb, of which they state that from seventy-five to one hundred and twenty-five minims (4.6–7.8 mils) may be exhibited in the course of twenty-four hours. The *dose* of the dried powder is commonly given as from two to three grains (0.13–0.2 Gm.), but probably much larger amounts can be safely taken.

Pumice. *Pumex*, N. F. *Pumice Stone. Obsidian.*—"A substance of volcanic origin, consist-

ing chiefly of complex silicates of aluminum, potassium, and sodium." *N. F. IV.*

A very light porous stone, found in the vicinity of active and extinct volcanoes, and believed to have been thrown up during their eruption. The spongy structure of pumice is believed to be due to the effects of aqueous vapor upon lava while in a fluid state. The pumice stone of commerce is said to be obtained chiefly from Lipari. It is used whole, in the manner of a file, for removing the outer surfaces of bodies, or for rubbing down inequalities, and, in the state of powder, for polishing glass, metals, stones, etc., purposes to which it is adapted by the hardness of its particles. (See *P. J.*, 1882.)

Pumice was admitted to the National Formulary IV for use in several preparations to assist in distributing the particles of extracts, tar and resins to facilitate solution. It is described as follows:

"Pumice occurs as very light, hard, rough, porous gray masses, or as a gritty, gray-colored powder. It is permanent in the air, odorless and tasteless. The dry masses usually float on water.

"Boil 10 Gm. of Pumice with 50 mils of distilled water for one-half hour, adding distilled water from time to time to maintain approximately the original volume and then filter; the filtrate is neutral to litmus, and one-half of this filtrate, when evaporated and the residue dried to constant weight at 110° C., yields not more than 0.01 Gm. of residue (*soluble substances*). The remaining half of the filtrate, after slightly acidulating with hydrochloric acid, does not yield a blue color with potassium ferrocyanide T.S. (*iron*).

"Boil 1 Gm. of Pumice with 25 mils of diluted hydrochloric acid for one-half hour, adding distilled water from time to time to maintain approximately the original volume, and then filter the liquid; the filtrate yields upon evaporating to dryness, igniting and quickly weighing, not more than 0.05 Gm. of residue." *N. F. IV.*

Punaria Ascochingæ.—This plant was said to belong to the *Compositæ* and was native in Argentine; was asserted to be free from alkaloids, but to contain a glucosidal resin which is its active principle. Zehden (*Med. Woch.*, 1906, No. 35) found it useful in *asthma* when the powder, made up into pastilles called *asthma carbon*, is burned and inhaled.

Holmes (*P. J.*, 1908, lxxx, 316) says there is no plant known by this name and that the same substance was introduced many years ago and was really obtained from *Brachycladi stuckertii.*

Purgatol. *Purgatin. Anthrapurpurine-diacetate. Diacetyl Ester of Anthrapurpurine,* or *Trioxyanthraquinone.* $C_{14}H_5(OH)(OC_2H_3O)_2O_2$.—This substance occurs as an orange-colored crystalline powder, melting at 175° to 178° C. (347°–352.4° F.), insoluble in water and in dilute acids, but slowly soluble in weak alkali and splitting up with development of a deep violet-red coloration.

Purgatol is said to be a laxative similar to emodin, to which it is chemically allied. It is absorbed to some extent, causing the urine to become red. It has been recommended in *chronic constipation* in *doses* of eight grains (0.5 Gm.), increased if necessary, and is said to act in from three to twelve hours without pain.

Pycnanthemum. *P. flexuosum* (Walt.) Bsp. (*P. linifolium* Pursh.) *Dysentery Weed.*—This American mint is popularly used in bowel complaints; its hot infusion is diaphoretic. (See *A. J. P.*, 1894, 65, 169; *Ph. Rund.*, 1896, 32.)

A volatile oil was obtained by E. R. Miller by distilling the leaves and flowering tops of *P. pycnanthemoides.* (See *Proc. Alabama Pharm. Assoc.*, 1910, 58.)

Pyocyanase.—This is the name which is given to a solution of bacterial proteids, obtained by the process of autolysis, from the *Bacillus pyocyaneus.* The method of preparation is as follows: The bacilli are grown in bouillon until they cease to multiply; this cessation of growth is believed to be due to the production of a ferment which eventually leads to a solution of the bodies of the bacteria. The bouillon is then filtered through porcelain filters to free it from any bacteria which may be present. This solution contains a substance which has the power of dissolving not only the *Bacillus pyocyaneus*, but many other forms of bacteria, including those which cause diphtheria, typhoid fever, streptococci, etc. The tubercle bacillus, however, does not appear to be affected by it. Muhsam (*D. M. W.*, 1908, xxxiv, 231) added one drop of *pyocyanase* to eighty minims (5 mils) of a bouillon culture of diphtheria and found that in twenty-four hours these germs were all destroyed. He also injected into guinea-pigs 2 mils of diphtheria culture to which was added at the time of inoculation from one to five drops of pyocyanase and found that in every instance the latter protected the animals against the acquirement of the disease.

Pyocyanase has been used as a local antibacterial agent in a number of conditions. It has been found serviceable when applied directly to the membranes in cases of *diphtheria*, it is stated that it is the only substance which is capable of sterilizing the mouth, it has also been employed with asserted good results in various other suppurative and infectious conditions of the mouth, nose and throat. Pringsheim (*Med. Klin.*, 1909, p. 1678) dissents from the chorus of praise and states that it is not superior in its practical effects to other disinfectants in common use. Bernbach (*M. M. W.*, 1908, lv, 120) finds that when injected subcutaneously it is followed by local redness, swelling and pain, and chill followed by a fever reaching as high at times as 40° C. (104° F.), which ends in five hours with a critical sweat.

Pyocyanase is applied either by means of a swab or an atomizer, from fifty to eight minims (3.0–5.0 mils) being used.

Pyoktanin Blue. *Methyl Violet. Penta and Hexa-methyl-para-rosaniline Hydrochloride.*—A violet crystalline powder soluble in 12 parts of alcohol, 50 parts glycerin and 75 parts water.

According to Liebrich, this is a mixture of aniline compounds. It is used as an antiseptic in the form of pencils or in a powder. *Pyoktanin yellow*, used for similar purposes, is considerably weaker in its effect. It also is used in the form of pencils or powder. The minimum *dose* of each is one grain (0.065 Gm.), while the maximum daily *dose* of the blue is ten grains (0.65 Gm.) and of the yellow, fifteen grains (1.0 Gm.). Methyl violet is also valuable as an indicator for detecting the presence of inorganic acids in organic acids, organic acids not affecting the color of its aqueous solution, while inorganic acids in exceedingly small proportion turn its solution bright green.

In Stilling's experiments a solution of pyoktanin in the strength of one to four thousand was sufficient to prevent the development of bacteria of putrefaction; the *Staphylococcus pyogenes aureus* was found to be very susceptible to the germicidal power of the methyl violet. Janicke, experimenting with the pathogenic organisms of pus, of

anthrax, of cholera, of typhus, and of pneumonia, found the activity of pyoktanin even greater than asserted by Stilling, and noticed a very remarkable difference in the susceptibility of different species of bacteria, making the further important observation that those bacteria that were most readily stained by the methyl violet were most readily influenced by it. On the other hand, Valude states (*Internat. Med. Congress*, 1890) that immersion for at least one hour in a 1 per cent. solution of pyoktanin was required to effect the same result on pathogenic bacteria as was caused in ten minutes by 1 to 4000 corrosive sublimate. The practical value in surgery of pyoktanin has been asserted by Stilling, by Sée and Morau (*Med. Mod.*, 1890) by Patterson, and by numerous other surgeons, but the remedy has not come into general use, probably because of its vigorous staining properties. It has, however, been used to a considerable extent in veterinary practice. Klein (*Berlin. Tierartz. Wochens.*, 1911) and others have reported favorably on its value in *foot and mouth disease*. It is also used in *doses* of one to eight grains (0.065–0.5 Gm.) in the treatment of *cholera* and *carcinoma*.

According to Führer (*A. E. P. P.*, 1908, lix, p. 161), methyl violet has an effect upon the heart similar in kind to that of digitalis, and methyl green, which is prepared from methyl violet, has no effect upon the heart, but acts upon the peripheral motor nerves as does curara.

Pyoktanin Mercury.—A combination of mercury with blue pyoktanin. It forms a violet powder almost insoluble in water and alcohol. It is used as antiseptic in *gonorrhea* in 1–2000 solutions and in *burns*, diluted with equal amounts of starch.

Pyoktanin Yellow. *Imino tetramethyl diamido diphenyl methane hydrochloride. Apyonin. Medicinal Auramine.*—This is a yellow powder insoluble in water and alcohol, used as an antiseptic in *skin diseases* and in ophthalmic practice. It is used as a dusting powder, 1 or 2 per cent., or 2 to 10 per cent. ointments.

Pyramidon. *Di-methyl-amino-phenyl-dimethyl-pyrazolon. Amidopyrine.* $C_{13}H_{27}N_3O$. *N. N. R.* 1917.—This is a derivative of antipyrine in which an H atom of the pyrazolon group is replaced by a dimethyl-amido group. It is said to be formed by reducing iso-nitroso-antipyrine and methylating the product so obtained. *Pyramidon* is a colorless crystalline powder, soluble in water to the extent of 1 in 10 (maximum of solubility is reached at 80° C., 176° F.), and practically tasteless. Pyramidon may be easily distinguished from antipyrine by its color reactions with various reagents. Ferric chloride gives a deep blue-violet fugitive color, and not the red of antipyrine. Nitrous acid gives a fugitive violet instead of the more permanent green of iso-nitroso-antipyrine. Nitric acid also gives a violet to amethyst coloration. In the urine pyramidon may best be detected by ferric chloride, although the color produced is no longer a pure blue, but Tokay red with a tinge of amethyst.

Filehne (*B. K. W.*, 1896) states that pyramidon resembles in its action antipyrine, and is equally efficient as an antipyretic and analgesic, but affirms that it is much more active and that its effects are more lasting than those of antipyrine. It is readily absorbed and is said to be eliminated through the kidneys in part unchanged, in part converted into *rubaronic acid*, and in part into a material which is colored deeply by ferric chloride and is probably *antipyryl urea*.

In a number of cases the urine has taken a pinkish hue after the use of pyramidon. This, by some, has been attributed to the formation of hematoporphyrin, but Apert asserts that it is due to the formation of decomposition products of the drug itself.

According to Ssadkowski, it is a stimulant to the heart and blood vessels, so that in *phthisis* with high arterial pressure it may produce *hemoptysis*. It has been used as an antipyretic and as an analgesic. As an antipyretic its influence is slow and continuing, and some observers assert that it is more prone than antipyrine and acetphenetidin to produce excessive sweating and collapse. It has been highly commended in *migraine*, *neuralgia*, and similar conditions; also in *asthma* of nervous origin. The *dose*, from five to ten grains (0.32–0.6 Gm.), may be repeated every three or four hours, not exceeding thirty grains (2.0 Gm.) in the twenty-four hours, administered in capsule or in aromatic solution.

Pyramidon Camphorate. *N. N. R.* 1917.—There are two combinations of camphoric acid with pyramidon on the market. The neutral pyramidon camphorate, $(C_{13}H_{17}N_3O)_2C_{10}H_{16}O_4$, is a white, crystalline powder, fusing between 80° and 90° C. (176°–194° F.), soluble in 15 parts water and 2 parts alcohol. The acid camphorate (*pyramidon bicamphorate*), $C_{13}H_{17}N_3O.C_{10}H_{16}O_4$, has a faintly acid reaction, fuses between 84° and 94° C. (183.2°–201.2° F.), and is soluble in twenty parts of water or four of alcohol. The purpose of these combinations is to overcome the tendency of pyramidon to produce excessive sweating, indeed, it is asserted that the bicamphorate is useful to control the *night sweats* of *phthisis*. The two salts are used for much the same purposes as pyramidon. *Dose*, of either, is eight to fifteen grains (0.5–1.0 Gm.).

Pyramidon Salicylate. *Pyramidonis Salicylas.* $C_{13}H_{17}N_3O.C_7H_6O_3$.—This substance has been proposed as a substitute for the older salicylates, and may be used in their stead in subacute and chronic cases. The *dose* is eight to twelve grains (0.5–0.78 Gm.).

Pyrantin. *P-ethoxyphenylsuccinimide. Phenosuccin.* $(CH_2CO)_2.N.C_6H_4.OC_2H_5$.—It is prepared by melting together *p*-amidophenetol hydrochloride or acetphenetidin with succinic acid and extracting with alcohol. It is colorless, crystallizes in needles melting at 155° C. (311° F.), is insoluble in ether, but soluble in 83.6 parts of boiling water and in 1317 parts of water at 17° C. (62.6° F.). Alkalies convert it into salts of *p*-ethoxyphenylsuccinamic acid, which are soluble in water. A. Piutti states that this drug possesses properties analogous to acetphenetidin. The sodium salt of this substance is marketed under the name of *soluble pyrantin*. Renzi and De Govanni have found it especially useful in acute *rheumatism* in *doses* of from fifteen to forty-five grains (1–3 Gm.) per day.

Pyranum. *Pyrenol. Thymol-sodium Benzoyl-oxybenzoate.*—This is a white, hygroscopic, crystalline powder with an aromatic odor and a sweetish taste. It dissolves readily in water, one part to five, and in alcohol, one part to ten. This substance, which apparently undergoes change in the system (salicylic acid and thymol having been detected in the urine after its administration), was brought forward by Schlesinger (*Th. M.*, Feb., 1903) as an antipyretic and antineuralgic. Fifteen grammes given to a healthy man in three days produced no other symptoms than sweating, and in the animal large doses caused only a slight fall in the arterial pressure. It was used in various

cases of chronic and acute *fevers;* was found to be superior to salicylic acid in acute *rheumatism,* and to have very remarkable analgesic properties. Burchand (*Ther. Geg.,* 1905) recommends *pyranum* in *hysteria* and *neurasthenia. Dose,* fifteen grains (1 Gm.) repeated up to forty-five grains (3 Gm.) in a day, if required.

Pyrazole. $C_3H_4N_2$.($\begin{matrix}CH=CH\\|\\CH=N\end{matrix}$>NH).—This compound has been prepared by acting upon epichlorhydrin with hydrazine in the presence of zinc chloride. It is a basic substance, crystallizing in needles, melting at 70° C. (158° F.), and boiling at 188° C. (370.4° F.). It is readily soluble in water, alcohol, and ether. All of the *pyrazole* derivatives were found by Tappeiner (*A. E. P. P.,* 1891) to act as paralyzants of the central nervous system. Only one of them, *phenylmethylpyrazolcarboxylic acid,* seems to promise value in practical medicine, on account of its extraordinarily active diuretic effects upon both the lower animals and man. Daily *dose,* from fifteen to thirty grains (1.0–2.0 Gm.).

Pyrenol, a white, crystalline, aromatic powder soluble in water and alcohol, said to be a compound of benoates, salicylates, and thymol, is a proprietary preparation used as an expectorant and antispasmodic.

Pyridine. C_5H_5N.—*Pyridine* is the first of a series of homologous bases which are found in coal tar naphtha, in shale oil, in peat tar, in tobacco smoke, and more especially in the product known as *Dippel's oil,* obtained by the distillation of bones and other animal matter. It has been used as an antiseptic and germicide, and is employed in Germany for "denaturing" alcohol for manufacturing uses. Pure pyridine is a colorless liquid, with a powerful and persistent odor, of sp. gr. 1.0033 at 0° C. (32° F.), and boils at 116° to 118° C. (240.8°–244.4° F.). It is miscible with water in all proportions, but is precipitated from its solution by excess of sodium hydroxide. It is also miscible with alcohol, ether, chloroform, benzene, and fatty oils. In toxic dose pyridine is a violent poison, producing cyanosis, methemoglobinemia, great muscular weakness from paralysis both of the motor centers and nerves, and finally death from failure of respiration. De Renzi asserts that in small doses it stimulates the heart, increases the blood pressure, and is a useful remedy in *angina pectoris.* It was first introduced into practical medicine, as a remedy for *asthma,* by Germain Sée, whose statement has since been confirmed by various clinicians. Sée employed it by exposing about a drachm upon a plate in a small room, in which the patient remained from twenty to thirty minutes, the process being repeated several times a day; or from five to ten minims in two ounces of water may be taken by anatomizer; or five minims may be inhaled directly. De Renzi has given it internally in the daily *dose* of six minims (0.3 mil) gradually increased to twenty-five (1.6 mils). Under the name of *pyrilin* is marketed a solution of *pyridin ethyl-phosphinate,* recommended in diseases of the air passages.

Pyridine Tricarboxylic Acid. $C_5H_2(COOH)_3N$. —This important derivative of pyridine may be prepared by the oxidation of methyl-pyridine (picoline), or is obtained from certain natural alkaloids, such as quinine, quinidine, and cinchonidine, by boiling with an alkaline solution of potassium permanganate. It forms prisms melting at 244° C. (471.2° F.). This substance is said to be an active antiseptic and antipyretic, and, according to Rademaker, in *malarial fever* even surpasses quinine, when given in dose of ten grains (0.65 Gm.) after the paroxysm. The same authority asserts that, when given in doses of from one to two grains (0.065–0.13 Gm.), it will arrest the paroxysm of spasmodic *asthma.* It has also been used in *typhoid fever* as an antipyretic, and as a specific in *gonorrhea,* when it is given by injection. (*Medical Herald,* June, 1887, 1888.) No accidents have been reported from its use.

Pyrosal. $C_9H_8O_5C_{11}H_{12}N_2O$.—*Antipyrine acetylsalicylate* forms colorless needles or plates of an acid but not bitter taste which are difficultly soluble in water. *Pyrosal* is said to contain about 50 per cent. of antipyrine, 36 per cent. of salicylic acid, and 14 per cent. of acetic acid. It is asserted to be broken up in the intestinal canal into its constituents, and to exert their influence in the human system, and has been used in *polyarthritis,* severe *influenza, febrile cystitis, migraine,* and *sciatica,* in *doses* of from eight to fifteen grains (0.5–1.0 Gm.), from two to six times daily.

Quamacai.—The wood of *Paullinia Thalictrifolia* (fam. *Sapindaceæ*), a native of Brazil, has been used in *beri-beri* and *rheumatic affections.* It is also used externally in diaphoretic baths.

Quebracho Colorado and *Quebracho Gum* are respectively the wood and the dried juice or aqueous extract of the *Schinopsis Lorentzii* (Gries.) Engl. (fam. *Anacardiaceæ*), a large tree growing in the Argentine Republic. The wood is very heavy, hard, and of a reddish-brown color. (See *A. J. P.,* 1879, p. 152; also Penzoldt, *loc. cit.;* P. J., xii.) *Quebracho colorado* has been used as a substitute for the true quebracho, but is essentially different from it, and probably is a simple astringent and gastro-intestinal stimulant, although Penzoldt claims that it is similar in its action, but much weaker than quebracho blanco. The extract, which contains about 70 per cent. of tannin, is extensively used in the tanning of leather. In appearance it is somewhat intermediate between kino and logwood extract. Perkin and Gunnel have determined the yellow coloring matter of the wood of quebracho colorado to be identical with *fisetin,* $C_{15}H_{10}O_6$, the coloring matter of young fustic, *Rhus Cotinus* L. It occurs in glistening yellow needles, dyeing similarly to quercitin, and yields compounds with mineral acids. Its benzoyl and acetyl derivatives have also been prepared. Fused with alkalies it yields protocatechuic acid and probably resorcinol. Ellagic and gallic acids have also been obtained from the wood, these being probably formed during the isolation of the fisetin. (*A. J. P.,* Nov., 1896, 626.)

Quercus. *N. F. IV* (*U. S. VIII*). *Oak. White Oak Bark. Stone Oak. Écorce de Chêne,* Fr. Cod. *Cortex Quercus,* P. G. *Eichenrinde,* G. *Quercia, Corteccia de quercia,* It.—"The dried bark of the trunk and branches of *Quercus alba* Linné (Fam. *Fagaceæ*), deprived of the periderm." *N. F.*

There are about sixty-five species of oak found in the United States. Many of these are applied to important practical purposes. *Quercus Robur,* or *European oak,* has a very wide distribution. It is the common British oak, constitutes a large part of the European forests, and has spread itself over almost the whole northern section of Asia and along the northern coast of Africa. There are two distinct varieties of it, one, *pedunculata,* with sessile or shortly stalked leaves and the acorns on

long peduncles; the other, *sessiflora*, with the leaf-stalks more or less elongated and the acorns either sessile or provided with a very short peduncle. The dried bark of the smaller branches of this tree were formerly recognized by the Br. Pharmacopœia under the name of *Quercus Cortex*.

Of all the American species, the *white oak* approaches the nearest, in the character of its foliage and the properties of its wood and bark, to *Q. pedunculata* of Great Britain. Its trunk and large branches are covered with a whitish bark, which serves to distinguish it from most of the other species. The leaves are regular and obliquely divided into oblong, obtuse, entire lobes, which are often narrowed at their base. When full grown, they are smooth and light green on their upper surface, and glaucous beneath. Some of the dried leaves remain on the tree during the whole winter. The acorns are large ovoid or ellipoidal, contained in rough, shallow, grayish cups, and supported singly or in pairs upon peduncles nearly 2.5 cm. in length.

The white oak abounds from Ontario to Maine and Minnesota, and extends southward. It is the most highly valued for its timber of all the American oaks, except the *live oak*, *Q. virginiana* Mill. (*Q. virens* Ait.), which is preferred in ship building. The bark is sometimes used for tanning, but the barks of the *red* and *Spanish oaks* are preferred. All parts of the tree, with the exception of the epidermis, are more or less astringent, but this property predominates in the fruit and bark.

White oak bark, deprived of its epidermis, is of a light-brown color, of a coarse, fibrous texture, and not easily pulverized. It occurs "in nearly flat pieces, from 2 to 10 mm. in thickness; externally light brown, becoming darker with age, rough-fibrous; fracture uneven, coarsely fibrous. Odor distinct; taste strongly astringent; not tingeing the saliva yellow when chewed. Quercus yields not more than 7 per cent. of ash." *N. F. IV.* The medicinal value of oak bark depends on the presence of a considerable proportion of tannin. The proportion of this ingredient varies with the size and age of the tree, the part from which the bark is derived, and even the season when it is gathered. It is most abundant in the young bark, and the English oak is said to yield four times as much in spring as in winter. H. Davy found the inner bark most abundant in tannin, the middle portion or cellular integument much less so, and the epidermis almost wholly destitute as well of this principle as of extractive. Kraemer examined the tannin of white oak bark (*A. J. P.*, 1890, p. 236) and assigned to it the formula $C_{29}H_{27}O_{13}$, which was later confirmed by Trimble (*Tannins*). The tannin yields upon sublimation a principle resembling pyrocatechin and upon fusion with potassium hydrate a phenol similar to protocatechinic acid. Dilute solutions of white oak tannin are colored olive-brown with ferric chloride T.S. and possess a slight fluorescence.

The tannic acid of the oak barks is known as *quercitannic acid*, and has, according to Löwe (*Zeit. An. Chem.*, 20, p. 208), two forms, one soluble in water, of the formula $C_{28}H_{28}O_{14}$, and the other difficultly soluble, $C_{28}H_{24}O_{12}$. Both are changed by the loss of water into *oak red*, $C_{28}H_{22}O_{11}$. Neither is a glucoside. Gerber discovered in European oak bark a peculiar bitter principle upon which he conferred the name of *quercin*. This quercin Husemann considers to have been only impure quercite (or oak sugar).

Quercus velutina Lam., or *black oak*, is one of our largest trees, frequently attaining the height of eighty or ninety feet. Its trunk is covered with a deeply furrowed bark, of a black or dark brown color. The leaves are ovate-oblong, pubescent, slightly sinuated with oblong, aculeate lobes. The fructification is biennial. The acorn is globose, flattened at top, and placed in a saucer-shaped cup.

Black oak bark has a more bitter taste than that of the other species, and may be distinguished also by staining the saliva yellow when it is chewed. Its cellular integument contains a coloring principle, capable of being extracted by boiling water, to which it imparts a brownish-yellow color, which is deepened by alkalies and rendered brighter by acids. Under the name of *quercitron*, large quantities of this bark, deprived of its epidermis and reduced to coarse powder, are sent from the United States to Europe, where it is used for dyeing wool and silk of a yellow color. The coloring principle is called *quercitrin*. Herzig (*J. Chem. S.*, 1893, 413) found that its composition is expressed by the formula $C_{21}H_{22}O_{12} + 2H_2O$, and this is confirmed by Rudolph. (*Ph. Post*, 1893, 529.) The reaction for its decomposition is

$$C_{21}H_{22}O_{12} + H_2O = C_{15}H_{10}O_7 + C_6H_{10}O_6$$

the products being *quercetin* and *isodulcite* in equal molecules.

Quercitrin forms yellowish crystals, which, pulverized, yield a citron-yellow powder. It is neutral in reaction, is odorless, and in the dry condition tasteless, but in hot aqueous or alcoholic solution has a bitter taste. It fuses at 160° to 200° C. (320°–392° F.) to a resinous mass. It is almost insoluble in cold water, sparingly soluble in hot water, and easily soluble in alcohol and alkaline solution. Besides this principle, the bark contains much *quercitannic acid;* but it is less used in tanning than the other barks, in consequence of the color which it imparts to the leather, and it was dropped from the U. S. P., 1890, on account of its decoction staining so decidedly.

Quercitrin has been found in various other plants, as in the leaves of *Ruta graveolens*, and the flower buds of *Capparis spinosa*, *Sophora japonica*, and *Æsculus Hippocastanum*, or horse chestnut. (*Chem. Gaz.*, May 2, 1859, p. 161.) As this principle is capable of assuming various colors under various chemical influences, the idea has been advanced that it might be the coloring principle of flowers.

Acorns, besides the bitter and astringent principles of the bark, contain a peculiar saccharine matter (*quercite*), which is insusceptible of the vinous fermentation. (*J. P. C.*, 3e sér., xx, 335.) They are sometimes used as a tonic or astringent, and a decoction made from roasted acorns has been long employed in Germany as a remedy in *scrofula*. Before roasting they should be deprived of their shells, and the cotyledons, according to Dausse, should lose, during the process, 28 per cent. of their weight. (*Ph. Cb.*, Oct. 9, 1850, p. 687.) From half an ounce to an ounce may be prepared and taken like coffee at breakfast (Richter).

The National Formulary IV admitted quercus mainly in order to provide a process for the fluid-extract, *Fluidextractum Quercus*, N. F., which was formerly in the U. S. VIII; it is made with a menstruum of five volumes of alcohol, four volumes of water and one volume of glycerin, followed by diluted alcohol. The medical value of oak-bark depends solely upon its tannin. Because of its cheapness it is often used where an external astringent wash is desired. Thus it is employed

as an injection in *leucorrhea* and *hemorrhoids*, as a wash for flabby *ulcers* and similar purposes.

Quietol. *Valeryl Oxybutyrin from Hydrate.* $C_{14}H_{27}O_4N.HBr$.—This substance forms lustrous crystals of valeric odor and bitter taste; soluble in warm water, alcohol, acetone, etc., and melting point 118° C. (244.4° F.). It is used as an antipyretic and hynotic in *doses* of ten grains (0.65 Gm.).

Quina Morada.—This drug, growing in Bolivia and the Argentine Republic, and there credited with the therapeutic values of cinchona is produced by *Pogonopus Tubulosus* (Rich.) K. Sch. (Fam. *Rubiaceæ*). It has been studied by Arata and Canzoneri, who find in it a blue fluorescent substance, *moradin*, and an alkaloid, *moradeine*. (*P. J.*, April, 1890.)

Quinacetine Sulphate. $(C_{27}H_{31}N_3O_2)_2H_2SO_4.H_2O$.—This is obtained by the reaction of certain organic compounds with methoxylated di-tetrahydro-chinolyl. It is colorless, odorless, and tasteless powder, and dissolves readily in acidulated water. It is antipyretic and anodyne.

Quinanaphthol. *Quinaphthol. Quinine-beta-naphthol-monosulphonate.* $C_{20}H_{24}O_2N_2.(OHC_{10}H_6.SO_3H)_2$.—This is a yellow crystalline powder, soluble in alcohol and water. It fuses at 185° to 186° C. (365°–366.8° F.), and contains 42 per cent. quinine. It is used in *typhoid fever, intestinal tuberculosis, dysentery* and *acute rheumatism* in *doses* of five to fifteen grains (0.3–1 Gm.).

Quinate of Urea. *Urol. Urea Quinate.* $C_7H_{12}O_6.2CO(NH_2)_2$.—A combination of two molecules of urea and one of quinic acid. It forms prismatic crystals melting at 106° to 107° C. (222.8°–224.6° F.). It is recommended by Van Noorden in *doses* of thirty to forty-five grains (2–3 Gm.) dissolved in a tumblerful of hot water, on rising, and going to bed, as a solvent for uric acid.

Quinate of Urotropin. *Quinotropin. Urotropin Quinate. Chinotropin. Hexamethylenamine Quinate.*—This quinine compound is furnished commercially in two forms, Quinotropin I, containing 73 per cent. quinic acid and 27 per cent. urotropin; Quinotropin II, containing 80 per cent. quinic acid and 20 per cent. urotropin. These compounds yield aqueous solutions of an acid, agreeable taste. According to Nicolaier and Hagenberg (see also De la Camp, *M. M. W.*, 1901, No. 30), quinotropin does not decrease the excretion of uric acid, but aids in its solution in the urine. *Dose*, Quinotropin I, twenty-five to fifty grains (1.6–3.2 Gm.) per day; Quinotropin II, fifty to seventy-five grains (3.2–5.0 Gm.) per day.

Quinic Acid. *Acidum Quinicum. Kinic Acid. Hexahydro-tetraoxybenzoic Acid.* $C_6H.H_6.(OH)_4COOH$.—Forms colorless, rhombic prisms, easily, soluble in water, difficultly soluble in strong alcohol, which fuse at 162° C. (324° F.). Found naturally in cinchona bark, in the coffee bean, and other sources. Led by the belief that the decrease in the elimination of uric acid, which is said to be produced by strawberries, is due to *quinic acid*, Weiss, of Basel, experimentally determined that quinic acid checks the formation of uric acid in the body, and was led to propose it and its salts as remedies in the treatment of *gout*. This theory of the action of quinic acid is certainly not established and of doubtful correctness, but has given rise to practical trials of quinates by various clinicians in gout with asserted good results. Quinic acid is converted in the system, first into benzoic, and second into hippuric acid. Various combinations of quinic acid have appeared in commerce, often under proprietary names.

Quinidine. *Quinidina. N. F. IV.*—"An alkaloid [$C_{20}H_{24}O_2N_2 = 324.21$], isomeric with quinine, obtained from the bark of various species of *Cinchona* (Fam. *Rubiaceæ*). Preserve it in well-closed containers, protected from light." *N. F.* "Quinidine occurs in acicular, white crystals or as an amorphous, white powder. When crystallized from alcohol it forms monoclinic prisms containing one molecule of alcohol which it slowly loses on exposure to air, and rapidly loses when heated to 100° C. When precipitated by ammonia water from an aqueous solution of a salt of Quinidine, washed and dried, it forms an amorphous powder. Odorless and having an intense and persistent bitter taste. When crystallized from an alcoholic solution, one gramme dissolves at 25° C. in about 32 mils of alcohol, 53 mils of ether, and 1.5 mils of chloroform; very slightly soluble in petroleum benzin and almost insoluble in water. One gramme of dried amorphous Quinidine dissolves at 25° C. in about 36 mils of alcohol, 67 mils of ether, and 1.7 mils of chloroform; very slightly soluble in petroleum benzin and almost insoluble in water. Quinidine melts at about 168° C. Incinerate 0.2 Gm. of Quinidine; no weighable residue remains. Its alcoholic solutions is dextrorotatory and its aqueous solution is alkaline to litmus. A solution of Quinidine in diluted sulphuric acid (1 in 1000) shows a strong blue fluorescence. Add a few drops of bromine T.S. to 10 mils of an aqueous solution of Quinidine (1 in 1000), made with the aid of sufficient diluted sulphuric acid to produce complete solution, and then follow with ammonia water in slight excess; the liquid acquires an emerald-green color. A solution of about 0.1 Gm. of Quinidine in 5 mils of sulphuric acid is not darker than pale yellow. Dissolve 0.5 Gm. of Quinidine in 10 mils of distilled water at 80° C., with just enough sulphuric acid to form a solution neutral to litmus paper, and add a neutral solution of 0.5 Gm. of potassium iodide in 5 mils of distilled water at 80° C. Agitate the mixture slightly, cool it to 15° C. and keep it at this temperature for one hour with occasional stirring. A white precipitate is formed (difference from *quinine*). Filter out the precipitate and add 2 drops of ammonia water to the filtrate; it does not cause more than a slight turbidity (*other cinchona bases*). Care must be taken to have the liquid perfectly neutral after the addition of the potassium iodide solution; if slightly acid, very dilute ammonia water must be added, drop by drop, with constant stirring until exactly neutral to litmus paper." *N. F. IV.* Various salts of quinidine such as the *sulphate* and *tannate* may be obtained. Quinidine is rarely prescribed in medicine. A syrup is recognized by the N. F. (See Part III). Its *dose* is the same as that of quinine, *i.e.*, one and a half grains (0.1 Gm.) as a tonic and fifteen grains (1 Gm.) daily as an antimalarial remedy.

Quinine Acetate. $C_{20}H_{24}O_2N_2.C_2H_4O_2$.—This occurs as fine, white crystals of a bitter, acid taste and characteristic acetic odor. It is soluble in water and alcohol, and is stated to be useful as a diuretic. *Dose*, one to fifteen grains (0.065–1.0 Gm.).

Quinine Acetyl Salicylate. *Quinine Aspirin. Xaxaquin.*—Acetyl salicylate of quinine, $CH_3.CO.O.C_6H_4.COOH.C_{20}H_{24}O_2N_2$, is a white, crystalline powder, sparingly soluble in water, more readily in alcohol and in chloroform. It has been used by Rivolta in *pleurisy*. Boshuwers has used it (*Ther. Neu.*, March, 1908) as a symptomatic remedy in

influenza and *tonsillitis*. The *dose* is three to ten grains (0.2–0.65 Gm.).

Quinine Æsculinate (Neutral). *Escoquinine.*—It is stated to be prepared by chemically combining quinine with a glucoside obtained from the Extract of Hippocastanium. It is a yellowish, amorphous, water insoluble powder, bitter tasting and containing 50 per cent. quinine. It is claimed to have been used with signal success in the treatment of *catarrh* and lung complications. *Dose*, one and one-half to three grains (0.096–0.2 Gm.).

Quinine Albuminate.—Yellowish-white scales, soluble in dilute hydrochloric acid and in acidified pepsin water. It is given for the tonic quinine effect, being agreeable to delicate patients. *Dose*, one to fifteen grains (0.065–1.0 Gm.).

Quinine Antimonate.—A white powder insoluble in water. It is used in the treatment of *rheumatism, gout, herpes*, etc. *Dose*, one and one-half to seven grains (0.096–0.45 Gm.).

Quinine Arrhenalate. *Quinine Methyl-arsenate. Quinine Monomethyl-arsenate.* $(C_{20}H_{24}O_2N_2)_2AsO.(OH)_2CH_3$.—This salt forms colorless, bitter crystals, fusing at 139° to 141° C. (282.2°–285.8° F.), which are insoluble in cold and slightly soluble in warm water.

Quinine Arsenate. *Quininæ Arsenas.* $2(C_{20}H_{24}O_2N_2).H_3AsO_4 + 8H_2O$.—Made by precipitating a solution of 10 parts of quinine hydrochloride in 200 parts of water with a solution of 3.9 parts of sodium arsenate dissolved in 100 parts of water. The precipitate is washed and purified by recrystallization. It forms white, prismatic crystals, slightly soluble in cold water, very soluble in hot water. The salt contains 69.39 per cent. of quinine and 12.30 per cent. of arsenic acid. *Dose*, one-fifteenth to one-eighth of a grain (0.004–0.008 Gm.).

Quinine Benzoate. *Quininæ Benzoas.* $C_{20}H_{24}O_2N_2.C_7H_6O_2$.—It may be made by neutralizing 3 parts of benzoic acid, dissolved in hot alcohol, with 8 parts of anhydrous quinine and crystallizing. The salt contains about 73 per cent. of quinine. Difficultly soluble in water, requiring about 370 parts for solution.

Quinine Borate. *Quininæ Boras.* $C_{20}H_{24}O_2N_2.H_3BO_3$.—Mix 10 parts of anhydrous quinine and 1.91 parts of boric acid with 20 parts of water, evaporate and powder the dried residue. The salt contains about 84 per cent. of quinine.

Quinine Bromate. *Quininæ Bromas.* $C_{20}H_{24}O_2N_2.HBrO_3$.—Made by salifying quinine with hydrobromic acid. It forms needle-like masses of crystals, is soluble in about 250 parts of cold water, freely in warm water and in alcohol.

Quinine Camphorate. $(C_{20}H_{24}O_2N_2)_2C_{10}H_{16}O_4$.—A white powder soluble in alcohol and insoluble in water. It possesses but little advantage over, or difference in properties from, the sulphate of quinine. *Dose*, one to ten grains (0.065–0.65 Gm.).

Quinine Carbonate. *Acid Carbonate of Quinine.* $C_{20}H_{24}O_2N_2.H_2CO_3 + H_2O$.—The carbonate is made by passing carbon dioxide through a mixture, in which freshly precipitated quinine is suspended, until all the quinine is dissolved; the solution is then evaporated and crystallized. In the form of fine, needle-like crystals, soluble in water and alcohol. It contains 73.66 per cent. of quinine. The neutral carbonate is described under the title *Aristochin*, see page 1262.

Quinine Chlorhydrophosphate. *Quininæ Chlorhydrophosphas.* $C_{20}H_{24}O_2N_2.HCl(H_3PO_4)_2 + 3H_2O$.—The salt is made by dissolving 35 parts of quinine hydrochloride in a mixture of 70 parts of 25 per cent. phosphoric acid and 9 parts of 12.5 per cent. hydrochloric acid and allowing the crystals to form during spontaneous evaporation. It is soluble in about 2 parts of water, having an acid reaction, and containing about 53 per cent. of quinine.

Quinine Chlorhydrosulphate. *Quininæ Chlorhydrosulphas.* $(C_{20}H_{24}O_2N_2)_2H_2SO_4(HCl)_2 + 3H_2O$.—Made by dissolving 10 parts of quinine sulphate in 3.3 parts of 25 per cent. hydrochloric acid and allowing the solution to crystallize during spontaneous evaporation. It forms colorless crystals, soluble in 1 part of water. The salt contains about 74 per cent. of quinine.

Quinine Chromate. *Quininæ Chromas.* $C_{20}H_{24}O_2N_2.H_2CrO_4 + 2H_2O$.—It may be made by precipitating 4 parts of quinine hydrochloride, in 100 parts of warm water, with 1 part of neutral potassium chromate, dissolved in 15 parts of water. The crystals are washed and purified by recrystallization from hot diluted alcohol. It forms yellow crystalline needles, almost insoluble in cold water, soluble in 160 parts of boiling water.

Quinine Diglycol Sulphate. *Tasteless Quinine. Insipin.*—This is a solution of quinine sulphate in ethylene glycol. It is stated to have the advantages over the ordinary salts of quinine not only in its comparative freedom from bitterness, but also in that it is less liable to cause toxic manifestations. It is used for children for the same purposes as quinine. *Dose*, fifteen to thirty grains (1.0–2.0 Gm.).

Quinine Eosolate. *Quininæ Eosolas.* $C_9H_7S_3O_{12}(C_{20}H_{24}O_2N_2)_2$.—This is the commercial name of the neutral quinine salt of *trisulpho-acetyl-creosote*. Very active anti-periodic properties have been claimed for it. *Dose*, three to eight grains (0.2–0.5 Gm.) three times a day.

Quinine Formate.—This forms white, glassy needles of a bitter taste. It is a stable salt, neutral and soluble in water, alcohol and chloroform, but insoluble in ether. It contains 87.6 per cent. quinine, and is used subcutaneously for the same purpose as other quinine salts, the *dose*, however, being slightly smaller.

Quinine Glycerophosphate. *Quininæ Glycerophosphas. N. F. IV. Kineurine.* $[(C_{20}H_{24}O_2N_2)_2PO_4H_2C_3H_7O_2 + 4H_2O = 892.60]$.—"The glycerophosphate of the alkaloid quinine. Preserve it in well-stoppered, amber-colored bottles." *N. F. IV. Quinine glycerophosphate* was admitted to the *N. F. IV* to be used as an ingredient in *Compound Elixir of Glycerophosphates*. It forms a white powder, soluble in hot water and alcohol, which contains 68 per cent. of quinine in combination with glycerophosphoric acid. It is described as follows: "Quinine Glycerophosphate occurs as fine, white crystalline needles or as a powder; odorless and having a very bitter taste. One gramme dissolves in about 850 mils of water, or 75 mils of alcohol at 25° C.; very soluble in boiling alcohol; very slightly soluble in chloroform or ether; soluble in 20 parts of a mixture of one volume of alcohol and two volumes of chloroform. Quinine Glycerophosphate slowly loses part of its water of crystallization at room temperature and when heated to 100° C. becomes anhydrous. Incinerate 0.2 Gm. of the salt; no weighable residue remains. The salt yields a clear solution with diluted sulphuric acid. An aqueous solution is not fluorescent, but becomes so upon the addition of a few drops of diluted sulphuric acid. Add

1 mil of bromine T.S. to 10 mils of a saturated aqueous solution of the salt, and then follow with 1 mil of ammonia water; the liquid acquires an emerald-green color. When the salt is heated with potassium bisulphate the odor of acrolein is given off. An aqueous solution of 0.1 Gm. of the salt in 10 mils of distilled water, made with the aid of acetic acid, does not produce a precipitate on the addition of ammonium oxalate T.S. (*calcium*). Dissolve 0.1 Gm. of the salt in 10 mils of diluted hydrochloric acid; the solution does not become more than faintly turbid upon the addition of a few drops of barium chloride T.S. (*sulphate*). Dissolve 0.1 Gm. of the salt in 10 mils of diluted nitric acid; the solution is not rendered more than faintly turbid on the addition of silver nitrate T.S. (*chloride*). Add a slight excess of ammonia water to a saturated aqueous solution of the salt, and filter; the clear filtrate does not show more than a slight turbidity with magnesia mixture T.S. (*phosphate*). Mix about 2.5 Gm. of the salt in a separatory funnel with 15 mils of distilled water, add 5 mils of ammonia water, shake with three successive portions of 25, 15 and 10 mils of chloroform, respectively, and evaporate the chloroform solutions to dryness on a water bath. Dissolve 1.5 Gm. of this dry residue in 25 mils of alcohol, add 50 mils of hot distilled water, neutralize the liquid with normal sulphuric acid V.S., using methyl red T.S. as indicator and evaporate the liquid to dryness on a water bath. Powder the residue, mix it with 20 mils of distilled water and maintain the temperature of the mixture at 65° C., for thirty minutes, agitating frequently. Now cool the mixture to 15° C., macerate it at this temperature for two hours with occasional shaking, then filter it through a dry filter, of from 8 to 10 cm. in diameter, into a dry test tube. Transfer 5 mils of this filtrate to a test tube and mix it gently (without shaking) with 7 mils of ammonia water, which must contain not less than 10 per cent. nor more than 10.2 per cent. of NH_3, must have a temperature of 15° C., and be added at once. A clear liquid is produced (*other cinchona alkaloids*). If the temperature during the maceration has been 16° C., add 7.5 mils of ammonia; if 17° C., add 8 mils." *N. F. IV.* This substance has been recommended as an antiperiodic in *doses* of five to ten grains (0.32–0.65 Gm.). The tonic *dose* is set down as one and one-half to three grains (0.096–0.2 Gm.).

Quinine Glycyrrhizinate.—A brown powder, soluble in alcohol and containing 25 per cent. quinine. It is particularly adapted for administration to children because of its slightly bitter taste. *Dose*, the same as of the sulphate.

Quinine Hypophosphite. [$C_{20}H_{24}O_2N_2HPH_2O_2 + 2H_2O = 426.31$]. *Quininæ Hypophosphis. N. F. IV.*—"The hypophosphite of the akaloid quinine. Preserve it in well-stoppered, amber-colored bottles." *N. F. IV.* "Quininde Hypophosphite occurs as fine, white, silky, glistening needles or prisms; odorless and having a very bitter taste. One gramme dissolves in about 35 mils of water, in 12.5 mils of alcohol, or in 27 mils of chloroform at 25° C.; almost insoluble in ether. Heated to 100° C., Quinine Hypophosphite becomes anhydrous; the anhydrous salt melts at about 181° C. At a higher heat it fuses to a black mass and evolves vapors of phosphuretted hydrogen. Incinerate 0.2 Gm. of the salt; no weighable residue remains. Add 1 mil of bromine T.S. to 10 mils of an aqueous solution of the salt (1 in 1000) and then follow with 1 mil of ammonia water; the liquid acquires an emerald-green color. Acidulate an aqueous solution of the salt (1 in 40) with a few drops of nitric acid, add silver nitrate T.S. and warm the liquid; a brown precipitate is formed, which, on standing, becomes black. Dissolve 0.1 Gm. of the salt in 10 mils of distilled water, and add a few drops of nitric acid; the solution is not rendered more than faintly turbid by the addition of silver nitrate T.S. (*chloride*). Dissolve 0.1 Gm. of the salt in 10 mils of distilled water, and add a few drops of hydrochloric acid; the solution is not rendered more than faintly turbid by the addition of barium chloride T.S. (*sulphate*). To test this salt for excessive amounts of *other cinchona alkaloids* proceed as directed under *Quininæ Glycerophosphas." N. F. IV.* This hypophosphite was admitted to the N. F. IV to be used in the *compound solution of hypophosphites.* The *dose* is the same as that of quinine sulphate.

Quinine Iodate. *Quininæ Iodas.* $C_{20}H_{24}O_2N_2.HIO_3$.—Made by dissolving freshly precipitated quinine in hydriodic acid, using molecular proportions, and afterwards evaporating and drying the salt. In small needle-like crystals, freely soluble in alcohol and in 700 parts of cold water. It contains about 63 per cent. of quinine.

Quinine Phenolsulphonate. *Quininæ Phenolsulphonas. Quinine Sulphocarbolate.* $C_{20}H_{24}O_2N_2[C_6H_4(OH)SO_3H]$.—Made by precipitating 10 parts of quinine sulphate, in 500 parts of water, by adding it to a boiling solution of 6 parts of barium phenolsulphonate, dissolved in 75 parts of water. The precipitate is washed and dried. A yellowish-white mass, melting when warmed, only slightly soluble in water, soluble in alcohol.

Quinine Sulphoguaiacolate. *Quinine Orthoguaiacol-sulphonate. Sulphoguaiacin.*—This occurs in yellowish, crystalline leaflets freely soluble in water but only sparingly so in alcohol or ether. It is stated to be actively antiseptic and is used in the treatment of various infectious diseases, as *influenza, tuberculosis, rheumatic fever, whooping cough,* etc. It is usually given either hypodermically or in suppository. The single *dose* should not exceed six to eight grains (0.4–0.5 Gm.), but it is stated that sixty grains (3.9 Gm.) may be given in the twenty-four hours.

Quinine Valerate. [$C_{20}H_{24}O_2N_2HC_5H_9O_2 + H_2O = 443.30$]. *Quininæ Valeras. N. F. IV.*—"The valerate of the alkaloid quinine. Preserve it in well-stoppered, amber-colored bottles." *N. F. IV.* "Quinine Valerate occurs as white, lustrous crystals, having an odor of valeric acid and an intensely bitter taste. It is sparingly soluble in cold water, soluble in hot water, becoming less soluble with age on account of loss of valeric acid; readily soluble in alcohol. Its aqueous solution is neutral or slightly alkaline to litmus. Add a few drops of bromine water to 10 mils of an aqueous solution of the salt (1 in 1000), then add an excess of ammonia water; an emerald-green color is produced. An aqueous solution of the salt, acidulated with sulphuric acid, exhibits a blue fluorescence and has the odor of valeric acid. Incinerate 1 Gm. of Quinine Valerate; not more than 0.1 per cent. of ash remains. About 0.1 Gm. of the salt dissolves in 5 mils of sulphuric acid without producing more than a light yellow color (*readily carbonizable impurities*). Ten mil portions of the cold, saturated aqueous solution of the salt do not give more than a slight turbidity with barium chloride T.S. when acidulated with hydrochloric acid (*sulphate*); nor with silver nitrate T.S. when

acidulated with nitric acid (*chloride*). To test this salt for excessive amounts of *other cinchona alkaloids* proceed as directed under *Quininæ Glycerophosphas.*" *N. F. IV.* This quinine salt was admitted to the National Formulary IV to be used as an ingredient in *Elixir of Quinine Valerate and Strychnine.* The amount of valeric acid in this elixir is entirely too small to have any therapeutic action and this criticism applies to the salt itself which is given in the same dose as quinine sulphate.

Quinoa.—The *Chenopodium Quinoa* Willd. (Fam. *Chenopodiaceæ*), is largely cultivated in Southern Peru and Southern Chili, often above the height at which barley and rye will ripen, for the sake of its seeds. These are about the size of white mustard seeds, but flatter, and afford a flour resembling somewhat oatmeal. The starch grains are very small, and constitute about 40 per cent. of the grain, which also contains 5 per cent. of sugar, 7½ of casein, and 11 of albumen and other protein compounds. One variety, the *red quinoa,* contains a bitter principle in the seed husks, and is used to some extent as an emetic and antiperiodic. (*A. J. P.*, 1872, 559.)

Quinoline. *Chinoline. Leucoline. Chinolin,* G. (C_9H_7N.)—This is an artificial alkaloid prepared by the destructive distillation of quinine or cinchonine with potassium hydroxide, and also synthetically by König's and Skraup's processes by the action of sulphuric acid and glycerin upon nitrobenzene and aniline, or a mixture of these two latter substances. *Chinoline* is a colorless, strongly refractive, oily liquid, having a specific gravity of 1.081 at 10° C. (50° F.) (Hoffmann), boiling at 235.6° C. (456.8° F.) without decomposition, the oily stain left on bibulous paper disappearing readily on exposure. Its odor is aromatic, resembling that of oil of bitter almond. It is sparingly soluble in cold water, more so in hot water, soluble in alcohol, and mixes in all proportions with ether, carbon disulphide, methyl alcohol, etc. It easily dissolves camphor and resin. It gradually turns reddish-brown in color on exposure to the air. It forms readily crystallizable salts with acids, the tartrate now being a commercial article; these salts are decomposed by contact with fixed alkalies and the peculiar odor of quinoline developed. Ekin (*P. J.*, Feb. 11, 1882) found a sample of commercial German chinoline to consist largely of a mixture of aniline and nitrobenzene, although labelled pure. *Quinoline tartrate,* $(C_9H_7N)_3.(C_4H_6O_6)_4$, is in the form of a whitish, micaceous, crystalline powder, melting at 125° C. (257° F.). It dissolves in 80 parts of cold water, in about 150 parts of alcohol, and in 300 parts of ether, having a peculiar pungent odor and a rather sharp, though not unpleasant taste. *Quinoline hydrochloride,* $C_9H_7N.HCl$, melts at 94° C. (201.2° F.) and sublimes unchanged. It dissolves in water, alcohol, and chloroform. *Quinoline salicylate,* $C_9H_7N.C_7H_6O_3$, is a white crystalline powder, soluble in water and glycerin, very soluble in alcohol, ether, vaseline, and fatty oils.

While quinoline was originally brought forward as a substitute for quinine, experience has shown that it possesses only feeble antiperiodic properties. It is, however, an active antipyretic and is also a powerful germicide. It is a depressant to the central nervous system and in 1 per cent. solution will prevent the coagulation of the blood. It is used chiefly as an antiseptic, especially in the treatment of *gonorrhea* for which purpose an 0.7 per cent. solution may be employed. Quinoline has been highly commended as a preservative for anatomical specimens. The formula adopted in the Erlangen Physiological Institute is: quinoline, 5 grammes; sodium chloride, 6 grammes; glycerin, 100 grammes; water, 900 grammes. The ordinary tar quinoline can be used. For physiological study of quinoline derivatives, see *Trans. College of Physicians of Edinburgh* (Laboratory), 1893; also Laidlaw (*Biochem. J.*, 1910, v, 243).

Quinoline Sulphocyanate or **Rhodanate.** *Quinine thiocyanate. Quinolinæ Sulphocyanas.*—A colorless or yellowish, crystalline powder, only slightly soluble in cold water and ether, but freely soluble in hot water and alcohol. The salt melts at about 137° C. (278.6° F.).

Radium. Ra = 226.4.—The discovery that certain substances are radio-active was made by Henri Becquerel in 1896, who showed that *uranium* was capable of affecting a photographic plate in the same way as light. Shortly after this, it was shown that a number of other substances were radio-active. The characteristics of radio-active bodies are four: (1) They affect photographic plates; (2) they produce phosphorescence in certain substances; (3) they cause the surrounding air to become a conductor of electricity; (4) they produce heat. In 1899 Madame Curie, while investigating the radio-activity of certain minerals, came to the conclusion that the uranium ore, known as *pitchblende,* must contain some substance more actively radiant than uranium itself. This led her to the separation of the element radium, which showed two million (2,000,000) times as much activity as uranium.

Radium is an elemental substance, possessing remarkable chemical and physical properties, discovered in pitchblende, a complex uranium ore, by Professor and Madame Curie of the University of Paris, in 1900.

After tedious and difficult experimentation involving the recrystallization, precipitation, and concentration of a ton of the ore down to a few decigrammes of purified product, a barium-like element was discovered which was many thousand times as active as uranium in its radio-activity, and which was therefore named radium by its discoverers. Radium is manufactured in several places in America at the present time, thus putting a stop to the shipment of uranium ores to Europe. The United States Government has taken an active interest in locating deposits of uranium bearing ores. The most valuable deposits have been found in Colorado so far. In testing specimens of unknown ores for radio-activity, the photographic plate is used and an exposure is made of the unopened plate with a small metal object placed between the ore sample and the plate. After leaving the objects in this relative position for twelve hours or more the plate is developed in the regular way and is examined for evidence of a photographic outline or image of the metal object. The extraction of radium salts from pitchblende and *carnotite,* another radium containing uranium ore, includes three stages. First the ores are roasted; the roasted ores are then treated with sulphuric and nitric acids which takes out the uranium compounds and leaves the radio-active metals behind as sulphates; the residue is then treated alternately with alkalies and acids and is finally separated by fractional precipitation as sulphate.

One ton of uranium residues furnishes from 17 to 22 pounds of radio-active barium residue, which upon final concentration yields a few drachms of

radium bromide of high radio-active power. The element radium has not yet been obtained.

Properties.—Radium gives off three groups of rays, which are known by the first letters of the Greek alphabet, *alpha*, *beta*, and *gamma rays*. The alpha and beta rays are universally acknowledged to be material substances, while the gamma rays are by some considered waves of ether, and by others as electrons. Besides these, in solution radium liberates a gaseous element which is known as *emanation*. This gas is formed in the radium while in the dry state, but is completely absorbed, and only given off from solutions of salts of the metal. The most widely accepted theory concerning the origin of these rays is that of Rutherford. According to this, radio-activity is a sign of atomic destruction, particles of matter being given off, and the element being changed into another form of element with a lower molecular weight. Thus, uranium gives off alpha particles, and the residue is *ionium;* this gives off alpha particles, the residue being radium. The decomposition of radium forms emanation, which in turn gives off alpha particles, forming a series of active deposits known as Radium A., Radium B., C., D., E., F. (Polonium), and eventually Radium G., which is by some believed to be identical with lead.

The alpha rays, which constitute about nine-tenths of the radiation of radium are positively charged electrons with a mass about four times that of hydrogen, moving with a velocity approximately one-tenth that of the light wave. By some they are supposed to be identical with the element *helium*, or rather to represent helium in the process of formation. Their power of penetration is relatively small. They can pass only through three inches of air, and are stopped by a heavy sheet of note-paper.

The beta rays are negatively charged electrons, and are by many believed to be identical with the cathode stream formed in a Crooke's tube. Their velocity is about equal to that of light, and their penetration is quite considerable, it requiring a sheet of lead one centimeter in thickness to certainly stop them.

The gamma rays form only about one per cent. of the total radiation. Of their nature comparatively little is known. Their penetration is extraordinary, exceeding that of the X-ray. Because of the fact that they are not deflected by a magnetic field it was formerly believed that they were non-material, but the theory has been brought forward that they are discrete particles, electrically neutral.

Emanation is constantly being formed in radium. It is absorbed by the salts of the metal when in a dry state, but is liberated when the salt is dissolved. It is a gaseous element, which may be liquefied at a temperature of −150° C. (−238° F.), and has an atomic weight of 222. When freshly liberated it is radio-active, but becomes exhausted within a relatively short time, one-half of its power being dissipated within four days. Any substance exposed to emanation becomes temporarily radio-active. This is due to a deposit of the solid matter into which emanation is transferred after giving off its alpha rays.

The approximate estimate of the radio-active power in given substances can be reached by the degree of its influence upon photographic plates or the degree of fluorescence imparted to a platinocyanide screen, but accurate measurements are based upon their ionizing power, that is, upon the degree of electrical conductivity they impart to the air. For this purpose, an apparatus known as the electroscope is employed. A *Curie* is the amount of emanation in equilibrium with one gramme of radium. A micro-curie is one-millionth of this and is equivalent to the amount of emanation in one milligramme of radium and equals 2500 "Maché units."

Most of the radium which is used therapeutically is in a more or less impure state, and it becomes necessary to have some knowledge of the radio-active power of any known specimen before it is used for medical purposes. Manufacturers of radium generally supply with each sample of the metal, a statement of its power, in which uranium is taken as the unit. For instance, pure radium has two million units, that is, it is two million times as radio-active as uranium. Specimens of over two-hundred-thousand units are suitable for medical uses.

Therapeutic Uses.—The medical value of radium depends in the first place upon the destructive action of the rays upon the certain pathological tissues, and secondly upon the alterations in functions which are produced by the internal administration of emanation. The widest use of radium has been as a destructive agent in various types of *neoplasms*. For this purpose it is applied in various forms of containers, the most popular being a sealed glass tube, which is enclosed within a thin aluminum capsule to protect it from breaking.

The earliest investigations of the action of radium rays upon living protoplasm appear to be those of Schwarz (*A. G. P.*, 1903), who showed that when hen's eggs were exposed to the metal there was a decomposition of the lecithin within them. London (*B. K. W.*, xliii) found that rabbits kept for two weeks in a cage on top of which was placed 25 mgm. of radium lost their hair, the ears necrosed and the sexual organs degenerated; he believes that the emanations have no effect on fibroid tissue. The alpha rays have considerable germicidal action, as apparently does also emanation, but neither of these have any great penetrative power, so that the anti-bacterial effect of radium is not likely to prove of practical utility.

When applied to the skin, radium produces no immediate effect, but lesions appear after considerable periods of incubation, which may be as long as two weeks. If the dose has been small there is merely redness, but after longer exposure an ulcer is formed which heals very slowly. Although there is left behind, when these ulcers heal, a white supple cicatrix, destruction to the hair folicles, sweat and subaceous glands may have been the result of the action of the rays upon the skin. It is possible, however, to profoundly influence the deeply lying structures with much less danger of causing dermatological injuries than with the X-rays. This can be accomplished by screening off the relatively superficially acting alpha and beta rays which allows the deeply penetrating gamma rays alone to act.

Radium has been used for the destruction of various *malignant growths*, and in a number of cases with good results. In any form of malignant tumor, however, in which operation is possible, while the radium treatment may be useful as an adjunct to the surgical, it should never offer an excuse for delaying operative interference. When, however, for any reason operation is impossible, the use of radium holds out hope for symptomatic relief, and in a certain proportion of cases, even for complete recovery. In the first

annual report of the London Radium Institute (*B. M. J.*, Jan. 25, 1913, p. 149), of 38 cases of *cancer of the breast* 35 were improved by the treatment, although in only a few instances did the carcinomous nodules disappear. In 39 cases of inoperable *cancer of the uterus* there were three apparently cured while in 19 there was relief of pain and arrest of the discharge and hemorrhage. The most striking results are obtained in cases of *rodent ulcers*. In these, provided the bones or cartilages have not been attacked, and the mucous membrane is not involved, strong hope for a complete cure may be held out. Out of 90 cases treated in the London Institute, 31 were apparently cured, and 41 improved. In *sarcoma* also, markedly beneficial results are often obtained. Other conditions in which benefit is sometimes seen from the radium treatment includes *lupus erythematosus, keloid, tuberculous glands, pruritus, leukemia,* and *nevi*. For further information on the use of radium in cancer, see symposium in *J. A. M. A.*, 1914, lxiii, p. 737. The dosage of radium is generally expressed in terms of pure radium and time. For instance, if the quantity of the salts equivalent to one milligramme of pure radium is to be applied for one hour, the dosage set is "one milligramme, hour." If an impure preparation is employed, as is usually the case, its activity must be calculated to that of pure radium. For instance, if the salt represent five-hundred-thousand units, it would require four milligrammes to exercise the same effect as one milligramme of pure radium.

Emanation when introduced into the system appears to have an influence upon the circulation, but especially upon metabolism. According to Loewi (*B. K. W.*, 1912, xlix, p. 198), the inhalation of emanation produces a contraction of the vessels of the lungs, and dilation of the vessels of the brain, with some tendency to lower the general blood pressure. The effect upon metabolism is shown in an increased elimination of uric acid. Although His (*B. K. W.*, xlviii, p. 197) found after the exhibition of radium marked diminution in the amount of uric acid in the blood, Fine and Chace (*J. P. Ex. T.*, 1914, vi, 219) could find no such change. Armstrong (*Practitioner*, 1912, lxxxviii, p. 156) and a number of German writers have described beneficial results from the drinking of water containing emanation, and also from the inhalation of the gas itself in *gout*.

While it seems evident that radium emanation has some marked effect on metabolism the precise nature of this alteration remains as yet obscure. Clinically, radium has been used internally in the treatment of *gout, arthritis deformans* and other diseases of the joints; in muscular *rheumatism,* in *sciatica, neuralgia* and other painful conditions. Some believe that the beneficial effects obtained by drinking mineral waters is due to their radium content; but while it is a fact that many of the famed medicinal springs are radio-active it remains to be shown that this explains their beneficial action. Indeed, the whole use of radium as an internal remedy is still in the experimental stage. An enumeration of the proprietary radium specialties, large numbers of which have been originated during the past few years, will be found in the *A. Ph. A. Year-book of Pharmacy*, 1912, p. 302.

Raisins. *Uva Passa. U. S.* 1870.—The dried ripe fruit of the *Vitis vinifera* L. (Fam. *Vitaceæ*), is no longer recognized by the Pharmacopœia. The grape vine itself is too well known to require description. Its leaves and tendrils are somewhat astringent, and were formerly used in *diarrhea, hemorrhages,* and other morbid discharges. The juice which flows from the stem was also thought to be possessed of medicinal virtues, and the idea still lingers among the vulgar in some countries. The unripe fruit has a harsh, sour taste, and yields by expression a very acid liquor, called *verjuice,* which was much esteemed by the ancients as a refreshing drink when diluted with water. It contains malic and tartaric acids, and an acid called *racemic acid,* a compound isomeric with tartaric acid, but differing from it in being optically inactive. M. A. Petit has ascertained that grape leaves contain 2 or 3 per cent. of glucose, and a quantity of acid varying from 1.3 to 1.6 per cent. Of the acid, tartaric acid constituted one-third, and most of this was in the form of cream of tartar. In a subsequent investigation, Petit found that the leaves contained a notable portion of both glucose and cane sugar. In one instance he obtained 1.58 per cent. of the latter and 1.749 of glucose. (*J. P. C.*, Jan., 1874, 41.) The seeds afford from 15 to 18 per cent. of a bland fixed oil, which is occasionally extracted. Fitz (*Ber. d. Chem. Ges.*, 1871, 442) has shown that it consists of the glycerides of *erucic acid,* $C_{22}H_{42}O_2$, stearic and palmitic acids, the first-named acid largely prevailing. The seeds further contained from 5 to 6 per cent. of tannic acid, which also exists in the skin of the fruit. The grape, when ripe, is among the most pleasant and grateful fruits, and is admirably adapted, by its refreshing properties, to febrile complaints. If largely taken, it proves diuretic and gently laxative. The ripe fruit differs from the unripe in containing more sugar and less acid, though never entirely destitute of the latter. The plant is a native of the southern shores of the Caspian Sea and Armenia, and has been cultivated in Europe and Northern Africa from the remotest antiquity, and is now spread over all the temperate civilized regions of the globe. The fruit is exceedingly influenced by soil and climate, and the varieties of the plant which have resulted from culture or situation are innumerable.

Several varieties of raisins are known in commerce. The best of the European fruit are the *Malaga raisins,* imported from Spain. They are large and fleshy, of a purplish-brown color and sweet, agreeable taste. Those produced in Calabria are similar. The *Smyrna raisins* are also large, but of a yellowish-brown color, slightly musky odor, and less agreeable flavor. They are originally brought from the coast of Syria. The *Corinthian raisins,* or *currants* as they are commonly called in this country, are small, bluish black, of a fatty appearance, with a vinous odor and a sweet, slightly tartish taste. Their name is derived from the city in the vicinity of which they were formerly cultivated. At present they are procured chiefly from Zante, Cephalonia, and the other Ionian Islands. In the older Pharmacopœias they are distinguished by the title of *uvæ passæ minores*. Within recent years the production of raisins in California has become an industry of the highest importance. These raisins are coming into large use in the United States and are rapidly replacing those obtained from Malaga; the importation of the latter decreased in the years between 1876 and 1900 at least 90 per cent. The ripe grapes are cut from the vines, spread out on a clay floor, and dried by exposure to the heat of the sun. The drying process usually requires about ten days' time. Artificial heat is used to dry them in rainy weather; sometimes the grapes are partially dried

on the vines; this is done by cutting the stalks of the ripe grapes half way through, and allowing the bunches to remain for a few weeks, a portion of the bark of the vine being removed also to facilitate the process. If it is desirable to remove the waxy bloom on the grapes, the bunches are steeped for a short time in weak alkaline solution, washed and then thoroughly dried.

Raisins usually contain more sugar than do recent grapes. This principle, indeed, is often so abundant that it effloresces on the surface or concretes in separate masses within the substance of the raisin. The average composition of the raisin is given as 32.02 per cent. water, 2.42 nitrogenous material, 0.59 fat, 54.56 sugar, 7.48 other nitrogenous organic matter, 1.72 wood fiber, and 1.21 ash. (König, *Nahrungs- und Genussmittel*, 3te Aufl., ii, 815.) The *sugar of grapes* (*glucose*) differs from that of the cane, being less sweet, less soluble in cold water and much less so in alcohol. In these respects it does not differ from artificial glucose, which is now made in enormous quantities and consumed in food products and candies; the artificial product is made by acting on starch with sulphuric acid (see page 517).

The chief medicinal use of raisins is to flavor demulcent beverages. Taken in substance they are gently laxative, but are also difficult of digestion, and, when largely eaten, sometimes produce unpleasant effects, especially in children.

Radish. *Raphanus sativus* L.—The juice of this well known plant has been used by Grumme in the treatment of *cholelithiasis* as an aid in preventing the formation of biliary calculi. His method is as follows:

White or black radishes are peeled, crushed in a suitable apparatus and the juice expressed. If the treatment is begun during or after an attack, the patient is made to drink on the first day half a cupful (100 mils) (or three and a half fluidounces) of the juice, then a whole cupful and later two cups (400 mils) (or fourteen fluidounces) daily. This amount is taken daily for two or three weeks, whereupon the dose is gradually decreased, until half a cupful is taken three times a week. This treatment is continued for six to eight weeks. When it is repeated, one cupful of juice is taken daily in the beginning, then half a cupful daily and later half a cupful every second day.

Saki reports the presence of an amylolytic enzyme in radish juice. (*J. P. C.*, 1906, 561.)

Sacher recommends the coloring matter from red radishes as a sensitive indicator in alkalimetry; the fresh peels are treated with alcohol and the solution is turned red with acids and green by alkalies.

Randia. *Randia dumetorum* Lam. (Fam. *Rubiaceæ*.)—The fruit of this East India shrub is used by the natives as a fish poison, and is said to act in man as an irritating emetic. According to the *Pharmacographia Indica*, each fruit contains about four grains (0.26 Gm.) of saponin, besides valeric acid. The tincture has been used by James Sawyer (*L. L.*, 1891) as an antispasmodic.

Ranunculus. *Crowfoot. Renoncule*, Fr. *Hahnenfuss*, G.—Most of the plants belonging to the genus *Ranunculus* have similar acrid properties, and, from their close resemblance, are confounded under the common name of *buttercup*. *R. bulbosus* L. was formerly in the Secondary List of the U. S. Pharmacopœia; but *R. sceleratus* L. had attracted more attention in Europe, and *R. acris* L. and *R. flammula* L. were recognized by the Dublin College. In all these species the plant itself is a violent irritant, producing when chewed excessive inflammation in the mouth and throat, and, when swallowed toxic gastritis which may be fatal. The acrid principle appears to be volatile; according to Bigelow, it is yielded to water in distillation. Clarus discovered, in *R. sceleratus* L., besides the acrid volatile oil, a nearly inert resin, and a narcotic principle called *anemonin* or *anemone camphor*, $C_{15}H_{12}O_6$. The volatile oil is soluble in ether, and is decomposed, on standing, into a white amorphous substance having acid properties (*anemonic acid*), $C_{15}H_{14}O_7$, and into anemonin. (*Brit. and For. Med.-Chir. Rev.*, 1859, 181.) Rochebrune states that he has separated from *R. aquatilis* L., *R. flammula L.*, *R. sceleratus* L. and *R. bulbosus* L., crystalline alkaloids to which he has given the name of *ranunculine*, although their identity is doubtful. These alkaloids are violent irritants and active cardiac poisons. (*Toxicolog. Africaine*, i.) Before the introduction of cantharides the green buttercup plants were much employed as vesicants.

Realgar. As_2S_2. *Red Orpiment.*—This is *arsenic disulphide*. It is found native in Saxony, Bohemia, Transylvania, and in various volcanic regions. *Realgar* is artificially made by melting arsenic trioxide with about half its weight of sulphur. Thus prepared, it is of a crystalline texture, of a beautiful ruby-red color, of a uniform conchoidal fracture, somewhat transparent in thin layers, and capable of being sublimed without change. Native realgar is said to be innocuous when taken internally, while that artificially prepared is poisonous, in consequence, according to Guibourt, of containing a little free arsenic trioxide. Realgar is used only as a pigment.

Red Chalk. *Reddle.*—A mineral substance of a deep red color, of a compact texture, dry to the touch, adhering to the tongue, about as hard as chalk, soiling the fingers when handled, and leaving a lively red trace when drawn over paper. It consists of clay and ferric oxide, and is intermediate between *bole* and *red ochre*, containing more ferric oxide than the former and less than the latter. It is used for drawing lines upon wood, etc., and is sometimes made into crayons by levigating and elutriating it, then forming it into a paste with mucilage of gum arabic, molding this into cylinders, and drying it in the shade. It has been used internally as an absorbent and astringent.

Regianin.—This is a principle obtained by Phipson from the nut of *Juglans regia*. It occurs in octahedral, prismatic, or feathery crystals, and gives with ammonia and other alkalies a reddish-purple solution, from which hydrochloric acid precipitates an amorphous powder, *regianic acid*. It is probably identical with the *nucin* obtained from green walnut shells.

Rennet. *Gastric Juice. Liquor Seriparus. Laabessenz*, G.—For a full account of the constitution of gastric juice and its properties the reader is referred to works upon physiology. The crude juice was applied by P. S. Physick to foul ulcers. *Rennet* is an aqueous or vinous infusion of the dried stomach of the calf, though that of the sheep or other animal would probably answer the same purpose. It is much used, as every one knows, for curdling milk, a property which it owes to a portion of the gastric secretion, retained and dried in the mucous tissue of the stomach. Whether the milk-curdling ferment is identical with the proteolytic ferment (pepsin)

is not yet definitely determined. George Ellis prepared *rennet wine* as follows: Take the stomach of a calf immediately after the animal has been killed, cut off and reject about three inches of the upper or cardiac portion, slit the stomach longitudinally, wipe it gently with a dry napkin so as to remove as little of the clean mucus as possible, then cut it into small pieces, the smaller the better, put it into a common wine bottle, fill the bottle with good sherry, and let it stand corked for three weeks. It is known to be good if a teaspoonful will coagulate half a pint of milk in two minutes at 37.7° C. (100° F.). The *dose* is a teaspoonful in a wineglassful of water, immediately after each meal. [See next article.)

Rennin. *Renninum. N. F. IV.*—Under this name the National Formulary IV has introduced in solid form, the milk-curdling principles from calves' stomachs. It possesses several advantages over liquid rennet and it is believed to retain its powers longer than the liquid form. It is described as follows:

"The partially purified milk-curdling enzyme obtained from the glandular layer of the stomach of the calf, *Bos taurus* Linné (Fam. *Bovidæ*), and capable of coagulating not less than 25,000 times its weight of fresh milk. Rennin of a higher coagulating power may be brought to the standard by admixture with sodium chloride and sugar of milk. Rennin deteriorates rapidly and must be kept in well-stoppered, amber-colored bottles, and stored in a cool place." *N. F. IV.*

"Rennin occurs as a grayish-white or yellowish-white powder, or as pale yellow grains or scales having a characteristic and slightly saline taste and a peculiar, not unpleasant odor. It is slightly hygroscopic.

"It is slowly soluble in water and in diluted alcohol, the solutions being more or less opalescent.

"When mounted in water or diluted alcohol and examined microscopically, it shows no cellular structure, and no blue coloration is produced on the addition of iodine T.S.

"*Assay.*—Mix 0.1 Gm. of Rennin with 50 mils of distilled water by stirring (vigorous shaking or violent agitation of this liquid must be avoided) and allow the liquid to stand for exactly fifteen minutes. Place 50 mils of cow's milk in a beaker about 12 cm. in height and 5 cm. in width, warm rapidly on a water bath to 43° C., add 1 mil of the Rennin solution and stir the mixture slowly for ten seconds. Maintain the temperature of the bath at 43° C. for ten minutes after the addition of the Rennin solution, remove the beaker from the bath and tip it to an angle of 45 degrees. The milk must have lost its fluidity to the extent of exhibiting a decidedly convex surface. An additional thirty seconds on the water bath produces a firm curd." *N. F. IV.*

Rennin was admitted to the National Formulary IV for the purpose of using it as an ingredient in making Compound Elixir of Pepsin and Rennin.

Resaldol. *Resorcin benzoyl carbonic acid ethyl ester (2,4-dioxybenzoyl-o-benzoic acid ethyl ester).* $C_{20}H_{14}O_5(CH_3CO)_2$.—*Resaldol* is made by acetylating the product of the reaction between chlormethyl-salicylic aldehyde and resorcinol. It is an amorphous yellowish-brown powder of an astringent taste, insoluble in water and dilute acids, but soluble in alkalies. According to Impens (*D. M. W.*, 1913, p. 1827), it acts much like cotoin (see p. 1344), over which it has the advantages of being tasteless and non-irritant. It is used in *tuberculous* and other forms of *enteritis.* The *dose* is eight grains (0.5 Gm.) several times a day.

Resalgin. *Antipyrine Resorcylate.* $(C_{11}H_{12}N_2O_2)_2.C_7H_6O_4$.—This occurs in crystalline needles soluble in 150 parts of cold water and 20 parts of boiling water, readily soluble in alcohol, ether, and chloroform. It is obtained by acting on antipyrine with potassium resorcylate. Forms colorless, odorless crystals melting at 110.5° C. (231° F.).

Betaresalgin, also called *resorcylalgin,* is obtained from betaresorcylic acid and antipyrine. It forms shiny white to pinkish crystals. It is soluble in alcohol, ether and chloroform and in 150 parts water. Melting point 115° C. (239° F.). It exercises both an antipyretic and an anodyne action.

Reseda. *Reseda Luteola* L. *Weld. Dyer's Weed. Herbe Jaune, Gaude,* Fr. *Wau, Gelbkraut, Harnkraut,* G. (Fam. *Resedaceæ.*)—An annual European plant, naturalized on roadsides and ballast from Massachusetts to Pennsylvania. The plant grows to a height of 6 dm., possesses alternate lanceolate leaves and small greenish-yellow flowers. It is inodorous, and has a bitter taste, which is very persistent. Volhard showed that allyl thiocyanate, $C_3H_5.SCN$ (volatile oil of mustard), was present in the root, and Chevreul obtained from it by sublimation a peculiar yellow coloring matter, which he called *luteolin.* Hlasiwetz and Pfaundler (1895) assign to it the formula $C_{15}H_{10}O_62H_2O$ and find it to be tetrahydroxyflavone. This forms yellow crystals of silky luster, insoluble in water, soluble in alcohol. It dissolves in alkalies with deep yellow color. It is used especially in silk dyeing. A. G. Perkin (*J. Chem. S.*, 1896) investigated the salts of luteolin, and called attention to the similarity of its properties to those of *fisetin.* In medicine it has been employed as a diaphoretic and diuretic, but it is now used only for dyeing purposes.

Resineon.—This is a volatile oil obtained from black tar oil by distillation and stated to be free of phenol. It boils at 148° C. (298.4° F.) and is used externally as a dressing for wounds and injuries and as an antiseptic in *skin affections.* A 1 to 8 ointment is applied by inunction in *chronic eczema.*

Resol.—A proprietary disinfectant said to be made by saponifying wood tar with potassium hydroxide and adding wood spirit.

Resopyrine. $C_{11}H_{12}N_2O + C_6H_4(OH)_2$.—Made by mixing solutions of 30 parts of antipyrine and 11 parts of resorcinol. A crystalline mass separates which should be recrystallized from alcohol. It is insoluble in water.

Resorbin.—An ointment vehicle made by emulsifying almond oil and water by means of a little yellow wax, gelatin, and soap, to which is added some lanolin. It is asserted that it greatly facilitates the absorption of medicaments.

Resorcinal.—*Resorcinal* is obtained by fusing equal parts of resorcinol and iodoform. It is a brown powder of iodine-like odor and used as a vulnerary and dermatic, as 20 per cent. dusting powder, or a 5 to 10 per cent. ointment.

Retamine. $C_{15}H_{26}N_2O$.—This is an alkaloid, crystallizing in long needles, melting at 162° C. (323.6° F.), with decomposition, which has been isolated by Battandier and Malosse from the young shoots and branches of *Retama sphærocarpa* Raf. (*Cytisus sphærocarpus* O. Kze.).

Retinol. *Codoil. Rosinol. Rosin Oil.* $C_{32}H_{16}$.—A product obtained by the distillation of rosin. It

forms a yellowish oil boiling at temperatures over 280° C. (536° F.). It is stated that *retinol* does not irritate the skin, is unaltered by light, is mildly antiseptic, does not become rancid, and is very inexpensive; qualities which, taken along with its extraordinary solvent power, bid fair to make it a valuable vehicle for ointments. Among the substances dissolved by it are: salol, 1–10; iodol, 1–50; naphthol, 1–50; thymol iodide, 1–50; camphor, 1–20; chrysophanic acid, 1–40; cocaine, 1–30; codeine, 1–40; and strychnine, 1–40. It is miscible in all proportions with oil of juniper, phenol, turpentine, alcohol, and ether. Resorcinol, if dissolved in glycerin, may be mixed with retinol, and so may iodoform if it be dissolved in a little ether. Iodol is dissolved, but soon precipitates as a resinous mass. Phosphorus is also dissolved, and the solution remains unchanged indefinitely. Retinol mixes readily with fats, oils, vaseline, lard, lanolin, glycerin, cacao butter, etc., and may be used in ointments. In cases where a liquid is not undesirable, retinol, owing to its antiseptic properties, can with great advantage replace these bodies. Upon the mucous membrane retinol seems to act as a mild stimulant antiseptic; it has been used with alleged excellent results locally in *otitis*, *vaginitis*, *rhinitis*, and other mucous diseases. Injections of it in *gonorrhea* are said to be remarkably effective. As a means of administering phosphorus it is especially recommended.

Rexotan.—This is a condensation product of tannin, urea and formaldehyde. It is in the form of a yellowish-brown powder, without odor or taste, insoluble in most of the ordinary solvents or in acid liquids, but decomposed by alkalies with the liberation of formaldehyde.

The advantage is claimed for this preparation, like many other of the organic compounds of tannin, that it is insoluble in cold water and dilute acids and, therefore, not dissolved in the stomach, but being easily soluble in solutions of the carbonates and phosphates exercises its astringent effect in the intestinal tract and further that in the intestines the formaldehyde is slowly liberated so that the drug exercises both an astringent and antiseptic action. It is used in the treatment of various types of *diarrhea* in *doses* of eight grains (0.5 Gm.) three to four times a day.

Rhamnus Cathartica. *N. F. IV. Buckthorn Berries. Baccæ Spinæ Cervinæ.*—"The dried, ripe fruit of *Rhamnus cathartica* Linné (Fam. *Rhamnaceæ*), without the presence of more than 5 per cent. of the unripe fruit or other foreign matter." *N. F.*

The *R. cathartica* Linn, or common buckthorn, grows in Europe along with *R. Frangula*, and has become naturalized in this country. Its bark is probably often sold for the official Frangula. It is distinguished by its more spreading, thorny habit, and its diœcious flowers, which are thickly clustered in the axils and have their parts in fours. The leaves are more acute, have their margins finely serrate and their lateral veins mostly proceeding from the proximal half of the midrib. The fruit is black.

The berries which are ripened in September, are of the size of a pea, round, somewhat flattened at top, black, smooth, shining, with four seeds in a green, juicy parenchyma. Their odor is unpleasant, their taste bitterish, acrid, and nauseous. Their blackish, expressed juice was formerly recognized in the Br. Ph. under the name of *Rhamni succus*. It is reddened by the acids, and from deep green is rendered light by the alkalies. Upon standing it soon begins to ferment, and becomes red in consequence of the formation of acetic acid. Evaporated to dryness, with the addition of lime or an alkali, it forms the color called by painters *sap-green*. The dried fruit of another species, *R. infectoria*, yields a rich yellow color, and is employed in the arts under the name of *French berries*.

The National Formulary IV describes buckthorn berries as follows:

"Flattened, globoid or ovoid, from 4 to 8 mm. in diameter; externally purplish-black, wrinkled from shrinking of the mesocarp in drying; three- to four-celled, each cell containing a brown, triangular-convex, seed-like nutlet; in the fully dried, ripe fruit the pedicel is usually lacking. Odor faint, unpleasant; taste at first sweetish, then nauseating and bitter; it colors the saliva purplish-red. When macerated in water the drupe readily assumes its original globular shape, about 1 cm. in diameter. The expressed pulp is colored red by acids and greenish-yellow by alkalies. Shake out an aqueous infusion of Rhamnus Cathartica with ether, separate the ethereal solution and shake it with 5 per cent. ammonia water; the ammonia solution assumes a cherry-red color. The unripe fruit, which is to be rejected, is green to greenish-brown, firm, furrowed, pedicel usually attached; very bitter; it colors the saliva greenish-yellow. Rhamnus Cathartica yields not more than 5 per cent. of ash." *N. F.*

The blackish, expressed juice of Buckthorn berries was formerly recognized in the Br. Ph. under the name of *Rhamni Succus*. It has the color, odor, and taste of the parenchyma, is reddened by the acids, and from deep green is rendered light green by the alkalies. Upon standing it soon begins to ferment, and becomes red in consequence of the formation of acetic acid. Evaporated to dryness, with the addition of lime or an alkali, it forms the color called by painters *sap-green*. The dried fruit of another species, *R. infectoria*, yields a yellow color, and is employed in the arts under the name of *French berries*.

Tschirch and Polacco, in 1900, investigated the constituents of buckthorn berries and found certain yellow coloring substances. The researches of N. Waljaschko and N. Krassowski since demonstrated that the fruits of *R. cathartica* contain the same yellow coloring matters as are contained in the fruits of *R. infectoria* and *R. tinctoria*, namely, *quercetin* and *rhamnin*, both existing in *R. cathartica* in the form of glucosides, which are split up by the action of an enzyme contained in the fruits: *Rhamnin*, for example, from the glucoside *xanthorhamnin*. The yellow coloring matters of Tschirch and Polacco, therefore, cannot be regarded as pure substances. They also extended the investigations of the former concerning the purgative substances contained in buckthorn fruits, with results confirming the theory advanced by Tschirch. They found the fruits to contain about 2 per cent. of emodin-substances and as cleavage products of the glucosides obtained by the action of ferments from the emodin-substances: *Emodin*, identical with *frangula emodin* and *rhamnosid;* the *emodin of rhamnoxanthin* ($C_{21}H_{20}O_9 + H_2O$), which is isomeric but not identical with frangulin; *rhamnonigrin*, and a resin like body containing emodin. Other constituents found in buckthorn berries are: fixed

oil, succinic acid, glucose, galactose, rhamnose, and a pentose, but of the four sugars only glucose was present in the free state, the others being derived from the glucosides. (*Ph. Ztg.*, 1909, No. 16, 159.) Tschirch and Bromberger (*Schw. Woch. f. Ch. v. Ph.*, 1912, p. 193) report the following constituents found in a 15 Kilo sample upon which they did considerable work: *Rhamno-sterin*, $C_{18}H_{28}O_2$; *rhamno-fluorin*, $C_{14}H_{12}O_6$; *emodin*, $C_{15}H_{10}O_5$; *iso-emodin*, $C_{15}H_{10}O_5$; *chrysophanol* $(C_{14}H_5O_2)CH_3(OH)_2$. A fluidextract and a syrup of buckthorn berries are contained in the N. F. (see Part III).

The *dose* of the dried berries is from ten to twenty grains (0.65–1.2 Gm.). Among other species of Rhamnus which have claimed attention are *R. Wightii*, W. & A., a common shrub of Madras and Bombay (*P. J.*, Feb., 1888), and *R. californica*, Eschsch. (*R. humboldtiana*, Roem. and Schult.), of Mexico, which S. E. Sosa states sometimes produces paralysis in children (*El Estudio*, 1890). (See also *Cascara Sagrada.*)

Rhigolene.—This name was given by H. J. Bigelow of Boston, to a very light, inflammable liquid, obtained by distilling petroleum, and separating the liquids of the lowest boiling point by redistillation, until one is obtained which boils at about 18° C. (64.4° F.). A degree of cold –9° C. (15.8° F.) is, according to Bigelow, obtained through the evaporation of this liquid by means of the common atomizer or "spray-producer." This is the chief use of the liquid, which may be employed in producing congelation of any part of the body preparatory to a surgical operation, or a great degree of cold for any other purpose. It should, when not in use, be kept in a cool place, in bottles tightly corked, or otherwise it will be rapidly evaporated. In a warm place it might break the bottles through its extreme volatility, unless the stopper should previously be driven out. The vapor is inflammable and care should be exercised in using it near a flame.

Rhizophora Mangle.—The red bark of the South American *mangrove tree* has been used for many years by the natives as a febrifuge but more recently Duque and Moreno (*S. M.*, 1905, p. 479) have claimed that it is a specific in *leprosy*. They administer a beginning *dose* of one fluidrachm (3.75 mils) of the fluidextract twice a day which is gradually increased until the patient is taking a fluidounce and a half (45 mils) daily.

Rhododendron. *Rhododendron Chrysanthemum* Pall. *Yellow-flowered Rhododendron. Rosebay. Snowrose. Rosage*, Fr. *Alpenrose, Schneerose, Gichtrose*, G. (Fam. *Ericaceæ.*)—The leaves of this rhododendron have long been employed in Siberia as a remedy in *rheumatism*, and to a less extent in *gout* and *syphilis*. They yield their virtue to water and alcohol, and, according to von Archangelski, contain three proximate principles; *rhododendrol*, $C_{10}H_{12}O_2$; *rhododendrin*, $C_{16}H_{22}O_7$; and a glucoside resembling digitalin and very toxic. The *dose* of the dried leaves is said to be two drachms (7.7 Gm.), given in infusion.

G. F. Kuehnel found in leaves of the "great laurel," *Rhododendron maximum* L., a common shrub in the Alleghenies from New York to Georgia, *arbutin*, *ericolin*, and *ursone*. (*A. J. P.*, 1885.)

Rhus.—The genus *Rhus* contains various species which have the property—probably even without direct contact—of so violently irritating susceptible skins as to produce severe dermatitis. Of these poisonous species there are six which are indigenous to the United States.

R. vernix L. (*R. venenata* DC.)—*Swamp Sumac, Poison Sumach, Poison Elder* is our most poisonous species. It is a handsome shrub or small tree, usually ten or fifteen feet high. The bark of the trunk is dark gray, of the branches lighter, of the extreme twigs and petioles pale to deep red. The leaves are pinnate, with three to six pairs of opposite leaflets, and an odd terminal one. These are oblong or oval, entire or slightly sinuate, acuminate, smooth, and, except the one at the end, nearly sessile. The flowers are polygamous, very small, greenish, and in loose or slender axillary panicles. The berries are small, roundish, and greenish white. The tree grows in swamps and low grounds from Canada to Carolina, and flowers in June and July. It was confounded by the older botanists with *R. vernicifera* DC., of Japan, the Japanese lacquer tree, which has similar poisonous properties. Its activity is said to depend upon *urushic acid.*

Rhus Michauxii Sargent (*R. pumila* Michx.) is a rare Southern species, growing in upper Carolina and Georgia, and not more than a foot in height. It is characterized by its pubescent branches and petioles, by its pinnate leaves, with many pairs of oval, nearly acuminate, incised-dentate leaflets, downy beneath, and by its silky fruit. According to Pursh, it is the most poisonous of the genus.

Rhus diversiloba Torrey and Gray (*R. lobata* Hooker) is found on our Pacific border. It is there generally known as *Poison Oak*, and closely resembles the common poison ivy or poison oak. (*R. Toxicodendron* L.)

Rhus Metopium L. (*Metopium Linnæa*, Engelm.), *Mountain Manchineel, Coral Sumac*, is a West Indian species, growing also in the "hummock" lands of Southern Florida. It is a small tree, the bark, when wounded, exuding a gum-resin (*hog gum*) to which medicinal properties are ascribed. The leaves are pinnate with fine leaflets. To the acid red fruit is due the name Coral Sumac. It is exceedingly poisonous.

Rhus Toxicodendron (*R. radicans* L.), *Poison Oak, Poison Ivy*, whose fresh leaves were formerly official in the U. S. Pharmacopœia under the name of *Rhus Toxicodendron*, U. S., 1890, is a woody vine climbing by numerous aerial rootlets to considerable heights and showing considerable variation. The leaves are 3-foliate, the leaflets being ovate or rhombic, 2.5 to 15 cm. long, entire or sparingly dentate or sinuate, acute or short-acuminate, the lateral sessile or short-stalked, are inequilateral, the terminal ones stalked. The flowers are green, 3 mm. broad, in loose axillary panicles, 2 to 8 cm. long; the fruit globose-oblong, whitish or cream colored, resembling that of *R. Vernix.*

The milky juice, of the poisonous species of *Rhus*, becomes black on exposure to the air, and leaves upon linen or other cloth a stain, which cannot afterwards be removed by washing with soap and water, or by alcohol either hot or cold, but deepens by age. It has been proposed as an indelible ink. Ether dissolves it; applied to the skin it frequently causes inflammation and vesication.

While there is a fairly general agreement that the toxic constituent of the poisonous species of Rhus is a non-volatile substance, there is much evidence that there is a volatile poison also in this plant. (Bessey, *A. J. P.*, 1914, p. 112.) Several authors are inclined to explain the poisoning which

results to sensitive persons who pass near Rhus plants without touching them, by saying that the poison resides in the pollen and the plant hairs. The latter may be carried by air currents or may be transported on clothes, or tools, or animals, which after brushing against the plant are able to transfer the poison to susceptible persons. Warren (*A. J. P.*, 1913, p. 548) was unable to detect a poisonous principle in the pollen grains of *Rhus Vernix*. See also Tschirch and Stevens, *A. J. P.*, 1906, p. 63. Besides the unidentifiable poisonous principle of rhus there is present an iron greening tannin, chlorophyll, wax, fixed oil, resin, sugar, albumen, pectin, gum, starch, and oxalic acid.

The poisonous rhus when taken internally appears to be possessed of narcotic besides irritant properties, vomiting, drowsiness, stupor, dilated pupils, convulsive movements, delirium, and fever having been present in poisoning by them. (*Am. J. M. S.*, April, 1866; also *M. Rep.*, Nov., 1867.) The tincture of rhus has been used especially by homeopathic practitioners in the treatment of *subacute* and *chronic rheumatism*, and the practice has found imitation.

Some years ago H. C. Wood made extended trials of the remedy, using a homeopathic tincture obtained from a homeopathic pharmacy, in various doses (homeopathic, small, and large), upon a large number of cases of *subacute, chronic*, and *acute rheumatism*, in the Philadelphia Hospital, but he was not able to perceive that the patients progressed more rapidly when taking it than when they were simply nursed. The best preparation would undoubtedly be a concentrated alcoholic tincture, made from the green drug; strength of one to four. The *dose*, of a 25 per cent. tincture given by H. C. Wood was from one to five minims (0.06–0.3 mil), three times a day. The solid extract is an ineligible preparation, owing to the extreme volatility of the active principle of the crude drug.

Rhus canadensis Marsh. (*R. aromatica* Ait) (Fam. *Anacardiaceæ*).—This indigenous plant, growing in dry soil from Maine and Southern Ontario to Florida and westward, has been highly recommended in the treatment of *nocturnal incontinence* of urine by a number of clinicians of repute. (See *G. H. M. C.*, 1889; also *Annals of Gynæc.*, 1890.) For elaborate description of the bark, see *Newer Materia Medica*. The adult *dose* is twenty or thirty minims (1.3–1.8 mils) of the fluidextract of the bark, three times a day, given in aromatized solution.

Rhus Glabra. *N. F. IV* (*U. S. VIII*). *Rhus Glabrum. U. S.* 1870. *Sumac Berries. Sleek. Scarlet. White Sumach. Shoe-make. Vinegar Tree. Sumac*, Fr. *Sumach*, G.—"The dried, ripe fruit of *Rhus glabra* Linné (Fam. *Anacardiaceæ*), without the presence of more than 5 per cent. of stems or other foreign matter." *N. F.*

Rhus glabra called variously *smooth sumach, Pennsylvania sumach*, and *upland sumach*, is an indigenous shrub from four to twelve feet or more in height. The leaves are upon smooth petioles, and consist of numerous opposite leaflets, with an odd one at the extremity, all of which are lanceolate, acuminate, acutely serrate, glabrous, green on their upper surface, and whitish beneath. In the autumn their color changes to a beautiful red. The flowers are greenish red, and disposed in large, erect, terminal compound thryses. The fruit is in clusters of small crimson berries.

The shrub is found in Canada and almost all parts of the United States, growing in old neglected fields, along fences, and on the borders of woods. The flowers appear in July, and the fruit ripens in the early part of autumn. The bark and leaves are astringent, and are largely used, especially the leaves, in tanning leather and in dyeing. The sumach for the manufacture of extract for tanners' use is largely cultivated in Virginia, where the annual crop reaches from 7000 to 8000 tons, and is collected at any time between the first of July and the appearance of frost.

The berries have a sour, astringent, not unpleasant taste, and are often eaten by the country people with impunity. They are described in the National Formulary IV as follows:

"Nearly globular, ovoid, more or less reniform, somewhat compressed, about 5 mm. in length and 2 mm. in diameter; externally dark red, velvety with short hairs, summit with remains of the short style, base occasionally with the five-cleft calyx and a short pedicel; endocarp, smooth, shiny, light red; one-celled, one-seeded; seeds dark brown, smooth. Inodorous; taste acidulous and slightly astringent. The powder is brownish-red, and, when examined under the microscope, exhibits irregular fragments; non-glandular hairs, more or less elliptical or ovoid or spatulate, about 0.15 mm. in length and from 0.045 to 0.08 mm. in width, filled with a pink or red cell sap in which occasionally occur rod-shaped crystals; glandular hairs with a short one-celled stalk and multicellular head, from 0.045 to 0.075 mm. in length; fragments of endosperm numerous; fragments of endocarp showing very small stone cells with irregularly thickened walls, readily determined by the use of aniline sulphate T.S. and sulphuric acid; fragments of embryo with rather small cells containing a fixed oil; occasional reddish colored fragments of epidermis and underlying spiral tracheæ of the mesocarp. Mix 1 Gm. of powdered Rhus Glabra with 10 mils of hot water, shake the mixture occasionally until cold, filter, and allow the filtrate to evaporate spontaneously in a watch crystal; numerous, feather-shaped crystals separate which polarize light strongly with a distinct play of colors. Rhus Glabra yields not more than 4 per cent. of ash." *N. F.*

W. J. Watson ascertained that free malic acid and acid calcium malate coexist in the berries, which contain also, upon the same authority, tannic and gallic acids, fixed oil, extractive, red coloring matter, and a little volatile oil. (*A. J. P.*, xxv, 194). A medicinal wine has been prepared from the fruit. (*M. S. R.*, Feb. 9, 1867.) For a paper on the relative proportion of the constituents found in the husk and seed portion of the fruit by Frankforter and Martin, see *A. J. P.*, 1904, 151.

Excrescences are produced under the leaves resembling Chinese galls in character, and containing large quantities of tannic and gallic acids. These have been used as a substitute for the imported galls by Walters of New York, who thought them in every respect preferable. They may be collected at little expense, as they are produced very abundantly, especially in the Western States.

Henry Trimble collected some galls from the leaves of *R. glabra* and found that they contained 61.70 per cent. of tannin, reckoned on the weight of the air-dried galls, or 70.90 per cent. of the weight of absolutely dry material. (*A. J. P.*, 1890, p. 564.)

From the experiments of Stenhouse (*A. J. P.*, xxxiv, 252), it appears that the tannic acid of

sumach is identical with that of galls, being, like it, resolved, under the influence of sulphuric acid, into glucose and gallic acid, and this change is supposed to take place spontaneously in sumach when long kept.

The percentage of tannin in Virginia sumach rises at times as high as 27 per cent., but falls a few per cent. below this as the season advances. Samples of leaves gathered along the Mississippi near Dubuque, Iowa, in July and August, yielded 16.36 per cent. and 15.75 per cent. respectively. (*A. J. P.*, 1888, p. 389.) The proportion of tannic acid in the European sumach falls from 6 to 8 per cent. below the percentage of the Virginia sumach, yet the European is much preferred by tanners and dyers. By using Sicilian sumach it is possible to make the finer white leathers so much used for gloves and fancy shoes, while by the employment of the American product the leather has a yellow color, apparently due to a coloring matter, which, according to Loewe, consists of quercitrin and quercitin, and exists in larger quantity in the American than in the Sicilian drug. Enormous quantities of a dark-red, semi-fluid, bitter, astringent extract are prepared in Virginia from sumach, and used both in America and in Europe. It is said to contain from 25 to 30 per cent. of tannin.

Recently the fruits of *Rhus glabra* have been replaced by those of the *Stag Horn Sumac* (*Rhus typhina* L.) This shrub is very abundant in the eastern United States. The fruits resemble those of rhus glabra both in form and size but are distinguished by being covered with needle-like crimson hairs which are frequently over 2 mm. long. For detailed description of the fruits of these two plants see Kraemer. (*A. J. P.*, 1913, p. 398.)

Sumach berries are astringent and refrigerant. A strong decoction, or the fluidextract diluted, affords a very effective and pleasant gargle in *angina*, especially in combination with potassium chlorate. *Fluidextractum Rhois Glabræ* was official in the U. S. VIII, but then deleted. It was admitted to the National Formulary IV with a slight alteration in the menstruum. The fluidextract affords an excellent astringent in relaxing *diarrheas* and other conditions where the tannin drugs are useful. The *dose* of the fluidextract is fifteen to thirty minims (1–2 mils).

Ricin is the name given by Kobert and Stillmark to the toxic constituent of castor beans (*Ricinus communis*). It belongs to the class of albuminoids and is of the character of an enzyme. It is a white powder which forms a turbid liquid in a 1 per cent. solution of sodium chloride. It has been proposed by Jacoby to detect the presence of pepsin in liquids by using *ricin*. (*M. R.*, 1907.) For a valuable paper by Finnemore and Deane read before the British Pharmaceutical Conference, 1905, see *M. R.*, 1906, 165. The toxic symptoms, which frequently do not come on for several hours after the ingestion of the poison, are due primarily to the intensely irritant action of the substance, and consist of diarrhea, with suppression of the urine, and frequently jaundice, probably from irritation of the mucous membrane of the biliary ducts. Müller (*A. E. P. P.*, 1899, xlii) states that the poison also has a direct action upon the medulla, leading to the fall of blood pressure and lessened respiratory activity.

The effects of ricin in many directions bear a striking resemblance to the effects of bacterial toxins. Thus, for example, it produces a leucocytosis and an agglutination of the red corpuscles. The most interesting, however, of these resemblances is the production of immunity and the formation of antitoxic substances.

Rimu Resin.—The resin of the *Dacrydium cupressinum* Solander, the New Zealand red pine or *rimu*, a large coniferous tree of New Zealand, is characterized by its rose color and its crystalline appearance. It is composed chiefly of a crystalline acid resin, *rimuic acid*. (*Chem. News*, lxxxviii, 20.)

Robinia. *Robinia Pseudo-Acacia* L. *Locust Tree. False Acacia. Robinier*, Fr. *Falsche Akasie*, G. (*Fam. Leguminosæ.*)—This well-known indigenous tree has a place in the materia medica of the eclectics. The bark of the root is the most active part, and is said to be tonic, and in large doses purgative and emetic. The root and inner bark are poisonous to cattle. The leaves, on the other hand, are said to offer a wholesome food for foraging animals. This would seem confirmed by the experiment of Paven, who failed to find in them any poisonous principles. (For an elaborate investigation of its histology, see *P. J.*, 67, 153.) F. B. Power and J. Cambier (*Ph. Rund.*, Feb., 1890) found an alkaloid identical with *choline;* also globulin and a phytalbumose, which produces purging and vomiting. It is precipitated by alkaloidal reagents. The bark also contains a poisonous albuminoid or enzyme, *robinalbin*, which, according to Kobert (*M. Bull.*, April, 1891), is similar to, but not identical with, ricin. Power (*P. J.*, Aug. 17, 1901) summarizes the results of a more detailed investigation of this bark. He names the poisonous proteid *robin* and states that it belongs to the class of nucleo-proteids. He finds evidences of one or more alkaloids; by hydrolysis he obtained *syringic acid*, $C_9H_{10}O_5$, and a red amorphous substance, *syringenin*. These products indicate the glucoside *syringin*, $C_{17}H_{24}O_9$. He also considers that *gluco-syringic acid*, $C_{15}H_{20}O_{10}$, may pre-exist in the bark. Power subsequently reaffirmed the presence of the protein, robin, in robinia bark, and confirms its toxic properties and enzymic action. (*A. J. P.*, 1913, 339.) Robin has emetic and purgative properties. Three cases of the poisoning of children by the root have been recorded. (*Ann. Thér.*, 1860, 64.) Z. T. Emery (*N. Y. M. J.*, Jan. 22, 1887) reports the poisoning of thirty-two boys from chewing the inner bark of the tree. The symptoms in the mildest cases were vomiting and flushed face, dryness of the throat and mouth, and dilated pupils. In the severest cases, to these were added epigastric pain, extremely feeble, intermittent heart action, and stupor.

Robinia Nicou Aubl., now known as *Lonchocapus Rufescens* Benth.—According to the researches of Geoffroy (*Annal. de l'Inst. botanico-geologique colon. de Marseille*, 1895), this leguminous plant, which is used in Guiana for the purpose of stupefying fish, contains an active principle, *nicoline* (C_3H_4O), which crystallizes in oblique, rhomboidal tables. It has been found by E. Boinet (*C. R. S. B.*, 1896, 10 s., iii) to produce in the lower animals a short primary stage of excitation, followed by one of stupor, great muscular relaxation, enfeeblement of sensibility, mydriasis, fall of temperature, cyanosis, and death through centric paralysis of the respiration, though there is also fall of arterial pressure. In the dog there was salivation and vomiting.

Rosa.—Of the genus *rosa* at least four species

have been, and probably to some extent are still, use in medicine—namely, *Rosa canina* L., *Rosa centifolia* L., *Rosa damascena* Mill., and *Rosa gallica* L.

Rosa canina.—The *Dog Rose, Wild Brier,* or *Hip Tree,* of Europe, is distinguished by its prickly stem and petioles, and ovate, smooth, rigid leaves. It has white or pale red flowers, having usually five obcordate fragrant petals. The fruit consists of a fleshy, hollow receptacle, bearing on its inner surface a number of hairy achenes. The ripe fruit, which is usually employed in the fresh condition, is ovoid, smooth, shiny and of a reddish color. The summit is crowned with 5-calyx teeth. Rose hips possess a pleasant, sweet, acidulous taste. It was formerly official in the British Pharmacopœia under the name of *Rosæ Caninæ Fructus.* It contains about 30 per cent. of sugar, combined with citric and malic acids, also salts of these acids, and a trace of tannin. It was used for the preparation of an acidulous confection. Vanillin has also been found present in the petals.

Rosa centifolia has prickly stems and the leaves consist of two or three pairs of leaflets, with an odd one at the summit, closely attached to the common footstalk, which is rough, but without spines. The leaflets are ovate, broad, serrate, pointed, and hairy on the under surface. The flowers are large, with many petals, generally of a pale red color, and supported upon peduncles beset with short bristly hairs. The varieties of *R. centifolia,* produced by its almost universal cultivation, are very numerous, but the plant is said to grow with single flowers in the eastern part of the Caucasus. It is very closely allied to *R. gallica,* some botanists maintaining that the species are really one. The petals, which were recognized by the U. S. P., 1890, as *pale rose,* are roundish-obovate and retuse, or obcordate, pink, fragrant, sweetish, slightly bitter, and faintly astringent. They contain volatile oil, malic and tartaric acids, tannin, fat, resin, sugar, and a coloring matter which seems to be identical with that of the red rose. They should be collected when the flower is fully expanded but has not begun to fall. Their fragrance is impaired but not lost by drying. They may be preserved for a considerable time by compressing them with alternate layers of common salt in a well-closed vessel, or beating them with twice their weight of that substance. A rose water is often prepared from them by distillation.

Rosa damascena is not known in the wild state, and is thought by some botanists to have been produced by cultivation by hybridizing *R. gallica* with *R. canina.* It is the rose which is cultivated in Turkey and yields the commercial *otto of rose.* (See *Oleum Rosæ,* p. 870.) It is a tall shrub with semi-double, light red to white flowers of moderate size, having several on a branch, though not clustered. Its volatile oil is the base of rose water.

Rosemary. *Rosmarinus. Folia Rosmarini, s. Roris Marini. Folia Anthos. Feuilles de Romarin,* Fr. Cod. *Rosmarin, Rosmarinblätter,* G. *Rosmarino,* It. *Romero,* Sp.—"The leaves of *Rosmarinus officinalis* (Fam. *Labiatæ*)." *U. S.,* 1880. *Rosmary* is a small evergreen shrub, with an erect stem, divided into many long, slender, ash-colored branches. The leaves are numerous, sessile, opposite, about 2.5 cm. long, rigid, linear, entire, obtuse at the summit, folded backward at the edges, of a firm consistence, smooth and green on the upper surface, whitish, woolly, and glandular beneath. The flowers are axillary, pale blue or white. The plant grows spontaneously in the countries which border on the Mediterranean, and is cultivated in the gardens of Europe and this country. The leaves, which have already been described, have a strong balsamic odor, which is possessed, but in a less degree, by all parts of the plant. Their taste is bitter and camphorous. These properties are imparted partially to water, completely to alcohol, and depend on the volatile oil. (See *Oleum Rosmarini,* p. 787.) The tops lose a portion of their sensible properties by drying, and become inodorous by age. Rosemary is gently stimulant, and has been considered emmenagogue. In the practice of this country it is scarcely used; but in Europe, especially on the continent, it enters into the composition of several syrups, tinctures, etc., to which it imparts its agreeable odor and excitant property. It is sometimes added to sternutatory powders, and is used externally in connection with other aromatics in the form of fomentation. In some countries it is employed as a condiment; and its flowers, which are much sought after by the bees, impart their peculiar flavor to the honey of the districts in which the plant abounds.

Rotten Stone. *Terra Cariosa.*—An earthy mineral, occurring in light, dull, friable masses, dry to the touch, of a very fine grain, and of an ash-brown color. It is obtained from Derbyshire, in England, and is used for polishing metals. For a particular account of it, see *A. J. P.,* 1860, 463.

Rourea. *Rourea oblongifolia* Hook. and Arn. (Fam. *Connaraceæ.*)—This Mexican creeper is affirmed to contain an alkaloid, and to act as a violent convulsant poison. (*El Estudio,* 1890.)

Rubia. *Garance,* Fr. *Krappwurzel, Färberröthe,* G. *Robbia,* It. *Rubia de tintoreros, Granza,* Sp.—Under this name the U. S. P. formerly recognized *madder, Rubia tinctorum* L. (Fam. *Rubiaceæ.*) The root of *dyer's madder* is perennial, and consists of numerous long, succulent fibers, varying in thickness from the size of a quill to that of the little finger, and uniting at the top in a common head, from which also proceed side-roots that run near the surface of the ground, and send up many annual stems. The quadrangular stems are furnished with short prickles by which they adhere to neighboring plants, upon which they climb. The leaves are arranged in whorls at the joints of the stem. The flowers are small, yellow and terminal. The plant is a native of Southern Europe. The root, which is dug up the third summer, enters commerce either in the form of the whole root deprived of its cuticle, or in the form of a reddish-brown powder. Madder has a weak, peculiar odor, and a bitterish, astringent taste, and imparts these properties, as well as a red color, to water and alcohol. It contains as its most important constituent *alizarin,* $C_{14}H_6(OH)_2O_2$, and with it as coloring matter of secondary importance *purpurin,* $C_{14}H_5(OH)_3O_2$. Besides these two technically important constituents there have been recognized *pseudopurpurin,* an orange dye color, and a yellow one (*xanthopurpurin*). These coloring matters, however, are probably decomposition products from glucosides existing in the fresh plant. Thus, alizarin is known to result along with glucose from the treatment with dilute acids of *rubianic* or *ruberythric acid,* $C_{26}H_{28}O_{14}$, according to the reaction:

$$C_{26}H_{28}O_{14} + 2H_2O = C_{14}H_8O_4 + 2C_6H_{12}O_6$$

The most interesting of the coloring substances is the *alizarin,* and this is now termed *dihydroxy-*

anthraquinone, $C_{14}H_8O_{14}$. This occurs as orange-red crystals, almost insoluble in cold water, but readily soluble in alcohol, ether, the fixed oils, and alkaline solutions. The alcoholic and aqueous solutions are rose-colored; the ethereal, golden yellow; the alkaline, violet and blue when concentrated, but violet-red when sufficiently diluted. A beautiful rose-colored lake is produced by precipitating a mixture of the solutions of alizarin and alum. Alizarin was recognized by Graebe and Liebermann in 1868 as a derivative of anthracene, $C_{14}H_{10}$—a hydrocarbon contained in coal tar—and in the same year they elaborated a method for preparing it commercially from anthracene. Upon this arose rapidly a great chemical industry, and the cultivation of madder, has, of course, decreased correspondingly.

Madder is used in *amenorrhea* and *dropsy*, and when taken into the stomach imparts a red color to the milk and urine, and to the bones of animals, without sensibly affecting any other tissue. The effect is observable most quickly in the bones of young animals, and in those nearest the heart. Under the impression that it might effect some change in the osseous system, it has been prescribed in *rachitis*, but without favorable result. *Dose*, about half a drachm (2.0 Gm.), repeated three or four times a day.

Rubidium.—Salts of *rubidium* may be obtained much more cheaply than in former years, on account of Erdmann's process for the recovery of these salts from the Stassfurt potash deposits. Several salts have been brought forward for use in practical medicine.

Rubidium iodide, RbI, which occurs in whitish crystals, freely soluble in water, has been recommended by Harnack, Neisser, and others as a substitute for potassium iodide, than which it is asserted to be better borne by the stomach. The dose is that of potassium iodide. G. Jacontini affirms that rubidium iodide is a specific in *coryza*.

Rubidium bromide, RbBr, may be used as a substitute for, and in the dose of, potassium bromide, than which it is said to be better borne, especially by feeble patients.

Rubidium and Ammonium Bromide ($RbBr + 3NH_4Br$).—A white or slightly yellowish, crystalline powder, readily soluble in water. Its taste is somewhat cooling at first, and pungently saline afterwards. This salt, one hundred parts of which contain thirty-six parts of rubidium bromide and sixty-four of ammonium bromide (NH_4Br) is used as a hypnotic in *doses* of from one to two drachms (3.9–7.7 Gm.) in a day.

Rubidium Sulphate. Rb_2SO_4.—This occurs as large, rhombic crystals with a taste resembling potassium sulphate. It is soluble in water and is stated to be a very active cathartic.

Rubus. *N. F. IV. Blackberry Bark. Bramble. Finger Berry, Ecorce de Ronce Noir*, Fr. *Brambeeren, Brombeerrinde*, G.—"The dried bark of the rhizome of *Rubus villosus* Aiton, *Rubus nigrobaccus* Bailey, or of *Rubus cuneifolius* Pursh (Fam. *Rosaceæ*)." *N. F.* Of the genus Rubus a large number of species are indigenous in the United States, where they are called by the various names of *blackberry, dewberry, cloudberry*, etc. Most of them are shrubby or suffruticose briers, with astringent roots and edible berries; some have annual stems without prickles. They are naturally divided into the *raspberries*, in which the edible fruit is composed of pulpy, one-seeded, coherent little drupes, separate from the dry receptacle, and the *blackberries*, in which the receptacle is juicy and coheres with the drupes to form the fruit. The National Formulary recognizes as the source of rubus only three species, but it is probable that others contribute to the bark of the markets. In fact, the U. S. Pharmacopœia of 1890 recognized officially *R. canadensis* L., and *R. trivialis* Michaux.

The blackberry root is branching, cylindrical from 0.5 to 2.5 cm. in thickness, and covered with a thin bark, which is externally of a light brownish or reddish-brown color, and in the dried root is wrinkled longitudinally. The dewberry root is usually smaller, without the longitudinal wrinkles, but with transverse fissures through the epidermis, and of a dark ash color, without any reddish tinge. Both are inodorous. The National Formulary IV describes blackberry bark as follows: "In elongated, tough, flexible quills or bands, from 3 to 6 mm. in diameter, the bark from 1 to 2 mm. in thickness; outer surface deep red-brown or dark gray-brown, occasionally blackish-brown, somewhat scaly; inner surface yellow or pale brown, strongly and coarsely long straight-striate; fracture tough-fibrous; readily splitting. Inodorous; taste strongly astringent and bitter. Rubus yields not more than 5 per cent. of ash." *N. F.* Blackberry bark was official in the U. S. VIII, but it was deleted, and the National Formulary IV admitted it under the name of Rubus. Its virtues are extracted by boiling water and by diluted alcohol, and depend chiefly upon tannin, which is an abundant constituent. The woody part of the roots is inert.

Dewberry and blackberry roots have long been a favorite domestic astringent remedy in *diarrheas*. Given in decoction, they are usually acceptable to the stomach, without being offensive to the taste. The decoction may be prepared by boiling an ounce of the smaller roots, or of the bark of the larger, in a pint and a half of water down to a pint, of which from one to two fluidounces (30 to 60 mils) may be given to an adult three or four times, or more frequently, during the twenty-four hours.

A fluidextract and compound elixir of rubus are in the N. F.

The fruit is official in the N. F. under the English title **Blackberries**, *N. F. IV. Rubi Fructus*. It is described by the N. F. as "The fresh, ripe fruit of varieties of *Rubus nigrobaccus* Bailey or *Rubus villosus Aiton* (Fam. *Rosaceæ*). An aggregate fruit, ovate to oblong, rounded or slightly pointed, composed of numerous, shining black drupelets attached to an esculent receptacle; pericarp externally smooth or with only a few hairs (*R. villosus*), mesocarps fleshy, juice purple-red, endocarps hard, black, surfaces deeply wrinkled." *N. F.*

The fruit of *Rubus Iodœus* is official in the N. F. under the English title **Raspberries**, *N. F. IV. Rubi Idæi Fructus*. They are described as "The fresh, ripe fruit of varieties of *Rubus Idœus* Linné or of *Rubus strigosus* Michaux (Fam. *Rosaceæ*). An aggregate fruit, globular or hemispherical with a concave depression at the base where separated from the receptacle, composed of twenty or more small, rounded-polygonal, succulent drupelets; pericarps externally red, hairs numerous; mesocarps fleshy, juice red; endocarps small stones with wrinkled surfaces. Odor characteristic, aromatic; taste pleasant, sweet, acidulous. For pharmaceutical purposes, Black Raspberries, the fresh ripe fruit of varieties of *Rubus occidentalis* Linné

(Fam. *Rosaceæ*), may be substituted either in part or wholly for Red Raspberries." *N. F. Rubus strigosus* has yielded to cultivation certain superior raspberries, especially those which have been known commercially as the Cuthbert and Hansall raspberries. *Rubus neglectus* Peck, the purple wild raspberry, with a fruit which varies from dark red or purple to yellowish in cultivation, has also yielded a commercial raspberry.

Raspberries are employed for the production of the N. F. syrup (see Part III).

The *Rubus occidentalis* L., *black raspberry* or *thimbleberry* of the Northern United States, which is also cultivated, is sometimes employed for the making of a raspberry syrup, but yields a very inferior product.

Rubus Chamæmorus L. *Cloud Berry. Baked-Apple Berry.* (Fam. *Rosaceæ.*)—This plant, which inhabits the northern portions of both continents, is largely employed in Northern Russia, in the form of an infusion of the berries or leaves, as a diuretic in *dropsy.* The fruits are about 2 cm. in diameter, of an amber color, and very juicy when ripe. Popoff found in it a crystallizable acid which is an essential diuretic, acting directly upon the renal secreting structures without affecting either cardiac action or arterial tension. (*Vrach.*, iv, 1886.)

Rumex. *N. F. IV. Yellow Dock. Curled Dock. Radix Lapathi.—Rumex* was official in the U. S., 1890, and has been admitted to the N. F. IV and is defined as "The roots of *Rumex crispus* Linné, or of *Rumex obtusifolius* Linné (Fam. *Polygonaceæ*), without the presence of more than 5 per cent. of stem bases." *N. F. IV.* The roots of rumex are officially described as "Usually split longitudinally or cut into transverse pieces about 2 cm. in length. The entire root, nearly simple, slightly tapering, with few if any rootlets, somewhat twisted, up to 30 cm. in length and 7 cm. in diameter, externally reddish-brown or grayish from adhering soil, finely annulate above, deeply wrinkled longitudinally, marked with small indented root scars which are often transversely elongated and with occasional stem scars or remains of stem, the latter being hollow and finely striated; leaf buds few, obconical; fracture short and dusty, somewhat fibrous. The transverse section exhibits a yellowish or brownish cortex and a whitish or yellowish wood which is finely radiate in the outer portion. When examined under the microscope, it exhibits a thick cortex with several layers of cork, beneath which is an interrupted row of stone cells; a distinct cambium; and vascular bundles with few fibers. The **powder**, when examined under the microscope, shows calcium oxalate crystals in rosette aggregates from 0.025 mm. to 0.06 mm. in diameter; numerous starch grains ellipsoidal or narrowly elongated, sometimes truncate, up to 0.025 mm. in length; stone cells from 0.04 mm. to 0.2 mm. in diameter, with walls somewhat lamellated, from 0.008 mm. to 0.025 mm. in thickness and with few simple pores; sclerenchymatous fibers few, thin-walled with simple pores; tracheæ up to 0.1 mm. in width with scalariform or reticulate thickenings of the wall; cork cells light brown. Rumex yields not more than 10 per cent. of ash." *N. F. IV.*

Several species of rumex have sour leaves, and are distinguished by the common name of *sorrel* from the others, which are called *dock.* Of the former, *Rumex Acetosa* L., or *common English sorrel*, formerly held a place in the London and Dublin Pharmacopœias. *R. Acetosella* L. is the common sorrel of our fields, though supposed to have been originally introduced from Europe. The leaves of both these plants are agreeably sour to the taste, and owe their acidity to acid potassium oxalate with a little tartaric acid. They quite lose this taste in drying. They are refrigerant and diuretic, and may be used advantageously as an article of diet in *scurvy.* For this purpose they are prepared in the form of salad. The juice of the leaves forms with water an agreeable acidulous drink, sometimes used in fevers. Taken very largely, the leaves are said to have produced poisonous effects. *R. scutatus* L., of Europe, Northern Africa, Asia Minor, and the Caucasus, also ranks among the sorrels (*French sorrel*).

Of the proper docks, the roots of *R. silvestris* Wallr., an European plant, and of *R. conglomeratus* Murr., *R. aquaticus*, *R. sanguineus* L., and *R. Patientia* L., belonging both to Europe and to the United States, may be employed indiscriminately with those of the *R. crispus* L., which was formerly recognized by the U. S. Pharmacopœia. *R. Britannica* L., and *R. obtusifolius* L., were formerly official. *R. Hydrolapathum* Hudson, which is the *R. aquaticus* of the old Dublin Pharmacopœia, is thought to be the *Herba Britannica* of the ancients, celebrated for the alleged cure of *scurvy* and diseases of the skin. The docks are herbaceous plants with perennial roots, and especially distinguished by the sheathing petioles of the leaves. The flowers are small, mostly green, and occur in terminal or axillary panicles.

Dock root, from whatever species derived, has an astringent, bitter taste, with little or no odor. The leaves of most of the species are edible when young, and are occasionally used like spinach. They are somewhat laxative, and form an excellent diet in scorbutic cases. The roots are used to dye a yellow color. According to J. H. Salisbury (*N. Y. Journ. Med.*, March, 1855), the petioles of the leaves contain nearly one per cent. of oxalic acid; the cortical part of the root, which is the most active, yielded, on analysis, starch, a little sugar, albuminous matter, gummy matter, bitter extractive, tannic acid of the kind which gives green precipitates with the salts of iron, lignin, and various salts. The root yields its virtues to water and to alcohol, but is injured by long boiling.

Dock root is astringent, gently tonic, and has been supposed to have alterative properties, making it useful in skin diseases and even *syphilis.* From the root of *R. Nepalensis* Wall., which is largely used in Madras as an astringent for medicinal purposes and for dyeing, O. Hesse has separated three crystalline substances to which he gives the names of *rumicin*, *nepalin*, and *nepodin.* (*P. J.*, lvi; also *Proc. A. Ph. A.*, 1896, 551.) According to Tutin and Clewer (*Trans. Chem. Soc.*, 1910, xcvii) the *R. Eckolianus* Meissner, a South African herb, contains chrysophanic acid, emodin, and allied products, and is mildly purgative. Tschirch and Weil found small quantities of *emodin* and *chrysophanic acid* with *lapathinic acid*, $C_{20}H_{18}O_{14}$, in the root of *R. obtusifolius.* (*A. de Pharm.*, 1912, No. 1, 20.) *R. aquaticus* and *R. Britannica* are the most astringent. The roots of some species unite a laxative with the tonic and astringent property, resembling rhubarb somewhat in their operation. Such are those of *R. crispus* and *R. obtusifolius;* and *R. alpinus* L., has in some parts of Europe the name of *mountain rhubarb.* This resemblance is not singular, as the two genera belong to the same natural family. A. Gilbert and P. Lereboullet have discovered a remarkable prop-

erty of *Rumex crispus*. For the roots of this plant are said to possess the power of taking up the iron present in the soil, and fixing it in the form of organic compounds of iron. By watering the plants with a solution of iron carbonate, roots are said to be obtained which contain 1.5 per cent. of iron. Rumex is said to give good results in the treatment of *chlorosis* and *anemia*. The authors gave the dried and powdered root during meals in doses of fifteen to forty-five grains (1–3 Gm.), in view of their good results they regard it as a valuable iron medicine. Dock root is given in powder or in decoction. Two ounces (62 Gm.) of the fresh root bruised, or one ounce (31 Gm.) of the dried, may be boiled in a pint (480 mils) of water, of which two fluidounces (60 mils) may be given at a *dose*, and repeated as the stomach will bear it. George G. Flemyng (*L. L.*, i, 1896) reported the death of two sisters, aged respectively five and six and a half years, preceded by symptoms of oxalic acid poisoning as the result of the ingestion of sorrel leaves.

Ruta.—Under this name the U. S. Pharmacopœia formerly recognized *Ruta graveolens* L.; *Rue; Rue odorante*, Fr.; *Garten-Raute*, G.; Ruta, It.; *Ruda*, Sp., (Fam. *Rutaceæ*). It is a low, shrubby plant, with several shrubby branching stems, which, near the base, are woody and covered with a rough, bark, but in their ultimate ramifications are smooth, green, and herbaceous. The leaves are fleshy, 2- to 3-pinnatified, the ultimate lobes or divisions being obovate-cuneate. The flowers are yellow, and disposed in a terminal branched cyme. The plant is a native of the south of Europe, locally established in pastures in the United States and cultivated in our gardens. The whole herb is active, and yields its properties to water and alcohol. The leaves have a strong, disagreeable odor, especially when rubbed. Their taste is bitter, hot, and acrid. When recent, and in full vigor, they have so much acrimony as to inflame and even blister the skin, if much handled; but the acrimony is diminished by drying. Their virtues depend chiefly on a volatile oil, which is contained in glandular vesicles, apparent over the whole surface of the plant. They contain, also, according to Bornträger, a peculiar acid which he calls *rutinic acid*, $C_{25}H_{28}O_{15}$ (or $C_{27}H_{32}O_{16}$, according to later writers). Rutinic acid is the coloring principle of rue, and has been found in various other plants; though, like quercitrin, yielding quercetin and sugar, it has been shown to be distinct. (*J. P. C.*, 1862, 165.)

Rue yields a very small proportion of a yellow or greenish volatile oil (*Oleum Rutæ, U. S.*, 1880), which becomes brown with age. According to Zeller, the yield from the fresh herb is 0.28 per cent., that from the seeds about 1 per cent. The oil has the strong unpleasant odor of the plant, and an acrid taste. Kane gives its sp. gr. at 0.837, its boiling point at 230° C. (446° F.). "A neutral reaction. Sp. gr. about 0.880. It is soluble in an equal weight of alcohol." *U. S.*, 1880. It consists mainly of an oxidized constituent, which Strecker proved to be *methyl-nonyl-ketone*, $CH_3.CO.C_9H_{19}$; that is, a ketone analogous to acetone, $CH_3.CO.CH_3$. This accounts for its yielding under treatment with oxidizing agents, pelargonic acid, $C_9H_{18}O_2$. The methyl-nonyl-ketone, when pure, is a colorless liquid, fluorescing blue, boiling at 225° C. (437° F.), and crystallizing at about 15° C. (59° F.). Schimmel & Co. (*Schim. Rep.*, 1892, 31) state that pure oil of rue consists of 90 per cent. of methyl-nonyl-ketone, and solidifies even at a moderate temperature to a solid, crystalline mass, and has the sp. gr. 0.837.

According to von Soden and Henle, *Algerian oil of rue* differs from the ordinary oil in that it is chiefly composed of *methyl-heptyl-ketone*, with but small quantities of *methyl-nonyl-ketone*. Its specific gravity at 15° C. (59° F.) is 0.842; and it does not solidify at −15° C. (5° F.). (*Ph. Ztg.*, 46.) Frederick B. Power and Frederic H. Lees (*Trans. Chem. Soc.*, 1902) have since published an elaborate investigation of a similar Algerian oil. They find 80 per cent. of the two ketones, methyl-heptyl-ketone and methyl-nonyl-ketone, 10 per cent. of the corresponding carbinols (alcohols), pinene, l-limonene, cineol, methyl salicylate, ethyl valerate, and some free fatty acids.

Rue is said to have been used by the ancients as a condiment. In modern times it has been employed in *hysteria, worms, colic*, and atonic *amenorrhea* and *menorrhagia*. Its medicinal activity depends upon its volatile oil, which is a powerful local irritant, causing, when applied to the skin persistently, burning, redness, and vesication, and when taken internally in large doses, violent gastric pains and vomiting, great prostration, confusion of mind, convulsive twitching, and in pregnant women, abortion. It has been considerably used in Europe for the production of criminal abortion, in a number of cases with fatal results. In a case of fatal poisoning in a man, reported by G. F. Cooper, there were vomiting, violent tormina and tenesmus, with bloody stools, great abdominal distention, with tenderness and severe strangury. (*Med. Exam.*, N. S., ix, 720.) The *dose* of the oil is from two to five minims (0.12–0.3 mil) every two or three hours. The rue itself is sometimes given in the *dose* of from ten to thirty grains (0.65–2.0 Gm.).

Ruthenium Chloride. *Ruthenium Sesquichloride.* Ru_2Cl_6.—A deliquescent, crystalline mass of a brownish-red color and soluble in water and stated to possess a high antiseptic value.

Ruthenium Red. *Ruthenium Oxychloride Ammoniated.* $Ru_2(OH)_2Cl_4.7(NH_3) + 3H_2O$.—A brownish-red powder, soluble in water. It is used as a microscopic stain and reagent for pectin, plant mucin, and gum. In bacteria staining there must be added to the *ruthenium red* a small amount of acetic acid.

Rye. *Secale cereale* L. (Fam. *Gramineæ.*) *Roggen*, G. *Leigle*, Fr. *Centeno*, Sp.—*Rye* is allied to wheat and barley. Its native country is somewhat doubtful, but is said to be found wild throughout the Mediterranean countries, extending to Central Asia. There are two prominent varieties known as "Winter" and "Spring" rye, the difference being due to cultivation mainly. Rye is now cultivated in all temperate latitudes. The average composition of rye as a cereal may be thus stated: fat, 1.43 per cent.; starch, 61.87 per cent.; sugar (as sucrose), 4.30 per cent.; albumen (insoluble in alcohol), 9.78 per cent.; nitrogenous matter (soluble in alcohol), 5.09 per cent.; cellulose, 3.23 per cent.; mineral matter, 1.85 per cent.; moisture, 12.45 per cent. (Sadtler, *Industrial Organic Chemistry*, 3d ed., p. 169.) *Rye flour* is used, in the dry state, as an external application to *erysipelatous inflammation* and other eruptive affections, the burning and unpleasant tingling of which it tends to allay, while it absorbs the irritating secretions. In the form of mush it is an excellent laxative article of diet, and, mixed with molasses, it may be given with great advantage in *hemorrhoids* and *prolapsus ani*,

connected with *constipation*. Rye carbonized by heat, with exclusion of the air, has been highly recommended as a tooth powder.

Sabadilla. *Cevadilla.*—The dried ripe seeds of *Schoenocaulon officinale* (Schlecht.) A. Gray [*Asagræa officinalis* (Cham. and Schlecht.) Lindl.], were recognized by the Br. Pharm. of 1885. At one time cevadilla was generally believed to be derived from *Veratrum Sabadilla* Schiede. The plant grows in the Andes of Mexico and in the mountains of Guatemala and Venezuela. It is also cultivated. The fruit is a capsule having three locules in each of which there are from three to four seeds. A resemblance, existing or supposed, between this fruit and that of barley is said to have given rise to the Spanish name cevadilla, which is a diminutive of barley. The seeds are elongated, pointed at each end, flat on one side and convex on the other, somewhat curved, 5 to 8 mm. long, wrinkled, slightly winged, black or dark brown on the outside, whitish within, hard, inodorous, and of an exceedingly acrid, burning, and durable taste.

Pelletier and Caventou first noted the presence of an alkaloid in cevadilla, which base they called *veratrine;* Meissner in the same year announced the presence of an alkaloid, *sabadilline*, $C_{34}H_{53}O_8N$, and Couërbe, Merck, and Weigelin all described what they considered as distinct bases; but its exact composition remained unsettled until Wright and Luff (*J. Chem. S.*, 33, 338) found in it three bases: (1) *cevadine*, $C_{32}H_{49}O_9N$, (agreeing with the base described by Merck as veratrine), crystallizing in needles or compact crystals, fusing at 205° C. (401° F.) (202° C. (395.6° F.), according to Merck), insoluble in water, easily soluble in alcohol and ether, and decomposed by hot alcoholic potash into *cevine*, $C_{27}H_{43}O_8N$ ($C_{27}H_{45}O_9N$, Flückiger), and *methyl-crotonic acid* (*cevadic acid* of Pelletier and Caventou), $C_5H_8O_2$; (2) *veratrine*, $C_{37}H_{53}O_{11}N$, obtained from the syrupy mother liquor from which the cevadine has crystallized (see p. 1194); (3) *cevadilline* or *sabadilline*, $C_{34}H_{53}O_8N$, obtained after the extraction of the veratrine with ether; it is insoluble in ether, slightly soluble in boiling benzene, and readily soluble in fusel oil, uncrystallizable, and appears to yield methyl-crotonic acid on treatment with alcoholic soda. For method of extracting the alkaloids, see *U. S. D.*, 19th ed., p. 1636.

Merck has since (*M. R.*, Jan., 1891, 3–9) isolated two new alkaloids from cevadilla, which he names *sabadine* and *sabadinine* respectively. The former has the formula $C_{29}H_{51}NO_8$, crystallizes from ether in short needles, and fuses at from 238° to 249° C. (460.4°–464° F.). It dissolves in concentrated sulphuric acid with a yellow color and a green fluorescence, which gradually disappears, while the liquid assumes a blood-red and then violet color. The alkaloid is sternutatory, although in a much less degree than veratrine. The second alkaloid crystallizes from ether in filiform needles, which begin to sinter at 160° C. (320° F.), but show no fixed fusing point. Concentrated sulphuric acid causes a permanent blood-red color. The formula is given as $C_{27}H_{45}NO_8$. This alkaloid is not sternutatory. Cevadilla yields about 0.3 per cent. of veratrine. (See *Veratrina*, p. 1194.)

Cevadilla is an acrid, drastic emeto-cathartic, operating occasionally with great violence, and in overdoses capable of producing fatal effects. Known in Europe as early as 1752, and formerly used to some extent as a tænicide, in *doses* of from five to twenty grains (0.32–1.3 Gm.), it was official solely as the source of veratrine. It is the principal ingredient of the *pulvis capucinorum*, sometimes used in Europe for the destruction of vermin in the hair.

According to E. Falk, 0.001 Gm. of pure cevadine will paralyze the frog; 0.01 Gm. will cause death from cardiac paralysis in rabbits; 0.02 Gm. per kilogramme produces paralysis, interrupted by tetanic spasms. Cevine was found to be much less poisonous than cevadine, though producing similar symptoms.

Sabbatia. *American Centaury. Centaurée Américaine*, Fr. *Sabbatie*, G.—The overground plant of *Sabatia* (*Sabbatia*) *angularis* (L.) Pursh. (Fam. *Gentianaceæ*), an herb found in rich soil throughout the Eastern and Central United States and Ontario. The stems are much branched, distinctly 4-angled, and from 3 to 9 dm. high. The leaves are ovate, 5-nerved, having a heart-shaped clasping base. The flowers are rose-pink and on drying become pinkish-brown. The fruit is a 2-valved capsule, dark brown and covered with a resin. It is more or less used in popular medicine as a tonic and antiperiodic. It is a simple bitter of some activity, and may very well be substituted for the foreign remedies of its class. Rodney H. True found American centaury adulterated with *Rhexia mariana*, also known as *deer grass* or *meadow beauty*. (*A. J. P.*, 1905, 213.) John F. Huneker found in *sabbatia* a small proportion of *erythrocentaurin*, $C_{27}H_{24}O_8$, previously discovered by Méhu, a French chemist, in *Erythræa Centaurium* Pers., of Europe.

In the Southeastern United States, the *Sabbatia Elliottii* Steud., or *Quinine flower*, and in the Southwestern United States the *Sabbatia campestris* Nutt. have been employed like the *S. angularis* in the North. According to Merck the *S. Elliottii* contains a glucoside, *sabbatin*, as its active principle. Of the *S. angularis* and the *S. campestris* the whole plant is used, the *dose* being a drachm (3.9 Gm.), given in the form of fluidextract or in decoction. Of the quinine flower, the root is employed; *dose*, of the fluidextract, one fluidrachm (3.75 mils); in intermittent fever to be repeated at short intervals.

Sabina. *U. S. VIII. Savin. Sabinæ Cacumina. Summitates* (*Herba*) *Sabinæ. Savine Tops. Sabine*, Fr. Cod. *Sevenbaum. Sadebaumspitzen. Sevenkraut*, G. *Sabina*, It., Sp.—"The tops of *Juniperus Sabina* Linné (Fam. *Coniferæ*)." *U. S. VIII. Juniperus Sabina* is an evergreen shrub from three to fifteen feet high, with numerous erect, pliant branches. The leaves, which completely invest the younger branches, are numerous, small, erect, firm, smooth, pointed, dark green, glandular in the middle, opposite, and imbricated in four rows. The fruit is a blackish-purple berry of an ovoid shape, and containing three seeds. The savin is a native of the south of Europe and the Levant, and grows wild in the neighborhood of the northwestern lakes of the United States.

The ends of the branches, and the leaves by which they are invested, are collected for medicinal use in the spring. When dried they are very much faded in color. They were officially described as "short, thin, subquadrangular branchlets bearing leaves which are rather dark green, in four rows, opposite, scale-like, ovate-lanceolate, more or less acute, appressed, imbricated, having on the back a shallow groove containing an oblong or roundish gland; odor peculiar, terebinthinate; taste disagreeable, resinous and bitter." *U. S.* They have a strong, heavy, disagreeable odor, and a

bitter, acrid taste. These properties, which are less striking in the dried than in the recent leaves, are owing to a volatile oil. The leaves impart their virtues to alcohol and to water. C. H. Needles found in them volatile oil, gum, tannic or gallic acid, resin, chlorophyll, fixed oil, bitter extractive, lime, and salts of potassium. (*A. J. P.*, xiii, 15.)

In America the tops of *Juniperus virginiana* L., or common *red cedar*, also commonly referred to as *savin*, are sometimes substituted in commerce for savin, which they resemble closely, but from which they can be distinguished by some of their leaves being obtuse or acutish and the fruits being smaller, purplish and containing fewer seeds. In Europe savin is said to be adulterated with the tops of *J. phœnicea* L., which contain volatile oil similar to that of *J. communis*. Such substitution is to be detected by the fact that in *J. phœnicea* the imbricated leaves occur in spirals of five, and the berries are large, shiny, and vary in color from yellow to reddish-yellow. In the mesophyll there occur large stone cells which are either single or in groups.

According to the more recent authorities, the proportion of volatile oil obtained from savin varies as much as from 1 to 2.5 per cent. The *oil of savine* (*Oleum Sabinæ, U. S. VIII*) is "a colorless or yellowish liquid, having a peculiar terebinthinate odor, and a pungent, bitter, and camphoraceous taste. Specific gravity: 0.903 to 0.923 at 25° C. (77° F.). The Oil is dextrogyrate, the angle of rotation varying between + 40° and + 60° in a 100 Mm. tube, at a temperature of 25° C. (77° F.). Soluble in about one-half volume or more of 90 per cent. alcohol." *U. S.* According to Schimmel & Co. (*Schim. Rep.*, April, 1897), its specific gravity is from 0.91 to 0.925, optical rotation + 45° to + 60°, and it contains *pinene*, $C_{10}H_{16}$, *cadinene*, $C_{15}H_{24}$, and an alcohol, $C_{10}H_{16}O$, *sabinol*, which is present both in the free state and as acetic ester. With iodine it becomes heated, detonates, and gives off yellow and violet-red vapors. (Flaschoff.)

Savin is highly irritant, and is supposed to have a special direction to the uterus. It has been much used in *amenorrhea* and *atonic menorrhagia*, and occasionally as a remedy for *worms*. Chapman strongly recommended it in *chronic rheumatism*, and it is employed in Germany, both internally and externally, in *chronic gout*. In overdoses it may produce dangerous gastro-intestinal inflammation, and it should therefore be used with caution. In no case should it be employed when much general or local excitement exists. In pregnancy it should always be given with great caution. As an external irritant, savin is useful, in the form of cerate, for maintaining a discharge from blistered surfaces; but as in this country savin ointment is often feeble, either from the age of the drug or from the substitution of red cedar, it has fallen into disrepute. In powder or infusion, savin is used in Europe as an application to *warts, indolent* or *gangrenous ulcers, psora*, and *tinea capitis*, and the expressed juice of the fresh leaves, diluted with water, is sometimes used for similar purposes. Powdered savin should not be used after it has lost the green color, characteristic of the fresh drug. The oil of savin is a powerful local irritant, producing, when persistently applied to the skin or the mucous membrane, violent inflammation. It has been much used for the purpose of producing criminal abortion, and in a number of such cases has caused death, the symptoms being violent abdominal pain, bloody vomiting and purging, diminution or suppression of urine, disordered respiration, unconsciousness, convulsions, and fatal collapse. Although Prochnow (*A. I. P. T.*, 1911, xxi, p. 316) has found that small doses of savin have a slight stimulating effect upon the uterus it is manifest that any abortifacient results must be due to general disturbance of the health rather than to any local action. The fluidextract is rarely used internally but the stated dose is from five to ten minims (0.3–0.6 mil). The *dose* of the oil of savin is from one to three minims (0.06–0.2 mil).

Fluidextract of Savin. Fluidextractum Sabinæ. U. S. VIII.—The U. S. VIII gave the following directions for the preparation of the fluidextract: "Savin, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, *a sufficient quantity*, to make *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Moisten the powder with *two hundred and fifty mils* [or 8 fluidounces, 218 minims] of Alcohol, and pack it firmly in a cylindrical percolator; then add enough Alcohol to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding Alcohol, until the Savin is exhausted. Reserve the first *nine hundred mils* [or 30 fluidounces, 208 minims] of the percolate, and evaporate the remainder, at a temperature not exceeding 50° C. (122° F.), to a soft extract; dissolve this in the reserved portion, and add enough Alcohol to make the Fluidextract measure *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]." *U. S. VIII*

Sabromin. *N. N. R.* 1917. *Dibrom-behenate of Calcium.* $(C_{22}H_{41}O_2Br_2)_2Ca$.—This is a white powder without taste or odor prepared by adding bromine to erucic acid, forming *dibrombehenic acid*, and then preparing the calcium salt of the latter. It is insoluble in alcohol, water and acetone, soluble in ether and chloroform, and contains after drying 29 per cent. bromine and 3.8 per cent. calcium. The clinical evidence is indisputable that this preparation is capable of exercising many of the therapeutic properties of the alkaline bromides, but there is considerable contradiction as to the extent to which it may replace the older salt. On the one hand, Von Mering (*M. K.*, iv, p. 1464) has found, despite the fact that it contains only one-half the amount of bromine that potassium bromide does, it is equal in power although slower in action, and Bratz and Schlokow (*D. M. W.*, 1909) assert that weight for weight *sabrominin* is more efficacious than potassium bromide. On the other hand, Ellinger and Kotake (*A. E. P. P.*, 1911, lxv) assert that if administered in large enough doses to obtain the bromide action, sabromin is injurious to the kidney, and Bittner (*Pr. M. W.*, 1910) found it of little use in *epilepsy*. It has been employed by many physicians with mostly favorable results in *hysteria, neurasthenia, insomnia, epilepsy*, and other conditions in which the bromides are habitually employed. The *dose* ordinarily given is from eight to thirty grains (0.5–2.0 Gm.).

Saccharosolval.—This preparation is a combination of ortho-oxybenzoic acid, trypsin, and the spinal marrow of oxen. It is administered in the treatment of *diabetes*, forty-five grains (3 Gm.) being given three times a day.

Safrol. *Safrolum. U. S. VIII. Synthetic Oil of Sassafras. Safrol*, Fr., G. $C_{10}H_{10}O_2 = 162.08$. —"The methylene ether of allyl pyrocatechol [C_6

$H_3.C_3H_5.(OOCH_2)$ 1 : 3 : 4], found in oil of sassafras, camphor oil, and other volatile oils, purified, if necessary, by repeated chilling and crystallization." *U. S. VIII. Safrol* is found in oil of sassafras often in the proportion of 80 per cent., but commercially it is obtained from the red oil of camphor, by fractional distillation, the portion boiling at about 230° C. (446° F.) contains the safrol, this is cooled and the crystals separated. (See *Oleum Sassafras*, p.790.) It was officially described as "a colorless or faintly yellow liquid with a sassafras-like odor. Specific gravity: 1.098 to 1.100 at 25° C. (77° F.). Boiling point: about 233° C. (451.4° F.). It is optically inactive. On cooling to –20° C. (–4° F.) or below, it solidifies to a mass of crystals, which do not melt below 11° C. (51.8° F.). Soluble in about an equal volume of strong alcohol, and in about 30 parts of 70 per cent. alcohol. Miscible in all proportions with ether and chloroform." *U. S. VIII.* Physiologically and therapeutically, safrol is equivalent to oil of sassafras. *Dose*, three to eight minims (0.2–0.5 mil).

Sagapenum.—This gum-resin, formerly highly esteemed, but at present very rarely met with even in Eastern commerce, is the concrete juice of a Persian plant, *Ferula Persica* Willd. (Fam. *Umbelliferæ*), related to those that yield galbanum. It is in irregular masses, composed of agglutinated fragments, slightly translucent, of a brownish-yellow, olive, or reddish-yellow color externally, paler internally, brittle, of a consistence somewhat resembling that of wax, and often mixed with impurities, especially with seeds more or less entire. An inferior variety is soft, tough, and of uniform consistence. It has an alliaceous odor less disagreeable than that of asafetida, and a hot, nauseous, bitterish taste. It softens and becomes tenacious by the heat of the hand. The effect of time and exposure is to harden and render it darker. It is inflammable, burning with a white flame and much smoke, and leaving a light spongy charcoal. Pure alcohol and water dissolve it partially, diluted alcohol almost entirely. Distilled with water it affords a small quantity of volatile oil, and the water is strongly impregnated with its flavor. According to Tschirch (*Harze und Harzbehälter*, 229), it contains 23.3 per cent. of gum; 19.2 per cent. of essential oil, containing sulphur; and 57.5 per cent. of a resin which is free from sulphur and melts at 74° to 76° C. (165.2°–168.8° F.). The ether soluble resin of *sagapenum* can be separated by saponification into *umbelliferone* and *sagaresitannol*, $C_{24}H_{37}O_4.OH$. This latter yields on oxidation *oxypicric acid*. The oil is pale yellow, very fluid, lighter than water, and of a disagreeable alliaceous odor. Sagapenum was formerly used in *doses* of from ten to thirty grains (0.65–2.0 Gm.) in *amenorrhea*, *hysteria*, etc.; also externally in plasters as a discutient.

Sage. *Salvia. U. S. VIII. Garden Sage. Meadow Sage. Save. Picked Sage. Sauge Officinale*, Fr. Cod. *Sauge*, Fr. *Folia Salviæ*, P. G. *Salbei*, G.—"The dried leaves of *Salvia officinalis* Linné (Fam. *Labiatæ*)." *U. S. VIII. Salvia officinalis*, or common garden *sage*, is a perennial plant, about two feet high, with a quadrangular, pubescent, branching, shrubby stem, furnished with opposite, petiolate, ovate-lanceolate, crenulate, wrinkled leaves, of a grayish-green color, sometimes tinged with red or purple. The flowers are blue, variegated with white and purple, and are disposed on long terminal spikes, in distant whorls, each composed of a few flowers, and provided with ovate, acute, deciduous bracts. The calyx is tubular and striated, with two lips, of which the upper has three acute teeth, the under two. The corolla is tubular, bilabiate, ringent, with the upper lip concave, and the lower divided into three rounded lobes, of which the middle is the largest. The filaments are supported upon short pedicels, to which they are affixed transversely at the middle.

Sage grows spontaneously in Southern Europe, and is cultivated abundantly in our gardens. There are several varieties, differing in the size and color of their flowers, but all possessing the same medicinal properties. The flowering period is in June, at which time the plant should be cut, and dried in a shady place. The leaves were officially described as "long and stoutly petiolate, the blade elliptical or ovate-oblong, 3 to 7 Cm. long, obtuse or subacute at the summit, rounded or subcordate at the base, finely crenulate, thick, grayish-green, very pubescent, especially on the under surface, conspicuously reticulate-veined; odor aromatic; taste aromatic, bitter, and somewhat astringent." *U. S. VIII.*

Both the leaves and the flowering summits have a strong, fragrant odor, and a warm, bitterish, aromatic, somewhat astringent taste. They abound in a volatile oil, which may be obtained separate by distillation with water. Muir (*J. Chem. S.*, 37, p. 678) found it to contain a terpene boiling at 156° C. (312.8° F.), another boiling at 171° C. (339.8° F.), *thujone*, $C_{10}H_{16}O$, a liquid boiling at from 197° to 203° C. (386.6°–397.4° F.), and ordinary camphor, $C_{10}H_{16}O$. In the fresh oil the first terpene predominates. On standing, the amount of *thujone* increases, and then the camphor. The oil from English leaves contains also a sesquiterpene, $C_{15}H_{24}$, of the boiling point 260° C. (500° F.). Wallach (*Ann. Ch. Ph.*, 1889) states that the first portions contain pinene and cineol, but the greater portion consists of thujone, $C_{10}H_{16}O$ (formerly called *salviol*). Ferrous sulphate strikes a black color with infusion of sage.

Sage unites slightly tonic, astringent, and aromatic properties. By the ancients it was highly esteemed; it is at present little used, except as a condiment, but has been given in *dyspepsia*, also for *colliquative sweats*. According to Cadéac and Meunier (*Lyons Méd.*, May, 1891), the volatile oil of sage is a violent epileptiform convulsant, resembling in its action the oil of absinthe, but less powerful.

The *dose* of the powdered leaves is from twenty to sixty grains (1.3–3.9 Gm.). *Dose*, of the infusion (one oz. in one pint of boiling water), two fluidounces (60 mils).

Although the *Salvia* officinalis was the only species of this genus which was recognized by the U. S. P. VIII, many other species share the feeble medicinal properties of sage. *S. pratensis* L., *S. Æthiopis* L., *S. glutinosa* L., and *S. Sclarea* L., or *clarry*, have been officially recognized in Europe, but are less agreeable than is *S. officinalis* and are not much used; the leaves of *S. Sclarea* are said to be introduced into wine in order to impart to it a muscatel taste. The infusion of the *Rocky Mountain sage*, probably *S. lanceolata* Willd., is affirmed by A. Comstock (*T. G.*, 1887, 660) to be valuable as a diaphoretic in *malarial* and *rheumatic fevers*, taken in the form of hot infusion, and when cold to be distinctly tonic and astringent. The *dose* of fluidextract is half a fluidrachm (1.8 mils).

The seeds of various sages contain enough farinaceous and mucilaginous material to make them useful as food. In the Western United States the

ordinary sages of the plains are highly esteemed for fattening cattle, which eat their ripened tops freely (these sages must be distinguished from the so-called "sage brushes" of the West, which belong to the genus *Artemisia*). *Chia* is the seeds of one or more species of *salvia* largely used in Mexico and Southern Arizona by the natives as food. It is affirmed that the variety known as *Chia pinoli* is yielded by *S. columbaria* (see *Report U. S. Geogr. Surveys, 100th Merid.*, vol. vi, 48). *S. Chia* was described in the Farmacopea Mexicana as a new species, yielding *chia*, but Mariano Báscena affirms (*La Naturaleza*, 1881) that the common chia-yielding sage of Mexico is *S. polystachya* Ort., while *Chia azul* is yielded by *S. patens* Cav. Guibourt is probably in error in ascribing chia to *S. hispanica* L. The chia seeds are used not only when crushed as food and for the making of mucilaginous poultices, but also for the preparation of a mucilaginous drink, prepared by adding a teaspoonful of the seed to a tumblerful of cold water, allowing it to stand for half an hour, sweetening and flavoring to taste. Chia seeds are described as follows: "The seed is oblong-ovate, somewhat flattish, from 1 to 8 mm. in length, at one end there is a small, dark line, forming a slight projection, which is the microphyle of the seed, and this, when exposed to moisture, opens in a star-shaped or scalloped manner, emitting the growing embryo. The seed is smooth and glossy, and is surrounded by a transparent epithelium, swelling very largely when in water. The testa is darkish-gray, striated with dark brown lines, running diagonally, and dotted, forming a very beautiful variegated surface; when pressed or crushed under a spatula it bursts at the hilum, exposing the cotyledons and the oil cells, leaving an oily stain upon paper. Internally the testa is dark, grayish-brown, perfectly smooth, glossy, and devoid of the external variegations or striæ. It contains the embryo, with the radical pointing towards the hilum, and a white, mucilaginous substance much resembling unrendered fat." (*A. J. P.*, May, 1882, 227–229.) The European species, *Salvia verticillata* L., *S. Verbenaca* L., *S. horminum* L. and *S. viridis* L., all indigenous to Central or Southern Europe, are also noted for the mucilaginous character of their seeds, and have on this account been employed to remove foreign substances from the eye. *S. Verbenaca* is sparingly naturalized in waste places in the Middle and Southern States.

Sago. *Sagou*, Fr. *Sago*, G., It. *Sagu*, Sp.—Under this name the U. S. P. formerly recognized the starch obtained from the *sago* palms. Numerous trees, inhabiting the islands and coasts of the Indian Ocean, contain a farinaceous pith from which is extracted the starch in enormous quantities. In India and the East Indies it is obtained from several palms, viz.: *Metroxylon Rumphii* Mart. and *M. lœve* Mart.

The fruit of the *Cycas circinalis*, according to J. van Donjen, contains a poisonous glucoside, *pakoëine*. (*P. J.*, May, 1903.)

According to H. von Rosenberg (*Proc. A. Ph. A.*, xxvii, 140), pith cells of these palms consist mostly of starch when the large leaves have fallen off and the flowers are just taking their place. At this time the tree is felled, and the trunk cut into billets six or seven feet long, which are split in order to facilitate the extraction of the pith. This is obtained in the state of a coarse powder, which is mixed with water in a trough having a sieve at the end. The water, loaded with farina, passes through the sieve, and is received in convenient vessels, where it is allowed to stand till the insoluble matter has subsided. It is then strained off, and the farina which is left may be dried into a kind of meal or molded into whatever shape may be desired. For the consumption of the natives it is usually formed into cakes of various sizes, which are dried, and extensively sold in the islands. The commercial "Pearl" sago is prepared by forming the meal into a paste with water, and rubbing it into grains. It is produced in the greatest abundance in the Moluccas, but of the finest quality on the eastern coast of Sumatra. The Chinese of Malacca refine it so as to give the grains a fine pearly luster. Malcolm states that it is also refined in large quantities at Singapore.

Pearl sago is that which is now generally used. It is in small grains, about the size of a pin head, hard, whitish, of a light brown color, in some instances translucent, inodorous, and with little taste. It may be rendered perfectly white by a solution of chlorinated lime. *Common sago* is in larger and browner grains, of more unequal size, of a duller aspect, and frequently mixed with more or less of a dirty looking powder.

An average palm about fifteen years old will yield from 300 to 400 kg. of sago starch.

Sago meal is imported into England from the East Indies. It is in the form of a fine amylaceous powder, of a whitish color, with a yellowish or reddish tint, and of somewhat musty odor.

Sago starch grains are oval or ovate and often truncated. As the article of commerce is partially cooked the grains are more or less altered. The individual grains usually show a large central area around which are the narrow, distinct altered lamellæ which are sometimes traversed by radiating fissures. The starch grains vary from 0.015 to 0.080 mm. in length. When examined by polarized light the grains show a distinct cross. At one time sago flour showed considerable amounts of stone cells, hairs and calcium oxalate crystals, but as the product is more highly refined in recent years, these impurities have been eliminated.

Common sago is insoluble in cold water, but by long boiling unites with that liquid, becoming at first soft and transparent, and ultimately forming a gelatinous solution. Pearl sago is partially dissolved by cold water, probably owing to the heat used in its preparation. Chemically considered, it is a very pure natural starch, as the nitrogenous matter rarely amounts to more than one per cent., and the ash to one-half per cent., the remainder being starch and moisture.

Potato starch is sometimes prepared so as to resemble bleached pearl sago, for which it is sold. But, when examined under the microscope, it exhibits larger granules, which are also more regularly oval or ovate, smoother, less broken, and more distinctly marked with lamellæ than are those of sago, and the hilum often cracks with two slightly diverging slits. Imitation sago is now made in the United States from various kinds of starch.

Sago is used exclusively as an easily digestible, non-irritating food. It is given in the liquid state, and in its preparation care should be taken to boil it long in water, and stir it diligently, in order that the grains may be thoroughly dissolved. Should any portion remain undissolved, it should be separated by straining. A tablespoonful to the pint of water is usually sufficient.

Sajodin. *N. N. R.* 1917. *Calcium mono-iodobehenate.* $(C_{22}H_{42}O_2I)_2Ca$.—This is prepared by treating erucic acid with hydriodic acid, which

yields monoiodobehenic acid. The combination of the latter with calcium, known as *sajodin*, is a white, odorless, tasteless powder containing 26 per cent. iodine. When heated it evolves iodine vapors and the residue, when dissolved and diluted hydrochloric acid with ammonium hydrate and ammonium oxalate added, will give a precipitate of calcium oxalate.

Because the salts of the fatty acids are not decomposed in the stomach this preparation passes uninjured into the intestinal canal and hence causes no irritation of the stomach. It is also claimed for it that when used for long periods of time it is much less liable to give rise to that disturbance of nutrition generally spoken of as iodism, but the claim at one time made for it that it was entirely free from the danger of unpleasant secondary actions has been shown by Kuttelwascher (*Pr. M. W.*, 1907) and others not to be true, although it appears to be better borne than the alkaline iodides. It seems also that it is somewhat more slowly absorbed than the ordinary iodides, probably because it is necessary to be broken up before its absorption. Delayed elimination which has been reported is probably due to the fact that it is absorbed more gradually than the alkaline iodides. There is abundant evidence that it is capable of replacing therapeutically the official forms of iodine and it has been widely used in all those conditions in which iodine is of service. The ordinary *dose* is from eight to fifteen grains (0.5–1.0 Gm.) three times a day, best given in the form of a powder which may be enclosed in gelatine capsules. It should not be administered in the form of pill or tablet.

Salacetol. *Salicyl-acetol. Salantol.* $C_6H_4(OH)CO.OCH_2CO.CH_3$.—A synthetic product, the ester of salicylic acid and acetylcarbinol, introduced as a substitute for salol, to avoid the elimination of phenol in the system. Crystallizes out of alcohol in white or pinkish needles, fusing at 71° C. (159.8° F.), slightly soluble in cold water and alcohol, readily soluble in ether, chloroform, and petroleum benzin. It may be used when salol is indicated, in *doses* of from thirty to forty-five grains (2.0–3.0 Gm.).

Salamander Alkaloids.—*Salamander maculosa*, and probably other newts, produce a poisonous secretion from the skin, from which Hoppe-Seyler and Zalesky separated an active body, *salamandarine*. E. S. Faust (*A. E. P. P.*, xliii) has secured crystalline salts from this body which produce in the lower animals restlessness, excited reflex activity, and convulsions ending in total paralysis. A second alkaloid, *salamandaridine*, was also separated by Faust.

Salen.—This preparation is a mixture of methyl and ethyl glycolic esters of salicylic acid. At ordinary temperatures it is a liquid, which congeals at 5° to 10° C. (41°–50° F.). It is readily soluble in alcohol, ether, castor oil and benzol, but insoluble in olive oil. It is used altogether for external applications, either full strength or diluted with its solvents.

Salep. *Tubera Salep*, P. G. *Salep*, Fr., G.—This name is given to the dried tubers of numerous species of the genus *Orchis*, and other allied genera of the *Orchidaceæ*. At present the *salep* of European commerce is prepared chiefly in the Levant, but to some extent in Germany and other parts of Europe. The German salep is said to be more translucent than the Levant.

Salep is in small, oval, irregular, ovoid or oblong tubers, rarely palmate, hard, horny, semitransparent, of a yellowish color, a feeble odor, and a mild mucilaginous taste. It is sometimes kept in the state of powder. In composition and relation to water it is closely analogous to tragacanth, consisting of a substance insoluble but swelling up in cold water (*bassorin*), of another in much smaller proportion, soluble in cold water, and of minute quantities of saline matters. It also occasionally contains a little starch. It is highly nutritive, and may be employed for the same purposes as tapioca, sago, etc. Its medieval and Oriental reputation as an aphrodisiac is unfounded. On account of its hardness, salep, in its ordinary state, is of difficult pulverization; but the difficulty is removed by macerating it in cold water until it becomes soft, and then rapidly drying it. *Royal salep*, said to be much used as a food in Afghanistan, has been identified by J. E. T. Aitchison as the product of *Allium Macleanii* Baker. (Fam. *Liliaceæ*.) (*P. J.*, Sept., 1889.)

E. Reeb stated that salep possesses, like diastase, the property of coagulating milk, which he attributes to *erythrodextrin*, but finds that this body, in distinction from diastase, will retain its coagulating property even after heating it to 100° C. (212° F.). (*Journ. der Pharm. v. Elsass-Lothringen*, 1912, No. 8.)

Sal-ethyl. *N. N. R.* 1917. *Ethyl-Salicylate.*—This proprietary ester is used after the manner of, and for the same purposes as, methyl salicylate. It is a colorless volatile fluid of pleasant odor and taste. Sp. gr. 1.184 and boiling at 231.5° C. (449° F.). The *dose* is five to fifteen minims (0.3–1 mil).

Salhypnone. $C_6H_4O(COC_6H_5)COOCH_3$.—A benzoyl-methyl-salicylic ester which occurs in colorless needles melting at 113° C. (235.4° F.), insoluble in water and sparingly soluble in alcohol and ether. It is a mild antiseptic.

Salibromin. $C_6H_2Br_2OH.COOHCH_3$. *Dibrom-salicylicmethyl Ester.*—This forms a white crystalline powder soluble in alkalies. It has been proposed as an antiseptic and antirheumatic in *doses* of eight grains (0.5 Gm.), four or five times daily.

Salicylamide. *Salamid.* $C_6H_4\begin{cases}OH\\CONH_2\end{cases}$.—This compound is prepared by the action of concentrated ammonia upon methyl salicylate. When purified, it occurs in colorless, thin, transparent plates, melting at 138° C. (280.4° F.), soluble in alcohol, ether, chloroform, and two hundred parts of water. W. B. Nesbitt finds that this substance, when given in toxic dose, paralyzes the motor nerves and centers, also the muscles, and has but little effect upon blood pressure. He believes that it is a safer remedy than salicylic acid, and has the advantage of greater solubility and more prompt action in smaller dose. Also, that it has analgesic and antipyretic properties which correspond. It may be given in *doses* of three grains (0.2 Gm.). The highest amount used was fifteen grains (1.0 Gm.), taken in nine hours. (*T. G.*, Oct., 1891.)

Salicyl Resorcin Ketone. *Tri-oxy-benzo-phenone.* $C_{13}H_{10}O_4$.—A reddish-white crystalline powder, but sparingly soluble in water. It has been suggested as an intestinal antiseptic and as an antirheumatic. The *dose* is five to fifteen grains (0.32–1.0 Gm.).

Salifebrin. *Salicylanilide.*—An antipyretic, made by heating together salicylic acid and acetanilide in molecular proportions. It is a color-

less permanent powder, insoluble in water, freely soluble in alcohol.

Saligallol. *Pyrogallol Di-salicylate.*—A resinous solid, soluble in two parts of acetone and fifteen parts of chloroform. Its solution in acetone has been used as an external application in skin diseases.

Saligenin, *Ortho-oxybenzyl alcohol,* $C_6H_4.OH.CH_2OH$, is the decomposition product of the glucoside *salicin.* Under the name of *antiarthrin,* a substance has been introduced into commerce which is said to be a combination product between *saligenin* and tannin. It readily undergoes decomposition. It has been used in chronic *rheumatism* and *gout* in *doses* of eight to twenty grains (0.5–1.2 Gm.) four to six times a day.

Salimenthol.—*Samol, Salicylic Ester of Menthol,* $C_6H_4(OH)COO.C_{10}H_{19}$, is an almost colorless fluid, insoluble in water, but miscible with alcohol, ether, chloroform and fatty oils in all proportions.

It is supposed to exercise the virtues of both of its constituents and is employed in various rheumatic and painful conditions by external application with the idea that it will act as a local anodyne by virtue of its menthol radical and being absorbed will exercise the analgesic effect of salicylic acid. It may be applied in the form of a 25 per cent. ointment. It has also been administered internally in *doses* of eight to fifteen drops (0.5–1.0 Gm.), generally enclosed in capsules.

Saliphen. *Saliphenin. Salicyl-p-phenetidin.* $C_6H_4(OC_2H_5)NH.C_6H_4(OH)CO$.—This substance is the product of a reaction between salicylic acid and phenetidin in the presence of phosphorus trichloride. It is in colorless crystals, which melt at 139.5° C. (283° F.); is insoluble in water, but soluble in boiling alcohol, acetone, ether, chloroform and glacial acetic acid. It possesses slight antifebrile properties.

Salipyrin. *N. N. R.* 1917. *Antipyrine Salicylate. Salazolon.* $C_{11}H_{12}N_2O.C_7H_6O_3$.—Prepared by the action of salicylic acid upon antipyrine, either at 100° C. (212° F.) or in solution. It occurs as a white, coarsely crystalline powder, odorless, with a somewhat sweetish taste. It is readily soluble in alcohol and in benzene, and crystallizes from the former in hexagonal tables with a melting point of 91.5° C. (196.7° F.). According to Guttmann and to Kollmann (*Internat. Klin. Rundsch.,* Sept., 1890; also *M. M. W.,* Nov., 1890), it is an active antipyretic and antirheumatic, which rarely produces toxic symptoms, although an eruption resembling that caused by antipyrine has been noted. Kollmann states that it sometimes causes vomiting, and the daily *dose* should not exceed forty-five grains (3.0 Gm.), and always be less than this in the beginning, as some individuals are intolerant of it. *Salipyrin* has been used to a considerable extent in all forms of *rheumatic diseases,* in *influenza,* in various *fevers,* in *migraine,* and in the whole class of diseases in which its component constituents have been found to be useful; also locally in *coryza.* Salipyrin has been very highly praised by Beuttner as a sedative antihemorrhagic remedy, in all forms of *metrorrhagia* not dependent upon severe organic disease, in threatened *abortion,* and in *dysmenorrhea.* The usual *dose* is from seven to fifteen grains (0.45–1.0 Gm.), in capsule or tablet, repeated every three or four hours, until not over 45 grains (3 Gm.) have been taken.

Salit. *Salicylic Ester of Borneol.* $C_{10}H_{17}O.CO.C_6H_4.OH$.—It occurs as an oily fluid, insoluble in water, but readily soluble in alcohol, ether, and oils. It is incompatible with alkalies and alkaline salts.

Salit is employed for the purpose of the endermic administration of salicylic acid in *neuralgia,* and acute and chronic *rheumatic disorders.* In a few instances its application has given rise to a slight irritation of the skin. It should generally be diluted with equal portions of olive oil, and one-half to one teaspoonful of the mixture applied with friction or by painting over the infected part and covering with an impermeable dressing.

Salitannol. $C_{14}H_{10}O_7$.—A condensation product of salicylic and gallic acids; it is a colorless powder, insoluble in water, ether, chloroform, and benzene, slightly soluble in alcohol, soluble in solutions of caustic alkalies. It is used as a surgical antiseptic.

Salithymol. *Thymol Ester of Salicylic Acid.* $C_6H_3(CH_3)(C_3H_7)O.COC_6H_4(OH)$.—This salt is prepared by acting on molecular quantities of sodium salicylate and thymol sodium with phosphorus trichloride. It is a colorless crystalline powder, of sweet taste, insoluble in water, very soluble in alcohol. It is used as an antiseptic. *Dose,* from fifteen to thirty grains (1–2 Gm.).

Salix. U. S. 1880.—*Willow-bark. Weidewinde,* G. *Ecorce de Saule,* Fr. Most of the species of the large genus *Salix* are possessed of similar medicinal properties. (For elaborate study of various willow barks see *Wellcome Chemical Research Laboratory Report,* No. 39.) *S. fragilis* L. or Crack Willow, which has been introduced into this country from Europe, is said by Sir James Smith to be the most valuable species. *S. purpurea* L., a European species, is stated by Lindley to be the most bitter, and *S. pentandra* L. is preferred by Nees von Esenbeck. Many native species are in all probability equally active with the foreign.

Salix alba L., the species formerly recognized by the U. S. Pharmacopœia, is the common European or *white willow.* It has sparingly escaped from cultivation, growing from New Brunswick and Ontario southward to Pennsylvania. It is a large tree with a rough grayish bark, the twigs being brittle at the base, and in this respect somewhat resembling *S. fragilis.* The leaves are pubescent on both surfaces and finely serrulate. It hybridizes with other species of *Salix.* It flowers in April and May, and the bark is easily separable throughout the summer. That obtained from the branches rolls up when dried into the form of a quill, from 0.5 to 1 mm. thick, has a brown, more or less finely warty periderm, is flexible, fibrous, and of difficult pulverization. The inner surface is brownish-white, and smooth, separating in thin layers. Willow bark has a feebly aromatic odor and a peculiar bitter astringent taste. It yields its active properties to water, with which it forms a reddish-brown decoction. Pelletier and Caventou found among its ingredients, tannin, resin, a bitter yellow coloring matter, a green fatty matter, gum, wax, lignin, and an organic acid combined with magnesia. The proportion of tannin is so considerable that the bark has been used for tanning leather. The characteristic constituent of all species of willow, however, is *salicin.* (See *Salicinum,* p. 0000.) Robert W. Beck (*A. J. P.,* 1891, 581) has determined the relative percentages of salicin and tannin as follows:

	Salicin.	Tannin.
Leaves of *S. lucida* Muhl	0.30 per cent.	6.48 per cent.
Bark of *S. lucida* Muhl	1.09 " "	3.58 " "
Bark of *S. alba* L.	0.56 " "	4.26 " "
Bark of *S. nigra* Marsh	0.73 " "	3.29 " "

Jowett and Potter made an examination of thirty-three samples of willow and poplar, and found in but one (*Salix discolor* Muhl.) the related glucoside *salinigrin*, which Jowett had previously discovered in an unknown sample of willow bark. This compound has the formula $C_{13}H_{16}O_7$, and on hydrolysis yields glucose and meta-hydroxybenzaldehyde. (*Wellcome Chem. Research Laboratory Report*, No. 28.) The bark of the willow is feebly tonic, but it is at present never employed in regular medicine.

Salix nigra Marsh. *Black Willow.*—This is a tree with a dark brown bark, and is noted for its rapid distribution along streams into which its brittle twigs fall, which strike root, forming new plants. It hybridizes with *Salix alba*. The younger Michaux states that this is a strong bitter, and according to various eclectic practitioners its green aments or floral buds are a very active sexual depressant, useful in *spermatorrhœa*, in all forms of *sexual excitement*, and in the nervous disturbances of the menstrual period. From twenty to thirty minims (1.3–1.8 mils) of the fluidextract are to be given four times a day.

The *Pussy Willow* (*Salix discolor* Muhl.) is a shrub growing in swamps and on moist hillsides of the northern United States. It is well known because of its silky downy catkins which appear in early spring before the leaves.

Salocoll. *Phenocoll Salicylate.* $C_6H_4(OC_2H_5)NH.COCH_2.NH_2C_7H_6O_3$.—This substance forms fine white crystalline needles of sweet taste and soluble in hot water. It combines the properties of phenocoll and salicylic acid, being used in *rheumatic affections* in *doses* of nine to fifteen grains (0.6–1.0 Gm.) several times daily.

Salocreol is a preparation containing an ester of the various phenols of beechwood tar. It occurs as a fluid of neutral reaction, oily consistence, brownish color, and is almost completely odorless. It is almost insoluble in water, easily soluble in the various alcohols, ether, or chloroform. It is saponified by the alkalies and alcohols, and on prolonged exposure also by glycerin. In saponified solutions the addition of a trace of ferric chloride produces the violet colors characteristic of phenol and salicylic acid in neutral solutions. It is affirmed that it is readily absorbed by the skin and does not irritate it or stain it permanently. It is used as a local application in *erysipelas* and *rheumatism*. From one to two fluidrachms (3.9–7.5 mils) may be applied at a dose.

Salophen. *N. N. R.* 1917.—*Acetylparaminophenol Salicylate,* $C_6H_4\begin{cases}OH\\COOC_6H_4.NH(C_2H_3O)\end{cases}$, is formed by the combination of salicylic acid with acetylparamidophenol, and contains 51 per cent. of salicylic acid. It forms small white crystalline scales melting at 187° C. (368.6° F.), and is almost insoluble in cold water; moderately soluble in alcohol and ether. In warm alkaline solution it undergoes decomposition into salicylic acid and acetylparamidophenol. According to Siebel (*Th. M.*, Jan., 1892), this reaction takes place in the intestines. It has been used by various clinicians in all forms of *rheumatic diseases* and is undoubtedly effective, though less certain in its action than are the simple salicylates. It is also used to some extent as an analgesic in the pains of nervous diseases, in *pruritus*, and also as an intestinal antiseptic. It should not be confounded with Saliphen.

Dose, ten to fifteen grains (0.65–1.0 Gm.); not more than seventy-five grains should be given daily.

Saloquinine. *N. N. R.* 1917. *Salochinin.* $C_6H_4.OH.CO.O.C_{20}H_{23}N_2O$.—*Quinine ester of salicylic acid* occurs in colorless crystals, insoluble in water, freely soluble in alcohol and ether, fusing at 130° C. (266° F.). Acids or strongly acid salts decompose it, splitting it up into its constituents. It is tasteless and is said not to disturb the digestion or to cause tinnitus aurium, although it is very slowly absorbed. It is said to contain 70 per cent. of quinine, and has been used successfully as an antiperiodic, but is reputed to be of special value in the treatment of malarial and other *neuralgias*, also in fulgurant pains, and has also been highly commended in *typhoid* and other *fevers* as an antipyretic. If in a fever it be administered directly after the cold bath, it begins to powerfully impress the system about the time the effect of the immersion is going off. It may be given in the single *dose* of from fifteen to thirty grains (1–2 Gm.), repeated within twenty-four hours in bad cases of *rheumatic affections*.

Saloquinine Salicylate. *Rheumatin.* $C_6H_4.OH.CO.O(C_{20}H_{23}ON_2).C_6H_4OH.COOH$.—A white, tasteless powder. Slightly soluble in water, readily in chloroform and ether. It is used in *neuralgia*, *rheumatism*, etc., in fifteen-grain (1 Gm.) *doses*.

Salubrol. *Tetra-bromo-methylene-di-antipyrine.* $C_{23}H_{24}O_2N_4Br_4$.—An inodorous orange-yellow powder, made by the action of bromine on methylantipyrine. It is non-poisonous, and is used as a local hemostatic and antiseptic and as a substitute for iodoform.

Salvarsan. *N. N. R.* 1917. *Arsen-phenol-amine-hydrochloride. Arsenobenzol.* "606." $HCl.NH_2.OH.C_6H_3.As:As.C_6H_3OH.NH_2HCl + 2H_2O$.—It is a yellow crystalline hygroscopic powder, easily decomposed in the air. It dissolves in water, yielding a solution with a slightly acid reaction. In administering it hypodermically, this acidity must be exactly neutralized. This is accomplished by the cautious addition of normal volumetric sodium hydroxide solution.

Salvarsan was introduced into medicine as the result of a long series of experiments by Professor Ehrlich. The plan of his research was to obtain some arsenical in which the element would be so firmly bound up that it could not be split off by the human organism and therefore would be nontoxic to man but which would retain its destructive action on protozoal parasites, especially the group known as *spirilli* to which belong the germs causing relapsing fever, sleeping sickness, and syphilis. While it seems demonstrated that a certain proportion of the salvarsan will be decomposed in the human body with the liberation of inorganic arsenic, to what extent this breaking up of the molecule takes place is as yet uncertain. Luithlen (*Z. P. C.*, 1913, xiii) maintains that the toxic symptoms sometimes caused by salvarsan are due to the action of the molecule as a whole and not to any arsenic which may be liberated. On the other hand, Hoke and Rihl (*Z. E. P. T.*, 1911, ix, p. 332) find that the toxic effects of salvarsan are precisely the same as those of arsenic poisoning. In whichever way it acts there is no doubt that in large dose it is poisonous and that, even in quantities not exceeding the ordinary therapeutic doses, it occasionally produces serious poisoning. Corlett (*J. A. M. A.*, 1913, lxi) has collected the reports of 126 deaths following its use and estimates the mortality as 1 in 18,000 injections.

As regards the curative powers of salvarsan the greatest interest has centered around its use in *syphilis*. While there is no room for doubt as to its beneficial effects in this disease it cannot be

considered as a certain cure for all cases. Indeed, Pusey maintains that it "Does not cure syphilis in any more cases than mercury does." (*J. A. M. A.*, October 5, 1912.) The general consensus is, however, that at least in the early stages its effects are not only more prompt than those of mercury, but also more certain. Craig (*A. In. M.*, 1911), in 225 cases, found a temporary disappearance of the Wassermann reaction in 70 per cent. and a permanent disappearance in about 55 per cent. It should be noted that the original idea that a single dose of salvarsan was sufficient has been entirely abandoned, and even its most ardent advocates administer from three to four doses. In the tertiary manifestations of *syphilis*, especially those involving the nervous system, the action of salvarsan has been less satisfactory, but recently good results have been claimed for the intraspinal injection of the drug in *locomotor ataxia*.

Salvarsan is useful in a large number of other diseases besides *syphilis*, especially those that are due to pathogenic protozoa, such as *relapsing fever, frambesia* and *filiariasis*. Good results have also been reported in *malaria, dysentery, pernicious anemia*, etc.

Salvarsan is usually administered either by intramuscular or by intravenous injection. It seems to be demonstrated that the sodium salt is less liable to produce unpleasant sequelæ than the acid preparation, and it is therefore preferable to neutralize the salvarsan before its injection. When sufficient alkali is added to exactly neutralize the salvarsan it is no longer soluble in water, but the resulting compound becomes dissolved by the further addition of caustic alkali. For practical purposes the salvarsan may be dissolved in a little water and a normal solution of sodium hydroxide added until the precipitate which is at first formed is redissolved, and to this may then be added as large an amount of physiological salt solution as a diluent as may be deemed necessary. The technic of the injection is so complex that it should be undertaken only by those who have had practical experience in its application. The doses which are used to-day are much larger than those employed when the drug was first introduced. From three to nine grains (0.2–0.6 Gm.) may be given for the first *dose*. The injections may be repeated at intervals of one or two weeks, the dose being increased or not, according to the circumstances in the individual case.

Under the name of *neo-salvarsan* has been introduced a compound of salvarsan with formaldehyde sulphoxylate. It contains approximately two-thirds as much arsenic as salvarsan. It is an orange-yellow powder with a characteristic odor, even more unstable in the air than is salvarsan. It is freely soluble in water. It was introduced as a substitute for salvarsan because its solutions do not require neutralization before injection. The dose of neo-salvarsan is about half again as large as that of the older preparation.

Salvarsan is contra-indicated in disorders of the circulatory apparatus, advanced degeneration of the central nervous system, certain forms of *bronchitis*, and severe cachexia of non-syphilitic origin.

The European War having interfered with the commerce in salvarsan, a number of preparations purporting to be chemically identical with salvarsan have been introduced under various names as *kharsivan* and *arsenobenzol*. *Neokharsivan* and *novarseno-benzol* are supposed to correspond with neo-salvarsan.

Samandera Bark.—This is the inner bark of *Samandera indica* Gärtn., a tree belonging to the family of *Simarubaceæ*, growing in Ceylon and the East Indies. It is intensely bitter, and probably contains quassin. For further particulars, see *P. J.*, 1872, 541.

Sanatol.—This is a disinfectant solution claimed to be an aqueous solution of the sulphonic acids of crude phenol with about 60 per cent. water and to possess powerful disinfecting properties. When analyzed by the Vienna City Laboratories it was found to be a solution of naphthalin and concentrated sulphuric acid.

Sandal Wood. *Santalum Album. White Sandal Wood.*—"The heart wood of *Santalum album* Linné (Fam. *Santalaceæ*)." *N. F. IV.*

White *sandal wood* was introduced into the N. F. IV to serve as an ingredient in *tincture of saw palmetto and santal* of the National Formulary. It is described as follows:

"In billets, pieces or chips of varying shapes and sizes, heavy, hard but splitting easily, color light yellow; transverse sections yellow to light reddish-brown, with alternating light and dark concentric zones nearly equal in diameter, with numerous pores and traversed by many very narrow medullary rays.

"When examined under the microscope, sections show the medullary rays from two to four rows wide, the cells thick-walled and radially marked; the wood wedges consisting largely of wood fibers with pointed ends, large parenchyma and thick-walled secretion vessels and cells containing single crystals of calcium oxalate; the oil in globules adhering to the walls of the ducts and parenchyma cells and especially rich in the medullary cells. Odor characteristic, aromatic, persistent; taste peculiar, strongly aromatic.

"Sandal Wood yields not more than 8 per cent. of ash." *N. F. IV.* For further information on sandalwood see *Oleum Santali*, Part I. It owes its therapeutic virtue entirely to the volatile oil it contains.

Sandarac. *Sandaraca. Gum Juniper. Sandaraque*, Fr. *Sandarak*, G.—A resinous substance obtained from the *Callitris quadrivalvis* Vent. (*Thuja articulata* Vahl.), an evergreen tree (fam. *Pinaceæ*) growing in the mountains of northwestern Africa.

Sandarac is a resinous exudation which occurs as a natural secretion in schizo-lysigenous reservoirs in the bark. It exudes naturally, but an increase in yield is obtained by cutting through the bark. The exuding resin hardens and is collected. It is sent by the natives to Mogador, Casablanca and Nazagan. From these points it is shipped to London, Trieste, Marseilles and Hamburg. It occurs in small, irregular, roundish oblong grains or tears, of a pale yellow color, sometimes inclining to brown, more or less transparent, dry and brittle, breaking into powder under the teeth, of a faint, agreeable odor increased by warmth, and of a resinous, slightly acrid taste. It melts with heat, diffusing a strong balsamic odor, and easily inflames. It is almost entirely soluble in ordinary alcohol, and entirely so in that liquid when anhydrous, and in ether. Heated oil of turpentine also dissolves the greater part of it, but very slowly. According to Unverdorben, it consists of three resins, varying in their relations to alcohol, ether, and oil of turpentine. The *sandaracin* of Geise, which remains after sandarac has been exposed to the action of ordinary alcohol, is a mixture of two of these resins. Tschirch (*Harze und Harzbehälter*, p. 276) has isolated and de-

scribed an acid, *sandaracolic acid*, $C_{44}H_{64}O_4(OH)COOH$, making up 85 per cent. of the natural resin and *callitrolic acid*, $C_{64}H_{82}O_5(OH)COOH$, of which 10 per cent. is present. In Australia and Tasmania Callītris trees grow in vast numbers, and produce a sandarac which is almost colorless, having highly refractive power, and a pleasant aromatic odor, becoming dark by age, and sometimes assuming a superficial mealiness. This Australian sandarac softens easily, but does not melt in boiling water, is gritty to the touch, and can scarcely be distinguished from the African drug. (*P. J.*, Jan., 1890.) For an elaborate description of Australian sandarach, see also *A. J. P.*, 1896, 215. Sandarach was formerly given internally, and entered into the composition of various ointments and plasters. At present it is used chiefly as a varnish and as incense; its powder, termed *pounce*, is rubbed upon paper to prevent ink from spreading after letters have been scratched out. It is sometimes adulterated with mastic, rosin and dammar. A false sandarach has been described by R. Haneke. It resembled the real article, being lemon-yellow in color, transparent, and the tears elongated and rounded at the tips. When chewed it broke into fine powder and stuck to the teeth, while it softened on the water bath and flowed together into a resinous mass. Examination showed it to consist largely of colophony. (*O. Z.*, liv.)

Sanicula. *Sanicula marylandica* L. *Sanicle*, Fr. *Sanikel*, G.—The root of this indigenous umbellifer is popularly known in some parts of the country by the name of *black snake-root*. It is fibrous and of an aromatic taste, and, according to C. I. Houck (*A. J. P.*, vol. xiv, 463), contains a volatile oil and a resin. It has been used in *intermittent fever*, and also in *chorea* by Zabriskie. *Dose* of powder to children eight years old, half a drachm (2.0 Gm.) three times a day. (*Am. J. M. S.*, n. s., xii, 374.)

Sanitas.—This name is given to a fluid prepared by forcing air through a mixture of Russian turpentine oil and water, heated at 60° C. (140° F.) for a period ranging from 4 to 12 days. Among the various oxidation products is a soluble camphor ($C_{10}H_{16}O_3$), remaining dissolved in the oil, also a peroxide. It is used as an application for *burns*, *sores*, and *skin diseases*, and as a general disinfectant for sick rooms.

Sanochinol. *Sanschinol.*—This quinine compound is asserted to be the product of the action of ozone on a solution containing 4 per cent. of quinine hydrochloride. It forms a yellowish-brown solution, and is recommended for administration in the treatment of *malarial fevers* and *tuberculosis*.

Sanoform. *Di-iodo-methyl Salicylate.*

$C_6H_2\begin{cases}\diagup COOCH_3\\ —OH\\ \diagdown I_2\end{cases}$.—This substance is obtained by the action of iodine on methyl salicylate. It is a crystalline, colorless, odorless, and tasteless powder, permanent in the light and air, and melting at 110° C. (230° F.), but may be heated up to 200° C. (392° F.) without decomposing. It is soluble in 200 parts of cold or 10 parts of hot alcohol, and readily in ether, chloroform, benzene, and carbon disulphide, but almost insoluble in water or glycerin. It contains 62.7 per cent. of iodine. It forms with caustic alkalies, salts which are sparingly soluble in water.

Sanoform, first introduced as a substitute for iodoform by A. Arnheim, would appear to afford an efficient antiseptic dressing for wounds. As it remains unchanged at high temperatures, it is readily sterilized, while its odorlessness gives it a great advantage over iodoform. Its absorption is extremely slow, as it does not appear in the urine after having been administered hypodermically until twenty-four hours have elapsed, and does not entirely disappear until after fourteen days. It is seemingly, therefore, less poisonous than iodoform. It may be used as a dusting powder or in the manufacture of a 10 per cent. gauze which can be sterilized by heating; or a 1 per cent. solution in collodion, or a 10 per cent. ointment may be employed. It has been employed with satisfaction in ophthalmic surgery by Radziejewski and by Jacobsohn.

Santalol Formaldehyde.—Formic aldehyde in combination with oil of sandalwood and some inorganic acid is the source of this product. It is a balsamic yellow fluid, which in the presence of water breaks up into its components. It is employed in the treatment of inflammatory conditions of the bladder and kidneys.

Santolina.—A composite plant, commonly called *Holy herb, Heiligenpflanzen, Cypress herb, Cypressenkraut* (*Santolina Chamæcyparissus* L.), is stated to have long been used popularly against the *round worm* in Scotland. It has been analyzed by T. Maben (*P. J.*, xvi, 301), who finds in it a volatile oil and a considerable percentage of resin, with a bitter principle, which he believes to be an alkaloid and the active principle of the drug. The decoction of the plant may be made by boiling half an ounce in a pint of water for half an hour, straining and making up to a pint. It is given in *doses* of five fluidounces (150 mils) to adults and half that quantity to children, repeated for four mornings, and then followed by a brisk cathartic.

Santonica. *U. S. VIII. Levant Wormseed. Turkestan, Aleppo, Alexandria*, or *European Wormseed. Santonici Semen. Semen Cinæ. Flores Artemisiæ. Semen Sanctum. Semen-contra Dalep. Semencine ou Barbotine*, Fr. Cod. *Flores Cinæ*, P. G. *Wurmsamen, Zitwersamen*, G. *Santonico*, It., Sp.—The dried unexpanded flowers of the *Artemisia Cina* Berg. (*A. pauciflora* (Ledebour) Weber) (Fam. *Compositæ*). This plant is a small, semi-shrubby perennial, from whose oblique, knotted rootstalks arise numerous leafy shoots and flowering stems. The glabrous and woody stems bear on their many branches numerous small (one inch long) bi- to multi-pinnatifid leaves, while the leaves of the flowering stems are very minute, the upper ones simple. The flower heads are small, numerous, one-tenth of an inch long, with from twelve to eighteen involucral scales, and from three to five flowers. The plant varies very greatly, and several species have been made out of its varieties. The plant grows in Persia and Turkestan and the flower-buds are collected in July and August. The Levant wormseed was officially described as "heads 2 to 4 Mm. long, oblong-ovoid, slightly flattened, obtuse, consisting of an involucre of about 12 to 18 closely imbricated, glandular scales with broad midribs, enclosing 4 to 5 rudimentary florets. *Santonica* has the appearance of a granular, yellowish-green or greenish-brown, somewhat glossy powder; odor strong, peculiar, somewhat camphoraceous; taste aromatic and bitter." *U. S. VIII.* Astolfi (*Ph. Ztg.*, 1893, 333) gives the following test for recognizing adulteration of santonica. 1 Gm. of the suspected drug is finely pulverized and then

agitated with 10 mils of absolute alcohol; the whole is heated to boiling, filtered, a piece of potassium hydroxide is added to the filtrate, which is then heated. If the drug is pure, the liquid will acquire a pronounced red color; if falsified, the color will be yellow; and if no santonica be present, the liquid will be colored but faintly, if at all.

Most of the wormseed of commerce comes from the steppes of the northern portion of Turkestan to the great Nizhni-Novgorod fair, whence it finds its way to Moscow and Western Europe. The export from this region has largely declined, because of the erection in Orenburg and Tschimkent of factories for the manufacture of santonin, which is now sent from there into commerce. The yearly consumption of santonin throughout the world is estimated at about twenty-five tons, and of this at least twelve tons are produced in the factories just spoken of. The santonin in the plants is said to reach its maximum proportion in July and August, and to disappear immediately after the flowering.

Attention was called by C. H. LaWall (*J. A. Ph. A.*, 1913, p. 596) to a variety of santonica that has appeared upon the market, which seems to be devoid of santonin or to contain not more than traces. He proposes a simple test which may be applied directly to the drug as a preliminary procedure and thus avoid the necessity of going through the long assay process if the sample is valueless: Place 5 Gm. of santonica (whole or ground) in a test tube, add 5 mils of spirit of nitrous ether and boil gently. No more color should be developed or not more than a slight greenish yellow color due to the solvent action of the spirit on the resins of the drug. Now add 10 drops of alcoholic solution of potassium hydroxide. In an active drug a rose red color is developed in direct proportion to the amount of santonin present.

Wormseed contains a volatile oil, but it owes its efficiency to *santonin.* (See *Santoninum.*) According to Merck, the mother liquors in the manufacture of santonin from the seeds of *Artemisia maritima* yield a crystalline principle, $C_{15}H_{18}O_4$, which has been named *artemisin.* It is freed from santonin by recrystallization from chloroform. It melts at 200° C. (392° F.), gradually turns yellow in the air, and is more readily soluble in water and in dilute alcohol than is santonin. It gives a fugitive carmine red color when heated with aqueous or alcoholic sodium hydroxide, and is apparently a *hydroxy-santonin.* (*P. J.*, 1896, 484.) *Dose*, of artemisin, one-six hundred and fortieth of a grain (0.0001 Gm.). The oil of santonica, according to Wallach (*Ann. Ch. Ph.*, ccxxv, 314; and ccxxvii, 277), consists chiefly of *cineol*, $C_{10}H_{18}O$, which is isomeric with borneol, and seems to be identical with the cajuputol of cajuput oil, together with some *dipentene.* Wormseed is rarely used in this country in substance. It is stated that artemisin is a powerful stimulant to the mucous membrane and muscles of the alimentary canal and that its addition to the simple bitters greatly increases their activity. *Dose*, of santonica, ten to thirty grains (0.65–2.0 Gm.). For a method of valuing santonica, by Dragendorff, see *Proc. A. Ph. A.*, xxvi, 229. For *Ehling's Process for Valuing Santonica*, see *U. S. D.*, 19th ed., page. 1085.

Santoninoxime. $C_{15}H_{18}O_2.N.OH$.—This substance was first prepared in 1889 by P. Guici (*Gazz. Chim.*, xix, 367) by digesting at nearly 80° C. (176° F.) for three days five parts of santonin, four parts of hydroxylamine hydrochloride, fifty parts of strong alcohol, and four parts of precipitated calcium carbonate. It crystallizes in white silky needles, melts at about 217° C. (422.6° F.), is very slightly soluble in hot water, and turns the plane of polarized light to the left. Coppola states that this substance is a safe and reliable substitute for santonin, to be given in *doses* about three times as large.

Santyl. *N. N. R.* 1917. $C_{15}H_{23}O.CO.C_6H_4OH$. —This preparation is the salicylic acid ester of santalol (the terpene alcohol of oil of sandalwood), occurring as a yellowish oil of pleasant balsamic odor and taste, having a specific gravity of 1.07 at 15° C. (59° F.), and boiling with decomposition at 121° to 126° C. (249.8°–258.8° F.). A number of authors have reported that *santyl* has distinct advantages over the oil of sandalwood and most of its compounds, especially in the treatment of *urethritis.* Its taste is less disagreeable than that of the oil; it is also apparently much less liable to disturb the stomach and some believe that it is more active as a disinfectant because of the salicylic acid constituent in its molecule. Kanitz (*Th. M.*, 1907) found that not only was it non-irritant to the alimentary tract or the kidneys, but that it contains a very marked power of alleviating the painful symptoms, and to an extent, to directly antagonize the urethral inflammation in *gonorrhea.* Menier (*B. K. W.*, 1907) has found the local application of santyl useful in *ozena.* Strassmann (*Derm. Cb.*, 1907, No. 6) has found it of much value in the treatment of *cystitis*, due to prostatic enlargement. The *dose* is fifteen to thirty minims (1–2 mils) three times a day given either in water or milk.

Sapindus.—Various tropical plants belonging to this genus of the *Sapindaceæ* contain saponin, and are largely used for cleaning purposes. The berries are commonly used, being called "*Soap berries.*" Thus, in India are employed the pulp of the fruit of *Sapindus Mukorossi* Gaertn., the capsules of *S. trifoliatus* L., and in South America the oil and seed vessels of *S. Saponaria* L. (*P. J.*, 1871, 585.) For the properties of saponin, see *Saponaria officinalis*, below. The fruits of *S. rarak* DC., according to O. May, contain saponin and a fixed oil. (*A. Pharm.*, 1906, 25.)

Sapium. *Sapium sebiferum* (L.) Roxb. *Chinese Tallow Tree. Tankawang Fat.*—This is a species of the family *Euphorbiaceæ*, cultivated in the Chinese provinces of Kiangse, Kiang-sou, and Chih-kiang for the sake of the fixed oil which covers the seeds, and is extracted by methods detailed in *A. J. P.*, 1872, 264. (See *P. J.*, June, 1872.) The "tallow" occurs in hard, brittle, opaque, white masses of about eighty pounds' weight. It consists chiefly of palmitin with a little stearin and is said to be nearly pure stearin. The oil is largely used for lighting purposes. The remnants of the nut are employed as fuel and as manure. (See also *P. J.*, 1883, 401, and 1887, 901.)

Saponaria. *Saponaria officinalis* L. *Soapwort. Bouncing Bet. Fuller's Herb. Sheep Weed. Saponaire. Savonnière*, Fr. *Seifenwurzel*, G. (Fam. *Caryophyllaceæ.*)—A perennial, herbaceous plant, having large rose-colored flowers, which are commonly double. It is common along roadsides and waste places in the United States. The rhizome and roots are employed. The rhizomes are cylindrical, from 5 to 12 cm. long and 5 to 12 mm. thick, outer surface being reddish-brown. The fracture is short and even. They are inodorous, and of a taste at first bitterish and slightly sweetish, afterwards somewhat pungent, continuing long,

and leaving a slight sense of numbness on the tongue. They impart to water the property of forming a lather when agitated, like a solution of soap, whence the name of the plant was derived. This property, as well as the medicinal virtues of the plant, resides in *saponin*, $C_{32}H_{54}O_{18}$. This principle constitutes, according to Bucholz, its discoverer, 34 per cent. of the dried root which contains also a considerable quantity of gum and a little bassorin, resin, and altered extractive, besides lignin and water. For description of *saponin*, see *Quillaja*. Saponin has been found in many other plants, among them some species of *Silene*, *Dianthus*, and *Lychnis*, in *Vaccaria vulgaris* Host., and in *Agrostemma Githago* L., all belonging to the fam. *Caryophyllaceæ*. (*J. P. C.*, 3e sér., x, 339; also *P. J.*, 1871, 585; *Australian Journ. Pharm.*, 1887.) Serious poisonings by the mixture of the seeds of *Agrostemma Githago* with wheat have been reported. (*D. M. W.*, 1903.) According to Augustine Henry, there are at least eleven species of trees whose products are used in China for washing purposes and probably contain saponin, which is also found to the extent of 10 per cent. in the seeds of the Chinese tea oil tree, and is left in such large proportion in the refuse after the extraction of the oil that the "tea seed cake" is used as a fish poison. (*Am. Drug.*, 1896.) In California the *Indian Soap Root, Chlorogallum pomeridianum* (Ker.) Kunth., is much used for washing clothes; it probably contains saponin. The fruits of various species of *Sapindus* are also rich in saponin and are used as detergents accordingly.

Saprol. *Disinfection Oil.*—A mixture of crude cresols, containing pyridine bases and hydrocarbons, used for disinfecting purposes. As it is inflammable, care should be exercised in its use.

Sarcocolla. *Sarcocolle*, Fr. *Fleischleimgummi*, *Fischleimgummi*, G.—A peculiar vegetable product, exuding spontaneously from *Penæa Sarcocolla* L. (now *P. fulcata* L.), and *P. mucronata* L. (Fam. *Penæaceæ*), small shrubs, growing at the Cape of Good Hope, in Ethiopia, Arabia, etc. *Sarcocolla* occurs in the form of small, roundish, irregular grains, somewhat spongy, sometimes agglutinated in masses, at times admixed with fine hairs, friable, opaque or semi-transparent, of a yellowish or brownish-red color, inodorous unless heated, when they have an agreeable odor, and of a peculiar, bitter, sweetish, and acrid taste. Sarcocolla, according to Pelletier, consists of 65.3 per cent. of a peculiar substance, considered by Thomson as holding an intermediate place between gum and sugar, and called *sarcocollin*, $C_{13}H_{23}O_6$, 4.6 of gum, 3.3 of a gelatinous matter having some analogy with bassorin, and 26.8 of lignin, etc. It is said to be purgative, but at the same time to produce serious inconvenience by its acrid properties. The Arabian physicians used it internally, and by the ancients it was employed as an external application to wounds and ulcers, under the idea that it possessed the property of agglutinating the flesh, whence its name.

Sarcosin. *Methylaminoacetic Acid. Methylglycocoll.* $CH_3NHCH_2CO_2H$.—This derivative of creatine occurs in deliquescent, transparent crystals of a sweetish taste, soluble in water and slowly soluble in alcohol. Melting point 210° to 215° C. (410°–419° F.). It is used in *uric acid diathesis* and *rheumatism*. *Dose*, eight to fifteen grains (0.5–1.0 Gm.).

Sarracenia. *Side-saddle Plant. Fly Trap. Pitcher Plant. Huntsman's Cup. Water Cup. Sarracenie*, Fr., G.—According to E. P. Porcher, the roots of *Sarracenia flava* L., and *S. variolaris* Michx., have long been used in the Southern United States in *dyspepsia*, and are tonic, laxative, and diuretic. Sheppard found them to contain lignin, coloring matter, resin, an acid salt of lime, and probably an alkaloid. Stan. Martin asserts that he has found in the root—(1) an alkaloid which he proposes to name *sarracenine;* (2) a resin; (3) a yellow coloring principle (probably identical with Schmidt's *sarracenic acid*); (4) extractive; (5) substances which constitute the framework of plants. Sarracenine is white, soluble in alcohol and ether, combines with acids to form salts, and with sulphuric acid forms handsome needles, which are bitter, and communicate this taste to its menstrua. (*Ann. Thér.*, 1866, 73.) E. Schmidt, however, found no alkaloid but discovered *sarracenic acid*. (*A. J. P.*, 1872, 213.) *Dose*, of tincture (two ounces in one pint), a fluidrachm (3.75 mils); of fluidextract, from ten to twenty minims (0.6–1.3 mils).

Sassy Bark. *Nkasa. Doom Bark. Casca Bark. Mancona Bark. Saucy Bark. Ecorce de Mançoine*, Fr. *Manconarinde*, G.—This bark is interesting chiefly from its employment by the natives of Western Africa as an ordeal in their trials for witchcraft or sorcery. (For details, see *P. J.*, lxv, 2.) This bark was first studied by C. A. Santos (*A. J. P.*, 1849, xxi, 97), and subsequently by Procter (*Ibid.*, xxiii, 301; xxiv, 195). It is obtained from *Erythrophleum guineense* Don, and is a large tree with spreading branches, doubly pinnated leaves, flowers in spike-like racemes, and leguminous fruit. The bark is in pieces more or less curved, with or without epidermis, in the former case somewhat fissured externally, of a dull red color diversified by whitish spots, brittle, presenting when cut transversely numerous fawn-colored spots surrounded by reddish-brown tissue, nearly inodorous, and of an astringent taste. A comprehensive description of *sassy bark* is given in the *Commentar zur oesterreichischen Pharmacopœia*, 1890, by Vogl; and in the *Résumé de la Matière Médicale et Toxicologique Coloniale*, by Corre and Lejuanne, the plant, fruit, seeds, etc., are carefully illustrated. Gallois and Hardy obtained the poisonous principle *erythrophleine* by making an alcoholic extract of the bark, exhausting this with water, evaporating, rendering this extract alkaline with ammonia, and treating with acetic ether. The alkaloid is a colorless, crystalline solid, soluble in water, acetic ether, alcohol, and amyl alcohol, insoluble in chloroform, benzin, and ether. In contact with sulphuric acid and black manganese oxide, a violet color (less intense than that produced with strychnine) is developed. Harnack and Zabrocki (*A. E. P. P.*, xv, 404) also prepared *erythrophleine*, and by the action of hydrochloric acid upon it obtained an acid they call *erythrophleic acid*, and a volatile alkaloid they call *mançonine*. The bark yields its virtues to water. Power and Salway examined sassy bark in 1912 and confirmed the presence of erythrophleine as described by Harnack. (*A. J. P.*, 1912, 337.)

According to the observations of Savage, made in Africa (*Charleston Med. Journ.*, 1859), sassy bark produces in the natives a feeling of constriction in the fauces, attended by prickling, and followed by numbness, with, after a toxic dose, stricture across the brow, severe pain in the head, coma, and death. The physiological action of erythrophleine has been studied by various observers, especially by E. Harnack and R. D. Zabrocki,

Gallois and Hardy, and Lauder Brunton, with results which are fairly concordant. Erythrophleine exercises a digitalis-like action on the circulation causing a slow, strong pulse, with a rise in the arterial pressure. These changes are certainly in great part due to the direct action upon the heart, but are also seemingly in part produced by a stimulating influence upon the muscle fibers or nerves in the walls of the arterioles. Purging was also noted as the result of an increased peristalsis, thought to be due to the local action of the poison. Vomiting is believed by Lauder Brunton to be the result of an influence upon the nerve centers, because it occurs when the alkaloid is given hypodermically. In fatal poisoning in the lower animals, convulsions are pronounced, and the respiration is also markedly affected. In 1888 L. Lewin asserted erythrophleine to be a powerful local anesthetic, whose action is more pronounced than that of cocaine. His paper gave rise to an extraordinary controversy, the outcome of which appears to be that, although the alkaloid is possessed of not very active anesthetic powers, it is for various reasons practically not useful. (See 17th edition, *U. S. D.*, p. 1739.) A solution of the strength of one-tenth of one per cent. is used as an application to the cornea.

Germain Sée asserts (*Méd. Mod.*, Dec., 1891) that, although sassy bark does not act well upon the heart, it gives great relief in *dyspnea*, the number of respirations being lessened and the inspirations being extraordinarily increased in depth. He gave of the alkaloid from one-fortieth to one-thirtieth of a grain (0.0016–0.002 Gm.); of the extract, from one-fourth to one-third of a grain (0.016–0.021 Gm.).

Satureja. *Satureja hortensis* L. *Summer Savory. S. Montana* L. *Winter Savory. Sarriette*, Fr. *Saturei. Bohnenkraut*, G.—An annual labiate plant resembling thyme in odor and flavor, growing spontaneously in the south of Europe, cultivated in our gardens as culinary herbs, and sparingly naturalized from New Brunswick to Michigan and southward.

Saururus. *Saururus cernuus* L. *Lizard's Tail.* (Fam. *Saururaceæ.*)—D. L. Phares, of Newtonia, Miss., considers this indigenous swamp plant of the Eastern and Central United States "laxative, antispasmodic, sedative, and slightly astringent"; useful in irritation of the kidneys, bladder, prostate, and urinary passages generally. The *dose* of the strong infusion was, with the plant either fresh or dried, from one to four fluidounces (30–120 mils) every fifteen or thirty minutes, or three or four times a day. (*A. J. P.*, 1867, 468.)

Saxifraga.—Garreau and Machelast have isolated from *S. crassifolia* L. and other species of this genus a crystallizable bitter substance, *bergenin.* It is obtained by boiling the stems of the plants with absolute alcohol, after the tannin has been removed by ether. It crystallizes in alcohol, has a bitter taste, melts at 140° C. (284° F.), and burns up completely at 300° C. (572° F.). It is soluble in 167 parts of 90 per cent. alcohol and in 830 parts of water, but is more soluble in these liquids at a boiling temperature; it is faintly acid to litmus, and is not changed by treatment with dilute sulphuric or hydrochloric acid, but by diluted nitric acid is converted into oxalic acid. Concentrated sulphuric acid decomposes it. Its formula is given as $C_6H_9O_3.H_2O$. Bergenin is asserted to be intermediate in its action between salicylic acid and quinine. (*A. Pharm.*, 1881, 293.) The rhizome of *Saxifraga ligulata* Wall., which is used in India in *dysentery*, has been found by David Hooper to contain about 16 per cent. of gallic and tannic acids, but no other active principles. (*P. J.*, Aug., 1888.)

Scarlet Red. *N. N. R.* 1917. *Amido-azotoluol-azo-β-naphthol. Biebreich scarlet. Rubrum Scarlatinum.* $CH_3C_6H_4.N : NC_6H_3(CH_3)N : N.C_{10}H_5.OH$.—In 1906 Fisher (*M. M. W.*, 1906, liii, 2041) discovered that the dye stuff known as scarlet red had the power of greatly stimulating the growth of epithelial cells. This observation was confirmed by Helmholz (*J. H. H. B.*, 1907, xviii, 365), and in 1908 Von Schmieden (*Cb. C.*, 1908, xxxv, 153) applied it practically for the purpose of stimulating epithelial growths in various surgical conditions, as *chronic ulcers, unhealthy granulations*, and the like. Since then it has been employed by a number of surgeons to stimulate the formation of skin not only in these conditions, but in *bed sores*, in unhealed *ulcers*, following extensive injuries or *burns*, and to promote skin formation after operations. It is usually applied in the form of an ointment containing from 4 to 8 per cent. of the curative agent. When the ulcer is very large it is recommended that the salve should be applied around the edges rather than over the whole surface of the denuded area. It has also been employed by Wolfrum and Cards (*M. M. W.*, 1909, p. 242) in the treatment of *corneal ulcers* after the loss of cornea whether due to injury or ulceration and by Rabaudi (*S. M.*, 1909, p. 344) in *sore nipples* and *erosions of the uterus.*

When the wound is suppurating profusely, scarlet red is of little value. It should be reserved for clean, dry ulcers which show little tendency to heal. It may be applied either in the form of the eight per cent. ointment or as a powder diluted with boric acid. It is not an entirely harmless remedy, for Lyle (*N. Y. M. R.*, Nov. 16, 1912) has reported a case of serious poisoning, characterized by nausea and vomiting, epigastric pain with fever following the application of scarlet red over extensive ulcerated surfaces. Irritation of the kidney has also been attributed to its use.

Amido-azotoluol.—The success which has followed the use of *scarlet red* in the treatment of wounds which refuse to become covered with epithelium led E. Hayward to test other dyes of allied chemical properties. He found that ortho-amido-azotoluol, a substance closely allied to scarlet red, was even more efficacious than scarlet red. Amido-azotoluol has the chemical formula $CH_3C_6H_4N.NC_6H_3(CH_3)(NH_2)$. Amido-azotoluol forms red crystals or a reddish-brown powder melting at 100° C. (212° F.). It is insoluble in water but readily soluble in alcohol, chloroform and ether. It is also soluble in fatty oils.

Several other compounds, closely allied chemically to scarlet red, have been employed for the same purpose. Among these are *pellidol* (*diacetyl-amido-azotoluol*), and *azodolen*, which is a mixture of equal parts of pellidol with an iodol compound called *iodolen.* Hayward (*M. M. W.*, 1909, p. 1836) asserts that *ortho-amido-azotoluol* is even superior in efficacy to scarlet red.

Schinus. *Schinus molle* L. (Fam. *Anacardiaceæ.*)—The *pepper tree* of South America yields a berry the size of a pea, having a flavor similar to a mixture of pepper and fennel. It has been introduced as a shade tree in Southern California. (*A. J. P.*, 1896, 215.) The leaves contain a volatile oil which is readily discharged, as after a rain when the air is filled with fragrance. Schimmel &

Co. examined the volatile oil distilled from the berries; it had the sp. gr. 0.850, the odor of phellandrene, and was soluble in alcohol. (*Ph. Rev.*, 1897, 114.) It has been used successfully in *gonorrhea* as a substitute for cubeb. The leaves, bark, and gum resin have been employed medicinally. (See *A. J. P.*, 1866, 1885, 1890; also *P. J.*, 1887.)

Schleich's Anesthetic Mixture.—In 1895 Schleich proposed the use of an anesthetic mixture based upon the theory that the ideal anesthetic should have a boiling point as near as possible to the temperature of the human body, so that elimination should take place from the lungs as rapidly as possible, with consequent immediate awakening from unconsciousness. He proposed the use of petroleum benzin as an inert diluent to lower the boiling point, but H. C. Wood, Jr., in a series of experiments (*P. M. J.*, April, 1899), proved that petroleum benzin acts both upon the heart and the vasomotor system as a paralyzant, and that its effect upon the respiratory center is even more powerful, while its anesthetic influence is exceedingly feeble. Clinical experience has confirmed his conclusions that the use of Schleich's mixture is attended by more danger than is that of either chloroform or ether, and the method has been abandoned.

The same surgeon has also introduced a method of local anesthesia which consists in injecting very dilute cocaine solutions between the layers of the skin. For details of this method, see Wood's *Therapeutics*, 14th ed., p. 52.

Scolopendrium. *Scolopendrium Scolopodendrium* (L.) Karst. *Asplenium Scolopendrium* L. *Phyllitis Scolopendrium* (L.) Newman. *Hart's Tongue.*—The fronds of this fern, which is indigenous both in Europe and America, have a sweetish, mucilaginous, and slightly astringent taste, and, when rubbed, a disagreeable oily odor. They were used as a deobstruent in visceral affections, as an astringent in *hemorrhages* and fluxes, and as a demulcent in pectoral complaints.

Scopola. *Scopolia. Belladonna Scopola. Scopola Belladonna. Japanese Belladonna* (incorrectly).—"The dried rhizome of *Scopola Carniolica* Jacquin (Fam. *Solanaceæ*), yielding, when assayed as directed below, not less than 0.5 per cent. of its alkaloids." *U. S. VIII.* The genus *Scopola* is the connecting link between *Atropa* and *Hyoscyamus*, resembling *Atropa* in leaf and flower and in the microscopical character of its rhizome, but differing in that its fruit is not a berry but is a pyxis resembling that of Hyoscyamus. For description of drug and its histological study, see Kraemer, *A. J. P.*, 1908, p. 459. The Japanese plant, *S. japonica*, is so closely allied to *S. carniolica* that its specific distinction is very doubtful; it has been separated upon the characters of the style being curved, the calyx-teeth unequal and the leaves less obovate and having much longer petioles than *S. Carniolica;* but Holmes has shown that the curved style occurs in *S. Carniolica. S. Carniolica* is a common plant in Bavaria, Austro-Hungary, and Southwestern Russia, usually in the hilly districts, where it grows in damp, stony places. Its general appearance is that of the belladonna, but it is much shorter, rarely growing above a foot in height, has thinner leaves, and is especially distinguished by its fruit being a transversely dehiscent capsule and by the presence of a distinct rhizome.

The rhizome was officially described as "of horizontal growth, more or less curved and shortly and sharply flexuous, cylindraceous and somewhat flattened vertically, occurring mostly in pieces from 2.5 to 7.5 Cm. long and 0.8 to 1.6 Cm. broad, often split before drying; upper surface marked with closely set, large, cup-shaped stem scars, margins irregularly contracted; externally varying from yellowish-brown to dark brownish-gray, finely and irregularly wrinkled longitudinally, obscurely annulate and more or less nodular-roughened; fracture short and sharp, exhibiting a yellowish-white bark, its corky layer dark brown, or pale brown, wood indistinctly radiate, and central pith rather horny; nearly inodorous; taste sweetish, afterwards bitterish and strongly acrid." *U. S. VIII.*

The Japanese rhizome is from 5 to 15 cm. long, about 1 cm. in diameter, rarely branched, cylindrical or slightly compressed, knotty, bent, with circular disk-like scars, of a pale brown color, not whitish when abraded, with a slightly mousy, narcotic odor, and a taste nearly free from bitterness. According to Thos. Greenish, the microscopical characteristics of the rhizome of *S. Carniolica* are very similar to those of belladonna root, the chief differences being that the bark is less thick, the dark line under the epidermis narrower, the vascular bundles neither so large nor so numerous, and the bundles of raphides less pronounced; the starch grains are also smaller and their shape less distinct. The structure of the rhizome of *S. japonica* was found to be the same as that of the European species. Kraemer (*loc. cit.*) has since shown that scopola possesses only reticulate tracheæ while in belladonna root the tracheæ possess both simple and bordered pores.

The alkaloid *scopolamine* (or *scopoleine*), $C_{17}H_{21}O_4N$, has been found to be the characteristic constituent of the root. (See p. 985.) Inactive scopolamine, $C_{17}H_{21}O_4N$, also known as *atroscine*, is present. It melts at 82° C. (179.6° F.), and yields by hydrolysis tropic acid and scopoline. Seward W. Williams states, as the result of the assay of many tons of the root of *Atropa belladonna* and of the rhizome of scopola, each of the best qualities occurring in the American market, that while the belladonna root yields on an average 0.50 per cent. of alkaloid, the scopola yields 0.58 per cent. See also *Proc. A. Ph. A.*, 1899, 285.

Fluidextract of Scopola, U. S. VIII, was made as follows: "Scopola, in No. 40 powder, *one thousand grammes* [or 35 ounces av., 120 grains]; Alcohol, Water, each, *a sufficient quantity*, to make about *one thousand mils* [or 33 fluidounces, 6½ fluidrachms]. Mix *eight hundred mils* [or 27 fluidounces, 24 minims] of Alcohol with *two hundred mils* [or 6 fluidounces, 366 minims] of Water, and, having moistened the powder with *three hundred and fifty mils* [or 11 fluidounces, 401 minims] of the mixture, pack it firmly in a cylindrical percolator; then add enough menstruum to saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and, having closely covered the percolator, macerate for forty-eight hours. Then allow the percolation to proceed slowly, gradually adding menstruum, using the same proportions of Alcohol and Water as before, until the Scopola is exhausted. Reserve the first *eight hundred mils* [or 27 fluidounces, 24 minims] of the percolate, and evaporate the remainder, at a temperature not exceeding 50° C. (122° F.), to a soft extract; dissolve this in the reserved portion, and mix thoroughly. Assay *ten mils* of this liquid as directed below; from the result thus obtained, ascertain by calculation the amount of mydriatic

alkaloids in the remainder of the liquid, and add to this enough menstruum to make each *one hundred mils* of the finished Fluidextract contain 0.5 Gm. of the mydriatic alkaloids from Scopola." *U. S. VIII.*

Assay.—"The method to be employed is identical with that given for Fluidextract of Belladonna Root (U. S. VIII), using *ten mils* of Fluidextract of Scopola." *U. S. VIII.*

Extract of Scopola, U. S. VIII, was made by evaporating the fluidextract and assaying it so that it contains 2 per cent. of mydriatic alkaloids. *Dose*, one-eighth to one-fourth of a grain (0.008–0.016 Gm.).

The physiological and medicinal properties of scopola are very similar to those of belladonna, but the crude drug has been scarcely used at all in internal medicine. It has been largely employed in America in the manufacture of belladonna plaster and much of the hyoscine of commerce in the last decade has been obtained from it. Its alkaloid *Scopolamine hydrobromide* is recognized in the United States Pharmacopœia. *Dose*, of the drug, one to two grains (0.65–0.13 Gm.); of the fluidextract, one-half to three minims (0.03–0.2 mil).

Scrophularia. *Scrophularia marilandica* L. (*S. nodosa* L.). *Figwort. Scrofula Plant. Scrofulaire*, Fr. *Kropfwurz. Kontenwurz*, G. (Fam. *Scrophulariaceæ.*)—This rather tall herb, having a square stem, opposite leaves and slender panicles of small, greenish-purple flowers, grows in rich open woods from New York to North Carolina and west to Kansas. Its leaves have when fresh a rank fetid odor, and a bitter, somewhat acrid taste; but these properties are diminished by drying. Water extracts their virtues, forming a reddish infusion, which is blackened by ferric sulphate. For histological study of root, see *P. J.*, 1896. Walz has obtained from it two proximate principles, which he names respectively *scrophularin* and *scrophularosmin*. (Mayer, *A. J. P.*, 1863, p. 295.) Figwort leaves were formerly considered tonic, diuretic, diaphoretic, discutient, anthelmintic, etc.; useful in *scrofula* and as a local application in *hemorrhoids*. Van de Moer (*P. J.*, 1896) affirms that the seeds are toxic, belonging to the digitalis group.

Scutellaria. *N. F. IV. Skullcap. Scullcap. Hoodwort. Madweed. Mad-dog* or *Sideflowering Scullcap. Blue Pimpernel. Hooded Willow-herb. Scutellaire*, Fr. *Helmkraut, Schildkraut*, G.—"The dried plant of *Scutellaria lateriflora* Linné (Fam. *Labiatæ*)." *N. F. Scutellaria* was official in the U. S. P. VIII, but was introduced into the N. F. IV.

Several species of scutellaria have attracted attention. *Scutellaria galericulata* L., which grows in wet places from Newfoundland to North Carolina and west to Nebraska, has a feeble, somewhat alliaceous odor, and a bitterish taste. It has been employed in intermittents, and externally in old *ulcers*. *S. integrifolia* L. is intensely bitter, and might probably be found useful as a tonic.

Scutellaria lateriflora is an indigenous, perennial herb, with a stem erect, much branched, quadrangular, smooth, and one or two feet high. The leaves are ovate, acute, dentate, subcordate upon the stem, opposite, and supported upon long petioles. The flowers are small, of a pale blue color, and disposed in long, lateral, 1-sided, leafy racemes. The plant grows in wet shaded places in the United States and Canada.

The dried tops are described as "about 50 cm. in length, smooth; stem quadrangular, branched; leaves opposite, petiolate, about 5 cm. in length, ovate-lanceolate or ovate-oblong, serrate; flowers about 6 mm. in length, in axillary one-sided racemes, with a pale blue corolla and bilabiate calyx, closed in fruit, the upper lip helmet-shaped. Odor slight; taste slightly bitter. Scutellaria yields not more than 12 per cent. of ash." *N. F.* H. Molisch and G. Goldschmidt (*Ph. Ztg.*, Dec. 4, 1901, 965) obtained from scutellaria and a number of other labiates an identical body, to which they gave the name *scutellarin*. It is present in all of the different scutellarias, being most abundant in the upper epidermis of the leaf, but found also in the roots, stems and flowers of the plant. It was further obtained from the leaves of *Galeopis Tetrahit* L., and of *Teucrium Chamaedrys* L. In *Scutellaria altissima* L., the presence of cinnamic and fumaric acids were also established. Scutellarin is obtained by boiling freshly gathered leaves for fifteen minutes in ten times their weight of water, filtering the decoction and adding from 1 to 2 per cent. of hydrochloric acid, which causes an abundant precipitate of scutellarin. If precipitation is effected from the hot solution, the scutellarin separates in the form of light yellow crystals. The formula $C_{10}H_8O_3$ has been assigned to scutellarin. Its alcoholic solution gives a red precipitate with lead acetate and an intense green color with ferric chloride, changing on heating to a red color if the reagent is not present in great excess; alcoholic potassium or sodium hydroxides, as also alkali acetates, produce reddish-yellow precipitates, which change to green on exposure to the air. Solution of barium hydroxide has the same effect. The green color is produced immediately if an oxidizing agent, such as chlorine or bromine water, is added.

Scullcap is as destitute of medicinal properties as a plant may well be, not even being aromatic. When taken internally, it produces no very obvious effects, and probably is of no remedial value, although at one time it was esteemed as a remedy in *hydrophobia*. It has also been used in *neuralgia* and *convulsive affections, chorea, delirium tremens*, and *nervous exhaustion* from fatigue or over-excitement. (*A. J. P.*, xxiii, 370; *N. J. M. R.*, v; *M. S. Rep.*, 1870.) *Dose*, thirty to ninety grains (2.0–5.8 Gm.)

Sedatin, *Para-valerylphenetidin*, is made by the action of phenetidin hydrochloride upon sodium valerate; it occurs in fine crystals It is soluble in hot alcohol, sparingly soluble in ether, chloroform, and petroleum benzine. It is said to act like antipyrine. (See *Valeridin*, p. 1656.)

Sedum. *Sedum acre* L. *Biting Stonecrop. Wall Pepper. Small Houseleek. Mossy Stonecrop. Joubarbe âcre, Poivre des Murailles*, Fr. *Mauerpfeffer, Steinkraut*, G. (Fam. *Crassulaceæ.*)—This European plant has escaped to some extent from the gardens and grows wild in New England. It is spreading moss-like, possesses small, very thick leaves and yellow flowers. It causes vomiting and purging, and applied to the skin produces inflammation and vesication. The fresh herb and the expressed juice have been used as an antiscorbutic, emetic, cathartic, and diuretic, and have been applied locally to old *ulcers, warts*, and other excrescences. Other species are less acrid, and are even eaten as salad in some parts of Europe. Such are *Sedum rupestre* L., and *S. album* L. *S. Telephium* L. was formerly employed externally to cicatrize wounds, and internally as an astringent in *dysentery* and *hemoptysis*, and is still esteemed by the common people in France as a vulnerary.

Ernst Mylius found in 100 parts of *Sedum acre* 2.2 parts of a soft, not acid resin, 12.80 parts of uncrystallizable sugar, and 12.40 parts of a soft acid resin, besides an alkaloid and inert substance. (*J. P. C.*, 4e sér., xvii, 81.)

Selenium. Se = 79.2.—This widely distributed element, discovered by Berzelius in 1817, belongs to the sulphur group, and its compounds occur in nature associated with sulphur compounds. It is most conveniently extracted from the lead chamber deposits of the sulphuric acid works. The presence of *selenium* in sulphuric acid has been objected to on account of its coloring substances yellow, even minute quantities present in sulphuric acid giving a yellow tint to cellulose. (*P. J.*, 1912, 47.) The physiological actions of the compounds of this metal have not been widely studied, but Chabrié and Sépicque (*C. R. A. S.*, cx) have shown that *selenous acid* is an irritant poison. According to Merck, a solution of selenous acid (0.5 per 100) is a valuable reagent for detecting alkaloids. (*M. R.*, 1900.) Wassermann (*D. M. W.*, 1911) from experiments upon mice reached the conclusion that selenium had a destructive action on *cancerous growths* which has led to some clinical trials of various compounds of the element, especially the combination of *eosin-selenium* and the colloidal forms known as *seleniol* and *electro-selenium*. The treatment must be regarded as still in an experimental stage.

Semecarpus. *Semecarpus venosa* (Fam. *Anacardiaceæ*), the *Tschongott Tree.*—The highly poisonous nature of the bark of this tree, which is a native of the Caroline Islands, is, according to Thoms and Mannich (*Ph. Ztg.*, 1902), due to the presence of *cardol* (*anacardic acid*).

Sempervivum. *Sempervivum tectorum* L. *Common Houseleek. Hen-and-Chickens. Grande Joubarbe*, Fr. *Hauswurz, Hauslauch, Dachwurz*, G. (Fam. *Crassulaceæ.*)—A succulent, perennial plant with imbricated leaves and cymes of rose-purple flowers. It is extensively cultivated. In Europe the bruised recent leaves of this plant are employed as a cooling application to burns and other external inflammations. The juice is said to cure *warts*.

Senecio. *N. F. IV. Life Root.—Senecio* was introduced into the N. F. IV. It is defined as follows: "The dried overground portions of *Senecio aureus* Linné (Fam. *Compositæ*), gathered when flowering." *N. F.* Various species of this composite genus have been domestically used in the treatment of *amenorrhea* both in Europe and America, and their value has been confirmed by various practitioners. (See *P. J.*, Dec., 1897.) The species specially used have been *Senecio vulgaris* L., *Common Groundsel, Seneçon*, Fr., *Kreutzkraut, Jacobskraut*, G.; an annual European plant introduced into this country and growing quite commonly in waste grounds, and the North American species, *S. aureus* L., commonly called *golden ragwort* or *liferoot* and growing in wet meadows in the Northern United States. It is described as follows: "Stems from 3 to 6 dm. in length, if entire bearing a basal rosette of leaves; sparingly clothed with successively smaller leaves and bearing at the summit several yellow heads in a loose corymb, white floccose when young, but mostly glabrous when expanded, radical leaves on long, slender petioles, mostly of rounded form from 5 to 7 cm. in breadth, the base often cordate, the summit rounded, the margin crenate-dentate; stem-leaves gradually changing from the shape of the radical leaves to lyrately-pinnate, then pinnatifid and sessile, and at length clasping, oblong, and incised; heads slender peduncled, from 12 to 25 mm. in breadth, the lance-linear involucral scales in about two series, closely appressed, rays about ten, bright-yellow, disk flowers very numerous, small, bearing a glabrous akene and a white pappus. Odor characteristically aromatic; taste bitter, slightly astringent and distinctly acrid and pungent. Senecio yields not more than 10 per cent. of ash." *N. F. IV.* The fluidextract is official in the N. F. IV and made from a menstruum of two volumes of alcohol and one volume of water. It is used in the *dose* of one fluidrachm (3.75 mils) three times a day.

In *S. vulgaris*, and in lesser amount also in *S. Jacobœa* L., Grandval and Lajoux (*Union Médicale du Nord-est*, xix, 1895) have found two alkaloids, *senecionine*, $C_{18}H_{26}NO_6$, which is slightly, and *senecine*, which is readily, soluble in ether. According to Wiet, senecionine is a paralyzant of the peripheral motor and sensory nerves, while Bunch has found that the alcoholic extract of *Senecio Jacobœa* is capable of producing a rise of the arterial pressure due to contraction of the arterioles, followed, if the dose has been large enough, by arterial dilatation with fall of pressure. (*B. M. J.*, 1900, ii, 212.) *Senecin* of the eclectic practitioners is made by precipitating the tincture with water and is not therefore a pure active principle.

The rhizomes of the Mexican species, *Senecio grayanus* Hemsl. and *S. cervariæfolius* Sch., constitute *maturin*, the plants being known as *matarique, maturin*, or *guerena*. They produce rise of temperature, dilatation of the pupil, and violent tetanic spasms. Henckel states that they contain a glucoside resembling digitalin. (*A. J. P.*, Jan., 1891; also *Nouv. Rem.*, 1888, and *P. J.*, March, 1889.) Several species of senecio, especially the *S. Jacobœa*, have been accused of causing poisoning in cattle which have eaten them. Cushny has found in the *S. Gladifolium* Watt two alkaloids, *senecifoline* and *senecifolidine*, which are actively poisonous, causing symptoms similar to those which have occurred in animals after eating the compound. The most characteristic pathological lesion was cirrhosis of the liver. The fluidextract of *S. vulgaris* has been recommended by Dalché and others in *dysmenorrhea* and *amenorrhea*. (*Bull. Med.*, 1904.)

Septoform is a condensation product of formaldehyde with members of the terpene, naphthalene, and phenol groups, prominent among which is *dioxynaphthylmethane*, $(C_{10}H_7O)_2.CH_2$. This preparation is offered in the form of a soap and also of an aqueous solution. It is said to be free from irritant properties and to be so strongly germicidal that a 1 per cent. solution will kill the cholera vibrio in five minutes, and the 3 per cent. solution the pus organism in three minutes. It has been chiefly used in veterinary practice, and for the disinfection of the hands (a 3 per cent. solution), or of instruments (5 to 10 per cent. solution). (*Th. M.*, xvi.)

Serums. *Normal Horse Serum. Normal Sheep Serum. Normal Goat Serum.* These liquids are obtained from the blood of the respective animals by inserting a large sterile needle into a vein and allowing the blood to flow through rubber tubing connected with the needle into covered vessels of one or more liters capacity. The blood is allowed to coagulate for about two days, either around a rod or other device previously inserted in the vessel, or spontaneously in the bottom of the container; the clot at the end of this period may be

squeezed free of serum by dropping a weight from the upper part of the vessel. The clot gathers in its meshes the red cells and the white cells of the blood, so that the fluid remaining to be siphoned off is a transparent liquid of a light yellowish brown color. This is called *blood serum.* If the clotting had been prevented by the addition of a citrate or oxalate and the blood cells separated by means of sedimentation, with or without centrifugation, the resulting fluid would be *blood plasma.* If, in the third place, the blood had been vigorously agitated by means of rough solid bodies such as pieces of broken glass in the container immediately upon being withdrawn from the animal, the fibrin or clot would have rapidly formed around these agitating bodies leaving the cells suspended in the fluid; such a fluid is called *defibrinated blood,* it resembles whale blood in appearance, but differs from it in having lost the property of spontaneous coagulation, it differs from serum in containing red blood cells and some white cells. The blood platelets and part of the white cells are destroyed by defibrination. All these operations must be carried out with an aseptic technic more strict than that of the surgical operating room, because blood and the fluids derived from it are excellent culture media for bacteria, and all bacterial contamination, whether pathogenic (disease causing) or not must be excluded. All the instruments and vessels must be sterilized—not by boiling—but in such a manner that even bacterial spores are destroyed. This requires dry heat at 170° C. (338° F.) for an hour and a half. Material such as rubber, which will not withstand this heat, may be sterilized by steam at 15 pounds pressure for half an hour, provided the boiler or autoclave is so arranged that all the air in the interstices of the material to be sterilized is withdrawn and replaced with saturated steam; the usual steam sterilization does not accomplish this.

Even with such precautions, serums are not usually considered safe unless preserved by the addition of some antiseptic, such as 0.5 per cent. phenol or cresol, or chloroform to saturation. As usually administered these quantities of preservative are without serious effect.

The serum of normal animals is used in therapeutics to promote clotting in *hemorrhage* or in hemorrhagic diseases. The other blood fluids described above are not available for this purpose—the plasma on account of its content of citrate or oxalate which prevents clotting, the defibrinated blood and whole blood on account of the red blood cells which they contain; the blood cells of another species might prove harmful to man. According to Howell's theory, clotting of the blood takes place when *thromboplastin,* contained in tissue cells or blood-platelets, is allowed to act on *antithrombin,* a substance normally present in the blood inhibiting clotting. *Prothrombin* is thus set free which then combines with the calcium of the blood in the formation of *thrombin* or *fibrin ferment.* This fibrin ferment in conjunction with the *fibrinogen* present in normal blood—forms the clot. It is thus seen that in blood serum most of the clotting factors have been partially or wholly used up in the production of the clot. Nevertheless, serum has seemed of value in many cases of hemorrhage, though there are other cases in which it is of no value. (See also under *Blood of Bullocks,* p. 1282.) Fresh serum is apparently more efficacious than old; it is therefore advisable to use serums whose date of production is stated. *Dose,* two and one-half to five fluidrachms (10–20 mils) hypodermically, or in urgent cases intravenously.

The occurrence of serum sickness and anaphylactic shock after injection of serum or its products has been mentioned under *Serum Antidiphthericum* (Part I, page 998). The same precautions should be taken in the use of normal serum. Horse serum appears to be less toxic—less likely to cause serum sickness than the serum of any other alien species, but in cases in which hypersensitiveness to horse serum is feared or proven, serum from the goat or sheep may be used. In hospitals freshly drawn rabbit serum, or whole human blood, is used for similar purposes.

No serum can be sold in interstate commerce except when produced in an establishment licensed by the Secretary of the Treasury. The requirements are those given under *Serum Antidiphthericum* U. S., except those for potency. There is no standard for the potency of normal serum.

Immune Serums.—This term includes the serum of animals in whose blood an immunity to any given bacterium or other harmful substance has been produced by the injection of that bacterium or harmful substance. This immunity may show itself in various ways. It is most notable, and most truly an immunity when, as in the case of antitoxic immunity, the serum actually protects another animal from the toxin or poison, or even cures the second animal if injected some time after the toxin. The word *toxin* can only be applied to those poisons which have the property of inciting such an immunity (*i.e.,* producing antitoxin) when injected into an animal in gradually increasing doses. The immunity may be antibacterial instead of antitoxic, that is, attacking the bacteria themselves rather than their soluble poisons or toxins. *Antibacterial immunity* in a serum may be manifest in its bactericidal or bacteriolytic properties; these two modes of action are generally taken as synonymous, but the term bactericidal refers especially to the killing of bacteria by the serum, as shown by tests of the numbers of bacteria present after its action, while bacteriolytic has reference to the gradual breaking up and dissolving of the bacteria as seen under the microscope. Antibacterial immunity is also sometimes demonstrable as a protective action, protecting for example guinea pigs which receive the immune serum against doses of the bacterium in question which kill other guinea pigs of the same weight not receiving the serum. Antibacterial immunity may be bacteriotropic or *opsonic,* which means that the serum in question in some way changes the special bacteria so that they are easily taken up and destroyed by the white blood cells. It is to be noted that immune serums are specific—that is, if antitoxic—they neutralize only the particular toxin which was used in their preparation, and no other; if antibacterial they have an antagonistic affinity for the exact species of bacterium with which the original animal was treated, and no other, or in some cases, only closely related bacteria. This fact of specificity is made of diagnostic use in the agglutinating property of immune serums (see Agglutination Test for Typhoid Fever, under *Diagnostic Tests,* p. 1360), and in their complement fixing power (see Complement Fixation Reaction for Syphilis, under *Diagnostic Tests,* p. 1359).

In the case of immune serums used for the treatment of disease this specificity is frequently so high as to be detrimental. Thus an antibacterial serum prepared from a given organism may be powerless against the same species of organism arising from other sources. In meningococcus,

streptococcus and pneumococcus infection this is particularly true. The organisms from different sources are called strains—and in spite of many different strains being used in the production of these serums, cases of meningitis, sepsis, or pneumonia occur in which the serums can be shown to have no influence against the infecting organism either in the body of the patient or in the laboratory. This is one of the causes of the poor success which has generally attended the use of serums other than diphtheria and tetanus antitoxin. Measures to overcome this difficulty have been taken, notably in anti-meningococcus and partially in anti-pneumococcus serum.

The material which is injected in the production of an immune serum is called the *antigen*, while the substance in the immune serum which gives rise to the different phenomena mentioned above—antitoxic, bacteriocidal, or bacteriolytic, protective, bacteriotropic or opsonic, agglutinative, complement fixing,—is called an *antibody*. Some workers hold that there is a different antibody for each function, while others take the view that a specific serum has only one antibody, with all these varied functions. It is certain, however, that in different serums these properties are present in different proportions, and consequently it is easier to conceive them as being exercised by different antibodies. Unfortunately, we have little means of knowing in a given case, which properties or which antibodies are the important ones in rendering a serum valuable to cure or prevent the infection in question, therefore we have no means of precisely measuring the worth of a serum.

Immune serums may be prepared against other substances than toxins and bacteria, as against foreign proteins, in which case a seventh property is apparent—that of precipitating the antigen used in its preparation. Blood cells of many other species also act as antigen for another series of immune serums; the antibody most apparent here is *hemolysin*, which dissolves the red corpuscles when added to the immune serum so that the corpuscles disappear and the fluid in which they were suspended takes on a clear red color (see Complement Fixation Reaction for Syphilis, under *Diagnostic Tests*, p. 1359).

All establishments manufacturing serums used in the prevention or treatment of human diseases are required to be licensed by the Secretary of the Treasury if the serums are sold in interstate commerce. The same requirements are prescribed as in the case of *Serum Antidiphthericum*, U. S. (Part I, p. 998), but unfortunately except in the case of diphtheria and tetanus antitoxins there are no potency standards for any serums, the reason is given above—the multiplicity of the antibodies and the uncertainty as to their relative importance.

Immune serums commonly contain preservatives and also are prone to cause serum sickness in the same way as antidiphtheric serum U. S. (q. v.). In this connection it is to be noted that the serums described in Part II are in general by no means as efficacious as the antitoxins, (Serum Antidiphthericum, U. S., and Serum Antitetanicum, U. S.), and further that they are usually to be administered in much larger quantities by the intravenous route if any benefit whatever is to be expected; the former consideration would cause one to hesitate if any possible danger were anticipated from their use, and the latter emphasizes the need of extreme caution unless hypersusceptibility to horse serum has been excluded.

Immune serums containing antibodies must be sharply distinguished from Vaccines (p. 1653) which contain antigen and force the human body to manufacture its own antibodies.

All serums lose in potency gradually and should be kept at a temperature between 4° C. and 15° C. (39.2–59° F.).

Antianthrax Serum (*Serum Antianthracum*). *N. N. R.* 1917.—This immune serum is prepared by injecting horses with gradually increasing doses of anthrax bacilli. The horses are then bled as described under Normal Horse Serum, p. 1602, and the serum collected. Considerable success has attended the use of this serum in the treatment of *anthrax* in animals, and some in man, if the serum happens to be a potent one and is administered early. *Dose*, 30 units to 100 mils intravenously or subcutaneously.

Antidysentery Serum (*Serum Antidysentericum*). *N. N. R.* 1917.—Certain bacilli, or groups of bacilli, have been found to be the cause of some forms of dysentery. These bacilli are classified generically as the dysentery bacillus, and are given various names, as *Shiga-Kruse* type, *Flexner* type, Strong type, Y type, according as their characteristics fall into one or another of these fairly well defined groups. Horses have been immunized by the injection of cultures of one or several of these types, and the serum used in the treatment of human *dysentery*. The results in many cases have been encouraging, giving a considerable reduction in mortality over similar cases treated without serum. Other reports have been negative; it appears that the type of bacillus used in immunizing the horse must be the same as that causing the particular infection, and further that infection with the Shiga-Kruse type is more benefited than infection with Flexner type. *Dose*, two and one-half to eleven fluidrachms (10–50 mils), subcutaneously or intravenously.

Antigonococcus Serum (*Serum Antigonococcicum*). *N. N. R.* 1917.—By injection of animals with gonococci, serum may be prepared which at times shows the properties of bacteriolysis, agglutination and complement fixation. Such serum has been used in the treatment of gonococcal infections, in part with favorable results. The serum seems to have no value in acute *gonorrheal urethritis*, and the lack of complete success in other cases may be due to the failure of antibodies to reach the seat of disease in sufficient concentration.

Antimeningococcus Serum. Antimeningitis Serum. Serum Antimeningococcicum. N. N. R. 1917.—The success attending the use of this serum in cases of *meningitis* caused by the *meningococcus* (*Diplococcus intracellularis meningitidis*) is one of the great triumphs of serum therapy, second only to the success of the antitoxins against diphtheria and tetanus. To immunize the horses used in producing the serum, cultures are injected, freshly killed, living, and partially disintegrated and dissolved. Unfortunately no definite standard has as yet been proven valid, by which the value of an antimeningococcus serum may be measured in the laboratory. More or less inert products are therefore frequently met with. Still another source of frequent failure of the serum lies in the fact, as described above, p. 1603, that there are many strains of the meningococcus, and the strain causing a given infection may be very different from any of those used in producing the serum; the specific antibodies fitting that particular strain would then be lacking and improvement could not be expected from the use of the serum.

The great step in advance in the use of antimeningococcus serum was in its application directly

to the seat of disease, instead of merely subcutaneously. The injection is made under the dural membrane of the spinal canal, that is, into the meningeal space. As in other successful serum treatment, early diagnosis and early application is necessary. The injection is best done without anæsthesia. The patient should be held firmly on his left side, with knees bent up nearly to the face, and with his back resting at the edge of the table or bed. The hands of the operator and the instruments must be sterilized. A stout needle with trocar at least 4 inches long should be used. The skin should be cleansed first, then treated with an antiseptic, such as tincture of iodin. The site for insertion of the needle is preferably the median line just below the fourth lumbar vertebra (on a line with the crests of the hip bone).

The needle is directed upward at an angle of about 35 degrees along the upper edge of the fifth lumbar spine until the point is felt to penetrate the dura, when the trocar is withdrawn and the spinal fluid allowed to flow out. This should be saved in a sterile container and examined microscopically. A turbid fluid, however, indicates meningitis and in case of doubt it is best to inject the serum. From forty-five to ten fluidrachms (3–50 mils) of serum (previously warmed) is slowly injected by gravity pressure, the amount being best determined by the fall in blood pressure according to Sophian's method. A drop of 20 millimeters is an indication to stop the injection at once. The injection should be repeated daily until the condition of the patient has definitely improved and the spinal fluid has been free from meningococci pus cells.

The amount of preservative in serum for intraspinal administration should not exceed 0.3 per cent. cresol or phenol. If the preservative is too concentrated, or if too much serum is injected, there is danger of collapse and even death. But the danger of the disease itself is much greater and no delay in instituting serum treatment should ensue by reason of fear on this ground.

Antiplague Serum. Yersin Serum.—The horse used for immunization receives killed cultures or living avirulent cultures of *Bacillus pestis* and finally living virulent ones. It is evident that such immunization must be carried out under special precautions in view of the danger involved in working with living plague bacilli. One virulent strain appears to be as effective as another. The resulting serum can be shown to have protective action on animals, but in the treatment of human *plague* only a moderate reduction in mortality is obtained—largely because the serum is not administered at the incipiency of the disease. *Dose,* 100 mils (three and one-third fluidounces) or more intravenously.

Antipneumococcus Serum. Serum Antipneumococcicum. N. N. R. 1917.—The pneumococcus (*Diplococcus pneumoniæ,* Weichselbaum) is present more often than any other organism as a causative factor in pneumonia. In one or more of its types it is found in about 60 per cent. of normal mouths or throats and may cause ordinary colds, severe grip-like infection, middle ear disease, ulcer of the eye, or meningitis. Serums have repeatedly been produced by immunizing animals against the pneumococcus, but the results have been variable. Römer, Neufeld, and Cole have conducted experimental investigations in serum therapy of *pneumonia;* it appears to be one requisite for success that the serum be produced by the use of the type of pneumococcus found in the patient to be treated. Certain of these types are more frequent than others and offer more promise. Other desiderata are that the serum be used early—on the first or second day of the disease if possible, and that large amounts—as much as 100 mils per dose—be injected intravenously. Local application in *corneal ulcer* and intraspinal administration in *meningitis* due to the pneumococcus have had some success.

Antistreptococcus Serum. N. N. R. 1917.—Many attempts have been made to produce therapeutically valuable antistreptococcus serum. In many commercial serums some antagonistic influence on streptococci can be demonstrated in the laboratory, but only rarely are authentic series of benefited cases reported. It seems to be necessary to introduce a large amount of the serum (100 mils or more) intravenously, and in such a serious disease as streptococcus infection the added strain on the eliminative mechanism caused by such quantities of foreign protein may turn the tide in the wrong direction. The Viennese reports of success with streptococcus serum therapy in severe cases of *scarlet fever* have not been confirmed in this country. The strong serum specificity of different strains of the bacterium may account for divergent results. The activity of antistreptococcus serum appears to be largely bacteriotropic.

Antivenomous Serums. Antivenins.—The snake poisons are true toxins and the serums prepared to combat them are true antitoxins. Theoretically, then, we should expect the excellent results of diphtheria and tetanus antitoxin to be duplicated in the serum treatment of *snake bites,* instead of the equivocal results of the antibacterial serums. Certain practical difficulties have interfered with such success. In the first place, the toxins of snake venoms are highly specific. Not only are there present in a given venom several different poisons, such as *hemorrhagins* (causing breaks in the blood vessels and consequent hemorrhages), *neurotoxin* (poisoning the vital center of the central nervous system), *coagulins* (causing clotting of the circulating blood), *hemolysins* (destroying the red blood cells), *hemoglutinins* (clumping the red blood cells)—but each of these is peculiar to its own species. Therefore to be effective, the serum must be derived from an animal immunized against the particular species of snake to be encountered. In the second place, very potent serums have not as yet been prepared—due largely to the difficulty in securing the antigen—snake venom—in large quantities. Thirdly, the serum must be on hand and used immediately.

In the case of the common North American poisonous snakes,—the rattlesnake, copperhead, and watermoccasin, hemorrhagins are the most important toxins. If antivenomous serums are available, they should be carried by the traveler and administered within a few minutes after the bite. Some time may be saved by the ligature cutting off the return flow of blood from the part affected. 100 mils or more of the antivenomous serum suited to the species of snake concerned should be injected intravenously, and more injected intramuscularly in the vicinity of the wound.

Sesamum. *Sesamum indicum* L. (Fam. *Pedaliaceæ.*)—The *benne* plant of our Southern States is annual, with a branching stem four or five feet high, and bearing opposite, petiolate leaves, varying considerably in their shape. The flowers are reddish-white, and stand solitarily upon short peduncles in the axils of the leaves. The fruit is

an oblong capsule, with small, oval, yellowish seeds.

There are some ten or twelve species referred to the genus *Sesamum*, the majority of which are natives of Africa. In India one or two species occur wild, one of these, *Sesamum indicum* L. (*S. orientale* L.), has been cultivated from time immemorial in various parts of Asia and Africa. From the latter continent it is supposed that seeds were brought by the negroes to the United States, where, as well as in the West Indies, it is now cultivated to a considerable extent. The plant above described will grow as far north as Philadelphia. The seeds are employed as food by the negroes, who parch them over the fire, boil them in broths, make them into puddings, and prepare them in various other modes. By expression they yield a fixed oil, which was introduced into the Pharmacopœia at the revision of 1880 and is official in U. S. IX. (See Part I.) Berjot obtained from the seeds 53 per cent. of oil by means of carbon disulphide. Rautenberg reported a series of severe poisonings from the intestinal injection of sesame oil. (*J. A. M. A.*, xlvii, p. 1962.) These accidents, he believes, are due to adulteration of the oil.

Benne Leaves.—These abound in a gummy matter, which they readily impart to water, forming a rich, bland mucilage, much used in the Southern States as a drink in various complaints to which demulcents are applicable, as in *cholera infantum, diarrhea, dysentery, catarrh, acute cystitis, strangury*, etc. The remedy has attracted attention also in the North, and has been employed with favorable results in Philadelphia. One or two fresh leaves of full size, stirred about in half a pint of cool water, will soon render it sufficiently viscid. With dried leaves hot water is used. The leaves also serve for the preparation of emollient cataplasms.

Sethia. *Sethia acuminata* Arn. (now *Erythroxylon lucidum* H. B. K.) (Fam. *Erythroxylaceæ.*)—The juice of this Ceylon plant or the powdered leaves —*dose*, fifteen grains (1.0 Gm.)—are affirmed to be an efficient vermifuge. (*P. J.*, April 7, 1883.)

Sida. *Mesbé. Sida rhombifolia* L.—*Queensland hemp* (Fam. *Malvaceæ*), *jelly leaf*, is largely used in Australia as a demulcent. It contains a large quantity of mucilage. The fluidextract has been asserted to possess expectorant properties and to be especially valuable in the treatment of *pulmonary tuberculosis*. Zink (*M. M. W.*, 1912), however, was unable to obtain evidence of any specific action in *tuberculosis*. *Sida paniculata* L. (*S. floribunda* H. B. K.), of Peru, which also contains a large quantity of mucilage, is said by Martinet to be a very active vermifuge, owing its powers, probably, to the extremely minute but very resisting spines which cover its leaves, the part used.

Siegesbeckia. *Siegesbeckia orientalis* L. (Fam. *Compositæ*).—This plant is used in the Mauritius Islands in *syphilis, leprosy*, and various skin diseases. A white, crystalline principle, *darutine*, has been discovered in it by M. L. Auffray. (*P. J.*, vol. xvi, 1047; also *B. M. J.*, June 25, 1887.)

Sienna. *Terra di Sienna.*—An argillaceous mineral, compact, of a fine texture, very light, smooth, and glossy, of a yellowish-brown or coffee color, leaving a dull orange trace when moistened and drawn over paper. By calcination it assumes a reddish-brown color, and is then called *burnt sienna*. In both the raw and burnt states it is used in painting. The best *sienna* is brought from Italy, but an inferior kind is found in England.

Silene. *Silene virginica* L. (Fam. *Caryophyllaceæ*). *Catchfly. Wild Pink.*—The wild pink, growing from Western New York to Minnesota and southward, was considered by the Indians poisonous and by Barton an anthelmintic. It is a slender herb having thin-spatulate or oblong-lanceolate leaves and deep crimson or scarlet flowers in a loose raceme.

Silex, Pulverized. *Silex Contritus* Lond. *Quartz.*—For mechanical purposes, in the making of aromatic waters, etc., the London Pharmacopœia formerly recognized under the name of *Silex Contritus* powdered *quartz;* but at present powdered purified talc, paper pulp and magnesium carbonate are employed. For details, see 17th edition, *U. S. D.*, p. 1741.

Pulverized silex is a harsh, white, tasteless powder, insoluble in water and most other solvents. Its sp. gr. is 2.66. In composition it is a *silicic oxide*, SiO_2. *Silicon* is an electro-negative element, which has been obtained in two allotropic states, called amorphous and crystalline silicon; the first corresponding to amorphous carbon and the second to crystallized carbon or the diamond, except that it is steel-gray in color. The second variety is hard enough to scratch glass but not topaz and has the sp. gr. 2.49. It is now made on a large scale as a product of the electric furnace, being used as a deoxidizing agent in the casting of some metals. Pure *silica* is easily prepared by acidulating commercial solution of sodium silicate with hydrochloric acid, heating and evaporating, and washing the precipitated silica.

Silk Peptone. *N. N. R.* 1917.—This is a preparation of peptone derived from silk and standardized to a nearly uniform optical rotatory power. It is white to a yellowish non-hygroscopic powder, easily soluble in water and used as a testing agent for peptolytic ferments in tissues or in stomach contents. It has no use in therapy.

Silphium. *Silphium laciniatum* L. *Polar Plant.* (Fam. *Compositæ.*)—The *rosin weed*, or *compass plant*, of Ohio, yields an oleoresin, which is said to be used in making chewing gum. (*A. J. P.*, 1881, 487.)

Silver Acetate. *Argenti Acetas.* $AgC_2H_3O_2$.—*Silver acetate* occurs in white crystals, soluble in about 100 parts of water at ordinary temperatures, freely soluble in hot water. It has been introduced by Zweifel (*Centralbl. f. Gynækologie*, 1900, No. 51) as a substitute for silver nitrate in the treatment of *ophthalmia* of new-born infants. He asserts that the one per cent. solution is in these cases much more effective than the older salt.

Silver Ammonio-chloride. *Argentii Ammonii-chloridum. Argentum Chlorato-ammoniatum.*—This substance is formed by saturating solution of ammonia, by the aid of heat, with silver chloride and allowing the liquid to cool in a stoppered bottle. It crystallizes in cubes. Silver ammonio-chloride has been used in the treatment of *chorea, epilepsy*, and *syphilis*, and as an anthelmintic, in *doses* of from one-twelfth to one and a half grains (0.005–0.1 Gm.). It is probably of little value.

Silver Atoxylate. *Argenti Atoxylas. Argatoxyl.* $NH_2C_6H_4As.O.AgO.OH$.—*Silver atoxylate* (*atoxylic silver*) is insoluble in water, and is the mono-silver salt of para-amino-phenylarsonic acid. According to Blumenthal, atoxylate of silver contains 23 per cent. of arsenic and 33 per cent. of silver. Silver atoxylate has been used chiefly to increase bodily resistance to infectious diseases. According to Rosenstein (*All. M. C.*, 1912) its beneficial effects are due in part to its bactericidal properties and in

part to a leukocytosis which it calls forth. It has been used in *puerperal septicemia, rheumatic fever, gonorrheal arthritis, scarlet fever, carbuncles,* and other infections. From five to six grains (0.3–0.4 Gm.) suspended in ten times as much olive oil may be injected intra-muscularly at intervals of from one to several days. The injections are often followed by abscess formation but it is stated that the abscesses formed are sterile.

Silver Caseinate. *Argonin. N. N. R.* 1917. *Argentum Casein.*—This is a white powder, of neutral reaction, prepared by mixing equivalent quantities of solutions of sodium caseinate and silver nitrate and precipitating with alcohol. It is readily soluble in warm or albuminous water, with difficulty in cold water. It is incompatible with acids and acid salts, but is not affected by chlorides. A 10 per cent. solution in warm water is said to be permanent in the dark. (A. Leibrecht, *Th. M.*, vii, 1895.) Fifteen grains (1 Gm.) of this substance contain as much silver as does one grain (0.065 Gm.) of silver nitrate. It makes a neutral solution in water, and has been very highly recommended by both German and American clinicians in the treatment of acute and chronic cases of *gonorrhea.* Its 10 per cent. solution causes no pain in acute gonorrhea. According, however, to the elaborate study of H. M. Christian, it is not of much service in the treatment of *posterior urethritis.* One hundred and sixty minims (10 mils) of a 2½ to 3 per cent. solution may in the acute stages of the disease be injected into the urethra and allowed to remain there for five minutes. A solution—0.3 ammonia water, 0.6 argonin, 100 of water—is said by R. Mayer to be much more powerful than argonin itself.

Silver Chloride. *Argenti Chloridum.* AgCl.—This is readily prepared by adding a solution of sodium chloride to one of silver nitrate, as long as it produces a precipitate. As first thrown down, it is a white, curdy substance, but it soon becomes discolored when exposed to the light. It is decomposed by solutions of the caustic alkalies, which convert it into oxide, but not by their carbonates. After the formation of the oxide in this way, the addition of sugar reduces it, and revives the silver. (Levol.) Silver chloride has been used in *syphilis, epilepsy, chronic dysentery* and *diarrhea,* and other diseases in which silver nitrate has been given, but is probably of no value. The *dose* is from one to two grains or more (0.065–0.13 Gm.), four or five times a day.

Silver Citrate. $Ag_3C_6H_5O_7$. *N. N. R.* 1917. *Itrol.*—This salt, which is almost insoluble in water, was introduced by Credé as a dusting powder for wounds. It is powerfully antiseptic and non-irritant. According to Marshall and Neave (*B. M. J.*, 1906, ii) it is a more powerful germicide than silver nitrate. It has been very highly recommended by Werler (*Derm. Zeit.*, vol. cxi) in the treatment of *urethritis,* as being a powerful gonococcocide and non-irritant to the mucous membrane. He employs a solution varying in strength from one part in four thousand to one in eight thousand, which is to be injected four times a day. Von Arlt (*Aerzt. Zentral-Zeit.*, 1905) employs it in various infectious conditions of the eye, such as gonorrheal *ophthalmia, trachoma* and the like. His method of using it is to dust the powder on the previously cleansed conjunctiva, and to rinse off after a few minutes, either with water or borax solution. Warler also commends it as a remedy in the treatment of chronic *cystitis.* Tilger and other surgeons have commended the remedy in the treatment of all forms of infected mucous membrane in saturated solution (1 in 3800). Pfonarlt (*W. M. W.*, 1908, No. 52) recommends the dusting of the conjunctiva with pure itrol in cases of *ophthalmia neonatorum, trachoma,* and other severe infections of the eyes, alleging that it is no more irritant than would be any insoluble foreign body. In using itrol, it should be remembered that it is easily decomposed, especially in the presence of organic matter, and should be kept well stoppered and protected from the light.

Silver Fluoride. *Tachiol. Arganti Fluoridum.* AgF = 126.88.—Mueller (*D. M. W.*, 1908) recommends this salt as an injection in *gonorrhea* in strengths of from 1 in 10,000 to 1 in 2000. Stronger solutions, he says, are locally irritant. The silver fluoride, as well as the silver silicofluoride (*isotachiol*), Ag_2SiF_6, have been suggested for the purpose of sterilizing drinking water. According to the experiments of Hetsch 5 Gm. per 1000 litres will destroy most of the bacteria, but when these were numerous 10 Gm. per 1000 litres are not sufficient, and the agent is therefore not suitable for this purpose.

Silver Gelatose. *N. N. R.* 1917. *Albargin.*—This substance, which is a compound of silver and gelatose, is a yellowish, shining, sometimes coarse powder which, in either cold or warm water, freely forms neutral dialyzable solutions. It contains 13 to 15 per cent. of silver. It is incompatible with tannin and chlorides which precipitate gelatose and silver, respectively. It affects albumin slowly and also precipitates cocaine solutions, but may be used with the alkaloid providing the double solution be freshly prepared at the time of administration. It is not quickly reduced by light, but should be preserved in amber-colored bottles. It was introduced by Bornemann (*Ther. Geg.*, March, 1901) for the treatment of *gonorrhea.* When there is much irritation, the 0.1 per cent. aqueous solution may be injected four or five times a day; in more chronic conditions the solution may be up to 2 per cent.

Silver Iodate. $AgIO_3$.—This is a white insoluble powder. It is used chiefly as antiseptic in various *catarrhs,* especially in *enteritis* and *gastritis.* The *dose* is from one-twelfth to one-sixth of a grain (0.005–0.01 Gm.).

Silver Iodide. *Argenti Iodidum. U. S.* 1890. AgI = 234.80.—This salt may be readily prepared by adding a solution of potassium iodide to one of silver nitrate, and washing and drying the precipitate, which should be kept in dark amber-colored vials, protected from light. This iodide is said to have three allotropic forms and a point of maximum density at about 116° C. (240.8° F.). (See paper by G. F. Rodwell, in *Chem. News,* xx, 288; xxi, 14.) The U. S. Pharmacopœia, 1890, described it as "a heavy, amorphous, light yellowish powder, unaltered by light, if pure, but generally becoming somewhat greenish-yellow, and having neither odor nor taste. Insoluble in water, alcohol, diluted acids, or in solution of ammonium carbonate, but soluble in about 2500 parts of stronger ammonia water. It is also dissolved by an aqueous solution of potassium cyanide, and by a concentrated solution of potassium iodide, and the resulting solutions yield a black precipitate with hydrogen sulphide test-solution or ammonium sulphide test-solution. When heated to about 400° C. (752° F.), the salt melts to a dark red liquid, which, on cooling, congeals to a soft, yellow, slightly transparent mass. When mixed

with ammonia water, it turns white, but regains its yellowish color upon being washed with water. If a small quantity of chlorine water to be agitated with an excess of the salt, the filtrate acquires a dark blue color on the addition of starch test-solution. *U. S.*, 1890.

Silver iodide in suspension has been recommended as an injection for gonorrheal *urethritis* by Siter and Uhle. For this purpose, it is generally prepared extemporaneously. The formula recommended by Wilbert (*A. J. P.*, 1906) is 2.2 Gm. of silver nitrate dissolved in 50 mils of mucilage of acacia and 45 mils of water and to this is added 2.2 Gm. of potassium iodide which is dissolved in 50 mils of water and thoroughly shaken. Such a suspension of silver iodide is marketed as *Silvodide*. J. C. and B. L. DeG. Peacock (*Proc. Penna. Pharm. Assn.*, 1916, p. 231) contribute a thorough review of the various methods for preparing this emulsion and conclude that mucilage of chondrus is the best suspending medium when thoroughly purified. For tests of purity, see *U. S. D.*, 19th ed., p. 1647. Silver iodide has been given in *doses* of one or two grains (0.065–0.13 Gm.) three times a day, in *epilepsy* and other chronic nervous diseases, but is devoid of value.

Silver Lactate. *N. N. R.* 1917. *Argenti Lactas. Actol.* $AgC_3H_5O_3 + H_2O$.—*Silver lactate* was introduced by Credé as a surgical germicide. It is affirmed that its injection renders an infected wound rapidly aseptic without much irritation. It is soluble in 15 parts of water, and may be used in very strong, even saturated, solution. D. A. Tilger finds that the application of the pure powder to the curetted infected sore causes only moderate burning pain of short duration and acts most happily. (*M. M. W.*, 1897.) Its therapeutic properties seem to be purely local, since E. Marx found that after injection of very large doses of it into animals it does not prevent the development of pathogenetic germs. It is almost certainly decomposed at the point of injection, but, unlike corrosive sublimate, it does not form an insoluble compound when brought in contact with tissues, and so is able to find its way through these tissues. Fifteen grains (1 Gm.) of it have been given hypodermically without more serious symptoms than some burning pain at the point of injection. According to Marx, a remarkable rise of temperature follows the use of it in very large doses. Actol has been used to a considerable extent in dentistry, decayed or decaying pulp being washed with a solution of the strength of 1 in 2000 and then dusted with itrol.

Silver Methylene Blue.—This silver salt occurs as a blue powder readily soluble in water and representing 20 per cent. of silver. According to Edelmann (*D. M. W.*, 1913, p. 2292) it is germicidal in strengths of 1 part in 160,000 and contrary to many other anti-bacterials, exercises a considerable disinfectant power in the blood, 1 part in 80,000 exhibiting a distinctly antiseptic action. Doses of 0.1 Gm. per kilo injected subcutaneously produce no toxic effects in rabbits. It has been used not only as a local application, but as an internal disinfectant in *septicemia, rheumatic fever* and other infectious diseases. The *dose* recommended is from two to six grains (0.13–0.4 Gm.), either subcutaneously or intramuscularly.

Silver Methylene-nucleinate. *N. N. R.* 1917. *Sophol. Silver formo-nucleinate.*—This is a dark yellow, tasteless, odorless powder, readily soluble in water. When heated it gives off formaldehyde, a residue of metallic silver being left behind. Its solutions are not stable. It contains 20 per cent. of silver.

Sophol is asserted to possess a powerful germicidal action without any irritant effect upon mucous membranes. According to Vollert (*Ther. Neu.*, July, 1906), a 0.37 per cent. solution of sophol is bacteriologically equivalent to a 1 per cent. of protargol. It has been used chiefly in ophthalmic conditions, especially *gonorrheal ophthalmia* and also in non-specific cases of *conjuctivitis* in strengths of from 5 to 10 per cent. While apparently of much value for the purpose of destroying bacteria located on the superficies of the conjunctiva, Dreser (*A. J. P.*, xviii) states that it is lacking in penetrating power and is less valuable than silver nitrate after the germs have passed through the epithelium.

The solutions should be freshly prepared, as on standing, formaldehyde is liberated which is likely to prove irritant.

Silver Nitrate Ammonia Albumose. *N. N. R.* 1917. *Hegonon.*—It is asserted to contain approximately 7 per cent. of silver organically combined. It is not precipitated by albumin or sodium chloride.

Hegonon has been employed as an antiseptic in *gonorrhea* by Klingmuller. (*M. M. W.*, 1910.) It may be used in strengths of 1 in 400 to 1 in 3000.

Under the title *Argentamin* the N. N. R., 1917, recognizes an 8 per cent. solution of silver nitrate in a 15 per cent. aqueous solution of ethylene diamine. It is a clear, strongly alkaline liquid, sp. gr. 0.97, which does not precipitate albumin or chlorides. On exposure to air it is liable to turn yellow, but can be cleared by filtration. Its use in medicine was proposed in 1894 by Jean Schaeffer. (*Zeitsch., f. Hyg. u. Infektions*, 1894, xvi, Bd. ii.) Hoor used it in a large number of eye cases; he asserts that it causes less pain and irritation than the silver nitrate, and penetrates deeper. He used a 5 per cent. solution in the eye from one to four times a day in the same cases as those in which silver nitrate is useful. According to Aschner (*Orv. hetil.*, 1895), it is well borne by the posterior urethra in as strong solution as 1 to 250; but the anterior urethra will not bear more than 1 to 2000. An aqueous solution containing 10 per cent. of argentamin with 30 per cent. of a 1 per cent. solution potassium bichromate has been used instead of silver nitrate as a stain for histological examination of the nerve tissues. (*Ph. Ztg.*, 1910, No. 43, 436.)

Silver Orthophosphate. *Silver Phosphate. Argenti Phosphas.* $Ag_3(PO_4)$.—This substance is prepared by dissolving silver in concentrated orthophosphoric acid; the vitreous mass which results, while still melted, is dissolved in water acidulated with phosphoric acid, yielding a permanent solution. Spretzka (*Rév. Med. Pharm.*, v, 292) asserts that it is a valuable remedy in *gonorrhea*. The injection should contain 0.025 to 0.05 per cent. of the salt, increasing gradually to 0.25 or even 0.5 per cent.

Silver Phenolsulphonate. *Argenti Phenolsulphonas. Silver Sulphocarbolate. Silberol.* $C_6H_4(OH)SO_3Ag$.—A crystalline powder containing 28 per cent. of metallic silver, soluble in water; proved to undergo spontaneous decomposition, but said to be more permanent than itrol. Originally introduced by Zanardi as having the antiseptic properties without the corrosive action of silver nitrate, silberol has been employed by various practitioners in the treatment of *gonor-*

rhea and *ophthalmic inflammations*, and as a germicide in ocular surgery. It is asserted that a 2 per cent. solution is well borne as an antiseptic after operations upon the eye; also that when it is used as a substitute for silver nitrate silberol must be employed in twice as concentrated solution.

Silver Picrate. *Silver tri-nitro-phenylate. Picratol.* $C_6H_2O(NO_2)_3Ag. + H_2O$.—This occurs as yellowish crystals and said to represent 30 per cent. of silver. It is soluble in 50 parts of water. It is used as an antiseptic in *gonorrhea* and other *catarrhs* in strengths of from one-half to two per cent.

Silver-potassium Cyanide. *Silver and Potassium Cyanide.*—This occurs as colorless crystals readily soluble in water and very sensitive to light. According to Philippson it is about equally as poisonous as potassium cyanide and very powerfully bactericidal. He has employed it for washing out the bladder and urethra. He employs solution ranging from 1 in 7000 to 1 in 1000.

Silver Protalbin. *Largin.*—This is a compound of silver and protalbin, which occurs as a whitish powder, soluble in water to the extent of 10.5 per cent., freely soluble in glycerin, blood serum, and peptone solution. Not precipitated by chlorides nor yet by albumin, and containing 11.1 per cent. of silver. In brown bottles it keeps unchanged indefinitely. Owing to the fact that it does not coagulate albumin its penetrating powers when brought in contact with the mucous membrane are very great, and it is claimed by many German clinicians that as a specific germicide in the treatment of *gonorrheal affections* it is pre-eminent. In male *gonorrhea* the strength of the injection should be one-fourth of one per cent., gradually increased up to two per cent. In women the parts may be irrigated with from a one-half to one per cent. solution, after which a 5 per cent. largin bougie may be held in position by a cotton plug for fifteen minutes and the part again irrigated with a 0.5 per cent. solution of largin. Largin is also largely used in the treatment of infectious *conjunctivitis* and catarrhal *corneal ulcers* in the form of gelatin tablets containing one per cent.

Silver Proteinate. *N. N. R.* 1917. *Novargan.*—This is a fine yellow powder, soluble, at ordinary temperatures, in twice its weight of water. It is stated to contain 10 per cent. of silver, and to be actively germicidal. It is markedly astringent, and practically non-irritant, even in relatively concentrated solution. It has been used in the treatment of various *gonorrheal diseases*, in strengths of from two to ten per cent.

Silver Quinaseptolate. *Argenti Quinaseptolas. Argentol.* $C_9H_5N.OHSO_3Ag$.—This substance is a yellow powder, sparingly soluble in water, which was introduced into medicine by Credé on account of its readily splitting up into oxyquinoline and metallic silver. Both septic matters and intestinal juices are said to produce this change. It has been employed either as a dusting powder or in the form of spray, or injection, 1 in 300 to 1000, in *chancres*, *gonorrheas*, and various other surgical infections. C. Cipriani asserts that it is a valuable intestinal antiseptic of which 15 grains (1 Gm.) may be given safely in the twenty-four hours if necessary. It is said also to be an active non-irritant antiseptic with marked hemostatic properties.

Silver, Soluble. *Argentum Solubile. Argentum Colloidale. Soluble Silver.—Colloidal Silver. N. N. R.* 1917.—Several allotropic modifications of silver were discovered by Carey Lea in 1891. One of these has been introduced into medicine. "Soluble Silver," so called, can be prepared by taking a mixture of 30 Gm. ferrous sulphate dissolved in 100 mils of water and 36 Gm. of crystallized sodium citrate dissolved in 140 mils of water and pouring this mixture with stirring into 100 mils of a 10 per cent. silver nitrate solution. After allowing the precipitate to settle, the supernatant liquid is poured off, the precipitate dissolved in water, and again precipitated with absolute alcohol. When dried, the colloidal silver is a bluish or green-colored mass, which dissolves in water with a deep red color, but is precipitated from its solution by the addition of salt solutions. It contains 97.2 per cent. silver. Chassevant and Posternak find the collargol of commerce does not contain more than eighty-seven per cent. of silver, the rest being albuminous matter. (*C. R. S. B.*, 1903, lv.)

There are at present two forms of so-called colloidal or soluble silver employed in medicine, one of which is prepared by chemical means, and the other by electrolytic methods. The manufacturers of the latter preparations claim that the therapeutic virtues of the electrically prepared colloidal silver are much more clearly established than those of the chemically prepared varieties.

Colloidal silver was introduced into medicine by Credé wih the idea that it would possess the germicidal properties of silver, and being nontoxic, might be used internally for the control of various bacterial infections. It has been used very extensively in the treatment of *septicemia, rheumatic fever, gonorrheal arthritis, diphtheria, cerebro-spinal meningitis*, and other infectious diseases. While a large number of clinicians have been enthusiastic in their praises of its efficacy, there is as yet no well-supported theory of its mode of action, and a number of careful observers have denied that it possesses any therapeutic virtues whatsoever. Whatever may be the real value of this remedy, it is evident that it does not act as Credé had expected, as an antiseptic in the blood. In the first place, Brunner has shown that its germicidal action is extremely feeble, and Cohn (*K. T. W.*, 1905) found that within forty-five minutes after its injection the silver had disappeared from the blood entirely. This same observer has stated further that it had neither prophylactic nor curative properties in rabbits, against infection with the staphylococci. On the other hand, Dunger (*M. M. W.*, 1907) found that its injection lead to pronounced leukocytosis, and his conclusions have received considerable confirmation. It is claimed also that colloidal silver acts, like other colloidal metals, as a catalytic agent, and thereby aids in the destruction of the toxins.

The beneficial effects, however, which have been attributed to the local application of colloidal silver in *rhinitis, cystitis* and *conjunctivitis*, would seem to indicate that under some circumstances it may exercise antibacterial properties. The evidence for and against the practical value of colloidal silver is so contradictory that it is impossible to determine its utility.

The most widely used preparations of colloidal silver are as follows:

Collargol. N. N. R. 1917.—This occurs in bluish-black scale-like pieces which, with 20 parts of distilled water, yield a brownish colloidal solution

which is permanent if protected from light and heat. It is asserted to represent over 80 per cent. of metallic silver. It may be injected intravenously in solutions of from 2 to 5 per cent. strength, administering an amount of the solution equivalent to one to five grains (0.065–0.32 Gm.) once or twice a day. It is also widely employed in the form of a 15 per cent. ointment, *Unguentum Credé*, of which one-half to one drachm (1.8–3.75 Gm.) is applied at a *dose*, being vigorously rubbed into the skin.

Electrargol, N. N. R. 1917, is marketed in bottles and in sealed tubes. The *dose* is eighty to one hundred and sixty minims (5–10 mils) injected intramuscularly or directly into a vein.

Cargentos, N. N. R., 1917.—This is a *colloidal silver oxide*, which is said to represent 50 per cent. of metallic silver.

Lysargine.—This form of colloidal silver occurs as steel-gray shining scales which are readily soluble in water.

Argoferment is a colloidal silver preparation manufactured by an electrolytic process.

Silver Thiohydrocarburo-sulphonate. *Argenti Thiohydrocarburo-sulphonas. Silver Sulphoichthyolate. Silver Ichthyol. Ichthargan. N. N. R.* 1917.—This compound of ichthyol-sulphonic acid and silver is a brown amorphous stable powder, freely soluble in water, glycerin and diluted alcohol, insoluble in alcohol, ether, and chloroform. Its aqueous solution blackens with exposure to light, and in concentrated solution it is precipitated by sodium chloride and by albumin, the albuminous precipitate being redissolved by an excess of albumin. It is said to contain about 30 per cent. of silver and 15 per cent. of sulphur.

Wood (*N. Y. M. J.*, 1903, lxxvii) found that, although ichthargan is much less poisonous, its physiological action is the same as that of silver nitrate. The germicidal power of ichthargan is certainly equal, and probably superior, to that of silver nitrate, and it is far less irritant. It is therefore, a very valuable remedy for local application in the treatment of various infectious conditions, especially those involving mucous membranes. In *tonsillitis* and *pharyngitis* it may be applied to the throat with a swab in strengths of from 5 to 10 per cent. In *urethritis* for injections, solutions of 1 in 500 to 1 in 3000 may be used; for irrigations from 1 in 2000, to 1 in 5000.

Unna (*Med. Klin.*, 1913) highly recommends the use of ichthargan in various *skin diseases*, especially *psoriasis* and *chronic eczema*. He uses an ointment varying in strength from 5 to 15 per cent.

In *eczema, ulcerations, phlegmons*, and in *lymphangitis*, the ointment varying from 1 to 15 per cent. is advised, well rubbed into the adjacent healthy skin, previously thoroughly cleansed, and also applied directly to the affected surface, if it be exposed. Ichthargan has also been administered internally with asserted excellent results for the relief of *gastritis* and especially of *gastric ulcer*. *Dose*, one-twentieth to one-eighth of a grain (0.003–0.008 Gm.) in half a fluidounce (15 mils) of water, on an empty stomach.

Silver Vitellin. *Argentic Vitellin. Argyrol. N. N. R.* 1917.—This substance is said to be produced by extracting gliadin from wheat, treating it in an autoclave with dilute hydrochloric acid under pressure, and obtaining thereby a white granular precipitate which is said to be of the nature of a vitellin, and then combining this with silver, the resulting product being a dark brown powder containing 30 per cent. of metal. *Silver vitellin* is so soluble that one ounce may be dissolved in three drachms of water.

Argyrol has been used chiefly in the treatment of *conjunctivitis* and *urethritis*, especially of the gonorrheal type. Its value in these conditions, however, certainly does not depend upon any direct bactericidal effect, for this is extremely feeble. Post and Nicoll (*J. A. M. A.*, 1910, lv) have found a 50 per cent. solution is not certainly fatal to bacteria, even after thirty minutes' exposure, which finding is in harmony with the conclusions of other investigators. On the other hand, many clinicians believe it to be a very valuable remedy in this class of cases, and it is possible that it has some therapeutic virtue at present not explained, perhaps, as some believe, owing to a solvent action upon the pus, or perhaps due to some decomposition caused by the secretions.

It is one of the least irritant of all the silver preparations, and may be used in the urethra in strengths of from 1 to 10 per cent., while in *gonorrheal ophthalmia* it has been employed in concentrations up to 30 per cent.

Simaruba.—Under this name the U. S. P. formerly recognized the bark of the root of *S. amara* Aublet (*S. officinalis* DC.) *Ecorce de simarouba*, Fr. *Simarubarinde, Ruhrrinde*, G. *Corteccia di Simaruba*, It. *Corteza de Simaruba*, Sp. (Fam. *Simarubaceæ.*) This is a tree of considerable height, having alternate branches, with a bark which in the old tree is black and somewhat furrowed, in the young is smooth, gray, and marked here and there with broad yellow spots.

Simaruba bark is in long pieces, from 4 to 12 cm. wide and 2 to 5 mm. thick, folded lengthwise, light, flexible, tenacious, very fibrous, externally of a light brownish-yellow color, rough, warty, and marked with transverse ridges, internally of a pale yellow. It is without odor, and of a bitter taste. It readily imparts its virtues, at ordinary temperatures, to water and alcohol. The infusion is at least equally bitter with the decoction, which becomes turbid as it cools. Its constituents, according to Morin, are a bitter principle identical with *quassin*, $C_{10}H_{12}O_3$, to which Gilling (*P. J.*, 1908, lxxxi) ascribes the formula, $C_{22}H_{30}PO_9$, a resinous matter, a volatile oil having the odor of benzoin, malic acid, gallic acid in very minute proportion, an ammoniacal salt, calcium malate and oxalate, some mineral salts, ferric oxide, silica, ulmin, and lignin.

It is a native of French Guiana and the Islands of Dominica, Martinique, St. Lucia, St. Vincent and Barbadoes, in the West Indies. A closely related species, having, however, dicœcious instead of monœcious flowers, flourishes in Jamaica, San Domingo, Bahama Islands, Panama and Guatemala, extending even to Florida; it is called in Jamaica *mountain damson*, and is known as *S. glauca* DC. (*S. officinalis* Macf., not DC.) The two species have probably identical medicinal properties. The bark of the root is the part employed, the wood being nearly tasteless and inert. The middle bark contains much resin. A decoction of the bark and leaves of *S. versicolor* St.-Hil. (*Cortex Paraibæ*), is employed in Brazil as an antidote for snakebites and in the treatment of *syphilis* and *tapeworm;* the powder is used against vermin.

Simaruba possesses the same tonic properties as other simple bitters. In large doses it is said to purge and vomit. On account of its difficult pulverization, it is seldom given in substance.

The best mode of administration is by infusion. The *dose* is from twenty grains to a drachm (1.3–3.9 Gm.).

Simulo.—The dried fruit of *Capparis coriacea* Burch., one of the *Capparidaceæ*, has been recommended as a palliative in *epilepsy;* also in *chorea.* (See *T. G.*, 1888, 1889; and *Th. M.*, Aug., 1888.)

Sirolin.—This is a syrup containing approximately 7 per cent. thiocol (see p. 1640). It has been used in the same class of pulmonic diseases as creosote. The adult *dose* is one fluidrachm (3.75 mils).

Sisymbrium. *Sisymbrium officinale* (L.) Scop. *Hedge Mustard. Herbe aux chantres, Tortelle,* Fr. *Wildersenf, Hederich,* G. (Fam. *Cruciferæ.*)—This annual, growing in Europe and in waste grounds in the United States, is said to be diuretic and expectorant, and has been recommended in chronic *coughs, hoarseness,* and ulceration of the mouth and fauces. The juice of the plant may be used mixed with honey or sugar, or the seeds may be taken in substance. *Sisymbrium Sophia* L., or the *flax weed,* a plant which grows sparingly in waste places in the United States, was formerly official. It is of a pungent odor when rubbed, and of an acrid, biting taste. W. Zopf attributes its poisonous qualities to a volatile alkaloid. (*Zeit. f. Nat. Pharm. Central.*, 1894, 494.) The herb has been used externally in *indolent ulcers* and the seeds internally in *worms,* calculous complaints, etc. *Diplotaxis muralis* DC., (*S. Murale* L.), a plant growing about Atlantic ports, has been used in France in *scurvy, scrofula,* and other cachetic affections, especially associated, in the form of a syrup, with potassium iodide. (*Ann Thér.*, 1863, 126.) Grazing sheep are said to be killed in Southern France by feeding on *Diplotaxis tenuifolia* DC., and human poisoning has occurred. This species is also sparingly localized like D. *muralis.* George Heyl has separated a toxic and apparently uncrystallizable alkaloid. (*Ap. Ztg.*, May 30, 1900.)

Sium.—*Sium cicutæfolium* Schrank (fam. *Umbelliferæ*), which grows in British America and the United States, particularly along the water courses of the valleys of the Pacific slope, and is the *hemlock water parsnip* of this country, is positively asserted to be poisonous. A. R. Porter and N. Rogers (*A. J. P.*, 1876, 348, 483) found in it an active resinous body, toxic to animals. *Oil of Sium cicutæfolium* is stated by Rabak to be found in the plant in the proportion of 0.5 per cent. It is yellow and has an odor resembling that of caraway. (*Mid. Druggist,* 1905, 5.) *S. Sisarum* L., or *skirret,* a plant of Chinese origin, cultivated in Europe, has a sweetish, somewhat aromatic root. The latter is used in much the same manner as the oyster plant and parsnip. It is supposed to be a useful diet in chest complaints.

Skimmia. *Skimmia japonica* Thumb. *Miramashikimi.* (Fam. *Rutaceæ.*)—From this dwarf-growing holly-like shrub, which is cultivated on account of its dark, shining, evergreen leaves and clusters of bright-red berries, Eykman separated a glucoside, *skimmin,* and a decomposition product, *skimmetin.* (*Abhandl. d. Tokyo Diagaku.*, No. 10, Tokyo, 1883.) J. Honda (*A. E. P. P.*, Oct., 1904), however, finds that the activity of the plant depends upon the presence of the crystalline alkaloid, *skimmianine.* It is a muscle poison, producing no primary excitement in the muscle, but an increasing paralysis, the influence of the alkaloid extending to involuntary muscles, such as the heart, so that in mammals arterial pressure is progressively decreased.

Skin Varnishes.—Unna has devised a series of preparations for forming thin coverings on the skin. We reproduce the most important formulas.

Bassorin Varnish.—The pure bassorin basis is obtained, according to Elliot, by passing tragacanth mucilage (15 to 100) through a filter heated by steam, evaporating, and mixing with glycerin. A similar basis may be prepared by stirring 5 parts powdered salep with 95 parts cold water until a smooth mucilage is obtained, then heating for half an hour on the steam bath. The salep basis contains less bassorin, but more starch.

Casein Varnish.—The casein obtained by coagulating skimmed milk with rennet at a temperature of from 35° to 40° C. (95°–104° F.) is washed and dried until it forms a yellowish-white, sandy powder soluble in alkaline solution. In preparing this varnish the casein is dissolved by means of borax. For 20 parts casein 2.5 parts borax and 77.5 parts water furnish a rapidly drying uniform covering material. The alkaline characters of the borax are masked by the casein. Admixtures of heavy pulverulent substances readily settle out of this basis, and it is requisite to distribute them by shaking. A varnish of casein and glycerin is prepared by dissolving the casein in 3 or 3.5 parts of ammonia water, adding a quantity of glycerin equal in weight to the casein, and heating to drive off the ammonia. The resulting mass mixed with twice its weight of boiling water gives an excellent permanent emulsion.

Amber Varnish.—Made by dissolving a mixture of amber and turpentine in alcohol. It must not be used as a vehicle for the application of zinc oxide.

Castor Oil and *Shellac Varnish.*—With 1 part shellac, 1½ parts castor oil, and 3 parts alcohol, a varnish is obtained which forms a good flexible covering easily removed by alcohol.

Canada Balsam and *Collodion Varnish.*—Sixteen parts collodion with 1 part Canada balsam furnish a material suitable for the application of pyrogallol, and it can be easily removed by alcohol.

Castor Oil and *Collodion Varnish.*—Eight parts collodion and 1 part castor oil.

Lead Ricinoleate Varnish.—One part lead oxide heated with 1½ parts castor oil to saponification, and mixed with 2 parts absolute alcohol, gives a good skin varnish.

Chrysarobin Amber Varnish.—One part chrysarobin and 20 parts amber dissolved in turpentine.

Pyrogallol Shellac Varnish.—One part pyrogallol, 1 part castor oil, 5 parts shellac, and 15 parts absolute alcohol.

Salicylic Acid, Canada Balsam, and *Collodion Varnish.*—One part Canada balsam, 10 parts collodion, and 3 parts salicylic acid.

Zinc Oxide, Castor Oil, and *Collodion Varnish.*—Two parts zinc oxide, 2 parts castor oil, and 16 parts collodion.

Zinc and *Lead Ricinoleate Varnish.*—Five parts lead ricinoleate, 8 parts zinc oxide, 8 parts absolute alcohol, and, lastly, 1 part each of collodion and ether.

Ichthyol Borax Casein Varnish.—Five parts sodium ichthyolate and 15 parts borax casein varnish.

Sulphur Glycerin Casein Varnish.—Five parts sulphur and 15 parts glycerin and casein varnish.

Zinc Oxide Salepbassorin Varnish.—Two parts zinc oxide and 18 parts salepbassorin varnish.

Zinc Ichthyol Tragacanth Bassorin Varnish.—One part sodium ichthyolate, 2 parts zinc oxide, and 17 parts tragacanth bassorin varnish.

Smalt. *Smalts. Azure.*—When the impure cobaltic oxide, obtained by roasting the native arsenide of that metal, is heated with sand and potassium hydroxide, the mixture melts, and a beautiful blue glass results, which, when reduced to powder, forms smalt or azure. It is used chiefly in painting, and for coloring glass and porcelain.

Sodium Argaricinate. $C_{14}H_{27}OH(COONa)_2$.—This salt occurs as a white, tasteless powder, used as an anhydrotic in *doses* of one and one-half to three grains (0.096–0.2 Gm.) taken at night.

Sodium and Silver Thiosulphate. *Sodii et Argenti Thiosulphas.*—This double salt may be prepared by dissolving freshly precipitated silver oxide in a solution of sodium thiosulphate and evaporating the solution. It is in the form of minute crystals of the formula $2Na_2S_2O_3 + Ag_2S_2O_3$, very soluble in water, but insoluble in alcohol, and possessing a sweet taste. Its solution, protected from the light, undergoes no change, and, when quite pure, does not discolor the skin or linen. Delioux states that this salt acts locally like silver nitrate, but more mildly: for *gonorrhea*, one or two parts in two hundred of water.

Sodium Anisate. $C_6H_4.OCH_3.COONa + \frac{1}{2}H_2O$. —A white, micro-crystalline, soluble powder, which has been used as a succedaneum for the salicylate as an antipyretic and antirheumatic. *Dose*, five to fifteen grains (0.32–1 Gm.).

Sodium Bisulphite. *Sodii Bisulphis. U. S. VIII. Acid Sodium Sulphite. Leucogen. Sulfite (Bi) de Soude*, Fr. Cod. *Natrium Bisulfurosum. Doppeltschweftigsaures Natron*, G. $NaHSO_3 = 104.08$.—*Sodium bisulphite* is prepared by thoroughly saturating a concentrated solution of sodium carbonate or bicarbonate with sulphurous acid gas, and collecting the crystals which form upon the cooling of the liquid. As found in commerce, it usually contains sodium thiosulphate and sulphate, and is not reliable; even when kept in well-stoppered bottles it will readily lose its crystalline character and the quantity of sulphurous acid gradually diminishes. The bisulphite, under the technical name of leucogen, is largely used in many industries. It serves as bleaching agent in washing wool, and in the steeping of grain, and in preserving meats and vegetable juices, because of its reducing and anti-fermentative character.

Properties.—It was officially described as in "opaque, prismatic crystals, or a granular powder, exhaling an odor of sulphur dioxide, and having a disagreeable, sulphurous taste. Exposed to the air, the salt loses sulphur dioxide, and is gradually oxidized to sulphate. Soluble in 3.5 parts of water, and in 70 parts of alcohol at 25° C. (77° F.); in about 2 parts of boiling water, and in 49 parts of boiling alcohol. When strongly heated, the salt decrepitates, emits vapors of sulphur and of sulphur dioxide, and leaves a residue of sodium sulphate. To a non-luminous flame it imparts an intense yellow color. Its aqueous solution gives an acid reaction with blue litmus paper. On the addition of the hydrochloric or sulphuric acid, an aqueous solution of the salt evolves sulphur dioxide, which is recognized by its odor, and by its blackening a strip of paper dipped into mercurous nitrate T.S. and held over the escaping gas. If 1 Gm. of Sodium Bisulphite be dissolved in 10 Cc. of diluted nitric acid, and the solution heated sufficiently to expel the gases, the liquid should not become turbid (absence of *thiosulphate*). If 1 Gm. of the salt be dissolved in 20 Cc. of diluted hydrochloric acid, and heated sufficiently to expel the sulphur dioxide, the remaining solution, after being restored to its original volume, should not respond to the Time-Limit Test for *heavy metals* (see PART III, Test No. 121). If to 50 Cc. of tenth-normal iodine V.S., measured from a burette into a glass-stoppered vial (of about 100 Cc. capacity), 0.25 Gm. of finely powdered crystals of Sodium Bisulphite be added, the solution allowed to stand for about an hour, and shaken at frequent intervals, then the addition of not more than 6.45 Cc. of tenth-normal sodium thiosulphate V.S. should be required to decolorize the solution." *U. S. VIII.*

This salt possesses germicidal properties, which the neutral salt does not, due to the liberation of sulphurous acid. It is used as an antiseptic in *gastric fermentation* and externally in parasitic *skin diseases. Dose*, five to ten grains (0.32–0.65 Gm.).

Sodium Boro-Salicylate. *Sodii Boro-salicylas.* —This is made by heating 125 parts of boric acid, 320 parts of sodium salicylate, and 700 parts of water in a flask until a syrupy liquid is produced; this solidifies on cooling, yielding a white product. It dissolves in water. It is used as an antiseptic and preservative.

Sodium Bromvalerate. *Valerobromin.*—This substance is a mixture of sodium bromide and sodium valerate in molecular proportions and occurs as a crystalline water-soluble mass. It is given in the treatment of nervous maladies, *epilepsy, hysteria, neurasthenia*, etc., in *doses* ranging from thirty to seventy-five grains (2–5 Gm.) daily. It is stated that it should not be administered at all to infants under six months old.

Sodium Caseinate. *N. N. R.* 1917. *Sodii Caseinas. Nutrose. Casein-natrium*, G.—A combination of casein and sodium hydroxide, just enough of the alkali being used to dissolve the freshly precipitated casein. The solution is evaporated *in vacuo*, the dry residue powdered, thoroughly washed with alcohol, and then with ether and dried. A white, amorphous powder, with little odor or taste, insoluble in alcohol and ether, slightly so in cold water, but readily soluble in hot water. It is considered to be a valuable food in intestinal and digestive disturbances, also in *anemia* and *scrofula.*

Sodium Chlorate. *Sodii Chloras. U. S. VIII. Natrium Chloricum. Chlorate de Soude*, Fr. Cod. *Natriumchlorat. Chlorsaures Natron*, G. *Clorato sodico*, Sp. $NaClO_3 = 106.46$.—"It should contain not less than 99 per cent. of pure Sodium Chlorate [$ClO_2.ONa$]. This salt should be kept in well-stoppered bottles, and *great caution should be observed* in handling it, as dangerous explosions are liable to occur when it is heated, or subjected to concussion or trituration with organic substances (cork, tannic acid, sugar, etc.), or with sulphur, antimon sulphide, phosphorus, or other easily oxidizable substances." *U. S. VIII.*

This salt, while manufactured on a large scale for use in the textile industries by the method described under *Potassii Chloras*, is sometimes prepared on a small scale by Whittstein's process, which consists in first preparing sodium bitartrate by adding a strong solution containing 9.5 parts of tartaric acid to a hot aqueous solution of 9 parts of sodium carbonate. The hot solution is mixed with one in which 8 parts of potassium chlorate have been dissolved. Potassium bitartrate separates, while sodium chlorate remains in solution. The filtered solution is evaporated and crystallized. If desired of absolute purity, it may be recrystallized from an alcoholic solution. Owing

to the facility with which this salt parts with its oxygen, the official cautionary direction should be borne in mind.

It occurs in "colorless, transparent crystals (principally cubes with tetrahedral facets), or a crystalline powder; odorless, and having a cooling, saline taste. Permanent in dry air. Soluble in about 1 part of water, and in about 100 parts of alcohol at 25° C. (77° F.); in 0.5 part of boiling water, and in about 40 parts of boiling alcohol; also soluble in about 5 parts of glycerin. When heated, the salt melts, then gives off oxygen (about 45 per cent. of its weight), and finally leaves a residue of sodium chloride, readily soluble in water, and yielding, with silver nitrate T.S., a white, curdy precipitate, insoluble in nitric acid. To a non-luminous flame it imparts an intense yellow color. An aqueous solution of Sodium Chlorate (1 in 20) is neutral to litmus paper. When a crystal of the salt is dropped into hydrochloric acid, the liquid assumes a deep greenish-yellow color, and emits the odor of chlorine. A saturated, aqueous solution should not be rendered turbid by sodium bitartrate T.S. (limit of *potassium*). The aqueous solution of the salt (1 in 20), upon the addition of 1 Cc. of ammonium sulphide T.S., should not develop a dark coloration (absence of *lead, copper*, etc.)." *U. S. VIII.*

Sodium chlorate has medicinal properties similar to those of potassium chlorate, while its greater solubility permits the use of stronger solutions. According to Brissaud, when given in daily doses of more than two drachms it is apt to produce albuminuria. In overdose it would probably cause symptoms not distinguishable from those caused by potassium chlorate poisoning. *Dose*, five to fifteen grains (0.32–1.0 Gm.).

Sodium Dithiosalicylate. $S(C_6H_3(OH)CO\,ONa)_2$. *Dithion I* and *II.*—These are two isomeric salts separable by means of sodium chloride solution, the dithion I being insoluble in the latter solution. Dithion I is a yellowish-white, amorphous, soluble powder employed mostly in veterinary practice as a dusting powder of antiseptic value. The dithion II is used like sodium salicylate as an antirheumatic and antipyretic, free it is said, from secondary action. *Dose*, thirty to sixty grains (2–4 Gm.).

Sodium Ethylate. *Sodii Ethylas. Ethylate of Sodium. Caustic Alcohol.* C_2H_5ONa.—This preparation was introduced by B. W. Richardson of England, as a caustic. He makes it by adding sodium in small pieces gradually to absolute alcohol, kept at a temperature of 10° C. (50° F.); hydrogen is evolved, and when, owing to the formation of the ethylate, the reaction slackens, the liquid is to be carefully heated to 37.7° C. (100° F.). Sodium is then cautiously added until the reaction ceases; the liquid is cooled to 10° C. (50° F.), and the same quantity of absolute alcohol added as was used in the beginning. (*P. J.*, 1878, 485.) *Sodium ethylate* is a white powder, frequently having a brownish tinge, dissolving in water with a hissing sound, having the property of splitting into alcohol and sodium hydroxide upon contact with even a small quantity of water or moist living tissue:

$$C_2H_5ONa + H_2O = C_2H_5OH + NaOH$$

Sodium ethylate does not appear to be of any value as an internal remedy. When, however, it comes in contact with moist tissue, owing to the liberation of its sodium, it acts as a very speedy and powerful caustic. It should always be used in alcoholic solution, and applied by means of a glass rod. It is said to cause very little pain, and has been specially employed for the destruction of *nævi*. (*L. L.*, Nov., 1878.) A *solution of sodium ethylate* was official in the Br., 1898, under the title *Liquor Sodii Ethylatis*. It was prepared as follows: "Sodium, clean and bright, 22 *grains* (Imperial) or 1 gramme; Absolute Alcohol, 1 *fl. ounce* (Imp. meas.) or 20 mils. Cautiously dissolve the Sodium in the Absolute Alcohol contained in a flask, the latter being kept cool by a stream of cold water." *Br.*, 1898.

It is described as "a colorless liquid of syrupy consistence, becoming brown by keeping. Specific gravity 0.867. When slightly heated it boils and gives off alcoholic vapors, leaving a white residue which, on being strongly heated, becomes charred. If the white residue be mixed with *water* and heated, it yields ethylic alcohol, and the solution, on evaporation, leaves a white residue consisting almost wholly of caustic soda. This solution should be recently prepared. It contains 18 per cent. of the solid substance, C_2H_5ONa." *Br.*, 1898. It may be made more conveniently by dissolving twenty grains of sodium ethylate in 80 grains of absolute alcohol. It is used solely as a caustic, and is said to produce very little pain. It should not be allowed to come in contact with water. Richardson states that it should always be kept in glass-stoppered bottles, in a cold place, as he has known it to explode when placed in warm situations. Gamberini and Monari (*R. T.*, 1892) assert that the 20 per cent. liniment made with olive oil, well rubbed in daily, will usually cure *psoriasis* in twenty days, and that the 10 per cent. aqueous solution is very valuable in the treatment of *lupus erythematosus*, applied after curetting.

Sodium Formate. *Sodii Formas. Ameisensaures Natrium*, G. $HCO_2Na + H_2O$.—Prepared by neutralizing formic acid with sodium carbonate. It occurs in colorless, rhombic prisms, which are inodorous, and have a saline, bitter taste. Sodium formate is very deliquescent and dissolves freely in water. *Dose*, one-half to three grains (0.032–0.2 Gm.).

Sodium Fructosate. $C_6H_{11}NaO_6$.—This substance forms a yellowish, extremely hygroscopic powder, and is employed in place of the usual physiological salt solution for sustaining the heart action. It has been stated that it gives a better action when about 50 per cent. calcium saccharate is added to it and the two dissolved in normal salt solution.

Sodium Metaborate. *Antipyonin.* $NaBo_2 + H_2O$.—*Sodium metaborate* is made by boiling borax and boric acid in water. It is also called *sodium tetraborate*. It occurs as a fine, white powder, greasy to the touch, freely soluble in water. This salt is non-poisonous, devoid of caustic action, and markedly antiseptic. It is probably therapeutically equivalent to borax, but has been especially recommended in a 2 to 50 per cent. solution, or blown in as a powder, by Jaenicke and by Kafemann in *acute* and *chronic otorrhea*. Roland attributes extraordinary effects to its insufflation in *keratitis, conjunctivitis*, and other inflammatory eye conditions.

Sodium Methyl Arsenate. *Di-sodium Methyl Arsenate. Sodii Methylarsenas.* $(OAsCH_3O_2Na_2 + 5H_2O.)$—This arsenic preparation occurs as a crystalline powder containing 27.37 per cent. arsenic, easily soluble in water and less so in alcohol. It is precipitated by alkaloids, with mercuric chloride it gives a reddish precipitate, and with

copper sulphate a green precipitate. It appears to be about equivalent in its physiological and therapeutic effects to sodium cacodylate (see page 1019), over which the advantage is claimed that it does not impart a garlicky odor to the breath that is characteristic of the cacodylates. The *dose* is from one-third to one grain (0.021–0.065 Gm.). It is also sold under various trade names, as *arrhenal, arsynal, neosarsycodile, stenosine,* etc.

Sodium Naphthol. *Naphthol Sodium.—β-Naphthol sodium (microcidine),* a white powder easily soluble in water, used as a non-caustic, non-poisonous antiseptic, said to be much stronger than phenol.

Sodium Nitrate. *Sodii Nitras. U. S. VIII. Nitrate of Soda. Cubic Nitre. Chili Saltpeter. Nitras (Azotas) Sodicus. Nitrum Cubicum. Azoate (Nitrate) de Soude,* Fr. Cod. *Nitre cubique Nitrate de Chili,* Fr. *Natrium Nitricum,* P. G. *Natriumnitrat. Chilesaltpeter,* G. *Nitrato di sodio,* It. $NaNO_3 = 85.01$.—"It should contain not less than 99 percent. of pure Sodium Nitrate [$NO_2.ONa$], and should be kept in well-stoppered bottles." *U. S. VIII.* This salt is imported from South America, where it is found naturally, especially in the desert of Atacama, forming beds of vast extent. The nitrate deposits have been found uniformly through a zone 250 geographical miles in length north to south, and two geographical miles in width east to west. It was estimated that the nitrate beds contained the enormous quantity of 99,031,525 tons. The salt has been found also largely in Brazil, in the province of Bahia, near the river San Francisco. (*A. J. P.,* Nov., 1861, 502.) For an account of the sodium nitrate deposits of Chili, see *Potassii Nitras.* The crude salt is in saline lumps, rather soft and friable, and damp on the surface. Its varieties are classified, according to their color and state of aggregation.

The importations of sodium nitrate into the U. S., in 1915, were 575,371 tons, valued at $16,280,510 and in 1916 were 1,072,833 tons, valued at $32,129,926.

"*Caliche,*" as the crude mineral is called, contains from 48 to 75 per cent. of sodium nitrate, from 20 to 40 per cent. of sodium chloride, and smaller amounts of sodium sulphate, calcium sulphate, potassium nitrate, and potassium and sodium iodate (from 0.059 to 0.175 per cent. of iodine). Occasionally calcium borate, associated with sodium borate, is found under the beds of the nitrate.

Sodium nitrate, when pure, is in "colorless, transparent, rhombohedral crystals, odorless, and having a cooling, saline, and slightly bitter taste. Hygroscopic in moist air. Soluble in about 1.1 parts of water, and in about 100 parts of alcohol at 25° C. (77° F.); in 0.6 part of boiling water, and 40 parts of boiling alcohol. When heated to 312° C. (593.6° F.), the salt melts without decomposition. At a higher temperature it evolves oxygen, and is reduced to nitrite. When Sodium Nitrate is heated with charcoal, the mixture deflagrates. To a non-luminous flame it imparts an intense yellow color. Its aqueous solution is neutral to litmus paper. If the aqueous solution be mixed in a test-tube with a drop of diphenylamine T.S., and sulphuric acid be carefully poured in, so as to form a separate layer, a deep blue color will appear at the line of contact. The aqueous solution of the salt (1 in 20), slightly acidulated with hydrochloric acid, should not respond to the Time-Limit Test for *heavy metals* (see PART III, Test No. 121). If to 10 mils of the aqueous solution of the salt (1 in 20) 1 mil of chloroform be added, and then chlorine water which has been diluted with an equal volume of water be introduced, drop by drop, with agitation, the chloroform should remain free from any violet tint (absence of *iodine*)." *U. S. VIII.* Like potassium nitrate, it deflagrates when thrown on the fire, but it is distinguished by giving rise to an orange-yellow flame, and by the rhomboidal shape of its crystals, those of niter being long six-sided prisms. It evolves ruddy fumes when warmed in a test-tube with sulphuric acid and copper wire. This salt has been praised as a remedy in *dysentery* (see 15th ed., *U. S. D.*), in the *dose* of from half an ounce to an ounce (15.5–31 Gm.) in the course of the day in dilute solution, but is at present very rarely, if ever, used in practical medicine.

Sodium Nitroferrocyanide. *Sodium Nitroprusside. Sodii Nitroferrocyanidum.* $Na_2Fe(CN)_5NO$.—This is one of the interesting series of salts, discovered py Playfair, called *nitroprussides,* which are produced, for the most part, by saturating *nitroferrocyanic acid,* formed by the action of nitric acid in potassium ferrocyanide, with different bases. The sodium salt is best obtained by the process of A. Overbeck, as follows: Dissolve four parts of powdered potassium ferrocyanide, contained in a flask, in five and a half parts of commercial nitric acid, diluted with an equal weight of water. After the action is completed, which generally occupies about ten minutes and is accompanied by a copious evolution of gases, heat the resulting coffee-brown liquid in a water bath, until a drop of it gives a dingy green instead of a blue precipitate with a solution of ferrous sulphate. Then allow the liquid to cool; whereupon the larger part of the potassium nitrate generated will be deposited in crystals. Pour off the green mother liquor from these, and separate the remaining potassium nitrate by repeated concentrations. Next, neutralize the liquid, while heated in a water bath, with sodium carbonate, taking care to add the carbonate so long as a pure blue precipitate is produced. Lastly, filter the solution, and set it aside for the formation of crystals, which must be washed with water, and dried between blotting paper. The salt is in the form of large, ruby-colored, prismatic crystals, resembling those of potassium ferricyanide. It is soluble in two and a half parts of cold water, and in less quantity of hot water. Its solution, exposed to sunshine, is decomposed, with evolution of nitric oxide gas, and deposition of Prussian blue, at the same time acquiring a green color. Sodium nitroprusside, as well as the other soluble nitroprussides, is a most delicate test for alkaline sulphides, with which it produces a violet color. It is used also as a test for acetone in urine and in several tests for the detection of formaldehyde.

Sodium Oleate. *Sodii Oleas. Eunatrol. N. N. R.* 1917.—*Sodium oleate* may be made by dissolving 10 parts of sodium hydroxide in alcohol and adding the solution to 100 parts of oleic acid and carefully evaporating the soap which is formed to dryness. It is a whitish mass or a white powder, dissolving freely in water and alcohol. It was at one time believed to be useful in cases of *gall stone. Dose,* from fifteen to forty grains (0.9–2.6 Gm.) daily in capsules.

Sodium Paracresotate. $C_6H_3(CH_3)-(OH)CO ONa$.—An analogue of sodium salicylate obtained through the action of phenol on paracresol alkali. *Sodium metacresotate* and *sodium orthocresotate*

are found in commerce. It forms an inodorous, colorless, bitter, soluble powder used in *gastric catarrh, acute rheumatism,* and *typhoid fever* in *doses* of two to twenty grains (0.13–1.30 Gm.).

Sodium Phenolsulpho-ricinate. *Sodii Phenolo-sulpho-ricinas* (25 per cent.).—This phenol compound has been highly recommended as a local application in *laryngeal tuberculosis* and *papilloma;* also in *ozena.* In the latter disease the pituitary membrane and the nasal ducts are first cleansed and subjected to vigorous daily frictions with the aid of a sound padded with wadding steeped in a solution of *sodium phenolsulphoricinate* (1 to 2 or 3 parts of water).

Sodium Phenyl Propiolate. *Theranol. Thermiol.* $C_6H_5.C : C.COONa$.—This differs in its chemical formula from sodium cinnamate in that it contains two atoms less of hydrogen. It is marketed in the form of a 25 per cent. solution, to which has been given the trade name of *thermiol.* This solution is employed as an inhalation in the treatment of laryngeal and pulmonary *tuberculosis.* It should be diluted to make 1 per cent. to 4 per cent. solution of the salt. (See Bulling, *M. M. W.,* 1905.)

Sodium Pyrophosphate. *Sodii Pyrophosphas. U. S. VIII. Natrium Pyrophosphoricum. Pyrophosphate de Soude,* Fr. Cod. *Natriumpyrophosphat,* G. *Pirofosfato sodico,* Sp. $Na_4P_2O_7 + 10H_2O = 446.24$.—"It should contain, in an uneffloresced condition, not less than 99 per cent. of pure Sodium Pyrophosphate $[(PO)_2O.(ONa)_4 + 10H_2O]$, and should be kept in well-stoppered bottles." *U. S. VIII.* This salt which was recognized by the U. S. VIII is prepared by heating sodium phosphate in a suitable vessel to redness. When sodium phosphate is subjected to a temperature of 44° C. (11.2° F.), it melts in its water of crystallization; if the heat be increased to 100° C. (212° F.), all the water will be dispelled, and but 40 per cent. of the original weight remain; at 300° C. (572° F.) it is converted into the tetrabasic phosphate or pyrophosphate. By dissolving this residue in water, filtering and crystallizing, the salt may be obtained.

It occurs in "colorless, transparent, monoclinic prisms, or a crystalline powder; odorless, and having a cooling, saline, and feebly alkaline taste; slightly efflorescent in warm air. Soluble in about 11.5 parts of water at 25° C. (77° F.), and in 1.1 parts of boiling water; insoluble in alcohol. When heated to 100° C. (212° F.), the salt loses its water of crystallization (40.35 per cent.) without previous fusion. At a higher temperature it fuses, forming a transparent liquid, which, on cooling, solidifies to a crystalline mass." *U. S. VIII.* An aqueous solution is feebly alkaline to litmus and to phenolphthalein. It may be distinguished from the orthophosphates by the facts that it gives a precipitate with silver nitrate T.S., and does not with ammonium molybdate even when heated. The action of this salt upon the human economy is probably that of the phosphate. It has been highly recommended for removing ink stains from colored cotton fabrics. It is said to remove the stains slowly without affecting the other colors.

Sodium Selenite. *Sodii Selenis.* Na_2SeO_3.—A white powder which freely dissolves in water. The aqueous 2 per cent. solution of *sodium selenite* stains bacteria red by the precipitation of *metallic selenium,* and has been highly recommended for the purpose of microscopic staining.

Sodium Silicate. *Sodii Silicas. Soluble Glass.* $Na_2SiO_3 + H_2O$.—*Sodium silicate* is made by fusing one part of silica, fine sand, or powdered flint, and two parts of dried sodium carbonate, mixed in powder, in an earthenware crucible, and pouring out the fused mass on a stone slab to cool. This is pulverized, and treated with boiling water, to dissolve the soluble part. The solution is filtered and concentrated, so as to form crystals on cooling. These are then purified by dissolving them in water heated to 37.7° C. (100° F.), filtering the solution, and concentrating it so that it may recrystallize. The commercial solution of sodium silicate usually contains about 20 per cent. of silica and 10 per cent. of soda. In contact with acids the solution undergoes decomposition. It is employed in fixing fresco colors by the process of stereochromy, as a cement in the manufacture of artificial stone, and as an addition to soaps, constituting the so-called *silicate soaps.* Sodium silicate has been employed as an antiseptic, in the treatment of chronic *urethritis, vaginitis,* etc., but R. Löwenhaupt asserts that when pure it is not antiseptic, any powers which it may seem to have being dependent upon the presence of free alkali in it. Sodium silicate has been suggested as a remedy in *pulmonary tuberculosis,* and Scheffer (*K. T. W.,* 1908) asserts that it has an influence upon mineral metabolism, and is a useful remedy in *arteriosclerosis.* He recommends a *dose* of from twenty-four to forty-five minims (1.6–3.0 Gm.) of the *liquor sodii silicatis* three times a day. It should be given well diluted. Zeller (*M. M. W.,* 1912) recommends the internal use of a mixture of sodium and potassium silicate in the treatment of *external cancers* in conjunction with an arsenical paste. The mixture he employed contained three-quarters of a grain (0.048 Gm.) of each of the silicates, and he gave it three times a day.

Under the name of *Liquor Sodii Silicatis* the U. S. Pharm., 1890, formerly recognized the solution of sodium silicate, describing it as "a semi-transparent, almost colorless, or yellowish, or pale greenish-yellow, viscid liquid, odorless, having a sharp, saline, and alkaline taste, and an alkaline reaction. Specific gravity, 1.300 to 1.400 at 15° C. (59° F.). A drop of the Solution, when held in a non-luminous flame, imparts to it an intensely yellow color. If a portion of the Solution, largely diluted with water, be supersaturated with nitric acid, a gelatinous or pulverulent, white precipitate of silic hydrate will be produced." The solution is used in the preparation of mechanical dressings by the surgeon in the same class of conditons for which plaster of paris is employed.

Sodium Silico-Fluoride. *Sodii Silico-fluoridum.* Na_2SiF_6.—When gaseous SiF_4, generated by the action of sulphuric acid upon fluorspar in the presence of broken glass, is passed into water, hydrogen silico-fluoride, H_2SiF_6, is formed. This acid, when neutralized by sodium hydroxide or carbonate, will yield the sodium salt. It is difficultly soluble in water. It is asserted for the *silico-fluoride of sodium* that its solution, *salufer,* is practically non-toxic and powerfully antiseptic. The powder is a strong irritant or a mild caustic. The solution affects steel instruments. Bokenham, in experiments upon bacteria, found that in order to kill them it was necessary for the solution to be at least as strong as one to seven hundred and fifty parts, and that the drug has toxic properties, 0.05 Gm. of it causing prolonged nausea, great slowing of pulse, and reduction of arterial pressure.

Sodium Stearate. *Sodii Stearas.* $NaC_{18}H_{35}O_2$.

—The pencils of this substance, which have been recommended by T. G. Unna for use in *sycosis* and other parasitic skin diseases, are made as follows: Sodium stearate, 6 Gm. (90 gr.); glycerin, 2.5 Gm. (30 min.); alcohol, sufficient to make 100 Gm. (4 fl. oz.). The affected part should be rubbed with the pencil five or six times daily.

Sodium Succinate. *Sodii Succinas. N. N. R.* 1917. $Na_2C_4H_4O_4 + 6H_2O$.—White crystals freely dissolving in water. *Sodium succinate* has been highly commended by Ch. F. Hope for *catarrhal jaundice. Dose*, fifteen to twenty grains (1.0–1.3 Gm.) every three or four hours.

Sodium Sulphobenzoate. *Sodii Benzosulphonas. Sodium benzosulphonate.* $C_6H_4(NaSO_3)COONa$.—Heckel (*C. R. A. S.*, cv, 896) asserts that *sodium sulphobenzoate* is a non-poisonous antiseptic, superior to phenol, and equal to mercurial solution in the antiseptic treatment of wounds; strength of solution about fifty grains in a quart. It has been employed by L. Webster Fox in subconjunctival injections.

Sodium Sulphocyanide. *Sodium Sulphocyanate. Sodium Rhodanide. Sodium Thiocyanate.* NaSCn.—Bentley and Le Roy have found that this salt had the power of rendering soluble insoluble salts of calcium and magnesium and have suggested its use in the treatment of *arterial sclerosis* and *urinary calculus.* They administered it in *doses* up to one grain (0.065 Gm.). The remedy has also been suggested as a substitute for the iodides, especially in the treatment of chronic nervous conditions.

Sodium Sulphomethylate. *Sodii Methylsulphonas. Sodium Methylsulphonate.* $CH_2(OH)SO_3Na + H_2O$.—According to Rabuteau, this salt in 240 grain (15.5 Gm.) *doses* produces catharsis without cramp. (*A. J. P.*, 1880, 220.)

Sodium Sulphoricinoleate. *Sodium Sulphoricinate. Oleite.*—This substance may be prepared from castor oil by treating it with sulphuric acid at a low temperature, when a compound of sulphuric and ricinoleic acids is formed. The free sulphuric acid being removed by washing, and any unchanged oil by ether, the resulting sulphoricinoleic acid is then neutralized by sodium hydroxide, the finished product being a brown transparent, jelly-like liquid, with little odor, having an acrid taste, and soluble in water, alcohol, chloroform, and essential oils. It has remarkable solvent powers, dissolving phosphorus, iodine, phenol, resorcinol, naphthalene and many other medicinal substances. The phenol solution, often incorrectly called phenol sulphoricinate is described below.

According to the experiments of Fred B. Kilmer (*Proc. A. Ph. A.*, 1890; *P. J.*, xx, 1890), its action upon mucous membranes, healthy and diseased skins, *cuts, burns*, etc., is highly soothing, and it may be taken internally or freely absorbed through the skin without danger. It would appear, therefore, to afford an excellent basis for ointments; but as productions made with it are very sticky, and often liable to harden, it is commonly best used by rubbing the substance with oleite, and then adding 50 per cent. of fatty base.

A mixture of sodium sulphoricinate and phenol is sold under the title *Phenolum Natro-sulphoricinicum* (*phenol sulphoricinate*). It is a yellowish, syrupy liquid, containing 25 per cent. of phenol and 75 per cent. of sodium sulphoricinate. The liquid itself mixes in all proportions with water, and has been especially commended as a local application in various *diseases of the skin* and in *tubercular* and other *ulcerations of the mucous membranes.* First, recommended by T. Heryng (*Th. M.*, 1896) as a local caustic application to *papilloma* and *ulcers* in the nasal and laryngeal passages, or diluted in various forms of chronic inflammation of the mucous membrane of the nose and larynx. These statements have been confirmed by various laryngologists. Prezedborski finds it of very great service both in *rhinitis atrophica* and *hypertrophica.* Berlioz (*B. G. T.*, 1890) especially recommends it in *diphtheria.* The 20 per cent. aqueous solution is to be applied locally to the throat four times a day and once or twice in the night. (*S. M.*, 1892.)

Sodium Sulphosalicylate. *Sodii Salicylsulphonas.* $C_6H_3(OH)\langle^{COOH}_{SO_3Na}$. *Sodium Salicylsulphonate.*—*Salicylsulphonic acid*, made by acting on salicylic acid with sulphuric acid, is partly neutralized with sodium carbonate. It occurs as a white crystalline powder, soluble in twenty-five parts of water, insoluble in alcohol and ether. It is used as a substitute for sodium salicylate. It is less powerful than the latter, but free from its after effects. *Dose*, ten to thirty grains (0.65–2.0 Gm.).

Sodium Sulphovinate. *Sodium Ethylsulphate.* $C_2H_4(OH)SO_3Na + H_2O$.—This salt occurs as a white, granular powder or in hexagonal tabular crystals, according to the method of its preparation. Its taste is cooling and rather aromatic, nearly destitute of bitterness. It is very deliquescent, and is soluble in 0.7 part of water.

When sulphuric acid is added to alcohol the temperature rises at once, and a certain proportion of sulphovinic acid is formed, but, as water is at the same time developed, the reaction is soon arrested by the dilution of the mass. The first practical method of overcoming the difficulty was afforded by the process of Limousin. Nineteen and a half ounces (avoirdupois) each of pure sulphuric acid, sp. gr. 1.715, and of concentrated alcohol, about 96°, are slowly introduced by means of two funnels (one for the alcohol and the other for the acid) into a third funnel arranged in a flask plunged into a freezing mixture or kept in a current of cold water, the flow of the two liquids into the flask being so regulated as to keep the alcohol in excess. The mixture is kept for four to five days at a temperature of from 20° C. (68° F.) to 25° C. (77° F.), then diluted with from nine to ten pints of distilled water, and carefully saturated with somewhat less than forty-eight ounces of pure barium carbonate in solution. When the point of saturation has been attained, the liquid is left to deposit the barium sulphate, and afterwards filtered. The solution of barium sulphovinate so obtained is saturated with between twenty-seven and twenty-nine ounces of pure sodium carbonate dissolved in four liters of distilled water. When no more precipitate is formed by the addition of the alkaline solution, and the liquid is neutral to test paper, the transformation of the barium sulphovinate into *sodium sulphovinate* is complete. The liquor, decanted and filtered, is evaporated in a water bath until it has the sp. gr. 1.33, and left to crystallize. The drained crystals are dried in an oven. For additional methods of making the salt, see *U. S. D.*, 19th ed., p. 1653.

Sodium sulphovinate is said to be a mild although active cathartic. According to Rabuteau, five drachms (19.4 Gm.) of it dissolved in three glasses of water will generally produce in the adult four or five liquid stools without pain. The *dose* for children is from two to three drachms (7.7–

11.6 Gm.). The pleasantness of its taste and action would render it a favorite purgative were it not for its high price and the difficulty of preserving it, all of the sulphovinates having a great tendency on exposure to the air to break up into alcohol and a salt of sulphuric acid.

Sodium Tartrate. *Sodii Tartras.* $Na_2C_4H_4O_6$. $2H_2O = 230.06$.—This salt, in crystals, has been recommended by Delioux as an agreeable purgative, almost without taste, and acting with a power equal to that of the magnesium sulphate in the *dose* of ten drachms. The *soda powders*, so much used in the United States, form an extemporaneous sodium tartrate, somewhat aërated with carbon dioxide. A *solution of sodium tartrate* has been used as a substitute for solution of magnesium citrate. It may be made by dissolving six drachms of tartaric acid in two fluidounces of water, and seven and a half drachms of sodium bicarbonate in seven fluidounces of water, mixing the solutions gradually and filtering; the filtrate should be poured into a strong twelve fluidounce bottle and two fluidounces of lemon syrup added slowly, so that it will sink to the bottom of the bottle without mixing very much with the solution; eighty grains of tartaric acid are to be added without agitating the bottle, which is to be corked at once securely and set aside in a cool place. The bottle is to be shaken just before the contents are administered.

Sodium Tellurite. Na_2TeO_3.—*Sodium tellurite* is a white powder sparingly soluble in water. The aqueous 2 per cent. solution of sodium tellurite stains bacteria black by the precipitation of *metallic tellurium*, and has been highly recommended for the purpose of microscopic staining.

Sodium Thiophene Sulphonate. $NaC_4H_3S_2O_3 + H_2O$.—A white powder containing about 33 per cent. of sulphur. It is soluble in water and is used either in a 5 to 10 per cent. solution or ointment in the treatment of *skin diseases*.

Sodium Valerate. *Sodii Valerianas. Sodii Valeras.* C_4H_9COONa.—This salt was dismissed from the U. S. Pharmacopœia in 1870, and from the British Pharmacopœia in 1898. For a process for preparing it, see *U. S. D.*, 19th ed., p. 1654. *Sodium valerate* is a deliquescent, very soluble salt, in snow-white masses, having the disagreeable odor of valeric acid, and a taste at first styptic, but afterwards sweetish. When heated to 140.5° C. (285° F.), it fuses without loss of acid, and upon cooling concretes into a white solid. It is little used medicinally, having been originally introduced into the Dublin Pharmacopœia in 1850 for the sole purpose of forming, by double decomposition, iron, quinine, and zinc valerates. *Dose*, as a nervous stimulant, one to five grains (0.065–0.32 Gm.).

Soja. *Glycine hispida* Maxim. (*Soja hispida* Moench.) *Soy Bean. Soja* or *Sahuca Bean. Miso.* (Fam. *Leguminosæ.*)—*Soja* is an important food plant and forage crop. It is an annual having hairy, trifoliate leaves, inconspicuous, violet-colored flowers, and forms broad legumes containing 2 to 5 seeds. The latter are compressed, spherical and vary from brownish-green to brownish-black. Meissel and Böcker (*A. J. P.*, 1885, 108) give the composition of soja bean as follows: water, 10 per cent.; soluble casein, 30; albumen, 0.5; insoluble casein, 7; fat, 18; cholesterin, etc., 2; dextrin, 10; starch, 5; cellulose, 5; ash, 5; traces of sugar and an amido compound. Stingl and Morawski (*Monatsschrift für Chemie*, April, 1886) have determined the presence in this bean of a ferment said to be one of the most powerful known in its action upon starch, two-thirds of which it converts into sugar and one-third into dextrin. Soja bean has been suggested as a diabetic food, but it contains upwards of 25 per cent. of carbohydrates.

Solanine. $C_{42}H_{75}O_{18}N$.—A physiologically active substance obtained from the sprouts of *Solanum tuberosum* L. (potato), and other *Solanaceæ*. It is classed both as a glucoside (because of its being decomposable into glucose), and also as an alkaloid (because of its basic properties). *Solanine* is in the form of a white, opaque powder, or of delicate acicular crystals, somewhat like those of quinine sulphate, though finer and shorter. It is inodorous, of a bitter taste, fusible at from 112.7° to 115.5° C. (235°–240° F.), decomposing at a slightly higher temperature with an odor of caramel, a sublimate of *solanidine* forming. It is scarcely soluble in water, soluble in alcohol and ether, and capable of neutralizing the acids. It is distinguished by the deep brown or brownish-yellow color which iodine imparts to its solution, and by its reaction with sulphuric acid, which becomes first reddish-yellow, then purplish-violet, then brown, and, lastly, again colorless, with the deposition of a brown powder. This test is said not to be interfered with by the presence of morphine. (*A. J. P.*, 1873, 484.) The salts which solanine forms with acids are mostly amorphous in character. The oxalate, chromate, and phosphate form crystalline crusts. The acid sulphate is said to be very stable, and is not decomposed by water even on heating, in contradistinction to the neutral salt. It is amorphous and very bitter.

The physiological action of solanine is very similar to that of the saponins. Perles (*A. E. P. P.*, 1889, xxvi) found that when mixed with the blood outside of the body it caused rapid coagulation with destruction of the blood corpuscles. In the frog it produced a centric paralysis, with later paralysis of the heart. In mammals it produced excitement, with tremors, followed by central paralysis, collapse, and death in deep coma, preceded by a fall of temperature which is so great as to be almost characteristic. Vomiting and diarrhea were frequently observed, and the urine contained albumin and often hemoglobin. After death inflammation of the gastro-intestinal mucous membranes, and also a parenchymatous and even hemorrhagic nephritis were found. According to Capparoni (*B. G. T.*, May, 1888), minute doses of solanine, while diminishing the rapidity of the heart's action, increase at the same time the arterial pressure.

In the researches of Max Perles, the action of *solanidine* was very similar to that of solanine, the chief difference between the two being that solanine is a violent local irritant, while solanidine seems free from local irritant properties.

Solanine has been used with asserted benefit by Capparoni (*B. G. T.*, May, 1888) and others, as an antispasmodic remedy in *asthma*, *bronchitis* and *cystitis*. It is also attributed with a sedative action on the central nervous system, and has been used by Capparoni in the treatment of ataxic pains. Waugh (*J. A. M. A.*, 1906) asserts that it is of great service in *epilepsy*.

Schmiedeberg (*A. E. P. P.*, 1899, xxxvi, 361) describes an epidemic of solanine poisoning from sprouted potatoes in which the symptoms were headache, colic, vomiting, diarrhea, dilated pupils,

first accelerated, then slowing of the pulse, mental confusion and sometimes unconsciousness.

The *dose* of solanine, as given by different writers, varies widely, probably because of varying degrees of purity of the drug employed.

Waugh states that of the pure alkaloid, the proper *dose* is one-twelfth of a grain (0.005 Gm.), but other writers have given much larger amounts.

Solanum.—The genus *Solanum* contains a number of species which are possessed of active physiological properties and some of which have been used to a considerable extent in medicine.

S. carolinense L. *Horse Nettle. Sand Brier. Poisonous Potato. Apple of Sodom.*—Under the name of *Solanum* the N. F. IV has made the berries of *S. carolinense* official and has introduced fluidextract of solanum made with a menstruum of two volumes of alcohol and one volume of water.

"The air-dried ripe fruit of *Solanum carolinense* Linné (fam. *Solanaceæ*)." *N. F. IV.*

"Globose, slightly depressed, somewhat shriveled and wrinkled in drying, from 0.8 to 2 cm. in diameter, orange-yellow, glabrous, fleshy, two-celled, many-seeded, calyx and pedicel usually persistent; calyx stellate pubescent, deeply five-lobed, the lobes ovate or ovate-lanceolate, acuminate and enclosing half or more of the berry; seeds orbicular, flat, yellow, smooth, shining. Odor pepper-like; taste bitter and acrid.

"Solanum yields not more than 6 per cent. of ash." *N. F. IV.*

This is a coarse perennial weed growing in waste sandy ground in the United States as far west as Iowa and as far south as Florida, and yields an orange-yellow berry which is said to be the most active part of the plant. For study of microscopic structure, see *A. J. P.*, vol. lxix. It has been examined by G. A. Krauss (*A. J. P.*, 1890, 601, and 1891, 65 and 216) and Harry Kahn (*A. J. P.*, 1891, 126). Krauss found two active principles corresponding probably to *solanine*, $C_{42}H_{75}NO_{15}$, and *solanidine*, $C_{41}H_{71}NO_2$, together with a characteristic organic acid to which he gives the name *solanic acid*. J. U. Lloyd believes that the alkaloid in this plant is not identical with solanine, and proposes to call it *solnine*. (*A. J. P.*, 1894, 61, and 1897, 76, 89, 108.) E. Q. Thornton (*T. G.*, xii, 1896) finds that in frogs this solanum produces stupor with tetanic spasms, not prevented by section of the cord. It is said to have long been used by the negroes of the South in the treatment of the so-called falling sickness, and in 1889 it was recommended by J. L. Napier as of value in *epilepsy*. H. C. Wood has found that, although when given by itself its usefulness is very limited, as an adjuvant to the bromides it lessens the size of the doses necessary to keep the convulsions in check. Not less than a fluidrachm (3.75 mils) of the fluidextract should be given three times a day. No unpleasant effects have been produced by it. The N. F. recognizes a fluidextract (see Part III).

S. aculeatissimum Jacq., known as *Apple of Sodom*, is indigenous to Brazil; the fruit yields traces of *solanine*.

S. bacciferum (?), of Jamaica, yields the so-called *Susumber berries*, which are habitually used as fruit by the natives, but Manners has recorded in the *Ed. M. J.*, 1867, fatal poisoning by these berries, death being preceded by dilated pupils and collapse. It is probable, however, that the berries were not true susumber berries but were the product of some other species of solanum.

S. Chenopodium F. Muell.—In this plant, which is a native of Queensland, C. E. Sage has found the alkaloid *solanine*. According to E. B. Ormerod the plant is useful in the treatment of *dysentery*. (*P. J.*, lxviii, 1902.)

Under the English title *Bittersweet* the *N. F. IV* recognizes "The dried stems and branches of *Solanum Dulcamara* Linné (Fam. *Solanaceæ*)." N. F. The Latin title is *Dulcamara*, the synonyms *Stipites Dulcamaræ*, *Tiges de Douce-amère* (*de Morelle grimpante*), *Douce amère*, Fr. *Bittersüss*, *Bittersüss-Stengel*, *Alpranken*, G. *Dulcamara*. *Dulcamara* is a climbing shrub with a woody branching stem and purplish, cymose flowers, with lemon-yellow anthers. The bright scarlet berries remain after the falling of the leaves. The plant grows in wet places and around dwellings and is common to Europe and North America, and in the United States grows from New England to Ohio. All portions of the plant are very active. Fatal results from the eating of the berries by a child have been recorded. (*P. J.*, 1861.) For medicinal purposes the plant should be gathered in the autumn after the fall of the leaf, and the extreme twigs should be selected. That grown in high and dry situations is said to be the best.

It is described in the N. F. as "In short sections about 5 mm. or less in thickness, cylindraceous, somewhat angular, longitudinally striate, more or less warty, usually hollow in the center; bark thin, externally pale greenish, or light greenish-brown, glabrous, marked with alternate leaf scars, internally green, the greenish or yellowish wood occurring in one or two concentric rings. Odor slight; taste bitter, afterwards sweet.

"The powder is greenish-yellow and, when examined under the microscope, exhibits tracheæ up to 0.05 mm. in diameter and with bordered pores; lignified wood fibers with few pores; non-lignified bast fibers with walls up to 0.02 mm. in thickness; fragments of cork cells; few, simple, unicellular hairs up to 0.8 mm. in length, and with the lumina distinct in the lower portions only; few starch grains, spheroidal, up to 0.012 mm. in diameter; sphenoidal crystals of calcium oxalate numerous, up to 0.007 mm. in length.

"Bittersweet yields not more than 6 per cent. of ash." *N. F. IV.*

The dried twigs are inodorous, though the stalk in the recent state emits, when bruised, a peculiar, rather nauseous odor. Their taste, which is at first bitter and afterwards sweetish, have given origin to the name of the plant.

Boiling water extracts all their virtues. These are supposed to depend, at least in part, upon the alkaloid *solanine*. Wittstein (1852) supposed another alkaloid, *dulcamarine*, to be present, but Geissler (1875) showed that this substance was a glucoside, and not an alkaloid, yielding on decomposition with dilute acids *dulcamaretin* and sugar. He assigned the formula $C_{22}H_{34}O_{10}$ to dulcamarine, and $C_{16}H_{26}O_6$ to dulcamaretin. (Flückiger, *Pharmacopgraphia*, 2d ed., p. 451.) (For account of *solanine*, see previous article.) Besides solanine, the stalks of *S. Dulcamara* contain, according to Pfaff, a peculiar principle to which he gave the name of *picroglycion*, indicative of the taste, at once bitter and sweet, which it is said to possess. This was obtained by Blitz, in the following manner: The aqueous extract was treated with alcohol, the tincture evaporated, the residue dissolved in water, the solution precipitated with lead subacetate, the excess of this salt decomposed by hydrogen sulphide, the liquor then evaporated to dryness, and the residue treated

with acetic ether, which yielded the principle in small isolated crystals by spontaneous evaporation. Frederick Davis (*Y. B. P.*, 1902) found the two alkaloids, *solanine* and *solanidine*, the glucoside *solanein*, and the bitter principle *dulcamarin*, in fresh specimens of the plant.

Dulcamara possesses feeble narcotic properties, with the power of increasing the secretions, particularly those of the kidneys and skin. George B. Wood observed, when the system was under its influence, a dark purplish color of the face and hands, and at the same time considerable languor of the circulation. In overdoses it produces nausea, vomiting, faintness, vertigo, and convulsive muscular movements. (*London Med. Gaz.*, 1850.)

Anaphrodisiac properties have been attributed to dulcamara, and it has also been employed with alleged benefit in chronic *rheumatism*. But its chief use has been in the treatment of scaly cutaneous eruptions, such as *lepra*, *psoriasis*, and *pityriasis*. A fluidextract is official in the N. F. (see Part III). Dulcamara may be given in *doses* of from thirty grains to a drachm (2–3.9 Gm.).

D. Freire has obtained from the fruit of *S. grandiflorum*, or wolf fruit, of Brazil, a toxic alkaloid, *grandiflorine*. (*C. R. A. S.*, cv.)

S. Jacquinii Willd. is used in India as a diaphoretic and expectorant.

S. Lycopersicum L. *Tomato Plant* (formerly termed the *Love Apple*).—The tomato is believed by many practitioners to be an injurious article of diet to gouty persons on account of the great acidity of the juice, an acidity which T. D. McElhenie has demonstrated to be due at least in part to citric, malic, and oxalic acids. (*A. J. P.*, 1872.) Solanine is said not to be present in the juice but has been found by George W. Kennedy (*P. J.*, 1873) in the herbaceous part of the plant. It probably also exists in the seeds. (*A. J. P.*, xxxiv.)

S. nigrum L. *Black*, or *Garden*, or *Common Nightshade. Duscle. Hound's Berry. Morelle.*—This is a simple leaved annual plant, growing widely in shaded and rich open ground throughout the United States. The leaves have been used in medicine in the treatment of *scrofulous dyscrasias*, and are said to produce diaphoresis when in overdose; also nausea, purging, and nervous disturbance. The poisonous properties commonly attributed to this plant are, however, to be doubted, since Dunal of Montpellier, states, as the result of numerous experiments, that the berries are not poisonous to man or the inferior animals; and the leaves are said to be consumed in large quantities in the Isles of France and Bourbon and in the Hawaiian Islands by the natives as food, having been previously boiled in water. In the latter case the active principle of the plant may have been extracted by decoction. Introduced by importers under the name of *jurubeba*, this plant was examined by Kobert and found to be inert. According to Peckoldt, however (*Ph. Rund.*, 1889), true jurubeba is *Solanum insidiosum* Mart., from which the results would have been more favorable. It is used in Brazil in *gonorrhea* and *syphilis*.

S. Pseudocapsicum L., or *Jerusalem* or *Winter Cherry*, a plant cultivated for greenhouse or house decoration when covered with its bright colored berries, yields a fruit whose resemblance to the common cherry is said to have led to its being eaten by children with fatal results.

S. rostratum Dunal. *Sand Bur. Buffalo Bur. Beaked Nightshade. Bull Nettle.*—This very prickly plant, which grows on the prairies from Nebraska to Mexico, and is noteworthy as having been the original food of the Colorado beetle or potato bug, has yielded to W. S. Amos an alkaloid. (*Notes on N. R.*, iv.)

Narcotic properties have been attributed to the leaves, stalks and unripe berries of *S. tuberosum* L., or common white potato, and the extract has been used in various diseases. Worsham, of Philadelphia, found the extract, in the quantity of nearly one hundred grains, to cause no sensible effect. (*Phila. Journ. of the Med. and Phys. Sciences*, vi, 22.)

A case is recorded of death in a girl of fourteen, from eating the unripe fruit of the potato. (*B. M. J.*, Sept. 3, 1859.) The prominent symptoms were partial stupor, speechlessness, jactitation, hurried breathing, lividness of the skin, cold sweats, very frequent and feeble pulse, and a constant spitting through the closed teeth of viscid frothy phlegm.

It is probable that the properties of the plant vary with the stage of growth, or with the place and circumstances of culture. C. Haaf found solanine in old potatoes which had begun to germinate, in the proportion of 0.16 in 500 parts, and in very young potatoes, deprived of their coating, precisely the same quantity. Fully ripe potatoes, which had not begun to sprout, gave a negative result. (*N. R. Pharm.*, 1864, p. 559.) Solanine has also been found in the germs of potatoes by Schmiedeberg. (*A. E. P. P.*, 1899, xxxvi, 361.)

Solidago. *Golden-rod. Verge d'Or*, Fr. *Goldruthe*, G.—There are very numerous species of this composite genus in the United States. Of these *S. odora* Ait., or the *Sweet Golden-rod*, was formerly official. *S. Virgaurea* L. [now *S. Raudii* (Porter) Britton], which occurs on dry or granitic soil in the northern United States and Europe, was formerly directed by the Dublin College. It is aromatic, astringent, in hot infusion diaphoretic, and is asserted to be diuretic. (*Rev. Gén. de Clin. et de Thérap.*, 1889.) For a study of the flowers of *S. bicolor* L., by Adam Conrath, see *A. J. P.*, 1873, 253. For an analysis of *S. rugosa* Mill., see *A. J. P.*, 1893, 122.

Soluble Mercury of Hahnemann. $NH_2(Hg_2)NO_3$.—This is prepared by adding, drop by drop, a diluted solution of ammonia to an equally diluted solution of mercurous nitrate, until the precipitate begins to be paler than at first. It is a black powder. When it has a gray color, the fact shows that too much ammonia has been employed in its precipitation. In this case $NH_2(Hg_2)NO_3$ yields $NH_2(Hg)NO_3 + Hg$. This preparation was included in the old French Codex. It has been used in *syphilitic* diseases.

Solurol. *Hyminic Acid. Nucleotinphosphoric Acid.* $C_{30}H_{46}N_4O_{15}.2P_2O_5$.—A yellow amorphous powder, easily soluble in water. It is used as an uric acid solvent in *gout*, *rheumatism* and similar affections. *Dose*, four to eight grains (0.25–0.5 Gm.).

Solution of Chlorinated Potassa. *Liquor Potassæ Chlorinatæ. Chlorure de Potasse*, Fr. *Chlorkalilösung*, G. *Javelle's Water. Eau de Javelle.*—This is prepared from potassium carbonate precisely as the solution of chlorinated soda is from sodium carbonate, and has an analogous composition. (See *Liquor Sodæ Chlorinatæ*, p. 655.) It is employed for taking out fruit stains, etc., from linen.

Solution of Dialyzed Iron. *Liquor Ferri Dialysatus. Liquor Ferri Oxychlorati*, P. G.—*Dialyzed solution of iron* was formerly recognized by the Br. Ph. It is made by treating a solution of ferric chloride with ammonia, whereby ferric hydroxide is precipitated, which by agitation is dissolved, placing the thick liquid in a dialyzer, and suspending this in water, which is to be constantly renewed so long as any traces of hydrochloric acid are found in it. The following process has been used in the United States: To one hundred parts of solution of ferric chloride, sp. gr. 1.26, thirty-five parts of ammonia water, sp. gr. 0.923, may be gradually added. The precipitate which almost immediately forms is redissolved, and the solution introduced into the dialyzer, which is then suspended upon the water, contained in a suitable vessel. When the water in the outer vessel ceases to produce a precipitate with silver nitrate, or to show an acid reaction, the preparation in the inner vessel is assayed by evaporating 10 mils to dryness on a water bath, to ascertain the amount of ferric oxychloride in solution; then the final solution is diluted so that it shall contain 10 per cent. of dry oxychloride.

Dialyzed iron is a colloidal solution of *ferric oxychloride* in water. The solution is of a transparent reddish-brown color, free from the usual astringent, styptic taste of iron preparations. It mixes in all proportions with distilled water, alcohol, syrup, and glycerin, but water containing any saline impurity is apt to cause precipitation. When gelatinization occurs, agitation with a small quantity of solution of ferric chloride will usually restore it to fluidity, care being observed not to add an excess. Contact with the alkalies should be avoided, even in minute quantity; indeed, it is best administered without addition of any kind, or simply diluted with distilled water.

The British Pharmacopœia formerly directed that its specific gravity should be 1.047, and "100 grains should afford a precipitate with a solution of ammonia which, washed, dried and ignited, weighs five grains." E. B. Shuttleworth (*Can. Pharm. Journ.*, Dec., 1877) recommends a solution which has the sp. gr. 1.040 and yielding 5 per cent. of residue when well dried on a water bath as the best for medicinal use. The specific gravity test can be relied upon, if the solution does not give a precipitate with silver nitrate or become of a blackish-blue color upon treatment with tannin, showing the absence of free ferric chloride. (See also *N. R.*, 1879, 46, for a new process by F. Schneider, from *S. W. P.*, 1878, 409.) There is good reason for believing that much of the so-called dialyzed iron formerly found in commerce was made by adding freshly precipitated ferric hydroxide to solution of ferric chloride until it ceased to be dissolved and then filtering the solution. (Scheffer, *A. J. P.*, March, 1878.) *Ferrum catalyticum*, or *catalytic iron*, used on the Continent, is probably made in this way.

Solution of dialyzed iron has been very highly praised as a ferruginous tonic free from astringency. It is capable of acting as an antidote to arsenic by virtue of the readiness with which it yields hydrated ferric oxide, but it is safer to depend upon the official antidote, ferric hydroxide with magnesium oxide (see p. 470). *Dose*, from one-half to one fluidrachm (1.3–3.75 mils).

Solution of Magnesium Bisulphite. *Liquor Magnesii Bisulphitis.*—George Archibald, having found that magnesium bisulphite is capable of arresting the butyric acid fermentation, proposed a solution of it as a remedy in *heartburn*. He prepared it by treating the magnesium carbonate with sulphurous acid, adding to an ounce of water sixteen grains of the sulphite thus formed, and passing sulphurous acid gas through the mixture until a clear solution is obtained. (*P. J.*, 3d series, ii, 502.)

Solutol.—An alkaline solution of sodium cresol in an excess of cresol. It is a transparent brownish liquid, miscible with water, and is used for disinfecting purposes.

Solveol.—A solution of sodium-cresylate in cresol. It is less caustic than solutol, is nearly odorless, of a neutral reaction, and miscible with water. It is used as surgical antiseptic, for dressings, and in spray apparatus.

Somatose.—This is an artificially digested meat albumin containing 51.6 per cent. of deutero- and 13.4 per cent. of hetero-albuminoses, 5 per cent. of peptone, 1 per cent. of moisture, and 5 per cent. of nutrient salts. A yellowish, odorless, and almost tasteless powder.

Iron Somatose is a similar preparation containing 2 per cent. of iron in combination.

Milk Somatose is a soluble nutrient prepared by the same digestive process from casein, containing 5 per cent. of tannin. It is a light yellowish powder, readily soluble in water.

Somnoform.—A proprietary anesthetic said to contain ethyl chloride 60 per cent., methyl chloride 35 per cent., ethyl bromide 5 per cent. Of late it has come into wide use in dental anesthesia, due to its thorough, yet fleeting action. While it has been stated that it possesses no unpleasant after-effects when properly administered, the numerous cases where stomachic disturbances have arisen after its use would lead one to doubt this statement. (For a study of its physiological action, see *B. M. J.*, 1903, 1.)

Sonatin.—This is a solution of benzoyl acid ($C_6H_5COC_6H_4COO$) in castor oil intended as a cheap and efficient substitute for the expensive balsam of Peru. It is claimed to be the equal of the latter in the treatment of many *skin diseases* where the balsam is indicated.

Sonchus. *Sonchus oleraceus* L. *Common Sow Thistle.* (Fam. *Compositæ.*)—A coarse weed, having runcinate-pinnatifid leaves clasping by a heart-shaped base and producing corymbs of pale yellow flowers in summer and autumn. This European plant is commonly found in waste places around dwellings in the United States. The brownish gum left after the evaporation of the juice of this plant is said to be a powerful hydragogue cathartic, in *doses* of from two to four grains (0.13–0.26 Gm.). Combined with aromatics or belladonna, it may be used instead of elaterium in *dropsy*. (*Med. Bull.*, July, 1888.) It has also been used as a so-called cure for the opium habit. (*Pac. Pharm.*, 1908, 113.)

Soot. *Fuligo Ligni.*—This well-known substance has a peculiar odor, and a bitter, empyreumatic, and disagreeable taste. Its composition varies according to the source and conditions of its formation. When obtained by the combustion of resinous materials it may contain oily distillation products soluble in ether; when obtained by the combustion of wood it may contain pyroligneous (acetic) acid and products peculiar to wood tar, such as creosote, guaiacol, and phenola. Of course mineral substances from the ash of the wood may also be present.

Soot was formerly official with the Edinburgh

College, and the Scotch physicians prescribed it as a tonic and antispasmodic. It has also been employed as an external remedy in skin diseases. (See *B. G. T.*, 1834; also 14th ed., *U. S. D.*) A few shovelfuls of it, thrown into privies or drains, effectually destroy their foul exhalations.

Sophora. *S. speciosa* Benth. *Coral Bean.*—From the poisonous seeds of this leguminous Texan tree, H. C. Wood obtained a volatile liquid alkaloid (*sophorine*) whose chloride is crystalline (see *A. J. P.*, 1878), and which, according to P. C. Plugge, is identical with cytisine. This same alkaloid probably exists in many species of the genus, as Parsons found a liquid alkaloid in *S. sericea* Nutt., *crazy-weed*, which grows in Colorado and Mexico (*Rep. Commissioner of Agricult.*, 1879, and *N. R.*, 1881, 67; see also Kalteyer and Neill, *A. J. P.*, 1866, 465), and Greshoff (*P. J.*, xxii). The latter found a poisonous alkaloid in the leaves of *S. tomentosa* L., the seeds and roots of which are used in Ceylon and Java as a remedy for *cholera*. Plugge, however (*A. Pharm.*, 1895), affirms that *matrine*, the alkaloid discovered by Nagai in *S. angustifolia*, is distinct from cytisine.

Sorbus. *Sorbus Aucuparia* L. (Now *Pyrus Aucuparia* (L.) Erhr.) *Mountain Ash. Rowan Tree. Sorbes*, Fr. *Eberesche, Vogelbeere*, G. (Fam. *Rosaceæ*.)—A small European tree extensively cultivated in the United States and becoming naturalized. Its fruit contains a peculiar kind of sugar called *sorbinose*, $C_6H_{12}O_6$, isomeric with levulose. It reduces Fehling's solution, but is not fermentable with yeast. Hofmann has also discovered two news acids, which he designates as *sorbic* and *parasorbic acids*, $C_6H_8O_2$. Sorbic acid forms colorless needle-like crystals fusing at 134.5° C. (274° F.), while parasorbic acid is a lactone-like body, which, on heating with concentrated acids or solid alkali, changes into sorbic acid. M. J. Boussingault has found in it a crystalline saccharine principle, *sorbitol*, isomeric with mannitol, melting, when anhydrous, at from 110° to 111° C. (230°–231.8° F.), when hydrated, at 102° C. (215.6° F.). Its formula is $C_6H_{14}O_6$. It does not undergo the vinous fermentation. (*P. J.*, 1872, 28.) The seeds of the fruit contain 22 per cent. of fixed oil. The fruit has been used in *scurvy*, and in infusion, as a remedy in *hemorrhoids* and *strangury*. All parts of the tree are astringent, and may be employed in tanning and dyeing black. *S. americana* Marsh. (now *Pyrus americana* (Marsh.) DC.), or *American Mountain Ash*, probably has similar virtues to the European species. Edwin Johanson found the fruit to yield from 4.92 to 6.6 per cent. of malic acid. (*Ph. Z. R.*, i, 1882.)

Sorghum.—A cane-like plant resembling Indian corn, from which it is distinguished by producing large heads of small grains. There are a number of varieties and these are usually distinguished as "saccharine" sorghums and "non-saccharine" sorghums. The former contain a sugary sap and are referred to *Andropogon arundinaceus* var. *saccharatus*. The latter are commonly known as *broom corn* or *Kaffir corn* and are varieties of *A. arundinaceus* var. *Durrha*. The saccharine sorghums are cultivated in the United States to some extent as a forage crop. They are not used in the manufacture of sugar, owing to the difficulty of effecting its crystallization. Broom corn has been cultivated in the United States since 1798 and is especially adapted to the manufacturer of brooms and brushes. In some of the semi-arid districts of the West it is reported that cattle have been poisoned from eating of the green sorghum, usually of a second growth. This is apparently due to the production of hydrocyanic acid in the leaves.

Sozal. *Aluminum Paraphenolsulphonate.* $(C_6H_4(OH)SO_3)6Al_2$.—This is obtained by dissolving aluminum hydrate in paraphenolsulphonic acid, or by double decomposition of aluminum sulphate and barium paraphenolsulphonate. It occurs in brownish crystalline grains having a weak phenol odor, but strongly astringent taste; easily soluble in water, glycerin, and alcohol, forming permanent solutions. It has been used as an antiseptic in place of iodoform. (*Ph. Ztg.*, 1892.)

Sozoiodolic Acid. *Sozoiodol. Diiodparaphenolsulphonic Acid, Crystalline.* $C_6H_2I_2(SO_3H)OH + 1\frac{1}{2}H_2O$.—This is a white glistening powder, odorless, of slightly acid taste, slightly soluble in cold water, more easily in hot water. It is decomposed on heating to 200° C. (392° F.), giving off violet vapors. It contains about 53 per cent. of iodine. It can be recognized by heating, or by adding sulphuric acid to it in hot solution, when iodine separates. Ferric chloride imparts a dark violet color to the aqueous solution; silver nitrate throws down a white precipitate of silver soziodol completely soluble in diluted nitric or sulphuric acid. For an outline of the process of manufacture, see *Squibb's Ephem.*, Feb., 1893. Soziodol is used as a local remedy, resembling somewhat iodoform in its range of usefulness. According to Langaard, 2 per cent. is sufficient to kill bacteria of pus; for wounds, a 10 per cent. mixture with powdered talc is advocated. Lassar praises it in *eczema, herpes tonsurans, impetigo*, etc.; it has also been much used in *otitis* and *rhinitis*. Langaard has found that fifteen-grain doses have no appreciable effect upon rabbits, and Bufalini gave twenty-two grains a day in *phthisis* without unpleasant effect. The soziodolates have also been called by the proprietary name of *Ronozol salts*. The following salts have been used:

Potassium sozoiodol, sparingly soluble; a desiccant indicated in *eczema*. It is usually employed with talc in the proportion of 1: 5 or 1: 6. *Zinc sozoiodol*, a local irritant in solutions of from 1: 20 to 1: 50; a caustic, in a solution of 1: 5. *Mercury sozoiodol*, a caustic, even in a solution of 1: 10. Miller affirms that its solution of 2½ per cent. kills the acarus of *scabies* in twenty-four minutes. It has been used as an antisyphilitic in *doses* of one grain (0.065 Gm.).

Schwarz recommends pills, each containing one-third of a grain of sozoiodol mercury and one-fifteenth of a grain of powdered opium. (*Th. M.*, 1908, 299.)

Sodium Sozoiodolate (*sodium soziodol*) occurs as colorless, inodorous, crystalline needles, soluble in about fifteen parts of water, also soluble in alcohol or glycerin. The finely powdered substance mixed with equal parts of sulphur is employed by insufflation in treating *diphtheria, laryngitis, nasal tuberculosis*, etc. It is also used in a 2 to 5 per cent. solution as an antiseptic douche or wash in *gonorrhea*.

Sozolic Acid. *Acidum Sozolicum. Orthophenolsulphonic Acid.* $C_6H_4(SO_3H)OH$.—Ortho and paraphenolsulphonic acids are both formed when phenol is dissolved in concentrated sulphuric acid; at medium temperatures the former is far more abundant, but it readily passes into the para compound on the application of heat. Sozolic acid has a very faint odor of phenol. It is readily soluble in water, alcohol, and glycerin, and is used so diluted as to contain from 3 to 10 per

cent. of the active principle. The orthophenolsulphonic acid in 33⅓ per cent. solution has received the trade name of *aseptol*. The ortho acid changes on heating into the isomeric paraphenolsulphonic acid, and this change takes place even in the aqueous solution of the former, a fact which should be remembered in the preparation of aseptol solutions.

E. Riegler (*W. M. Bl.*, xviii, 1895) proposes aseptol as a test for albumin in urine. One part in 20,000 causes coagulation; the precipitate with albumin does not disappear with heat. The solutions of albuminose and peptones are also precipitated, but the precipitates of these disappear with heat. The solution of aseptol undergoes decomposition when exposed to light.

Schiff and Beilstein asserted that phenolsulphonic acid acts like tannic and gallic acids, precipitating albumen and alkaloids, and being capable of replacing gallic acid in the making of leather and in pharmacy. There is, however, no sufficient reason for believing that the substance can be used in medicine in the place of the vegetable acids named. It has also been asserted that phenolsulphonic acid is a powerful antiseptic, but in a careful series of comparative experiments, F. A. Tucker (*Notes on New Remedies*, 1892) found that it had not more than one-third the antiseptic power of phenol.

Spartium. *Spartium junceum* L. *Spanish Broom.* (Fam. *Leguminosæ.*)—A small shrub, indigenous in the south of Europe, and cultivated in our gardens as an ornamental plant. The flowers are large, yellow, and of an agreeable odor. Spanish broom, in its medicinal properties closely resembles *Scoparius*, but appears to be from five to six times more active, 6 Gm. of the dried plant, given in infusion, having produced very violent poisoning; serious results have been produced by the substitution of the Spanish for the true broom. The dried flowers are readily differentiated, those of the *true broom* having a small, bell-shaped calyx with two unequal lobes, the upper of which is bidentate, the lower minutely tridentate, and the style always rolled, while in *Spartium junceum* the calyx is deeply cleft to the base on one side only, and the style is deeply rolled.

The symptoms produced by overdoses are vomiting and purging, with renal irritation. The seeds have been used to a considerable extent in *dropsy* in *doses* of from ten to fifteen grains (0.65–1.0 Gm.) three times a day in the form of tincture.

Sphæranthus. *Sphæranthus indicus* L. (Fam. *Compositæ.*)—An herbaceous plant having winged stems and widely distributed in Africa, Asia and Australia. It is used as a general tonic, deobstruent, alterative, and aphrodisiac, under the names of *Mundi Gorakhmundi*, *Murmuria*, and *Kottakkarandai*. Dymock has found it in a deep cherry-colored essential oil.

Spider Poisons.—The popular belief that certain spiders have the power of poisoning small animals, and even man, has received confirmation, and an active principle, *arachnolysin*, has been separated by Sachs and found to have a powerful hemolytic action upon the blood of rabbits and cats but not to affect dogs and guinea-pigs. (See Kobert, *Giftspinnen*, 1901; *S. Jb.*, Bd. 274, 178.)

Spilanthes. *Spilanthes Acmella* Murr. (*S. oleracea* L.) *Para Cress. Cresson de Para*, Fr. *Parakresse*, G. (Fam. *Compositæ.*)—A plant of India, used as a masticatory for *toothache;* when chewed it produces a copious salivation. (*A. J. P.*, xliv, 323.)

Spiracin. *Methyl-carboxyl-salicylic Acid.*—It forms a white crystalline powder, insoluble in water. It is used for the same purposes as the salicylates in *doses* of ten to fifteen grains (0.6–1 Gm.).

Spiræa.—Many if not all of the species of this genus contain a colorless volatile oil, very similar to the oil of gaultheria, but composed mainly of salicylic aldehyde, with only smaller amounts of methyl salicylate. The species which have been submitted to actual analysis are the *Spiræa Ulmaria* L. (*Filipendula Ulmaria* (L.) Maxim.), commonly known as *Queen of the Meadow*, or *Meadow-sweet*—a European plant which has been introduced into this country; also the European species *S. lobata* Jacq. and the species *S. Filipendula* L. (*Filipendula vulgaris* Moench.), which grows in Southern Europe and Northern Africa. A yellow, crystalline powder of a bitter taste, insoluble in water, slightly so in alcohol, readily soluble in ether, and having an acid reaction. *Spiræic acid* (now recognized as salicylic acid) (*J. Pr. Chem.*, xix) was separated from the flowers of *S. Ulmaria* by Löwig and Weidmann, and has been found by Rochebrune in the flowers of *S. Filipendula* L.

The roots of probably most of the species contain tannic acid, gallic acid, and when fresh some of the volatile oils. (*A. J. P.*, 1887.) The root of *Spiræa tomentosa* L. (*Hardhack, Steeplebush*, or *Whitecap*), was formerly recognized in the U. S. Pharmacopœia. It is an indigenous shrub growing in low grounds from New Brunswick and Nova Scotia to the mountains of Georgia and westward. The stems and lower surfaces of the ovate-lanceolate, serrate leaves are whitish and tomentose. The rose-colored flowers are disposed in terminal, compound, crowded spikes or racemes.

The flowers of *Spiræa* possess to a very feeble extent the medicinal virtues of salicylic acid, and have been used as diuretic and tonic in the form of decoction. The roots are astringent, and have been used in the treatment of *diarrhea* in *doses* of from five to twenty grains (0.32–1.3 Gm.) of the aqueous extract repeated *pro re nata*.

Spiroform. *Vesipyrin. Acetyl Salol. Acetylphenyl-o-oxybenzoic Acid. Acetyl Salicylic Phenyl Ester.* $C_6H_4(OCH_3CO)COOC_6H_5$.—A tasteless, odorless powder, insoluble in water, readily decomposed by alkalies. This substance acts in the body much like phenyl salicylate; it passes through the stomach unchanged, but is broken up in the intestines, liberating salicylic acid. It was originally introduced as a urinary antiseptic, but has also been employed as an antirheumatic and analgesic. The *dose* is from eight to fifteen grains (0.5–1.0 Gm.).

Spirosal. *N. N. R.* 1917. *Mono-glycol Salicylate.* $C_6H_4OH.CO.O(CH_2.CH_2.OH)$.—It occurs as an almost colorless and odorless liquid, freely miscible with alcohol, and with eight parts of olive oil. It has been brought forward as a means of administering salicylic acid endermically. According to Schoenheim (*Med. Klin.*, 1907) it is more rapidly absorbed through the skin than the other preparations of salicylic acid intended for percutaneous absorption, and a number of clinicians have reported favorably upon its application in various forms of *rheumatism*. It has also been suggested for the treatment of *furunculosis* of the external auditory canal. It is applied either un-

diluted, or mixed with equal parts of alcohol, about a drachm at a *dose*, well rubbed into the skin, and then covered with impermeable dressing.

Sponge. *Spongia. Spongia officinalis. Eponge*, Fr. *Schwamm. Badeschwamm*, G.—The sponge is "a flexible, fixed, torpid, polymorphous animal, composed either of reticular fibers or masses of small spires interwoven together, and clothed with a gelatinous flesh, full of small mouths on its surface, by which it absorbs and ejects water." Until recently sponges were classified as colonial *Protozoa*, the lowest group of animals, but they are now brought under a separate phylum known as *Porifera* (or *Spongiaria*) a name applied to them because of their abundance of water pores. The latter are of two kinds, both opening into the digestive canals and ramifying passages of the sponge. Some of these are large, but most of them are small, being in the nature of inhalent pores or inlets for admitting the water. The current through these pores is a constant one which is induced by countless flagella which occur in definite enlargements on the canals and known as ciliated chambers. This current contains the minute organisms which are carried to the digestive cavities and upon which the animal feeds. Through these canals oxygen is distributed, the waste matters eliminated and fertilization of the eggs is effected. Sponges inhabit the bottom of the sea, where they are fixed to rocks or other solid bodies, and are most abundant within the tropics. They are collected chiefly in the Mediterranean and Red Seas, the West Indies and the coast of Florida and Central America. In the Grecian Archipelago, Crete, Cyprus, on the coast of Asia Minor, Syria, Barbary and the Bahama Islands, sponge fisheries constitute a very important industry. Formerly most of the sponges used in the United States were brought from the Mediterranean waters, but since 1852 the Bahamas and the coast of Florida have furnished much of the commercial supply. When collected they are enveloped in a gelatinous coating, which forms part of the animal. For details of fishery and preparation, see *P. J.*, xx. Large quantities of the coarser kinds are imported from the Bahamas, but the finest and most esteemed are brought from the Mediterranean, especially from the coast of Syria. Recently the cultivation of sponges has been undertaken on an extensive scale. Small fragments are cut under water from the live sponge, and fixed upon a sandy bottom by means of skewers. In three years they will have grown sufficiently to be marketable.

Sponge, as found in commerce, is in yellowish-brown masses of various shapes and sizes, light, porous, elastic, and composed of fine, flexible, tenacious fibers, interwoven in the form of cells and meshes. It usually contains numerous minute fragments of coral or stone, or small shells, from which it must be freed before it can be used for ordinary purposes. Sponge is prepared by macerating it for several days in cold water, beating it in order to break up the concretions which it contains, and dissolving what cannot thus be separated of the calcareous matter by hydrochloric acid diluted with thirty parts of water. By this process it is rendered perfectly soft, and fit for surgical use. It may be bleached by steeping it in water impregnated with sulphurous acid, or by exposure in a moist state to the action of chlorine. It is stated that sponges which have been soaked in pus and infectious matters will recover their primitive condition by soaking in a 4 per cent. solution of potassium permanganate, then in a 25 per cent. solution of official sulphurous acid, and finally thorough washing in an abundance of water. (*A. J. P.*, xliv, 355.) When intended for surgical purposes, the softest, finest, and most elastic sponges should be selected; for forming *burnt sponge* the coarser will answer equally well. According to Hatchett, the chemical constituents of sponge are gelatin, coagulated albumin, common salt, and calcium carbonate. Magnesia, silica, iron, sulphur, and phosphorus have been detected in it, as also iodine and bromine, combined with sodium and potassium. From the experiments of Croockewit, it would appear that sponge is closely analogous to, if not identical with, the *fibroïn* and *sericin* of silk, differing from it only in containing iodine, sulphur, and phosphorus. (*Ann. Ch. Ph.*, xlviii, 43.) Schlossberger, however, has shown that it is distinct, in its very slight solubility in ammoniacal solution of copper hydroxide and in its yielding leucine and glycocoll when treated with diluted sulphuric acid, while sericin yields under similar treatment tyrosine and serin. He names the principle *spongin*.

Sponges are used for mechanical purposes only. *Sponge tent* is employed for dilating sinuses. This is prepared by dipping sponge into melted wax, compressing it between two flat surfaces till the wax hardens, and then cutting it into pieces of a proper form and size. By the heat of the body the wax becomes soft, and the sponge, expanding by the imbibition of moisture, gradually dilates the wound or sinus in which it may be placed. When a conical sponge tent of uniform caliber is required, as for dilating the uterine cavity, a better plan is to cut the sponge into a conical shape while fresh and compress when moist, by winding it carefully with a fine tightly drawn cord, removing the cord when perfectly dry, and dipping the tent into melted wax, so as to get a thick coating. For other modes of preparing sponge tent, as well as of saturating the sponge at the same time with substances calculated to make a remedial impression, as phenol, alum, lead acetate, etc., see *A. J. P.*, 1868, 410; 1869, 446.

Spongia Usta, *Burnt Sponge*, was formerly official (*Spongia Usta*, U. S. 1850), but is no longer used in medicine. For method of preparation, analysis, and therapeutic properties, see 16th edition, *U. S. D.*

Statice. *Statice Limonium* (L.) Gray. [Now *Limonium carolinianum* (Walt.) Britt.] *Marsh Rosemary. Ink Root. Sea Lavender. Romarin des Marais, Lavande triste*, Fr. *Strandnelke*, G. (Fam. *Plumbaginaceæ.*)—It is an indigenous maritime plant with a perennial, very astringent, root, sending up annually tufts of leaves, which are obovate or cuneiform, entire, obtuse mucronate, smooth, and on long foot-stalks.

Marsh rosemary grows in the salt marshes along the sea coast from Labrador to Texas, and flowers from July to September. The root, which was formerly in the Secondary List of the U. S. Pharmacopœia, is large, spindle-shaped, or branched, fleshy, compact, rough, and of a purplish-brown color. It is bitter and extremely astringent, but odorless. It contains tannic acid (12.4 per cent.), volatile oil, resin, and other substances. (*A. J. P.*, xiv, 116.) *Statice* is powerfully astringent, and in some parts of the United States, particularly in New England, is much employed, especially as a local application, in de-

coction, to aphthous and ulcerative affections of the mouth and fauces.

In Brazil and Buenos Ayres the roots of *S. brasiliensis* Boiss. are employed under the name of *Buaycura* or *Guaycura*. (*P. J.*, 1878, ix, 466.) For a description of the physical and chemical characteristics of the root, see *P. J.*, vol. xv, 86. In Russia and Spain the very large roots of *S. latifolia* Sm. are used for tanning, and in Morocco the roots of *S. mucronata* L. are stated to be employed, under the name of *safrifa*, as a nervine.

Steresol.—An antiseptic varnish made by dissolving purified shellac 270 parts, benzoin 10 parts, balsam of Tolu 10 parts, phenol in crystals 100 parts, oil of cinnamon 6 parts, saccharin 6 parts, in sufficient alcohol to make 1000 parts. It permits of asepsis of mucous surfaces, and is adapted for use where it is impossible to apply bandages.

Sterisol. *Steriosol.*—According to Aufrecht, this liquid contains formaldehyde, sodium chloride, potassium phosphate, sugar of milk, and water. It is used as an antiseptic.

Sticta. *Lungmoss. Lungwort.*—The lichen *Sticta pulmonaceæ*, a native of Europe, used largely by the natives in the treatment of *pulmonary complaints*. It owes its activity chiefly to *stictic acid*, which is bitter and possesses a powerful astringent action.

Stipa.—According to Gillespie (*B. M. J.*, Oct., 1898), a number of species of this genus of grasses are actively poisonous, and have caused death in horses and other domestic animals. Of such character especially are *Stipa viridula* Trin., *Stipa inebrians* Hance, and *Stipa sibirica* Lam., of the Russian steppes. A few experiments made with *Stipa viridula* Trin., a plant growing in the prairies and meadows from western Minnesota to the Dakotas and southernward, indicated that it acts powerfully upon the brain and spinal cord.

Stipa Vaseyi Scribner.—According to Vernon Bailey this grass, which grows on the mountains of California, is a very active narcotic, producing in animals, which graze upon it, sleep lasting for a week or longer. (See Farwell, *Merck's Rep.*, 1911, p. 271.)

Stovaine. *N. N. R.* 1917. *Amylene AB. Hydrochloride.* (*Hydrochloride of Benzoyl-dimethylamino-propanol*, $CH_3CH_2C(C_6H_5COO)(CH_3)CH_2N(CH_3)_2HCl$.—It is closely related to alypin (see page 1239). It crystallizes in small, brilliant scales, melting at 175° C. (347° F.), and is very soluble in water. It shows most of the reactions of cocaine, which is also a benzoyl derivative.

This substance which has been advertised by methods approaching that employed by the mountebank has been used as a local anesthetic especially for the production of the so-called *spinal anesthesia* by a very large number of surgeons. In the experiments of LeBrocq (*B. M. J.*, March 27, 1909) it was found that if the toxicity of cocaine represented 1 that of stovaine would be 0.625 and that of eucaine 0.414; in other words it stands midway between cocaine and eucaine in danger. He also found that it was locally irritant, its injection being followed by intense hyperemia and even local sloughing. As confirmatory of this local irritant effect are the changes which have been found in the spinal cord from its lumbar injection. Pauterier and Simon (*Bull. Hop. Par.*, 1907) report a case of meningitis following spinal anesthesia with the agent and Spiller and Leopold (*J. A. M. A.*, 1910, liv, p. 1840) caused intense degeneration of the posterior columns of the cord by repeated injections in the lower animals. In 1907 Chaput (*Press. Med.*, 1907) collected statistics of 3174 spinal anesthesias with stovaine with six deaths, mortality of about one in 530. In the same year, however, Torrance collected 5532 cases with but 3 deaths. It is evident that the mortality of spinal anesthesia from stovaine is higher than that of general anesthesia with ether or chloroform. Schwarz (*Cb. C.*, 1907) reported signs of renal irritation in 78 per cent. of cases anesthetized by this method, but Hosemann (*Cb. C.*, 1908, xxxv, 60), in a series of sixty cases, noted mild irritation of the kidney in only ten cases, in none of which was there permanent injury.

As a local anesthetic stovaine has the advantage over cocaine of being somewhat less toxic, of not dilating the pupil or causing vascular constriction, and of withstanding boiling temperatures. Weight for weight, it is probably the most powerful anesthetic of all the cocaine substitutes, according to LeBrocq, surpassing even cocaine itself. For local anesthesia it is generally employed in a 1 per cent. solution of which sixteen to fifty minims (1–3 mils) may be injected, according to the size of the area it is desired to render insensible. For spinal anesthesia it is recommended to be used in strengths of from 3 to 10 per cent., injecting a quantity of this solution equivalent to from 0.032 to 0.065 Gm. of the drug.

Strontium Acetate. $Sr(C_2H_3O_2)_2 + \frac{1}{2}H_2O$.—This is a white crystalline powder, soluble in water. It is said to possess anthelmintic properties. It is given in *doses* of from ten to thirty grains (0.65–2.0 Gm.) twice a day.

Strontium Arsenite. $Sr(AsO_2)_2 + 4H_2O$.—A white powder soluble in water. It possesses the therapeutic virtues of arsenic, but has no advantages over the official preparation. The *dose* is from one-thirtieth to one-fifteenth of a grain (0.002–0.004 Gm.).

Strontium Carbonate. *N. F. IV. Strontii Carbonas.*

"It contains, when dried to constant weight at 100° C., not less than 99 per cent. of $SrCO_3$ (147.62)." *N. F.*

"Strontium Carbonate occurs as a white powder, odorless and tasteless. It is insoluble in water; dissolved with effervescence by diluted hydrochloric, nitric, or acetic acid; the addition of diluted sulphuric acid to these solutions produces a white precipitate. One Gm. of the salt yields a clear, or not more than slightly turbid, solution, with 10 mils of diluted hydrochloric acid (*sulphate*). A solution of 0.1 Gm. of the salt in 10 mils of distilled water made with the aid of nitric acid does not immediately become more than slightly opalescent on adding silver nitrate T.S. (*chloride*). Dissolve 1 Gm. of Strontium Carbonate in distilled water with the aid of a slight excess of acetic acid, dilute to 100 mils and to 10 mils of this solution add 5 drops of potassium dichromate T.S.; no turbidity develops within five minutes (*barium*). Shake 2 Gm. of the salt with 25 mils of distilled water, filter, evaporate the filtrate and dry the residue at 100° C.; it weighs not more than 0.01 Gm. (*soluble substances*). A solution of the salt in a slight excess of diluted hydrochloric acid does not respond to the Test for heavy metals.

"*Assay.*—Dissolve about 1.5 Gm. of Strontium Carbonate, dried to constant weight at 100° C. and accurately weighed, in 30 mils of normal

hydrochloric acid V.S. and titrate the excess of acid with normal sodium hydroxide V.S., using methyl orange T.S. as indicator. It shows in the dried salt not less than 99 per cent. of $SrCO_3$.

"Each mil of normal hydrochloric acid V.S. consumed is equivalent to 0.07381 Gm. of $SrCO_3$. Each gramme of Strontium Carbonate requires not less than 13.4 mils of normal hydrochloric acid V.S." *N. F.*

It is not used medicinally, but was introduced into the N. F. for the preparation of the compound elixir of formates.

Strontium Lactate. *Strontii Lactas. U. S.* 1890. $Sr(C_3H_5O_3)_2.3H_2O = 319.76$.—This salt may be prepared by the process of Thumann. (See *U. S. D.*, 19th ed., p. 1661.) *Strontium lactate* is "a white, granular powder, or crystalline nodules, odorless, and having a slightly bitter, saline taste; permanent in the air. Soluble in about 4 parts of water at 15° C. (59° F.), and in less than 0.5 part of boiling water. The solution saturated at a boiling heat remains liquid for many hours, even after being cooled to 0° C. (32° F.). Soluble in alcohol. When heated to 110° C. (230° F.), the salt loses its water (16.9 per cent.). At a higher temperature it first fuses, then is decomposed, giving off inflammable vapors, and leaves a residue of strontium carbonate and carbon, which, on the addition of hydrochloric acid, effervesces and communicates an intense, red color to a nonluminous flame. The aqueous solution (1 in 20) is slightly acid to litmus paper." *U. S.*, 1890. It gives the characteristic reactions of the soluble salts of strontium and the lactates. The absence of barium may be shown by potassium dichromate T.S., which should produce no turbidity. For further tests of purity, see *U. S. D.*, 19th ed., p. 1662.

Uses.—Strontium lactate was originally brought forward by J. V. Laborde, who found it to have a distinct diuretic action. His researches led to clinical studies of the drug by German Sée, Paul, Dujardin-Beaumetz, and others. It is asserted that strontium lactate is an extremely successful remedy in the treatment of *nephritis* and chronic *albuminuria*, the urine being increased, the albumin lessened or entirely removed, and the genéral nutrition improved. The experiments, however, of Wood and Arnold (*Phila. Monthly Med. Journ.*, April, 1899) have shown that only infinitesimal amounts of the drug are absorbed from the intestines. Upon the intestinal canal the lactate is asserted to exert a very favorable influence. Strontium lactate has also been tried with alleged good results in the treatment of *rheumatism* and *gout*, it being affirmed that it increases the nitrogenous elimination and causes disappearance of the urates. *Dose*, from ten to thirty grains (0.65–2.0 Gm.) three times a day in solution.

Strontium Phosphate. $Sr_3(PO_4)_2$.—A white, tasteless powder, soluble with decomposition in acids. Nutritive and tonic. It is used in the treatment of *phthisis* and other wasting diseases, as a tissue builder, asserted to be superior to calcium phosphate. (Labordé.) *Dose*, ten to thirty grains (0.6–2.0 Gm.).

Strontium Sulphide. *Strontii Sulphidum.* SrS.—This substance has been used to some extent as a depilatory, in accordance with the following method: A powder of 2 parts strontium sulphide, 3 parts of zinc oxide, and 3 parts of powdered starch, kept dry until used, is formed into a paste with warm water and allowed to remain upon the surface from which the hair is to be removed from one to five minutes, being taken off so soon as pronounced pain or any evidences of caustic action are perceptible. The surface should then be gently but firmly scraped with a blunt edge like that of a paper knife, then washed well with warm water, and treated with an emollient.

Strychnine Arsenate. *Strychninæ Arsenas.*—*Strychnine arsenate* has been introduced as a means of obtaining the effects of its constituents. It is especially praised by Coriveaud (*K. T. W.*, 1909) in the treatment of *bronchial asthma* and other pectoral complaints. The *dose* is one sixty-fourth of a grain, increased to one-fifteenth (0.001–0.004 Gm.). (*W. M. Bl.*, Sept., 1886.)

Strychnine Glycerophosphate. *N. F. IV. Strychninæ Glycerophosphas. Strychnine Glycerinophosphate.*—This strychnine salt was introduced into the N. F. IV to be used in making the compound elixir of glycerophosphates.

"The glycerophosphate $[(C_{21}H_{22}O_2N_2)_2PO_4H_2(C_3H_7O_2) + 6H_2O = 948.60]$ of the alkaloid strychnine. Preserve it in well-stoppered bottles." *N. F.*

"Strychnine Glycerophosphate occurs in white, rhombic crystals or as a white powder; odorless; having at first a faint, sweet taste, afterward becoming intensely bitter. One gramme dissolves in about 350 mils of water, the solution being neutral or slightly alkaline to litmus; also in about 310 mils of alcohol; slightly soluble in chloroform, and very slightly soluble in ether. On incinerating 0.2 Gm. of the salt it yields no weighable residue. The addition of sulphuric acid to the salt produces no color, or at most only a slight yellowish coloration, but on subsequently adding a fragment of potassium dichromate a deep blue color is obtained, which changes to deep violet, then to purplish-red, cherry-red and finally to orange or yellow. Add ammonia water in slight excess to a saturated aqueous solution of the salt; a white precipitate is formed which is readily soluble in chloroform. A saturated aqueous solution of the salt, acidulated with diluted nitric acid, is not rendered more than faintly turbid on the addition of silver nitrate T.S. (*chloride*). A saturated aqueous solution of the salt, acidulated with hydrochloric acid, shows not more than a slight turbidity on the addition of barium chloride T.S. (*sulphate*). Add a slight excess of ammonia water to an aqueous solution of the salt and filter the mixture; the filtrate shows not more than a slight turbidity with magnesia mixture T.S. (*phosphate*)." *N. F.*

It has no advantages medicinally over other strychnine salts.

Strychnine Valerate. *N. F. IV. Strychninæ Valeras.*—This salt was introduced into the National Formulary to be used in elixir of strychnine valerate, a preparation of doubtful utility since the amount of valeric acid present can have no useful therapeutic action in a teaspoonful *dose* which contains only one-hundredth of a grain of the strychnine valerate and the latter contains only two-thirds of its weight of strychnine.

"The valerate $[C_{21}H_{22}O_2N_2.HC_5H_9O_2 = 436.28]$ of the alkaloid strychnine. Preserve it in well-stoppered, amber-colored vials." *N. F.*

"Strychnine Valerate occurs as a white crystalline powder, having an odor of valeric acid and an intensely bitter taste. It is sparingly soluble in water, becoming less soluble on keeping, through the loss of valeric acid; soluble in alcohol or chloroform; slightly soluble in ether. Its saturated

aqueous solution is neutral or slightly alkaline to litmus. Dissolve about 0.05 Gm. of Strychnine Valerate in 2 mils of sulphuric acid; no more than a faint yellowish color appears, but on adding a fragment of potassium dichromate a deep violet color is produced which changes to orange or yellow. When sulphuric acid is added to the salt, the odor of valeric acid is evolved. Incinerate 1 Gm. of Strychnine Valerate; the ash does not exceed 0.1 per cent. Ten mil portions of an aqueous solution of the salt (1 in 100) are not affected at once by barium chloride T.S. when acidulated with hydrochloric acid (*sulphate*) nor by silver nitrate T.S. when acidulated with nitric acid (*chloride*). About 0.02 Gm. of the salt, moistened with nitric acid, may be colored yellow, but not red or reddish (*brucine*)." *N. F.*

The average *dose* of strychnine valerate is given as one-fortieth of a grain (0.0015 Gm.).

Strychnos Potatorum L. *Chilbinj. Clearing Nuts. Indian Gum Nuts.* (Fam. *Loganiaceæ.*)—The nuts of this species of *Strychnos* are very largely used in some parts of India for clearing muddy water, and are stated to have found their way into American commerce. (*A. J. P.*, 1871.) The fruit is also employed by the native practitioners of Hindostan, under the name of *nirmali*, as an emetic and in *dysentery*. They do not contain strychnine. In clearing water, one of the dried nuts is rubbed hard for a short time around the inside of the earthen water pot; on settling, the water is left pure and tasteless. The seeds contain a large quantity of an albuminous principle, upon which their virtues probably depend. The tree, which grows to a very large size, produces a shining, black, one-seeded berry (that of the nux vomica being many-seeded). The seeds are described (*P. J.*, 1871, 44) as broadly lenticular, about half an inch in diameter and a quarter of an inch in thickness, of a dirty whitish-gray color, and covered with a thick coating of delicate appressed hairs. These are so small that the seed to the naked eye looks mealy. Under the microscope the hairs are seen to be agglutinated in groups of from three to six, and to consist each of a single pointed cylindrical cell.

Stylophorum. *Stylophorum diphyllum* (Michx.) Nuttall. (Fam. *Papaveraceæ.*)—This plant, commonly known as "*Celandine Poppy*," is found in damp woods from western Pennsylvania to Wisconsin and Tennessee. In its foliage and flowers it resembles *Chelidonium majus*. According to E. Schmidt, the root contains *chelidonine*, with a second alkaloid closely related to, if not identical with, *chelerythrine*. (*A. J. P.*, 1888.)

Styptic Collodion. *N. F. IV* (*U. S. P. VIII*). *Collodium Hæmostaticum, Styptic Colloid, Xylostyptic Ether. Collodion styptique, Collodion au tannin*, Fr.; *Tannin-Kollodium*, G. (See under *Collodium Stypticum*, Part III.)—When applied on wounded or abraded surfaces, it soon loses the ether and alcohol, and a firm coating is left, in which, besides the tannin and colloidal substances, are the coagulated blood and secretions from the surface, forming a covering for the part by which the air is excluded. The liquid is applied with a camel's hair brush, or by means of cotton saturated with it, to the edges of the wounds closed by stitches, to ulcerated surfaces, and bleeding parts. If it be desired to make a special impression on the diseased surface, phenol, creosote, iodine, morphine, etc., may be incorporated with the styptic fluid.

Styptic Colloid (Carbolized).—In this preparation advantage is taken of the antiseptic and styptic properties of phenol, and a very effective hæmostatic results. It is made by adding ten per cent. of phenol to styptic collodion.

Stylosanthes. *Stylosanthes biflora* (L.) B. S. P. (Fam. *Leguminosæ.*)—This low, branching perennial has wiry stems, 3-foliate leaves and small yellow flowers. It is found in the pine barrens of the Eastern and Central United States and it is asserted that it possesses the power of relieving abdominal uterine pains during the latter months of gestation, and is also a uterine tonic during parturition. *Dose*, of the fluidextract, from ten to twenty minims (0.6–1.3 mils) three times a day.

Styrone. *Cinnamic Alcohol. Styryl Alcohol.* $C_6H_5.CH : CH.CH_2.OH$.—A *beta-phenyl-allyl alcohol* appearing either as an aromatic oily fluid, boiling at 250° C. (482° F.), or a crystalline solid, forming white needles soluble in alcohol and fusing at 25° to 30° C. (77°–86° F.). The fluid is used in *otitis media* and the crystals as a deodorant and antiseptic either in the dry form or in a glycerin solution.

Subcutin.—This compound of paraphenolsulphonic acid with paramido-benzoic acid has been brought forward by Ritsert as non-toxic, distinctly germicidal, and locally anesthetic. It is a white, crystalline powder, soluble to the extent of 1 per cent. in cold water, and two and one-half per cent. in tepid water. For hypodermic use to this solution is added about 1 per cent. of ordinary salt. It is stated that it is especially adapted to the production of infiltration anesthesia.

Sublamine. *Hydrargyri Sulphas Æthylenediaminata. N. N. R.* 1917. $HgSO_4.2C_2H_4(NH_2) + 2H_2O$.—This is a white powder, soluble in water, composed of one molecule of mercuric sulphate and two molecules of ethylenediamine, and contains about 43 per cent. of mercury. It was originally brought forward as a non-irritant germicide of exceptional penetrative power, and especially useful for the purpose of disinfecting the hands and skin; used in solution varying from 1 to 1000 up to 1 to 200. It has also been highly commended in 1 to 300 for sterilizing suture silk by boiling.

Sublamine has also been employed to some extent for the hypodermic administration of mercury; it is affirmed by Schuftan, when given hypodermically, to be more active than corrosive sublimate, probably because it does not coagulate albumin. It is incompatible with sodium chloride and should not be exposed to the air.

Sublimo-Phenol. *Phenolated Mercuric Chloride. Chloro-phenolate of Mercury.*—Colorless crystals produced by precipitation when solutions of mercuric chloride and potassium phenolate are mixed. It is easily soluble in fused phenol or boiling aqueous or alcoholic solutions of phenol. It is used in antiseptic surgery.

Succinic Acid. *Acidum Succinicum. Sal Succini Volatile. Acide succinique*, Fr. *Bernsteinsäure*, G. $H_2C_4H_4O_4$.—This acid is obtained by distilling amber. The product is an aqueous solution of *succinic acid*, associated with empyreumatic oil. (See *Amber* and *Oil of Amber*, page 1239.) By filtering the liquor the solution of the impure acid passes through, while the oil is absorbed by the paper. The acid may be purified by boiling the solution with nitric acid, diluted with twice its bulk of water, and then evaporating to crystallize: should the crystals not be colorless, the treatment with nitric acid must be repeated until they are so. Succinic acid is made artificially by the action of nitric acid on the fatty acids, and

may be produced in a great many ways from various substances. Thus, it is invariably formed in small amount in the alcoholic fermentation of sugar. Desaignes obtained it more advantageously from calcium malate subjected to fermentation excited by casein. The malate was converted into calcium succinate, which was then decomposed by sulphuric acid, so as to yield succinic acid. For the details of the process for obtaining succinic acid from calcium malate, see the paper of E. J. Kohl, in *A. J. P.*, vol. xxviii, July. Succinic acid, when pure, is in white, transparent crystals having no odor and a somewhat acrid taste. It dissolves in five times its weight of cold and twice its weight of boiling water. It is less soluble in alcohol and very sparingly so in ether. Nitric acid is without action on it. It melts at 182° C. (359.6° F.), and boils without alteration at 235° C. (455° F.). It sublimes, however, at a much lower temperature. According to Wackenroder, it is sometimes adulterated with tartaric acid soaked in oil of amber. Succinic acid, though formerly official, is at present seldom used in medicine. It has been ascertained to be a product of vital action, having been detected by Heintz in the colorless liquid found in hydatid cysts of the liver. (See *J. P. C.*, Sept., 1850.) One of its salts, *ammonium succinate*, $(NH_4)_2C_4H_4O_4$, made by supersaturating succinic acid with ammonia, evaporating and crystallizing, has been used with alleged great success in *delirium tremens*. This salt is occasionally used as a precipitant of ferric oxide. For a description of *sodium succinate*, see page 1616.

Succus Pomorum. *N. F. IV. Fresh Apple Juice.*—"The freshly expressed juice of sound, ripe, sour apples, the fruit of cultivated varieties of *Pyrus Malus* Linné (Fam. *Rosaceæ*)." *N. F. IV.* Fresh apple juice is used in making the N. F. *Ferrated Extract of Apples.*

Sucramine.—This substance, which has been exploited in France as a new sweetening agent, is said to be simply the ammonium salt of saccharin.

Sulfogenol.—Crude mineral oil obtained from a bituminous shale, by dry distillation, is saturated with sulphur and sulphonated by means of strong sulphuric acid. *Sulfogenol* is the ammonium compound of this sulphonated product. It possesses the same properties as ichthyol, but with a less disagreeable odor and taste, and is soluble in water and alcohol.

Sulfosote. *Potassium creosotic-sulphonate*, or a mixture of *guaiacol- and cresol-sulphonates of potassium.*—Under its proprietary name, *sulfosote* is supplied in the form of a syrup, of which the *dose* is said to be, for the adult, three fluidrachms (11.25 mils). It has been used in various forms of pulmonic disease for the treatment of which creosote is advisable.

Sulphaldehyde. *Thioaldehyde. Thioacetaldehyde.*—It is made by the action of hydrogen sulphide upon acetaldehyde in aqueous solution. An oil is obtained which solidifies at low temperatures. According to Lusini (*Nouv. Rem.*, 1890), this substance acts on the lower animals as a powerful hypnotic.

Sulphaminic Acid. *Amido-sulphonic Acid.* NH_2SO_2OH.—This occurs as colorless crystals, freely soluble in water. Emmerich (*M. M. W.*, 1912), on the theory that the irritant toxin of *cholera* is nitrous acid, recommended the use of *sulphaminic acid* in the treatment of this disease. A tablespoonful of a one per cent. solution may be given every hour.

Sulphaminol. $C_6H_4\langle{}^{S_2}_{NH}\rangle C_6H_3.OH$. *Thio-oxydiphenylamine.*—This compound is made by the action of sulphur upon the salt of metaoxydiphenylamine. It is a greenish-yellow powder free from odor and taste, readily soluble in alkalies, more difficultly so in alkaline carbonates, quite insoluble in water. When heated it turns brown, and melts at 155° C. (311° F.). It is asserted that this substance is harmless (see a paper by Kobert, *Journ. de Méd.*, Sept., 1890), and that when taken internally it is split up in the organism into oxydiphenylamine and sulphuric acid compounds. It has been used as an antiseptic dusting powder. Various compound solutions of it have been employed as local applications to the mucous membranes of the nose and larynx, such as *sulphaminol menthol, s. eucalyptol*, etc. Internally, it has been given in *doses* of from four to five grains (0.26–0.32 Gm.); externally, it may be used in powder or oily solutions.

Sulphanilic Acid. *N. N. R.* 1917. $C_6H_4(NH)_2(HSO_3)$ 1 : 4. *Para-amino-benzene-sulphonic Acid.*—It occurs as colorless crystals, slightly soluble in water and insoluble in alcohol and ether and efflorescent in the air. Internally it has been recommended in the treatment of chronic *catarrh* in *doses* of 10 to 30 grains (0.6–2.0 Gm.), although it is of doubtful value. Its most important use is in Ehrlich's diazo-reaction for typhoid urine. Under the name of *Nizin*, tablets containing 0.13 gramme of sulphanilate of zinc are marketed and asserted to possess both astringent and antiseptic properties.

Sulphoform. *Triphenylstibine Sulphide.* $(C_6H_5)_3SbS$.—According to Kaufmann (*Ber. d. Chem. Ges.*, 1908, xli), this compound liberates its sulphur with extreme ease; hydrogen dioxide causes a separation of the sulphur and oxidization to sulphuric acid, and the antimony being oxidized to antimony oxide which combines with the sulphuric acid, this reaction taking place almost quantitatively at a temperature of 36° C. (96.8° F.). He states that *sulphoform* is more than one hundred times as efficacious as ordinary sulphur as a reducing agent. Joseph (*Derm. Cb.*, 1910, xiv) has found it a very useful remedy for *seborrheic alopecia*, and also of service in *eczema* and other *skin diseases*. He uses an ointment containing from five to twenty per cent. of sulphoform.

Sulpholeic Acid and Sulpholeates.—Sulpholeates or salts produced by the combination of alkalies with sulpholeic acid, have come into use on account of their ability to dissolve many substances or hold them in suspension as emulsifying agents. Sulpholeic acid is prepared as follows: Castor, almond or other fixed oil is gradually mixed with 30 or 40 parts of concentrated sulphuric acid, the mixture being cooled, if necessary, with ice, to prevent a rise of temperature above 50° C. (122° F.). The reaction, which at first is quite violent, is allowed to go on for from six to twelve hours, after which the mixture of acid and glycerin is decanted, the residue mixed with 100 parts of water, and this, after stirring, is also decanted. The resulting sulpholeic acid is converted into *alkaline sulpholeate* by the addition of a hydroxide or carbonate of the required alkali. From this combination pure sulpholeic acid is obtained by careful decomposition with sulphuric acid, and agitation with purified benzin or ether, which leaves the acid on evaporation pure and anhydrous. (*Ph. Rund.*, 1885, p. 154.) According to A. Mueller Jacobs, when concentrated and in as pure a state as possible, the sulpholeates, as

well as the free sulpho-acids themselves, mix readily and completely with a great variety of organic compounds, for instance with liquid hydrocarbons, particularly those of low boiling point, with chlorine, iodine, and bromine derivatives of the same, with ethers and alcohols, with organic sulphur compounds, such as carbon disulphide, oil of mustard, mercaptan, etc., and with all essential oils. They also dissolve varying quantities of sulphur, iodorform, solid hydrocarbons, such as naphthalene, naphthol, anthracene, and paraffin, the terpenes and camphenes. These liquid mixtures of sulpholeates and other bodies have the property of forming emulsions or even clear solutions with water. The limit of the miscibility (in form of emulsion) or solubility varies considerably, and depends both on the degree of concentration of the sulpholeate serving as a menstruum, and on certain little understood properties of the substances mixed with it.

This peculiar behavior of the sulpholeates and particularly of the sulpho-ricinoleate of alkalies, towards many otherwise insoluble or difficultly soluble substances, as well as their pronounced saponaceous character and the great readiness with which they take up and combine with liquids, is said to render them eminently suitable for various technical and medicinal uses.

The liquid alkaline salt which forms the solvent is termed *polysolve* by A. Mueller Jacobs, who believes that the sulpholeate mixtures will be found excellent solvents for substances the employment of which in a concentrated condition is accompanied by certain untoward effects, or may serve as vehicles in place of vaseline, oils, glycerin, etc., in perfumery, soap making or pharmacy. (*Am. Drug.*, 1884, p. 22.)

Sulphopyrine. *Antipyrine para-aminobenzene-sulphonate. Antipyrine Sulphanilate.*—It is a white, crystalline powder, without odor, readily soluble in water, insoluble in alcohol. Although originally introduced as a substitute for antipyrine, Neumann (*All. W. M. Z.*, 1906, p. 813) has found that this drug has the power of preventing the appearance of that congery of symptoms commonly known as *iodism*. It is also used in *coryza*. The *dose* he employed was fifteen grains (1 Gm.) three times a day.

Sulphoid. *Sulfidal. Colloidal Sulphur.*—It is made by passing hydrogen sulphide through a solution of sulphurous acid and has been used in the treatment of various *skin diseases* as a substitute for the ordinary form of sulphur. According to Joseph (*Derm. Ob.*, 1907), it is distinctly superior to the insoluble forms of sulphur. In *acne* he employed a paste or ointment containing 10 per cent. of *sulphoid* and 2 per cent. of salicylic acid, in *alopecia seborrheacia* and *eczema squamosum* a 10 per cent. solution in water either with or without glycerin.

Sulphur Iodide. *Sulphuris Iodidum. U. S. VIII, Br.* 1898. *Sulfur Iodatum. Ioduretum Sulfuris. Iodure de Soufre*, Fr. *Jodschwefel*, G.—This compound is chemically regarded as *iodine disulphide*, I_2S_2, or, as sometimes stated, *sulphur subiodide*. *Sulphur iodide* is in "brittle masses of a crystalline fracture and a grayish-black, metallic luster, having the odor of iodine and a somewhat acrid taste. Almost insoluble in water; soluble in about 60 parts of glycerin; very soluble in carbon disulphide. Alcohol, ether, and a solution of potassium iodide dissolve the iodine, leaving the sulphur. Continued boiling with water vaporizes all of the iodine, leaving about 20 per cent. of sulphur as residue. On exposing Sulphur Iodide to the air, it gradually loses iodine. On heating it, some iodine sublimes at first; at a somewhat higher temperature a sublimate is formed, containing both iodine and sulphur. At a still higher temperature, the whole is volatilized, leaving only a trace of residue. If 0.5 Gm. of finely pulverized Sulphur Iodide, together with 1 Gm. of potassium iodide, be dissolved in 20 mils of water (the sulphur separating), not less than 28 mils of tenth-normal sodium thiosulphate V.S. should be required for complete decolorization of the mixture, using starch T.S. as indicator." *U. S. VIII.*

The process of the U. S. VIII of the U. S. Pharmacopœia for this salt was as follows: "Washed Sulphur, *twenty grammes* [or 308 grains]; Iodine, *eighty grammes* [or 2 ounces av., 360 grains]. Mix the Sulphur and Iodine thoroughly by trituration; introduce the mixture into a flask, close the orifice loosely, and, by means of a water-bath, gradually and with occasional agitation apply a heat not exceeding 60° C. (140° F.), until the ingredients combine and become of a uniformly dark color throughout. Then increase the heat to the boiling point of the water, so as to fuse the mass. Should any Iodine have sublimed and condensed on the glass, incline the flask so as to combine the Iodine with the fused mass, and then pour the latter upon a porcelain plate or other suitable cold surface. When it is cold break the product into pieces of suitable size, and keep them in a glass-stoppered bottle, in a cool place." *U. S. VIII.*

Its solution in glycerin would probably prove useful, in some cases, as a substitute for the ointment of this iodide. It is rapidly decomposed, when in a state of powder, upon the addition of several of the volatile oils, violet vapors of iodine being evolved, and the odor of sulphur perceived. Sulphur iodide has been very usefully employed as an external remedy in various skin diseases, such as *tinea capitis, lupus, lepra*, etc., applied in the form of ointment. *Ointment of sulphur iodide*, formerly official in the British Pharmacopœia, was made by mixing together 1 part of sulphur iodide, one part of glycerin and 23 parts of benzoinated lard. Internally, it has been used with alleged advantage in human *glanders*. (Bourdon, of Paris, *Ann. Thér.*, 1858, 239.)

Sulphoricinic Acid.—This is made by the action of from 30 to 40 per cent. sulphuric acid upon castor oil at a temperature not exceeding 50° C. (122° F.), care being taken to avoid the evolution of sulphur dioxide. On the addition of water, sulphoricinic acid with unchanged oil separates in an oily layer from the aqueous solution of acid below. This substance is a powerful local irritant. Berliox states that the acid and its soluble salts are actively antiseptic and deodorizant; useful as a local application in *ozena* and other affections. (*S. M.*, March 11, 1891.) *Sodium sulphoricinate* is described on page 1616. The commercial product made by the action of strong sulphuric acid upon castor oil is known as *Turkey Red Oil*, and is used as a hydrolizing agent in the manufacture of fatty acids and glycerin from fixed oils by the so-called Twitchell process.

Sulphosalicylic Acid. *Salicyl-sulphonic Acid.* $C_6H_3SO_3H.OH.COOH$.—Made by acting upon salicylic acid with strong sulphuric acid. It is in the form of white acicular crystals, soluble in water and alcohol. *Sulphosalicylic acid* is used, like sodium salicylate, in rheumatism, but its chief value lies in its use as a reagent to detect the

presence of proteids of all kinds. Egg-albumin (1 in 12,500) can be detected by this reagent, forming a dense, white precipitate which is not redissolved on boiling. It is used to detect albumin, peptones, globulins and fibrin. Albumoses and peptones redissolve when boiled, but again separate on cooling.

Sweet Pellitory.—The root of *Tanacetum umbelliferum* Boiss. (Fam. *Compositæ*), of India, according to David Hooper, contains pyrethrine in minute proportions with fat and wax, an organic acid which is a pigment, glucose, and inulin. (*P. J.*, xxi, 1890.)

Swietenia. *Swietenia febrifuga* Roxb. (*Soymida febrifuga* Juss.) *Rohan Bark.* (Fam. *Meliaceæ.*)—The bark of this East Indian tree contains a bitter principle and is said to be much used as an antiperiodic in half drachm (2 Gm.) *doses*. The extract is used in *dysentery* like kino.

Swietenia Mahogoni Jacq., or *mahogany tree*, which grows in the West Indies and other parts of tropical America, has also a bitter, astringent bark, containing catechin. (*Bull. Soc. Chim. Paris*, xxiv, 118.) The oil of the seeds is said to be used as a purgative in the West Indies. The bark of *S. senegalensis* Desv. (*Khaya senegalensis* A. Juss.), *Juribali bark*, is used on the coast of Africa in the cure of *intermittents*, and Caventou extracted an alkaloid from it. (*Am. J. M. S.*, N. S., xx, 168.)

Symphorol. *Symphoral. Sodium, Lithium*, or *Strontium Caffeine-sulphonates.*—The name *symphorol* is applied to either of the salts above mentioned. They are colorless, odorless, bitter powders. The sodium salt is used as a diuretic in *doses* of fifteen grains (1 Gm.) several times a day.

Symphytum. *Symphytum officinale* L. *Comfrey. Blackwort. Briussewort. Radix Symphiti. Radix Consolidæ Majoris. Consoude*, Fr. *Schwarzwurz, Beinwurz*, G.—A perennial, European plant often cultivated. Its root is spindle-shaped, branched, often more than 2.5 cm. thick and 3 dm. long, externally smooth and blackish, internally white, fleshy, and juicy. By drying it becomes wrinkled, of a firm, horny consistence, and of a dark color within. It is almost inodorous, and has a mucilaginous, feebly astringent taste. Titherley and Coppin in 1912 found 0.8 per cent. of *allantoin*, $C_4H_6N_4O_3$, in the rhizome. It contains mucilage in great abundance (according to Lewis, more than althæa root), and a little tannin. It was formerly highly esteemed as a vulnerary. According to Macalister (*B. M. J.*, Jan. 6, 1912), *allantoin*, in aqueous solution in strengths of 0.3 per cent. has a powerful action in hastening epithelial formation, and is a valuable remedy not only in external ulceration, but also in *ulcers of the stomach* and duodenum. Comfrey is a demulcent, and is used domestically in *chronic catarrhs, consumption*, and other lung diseases.

Symplocos. *Symplocos racemosa* Roxb. (Fam. *Styraceæ.*)—The bark of this East Indian tree is said to be a mild astringent, and especially useful in *menorrhagia*. (*P. J.*, Sept. 24, 1881.)

Synanthrose. *Lævulin.* $C_6H_{10}O_5$.—This is a carbohydrate, isomeric with inulin, discovered by O. Popp in *Helianthus tuberosus* L. (fam. *Compositæ*). For details, see Tollens, *Kohlenhydrate*, 198.

Syringa. *Syringa vulgaris* L. *Common Lilac.* (Fam. *Oleaceæ.*)—The leaves and fruit of this common garden plant have a bitter and somewhat acrid taste, and have been used as tonics and antiperiodics. Petroz and Robinet found in the fruit a sweet and a bitter principle. The latter was afterwards obtained pure by Meillet, who gave it the name of *lilacin*, and by Bernays, who called it *syringin*. It has been investigated by Kromayer (*A. Pharm.* (2), cxiii, 19), who established its glucosidal character, gave it the formula $C_{17}H_{24}O_9 + H_2O$, and showed it identity with the *ligustrin* of Polex. It forms long, white, stellate needles, which are tasteless, easily soluble in hot water and alcohol, insoluble in ether. The crystals become anhydrous at 115° C. (239° F.), and fuse at 212° C. (413.6° F.). As an antipyretic and antiperiodic drug it is said to be very valuable, especially when administered in the relapsing fevers of *malaria*. On heating with dilute acids its breaks up into *syringenin*, $C_{11}H_{14}O_4$, and a fermentable glucose. The *syringenin* (which has been recognized as *oxymethyl coniferin*) is a light, rose-red amorphous mass, soluble in alcohol, insoluble in water and ether.

Syrup of Ferrous Bromide. *Syrupus Ferri Bromidi, U. S.* 1880. *Syrup of Bromide of Iron.*—"A syrupy liquid containing 10 per cent. of Ferrous Bromide. It is made from bromine and iron by a process analogous to that for syrup of ferrous iodide. Ferrous bromide has been recommended as a sedative chalybeate tonic, and has been especially praised by Jacob Da Costa in *chorea*. In an extended trial of it by H. C. Wood, it failed entirely to be of service. It is not an eligible chalybeate. *Dose*, of the syrup, from one-half to one fluidrachm (1.8–3.75 mils), equal to about four to eight grains of the bromide.

Tacamahac. *Tacamahaca.*—These names are applied to a resinous substance which is sometimes substituted for or admixed with Elemi resin. There are two classes of these products: (1) one having an odor resembling Elemi and including the *East Indian Tacamahac* which is probably obtained from *Calophyllum Inophyllum* L. (Fam. *Guttiferæ*), and *Bourbon Tacamahac*, obtained probably from *C. Tacamahaca* Willd. The West Indian and East Indian *Resin Anime* is a product of one of the Burseraceæ; (2) a second class having an odor of incense and including *Cayenne Incense*, obtained probably from *Icica heptaphylla* Aubl. (now *Protium heptaphyllum* March. (Fam. *Burseraceæ*), a West Indian Tacamahac obtained from *Protium heptaphyllum* and related species. There are also several gums and resins of this same character which are obtained from *Bursera gummifera* L. and other plants of the Burseraceæ. The resinous substance derived from *Bursera tomentosa* Triana, a tree of considerable size, of the Fam. *Burseraceæ*, growing in the island of Curaçoa and in Venezuela, is in irregularly shaped pieces of various sizes. The color is usually light yellowish or reddish-brown, but in the larger masses is more or less diversified. The pieces are in general translucent, though frequently covered with powder upon their surface, so as to render them apparently opaque. They are heavier than water, brittle, and pulverizable, yielding a pale yellow powder. Their odor is resinous and agreeable, their taste bitter, balsamic, and somewhat acrid. Exposed to heat, they melt and exhale a stronger odor. Tacamahac is partially soluble in alcohol, and completely so in ether and the fixed oils. It consists of resin with a little volatile oil.

The East Indian tacamahac and called *tacamahaca orientale*, or *tacamahaca in testis*, comes into the market in gourd shells covered with rush leaves. It is of a pale yellow color inclining to green, slightly translucent, soft, and adhesive, of an

agreeable odor, and an aromatic bitterish taste. It is at present very rare in commerce. The tree which yields this resin produces a drupe, about as large as a plum, from the seeds of which 50 per cent. of a greenish-yellow fixed oil is obtained by expression, which is used in India for lamps, and as a local application in the *itch*. (*J. P. C.*, 1861, 23.) Guibourt describes several other varieties of tacamahac, which, however, are little known. Among them is a soft, adhesive, dark, green oleoresin (*J. P. C.*, 3e sér., xxiv, 396), said to be procured from the *Calophyllum Tacamahaca* Willd., growing in the islands of Réunion and Madagascar. (See also Pennetier, *Matières Premières*, 642.)

Tacamahac was formerly highly esteemed as an internal remedy, but is now used only in ointments and plasters. Its properties are analogous to those of the turpentines. It is sometimes used as incense.

Tachia. *Tachia guianensis* Aubl.—The root of this tree (Fam. *Gentianaceæ*), is used under the name of *Caferana*, in Brazil, as an antiperiodic and tonic. According to Peckoldt it contains an organic, crystalline substance, *caferanine*. (See *Merck's Bericht*, 1889; also *Ber. d. Chem. Ges.*, 1899, No. 7.)

Taka Diastase.—This ferment discovered by Takamine is formed by the action of a fungus (*Moyashi; Aspergillus Oryzæ* Cohn., *Eurotium Oryzæ* Ahlburg; for description, see *A. J. P.*, 1898, 137) upon steamed rice, and is used in Japan, where it is known by the name of *koji*, in the preparation of the national intoxicating beverage *sake*. It has also been employed to act upon maize in the making of whisky. It is a yellowish-white, highly hygroscopic powder, almost tasteless, freely soluble in water. It is capable, under proper conditions, of converting one hundred times its weight of starch in ten minutes into glucose. Its action and therapeutic uses are the same as those of diastase from malt. (See p. 403.) It should be given in the middle of the meal, in *doses* of from five to ten grains (0.32–0.65 Gm.), in capsules; or, after the meal, in slightly alkaline solution.

Tamaquare.—A fluid preparation from a Brazilian Myrospermum, which is miscible with alcohol, does not dry and possesses an unctuous consistency. It is used in certain diseases of the eye, petrolatum being used as the vehicle. From a three to a ten per cent. ointment is the usual strength.

Tanformal.—This is claimed to be a chemical combination of tannin, phenol, and formaldehyde. It forms an aromatic, brown powder, insoluble in water and decomposed by alkalies. It is said to be insoluble in the acid gastric juice and soluble in the intestinal juices, and therefore useful as an intestinal astringent and antiseptic. *Dose*, eight to thirty grains (0.5–2.0 Gm.).

Tanghinia. *Ordeal Bean of Madagascar.—Tanghinia venenifera* Poir. (*Cerbera Tanghin* Hook.) (fam. *Apocynaceæ*), has been investigated, and, according to C. E. Quinquaud, is both a respiratory and a cardiac poison. (*C. R. A. S.*, cl, 534; see also *T. G.*, vol. ii, 610.) The active principle, *tanghinin*, occurs in colorless lustrous scales, efflorescing in the air, having a bitter and sharp taste, soluble in alcohol, ether, and acetic acid.

Tang-kui or **Man-mu.**—Under the name of *tangkui* the Chinese have used for a long time a root obtained from some umbelliferous plant closely allied to the *Levisticum officinale*, which, according to Lezenius (*Ph. Centralh.*, 1910, p. 221), is probably from the *Ligusticum acutilobum*. A fluidextract of this root has been introduced into European medicine under the name of *eumenol* and is recommended by a number of authors in the treatment of *dysmenorrhea* and other uterine complaints. The *dose* of this fluidextract is one tablespoonful three times a day. Bufalini, having searched in vain for an active alkaloid, believes that the activity of the substance depends upon an ethereal oil.

Tannalbin. *Tannin Albuminate. N. N. R.* 1917.—This compound, suggested by Gottlieb, is made by adding to ten parts of a 10 per cent. solution of albumin, six and a half parts of a 10 per cent. solution of tannin; the precipitate is collected, washed, pressed, and dried by exposure to heat (about 110° C., 230° F.) for six hours. It contains about one-half its weight of tannin. It is a light brown powder, insoluble in water and in the gastric juice, tasteless, odorless, and not at all irritant to the mucous membranes. As an astringent it is very feeble, but, as the tannic acid is probably liberated in the intestines, it is a valuable remedy in the treatment of *chronic diarrhea* dependent upon intestinal relaxation, and has even been used with asserted satisfaction when there were intestinal catarrh and ulceration. It does not disturb the digestion, but has been highly commended in *gastric catarrh* with excessive secretion of mucus. *Dose*, from fifteen to thirty grains (1–2 Gm.), three to six times a day, in capsule or powder.

Tannalum. *Tannal. Basic Aluminum Tannate.* $Al(OH)_2(C_{14}H_9O_9) + 5H_2O$.—This is a brownish-yellow powder, insoluble in water, which has been especially commended by Heymann as a mild, astringent, non-irritant substance, to be used as a dusting powder or by insufflation in diseases of the nasal and laryngeal mucous membranes. By the action of tartaric acid it becomes converted into the so-called *soluble tannal*, $Al(C_4H_4O_6)(C_{14}H_9O_9) + 3H_2O$, also used locally.

Tannargan. *Tanargentan.*—This compound occurs as a dark gray, insoluble powder. It is formed by the interaction of silver nitrate, albumen, and tannic acid, and is said to contain 10 per cent. of silver. It has been used as an intestinal disinfectant in cases of *gastro-enteritis*, *typhoid fever* and *intestinal tuberculosis*, but is employed more in veterinary than human practice. The *dose* for a man is four to eight grains (0.25–0.5 Gm.) two or three times a day.

Tannigen. *Tannyl Acetate. N. N. R.* 1917. $C_{14}H_8(COCH_3)_2O_9$.—This compound, which is prepared by the action of acetic anhydride or acetyl chloride upon tannin, is the diacetic ester of tannic acid. It is a yellowish-gray, tasteless and odorless, slightly hygroscopic powder, which can be heated to 180° C. (356° F.), without alteration; insoluble in cold water, readily soluble in alcohol, dissolving in diluted solution of sodium phosphate, soda, or borax, with the production of a yellowish-brown color. It has been used as a mild astringent in chronic *diarrheas*, *especially* in such as often accompany *phthisis*, and as a local application by insufflation in chronic *rhinitis* and *laryngitis*. *Dose*, from ten to fifteen grains (0.65–1.0 Gm.) three or four times a day, in capsules; to children it may be given spread on bread and butter.

Tannisol.—This is prepared by heating tannin with a 35 per cent. formaldehyde solution on a steam bath until a pulverizable mass results. It is then dried until all the excess of formaldehyde is driven off. It forms a reddish-brown powder, inodorous and tasteless, and soluble only in alkaline

fluids. Similar to other tannin preparations of this type it is used as an astringent antiseptic in *doses* ranging from two to eight grains (0.12–0.5 Gm.).

Tannobromine.—This is a reddish or yellowish powder, resulting from the action of formaldehyde on dibrom-tannin. It is sparingly soluble in water, readily so in alkaline solution or in alcohol. It is used in the treatment of *scalp diseases.*

Tannocasum.—Casein and tannin in combination in the form of yellowish, flaky powder constitute this product. It is employed largely as an intestinal astringent in *doses* ranging from eight to thirty grains (0.5–2.0 Gm.).

Tannochrom is found in commerce as a gray insoluble powder containing fifty per cent. of a compound of chromium bitannate and resorcinol; a fifty per cent. solution is also used which is miscible with water, alcohol and glycerin. The powder is used in the treatment of *eczema* and other skin diseases, and the liquid in one-fourth to one-half per cent. solution in *gonorrhea.*

Tannocol. *Gelatin-tannate.*—This is a tasteless, odorless powder, containing about 50 per cent. of tannic acid, having the same therapeutic properties and applications as tannalbin. It is claimed by Rosenheim that it is superior to that substance in being cheaper, of greater constancy of constitution, and less easily affected by the gastric juices. In the intestines it is decomposed by the alkaline secretions and tannic acid is liberated. *Dose,* fifteen to thirty grains (1–2 Gm.).

Tannoform. *N. N. R.* 1917. *Helgotan. Methylene Ditannin.* $CH_2(C_{14}H_9O_9)_2$.—A new class of bodies has been prepared by Merck which are termed *tannoforms,* and which consist of combinations between the various characteristic tannins and formaldehyde. These bodies are formed by adding a solution of formaldehyde gas to a purified plant extract containing the plant tannin, in the presence of hydrochloric acid. The further nomenclature of the tannoforms depends upon the name of the plant from which the particular tannin is derived.

The condensation product of gallotannic acid and formaldehyde, which is termed simply tannoform, is made by dissolving five grammes of tannin in about fifteen kilogrammes of hot water, adding three kilogrammes of 30 per cent. formaldehyde, and then adding concentrated hydrochloric acid until no further precipitate is thrown down. This requires about twelve to fifteen kilogrammes of acid. The precipitate is then washed with water and dried at a low temperature.

Tannoform occurs as a light, pinkish powder which decomposes at about 230° C. (446° F.). It is dissolved by alcohol and is insoluble in all the usual organic solvents; but is soluble in diluted ammonia, sodium or potassium hydroxide solutions, giving a brownish-red solution, from which it is again precipitated upon the addition of an acid. When warmed with concentrated sulphuric acid it dissolves with a brown color, turning on further heating to green, and then to blue. This green or blue solution gives a blue color with alcohol, which on standing some time turns to a wine-red, and on dilution with soda solution to a grass-green color.

Tannoform has been used with alleged good results in *enteritis* and other forms of *diarrhea.* It is asserted that the drug is decomposed by the intestines, the tannic acid radical acting as an astringent, and the formaldehyde as an antiseptic. It is, however, more frequently employed as a local remedy in the treatment of *eczema, bed sores,* etc. In *hyperidrosis of the feet,* well rubbed in between the toes over night, it will often give relief of considerable duration, but has the disadvantage of staining the skin brown. It has also been used externally to control night sweats. *Dose,* from five to fifteen grains (0.32–1.0 Gm.), in capsule, from three to six times a day.

Tannoguaiaform is a compound of tannic acid, guaiacol and formaldehyde. It is odorless and tasteless and has been recommended as an intestinal astringent and antiseptic particularly suited to the treatment of intestinal tuberculosis, as it probably liberates formaldehyde in the intestines. Care should be used in prescribing it. *Dose,* eight to fifteen grains (0.5–1.0 Gm.).

Tannon. *N. N. R.* 1917. *Tannopin,* $(CH_2)_6N_4(C_{14}H_{10}O_9)_3$, is a condensation product of tannin and hexamethylenetetramine. It is a light brown, tasteless and odorless, non-hygroscopic powder, insoluble in water, weak acids, spirit, and ether, but dissolving slowly in dilute alkaline solution. It has been used by Schreiber (*D. M. W.,* 1897) in *diarrhea* in *doses* of fifteen grains (1.0 Gm.) from three to four times a day.

Tannosal. *Creosote Tannate. Creosal.*—While the manufacturers of this preparation claim that it is a definite chemical compound yet it has been stated that it is a simple mixture of creosote and tannic acid. It occurs as a brown, amorphous powder, soluble in water, smelling slightly of creosote and containing about 60 per cent. of the latter. It splits up into its constituents in the small intestine and is consequently proposed as a valuable remedy in the treatment of *phthisis. Dose,* five to twenty grains (0.33–1.3 Gm.).

Tannothymal.—This substance which is a condensation product of thymol, formaldehyde and tannin, occurs as a yellowish to reddish powder, practically insoluble in water and dilute acids, but decomposed by dilute alkalies.

It has been used as an astringent antiseptic in the treatment of *diarrhea.* The *dose* is eight to fifteen grains (0.5–1.0 Gm.) three times a day.

Tannyl.—It is said to be a compound of tannin with oxychlor-casein. It is a grayish-brown powder, insoluble in water, and unaffected by the gastric juice.

According to Salkowski, oxychlor-casein has a marked action as an intestinal disinfectant, but by itself is not useful, because it is destroyed by the gastric juice. Combined with tannin, however, it is capable of reaching the intestinal tract in a still active form. Umber (*Ther. Geg.,* 1908) has used *tannyl* with asserted success in the treatment of *diarrhea,* not only when due to ordinary *enteritis,* but even in tuberculous cases.

The *dose* of tannyl is from fifteen to forty-five grains (1–3 Gm.).

Tansy. *Tanacetum. U. S.* 1890.—Under this name the U. S. Pharmacopœia formerly recognized the tops and leaves of the *Tanacetum vulgare* L., a perennial herbaceous plant rising two or three feet in height, which is cultivated in our gardens, although growing wild in the roads and in old fields. It was originally introduced from Europe. It is in flower from July to September.

Tansy was officially described as follows: "Leaves about 15 Cm. long; bipinnatifid, the segments oblong, obtuse, serrate or incised, smooth, dark green, and glandular; flower-heads corymbose, with imbricated involucre, a convex, naked receptacle, and numerous yellow, tubular florets." *U.*

S., 1890. The odor is strong, peculiar, and fragrant, but much diminished by drying; the taste is warm, bitter, somewhat acrid, and aromatic. These properties are imparted to water and alcohol. According to Leppig (*Inaug Dis.*, Dorpat, 1882), both the flowers and the leaves contain the following constituents: *tanacetin*, tannic acid (*tanacetum-tannic acid*), traces of gallic acid, volatile oil, a wax-like substance, albuminoids, tartaric, citric, and malic acids, traces of oxalic acid, a lævogyrate sugar, resin, metarabic acid, parabin, and woody fiber. Of these the most important are the bitter principle *tanacetin*, to which Leppig gives the formula $C_{11}H_{16}O_4$, and which forms a very hygroscopic, brownish, amorphous mass, easily soluble in alcohol and in water, insoluble in ether. It possesses a taste at first characteristically bitter like willow bark, and then cooling and caustic. The essential oil was investigated by Bruylants (*Ber. d. Chem. Ges.*, xi, 449), according to whom it consisted of a terpene, $C_{10}H_{16}$, boiling at from 155° to 160° C. (311°–320° F.), of which 1 per cent. only is present, an aldehyde, $C_{10}H_{16}O$, boiling at from 195° to 196° C. (383°–384.8° F.), of which 70 per cent. was obtained, and an alcohol (borneol), $C_{10}H_{18}O$, boiling at from 203° to 205° C. (397.4°–401° F.), of which 26 per cent. was present. Semmler (*Ber. d. Chem. Ges.*, xxv, 3343, 3352, 3513) has specially investigated the constituent boiling at 195° C. (383° F.), and having the composition $C_{10}H_{16}O$. He finds it to be not an aldehyde, but a ketone, and calls it *tanacetone*. It is identical with the ketone found in sage oil, wormwood oil, and thuja oil. As it was first identified in this last-named oil by Wallach, and named by him *thujone*, this name is now applied to it to the exclusion of the other. (See also *Schim. Rep.*, April, 1893, and April, 1897; and Gildemeister and Hoffmann, *Aetherische Oele.*)

Tansy adds to the medicinal properties of the aromatic bitters those of an irritant narcotic. It has been recommended in *intermittents*, *hysteria*, and *amenorrhea*, but in this country is little employed in regular practice. The seeds are said to be most effectual as a vermifuge. Tansy has been used to a considerable extent as a domestic abortifacient, but is not only very uncertain, but also very dangerous in its action, and has in varicus cases produced death. The symptoms caused by it have been abdominal pain, vomiting, violent epileptic convulsions often followed by profound coma, dilated pupils, great disturbances of respiration, frequent and feeble pulse, and death, which has been said to be from heart failure, but is probably the outcome of a paralytic asphyxia. The minimum fatal dose can scarcely be considered to have been positively ascertained, but a fluidrachm (3.75 mils) of the oil is said to have caused death, although recovery in one case occurred after taking half a fluidounce. Tansy tea has also caused death. (For cases, see *Am. J. M. S.*, xvi, xxiii, xxiv; *J. P. C.*, April, 1870; *J. A. M. A.* xlvii, p. 509.) Post-mortens have been reported in which no inflammation of the gastro-intestinal mucous membranes could be discovered.

The *dose* of the powder is from thirty grains to a drachm (2.0–3.9 Gm.) two or three times a day; but the infusion is more frequently administered.

Tapioca.—Under this name the U. S. P. formerly recognized the starch grains obtained from the bitter cassava (*Manihot utilissima* Pohl), and the sweet cassava (*M. palmata* var. *Aipi* Pohl) (Fam. *Euphorbiaceæ*). The starch is extracted from the thickened root and is known in commerce by the names of *Cassava*, *Tapioca* or *Manioca Starch*, and as *Bahia*, *Rio* or *Para Arrowroot*. The plant is cultivated in Brazil and other parts of tropical America. It is also grown in Florida and other of the Southern States. In the production of the starch from the bitter cassava the hydrocyanic acid which is present in fresh roots is entirely eliminated by the process of washing and drying.

The root of the *sweet* cassava may be eaten with impunity; that of the *bitter*, which is the most extensively cultivated, abounds in an acrid, milky juice, which renders it highly poisonous if eaten in the recent state. Henry and Boutron Chalard affirm that the bitter cassava contains hydrocyanic acid (*J. P. C.*, xxii, 119), but Peckdolt claims that its poisonous effects are due to *manihotoxine* (*Ph. Rund.*, iv, 1890).

The preparation of tapioca in Malacca is thus described by James Collins: The fresh rootstocks are thoroughly washed in tubs in a constant stream of water by the Chinese, and then peeled like turnips; they are then sliced in one machine and pulped in another, the pulp being removed in cane baskets to large wooden frames, with calico bottoms; a powerful stream of water is allowed to fall upon the pulp, a sifting motion being communicated to the strainer; as the starch is washed out, it is received into inclined troughs, and, while in a state of suspension, run into settling vats. There it is stirred and washed, and, while moist, it is removed to the drying room. Two kinds of tapioca are prepared. The flour is made by heating slightly by fires placed underneath; it is constantly stirred and turned over with iron shovels, to prevent agglutination and insure equal drying. Granular tapioca is made as follows: A long range of quallies, or small, shallow iron pans, are slightly tilted forward on ledges of brickwork, and heated with a wood fire. Each operator has a quallie and fire to himself. Taking a quantity of damp starch, he stirs it round and round with an iron shovel, and the heat is sufficient to cause the tapioca to become agglutinated together in small masses, and coated with dextrin. The drying is done with great skill over an open fire. (*C. D.*, 1884.)

Tapioca is in irregular, hard, white, rough grains, possessing little taste, partially soluble in cold water, and affording a fine blue color when iodine is added to its filtered solution. The partial solubility in cold water is owing to the rupture of the starch granules by heat. Examined under the microscope, the granules appear somewhat plano-convex or bell-shaped and more or less compound. The individual grains vary from 0.006 to 0.030 mm. in diameter and have a distinct central circular or radiating cleft. They polarize light strongly, showing a distinct cross. *Tapioca meal*, called sometimes *Brazilian arrow-root*, and by the French *moussache*, is the fecula dried without heat. Its granules are identical with those already described. Being nutritious, and the same time easy of digestion and destitute of irritating properties, tapioca forms an excellent diet for the sick and convalescent. It is prepared for use by boiling it in water. Lemon juice and sugar are usually grateful additions, and in *low states of disease* or cases of *debility* it may be impregnated with wine and nutmeg or other aromatic.

A factitious tapioca is found in commerce, consisting of very small, smooth, spherical grains, and

supposed to be prepared from potato starch. It is sold under the name of *pearl tapioca.*

Cassaripe is the thickened gum obtained from the root of the bitter cassava, which is said to be innocuous and so actively antiseptic as to be habitually used in Brazil for the preservation of meat. According to S. D. Risley (*Phila. Med. Journ.*, 1899), the 10 per cent. ointment of cassaripe is useful in *suppurating conjunctivitis* and *ulcers* of the *cornea*, applied with gentle massage three or four times a day.

Taxus. *Taxus baccata* L. *Yew Tree. If commun*, Fr. *Eibe*, G. (Fam. *Taxaceæ.*)—The fruit of this handsome evergreen appears to be a deadly poison. In a fatal case the child was found semicomatose, with convulsions, a cold and clammy skin, difficult respirations, dilated pupils, and making attempts at vomiting. The poison is probably in the seeds. (See 16th edition, *U. S. D.*; also James Thompson, *L. L.*, 1868, 530. For fatal cases in adults, see *M. T. G.*, 1870, ii; also *L. L.*, 1870, 471; also *P. J.*, viii, 361.) W. Marmé obtained from yew seeds and leaves an alkaloid, $C_{37}H_{51}NO_{10}$, to which the name of *taxine* has been given. It was a white, poisonous, crystalline powder, only slightly soluble in water, easily soluble in ether, alcohol, chloroform, benzene and carbon disulphide, but not in petroleum benzin. It fused at 80° C. (176° F.). With concentrated sulphuric acid it gave a red color, but dissolved without color in nitric and phosphoric acids. (*A. J. P.*, 1876, 353.) For Vreven's method of isolating taxine, see *P. J.*, 1896, 215. Amato and Capparelli (*Gazz. Chim.*, x, 349) prepared from the leaves a volatile alkaloid, which was soluble in cold sulphuric acid with yellow color, becoming red on heating. They also isolated a nitrogenous crystalline and colorless principle, fusing at from 86° to 87° C. (186.8°–188.6° F.), soluble in alcohol, insoluble in water, named *milossin.*

Lefebvre (*A. Pharm.*, ccxlv, 486) has isolated from the twigs of the yew a crystalline glucoside to which he gives the name "*taxicatin.*" It had the formula of $C_{13}H_{22}O_7 + 2H_2O$ and a melting point of 165° C. (329° F.).

Tayuya.—The root of the *Dermophylla* (*Cayaponia*) *pendulina* Manso (Fam. *Cucurbitaceæ*), is used in Brazil, under the name of *tayuya*, in *syphilis*, etc. (*N. R.*, 1877, 234); also, under the same name, the root of the *Trianosperma ficifolia* Mart. (*Cayaponia Martiana* Cogn.), also of the Fam. *Cucurbitaceæ* (*P. J.*, x, 667), and probably various other roots. In *C. ficifolia* Cogn. two alkaloids, *trianospermine* and *trianospermitine*, and a bitter principle, *tayuyin*, have been found by Peckoldt (*P. J.*, x, 667), and in *T. dermophylla* a green resin, bitter extractive, and tannic acid were found by the same investigator. (*B. G. T.*, lxxxiv, xci. See also *Proc. A. Ph. A.*, xxiv.)

Tea. *Thé*, Fr. *Thee*, G.—The plant which furnishes *tea—Thea sinensis* L. (Fam. *Theaceæ*)—is an evergreen shrub. It has numerous alternate branches, furnished with elliptical-oblong or lanceolate, short petiolate, pointed leaves, which are serrate except at the base, smooth on both sides, green, shining, pinnately veined and having a prominent midrib. They are two or three inches long, and from half an inch to an inch in breadth. The flowers are either solitary or supported, two or three together, at the axils of the leaves. They are of considerable size, not unlike those of the myrtle in appearance, consisting of a short green calyx with five or six lobes, of a corolla with from four to nine large unequal snow-white petals, of numerous stamens with yellow anthers and connected at their base, and of a pistil with a three-parted style. The fruit is a three-locular and three-seeded capsule.

There are two principal varieties of *T. sinensis*, viz. *viridis* L., which is a large spreading shrub, having light green lanceolate leaves from 12 cm. long to 4 cm. wide; and a second variety, *Bohea* L., which is an upright shrub with dark-green elliptical leaves 6 cm. long and 3 cm. wide. The flowers of the latter occur in groups of two or three, whereas in *viridis* they are single. There are a great many varieties of tea, on the market, and their trade value is influenced by the peculiarities of mother plant and climate and the degree of ripeness and preparation of the leaves. As a rule only the youngest leaves are gathered. The so-called black and green teas are due to the method of preparation of leaves. In the first the chlorophyll is destroyed, whereas in the latter it is unaffected. Winton gives the following characters as common to all tea leaves: "The firm, rather thick texture; the glossy upper surface; the short stem into which the base of the leaf tapers; the thick margins, rolled a little towards the inner surface, with cartilaginous teeth; the veins which branch from the midrib at angles usually greater than 45 degrees, and at some distance from the margin form loops uniting adjoining ribs. The teeth on the margin of the leaf are shrunken multicellular glands which break off readily from the old leaves." (For discussion of microscopical characteristics, see Winton and Moeller, "The Microscopy of Vegetable Foods."

The tea plant is a native of China and Japan, and is cultivated in both countries, but most abundantly in the former. It has been more recently cultivated in India (Assam), Ceylon, Java and in South Carolina. In Japan it forms hedge rows around the rice and corn fields; in China, whence immense quantities of tea are exported, whole fields are devoted to its culture. It is propagated from the seeds. For particulars as to the cultivation of tea, see *P. J.*, 1871, 386.

(An elaborate article on tea, with methods of cultivation, etc., by Wm. B. Marshall, U. S. Nat. Museum, will be found in *A. J. P.*, 1903, p. 79.)

The odor of the tea leaves themselves is very slight, and it is customary to mix with them the flowers of certain aromatic plants, as those of the orange, different species of jasmine, the rose, *Osmanthus fragrans* Lour. (*Olea fragrans* Thumb.), of the *Oleaceæ*, and *Camellia Sasangua* (Thumb.?), in order to render them pleasant to the smell. The flowers are afterwards separated by sifting or otherwise. (See *P. J.*, xv, 112.) Under the name of *flowers of tea* was at one time sold a waste product consisting of the hair of young leaves, but the flowers themselves have been used to make a beverage. (*P. J.*, lxxi, p. 453.)

Bush Tea and *Honig Thee*, used at Cape Colony, South Africa, as a substitute for tea, are the dried leaves and tops of several species of *Cyclopia*, among which are *C. subternata* Vog., *C. latifolia* DC., *C. genistoides* Vent. and *C. sessiliflora* Eckl. and Zeyh. (Fam. *Leguminosæ.*) According to the analysis of Henry G. Greenish, they do not contain theine, but a glucosidal body, *cyclopin*, $C_{25}H_{28}O_{13}$. (*P. J.*, xi, 549.)

The United States imported in 1915, 96,987,942 pounds of tea, valued at $17,512,619. The largest consumer is the United Kingdom, which in 1914 took 317,664,000 pounds, and the next Russia,

which took 166,064,003 pounds. Numerous varieties exist in commerce, differing in the shape communicated by rolling, in color, in flavor, or in strength; but they may be all arranged in the two divisions of *green* and *black teas*, which, at least in their extremes, differ so much in properties that it is difficult to conceive that they are derived from the same species.

Under the name of *tea oil* there has appeared in the London markets a Chinese fixed oil said to be derived from *Camellia drupifera* Lour. (*C. oleifera* Wall.), a detailed description of which, with tests, may be found in the *P. J.*, vol. xvi, 634. A similar oil is prepared in Japan from the seeds of *Camellia japonica* L. (*Ibid.*, 637, 764.)

Green tea is characterized by a dark green color, sometimes inclining more or less to blue or brown. It has a peculiar, refreshing, somewhat aromatic odor, and an astringent, slightly pungent and agreeably bitterish taste. Its infusion has a pale greenish-yellow color, with the odor and taste of the leaves. According to Warington, who examined numerous varieties of tea carefully, both by the microscope and chemical tests, many of the green teas imported into Great Britain owe their color to a powdery coating, consisting of calcium sulphate and Prussian blue; others to a mixture of these with a yellowish vegetable substance; and others, again, to calcium sulphate alone. (*P. J.*, iv, 37.) *Black tea* is distinguished by a dark brown color. It is usually less firmly rolled and lighter than the green, and contains the petioles of the plant mingled with the leaves. Its odor is fainter, and of a somewhat different character, though still fragrant. Its taste, like that of green tea, is astringent and bitterish, but is less pungent, and to many persons less agreeable. To hot water it imparts a brown color, with its sensible properties of taste and odor. These vary exceedingly in degree in the different varieties, and some black teas are almost wholly destitute of aromatic or agreeable flavor. According to Blyth, green tea is prepared from young leaves which are roasted over a wood fire within an hour or two after being gathered; while the black tea leaves, on the other hand, are allowed to lie in heaps for ten or twelve hours after they have been plucked, during which time they undergo a sort of fermentation; the leaves then pass through certain processes, and are slowly dried over charcoal fires. (Wynter Blyth, *Foods, Composition and Analysis*, 1903.) A sophisticated tea is largely exported from China, consisting of powdered tea mixed with sand and other earth, and agglutinated with gum; that which is to pass for black being colored with plumbago, and the green with the coating above referred to. On analysis, these teas were found to afford from 35 to 45 per cent. of ashes, while the genuine yields only 5 per cent. A very full account of the adulteration of tea and the methods for the detection of the same may be found in Allen, *Com. Org. Anal.*, 2d edition.

The analyses below[1] by Y. Kozai (*Bulletin No. 7, Imperial College of Agriculture*, Japan) have a special value, owing to the author's knowledge of tea manufacture. Unusual precautions were taken in sampling the leaves, to insure strictly parallel specimens being taken. The figures refer to the moisture-free leaves in each case.

[1] Analyses of Tea (percentage composition).

	Unprepared Leaves.	Green Tea.	Black Tea.
Caffeine or Theine	3.30	3.20	3.30
Ether Extract	6.49	5.52	5.82
Hot-water Extract	50.97	53.74	47.23
Tannin (as Gallotannic Acid)	12.91	10.64	4.89
Other Nitrogen Free Extract	27.86	31.43	35.39
Crude Protein	37.33	37.43	38.90
Crude Fiber	10.44	10.06	10.07
Ash	4.97	4.92	4.93
Albuminoid Nitrogen	4.11	3.94	4.11
Caffeine Nitrogen	0.96	0.93	0.96
Amido-nitrogen	0.91	1.13	1.16
Total Nitrogen	5.97	5.99	6.22

Rochleder found also a peculiar acid, which he calls *boheic acid*, $C_7H_{10}O_8$. According to Stenhouse, the tannin of tea, though always accompanied by a little gallic acid, differs essentially from that of galls; not being, like it, a glucoside, but yielding, under the influence of sulphuric acid, a dark brown substance, almost insoluble in water. (See *A. J. P.*, 1862, 254.) For article on the methods of analysis of tea and a series of analyses of different varieties, see *A. J. P.*, 1887, 626. The volatile oil is citron-yellow, lighter than water, has a strong odor of the tea plant, solidifies easily by cold, and resinifies on exposure to air. It is probably one of the principles upon which depend the effects of tea upon the nervous system. Hence old teas are less energetic than the recently imported; and it is said that the fresh leaves have often produced dangerous effects in China. Nevertheless, the tannic acid is not without influence upon the system; and it is not improbable that the extractive contributes to the peculiar influence of this valuable product. Of these active ingredients, the volatile oil, tannic acid, and extractive are found most largely, according to the analysis of Mulder, in the green tea. *Theine*, $C_8H_{10}N_4O_2$, is a crystallizable principle discovered by Oudry. It was afterwards proved by Jobst to have the same composition as caffeine (see page 247). Kossel discovered, in 1888, a related principle, *theophylline* (*dimethylxanthine*), but only in very small amounts. It is now made synthetically and is official. (See *Theophyllina.*)

The proportion of theine found in tea varies considerably, the general range being from three to four per cent. India and Ceylon tea usually contain slightly more than four per cent.

Tea is astringent and gently excitant, and exerts a decided influence over the nervous system, evinced by the feelings of comfort and even exhilaration which it produces, and the unnatural wakefulness to which it gives rise when taken in unusual quantities or by those unaccustomed to its use. It is almost exclusively used as a beverage. Taken moderately, and by healthy individuals, it may be considered as practically harmless; but long continued in excessive quantity it is capable of inducing unpleasant nervous and dyspeptic symptoms. Green tea is decidedly more in-

jurious in these respects than black, and should be avoided by dyspeptic individuals, and by those whose nervous systems are peculiarly excitable. It is rarely used as a medicine, but the infusion is popularly employed to relieve neuralgic headaches.

Tegmin.—Under this name a surgical dressing has been recommended; it is an emulsion made from yellow wax, one part; acacia, two parts; water, three parts; it also contains 5 per cent. of zinc oxide and a little wool fat. It is used as a protective and vehicle for skin remedies.

Telfairia Pedata Hook. (Fam. *Cucurbitaceæ.*)—The seeds of this East African plant yield a deep yellow fragrant oil, of specific gravity 0.918, containing *telfairic acid.* (*Chem. Zeit. R.*, xxiv, 24.)

Tellurium. (Te. Atomic weight, 127.5.)—The first physiological investigations as to the action of tellurium were made by Hansen (*Chem. Gaz.*, 1854), who found that the *potassium tellurate* produces in dogs vomiting, with stupor, and that in the dose of one grain three times a day it causes in man cardiac oppression, nausea, some salivation, with a pronounced garlic-like odor of the breath. These investigations have been extended and confirmed by William J. Gies (*M. A.*, June, 1901), who found that in doses of one-third of a grain per kilogramme sodium tellurate caused in the dog vomiting, diarrhea, unconsciousness, paralysis, convulsions, and death, with pronounced inflammatory changes in the intestines and kidneys similar to those seen after arsenic. Characteristic was the pigmentation of all parts of the body by metallic tellurium. During life the brown or greenish discoloration of urine and the very pronounced garlicky odor of the breath were almost diagnostic. The continuous administration of minute doses had no effect upon metabolism, but if the amount ingested was increased, gastro-intestinal irritation with restlessness soon appeared. Tellurium was found in the feces, urine, breath, and skin secretions. In man drowsiness, nausea and constipation seemed to result from the remedy, given in doses up to half a grain. There was also a marked anhidrotic action, even in healthy men, appearing fifteen minutes to one hour after the ingestion of the dose. Potassium tellurate is an efficient remedy for the arrest of *colliquative sweating*, but the pronounced alliaceous odor which it imparts to the breath, and even to the perspiration, greatly interferes with its use. *Dose* of potassium or sodium tellurate, one-sixth to one-half of a grain (0.01–0.032 Gm.).

Tellurous acid and its potassium salt have been recommended by Gosio (*Zeit. Hyg. u. Inf.*, 1905, li, 65) as an indicator of the presence of living bacteria, especially in sera. He asserts that it is harmless to the human and is reduced by growing bacteria giving rise to color change.

Tephrosia. *Tephrosia virginiana* (L.) Pers. *Turkey Pea. Wild Pea. Catgut. Goat's Rue. Hoary Pea. Devil's Shoestring. Tephrosie*, Fr., G. (Fam. *Leguminosæ.*)—Several species of *Cracca* and *Tephrosia* are employed in different parts of the world, though unknown in general commerce. They are leguminous plants, shrubby or herbaceous, with odd-pinnate leaves and white or purplish racemed flowers. They are generally possessed of cathartic properties, their leaves or roots being employed. Plugge (*Proc. A. Ph. A.*, 1897, 560) examined the root of *T. macropoda* and found a poisonous active principle, not identical with cytisine.

Hanriot isolated from *T. vogellii*, a crystalline principle, *tephrosin*, which occurs in small glistening crystals which are almost insoluble in water, slightly soluble in alcohol or glycerin, more readily soluble in acetone, and freely soluble in chloroform. Its formula is $C_{34}H_{26}O_{10}$. *Tephrosal*, $C_{10}H_{16}O$, is a volatile, aromatic liquid, slightly soluble in water, more readily soluble in alcohol, ether, benzin, and chloroform. (*T. C.*, li, 302.)

Tephrosia virginiana L. grows in most parts of the Eastern United States. It is a foot or two high, with pubescent stems and leaves and handsome terminal flowers. (See Griffith's *Med. Bot.*, 237.) The roots, which are slender, long, and matted, are tonic and aperient, and are said to have been used by the Indians as a vermifuge, given in the form of decoction.

According to Holmes (*P. J.*, 1910, lxxxiv) the *T. vogelii* is used in Africa as a fish poison. Its toxicity seems to be due to the neutral principle, *tephrosin*. There is no evidence as to its noxiousness for human beings.

Terpinol.—This is not a simple body, but a mixture of terpenes with variable proportions of an alcohol, *terpineol*, $C_{10}H_{17}OH$. It forms a colorless oily substance with a hyacinthine odor; it is produced by boiling terpin with diluted mineral acids. It is insoluble in water, but readily soluble in alcohol and ether. Terpinol has been used in chronic *bronchial catarrh*, and is especially commended by Lazarus when there is much irritation of the membrane with scanty secretion. Janowsky states that it is a valuable remedy in *hemoptysis*. The *dose* is three to five minims (0.2–0.3 mil) at intervals of from one to four hours, administered in capsules.

Terraline. *Terroline.*—A liquid proprietary petroleum product, odorless and tasteless, used internally in emulsions, in the *dose* of from one to two fluidrachms (3.75–7.5 mils). See *Petrolatum Liquidum* (Part I).

Testa Præparata. *Prepared Oyster-shell. Magistère de Coquilles (d'écailles) d'Huîtres*, Fr. *Präparirte Austerschalen*, G.—"Take of Oyster-shell *a convenient quantity*. Free the Oyster-shell from extraneous matter, wash it with boiling water, and, having reduced it to a fine powder, treat this in the manner directed for Prepared Chalk." *U. S.*, 1870. Prepared oyster-shell differs from prepared chalk in containing animal matter, which, being very intimately blended with calcium carbonate, is supposed by some physicians to render the preparation more acceptible to a delicate stomach. It is given as an antacid in *diarrhea*, in the *dose* of from ten to forty grains (0.65–2.6 Gm.) or more, frequently repeated. A preparation was introduced into use in this country, under the name of *Castillon's powders*, consisting of sago, salep and tragacanth, each, in powder, *a drachm*, prepared oyster-shell, *a scruple*, and sufficient cochineal to give color to the mixture. A drachm of this is boiled in a pint of milk, and the decoction used *ad libitum* as a diet in chronic bowel affections.

Tetra-ethyl Ammonium Hydroxide. $N(C_2H_5)_4OH$.—This occurs as colorless hygroscopic crystals, alkaline in reaction and is used in *articular rheumatism* and *uric acid diathesis*. The 10 per cent. solution is used in *doses* of five to twenty minims (0.3–1.3 mils).

Tetragastris. *Tetragastris panamensis* (Engl.) O. Kuntze. *Bois Cochon*, or *Sucrier de Montagne*, Fr. (Fam. *Burseraceæ.*)—This native of Panama has been examined by Gaucher, Combemale and

Marestang (*France Méd.*, October, 1888), who find in it an alkaloid and a resin. The extract of the root and stems produces in the guinea pig rapid and considerable lowering of temperature, progressive paralysis, general convulsions, dilatation of the pupils, respiratory irregularity and cardiac paresis. The alkaloid was found to be a convulsive agent, acting upon the spinal cord. The resin, which seemed much more active than the alkaloid, acted as a paralyzant.

Tetramethylammonium. $N(CH_3)_4$.—Several salts of this base have been prepared. *Tetramethyl ammonium hydroxide*, $N(CH_3)_4.OH$, occurs in deliquescent crystals which are freely soluble in both water and alcohol, but it is usually marketed in the form of a 10 per cent. solution. This caustic alkaline liquid has a strong affinity for carbon-dioxide. It has been used in *rheumatism* in *doses* of ten to fifteen minims (0.6–0.9 mil.). Tetramethylammonium bromide, chloride, and iodide have been made.

Tetranthera.—From the bark of the lauraceous plant, *T. citrata* Nees (now *Litsea citrata* Blume), J. D. Filippo has extracted an alkaloid, *laurotetanine*. (See *A. Pharm.*, 1898, 601.)

Charabot and Lalone examined the volatile oils from various parts of *Tetranthera* (*Litsea citrata*). The oil from the bark has the sp. gr. 0.8673 at 15° C. (59° F.), that from the leaves 0.9013 at 15° C. (59° F.) and that from the fruits 0.8872 at 15° C. (59° F.). (*P. J.*, 1908, 351.)

Tetronal. *Diethyl-sulphone-diethyl-methane.* $(C_2H_5)_2C(C_2H_5SO_2)_2$.—This occurs as a white crystalline powder, insoluble in water, soluble in alcohol and fusing at 85° C. (185° F.). The effects of this compound are practically the same as the closely allied *Sulphonethylmethane*. (See p. 1080.) Although the introducers of this group of drugs, Baumann and Kast (*A. E. P. P.*, 1892, xxxi) classed tetronal as the most powerful of the group it has failed to achieve the popularity of the official representatives. The *dose* is from eight to fifteen grains (0.5–1 Gm.).

Teucrium. *Teucrium Chamædrys* L. *Germander. Chamædrys. Petit Chêne*, Fr. *Edlar, Gamanderlein, Frauenbiss*, G.—A small European labiate, which has been employed as a mild corroborant in *uterine, rheumatic, gouty* and *scrofulous affections* and *intermittent fevers*. Germander was an ingredient in the *Portland powder*, noted as a remedy in gout. This powder, according to the original prescription, consisted of equal parts of the roots of *Aristolochia rotunda* L. and *Gentiana lutea* L. of the tops and leaves of *Teucrium Chamædrys* and *Erythræa Centaurium* (L.) Pers. and of the leaves of *Ajuga Chamæpitys* Schreb., or *ground pine*. The *dose* was a drachm every morning before breakfast for three months, then forty grains for three months, afterwards half a drachm for six months, and finally half a drachm every other day for a year. (Parr.)

Two other species of *Teucrium* have been used in medicine,—*T. Marum* L., *cat thyme*, or *Syrian herb mastich*, indigenous in the south of Europe, and *T. Scordium* L., or *water germander*, growing in the higher latitudes of the same continent. The former is a warm, stimulating, aromatic bitter, and has been recommended in *hysteria, amenorrhea* and *nervous debility;* the latter has the odor of garlic and a bitter, somewhat pungent taste, and was formerly highly esteemed as a corroborant in *low forms of disease;* but neither of them is now much employed. *T. Marum* is an errhine, and was formerly an ingredient of the *Pulvis Asari Compositus*.

A plant said to have been used advantageously in *cholera* in the Levant, a specimen of which was sent to Paris, proved to be *Teucrium Polium* L. (*J. P. C.*, xv, 352.) Moorhof (*Ph. Cent.*, 1893, 89) prepared a purified liquid extract from *T. Scordium*, and named it *teucrin*, which he recommends in the treatment of fungoid diseases and abscesses.

The *dose* of either of the three species is about half a drachm (2.0 Gm.).

Tfol is an argillaceous earth, containing free gelatinous silica, which is largely used in Northern Africa as a substitute for soap. It has been strongly recommended by Lahache for the purpose of emulsifying tar oil and for disinfecting purposes.

Thalictrum.—It appears probable that many species of this genus (Fam. *Ranunculaceæ*) have active medicinal or toxic properties. In 1879 Henriot and Doassans asserted that they had separated from the roots of the *Thalictrum macrocarpum* Gren., a shrub of the Pyrenees, a crystalline yellow substance, having very pronounced toxic principles, analogous to those of curare; and subsequently stated (*C. R. S. B.*, 1880) that this substance really consists of two principles,—an alkaloid, *thalictrine*, obtained in the form of prismatic needles, insoluble in water, soluble in alcohol, forming crystalline salts with acids, and *macrocarpin*, a yellow crystalline body, soluble in water, representing the coloring principle of thalictrum. Subsequently *berberine* was found by Doassans and Mousset in *Thalictrum flavum* L., *Fen Rue* or *Monk's Rhubarb*, a shrub widely distributed in Europe and Asia, macrocarpin being, according to this authority, very closely allied to berberine, but differing in that its color is not affected by ammonia. Rochebrune (*Toxicolog. Africaine*, i) has found both thalictrine and macrocarpin in the roots of *Thalictrum glaucum* Desf., of Spain. Thalictrine he states to be a very active cardiac poison, producing loss of power, convulsive movements, irregularity and depression of the heart's beat, and finally death in some cases in convulsions. According to Rochebrune, thalictrine also exists in the African species *Thalictrum rhynchocarpum* Q. Dillon and A. Rich.

Thalline. *Tetrahydroparaquinanisol* or *Tetrahydroparamethyloxyquinoline.* $C_9H_6H_4N(OCH_3)$.—The term *anisol* is applied to the methyl ether of phenol, and it is therefore methyloxybenzene. Skraup's synthesis of quinoline, C_9H_7N, was effected by heating aniline or amidobenzene with nitrobenzene, glycerin and sulphuric acid. By taking instead paramidoanisol, paranitroanisol, glycerin and sulphuric acid, Skraup obtained paraquinanisol, $C_9H_6N(OCH_3)$. This is then treated with tin and hydrochloric acid, when it takes up four atoms of hydrogen and becomes $C_9H_6H_4N(OCH_3)$. The name *thalline* was given to this base because of the deep green color produced by ferric chloride and other oxidizing agents. The base thalline is obtained in well-formed rhombic crystals, which fuse at 40° C. (104° F.) and recrystallize on cooling. It shows a neutral reaction and has a characteristic aromatic odor resembling that of coumarin. It is soluble in water, alcohol, and ether.

Thalline sulphate is a white crystalline powder which loses its two molecules of water of crystallization at 100° C. (212° F.) and melts at 110° C. (230° F.). It is soluble in five times its

weight of cold water and freely soluble in boiling water, soluble in 100 parts of alcohol. Both solutions turn brownish on exposure to air and light. The odor of the sulphate recalls that of anisol. *Thalline tartrate* is a white crystalline powder, fusing at 155° C. (311° F.) and possessing a coumarin-like odor. It is soluble in ten parts of water and hardly soluble in alcohol. Its aqueous solution has an acid reaction.

Thalline tartrate and sulphate are medicinally equivalent. They are powerful antipyretics, acting also, when in sufficient dose, as depressants both upon the vasomotor system and upon the heart, and, according to A. Robin, checking tissue waste in the body and having a very marked tendency to attack the red blood corpuscles. These salts have been used in practical medicine, in *doses* of from four to eight grains (0.26–0.5 Gm.), but are so prone to produce disagreeable symptoms, such as marked cyanosis, vomiting, diarrhea, albuminuria, etc., that their employment has been abandoned. According to Kreis, in from 4 to 4½ per cent. solution they are active germicides, and the frequent use of urethral injections of the 1 to 2 per cent. solution has been found very useful in *chronic gonorrhea*. Moncorvo states that thalline is an active hemostatic.

Thalline Periodide. *Thalline Periodosulphate.*—An iodine addition product of thalline sulphate. It occurs as black crystals soluble in alcohol. It has been used in the treatment of *carcinoma*, three to four grains (0.2–0.25 Gm.) being given in pill form every two or three hours. In cases where functional activity of the epidermal glands has ceased, pilocarpine in slight doses is given at the same time.

Thalline Salicylate. $C_{10}H_{13}NO.C_7H_6O_3$.—This occurs as a reddish, crystalline powder, soluble in alcohol and administered as an antiseptic and antipyretic in the treatment of *gonorrhea, typhoid fever*, etc. *Dose*, three to eight grains (0.2–0.5 Gm.).

Thallium. (Tl. Atomic weight, 204.0.)—This metal, discovered by spectrum analysis, has been found to prevail widely in nature. The credit of its discovery by Crookes in 1861 has been disputed by Lamy. Although the absorption of the salts of thallium appears to be slow they are certainly distributed everywhere, their presence having been recognized by Lamy by the green spectroscopic line in all the tissues of poisoned animals.

Thallium is an active poison, according to Swain and Bateman (*J. Bi. Chem.*, Jan., 1910), only slightly less toxic than arsenic. Moreover, it is distinctly accumulative in its effect, so that small doses repeated over periods of time may produce serious intoxication. The symptoms of acute poisoning in the lower animals by thallium are a disordered muscular action, as shown by tremors, inco-ordination, gradually increasing paralysis. Often, also, there is evidence of irritation of the intestinal tract, with vomiting and diarrhea. The pupils are dilated, there is salivation, conjunctivitis, with free mucous secretion, diuresis, embarrassment of respiration and more or less weakness of circulation. Death occurs in coma and is due to respiratory failure. After death there may be found some effusion of blood and inflammation of the lungs and intense congestion of the bowels, pericardial effusion and ecchymosis of the heart surface.

Cases of poisoning are uncommon in man, but Ballard (*Reports of the Boston City Hospital*, 1902) has recorded a case in which, after between two to four grains which were taken in the course of a week, there were produced diarrhea, muscular weakness and tenderness over the nerve trunks. As both lead and arsenic were found in the urine, however, it was doubtful how far the symptoms were due to the thallium. Olmer and Tian (*C. R. S. B.*, lxv, p. 742) report a case in which, after application of a paste of acetate of thallium to the chest, there were pains in the extremities, stomatitis, albuminuria and widespread alopecia. The loss of hair has been an almost constant symptom of human poisoning, and also occurs, according to Swain and Bateman, in the lower animals.

Sabouraud (*Revue Internationale de Medecin*, 1912) has recommended an ointment containing 1 per cent. of thallium acetate as a depilatory.

That thallium can produce widespread general neuritis is strongly indicated by the violent pains, especially of the legs, which have been noted by Lamy, by Combemale, and other observers, and also by the muscular atrophy which appears to be pronounced in chronic poisoning by the drug in the lower animals. Curci, indeed, claims that thallium is exclusively a muscle poison, and as long ago as 1874 Rabuteau recorded that after death from thallium the muscles did not respond to irritation. (See *Ed. M. J.*, 1874.)

Pozzi and Courtade assert that in some cases thallium causes swelling of the gums with a blue line at the junction with the teeth, but this symptom seems not to have been noticed by other observers. In 1898 Combemale claimed that in *doses* of one and a half grains (0.096 Gm.), given at bedtime, thallium acetate is a valuable remedy in the *colliquative sweats* of phthisis; that it is effective has been proved by Huchard and others; but in many cases it has produced severe peripheral pains, loss of hair, abdominal disturbance, and other very disagreeable symptoms.

Thanatol. *Guæthol. Ajacol. Pyro-catechin-mono-ethyl-ester.* $C_6H.OC_2H_5.OH$.—This is an oily liquid, homologous with guaiacol and having similar medicinal properties. (See p. 1415.)

Thapsia. *T. garganica* L. *Thapsie, Faux Fenouil*, Fr.—An umbelliferous plant, growing in Southeastern Europe, and well known to the ancients, named from the isle of Thapsos, where it was obtained. Theophrastus speaks of its root as emetic and purgative. After long neglect this plant has obtained a foothold in the French Codex, which recognizes a *Resina Thapsiæ* prepared by exhausting the bark of the root with alcohol and evaporating to a soft extract. From this extract the Codex further directs that an *Emplastrum Thapsiæ* shall be so prepared as to contain 7 per cent. of the resin combined with yellow wax, turpentine and colophony. The bark of the root and the resin are both objects of commerce. The bark is described by Stanislaus Martin as almost always doubly quilled, unless where altogether in small fragments, exteriorly rugose with the epidermis here and there detached in patches larger or smaller, and of a deep brown color, interiorly smooth and whitish and of a fibrous fracture. The size of the pieces varies, the largest not exceeding 6 dm. in length and 2.5 in width. It is said that great care is necessary, in removing the root from the bales, not to be injured by the powder which escapes, and which causes itching and swelling of the face and hands. By submitting *thapsia* to the successive action of alcohol and ether Pressoir obtained two resins. (*J. P. C.*, 4e sér., xi, 328.) Canzoneri finds that

the ethereal extract is an amber-colored syrupy resin possessing vesicating properties. From it he has obtained two acids, *octoic* or *caprylic* acid, and *thapsic* acid, besides a neutral non-nitrogenous vesicating substance. (See *A. J. P.*, vol. xiv, 325.) Cazenave objects to the plaster prepared from the resin and kept in masses, as it deteriorates by time. He proposes the following method of preparing a plaster extemporaneously when wanted. Dissolve the resin in alcohol and with the aid of a brush spread it on a suitable recipient, which may be of ordinary plaster, waxed taffetas, or simply gummed paper. A single layer is sufficient for the purpose of an active revulsion, but the effect may be increased at pleasure by increasing the number of layers. (*J. P. C.*, 1868, 29.) The French thapsia plaster is an exceedingly active counter-irritant, producing much inflammation of the skin with an eczematous eruption and intolerable itching and, if the application be maintained, finally an ulcerated and suppurated surface, which on healing leaves behind it pronounced scars. The therapeutic action of the plaster is that of a severe counter-irritant.

The resin from the root of *Thapsia Sylphium* St.-Laz., an Algerian plant, which most botanists believe to be a simple variety of *T. Garganica* L. is, according to Herlaut, more active than that of the official plant. (*Proc. A. Ph. A.*, xxvi, 250.) Heckel and Schlagdenhauffen (*N. R.*, June and July, 1887) find in the root of *Thapsia villosa* L. a vesicant resin, which acts more slowly and gently than does that of *T. Garganica*.

Theobromine Preparations.—The alkaloid *theobromine* (see p. 1122), which is itself insoluble in water, unites with several of the earthy metals to form soluble compounds. Advantage of this fact has been taken by manufacturers to place upon the market a large number of soluble preparations of theobromine. The majority of these preparations have the same range of therapeutic usefulness as the official theobromine and sodium salicylate.

Theobromine Acetyl-salicylate. $C_7H_8N_4O_2$. $C_9H_8O_4$.—A white crystalline powder, soluble in alcohol and insoluble in water. It has been stated that this combination of theobromine shows better results as a rapid acting diuretic than the other salts of the same base. *Dose*, five to fifteen grains (0.33–1.0 Gm.).

Theobromine Barium and Sodium Salicylate. Barutin.—This is a white, amorphous powder with a sweetish alkaline taste and soluble in about twenty parts of water. It represents about 25 per cent. of theobromine and 17 per cent. of barium. Carbonic acid causes a precipitation. *Dose*, three to eight grains (0.2–0.5 Gm.), which should be given well diluted.

Theobromine Lithium. Theobromose. $C_7H_7O_2N_4Li$.—It occurs as fine needle-like crystals, which are soluble in about one-half their weight of water. The solution is readily decomposed by atmospheric carbonic acid. It is used as a diuretic.

Theobromine and Lithium Benzoate. N. N. R. 1917. *Uropherin B.* $LiC_7H_7O_2N_4 + LiC_7H_5O_2$.—A white powder, soluble in five parts of water, representing 47 per cent. of theobromine. Precipitated by carbonic acid. Is stated to be more actively diuretic than other salts of theobromine. *Dose*, five to fifteen grains (0.3–1 Gm.).

Theobromine and Lithium Salicylate. N. N. R. 1914. *Uropherin S.* $LiC_7H_7O_2N_4 + LiC_7H_5O_3$.—Properties and uses the same as those of *Uropherin B.*, but it is somewhat more prone to disturb the stomach.

Theobromine and Sodium Acetate. N. N. R. 1917. *Aguirin. Theonacet.* $C_7H_7O_2N_4Na + NaC_2H_3O_2$.—A white, hydroscopic, alkaline powder, representing 60 per cent. of theobromine, readily soluble in water, forming a strongly alkaline solution which is incompatible with most inorganic salts, causes precipitation of alkaloid from solutions of their salt, darkens calomel, reduces potassium permanganate solution and is precipitated by carbon dioxide. The dry substance becomes pasty when triturated with chloral hydrate, phenol or piperazin. It is incompatible with carbonated beverages, acids, saccharin and mucilaginous liquids, alkaloids and alkaloidal reagents generally. Used as a diuretic. *Dose*, five to fifteen grains (0.3–1 Gm.) in solution.

Theobromine Salicylate. $C_7H_8O_2N_4.C_7H_6O_3$.—This forms fine white needle-like crystals of a bitter taste, acid in reaction and fairly soluble in water. *Dose*, five to fifteen grains (0.3–1 Gm.).

Theobromine and Sodium Benzoate.—A white soluble powder, representing 47 per cent. of theobromine. *Dose*, eight to fifteen grains (0.5–1.0 Gm.).

Theobromine and Sodium Citrate. Urocitral.—A white, alkaline powder, moderately soluble in water, representing 45 per cent. of theobromine. *Dose*, eight to fifteen grains (0.5–1.0 Gm.) several times a day.

Theobromine Sodium Formate. Thephorin. N. N. R. 1917. $NaC_7H_7O_2N_4 + NaCHO_2 + H_2O$.—A white, alkaline, bitterish powder, soluble in 10 parts of water and representing 62.5 per cent. of theobromine. Used as a diuretic. It is asserted to be more irritant to the kidneys than other theobromine salts, and must be used with caution in *nephritis*. *Dose*, five to eight grains (0.3–0.5 Gm.).

Theobromine and Sodium Iodide. Sodium Iodotheobromate. Eustenin. $C_7H_7O_2N_4Na.NaI$.—This is a white, hygroscopic powder, freely soluble in water, but decomposed with precipitation by carbonic and other acids. It represents 51 per cent. of theobromine and 42.6 per cent. of sodium iodide. It is believed to combine the therapeutic effects of these two drugs and is recommended especially as an anti-sclerotic in arterial degenerations, *angina pectoris, chronic nephritis* and similar conditions. The *dose* is eight to fifteen grains (0.5–1.0 Gm.) several times a day.

Theobromine Sodium Iodo-salicylate. Iodotheobromine.—This ambitious powder attempts to combine the actions of theobromine, the iodides and the salicylates. It occurs as a white powder, which is soluble in hot water. It has been recommended chiefly in aortic insufficiency. *Dose*, five to eight grains (0.3–0.5 Gm.).

Theobromine and Sodium Lactate.—A white hygroscopic alkaline powder, soluble in sixteen parts of water, readily decomposed by atmospheric carbonic acid.

Theobromine and Sodium Sulphate.—A white powder soluble in water and containing about 50 per cent. theobromine. It is used like other theobromine salts.

Theoform (not to be confounded with *thioform*).—This is a proprietary name of a condensation product of theobromine and formaldehyde with the addition of citric acid as a preservative. It occurs as a white, bitter powder representing 4 per cent. of theobromine and is soluble in water. *Dose*, fifteen grains (1 Gm.).

Theophylline Compounds.—Although theophylline is now official, it is more frequently employed in the form of one of its soluble compounds. The following are upon the market:

Theophylline Ethylene Diamine. Euphyllin.—This is a white crystalline substance, freely soluble in water and representing 78 per cent. of theophylline. The *dose* recommended is from one and a half to three grains (0.1–0.2 Gm.).

Theophylline Sodium Acetate. Acet-theocin Sodium. N. N. R. 1917. $NaC_7H_7O_2N_4 + NaC_2H_3O_2 + H_2O$.—This is a white, crystalline powder, representing approximately 60 per cent. of theocin, soluble in twenty parts of water. It is used as a diuretic in *doses* of three to five grains (0.2–0.3 Gm.) several times a day.

Theophylline Sodium Salicylate. $C_7H_7O_2N_4Na.C_6H_4.OH.COONa$.—This is soluble in fourteen parts of water. Its doses and uses are the same as the preceding.

Theophylline Sodium Formate. N. N. R. 1917. *Thephorin.* $C_7H_7O_2N_4Na.HCOONa + H_2O$.—This occurs as a white powder soluble in water and possessing valuable diuretic properties. *Dose*, eight to fifteen grains (0.5–1 Gm.).

Thermifugin. *Sodium-methyltrihydroxyquinoline Carbonate.* $C_9H_3(CH_3).NCOONa$.—A water-soluble powder of a white or a yellowish-white color. It is used as an analgesic and antipyretic in four grain (0.26 Gm.) *doses*.

Thermin. *Tetrahydro-β-naphthylamine Hydrochloride.* $C_{10}H_7.H_4.NH_2.HCl$.—The tetrahydro addition compound is formed when metallic sodium is caused to act upon naphthylamine in boiling amyl alcohol solution. It is a colorless to reddish-white crystalline powder, soluble in water, alcohol and amylic alcohol. The hydrochloride has been brought forward by Filehne of Breslau, as a local mydriatic of extraordinary power.

Jonescu (*A. E. P. P.*, 1909, lx, p. 345) has shown that tetra-hydronaphthylamin causes dilatation of the pupil by stimulating the sympathetic nerves and that the dilatation follows either the local installation or the subcutaneous injection of the drug; that it causes marked constriction of the blood vessels, chiefly by acting upon the vasomotor centers, although he believes the peripheral nerves to the vessels are also affected. The rise in temperature which it causes he attributes to a direct action upon the heat centers. According to Feri (*A. I. P. T.*, 1911, xxi, p. 27) there is in poisoning by *thermin* an increase in heat production with lessened heat dissipation which differentiates at once the fever it produces from that seen, for example, in infectious diseases. According to Sacharoff (*Z. E. P. T.*, vii, p. 225) the spasm of the blood vessels of the skin is in part responsible for this rise of temperature by preventing the dissipation of the excessive caloric. Thermin appears to cause a non-maximum dilation of the pupil and does not destroy the light reflexes. It is used as a mydriatic in strengths of from 1 to 5 per cent.

Thermodin. *N. N. R.* 1917. *Acetyl para-ethoxy-phenyl-urethane.* $C_6H_4(OC_2H_5)N(COCH_3)COOC_2H_5$.—A derivative of urethane in the form of a colorless, crystalline powder, fusing at from 86° to 88° C. (186.8°–190.4° F.), insoluble in water. It is used as an antipyretic in *doses* of from five to fifteen grains (0.32–1.0 Gm.).

Thermol. *Acetyl-salicyl-phenetidin. A-s-phen.* $C_{17}H_{17}NO_4$.—This substance is a white, crystalline, odorless, tasteless powder, which is claimed to be a harmless and active antipyretic and analgesic and as such has been used to a considerable extent in *typhoid fever, neuralgia, dysmenorrhea, migraine*, etc.; also as an antispasmodic in *whooping cough*. *Dose*, three to fifteen grains (0.2–1.0 Gm.).

Thevetia. *Yccotli.*—Inhabiting the damp, hot valleys of the Mexican Cordilleras is a large tree belonging to the *Apocynaceæ*, whose fruits are known by the natives as *huesos ó codos de fraile*, or *friar's elbow bones*, and are used as a topical application in *hemorrhoids*. The tree is the *Thevetia Jccotli* A. DC. In the seeds Herrera found a glucoside, *thevetin*. (*A. J. P.*, 1877, 145.) Closely allied to *T. Yccotli* is *T. nereifolia* Juss., a tree which probably grows also in Mexico, but has been found by botanists chiefly, if not solely, in the West Indian Islands, Colombia, Peru and other parts of South America. De Vrij very many years ago discovered in its seeds a glucoside which was closely studied by Blas. (*Neues Jahrb. f. Pharmacie*, Bd. xxxiv, 1854, 1.) He gave it the name of *thevetin* and the formula $C_{54}H_{84}O_{24}$ and believed it to be identical with *cerberin*, previously found by Oudemann in *Cerbera Odallam* Ham., also an apocynaceous plant, but Plugge (*A Pharm.*, 1893, 10) after a thorough study found that cerberin was not identical with either tanghinin or thevetin. With the former it is isomeric, showing the same percentage composition, but has different crystalline form and melting point—cerberin 192° C. (377.6° F.), tanghinin 182° C. (359.6° F.). From thevetin it differs not only in composition, but in the nature of the decomposition products. Cerberin, $C_{27}H_{40}O_8$, is decomposed into *cerberetin*, $C_{19}H_{26}O_4$, a citron-yellow amorphous powder melting at 85.5° C. (186° F.), and glucose, while thevetin, $C_{54}H_{84}O_{24}$, is split into *theveresin*, $C_{48}H_{70}O_{17}$, a white powder, and glucose.

Merck (*Jahresb. für*, 1892, 57) described a glucoside *cerberin* to which he gives the formula $C_{25}H_{38}O_{12}$, which name he changed to *cerberid* in 1911. He states that it was obtained from a Mexican plant, probably *Thevetia Yccotli*. Whether this glucoside is identical with the thevetin of Blas cannot be definitely stated. Blas found that the thevetin of De Vrij boiled in diluted sulphuric acid splits into glucose and *theveresin*, which has the formula $C_{48}H_{70}O_{17}$. Thevetin occurs in minute crystals, odorless, of a bitter taste, slightly soluble in cold water (twelve parts), freely so in boiling water, diluted and strong alcohol, acetic acid, insoluble in ether. Its most characteristic reaction appears to be its dissolving in concentrated sulphuric acid, with the production of a reddish-brown color, changing to a cherry-red, and after some hours to a violet color. In commerce it occurs as a yellowish-white, amorphous bitter powder, easily soluble in water and alcohol. Theveresin is only slightly soluble in boiling water. These substances are active poisons. *Thevetosin*, a crystalline glucoside, was made by Herrera from the seeds of *T. Yccotli*. It is a cardiac poison. (*M. R.*, 1911.) A number of cases of poisoning by the seeds of the East Indian thevetia has occurred; the symptoms have been repeated vomiting, a slow, very feeble pulse, delirium, convulsive movements and coma. The physiological action of the thevetin from *T. nereifolia* has been investigated chiefly by König. (*A. E. P. P.*, Bd. v, 228.)

David Cerna finds that the glucoside of *T. Yccotli* (*P. M. T.*, ix, 396) with sulphuric acid

affords a clear greenish-yellow solution gradually passing to brown and brownish-violet and finally becoming a permanent cherry-brown color, which changes on the addition of potassium bicarbonate to an emerald-green; also that it is in moderate doses stimulant both to the circulation and respiration, but finally paralyzes the heart muscle and the respiratory apparatus; that it causes cerebral convulsions and spinal paralysis, abolishing sensation and reflex activity before voluntary movement by an influence upon the sensory nerves or spinal tract. Zotos N. Zotos (*In. Dis.*, Dorpat, 1892) states that *cerberin* belongs physiologically to the digitalin group.

Thialdine. $C_6H_{13}NS_2$.—This substance, obtained when hydrogen sulphide acts upon aldehyde-ammonia in aqueous solution, forms crystals melting at 43° C. (109.4° F.), which are but slightly soluble in water, more easily in alcohol. It has been investigated by Lusini, who found it a general paralyzing agent, acting powerfully upon the heart, which it arrests in diastole; while *carbothialdine*, $C_5H_{10}N_2S_2$, formed by the action of carbon disulphide in alcoholic solution upon aldehyde-ammonia, acts as a tetanizing agent and does not affect the heart. (See *Nouv. Rem.*, Nov., 1890.)

Thigenol. *N. N. R.* 1917.—This proposed substitute for ichthyol is said to be the sodium salt of a sulphonic acid of a synthetic sulphur oil, and has been used in 20 per cent. ointment for the treatment of *dermatitis, prurigo* and other diseases of the skin. (*K. T. W.*, 1902, No. 6.)

Thilanin.—This substance is said to be made by the action of sulphur upon lanolin. It is of the consistence of lanolin, of a brownish color and peculiar odor. It is said not to be irritating, and has been used without dilution with asserted excellent results in *chronic eczema* and other *skin eruptions* in which uncombined sulphur has been employed.

Thilaven. *Thiozine.* $C_5H_7S_3C_2CH_2C_5H_9O_2$.—This is a solution of linalyl-acet-thiozone in alkaline theozone. It occurs as a dark brown fluid with an alkaline reaction and a pleasant lavender-like odor. It contains 5 per cent. of sulphur, of which it is claimed about one-sixth is in a form readily absorbable through the skin. It has been used for similar purposes to ichthyol by Knorr (*Med. Klin.*, 1910) with satisfactory results.

Thiocol. *N. N. R.* 1917. *Potassium Guaiacol Sulphonate. Orthocoll.* $C_6H_3.(OCH_3)OH.SO_3K$.—This is a fine white powder, having a taste at first bitter and afterwards sweetish; readily soluble in water, sparingly so in alcohol; containing about 60 per cent. of guaiacol. It is pleasant to the taste and not irritant to the gastric or other mucous membranes. Its freedom from odor, ready absorption and non-irritant action on the mucous membrane are among its recommendations that have been reported by its introducers. The original commendation of it by C. Schwartz (*K. T. W.*, 1898), in *tuberculosis, chronic bronchitis* and *intestinal catarrh*, has been confirmed by various clinicians. Cole (*Practitioner*, November, 1911) finds its effects about the same as those of creosote, over which it has the great advantage of being practically tasteless and much less likely to irritate the stomach. It occasionally produces a rash which, however, disappears quickly when the remedy is stopped. The *dose* is eight to twenty grains (0.5–1.2 Gm.).

Thioform. *Basic Bismuth Dithiosalicylate.* $2(S.C_6H_3[OH]COOBiO) + Bi_2O_3 + 2H_2O$ (not to be confounded with theoform).—A yellowish-brown powder containing 72 per cent. bismuth oxide. It is used as an antiseptic dusting powder in *eczema, erysipelas, psoriasis*, etc.

Thiol. *N. N. R.* 1917.—This is a thin, dark brown, neutral liquid, with an odor somewhat like that of Russia leather, having a specific gravity of from 1.082 to 1.089; its aqueous solution is transparent, froths when shaken, and is not precipitated by strong alcohol; it is also feebly soluble in glycerin. On evaporation, liquid thiol yields about 40 per cent. of dried thiol. It is prepared from paraffin oils of from 0.89 to 0.90 sp. gr., which are treated with sulphur at high temperatures. The unsaturated hydrocarbons (olefins, etc.) are alone attacked, and these are then extracted by suitable solvents from the saturated hydrocarbons. They are then acted upon by concentrated sulphuric acid at low temperatures, and the thiol separated out by the addition of ice. It may then be evaporated *in vacuo* to either *thiolum liquidum* or *.thiolum siccum.*

It is asserted that thiol possesses the remedial properties of ichthyol, to which it is superior on account of its being odorless. It has been used in the treatment of superficial and deep inflammations, as in *eczema* and *syphilitic ulcers* and in various joint conditions as *sprains, rheumatism* and the like. Kretzomer states that painted along the nerve in cases of *acute sciatica*, it produces immediate relief. (*All. M. C. Z.*, 1909.)

The liquid is used in the form of a solution or ointment; the dried thiol is sometimes employed as a powder. In *rheumatism* thiol has been given internally in *doses* of from five to ten minims (0.3–0.6 mil), or the dried preparation in *doses* of from one to two grains (0.065–0.13 Gm.).

Thiolinic Acid.—This is a darkish-green extract-like mass, having the odor of mustard, which has been called *sulphurated linseed oil.* It is insoluble in water; soluble in alcohol. Its alkaline combinations, especially with the sodium salts, have been recommended as substitutes for thiol and ichthyol.

Thionine. *Lauth's Violet.*—The oxidation product of *imidamidoiodiphenylimide*, $C_{12}H_{10}N_3SCl$. A greenish-black powder, having a metallic luster. It dissolves easily in water, imparting to the solution an intense violet color. It is used as a microscopic stain for nuclei and also in metachromatic investigations (for mast cells, mucus, etc.).

Thiophene (C_4H_4S) was recognized by Victor Meyer in 1883 as being an invariable accompaniment of benzene as produced from coal tar, and because of the similarity of properties, adhering very closely to it through all reactions. It can be separated by shaking the benzene with one-tenth of its bulk of concentrated sulphuric acid until the addition of a little isatine no longer produces a blue color (indophenin reaction). Steinkopf obtained a 40 per cent. yield of *thiophene* by passing acetylene over pyrites heated to 300° C. (572° F.). (*Chem. Trade Jour.*, 1911, 394.) Thiophene is a colorless, mobile oil, of faint odor, and boils at 84° C. (183.2° F.). Just as benzene is accompanied in coal tar by toluene, xylene and higher homologues, so thiophene is accompanied by *thiotolene* (*methyl-thiophene*), $C_4H_3S.CH_3$ and *thioxene* (*dimethyl-thiophene*), $C_4H_2S.(CH_3)_2$. Thiophene and its homologues yield a large number of brilliant dye colors analogous to those derived from benzene. It was

first physiologically tested by A. Heffter (*A. G. P.*, 39, 420), who found that it appeared in the urine, and lessened the elimination of sulphuric acid in the urine. E. Spiegler (*Th. M.*, Feb., 1892) has employed in *skin diseases*—1, *Sodium thiophene sulphonate*, $C_4H_3S—NaSO_3$; 2, *Thiophenediiodide*, $C_4H_2I_2S$. The first of these compounds is a white crystalline powder, containing 33 per cent. of sulphur, having a feeble, disagreeable odor. It was found in the form of an ointment to act very well in *prurigo* with *eczema*. Thiophenediiodide occurs in tabular crystals, melting at 40.5° C. (105° F.), having a characteristic, not disagreeable odor, insoluble in water, but very feebly soluble in ether, chloroform and warm alcohol, soluble with difficulty in cold alcohol; containing 75.5 per cent. of iodine and 9.5 per cent. of sulphur. It was found to be antiseptic and is one of the compounds suggested as a substitute for iodoform. The *tetrabromide of thiophene*, C_4Br_4S, obtained by the complete bromination of theophene, is recommended as an antiseptic. It occurs as a yellow crystalline powder soluble in alcohol.

Thioresorcin. $C_6H_4(OS)_2$.—A yellowish-gray powder, insoluble in water, made by fusing together one molecule of resorcinol and two molecules of sulphur. It has been recommended as a substitute for iodoform, but has given rise to unpleasant symptoms.

Thiosinamine. *N. N. R.* 1917. *Rhodallin Allylthio-urea. Allylsulpho-urea. Allylsulphocarbamide.* $(NH_2).CS.NHCH_2.CH : CH_2$.—This occurs in colorless, monoclinic or rhombic crystals, of a bitter taste and feeble garlic-like odor. It is moderately soluble in water, very soluble in alcohol and ether. It possesses no bactericidal properties.

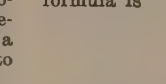
Under the name of *Fibrolysin* a 15 per cent. solution of the double salts of *thiosinamine* and *sodium salicylate* is marketed in the form of ampuls, containing 2.3 mils of the solution. This solution decomposes rapidly on exposure to the air.

Thiosinamine was introduced into medicine by Von Hebra (*Internat. Klin. Rundschau*, September, 1905) in the treatment of various conditions accompanied with formation of fibrous tissue. He states that after its injection there is a temporary reduction in the number of leukocytes, followed by pronounced hyper-leukocytosis which persists for a considerable period of time. The occurrence of leukocytosis has been pretty generally confirmed by a number of authorities, some of whom have attributed the beneficial effects of the drug to this action. Starkenstein, however (*Th. M.*, 1910), believes that it is due to a power of encouraging the hydrolysis of collagen into gelatin, thereby leading to the softening of the connective tissue. While there is some contradiction of opinion among those who have investigated the action of this drug clinically, there is considerable evidence that it is often a remedy of great service in aiding in the absorption of connective tissue. Among the conditions in which this remedy has received recommendation may be mentioned excessive scarring as from *burns*, *keloids*, *urethral* and *œsophageal strictures*, and various other forms of cicatricial formations. Besides these, asserted benefit has been reported in sclerotic conditions of the ear attended with *deafness*, and in sclerosis of the central nervous system as *locomotor ataxia*, and in *arterial fibrosis*. The remedy, whatever may be said of its efficacy, is not entirely invocuous. A number of instances of excessive reaction, attended with chills and sweating following by fever, have been reported, and Pritchard reports a case of *purpura hemorrhagica*, which ended fatally, following 18 injections.

Thiosinamine may be administered by the mouth, in *doses* of one-half to two grains (0.03–0.12 Gm.) several times a day; for hypodermic use it may be dissolved in alcohol or glycerin. Fibrolysin is marketed only in the form of hermetically sealed vials each of which represents five grains (0.2 Gm.) of thiosinamine. The contents of one of these vials may be injected at one *dose* daily, or on alternate days.

Iodolysin is a compound said to contain 43 per cent. of thiosinamine and 47 per cent. of iodine. The advantage is claimed over other preparations that it is non-irritant and is especially suitable for hypodermic injection. Whitehorn-Cole (*F. Th.*, 1910, p. 69) reports favorably upon its use in *rheumatic arthritis*. The *dose* is from five to eight grains (0.32–0.5 Gm.).

Thiosinamine-ethyl-iodide. *Tiodine.* $C_6H_{13}N_2SI$.—Under the name of *tiodine*, the compound resulting from heating thiosinamine with ethyl-iodide has been introduced into medicine. Its formula is



It forms colorless crystals readily soluble in water and alcohol. It has been used for the same class of cases as thiosinamine, especially, however, for the relief of lesions of the central nervous system. Its injection is stated to be painless. It may be administered either by mouth or hypodermically. The *dose* is from one and one-half to three grains (0.1–0.2 Gm.), if by the mouth several times a day, if hypodermically, every other day.

Thorium.—*Thorium dioxide* has been used as a substitute for bismuth subnitrate in making X-ray pictures of the alimentary tract. According to Kaestle (*M. M. W.*, 1908), it is absolutely inert physiologically, and is very opaque to the X-ray. S. Tracey has used the antiseptic action of a current of air passed over heated thorium oxide in the treatment of *tuberculosis* with apparently beneficial results.

Thorium Nitrate. $Th(NO_3)_4 + 4H_2O$.—It forms white, aggregate crystals which are very soluble in water. Depending on the fact or the belief that thorium salts are radio-active much attention has been called to this salt as being the most advantageous of the thorium salts for utilization. A solution of the nitrate has been employed in the treatment of parasitic skin diseases and a weak solution has been administered internally in the treatment of *rheumatism*.

Thiuret. $C_6H_7N_3S_2$.—A sulphurated compound made by the oxidation of *phenyl-dithiobiuret;* it is a bulky, inodorous, crystalline powder, insoluble in water, soluble in alcohol and ether, easily decomposed by alkaline solutions with liberation of sulphur. It is used as a substitute for iodoform.

Thuja. *N. F. IV. Arbor Vitæ. White Cedar.*—"The recently dried, leafy young twigs of *Thuja occidentalis* Linné (Fam. *Pinaceæ*), with stems not over 4 mm. in diameter, and without the presence of more than 1 per cent. of foreign substances." It is specifically characterized by the appressed-imbricated leaves, the pointless cone-scales, and the broad wings etxending all around the seeds. It attains a height of 20 m., and grows in swampy grounds from Pennsylvania northward and west-

ward, often forming extensive "cedar swamps." In Canada and the extreme northern parts of the United States it is commonly called *white cedar*, a name sometimes applied to *Chamæcyparis thyoides* (L.) B. S. P., which latter is more properly called *Southern white cedar*. The wood is reddish, soft, fine-grained, and very durable. The leaves, or small twigs invested with the leaves, have an agreeable, balsamic odor, specially when rubbed, and a strong, balsamic, camphoraceous, bitter taste. The twigs are described as "fan-shaped, flattened, bearing the scale-like leaves appressed in four rows; leaves of the edges boat-shaped, the intermediate flat, those at the tips of the twigs very broad, the lower elongated, all bearing conspicuous glands on the back. Odor strongly balsamic, aromatic and pungent; taste camphoraceous, terebinthinate and bitter. Thuja yields not more than 7 per cent. of ash." *N. F.* A. Kawalier, of Vienna, found in them volatile oil, a bitter principle called *pinipicrin*, $C_{22}H_{36}O_{11}$, which occurs also in *Pinus sylvestris*, sugar, gelatinous matter, a variety of wax, resin, and tannic acid; also a peculiar crystallizable coloring principle, *thujin*, to which he gives the formula $C_{20}H_{22}O_{12}$. It is of a citron-yellow color and an astringent taste, soluble in alcohol, inflammable, and when its alcoholic solution is heated with diluted hydrochloric or sulphuric acid it splits up into glucose and *thujigenin*,

$$C_{20}H_{22}O_{12} + H_2O = C_6H_{12}O_6 + C_{14}H_{12}O_7$$

and by continuing the reaction another molecule of water is taken up by the latter and *thujetin*, $C_{14}H_{14}O_8$, is formed. Thujetin is possibly identical with quercetin. When thujin is heated with barium hydroxide, instead of thujetin is obtained another product, *thujetic acid*, $C_{28}H_{22}O_{13}$. The same chemist determined that the tannic acid of this plant is identical with *pinitannic acid*, which he had previously obtained from the leaves of *Pinus sylvestris* L. (See, for details, *Chem. Gaz.*, Nos. 392, 393, 1859.) According to Hübschmann, the leaves and twigs of *Thuja occidentalis* yield also 1 per cent. of an essential oil of sharp, camphor-like taste, sp. gr. 0.925, boiling point from 190° to 206° C. (374°–402.8° F.), and easily soluble in alcohol. According to *Schim. Rep.*, April, 1897, thuja oil (*oil of white cedar*) contains pinene, fenchone, thujone, and probably carvone.

F. K. Bailey has reported a case of poisoning in a girl, aged fifteen, who took sixteen drops of the oil of white cedar, and directly afterwards fell unconscious, with clonic spasms followed by epileptiform convulsions lasting at intervals for several hours. Long-continued irritation of the stomach resulted. (*N. R.*, 1872.)

In the form of decoction, thuja has been used in *intermittent fever*, and, according to Schoepf, in *coughs*, *fevers*, *scurvy*, and *rheumatism*, and as an emmenagogue. Made into an ointment with lard or other animal fat, the leaves are said to form a useful local application in rheumatic complaints. Sicard and Larue (*Gaz. des. Hôp.*, 1909) assert that the injection of the tincture of thuja into warts will cause their rapid disappearance. A yellowish-green volatile oil, which may be obtained from the leaves by distillation, has been used with success in *worms*. According to Hildebrand both fenchone and thujone act as stimulants to the heart muscle. (*A. E. P. P.*, xlviii.) According to Prochnow (*A. I. P. T.*, xxi, p. 314) the infusion of thuja has a stimulating effect upon the isolated uterus similar to that of hydrastis. The *dose* of the fluidextract made with alcohol is half a fluidrachm (2 mils) from three to six times a day.

Thymacetin. $C_6H_2(CH_3)C_3H_7\left\{\begin{matrix}OC_2H_5\\NH(C_2H_3O)\end{matrix}\right.$.—This is a white, crystalline powder, slightly soluble in water, having the same chemical relation to thymol that phenacetin has to phenol. According to Jolly (*Cb. G. T.*, Feb., 1892), it is a very valuable analgesic and hypnotic. *Dose*, from three to fifteen grains (0.2–1.0 Gm.), best given in capsules.

Thyme. *N. F. IV. Thymus. Common or Garden Thyme.*—"The dried tops of *Thymus vulgaris* Linne (Fam. *Labiatæ*), collected when the plant is in flower." *N. F.* It is extensively grown in the United States for flavoring purposes. It is also used to some extent in medicine. The N. F. description is as follows: "Stems quadrangular, about 0.5 mm. in diameter, grayish-brown or purplish in color, pubescent, nodes from 5 to 20 mm. apart, occasionally with the opposite leaves attached; leaves linear, linear-lanceolate, or ovate-oblong, from 0.5 to 4 mm. in length and from 0.5 to 2 mm. in breadth, summit acute, base obtuse tapering into a petiole from 0.5 to 2 mm. in length, margin revolute, upper surface grayish-green, puberulent, with numerous one-celled, thick-walled, non-glandular hairs; lower surface grayish, pubescent, with non-glandular, one- to four-celled, thick-walled, rough simple hairs, up to 0.135 mm. in length and usually curved at the first joint in the bases; numerous compound glandular secreting hairs, with short one-celled stalk occurring chiefly on the upper surface and depressed in the cuticle, which give the leaf a glandular-punctate appearance; inflorescence in about twelve-flowered axillary whorls; flowers polygamous, calyx tubular, about 4 mm. in length, ovoid or slightly curved on the lower side near the base, from nine- to twelve-nerved, pubescent, the throat bearded with longitudinally striated, straight simple hairs up to 1 mm. in length, bilabiate, upper lip three-toothed, lower lip with two hairy, ascending, attenuate divisions, corolla about twice as long as the calyx, purplish, smooth within, slightly pubescent without, upper lip emarginate, lower spreading and three-lobed, stamens slightly didynamous and exserted, stigma bifid; nutlets about 0.5 mm. in diameter, spheroidal and finely tuberculate. Odor agreeable, aromatic; taste aromatic and warming. Thyme yields not more than 14 per cent. of ash." *N. F.*

Thyme owes its therapeutic virtues to its volatile oil. (See *Oleum Thymi*, PART I). It is occasionally used in domestic medicine, like other aromatic plants, in the form of a hot infusion as a diaphoretic. *Fluidextract of Thyme N F. IV* is made with a menstruum of 10 volumes of glycerin, 25 volumes of alcohol and 65 volumes of water followed by 1 volume of alcohol and 3 volumes of water. The *dose* is one fluidrachm (4 mils).

Thymidol. *Methyl-propyl-phenol-menthol.*—This is stated to be a condensation product of thymol and menthol. It is used in preparing antiseptic washes for the mouth and nose, and also for filling tooth cavities.

Thymoform. *Thymoloform.* $CH_2:(C_6H_3[CH_3][C_3H_7]O)_2$.—It is made by heating 100 parts of thymol with 100 parts of a 40 per cent. solution of formaldehyde and gradually stirring in 100 parts of concentrated hydrochloric acid. It is in the form of a yellowish, tasteless powder, having a faint odor of thymol. It is readily soluble in alcohol, ether, chloroform and olive oil, but insoluble

in water, petroleum, benzin, and glycerin. It is used as an antiseptic dusting powder.

Thymol Carbonate. *Thymol Urethane. Thymolcarbonic Ether. Thymotal. Tyratol.* CO $(NH_2)O.C_{10}H_{13}$.—J. F. Pohl, by the same process by which guaiacol is converted into guaiacol carbonate, has produced from thymol a nearly tasteless, colorless, crystalline compound of neutral reaction, fusing at 49° C. (120.2° F.). It is slightly soluble in water, but is decomposed by the alkaline juices of the intestine, thymol being liberated. It is claimed that this substance is as effective as thymol against the *anchylostoma*, and, owing to its not dissolving in the stomach, is much less apt to produce disagreeable symptoms. (*A. J. P.*, March, 1901, 143.) *Dose*, for adult, thirty grains (2 Gm.) three times a day for four days, followed by brisk purgation.

Thyresol. *N. N. R.* 1917. $C_{15}H_{23}O.CH_3$.—The *methyl ether of santalol* is an almost colorless fluid. Sp. gr. 0.93–0.94, boiling point 149°–156° C. (287.6°–312.8° F.) at 16 mm. pressure. The preparation is practically insoluble in water, but dissolves to a clear fluid in all proportions in alcohol, ether, and oils. It has a slight sandal-wood odor. It has been used by Knauth (*D. M. W.*, 1909), and others, as a substitute for santalol in the treatment of *urethritis*. According to Knauth it is not split up in the organism but appears in the urine in combination with glycuronic acid.

Tilia. *Linden Tree.*—The dried flowers of *Tilia curopæa L.*, and of other species of *tilia* (Fam. *Tiliaceæ*), are official in the German Pharmacopœia under the head of *Flores Tiliæ*. The flowers are yellowish or greenish-white having 5 sepals and 5 petals. The 5 original stamens, by chorisis have each developed a cluster and at the base occurs in addition, a spatulate petal-like body opposite each of the petals. The pistil has a 5-locular ovary which is surmounted by a single style and a 5-toothed stigma. The flowers contain a colorless, fragrant, volatile oil. The bark has been said to contain a neutral body, *tiliadin*, and a glucoside, *tilicin*. (See *A. J. P.*, 1890; *P. J.*, 66, 105.) The infusion is used as a household remedy to relieve hysteria and indigestion.

Timbo.—This name is applied in Brazil to various sapindaceous plants, used as fish poisons. Among these is *Serjania curassavica*, Radlk. (*Paullinia pinnata* L.), in which Stanislaus Martin (*B. G. T.*, xcii) has found an alkaloid, *timbonine;* F. Pfaff have obtained from a *timbo* of unknown origin two alkaloids, *timboin* and *anhydrotimboin*, also an oily compound, *timbol*. (*A. J. P.*, Nov., 1891.)

Tin. (Sn. At. wt., 118.1.) *Stannum. Etain*, Fr. *Zinn*, G.—This was recognized in the old Edinburgh and Dublin Pharmacopœias, and in the U. S. of 1850, but is no longer official. It has, however, too long ranked among recognized remedies to be passed without notice. Tin is one of the metals which have been known from the earliest ages. It exists generally as an oxide (in *stone* and *wood tin*), rarely as a sulphide (*tin pyrites*), and is by no means generally diffused. It is found in England, Spain, Germany, Bohemia, and Hungary, in Europe, and sparingly in some parts of the United States; in the island of Banca and the Peninsula of Malacca in Asia; in Bolivia, and at Durango in Mexico. The mines of Banca furnish the purest tin. The metal is extracted from the native oxide. When this occurs in its purest state, in detached roundish grains, called *stream tin*, the reduction is effected by heating with charcoal. When the common oxide, called *mine tin*, is reduced, it requires to be freed, by pounding and washing, from the adhering gangue; after which it is roasted to drive off sulphur, arsenic, and antimony, and finally reduced in furnaces by means of stone coal. The metal, as thus obtained, is called *block tin*, and is not pure. The purest kind of tin known in commerce is called *grain tin*. The world's production of tin for 1915 was 112,281 tons, the largest producers being Malaga, Bolivia, and Banca in the order named.

Tin is a malleable, rather soft metal, of a silver-white color. It may be beaten out into thin leaves, called *tin foil*. It undergoes a superficial tarnish in the air. Its taste is slight, and when rubbed it exhales a peculiar odor. Its ductility, and tenacity are small; when bent to and fro, it emits a cracking noise, which is characteristic. Its sp. gr. is 7.29, melting point 235° C. (455° F.), and it volatilizes at a white heat. It forms two oxides. The *stannous oxide*, SnO is of a grayish-black color. When perfectly pure it has, according to Roth, a red color. *Stannic oxide*, SnO_2, or *dioxide*, froms two hydrates, both being acids—*stannic acid*, $SnO_2.H_2O$, and *metastannic acid*, $Sn_5O_{10}.5H_2O$, or $(H_2SnO_3)_5$.

The tin of commerce is often impure, being contaminated with other metals, introduced by fraud or present in consequence of the mode of extraction from the ore. A high specific gravity is an indication of impurity. When its color has a bluish or grayish cast, the presence of copper, lead, iron, or antimony may be suspected. Arsenic renders it whiter, but at the same time harder, and lead, copper, and iron cause it to become brittle. Pure tin is converted by nitric acid into a white powder (*metastannic acid*), without being dissolved. Boiled with hydrochloric acid, it forms a solution which yields a white precipitate with potassium ferrocyanide. A blue precipitate with this test indicates iron, a brown one copper, and a violet-blue one both iron and copper. If lead be present, a precipitate will be produced by magnesium sulphate. The Malacca and Banca tin and the English grain tin are the purest kinds found in commerce. Banca tin, from analyses by Mulder, appears to be particularly pure, containing only one twenty-fifth of one per cent. of foreign metals. Block tin and the metal obtained from Germany are usually of inferior quality.

Tin enters into the composition of bronze, bell metal, pewter, and plumber's solder. It is used also in making tin plate, which is sheet iron coated with tin, in making tin amalgam for silvering looking glasses, and in forming the *solution of stannous chloride* (*bichloride of tin*), a combination essential for the dyer's use. It is employed in fabricating various vessels and instruments useful in domestic economy and the arts. Being unaffected by weak acids, it forms a good material for vessels intended for boiling operations in pharmacy. A *false tin foil* is considerably used at present, made by coating lead with tin, and then rolling it out into thin sheets. As tin foil is employed for enclosing medicinal powders and perishable articles of food and medicine, care should be taken not to use this substituted preparation.

Powder of Tin. Stanni Pulvis.—For directions for making, see 16th edition, *U. S. D. Powder of tin* was used as a mechanical anthelmintic, but has very properly gone out of vogue. The *dose* is half an ounce, mixed with molasses, given for several successive mornings, and then followed by a brisk cathartic purge. In the *J. P. C.*, 4e sér., xix,

78, is reported a death believed to have been caused by tin. Pattengo (*A. E. P. P.*, xvii, 1886) confirms the old statement of Orfila that the metal is of no therapeutic value. Three-fourths of a grain of the chloride intravenously injected into a dog suffice to cause trembling, Cheyne-Stokes respiration, opisthotonos, and death. *Stannous chloride*, or *chloride of tin*, is a violent irritant and mild caustic. Chemically pure tin, given internally, is probably not absorbed. (See 16th edition, *U. S. D.*)

Tinospora. *Br. Add.* 1900.—"The dried stem of *Tinospora cordifolia* Miers (Fam. *Menispermaceæ*), collected in the hot season." *Br. Add.*, 1900. *Tinospora* has long been used in India as a medicine and in the preparation of a starch known as *gilæ-ka-sat* or as *palo*. It is said to be a tonic, antiperiodic, and a diuretic. Flückiger obtained from it traces of an alkaloid and a bitter glucoside. The Br. Add., 1900, recognized an *infusion* (*Infusum Tinosporæ* Br. Add., 1900, two ounces to the pint), *dose* one-half to one fluidounce (15–30 mils); a *tincture* (*Tinctura Tinosporæ* Br. Add., 1900, four ounces to the pint), *dose*, one-half to one fluidrachm (1.8–3.75 mils); and a *concentrated solution* (*Liquor Tinosporæ Concentratus* Br. Add., 1900), *dose*, one-half to one fluidrachm (1.8–3.75 mils). *Tinospora crispa* Miers, which is abundant in the Philippines, is used freely by the natives under the name of *makabuhay* (that is, "You may live"), as a panacea, especially valuable in *general debility*, in chronic *rheumatism*, and in *malarial fevers*. It may be prepared in the same way and given in the same doses as *Tinospora cordifolia*.

Tissa. *Tissa rubra* (L.) Brit. [now *Spergularia rubra* (L.) J. and C. Presl.], is a native of Malta, Sicily, and Algiers, and is found growing in dry, sandy soil from Quebec to Virginia. It has long been used as a popular remedy in diseases of the bladder. It was shown by F. Vigier (*J. P. C.*, 1879, ii, p. 371) to contain a resinous aromatic substance which is probably its active principle. It is strongly recommended by Bertherand in *calculous diseases* and acute and chronic *cystitis*. The aqueous extract may be given in *doses* of thirty grains (2.0 Gm.); or the fluidextract, *dose*, a fluidrachm (3.75 mils), three or four times a day.

Titanium. Ti = 48.1.—A hard, gray-colored metal in powdery fragments, specific gravity 3.589. It is soluble in warm hydrochloric acid. Pick (*Med. Klin.*, 1911) has used various salts of *titanium*, especially the sulphate and salicylate, with asserted benefit as local remedies in the treatment of *eczema*, *lupus*, *rhinitis* and *conjunctivitis*. On the skin he uses solutions of from one-quarter to one-half per cent. of titanium sulphate, which must be freshly made, as the salt is decomposed by water. For mucous membranes the solution may vary in strength from one-twentieth to one-tenth of one per cent.

Tobacco. *Tabacum. U. S.* 1890. *Nicotiana Tabacum* L.—The Virginia *tobacco* plant is an annual with a large, fibrous root, and an erect, round, hairy, viscid stem, which branches near the top, and rises from three to six feet in height. The leaves are numerous, alternate, sessile, and somewhat decurrent, very large, ovate-lanceolate, pointed, entire, slightly viscid, of a pale green color, and have a narcotic odor. The seeds, examined by F. M. Brandt, yielded no narcotic principle, though a protein-like substance contained in them was thought by its decomposition to produce nicotine. (*Neues, Jahrb. für Pharm.*, xxi, 42.) William Procter also failed to find nicotine in the seeds. (*Proc. A. Ph. A.*, 1858, 296.)

There is good reason to believe that this plant is a native of tropical America, where it was found by the Spaniards upon their arrival. It is at present cultivated in most parts of the world, and nowhere more abundantly than within the limits of the United States. Virginia is, perhaps, the region most celebrated for its culture. The young shoots, produced from seeds thickly sown in beds, are transplanted into the fields during the month of May, and set in rows with an interval of three or four feet between the plants. Through the whole period of its growth the crop requires constant attention. The development of the leaves is promoted by removing the top of each plant and thus preventing it from running into flower and seed. The harvest is in August. The ripe plants, having been cut off above their roots, are dried under cover, and then stripped of their leaves, which are tied in bundles and packed in hogsheads. While hung up in the drying houses, they undergo a curing process, consisting in exposure to a considerable degree of heat, through which they become moist, or, in other words, are said to sweat, after which they are dried for packing.

Other species also of *Nicotiana* are said to be cultivated, especially *N. rustica* L., which yields the Turkish tobacco and is said to have been the first introduced into Europe, and is thought to have been cultivated by the aborigines of this country, as it is naturalized near the borders of some of our small Northern lakes. The *N. quadrivalvis* of Pursh affords tobacco to the Indians of the Missouri and Columbia Rivers; and *N. fruticosa*, a native of China, was probably cultivated in Asia before the discovery of this continent by Columbus. Besides these there are *N. Persica* L., cultivated in Persia, and is the source of Persian tobacco; *N. repanda* Willd., cultivated in Central and Southern North America; *N. Bigelovii* Wats., of North America. It is very doubtful, however, whether these plants furnish any large part of the commercial tobacco. Latakia tobacco seems to be the product of the *N. Tabacum*, and Senator Vidal asserts that *N. repanda* is not found in Cuba, *N. Tabacum* being the only species there cultivated. (*P. J.*, viii, 710.) Again, the Persian and Turkish tobacco sold under the name of *tumbeki*, which has been variously attributed to *N. Persica* and to *N. rustica*, is in all probability the product of *N. Tabacum*. (*Kew Bulletin*, April, 1891.)

The total annual production of tobacco throughout the world at present is estimated at 1,000,000 tons, of which Asia furnishes 350,000, America 300,000, Europe 250,000, and the rest of the world 100,000 tons. (*Zeit. für Angew. Chem.*, 1905, p. 1623.)

Tobacco, as it occurs in commerce, is of a yellowish-brown color, a strong narcotic penetrating odor which is wanting in the fresh leaves, and a bitter, nauseous, and acrid taste. These properties are imparted to water and alcohol. They are injured by long boiling, and the extract is, therefore, relatively feeble. An elaborate analysis of tobacco was made by Vauquelin, who discovered in it among other ingredients, an acrid, volatile, colorless liquid, slightly soluble in water, very soluble in alcohol, and supposed to be the active principle. It was separated by a complicated process, of which, however, the most important step was the distillation of tobacco juice with potassium hydroxide. In the results of this distillation Vauquelin recognized alkaline properties, which he ascribed to ammonia, but which were, in part at

least, dependent upon the acrid principle above mentioned. To this principle the name of *nicotine* was given; but its alkalinity was ascertained by two German chemists, Posselt and Reimann. The nicotine obtained by Vauquelin and by Posselt and Reimann was a colorless, volatile liquid, and, as subsequently ascertained by Henry and Boutron, was in fact an aqueous solution of the alkaline principle in connection with ammonia. It was reserved for these chemists to obtain nicotine in a state of purity. It exists in tobacco combined with an acid in excess, and in this state is not volatile. It is easily extracted from tobacco by means of alcohol or water as a malate, from which the alkaloid can be separated by shaking it with caustic soda solution and ether. The ether is then expelled by warming the liquid, which finally has to be mixed with slaked lime and distilled in a stream of hydrogen, when the nicotine begins to come over at about 200° C. (392° F.). The percentage of nicotine in tobacco varies considerably—from 1.62 per cent. in Havana tobacco and 2 per cent. in Maryland tobacco to 6 per cent. in Virginia tobacco and 8 per cent. in Kentucky tobacco. For a mode of estimating the proportion of nicotine in tobacco, see Harrison and Self, *P. J.*, June 1, 1912. For an analysis of the ashes of Virginia tobacco, by McD. Irby, of New Orleans, and J. A. Cabell, of Virginia, see *Chem. News* (Sept. 4, 1874, 117). For Liecke's and Schloessing's methods of estimating nicotine, see 17th edition, *U. S. D.*, p. 1346. For Kosutany's method, see *Z. An. Chem.*, 1893, 277.

Nicotine. (*Nicotina* or *Nicotia.*) β-pyridyl-α-methyl-pymolidine.—This is a colorless or nearly colorless fluid, of the sp. gr. 1.027, boiling at 247° C. (476.6° F.), and not solidifying at −10° C. (14° F.); having a faint odor when cold; of an exceedingly acrid, burning taste, even when largely diluted; entirely volatilizable, and, in the state of vapor, very irritant to the nostrils, with an odor recalling that of tobacco; inflammable; very soluble in water, alcohol, ether, the fixed oils, and oil of turpentine; strongly alkaline in its reaction, and capable of forming crystallizable salts with the acids. These salts are deliquescent, having a burning and acrid taste, and, like the salts of ammonia, lose a portion of their base by heat. While nicotine has not been prepared synthetically as yet, two isomeric bases, *isonicotine* and *nicotidine*, have been prepared. On treatment with oxidizing agents, nicotine yields *nicotinic* or *β-pyridinecarboxylic acid*, $C_5H_4N.COOH$. In its action on the animal system it is one of the most virulent poisons known. A drop of it, in the state of concentrated solution, is sufficient to destroy a dog, and small birds perish at the approach of a tube containing it. Tannin forms with it a compound of but slight solubility, and might be employed as an antidote. Nicotine exists in tobacco in small proportion; it has been found in the seeds, and, in very small proportion, in the root. There can be little doubt that tobacco owes its activity to this alkaloid, which has also been criminally employed as a poison. (*N. Y. Jour. of Med.*, N. S., ix.) Nicotine has the remarkable property of resisting decomposition amid the decaying tissues of the body, and was detected by Orfila in the bodies of animals destroyed by it two or three months after their death. Mayer concluded from his experiments that nicotine is the active principle in all parts of the plant both before and after curing. (*Proc. A. Ph. A.*, 1865.)

Although Thoms (*A. J. P.*, 1900, p. 227) was unable to detect any nicotine in tobacco smoke, there is no room for doubt that it is present in sufficient amount to be injurious. Lehmann (*P. J.*, Sept. 18, 1909) finds that about 95 per cent. of the nicotine in tobacco passes over into the smoke, and Toth (*Chem. Ztg.*, 1909, p. 866) has shown that the large proportion of nicotine exists in the smoke in uncombined state.

When distilled at a temperature above that of boiling water, tobacco affords an empyreumatic oil, which Brodie proved to be a most virulent poison. It was official in the U. S. P., 1870, under the name of *Oleum Tabaci: Oil of Tobacco.* A single drop, injected into the rectum of a cat, occasioned death in about five minutes, and double the quantity, administered in the same manner to a dog, was followed by the same result. This oil is of a dark brown color and an acrid taste, and has a very disagreeable odor exactly resembling that of tobacco pipes which have been much used. It has been stated to contain nicotine. (*Ann. Ch. Phys.*, 3e sér., ix, 465.)

It is quite certain that tobacco leaves undergo considerable chemical changes during the processes of curing and preparation for use. Thus, the characteristic odor of ordinary tobacco is entirely different from that of the fresh leaves, and must be owing to the generation of a new volatile principle. The proportion of nicotine is probably slightly diminished by the process of "curing." (See Mayer, *Proc. A. Ph. A.*, 1865.)

Medicinal Properties and Uses.—Tobacco is locally irritant. Snuffed up the nostrils, it excites violent sneezing, and a copious secretion of mucus; chewed, it irritates the mucous membrane of the mouth and increases the flow of saliva; when injected into the rectum, it sometimes operates as a cathartic; and the alkaloid nicotine injected into the cellular tissue of animals evidently produces much pain. In large doses, or in persons unaccustomed to it, tobacco produces severe nausea, sometimes vomiting, accompanied with profuse perspiration, and great muscular weakness. The alkaloid nicotine is a virulent poison. It primarily excites, and secondarily paralyzes, the ganglia upon the sympathetic nerves, stimulates the intestinal muscles, and, in sufficient quantities, has a paralytic action upon the motor nerves. As a result of its action upon the sympathetic ganglia, it causes contraction of the blood-vessels with marked increase in the blood pressure, followed, after large doses, with vascular dilatation and fall of pressure. The pulse rate is at first decreased, later becomes rapid. There is primary increase in the secretion of the salivary and probably of the other glands, followed, after large doses, by paralysis of secretions.

The use of tobacco was adopted by the Spaniards from the American Indians. In the year 1560 it was introduced into France by the ambassador of that country at the court of Lisbon, whose name—Nicot—has been perpetuated in the generic title of the plant. Sir Walter Raleigh is said to have introduced the practice of smoking into England. In the various modes of smoking, chewing, and snuffing, the drug is now largely consumed in every country on the globe. It must have properties peculiarly adapted to the propensities of our nature to have thus surmounted the first repugnance to its odor and taste and to have become the passion of so many millions. Whether or not nicotine plays any part in the pleasurable effects of tobacco is, despite considerable research and discussion, unsettled, but it is generally agreed that the evil

effects of excessive indulgence are due to this alkaloid. The most important disturbances produced are in the digestive and circulatory organs. As a result of the disturbed innervation of the heart, palpitation and cardiac irregularities are common, and the vascular contraction is generally regarded as one of the causes of arterial degenerations.

Formerly much used as a relaxant, tobacco has been superseded by safer and more efficacious remedies, so that it is at present never employed in medicine, except occasionally in *chronic asthma.* It should always be borne in mind that its active principle is absorbed readily by the skin, and that serious or even fatal poisoning may result from its too free application to the surface of the body. A case of death is on record, occurring in a child eight years old, in consequence of the application of the expressed juice of the leaves to the head, for the cure of *tinea capitis.* Death has also been produced by the inhalation of the smoke.

From five to six grains (0.32–0.4 Gm.) of powdered tobacco will generally act as an emetic; but should never be used for this purpose.

Toddalia. *Br. Add.* 1900.—"The dried root-bark of *Toddalia aculeata* Lam." (Fam. *Rutaceæ.*) This climbing shrub, known also as *Lopez root,* growing in East Africa, Madagascar, the subtropical Himalayas, Ceylon, and the Philippines, is a tonic stomachic, containing a resin and a volatile oil, which may be readily obtained from the leaves by distillation. This oil has the odor of citron peel, and a bitter, aromatic taste. See also *Schim. Rep.,* 1906, 82, and 1912, 121. The British Addendum recognized an *infusion* (*Infusum Toddaliæ,* two ounces to a pint), *dose,* one to two fluidounces (30–60 mils); also a *concentrated solution* (*Liquor Toddaliæ Concentratus,* Br. Add., 1900), *dose,* from one-half to one fluidrachm (1.8–3.75 mils).

Tolypyrine. *Tolyantipyrine. Paratolyl-dimethyl-pyrazole.* $C_{12}H_{14}ON_2$.—This compound occurs in colorless crystals soluble in water and alcohol, insoluble in ether, and is used like antipyrine as an antipyretic in *doses* of from eight to thirty grains (0.5–2.0 Gm.).

Tolysal. *Tolypyrine Salicylate.* ($C_{12}H_{14}N_2O$ $C_7H_6O_3$.)—This has been used in *rheumatism. Dose,* ten to fifteen grains (0.6–1 Gm.).

Tonga.—*Tonga Bark* is a composition of unknown barks compounded by the natives of the Feejee Islands for medicinal purposes. The plants from which this remedy is derived are believed to be *Premna taitensis* Schan. (Fam. *Verbenaceæ*), and *Epipremnum mirabile* Schott. (Fam. *Araceæ.*) According to Moeller (*Ph. Centrh.*), the latter is not a source of tonga. (*A. J. P.,* 1881, 439.) It was introduced to the notice of the medical profession by Sydney Ringer and Wm. Murrell, of London, as a remedy for *neuralgia.* (*L. L.,* ii, 1880.) Merck reports the presence of *tongine* and a volatile oil in tonga. (*Merck's Index,* 1907.) The natives are said to steep the bundle as prepared by them for twenty minutes in half a tumberful of cold water, and then, squeezing it dry, drink the infusion, preserving the bundle in a dry place for further use. A fluidextract has been put upon the market, and evidence of its value brought forward, but we have known a fluidrachm of this extract to be given every two hours for two days without obvious effect; the *dose* usually recommended is half a fluidrachm (1.8 mils).

Tonka Bean. *Fève Tonka,* Fr. *Tonka-bohnen,* G.—The seeds of *Coumarouna odorata* of Aublet, a large tree growing in Guiana and Northern Brazil which yields the Dutch Tonka Bean; and of *C. appositifolia* (Aubl.) Tanb, which is the source of the English tonka bean. The fruit is an oblong-ovate pod, enclosing a single seed, from 3 to 4 cm. long and about 1 cm. wide, usually somewhat compressed, with a dark brown, wrinkled, shining, thin, and brittle skin, and a light brown, oily kernel. The seed has a strong, agreeable, aromatic odor, and a bitterish, aromatic taste. Its active constituent is a crystallizable, odorous substance, called *coumarin* or *cumarin,* $C_9H_6O_2$ (see page 1345). It is the anhydride of *coumaric acid,* $C_9H_8O_3$. It is capable of sublimation; but, to obtain it in crystals in this way, a low temperature is necessary. (Waddington, *P. J.,* 1868, 410.) This substance is sometimes found in a crystalline state, between the two lobes of the kernel. Coumarin appears to be a widely spread substance which has been found in many species of plants, notably in species of *Melilotus* (fam. *Leguminosæ*), sweet vernal grass (*Anthoxanthum odoratum* L.), and related grasses, and *Trilisa odoratissima* (Walt.), Cass. (*Liatris odoratissima* Willd.) (fam. *Compositæ*), a plant sometimes used to protect woollens from moths. (*A. J. P.,* 1859, 556; also 1899, 133; see also *Chem. Gaz.,* 1852; *D. C.,* Nov., 1887.) Gössmann obtains coumarin in the following manner. The beans, cut finely, are heated for a long time with an equal bulk of alcohol of specific gravity 0.863, nearly to boiling, and, the tincture being decanted, the residue is treated in the same manner. The tinctures are mixed, the alcohol distilled off until turbidness appears, when four times the bulk of water is added, which precipitates coumarin and fatty matter. The precipitate is then heated to boiling, and the liquid passed through a moistened filter. The fatty matter remains on the filter, and the hot solution which passes deposits the coumarin on cooling. More may be obtained by concentrating the liquid, and may be purified by animal charcoal. One pound of the beans yielded 108 grains of coumarin. Coumarin has been prepared synthetically by heating salicylic aldehyde with sodium acetate and acetic anhydride, whereby *acetocoumaric acid* is formed, which decomposes further into acetic acid and coumarin. It has also been obtained by the action of phenol upon the malic acid. Tonka bean is used to adulterate tincture and extract of vanilla and to flavor snuff, being either mixed with it in the state of powder or put entire into the snuff box. Coumarin adulterated with acetanilid has been found in the market. (*Schim. Rep.,* 1893, 67.) *Tonquin butter* is an article of commerce in Holland. It is the fatty substance of tonka beans; it was analyzed by M. Duyk, it has the sp. gr. of 0.888, melting point is 28° C. (82.4° F.), saponification number 25.7. (*Rep. de Pharm.,* 1908.)

Ellinger (*A. E. P. P.,* 1908, Suppl.) found the fatal dose of coumarin for the rabbit to be 0.3 Gm. per kilo. He confirmed the statement of Köhler (*Cb. M. W.,* 1875) that it acted as a narcotic, but could not find evidence of cardiac depression. The fluidextract of the bean has been used with asserted advantage in *whooping cough* in *doses* equivalent to from five to eight grains (0.32–0.5 Gm.) for children five years old. (*A. J. P.,* 1869, 27.)

Tormentil. *Rhizoma Tormentillæ,* P. G. *Tormentille,* Fr. *Tormentillwurzel,* G. *Tormentilla,* It. *Tormentila,* Sp.—Various species of the rosaceous genus *Potentilla* have been employed in medicine. (See *A. J. P.,* 1875, 109.) It is asserted

that our common *P. canadensis* L. is a valuable sudorific and diuretic.

Potentilla Tormentilla Neck. (*Tormentilla erecta* L., *T. officinalis* Curt.)—The tormentil, or *septfoil*, which was formerly in the Secondary List of the U. S. Pharmacopœia, is a small perennial plant of Europe and Asia. All parts of the plant are astringent, especially the rhizome, which is the part employed. The rhizome of *tormentil* is cylindrical, somewhat fusiform, branching and more or less curved, from 2.5 to 8 cm. long, and from 0.5 to 1.5 cm. thick, brown or blackish externally, and reddish within. It has a slight aromatic odor and a very astringent taste. It contains a red coloring principle, soluble in alcohol, but insoluble in water, and considerable quantities of a peculiar tannin (*tormentil-tannic acid*, $C_{26}H_{22}O_{11}$). Rembold found that tormentilla red has the same composition as rhatany red, and yields the same products of decomposition when fused with potassium hydroxide. He also obtained *kinovic acid*, $C_{24}H_{38}O_4$, and small quantities of *ellagic acid*, $C_{14}H_6O_8$. (*A. J. P.*, 1868, 311; from *Ann. Chem.*, cxliv, 5.) The root is said to be used for tanning leather in the Orkneys and Western Islands of Scotland, and for staining leather red by the Laplanders. Tormentil is a simple and powerful astringent, applicable to all cases of disease in which this class of medicines is indicated. It may be given in substance, decoction, or extract. The *dose* of the powder is from thirty grains to a drachm (2.0–3.9 Gm.).

Toxicodendron Capense Thunb. (Fam. *Euphorbiaceæ.*)—The fruits of this South African species are said to be used for the poisoning of hyenas. They have been investigated by von Engelhardt (*Kobert's Arbeiten*, 1892), who finds in them a neutral, bitter principle, *hyananchin*, which is a powerful poison, resembling strychnine in its physiological action, from which, however, it differs in that it powerfully affects the cerebrum. The convulsions which it produces are of central origin, the poison having no action upon the nerve trunks or the muscles.

Toxylon. *Maclura pomifera* (Raf.) Schneider. (*Maclura aurantiaca* Nutt.) (Fam. *Moraceæ.*) *Osage Orange.*—The bark of the root of this tree, which is indigenous in the Southern United States, is said to be considerably used in making a yellow dye. Alex. King has found in it *moric* and *moritannic acids*. (*A. J. P.*, xlvi, 257.)

Toxynon. *Sodium-acet-amino-mercury benzoate.*—This mercurial preparation, according to Gutmann (*B. K. W.*, 1913), contains 48 per cent. of mercury. He recommends it for intravenous injection in the treatment of *syphilis*. The *dose* is one and one-half to three grains (0.096–0.2 Gm.) every alternate day.

Tradescantia Erecta Jacq. (Now *Tinantia fugax* Scheidw.) (Fam. *Commelinaceæ.*)—The natives of South America used an extract of this plant as a hæmostatic in cock-fights and it has lately been introduced into medicine, being especially recommended in *hemorrhages of the ear and the upper air passages*. Nothing definite is known of its actual composition and its styptic virtue has been ascribed, by some, to its tannin content. For description of *Commelina communis*, a perennial herb of the United States, see Preston, *A. J. P.*, 1898, p. 321.

Tragoponic Acid.—This was found by Rademaker and Fisher in the seeds of *Tragopogon porrifolius* L. (Fam. *Compositæ.*) *Salsify*, more commonly known as *oyster plant*, is the plant which furnishes the edible root. (See *Nat. Drug.*, July 23, 1886, 47.)

Traumatol. *Iodocresine. Iodocresol.* $C_6H_3I.(CH_3)OH$.—This occurs as a purplish-red or yellow powder; it is obtained by acting on cresol with iodine, and is used as a substitute for iodoform.

Tribrom Beta-naphthol. $C_{10}H_4Br_3OH$.—This occurs as a greyish crystalline powder, readily soluble in alcohol, ether and the alkalies. Lehmann (*Beitr. Klin. Chir.*, 1911, xlvii) has used it for the purpose of disinfecting the hands of the surgeon. He uses an alcoholic solution containing 0.5 per cent.

Tribromhydrin. (*Tribromhydrinum. Allyl Tribromide, Tribromaliyl, Tribrompropane, Propargyl Tribromide.* $CH_2Br.CHBr.CH_2Br$.—This substance is a colorless or faintly yellowish liquid at the ordinary temperature, but solidifying when cooled below 10° C. (50° F.) to a mass having a specific gravity of 2.430 at 15° C. (59° F.). Its boiling point is about 220° C. (428° F.) and is soluble in alcohol or ether. It has been recommended by De Fleury as a nerve sedative in *hysteria, asthma, whooping cough*, and other nervous disorders. It may be administered by mouth in capsules containing each five drops (0.25 mil), of which one or two may be given several times a day. It has also been employed subcutaneously in two to three minim (0.12–0.2 mil) doses in 20 minims of ether. (*Ph. Post*, Dec., 1888.)

Tribromphenol. $C_6H_2Br_3.OH$.—*Tribromphenol* is prepared by shaking a solution of phenol with bromine water. It occurs in the form of soft, white, colorless needles, melting at 95° C. (203° F.), and subliming undecomposed at a higher temperature. It is soluble in alcohol, ether and chloroform, and soluble with difficulty in glycerin, liquefied phenol, water and weak alcohol. In caustic alkaline solutions it is readily soluble, and from them it is separated unaltered by acids.

As pointed out on page 0000, the introduction of a halogen into its molecule increases the antibacterial properties of phenol. Bechold and Ehrlich (*Cb. C.*, 1906, xlvii) have found that tribromphenol will inhibit the growth of bacteria when present in 1 part in 10,000. Grimm, who recommends tribromphenol as a surgical antiseptic, states that a half per cent. solution will kill the bacteria of putrefaction in an hour.

Tribromphenol-bismuth. *Xeroform.* $Bi_2O_3(C_6H_2Br_3OH)$.—This is a yellowish-green, insoluble, almost odorless and tasteless powder, which, according to its manufacture, is a chemical combination of equal amounts of bismuth and tribromphenol, containing about 50 per cent. of bismuth oxide.

Xeroform has been widely used as a substitute for iodoform in various surgical procedures. The advantages claimed for it are that it is not only practically odorless, it is also non-toxic, and that it exercises a more powerful antiseptic effect. It appears also to possess to a considerable degree the analgesic action, as well as the desiccating and antiseptic effect of iodoform on *wounds*. It has also been employed as a substitute for the salts of bismuth in the treatment of *enteritis, gastric ulcer* and similar conditions. For the latter purpose it is administered in *doses* of from 8 to 15 grains (0.5–1.0 Gm.).

Tribromphenol Bromide. $C_6H_2Br_3OBr$.—E. W. Lewis finds that the melting point usually attributed to this substance 47.8° C. (118° F.), is much too low, and tnat it may be raised to

148° to 149° F. (64.4°–65° C.) by recrystallizing the compound from ethyl acetate; moreover, while, as usually stated, the substance of low melting point gives off bromine on heating at about 125° F. (51.7° C.), the purified material begins to lose bromine before melting at about 145° F. (62.8° C.). *Tribromphenol bromide* is made by adding 2 to 4 Gm. of phenol dissolved in water to bromine water containing 19 Gm. of bromine. After each addition of phenol the bottle is vigorously shaken, and when all of the phenol is added the mixture is set aside in a dark place for three days; the precipitate is then collected, drained on a porous earthenware tile and dried over sulphuric acid; the precipitate is then dissolved in warm ethyl acetate and the solution on cooling deposits the crystals. The crystals of tribromphenol bromide belong to the orthorhombic system. It forms citron-yellow scales which are insoluble in water, ether, cold alcohol and alkalies. On boiling with alcohol it is decomposed and tribromphenol results.

Triferrin, *N. N. R.* 1917, or *paranucleinate of iron*, contains about 22 per cent. of iron as well as 2.5 per cent. of organically combined phosphorus and is prepared from casein of cow's milk by digestion and precipitation by means of ferric salts. *Triferrin* is freely and completely soluble in a weak solution of sodium hydroxide, but it is insoluble in diluted hydrochloric acid having the acid strength of normal gastric juice. *Dose*, five grains (0.32 Gm.).

Trifolium. *N. F. IV. Red Clover Blossoms.*—"The dried inflorescence of *Trifolium pratense* Linné (Fam. *Leguminosæ*)." *N. F.* It is described in the N. F. as "Heads are ovoid with rounded summit, mostly from 12 to 25 mm. in length and breadth, shriveled, purplish and more or less brown from drying, consisting of many small papillonaceous flowers, crowded together and clothed at the base with broad, pointed, ciliate stipules of a pale green color with darker veins and which may or may not be accompanied by diminutive trifoliate leaves. The individual flowers are from 12 to 15 mm. in length, longer than the four nearly equal teeth and shorter than the narrower fifth tooth, calyx-teet subulate, tapering; petals united into a tube below, the standard longer than the wings, but when recurved appearing shorter; stamens diadelphous (nine and one); style slender. The odor is faintly aromatic and somewhat tea-like, the taste being sweetish, then slightly bitter. Trifolium yields not more than 10 per cent. of ash."

Red clover blossoms were introduced into the N. F. IV and are used to make the fluidextract (see Part III). For the results of a research of the constituents of *T. pratense* by Power and Solvay, see *C. D.*, 1910, 273. Clover has, by the superstitious, been supposed to possess alterative properties. It also enters into the composition of some antiasthmatic cigarettes. There is, however, no sufficient reason to suspect it of any medicinal virtue.

Trigemin. *Dimethyl-amido-antipyrin-butyl-chloral hydrate.* $C_{17}H_{24}N_3O_3Cl_3$.—A product of the action of butyl chloral hydrate on pyramidon, forming long white needles, fusing at 85° C. (185° F.) and possessing a delicate aromatic odor and a mild taste. It has been used as an analgesic in all those forms of pain for which the coal-tar derivatives are valuable. It is incompatible with spirit of nitrous ether, acacia and most of the chemicals that are so with antipyrin. The *dose* is from three to fifteen grains (0.2–1.0 Gm.).

Trigonella. *Greek Hay Seed. T. Fœnum-græcum* L. *Fenugreek. Semen Fœnugræci*, P. G. *Bockshornsamen*, G.—A European annual leguminous plant cultivated in Southern Europe, Northern Africa and India for its seeds. These are oblong-cylindrical, somewhat compressed, obliquely truncated at each extremity, 3 to 5 mm. in length, brownish yellow externally, internally yellow and marked with an oblique furrow running half their length. They have a strong peculiar odor resembling that of elm bark, and an oily, bitterish, farinaceous taste, and contain fixed and volatile oils, mucilage, bitter extractive and a yellow coloring substance. E. Jahns (*Ber. d. Chem. Ges.*, xviii, 2518–2523) has obtained *choline*, $C_5H_{15}NO_2$, and *trigonelline*, $C_7H_7NO_2$. The yield of the former was 0.05 per cent., and of the latter 0.13 per cent. Trigonelline is isomeric and probably identical with pyridine-betaine. By heating trigonelline with concentrated solution of potassium hydroxide, a distillate is obtained which appears to contain pyridine. An ounce of the seeds, boiled in a pint of water, renders it thick and slimy. They yield the whole of their odor and taste to alcohol. On the continent of Europe they are employed in the preparation of emollient cataplasms, enemata, ointments and plasters. They are never used internally for human beings, but the ground seeds are used to an enormous extent in the manufacture of cattle powders or condition powders and to give a maple flavor to confectionery.

Tri-iodophenol Bismuth.—Because of the success of tribromphenol-bismuth the homologous iodine compound has been introduced under the name of *neoform*. It is a yellow powder insoluble in all the ordinary solvents and is used as a surgical dusting powder.

Trillium. *N. F. IV. Beth Root. Birth Root. Wake Robin. Trillium*, Fr., G.—"The dried rhizomes of *Trillium erectum* Linné and closely allied species of *Trillium* (Fam. *Liliaceæ*)." *N. F.*

It is described in the N. F. as follows: "Rhizome oblique, globular, oblong or obconical, truncate, below, terminated by a small bud surrounded by a sheath of scarious leaf bases, annulated by leaf scars and fissured by stem scars. It is from 0.6 to 5 cm. in length and from 0.6 to 2.5 cm. in width, more or less compressed laterally, rootlet scars in several concentric rows on the under side in the upper portions. Externally yellowish to reddish-brown; internally of a pale yellow; fracture somewhat uneven with a more or less spongy appearance. Odor distinct; taste bitter and acrid with a sensation of warmth in the throat and when chewed causing an increased flow of saliva. Trillium yields not more than 5 per cent. of ash."

The indigenous species, *T. erectum* L. is said to have been employed by the aborigines, and also used by the early settlers; it still has some vogue under the name of *beth root* as an astringent and tonic expectorant; also in *hemorrhages* and to hasten *parturition* and as a local irritant in *skin diseases*. *Dose*, of powdered root, a drachm (3.9 Gm.) three times a day. E. S. Wayne found in it a substance supposed to be saponin. It is said also to contain volatile oil and tannic acid. D. J. Prendergast believes that the *Trillium erectum* contains a glucoside similar to convallamarin. (*Am. Drug.*, Nov., 1887.) For details, see 16th edition, *U. S. D.* Vivian I. Reid (*A. J. P.*, 1892, 67) found a small quantity of fixed oil, saponin to the extent of 4.86 per cent. and an acid crystalline principle which is colored purplish-brown by sulphuric acid and light green with sulphuric acid and potassium dichromate.

This rhizome was introduced into the N. F. IV to use in the preparation of the *fluidextract of trillium* with three volumes of alcohol and one volume of water. The fluidextract is an ingredient in *compound elixir of viburnum opulus.*

Trimethylamine. *Secaline.* $CH_3CH_3CH_3N$.—This substance which has been so often confused with propylamine (see p. 1563) is a colorless liquefiable gas of a fishy ammoniacal odor, soluble in water and alcohol and having at 0° C. (32° F.) specific gravity of 0.673, boiling at 9° to 10° C. (48.2–50° F.) and possessing extremely toxic properties. It was first prepared by Wertheim in 1850 from narcotine and was given the name *metacetamine.* The common method of preparing this substance of the present time is by the action of ammonia gas on methyl iodide. The aqueous solution of *trimethylamine* is often miscalled "propylamine," which is a primary compound of ammonia [monamine (which see)], whereas the trimethylamine is a tertiary compound ammonia (triamine). It is not used medicinally.

The hydrochloride, $(CH_3)_3NHCl$, is used as an odorous addition to bait, to lure fish.

Triosteum. *T. perfoliatum* L. *Horse Gentian. Bastard Ipecac. Tinker's Weed. Wild Coffee. Fever Root. Feverwort. Wild Ipecac. Racine de Trioste,* Fr. *Dreisteinwurzel,* G. (Fam. *Caprifoliaceæ.*)—This plant is found in rich woods from Massachusetts to Alabama and westward to Nebraska, preferring a limestone soil and shady situations. The rhizome or root, the part used, is horizontal, long, about 15 mm. in diameter, thicker and tuberculated near the origin of the stem, of a yellowish or brownish color externally, whitish within, and furnished with fibers which may be considered as branches of the main root. When dry it is brittle and easily pulverized. On microscopic examination, numerous crystals of calcium oxalate are to be seen. It has a sickening odor, and a bitter, nauseous taste. It is said to contain an alkaloid which Andree believed to be identical with emetine, but which Hartwich has shown to be different. It yields its active properties to both water and alcohol. Triosteum is cathartic, and in large doses emetic and perhaps diuretic. The bark of the root may be given in *doses* of twenty to thirty grains (1.3–2.0 Gm.), or the extract in half the quantity. For uses, see *A. J. P.,* 1891, 326.

Triphenin. *Propionyl-phenetidin.* $C_6H_4.C_2H_5O.NH.(CH_3.CH_2.CO)$.—A homologue of phenacetin made by boiling a mixture of paraphenetidin with propionic acid; it forms colorless, odorless crystals, using at 120° C. (268° F.), of feebly bitter taste, soluble in 2000 parts of water and its incompatibles are the same as those of phenacetin.

Triphenin has been used to a limited extent as an antipyretic in *typhoid fever, pneumonia,* and other acute affections, and also as an analgesic for nervous pains. Its range of action is precisely that of phenacetin. *Dose,* eight to fifteen grains (0.5–1.0 Gm.).

Tripoli. *Terra Tripolitana.*—An earthy mineral, of a whitish, yellowish, or pale straw color, sometimes inclining to red or brown, usually friable, often adhesive to the tongue, and presenting the aspect of argillaceous earth, though differing from clay by the roughness and hardness of its particles, and by not forming a paste with water. The *Venice tripoli* is said to come from Corfu. Tripoli is sometimes artificially prepared by calcining certain argillites. It is used for cleaning and polishing metals.

Trompatila.—This is the stem and branches of *Bouvardia triphylla* Salisb. (fam. *Rubiaceæ*), a Mexican plant used by the natives for *hydrophobia.* (*A. J. P.,* 1874, 51.)

Tropacocaine. *N. N. R.* 1917. *Benzoyl-pseudotropeine.* $C_8H_{14}NO.C_7H_5O$.—This compound, belonging chemically to the class of *Tropeines* (see *Atropine*), was isolated by Geisel from a narrow-leaved coca plant from Java. (*Ber. d. Chem. Ges.,* xxiv, p. 2336.) It is obtained as an oil, which when quite dry solidifies in radiating crystals, melting at 49° C. (120.2° F.). It has a strong alkaline reaction, and is easily soluble in alcohol, ether, chloroform, benzene, and petroleum benzin. The *hydrochloride,* being freely soluble in water, is usually preferred to the base. It is decomposed by heating with hydrochloric acid into benzoic acid and pseudotropine, $C_8H_{15}NO$.

Tropacocaine resembles cocaine in its stimulant action upon the nerve centers, and also in its local anesthetic action. It differs from cocaine, however, in that it does not cause local constriction of the blood vessels, and that it has very little influence upon the pupil. It is also decidedly less toxic than cocaine. It has been used chiefly in the so-called spinal anesthesia and a large number of surgeons have reported favorably upon it. A *dose* of one grain (0.06 Gm.) is ordinarily recommended, although a number of authors have used larger quantities without evil effects. Tropococaine has been used also as a local anesthetic in ophthalmic and pharyngological practice. It possesses an advantage over cocaine in being more stable in solution and easily sterilizable.

Trypan Blue. *Diamine blue. Congo blue. Azidin blue. Niagara blue. Sodium salt of tolidin-disazo-bi-l-amido-8-naphthol-3, 6-disulphonic acid.*—It has been used as a dyestuff. Recently a purified form of this dye has been brought forward as a therapeutic remedy in various protozoan infections. It occurs as a bluish-gray powder which forms in water a deep violet-blue solution. It is almost insoluble in alcohol and quite so in ether. We do not know of any reports of its use in human beings, but Evers, Zengel (*B. Thier W.,* 1913) and others have reported rapid cures of both *malaria* and *trypanosomiasis* in the lower animals.

Trypan Red. *Sodium salt of ortho-benzidine-mono-sulpho-acid-disazo-bi-2-naphthylamine-3.6-sulpho-acid.* $C_{10}H_4(NaSO_3)_2NH_2N.N(C_6H_4)(C_6H_3)NaSO_3N.NC_{10}H_4(NaSO_3)_2NH_2$.—By *trypan red* is meant a coloring matter allied to *benzo-purpurin B,* or to *Brilliant Congo R.* It is a reddish-brown powder, soluble in water. The aqueous solution is not altered by the addition of acetic acid, but on the addition of a sufficient quantity of hydrochloric acid, the free sulpho-acid is eliminated in blue flakes.

This was brought forward by Ehrlich and Shiga (*B. K. W.,* 1904) as a useful remedy in experimental, and a hopeful remedy in human *trypanosomiasis.* Jaboulay and one or two other French writers (*Lyons Medicale,* 1905) have used it hypodermically in the treatment of *cancers* with asserted extraordinary benefit, but the remedy has failed to come into general use. Eight grains (0.5 Gm.) of the remedy may be injected hypodermically, dissolved in 40 mils of physiological salt solution, at intervals of from two to ten days.

Tulipine.—An alkaloid extracted from the garden tulip, *Tulipa* and of which there are a number

of classes depending upon the order of their flowering. It is said to be a cardiac poison, with remarkable sialagogue properties. (*Nouv. Rem.*, 1886.) Under the name of *chielin* there has been put upon the market a brownish thick extract-like substance of an agreeable odor, easily soluble in water, said to be derived from the bulb of the tulip and to be non-poisonous. It has been highly recommended by H. Heyman as a soothing application in various forms of inflammatory skin diseases. (*D. M. W.*, August, 1902.)

Tumenol.— *N. N. R.* 1917. A dark brown or brownish-black liquid, of a syrupy consistence, which is made from bituminous shale oils. These are agitated with sodium hydroxide solution to remove phenols and then with sulphuric acid to remove pyridine and other bases. The oil is then treated with fuming sulphuric acid. The dark syrupy liquid which separates is washed with water and dissolved in sodium hydroxide. From this solution ether extracts *tumenol oil.* Hydrochloric acid, on the other hand, if added to the sodium hydroxide solution, throws down *tumenol-sulphonic acid.* A mixture of these two substances constitutes *tumenol venale*, a soft, resinous, odorless mass. A. Neisser (*D. M. W.*, 1891) highly commends tumenol as a local application in *eczema* and as having extraordinary powers over the itching of *prurigo, parasitic dermatitis* and other *skin affections.* He uses a lotion made with equal parts of ether, rectified spirit and water or glycerin and 10 per cent. of tumenol.

Turicin.—A compound of tannin (21 per cent.) with glutenin, which forms a fine inodorous, tasteless, flesh-colored powder, insoluble in water and dilute acids. Weak alkalies impart to a solution of *turicin* a rose-red color and the stronger alkalies a blood-red color. It is employed as an intestinal astringent in five to fifteen grain *doses.* It is incompatible with iron and alkalies, acacia and arsenic solutions.

Tussol. *Antipyrine Mandelate* (*Phenyl-glycolate*). $C_{11}H_{12}N_2O.C_6H_5CH(OH)COOH$.—It forms a white powder, fusing at 52° to 53° C. (125.6°–127.4° F.), is soluble in water and incompatible with most of the substances that are incompatible with antipyrine. It is recommended in the treatment of *whooping cough* in the following *doses:* for children under one year, from three-fourths to one and a half grains (0.048–0.096 Gm.); from two to four years, four to six grains (0.26–0.4 Gm.).

Tutty. *Tutia. Impure Oxide of Zinc.*—This oxide is formed during the smelting of lead ores containing zinc. It is deposited in the chimneys of the furnaces, in the form of incrustations, moderately hard and heavy, and studded over with small protuberances of a brownish color on the outside and yellowish within. As it occurs in commerce, the pieces occasionally present a bluish cast, from the presence of small particles of metallic zinc. Sometimes a spurious substance is sold for *tutty*, consisting of a mixture of blue clay and copper filings, made into a paste with water and dried on an iron rod. It is distinguished from the genuine tutty by its diffusing in water and exhaling an earthy odor, and by its greater friability. Tutty is used solely as an external desiccant. To fit it for medicinal use it must be reduced to fine powder, which is dusted over the affected part, or applied in the form of an ointment.

Tylophora Leaves. *Tylophoræ Folia. Br. Add.* (Fam. *Asclepiadaceæ.*)—The dried leaves of *Tylophora asthmatica* (L.) Wight and Arnott, are used in certain parts of India as a poison for vermin, and have been used with fatal results as a poison. *Tylophora asthmatica*, which grows in Bengal, Burmah and Ceylon, has been known in Indian medicine since 1780, and has been largely used in both the civil and the military medical service of Madras. It is officially described as "petiolate, entire, from two to five inches (five to twelve and a half centimeters) long and from three-quarters of an inch to two and one-half inches (eighteen to sixty-five millimeters) broad, lanceolate-ovate or ovate or subrotund in outline, somewhat cordate at the base, abruptly acuminated; rather leathery in texture, glabrous on the upper surface, and finely downy on the lower; of a brownish-green color, which is paler on the lower surface. Odor slightly aromatic; almost devoid of taste." *Br. Add.*

David Hooper has separated from this drug an alkaloid, *tylophorine*, soluble in ether and alcohol, but scarcely so in water; forming crystalline salts, and striking with nitric acid a purplish-red color, with Fröhde's reagents a deep sap-green, and with potassium dichromate and sulphuric acid a dirty violet. Tylophora resembles in its activity ipecac, and is used as a substitute for that drug in *bronchitis* and in *dysentery.* In *doses* of from twenty to thirty grains (1.3–2.0 Gm.) it is used as an emetic. The expectorant *dose* is from one-half to two grains (0.032–0.13 Gm.).

Tyramine. *N. N. R.* 1917.—One of the active bases which was found in ergot by Barger and Dale was *para-hydroxy-phenyl-ethylamine*, which had previously been found by Barber and Walpole as one of the decomposition products in putrid meat infusion. This base is now prepared synthetically, and marketed under the trade-name of "*tyramine.*" In a general way the physiological action of tyramine is similar to that of epinephrine, but it is very much less powerful, and produces practically no effect when applied locally to the mucous membranes. It is recommended only as an internal remedy, as a circulatory stimulant in *shock* and *collapse* and as a uterine stimulant. There is not sufficient clinical evidence to justify a conclusion as to its practical usefulness. The *dose* is from one-third to one grain (0.02 to 0.065 Gm.).

Ulex. *Ulex europœus* L. (Fam. *Leguminosæ*), is the common *furze, gorse,* or *whin* so conspicuous in the waste places and by the roadsides of Great Britain, from its spiny branches and bright yellow flowers situated on the spines, either solitary or in pairs. The young tops are fed to cattle and horses, but the food value has been questioned. The leaf buds have been used as a substitute for tea and the flowers yield a beautiful yellow dye. In the seeds of this plant, A. W. Gerrard has found an alkaloid, *ulexine.* In 1890 Kobert (*D. M. W.*, 1890), as the result of an elaborate physiological study, came to the conclusion that ulexine and cytisine are identical. The suggestion has given rise to a considerable chemico-physiological discussion, a brief abstract of which may be found in *P. J.*, Feb., 1891. Kobert found indications of a second alkaloid in ulex. Partheil (*A. Pharm.*, 1892, 448; 1894, 486) and Plugge (*A. Pharm.*, 1894, 444) are in accord as to the identity of ulexine and cytisine. Ulexine has been used in cardiac *dropsy. Dose*, from one-fifteenth to one-twentieth of a grain (0.004–0.003 Gm.).

Ulmaren is the name given by Bourcet to a

mixture of the salicylic acid esters of the higher aliphatic alcohols. It has been stated to contain 75 per cent. of salicylic acid. *Ulmaren* is described as a heavy, pale yellowish-red, refractive, neutral, or weakly acid liquid, of pleasant, faint odor recalling salol, and burning taste. Its sp. gr. at 15° C. (59° F.) is 1.06; and its boiling point lies between 237° C. and 242° C. (458.6°–467.6° F.). It crystallizes from an equal volume of petroleum benzin, and is almost insoluble in water, but is soluble in alcohol, ether and chloroform. Animal experimentation (*Th. M.*, 1903, xvii) showed that in moderate doses it is well taken, but if given in large doses by the mouth causes in the dog vomiting and purging, and in the rabbit a dose of 0.07 Gm. per kilogramme intraperitoneally injected, caused death from asphyxia. It is recommended to be used as an external application in *rheumatic* and *neuralgic* diseases, as well as in *gout*, either to be painted on the part and covered with waxed paper or used in the form of an ointment made up with lanolin, in which case it should be present in the proportion of 30 per cent. After epidermatic application the salicylic acid reaction may be demonstrated in the urine in three hours and lasts for three days. It is affirmed to have marked analgesic, antipyretic and antirheumatic powers. (*B. G. T.*, June, 1903.) *Dose*, fifteen to forty-five grains (1–3 Gm.); externally thirty to sixty grains (2–3.9 Gm.).

Ultramarine. *Outremer*, Fr. *Ultramarin*, G.—This fine blue pigment was formerly obtained from *lapis lazuli*, or *lazulite*, a mineral of Siberia. It is now prepared artificially on a very large scale. In preparing it, a mixture of soft clay with sodium sulphate, charcoal, caustic soda and sulphur is heated in crucibles. In this way a colorless compound is first produced, termed white ultramarine. This, however, soon becomes of a green color. The green ultramarine thus obtained, which is also used as a color, is then mixed with sulphur and heated. The sulphur takes fire and is allowed to burn in the air, when the product becomes of a fine blue color. (*Roscoe and Schlorlemmer*, vol. ii, 459.) It is thought to be a compound of aluminum and sodium silicates with sodium polysulphide, although the sulphur present is retained in two conditions, part being deposited when ultramarine is treated with acids and part escaping as hydrogen sulphide.

Umbellularia. *Umbellularia californica* (Arn.) Nutt. *California Laurel. California Sassafras. Spice Tree.* (Fam. *Lauraceæ*).—The leaves of this California tree are employed in *neuralgic headaches*, and in *intestinal colic* and *atonic diarrhea;* also externally as a mild counter-irritant. Stillman and O'Neill (*N. R.*, 1883) obtained from the seeds a new acid, *umbellulic acid*. The leaves are said also to contain about 4 per cent. of a volatile oil, having a specific gravity of 0.936, a warm camphoraceous taste, and a strong pungent odor. Burse has separated from the oil by fractional distillation *umbillol*, an oil having the formula $C_9H_{12}O$, which dissolves in concentrated sulphuric acid with red color, and is narcotic. (*Ap. Ztg.*, xi.) According to Schimmel & Co. (*Schim. Rep.*, April, 1897), it also contained *cineol*, $C_{10}H_{18}O$. It is probable that the volatile oil is a strong local anesthetic, as it has been found to act rapidly when brought in contact with exposed pulp or sensitive dentine. The fluidextract has been used in *doses* of from ten to thirty minims (0.6–1.8 mils).

Umber. *Terra Umbra.*—A mineral of a fine compact texture, light, dry to the touch, shining when rubbed by the nail, and of a fine pale brown color, which changes to a peculiar beautiful deep brown by heat. According to Klaproth, it contains 13 parts of silica, 5 of alumina, 48 of ferric oxide, 20 of manganese, and 14 of water in 100. *Burnt umber*, as well as the mineral in its unaltered state, is used in painting. The umber of commerce is said to be brought chiefly from the island of Cyprus.

Uranium.—U = 238.5. The salts of the metal uranium are violent poisons, producing not only severe *gastro-enteritis* and *nephritis*, but alst acting specifically on the hemoglobin of the blood, affecting its oxygenating powers. (See *P. J.*, Sept., 1890; Oct. 30, 1897.) They have been carefully investigated by Jacob Woroschilsky (*Arbeiten d. Pharm. Inst.*, Dorpat, v. 1890), who finds that they are violent poisons, though acting slowly, especially when given subcutaneously, small toxic doses producing death almost as rapidly as larger ones. In the lower animals, 1 milligramme of the oxide per kilogramme will produce an intense parenchymatous nephritis, followed by violent inflammation of the intestines. There is marked elevation of the blood pressure and widespread degeneration of the tissues, especially of the blood vessels. In mild cases of poisoning a transient glycosuria is a primary symptom.

Uranium calcium phosphate, according to Churchward (*L. L.*, 1911, i, p. 660), is radioactive and may be used instead of radium in the treatment of *rodent ulcers*.

Jackson (*A. J. Phys.*, 1910, xxvi, p. 381) finds that *sodium-uranium tartrate* causes a slight rise in the blood pressure and some increase in the respiration; it destroys the coagulability of the blood, but does not affect its oxygen carrying power.

Urasol. *Acetyl-methylene-disalicylic Acid. Afsal.* $CH_2(C_6H_3{<}^{OC_2H_3O}_{COOH})_2$.—This substance is said to be formed from about 75 per cent. of salicylic acid, 16 per cent. of acetic acid, and 8 per cent. of formaldehyde. It occurs as a yellowish-white powder, insoluble in water, soluble in ether and alcohol, and is incompatible with acids and with iron compounds It has been used in *doses* of five to eight grains (0.32–0.5 Gm.), given in capsules, in *muscular rheumatism*, irregular *gout*, and as an antiseptic in *cystitis* and other inflammations of the genito-urinary tract.

Urea. *N. N. R.* 1914. *Carbamide. Urée*, Fr. *Harnstoff*, G. $CO(NH_2)_2$.—For an account of the physical and chemical properties of *urea*, the reader is referred to treatises upon physiology. Urea has been employed in practical medicine as a hydragogue diuretic in the treatment of *dropsies* and as a tonic alterative in *phthisis*. (*L. L.*, December, 1901.) *Dose*, ten grains (0.65 Gm.) every six hours; increase *pro re nata*. Urea is incompatible with chloral hydrate and lead acetate.

A new and convenient method of determining urea has been found in an enzyme called *urease*, which exists in the soy bean as well as in other leguminous seeds. It readily converts urea into ammonium carbonate by the following hydrolytic reaction:

$$CO{<}^{NH_2}_{NH_2} + 2H_2O = CO{<}^{ONH_4}_{ONH_4}$$

In its use for the quantitative determination of urea the natural alkalinity of the urine must first be determined, which is then compared with the alkalinity of a specimen of the urine which has been treated with the enzyme.

Thio-urea is a substance in which one atom of oxygen in a molecule of urea is replaced by an atom of sulphur, $CS\langle^{NH_2}_{NH_2}$ or C_4N_2S. According to Paul Binet (*Rev. Méd. de la Suisse Rom.*, 1893), it is a very active poison, paralyzing the nerve centers, but leaving intact the peripheral nerves and the muscles. It is used commercially as a photo fixing agent and to remove stains from negatives.

Ureabromine. *Bromo-calcium Urea.* $CaBr_2.4CO(NH_2)_2$.—This occurs as colorless, odorless crystals, freely soluble in both water and alcohol, with a melting point of 186° C. (366.8° F.) and representing 36 per cent. of bromine. It is incompatible with chloral hydrate, potassium iodide and acids. It has been used by Fischer and Hoppe (*B. K. W.*, 1911) with asserted remarkable results in spasmodic conditions of children, especially in *epilepsy*. He attributes this effect not only to the bromine, but also to the readily absorbable calcium it contains. The *dose* for the adult is from thirty to sixty grains (2–4 Gm.).

Urechites. *Urechites suberecta* Jacq. *Savannah Flower. Yellow-flowered Nightshade.*—This is an apocynaceous plant, which grows abundantly in the West Indian Islands and to some extent in Florida, is said to be used in Jamaica by the negroes as a poison. The symptoms which it produces are violent vomiting and purging, with convulsions. J. J. Bowrey (*J. Chem. S.*, June, 1878) has isolated from it two glucosides, *urechitin* and *urechitoxin*, having respectively the formula $C_{28}H_{42}O_8$ and $C_{13}H_{20}O_5$. Isaac Ott (*T. G.*, 1880) finds the plant to be a powerful cardiac poison, first increasing and then depressing the arterial pressure, and finally, if the dose be large enough, killing by producing cardiac arrest. The results reached by Ott are in accord with those of Ralph Stockman (*Laborat. Rep., Royal College of Physicians*, Edinburgh, vol. iv, 1892), who finds that both of the glucosides are very active poisons belonging to the digitalis group. On the other hand, Vowinkie came to the conclusion that even small doses of the plant depress the heart, and experiments made upon man by Bowrey show that in large doses the drug produces nausea, vomiting, general depression, great perspiration, and slight swelling of the pulse. Stockman (*Rev. de Clin. et de Thér.*, June 29, 1892) found that the leaves contain a toxic alkaloid, which he calls *urechitine*, $C_{28}H_{42}O_8 + H_2O$, and a glucoside, *urechitonin*, which is less toxic. In Jamaica the drug is said to have been used in the treatment of *intermittent* and other *sthenic fevers*. The *dose* of the fluidextract is from two to ten minims (0.12–0.6 mils).

Urobiline. *Hydrobilirubin.* $C_{32}H_{40}O_7N_4$.—This biliary pigment, prepared from urine, occurs as a brown resinous mass soluble in alcohol, ether, chloroform, and alkaline solution. It has been proposed by Th. Roman and G. Delluc as a reagent for zinc. A few drops of a solution of urobiline in chloroform, 2 mils of which are mixed with 5 mils of absolute alcohol, will cause a green fluorescence in an alkaline solution containing zinc. (See also *D. M. W.*, 1913, No. 10.)

Urol. *Urea Quinate.* $C_7H_{12}O_{6\cdot2}[CO(NH_2)_2]$.—A chemical combination of one molecule of quinic acid and two molecules of *urea*. It forms very soluble, colorless prismatic crystals fusing at 106° to 107° C. (221.8°–224.6° F.). It is employed in the treatment of *gout, gravel* and *uric acid diathesis* in *doses* of thirty to forty-five grains (2–3 Gm.). This amount is to be dissolved in warm water and taken either on rising or when retiring. It is incompatible with acids.

Ursal.—A compound of urea and salicylic acid, used as a substitute for sodium salicylate.

Urtica. *Ortie brûlante*, Fr. *Brennessel*, G.—Various species of this genus (Fam. *Urticaceæ*) are furnished with poisonous stinging hairs. *Urtica gigas* A.Cunn. (now *Laportea gigas* Wedd.), of Eastern Australia is said frequently to kill horses, and to produce in man a sting whose impression lasts for months. (*N. R.*, 1875.) It has generally been thought that the virulence of the hairs is due to the presence of free formic acid (*A. J. P.*, xxii), and David Hooper (*P. J.*, April, 1887) has demonstrated the presence of formic acid, or a substance very closely allied to it, in the hairs of the *Nilgri nettle* (*Girardinia palmata* Gaudich.). Nevertheless, it does not seem probable that formic acid is the poison. G. Haberlandt believes it to be a non-volatile albuminoid, and L. Reuter has obtained from several nettles a glucoside. (*A. J. P.*, Jan., 1890.) Oddi and Lomonaco (*Rif. Med.*, April, 1892) isolated from the common nettle a crystalline alkaloid, and found that in mammals the extract acts powerfully upon the vasomotor system, and in frogs causes centric paralysis with diastolic cardiac arrest.

U. dioica L., or *common nettle*, and *U. urens* L., or *dwarf nettle*, European plants naturalized in waste places to some extent in the United States, have been used in medicine as local irritants, as diuretics (*A. J. P.*, 1866), and especially for the purpose of arresting *uterine hemorrhage*. The fluidextract may be given in *doses* of half a fluidrachm (1.8 mils) or a decoction of the strength of an ounce to a pint in teacupful doses. Under the name of *brandol* is marketed a preparation used in the treatment of *burns* and *wounds;* it is a liquid consisting of 93 per cent. infusion of urtica, 2 per cent. picric acid and 5 per cent. glycerin.

Ustilago. *U. S.* 1880. *Corn Smut.*—The genus *Ustilago* belongs to the *Ustilaginaceæ*, all the members of which generally develop their spores in the ovary or anthers of the host plant, forming a slimy mass, which in maturing becomes a black dust made up of spores. They produce the *smut* in cereals. *Ustilago Maydis* (DC.) Tul. is produced on the stems, the pistils (corn grains), and the male inflorescence (tassel) of the Indian corn. It is specifically characterized by its minute spherical spores, about 0.007 mm. in diameter. It is abundant in the United States. Upon the corn the smut appears in masses, varying in size from a cherry to a child's head. These masses are smooth, irregularly globose, or sometimes lobulated, having at first a livid, bluish tint, and then becoming blackish, and finally bursting and emitting the black contents, consisting of innumerable globose very minute spores, each of which is covered with beautiful little pointed processes. In a dried state the masses are blackish and covered with a black powder.

C. H. Cressler found in ustilago an alleged alkaloid, *secaline* (*trimethylamine*), besides a thick, viscid, fixed oil and a resin soluble in ether, but not in alcohol. (*A. J. P.*, 1861, 306.) Rademaker and Fischer (*Nat. Drug.*, 1887, 296) believed that

they had discovered a white, bitter alkaloid, *ustilagine*, soluble in ether, while H. B. Parsons decided that the fixed oil contained an acid which he provisionally named *sclerotic acid;* also an amine-like volatile substance extracted by ether. (*N. R.*, March, 1882; also *West. Drug.*, 1894.) A. W. Balch (*Journ. Boston Soc. Med. Sci.*, March, 1901) was not able to find any active substance in the smut.

The belief that corn smut is an abortifacient to the lower animals (*A. J. P.*, Sept., 1861) appears to be without foundation, as in the experiments made by the United States Department of Agriculture in 1898 (*Farmers' Bulletin*, No. 69) no effect was produced by corn smut given to pregnant cows. The experiments of James Mitchell (*T. G.*, ii, 223) that ustilago abolishes sensation, reflex action, and later general motor power in the frog, is contradicted by the results of Balch, who also found that enormous doses of the substance have no effect upon the color of the cock's comb. In *doses* of one to two drachms (3.9–7.7 Gm.) it has been claimed by W. A. N. Dorland that the fluidextract markedly increases the severity and frequency of the uterine pains in human labor. The whole drift of our present evidence is to show that ustilago is probably inert.

Uzara. *Uzaron.*—Under this name the root of an undetermined African plant, probably belonging to the *Asclepiadaceæ*, has been used both by the natives and European physicians in the treatment of *dysentery*, especially of the amœbic variety. Guerber and Frey (*A. E. P. P.*, 1913, lxxv, p. 75) have determined that it contains neither alkaloid nor tannin, but does contain non-nitrogenous glucosides which have a digitalis-like action upon the heart and diminish peristalsis of the intestines. It appears to owe its virtues in part to its amœbicidal action, but in part also to its effect upon the intestinal muscles.

Vaccines. *Bacterins.*—Efficient vaccine therapy is much older than serum therapy. The word vaccine takes its origin from the Latin *vacca*, cow, and Jenner's publication of 1798, "*An Inquiry into the Causes and Effects of Variola Vaccinae.*" (See Part I, *Virus Vaccinicum*, U. S. *Vaccine Virus*, p. 1203.) Vaccination against smallpox is still our most reliable method of immunization against an infectious disease. Pasteur later applied the term vaccine to his attenuated anthrax virus, and Sir Almroth Wright has still further extended it in his "*bacterial vaccines*" to cover killed cultures of micro-organisms injected into man for the cure as well as the prevention of disease. Strictly, vaccine should mean only one thing, the virus of vaccinia or cow pox.

The various products treated below have this in common, that they are disease producers so modified as to be comparatively harmless, and are used to immunize against the disease which in their virulent form they cause.

This immunization may be either to prevent infection or to ameliorate, or cure, an already existing infection. Vaccines, then, are classed as *antigens*, while serums represent *antibodies*. In receiving a vaccine, the patient is called upon to manufacture his own antibodies. This fact is not to be lost sight of, particularly in serious illness. By vaccine treatment there is being introduced into the body material more or less similar to those invaders which the body forces are already striving to overcome. The balance in the struggle may be a narrow one, and such a load, though well intended, may turn the battle in the wrong direction. On the other hand, for preventive immunization, vaccine therapy has the advantage that the antibodies produced in the patient's own serum are more stable than when introduced in foreign serum and, furthermore, that the cells of the body as well as the blood fluid may be brought into the defensive line.

The greater part of these vaccines are bacterial vaccines. These are suspensions of killed bacteria in physiological saline solution, with 0.25 to 0.5 per cent. phenol or cresol as preservative. The bacteria are grown on a solid medium, such as agar, are washed off with the saline solution, and the killing is usually accomplished by heating one hour at 53° to 60° C. (127.4°–140° F.), though strong antiseptics may be used for this purpose.

The number of organisms per mil is estimated by direct counting in a microscopic chamber, by comparison with the number of blood cells in normal human blood, or by relative density; saline solution is then added to reduce the suspension to the desired strength. When in the final containers tests are made to insure sterility.

"*Stock vaccines*" are prepared from strains of the different organisms carried in stock by the producer. "*Autogenous vaccines*" are made up from the actual cultures obtained from the patient to be treated and are usually preferred (see remarks on specificity, under *Immune Serum*, p. 1603). Nevertheless, on account of the delay and expense of obtaining and isolating the patient's own strain, stock vaccines are often used. For prophylactic immunization, of course, stock vaccines are necessary.

Aside from prophylaxis (*typhoid fever, cholera*) the success in bacterial vaccine therapy seems to have been attained in chronic, sluggish, localized infections.

Bacterial vaccines deteriorate with age—how much we are unable to tell until we have a measure of their potency. They should, however, be kept at 4° to 15° C. (39°–59° F.) and be used within a short time—probably three or four months—of their preparation.

Rabies Vaccine. N. N. R. 1917. *Antirabic Virus. Pasteur Treatment.*—The prevention of *hydrophobia* in persons bitten by rabid animals is one of the debts owed by the world to Pasteur. While formerly 15 per cent. of such unfortunate people contracted rabies and died, the mortality now in treated cases is less than 1 per cent. usually and in some institutes almost zero. The treatment is in a sense a preventive one. It is instituted after the bite, but before symptoms have developed. On account of the long incubation period in rabies there is then opportunity to acquire immunity in most cases.

The dried cord method of Pasteur, which is still the most used on account of its long successful history, consists in daily hypodermic injections of portions of the dried spinal cord of rabid rabbits.

The rabbits have been inoculated intradurally with "fixed virus," that is, a virus whose incubation period has been shortened and fixed at five to seven days by passage from rabbit to rabbit through a long series. The usual incubation period of "street virus," or rabies as it occurs naturally, is from 12 to 90 days. In this process of fixation the virus gradually loses its virulence for man. The cords of the rabbits are dried for various lengths of time over caustic potash in an aseptic manner; if dried for 6 days, the cord is

called a "6-day cord." The treatment is begun with cords dried the longest time; originally Pasteur began with a 14-day cord, but the tendency has been to use cords dried fewer and fewer days, as the fixed virus has been found practically innocuous for man. The treatment lasts about 21 days, a piece of cord 5 millimeters long is emulsified in 2.5 mils salt solution and injected each time. Other modifications of the Pasteur treatment are the injection of weak dilutions of the fresh fixed virus (Högyes), the carbolization of the virus (Fermi), attenuation by dialysis (Cumming) or by drying while frozen (Harris). The virus should be prepared as few hours as possible before its use.

Acne Bacillus Vaccine. *N. N. R.* 1917.—The acne bacillus is a short rod, not decolorized by Gram's stain, growing only in the absence of oxygen, and even sluggishly then. The vaccine prepared from it is used in cases of *acne* in which the bacillus is found and which do not improve under the usual staphylococcus vaccine. The usual *dose* is about 5,000,000 killed bacteria.

Cholera Vaccine. *N. N. R.* 1917.—The cholera vibrio is the cause of *Asiatic cholera.* It is a curved rod, decolorized by Gram's stain, a rapid grower, and prefers an alkaline medium. The vaccine is used prophylactically with good success in Japan. The following results with the vaccine are reported by the Japanese Imperial Institute:

	Case rate per 100,000	Case mortality rate per cent.
Inoculated	55	39.5 per cent.
Uninoculated	70	74.5 per cent.

Gonococcus Vaccine. *N. N. R.* 1917.—The gonococcus is a thick, coffee-bean shaped organism occurring in pairs. It is decolorized by Gram's stain and is difficult to grow, even on media which contain one of the body fluids. In *gonorrheal urethritis, vaginitis,* and *ophthalmia* no benefit is to be expected from vaccine treatment. Some favorable influence is frequently exercised by the vaccine in cases of *gonorrheal arthritis.* The *doses* used are 5,000,000 (freshly isolated cultures) to 1,000,000,000 (old strains).

Pertussis Bacillus Vaccine. *N. N. R.* 1917.—The pertussis bacillus, or bacillus of Bordet-Gengou, is the cause of *whooping-cough.* It is a very small Gram-negative rod, growing at first only on special media. The vaccine prepared from this organism is used both as a preventive and in the treatment of whooping-cough. In the former case three doses of 50,000,000 to 2,000,000,000 are given a week apart. For treatment, the *doses* range from 50,000,000 to 2,000,000,000 every two to four days. It is reported that the vaccine treatment makes the attack milder and in particular shortens the course of the disease.

Plague Bacillus Vaccine. *N. N. R.* 1917. *Haffkine Prophylactic.*—The bacillus of *bubonic plague,* or *Bacillus pestis,* is a short, Gram-negative rod which has a tendency to take up the stain more intensely at the ends, leaving a relatively light staining central portion. It grows fairly well on ordinary laboratory media and is one of the most virulent bacteria known, since it will easily cause a fatal infection by mere contact with the abraded skin. The vaccine is used with fair success as a preventive—those inoculated being less prone to the disease than the uninoculated in the same community and having relatively milder attacks if not entirely protected. Though the prophylactic is useful for travelers through badly infected territory, reliance in a plague outbreak is to be placed in eradicative measures rather than in Haffkinization of the population.

Staphylococcus Vaccines. *N. N. R.* 1917.—There are three species or varieties of staphylococci concerned in human disease, the *Staphylococcus albus,* which produces a white growth on solid media; the *Staphylococcus aureus,* which produces golden yellow, and the *Staphylococcus citreus,* giving a lemon yellow. The first of these is the usual cause of the relatively mild skin pimples and boils; the second is more likely to be encountered in more severe abscesses and carbuncles, while the third is relatively rare. All are large round organisms, Gram positive and tending to a tessellated arrangement; rapid growth is obtained on all ordinary media. It is with these organisms that the most striking successes of vaccine therapy have been made, particularly in *furunculosis.* If possible, the vaccine should be autogenous, but cure is frequent with stock vaccines. Some cases will not respond even to autogenous vaccines. The initial *dose* is usually 20,000,000 to 100,000,000, repeating with an increase every four or five days until a slight reaction is obtained, then proceeding more slowly until a cure is effected. As with other methods of treating this affection, relapses are not infrequent; more intensive and prolonged treatment is then indicated. *Sycosis vulgaris, pustular acne, carbuncles, abscesses* are all amenable to vaccine therapy to a greater or less degree, but, especially in the two latter, surgical measures should not be neglected.

Streptococcus Vaccine.—There is difference of opinion regarding the unity or the plurality of the disease producing types of streptococci. The usual *Streptococcus pyogenes* is a round or oval organism. Gram positive, tending to be arranged in chains, and to divide with the line of division at right angles with the chain; the cocci often appear in pairs. This organism grows less readily and in smaller colonies than the staphylococcus. The streptococci forming long chains (*Streptococcus longus*) are thought to be more pathogenic than those with short chains (*Streptococcus brevis*). On blood agar the colonies have a clear halo, due to hemolysis (*Streptococcus hemolyticus*). Other strains (called *Streptococcus viridans*) produce greenish colonies under like conditions; these latter are found in infections such as *endocarditis* and *arthritis,* while the hemolytic strains occur in the virulent, pyogenic *phlegmons* and fatal *septicemias.* Another form, *Streptococcus mucosus,* produces a mucoid growth, and has a capsule like the pneumococcus.

The name *Streptococcus rheumaticus* is given to the streptococci found in *rheumatism, Streptococcus erysipelatus* to those of *erysipelas,* and some suppose a particular streptococcus to be the causative agent in *scarlet fever.* The evidence for the latter is poor, the streptococci found in this disease and responsible for the greater number of the complications being probably secondary invaders.

On account of our inability to treat the greater part of the streptococcal infections directly, this has been a favorite field for vaccine therapy, but the results are far from convincing. Russian reports of successful prophylaxis of scarlet fever by the use of streptococcus vaccine have not been confirmed in this country. Occasional favorable results are obtained in the treatment of one or another conditions of streptococcal invasions, espe-

cially if attention is paid to strain specificity and the tendency of the organisms to decrease in pathogenicity and immunizing power under artificial cultivation.

Streptococcus and Prodigiosus Vaccine. N. N. R. 1917. *Toxins of Erysipelas and Prodigiosus. Coley's Fluid.*—This suspension, used in the treatment of inoperable *sarcoma*, is practically a bacterial vaccine prepared from *Streptococcus pyogenes* and *Bacillus prodigiosus*. Due to the latter, the fluid has a reddish tint. An analysis of the reported cases in which it has been used indicates that it is probably of some value in the field for which it is recommended.

Typhoid Bacillus Vaccine. N. N. R. 1917. *Typhoid Vaccine. Typhoid Prophylactic.*—The typhoid bacillus, or *bacillus of Eberth*, is an actively motile rod, sometimes very short, sometimes by the end-to-end arrangement of several individuals, long and filamentous, Gram-negative and growing readily on ordinary media. It is the cause of *typhoid fever*—in German *typhus*, but to be distinguished from true typhus fever, or *typhus exanthematicus*. As the staphylococcus vaccines are the best examples of vaccine therapy, so typhoid vaccine is the best example of prophylaxis by bacterial vaccine. Treatment of *typhoid fever* by vaccines, while yielding some slightly encouraging results, is often dangerous on account of the severity of the general infection. Attempts to rid typhoid carriers of their bacilli by vaccine therapy are occasionally successful, usually not.

In 1896 Pfeiffer and Kolle in Germany and Wright in England began work on typhoid immunization. The German vaccine was grown on solid medium-agar—the English in broth and heated to 60° C. (140° F.). Later Leishman found that heating to 53° to 54° C. (127.4°–129.2° F.) was sufficient and gave better immunization. The English used one injection at first, then two, eight days apart. Kolle advised three. The method of the American army, instituted by Russell, followed the agar cultures and the triple dose of Kolle, but used Leishman's strain and temperature. The results in the United States Army are well known and striking; together with improved sanitation, the compulsory vaccination has practically eliminated typhoid. In the 1898 camp at Jacksonville, before vaccine protection, there were 10,759 troops and 248 deaths from typhoid. In the camp at San Antonio covering a similar period in 1911, after vaccination, there were 12,801 troops and no deaths from typhoid.

The vaccine is a suspension containing one billion bacilli per mil. The injections are given seven to ten days apart, the first being one-half mil, the second and third one mil, hypodermically. Reactions both local and febrile are often seen within forty-eight hours, more frequently with some lots of vaccine than with others. It appears that the intensity of reaction given by a given lot of vaccine may bear some relation to its immunizing power. The vaccine produces agglutinines (positive Widal test) in men and animals injected, also bacteriotropism or opsonin against the typhoid bacillus. Typhoid vaccine probably becomes more or less inactive after a few months and should be kept at a temperature between 4° and 15° C. (39.2°–59° F.) in the dark.

The protection given by the vaccine is not absolute nor life-long, but for three years it is usually sufficient to resist all ordinary intensities of infection, and some immunity doubtless persists through life. Even when the vaccinated do chance to contract the disease, their attack is generally much milder than in the unvaccinated.

There have been combined with the typhoid vaccines in some instances vaccines against infection with *paratyphoid bacillus A* and *paratyphoid bacillus B*. These two infections, though generally milder, resemble typhoid in their symptoms and in the types of causative organism. It appears that immunization against all three diseases can go on simultaneously.

Pollen Extract. N. N. R. 1917. *Hay Fever Vaccine.*—This product is included with the vaccines because it depends on an immunological response on the part of the person receiving treatment. Hay fever and rose cold are probably caused by the irritant action of the pollen of certain plants on the ocular and respiratory mucous membranes of especially sensitive individuals. By skin inoculation it is often possible to determine to what pollens a person is sensitive. The administration of pollen extract is an attempt to decrease their sensitiveness, in other words, to immunize the patient against the pollen. The Gramineæ or grasses are chiefly concerned in the production of rose cold (June cold), and the Compositæ in that of *Hay fever* or autumnal catarrh. Pollen extracts have been prepared from each of these two great classes and favorable reports from treatment are not uncommon. The extract is usually given in a long series of injections, preferably before the symptoms of the year appear. The extract is unstable and should be used when freshly prepared. Severe reactions may also occur with potent extract unless the symptoms are watched and the increase in dosage made gradually.

Vaccinium. *Vaccinium crassifolium* Andr. (Fam. *Vacciniaceæ.*)—The leaves of this American shrub are said to be astringent and diuretic, and capable of replacing uva ursi. *Dose*, of the fluidextract, from a half to one fluidrachm (1.8–3.75 mils).

Valamin. *Iso-valerianic-ester of Amylene Hydrate.* $(CH_3)_2C_2H_5.COOC_5H_9$.—It occurs as a colorless liquid sparingly soluble in water with a taste and odor suggesting that of valeric acid. It is used as a nerve sedative and mild hypnotic in *doses* of from four to fifteen grains (0.25–1 Gm.).

Valeric Acid. *Valerianic Acid. Acidum Valericum. Acidum Valerianicum. Isopropylacetic Acid.* $HC_5H_9O_2$. Mol. wt., 102.08. *Acide valérianique, Acide valérique*, Fr. *Valeriansäure, Baldriansäure*, G. *Acido valerianico, It.*, Sp.

In the 1860 U. S. revision this acid was transferred from the Preparations to the Materia Medica list; in that of 1880 it was dropped entirely.

For modes of preparing valeric acid from the oil and roots of valerian, the reader is referred to the article on Valerian in this work, and for other methods of producing valeric acid, see *U. S. D.*, 19th ed., p. 1688. It is prepared also from amyl alcohol by reaction with a mixture of potassium dichromate and sulphuric acid, as the first step in the preparation of sodium valerate.

Valeric acid (originally valerianic acid) received its name from having been found in the oil distilled from the root of *Valeriana officinalis* L. (Fam. *Valerianaceæ*). It was first obtained in 1817 by Chevreul from the oil of the dolphin, and received the name of *delphinic acid*, which, however, upon the discovery of its identity with the acid afterwards obtained by Pentz from valerian, was superseded by its present title. It has been

obtained also from the bark and fruit of *Viburnum Opulus* L. and other species of *Viburnum* (Fam. *Caprifoliaceæ*), the sap wood of the European elder (*Sambucus nigra* L.) (Fam. *Caprifoliaceæ*), the root of *Angelica Archangelica* L. (*Archangelica officinalis* Hoffm.) (Fam. *Umbelliferæ*), and from various organic products of the vegetable and animal kingdom.

Valeric acid is a colorless liquid, of an oily consistence, a repulsive odor, resembling, however, that of valerian, and a pungent, sour, acrid, disagreeable taste. Its sp. gr. is 0.937 for the synthetic acid and 0.931 for the natural. It is soluble in thirty parts of cold water, and when agitated with water takes up about 20 per cent., without losing its oily consistence, and rises to the surface of the liquid. Alcohol and ether mix with it in all proportions. It is very soluble in strong acetic acid and dissolves camphor and some resins. It forms salts with the alkalies and reddens litmus paper strongly, but the blue color gradually returns in a warm place. For tests of purity by Mossler, see *P. J.*, 1911, 175.

The virtues of valerian have been attributed to valeric acid and the latter has therefore been used as a nerve sedative, but it is probably inert. The customary *dose* is from three to ten minims (0.2–0.6 mil).

Valeridin. *Valerydin. Sedatin. Iso-valeryl-p-phenetidin.* $C_6H_4\begin{cases}NHCOC_4H_9\\OC_2H_5\end{cases}$.—This substance occurs as white, glistening needles, which are readily soluble in alcohol or chloroform, difficultly soluble in ether, and almost insoluble in water. It is obtained by heating isovaleric acid with p-phenetidin. C. Erdmann (*Ph. Ztg.*, xliii) commends this substance in *doses* of from eight to fifteen grains (0.5–1.0 Gm.) a day, as a succedaneum for valeric acid, and as being very serviceable in *migraine, neuralgia* and *hysteria.*

Validol. *N. N. R.* 1917. *Menthyl Valerate.* $CH_3.CH_2.CH_2.COO.(C_{10}H_{19})$.—*Validol* is a clear, colorless liquid, of a mild, pleasant odor, and slightly bitter taste, said to contain 30 per cent. of menthol combined chemically with 70 per cent. of valeric acid. It was originally proposed by Schwersenski (*Th. M.*, 1897) as being locally nonirritant and affording a means of exhibiting menthol; for its local action in *pruritus, gastralgia, coryza,* various mucous inflammations, and as an antispasmodic in *migraine, neurasthenia, hysteria* and other neuroses. Validol has also been used as an antiemetic, for the relief of *sea-sickness* and in other forms of *nausea.* It is stated to be specially eliminated through the urine, to which it imparts a peculiar odor. *Dose,* five to twenty minims (0.3–1.3 mils); locally 10 to 15 per cent. ointment is recommended.

Validolum Camphoratum is a 10 per cent. solution of camphor in validol.

Valofin.—This is stated to be a combination of peppermint extract with *valeryl ethylate* and ammonium valerate. It has an agreeable odor and is so concentrated that a teaspoonful when mixed with a cupful of warm water will represent an infusion of peppermint and valerian. It is used as a nerve sedative in *doses* of from fifteen to thirty minims (1–2 mils).

Valonia. *Acorn Cups. Valloné, Vélanède, Gallon,* Fr. *Knoppern, Walonen,* G.—The great cups of the acorns of the *Quercus Aegilops* L. (Fam. *Cupuliferæ*), a native of Bosnia, contain a very large percentage of tannin. They are extensively exported for dyeing and tanning, and have been employed as an astringent in *diarrhea.*

Valyl. *N. N. R.* 1917. *Valeric Acid Diethylamide.* $C_4H_9.CO.N(C_2H_5)_2$.—It occurs as a colorless liquid having a characteristic odor and burning taste, and boiling at 210° C. (410° F.). According to Kionka (*D. M. W.*, xxvii, 1901), valyl produces cerebral excitement, attended with convulsions, probably of cerebral origin, as there is no increased reflex activity. It is said primarily to increase the blood pressure and to have little action upon the heart or respiration. It is somewhat irritant, but may be given in four per cent. aqueous solution, and has been used as a substitute for valerian in *hysterical* and allied *neuroses. Dose,* four to fifteen grains (0.26–1.0 Gm.) three times a day, preferably administered with an equal amount of tallow in gelatin capsules.

Vanadic Acid. *Acidum Vanadicum.* (*Meta-vanadic Acid,* HVO_3.)—Forms golden-yellow scales, which are only slightly soluble. According to Le Blond and C. David, *vanadic acid* is actively antiseptic, and very useful in solutions for the skin, 0.05 in 1000; for gynecological use, 0.17 in 1000.

Sodii Vanadas. Sodium Vanadate. $NaVO_3$. This is a yellowish-white powder, freely soluble in hot water.

Ferri Vanadas. Iron Meta Vanadate. $Fe_3(VO_3)_6$.—A dark, grayish-brown powder, almost insoluble in water.

Lithii Vanadas. Lithium Meta Vanadate. $LiVO_3 + H_2O$.—A yellowish-white crystalline powder, freely soluble in water.

The meta vanadates are used in preference to the ortho, pyro, etc., due to their stability in solutions. They are incompatible with acids, the latter imparting to their solutions a yellowish-red color.

In the arts vanadic acid is used in various oxidizing processes as a carrier of oxygen, effecting by its presence the more efficient action of other oxidants, as in the aniline black formation, where a small amount of ammonium vanadate is capable of taking the place of large amounts of chlorates and similar oxidizing agents. It is also used in vanadium inks.

According to Jackson (*J. P. Ex. T.*, 1912, iv, p. 1) sodium orthovanadate, when injected in large doses, produces a slight rise in the general blood pressure, which is due to constriction of the vessels of the abdominal region, increased peristalsis of the intestinal tract, salivation, vomiting and diarrhea, more or less spasm of the bronchial muscles, and death from respiratory failure.

According to Dutton (*J. A. M. A.*, June 3, 1911), workers in industries in which vanadium is used, suffer from a form of *chronic poisoning,* the most important results of which are congestion of the lungs and of the kidneys, and sometimes *hemorrhagic nephritis* and also irritation of the gastro-intestinal tract. *Anemia* is an early symptom, and there is usually a dry cough, loss of appetite, emancipation and albuminuria.

The vanadates have been used in *anemia, tuberculosis* and a host of other chronic diseases, but are probably without therapeutic virtue. The usual *dose* of sodium or lithium meta vanadate is from one-sixtieth to one-fifteenth of a grain (0.001–0.004 Gm.).

Under various names, as *vanadiol, oxylasine,* etc., various proprietary preparations containing vanadium have been introduced for which extraordinary therapeutic properties were claimed. The

evidence in support of these claims, however, is extremely unsatisfactory.

Vandellia. *Vandellia diffusa* L. (Fam. *Scrophulariaceæ.*)—This is an herb of Paraguay, said to be used by the natives as an emetic. (*P. J.*, 1872, 849.)

Vanilla. *N. F. IV* (*U. S. P. VIII*). *Vanilla Bean. Vanille,* Fr. Cod. *Fructus Vanillæ,* P. G. *Vanille,* G.—"The cured, full-grown, unripe fruit of *Vanilla planifolia* Andrews (Fam. *Orchidaceæ*)." *N. F.*

Vanilla planifolia is a fleshy, dark green, perennial climbing plant, with a very long, smooth, dark green stem, much branched, and furnished at the nodes with aerial roots, which cling to the tree or the wooden framework supporting the plant. The dark green, tough leaves are alternate, oval, sessile, attenuate at the apex, fleshy and veinless. The pale greenish-yellow, sessile flowers are about two inches in diameter, and occur in loose, axillary racemes of eight or ten. The fruit is a slender pod, seven or eight inches long, filled with an oily mass containing numerous small, black, shining seeds.

This plant is a native of the West Indies, Mexico and South America, but is now extensively cultivated. The plant does well from the sea-level up to two thousand feet of altitude, requiring for its perfection, however, a moist, hot climate, with an habitual dry summer spell which seems to be necessary to bring good flowering. It is propagated by means of cuttings, sometimes two or three feet in length, but preferably from ten to twelve feet long, taken from growing shoots; these are planted after the dry season is over and should produce flowers in two years. Preferably placed upon trees, but sometimes on long stakes, trellises, wire supports, etc., the slip is placed with one end on the ground, covered with leaves or some light top dressing. In many cases the vines are planted so closely as scarcely to leave room for cultivators to pass, but it has been found that under these circumstances the vanilleries are especially liable to destructive fungous diseases. As the flower does not fertilize itself, fertilization (pollination) by hand is necessary; it is usually performed by women and children. It is said that a fairly trained workman can fecundate over one hundred flowers per hour. In most localities not more than thirty fertilized flowers should be left to a plant. The pods reach their full size in from five weeks to eight months, according to the altitude of the locality and to the amount of shade. The first indication of ripening is a slight yellowing of the whole pod; as soon as this occurs the pods should be picked, and sorted, and the curing process commenced. If left to ripen further the pods are prone to split and otherwise deteriorate. For the purpose of curing them the pods are kept in a heated room for some days (about 110° F.), then transferred to a cooler one (90° F.), and finished at ordinary temperature. During the process, which lasts some months, there is a loss of 70 to 80 per cent. of weight. For details as to culture, see *Bulletin* 21, 1898, U. S. Department of Agriculture, Division of Botany. The practice of curing the beans by placing them under blankets in the sun is still in vogue, but that of using a regulated artificial heat is more certain, and it is the modern method.

When thoroughly cured the beans are sorted and tied into bundles, which are wrapped in sheet lead or placed in small metallic boxes. In doing this it is essential that the bundle be wrapped in a thin vegetable parchment paper, as chemical action occurs when the beans come in contact with the metal.

Fruits which have not been picked early enough are inferior and are frequently cut into short pieces and sold as "cuts." If by chance the fruit should be picked too early the quality of the resulting product is distinctly inferior. The fruit as first picked has no aroma, the *vanillin* during the process of curing being produced from the glucoside *coniferin* in the interior of the fruit. This was shown to be converted into *coniferyl alcohol* and glucose, and the former of these subsequently changed into vanillin.

The cultivation of vanilla has extended from South America throughout the tropics, so that at present, although the wild plant is abundant in the Mexican States of Vera Cruz and Oaxaca the vanilla of the markets comes almost exclusively from vanilleries. Holland is supplied from Java plantations; France from Tahiti, Madagascar, Réunion, Guadeloupe, and other of her colonies. From Mauritius and the Seychelles the product goes to London. In the markets most of the varieties are known by the name of the country in which they are produced. The finest of the varieties is the Mexican, although of recent years the Bourbon beans have so improved that they almost rival it in strength and flavor. At present the Mexican bean is sold at somewhat less than double the price of the Bourbon; the Bourbon at almost double the price of the Tahiti, the latter bean being commonly much injured by carelessness in the process of curing.

Of *Mexican vanilla,* the first quality occurs in pods from 15 to 20 cm., long, flattened, 6 to 8 mm. in diameter, with the lower end slightly attenuated, the upper end gradually tapering for about a quarter of the length of the pod, usually curved and slightly twisted near the point. The color is dark brown, the pods fairly plump, the surface ridged longitudinally, and with an incrustation of fine crystals beginning at the ends, gradually extending; when fresh somewhat viscid, but always roughish to the touch. For an interesting account of the Mexican vanilla plant by Charles E. Hires, see *A. J. P.*, 1893, 576.

Of the Mexican vanillas the most valuable variety, called *ley,* or *vainilla mansa,* by the Spaniards, consists of cylindrical, somewhat flattened pods, six or eight inches long, three or four lines thick, nearly straight, narrowing towards the extremities, bent at the base, shining and dark brown externally, wrinkled longitudinally, soft and flexible, and containing within their tough shell a soft black pulp, in which numerous minute, black, glossy seeds are embedded. It has a peculiar, strong, agreeable odor, and a warm, aromatic, sweetish taste. The interior pulp portion is most aromatic. In it are more or less numerous, minute crystals. Another variety, called *vainilla simarona* by the Spaniards, is smaller, of a lighter color, and less aromatic. The pods are said to be very dry and to contain no vanillin. (*Nueva Farmacopea Mexicana.*) According to Schiede, it is yielded by a distinct species, the *Vanilla sylvestris* Schiede. A third variety is the *vainilla pompona* of the Spaniards (*boba vainilla,* or *plátano vainilla*). In this, the pods are from 12 to 18 cm. long, from 12 to 18 mm. broad, shaped somewhat like a plantain, almost always open, very dark brown or nearly black, soft, viscid, and of a strong odor. Schiede states that it is the product

of the *Vanilla Pompona* Schiede. The variety *vainilla vezacate* is said to be derived from pods gathered long before maturity. (*Nueva Farmacopea Mexicana.*) The *vainilla pompona* of the Spaniard is evidently the *vanillons* of European commerce, which are usually from 10 to 13 cm. long and from 15 to 25 mm. in diameter, frequently sharply angled, brown to red-brown in color, usually split open and free from efflorescence. Owing to the transverse markings by twine with which they have been wrapped during the process of curing, the beans have a peculiar twisted appearance. Their odor, which resembles that of heliotrope, is due to the presence in them of *heliotropin*, in lieu of *vanillin*.

Bourbon vanilla, produced in the Isle of Réunion to the amount of 200,000 pounds a year, resembles Mexican vanilla, but is scarcely so long in the tapering portions, is of a dark-brown almost black color, is not so firm as the Mexican, has the surface smooth and waxy, and soon becomes covered with a coating of acicular crystals known as "frost." The odor of this vanilla is said to resemble that of Tonka bean rather than that of Mexican vanilla.

The *Seychelles* and *Mauritius vanilla* (*inferior Bourbon* of the trade) has the pods about six inches in length, not over a quarter of an inch in width, and characterized by the pale color, the faint odor, and a smooth but not waxy surface.

South American or *Guadeloupe vanilla* resembles the Mexican bean, but is usually recognizable, when the bean is entire, by the latter being broad and flattened, usually half an inch or more wide, slightly tapering at the lower end, and at the upper sharply attenuated an inch or so at the point. It has a reddish-brown color, and is of a rank odor. It is very pulpy, with a surface intermediate in feel between the Bourbon and the Mexican, and having but few crystals. One variety of this vanilla, sold under the name of *vanillons*, has the odor of heliotrope and is much used by perfumers and tobacco manufacturers.

Tahiti vanilla, "*transplanted Mexican vanilla*," has its pods from six to seven inches long, flat, from three-eighths to half an inch wide, with a reddish-brown color. They are almost destitute of vanilla flavor, and have an odor suggesting heliotrope. It is said they contain piperonal and also vanillin. (*Ph. Cb.*, 45.)

Java vanilla, which is almost exclusively consumed in Holland, has a pod from four to six inches long, with a flavor as fine as that of the Mexican bean, and a much stronger odor.

Vanilla pods are described by the N. F. as: "Pods linear, flattened, from 15 to 35 cm. in length and from 5 to 9 mm. in breadth: summits terminating in flat circular scars; gradually tapering, more or less bent and curved or hooked at the bases, or in the Tahiti variety, broad in the middle and tapering towards either end, the base closely resembling the summit; externally blackish-brown, longitudinally wrinkled, moist-glossy; occasionally with an efflorescence of vanillin in the form of acicular crystals or monoclinic prisms; frequently with narrow, elliptical or irregular, more or less wrinkled, dark-brown patches of cork; occasionally split into three parts near the tip, flexible and tough, one-celled, containing a blackish-brown pulp and numerous blackish-brown seeds; the latter being flattened, irregularly triangulate or nearly circular in outline, reticulate and varying from 0.25 to 0.3 mm. in diameter. Odor and taste characteristic and very agreeable. Under the microscope, transverse sections of the pods of Vanilla show an epidermis with a somewhat thickened outer cuticularized layer having occasionally rounded or conical masses of an excretion of a gum-like substance; a layer of collenchyma of one or two rows of cells; a thick sarcocarp composed of parenchyma cells in which are imbedded an interrupted circle of fibro-vascular bundles; the parenchyma cells are deeply undulate in outline and usually contain a thin protoplasmic layer enclosing numerous oily globules or may contain bundles of raphides of calcium oxalate; the individual crystals varying from 0.2 to 0.4 mm. in length; some of the parenchyma cells are specially modified and distinguished by their somewhat thickened walls with long, oblique, slit-like pores or the thickening may extend in the form of broad, spiral bands; in the fibro-vascular bundles the phloem is central, being more or less surrounded by a few tracheæ, the walls possessing slit-like pores or spiral thickenings, and at the outside of the bundle is a closed circle of sclerenchymatous fibers, the walls being thin, strongly lignified, provided with numerous, transverse, simple pores, the outer wall of the outer row of fibers being irregular or sinuate; from the inner walls of the endocarp arise the placentæ bearing numerous brownish-red or blackish seeds, and from the cells of the endocarp also arise numerous long, nearly straight hairs, the ends being rounded, the hairs being more or less matted together by a gummy or resinous mass in which some of the seeds are held; in mounts made in hydrated chloral T.S. or potassium hydroxide T.S., the immature, brownish-red seeds show a deeply reticulate seed-coat, with cells of an oblong-polygonal form in surface view. Place a few of the crystals, occurring as an efflorescence on the fruit, on a microscope slide or watch crystal and add a drop of phloroglucinol T.S. and hydrochloric acid; the solution immediately acquires a carmine-red color (distinction from *benzoic acid*). The amount of extractive yielded to dilute alcohol should not be less than 12 per cent. Vanilla yields not more than 6 per cent. of ash." *N. F.*

Transverse sections of the pods of vanilla show an epidermis with a somewhat thickened outer cuticularized layer having occasionally rounded or conical masses of an excretion of a gum-like substance; a layer of collenchyma of one or two rows of cells; a thick sarcocarp composed of parenchyma cells in which are imbedded an interrupted circle of fibro-vascular bundles; the parenchyma cells are deeply undulate in outline and usually contain a thin protoplasmic layer enclosing numerous oily globules or may contain bundles of raphides of calcium oxalate; the individual crystals varying from 0.2 to 0.4 mm. in length; some of the parenchyma cells are specially modified and distinguished by their somewhat thickened walls with long, oblique, slit-like pores or the thickening may extend in the form of broad, spiral bands; in the fibro-vascular bundles the phloem is central, being more or less surrounded by a few tracheæ, the walls possessing slit-like pores or spiral thickenings, and at the outside of the bundle is a closed circle of sclerenchymatous fibers, the walls being thin, strongly lignified, provided with numerous, transverse, simple pores, the outer wall of the outer row of fibers being irregular or sinuate; from the inner walls of the endocarp arise the placentæ bearing numerous brownish-red or blackish seeds and from the cells

of the endocarp also arise numerous long, nearly straight hairs, the ends being rounded, the hairs being more or less matted together by a gummy or resinous mass in which some of the seeds are held; in mounts made in hydrated chloral T.S. or potassium hydroxide T.S., the immature, brownish-red seeds show a deeply reticulate seed-coat, with cells of an oblong-polygonal form in surface view.

A characteristic test for the vanillin crystals which occur as an efflorescence on the fruit is as follows: On a microscope slide or watch crystal, place a few crystals and add a drop of phloroglucinol T.S. and hydrochloric acid; the solution immediately acquires a carmine-red color (distinction from *benzoic acid*). The amount of extractive which vanilla of good quality yields to dilute alcohol should not be less than 12 per cent. Nor should it yield more than 6 per cent. of ash.

Vanilla beans from which the vanillin has been removed by means of a solvent are sometimes offered for sale. The fraud is to be detected by the absence of flavor and odor. Such beans, and also beans of an inferior quality, are sometimes "improved" in appearance and in odor by the use of benzoic acid. For the detection of this fraud the pharmacist should avail himself of the fact that while the crystals of benzoic acid are flattened and rhomboidal and generally lie upon the bean, those of vanillin are usually acicular and stand out at right angles from the surface of the fruit. The absence of the crystalline coating on the vanilla beans seems to be no proof of inferiority, for Henri Lecomte affirms that it is not rarely absent in the best Mexican bean. (*B. Sc. Pharm.*, 1901.)

According to Bucholz, vanilla does not yield volatile oil when distilled with water, and the aroma appears to depend on chemical changes which may take place during and after the curing of the fruit. Many years since, vanilla was analyzed by Bucholz and Vogel, the former of whom found in it a disagreeable-smelling fixed oil, a soft resin having a feeble odor of vanilla when heated, a bitterish extractive resembling tannin, sugar, starch and benzoic acid. But the characteristic odorous principle was not isolated until Gobley obtained *vanillin* by acting on vanilla with solvents (see *Vanillinum*). Although the latter substance has been largely manufactured, it does not take the place of the preparations of vanilla, the flavor and odor of the latter being greatly preferred. It passes with water in distillation. If vanilla, finely divided, be distilled with water, a turbid liquid passes, which becomes clear by agitation with ether, and the ether on evaporation yields crystals of vanillin. Vanilla, in the fresh state in which it is gathered, does not in the least possess the characteristic fragrant odor. H. Lecomte (*J. P. C.*, 1903, 343) studied the conditions which bring about the formation of vanillin. According to his researches, there exist in the vanilla plant two ferments, which differ in a marked degree from each other in their functions. The one, an oxydase, is present in the individual organs of the plant, such as the leaves, shoots and their aqueous extracts, in the green and ripe fruit, and in the prepared commercial fruit. Lecomte detected it in the organs of plants of different origin, by means of G. Bertrand's reactions. At the same time, the presence of manganese salts was observed in all products, which renders it not impossible that they stand in some relation to the above-named ferment. The second ferment is contained in the sap of the vanilla, and acts as a hydrolyzing ferment. With regard to the mechanical treatment of vanilla, it would appear in the first instance as if it counteracted the function of the ferment. It consists, as is well known, of the immersion of the fruit during twenty seconds in water at 85° C. (185° F.), a manipulation which might bring about the destruction of the ferment. But the author has convinced himself that a temperature of about 50° C. (122° F.), such as the interior of the fruit probably only reaches during the short duration of the process, really promotes the function of the oxydase. Both ferments, the oxydase as well as the one possessing the hydrolytic action, appear to be necessary for the formation of vanillin in the plant, and their action may possibly be explained thus: During the preparation, the coniferin produced by the plant is split up into glucose and coniferyl alcohol. This process would explain also the occurrence of grape-sugar in vanilla. The oxydase then converts the coniferyl alcohol into vanillin. Tiemann and Haarmann obtained from Mexican vanilla 1.69 per cent. of vanillin, from Réunion vanilla 2.48 per cent., from Java vanilla 2.75 per cent. Stokeby found in vanilla, resin, wax, a fixed oil, a brown resinous matter, tannic acid changing the salts of iron to green, gum, sugar, phosphates and sulphates: hydrochloric acid separated from it oxalic acid, and potassium hydroxide, humic acid. (*J. P. C.*, 4e sér., iii, 76, 1866; see also paper by Clay W. Holmes, *Proc. A. Ph. A.*, 1887, 526.)

(See *Vanillinum*, PART I.)

Vanilla is used in the N. F. IV in making the *tincture of vanilla* (10 per cent. with a menstruum of alcohol and water), which is used as a flavoring agent in *elixir of ammonium valerate*, *elixir of hops*, *elixir of strychnine valerate* and *syrup of the bromides*.

Vanilla Poisoning.—Many years ago Orfila reported cases of violent gastro-intestinal irritation from eating vanilla ices, and since then others have reported similar instances of poisoning. In 1886 Vaughan in the investigation of an ice cream which had caused serious poisoning in eighteen persons found that the vanilla used to flavor it, in doses of 30 drops failed to produce any symptoms in either himself or his assistants, and he was able to separate the ptomaine tyrotoxicon, which he had previously found in other milk food (see *A. J. P.*, xvi, p. 452). It is highly probable that many of these cases are due to ptomaine poisoning rather than vanilla poisoning; but if the one reported by Rosenthal (*P. J.* xv, p. 24) be accurately stated it must be allowed that in some instances the vanilla itself is at fault. In this connection the reports of Claverie (*J. P. C.* Supp. 1908, xxv) of violent dermatitis in workmen handling vanilla beans is of interest. He attributes the symptoms to the oily exudate of the vanilla pods.

Vanillin Mercury. $(C_6H_3(OCH_3)(COH)O)_2Hg$.—This mercurial combination occurs as a white powder, tasteless and possessing a slight vanilla odor. It is insoluble in water, but soluble in dilute acids and has a mercury content of forty per cent. It is administered in the treatment of *syphilis*, both internally and hypodermatically.

Vasogen. *Vaselinum Oxygenatum.*—This is a feebly alkaline, yellow-brown fluid, of a peculiar but not disagreeable odor and taste, which readily emulsifies with water. It is said to be "oxygenated vaseline or petrolatum," and again that "it con-

tains about 25 per cent. of olein, saponified with anhydrous ammonia, and mixed with vaseline and vaseline oil." *Vasogen* serves as a vehicle for ointments whose active ingredients, it is said, are absorbed with great rapidity from the skin. There have been offered camphor vasogen, 33½ per cent.; iodine vasogen, from 3 to 10 per cent.; menthol vasogen, 2 per cent., and the list might be extended almost indefinitely.

There is a class of proprietary preparations of similar composition known as *petrogens* and there is also a group of preparations in the N. F. IV known as *petroxolins*, which are very similar.

Veratrole. *Pyrocatechin-di-methyl ester.* $C_6H_4(OCH_3)_2[1:2]$.—This is made by acting upon veratric acid with baryta in the presence of heat. It occurs as colorless crystals which melt at 23° C. (73.4° F.), and are soluble in alcohol, ether and the fixed oils. It is supposed to resemble guaiacol in its physiological action as it does in its composition. It is especially employed locally, mixed with equal parts of tincture of iodine in the treatment of intercostal *neuralgia*. It has also been administered internally in *tuberculosis* in *doses* of two grains (0.12 Gm.).

Verbascum. *Verbascum Thapsus* L. *Mullein. Flores Verbasci*, P. G. *Bouillon blanc, Molène*, Fr. *Wolkraut, Königskerze*, G. (Fam. *Scrophulariaceæ*.—The ordinary mullein weed is too well known to need description. As remedial agents both leaves and flowers have been employed. *Mullein Flowers* (*Verbasci Flores*) are official in the *N. F. IV* and are described as "the dried corollas, with adhering stamens, of *Verbascum phlomoides* Linné or of *Verbascum thapsiforme* Schraeder (Fam. *Scrophulariaceæ*). Preserve the flowers in tightly-closed containers. Corolla light-yellow, the outer surface grayish with a fine, soft, woolly indumentum, the inner surface sparsely hairy and finely veined; tube of the corolla only 1 or 2 mm. in length and almost equally broad, the limb from 14 to 30 mm. in breadth, between wheel-shaped and saucer-shaped, obscurely two-lipped, the unequal lobes rounded-obovate. Stamens five, borne on the base of the corolla, shorter than the corolla, two of them longer than the other three, the filaments thick and fleshy, more or less pilose, especially the three shorter ones, usually orange colored. Stamen-hairs cylindrical, unicellular, non-branching, surface minutely reticulate, apex rounded, frequently enlarged. Pollen grains smooth, triangular and more or less rounded, from 0.025 to 0.03 mm. in diameter. The flowers impart a yellow color to boiling water, and a rather permanent green color with dilute sulphuric acid, the latter color becoming brown upon the addition of alkalies. Odor peculiar, agreeable; taste mucilaginous, not agreeable. Mullein Flowers yield not more than 6 per cent. of ash." *N. F. Mullein Leaves* (*Verbasci Folia*) are official in the *N. F. IV* and are described as "the dried leaves of *Verbascum Thapsus* Linné (Fam. *Scrophulariaceæ*), and of other species of *Verbascum*. Obovate with narrowed base, or varying to oblong or oblong-lanceolate, without a true petiole, obtuse or tending toward acuteness at the summit, from 1 to 6 dm. in length and from 3 to 15 cm. in breadth; very thick, rather tough, light yellowish-gray or greenish-gray, densely long-tomentose, with numerous, multicellular, branching, non-glandular hairs. Nearly odorless; taste mucilaginous and slightly bitter. Verbascum yields not more than 14 per cent. of ash." *N. F.*

Mullein leaves are demulcent and emollient, and are thought to possess anodyne properties, which render them useful in pectoral complaints. On the continent of Europe, an infusion of the flowers, strained in order to separate the rough hairs, is considerably used in mild *catarrhs*. An oil, produced by saturating olive oil with mullein flowers, during prolonged exposure to the sun, is used as a local application in Germany for *piles* and other *mucous membrane inflammations*. The mullein oils sold in pharmacies are of this nature, or some of them alcoholic tinctures. The dried leaves are sometimes smoked to relieve irritation of the respiratory mucous membranes; fomentations with mullein leaves also have some repute as anodynes. Internally, the decoction (an ounce to the pint, flowering tips) may be taken in the quantity of from four to six fluidounces.

According to L. Rosenthal (*P. J.*, July, 1902), the seeds of *Verbascum sinuatum* L., which are used in Greece as a fish poison, contain 6.13 per cent. of saponin. Traces of the same substance were found in the fruits of *V. phlomoides* L. and *V. thapsiforme* Schrad.

Verbascum flowers were introduced in the N. F. IV as one of the ingredients in *Pectoral species*, and the leaves in *Fluidextract of mullein leaves* made with diluted alcohol.

Dose, one to two drachms (3.9–7.8 Gm.).

Verbena. *N. F. IV. Blue Vervain.*—"The dried overground portion of *Verbena hastata* Linné (Fam. *Verbenaceæ*), collected when flowering." The plant is a tall shrub growing in damp situations throughout the United States. "In broken or cut pieces; stem stout, obtusely quadrangular, rough, pubescent; leaves opposite, petioles from 12 to 25 mm. in length, blades from 6 to 12 cm. in length, lanceolate, acuminate, acute, coarsely and sharply serrate or the lower hastate lobed, deep green above, paler beneath, conspicuously veined; flowers in terminal interrupted panicles of spikes, spikes erect cylindraceous, densely flowered, each flower subtended by a lanceolate acute bract; calyx adherent, little more than half the length of the corolla, tubular, five-lobed, the mouth slightly oblique; corolla small, bright blue, salver-form tube externally pubescent, sub-equally five-lobed; stamens adnate to the corolla tube, included, didynamous; fruit dividing at maturity into four one-seeded parts. Odor heavy, especially if dampened; taste bitter and disagreeable. Verbena yields not more than 10 per cent. of ash." *N. F.* The *fluidextract of verbena* is official in the N. F. (See Part III.) There is no reason to suspect it of medicinal virtue. The *dose* stated in the N. F. is fifteen grains (1 Gm.).

Verditer.—Two preparations of copper, employed as pigments, are known by this name in commerce, and are distinguished by the epithets of blue and green. *Blue verditer* is prepared in London from the solution of copper nitrate obtained in precipitating silver by copper. According to Gray, this solution is poured while hot upon whiting calcium carbonate, and the mixture stirred every day till the liquor loses its color, when it is decanted, and fresh portions added till the proper color is obtained. By a process for procuring this pigment, invented by Pelletier, the solution of copper nitrate is decomposed by quicklime, and the precipitate, after being washed, is incorporated intimately with another portion of quicklime. By the former process, a copper carbonate is obtained; by the latter, a mixture of copper and calcium hydroxides. *Green verditer*

is prepared by precipitating a solution of copper nitrate by chalk or a white marl, and consists of copper carbonate mixed with an excess of the calcareous carbonate.

Veronal Sodium. *Sodium dimethylbarbiturate.* $Na(C_8H_{11}O_3N_2)$. *Sodium Veronal. Medinal.*—This preparation has the advantage over veronal that it is much more soluble in water, it requiring only six times its weight to dissolve it, according to Puckner and Hilfert. (*J. A. M. A.*, Jan. 23, 1909.)

Because of its freer solubility, medinal acts more promptly than veronal. It may be used for the same purposes as veronal in *doses* of five to fifteen grains (0.3–1 Gm.). Munk (*Med. Klin.*, iv, p. 1834) has also employed it hypodermically in the form of a ten per cent. solution. The injections are somewhat painful, because of the large volume of the injection.

Vernonia. *Vernonia anthelmintica* Willd. (Fam. *Compositæ.*)—This is an East Indian plant, whose black, bitter, and nauseous seeds have a high reputation in Ceylon as an anthelmintic in *doses* of sixty grains (3.9 Gm.). (*P. J.*, April, 1883; also *Ph. Rev.*, 1896, 274.)

Veronica. *Veronica officinalis* L. *Speedwell. Véronique mâle*, Fr. *Ehrenpreis*, G. (Fam. *Scrophulariaceæ.*)—Several species of *veronica*, common to Europe and this country, have been medicinally employed. Of these, *V. officinalis* L., and *V. Beccabunga* L., or European *brooklime*, are the most conspicuous. *V. officinalis* has a bitterish, warm, and somewhat astringent taste. Enz found in it a bitter principle soluble in water and alcohol, but scarcely so in ether, and precipitated by the salts of lead, but not by tannic acid; an acrid principle; red coloring matter; a variety of tannic acid producing a green color with ferric salts, a crystallizable fatty acid, with malic, tartaric, citric, acetic, and lactic acids; mannite; a soft, dark green, bitter resin. Mayer, of New York, found evidences of an alkaloid and of a saponaceous principle. (*A. J. P.*, 1863, 209.) Vintilesco found a glucoside in *V. officinalis* and *V. chamædris*. (*J. P. C.*, 1910, No. 4.) The plant has been considered diaphoretic, diuretic, expectorant, tonic, etc., and was formerly employed in *pectoral* and *nephritic complaints, hemorrhages, diseases of the skin*, and in the treatment of *wounds*. *V. Beccabunga* was used in the fresh state in *scurvy*.

Viburnum Opulus. *N. F. IV (U. S. P. VIII). High Bush Cranberry Bark. Cramp-bark. Wild Guelderrose. Cherry-wood. Red or Rose Elder. Pincushion Tree. Squaw Bush; in cultivation Snowball Bush. Obier*, Fr. *Wasserholderrinde. Wasserschwelke*, G.—"The dried bark of *Viburnum Opulus* Linné var *americanum* (Miller) Aiton (Fam. *Caprifoliaceæ*), without the presence of more than 5 per cent. of wood and other foreign matter." *N. F.*

Viburnum Opulus, cranberry tree or *high bush cranberry*, belongs to the section of the genus which has peduncled cmyes, light red, acid, roundish drupes, with very flat orbicular not sulcate stones, palmately veined leaves, and scaly winter buds. It is a large bush, reaching the height of ten feet, growing in low grounds from New Brunswick far westward, and southward to Pennsylvania. The leaves are from three- to five-ribbed, strongly three-lobed, broadly wedge-shaped or truncate at the base, with the spreading pointed lobes mostly toothed in the sides and entire in the sinuses. The petioles bear two glands at the apex. The *snow-ball tree*, or *Guelder rose*, is a variety in which the whole inflorescence has been turned into a mass of showy sterile flowers.

"In strips, or occasionally in quills or chip-like fragments, the bark attaining a thickness of 3 mm.; outer surface of the thinner pieces of a light gray color with crooked, longitudinal, purplish-brown stripes and very small brown lenticels, the thicker pieces purplish-red or occasionally blackish, except when very young, and more or less finely fissured or thinly scaly; inner surface varying in color from yellowish to rusty-brown, with very short oblique striæ, except where the outer wood layer adheres; fracture short and weak, the fractured surface mostly whitish, varying to pale brown in the inner layer, rusty brown in the outer layer, covering the green tangential layers of phelloderm. Odor strong and characteristic; taste mildly astringent and decidedly bitter. Under the microscope, sections of Viburnum Opulus show as outer corky layer, of five to twenty-five rows of cells, the walls being nearly colorless, frequently thickened on the inner surface, individual cork cells from 0.015 to 0.045 mm. in radial diameter and from 0.030 to 0.075 mm. in tangential diameter; outer bark of about ten rows of cells containing a brownish-yellow, amorphous substance, small starch grains or chloroplastids; medullary rays one to two cells in width, usually not more than one-cell wide; inner bark with occasional groups of bast fibers composed of one to ten cells, the walls being very thick, non-lignified, lamellated and finely porous; adhering wood with large tracheæ having scalariform or reticulate thickenings, and being surrounded by wood fibers with thick lignified walls; starch grains, mostly in cells of parenchyma and medullary rays, either single or compound, the individual grains not exceeding 0.006 mm. in diameter; calcium oxalate in rosette aggregates, 0.015 to 0.04 mm. in diameter, numerous fragments of parenchyma cells, the lumina filled with a reddish-brown amorphous substance. The powder of Viburnum Opulus is light grayish-brown, consisting of irregular fragments; polygonal cork cells, with thin, colorless walls; parenchyma with rosette aggregates of calcium oxalate, from 0.015 to 0.04 mm. in diameter; starch grains very small and mostly in parenchyma cells; fragments of parenchyma containing a brownish-yellow amorphous substance; occasional tracheal fragments associated with lignified wood fibers, bast fibers and stone-cells." *N. F.*

For studies of Viburnum barks, see *A. J. P.*, 1895, 378, 394; also *Ph. Post.* 35, 773, Gibson (*Proc. Indiana Pharm. Assoc.*, 1900, 112) believes that there is a glucoside present in the bark of *V. Opulus;* he describes it as resinous, greenish in color, soluble in alcohol, slightly soluble in water.

The berries of this plant are used to a considerable extent as a substitute for the ordinary cranberry, and are antiscorbutic, but there is no sufficient reason to believe the bark has any medicinal properties of any kind. *V. obovatum* Walt., a tree shrub growing from Virginia southward, is said to be an antiperiodic. (*A. J. P.*, 1878.) Viburnum opulus was dismissed from the U. S. P. IX, but introduced in the N. F. IV. It is used in making *Fluidextract of Viburnum Opulus* with a menstruum of 2 volumes of alcohol and 1 volume of water. *Compound Tincture of Viburnum*, and *Compound Elixir of Viburnum Opulus*. *Dose*, thirty to sixty grains (2.0–3.9 Gm.).

Vieirine.—This substance is obtained from the bark of the *Remijia Velloxii*, DC. (Fam. *Rubiaceæ*), of Brazil. It is used in Brazil in *doses* of from one to four grains (0.065–0.26 Gm.) repeated *pro re nata*, as a tonic and as an antiperiodic in place of quinine.

Vienna Paste. *Potassa Cum Calce. U. S.* 1890. *N. F. IV. Potassa with Lime.*—This is official in the N. F. IV (see Part III). It is "a grayish-white powder, deliquescent, having a strongly alkaline reaction, and responding to the tests for calcium and potassium. It should be soluble in diluted hydrochloric acid without leaving more than a small residue." *U. S.*, 1890. It should not effervesce on the addition of an acid. It is prepared for use by being made up into a paste with a little alcohol. The paste is applied for ten or fifteen minutes to the part to be cauterized, exactly as with potassium hydroxide, than which escharotic it is more manageable, being slower in its operation, and less deliquescent. Filhos has improved this caustic by forming it into sticks. To prepare it thus, the potassium hydroxide is perfectly fused in an iron spoon, and one-third of its weight of quicklime is added in divided portions, the whole being stirred with an iron rod. The fused mass is then run into lead tubes, closed at one end, about three inches long, and from a quarter to half an inch in diameter in the clear. The sticks are kept, still enclosed in the lead tubes, with the open end downward, in thick glass tubes, containing some powdered quicklime, and closed with a cork, between which and the stick some cotton is put to steady the caustic. When employed, as much of the caustic is uncovered at the end by scraping off the lead, as it is proposed to use.

Viferral. *Polychloral.*—A polymerization product of chloral and pyridin. It forms a white powder of disagreeable taste and fuses at 153° to 155° C. (307.4°–311° F.). Alkalies react on it, splitting it up into chloroform and formic acid. When heated with dry potassium hydroxide it develops the unpleasant isonitril odor. It is slightly soluble in cold and readily so in hot water. It is used as a hypnotic, asserted to be superior to chloral, due to its non-toxicity. *Dose*, twelve to fifteen grains (0.8–1.0 Gm.).

Vinca.—Under this name are included *V. major* L., *Greater Periwinkle*, and *V. minor* L., *Lesser Periwinkle* (Fam. *Apocynaceæ*). It is said to be very useful in arresting *menorrhagic* and other *hemorrhages*. (*P. J.*, 1871, 961; *Ibid.*, 1873, 963; also *A. J. P.*, 1872.)

Vincetoxicum. *V. officinale* Moench. (now more properly *Cynanchum Vincetoxicum* (L.) Pers. *White Swallow-wort. Vincetoxicum. Asclépiade, Dompte-venin, Hirundinaire*, Fr. *Schwalbenwurz, Giftwende*, G.—A perennial, herbaceous European plant, the root of which was formerly esteemed a counterpoison, and hence the botanical name. It has a bitterish, acrid, taste, and, when fresh, a disagreeable odor, which is diminished by drying. Kubler found a glucoside, *vincetoxin*, $C_{50}H_{82}O_{20}$, which he states differs from *condurangin* which other investigators asserted to be identical. (*A. Pharm.*, 1908, 659.) Taken internally, especially in the recent state, it excites vomiting, and is capable, in larger quantities, of producing dangerous, if not fatal, inflammation of the stomach. Feneulle found in the root a principle analogous to emetin. It has been used in *skin diseases* and *scrofula*.

Vinegar. *Acetum.*—*Vinegar* is produced by the acetous fermentation in infusion of mixed malted and unmalted grain, or of various fruit juices. Any substance which is capable of undergoing the alcohol fermentation is further liable, under the influence of a microscopic plant, *Mycoderma aceti*, first described by Pasteur, and exposure to the air at a temperature between 24° C. (75° F.) and 35° C. (95° F.), to undergo further change with oxidation, which converts the alcohol into acetic acid. Practically for success there should not be more than 12 per cent. of alcohol in the original fluid. The mycoderm may exist as a pellicle composed of extremely small cells (micrococci) in contiguous rows, or finally enveloped in a glue-like mass, or it may be in the form of rod-like cells (bacilli) more or less dispersed through the fluid. There are a number of other organisms which oxidize alcohol into acetic acid, viz., *Bacterium aceti*, *B. Pasteurianum*, *B. Kuetzingianum*, *B. Oxydans*, and *B. Industrium*.

In the quick *German process* for making vinegar a mixture of one part of 80 per cent. alcohol, four or six parts of water, and one-thousandth of honey or extract of malt, at a temperature of 24° C. (75° F.) to 35° C. (95° F.), is allowed to percolate through beech shavings, previously steeped in vinegar, and contained in a deep oaken tub, in which is a wooden diaphragm perforated with numerous small holes, loosely filled with packthread about six inches long. It is essential to the success of the process that a current of air shall pass through the tub. In order to establish this current, eight equidistant holes are pierced near the bottom of the tub, forming a horizontal row, and four glass tubes are inserted vertically in the diaphragm, of sufficient length to project above and below it. The air enters by the holes below, and passes out by the tubes. Although the air is necessary for the furnishing of oxygen, acetification consisting chiefly in the oxidation of the alcohol, the beech shaving and similar articles chiefly aid in the process by affording surface upon which the mycoderms can grow. During the process the temperature rises to 37° C. (100° F.) or 40° C. (104° F.), and remains nearly stationary while the process is going on favorably. The liquid is drawn off by a discharge pipe near the bottom, and must be passed three or four times through the tub before the acetification is completed, which generally occupies from twenty-four to thirty-six hours. According to Wimmer, pieces of purified charcoal, about the size of a walnut, may be advantageously substituted for the beech shavings in the process.

In 1862, Pasteur substituted for the German process the sowing of the mycoderm upon the surface of a mixture of wine and vinegar, or of water, alcohol (2 per cent.), and acetic acid (1 per cent.) adding alcohol daily in small quantities after about half that contained in the original liquid had been converted into acetic acid, until a vinegar of sufficient strength was produced. The *French process* was improved in 1869 by Laugier, and it was subsequently further elaborated by Emanuel Wurm. (For details, see *P. J.*, xi, 133.)

In England, vinegar is made from the infusion of malt. The fermented wort is caused to fall in a shower upon a mass of fagots of birch twigs occupying the upper part of a large vat, and, after trickling down to the bottom, is pumped up repeatedly to the top, to be again allowed to fall, until the acetification is completed. This mode of

oxidizing the alcohol in the fermented wort has the advantage of rendering insoluble certain glutinous and albuminous principles, which, if not removed, would cause a muddiness in the vinegar and make it liable to spoil.

In the United States, vinegar is largely made by the German method of oxidizing very diluted alcohol, and is called *spirit vinegar;* it is often prepared from cider—*cider vinegar.* The cider is placed in barrels (with their bung holes open) which are exposed during the summer to the heat of the sun. The acetification is completed in the course of about two years. The progress of the fermentation, however, must be watched, and as soon as perfect vinegar is formed, it should be racked off into clean barrels. Without this precaution, the acetous fermentation would run into the putrefactive, and the vinegar spoiled. Cider vinegar contains no aldehyde. It contains malic acid, and therefore yields a precipitate with lead acetate. The want of such a precipitate indicates that the alleged cider vinegar is a manufactured substitute, although a fictitious article might yield a similar precipitate.

Vinegar may be clarified, without impairing its aroma, by throwing about a tumberful of boiling milk into from fifty to sixty gallons of the liquid, and stirring the mixture. This operation also makes red vinegar pale.

The series of changes which occur during the *acetous fermentation* is called *acetification.* During its progress there is a disengagement of heat; the liquor absorbs oxygen and becomes turbid; filaments form, and upon the completion of the fermentation, form a pultaceous mass, leaving a clear liquor containing the acetic acid. The explanation of Liebig is that the alcohol loses two atoms of hydrogen as the first effect of oxidation, and becomes aldehyde, and this, by the absorption of one atom of oxygen, becomes acetic acid ($C_2H_3O.OH$). Thus the conversion of alcohol into acetic acid consists in, first, the removal of two atoms of hydrogen, and afterwards the addition of one atom of oxygen. The following equations represent this change:

$$C_2H_6O + O = C_2H_4O + H_2O$$
$$C_2H_4O + O = C_2H_4O_2$$

Aldehyde is a colorless, inflammable, ethereal liquid, having a pungent taste and odor. Its specific gravity is 0.79. It absorbs oxygen gradually, and is thus converted into acetic acid, as just stated. Its property of absorbing oxygen gives it a reducing power like that possessed by glucose. Hence it responds to Fehling's test for that substance (PART III). It is characterized by its forming a crystalline compound with ammonia, and also with alkaline bisulphites; it is polymerized by the action of acids and some other reagents, and thus yields *paraldehyde* $(C_2H_4O)_3$, a liquid boiling at 124° C. (255° F.). The name aldehyde alludes to its relation to alcohol, *alcohol dehydrogenated.* Its aqueous solution is decomposed by potassium hydroxide with formation of *aldehyde resin.* This is a soft, light brown mass, which, heated to 100° C. (212° F.), gives off a nauseous soapy odor.

Properties.—Vinegar, when good is of an agreeable, penetrating odor, and a pleasant acid taste. According to Magnes-Lahens, wine vinegar always contains a little aldehyde. The better sorts of vinegar have a grateful aroma, probably due to the presence of an ethereal substance, perhaps acetic ether. The color of vinegar varies from pale yellow to deep red. When long kept, especially if exposed to the air, it becomes ropy, acquires an unpleasant odor, putrefies, and loses its acidity.

The essential ingredients of vinegar are acetic acid and water; but, besides these, it contains various other substances, derived from the particular vinous liquor from which it may have been prepared. Among these may be mentioned coloring matter, gum, starch, gluten, sugar, a little alcohol, and frequently malic and tartaric acids, with a minute proportion of alkaline and earthy salts. Vinegar should be devoid of lead and copper and of free sulphuric acid, as shown by its not being discolored by hydrogen sulphide, and yielding no precipitate when boiled with a solution of calcium chloride, and of such a strength that a fluidounce would require, for neutralization, not less than thirty-five grains of potassium bicarbonate. After neutralization it should be free from acrid taste, indicating the absence of acrid substances, the taste of which may have been concealed by that of the acetic acid.

Malt Vinegar (*Acetum Britannicum*) has a brown color, and a sp. gr. from 1.006 to 1.019. The strongest kind, called *proof vinegar,* contains from 4.6 to 5 per cent. of acetic acid. That of British manufacture usually contains sulphuric acid, which the manufacturer is allowed by law to add in a proportion not exceeding one part in a thousand; but if the vinegar be properly made it does not require to be thus protected.

Malt Vinegar is "a liquid of a brown color and peculiar odor. Specific gravity 1.017 to 1.019. 445.4 grains by weight (1 fluidounce) of it require about 402 grain-measures of the volumetric solution of soda for their neutralization, corresponding to 5.41 per cent. of real acetic acid, $HC_2H_3O_2$. If ten minims of solution of barium chloride be added to a fluidounce of the vinegar, and the precipitate, if any, be separated by filtration, a further addition of the test should give no precipitate. Sulphuretted hydrogen causes no change of color." *Br.,* 1885.

Wine Vinegar (*Acetum Gallicum*) is nearly one-sixth stronger than pure malt vinegar. It is of two sorts, the white and the red, according as it has been prepared from white or from red wine. *White wine vinegar* is usually preferred. *Red wine vinegar* may be deprived of its color, and rendered limpid, by being passed through animal charcoal. Under the name of wine vinegar or white wine vinegar the so-called distilled vinegar is sometimes sold. This is made, not by distillation of vinegar as the name indicates, but by the distillation of a weak alcoholic liquid produced by the fermentation of molasses with yeast and the subsequent acetification of the weak alcohol by percolation through beechwood shavings impregnated with mycoderma aceti.

The best test for the detection of free inorganic acids is a weak solution of methyl violet which turns green in the presence of free inorganic acids, but remains unaffected by organic acids.

Distilled Vinegar (*Acetum Destillatum; Vinaigre distillé, Oxéolat simple,* Fr.; *Destillirter Essig,* G.) was official in the U. S. Pharmacopœia, 1870, and was prepared by obtaining seven pints of distillate from eight pints of vinegar placed in a glass retort, the one pint left in the retort retaining the fixed impurities, salts, etc. One hundred grains should saturate not less than seven and six-tenths grains of potassium bicarbonate.

Adulterations.—The principal foreign substances which vinegar is liable to contain are sulphuric and sulphurous acids, and copper and lead, derived from improper vessels used in its manufacture. Tin has been found in it after standing a short time in tin vessels.

Barium chloride is not a suitable test for the presence of free sulphuric acid, as it will cause a precipitate with sulphates, which are often found in vinegar when no free sulphuric acid is present.

By far the most dangerous impurities in vinegar are copper and lead. The former may be detected by a brownish precipitate on the addition of potassium ferrocyanide to the concentrated vinegar; the latter, by a blackish precipitate with hydrogen sulphide, and a yellow one with potassium iodide. Pure vinegar is not discolored by hydrogen sulphide. According to Chevallier, wine vinegar which has been strengthened with acetic acid from wood sometimes contains a minute proportion of arsenic, which is probably derived from arseniferous sulphuric acid, employed in preparing the acetic acid. (For an examination of samples of commercial vinegar by F. G. Ryan, see *A. J. P.*, 1899, p. 71; see also Leach's *Food Analysis*, 3rd edition.)

Vinegar has feeble antiscorbutic properties, but is at present used as a medicine only for its local astringent properties, and in the form of an enema diluted with three times its bulk of water to kill *seat worms*. In the *dermatitis* produced by exposure to the sun, made into a paste with glycerin, bismuth, and starch, it is very effective. In *hematemesis* one ounce to a tumbler of water often acts very advantageously, and may be taken freely. At one time vinegar was largely used in pharmacy as a menstruum, but on account of its tendency to undergo decomposition it has been replaced by diluted acetic acid in both the American and British Pharmacopœias.

Vinegar of Ipecacuanha. *Br.* 1898. *Acetum Ipecacuanhæ.*—"Liquid Extract of Ipecacuanha, 1 fluidounce (Imperial measure) or 50 mils; alcohol (90 per cent.), 2 fluidounces (Imperial measure) or 100 mils; Diluted Acetic Acid, 17 fluidounces (Imperial measure) or 850 mils. Mix; filter, and, if necessary, add sufficient diluted acetic acid to produce one pint (Imperial measure) or one thousand mils of the Vinegar of Ipecacuanha." *Br.*, 1898. Diluted Acetic Acid is a good menstruum for ipecacuanha, and this vinegar will doubtless prove effective as an expectorant. (For uses see *Ipecacuanha.*) *Dose*, five to forty minims (0.3 to 2.5 mils).

Vioform. *Nioform.* $C_9H_5NOHICl$. *N. N. R.* 1917.—*Iodo-chloroxyquinoline* was introduced as a substitute for iodoform in surgery. It is a greenish-yellow, almost odorless, bulky, insoluble powder. According to the researches of E. Tavel, it is less toxic than iodoform, especially when brought in local contact with wounds, and is also more actively germicidal than is iodoform. Locally it is not at all irritant. (See *S. Jb.*, Bd. 267, p. 133; Bd. 272, p. 163.)

Viola. *Violet.*—The genus *Viola* (Fam. *Violaceæ*) includes numerous species, many, perhaps all of which are possessed of analogous medicinal properties. *Viola tricolor* L., the *Heart's-ease, Pansy,* or *Johnny-jump-up* of the gardens, was formerly recognized by the U. S. Pharmacopœia; while *V. odorata* L., and *V. pedata* L., have held places in both the British and the United States Pharmacopœias.

V. odorata L. (*Violette, Violette odorante,* Fr.; *Wohlriechendes Veilchen, Veilchen,* G.; *Violetta,* It.; *Violeta,* Sp.), the common violet of Europe, resembles very closely the American blue violet, *V. cucullata* Ait., from which, however, it is at once distinguished by its delicious fragrance. It is the *sweet violet* of our gardens. *V. pedata* L., is an indigenous, stemless violet, characterized by its large blue or variegated beardless flowers, and its deeply three- to five-divided, pointed pedate leaves.

The flowers of *V. odorata* yield their odor and their slightly bitter taste to boiling water. Their infusion affords a delicate test for acids and alkalies, being reddened by the former and rendered green by the latter. Their odor is destroyed by desiccation, and the degree to which they retain their fine color depends upon the care used in collecting and drying them. They should be gathered before being fully blown, deprived of their calyx, and rapidly dried, either in a heated room or by exposing them to a current of very dry air. The flowers of other species are often mingled with them, and, if of the same color, are equally useful as a chemical test.

In the root, leaves, flowers, and seeds of *Viola odorata,* Boullay discovered an alkaloid, *violine,* allied to emetine, but possessing distinct properties. It exists in the plant combined with malic acid. Orfila asserts that it is exceedingly active and even poisonous. It is probably found in other species of *viola.* Mandelin (*Jahresb.*, 1883) obtained a glucoside analogous to quercitrin, which he names *viola-quercitrin.* It crystallizes out of hot water in fine yellow needles. When boiled with diluted acids, it is decomposed into *quercetin, isodulcite* and a fermentable glucose,

$$C_{27}H_{30}O_{16} + 3H_2O = C_6H_{14}O_6 + C_6H_{12}O_6 + C_{15}H_{10}O_7$$

he also obtained salicylic acid from several species of viola. (*A. J. P.*, 1882, 10.) Kraemer (*Inaug. Diss.*, Marking, 1896) detected methyl salicylate and this was later confirmed by Schimmel & Co. See also Gadd's article, *Y. B. P.*, 1905, 466.

The herbaceous parts of various species of violets are mucilaginous, emollient, and slightly laxative, and have been used in *pectoral, nephritic,* and *cutaneous diseases.* In Europe a syrup prepared from the fresh flowers of *Viola odorata* is employed as an addition to demulcent drinks, and as a laxative for infants. The root, which has a bitter, nauseous, slightly acrid taste, acts in the *dose* of from thirty grains to a drachm (2.0–3.9 Gm.) as an emetic and cathartic. It is probable that the same property is possessed by the roots of all the violets, as it is known to be by several species of *Ionidium,* which belongs to the same family. The existence in small proportion of the emetic principle in the leaves and flowers accounts for their expectorant properties.

Virginia Creeper. *Psedera quinquefolia* (L.) Greene (*Parthenocissus quinquefolia* (L.) Planch. *Ampelopsis quinquefolia* Michx.) *American Ivy. Vigne vierge,* Fr. *Wilder Wein, Amerikanischer Epheu,* G.—The bark twigs of this indigenous, woody creeper of the fam. *Vitaceæ* have been used by the eclectics as an alterative, tonic, and expectorant. They contain tartaric acid and potassium and calcium tartrates, albumen, sugar, pyrocatechin, and some other principles. McCall employed the bark collected late in the fall in *dropsy,* with asserted very good results. (*Penins. and Independ. Med. Journ.*, June, 1858.) In two cases

of poisoning reported by Bernays, the symptoms were violent vomiting and purging, collapse, and deep sleep, with dilated pupils. (*P. J.*, vii.)

Viscum. *Viscum album* L. *Mistletoe. Gui de Chêne, Gillon,* Fr. *Mistel,* G. (Fam. *Loranthaceæ.*)—A European evergreen, parasitic shrub growing on various trees, particularly the apple and other fruit trees, and forming a pendent bush from two to five feet in diameter. The plant is famous in the history of Druidical superstition. In the religious rites of the Druids, the mistletoe of the oak was employed, and hence was afterwards preferred when the plant came to be used as a remedy; but it is in fact identical in all respects with those which grow upon other trees. (*P. J.*, 1897, 289.) The fresh bark and leaves have a peculiar, disagreeable odor, and a nauseous, sweetish, slightly acrid and bitterish taste. *Viscin,* which forms the glutinous constituent in the berries, leaves, and stalks of the mistletoe, is the principal constituent of *birdlime.* Crude viscin may be obtained by kneading the finely bruised mistletoe bark with water, as long as anything is dissolved, and removing the ligneous impurities mechanically. A purer product may be obtained by boiling the crude product in strong alcohol, macerating the residue with ether, evaporating the ethereal extracts, purifying these extracts by kneading first with alcohol and then with water. The formula $C_{20}H_{48}O_8(C_{20}H_{32} + 8H_2O)$ has been given to it by Reinsch. Pawlevsky (*Bull. Soc. Chim.* (2), 34, 348) obtained from mistletoe a crystallizable acid, slightly soluble in water, insoluble in alcohol and ether, fusing at from 101° to 103° C. (213.8°–217.4° F.), to which he gave the formula $CH_3O_3.OH$. The berries, which are white, and about the size of a pea, abound in the peculiar viscid principle, and are sometimes used in the preparation of birdlime, of which this principle is the basis. Mistletoe is said to be productive of vomiting and purging when largely taken. The berries caused in a child three years old vomiting and prostration, coma, a fixed and somewhat contracted pupil, and convulsive movements. (*Ann. Thér.*, 1859, 36.) A fatal case is recorded. (*M. T. G.*, 1867, 26.) The plant was formerly looked upon as a powerful nervine, but it is now out of use. The leaves and wood were given in the *dose* of a drachm (3.9 Gm.) in substance. *Viscum* has been recommended by Gaultier (*S. M.*, 1907) for the reduction of high blood pressure in *arterio-sclerosis* and other conditions of excessive arterial tension. But Dossin (*A. I. P. T.*, 1911, xxi, p. 432) finds that the lowering of blood pressure is of but short duration and is preceded by a rise and concludes, therefore, that the drug is not clinically useful for this purpose. Gaultier employed a watery extract in *doses* of 3 grains (0.2 Gm.) daily. According to P. Riehl (*D. M. W.*, xxvi, 1900), viscin affords an excellent basis for the making of applications to the skin, a benzene viscin solution mixed with starch affording an excellent plaster mass.

The *American Mistletoe* is the *Phoradendron flavescens* (Pursh) Nutt. It is a woody parasite, growing upon the branches of deciduous trees from New Jersey to Florida and westward. It is probably the plant reported as growing upon the elm, by which several children were poisoned. (Henry Dye, *Memphis Med. Recorder,* iv, 344.) The prominent symptoms were vomiting and great thirst followed by frequent discharge of bloody mucus from the bowels, with tenesmus. One of the children was found in a collapsed state, in which death took place. Dye states also that, in other instances, as he had been informed, children had eaten the *berries* without any ill effect. In the western part of the United States *Arcenthobium Americanum* Nutt., and *Phoradendron juniperinum* Englm., are also known under the name of mistletoe. Crawford (*J. A. M. A.*, 1911, lvii) has found that the extract of *P. flavescens* or the *P. juniperinum,* when injected into the blood stream, produces a sharp rise in the blood pressure similar to that produced by epinephrine. He also succeeded in isolating an active base, the composition of which, however, he did not satisfactorily determine, but suggests that it may be phenylethylamine. W. H. Long, confirmed by Lee Payne (*North Carolina Med. Journ.*, vol. vii, 253) asserts (*New Prep.*, ii, 31) that the American mistletoe is a very certain oxytocic, and very efficacious in arresting post-partum and other varieties of *uterine hemorrhage.* He gives a fluidrachm (3.75 mils) of the fluidextract every twenty minutes in labor until the effect is produced; every four to six hours in *menorrhagia.* Dalassus proposes a formula for an aqueous *extract of mistletoe.* Five hundred parts of the ground, dry, young twigs and leaves are infused for 12 hours in 3000 parts of boiling water, expressed and the residue treated with 1500 parts of boiling water. The united liquids are then evaporated to the consistence of an extract. *Syrup of mistletoe* is made by dissolving 1 part by weight of the above extract in 10 parts by weight of boiling water and adding 990 parts of simple syrup.

Vitex.—The various species of this genus have been attributed by the ancients with wonderful powers, and the *V. trifolia* is still used occasionally for medicating baths.

Warburg's Tincture.—This famous remedy, at first a proprietary medicine, afterwards by the voluntary act of its inventor had its formula revealed. It is now official in the N. F. IV (see Part III). There is so much testimony as to its extraordinary virtues in the severe *remittent* and *pernicious malarial fevers* of India that its powers can scarcely be questioned. After the bowels of the patient in the acutest stage of the disorder have been freely opened, a half ounce of the tincture is given undiluted, all drink being withheld, and at the end of three hours a second half ounce is given in a similar manner. Soon after the second dose a violent, aromatic perspiration comes on, and the fever is usually broken. The remedy is also commended in *collapse* without organic disease. The formula given by Warburg is as follows: Socotrine aloes 1 lb.; rhubarb, angelica fruit, confection of Damocratis, each 4 oz. troy; elecampane, saffron, fennel, prepared chalk, each 2 oz. troy; gentian, zedoary, cubebs, myrrh, camphor, agaric, each, 1 oz. troy. Digest the whole with 500 oz. proof spirit in a water bath for 12 hours express, add 10 oz. sulphate of quinia, dissolve by the aid of a water bath, cool, and filter.

It is evident that *Warburg's tincture* contains various substances which are inert, but the practical difficulty is to determine as to what its extraordinary value anti-malarial powers are really due. The formula of Hager—quinine sulphate 1 part, spirit of camphor 2 parts, elixir proprietatis (P. G.), 22 parts, alcohol, 16 parts—does not seem to us to at all represent the tincture. The formula used in the U. S. army, with asserted excellent results in Cuba, has the advantage of yielding a product in tablets, which is as follows: Aqueous extract aloes, 224 grains; rhubarb, 448 grains; angelica seed, 448 grains; elecampane, 224 grains; saffron (Spanish), 224 grains; fennel, 224 grains;

gentian, 112 grains; zedoary root, 112 grains; cubeb, 112 grains; myrrh, 112 grains; white agaric, 112 grains; camphor, 112 grains; quinine sulphate, 1280 grains. Exhaust with eight pints of diluted alcohol, or divide into 1024 tablets.

The confection of Damocratis, in the original, which was a combination of thirty aromatic substances mostly obsolete, may be found in the 19th ed., *U. S. D.*, p. 1695. It is contained in the formula in such small amount that it is hardly possible that it could have any effect. (See also *Tinctura Antiperiodica*, N. F., Part III.)

The National Formulary has revised the formula of Warburg's tincture and there are two tinctures, one with and one without aloes.

Dose.—The dosage of Warburg's tincture depends on the kind used—whether with aloes or without—and the intended purpose, and varies from 4 mils (1 fluidrachm) to 15 mils (4 fluidrachms). The larger quantity is given when Dr. Warburg's original directions are followed for administering the remedy in remittent fevers. These directions were as follows: "One-half ounce to be given alone, without dilution, after the bowels have been evacuated by any convenient purgative, all liquids being withheld. After three hours another half ounce is to be given."

White Ash Bark. *N. F. IV. Fraxinus.*—It is described as "the dried bark of *Fraxinus americana* Linné (Fam. *Oleaceæ*) and probably of other species of *Fraxinus*, deprived of the corky layer. In flat pieces of varying length and width, from 3 to 6 mm. in thickness, externally yellowish or pale brown, sometimes with ridges of a warty nature and fissures of a grayish-brown color with markings of lichens; inner surface, pale brown to yellowish, longitudinally striate; fracture very uneven, fibrous. Odor faintly aromatic; taste bitter, weakly acrid. Fraxinus yields not more than 10 per cent. of ash." *N. F.* A large forest tree of the northern United States and Canada. It contains a volatile oil, an alkaloid and several resins. The bark has been used in *dysmenorrhea* by Charles P. Turner and others. A *wine* is official in the N. F. (see Part III).

Fraxinus excelsior L. *Frêne*, Fr. *Esche*, G. *Fresco*, Sp. (Fam. *Oleaceæ.*)—The bark of the *Common European Ash* occurs in quills and is of a grayish or grayish-green color. It is bitter and astringent, and at one time was employed in the treatment of *intermittent fever.* It contains a crystalline glucoside and a bitter principle, and a fixed oil obtained from the seeds. (*Chem. Ztg.*, 1911, 478.) The leaves have long been used in *rheumatic affections* and *gout.* Garot has shown that they contain 16 per cent. of *calcium malate.* (See *J. P. C.*, 3e sér., xxiv, 311; also 4e sér., xii, 60.) *Dose*, an ounce (31 Gm.), infused in half a pint (236 mils) of boiling water, three times a day. (See *Am. J. M. S.*, N. S., xxv, 492.)

White Pine Bark. *N. F. IV. Pinus Alba.*—"The dried inner bark of *Pinus Strobus* Linné (Fam. *Pinaceæ*)." *N. F.* "In flat pieces of variable size and from 1 to 3 mm. in thickness; outer surface varying from a pale pinkish-white when fresh, to a light or rather deep yellowish-brown on keeping, occasionally with small patches of the gray-brown periderm adhering; more or less cottony, and often showing small scattered pits; inner surface either lighter or darker than the outer, finely striate; fracture tough, fibrous; transverse section showing an outer yellowish and an inner whitish band. Odor slight, terebinthinate; taste slightly mucilaginous, bitter, sweet and astringent. The powdered drug, when examined under the microscope, exhibits numerous rounded or oval, simple starch grains, up to 0.03 mm. in diameter, some having a cleft or fissure through the center; few monoclinic prisms of calcium oxalate about 0.02 mm. in diameter; resin in reddish-brown, angular masses; thin-walled parenchyma cells, isodiametric to elongated, many containing starch grains; tracheids very few or absent. White Pine Bark yields not more than 3 per cent. of ash." *N. F. IV.*

This bark was introduced into the N. F. IV for the purpose of making *Compound Syrup of White Pine* and *Compound Syrup of White Pine with Morphine.* The differentiation of these two syrups was a wise step in the last revision; but in our opinion it would have been wiser to have dropped *white pine* and all of the preparations; the syrup containing morphine has long been used and has no doubt contributed its share towards cultivating the morphine habit.

Whiting.—This is essentially the same as prepared chalk, being made by the pulverization and elutriation of crude chalk. It is used as a coarse paint, and for various purposes in the arts, for which calcium carbonate is requisite. *Paris white* is a variety of the same material.

Winter's Bark. *Wintera.*—The bark of *Drimys Winteri* Forst. *Cortex Winteranus. Ecorce de Winter, Cannelle de Magellan*, Fr. *Winter's Zimmt*, G. (Fam. *Magnoliaceæ.*)—For descriptions of tree, see *U. S. D.*, 16th edition. The tree is a native of the southern parts of South America, growing along the Strait of Magellan, and extending as far north as Chile. According to Martius, it is found also in Brazil. The bark of the tree was brought to England, in the latter part of the sixteenth century, by Captain Winter, who attended Drake on his voyage round the world, and while in the Strait had learned its aromatic and medicinal properties. Since this period, from time to time various barks have appeared in European commerce as *Winter's bark*, although not any that was the genuine bark. Among those in the London market was at one time the bark of *Cinnamodendron corticosum* Miers. (Fam. *Canellaceæ*), of Jamaica, which is pungent like true Winter's bark, but is of a much paler brown color, and resembles canella bark except in the absence of the chalky-white inner surface. More recently this bark has been replaced by the bark of *Croton Malambo* Karst. (Fam. *Euphorbiaceæ*), which resembles in color and thickness the bark of the Cinnamodendron, but has a bitter taste and a calamus-like flavor. For the description of a specimen which was in possession of George B. Wood many years since, see *U. S. D.*, 19th ed., p. 1696. P. N. Arata and F. Canzoneri (*P. J.*, June 14, 1890) describe a bark which they assert to be a genuine Winter's bark from the Strait of Magellan. From this they separated a volatile oil by distilling the bark with water, exhausting the distillate with petroleum, and distilling off the solvent. The crude oil, amounting to 0.64 per cent. of the weight of the bark employed, was a mixture of several substances. *Winterene*, $C_{15}H_{24}$, is the essential oil separated from this by fractional distillation. It is readily oxidized on exposure to the air, becoming yellow. The formula $C_{25}H_{40}$ was calculated from the ultimate analysis and vapor density, but the authors consider that the ready oxidizability of winterene and its analogy to similar essences point rather to the formula $C_{15}H_{24}$, which would place it in the group of sesquiterpenes, such as

cedrene, cubebene, etc. The presence of tannic acid and ferric oxide, according to Henry, serves to distinguish Winter's bark from *Canella alba*, with which it has often been confounded. The bark above described as commercial Winter's bark is destitute of both tannic acid and ferric oxide, and cannot therefore be the bark examined by Henry.

The bark of the *Drimys granatensis* L. f. (now regarded as identical with *D. Winteri* Forst.), has been imported into London under the name of *Merida coto*, and it has been stated that it contains *cotoin*. It occurs in short pieces of a yellowish-gray color, traversed longitudinally by hard cellular layers, which distinguish it at once from coto and paracoto bark. Its odor resembles that of true coto, but is more feeble. A careful chemical study of it by O. Hesse (*P. J.*, vol. iv) shows that it contains no cotoin, but a crystalline substance, $C_{18}H_{14}O_4$, to which the name of *drimin* was given. From the leaves Hesse obtained a wax alcohol, *drimol*, $C_{28}H_{58}O_2$. As *Drimys granatensis* L. f., is recognized as *D. Winteri* Forst., it is plain that Merida coto must be looked upon as a form of Winter's bark coming from Venezuela.

Winter's bark is a stimulant aromatic tonic, and was employed by Winter as a remedy for *scurvy*. It may be used in half-drachm (2.0 Gm.) *doses* for similar purposes with cinnamon or canella alba, but is scarcely known in the medical practice of this country. *Drimys chilensis* of De Candolle, growing in Chile, yields a bark having similar properties (Carson, *A. J. P.*, xix, 81); also *D. aromatica* F. Muell., of Australia. (*P. J.*, xxi.)

Wistaria. *Wistaria chinensis* DC. (*Kraunhia chinensis.*) (Fam. *Leguminosæ.*)—Ottow (*P. J.*, Oct., 1886) has obtained from this ornamental leguminous woody climber a crystalline poisonous glucoside, *wistarin*.

Withania. *Withania coagulans* Dun. (Stocks.) *Vegetable Rennet.* (Fam. *Solanaceæ.*)—This shrub, common in Afghanistan and East India, has the property of coagulating milk, and has been used for preparing a vegetable rennet ferment for making cheese. Sheridan Lea found upon examination that the substance which possesses the coagulating power is a ferment closely resembling animal rennet. The active principle is soluble in glycerin, and can be extracted from the seeds by this solvent; the extract possesses strong coagulating powers even in small amounts. Alcohol precipitates the ferment body from its solutions, and the precipitate, after washing with alcohol, may be dissolved again without having lost its coagulating powers. The active principle of the seeds will cause the coagulation of milk when present in very small quantities, the addition of more of the ferment simply increasing the rapidity of the change. The coagulation is not due to the formation of acid by the ferment. If some of the active extract be made neutral or alkaline, and added to neutral milk, a normal clot is formed, and the reaction of the clot remains neutral or faintly alkaline. The clot formed by the action of the ferment is a true clot, resembling in appearance and properties that formed by animal rennet, and is not a mere precipitate. Lea prepared an active extract, applicable for cheese making purposes, by grinding the dry seeds very finely in a mill, and extracting them for twenty-four hours with such a volume of 5 per cent. sodium chloride solution that the mass is still fluid after the absorption of water by the fragments of the seeds as they swell up. From this mass the fluid part may be readily separated by using a centrifugal machine (such as is used in sugar refining), and it can then be easily filtered through filter paper; without the centrifugal machine the separation of the fluid from the residue of the seeds is tedious and imperfect; forty grammes of the seeds treated as above, with 150 mils of 5 per cent. sodium chloride solution, gave an extract of which 0.25 mil clotted 20 mils of milk in twenty-five minutes, and 0.1 mil clotted a similar portion of milk in one hour. When added in these proportions the curd formed is quite white. The presence of the coloring matter is, however, perhaps on the whole unimportant, since even if a larger quantity of the ferment extract is added in order to obtain a very rapid coagulation, the coloring matter is obtained chiefly in the whey, the curd being white; by adding sufficient common salt to make the percentage up to 15 per cent., and alcohol up to 4 per cent., the preparation would retain its activity very well. (*P. J.*, 1884, 606.)

Wrightia. *Wrightia zeylanica* R. Br. (*W. antidysenterica* R. Br.) (Fam. *Apocynaceæ.*)—Under the names of *Conessi bark, Tellicherri bark*, and *Codaya pala*, a spongy, rusty-colored, bitter bark of this apocynaceous tree was formerly used in Europe as a remedy in *dysentery* and *diarrhea*, and is said still to be largely employed by the native practitioners of India. Stenhouse obtained from the seeds, besides a fixed oil which they contain in large quantity, a non-crystalline alkaloid, called by him *wrightine*, which seems to be the same substance previously described by Hains under the name of *conessine*. (*P. J.* (2), vi, 432.) The alkaloid conessine is now a commercial product prepared by Merck, and the formula $C_{24}H_{40}N_2$ is given it. It occurs in delicate, white, interlaced masses of crystals, melting at 121° C. (249.8° F.), sparingly soluble in water, readily so in alcohol. A small quantity rubbed with a few drops of concentrated sulphuric acid affords on the addition of nitric acid a golden and finally orange-yellow color. We are not aware that the medicinal properties of this have been investigated.

A species of the allied genus *Holarrhena* (*H. africana* A. DC.), is stated by German missionaries to be used in parts of tropical Africa in *dysentery*. Polstorx and Schirmer (*Ber. d. Chem. Ges.*, 1886, 78) prepared the alkaloid both from *Holarrhena africana* and from *Wrightia zeylanica*, finding it to be identical in the two cases. When oxidized by iodic acid in sulphuric acid solution, conessine is changed to *oxyconessine*, $(C_{12}H_{20}NO.)_2$.

Wurrus.—Under the name of *Vars, Wars*, or *Wurrus*, a powder somewhat similar to kamala has been used as an anthelmintic in Southern Arabia, and exported into commerce from Aden. It is believed to be the product of *Flemmingia Grahamiana* W. et Arn. (Fam. *Leguminosæ.*) (*P. J.*, Sept., 1887.) It is composed of cylindrical or subconical grains, 170 to 200 mm. long by 70 to 100 broad, with oblong resin cells arranged perpendicularly in three or four tiers.

Xanol.—This is a *caffeo-sodium salicylate*. The salicylic radical is said to be obtained from *natural wintergreen oil*. It forms a very soluble white powder which is decomposed by acids. It is used as a vasomotor heart tonic and diuretic.

Xanthium.—Guichard believes that he has found an alkaloid in the *X. spinosum* L. (*P. J.*, vii, 249.) In the *Xanthium Strumarium* L., *Cocklebur* or *Clotbur*, which is common both in Europe and in America, A. Zander believes that he has found a glucoside, *xanthostrumarin*. M.

V. Cheatham thinks that there is a second active principle. (See *A. J. P.*, vol. xi, 271; vol. xiv, 134.) Clotbur is stated to be an active styptic, both local and general. *Dose*, of the fluidextract, from one to two fluidrachms (3.75–7.5 mils).

Xanthorrhiza. *Yellow-root. Shrub Yellow-root. Xanthorrhiza apiifolia* L'Her. (Fam. *Ranunculaceæ.*)—This is a low shrub, with a horizontal rhizome, which sends off numerous suckers. The stem is simple, about 5 mm. thick, with a smooth bark and bright yellow wood. The leaves, are compound, consisting of several ovate-lanceolate, acute, doubly serrate leaflets, sessile upon a long petiole, which embraces the stem at its base. The flowers are small, purple, and, disposed in long, drooping, divided racemes, placed immediately below the first leaves. Yellow-root grows from Southern New York to Georgia and west to Kentucky. It flowers in April. The root was formerly in the Secondary List of the U. S. Pharmacopœia, but the bark of the stem possesses the same virtues. The root is from 7 cm. to 1 dm. in length, and about 12 mm. thick near the stem. It shrinks somewhat in drying, and, as found in commerce, is in slender pieces of various lengths, wrinkled longitudinally, with a light yellowish-brown, easily separable epidermis, a thick, hard, bright yellow woody portion, and a very slender central pith. It is inodorous, and of a simple but extremely bitter taste. It imparts its color and taste to water. The infusion is not affected by ferric salts. J. Dyson Perrins found *berberine* in it. (*P. J.*, May, 1862.) Samuel S. Jones believed that he had proved the existence in the drug of a second alkaloid. (*A. J. P.*, vol. xvi, 1861.) *Xanthorrhiza* possesses properties closely analogous to those of calumba, quassia, and other simple tonic bitters, and may be used for the same purposes and in the same manner. Woodhouse employed it in the *dose* of forty grains (2.6 Gm.).

Xanthorrhœa Resins. *Gum Acaroides. Gum Acroides. Grass-tree Gum. Botany Bay Gum.*—Yellow and reddish resinous substances, the products of *Xanthorrhœa hastilis* R. Br. and *X. australis* R. Br. (fam. *Liliaceæ*), have been introduced into England from Australia. They are obtained by spontaneous exudation from the stems of the plants, which are usually shrubs. The *yellow variety* (from *X. hastilis*) is in tears, in flattish pieces having on one side the mark of the stem, or in masses of various size and irregular shape. It has a reddish-yellow color, resembling gamboge when broken, and when heated emits a fragrant odor like that of Tolu balsam. It contains resin, cinnamic and benzoic acids, and a trace of volatile oil, and may therefore be ranked among the balsams. When heated with nitric acid, it yields a large proportion of picric acid. In medicinal properties it is said to bear a close resemblance to storax and the balsam of Tolu. A tincture, made in the proportion of two ounces to a pint of alcohol, may be given in the *dose* of one or two fluidrachms. The *red variety* (from *X. australis* R. Br.) resembles dragon's blood in color, and appears to be analogous to the other variety in properties. (See *A. J. P.*, 1881; also *A. J. P.*, vol. xv, and *D. C.*, 1895, 83.) These resins have been introduced as a shellac substitute in varnish making.

Xanthoxylum Berries. *Xanthoxyli Fructus. N. F. IV. Prickly Ash Berries.*—"The fruit of *Zanthoxylum americanum* Miller (*Northern Prickly Ash*), or *Zanthoxylum Clava-Herculis* Linné (*Southern Prickly Ash*) (Fam. *Rutaceæ*)." *N. F. IV.*

Prickly ash berries were introduced in the N. F. IV to be used as an ingredient in *compound fluidextract of stillingia* N. F. IV, made with a menstruum of 25 volumes of glycerin, 50 volumes of alcohol and 25 volumes of water, finishing with diluted alcohol. The berries are described as "Capsules with short stalks (*X. americanum*) or without stalk (*Z. Clava-Herculis*); when fresh, ellipsoidal, fleshy, gray-brown, when dry, dehiscent; carpels two, convex, summit short pointed; seeds one or two oblong, black, shining, and wrinkled from drying. The carpels have a pungent, warm, aromatic taste and on chewing leave a tingling sensation on the tongue; when breathed upon they emit a faintly aromatic odor resembling that of citral. Prickly Ash Berries yield not more than 7 per cent. of ash." *N. F. IV.*

Xylene. *Xylol. Xylène*, Fr. *Xylol*, G. $C_6H_4(CH_3)_2$.—There are three isomeric hydrocarbons of this name, the ortho-, meta-, and para-xylene respectively, all contained in coal tar. A mixture of them was first extracted from naphtha by Hugo Müller, and was brought forward by Zuelzer as a specific in *smallpox*, but is useless. (*P. J.*, 1872, 623.) It is largely used as a solvent by microscopists.

Xylochloral.—A compound of chloral and *xylose* (*wood sugar*, $C_6H_{10}O_5$), analogous with chloralose. It forms colorless soluble scaly fragments fusing at 132° C. (269.6° F.). It has been used as a hypnotic. *Dose*, ten to fifteen grains (0.6–1.0 Gm.).

Xylenol Orthosalicylate. *Orthoxylenol Salol.* $C_8H_9C_7H_5O_3$.—A neutral white powder devoid of odor and taste. It is employed as an internal antiseptic and antirheumatic. The metaxylenol salol is used for the same purposes as the ortho compound. *Dose*, two to six grains (0.12–0.36 Gm.).

Yeast. *Cerevisiæ Fermentum Compressum*, N. F. *Compressed Yeast. Fœx medicinalis. Hefe, Bierhefe*, G. *Levure*, Fr.—The ferment obtained in brewing beer, and produced by *Saccharomyces* (*Torula* Turpin) *cerevisiæ* Meyen, was dismissed from the U. S. Pharmacopœia in 1880, from the British in 1898. Two well-marked varieties of the *Saccharomyces cerevisiæ* have been recognized. The one is the most active at the ordinary temperature (16°–20° C., 60.8°–68° F.), and carries through its fermentative work in from three to four days; the other works at a lower temperature (6°–8° C., 42.8°–46.4° F.), and the fermentation is much slower. The first placed in a saccharine liquid is carried by the carbon dioxide which it liberates to the surface of the liquid, where it continues its activity; it is, therefore, known as a *surface* or *top yeast*. The second, on the contrary, is not carried up, and rests during its entire activity on the bottom of the fermenting vessel, and is hence called a *bottom yeast*. Two quite distinct methods of beer brewing are practised, depending upon the use of the one or the other of these varieties of yeast. (For fuller information as to the nature of *yeast* and its conditions of culture and activity, see Sadtler's *Industrial Organic Chemistry*, Philadelphia, 3d ed., 1900, 185 *et seq.*)

Yeast is a flocculent, frothy, somewhat viscid semi-fluid, of a dirty yellowish color, a sour vinous odor, and a bitter taste. Exposed to a moderate heat it loses its liquid portion, becomes dry, hard, and brittle, and may in this state be preserved for a long time, though with the loss of much of its

peculiar power. *Yeast cakes* are made by putting yeast into sacks, washing it with water, then submitting it to pressure, and ultimately drying it; *compressed yeast*, the undried product, is now largely used.

Yeast is insoluble in alcohol or water. Its ultimate composition, according to Schlossberger (*Ann. Ch. Ph.*, 51, 199), is carbon 49.9 per cent., hydrogen 6.6 per cent., nitrogen 12.1 per cent., and oxygen 31.4 per cent. Its proximate constituents are albuminoids, cellulose, fats, and resinous substances.

The chief function of yeast is the inducing of the vinous fermentation, in which are produced alcohol and carbon dioxide, and various other substances in smaller or larger proportions. Pasteur has shown that while from 94 to 95 per cent. of the sugar decomposes into ethyl alcohol and carbon dioxide, the other 5 or 6 per cent. decomposes by secondary reactions, yielding glycerin from 2.5 to 3.6 per cent. and succinic acid from 0.4 to 0.7 per cent. The higher homologues of ethyl alcohol are also produced in small amount, forming fusel oil or raw spirit.

Yeast consists of numerous cells, irregular, roundish, or cylindrical in shape, separate, joined into rows, or budding one from the other. It is most probable that the yeast plant is the mycelium, or early vegetative stage, of more than one species of mucor or mould; and some authorities recognize various species of the yeast fungus. The name *Torula cerevisiæ* was first given to the yeast plant, which was subsequently called *Mycoderma vini;* Reess, in his elaborate work (*Alkoholsgährungspilze*, Leipsic, 1870), made a distinct genus of it, *Saccharomyces*, including many species.

The wine-producing yeasts are varieties of the species *Saccharomyces ellipsoideus.*

Compressed Yeast is official in the N. F. IV under the title *Cerevisiæ Fermentum Compressum.* It is described as "the moist, living cells of *Saccharomyces cerevisiæ* Meyen (Fam. *Saccharomycetaceæ*) or of other species of *Saccharomyces*, combined with a starchy or absorbent base. White or yellowish-white, soft and easily broken masses, having a characteristic, slightly sour odor, and not more than a faintly acid reaction to litmus. When examined under the microscope, numerous oidium and mycoderma cells and starch grains are visible. Compressed yeast must not be used unless fresh, and free from mildew and musty or foul odors." *N. F.*

According to Albert Buchner and Rapp, a dried yeast which retains its activity on keeping is obtained as follows: The yeast is freed from water as much as possible by expression, immersed in acetone and rubbed through a sieve. The acetone is decanted, renewed, again decanted, and the residue collected by the aid of a suction filter, then treated with ether for three minutes, and this removed in the same way, after which the the yeast is spread out to dry, the drying being completed at a temperature of 45° C. (113° F.). Dried yeast, so obtained, is an almost white powder. (*Ph. Centralh.*, 1903, 36.)

According to Casagrandi, *Saccharomyces ruber*, previously discovered by Demme, produces a *red yeast* which ferments glucose very readily, developing a red pigment. This saccharomyces was found pathogenic to various animals, and when put into milk so modified that liquid as to convert it into a pronounced intestinal irritant. (*P. J.*, Jan., 1898.) A number of yeasts are used in China and Java whose fundamental plants are different from those of the European yeast. See *P. J.*, vol. xlvii.

Yeast has been very widely employed, not only as a folk remedy, but also by the medical profession, in the treatment of various infectious conditions, especially of the skin. On the whole, there is strong clinical evidence of its usefulness in *furunculosis, acne* and the like. There is no generally accepted explanation of its mode of action. Certain investigators have believed it to exercise a direct bactericidal effect, but Tsuru (*W. K. R.*, 1909) found that this action was only exerted by growing yeast, and believed that the effect was due to the production of alcohol and various acids, during the process of fermentation. Abraham (*Monatsschrift fur Geburtsh. u. Gyn.*, 1910, No. 1) dissents from this conclusion, because he found that living yeast exercised an antibacterial effect, even in the absence of sugar. Even although yeast possessed active germicidal properties, this could not explain the benefit which has followed its internal administration. Some writers believe that this action is due to the high nuclein content, the latter acting as a stimulant to the formation of leucocytes. (See p. 1512.)

A possible explanation of the therapeutic benefit of yeast has been suggested by the experiments of Walzou and Sacharow, who found that it increased the opsonic index of dogs for staphylococci and streptococci. Plantier (*S. M.*, 1907) has had excellent results with the local application of yeast in the treatment of *burns.* He spreads a thick paste of the ferment upon strips of gauze which are applied to the denuded area, being renewed every two or three days. The preparation which is generally preferred by clinicians is the semi-liquid *brewer's yeast.* This has been employed internally in *doses* of from one to two ounces (30 to 60 mils) several times a day. It has also been used locally, especially in vaginal infections.

Of the N. F. compressed yeast from one to three teaspoonfuls (4–11 Gm.) may be given three times a day; of the liquid, brewer's yeast, two to four ounces (60–120 mils).

Dried yeast has been much used in France and it is probable that the ordinary *yeast cake* of American bakers may well be substituted for yeast.

A large number of preparations of yeast have been placed upon the market under various trade names. Among these the following may be mentioned: *Ceridin (cerolin). Dose,* one and a half to three grains (0.1 to 0.2 Gm.). *Bajuvarin* is a preparation of yeast which is used both internally and locally by veterinarians. *Fermentine* is a preparation of yeast containing benzoin, used principally for local application. *Fermocyl.* A mixture of dried yeast, pancreas and sodium phosphate, marketed in the form of tablets, each corresponding to about 30 grains (2 Gm.) of the fresh yeast. Used in diabetes. *Furunculin. Dose,* ten to thirty grains (0.65–2 Gm.). *Levuretin, Levurin,* and *Leuvurinose* are proprietary forms of dried beer yeast; any of them may be given in doses of one drachm (3.9 Gm.). *Mycodermin.* Marketed only in pills. *Dose,* 2 to 4 pills. *Trygase. Dose,* one teaspoonful. *Zymin* is a dried yeast which is marketed either as a powder, intended for external use, or in the form of tablets each of which contains fifteen grains (1 Gm.).

Xerase. N. N. R. 1917. This is stated to be a mixture of yeast and kaolin with glucose and salts. This is a yellowish-gray powder, asserted to possess not only absorbent but also bactericidal powers. It is intended for local application, especially in *gonorrhea* of women.

Cerolin. N. N. R. 1917. A fatty substance derived from yeast, asserted to represent the specifically active constituent of yeast. It is a yellowish to a brownish semifluid with an odor resembling that of yeast. It is used in the treatment of *furunculosis, acne* and *scurvy,* possessing also a laxative action. *Dose,* one and a half to five grains (0.096–0.32 Gm.). Pills of cerolin, each containing one and one-half grains (0.1 Gm.), are also on the market.

Yohimbine.—This is an alkaloid which is obtained from the bark of *Corynanthe Yohimbi* Schum., a rubiaceous tree growing in the Southern Cameroons district in Africa. The bark comes into commerce in flattened or slightly quilled pieces 75 cm. long to 4 to 8 mm. thick, with an external corky layer of a gray-brown color covered with isolated lichens. It shows numerous longitudinal and transverse fissures like some old specimens of cinchona bark. The transverse fracture is of a uniform yellowish-brown color, and presents short, soft fibers like rough velvet. The taste is bitter.

The alkaloid has been obtained in white needles melting at 234° C. (453.2° F.) and having the composition $C_{23}H_{32}N_2O_6$.

The salt of this base that is ordinarily used is the hydrochloride, being preferable on account of its solubility and high percentage of the alkaloid.

It was originally investigated by Oberwarth and Loewy (*V. A. P. A.,* cliii, and *B. K. W.,* No. 42, 1900), who found it to be in animals and also in man a very active excitant to the sexual organs and functions. On the other hand, Kravkoff, as the result of experiments upon the lower animals and upon man, concluded that it has no aphrodisiac effects and frequently produces nausea, salivation, irritability, and other disagreeable results.

Muller (*A. I. P. T.,* 1907, p. 65) found that *yohimbine,* in small doses stimulated, and in large doses depressed, the respiratory center. If lethal doses are given the heart continues beating after the respiration has ceased. Small doses have little effect upon the blood pressure, but moderate-sized doses caused a slight rise in the blood pressure with local dilatation of the vessels of the pelvic organs. He believes that its aphrodisiac action is due to an increase in the excitability of the lower centers in the spinal cord. On the other hand, many authors believe that its effect is due to the hyperemia produced. Toff (*D. M. W.,* 1904) has found it useful because of this effect in scanty or *irregular menstruation.*

It has been used by numerous clinicians in *neurasthenic impotence,* with reports which are generally favorable to its influence. (For literature, see *M. R.,* 1901, 1902.) It is said to be of no value when the impotence depends upon organic nerve trouble, and to be harmful when it is caused by chronic inflammatory disease of the sexual organs or of the prostate gland. *Dose,* of the hydrochloride, 0.005 Gm. (one-twelfth grain), either in tablet or solution, three or four times a day. Yohimbine has also been employed in a 1 per cent. solution hypodermically.

Zea. *N. F. IV (U. S. P. VIII). Corn Silk. Stigmata Maydis. Filament de Mais,* Fr. *Maispistille,* G.—"The fresh styles and stigmas of *Zea Mays* Linné (Fam. *Gramineæ*)." N. F.

This drug is the so-called "silk" of the ear of ordinary Indian corn or maize, cultivated in the warmer temperate and subtropical countries of the world. It consists of "slender filaments from 10 to 20 cm. in length, and about 0.4 mm. in diameter; of a light green, purplish-red, yellow or light brown color; stigmas bifid, the segments very slender, frequently unequal and from 0.4 to 3 mm. in length. Under the microscope, the styles are seen to consist for the most part of parenchyma and two parallel, vascular bundles with narrow, spiral or annular tracheæ; the epidermal cells are rectangular, many of these being extended into multicellular hairs, the latter being from 0.2 to 0.8 mm. in length, the basal portion consisting of two to five united cells, the upper portion being usually unicellular; the cells of the hairs are rich in cytoplasm and usually contain a small, spherical nucleus; the purplish-red styles contain a purplish-red cell sap. Digest a small portion of the fresh styles and stigmas in diluted alcohol and filter; a pale purplish-red solution is produced, separate portions of which, on the addition of acids, become distinctly purplish or yellowish-red; on the addition of alkalies, green; on the addition of ferric chloride T.S., olive-green changing to greenish-brown; and on the addition of an aqueous solution of alum, bluish or purplish, the color being quite permanent." *N. F.* Rademaker and Fischer (*A. J. P.,* 1886, p. 369) determined the presence of 2.25 per cent. of *maizenic acid* in dried corn silk. It was first described, however, by Vautier. It is freely soluble in water, alcohol and ether, but insoluble in benzin. Rademaker and Fischer found, in addition to the acid, fixed oil, resin, chlorophyll, sugar, gum, extractive, albuminoids, phlobaphene salt, cellulose and water.

Used as a mild stimulant diuretic, useful in *acute* and *chronic cystitis* and in the bladder irritation of *uric acid* and *phosphatic gravel.* It has also been employed in *gonorrhea,* and has been affirmed by Landreux to be a useful diuretic and even cardiac stimulant in the *dropsy of heart disease.* It probably is, however, of little value.

Concerning the activity of *maizenic acid* we have little definite knowledge, but it probably represents whatever physiological power the drug possesses; it has been given in the *dose* of one-eighth of a grain (0.008 Gm.).

Corn silk was official in the U. S. VIII but dismissed from the U. S. IX. It was introduced in the N. F. IV. The fluidextract of zea N. F. is made with a menstruum of diluted alcohol.

Dose, one to three drachms (3.9–11.6 Gm.).

Zebromal.—The *dibrom-cinnamic-ethyl-ester,* $C_6H_5.CHBr.CHBr.COOC_2H_5$, occurs as a white crystalline powder, soluble in alcohol with the fatty oils, but not in water. It has been suggested by Ellinger and Kotake (*A. E. P. P.,* 1911, lxv, p. 87) as a substitute for the alkaline bromides in *epilepsy,* but we know of no clinical reports of its efficacy.

Zedoary. *N. F. IV. Zedoaria. Radix Zedoariæ. Rhizoma Zedoariæ,* P. G. *Zedoarie,* Fr. *Zitterwurzel,* G.—"The dried rhizome of *Curcuma Zedoaria* (Bergius) Roscoe (Fam. *Zingiberaceæ*)." *N. F.* There are two kinds of zedoary, the long and the round, distinguished by the old official titles of *radix zedoariæ longæ* and *radix zedoariæ rotundæ.* Both kinds come from the East Indies. The *long zedoary* is in slices, from 2.5 to 7.5 cm. in length, and from 1 to 2.5 cm. thick, obtuse at the extremities and exhibiting the remains of the radical fibers. The *round* is commonly seen in communities, and is "usually cut into transverse rounded sections, twisted and wrinkled, from 1 to 4 cm. in diameter, and from 5 to 10 mm. in thickness; externally grayish-brown, hairy, rough, with few root scars;

transverse surface pale reddish to gray-brown; a distinct, dark circular endodermis, which is from 2 to 5 mm. in width, separates the cortex; the stele contains numerous, orange-colored resin cells and irregularly distributed, lighter colored wood bundles which are fewer in the cortex; fracture short, somewhat mealy and waxy. Odor aromatic, camphor-like; taste aromatic, warm, slightly bitter. Under the microscope, sections show a thick cork, a thin epidermis with numerous characteristic hairs, thick-walled, one- to six-celled, up to 1 mm. in length and often thicker in the middle than at the base; the parenchyma of the cortex and of the central cylinder rich in starch; secretion cells isodiametric with suberized walls, contents colorless or yellowish; the endodermis of small, thin-walled quadratic cells, the fibro-vascular bundles collateral, more numerous in the central cylinder and nearer the endodermis; few bast fibers in the cortex and no crystal cells. The powder contains numerous starch-grains which are ovoid, from 0.02 to 0.07 mm. in length and from 0.007 to 0.03 mm. in thickness, having the point of origin of growth in the smaller end of the grain; numerous characteristic, thick-walled hairs; rich in parenchyma; very few bast fibers; no calcium oxalate crystals or stone cells. Zedoary yields not more than 7 per cent. of ash." *N. F.*

Zedoary yields a volatile oil, when distilled with water, and contains a pungent soft resin and bitter extractive.

Zedoary was introduced into the N. F. IV and is used as an ingredient in *bitter tincture of zedoary, antiperiodic pills, antiperiodic pills without aloes, bitter tincture, antiperiodic tincture and antiperiodic tincture without aloes.*

Zedoary is a warm, stimulating aromatic, useful in flatulent colic and debility of the digestive organs. It is rarely employed, as it produces no effects which cannot be as well or better obtained from ginger. The *dose* is from ten grains to half a drachm (0.65–2.0 Gm.).

Zerechtit. *Tschuking. Landtia Schimperi* Benth. and Hook. (*Ubicea Schimperi* J. Gay *Arctotis Schimperi* O. Kze.)—The leaves, flowers and fruit of an Abyssinian composite. (See *Proc. A. Ph. A.*, xxvi, 228.)

Zerumbet. *Cassumuniar.*—Under these names an East Indian root was formerly used, having some analogy in sensible and medicinal properties to ginger, and ascribed to the *Zingiber Zerumbet* of Roscoe. By some authors the zerumbet has been erroneously confounded with the round zedoary. Geiger describes it as in pieces of the size of a fig or larger, externally grayish-brown and wrinkled, internally yellowish, hard and tough, of a biting, aromatic taste and a spicy odor.

Zimphen. *Sodium Metaoxycinnamate.*—This forms yellow crystals. Soluble in alcohol and but sparingly soluble in water. It is employed internally as a general antiseptic. *Dose,* eight grains (0.5 Gm.) before meals.

Zinc and Potassium Cyanide. *Zinci et Potassii Cyanidum.* $K_2Zn(Cn)_4$.—Made by adding zinc cyanide to solution of potassium cyanide, evaporating and crystallizing. The salt possesses a sweet and metallic taste and is used for the same purposes as zinc cyanide in from one-eighth to one-half grain (0.008–0.032 Gm.) *doses.*

Zinc Borate. *Zinci Boras.* $ZnB_4O_7 + 7H_2O$.—Prepared by mixing an aqueous solution of zinc sulphate (1 in 10) with one of borax (1 in 25), and collecting the precipitate. Used as an antiseptic dusting powder.

Zinc Bromide. *Zinci Bromidum. U. S. VIII. Zincum Bromatum. Bromure de Zinc,* Fr. *Bromzink, Zinkbromid,* G. *Bromuro zincico,* Sp. $ZnBr_2 = 225.21$.—"It should contain, when anhydrous, at least 97 per cent. of pure Zinc Bromide, and should be kept in small, glass-stoppered bottles." *U. S. VIII.*

Zinc bromide may be made either by the direct combination of zinc and bromine, or by dissolving zinc in a solution of hydrobromic acid. L. Lyons proposes to make this salt by dissolving potassium bromide and crystallized zinc sulphate, each, in the smallest quantity of hot water and mixing while hot. When the mixture has cooled, twice its bulk of alcohol is added and the whole filtered through asbestos to separate the potassium sulphate. The filtrate is then evaporated to dryness.

It is "a white, or nearly white, granular powder; odorless, having, even in dilute solutions, a sharp, saline and metallic taste. Very deliquescent. Readily soluble in water and alcohol. When heated to 394° C. (741.2° F.), the salt fuses, and, with a careful increase of heat, may be sublimed in the form of needle-shaped prisms. Its aqueous solution gives a slightly acid reaction with blue litmus paper." *U. S. VIII.*

It responds to the tests for zinc and for hydrobromic acid. The absence of iodides may be shown by adding to 10 mils of the aqueous solution of the salt (1 in 20) 1 mil of chloroform, then chlorine water (which has been diluted with an equal volume of water), cautiously introduced, drop by drop, with constant agitation, the liberated bromine will dissolve in the chloroform, imparting to it a yellow to orange color, free from any violet tint (absence of *iodide*).

"The aqueous solution of the salt (1 in 20), to which sufficient hydrochloric acid has been added to insure a clear solution, should not respond to the Time-Limit Test for *arsenic, cadmium, lead,* and *copper* (see U. S. P. VIII, Test No. 121); in applying this test the addition of ammonia water should be omitted. Another portion of this aqueous solution should not be rendered turbid by the addition of barium chloride T.S. (absence of *sulphate*). Five Cc. of the aqueous solution of the salt (1 in 10) should not respond to the Modified Gutzeit's Test for *arsenic.*" *U. S. VIII.*

Zinc bromide is capable in excessive doses of acting as an irritant poison. It has been commended in *epilepsy,* but is of no value.

Dose, one to two grains (0.065–0.13 Gm.).

Zinc Cyanide. *Zinci Cyanidum.* $Zn(Cn)_2$.—This cyanide is precipitated as a white insoluble powder, by adding cautiously, until it ceases to produce a precipitate, a recently filtered solution of potassium cyanide to a solution of zinc sulphate. It is used in Germany as a substitute for hydrocyanic acid, and is said to be anthelmintic. It has been recommended by Lashkevich in *cardiac neuroses* in doses of from one-tenth to one-eighth grains (0.006–0.008 Gm.) three times a day. It has been employed in *epilepsy, chorea* and *neuralgia,* in several *painful affections of the stomach* and in the *colics* attendant on *difficult menstruation.* The *dose* is a quarter of a grain (0.016 Gm.), gradually increased to a grain and a half (0.096 Gm.), given in mixture. It is official in the French Codex.

Zinc Ferrocyanide. *Zinci Ferrocyanidum.* $Zn_2Fe(Cn)_6 + 3H_2O$.—Formed by double decomposition between hot solutions of potassium ferrocyanide and zinc sulphate. It is precipitated as

a white powder. It has similar medicinal properties to those of the cyanide, and is used in the same diseases. The *dose* is from one to four grains (0.065–0.26 Gm.), given in pill. (See *Zinc Cyanide*, p. 1671.)

Zinc Iodide. *Zinci Iodidum. U. S. VIII. Zincum Iodatum. Iodure de Zinc*, Fr. *Zinkjodid, Jodzink*, G. $ZnI_2 = 319.21$.—"It should contain, when anhydrous, not less than 98 per cent. of pure Zinc Iodide, and should be kept in small, glass-stoppered bottles protected from light." *U. S. VIII.*

This iodide may be formed by digesting an excess of zinc, in small pieces, with iodine diffused in water. Combination takes place and, by evaporation, a deliquescent, very soluble saline mass is obtained, having a metallic styptic taste, resembling that of zinc sulphate. It may also be obtained by heating in a flask a mixture of 20 parts of zinc and 170 of iodine, and subliming into a vial. Thus prepared, it is in the form of white needles. This salt is very liable to spontaneous decomposition.

Properties.—It is "a white, or nearly white, granular powder; odorless, and having a sharp, saline and metallic taste. Very deliquescent, and, upon exposure to air and light, becoming brown from liberated iodine. Readily soluble in water, alcohol, or ether. When heated to about 446° C. (834.8° F.), the salt fuses to a colorless liquid, and at a higher temperature sublimes, forming quadratic needles, while a small part is decomposed and leaves a residue of zinc oxide. Its aqueous solution reddens blue litmus paper. An aqueous solution of the salt (1 in 20) yields a white gelatinous precipitate with potassium ferrocyanide T.S., and a pure white precipitate with ammonium sulphide T.S. With silver nitrate T.S. it yields a pale yellow precipitate, insoluble in ammonia water; with mercuric chloride T.S., a red precipitate, soluble in potassium iodide T.S. The aqueous solution of the salt (1 in 20), to which sufficient diluted hydrochloric acid has been added to insure a clear solution, should not respond to the Time-Limit Test for *arsenic, cadmium, lead,* and *copper* (see U. S. P. VIII, Test No. 121); in applying this test the addition of ammonia water should be omitted. Another portion of the aqueous solution should not be rendered turbid upon the addition of barium chloride T.S. (absence of *sulphate*). If ammonium carbonate T.S. be added to the aqueous solution of the salt (1 in 20), a pure white precipitate will form, which should redissolve completely in an excess of the reagent. Five Cc. of the aqueous solution of the salt (1 in 10) should not respond to the Modified Gutzeit's Test for *arsenic* (see U. S. P. VIII, Test No. 17). If 1 Gm. of Zinc Iodide be mixed with 5 Cc. of distilled water, and sufficient ammonia water be added to redissolve the precipitate formed, followed by a solution of 1.5 Gm. of silver nitrate in 10 Cc. of water, then, after shaking and filtering, the filtrate should not be rendered more than slightly turbid by the addition of an excess of nitric acid (limit of *chloride*). If 0.5 Gm. of dry Zinc Iodide be dissolved in 20 Cc. of water, and if 35 Cc. of tenth-normal silver nitrate V.S., 5 Cc. of nitric acid, and 3 Cc. of ferric ammonium sulphate T.S. be added, and the mixture well shaken, then the addition of not less than 3.4 Cc. nor more than 4 Cc. of tenth-normal potassium sulphocyanate V.S. should be required to give a permanent reddish-brown tint to the solution." *U. S. VIII.*

Zinc iodide was proposed by Barlow as an alterative remedy in *chorea, scrofula* and *hysteria* (*M. T. G.*, Nov., 1853), but has failed to come into general use. The best form of administration is in *syrup*, to protect it from change. (See p. 1353, *U. S. D.*, 19th ed.) Zinc iodide has been used as an external application. A solution containing from one to two grains (0.065–0.13 Gm.) to the fluidounce (30 mils) of water has been used as an astringent injection in *gonorrhea.*

Dose, one-half to two grains (0.032–0.13 Gm.).

Zinc Lactate. *Zinci Lactas.* $Zn(C_3H_5O_3)_2 + 3H_2O$.—This salt is used by Herpin in *doses* of two grains (0.13 Gm.), three times a day, gradually increased to ten grains (0.65 Gm.) a day, as a substitute for zinc oxide in *epilepsy.* For its physical properties and methods of preparation see 16th edition *U. S. D.*

Zinc Permanganate. *N. N. R.* 1917. *Zinci Permanganas. Zinkpermanganat, Uebermangansaures Zink*, G. $Zn(MnO_4)_2 + 2H_2O$.—Made by precipitating barium permanganate with zinc sulphate, using exact molecular proportions. It forms almost black deliquescent crystals, giving off oxygen even more readily than does potassium permanganate. It is incompatible with peroxides, acids, ammonia and hypophosphites, and must not be triturated with organic substances. It is used as an astringent and antiseptic application.

Zinc Peroxide. *Zinc Perhydrol. Zinconal.*—A mixture stated to contain equal parts of *zinc peroxide* and zinc oxide, has been introduced as an antiseptic dusting powder in the treatment of *wounds* and *ulcers.* It is a white insoluble powder and its value appears to depend upon the slow formation of hydrogen dioxide. It may be used either in the form of a dusting powder or as an ointment in strengths of 25 to 50 per cent.

Zinc Phosphate. *Zinci Phosphas. Trizincic Orthophosphate.* $Zn_3(PO_4)_2 + 4H_2O$.—Barnes, of London, has brought forward this salt of zinc as having special advantages over other salts of the same metal in the treatment of *nervous diseases*, peculiarly useful in the *insanity* occurring in the convalescence from fevers, in which he associates it with quinine, and in *epilepsy* attended by *disorder of the uterine functions.* Zinc phosphate may be prepared by the mutual reaction of zinc sulphate and an alkaline phosphate. Zinc phosphate is a white powder, insoluble in water but soluble in acids.

Zinc Phosphide. *Zinci Phosphidum. U. S.* 1890. $Zn_3P_2 = 258.19$.—According to Hager, *zinc phosphide* was first prepared by Marggraf in 1740. It was formerly made by fusing, in a bath of iron filings, 74 parts of pure zinc, and adding gradually, in small pieces, 26 parts of dry phosphorus. This process gives good results only in small quantities (10 to 20 Gm.). A more recent process is to pass vapors of phosphorus in a current of dry hydrogen over fused zinc. The product is a spongy, gray mass, of metallic appearance, containing rhomboidal crystals, and when powdered resembling somewhat reduced iron. The particles of metallic zinc should be separated. Its sp. gr. is 4.72. "Zinc phosphide should be kept in small, glass-stoppered vials." *U. S.*, 1890.

It occurs as "a gritty powder of a dark gray color, or crystalline fragments of a dark, metallic luster, and having a faint odor and taste of phosphorus. In contact with the air it slowly emits phosphorous vapor. Insoluble in water or alcohol. Soluble in diluted hydrochloric or sulphuric acid with evolution of hydrogen phosphide. When

strongly heated, with exclusion of air, it melts and finally sublimes. When heated in air, it becomes oxidized to zinc phosphate. If 0.5 Gm. of zinc phosphide be dissolved in 15 Cc. of diluted hydrochloric acid, heat being applied to expel all of the hydrogen phosphide gas, a clear solution should result, leaving no residue (absence of *insoluble impurities*). A portion of this solution should yield a pure white precipitate with potassium ferrocyanide test-solution (absence of *iron* or *copper*); or with ammonium sulphide test-solution (absence of *lead* or *copper*). If another portion of this solution be mixed with an equal volume of hydrogen sulphide test-solution, no color or turbidity should appear (absence of *arsenic, cadmium, lead, copper,* etc.)." For a method of assay of zinc phosphide, see *N. R.*, June, 1879.

It has been proved by direct experiment upon animals, as well as by clinical experience, that zinc phosphide affects the system physiologically and therapeutically in exactly the same manner as does phosphorus, and it is employed in medicine as a substitute for that element. Theoretically, each grain of the phosphide contains nearly a quarter of a grain of phosphorus. It is asserted in the journals to have been administered in doses of one or even two grains; but of the pure salt such amounts would be extremely dangerous; the commencing *dose* is one-twentieth of a grain (0.003 Gm.).

Zinc Salicylate. *Zinci Salicylas. Zinksalicylat,* G. $Zn(C_6H_4.OH.COO)_2 + 3H_2O$.—Made by boiling together molecular proportions of sodium salicylate and zinc sulphate, cooling, washing the crystals and recrystallizing from hot water. In the form of long satiny needle-like crystals, having a sweet but astringent and bitter taste. It is soluble in about 20 parts of cold water. Zinc salicylate is an astringent and antiseptic, a solution (one-fifth to one per cent.) is used in *ophthalmia* and *gonorrhea.* It is incompatible with iron compounds and with mineral acids.

Zinc Subgallate. *Zinci Subgallas.*—An odorless powder containing 44 per cent. of zinc oxide and 56 per cent. of gallic acid. Internally it is used in intestinal disorders as an antiferment in *doses* of from one-half to four grains (0.032–0.26 Gm.). It is incompatible with iron compounds and with alkaloidal salts. Externally it has been used in *skin diseases.*

Zinc Sulphite. *Zinci Sulphis.* $ZnSO_3 + 2H_2O$. —Made by precipitating a solution of zinc sulphate with sodium sulphite, collecting, washing and drying the precipitate. A white crystalline powder, soluble in about 600 parts of water.

Zincopyrin. *Phenyl-dimethyl-pyrazolone Zinc Chloride.* $(C_{11}H_{12}N_2O)_2ZnCl_2$.—It is a double salt made with one molecule of zinc chloride and two of antipyrine. It occurs as shining scales soluble in about 20 parts of water. It is used as a caustic in inoperable *cancers.*

Zirconium. Zr = 90.6.—*Zirconium dioxide* is a heavy white insoluble powder which has been used by Kaestle (*M. M. W.*, 1909) for making X-ray examinations of internal organs. According to this author it is the most opaque substance available except thorium oxide and has the advantage of being much cheaper.

Zizyphus. *Zizyphus sativa* Gaertn. (*Z. vulgaris* Lamarck.) *Jujube,* Fr. *Brustbeeren, Judendornbeeren,* G.—A shrub, or small tree, of the Fam. *Rhamnaceæ,* growing on the shores of the Mediterranean, and cultivated in Italy, Spain, and the south of France. The fruit is the part used. This consists of oval drupes, of the size of a large olive, with a thin, coriaceous, red or reddish-brown skin, a yellowish, sweet, acidulous pulp, and an oblong, pointed stone in the center. These have the name of *jujubæ.* By drying, their pulp becomes softer and sweeter, and acquires a vinous taste, evincing the commencement of fermentation. They are nutritive and demulcent, and are used in the form of decoction in *pectoral complaints. Jujube paste* consists properly of gum arabic and sugar, dissolved in a decoction of this fruit and evaporated to the proper consistence. As a demulcent it is in no respect superior to a paste made with gum arabic and sugar alone, and the preparation formerly sold in this country under the name contains in fact none of the fruit. The fruits of two other species, *Z. Lotus* Lam., growing in the north of Africa, and *Z. Jujuba* Lam., a native of the East Indies, possess properties similar to those of the *Z. sativa* and are used as food by the inhabitants of the countries where they grow. The *Zizyphus Jujuba* is stated by Bosisto (*A. J. P.*, 1886) to be one of the main sources of stick-lac, from which shellac is manufactured.

Zygadenus. *Death Comas.*—One or more species of this liliaceous genus, found in the Western United States, are highly toxic to grazing animals, notably to sheep. H. S. Goodell affirms that he has seen violent convulsions produced by the juice of *Z. venenosus* Watson. Slade (*A. J. P.*, 1905, p. 262) obtained an alkaloid from *Z. venenosus,* which resembled veratalbine. Heyl and others (*J. A. C. S.*, 1911 and 1913) obtained an alkaloid from the leaves of *Z. intermedius, zygadenine,* which resembled veratrine.

Zymoidin.—A powder said to be composed of zinc oxide, bismuth oxide, aluminum oxide, iodine, boric acid, carbolic acid, gallic acid, salicylic acid, quinine, and other ingredients. It is used as an antiseptic and dusting powder.

PART III

SECTION I

In this division are included the subjects formerly embraced in the Appendix of this work, with the addition of the official tests and various tables, and an abstract of the preparations of the National Formulary.

Reagents, Test Solutions, and Volumetric Solutions

U. S. P. Ninth Decennial Revision

The constant reference to tests in the previous pages, and the adoption of volumetric test solutions in the U. S. Pharmacopœias, and the British Pharmacopœia, necessitate the insertion of the official reagents and solutions used in the quantitative and qualitative tests. Great care should be used, in preparing these tests and selecting the reagents, to see that they come fully up to the official requirements, as the whole value of the test depends upon the purity of the reagent and the accuracy with which the solution has been made.

INTRODUCTORY

Official Substances as Reagents.—Latin official names are not used as titles in the following list, the English names being preferred. Some official substances (chemicals, chemical solutions, etc.) are sufficiently pure to be used as reagents, if they comply with the tests of purity prescribed by the Pharmacopœia. In the case of other official substances, the presence of certain impurities, though immaterial for their use as medicines, renders them unsuitable for employment as reagents. Whenever a greater degree of purity is required than is provided for by the text of the Pharmacopœia, it will be specially mentioned in the following list.

Abbreviations and Signs Used:

T.S. = Test Solution.

V.S. = Volumetric Solution.

$\frac{N}{1}$ = Normal (see under "Volumetric Solutions," page 1692).

$\frac{N}{2}$ = Half-normal; $\frac{N}{10}$ = Tenth-normal; $\frac{N}{50}$ = Fiftieth-normal; $\frac{N}{100}$ = Hundredth-normal; $\frac{N}{200}$ = Two-hundredth-normal.

$\frac{2N}{1}$ = Double-normal (sometimes written: 2N).

Keeping of Reagents.—Preserve reagents in bottles made of glass as free as possible from lead or arsenic and closed by well-ground glass stoppers or, in certain cases, rubber stoppers. Ground glass stoppers of bottles containing alkali hydroxides, ammonium sulphide, ammonia water, and other substances of alkaline reaction, which rapidly attack ground glass surfaces, are to be coated with a thin film of petrolatum.

Keep reagents which are easily affected by light, such as hydrogen sulphide T.S., ammonium sulphide T.S., chlorine water, silver nitrate T.S., etc., in bottles made of dark amber-colored glass.

NOTE.—As some of the following test solutions are in certain cases directed to be used in definite quantities, it is important that they always be prepared of the *exact strength prescribed* and measured at the standard temperature of 25° C. (77° F.).

Water, whenever required or mentioned as a solvent in the tests given in the Pharmacopœia, or in the preparation of any reagent, is always understood to be *distilled water*.

Reagents and Test Solutions

The reagents are arranged in alphabetical order and the test solutions are usually mentioned in connection with the principal chemical or other substance from which they are prepared.

Acetic Acid.—Use the official acetic acid (see page 14).

Acetic Anhydride (Acetic Acid Anhydride), $(CH_3.CO)_2O$.—A colorless, mobile, refractive liquid of pungent acetic odor, boiling at about 137° C. (278.6° F.). Specific gravity about 1.07 at 25° C. (77° F.). When poured into water it sinks at first, but gradually dissolves, forming acetic acid. Dilute 1 mil with about 50 mils of distilled water, add 5 mils of nitric acid, and mix well; the solution gives no reaction upon the addition of silver nitrate T.S. (*hydrochloric acid*). Evaporate 10 mils of acetic anhydride to dryness, completing the drying at 110° C. (230° F.); the residue weighs not more than 0.5 milligrammes (*non-volatile matter*).

Dissolve 10 mils of acetic anhydride accurately weighed in sufficient distilled water to measure 100 mils and titrate 10 mils of this with normal potassium hydroxide V.S., using phenolphthalein T.S. as indicator; not less than 19.3 mils is required to neutralize 1 Gm. of acetic anhydride. Preserve acetic anhydride in glass-stoppered vials in a cool place.

Acetone.—Use the official acetone (see page 9).

Albumen Test Solution.—Carefully separate the white of a strictly fresh hen's egg from the yolk, shake it thoroughly with 100 mils of distilled water, and filter. This solution must be freshly made when required.

Alcohol, 94.9 per cent.—Use the official alcohol (see page 108) containing not less than 94.9 per cent., by volume, of C_2H_5OH at 15.6° C. (60° F.). Alcohol of lower strength is prepared as follows:

Alcohol, 90 per cent.—Mix 51 mils of alcohol (see page 108) with 3 mils of distilled water. The specific gravity of the mixture is 0.834 at 15.6° C. (60° F.), corresponding to 90 per cent., by volume, of C_2H_5OH.

Alcohol, 80 per cent.—Mix 45.5 mils of alcohol (see page 108) with 9.5 mils of distilled water. The specific gravity of the mixture is 0.864 at 15.6° C. (60° F.), corresponding to 80 per cent., by volume, of C_2H_5OH.

Alcohol, 70 per cent.—Mix 38.6 mils of alcohol (see page 108) with 15 mils of distilled water. The specific gravity of the mixture is 0.890 at 15.6° C. (60° F.), corresponding to 70 per cent., by volume, of C_2H_5OH.

Alcohol, Dehydrated, C_2H_5OH.—Use the official dehydrated alcohol (see page 107), containing not less than 99 per cent., by volume, of C_2H_5OH.

Ammonia, Spirit of.—An alcoholic solution of ammonia (NH_3) containing 10 per cent., by weight, of the gas. It responds to the tests for purity given under ammonia water (see page 167).

Ammonia Test Solution.—Use the official ammonia water (see page 166).

Ammonia Carbonate Test Solution.—Dissolve 20 Gm. of ammonium carbonate (see page 130) in a mixture of 20 mils of ammonia water and 65 mils of distilled water, and add sufficient distilled water to measure 100 mils.

Ammonium Chloride Test Solution.—Dissolve 10 Gm. of ammonium chloride, NH_4Cl (see page 132), in sufficient distilled water to measure 100 mils. In addition to the tests prescribed for this salt under ammonium chloride (see page 133), the following must be complied with when employed in the test for lead under citric acid, tartaric acid, potassium bitartrate, or potassium and sodium tartrate. Dissolve 3 Gm. of the salt in 10 mils of distilled water acidified with 1 drop of diluted hydrochloric acid in a test tube of colorless glass having an internal diameter of 2 cm., add 10 mils of hydrogen sulphide T.S., which must be perfectly clear and colorless, and mix well. The liquid must show no discoloration when viewed downward against a white surface.

Ammonium Molybdate Test Solution.—Mix 6.5 Gm. of finely powdered molybdic acid (see page 1685) with 14 mils of distilled water and 14.5 mils of stronger ammonia water to effect solution. Cool and slowly add the solution, in small portions with agitation, to a well cooled mixture of 32 mils of nitric acid and 40 mils of distilled water. Allow the solution to stand for twenty-four hours and then filter through asbestos.

Preserve the test solution in the dark, and, if a sediment should form in it after some days, carefully decant the clear solution. This solution should be tested at frequent intervals. Add 2 mils of sodium phosphate T.S. to 5 mils of the reagent; an abundant yellow precipitate forms either at once or upon slight warming. If only a slight precipitation or yellow opalescence results, the reagent must be rejected. When employed as a reagent, ammonium molybdate T.S. is always added in large excess to the solution being tested, the latter having previously been strongly acidified with nitric acid.

Ammonium Nitrate, NH_4NO_3.—Colorless crystals, soluble in less than their own weight of water, and in about 10 parts of alcohol. This salt when used as a reagent conforms to the tests for purity given under ammonium chloride (see page 132) and in addition responds to the following tests: Ten mil portions taken separately of an aqueous solution of the salt (1 in 10), acidulated with a few drops of nitric acid, yield no turbidity on the addition of a few drops of silver nitrate T.S. (*chloride*) or a few drops of barium nitrate T.S. (*sulphate*). Dissolve 1 Gm. of ammonium nitrate in 10 mils of distilled water, add a few drops of potassium iodide T.S., 1 mil of acetic acid and a few drops of starch T.S.; no blue color is produced (*nitrite*).

Ammonium Oxalate Test Solution.—Dissolve 4 Gm. of crystallized ammonium oxalate, $(NH_4)_2C_2O_4+H_2O$, in sufficient distilled water to measure 100 mils, or dissolve 3.548 Gm. of purified oxalic acid (see page 1686) in 90 mils of distilled water, add 13 mils of ammonia water, boil to expel any excess of ammonia, and dilute with distilled water to make 100 mils.

Evaporate 50 mils of the test solution and ignite the residue, or ignite 2 Gm. of the salt; it leaves not more than 0.02 Gm. of residue (*fixed impurities*). The precipitate produced by the addition of silver nitrate T.S. or by barium chloride T.S., when added to 25 mils of the test solution, dissolves without residue upon the addition of nitric acid (*chloride and sulphate*).

Ammonium Polysulphide Test Solution.—A yellow liquid, made by dissolving a small quantity of the official precipitated sulphur (see page 1083) in colorless ammonium sulphide T.S.

Ammonium Sulphate, $(NH_4)_2SO_4$.—This salt must respond to the following tests for purity: Two Gm. yields not more than 0.002 Gm. of residue on ignition (*fixed impurities*). Five mils of an aqueous solution of the salt (1 in 10) does not respond to the Test for heavy metals (see Test No. 3). Five mils of a similar solution shows no turbidity upon the addition of nitric acid and silver nitrate T.S. (*chloride*). Another 5 mils of the solution (1 in 10) is not colored red upon the addition of 1 mil of hydrochloric acid and 1 drop of ferric chloride T.S. (*sulphocyanate*). This salt may be prepared by cautiously neutralizing ammonia water with sulphuric acid, which has been previously diluted with about two volumes of distilled water, evaporating and crystallizing. During the evaporation, the solution should be tested with litmus paper, from time to time adding more ammonia if necessary to keep the liquid alkaline.

Ammonium Sulphide Test Solution.—Saturate 3 parts of ammonia water (see page 166) with hydrogen sulphide, prepared as directed on page 1682, and add to the solution (which now contains ammonium hydrogen sulphide, NH_4HS) 2 parts of ammonia water, which converts the greater portion of the ammonium hydrogen sulphide into ammonium sulphide, $(NH_4)_2S$. Ten mils of the clear ammonium sulphide T.S., when evaporated to dryness and then gently ignited, leaves a residue weighing not more than 0.005 Gm. (*non-volatile matter*). It is not rendered turbid either by magnesium sulphate T.S. (*free ammonia*), or by calcium chloride T.S. (*ammonium carbonate*). Protect it from air and light by keeping it in small, dark amber-colored bottles, in a cool, dark place. As soon as a notable deposit of sulphur has made its appearance in the solution reject it.

Ammonium Vanadate (Ammonium Metavanadate), NH_4VO_3.—A white crystalline powder, soluble in about 100 parts of cold water and readily soluble in boiling water, forming a yellow liquid. This color is due to partial decomposition through loss of ammonia. When heated the salt assumes a yellow color which changes to brown, then reddish-brown, as the temperature rises.

Amyl Alcohol, $C_5H_{11}OH$.—A colorless, oily liquid having a penetrating characteristic odor, boiling between 128° and 132° C. (262.4° and 269.6° F.); soluble in 40 parts of water at 25° C. (77° F.); miscible with alcohol, ether, chloroform, carbon disulphide, petroleum benzin, benzene, or fixed or volatile oils. Ten mils of amyl alcohol, when evaporated to dryness on a water bath, yields not more than 0.0005 Gm. of residue.

Aniline (Phenylamine), $C_6H_5NH_2$.—When freshly distilled, aniline is a colorless, strongly refractive, oily liquid, having a peculiar, aromatic odor and a pungent, burning taste. Upon exposure to the light and air, it rapidly assumes a reddish-brown color. Specific gravity, about 1.02 at 25° C. (77° F.). Aniline distils completely between 182° and 184° C. (359.6° and 363.2° F.). It is soluble in alcohol, ether, or the fixed or volatile oils. With acids, it forms soluble crystalline salts. When added to an aqueous solution of calcium or sodium hypochlorite, a blue or purple color is produced. Preserve it in amber-colored bottles.

Aniline Sulphate, $(C_6H_5NH_2)_2H_2SO_4$.—Add gradually 10 Gm. of aniline, $C_6H_5NH_2$, to about 7 Gm. of sulphuric acid, stirring constantly. Dissolve the resulting solid mass in sufficient boiling diluted alcohol and set it aside for crystallization. Collect the crystals upon a filter, and, after draining them, recrystallize the salt from diluted alcohol. Collect the crystals on a filter and finally dry them in a desiccator. Aniline sulphate forms white crystals very soluble in water, less soluble in diluted alcohol, and slightly soluble in alcohol.

Aniline Sulphate Test Solution.—Dissolve 5 Gm. of aniline sulphate in 40 mils of distilled water, add 51 mils of diluted alcohol (see page 110) and sufficient distilled water to make 100 mils.

Arsenic Acid (Ortho-arsenic Acid), $H_3AsO_4+\frac{1}{2}H_2O$.—In white crystals or as a crystalline mass, very hygroscopic, readily soluble in water and alcohol. It fuses at about 100° C. (212° F.), becoming anhydrous at 110° C. (230° F.). At higher temperatures, it is converted into the pyro-acid and, finally, at 200° C. (392° F.) into the meta-acid. The addition of silver nitrate T.S. to an aqueous solution of arsenic acid, followed by the gradual addition of ammonia water, drop by drop, produces a red-brown precipitate which is readily soluble in a slight excess of ammonia water. With magnesia mixture T.S., arsenic acid solutions give a white crystalline precipitate. One mil of an aqueous solution of the salt (1 in 10) after neutralizing with sodium carbonate does not decolorize 1 drop of iodine T.S. (*arsenous oxide*). To 10 mils of a solution of ferrous sulphate (1 to 10) add 0.5 mil of an aqueous solution of arsenic acid (1 in 10) and float this over concentrated sulphuric acid contained in a test tube; no brown ring is formed at the zone of contact (*nitric acid*).

Arsenic Acid Test Solution, Concentrated.—For use in the assay for eucalyptol prepare this solution by dissolving 85 Gm. of crystalline arsenic acid (see above) in sufficient distilled water to make the product weigh 100 Gm. This solution has a specific gravity of about 2.173 at 25° C. (77° F.). The test solution may also be prepared by adding 56 Gm. of arsenic trioxide, in small portions, to 60 mils of nitric acid contained in a porcelain evaporating dish, stirring continuously and warming gently to assist the evolution of nitrous vapors. When all of the arsenic trioxide has been added, evaporate to a syrupy consistence, add about 25 mils of distilled water and again evaporate, and then repeat this operation once more. Finally dilute with distilled water until the solution weighs 100 Gm. This solution must comply with the tests for identity and purity given under *Arsenic Acid* (see above). If the tests indicate the presence of arsenous oxide, more nitric acid must be added and the evaporation repeated. If nitric acid is present, the solution should be repeatedly diluted and evaporated.

Arsenic Trioxide (Arsenous Oxide), As_2O_3.—For use in the Arsenic Test use arsenic trioxide which complies with the description and tests given in Part I (see page 192).

Asbestos.—The anhydrous, silky, well-matted variety (not serpentine), commercially known as "Asbestos Wool," which when moistened readily wads when rolled between the fingers. For use as a filtering medium for the "Gooch" crucible, remove the soluble matter by boiling it for one hour with diluted hydrochloric acid, and washing it with boiling water, by decantation, until free from acid. Finally transfer it to a wide-mouthed bottle containing distilled water. When desired for use, shake the mixture and pour it into a Gooch crucible which is attached to a suction pump, distributing the asbestos uniformly over the bottom in a layer sufficiently thick to retain a precipitate.

Azolitmin.—See under *Indicators* (page 1707).

Azolitmin Test Solution.—See under *Indicators* (page 1707).

Azur II (Azur Blue II, Methylene-Azur II).—A mixture of equal parts of the chlorides of methylene blue (tetramethylthionine) and methylene-azur (methylene blue sulphonate). A dark green powder, entirely soluble in water with a deep blue color, less soluble in alcohol and slightly soluble in chloroform; insoluble in ether. The addition of tannic acid T.S. to an aqueous solution of azur II (1 in 1000) produces a blue precipitate. The addition of a few drops of hydrochloric acid to a mixture of 5 mils of an aqueous solution of this dye (1 in 1000) and 0.5 Gm. of zinc dust causes decolorization. When the decolorized mixture is filtered, and solution of hydrogen dioxide is added, the deep blue color is restored (reduction to leuco base and reoxidation). The addition of either hydrochloric acid or ammonia water to an aqueous solution of azur II (1 in 1000) produces no change. The addition of sodium hydroxide T.S. to an aqueous solution of azur II (1 in 1000) produces a violet coloration; upon heating the solution a violet precipitate is formed. The addition of potassium iodide T.S. to an aqueous solution of the dye (1 in 1000) produces a violet precipitate; the addition of potassium dichromate T.S. produces a red-violet precipitate. Azur II dissolves in concentrated sulphuric acid with a bright green color [distinction from *methylene violet* (dimethylthionolin)]; upon cautiously diluting with distilled water the solution assumes a blue color, remaining clear. Acidulate an aqueous solution of azur II (1 in 1000) with a few drops of hydrochloric acid, then shake it with ether, remove the ethereal layer, and shake it with a diluted solution of sodium hydroxide T.S.; the latter remains uncolored (distinction from *azur II-eosin*).

Azur II-Eosin.—A mixture of methylene blue eosin (methylene blue eosinate) and methylene-azur-

eosin (methylene blue sulphone-eosinate). A dark green powder only very slightly soluble in water, more readily soluble in alcohol or glycerin. A warm saturated aqueous solution of azur II-eosin (about 1 in 2000) possesses a blue color with intense shading into violet. Highly dilute solutions possess a slight, greenish opalescence. Its solutions in alcohol or glycerin possess the same color with a strong yellowish-green fluorescence. A saturated aqueous solution of azur II-eosin is precipitated upon the addition of tannic acid T.S. The addition of zinc dust and ammonia water to an aqueous solution of this dye causes decolorization. When filtered, the colorless filtrate, upon standing in the air, quickly assumes a blue color (reduction to a leuco base and reoxidation to original color). A hot, saturated and filtered, aqueous solution of azur II-eosin assumes a pale blue color upon the addition of hydrochloric acid, and the dye separates in blue flocculles. If this acid solution is agitated with ether and the ethereal layer removed and shaken with diluted sodium hydroxide T.S., the latter assumes an eosin color (distinction from *azur II*). The addition of sodium hydroxide T.S. to a saturated aqueous solution of azur II-eosin intensifies its violet color. Azur II-eosin dissolves in concentrated sulphuric acid with a deep green color which, upon dilution with water, changes to a blue, a portion of the dye (eosin) separating in flocculles (distinction from *azur II*).

Barium Chloride, $BaCl_2+H_2O$.—Transparent crystals, easily soluble in water, almost insoluble in alcohol or concentrated hydrochloric acid. An aqueous solution of the salt (1 in 20) is neutral and does not respond to the Test for heavy metals (see Test No. 3). Dissolve 2 Gm. of barium chloride in 100 mils of distilled water, add 2 mils of hydrochloric acid, heat to boiling, then add a slight excess (about 10 mils) of diluted sulphuric acid, set it aside for twelve hours, and filter. The clear filtrate, on evaporating and igniting, yields a residue weighing not more than 0.002 Gm. (*other fixed bases*). Shake 1 Gm. of the finely powdered salt with 20 mils of dehydrated alcohol during five minutes and filter; the filtrate on evaporation and ignition yields not more than 0.002 Gm. of residue (*strontium and calcium*).

Barium Chloride Test Solution.—Dissolve 10 Gm. of barium chloride in sufficient distilled water to measure 100 mils.

Barium Hydroxide, $Ba(OH)_2+8H_2O$.—White crystals, soluble in about 20 parts of cold water and 3 parts of boiling water. The salt readily absorbs carbon dioxide from the air, forming an insoluble carbonate, hence aqueous solutions are more or less turbid. A solution of 1 Gm. of barium hydroxide in 50 mils of distilled water and 5 mils of nitric acid shows no opalescence upon the addition of silver nitrate T.S. (*chloride*). Dissolve 2 Gm. of the salt in 100 mils of distilled water, add 5 mils of hydrochloric acid, heat to boiling, then add a slight excess of diluted sulphuric acid, set it aside for twelve hours, and filter; the clear filtrate, on evaporating and igniting, yields a residue weighing not over 0.003 Gm. (*other fixed bases*). The solution of 1 Gm. of barium hydroxide in 20 mils of distilled water rendered acid with hydrochloric acid, does not respond to the Test for heavy metals (see Test No. 3). One Gm. of barium hydroxide dissolved in 100 mils of distilled water requires not less than 6.3 mils of normal hydrochloric acid V.S. for neutralization, using methyl orange T.S. or methyl red T.S. as indicator. Each mil of normal hydrochloric acid V.S. corresponds to 0.157755 Gm. of barium hydroxide [$Ba(OH)_2+8H_2O$].

Barium Hydroxide Test Solution.—A saturated solution of barium hydroxide (see above) in recently boiled distilled water. This solution rapidly absorbs carbon dioxide from the air. Prepare a fresh solution when required for use.

Barium Nitrate, $Ba(NO_3)_2$.—Colorless crystals, soluble in 20 parts of cold water and 2.8 parts of boiling water; its solution is neutral to litmus. The addition of silver nitrate T.S. to an aqueous solution of the salt (1 in 20) produces no change (*chloride*). Barium nitrate meets the requirements of the tests for "other fixed bases" and "heavy metals" given under *Barium Chloride* (see above).

Barium Nitrate Test Solution.—Dissolve 5 Gm. of barium nitrate in sufficient distilled water to measure 100 mils.

Beef Extract (Meat Extract).—Use extract of beef complying with the tests of the U. S. Department of Agriculture, preferably the kind known as "Liebig's."

Benzene (Benzol or Benzole).—Benzene, C_6H_6, is a colorless, transparent, inflammable liquid of a peculiar, aromatic odor; specific gravity about 0.876 at 25° C. (77° F.); congealing at about 5.2° C. (41.4° F.); boiling between 79° and 80.4° C. (174.2° and 176.7° F.). It is insoluble in water, but soluble in 4 parts of alcohol and also in ether. When equal volumes of benzene and concentrated sulphuric acid are shaken together, the latter is not colored. Shake 2 mils of benzene with 0.5 mil of sulphuric acid and 1 drop of fuming nitric acid; no green or blue tint is produced (*thiophene*).

Benzidine (Paradiaminodiphenyl), $(C_6H_4)_2(NH_2)_2$.—A white or slightly reddish crystalline powder. It is very slowly soluble in cold water, more readily in boiling water; soluble in alcohol and in ether. It melts at about 128° C. (262.4° F.). On adding a few drops of barium chloride T.S. to a solution of 1 Gm. of benzidine in 50 mils of distilled water acidulated with 5 mils of hydrochloric acid, no turbidity is produced (*sulphate*). One Gm. of benzidine upon ignition leaves no weighable residue.

Benzin (Petroleum Benzin).—Use the official purified petroleum benzin.

Beta-iminazolyl-ethylamine Hydrochloride.—Used in standardizing solution of the pituitary body (see page 646).

Blood Serum.—The serum filtered from the clotted blood of the horse or ox.

Bromine, Br.—Preserve it in a glass-stoppered bottle in a cool place, the bottle being enclosed in a larger vessel with the space between filled with some substance (as calcium hydroxide) capable of absorbing and combining with any vapors which might be given off. A heavy, dark brownish-red, mobile liquid, evolving, even at ordinary temperatures, reddish fumes, highly irritating to the eyes and lungs, and having a peculiar, suffocating odor; resembling that of chlorine. Specific gravity about 3.1 at 25° C. (77° F.). Boiling point, about 63° C. (145.4° F.). Bromine is soluble in 90 times its volume of water at 25° C. (77° F.); freely soluble in alcohol or ether (with gradual decomposition of these solvents); also soluble in chloroform, carbon disulphide, or carbon tetrachloride with a deep reddish-yellow color. On exposure to air or to heat, it is volatilized. Bromine destroys the color of solutions of litmus or indigo, and imparts a yellow color to starch T.S. Add 5 mils of bromine to an excess of potassium hydroxide T.S.; it combines to form a permanently clear liquid, without the separation of oily drops (*organic bromine compounds*). Shake 10 mils of a saturated aqueous solution of bromine with a slight excess of reduced iron until it becomes nearly colorless; the filtered liquid, on the addition of 5 drops of ferric chloride T.S. and of 5 drops of starch T.S., does not assume a blue color (*iodine*).

Bromine Test Solution (Bromine Water).—A saturated aqueous solution of bromine prepared by adding 3 mils of bromine to 100 mils of cold distilled water contained in a glass-stoppered bottle, the stopper of which should be lubricated with petrolatum. Keep this reagent in a cool place, protected from light, and shake it well, allowing the excess of bromine to settle, before using.

Cadmium and Potassium Iodide.—A mixture of equal weights of cadmium iodide and potassium iodide (see page 902) may be employed. A white powder readily soluble in water or alcohol. Upon keeping it acquires a yellowish color. Dissolve 1 Gm. of the powder in 20 mils of distilled water, add 5 mils of potassium hydroxide T.S., and filter the solution; the filtrate yields no precipitate with hydrogen sulphide T.S. either before or after acidulating with hydrochloric acid (*foreign metals*). An aqueous solution of the salt (1 in 20) prepared with distilled water, which has been previously boiled and cooled, gives no blue color upon the addition of starch T.S. (*free iodine*).

Cadmium Chloride, $CdCl_2+2H_2O$.—Small white crystals which effloresce in dry air and are soluble in about 0.7 part of cold or hot water. An aqueous solution of the salt gives a yellow precipitate with ammonium sulphide T.S. which is insoluble in an excess of the reagent.

Cadmium Chloride Test Solution.—Dissolve 10 parts of cadmium chloride in sufficient distilled water to make 100 parts.

Cadmium Iodide, CdI_2.—Colorless to yellowish, glossy scales, soluble in 1.1 parts of cold water and in 0.75 part of boiling water, readily soluble in alcohol. Solutions of this salt, upon the addition of alkali hydroxides, yield a white precipitate of cadmium hydroxide insoluble in an excess of the reagent; the precipitate produced by the addition of ammonia water is soluble in an excess of the reagent. Hydrogen sulphide T.S. or ammonium sulphide T.S. added to an aqueous solution of the salt yields yellow cadmium sulphide which is insoluble in an excess of the latter reagent. Add 10 mils of potassium hydroxide T.S. to a solution of 1 Gm. of cadmium iodide in 20 mils of distilled water, and filter; the filtrate yields no precipitate with hydrogen sulphide T.S. either before or after acidulating with hydrochloric acid (*foreign metals*).

Calcium Chloride Test Solution.—Dissolve 10 Gm. of calcium chloride (see page 254) in sufficient distilled water to measure 100 mils.

Calcium Hydroxide Test Solution (Lime Water), a nearly saturated, aqueous solution of calcium hydroxide, $Ca(OH)_2$.—Use lime water (see page 630).

Calcium Sulphate Test Solution.—Introduce pulverized transparent crystals of native gypsum (selenite), ($CaSO_4+2H_2O$), into a bottle nearly filled with distilled water, agitate it at intervals for twelve hours, and decant the clear, saturated solution when required. One part of gypsum requires about 400 parts of water for solution at 25° C. (77° F.). The test solution may also be made by shaking together 1 Gm. of calcium carbonate and 200 mils of distilled water, containing 5 mils of diluted sulphuric acid. When the acid is completely neutralized filter the mixture.

Canada Turpentine.—A liquid oleoresin obtained from *Abies balsamea* (Linné) Miller (Fam. *Coniferæ*). Viscid, pale yellowish or greenish-yellow, transparent; odor agreeable, taste terebinthinate, bitter, and slightly acrid; it is completely soluble in ether, chloroform, or benzene. When exposed to the air, Canada turpentine gradually dries and forms a transparent varnish; it solidifies on being mixed with 20 per cent. of its weight of magnesium oxide previously moistened with water.

Carbon Disulphide, CS_2 (Carbon Bisulphide).—Preserve in partially filled, well-stoppered bottles, or in tin cans, in a cool place, remote from flame or fire. A clear, colorless, highly-refractive liquid, very volatile, having a strong, characteristic but not fetid odor, and a sharp, aromatic taste. Specific gravity between 1.256 and 1.257 at 25° C. (77° F.). Soluble in about 530 parts of water at 25° C. (77° F.); very soluble in alcohol, ether, chloroform, or fixed or volatile oils. Carbon disulphide vaporizes rapidly at the ordinary temperature, is highly inflammable, boils between 46° and 49° C. (114.8° and 120.2° F.), and when ignited, burns with a bluish-white flame, producing carbon dioxide and sulphur dioxide. It does not affect the color of blue litmus paper moistened with water (*sulphur dioxide*). Twenty mils when allowed to evaporate spontaneously in a glass dish and finally on a water bath leaves not more than 0.001 Gm. of residue (*dissolved sulphur*). No discoloration is produced in 10 mils of lead acetate T.S. after agitating with 25 mils of carbon disulphide, when viewed from above in a test tube of about 2 cm. in diameter (*hydrogen sulphide*).

Carbon Tetrachloride, CCl_4.—A colorless, heavy liquid, of characteristic odor; non-inflammable; specific gravity about 1.58 at 25° C. (77° F.), boiling point between 76° and 77° C. (168.8° and 170.6° F.). It is immiscible with water, but miscible with dehydrated alcohol, ether, or fixed or volatile oils. Shake 10 mils with 20 mils of distilled water and allow the liquids to separate completely; the water remains neutral to litmus, and becomes not more than slightly opalescent on the addition of silver nitrate T.S. (*chloride*), and is not colored by potassium iodide T.S. (*chlorine*). Twenty-five mils when evaporated on a water bath leaves not more than 0.0005 Gm. of residue (*non-volatile matter*). To 10 mils of a solution of potassium hydroxide in dehydrated alcohol (1 in 10), add 10 mils of carbon tetrachloride; after standing for one hour, acidify with acetic acid and add 1 mil of copper sulphate T.S.; no yellow precipitate appears within two hours (*carbon disulphide*).

Carmine.—A lake color obtained from cochineal by the precipitation of its aqueous infusion with inorganic salts and albumen. Bright red, light and friable lumps, insoluble in cold water and acids, partially soluble in hot water, soluble in ammonia water with a dark red color. When dried at 100° C. (212° F.), 1 Gm. of carmine loses not more than 0.25 Gm. in weight; the residue ignited cautiously in a porcelain crucible, leaves not more than 0.12 Gm. of ash. During the ignition no odor like that of phenol or bromine is perceptible (*aniline colors*). Excepting for a few floccules, 0.15 Gm. of carmine dissolves completely in a mixture of 5 mils of ammonia water and 20 mils of distilled water.

Chlorine Test Solution (Chlorine Water).—Place 10 Gm. of manganese dioxide (see page 680) in a flask connected by a suitable tube with a small wash bottle containing 50 mils of water, and connect this with a bottle having a capacity of 1000 mils and containing 400 mils of distilled water which has previously been boiled and allowed to cool. Add to the dioxide in the generating flask 25 mils of hydrochloric acid, previously diluted with 25 mils of water, and apply a gentle heat by means of a sand bath. Conduct the generated chlorine through the water contained in the wash bottle into the bottle containing the distilled water, which should be loosely stopped with cotton and kept, during the operation, at a temperature of

about 10° C. (50° F.). When the air has been entirely displaced by the gas, disconnect the bottle from the apparatus, and, having inserted the stopper, shake the bottle, loosening the stopper from time to time, until the gas ceases to be absorbed. If necessary, reconnect the bottle with the apparatus, and continue passing the gas and agitating, until the distilled water is saturated. Finally, pour the chlorine water into small, dark amber-colored, glass-stoppered bottles, which should be completely filled, and preserve them in a dark and cool place.

Chlorine Water, even when kept from light and air, is apt to deteriorate. When it is required of full strength, it should be freshly prepared.

Chloroform, $CHCl_3$.—Use chloroform (see page 323).

Cobaltous Chloride, $CoCl_2+6H_2O$.—Rose-colored, monoclinic crystals, nonhygroscopic, soluble in water or alcohol. Dissolve 2 Gm. of the salt in about 100 mils of distilled water, completely precipitate the cobalt by the addition of an excess of ammonia water followed by ammonium sulphide T.S., and filter; the filtrate, after evaporation and ignition, leaves not more than 0.008 Gm. of residue (*alkali salts*). Add 3 Gm. of sodium cyanide to a solution of 1 Gm. of cobaltous chloride, in about 20 mils of distilled water, boil until the solution acquires a yellow color and filter it; on the addition of about 1 mil of bromine followed by sufficient potassium hydroxide T.S. to render the solution strongly alkaline no brown color develops (*nickel*). No coloration is produced in a solution of 2 Gm. of the salt in 100 mils of distilled water, to which 2 mils of nitric acid has been added, upon the addition of hydrogen sulphide T.S. (*lead and copper*).

Cobaltous Chloride Test Solution.—Dissolve 2 Gm. of cobaltous chloride with the aid of 1 mil of hydrochloric acid in sufficient distilled water to measure 100 mils.

Cochineal Test Solution.—See under *Indicators* (page 1707).

Congo Red.—See under *Indicators* (page 1707).

Congo Red Test Solution.—See under *Indicators* (page 1707).

Copper, Metallic, Cu.—In the form of wire, foil, or turnings.

Cupric Acetate, $Cu(C_2H_3O_2)_2+H_2O$.—Bluish-green crystals, having an acetous odor, soluble in water or alcohol. An aqueous solution of the salt (1 in 20), mixed with a few drops of hydrochloric acid, is not rendered more than slightly turbid at once, upon the addition of a few drops of barium chloride T.S. (*sulphate*). In other respects it meets the tests for purity directed under *Cupri Sulphas* (see page 393).

Cupric Acetate Test Solution.—Dissolve 1 part of cupric acetate in sufficient distilled water to make 1000 parts. Should the solution become cloudy, add acetic acid, drop by drop, until it becomes clear.

Cupric Ammonium Sulphate Test Solution.—A solution of cupri-tetrammonium sulphate, $Cu(NH_3)_4SO_4+H_2O$. To copper sulphate T.S. add ammonia water, drop by drop, until the precipitate at first formed is nearly, but not completely, redissolved, then filter. This solution should be freshly made when required.

Cupric Sulphate Test Solution.—Dissolve 10 Gm. of copper sulphate (see page 393) in sufficient distilled water to measure 100 mils.

Cupric Tartrate Test Solution.—See Volumetric Solutions (page 1694).

Curare.—Curare is an impure vegetable extract prepared by the Indians of South America and used by them as an arrow poison. Its composition is not entirely known, and different specimens of curare vary, depending upon the special variety of plant used in its manufacture. The most important source of curare is the bark of several varieties of *Strychnos*, the species most commonly employed being *S. Castelnæi*, Wedd., *S. Toxifera, or S. Crevauxii.* In addition to the extract of these barks other substances are added to impart consistence, to mislead, or perhaps from superstitious considerations. Commercial curare is a brownish or black, shining resinoid mass, possessing a very bitter taste. About 75 per cent. is soluble in cold water and it is almost completely soluble in diluted alcohol.

Dimethylaminoazobenzene (Butter Yellow), $C_6H_5N : N.C_6H_4N(CH_3)_2$.—It forms yellow plates melting between 115° and 117° C. (239° and 242.6° F.). It is insoluble in water, soluble in alcohol; soluble in hydrochloric acid with a red color from which solution sodium hydroxide T.S. in excess precipitates the orange-yellow base. The solution of this dye in sulphuric acid is yellow and changes to red on dilution with water.

Diphenylamine, $(C_6H_5)_2NH$.—In the form of grayish-white or colorless crystals, of a peculiar, aromatic odor, melting between 53° and 54° C. (127.4° and 129.2° F.); slightly soluble in water, more soluble in acids. It is used either in the dry state, or in solution in sulphuric acid, as a test for nitric acid (in sulphuric acid, water, etc.), or for chlorine (in hydrochloric acid). To test a solution for the presence of nitric acid, a small portion of it is carefully poured down the side of a test tube, slightly inclined and containing a few mils of diphenylamine T.S. so as to form a layer over the latter. The presence of nitric acid is shown by a deep blue color at the zone of contact. A similar reaction is also produced by the presence of hypochlorites, chlorates, chromium trioxide, ferric salts, and similar oxidizing agents.

Diphenylamine Test Solution.—Dissolve 0.5 Gm. of diphenylamine in 100 mils of concentrated sulphuric acid (see page 1692) diluted with 20 mils of distilled water. The solution should be colorless.

Eosin A (Yellowish Eosin), $O[C_6H(Br_2O)_2Na]C.C_6H_4COONa$.—The sodium salt of tetra-brom-fluorescein. Fine red crystals of bluish, glossy luster, or a brownish-red powder; readily soluble in water, less soluble in alcohol and insoluble in ether. A concentrated aqueous solution of eosin A has a deep brownish-red color while a dilute solution (1 in 500) is yellowish-red with a greenish fluorescence. The alcoholic solutions show a yellowish-green fluorescence. The addition of tannic acid T.S. to an aqueous solution of eosin A (1 in 500) produces no change. When about 0.5 Gm. of zinc dust, followed by 5 mils of ammonia water, is added to 5 mils of an aqueous solution of eosin A (1 in 500) and the mixture agitated, rapid decolorization takes place. When this mixture is filtered, the addition of solution of hydrogen dioxide to the filtrate restores the pink color of the solution. The addition of hydrochloric acid to an aqueous solution (1 in 500) causes an orange precipitate which, upon agitating with ether, yields a yellow solution. This solution is decolorized upon agitating it with a dilute solution of an alkali. The addition of sodium hydroxide T.S. intensifies the color of an aqueous solution of eosin A (1 in 500). Eosin A dissolves in concentrated sulphuric acid (see page 1692) with a yellow color and, when this solution is cautiously diluted with distilled water, a yellowish-red precipitate is produced.

Ether.—Use ether (see page 96). It should be neutral to moistened litmus paper.

Ether, Dehydrated, $(C_2H_5)_2O$.—Specific gravity not greater than 0.7115 at 25° C. (77° F.), it distils between 34° and 36° C. (93.2° and 96.8° F.). Add a very small quantity of powdered rosaniline acetate (see page 1688), dried at 100° C. (212° F.), to 10 mils of dehydrated ether, contained in a dry glass cylinder, stopper and shake it. No coloration results (*water or alcohol*). Add some dry tannic acid to 10 mils of dehydrated ether, contained in a dry glass cylinder, stopper and shake it; the tannin does not agglutinate or form a syrupy deposit (*water or alcohol*). Twenty mils of dehydrated ether, when permitted to evaporate spontaneously, leaves no perceptible residue, and upon rinsing the vessel with distilled water, the latter does not distinctly affect litmus paper. If the ether shows the presence of traces of moisture it should be shaken with pieces of anhydrous calcium chloride.

Ethyl Acetate (Acetic Ether), $CH_3.COOC_2H_5$.—A transparent, colorless liquid, of fragrant, acetous odor; inflammable; soluble in about 10 parts of water at 25° C. (77° F.); miscible in all proportions with alcohol, ether, or volatile oils. Specific gravity: 0.893 to 0.898 at 25° C. (77° F.); boiling point from 72° to 77° C. (161.6° to 170.6° F.). On evaporating 10 mils of ethyl acetate on a water bath no weighable residue remains (*non-volatile matter*). Ethyl acetate does not immediately redden blue litmus paper. Evaporate a portion of ethyl acetate spontaneously from clean, odorless blotting paper; the final odor, after that of the ester ceases to be noticeable, is not that of foreign esters (*butylic or amylic ester*). Agitate 25 mils of ethyl acetate with 25 mils of a saturated aqueous solution of calcium chloride and permit it to stand for complete separation; the volume of the latter does not increase more than 0.5 mil (*alcohol or water*). Mix 20 mils of ethyl acetate with a solution of 20 Gm. of sodium hydroxide in 50 mils of distilled water, allow the mixture to stand, agitating occasionally, or heat it gently under a reflux condenser, until a homogeneous liquid results, and then distil about 25 mils. This distillate complies with the test for absence of methyl alcohol under *Alcohol*. When 5 mils of ethyl acetate is poured over 5 mils of sulphuric acid, no coloration is produced at the zone of contact of the two layers (*amyl alcohol or other carbonizable impurities*).

Ferric Ammonium Sulphate, $FeNH_4(SO_4)_2+12H_2O$.—Pale violet, octahedral crystals, without odor, and having an acid, styptic taste; efflorescent on exposure to the air. Soluble in 2.7 parts of water at 25° C. (77° F.) and in 0.8 part of boiling water; insoluble in alcohol. The addition of 0.5 mil of nitric acid to 10 mils of a solution of the salt (1 in 20); followed by a few drops of silver nitrate T.S., produces no turbidity (*chloride*). The addition of a few drops of a freshly prepared solution of potassium ferricyanide T.S. to a solution of the salt (1 in 20) does not produce a blue or green color (*ferrous salt*).

Ferric Ammonium Sulphate Test Solution.—Dissolve 10 Gm. of ferric ammonium sulphate in sufficient distilled water to measure 100 mils.

Ferric Chloride Test Solution.—Dissolve 10 Gm. of ferric chloride (see page 464) in sufficient distilled water to measure 100 mils.

Ferrous Sulphate Test Solution.—Dissolve a clear crystal of ferrous sulphate (see page 472) in about 10 parts of distilled water which has been previously boiled to expel air. This solution is to be freshly prepared immediately before use.

Ferrous Sulphate (Acid) Test Solution.—Dissolve 7.5 Gm. of clear crystals of ferrous sulphate (see page 472) in 90 mils of distilled water which has been previously boiled to expel air, and then add sufficient sulphuric acid (see page 64) to measure 100 mils. This solution is to be freshly prepared immediately before use.

Ferrous Sulphide, FeS.—A heavy solid, in the form of black or brownish-black irregular masses, or cast into sticks, soluble in diluted sulphuric or diluted hydrochloric acid, with copious evolution of hydrogen sulphide.

Filter Paper, Quantitative.—For the Mercuric Bromide Test Paper of the Arsenic Test use Schleicher and Schüll's No. 589 (Blue Ribbon), or Swedish O. filter paper or other makes of like surface, quality and ash (see Arsenic Test, page 1709).

Fluorescein (Resorcinolphthalein).—A derivative [$C_{20}H_{12}O_5$ or $O(C_6H_3OH)_2C.C_6H_4COO$] of resorcinol obtained by the condensation of resorcinol and phthalic anhydride. Fluorescein occurs as a yellowish-red to dark-red powder; odorless and tasteless. It is very slightly soluble in water or ether, soluble in alcohol. Fluorescein dissolves in solutions of alkali hydroxides or carbonates, forming a liquid which appears red when observed in transmitted light and fluorescent bright-green in reflected light. An alkaline solution of fluorescein, even when highly diluted, shows a greenish-yellow fluorescence, which is discharged by the addition of a slight excess of acid. Incinerate 1 Gm. of fluorescein; the ash does not exceed 0.0025 Gm. Heat about 1 Gm. of fluorescein at a temperature below a red heat until it is completely carbonized, then boil the powdered residue with 10 mils of diluted hydrochloric acid for five minutes, filter and wash the residue with 10 mils of distilled water. The combined filtrate, when boiled with a few drops of nitric acid, and supersaturated with ammonia and filtered, if necessary, remains clear upon the addition of an equal volume of hydrogen sulphide T.S. (*zinc*). Shake about 1 Gm. of fluorescein with 20 mils of distilled water and filter; one drop of tenth-normal sodium hydroxide V.S. imparts to 10 mils of the filtrate a bright green fluorescence. The addition of a drop of ferric chloride T.S. to the remaining portion of the filtrate does not produce a bluish coloration (*resorcinol and various other phenolic compounds*).

Fuchsin (Basic Fuchsin, Magenta, Rubin, Rosaniline).—The hydrochloride or acetate of rosaniline (triamido-diphenyl-tolyl-carbinol) frequently with the same salts of para-rosaniline (triamido-triphenyl-carbinol). In well-developed crystals or irregular crystalline fragments of a glossy, greenish-bronze luster. Soluble in water, alcohol, or amyl alcohol. An aqueous solution (1 in 500), upon the addition of tannic acid T.S., yields a red precipitate. The addition of about 0.5 Gm. of zinc dust (see page 1692), and 10 mils of ammonia water to 10 mils of an aqueous solution of fuchsin (1 in 500) produces decolorization when the mixture is well shaken. Place a few drops of this decolorized solution on filter paper, and then add near by a few drops of hydrochloric acid; the zone where the two neutralizing fluids meet assumes a red color. Sulphurous acid (see page 1692), when added slowly, with agitation, to an aqueous solution of fuchsin (1 in 500) causes decolorization. The original color is restored upon the subsequent addition of a solution of formaldehyde. Upon slowly adding hydrochloric acid, to an aqueous solution of fuchsin (1 in 500), the red color gradually changes to a brownish-red which subsequently changes to a yellow when the reagent is in

excess. The addition of sodium hydroxide T.S. to an aqueous solution of fuchsin (1 in 500) precipitates the red colored free base. Finely pulverized fuchsin dissolves in concentrated sulphuric acid (see page 1692) with a yellow to yellowish-brown color, which solution, upon the cautious addition of distilled water, becomes yellow to colorless.

Fuchsin, Acid (Acid Magenta, Acid Rubin, Fuchsin S).—Chiefly the acid sodium salt of fuchsin di- and tri-sulphonic acids. Acid fuchsin occurs as metallic, greenish, glistening granules or as a greenish-brown crystalline powder; soluble in water, forming a cherry-red solution, very slightly soluble in alcohol; insoluble in ether. The addition of tannic acid T.S. to an aqueous solution of acid fuchsin (1 in 500) produces no precipitation (*acid color*). The addition of about 0.5 Gm. of zinc dust and 5 mils of ammonia water to 10 mils of an aqueous solution of acid fuchsin (1 in 500) produces decolorization when the mixture is well shaken. When this mixture is filtered, the addition of hydrochloric acid to the colorless filtrate restores its original red color. This solution, when agitated with ether, imparts no color to the latter (*phthaleins*). The addition of sodium hydroxide T.S. to an aqueous solution of the salt (1 in 500) almost decolorizes the solution. The addition of hydrochloric acid to an aqueous solution (1 in 500) produces no change. It dissolves in concentrated sulphuric acid with a yellow to brownish-red color and this solution, upon the cautious addition of distilled water, changes to its original fuchsin-red color.

Fuchsin-Sulphurous Acid Test Solution.—To a solution of 0.5 Gm. of fuchsin and 9 Gm. of sodium bisulphite (see page 1689) in 500 mils of distilled water, add 10 mils of hydrochloric acid. The quantity of sulphurous acid present should be about 5 Gm. Preserve the solution in well-stoppered bottles protected from light.

Gelatin Test Solution.—Dissolve 1 Gm. of gelatin (see page 509) in 50 mils of distilled water, with the aid of a gentle heat, and filter if necessary. This solution is to be freshly made when wanted for use.

Glass Wool (Spun Glass).—Fine threads of spun glass. Two Gm. of glass wool when digested on a bath of boiling water for one-half hour with 100 mils of diluted hydrochloric acid, the mixture filtered and the filtrate evaporated to dryness and then dried at 110° C. (230° F.), leaves not more than 0.01 Gm. of residue (*soluble matter*). Boil 1 Gm. of glass wool for a few minutes with a mixture of 25 mils each of diluted nitric acid and distilled water; filter, evaporate the filtrate to dryness, and treat the residue with 10 mils of distilled water and again filter it; the filtrate is not affected by the addition of hydrogen sulphide T.S. (*lead*).

Glucose, Dry (Dextrose, d-glucose), $C_6H_{12}O_6$.—A white, anhydrous powder which complies with the tests for identity and purity given under "*Glucosum*."

Gold Chloride (Chlorauric Acid), $AuCl_3HCl+4H_2O$.—Yellow, very hygroscopic crystals which contain about 48 per cent. of metallic gold, when assayed by moistening a weighed portion of the crystals with a slight excess of ammonium oxalate T.S., evaporating to dryness, igniting and weighing the residue. The metallic gold thus obtained does not give a positive reaction upon heating with diluted hydrochloric acid, filtering and testing the solution with either hydrogen sulphide T.S., dry glucose, or ammonium sulphide T.S.

Gold Chloride Test Solution.—Dissolve 1 Gm. of gold chloride in 30 mils of distilled water.

Gold Chloride Test Solution, Diluted.—This solution is used as a standard for the assay of Dried Suprarenals (see page 1093), and must contain 0.1 Gm. of metallic gold in each 100 mils. Accurately measure 10 mils of gold chloride test solution (see above) into a weighed porcelain crucible, add about 1 Gm. of ammonium oxalate T.S. and evaporate it to dryness; then cautiously ignite the residue until no further loss in weight occurs, and weigh. Calculate the exact amount of metallic gold present in the solution which has been assayed and then dilute the remainder with a sufficient quantity of distilled water to make each 100 mils contain 0.1 Gm. of metallic gold.

Hematein, $C_{16}H_{12}O_6$.—A product of the oxidation of hematoxylin, occurring in reddish-brown plates of a greenish metallic luster; very slightly soluble in cold water, alcohol or ether, insoluble in chloroform. It is soluble in ammonia water with a brownish-violet color and in diluted solutions of the caustic alkalies with a bright red color.

Hematoxylin and Hematoxylin Test Solution.—See under *Indicators* (page 1707).

Hydrated Chloral Test Solution.—A concentrated aqueous solution prepared by dissolving 3 parts of hydrated chloral (see page 319) in 2 parts of distilled water.

Hydrochloric Acid, Concentrated, for Tests, HCl.—An acid of specific gravity between 1.170 and 1.184 at 25° C. (77° F.) (35 to 38 per cent.), which must respond to the following tests of purity: Evaporate 100 mils of the acid to about 5 mils, dilute it with 10 mils of distilled water, and add a few drops of barium chloride T.S.; no precipitate occurs within twelve hours (*sulphuric acid*). Evaporate 50 mils of the acid to dryness on a water bath; not more than 0.002 Gm. of non-volatile residue remains (*non-volatile solids*). Add 5 mils of the concentrated acid, diluted with 50 mils of distilled water, to a solution of 1 drop of tenth-normal iodine V.S. in 50 mils of distilled water to which a few drops of starch T.S. have been added; no decolorization occurs (*sulphurous acid*). Dilute 10 mils of the acid with about 100 mils of warm distilled water (at about 50° C. (122° F.)) and thoroughly saturate it with hydrogen sulphide; no dark coloration or precipitate forms either before or after neutralizing with ammonia water and adding a few drops of ammonium sulphide T.S. (*heavy metals*). Two mils of the acid, diluted with 10 mils of distilled water, when subjected to the Arsenic Test (No. 1) produces a stain not greater than that produced by the zinc.

Hydrogen Sulphide, H_2S.—A gas generated by treating ferrous sulphide (see page 1681) with diluted sulphuric acid, and washing the gas as directed below under the Test Solution.

Hydrogen Sulphide Test Solution (Hydrosulphuric Acid).—A saturated, aqueous solution of hydrogen sulphide. To prepare about 1000 mils of the solution, treat 20 Gm. of ferrous sulphide in a suitable apparatus with a mixture of 20 mils of sulphuric acid (see page 64) and 250 mils of distilled water, pass the gas through a drying tube filled with granulated calcium chloride, then from this through a tube of about 8 millimeters diameter and 40 centimeters in length, which contains about 5 Gm. of coarsely pulverized iodine mixed with glass wool (see above), and finally through a wash bottle which contains a small quantity of potassium iodide T.S. The gas thus purified is conducted nearly to the bottom of a bottle of the capacity of about 1500 mils containing 1000 mils of cold distilled water. Shake the bottle occasionally to facilitate

the solution of the gas. When the gas is no longer absorbed, transfer the solution to small, dark amber-colored bottles, fill nearly to the top; pass a stream of purified hydrogen sulphide for a few minutes through each, and then at once stopper them tightly, and preserve them afterwards in a cool and dark place. Do not use this solution unless it retains a strong odor of hydrogen sulphide, and, when added to an equal volume of ferric chloride T.S. produces at once a copious precipitate of sulphur.

Indicators.—See special list, page 1707.

Indigo Carmine Test Solution.—Dissolve 1 Gm. of sodium indigotindisulphonate (see page 1031) in 150 mils of distilled water.

Iodeosin and Iodeosin Test Solution.—See under *Indicators* (page 1708).

Iodine, Purified.—Heat powdered iodine (see page 588) in a porcelain dish placed on a water bath for twenty minutes, and stir it constantly with a glass rod, so that adhering moisture, cyanogen iodide, and most of the iodine bromide and iodine chloride, if present, may be vaporized, then transfer the iodine to a porcelain or other non-metallic mortar, and triturate it with about 5 per cent. of its weight of dry potassium iodide, so as to decompose any remaining iodine bromide and iodine chloride. Then return the mixture to the dish, cover it with a glass funnel, and heat the dish carefully on a sand bath. Detach the sublimed iodine, powder it and then dry for twenty-four hours over calcium chloride. Keep the product in well-stoppered bottles, in a cool place. One Gm. of iodine, thus purified, leaves no weighable residue when sublimed.

Iodine Test Solution.—Dissolve 1 Gm. of iodine (see page 588) and 3 Gm. of potassium iodide (see page 902) in 50 mils of distilled water.

Iodo-bromide Test Solution.—(See Iodine Absorption Value Test No. 8.) Dissolve 13.2 Gm. of powdered iodine (see page 588) in 1000 mils of glacial acetic acid (see page 13) with the aid of a gentle heat, if necessary to facilitate solution. Cool the solution to 25° C. (77° F.) and determine the iodine content in 20 mils of the solution by means of tenth-normal sodium thiosulphate V.S.; then add to the solution a quantity of bromine (see page 1678) molecularly equivalent to that of the iodine present (3 mils being the usual approximate amount). Keep the solution in glass-stoppered bottles, protected from light.

Iron, Metallic, Fe.—Bright and perfectly clean iron in the form of wire, sheet, filings, or powder (electrolytically reduced). For making solutions of pure iron salts, fine, thin, bright wire (so-called "florist's" or "piano wire") is used. For detecting copper use bright pieces of sheet iron or steel needles.

Lævo-methylamino-ethanol-catechol, $C_9H_{13}O_3N$.—A nearly white to light brown micro-crystalline powder. Very slightly soluble in water; almost insoluble in alcohol (90 per cent.), in ether, and in chloroform. Combines with acids to form salts which are readily soluble in water and in alcohol (90 per cent). Melts, with partial decomposition, between 205° and 212° C. (401° and 413.6° F.). Alkaline to moistened litmus paper. A dilute, slightly acidified solution gives with a trace of ferric chloride an emerald-green color which is changed to purple or carmine by the cautious addition of a dilute solution of sodium hydroxide. It readily reduces solution of gold chloride and gradually develops a characteristic, unpleasant odor when a small quantity is mixed with five times its volume of sodium hydroxide T.S. It yields no precipitate with potassio-mercuric iodide T.S. (*absence of most alkaloids*). No weighable ash is obtained on ignition of 0.2 Gm.

Lead Acetate Glass Wool.—Immerse glass wool (see page 1682) in a mixture of equal parts of lead acetate T.S. and distilled water and remove the excess of liquid by pressing it between filter paper. Prepare the glass wool, as just described, immediately before it is required in the test.

Lead Acetate Test Paper.—Immerse strips of heavy white filter paper, 6 cm. in width and 8 cm. in length, in a mixture of equal parts of lead acetate T.S. and distilled water, drain off the excess of liquid and dry the paper on glass in an oven at 100° C. (212° F.), avoiding contact with metal.

Lead Acetate Test Solution.—Dissolve 10 Gm. of clear, transparent crystals of lead acetate (see page 872), free from adhering lead carbonate, in sufficient distilled water to measure 100 mils. Preserve the solution in well-stoppered bottles.

Lead Acetate Test Solution, Alcoholic.—Dissolve 3 Gm. of clear transparent crystals of lead acetate (see page 872), free from adhering lead carbonate, in sufficient alcohol to measure 100 mils. Preserve the solution in well-stoppered bottles.

Lead Acetate Test Solution, Basic.—Use the official solution of lead subacetate (see page 650).

Lead Nitrate, $Pb(NO_3)_2$.—Colorless, octahedral crystals, transparent or opaque. Soluble in 1.85 parts of water at 25° C. (77° F.), in 0.75 part of boiling water, and almost insoluble in alcohol. Lead nitrate responds to the tests of identity for lead and freedom from foreign metals directed under *Plumbi Acetas* (see page 872).

Lead Peroxide (Lead Dioxide), PbO_2.—A dark brown powder containing not less than 90 per cent. of lead peroxide. Insoluble in nitric acid; when warmed with hydrochloric acid, it is converted into lead chloride with the evolution of chlorine; when heated alone or with sulphuric acid, lead peroxide gives off oxygen. It is dissolved by concentrated solutions of potassium or sodium hydroxide. Dissolve by agitation about 0.5 Gm. of finely powdered lead peroxide, previously dried to constant weight at 100° C. (212° F.) and accurately weighed, in a solution of 1.5 Gm. of potassium iodide (see page 902) and 12 Gm. of sodium acetate (see page 1010), in 8 mils of glacial acetic acid (see page 13) diluted with an equal volume of distilled water. Should the resulting solution be turbid, add further small portions of sodium acetate until clear. Then determine the liberated iodine by titrating with tenth-normal sodium thiosulphate V.S., starch T.S. being used as indicator. It shows not less than 90 per cent. of PbO_2. Each mil of tenth-normal sodium thiosulphate V.S. is equivalent to 0.01195 Gm. of PbO_2.

Lime, Freshly Slaked.—To prepare freshly slaked lime for the Opium Assay, drop upon a convenient quantity of lime one-third of its weight of water, cover it and allow it to stand until the lime is slaked and cooled.

Litmus Paper and Test Solution.—See under *Indicators* (page 1708).

Magnesia Mixture Test Solution.—Dissolve 5.5 Gm. of magnesium chloride, and 7 Gm. of ammonium chloride (see page 133) in 65 mils of distilled water, add 35 mils of ammonia water (see page 166), set the mixture aside for a few days in a well-stoppered vessel, and filter. If not perfectly clear, filter the solution before using.

Magnesium Chloride, $MgCl_2+6H_2O$.—White, deliquescent crystals, soluble in about 0.6 per cent. of cold water and about 5 parts of alcohol, leaving no insoluble residue. Ten mils of an aqueous solution (1 in 20) shows no precipitate upon the addition of a few drops of diluted sulphuric acid (*barium*), nor after the addition of 10 mils of ammonium chloride T.S. followed by a few drops of ammonia water and 5 mils of ammonium oxalate T.S. (*calcium*), nor after the addition of ammonium sulphide T.S. (*heavy metals*).

Magnesium Sulphate Test Solution.—Dissolve 10 Gm. of magnesium sulphate (see page 677) in sufficient distilled water to measure 100 mils.

Manganese Sulphate, $MnSO_4$.—Containing from 4 to 5 molecules of water of crystallization (depending on the temperature at which it is crystallized), forming pale rose-red crystals, slightly efflorescent in the air, soluble in about 1 part of water, insoluble in alcohol. Its aqueous solution (1 in 20) yields with barium chloride T.S. a white precipitate insoluble in hydrochloric acid, and with ammonium sulphide T.S. a salmon colored precipitate. Dissolve 1 Gm. of the salt in 50 mils of distilled water, add 0.5 mil of hydrochloric acid (see page 33) and a few drops of chlorine water (see page 1679), boil for a few minutes and cool. On now adding 1 mil of potassium sulphocyanate T.S. to this solution no red color is produced. Dissolve 1 Gm. of the salt in 50 mils of distilled water, add about 10 mils of ammonium chloride T.S., heat to boiling, and precipitate the manganese with ammonium sulphide T.S., continuing the heating until the precipitate acquires a greenish color, then filter, evaporate the filtrate to dryness and ignite; not more than 0.5 per cent. of residue remains (*calcium, magnesium, or alkali metals*).

Manganese Sulphate Test Solution.—Dissolve 10 Gm. of manganese sulphate in 50 mils of distilled water, and add sufficient diluted sulphuric acid to make 100 mils.

Mercuric Bromide, $HgBr_2$.—White rhombic needles or prisms or lustrous scales or a granular, crystalline powder, fusing at about 325° C. (617° F.) and subliming without decomposition. Soluble in 200 parts of water at 25° C. (77° F.) and in 25 parts of boiling water; readily soluble in boiling alcohol.

Mercuric Bromide Test Paper.—Cut stiff, heavy quantitative filter paper (see Filter Paper, Quantitative, page 1681) into strips 3 mm. in width and about 12 cm. in length. Immerse these strips for five minutes in alcoholic mercuric bromide T.S. (see below). Remove the excess of solution by pressing the strips between filter paper and then dry them quickly on glass in an oven heated to 100° C. (212° F.). Place the strips at once in a wide-mouthed bottle and stopper it securely.

Mercuric Bromide Test Solution, Alcoholic.—Dissolve 5 Gm. of mercuric bromide in 100 mils of alcohol, employing a gentle heat to facilitate solution. Keep it in glass-stoppered bottles protected from the light.

Mercuric Chloride Test Solution.—Dissolve 5 Gm. of corrosive mercuric chloride (see page 552) in sufficient distilled water to measure 100 mils.

Mercuric Nitrate Test Solution, $Hg(NO_3)_2$.—Mix 45 Gm. of nitric acid (see page 48) with 15 mils of distilled water and dissolve 40 Gm. of red mercuric oxide (see page 562) in the mixture. Keep the solution in glass-stoppered bottles.

Mercuric Potassium Iodide Test Solution (Mayer's Reagent).— Dissolve 1.358 Gm. of corrosive mercuric chloride (see page 552) in 60 mils of distilled water, and 5 Gm. of potassium iodide (see page 902) in 10 mils of distilled water. Mix the two solutions, and then add sufficient distilled water to measure 100 mils.

Mercuric Potassium Iodide Test Solution, Alkaline (Nessler's Reagent).—Dissolve 10 Gm. of potassium iodide (see page 902) in 10 mils of distilled water, and add gradually in portions a saturated aqueous solution of corrosive mercuric chloride (see page 552) with constant agitation, until a slight red precipitate remains undissolved; to this mixture add 30 Gm. of potassium hydroxide (see page 899) and, when solution has taken place, 1 mil more of the saturated aqueous solution of mercuric chloride. Dilute this solution with distilled water until it measures 200 mils. Allow the precipitate to subside, and draw off the clear fluid. Two mils of this reagent, when added to 50 mils of distilled water containing 0.05 milligramme of ammonia, produces at once a yellowish-brown coloration.

Mercurous Nitrate Test Solution, $HgNO_3$.—Mix 10 Gm. of pure mercury (see page 565) with 5 mils of nitric acid (see page 48) and 5 mils of distilled water, in a porcelain evaporating dish and set it aside for twenty-four hours in a cool, dark room. Separate and drain the crystals of mercurous nitrate, and dissolve them in 100 mils of distilled water. Preserve the solution in a dark amber-colored bottle in which a small quantity of mercury has been placed.

Methyl Orange and Methyl Orange Test Solution.—See under *Indicators* (page 1708).

Methyl Red and Methyl Red Test Solution.—See under *Indicators* (page 1708).

Methyl Violet 6B (Paris Violet 6B).—A mixture of penta- and hexa-methyl-para-rosaniline chlorides. A very dark greenish powder which dissolves readily in water or alcohol, yielding a deep violet solution. Its solution in alcohol or chloroform has a deeper blue color than the aqueous solution. Insoluble in ether. An aqueous solution of methyl violet (1 in 500) when added drop by drop to tannic acid T.S. forms a deep blue precipitate (*basic color*). The addition of a few drops of hydrochloric acid to a mixture of about 0.5 Gm. of zinc dust and 5 mils of an aqueous solution of methyl violet (1 in 500) causes rapid decolorization. Place a few drops of this decolorized solution near a few drops of ammonia water on filter paper; the zone of contact assumes a blue color. Add hydrochloric acid slowly, drop by drop, with agitation, to an aqueous solution of the salt (1 in 500); the violet color gradually changes to blue-green, green and finally to brownish-yellow, the solution remaining clear. Upon gradually diluting this solution with distilled water, the color changes take place in the reverse order. Add 5 mils of sodium hydroxide T.S. to 5 mils of an aqueous solution of methyl violet (1 in 500); a blue precipitate gradually forms and upon heating, the mixture becomes colorless and deposits white floccules. Concentrated sulphuric acid dissolves methyl violet with an orange to brownish-red color; upon slowly diluting this solution with distilled water, the solution assumes a brown, then green, and finally a blue color. Incinerate 1 Gm. of methyl violet; not more than 0.01 Gm. of ash remains.

Methylene Green (Mono-nitro-methylene blue, Tetra-methyl-mono-nitro-thionin-chloride), $(CH_3)_2 N.C_6H_3 : N(S)C_6H_2(NO_2).N.(CH_3)_2Cl$.—A very dark brown to gray-black powder; soluble in water and slightly soluble in alcohol, yielding greenish-blue solutions. An aqueous solution of methylene green (1 in 500) yields a precipitate upon the addition of tannic acid T.S. The addition of 0.5 Gm. of zinc dust and

5 mils of ammonia water to 10 mils of an aqueous solution of the salt (1 in 500) and warming the resulting mixture causes decolorization. Add a few drops of solution of hydrogen dioxide to the decolorized liquid, keeping the solution alkaline; a violet color is produced. The addition of hydrochloric acid to an aqueous solution of methylene green (1 in 500) produces no change; sodium hydroxide T.S. produces a violet precipitate which dissolves upon heating (distinction from *methylene blue*). Methylene green dissolves in sulphuric acid with a green color and on cautiously diluting this solution with distilled water it changes to greenish-blue.

Molybdic Acid, H_2MoO_4.—A white to yellowish-white powder, containing about 85 per cent. of molybdic anhydride (MoO_3). One Gm. of molybdic acid yields a clear solution with 10 mils of ammonia water; the addition of an equal volume of hydrogen sulphide T.S. produces a greenish-yellow color but no brownish-yellow color or precipitate (*heavy metals*). Pour a solution of 10 Gm. of molybdic acid in about 25 mils of ammonia water into a mixture of 75 parts of nitric acid (see page 48), and 75 parts of distilled water and set it aside for twelve hours at about 40° C. (104° F.); no yellow precipitate appears (*phosphoric acid*). Prepare a solution of about 0.5 Gm. of molybdic acid, accurately weighed, in 50 mils of distilled water by the aid of about 3 mils of ammonia water, warming it to facilitate solution. Make this solution acid with acetic acid, dilute it further with 200 mils of distilled water, and heat to boiling; then add 30 mils of an aqueous solution (1 in 20), containing lead acetate (see page 872), cover the beaker and boil the liquid for several minutes, stirring occasionally to facilitate granulation of the precipitate. Wash the precipitate by decantation ten times, using 50 mils of boiling distilled water each time; collect the precipitate in a previously ignited and tared Gooch crucible containing a layer of asbestos (see page 1677), again wash the precipitate with boiling distilled water until the washings cease to react with hydrogen sulphide T.S., and ignite to constant weight. The amount of lead molybdate ($PbMoO_4$) obtained, multiplied by 0.39226, gives the amount of molybdic anhydride (MoO_3) present.

Naphthylamine (Alpha) Hydrochloride, $C_{10}H_7.NH_2.HCl$.—A white crystalline powder which turns bluish on exposure. Soluble in water, alcohol, or ether. For tests of identity see below, under Betanaphthylamine.

Naphthylamine (Alpha) Hydrochloride Test Solution.—Boil 0.5 Gm. of alpha-naphthylamine hydrochloride with 100 mils of distilled water, for ten minutes, keeping the volume constant and finally filter it through cotton. Employ only freshly distilled water in preparing this reagent, which must be kept in well-stoppered bottles, protected from light.

Naphthylamine (Beta) Hydrochloride, $C_{10}H_7.NH_2.HCl$.—White to yellowish, glossy scales, or flakes, soluble in about 50 parts of water and readily soluble in alcohol. The addition of one drop of ferric chloride T.S. to 10 mils of an aqueous solution of betanaphthylamine hydrochloride (1 in 100) does not produce a violet color (*alpha-naphthylamine*); the addition of a small crystal of sodium nitrite to an aqueous solution of betanaphthylamine hydrochloride (1 in 100) produces an orange precipitate, not a dark red precipitate (distinction from *alpha-naphthylamine*).

Nitric Acid, HNO_3.—Use the official nitric acid (see page 48).

Nitric Acid, Diluted.—Add 50 Gm. of nitric acid (see page 48) to 290 Gm. of distilled water. It contains not less than 9.5 per cent. nor more than 10.5 per cent. of HNO_3. Diluted nitric acid to which an equal volume of distilled water has been added is not affected upon the addition of barium nitrate T.S. (*sulphuric acid*), or of silver nitrate T.S. (*hydrochloric acid*). Dilute about 20 mils of diluted nitric acid, accurately weighed, with 10 mils of distilled water and titrate with normal potassium hydroxide V.S., methyl orange T.S. being used as indicator. It shows not less than 9.5 per cent. nor more than 10.5 per cent. of HNO_3.

Nitric Acid, Fuming.—Use the commercial red fuming acid, if it is of a specific gravity between 1.48 and 1.52 at 25° C. (77° F.). Preserve it carefully in glass-stoppered bottles, in a cool place. It should conform to the tests for purity given under *Acidum Nitricum*.

Oil of Cedarwood (for use with the microscope).—For clearing microscopic sections, a selected commercial distilled oil from the wood of the Red Cedar, *Juniperus Virginiana* Linné (Fam. *Pinaceæ*) should be used. Such oil should have a refractive index of about 1.504 at 20° C. (68° F.). For use with homogeneous immersion lenses, a specially prepared oil is required, having a refractive index of exactly 1.515 at 18° C. (64.4° F.).

Orange G (The sodium salt of azo-benzene-beta-naphthol disulphonic acid), $C_6H_5.N : N.C_{10}H_4(OH)(SO_3Na)_2(2.6.8)$.—Orange to brick-red powder, or dark red crystals; readily soluble in water, yielding an orange-yellow solution, slightly soluble in alcohol, insoluble in ether or chloroform. The addition of tannic acid T.S. to an aqueous solution of orange G (1 in 500) causes no precipitation (*acid color*). The addition of hydrochloric acid to a mixture of 0.5 Gm. of zinc dust and 10 mils of an aqueous solution of the color (1 in 500) produces decolorization. When filtered, the colorless filtrate, on standing exposed to the air does not regain its original color (presence of *azo-group*). When heated, orange G does not deflagrate (distinction from *nitro colors*). The addition of barium or calcium chloride T.S. to a concentrated aqueous solution of orange G produces a colored, crystalline precipitate. The addition of hydrochloric acid to an aqueous solution of the dye (1 in 500) produces no change; the addition of sodium hydroxide T.S. to a similar solution produces a yellowish-red to a bordeaux color but no precipitation. Orange G dissolves in concentrated sulphuric acid with an orange to yellowish-red color; no change in color results upon diluting the solution cautiously with distilled water.

Orcin (Orcinol; Dihydroxy-methyl-benzene 1.3.5.), $C_6H_3(CH_3).(OH).(OH).+H_2O$.—In the form of monoclinic prisms, white with a reddish tint, which fuse at about 58° to 60° C. (136.4° to 140° F.). Orcin has an intensely sweet and astringent taste; very soluble in hot water, less soluble in cold water, readily soluble in alcohol or ether. The anhydrous substance fuses between 106° and 108° C. (222.8° and 226.4° F.). Anhydrous crystals are deposited from an ether solution. When exposed to light or air the crystals assume a reddish-brown color. The addition of a few drops of ferric chloride T.S. to an aqueous solution of orcin (1 in 20) produces a deep blue color. Warm 10 mils of an aqueous solution of orcin (1 in 10) with 10 mils of sodium hydroxide T.S. and add a few drops of chloroform; the solution assumes a purple-red color then bright red, and, after diluting with distilled water, shows an intense, greenish-yellow fluorescence. Aqueous solutions of orcin (1 in 20) tested separately do not yield precipitates upon the addition of test

solutions of either mercuric chloride, cupric sulphate, tannic acid or lead acetate; with basic lead acetate T.S., a white precipitate is obtained (characteristic of *resorcinol derivatives*). Dissolve about 1.3 Gm. of orcin, accurately weighed, in sufficient distilled water to measure 1000 mils. Introduce 25 mils of this solution, 25 mils of tenth-normal bromine V.S. and 50 mils of distilled water into a glass-stoppered flask of about 300 mils capacity, and then add 25 mils of dilute sulphuric acid T.S. After thoroughly agitating the mixture, set it aside for ten minutes, then cautiously lift the stopper, quickly introduce 2 Gm. of potassium iodide and close the flask at once. Agitate the solution and, after five minutes, determine the liberated iodine by means of tenth-normal sodium thiosulphate V.S.; conduct a blank experiment, omitting the addition of the solution of orcin and note the number of mils of tenth-normal sodium thiosulphate V.S. consumed. The difference in mils of tenth-normal sodium thiosulphate V.S. required in the original titration and the blank test, when multiplied by 0.002068, gives the quantity of anhydrous orcin present, which corresponds to not less than 85 per cent.

Ouabain.—Crystallized ouabain, frequently, though erroneously, referred to as crystallized strophanthin, or g-strophanthin Thoms. Ouabain is a glucoside, $C_{30}H_{46}O_{12}+9H_2O$, obtained from the wood of *Acocanthera Ouabaio* Cathelineau, or from the seed of *Strophanthus gratus* Franchet. It occurs as colorless, quadratic crystals of bitter taste. It is easily soluble in hot water, soluble in 100 parts of cold water and in about 30 parts of dehydrated alcohol and in 30 parts of amyl alcohol; slightly soluble in acetic ether, ether or chloroform. A solution of 0.01 Gm. of ouabain in 1 mil of distilled water, poured over a layer of concentrated sulphuric acid colors the latter from pink to red and the aqueous layer is colored green. Heated to 105° C. (221° F.), it loses about 20 per cent. of water. The ouabain thus dried melts between 187° and 188° C. (368.6° and 370.4° F.). On igniting 0.2 Gm. no weighable ash remains. Heating with diluted hydrochloric or sulphuric acid produces hydrolytic cleavage, yielding a body which is identical with rhamnose.

Oxalic Acid, Purified, $H_2C_2O_4+2H_2O$.—Colorless, uneffloresced crystals, soluble in 10 parts of cold water, in about 3 parts of boiling water and in 2.5 parts of alcohol. Ten Gm. when ignited leaves not more than 0.005 Gm. of residue (*non-volatile matter*). Dissolve 2 Gm. of oxalic acid and about 3 Gm. of potassium hydroxide in 30 mils of distilled water, add to this solution about 15 drops of Nessler's Reagent (see page 1684), no brownish-red coloration develops when compared with a blank test, omitting the oxalic acid (*ammonium compound*). Preserve it in well-stoppered bottles.

Oxalic Acid Test Solution.—Dissolve 5 Gm. of purified oxalic acid (see above) in sufficient distilled water to measure 100 mils.

Palladous Chloride, $PdCl_2$.—A dark brown, hygroscopic mass, readily soluble in water.

Palladous Chloride Test Solution.—Dissolve 0.5 Gm. of palladous chloride in sufficient distilled water to measure 10 mils. Preserve the solution in a glass-stoppered bottle.

Paradimethylaminobenzaldehyde (Dimethyl-p-amino-benzaldehyde), $(CH_3)_2N.C_6H_4.CHO$.—Colorless scales fusing at 73° C. (163.4° F.); soluble in hot water. The addition of an alcoholic solution of benzidine (1 in 100) to a slightly acidified solution of paradimethylaminobenzaldehyde produces a brick-red precipitate after standing.

Peptone (Beef Peptone).—The dried product of the pancreatic digestion of meat. A yellow powder of a slightly bitter but not disagreeable taste and an odor resembling that of meat extract. Soluble in all proportions in water, yielding a yellowish-brown liquid of faintly acid reaction. Slightly soluble in diluted alcohol, insoluble in alcohol or ether. An aqueous solution of peptone (1 in 20), upon the addition of tannic acid T.S. or mercuric chloride T.S., yields a precipitate. On the addition of 0.5 mil of potassium hydroxide T.S. to an aqueous solution of peptone (1 in 20), followed by a solution of copper sulphate (1 in 50), added drop by drop with agitation, an intense, red-violet color is produced (biuret reaction). Pour an aqueous solution of peptone (1 in 20) into an excess of alcohol, allow the resulting precipitate to settle and decant the clear supernatant liquid; the residue left on evaporating this liquid is completely soluble in alcohol and no coagulation occurs. One Gm. of peptone dissolves in 20 parts of water with but slight turbidity. When an aqueous solution of peptone (1 in 200) is heated to boiling, no precipitation occurs; the addition of nitric acid does not cause turbidity (*coagulable albumin*). Saturate an aqueous solution of peptone (0.5 Gm. in 20 mils) with powdered zinc sulphate; not more than a slight flocculent precipitate appears (*proteoses*). Dry 1 Gm. of peptone at 100° C. (212° F.), it loses not more than 7 per cent. in weight; ignite this dried product; not more than 0.005 Gm. of ash remains. Peptone contains not less than 12.5 per cent. of nitrogen when determined by the Kjeldahl method, corresponding to about 78 per cent. of pure peptone.

Phenoldisulphonic Acid Test Solution (Phenol-disulphonic acid), $C_6H_3(OH)(SO_3H)_2$.—Mix 37 parts of sulphuric acid (see page 64) with 3 parts of phenol (see page 838) in a flask of suitable capacity and heat in a bath of boiling water for six hours. Transfer the product to a glass-stoppered bottle while still fluid, and when desired for use, warm on a water bath until liquefied.

Phenolphthalein Test Solution.—See under *Indicators* (page 1709).

Phenylhydrazine, $C_6H_5.NH.NH_2$.—A colorless, or slightly yellowish, highly refractive liquid, boiling between 241° and 243° C. (465.8° and 469.4° F.), congealing, when cold, to monoclinic plates fusing at about 19° C. (66.2° F.). Phenylhydrazine is slightly soluble in cold water, more soluble in hot water and readily soluble in alcohol or ether. Its solutions rapidly absorb oxygen from the air, becoming brown. Shake 2 mils of phenylhydrazine with 20 mils of 5 per cent. acetic acid; a clear solution results.

Phenylhydrazine Dihydrochloride, $C_6H_5NH.NH_2.2HCl$.—A white crystalline powder, readily soluble in water, but slowly soluble in alcohol. It melts at about 200° C. (392° F.). Add to an aqueous solution of phenylhydrazine dihydrochloride (1 in 10) sufficient sodium hydroxide T.S. until the reaction is alkaline; upon the addition of copper sulphate T.S., a dense red precipitate is formed. An aqueous solution of the salt (1 in 20) has an acid reaction and is clear and colorless. One Gm. of the salt when ignited leaves no weighable residue.

Phenylhydrazine Hydrochloride, $C_6H_5.NH.NH_2.HCl$.—Silky scales melting at about 225° C. (437° F.). Readily soluble in water or alcohol. Its aqueous solution is clear and free from suspended particles.

Phloroglucinol, $C_6H_3(OH)_3+2H_2O$—A white to cream colored crystalline powder, readily soluble in water, alcohol, or ether. When rapidly heated, it melts between 217° and 219° C. (422.6° and 426.2° F.),

or when slowly heated, between 200° and 209° C. (392° and 408.2° F.). Introduce a few crystals of phloroglucinol in a test tube with about 1 mil each of sulphuric acid and acetic anhydride and heat in boiling water for from five to ten minutes; no blue color develops (*diresorcinol*).

Phloroglucinol Test Solution.—Prepare a 3 per cent. solution of phloroglucinol in alcohol. Keep the solution protected from light.

Phosphotungstic Acid, $P_2O_5.24WO_3+xH_2O$.—White to yellowish-green crystals efflorescing slightly in air. Readily soluble in water or alcohol and slightly soluble in ether. To a solution of 1 Gm. of phosphotungstic acid in 10 mils of distilled water, add 0.1 Gm. of sodium chloride and about 3 drops of indigo T.S. followed by about 10 mils of sulphuric acid, cautiously added; then allow the liquid to stand for ten minutes, the blue color does not disappear (*nitrate*). When 1 Gm. of phosphotungstic acid is dissolved in 10 mils of distilled water and boiled, and a small piece of sodium hydroxide added (about 2 Gm.) and the solution warmed, ammonia is not evolved (*ammonium salts*).

Picric Acid Test Solution.—See page 1692.

Platinic Chloride (Chloroplatinic Acid), $H_2PtCl_6+6H_2O$.—A brownish-red, hygroscopic, crystalline mass, soluble in water, alcohol, or ether, with a yellow color. One Gm. is completely soluble in 10 mils of dehydrated alcohol. Its aqueous solution should be yellow and not brownish. When platinic chloride is strongly ignited in a porcelain crucible, not less than 37.6 per cent. of residue remains. Digest this residue with about ten times its weight of a mixture of five volumes of nitric acid and ten volumes of distilled water on a water bath for fifteen minutes, filter, evaporate to dryness and ignite to constant weight; a residue not exceeding 0.15 per cent. of the platinic chloride taken remains (*other metals*).

Platinic Chloride Test Solution.—Dissolve 2.6 Gm. of platinic chloride in 20 mils of distilled water.

Potassio-Mercuric Iodide Test Solution.—See page 1684.

Potassium Bitartrate, $KHC_4H_4O_6$.—Purify potassium bitartrate (see page 887), to render it suitable for standardizing volumetric solutions of potassium and sodium hydroxide, as follows: To 100 Gm. of the salt, contained in a beaker, add a mixture of 85 mils of distilled water and 25 mils of diluted hydrochloric acid; place the covered beaker on a water bath and digest the mixture, with occasional stirring for three hours. Quickly cool the mixture, drain the solution from the precipitate, wash the latter by affusion and decantation with two successive portions of 100 mils each of distilled water, collect the precipitate on a plain filter, and continue the washing with cold distilled water until the filtrate, after adding a few drops of nitric acid, ceases to become opalescent upon the addition of silver nitrate T.S. Then dissolve the precipitate of potassium bitartrate in the smallest possible volume of boiling distilled water (about 1500 mils), filter, and constantly stir the filtrate while being rapidly cooled. When the mixture is cold, collect the crystalline precipitate on a plain filter, wash it with 300 mils of cold distilled water, and, after thoroughly draining, dry it at 120° C. (248° F.) until of constant weight. Preserve it in dry, securely stoppered bottles. Purified potassium bitartrate is employed for standardizing normal and tenth-normal potassium and sodium hydroxide V.S.

Potassium Bromate, $KBrO_3$.—White cubical crystals or a granular crystalline powder, having a pungent, saline taste. Soluble in 15.5 parts of water at 25° C. (77° F.), and in 2 parts of boiling water, slightly soluble in alcohol. An aqueous solution has a neutral reaction, and does not at once produce a yellow color upon the addition of diluted sulphuric acid (*bromide*). When heated to 350° C. (662° F.), the salt undergoes decomposition with the evolution of oxygen. Potassium bromate should not be triturated or heated with organic or easily oxidizable substances. The addition of nitric acid or sulphuric acid to the salt causes decomposition with the evolution of bromine. Dissolve 0.1 Gm. of potassium bromate, dried at 100° C. (212° F.) and 3 Gm. of potassium iodide, in about 25 mils of distilled water contained in a glass-stoppered bottle of suitable size, and, after the addition of 5 mils of hydrochloric acid, stopper the bottle securely, and set aside for ten minutes. Not less than 35.85 mils of tenth-normal sodium thiosulphate V.S. is required to discharge the color, corresponding to 99.8 per cent. of $KBrO_3$.

Potassium Carbonate Test Solution.—Heat about 15 Gm. of potassium carbonate (see page 892) in a crucible, gradually raising the temperature to 130° C. (266° F.), cool it in a desiccator, weigh off 10 Gm. of the residue, and dissolve it in sufficient distilled water to measure 100 mils.

Potassium Chromate, K_2CrO_4.—Yellow rhombic crystals, soluble in 1.6 parts of water, insoluble in alcohol. Add a few drops of silver nitrate T.S. to 10 mils of an aqueous solution of the salt (1 in 10) followed by 10 mils of nitric acid, and warm to about 50° C. (122° F.), no turbidity appears (*chloride*). Another 10 mils of a solution of the same strength when mixed with an equal volume of diluted hydrochloric acid does not become turbid after the addition of barium chloride T.S. (*sulphate*). Ten mils of an aqueous solution of salt (1 in 10) does not become turbid upon the addition of 5 mils of ammonia water, followed by 2 mils of ammonium oxalate T.S. (*alkali earths*). A solution of 0.1 Gm. of the salt in 20 mils of distilled water does not become red upon the addition of a few drops of phenolphthalein T.S. (*free alkali*).

Potassium Chromate Test Solution.—Dissolve 10 Gm. of potassium chromate in sufficient distilled water to measure 100 mils.

Potassium Dichromate, Purified (Potassium Bichromate), $K_2Cr_2O_7$.—This salt must conform to the following tests before it can be used in the preparation of the tenth-normal volumetric solution: To a solution of 5 Gm. of the salt in 100 mils of distilled water, add 30 mils of concentrated hydrochloric acid (see page 1682), followed by 5 mils of barium chloride T.S.; no turbidity appears after standing twelve hours (*sulphate*). To a solution of 5 Gm. of the salt in 60 mils of distilled water add 1 mil of ammonium chloride T.S. followed by ammonia water until alkaline (about 10 mils) and boil the liquid; no precipitation takes place after standing twelve hours (*aluminum*). The further addition of ammonium oxalate T.S. to the solution, which should still be alkaline, produces neither turbidity nor the slightest precipitation after standing twelve hours (*alkali earths*). Add 10 mils of nitric acid to a solution of 1 Gm. of the salt in 20 mils of distilled water and heat it to about 50° C. (122° F.); no turbidity develops within five minutes after the addition of a few drops of silver nitrate T.S. (*chloride*).

Potassium Dichromate Test Solution.—Dissolve 10 Gm. of purified potassium dichromate in sufficient distilled water to measure 100 mils.

Potassium Ferricyanide, $K_3Fe(CN)_6$.—Dark red crystals soluble in about 2.5 parts of cold water and in 1.5 parts of boiling water. Its aqueous solution undergoes decomposition upon standing, hence its solu-

tions must be freshly made when required for use. Potassium ferricyanide when added to ferrous salts yields a blue precipitate (Turnbull's Blue); when added to solutions of ferric salts it yields clear brown solutions.

Potassium Ferricyanide Test Solution.—Dissolve 1 part of potassium ferricyanide in about 10 parts of distilled water. This solution should be freshly made when required, as it undergoes decomposition with formation of ferrocyanide on standing. A freshly prepared aqueous solution mixed with ferric chloride T.S. which has been well diluted with distilled water shows a brown tint, free from turbidity or a shade of green.

Potassium Ferrocyanide, $K_4Fe(CN)_6+3H_2O$.—Yellow, soft, transparent crystals which are slightly efflorescent on exposure to air. Readily soluble in hot or cold water, insoluble in alcohol. A freshly prepared aqueous solution of the salt (1 in 20) is neutral to litmus; such a solution yields a blue precipitate with solutions of ferric salts, a reddish-brown precipitate with copper sulphate T.S., and a white precipitate with lead acetate T.S. or silver nitrate T.S.

Potassium Ferrocyanide Test Solution.—Dissolve 10 Gm. of potassium ferrocyanide in sufficient distilled water to measure 100 mils.

Potassium Hydroxide Test Solution.—Use the official solution of potassium hydroxide (see page 654).

Potassium Hydroxide Test Solution, Alcoholic.—Use the half-normal alcoholic potassium hydroxide V.S. (see page 1698).

Potassium Hydroxide Test Solution, Special.—This solution is to be prepared of the same strength as *Liquor Potassii Hydroxidi*, employing potassium hydroxide which, in addition to the tests prescribed under *Potassii Hydroxidi*, complies with the following: Dissolve 1 Gm. of the potassium hydroxide in 20 mils of distilled water, in a test tube about 2 cm. in diameter, add 5 mils of nitric acid, followed by a few drops of silver nitrate T.S.; not more than a slight opalescence is produced.

Potassium Iodide Test Solution.—Dissolve 20 Gm. of potassium iodide (see page 902) in sufficient distilled water to measure 100 mils, and preserve the solution in dark, amber-colored, well-stoppered bottles. The solution should be frequently renewed.

Potassium Nitrate, KNO_3.—In addition to the tests prescribed for Potassii Nitras (see page 905), this salt, for use as a reagent, must conform to the following tests: To a solution of 1 Gm. of potassium nitrate in 20 mils of distilled water, add 1 mil of nitric acid followed by a few drops of silver nitrate T.S.; no opalescence results (*chloride*). To a solution of 2 Gm. of the salt in 50 mils of distilled water, add 1 mil of hydrochloric acid, followed by barium chloride T.S.; no precipitate forms after standing for several hours (*sulphate*).

Potassium Permanganate Test Solution, $KMnO_4$.—Use the tenth-normal potassium permanganate V.S. (see page 1700).

Potassium Sulphate, K_2SO_4.—Hard, colorless, transparent prisms, or a white powder, odorless and having a somewhat bitter saline taste; permanent in the air. Soluble in about 9 parts of water at 25° C. (77° F.) and in 4 parts of boiling water. A saturated aqueous solution of the salt, which is neutral to litmus, yields a white, crystalline precipitate with an excess of sodium bitartrate T.S. An aqueous solution of the salt (1 in 20) yields with barium chloride T.S. a heavy white precipitate, insoluble in hydrochloric acid. An aqueous solution of potassium sulphate (1 in 20), slightly acidulated with hydrochloric acid, does not respond to the Test for heavy metals (see Test No. 3). Five mils of an aqueous solution of the salt (1 in 30) does not exceed the limit for arsenic when subjected to the Test for arsenic (see Test No. 1).

Potassium Sulphate Test Solution.—Dissolve 1 Gm. of potassium sulphate in sufficient distilled water to measure 100 mils.

Potassium Sulphocyanate (Potassium Thiocyanate), KCNS.—Colorless, hygroscopic, prismatic crystals. Readily soluble in less than its own weight of water; soluble in 10 parts of boiling dehydrated alcohol, yielding a clear solution. An aqueous solution of the salt (1 in 20) does not become turbid upon the addition of a few drops of concentrated hydrochloric acid (see page 1682), followed by barium chloride T.S. (*sulphate*). An aqueous solution of the salt (1 in 20), after the addition of 1 mil of diluted hydrochloric acid, remains colorless (*iron*), and does not respond to the Test for heavy metals (see Test No. 3).

Potassium Sulphocyanate Test Solution.—Use the tenth-normal potassium sulphocyanate V.S. (see page 1701).

Pyrogallol Test Solution, Alkaline.—Dissolve 0.5 Gm. of pyrogallol (see page 923) in 2 mils of distilled water and 12 Gm. of potassium hydroxide (see page 899) in 8 mils of distilled water. Mix the solutions immediately before using.

Resorcinol Test Solution.—Dissolve 1 Gm. of resorcinol (see page 947) in sufficient concentrated hydrochloric acid (see page 1682) to make 100 mils.

Rosaniline, Acetate, $C_{19}H_{18}N_3.C_2H_4O_2$.—The acetate of rosaniline (see *Fuchsin*, page 1681). Rosaniline acetate complies with all of the tests of identity and purity given under *Fuchsin*.

Rosolic Acid and Rosolic Acid Test Solution.—See under *Indicators* (page 1709).

Sawdust, Purified.—Moisten 1000 Gm. of oak sawdust, in approximately No. 20 powder, with water, pack in a cylindrical percolator and pour on enough of a 1 per cent. solution of sodium hydroxide to saturate the powder and leave a stratum above it.

When the liquid drops from the percolator, close the lower orifice and macerate the sawdust during twenty-four hours. Then proceed to percolate slowly until the alkaline percolate measures 5000 mils. Now continue the percolation with 4000 mils of 1 per cent. hydrochloric acid and then with water until the acid is all removed and the percolate is neutral. Finally dry the powder.

Selenous Acid, H_2SeO_3.—Colorless, prismatic or granular crystals, efflorescent in dry air and hygroscopic in moist air; readily soluble in water or alcohol. Red amorphous selenium is precipitated from aqueous solutions of selenous acid upon the addition of stannous chloride T.S. or sulphurous acid.

Silver Ammonium Nitrate Test Solution.—Dissolve 1 Gm. of silver nitrate (see page 182) in 20 mils of distilled water, and add ammonia water, drop by drop, agitating the mixture, until the precipitate first produced is almost, but not entirely, redissolved. Filter the solution and preserve it in dark amber-colored and well-stoppered bottles.

Silver, Metallic, Ag.—In the form of foil, wire or powder. Dissolve 2 Gm. of the metal in the smallest

possible quantity of nitric acid (see page 45) previously mixed with an equal volume of distilled water; no residue remains and the solution, after warming to remove the oxides of nitrogen, and diluting with fifty volumes of distilled water, remains colorless and clear. Add sufficient hydrochloric acid to this solution heated to boiling to precipitate the silver, filter, evaporate the filtrate to dryness and gently ignite the residue; not more than 0.0005 Gm. of residue remains (*foreign metals*), allowance being made for the non-volatile matter present in the water, reagents and extracted from the filter paper.

Silver Nitrate Test Solution.—For ordinary purposes, use the tenth-normal silver nitrate V.S. (see page 1702).

Silver Sulphate, Ag_2SO_4.—Small, white, anhydrous, lustrous rhombic crystals soluble in about 87 parts of cold water. It should correspond to the tests for purity given under *Argenti Nitras* (see page 183).

Silver Sulphate Test Solution.—Mix 1 Gm. of silver sulphate with 100 mils of distilled water in a glass-stoppered bottle and shake the mixture thoroughly. Decant the clear liquid when required for use. Alternative process: Dissolve 1 Gm. of silver nitrate (see page 182) in 0.5 mil of warm distilled water, and add 1.5 mils of sulphuric acid (see page 64); on cooling, small transparent crystals of silver sulphate, Ag_2SO_4, separate. Pour off the acid liquid carefully, wash the crystals repeatedly by decantation with cold distilled water, transfer them to a bottle, add 100 mils of distilled water, and shake thoroughly until the liquid is saturated. For use, decant a sufficient quantity of the solution.

Sodium Acetate, Anhydrous, CH_3COONa.—Heat sodium acetate (see page 1010) gently in a porcelain dish until fusion takes place and the salt becomes a pasty mass, then gradually increase the temperature, with caution, stirring constantly, until it again fuses, and continue the heat until a dry powder results. Care must be taken to avoid charring and the salt must be constantly stirred to prevent the adhesion of the mass to the sides of the dish.

Sodium Acetate Test Solution.—Dissolve 10 Gm. of sodium acetate (see page 1010) in sufficient distilled water to measure 100 mils.

Sodium Bisulphite, $NaHSO_3$.—It contains not less than 90 per cent. of $NaHSO_3$. Opaque, prismatic crystals, or a granular powder, having the odor of sulphur dioxide, and a disagreeable, sulphurous taste. Exposed to the air, the salt loses sulphur dioxide, and is gradually oxidized to sulphate. Soluble in 3.5 parts of water, and in 70 parts of alcohol at 25° C. (77° F.). Dissolve 1 Gm. of sodium bisulphite in 10 mils of diluted nitric acid and heat the solution sufficiently to expel the gases; the liquid does not become turbid (*thiosulphate*). Dissolve 1 Gm. of the salt in 20 mils of diluted hydrochloric acid, and heat it sufficiently to expel the sulphur dioxide; the remaining solution, after being restored to its original volume, does not respond to the Test for heavy metals (see Test No. 3). Transfer about 0.2 Gm. of sodium bisulphite, accurately weighed, to a glass-stoppered flask containing 50 mils of tenth-normal iodine V.S., and allow to stand with occasional agitation, until the salt is dissolved. Then titrate the excess of iodine with tenth-normal sodium thiosulphate V.S. It shows not less than 90 per cent. of $NaHSO_3$. Each mil of tenth-normal iodine V.S. corresponds to 0.005204 Gm. of $NaHSO_3$.

Sodium Bisulphite Test Solution.—Dissolve 30 Gm. of sodium bisulphite in sufficient distilled water to measure 100 mils. Should the solution possess a strong odor of sulphur dioxide, add a 20 per cent. aqueous solution of sodium hydroxide, drop by drop, until the odor becomes scarcely perceptible. The solution must be freshly prepared when needed.

Sodium Bitartrate, $NaHC_4H_4O_6+H_2O$.—White rhombic crystals or powder, soluble in 9 parts of cold and 1.8 parts of boiling water. When assayed and tested as directed under *Potassii Bitartras* (see page 887), it complies with the standards of purity there required. One mil of normal potassium hydroxide V.S. corresponds to 0.19006 Gm. of sodium bitartrate ($NaHC_4H_4O_6+H_2O$).

Sodium Bitartrate Test Solution.—Dissolve about 9 Gm. of sodium bitartrate in 100 mils of distilled water. Alternative method: To a solution of 3.5 Gm. of tartaric acid (see page 78) in about 80 mils of boiling distilled water, add gradually in small portions monohydrated sodium carbonate (see page 1023) until the solution has a neutral reaction to litmus paper. To the solution add 3.5 Gm. of tartaric acid, filter, and add sufficient distilled water to make the solution measure 100 mils. This solution must be freshly prepared when required.

Sodium Carbonate.—Use monohydrated sodium carbonate (see page 1023).

Sodium Carbonate, Anhydrous, Na_2CO_3.—This is prepared from sodium bicarbonate (see page 1014) which, in addition to the official requirements for purity, must conform to the following more rigorous tests before it can be employed for standardizing volumetric solutions of hydrochloric and sulphuric acids.

To a filtered solution of 5 Gm. of sodium bicarbonate in 100 mils of distilled water add an excess (5 mils) of concentrated hydrochloric acid (see page 1682), heat it to boiling, and then add 1 mil of barium chloride T.S. No cloudiness or precipitate forms within twelve hours (*sulphate*). To a solution of 1 Gm. of the bicarbonate in 30 mils of distilled water add 3 mils of nitric acid (see page 45); the solution remains clear, now heat it to boiling, and add 1 mil of silver nitrate T.S.; no opalescence appears within fifteen minutes (*chloride*). To 10 Gm. of sodium bicarbonate and about 50 mils of distilled water contained in a beaker of about 250 mils capacity, add slowly with stirring, about 30 mils of concentrated hydrochloric acid (see page 1682), taking care to avoid loss through violent effervescence. Filter, wash the beaker and filter with distilled water, transfer the filtrate and washings to a platinum dish, evaporate to dryness on a water bath and dry the residue for four hours at 120° C. (248° F.). Now add to the dried residue about 20 mils of distilled water and about 5 mils of concentrated hydrochloric acid (see page 1682), again evaporate to dryness and dry as before. Finally dissolve the residue in 3 mils of concentrated hydrochloric acid (see page 1682) and 50 mils of distilled water; the resulting solution remains perfectly clear upon standing (*silica*). To a solution of 1 Gm. of the bicarbonate in 15 mils of distilled water, add 2 mils of concentrated hydrochloric acid (see page 1682) followed by 2 drops of nitric acid (see page 45) and boil the solution; it is not reddened upon the addition of potassium sulphocyanate T.S., a blank test being carried out at the same time (*iron*).

Take any suitable quantity of sodium bicarbonate complying with the foregoing tests, place it in a platinum vessel and heat it in an air or sand bath for one-half hour at from 270° to 280° C. (518° to 536° F.) (not over 300° C. (572° F.)). Finally cool the salt in a desiccator and, before it is quite cold, transfer it to a dry, glass-stoppered bottle.

Sodium Carbonate Test Solution.—Dissolve 10 Gm. of monohydrated sodium carbonate (see page 1023) in sufficient distilled water to measure 100 mils.

Sodium Chloride, NaCl.—In addition to the requirements and tests prescribed for this salt under *Sodii Chloridum* (see page 1024), it is required to conform to the following more rigorous tests before it can be used in the preparation of tenth-normal sodium chloride V.S. To a solution of 3 Gm. of sodium chloride in 80 mils of distilled water, add 1 mil of concentrated hydrochloric acid (see page 1682), heat it to boiling, and add about 5 mils of barium chloride T.S.; no precipitation of barium sulphate takes place within twenty-four hours (*sulphate*). To a solution of 3 Gm. of sodium chloride in about 10 mils of distilled water, add 5 mils of ammonia water and 5 mils of sodium phosphate T.S.; no precipitation takes place within twelve hours (*magnesium salts*). Dissolve 5 Gm. of the salt in 80 mils of distilled water, heat the solution to boiling, and add 5 mils of ammonium oxalate T.S.; no precipitate is produced within twelve hours (*calcium*); nor is this solution affected by the addition of sodium carbonate T.S.; nor is a freshly prepared solution of the same concentration affected by the addition of sodium sulphide T.S. (*alkali earths and heavy metals*). To a solution of 1 Gm. of sodium chloride in 10 mils of distilled water, add 5 mils of sodium cobaltic nitrite T.S.; no precipitation occurs after twenty-four hours (*potassium*). The addition of Nessler's Reagent (see page 1684) to a solution of 3 Gm. of sodium chloride produces no yellow coloration (*ammonium salts*).

Sodium Cobaltic Nitrite Test Solution.—Dissolve 4 Gm. of cobaltous chloride (see page 1680) and 10 Gm. of sodium nitrite (see page 1032) in about 50 mils of distilled water, add 2 mils of acetic acid (see page 13) and dilute with sufficient distilled water to measure 100 mils. A few drops of acetic acid should be added to the solution from time to time. The reagent must not be kept longer than three months. Should any precipitate form on standing, filter the solution.

Sodium Cyanide Test Solution.—Dissolve 1 Gm. of sodium cyanide (see page 1027) in sufficient distilled water to measure 10 mils. This solution must be freshly prepared when required.

Sodium Hydroxide Test Solution, NaOH.—Use the official solution of sodium hydroxide (see page 660).

Sodium Hypobromite Test Solution.—To a solution of 40 Gm. of sodium hydroxide (see page 1028) in about 150 mils of distilled water add 10 mils of bromine (see page 1678) and, after solution has taken place, add sufficient distilled water to measure 200 mils. This solution must be freshly prepared when required for use.

Sodium Nitroprusside, $Na_2Fe(NO)(CN)_5+2H_2O$.—Transparent, dark red rhombic crystals, soluble in about 2.5 parts of water. With soluble sulphides it gives an intense, violet coloration. Solutions of sodium nitroprusside must be freshly prepared when required for use.

Sodium Nitroprusside Test Solution.—Dissolve 1 part of sodium nitroprusside in 19 parts of distilled water immediately before using.

Sodium Oxalate, $Na_2C_2O_4$.—A white crystalline powder, 1 Gm. of which dissolves in about 34 mils of water at 25°C. (77° F.), and about 16 mils of boiling water. When used for the standardization of tenth-normal potassium permanganate V.S., sodium oxalate should comply with the following tests for purity and be dried to constant weight at 105° C. (221° F.). When dried to constant weight at 105° C. (221° F.) sodium oxalate loses not more than 0.03 per cent. in weight (*moisture*). Introduce into a conical Jena or other flask of like quality 2 Gm. of sodium oxalate, add 150 mils of distilled water and 0.2 mil of phenolphthalein T.S., boil until the volume is reduced to about 100 mils, then cool while passing a current of air free from carbon dioxide through the solution. If the solution is red, not more than 0.2 mil of fiftieth-normal sulphuric acid V.S. is required to render it colorless. If the solution is colorless, not more than 0.2 mil of fiftieth-normal potassium hydroxide V.S. is required to produce a pink color. Sodium oxalate yields an almost perfectly clear solution and contains not more than 0.01 per cent. of matter insoluble in water. Convert 10 Gm. of the salt into carbonate by ignition in a platinum crucible using an alcohol burner, dissolve the residue in distilled water by the aid of sufficient nitric acid to impart a distinctly acid reaction, heat to boiling, filter and divide into two parts. To one part, add barium nitrate T.S. and set aside for twelve hours; not more than a barely perceptible cloudiness results (*sulphate*). The remaining portion, after the addition of silver nitrate T.S., does not yield more than a faint opalescence (*chloride*). Ignite 5 Gm. of the salt to carbonate, dissolve the residue in distilled water, acidify with acetic acid and filter; after the addition of a few drops of sodium cobaltic nitrite T.S. to the filtrate it should not yield more than a faint trace of precipitate after standing for several hours (*potassium*). Ignite 5 Gm. of the salt, dissolve the residue in distilled water acidify with hydrochloric acid and filter; the filtrate does not yield a coloration upon the addition of potassium sulphocyanate T.S. (*iron*). Heat 1 Gm. of the salt in a test tube, which has previously been rinsed with sulphuric acid, with 10 mils of sulphuric acid until fumes of sulphur trioxide appear; no discoloration of the acid is produced (*foreign organic bodies*).

Sodium Phosphate Test Solution.—Dissolve 10 Gm. of sodium phosphate, in clear crystals (see page 1035), in sufficient distilled water to measure 100 mils.

Sodium Phospho-tungstate Test Solution (Sodium Phospho-wolframate).—To a solution of 20 Gm. of sodium tungstate in 100 mils of water, add sufficient phosphoric acid (see page 54) to impart a strong acid reaction, filter and preserve it in an amber-colored, glass-stoppered bottle. Decant the solution from any sediment which may form.

Sodium Sulphide, Na_2S+9H_2O.—Colorless, or nearly colorless, transparent crystals, of sulphuretted odor, readily soluble in water, yielding a clear solution which is alkaline to litmus.

Sodium Sulphide Test Solution.—Dissolve 10 Gm. of sodium sulphide in sufficient distilled water to measure 100 mils; filter the solution if necessary. Sodium sulphide T.S. may be used in all instances where ammonium sulphide T.S. is directed, but must be freshly prepared when required for use.

Sodium Tartrate, Neutral, $Na_2C_4H_4O_6+2H_2O$.—Transparent crystals soluble in 2.6 parts of water at 25° C. (77° F.); insoluble in alcohol. It complies with the standards for purity required under *Potassii et Sodii Tartras* (see page 898); each mil of half-normal sulphuric acid V.S. corresponds to 0.057515 Gm. of $Na_2C_4H_4O_6+2H_2O$.

Sodium Tartrate Test Solution.—Dissolve 10 Gm. of neutral sodium tartrate (see above) in sufficient distilled water to measure 100 mils. Alternative method: To a hot solution of 6.5 Gm. of tartaric acid (see

page 78) in about 80 mils of boiling distilled water, add gradually, in small portions, monohydrated sodium carbonate (see page 1023) until the solution has a neutral reaction to litmus paper; after filtering and cooling add sufficient distilled water to measure 100 mils.

Sodium Thiosulphate, $Na_2S_2O_3+5H_2O$.—In addition to the tests prescribed for this salt under *Sodii Thiosulphas* (see page 1043) it is required to conform to the following more rigorous tests before it can be used in preparing the standard volumetric solution. Add iodine T.S., drop by drop, to a solution of the salt (1 in 20) in distilled water until it retains a faint but permanent yellow color; no turbidity is produced upon the addition of barium chloride T.S. (*sulphate and sulphite*). The addition of phenolphthalein T.S. to 10 mils of an aqueous solution of the salt (1 in 10) produces no pink coloration (*free alkalies*).

Sodium Thiosulphate Test Solution.—Use tenth-normal sodium thiosulphate V.S. (see page 1704).

Sodium Tungstate (Sodium Wolframate), $Na_2WO_4+2H_2O$.—Colorless prisms or plates, soluble in about 4 parts of Water, forming a solution which is alkaline to litmus. Evaporate a solution of 1 Gm. of sodium tungstate in 10 mils of distilled water and 10 mils of concentrated hydrochloric acid (see page 1682) to dryness on a water bath and then heat it for half an hour at 120° C. (248° F.). Treat the residue with 20 mils more of the hydrochloric acid, evaporate and heat as before, and repeat the operation three times. After cooling, digest the residue with a solution of ammonium nitrate (1 in 10) to which a few drops of nitric acid have been added, transfer it to a filter, wash the insoluble tungstic acid with diluted nitric acid, dry, ignite and weigh. (It is preferable to moisten this residue with a few drops of nitric acid and repeat the ignition.) This residue weighs not less than 0.69 Gm.

Stannous Chloride, $SnCl_2+2H_2O$.—Colorless crystals, readily soluble in water or alcohol. When in contact with the air or excess of water, the salt readily forms a basic chloride, hence, when dissolved, its solution should be acidulated with hydrochloric acid. When tested for arsenic as directed under the Test for arsenic (see Test No. 1), 0.3 Gm. of stannous chloride produces no stain. A solution of 2 Gm. of stannous chloride, in 1 mil of distilled water and 0.5 mil of hydrochloric acid, does not become opalescent on diluting with 20 mils of distilled water (*lead*). Alternative method: Heat tin (see page 1692) for several days with concentrated hydrochloric acid (see page 1682) upon a water bath, taking care that the metal is in excess. When the acid has become saturated, pour off the clear fluid from the undissolved tin or precipitate, filter it while still hot through asbestos and set it aside until crystallization takes place. Break up the crystals, drain, and dissolve them at once as directed under the Test Solution.

Stannous Chloride Test Solution.—Dissolve 1 Gm. of stannous chloride crystals (see above) in 10 mils of distilled water to which a few drops of hydrochloric acid have been added to prevent the precipitation of basic chloride, and preserve the solution in a glass-stoppered bottle in which a fragment of tin (see page 1692) has been placed. The solution must be renewed at frequent intervals.

Stannous Chloride Test Solution, Acid.—Dissolve 40 Gm. of stannous chloride crystals (see above) in 60 mils of concentrated hydrochloric acid (see page 1682) and preserve it in a glass-stoppered bottle.

Stannous Chloride Test Solution, Saturated.—(For Bettendorf's Arsenic Test, see Test No. 2.) Prepare a saturated solution of stannous chloride crystals (see above) in concentrated hydrochloric acid (see page 1682) or evaporate a solution prepared from metallic tin by the alternative method under *Stannous Chloride* (see above) to a specific gravity of about 2.00 at 25° C. (77° F.). After filtering the solution through asbestos it is transparent and has not more than a pale yellow color.

Starch (Potato).—The starch grains separated from the tubers of *Solanum tuberosum*, Linné (Fam. *Solanaceæ*). In a more or less finely granular powder, consisting of starch grains varying in shape from somewhat spherical or ellipsoidal to characteristic, with a few two- or three-compound grains; the individual grains with a circular point of origin of growth and distinct excentral lamellæ, the larger characteristic grains varying from 0.05 to 0.125 mm. in length, and under the micropolariscope showing a distinct cross and a strong play of color when a selenite plate is used.

Starch Test Solution.—Triturate 1 Gm. of corn starch (see page 142) with 10 mils of cold distilled water, add sufficient boiling distilled water with constant stirring to make about 200 mils, then boil the mixture for a few minutes until a thin, translucent fluid is obtained. This solution must be freshly prepared and filtered when required.

Succinic Acid, $H_2C_4H_4O_4$.—An organic acid obtained through the destructive distillation of amber or made synthetically. It forms colorless monoclinic prisms, soluble in about 20 parts of water, 2 parts of boiling water, 10 parts of alcohol, or 18 parts of acetone; very slightly soluble in ether and insoluble in chloroform or benzene. Succinic acid melts at about 182° C. (359.6° F.).

Sulphanilic Acid (Para-amidobenzenesulphonic Acid), $C_6H_4(NH_2)(SO_3H)1:4+2H_2O$.—Colorless, acicular, efflorescent crystals. When strongly heated, it carbonizes. Soluble in about 150 parts of cold water and insoluble in alcohol or ether.

Sulphanilic Acid Test Solution.—Dissolve 0.5 Gm. of sulphanilic acid in a mixture of 15 mils of glacial acetic acid and 135 mils of freshly distilled or recently-boiled distilled water. This reagent must be kept in well-stoppered bottles.

Sulpho-Salicylic Acid, $C_6H_3(OH)(SO_3H).COOH$.—Colorless, anhydrous needles very soluble in water and alcohol. It melts at about 120° C. (248° F.).

Sulphuric Acid.—Sulphuric acid of the purity required by the Pharmacopœia (see page 64), with a specific gravity of 1.832 at 25° C. (77° F.), will be satisfactory as a reagent unless otherwise directed.

Sulphuric Acid, Fuming, $H_2SO_4+SO_3$.—A heavy, fuming, oily liquid, sometimes slightly colored, containing from 14 to 16 per cent. of free sulphur trioxide corresponding to from 84.2 to 84.6 per cent. of total sulphuric anhydride, with a specific gravity of from 1.869 to 1.875 at 25° C. (77° F.). Great caution should be exercised in handling fuming sulphuric acid. Render the acid homogeneous by shaking vigorously, then transfer several mils to a glass-stoppered weighing flask and weigh accurately. Remove about 1 mil of the acid to a dish containing from 30 to 40 mils of distilled water and again accurately weigh the flask, thus noting the quantity of acid taken for the assay. Titrate the solution of the acid in the dish with normal potassium hydroxide V.S., using methyl orange T.S. as indicator. One mil of normal potassium hydroxide V.S. corresponds to 0.040035 Gm. of sulphuric anhydride (SO_3). The percentage of SO_3 thus found, when subtracted from 100, represents the water present, for each 18.02 parts of which, 80.07 parts of SO_3

are required for the formation of H_2SO_4. After allowing for all of the water in this manner, the remaining SO_3 may be termed free SO_3.

Sulphuric Acid, Purified and Concentrated, for Tests, H_2SO_4.—When concentrated sulphuric acid is specified in a test, it is intended that the strongest purified acid of a specific gravity of not less than 1.834 at 25° C. (77° F.), be employed. In addition to the tests prescribed for this acid under *Acidum Sulphuricum* (see page 67), it is required to conform to the following more rigorous tests before it can be employed as a reagent: Dilute 1 part of the acid with 4 parts of distilled water; no stain is produced by 25 mils of this diluted acid when subjected to the Test for arsenic (see Test No. 1). Dilute 1 mil of the acid with 9 mils of distilled water, cool and pour it so as to form a layer over 5 mils of diphenylamine T.S. (see page 1680); no blue color appears at the zone of contact (*nitric acid*). Upon carefully pouring about 2 mils of hydrochloric acid, in which a particle of sodium sulphite has been dissolved, over about 2 mils of the concentrated sulphuric acid, no reddish zone appears and no precipitate forms (*selenium*).

Sulphurous Acid.—An aqueous solution containing not less than 6 per cent. of sulphur dioxide. Ten mils of this solution, when mixed with 10 mils of dilute sulphuric acid (see under Arsenic Test, page 1709) and evaporated on a water bath until free from sulphur dioxide, does not produce a stain when subjected to the Test for arsenic (see Test No. 1). Introduce about 2 mils of the acid into a flask containing 10 mils of distilled water, previously tared with its contents, stopper and weigh accurately. To this add 50 mils of tenth-normal iodine V.S., allow to stand five minutes, then titrate the excess of iodine with tenth-normal sodium thiosulphate V.S. It shows not less than 6 per cent. of SO_2. Each mil of tenth-normal iodine V.S. corresponds to 0.003204 Gm. of SO_2.

Tannic Acid Test Solution.—Dissolve 1 Gm. of tannic acid (see page 75) in 1 mil of alcohol, and add sufficient distilled water to measure 10 mils. This test solution should be freshly prepared when needed.

Tartaric Acid Test Solution.—Dissolve 1 part of tartaric acid (see page 78) in 3 parts of distilled water. This solution must be frequently renewed.

Tin, Sn.—Metallic tin in the granulated or mossy condition. Digest 5 Gm. of tin with 40 mils or a sufficient quantity of nitric acid (see page 45) on a bath of boiling water until entirely converted into a white powder, then evaporate it to dryness. Stir the residue with 25 mils of diluted nitric acid (see page 50) and 25 mils of distilled water, and filter. To the filtrate add 1 mil of diluted sulphuric acid and evaporate it as far as possible upon a water bath, and then add 10 mils of distilled water; no weighable residue remains undissolved (*lead*). When converted into stannous chloride (see page 1691), it complies with the tests directed under that salt.

Toluol (Toluene, Methyl Benzene), $C_6H_5.CH_3$.—A colorless, refractive, inflammable liquid of peculiar aromatic odor; specific gravity about 0.865 at 25° C. (77° F.), boiling between 110° and 112° C. (230° and 233.6° F.). Miscible with alcohol, ether, chloroform, carbon disulphide, or petroleum benzin. It dissolves phosphorus, iodine, fats, or oils.

Trinitrophenol Test Solution (Picric Acid Test Solution), $C_6H_2(NO_2)_3.OH$.—Dissolve 1 Gm. of trinitrophenol (see page 1164) in 100 mils of distilled water by the aid of heat. Cool the solution and filter it if necessary.

Turmeric Paper and Tincture.—See under *Indicators* (page 1709).

Xylol (Xylene, Dimethyl Benzene), $C_6H_4(CH_3)_2$.—A mixture of ortho-, meta-, and para-xylene obtained through the distillation of coal tar naphtha. A colorless liquid of an odor resembling benzene. It boils between 136° and 140° C. (276.8° and 284° F.) specific gravity about 0.850 at 25° C. (77° F.); insoluble in water, but soluble in alcohol, ether, or chloroform.

Yeast.—Use the commercial compressed yeast cake.

Zinc, Zn.—Pure metallic zinc (see page 1216).

Zinc for the Arsenic Test.—Zinc in mossy or globular form, the latter about 3 to 6 mm. in diameter, known as No. 7 Shot Zinc. This must conform with the tests for purity as given under *Zincum* and in addition the following: The stain from 8 Gm. of zinc, when determined by a blank experiment as directed under the Test for arsenic (see Test No. 1), should scarcely be perceptible. Introduce 10 Gm. of the zinc into a flask of about 250 mils capacity, proved with a perforated rubber stopper and a rubber-valve tube, and containing 60 mils of distilled water, 15 mils of concentrated sulphuric acid for tests (see above) and 1 drop of copper sulphate T.S. When the reaction slackens, place the flask on a water bath and warm until solution of the zinc is complete. At once begin to add tenth-normal potassium permanganate V.S., drop by drop, with agitation, until the solution assumes a faint pink tint which remains permanent for one-half minute. Not more than 1.4 mils of tenth-normal potassium permanganate V.S. is required, indicating not over 0.08 per cent. of oxidizable matter, calculated as metallic iron (Fe).

Zinc Dust (Powdered Zinc).—Zinc in the form of a fine gray powder.

Zinc Oxide, ZnO.—When used in the assay of phosphoric acid, the phosphates or the hypophosphites, it must comply with the tests given under *Zinci Oxidum* (see page 1211) and also the following: Dissolve 1 Gm. of zinc oxide in 20 mils of distilled water and 5 mils of nitric acid in a test tube about 2 cm. in diameter and add a few drops of silver nitrate T.S.; not more than a slight opalescence is produced.

Volumetric Solutions

(U. S. P. IX)

It is absolutely necessary that the measuring vessels employed in the operations of volumetric analysis, consisting of burettes, flasks, mixing cylinders, pipettes, etc., shall agree among themselves accurately in their graduation at the standard temperature selected. All volumetric solutions should be prepared at the standard temperature of 25° C. (77° F.) and used in titrations, if practicable, at that standard temperature. If titrations are made at any other temperature, a volumetric solution should be used which has been standardized for such temperature. In case graduated apparatus calibrated at 25° C. (77° F.) is not procurable volumetric solutions may be prepared at the temperature for which the apparatus in hand was graduated (*e.g.*, 15° C. (59° F.) or 20° C. (68° F.)), and all such volumetric solutions should be marked to indicate the

temperature which has been used. Such solutions must be used as above stated at such standard temperature, care being taken that all graduated apparatus used be standardized at the same temperature.

Units of Capacity.—The units of volume employed by the Pharmacopœia must accord with its standard liter at 25° C. (77° F.) which represents the volume occupied by 996.04 Gm. of distilled water, weighed in air with brass weights, at a temperature of 25° C.[1] (77° F.) and barometer at 760 mm. To secure uniformity among the various forms of apparatus employed, the standard specifications of the U. S. Bureau of Standards should be adhered to as closely as possible, excepting that the temperature here adopted is 25° C. (77° F.). The tables for calibrating graduated apparatus will be found on page 1790.

Measuring Flasks.—Standard measuring flasks are calibrated to contain, when filled to the mark, 1000, 500, 250, 200 or 100 mils at 25° C. (77° F.). The necks must be of uniform calibre, and measure in diameter not less than 14 mm. nor more than 20 mm. for 1000 mil capacity; from 12 mm. to 18 mm. for 500 mil capacity; from 10 mm. to 15 mm. for 250 mil capacity and from 8 mm. to 12 mm. for 100 mil capacity. The capacity mark on any of these flasks should not be less than 6 cm. distant from the mouth and not less than 2 cm. from the base of the neck.

Cylinders.—These should be graduated to contain their respective volumes at the standard temperature. Their inside diameter must not be more than one-fifth the graduated length.

Transfer Pipettes.—These should be graduated to deliver at standard temperature the exact volume of fluid indicated. The suction stem should be at least 16 cm. long, and the delivery tube not less than 3 cm. nor more than 25 cm. long. The inside diameter at the capacity mark must not be less than 2 mm. and not exceed 4 mm. for those of 25 mil capacity. The capacity mark should not be more than 6 cm. from the bulb. The outlet of any transfer pipette should be of such size that the free outflow shall last not more than 1 minute, nor less than 15 seconds for 5 mils, 20 seconds for 10 mils and 30 seconds for 50 mils. After filling, the fluid adhering to the outside should be wiped from the stem; then when draining the contents, the pipette should be held in a vertical position; finally, to complete the emptying, the tip of the pipette should be held against the side of the vessel, permitting the last portions of the fluid to flow out by gravity. Pipettes should never be drained by blowing into them.

Burettes.—These must be provided with glass stop-cocks and be graduated for use at the standard temperature. Burettes provided with rubber tubes and pinch-cocks in place of glass stop-cocks may be used for potassium and sodium hydroxide V.S. The tips should be gradually tapered from 2 to 3 cm. in length and slightly bent. The rate of outflow should be regulated so that not less than 2 seconds should be consumed for each mil of the length of the column delivered. When completing titration, the tip of the delivery tube should be touched with the wet surface of the receiving vessel to complete the emptying.

General Directions.—All bottles in which volumetric solutions are to be kept, as well as the burettes or pipettes in which they are to be measured, should, prior to use, be thoroughly cleaned and rinsed first with distilled water, and then with two or three small portions of the solution that they are to contain. In all apparatus where the surface of the fluid is limited by a meniscus, the reading must be made from the lowest point of the meniscus unless the liquid is too opaque to permit exact observation of that point. It is of the utmost importance that the inner surface of all measuring apparatus shall be free from any suggestion of greasiness.

Normal volumetric solutions $\left(\frac{N}{1}\right)$ are those which contain in 1000 mils, in any stated reaction, the chemical equivalent of one gramme of hydrogen. If the molecule of the reagent is univalent, one liter will contain a weight in grammes equal to the molecular weight of the reagent; if bivalent, a weight in grammes equal to one-half its molecular weight; if trivalent, a weight in grammes equal to one-third its molecular weight. Thus, hydrochloric acid, HCl = 36.47, having but one H atom replaceable by a basic element, has 36.47 Gm. of HCl in 1000 mils of the normal volumetric solution; while sulphuric acid, $H_2SO_4 = 98.09$, having two replaceable H atoms, contains only one-half this number, or 49.045 Gm. of H_2SO_4 in 1000 mils of its normal solution. Potassium hydroxide, KOH = 56.11, has but one K to replace one H in acids, hence its normal solution contains 56.11 Gm. of KOH in one liter. Again, one molecule of potassium dichromate ($K_2Cr_2O_7 = 294.20$) in oxidation liberates three atoms of oxygen which are capable of oxidizing six atoms of ferrous to ferric iron. Therefore, each molecule of the dichromate, yielding three atoms of oxygen, is equivalent to six atoms of hydrogen. Hence, the normal solution should contain $\frac{294.20}{6}$ or 49.0333 Gm. in 1000 mils. Two molecules of potassium permanganate, $2KMnO_4 = 316.06$, in oxidation, give off five atoms of O, which are equivalent to ten atoms of H; hence its normal solution should contain $\frac{316.06}{10}$ or 31.606 in 1000 mils. Solutions containing in 1000 mils one-tenth of the quantity of the active reagent in the normal solution are called tenth-normal $\left(\frac{N}{10}\right)$ (normality = 0.1); those containing one-hundredth, hundredth-normal $\left(\frac{N}{100}\right)$ (normality = 0.01) those containing one-fiftieth, fiftieth-normal $\left(\frac{N}{50}\right)$ (normality = 0.02); those containing twice the amount, double-normal $\left(\frac{2N}{1}\right)$ (normality = 2); half the amount, half-normal $\left(\frac{N}{2}\right)$ (normality = 0.5). Solutions containing quantities of the active reagent having no simple relation to the molecular weight are called empirical.

Use of Empirical Solutions.—All standard volumetric solutions are liable to deteriorate in time, some very slowly, others rapidly, especially when not properly preserved. To restore the titer of such solutions (that is, to make them exactly normal, tenth-, or hundredth-normal, as the case may be) each time they are to be used, involves an unnecessary waste of time. If one accurately standardized solution be always available, it is not necessary that the other volumetric solutions employed in conjunction with it be adjusted to exactly correspond, mil for mil, so long as the *exact* ratio is known at standard temperature. The percentage strength of any empirical solution as compared with a standard volumetric solution is ascertained by experiment, then the number of mils of the empirical solution consumed in the titration of the substance is multiplied by its percentage strength, which product represents the equivalent volume of the true standard solution.

[1] 500 mils would weigh 498.02 Gm.; 250 mils, 249.01 Gm.; 100 mils, 99.604 Gm.

Example: One gramme of potassium carbonate required for neutralization 22 mils of an empirical solution of hydrochloric acid. In a trial experiment, 16 mils of this weak solution was required to neutralize 10 mils of a standard normal potassium hydroxide V.S. The former was therefore of 62.5 per cent. strength (for 16 : 10 : : 100 : x. $x = 62.5$), hence the 22 mils of empirical solution consumed represents 13.75 mils (62.5 per cent. of 22) of standard normal hydrochloric acid V.S. Therefore since 1 mil of $\frac{N}{1}$ hydrochloric acid V.S. = 0.0691 Gm. of K_2CO_3, 13.75 mils would be equivalent to 13.75×0.0691 or 0.9501 + Gm. of potassium carbonate.

Adjustment of titer of volumetric solutions which are above strength. Titrate 25 mils of the strong solution, with a carefully standardized corresponding solution, which must be of the same standard temperature. The number of mils of the latter consumed, divided by 25, will give the factor to be employed in adjusting the strength of the former.

Example: 25 mils of a " strong " normal solution of hydrochloric acid required 27.25 mils of standard normal potassium hydroxide V.S. for neutralization. The correcting factor is therefore $27.25 \div 25 = 1.09$. If the " strong " solution measures 875 mils its volume must be made up with distilled water to $875 \times 1.09 = 953.75$ mils. Add therefore to the " strong " solution $953.75 - 875 = 78.75$ mils of distilled water. After the solution is thus diluted, its titer should be verified by the titration of 25 mils with the standard normal potassium hydroxide V.S., the measurements in each case being made at 25° C. (77° F.) (or at least at the same temperature). It should require exactly 25 mils of the latter for neutralization. If this is not the case, either a new adjustment must be made, or else the new correction factor must be plainly written on the label of the bottle, and the required correction made whenever the solution is used.

Alkaline Cupric Tartrate Volumetric Solution

[Fehling's Solution]

A. The Copper Solution.—Dissolve 34.66 Gm. of carefully selected, small crystals of cupric sulphate (*Cupri Sulphas*, U.S.P.), showing no trace of efflorescence or of adhering moisture, in a sufficient quantity of distilled water to make the solution measure exactly 500 mils at standard temperature. Keep this solution in small, well-stoppered bottles.

B. The Alkaline Tartrate Solution.—Dissolve 173 Gm. of crystallized potassium and sodium tartrate (*Potassii et Sodii Tartras*, U.S.P.) and 50 Gm. of sodium hydroxide (*Sodii Hydroxidum*, U.S.P.) in a sufficient quantity of distilled water to make the solution measure exactly 500 mils at standard temperature. Keep the solution in small, rubber-stoppered bottles. For use, mix exactly equal volumes of the two solutions at the time required.[1]

One Mil of the Mixed Solution is the equivalent of:

	Gramme.
Cupric Sulphate, crystallized, $CuSO_4 + 5H_2O$	0.03466
Cupric Tartrate, $CuC_4H_4O_6 + 3H_2O$	0.03688
Cane Sugar, $C_{12}H_{22}O_{11}$ (after inversion)	0.00475
Glucose, anhydrous, $C_6H_{12}O_6$	0.00500
Milk Sugar, anhydrous, $C_{12}H_{22}O_{11}$	0.00678

Tenth-Normal Barium Hydroxide Volumetric Solution

$Ba(OH)_2 + 8H_2O = 315.51$ 15.776 Gm. in 1000 mils

Dissolve about 18 Gm. of crystallized barium hydroxide in 1000 mils of recently boiled and cooled distilled water, and, if necessary, filter the solution quickly.

Introduce 25 mils of tenth-normal sulphuric acid V.S. or preferably tenth-normal hydrochloric acid V.S. into a flask, add 3 drops of phenolphthalein T.S., and run in the barium hydroxide solution from a burette, provided with a soda-lime tube, reducing the flow to drops towards the end, until a pale pink color is produced which no longer disappears on shaking the liquid for about ten seconds. Note the number of mils of the barium hydroxide solution consumed, and, if the solution is too concentrated, dilute the remainder of the solution with freshly boiled and cooled distilled water, so that equal volumes of the barium hydroxide solution and of tenth-normal sulphuric or hydrochloric acid at 25° C. (77° F.) exactly neutralize each other.

Note.—This solution absorbs carbon dioxide from the air very rapidly, thereby changing its titer. It should, therefore, be preserved in rubber-stoppered bottles provided with a soda-lime tube (see under normal potassium hydroxide V.S.). This solution must also be standardized each time before using.

One Mil of Tenth-Normal Barium Hydroxide V.S. is the equivalent of:

	Gramme.
Barium Hydroxide, $Ba(OH)_2 + 8H_2O$	0.015776
Ammonium Benzoate, $NH_4C_7H_5O_2$	0.013908
Ammonium Salicylate, $NH_4C_7H_5O_3$	0.015508
Benzoic Acid, $C_7H_6O_2$	0.012205
Hydrochloric Acid, HCl	0.003647
Salicylic Acid, $C_7H_6O_3$	0.013805
Sulphuric Acid, H_2SO_4	0.0049045

[1] The accuracy of this solution when employed in titration may be verified as follows: To a solution of 0.95 Gm. of pure cane sugar in about 50 mils of distilled water, add 2 mils of hydrochloric acid and heat at 70° C. (158° F.) for ten minutes. After neutralizing with sodium carbonate, dilute the solution to 1000 mils. Fifty mils of this dilution should reduce the copper in exactly 10 mils of the solution.

Tenth-Normal Bromine Volumetric Solution

[KOPPESCHAAR'S SOLUTION]

Br = 79.92. 7.992 Gm. in 1000 mils.

Dissolve 3 Gm. of potassium bromate (see page 1687) and 50 Gm. of potassium bromide in sufficient distilled water to measure 1000 mils at or near 25° C. (77° F.). Transfer 20 mils of this solution at standard temperature, by means of a pipette, to a bottle having a capacity of about 250 mils, and provided with a glass stopper; add 75 mils of distilled water and 5 mils of hydrochloric acid (see page 33) and immediately insert the stopper. Shake the bottle a few times, then remove the stopper just sufficiently to quickly introduce 5 mils of potassium iodide T.S., taking care that no bromine vapors escape, and immediately stopper the bottle. Agitate the bottle thoroughly, remove the stopper and rinse it and the neck of the bottle with a little distilled water so that the washings flow into the bottle, and then add from a burette tenth-normal sodium thiosulphate V.S. until the solution is only slightly yellow, then add a few drops of starch T.S. and continue the addition of the tenth-normal sodium thiosulphate V.S. until the blue color is just discharged. Note the number of mils of the sodium thiosulphate V.S. thus consumed, and then dilute the bromine solution so that equal volumes of it and of tenth-normal sodium thiosulphate V.S. will exactly correspond to each other under the conditions mentioned above. Keep the solution in dark amber-colored, glass-stoppered bottles.

EXAMPLE: Assuming that the 20 mils of the bromine solution have required 22.5 mils of the sodium thiosulphate V.S. to completely discharge the iodine tint, then each 20 mils of the bromine solution must be diluted to 22.5 mils. Thus, if 960 mils of the solution remain, it must be diluted with distilled water to measure 1080 mils. After the solution is thus diluted, a new trial should be made in the manner above described, in which 25 mils of the tenth-normal sodium thiosulphate V.S. should just discharge the tint of the iodine liberated by the bromine set free from 25 mils of the standard bromine solution.

One Mil of Tenth-Normal Bromine V.S. is the equivalent of:

	Gramme.
Bromine, Br	0.007992
Orcin, $C_7H_6(OH)_2$	0.002068
Phenol, C_6H_5OH	0.001568
Resorcinol, $C_6H_4(OH)_2$	0.001834
Sodium Phenolsulphonate, anhydrous, $NaC_6H_5O_4S$	0.004903
Sodium Phenolsulphonate, crystallized, $NaC_6H_5O_4S+2H_2O$	0.0058035

Normal Hydrochloric Acid Volumetric Solution

HCl = 36.47. 36.47 Gm. in 1000 mils.

Mix 110 mils of hydrochloric acid (*Acidum Hydrochloricum*, U.S.P.) with sufficient distilled water to measure 1000 mils. Of this liquid (which is still too concentrated) carefully measure, at standard temperature from a burette, 25 mils into a flask or porcelain dish, and, after diluting with about double its volume of distilled water, add 2 drops of methyl orange T.S., then gradually add from a burette a freshly standardized normal potassium hydroxide V.S. at the same temperature, until the red or pink tint of the solution changes, after continuous shaking or stirring, to a permanent pale yellow. Note the number of mils of potassium hydroxide V.S. consumed, and then dilute the acid solution so that equal volumes of this and of the normal potassium hydroxide V.S. neutralize each other at 25° C. (77° F.).

EXAMPLE: Assuming that 25 mils of the acid solution first prepared required exactly 27.5 mils of normal potassium hydroxide V.S., each 25 mils of the former must be diluted to 27.5 mils or the whole of the remaining acid solution in the same proportion at standard temperature. Thus, if 950 mils should remain, 95 mils of distilled water must be added. After the liquid is thus diluted, a new trial should be made in the manner above described, in which 25 mils of the acid solution should require for neutralization exactly 25 mils of normal potassium hydroxide V.S. If necessary, a new adjustment should then be made to render the correspondence perfect at standard temperature.

ALTERNATIVE METHOD.—Normal hydrochloric acid V.S. may be standardized as directed under normal sulphuric acid V.S., employing the alternative method.

One Mil of Normal Hydrochloric Acid V.S. is the equivalent of:

	Gramme.
Hydrochloric Acid, HCl	0.03647
Barium Hydroxide, $Ba(OH)_2+8H_2O$	0.15776
Calcium Carbonate, $CaCO_3$	0.050035
Calcium Hydroxide, $Ca(OH)_2$	0.037045
Calcium Oxide, CaO	0.028035
Potassium Hydroxide, KOH	0.05611
Sodium Borate, anhydrous, $Na_2B_4O_7$	0.1010
Sodium Borate, crystallized, $Na_2B_4O_7+10H_2O$	0.19108
Sodium Cacodylate, anhydrous, $Na(CH_3)_2.AsO_2$	0.1600
Sodium Hydroxide, NaOH	0.04001

NOTE: Normal hydrochloric acid is in every respect equivalent in neutralizing power to normal sulphuric acid (see page 1704), and may be employed, except in special cases, for the same purposes.

Half-Normal Hydrochloric Acid Volumetric Solution

HCl = 36.47. 18.235 Gm. in 1000 mils.

Dilute 500 mils of normal hydrochloric acid V.S. at 25° C. (77° F.) with sufficient distilled water to measure at the same temperature exactly 1000 mils.

One Mil of Half-Normal Hydrochloric Acid V.S. is the equivalent of:

	Gramme.
Hydrochloric Acid, HCl	0.018235
Benzaldehyde, C_7H_6O	0.0530
Calcium Lactate, $Ca(C_3H_5O_3)$, anhydrous	0.05454
Cinnamic Aldehyde, C_9H_8O	0.033015
Citral, $C_{10}H_{16}O$	0.076
Lithium Salicylate, $LiC_7H_5O_3$	0.07199
Magnesium Hydroxide, $Mg(OH)_2$	0.0148
Potassium Acetate, $KC_2H_3O_2$	0.04906
Potassium Bicarbonate, $KHCO_3$	0.050055
Potassium Bitartrate, $KHC_4H_4O_6$	0.09407
Potassium Carbonate, anhydrous, K_2CO_3	0.03455
Potassium Citrate, anhydrous, $K_3C_6H_5O_7$	0.051057
Potassium Citrate, crystallized, $K_3C_6H_5O_7+H_2O$	0.05406
Potassium Hydroxide, KOH	0.028055
Potassium and Sodium Tartrate, anhydrous, $KNaC_4H_4O_6$	0.052533
Potassium and Sodium Tartrate, crystallized, $KNaC_4H_4O_6+4H_2O$	0.07055
Sodium Acetate, anhydrous, $NaC_2H_3O_2$	0.04101
Sodium Acetate, crystallized, $NaC_2H_3O_2+3H_2O$	0.068035
Sodium Benzoate, $NaC_7H_5O_2$	0.07202
Sodium Bicarbonate, $NaHCO_3$	0.042005
Sodium Carbonate, anhydrous, Na_2CO_3	0.026500
Sodium Carbonate, monohydrated, $Na_2CO_3+H_2O$	0.031005
Sodium Citrate, anhydrous, $Na_3C_6H_5O_7$	0.04301
Sodium Citrate, crystallized, $Na_3C_6H_5O_7+2H_2O$	0.04901
Sodium Glycerophosphate, $Na_2C_3H_7PO_6$	0.10805
Sodium Hydroxide, NaOH	0.020005
Sodium Salicylate, $NaC_7H_5O_3$	0.08002
Sodium Tartrate, neutral, $Na_2C_4H_4O_6+2H_2O$	0.057515
Strontium Salicylate, anhydrous, $Sr(C_7H_5O_3)_2$	0.09043
Strontium Salicylate, crystallized, $Sr(C_7H_5O_3)_2+2H_2O$	0.099435

Tenth-Normal Iodine Volumetric Solution

I = 126.92. 12.692 Gm. in 1000 mils.

Tenth-normal iodine V.S. may be prepared according to either of the following methods:

I. Dissolve 12.692 Gm. of purified iodine (see page 1683) in a solution of 18 Gm. of potassium iodide in 300 mils of distilled water. Then add sufficient distilled water to make the solution measure exactly 1000 mils at standard temperature. Transfer the solution to glass-stoppered bottles. Unless freshly prepared, its strength should always be determined anew at the time it is used.

II. Tenth-normal iodine V.S. may also be prepared as follows:

Dissolve about 14 Gm. of iodine (*Iodum*, U.S.P.) in a solution of 18 Gm. of potassium iodide (*Potassii Iodidum*, U.S.P.) in about 300 mils of distilled water, diluting finally to 1000 mils. Carefully measure from a burette 25 mils of this solution (which is too concentrated), into a flask, then add gradually and cautiously from a burette tenth-normal sodium thiosulphate V.S. (shaking constantly), until the color of the solution is but slightly yellow, then add a few drops of starch T.S. and continue the addition of the tenth-normal sodium thiosulphate V.S. until the blue color is just discharged. Note the number of mils of the sodium thiosulphate V.S. consumed, and then dilute the iodine solution so that 25 mils will require for decolorization exactly 25 mils of the tenth-normal sodium thiosulphate V.S. at standard temperature.

One Mil of Tenth-Normal Iodine V.S. is the equivalent of:

	Gramme.
Iodine, I	0.012692
Acetone, $(CH_3)_2CO$	0.0009675
Antimony and Potassium Tartrate, crystallized, $K(SbO)C_4H_4O_6+\frac{1}{2}H_2O$	0.016617
Arsenic, in arsenous compounds, As	0.003748
Arsenic Iodide, AsI_3	0.022786
Arsenic Trioxide (Arsenous Acid), As_2O_3	0.004948
Calcium Sulphide, crude, CaS	0.003607
Iron, Fe	0.002792
Mercurous Chloride, HgCl	0.023606
Mercurous Iodide, HgI	0.032752
Mercury (in mercurous compounds), Hg	0.02006
Potassium Sulphite, crystallized, $K_2SO_3+2H_2O$	0.009715
Sodium Bisulphite, $NaHSO_3$	0.005204
Sodium Sulphite, anhydrous, Na_2SO_3	0.006304
Sodium Thiosulphate, anhydrous, $Na_2S_2O_3$	0.015814
Sodium Thiosulphate, crystallized, $Na_2S_2O_3+5H_2O$	0.024822
Sulphur Dioxide, SO_2	0.0032035

Tenth-Normal Oxalic Acid Volumetric Solution

$H_2C_2O_4+2H_2O=126.05$. 6.3025 Gm. in 1000 mils.

Dissolve 6.45 Gm. of purified oxalic acid (see page 1686) in sufficient distilled water to measure 1000 mils. Into a flask accurately measure from a burette 25 mils of a freshly standardized tenth-normal potassium hydroxide V.S., dilute with about 20 mils of distilled water, add 3 to 5 drops of phenolphthalein T.S. and heat it to boiling. From a burette gradually add the oxalic acid solution (which is still too concentrated) until the red tint of the alkali solution fails to reappear after vigorous shaking and boiling. Note the number of mils of the oxalic acid solution consumed, and then dilute it so that equal volumes of this and of the tenth-normal potassium hydroxide V.S. neutralize each other at standard temperature. This volumetric solution deteriorates on standing, hence must be frequently renewed or restandardized.

NOTE: Tenth-normal oxalic acid V.S. is in every respect equivalent in neutralizing power to any other tenth-normal acid V.S. with either litmus or phenolphthalein T.S. as indicator. Its specific use, however, is in standardizing or determining an excess of tenth-normal potassium permanganate V.S.

One Mil of Tenth-Normal Oxalic Acid V.S. is the equivalent of:

	Gramme.
Oxalic Acid, crystallized, $H_2C_2O_4+2H_2O$	0.0063025
Ammonia Gas, NH_3	0.0017034
Calcium Carbonate, $CaCO_3$	0.0050035
Calcium Hydroxide, $Ca(OH)_2$	0.0037045
Calcium Oxide, CaO	0.0028035
Lead, Pb	0.010355
Lead Acetate, $Pb(C_2H_3O_2)_2$	0.016257
Lead Oxide, PbO	0.011155
Lead Peroxide, PbO_2	0.011955
Lead Subacetate, $Pb_2O(C_2H_3O_2)_2$	0.013706
Manganese Dioxide, MnO_2	0.0043465
Potassium Hydroxide, KOH	0.005611
Potassium Permanganate, $KMnO_4$	0.0031606
Sodium Hydroxide, NaOH	0.004001

Tenth-Normal Potassium Dichromate Volumetric Solution

$K_2Cr_2O_7=294.20$. 4.9033 Gm. in 1000 mils.

Dissolve 4.9033 Gm. of purified potassium dichromate (see page 1687), which has been pulverized and dried to constant weight at 120° C. (248° F.), in sufficient distilled water to measure exactly 1000 mils at standard temperature. When used as an oxidizing agent in titration to convert ferrous into ferric salts, or to liberate iodine from potassium iodide, the solution just mentioned (containing 14.710 Gm. in 1000 mils) has the effect of a $\frac{3N}{10}$ volumetric solution, and a solution of one-third of this strength, containing 4.9033 Gm. in 1000 mils, has the value of a tenth-normal solution, and is the equivalent of an equal volume of tenth-normal potassium permanganate V.S., or, in the case of iodine liberated from potassium iodide, it is the equivalent of an equal volume of tenth-normal sodium thiosulphate V.S. For titrating iron in ferrous compounds, it is used in the following manner. Introduce the aqueous solution of the ferrous salt into a flask and, if it is not already acid, render it so with sulphuric acid. Now add gradually tenth-normal potassium dichromate V.S. from a burette with agitation until a drop taken out upon a white surface no longer becomes blue when mixed with a drop of freshly prepared potassium ferricyanide T.S. Tenth-normal potassium dichromate V.S. may also be used in conjunction with potassium iodide (from which it liberates iodine) and sulphuric acid, for adjusting the titer of sodium thiosulphate V.S., and thus that of the iodine V.S.

One Mil of Tenth-Normal Potassium Dichromate V.S. is the equivalent of:

	Gramme.
Potassium Dichromate, $K_2Cr_2O_7$	0.0049033
Ferrous Carbonate, $FeCO_3$	0.011584
Ferrous Sulphate, anhydrous, $FeSO_4$	0.015191
Ferrous Sulphate, crystallized, $FeSO_4+7H_2O$	0.027802
Iron, in ferrous compounds, Fe	0.005584
Sodium Thiosulphate, $Na_2S_2O_3+5H_2O$	0.024822

Normal Potassium Hydroxide Volumetric Solution

$KOH=56.11$. 56.11 Gm. in 1000 mils.

Dissolve 75 Gm. of potassium hydroxide (see page 899) in sufficient recently boiled distilled water to measure about 1050 mils and fill a burette with a portion of this liquid. Into a flask of the capacity of about 300 mils, introduce 4.7035 Gm. of potassium bitartrate (which has been purified and dried as directed on page 1687) followed by 15 mils (accurately measured at 25° C. (77° F.)) of the potassium hydroxide solution which is being prepared and 80 mils of distilled water. Heat the solution to boiling, add from 3 to 5 drops of phenolphthalein T.S. and then cautiously, at standard temperature from a burette, further portions of the potassium hydroxide solution. Agitate the flask frequently, boil the liquid toward the end of the operation and reduce the flow of potassium hydroxide solution to drops, until the red color produced by its influx no longer disappears on shaking, and the liquid is not deeper in color than a pale pink. Note the total number of mils of the potassium hydroxide solution consumed, and then dilute the remainder of the solution so that exactly 25 mils of the diluted liquid, at standard temperature. shall be required to neutralize 4.7035 Gm. of the purified and dried potassium bitartrate.

EXAMPLE: Assuming that 20 mils of the stronger solution of potassium hydroxide first prepared had been consumed in the trial, then each 20 mils must be diluted to 25 mils or the whole of the remaining solution in the same proportion at standard temperature. Thus, if 1000 mils should be still remaining, this must be diluted with water to 1250 mils. After the liquid is thus diluted, a new trial should be made in the manner above described, in which 25 mils of the diluted solution should exactly neutralize 4.7035 Gm. of potassium bitartrate at standard temperature. If necessary, a new adjustment should then be made to render the correspondence perfect.

ALTERNATIVE METHOD.—Normal potassium or sodium hydroxide V.S. may be standardized against normal sulphuric acid V.S. which has been standardized by its alternative method, employing the trial solution directed in the first paragraph. Measure accurately 25 mils of this solution, at standard temperature, from a burette into a flask, add 2 drops of methyl orange T.S. or methyl red T.S., and afterwards from a burette the standard normal sulphuric acid V.S. at the same temperature, shaking after each addition, and, toward the end of the operation, reducing the flow to drops, until the yellow tint of the solution changes to a permanent rose after shaking. Note the number of mils of normal sulphuric acid V.S. consumed. Then dilute the potassium hydroxide solution so that 25 mils of this and 25 mils of the normal sulphuric acid V.S., at standard temperature, exactly neutralize each other.

NOTE: Solutions of caustic alkalies absorb carbon dioxide from the atmosphere, and thereby change their titer when used with litmus T.S., or phenolphthalein T.S. (in cold solution), as indicator (methyl orange T.S. is not affected by the presence of carbonic acid). Hence the volumetric solutions should be preserved in bottles provided with well-fitting rubber stoppers, or, better still, these should be provided with the tubes filled with soda-lime (a mixture of caustic soda and lime); the tubes pass through a perforation in the rubber stoppers and thus absorb the carbon dioxide and prevent its access to the solution. If the solution is kept in a burette for more than a few minutes, the same provision with a soda-lime tube should be observed. In place of potassium hydroxide V.S., sodium hydroxide V.S. (see page 1703) may be used, in the same manner and in the same quantity.

One Mil of Normal Potassium Hydroxide V.S. is the equivalent of:

	Gramme.
Potassium Hydroxide, KOH	0.05611
Acetic Acid, $HC_2H_3O_2$	0.06003
Acetic Acid Anhydride, $(CH_3CO)_2O$	0.05102
Ammonia Gas, NH_3	0.01703
Ammonium Chloride, NH_4Cl	0.05350
Boric Acid, H_3BO_3	0.06202
Citric Acid, crystallized, $H_3C_6H_5O_7+H_2O$	0.07003
Formaldehyde, CH_2O	0.03002
Hydrated Chloral, $C_2HOCl_3+H_2O$	0.1654
Hydriodic Acid, HI	0.12793
Hydrobromic Acid, HBr	0.08093
Hydrochloric Acid, HCl	0.03647
Hypophosphorous Acid, HPH_2O_2	0.06606
Lactic Acid, $HC_3H_5O_3$	0.09005
Nitric Acid, HNO_3	0.06302
Oxalic Acid, crystallized, $H_2C_2O_4+2H_2O$	0.063025
Paraformaldehyde, $(CH_2O)_3$	0.03002
Phosphoric Acid, H_3PO_4 (to form K_2HPO_4; with phenolphthalein)	0.04903
Potassium Bitartrate, $KHC_4H_4O_6$	0.18814
Sodium Bitartrate, $NaHC_4H_4O_6+H_2O$	0.19006
Sodium Hydroxide, NaOH	0.04001
Sulphuric Acid, H_2SO_4	0.049045
Sulphuric Anhydride, SO_3	0.040035
Tartaric Acid, $H_2C_4H_4O_6$	0.07503
Trichloracetic Acid, $HC_2O_2Cl_3$	0.16339

Half-Normal Potassium Hydroxide Volumetric Solution

KOH = 56.11. 28.055 Gm. in 1000 mils.

Dilute 500 mils of freshly standardized normal potassium hydroxide V.S., at standard temperature, with sufficient recently boiled distilled water at the same temperature to measure exactly 1000 mils. This solution may also be prepared and standardized directly with potassium bitartrate, as directed under normal potassium hydroxide V.S., employing for this purpose 2.3518 Gm. of the former and a solution of about 35 Gm. of potassium hydroxide (*Potassii Hydroxidum*, U.S.P.) in 1000 mils of distilled water. Twenty-five mils of half-normal solution, at standard temperature, should exactly neutralize 2.3518 Gm. of potassium bitartrate (see page 1687). The solution may also be standardized by comparison with half-normal sulphuric acid V.S., employing methyl orange T.S. as indicator.

NOTE: The same precautions should be taken for protecting this solution from carbon dioxide of the air as are directed under normal potassium hydroxide V.S.

One Mil of Half-Normal Potassium Hydroxide V.S. is the equivalent of:

	Gramme.
Potassium Hydroxide, KOH	0.02806
Acetic Acid, $HC_2H_3O_2$	0.03002
Boric Acid, H_3BO_3	0.03101
Citric Acid, crystallized, $H_3C_6H_5O_7+H_2O$	0.03502

	Gramme.
Hydriodic Acid, HI	0.06397
Hydrobromic Acid, HBr	0.04047
Hydrochloric Acid, HCl	0.01824
Hypophosphorous Acid, HPH_2O_2	0.03303
Lactic Acid, $HC_3H_5O_3$	0.04503
Nitric Acid, HNO_3	0.03151
Oxalic Acid, crystallized, $H_2C_2O_4+2H_2O$	0.03153
Phosphoric Acid, H_3PO_4 (to form K_2HPO_4, with phenolphthalein)	0.02452
Potassium Bitartrate, $KHC_4H_4O_6$	0.09407
Sodium Bitartrate, $NaHC_4H_4O_6+H_2O$	0.09503
Sodium Hydroxide, NaOH	0.020005
Sulphuric Acid, H_2SO_4	0.024523
Sulphuric Anhydride, SO_3	0.02002
Tartaric Acid, crystallized, $H_2C_4H_4O_6$	0.03751
Trichloracetic Acid, $HC_2O_2Cl_3$	0.08170

Tenth-Normal Potassium Hydroxide Volumetric Solution

KOH = 56.11. 5.611 Gm. in 1000 mils.

Dilute 100 mils of freshly standardized normal potassium hydroxide V.S., at standard temperature, with sufficient recently boiled distilled water at the same temperature to measure exactly 1000 mils. This solution may also be prepared and standardized directly with potassium bitartrate, as directed under normal potassium hydroxide V.S., employing for this purpose 0.9407 Gm. of the bitartrate and a solution of about 7.5 Gm. of potassium hydroxide (*Potassii Hydroxidum*, U.S.P.) in 1000 mils of distilled water. Fifty mils of tenth-normal solution, at standard temperature, should exactly neutralize 0.9407 Gm. of potassium bitartrate (see page 1687). This solution may also be standardized by comparison with tenth-normal sulphuric acid V.S., employing methyl orange T.S. as indicator.

NOTE: The same precautions should be taken for protecting this solution from carbon dioxide of the air as are directed under normal potassium hydroxide V.S.

One Mil of Tenth-Normal Potassium Hydroxide V.S. is the equivalent of:

	Gramme.
Potassium Hydroxide, KOH	0.005611
Betaeucaine Hydrochloride, $C_{15}H_{21}O_2N.HCl$	0.028365
Lactic Acid, $HC_3H_5O_3$	0.009005
Potassium Bitartrate, $KHC_4H_4O_6$	0.018814
Sulphuric Acid, H_2SO_4	0.0049045

Fiftieth-Normal Potassium Hydroxide Volumetric Solution

KOH = 56.11. 1.1222 Gm. in 1000 mils.

Dilute 20 mils of a freshly standardized normal or preferably 200 mils of tenth-normal potassium hydroxide V.S., at standard temperature, with sufficient recently boiled distilled water at the same temperature to measure exactly 1000 mils. Verify the titer of this solution by titrating 0.1881 Gm. of potassium bitartrate (see page 1687) which should require for neutralization exactly 50 mils of the volumetric solution. This standard solution is employed in conjunction with the tenth-normal sulphuric acid V.S. in the titration of alkaloids, with hematoxylin, cochineal, methyl red, or iodeosin T.S. as indicators. The relative value of these two volumetric solutions should be determined each time, using the indicator employed in the alkaloidal assay.

NOTE: The same precautions should be taken for protecting this solution from carbon dioxide of the air as are directed under normal potassium hydroxide V.S. It should be renewed at frequent intervals.

One Mil of Fiftieth-Normal Potassium Hydroxide V.S. is the equivalent of:

	Gramme.
Potassium Hydroxide, KOH	0.0011222
Potassium Bitartrate, $KHC_4H_4O_6$	0.0037628
Sulphuric Acid, H_2SO_4	0.0009809

Hundredth-Normal Potassium Hydroxide Volumetric Solution

KOH = 56.11. 0.5611 Gm. in 1000 mils.

Dilute 10 mils of normal or preferably 100 mils of tenth-normal potassium hydroxide V.S., at standard temperature, with sufficient recently boiled distilled water at the same temperature to measure exactly 1000 mils. Verify the titer of this solution by titrating 0.0941 Gm. of potassium bitartrate (see page 1687), which should require for neutralization exactly 50 mils of the volumetric solution at standard temperature. This solution must be frequently renewed.

One Mil of Hundredth-Normal Potassium Hydroxide V.S. is the equivalent of:

	Gramme.
Potassium Hydroxide, KOH	0.0005611
Potassium Bitartrate, $KHC_4H_4O_6$	0.0018814
Sulphuric Acid, H_2SO_4	0.00049045

Half-Normal Alcoholic Potassium Hydroxide Volumetric Solution

KOH = 56.11. 28.055 Gm. in 1000 mils.

Dissolve from 2 to 3 Gm. of silver nitrate in 5 mils of distilled water and add the solution to 1200 mils of alcohol (*Alcohol*, U.S.P.) in a glass-stoppered bottle, and mix thoroughly. Dissolve about 5 Gm. of potassium hydroxide (see page 899) in 25 mils of warm alcohol, cool the solution, and pour it slowly without stirring, into the alcoholic solution of silver nitrate. Let the mixture stand until the precipitated silver oxide has settled, filter and distil. Dissolve about 35 Gm. of potassium hydroxide (see page 899) in 20 mils of distilled water and add sufficient alcohol, purified as directed above, to measure 1000 mils. Let the solution stand in a glass-stoppered or rubber-stoppered bottle for one day, then quickly decant the clear, supernatant solution into a bottle provided with a well-fitted rubber stopper. Into a flask of the capacity of about 300 mils introduce 2.3518 Gm. of potassium bitartrate, which has been purified and dried, as directed on page 1687, and about 100 mils of distilled water. Heat the solution to the boiling point, add about 5 drops of phenolphthalein T.S., then run in cautiously at standard temperature from a burette the potassium hydroxide solution prepared as above, keeping the liquid hot and frequently agitating the flask, and, toward the end of the operation, reducing the flow to drops until the red color produced by its influx no longer disappears on shaking, and the liquid is not deeper than pale pink. Note the number of mils of the alcoholic potassium hydroxide solution consumed, and then dilute the remainder of the solution with alcohol purified as directed above, so that exactly 25 mils of the diluted liquid, at standard temperature, shall be required to neutralize 2.3518 Gm. of potassium bitartrate.

Half-normal alcoholic potassium hydroxide V.S. may also be standardized as follows: Of the above described concentrated alcoholic potassium hydroxide solution, carefully measure, at standard temperature, from a burette 30 mils into a flask, and, after diluting with about 50 mils of distilled water, add about 5 drops of phenolphthalein T.S., heat to boiling temperature, and add from a burette half-normal hydrochloric acid V.S., at standard temperature, frequently agitating the flask, and, toward the end of the operation, reducing the flow to drops until the red color of the liquid is just discharged. Note the number of mils of the half-normal hydrochloric acid V.S. consumed, and then dilute the remainder of the solution with the purified alcohol so that 25 mils of this and 25 mils of half-normal hydrochloric acid V.S., at standard temperature, neutralize each other. Should half-normal hydrochloric acid V.S. not be available, standardization can be carried out in the same manner with normal hydrochloric acid V.S., two volumes of the alcoholic potassium hydroxide being made to correspond with one volume of the normal acid.

NOTE: This solution should be kept in bottles provided with well-fitted rubber stoppers and protected from the light. Owing to the readiness with which this standard solution loses its titer blank tests should be performed whenever it is employed in titrations. It is important that this volumetric solution be standardized at the temperature at which it is used.

One Mil of Half-Normal Alcoholic Potassium Hydroxide V.S. is the equivalent of:

	Grams.
Potassium Hydroxide, KOH	0.028055
Borneol, $C_{10}H_{18}O$	0.07707
Bornyl Acetate, $C_{10}H_{17}.C_2H_3O_2$	0.09808
Menthol, $C_{10}H_{20}O$	0.07808
Menthyl Acetate, $C_{10}H_{19}.C_2H_3O_2$	0.09909
Methyl Salicylate, $CH_3.C_7H_5O_3$	0.07603
Potassium Bitartrate, $KHC_4H_4O_6$	0.09407
Santalol, $C_{15}H_{26}O$	0.111105

Tenth-Normal Potassium Permanganate Volumetric Solution

$KMnO_4$ = 158.03. 3.1606 Gm. in 1000 mils.

Introduce about 3.3 Gm. of crystallized potassium permanganate (*Potassii Permanganas*, U.S.P.) into a flask, add 1000 mils of distilled water, and boil for about five minutes. Close the flask with a plug of purified absorbent cotton, and set it aside for at least two days, so that suspended matter may deposit. After the lapse of this time, pour off the clear portion of the solution into a glass-stoppered bottle. The water to be employed for diluting this solution (which is still too concentrated) should be prepared as directed under distilled water (*Aqua Destillata*, U.S.P.), adding, however, about 1 Gm. of potassium permanganate to each liter of water in the retort before beginning the distillation.

The solution may be standardized as follows:

I. Introduce about 0.3 Gm. of sodium oxalate (see page 1690), previously dried to constant weight at 110° C. (230° F.) and accurately weighed, into a beaker of about 400 mils capacity. Dissolve the salt in 250 mils of distilled water, heated to 85° C. (185° F.) and add 5 mils of concentrated sulphuric acid (see page 1692) diluted with an equal volume of distilled water. To this solution, kept at 85° C. (185° F.), add, from a burette, the permanganate solution to be standardized, stirring vigorously and continually with a thermometer, the solution being added not faster than at the rate of from 10 to 15 mils per minute. The last 0.5 to 1 mil of the solution required must be added, drop by drop, with particular care to see that each drop is fully decolorized before introducing the next. When the solution has assumed a faintly pink tint (remaining permanent for thirty seconds), the titration should cease. The excess of permanganate solution required to cause an end-point color must be estimated by matching the color of the liquid being tested with a measured quantity of the same permanganate solution in another beaker containing the same volumes of hot distilled water and sulphuric acid. Note the number of mils of the permanganate solution consumed in the trial titration and deduct from this volume the amount of permanganate solution required to produce the same tint in the water and acid mixture; the difference represents the number of mils of the permanganate solution required to reach the exact end-point in the trial titration.

Each 0.0067 Gm. of sodium oxalate is equivalent to 1 mil of tenth-normal potassium permanganate V.S. The number of grammes of sodium oxalate taken, when multiplied by 149.2537, indicates the number of mils of tenth-normal potassium permanganate V.S. required. The solution may now be adjusted to exactly tenth-normal strength or the factor may be determined and the solution employed empirically. In the former instance note the number of mils of the trial permanganate solution consumed, then dilute it so that the volume of diluted solution corresponds to that obtained by calculation from the sodium oxalate taken.

EXAMPLE: Assuming that 0.25 Gm. of sodium oxalate was taken, and 35.2 mils of the trial potassium permanganate solution was consumed. Then $0.25 \times 149.2537 = 37.313$, and therefore 35.2 mils (or 352 mils) of the trial potassium permanganate solution are diluted to 37.3 mils (or 373.13 mils). The factor of this trial solution for use as an empirical solution may be determined by dividing the number of mils of the trial permanganate solution consumed, by the number of mils representing the true equivalent volume (product of 149.2537 × the grammes of sodium oxalate used). $37.313 \div 35.2 = 106.00$, which is the percentage strength of the solution based upon the true tenth-normal V.S.

II. Tenth-normal potassium permanganate V.S. may also be standardized as follows:

To a solution of about 1 Gm. of potassium iodide (*Potassii Iodidum*, U.S.P.) in 10 mils of diluted sulphuric acid contained in a flask, slowly add from a burette 25 mils of the potassium permanganate solution to be standardized; mix well, then dilute the mixture at once with about 200 mils of distilled water. Add slowly an accurately standardized tenth-normal sodium thiosulphate V.S. from a burette, shaking the mixture vigorously, until the liquid is but slightly yellow, then add a few drops of starch T.S. and continue the addition of the tenth-normal sodium thiosulphate V.S. until the blue color is just discharged. Note the number of mils of the latter consumed, then dilute the permanganate solution so that 25 mils of the solution corresponds to 25 mils of the tenth-normal sodium thiosulphate V.S. under the same conditions at standard temperature. At least three careful titrations should be made, accepting the average, before diluting.

EXAMPLE: Assuming that 25 mils of the tenth-normal sodium thiosulphate V.S. was required to decolorize the iodine liberated by 20 mils of the permanganate solution, then each 20 mils of the potassium permanganate solution remaining must be diluted with the specially prepared distilled water to 25 mils, or the whole of the remaining solution in the same proportion. Thus, if 920 mils remain, it should be diluted, at standard temperature, to measure 1150 mils. After the potassium permanganate solution is thus diluted, a new trial should be made in the manner above described, in which 25 mils of this solution should require exactly 25 mils of the tenth-normal sodium thiosulphate V.S. to decolorize the mixture.

NOTE: When potassium permanganate V.S. is to be prepared for immediate use, this may be done as follows: Dissolve about 3.3 Gm. of crystallized potassium permanganate in 1000 mils of recently boiled and cooled distilled water. Then standardize this by either of the above methods and dilute accordingly with recently boiled and cooled distilled water. Potassium permanganate V.S. made by this method, without the preliminary boiling and standing, deteriorates readily, hence the titer should be verified each time it is used. Potassium permanganate V.S. should be kept in well-closed glass-stoppered bottles, and burettes provided with glass stop-cocks must be employed in titrating with it. This solution should be restandardized frequently.

One Mil of Tenth-Normal Potassium Permanganate V.S. is the equivalent of:

	Gramme.
Potassium Permanganate, $KMnO_4$	0.0031606
Calcium Oxide, CaO (as oxalate)	0.0028035
Ferrous Carbonate, $FeCO_3$	0.011584
Ferrous Oxide, FeO	0.007184
Ferrous Sulphate, anhydrous, $FeSO_4$	0.015191
Ferrous Sulphate, crystals, $FeSO_4+7H_2O$	0.027802
Hydrogen Dioxide, H_2O_2	0.0017008
Iron, in ferrous compounds, Fe	0.005584
Oxalic Acid, crystallized, $H_2C_2O_4+2H_2O$	0.0063025
Oxygen, O	0.0008
Potassium Chlorate, $KClO_3$	0.0020427
Sodium Chlorate, $NaClO_3$	0.0017743
Sodium Nitrite, $NaNO_2$	0.0034505
Sodium Oxalate, $Na_2C_2O_4$	0.0067

Tenth-Normal Potassium Sulphocyanate Volumetric Solution

[VOLHARD'S SOLUTION]

KCNS = 97.18. 9.718 Gm. in 1000 mils.

Dissolve 11 Gm. of crystals of potassium sulphocyanate (see page 1688) in 1000 mils of distilled water. This solution is too concentrated and has to be adjusted so as to correspond in strength exactly with tenth-normal silver nitrate V.S. For this purpose, introduce into a flask 10 mils of tenth-normal silver nitrate V.S., 3 mils of ferric ammonium sulphate T.S., and 3 mils of nitric acid (free from nitrous compounds) and dilute the liquid with about 100 mils of distilled water. To this mixture add the sulphocyanate solution from a burette in small portions at a time. At first, a white precipitate of silver sulphocyanate appears, then every drop falling from the burette is surrounded by a deep brownish-red color produced by ferric sulphocyanate which disappears on vigorous shaking of the flask as long as any of the silver nitrate remains unchanged. When all of the silver has been converted into sulphocyanate, a single additional drop of the potassium sulphocyanate solution produces a brownish-red color which no longer disappears on shaking, but communicates a perceptible pale reddish-brown tint to the contents of the flask. Note the number of mils of the potassium sulphocyanate solution used and, after having confirmed the accuracy of the titration, dilute the whole of the remaining solution so that equal volumes of this and of the tenth-normal silver

nitrate V.S., at standard temperature, will be required to produce the permanent reddish-brown tint. (The same depth of pale reddish-brown tint to which the volumetric solution is adjusted must be attained when the solution is used for volumetric assays.) After the dilution, a new trial should be made, in which 25 mils of tenth-normal silver nitrate V.S., at standard temperature, 5 mils of ferric ammonium sulphate T.S., 5 mils of nitric acid, and 200 mils of distilled water are used, and there should be required of the potassium sulphocyanate solution, exactly the same number of mils as of the silver nitrate solution, at standard temperature, to produce the same depth of a permanent pale reddish-brown tint. If necessary a new adjustment should be made to render the correspondence perfect.

One Mil of Tenth-Normal Potassium Sulphocyanate V.S. is the equivalent of:

	Gramme.
Potassium Sulphocyanate, KSCN	0.009718
Mercuric Iodide, HgI_2	0.022722
Mercuric Nitrate, $Hg(NO_3)_2$	0.016231
Mercuric Oxide, HgO	0.01083
Mercury, Hg	0.01003
Silver, Ag	0.010788
Silver Nitrate, $AgNO_3$	0.016989
Silver Oxide, Ag_2O	0.011588

Tenth-Normal Silver Nitrate Volumetric Solution

$AgNO_3 = 169.89.$ 16.989 Gm. in 1000 mils.

Into a flask containing 10.788 Gm. of silver (see page 1688), and provided with a small funnel inserted into the neck to prevent loss by spurting, introduce gradually about 30 mils of nitric acid (*Acidum Nitricum*, U.S.P.) or sufficient for complete solution. After thoroughly rinsing the funnel inside and outside, transfer the solution, which should be clear, with the rinsings of the flask to a beaker or porcelain dish and evaporate it to dryness on a water bath, carefully protecting the vessel from dust. Then after drying in an air-oven at about 120° C. (248° F.) for ten minutes, dissolve the residue in sufficient distilled water to measure exactly 1000 mils at standard temperature. Keep the solution in dark amber-colored, glass-stoppered vials, carefully protected from dust and sunlight.

NOTE: Titration by tenth-normal silver nitrate V.S. may be conducted in various ways, adapted to the special preparation to be tested.

A. The titration of soluble chlorides and bromides.—To the strictly neutral (to litmus) solution of an accurately weighed quantity of the salt contained in either a porcelain dish or a flask placed on a white surface add sufficient potassium chromate T.S. to impart a yellow tint, then slowly add the tenth-normal silver nitrate V.S. from a burette, stirring or agitating constantly until the mixture acquires a permanent red tint, due to the formation of red silver chromate. This method is only suitable for neutral solutions.

B. The titration of free hydrobromic, hydrochloric, and hydriodic acids or their salts in acid solution, known as the Volhard, Thiocyanate, or Sulphocyanate method of residual titration.—Add an accurately measured excess of tenth-normal silver nitrate V.S. to the solution of the halogen acid or its salt, and then acidify with nitric acid, and add a few mils of ferric ammonium sulphate T.S.; then determine the uncombined excess of the silver nitrate V.S. by titrating back with tenth-normal potassium sulphocyanate V.S., the end-reaction being the formation of a permanent pale reddish tint. The volume of the silver nitrate V.S. originally added, less that of the potassium sulphocyanate V.S. consumed, will give the number of mils of the former which were required for the precipitation of the halogen. The quantity of nitric acid added should be sufficient to remove the yellow color produced by the addition of the indicator.

C. Titration until the first appearance of a permanent precipitate.—This method is applicable in the estimation of the alkali cyanides and hydrocyanic acid. When the solution is used by this method, it is a fifth-normal instead of a tenth-normal solution.

One Mil of Tenth-Normal Silver Nitrate V.S. is the equivalent of:

	Gramme.
Silver Nitrate, $AgNO_3$	0.016989
Allyl Iso-thiocyanate, C_3H_5SCN	0.004956
Ammonium Bromide, NH_4Br	0.009796
Ammonium Chloride, NH_4Cl	0.005350
Ammonium Iodide, NH_4I	0.014496
Arsenous Iodide, AsI_3	0.015191
Bromine, Br	0.007992
Calcium Bromide, anhydrous, $CaBr_2$	0.0099955
Calcium Bromide, $CaBr_2+2H_2O$	0.0011798
Calcium Chloride, anhydrous, $CaCl_2$	0.00555
Calcium Chloride, $CaCl_2+2H_2O$	0.0073511
Calcium Hypophosphite, $Ca(PH_2O_2)_2$	0.002836
Chlorine, Cl	0.003546
Ferrous Bromide, anhydrous, $FeBr_2$	0.010784
Ferrous Iodide, FeI_2	0.015484
Hydriodic Acid, HI	0.012793
Hydrobromic Acid, HBr	0.008093
Hydrochloric Acid, HCl	0.003647
Hydrocyanic Acid, HCN, to first formation of precipitate	0.005404
Hydrocyanic Acid, HCN, potassium chromate as indicator	0.002702
Iodine, I	0.012692

	Gramme.
Lithium Bromide, LiBr	0.008686
Lithium Chloride, LiCl	0.004240
Phosphoric Acid, H_3PO_4	0.0032687
Potassium Bromide, KBr	0.011902
Potassium Chloride, KCl	0.007456
Potassium Cyanide, KCN, to first formation of precipitate	0.013022
Potassium Hypophosphite, KPH_2O_2	0.003472
Potassium Iodide, KI	0.016602
Potassium Nitrate, KNO_3	0.010111
Potassium Sulphocyanate, KCNS	0.009718
Sodium Bromide, NaBr	0.010292
Sodium Chloride, NaCl	0.005846
Sodium Cyanide, NaCN, to first formation of precipitate	0.009802
Sodium Hypophosphite, $NaPH_2O_2+H_2O$	0.0035357
Sodium Iodide, NaI	0.014992
Sodium Nitrate, $NaNO_3$	0.008501
Sodium Phosphate, anhydrous, Na_2HPO_4	0.004735
Sodium Phosphate, crystallized, $Na_2HPO_4+12H_2O$	0.011941
Strontium Bromide, $SrBr_2+6H_2O$	0.017779
Strontium Chloride, $SrCl_2+6H_2O$	0.013332
Strontium Iodide, SrI_2+6H_2O	0.022479
Zinc Chloride, $ZnCl_2$	0.0068145

Hundredth-Normal Silver Nitrate Volumetric Solution

$AgNO_3=169.89.$ 1.6989 Gm. in 1000 mils.

Dilute, at standard temperature, exactly 100 mils of tenth-normal silver nitrate V.S. with sufficient distilled water at the same temperature to measure 1000 mils.

This solution should be kept in glass-stoppered, amber-colored bottles which have been rinsed with nitric acid and then with hot distilled water until all traces of the acid have been removed.

One Mil of Hundredth-Normal Silver Nitrate V.S. is the equivalent of:

	Gramme.
Sodium Chloride, NaCl	0.0005846

Tenth-Normal Sodium Chloride Volumetric Solution

$NaCl=58.46.$ 5.846 Gm. in 1000 mils.

Dissolve 5.846 Gm. of sodium chloride (see page 1690) in sufficient distilled water to measure exactly 1000 mils at standard temperature.

Tenth-normal sodium chloride V.S. should correspond, volume for volume, with tenth-normal silver nitrate V.S., by titrating 20 mils of the former with the latter, using potassium chromate as indicator.

One Mil of Tenth-Normal Sodium Chloride V.S. is the equivalent of:

	Gramme.
Sodium Chloride, NaCl	0.005846
Silver, Ag	0.010788
Silver Nitrate, $AgNO_3$	0.016989
Silver Oxide, Ag_2O	0.011588

Double-Normal Sodium Hydroxide Volumetric Solution

$NaOH=40.01.$ 80.02 Gm. in 1000 mils.

Dissolve 90 Gm. of sodium hydroxide (*Sodii Hydroxidum*, U.S.P.) in sufficient recently boiled distilled water to measure about 1000 mils.

For the standardization of this trial solution of sodium hydroxide proceed as directed under normal potassium hydroxide V.S. (see page 1697); each 25 mils of the volumetric solution, at standard temperature, should exactly neutralize 9.407 Gm. of potassium bitartrate (see page 1687) or 50 mils of normal sulphuric acid V.S. (see page 1704).

NOTE: The same precautions should be taken for protecting this solution from the carbon dioxide of the air as are prescribed for normal potassium hydroxide V.S. (see page 1697).

Normal Sodium Hydroxide Volumetric Solution

$NaOH=40.01.$ 40.01 Gm. in 1000 mils.

Dissolve 50 Gm. of sodium hydroxide (*Sodii Hydroxidum*, U.S.P.) in sufficient recently boiled distilled water to measure about 1050 mils. For the standardization of this trial solution of sodium hydroxide, proceed as directed under normal potassium hydroxide V.S. (see page 1697); 25 mils of the volumetric solution, at standard temperature, must exactly neutralize 4.7035 Gm. of potassium bitartrate or 25 mils of normal sulphuric acid V.S. (see page 1704).

NOTE: The same precautions should be taken for protecting this solution from the carbon dioxide of

the air as are prescribed for normal potassium hydroxide V.S. (see page 1698). This solution may be employed in place of the normal potassium hydroxide V.S. (see page 1697), volume for volume.

One Mil of Normal Sodium Hydroxide V.S. is the equivalent of:

	Gramme.
Sodium Hydroxide, NaOH	0.04001
Boric Acid, H_3BO_3	0.06202
Formaldehyde, CH_2O	0.03002
Trichloracetic Acid, $HC_2O_2Cl_3$	0.16339

Tenth-Normal Sodium Thiosulphate Volumetric Solution

$Na_2S_2O_3+5H_2O=248.22.$ 24.822 Gm. in 1000 mils.

Dissolve 30 Gm. of sodium thiosulphate (see page 1691) in sufficient distilled water, previously boiled for twenty minutes in a flask of hard glass and quickly cooled, to measure 1000 mils. This trial solution, which is too concentrated, is standardized as follows:

To 25 mils of tenth-normal potassium dichromate V.S., accurately measured, at standard temperature, into a glass-stoppered flask of about 500 mils capacity, add about 2 Gm. of potassium iodide (*Potassii Iodidum*, U.S.P.) (free from iodate), followed by 10 mils of diluted sulphuric acid. Rinse the walls of the flask cautiously with about 200 mils of cold distilled water poured in carefully so as not to mix, thus protecting the lower layer from loss of iodine. Stopper the flask securely and set it aside for half an hour in a dark place, then carefully rinse the stopper and sides of the flask with distilled water and add slowly the trial solution of sodium thiosulphate, at standard temperature, while rotating the flask gently. When the solution has assumed a yellowish-green color, add starch T.S. and then reduce the flow of the sodium thiosulphate solution to drops, constantly shaking until the blue color of the mixture changes to a light green; note the number of mils of the trial sodium thiosulphate solution consumed. Then dilute the sodium thiosulphate solution with distilled water which has been previously boiled for twenty minutes so that equal volumes of it and the tenth-normal potassium dichromate V.S. will exactly correspond to each other under the above conditions, at standard temperature.

NOTE: The same precautions should be taken for keeping and protecting this solution from the carbon dioxide of the air as are directed under normal potassium hydroxide V.S. (see page 1698).

One Mil of Tenth-Normal Sodium Thiosulphate V.S. is the equivalent of:

	Gramme.
Sodium Thiosulphate $Na_2S_2O_3+5H_2O$	0.024822
Bromine, Br	0.007992
Chlorine, Cl	0.003546
Chromium Trioxide, CrO_3	0.003333
Copper Sulphate, anhydrous, $CuSO_4$	0.015964
Copper Sulphate, crystallized, $CuSO_4+5H_2O$	0.024972
Iodine, I	0.012692
Iodine, I (Thymol Iodide)	0.002115
Iron, Fe, in ferric salts	0.005584
Lead Peroxide, PbO_2	0.01195
Potassium Bromate, $KBrO_3$	0.0027837
Potassium Dichromate, $K_2Cr_2O_7$	0.0049033
Sodium Arsenate, anhydrous, Na_2HAsO_4	0.0092985
Sodium Arsenate, crystallized, $Na_2HAsO_4+7H_2O$	0.015604

Two-Hundredth-Normal Sodium Thiosulphate Volumetric Solution

$Na_2S_2O_3+5H_2O=248.22.$ 1.2411 Gm. in 1000 mils.

Dilute exactly 25 mils, at standard temperature, of tenth-normal sodium thiosulphate V.S. with sufficient distilled water at the same temperature and recently boiled for twenty minutes to measure 500 mils. If desired, this solution may be standardized in the manner described under tenth-normal sodium thiosulphate V.S. (see above), employing 5 mils of tenth-normal potassium dichromate V.S. which should require for the decolorization of the liberated iodine, 100 mils of the two-hundredth-normal sodium thiosulphate V.S. The same precautions should be observed in the preservation of this solution as directed under tenth-normal sodium thiosulphate V.S.

One Mil of Two-Hundredth-Normal Sodium Thiosulphate V.S. is the equivalent of:

	Gramme.
Sodium Thiosulphate, $Na_2S_2O_3+5H_2O$	0.0012411
Iodine, I	0.0006346
Iodine, I (from Thyroid Glands)	0.0001058

Normal Sulphuric Acid Volumetric Solution

$H_2SO_4=98.09.$ 49.045 Gm. in 1000 mils.

Carefully mix 30 mils of pure, concentrated sulphuric acid (*Acidum Sulphuricum*, U.S.P.) with sufficient distilled water to measure about 1050 mils, and allow the liquid to cool to 25° C. (77° F.). Measure from a burette 25 mils of this liquid (which is yet too concentrated) into a flask, add about 50 mils of distilled water and 2 drops of methyl orange T.S. and afterwards, from a burette, a freshly standardized normal

potassium hydroxide V.S., shaking after each addition, and toward the end of the operation reducing the flow to drops, until the red tint of the solution changes to a permanent pale yellow after thorough shaking. Note the number of mils of normal potassium hydroxide V.S. consumed. Then dilute the sulphuric acid solution so that equal volumes of this and of normal potassium hydroxide V.S., at standard temperature, exactly neutralize each other.

ALTERNATIVE METHOD.—The diluted trial acid may be directly standardized as follows: Weigh accurately about 2 Gm. of anhydrous sodium carbonate (prepared as directed on page 1689), dissolve it in 100 mils of distilled water contained in a flask, add from 2 to 3 drops of methyl orange T.S., then run in, little by little, from a burette the acid solution to be standardized. Agitate the flask after each addition, reducing the flow of the acid to drops toward the end of the titration; the termination of the operation or exact saturation is indicated by a change in the color of the solution from orange to red or pink. A second or third trial should be made with other weighed portions of the sodium carbonate and in each experiment the number of mils consumed should be accurately noted and the results should agree closely. One gramme of anhydrous sodium carbonate requires for exact neutralization 18.868 (18.8679) mils of normal sulphuric acid V.S. at standard temperature.

EXAMPLE: 2.25 Gm. of anhydrous sodium carbonate required 37.6 mils of the trial acid for neutralization,[1] then:

$$42.453 : 37.6 :: 100 : x \quad x = 88.57 \text{ mils}$$

In a second trial 2.12 Gm. of the soda required 35.43 mils of the trial acid for neutralization, then:

$$40.00 : 35.43 :: 100 : x \quad x = 88.575$$

The acid may now be adjusted by measuring 885.72 mils (average) into a graduated liter flask and filling to the liter mark with distilled water at standard temperature. A new adjustment must be made to prove the accuracy of the standardization, using about 3 Gm., accurately weighed, of the sodium carbonate.

One Mil of Normal Sulphuric Acid V.S. is the equivalent of:

	Gramme.
Sulphuric Acid, H_2SO_4	0.049045
Ammonia Gas, NH_3	0.01703
Ammonium Acetate, $NH_4C_2H_3O_2$	0.07707
Ammonium Carbonate, $(NH_4)_2CO_3$	0.04804
Ammonium Carbonate (U.S.P.), $NH_4HCO_3.NH_4NH_2CO_2$	0.052373
Calcium Hydroxide, $Ca(OH)_2$	0.037045
Calcium Oxide, CaO	0.028035
Lead Acetate, crystallized, $Pb(C_2H_3O_2)_2+3H_2O$	0.18960
Lead Subacetate, assumed as $Pb_2O(C_2H_3O_2)_2$	0.13706
Lithium Carbonate, Li_2CO_3	0.03694
Lithium Salicylate, $LiC_7H_5O_3$	0.14398
Magnesium Carbonate, $(MgCO_3)_4Mg(OH)_2+5H_2O$	0.04857
Magnesium Oxide, MgO	0.02016
Potassium Acetate, $KC_2H_3O_2$	0.09812
Potassium Bicarbonate, $KHCO_3$	0.10011
Potassium Bitartrate, $KHC_4H_4O_6$	0.18814
Potassium Carbonate, anhydrous, K_2CO_3	0.06910
Potassium Citrate, crystallized, $K_3C_6H_5O_7+H_2O$	0.10812
Potassium Hydroxide, KOH	0.05611
Potassium and Sodium Tartrate, $KNaC_4H_4O_6+4H_2O$	0.14110
Sodium Acetate, $NaC_2H_3O_2+3H_2O$	0.13607
Sodium Bicarbonate, $NaHCO_3$	0.08401
Sodium Borate, crystallized, $Na_2B_4O_7+10H_2O$	0.19108
Sodium Carbonate, anhydrous, Na_2CO_3	0.0530
Sodium Carbonate, monohydrated, $Na_2CO_3+H_2O$	0.06201
Sodium Hydroxide, $NaOH$	0.04001
Sodium Salicylate, $NaC_7H_5O_3$	0.16004
Zinc Oxide, ZnO	0.040685

Half-Normal Sulphuric Acid Volumetric Solution

$H_2SO_4 = 98.09.$ 24.5225 Gm. in 1000 mils.

Dilute 500 mils of normal sulphuric acid V.S. at standard temperature with sufficient distilled water at the same temperature to measure 1000 mils.

This standard solution is chiefly employed in the titration of the organic salts of sodium and potassium in conjunction with methyl orange T.S. as indicator. For this purpose a special experiment should be made in which an accurately measured volume of 10 mils of normal potassium hydroxide V.S. should, after adding 2 drops of methyl orange T.S., require exactly 20 mils of the half-normal sulphuric acid V.S., at standard temperature, for neutralization. If necessary, an adjustment should be made to render the correspondence perfect.

One Mil of Half-Normal Sulphuric Acid V.S. is the equivalent of:

	Gramme.
Sulphuric Acid, H_2SO_4	0.024523
Ammonia Gas, NH_3	0.008515
Lithium Citrate, anhydrous	0.034977

[1] 2.25 Gm. of anhydrous sodium carbonate requires $2.25 \times 18.868 = 42.4528$ mils of normal sulphuric acid V.S.

	Gramme.
Lithium Citrate, crystallized, $Li_3C_6H_5O_7+4H_2O$	0.04699
Lithium Salicylate, $LiC_7H_5O_3$	0.07199
Potassium and Sodium Tartrate, anhydrous, $KNaC_4H_4O_6$	0.05253
Potassium and Sodium Tartrate, crystallized, $KNaC_4H_4O_6+4H_2O$	0.07055
Potassium Acetate, $KC_2H_3O_2$	0.04906
Potassium Bicarbonate, $KHCO_3$	0.050055
Potassium Bitartrate, $KHC_4H_4O_6$	0.09407
Potassium Citrate, anhydrous, $K_3C_6H_5O_7$	0.051057
Potassium Citrate, crystallized, $K_3C_6H_5O_7+H_2O$	0.05406
Potassium Hydroxide, KOH	0.02806
Sodium Acetate, anhydrous, $NaC_2H_3O_2$	0.04101
Sodium Acetate, $NaC_2H_3O_2+3H_2O$	0.068035
Sodium Benzoate, $NaC_7H_5O_2$	0.07202
Sodium Bicarbonate, $NaHCO_3$	0.04200
Sodium Carbonate, anhydrous, Na_2CO_3	0.02650
Sodium Carbonate, monohydrated, $Na_2CO_3+H_2O$	0.031005
Sodium Citrate, anhydrous, $Na_3C_6H_5O_7$	0.04301
Sodium Citrate, crystallized, $Na_3C_6H_5O_7+2H_2O$	0.04901
Sodium Salicylate, $NaC_7H_5O_3$	0.08002
Sodium Tartrate, neutral, $Na_2C_4H_4O_6+2H_2O$	0.057515

Tenth-Normal Sulphuric Acid Volumetric Solution

$H_2SO_4=98.09$. 4.9045 Gm. in 1000 mils.

Dilute 100 mils of normal sulphuric acid, at standard temperature, with sufficient distilled water at the same temperature to measure 1000 mils.

ALTERNATIVE METHOD.—Mix about 5 mils of concentrated sulphuric acid (specific gravity 1.826 at 25° C. (77° F.)) with sufficient distilled water to measure about 1100 mils, and allow it to cool to 25° C. (77° F.). Standardization should be carried out as directed under the alternative method for normal sulphuric acid V.S. (see page 1704), employing about 0.3 Gm. of anhydrous sodium carbonate (see page 1689), accurately weighed, with methyl orange T.S. as indicator. One decigramme of anhydrous sodium carbonate should require for neutralization 18.868 (18.8679) mils of the tenth-normal acid V.S. at standard temperature. This standard solution is employed in conjunction with the fiftieth-normal potassium hydroxide V.S. in the titration of alkaloids, with cochineal, iodeosin, methyl red, or hematoxylin T.S. as indicator. For this purpose a special experiment should be made, in which an accurately measured volume of 10 mils of the tenth-normal sulphuric acid, after adding a sufficient quantity of the indicator to be employed, should require 50 mils of the fiftieth-normal potassium hydroxide V.S. at standard temperature for complete neutralization.

One Mil of Tenth-Normal Sulphuric Acid V.S. is the equivalent of:

	Gramme.
Sulphuric Acid, H_2SO_4	0.0049045
Aconite, ether soluble alkaloids	0.0645
Aconitine, $C_{34}H_{47}O_{11}N$	0.064539
Atropine, $C_{17}H_{23}O_3N$	0.028919
Brucine, $C_{23}H_{26}O_4N_2$	0.039423
Calcium Hydroxide, $Ca(OH)_2$	0.0037045
Cephaeline, $C_{14}H_{19}O_2N$	0.023316
Cinchonidine, $C_{19}H_{22}ON_2$	0.029420
Cinchonine, $C_{19}H_{22}ON_2$	0.029420
Cocaine, $C_{17}H_{21}O_4N$	0.030318
Coniine, $C_8H_{17}N$	0.012715
Emetine, $C_{15}H_{21}O_2N$	0.024718
Hydrastine, $C_{21}H_{21}O_6N$	0.038318
Ipecac, Ether Soluble Alkaloids of	0.0240
Morphine, anhydrous, $C_{17}H_{19}O_3N$	0.028516
Morphine, crystallized, $C_{17}H_{19}O_3N+H_2O$	0.030318
Mydriatic Alkaloids, Combined	0.02892
Nux Vomica, Combined Alkaloids of	0.0364
Physostigmine, $C_{15}H_{21}O_2N_3$	0.027520
Pilocarpine, $C_{11}H_{16}O_2N_2$	0.020815
Potassium Hydroxide, KOH	0.005611
Quinine, anhydrous, $C_{20}H_{24}O_2N_2$	0.032421
Sodium Carbonate, anhydrous, Na_2CO_3	0.00530
Strychnine, $C_{21}H_{22}O_2N_2$	0.033420
Zinc Oxide, ZnO	0.0040685

Fiftieth-Normal Sulphuric Acid Volumetric Solution

$H_2SO_4=98.09$. 0.9809 Gm. in 1000 mils.

Dilute 20 mils of normal sulphuric acid V.S., or preferably 200 mils of tenth-normal sulphuric acid V.S., at 25° C. (77° F.), with sufficient distilled water at the same temperature to measure 1000 mils. The strength of this solution must be adjusted so that 25 mils of it will exactly neutralize 25 mils of a recently

standardized fiftieth-normal potassium hydroxide V.S., at standard temperature, cochineal, iodeosin, methyl red, or hematoxylin T.S. being used as indicator.

One Mil of Fiftieth-Normal Sulphuric Acid V.S. is the equivalent of:

	Gramme
Sulphuric Acid, H_2SO_4	0.0009809
Aconitine, $C_{34}H_{47}O_{11}N$	0.012907
Atropine, $C_{17}H_{23}O_3N$	0.0057838
Cinchona, Combined Alkaloids of	0.0061841
Cinchonidine, $C_{19}H_{22}ON_2$	0.605884
Cinchonine, $C_{19}H_{22}ON_2$	0.005884
Cocaine, $C_{17}H_{21}O_4N$	0.0060636
Coniine, $C_8H_{17}N$	0.002543
Hydrastine, $C_{21}H_{21}O_6N$	0.0076636
Ipecac, Combined Alkaloids of	0.0048034
Morphine, anhydrous, $C_{17}H_{19}O_3N$	0.0057032
Morphine, crystallized, $C_{17}H_{19}O_3N+H_2O$	0.0060636
Physostigmine, $C_{15}H_{21}O_2N_3$	0.005504
Pilocarpine, $C_{11}H_{16}O_2N_2$	0.004163
Quinine, anhydrous, $C_{20}H_{24}O_2N_2$	0.0062842
Strychnine, $C_{21}H_{22}O_2N_2$	0.006684

Indicators

(U. S. P. IX)

NOTE: Each test solution used as indicator must be examined as soon as prepared, and afterwards, from time to time, as to its neutrality. If necessary, it is brought, by the cautious addition of highly diluted sulphuric acid or of a very dilute solution of an alkali, to such a point that when three drops of it are added to 25 mils of distilled water, a few drops of a hundredth-normal acid or alkali V.S., respectively, will distinctly develop the appropriate tints. Tests solutions are injured by exposure to light, and it is best to preserve them in dark amber-colored vials. Keep test papers in dark bottles.

Azolitmin.—A purified coloring matter from litmus. In very dark to black-violet scales or as a reddish-brown powder, slightly soluble in water, insoluble in alcohol or ether. To test its relative sensitiveness, prepare a solution of 0.1 Gm. of azolitmin in 40 mils of distilled water by the aid of a gentle heat, then add 10 mils of alcohol and filter the liquid when cold. To about 50 mils of distilled water, which has previously *been boiled* (to free it from dissolved carbonic acid) and quickly cooled, add 0.1 mil of the trial solution; the resulting bluish-red solution assumes at once a distinctly red color upon the addition of 3 drops of fiftieth-normal sulphuric acid V.S. and under the same conditions a bluish-violet color upon the addition of 0.5 mil of hundredth-normal sodium hydroxide V.S.

Azolitmin Test Solution.—Dissolve 1 Gm. of azolitmin in 80 mils of distilled water and 20 mils of alcohol in a flask and sterilize the solution by heating it in a current of steam for one hour.

Cochineal Test Solution.—Macerate 1 Gm. of unbroken cochineal (see page 363) during four days with 20 mils of alcohol and 60 mils of distilled water, then filter. The color of this test solution is turned violet by alkalies, and yellowish-red by acids. Cochineal T.S. is useful in titrating alkaloids, inorganic acids, ammonia, the alkalies, and alkaline earths. The presence of salts of iron, aluminum, or copper must be avoided. This indicator is useless for titrating organic acids.

Congo Red (Dianil Red, Kosmos Red Extra).—The sodium salt of benzidin-diazo-bis-1-naphthylamine-4-sulphonic acid, $(C_6H_4N : N.C_{10}H_5(NH_2)SO_3Na)_2$. A brownish-red powder, readily soluble in warm water, yielding a blood-red solution; slightly soluble in cold water, insoluble in ether or chloroform. The addition of tannic acid T.S. to an aqueous solution (1 in 20) intensifies the color of congo red but causes no precipitation (reaction for *basic color*). The addition of 5 mils of stannous chloride T.S. to 10 mils of an aqueous solution of congo red (1 in 10), followed by agitation and warming on a water bath, produces a violet precipitate. When filtered, the colorless filtrate does not again assume its red color when exposed to the air (test for *azo-group*). The addition of a 15 per cent. solution of sodium hydroxide to an aqueous solution of congo red (1 in 200) produces no change. The addition of hydrochloric acid to an aqueous solution of this dye (1 in 200) produces a violet precipitate. Concentrated sulphuric acid dissolves congo red with a slate blue color and, upon the cautious addition of distilled water, a blue precipitate is produced.

Congo Red Test Solution.—Dissolve 0.5 Gm. of congo red in 90 mils of distilled water and add 10 mils of alcohol. Add 2 or 3 drops of congo red test solution to 100 mils of distilled water contained in a porcelain dish; the red color of this solution changes to violet upon the addition of one drop of fiftieth-normal sulphuric acid V.S., and again changes to red upon the further addition of one drop of fiftieth-normal potassium hydroxide V.S. (*relative sensitiveness*).

Hematoxylin (Hydroxybrasilin), $C_{16}H_{14}O_6+3H_2O$.—A crystalline substance derived from the heartwood of *Hæmatoxylon Campechianum* Linné (Fam. *Leguminosæ*). Colorless to yellowish prisms; very slightly soluble in cold water or ether, readily soluble in hot water or alcohol. When exposed to light, hematoxylin acquires a red color and yields yellow solutions. In ammonia water or in carbonated or caustic alkali solutions it yields a purple solution. Keep hematoxylin and its solution protected from light and air. When dissolved in aqueous solutions of the following salts, hematoxylin develops the colors indicated: in alum solution a red color; in stannous chloride solution a rose color; in solutions of copper salts a greenish-gray color; and it gradually turns black in potassium dichromate solution.

Hematoxylin Test Solution.—Dissolve 0.02 Gm. of hematoxylin in 10 mils of alcohol. Use about 5 drops for each titration. This indicator assumes a yellow to orange color in acid solutions, and a violet to purple color in alkaline solutions. The titration is complete when the change in color remains permanent upon the addition of one drop of the volumetric solution after stirring the liquid.

Iodeosin (Tetraiodofluorescein), $C_{20}H_8I_4O_5$.—A scarlet, crystalline powder, soluble in alcohol with a deep red color and in ether with a yellowish-red color. It is insoluble in water containing a trace of hydrochloric acid. It is not suitable for use as an indicator unless a test solution prepared from it (see below) will stand the following test of sensitiveness: Into a well-rinsed, colorless, glass-stoppered flask, introduce 100 mils of distilled water containing 5 drops of iodeosin T.S. followed by about 30 mils of ether. Then add drop by drop from a burette hundredth-normal hydrochloric acid V.S., vigorously shaking it after the addition of each drop until the aqueous layer just becomes colorless. After the addition of 5 more drops of the iodeosin T.S. and again shaking, the aqueous layer does not acquire a pink color; should it do so, the color must be discharged upon the addition of 1 drop of hundredth-normal hydrochloric acid V.S. (test of *sensitiveness*).

Iodeosin Test Solution.—Dissolve 0.1 Gm. of iodeosin in 100 mils of alcohol. This indicator becomes colorless in acid solutions, changing to pink in alkaline solutions. Dilute the solution to be titrated with distilled water to about 100 mils, in a 200 mil flask, add 20 mils of ether and 5 drops of the iodeosin T.S., cork and shake it well. Then add the volumetric alkali solution gradually, shaking it well after each addition. The titration is complete when the lower aqueous solution retains a faint pink color after shaking thoroughly. For assaying alkaloidal residues, dissolve the latter in a measured excess of volumetric acid solution, and transfer the acid solution to a 200 mil flask, washing the container well with distilled water until the contents of the flask measure about 100 mils. Then proceed as above. Frequently a scum forms between the ethereal and aqueous layer, in which case this assumes a pink color before the latter.

Litmus Paper and Test Solution.—Exhaust powdered litmus with three separate and successive portions (each equal to about 4 times its weight) of boiling alcohol (which removes the undesirable color erythrolitmin), each extraction lasting for about one hour. After draining off the alcohol, digest the residue with about an equal weight of cold water and filter. (This blue solution, which contains some alkali, after being acidulated, may be used to make red litmus paper.) Finally, extract the residue with about 5 times its weight of boiling distilled water, and, after thoroughly cooling, filter. The addition of 1 drop of hundredth-normal acid or alkali V.S. to 50 mils of distilled water containing 5 drops of the indicator produces a distinct change in color. Preserve the filtrate, as a test solution, in wide-mouthed bottles stoppered with loose plugs of purified cotton so as to exclude dust but admit air. The latter must be free from acid or ammoniacal vapors. The blue color of litmus test solution is changed by acids to red, and this red color by the addition of alkalies is restored to blue.

Litmus Paper, Blue.—Impregnate with the test solution just described strips of white filter paper, and dry them by suspending them on lines of clean twine, in an atmosphere free from acid or ammoniacal vapors. This paper must quickly respond to a two hundred and fiftieth-normal acid V.S.

Litmus Paper, Red.—Prepare this with the same kind of paper and in the manner described under *Litmus Paper, Blue,* having added to the test solution used to impregnate the paper just sufficient of a highly diluted solution of hydrochloric acid to impart to it a faint red tint. Neither blue nor red litmus paper should have an intense color. Preserve the test paper in bottles, so as to exclude dust and acid or ammoniacal vapors. This paper must quickly respond to a two hundred and fiftieth-normal alkali V.S.

Methyl Orange (Helianthin, Orange III, Tropæolin D., Dimethylaniline Orange). The sodium salt of paradimethylaminoazobenzene sulphonic acid, $(CH_3)_2\text{-}N\text{-}C_6H_4\text{-}N=N\text{-}C_6H_4.SO_3Na$.—An orange-yellow powder, readily soluble in hot water, the solution on cooling separating golden-yellow scales. Slightly soluble in cold water, yielding an orange-yellow solution. Insoluble in alcohol. An aqueous solution (1 in 500), upon the addition of hydrochloric acid, yields a red precipitate soluble in excess of the acid with a deep red color. The addition of calcium chloride T.S. to the aqueous solution of methyl orange (1 in 500) precipitates the insoluble calcium salt. The addition of solution of lead subacetate (*Liquor Plumbi Subacetatis,* U.S.P.) precipitates the coloring matter from an aqueous solution. Sulphuric acid dissolves methyl orange with a blood-red color.

Methyl Orange Test Solution.—Dissolve 1 Gm. of methyl orange (see above) in 1000 mils of distilled water. Excessive quantities of this indicator should be avoided in titration; from 1 to 3 drops are sufficient for a volume of from 50 to 100 mils, or add just enough to impart a faint tint to the solution, which if alkaline or neutral will assume a pure yellow, if faintly acid, an orange, and when strongly acid, a rose red color. The solution must comply with the following requirements for sensitiveness as an indicator: To 100 mils of distilled water, contained in a flask of Jena glass, add 1 drop of the Test Solution; the pale yellow color of the solution, upon the addition of 0.5 mil of hundredth-normal sulphuric acid V.S. changes to a rose color; the yellow color will be restored upon the further addition of 0.5 mil of hundredth-normal potassium hydroxide V.S. Methyl orange is suitable for titrating inorganic acids, alkalies, alkali carbonates or bicarbonates. It is not to be employed in titrating organic acids, nor in alcoholic or boiling solutions. This indicator gives a yellow color with alkalies and rose color with acids.

Methyl Red (Paradimethylaminoazobenzeneorthocarboxylic acid), $(CH_3)_2\text{-}N\text{-}C_6H_4\text{-}N=N\text{-}C_6H_4.COOH$.—Violet crystals, very slightly soluble in cold water, yielding a red solution, readily soluble in alcohol and glacial acetic acid. When dissolved in sulphuric acid, methyl red shows the same color change as methyl orange. The applications of methyl red as indicator are the same as those of methyl orange, except that when titrating solutions containing carbonates it should not be used (see above).

Methyl Red Test Solution.—Dissolve 0.2 Gm. of methyl red in 100 mils of alcohol. As an indicator from 1 to 3 drops are sufficient for a volume of 100 mils, or add just sufficient to impart a faint tint to the solution, which if alkaline will assume a pure yellow, and when faintly acid a rose-red, or when strongly acid a violet-red color. The solution must comply with the following requirements for sensitiveness as an indicator: To 100 mils of distilled water which has been freed from carbon dioxide by boiling in a flask of hard glass, add 2 drops of methyl red T.S.; the yellowish-red color of 50 mils of this solution is changed to pure yellow by the addition of 2 drops of hundredth-normal potassium hydroxide V.S., and the color of the other 50 mils is changed to red by 2 drops of hundredth-normal hydrochloric acid V.S. Methyl red T.S., which is not affected by neutral salts, may be used in all instances where methyl orange is indicated, except where carbon dioxide is present; its end-points are sharper than those of methyl orange and it is far more sensitive in the titration of very dilute solutions of weak bases, surpassing hematoxylin or iodeosin in the titration of alkaloids.

Phenolphthalein Test Solution.—Dissolve 1 Gm. of phenolphthalein (see page 843) in 100 mils of alcohol. About 3 drops are sufficient for 50 mils of the solution to be titrated; it gives a red color with alkali hydroxides or carbonates, and acids render the solution colorless. The test solution must comply with the following requirements for sensitiveness as an indicator: From 3 to 5 drops of the test solution are added to 300 mils of distilled water which has been previously boiled and cooled in a flask of Jena glass; this solution is colored red by the addition of not more than 0.5 mil of hundredth-normal potassium hydroxide V.S. Phenolphthalein may be employed in hot titrations. It is not suitable as an indicator for ammonia nor in the presence of large quantities of ammonium salts, but is largely used for organic acids, alkali hydroxides, and for carbonates and bicarbonates in boiling solutions.

Phenolphthalein Paper is prepared by impregnating white, unsized paper with the test solution and drying it.

Rosolic Acid, Corallin.—Amorphous reddish-brown powder or lumps, the latter having a greenish, metallic luster, consisting chiefly of the compound $C_{20}H_{16}O_3$, isomeric with methylaurin and homologous with aurin. Rosolic acid is soluble in alcohol and insoluble in water.

Rosolic Acid Test Solution.—Dissolve 1 Gm. of rosolic acid in 10 mils of diluted alcohol, and add enough distilled water to make 100 mils. Of this solution, about 0.5 mil is used for 100 mils of solution to be titrated. Its color is pale yellow, unaffected by acids, but turning to rose with alkalies. The solution must comply with the following requirements for sensitiveness as an indicator: To 100 mils of distilled water, add 2 drops of the test solution; the pale yellow color of this solution, upon the addition of 0.5 mil of hundredth-normal potassium hydroxide V.S., changes to a rose-red; the yellow color will be restored upon the further addition of 0.5 mil of hundredth-normal sulphuric acid V.S. Ammoniacal solutions are to be highly diluted when titrated with this indicator. It is useful for mineral but useless for organic acids, except oxalic.

Turmeric Tincture.—Digest any convenient quantity of ground turmeric root (from Curcuma longa Linné, Fam. *Scitaminaceæ*) repeatedly with small quantities of distilled water and discard the liquids. Then digest the dried residue for several days with six times its weight of alcohol, and filter.

Turmeric Paper.—Impregnate white, unsized paper with the tincture, and dry it. The tincture, as well as the paper, turns brown with alkalies, and the original yellow color is restored by acids, with the exception of boric acid, which, especially in the presence of hydrochloric acid, turns the color to reddish-brown, which is changed to bluish-black by ammonia.

General Tests

(U. S. P. IX)

Under this head are placed tests which are frequently duplicated throughout this Pharmacopœia. In order to save space they are here grouped together and in the text are referred to by number.

1. Arsenic Test

(U. S. P. IX)

Test Apparatus.—Prepare several generators, equipped with tubes, etc., as described below. Select as a generator a bottle of about 50 mils capacity, having a mouth about 2.5 cm. in diameter, and provide a well-fitting rubber stopper, suitably perforated. In the perforation in this stopper insert a vertical exit tube about 13 cm. in total length and 1 cm. in diameter throughout the upper portion (for about 10 cm.) and constricted at its lower extremity to a tube of about 3 cm. in length and about 5 mm. in diameter. This latter tube should extend but slightly below the stopper. In the lower part of the wider exit tube insert a small pledget of dry glass wool (see page 1682) and then a strip of the freshly prepared but dry lead acetate test paper (see page 1683) rolled into a coil, and above this a plug of the moist (not wet) lead acetate glass wool (see page 1683). In the upper extremity of this tube insert, through a perforated cork stopper, a glass tube 12 cm. in length, having an internal diameter of about 3 mm. Place the mercuric bromide test paper (see page 1684) in this tube, bending or creasing the upper portion of the strip so that it will retain its position. The strip should extend within about 2 cm. of the perforated cork stopper and must not be introduced into the tube until ready to start the test. This tube should be thoroughly cleaned and dried each time it is used.

Standard Arsenic Test Solution.—Dissolve 0.1 Gm. of arsenic trioxide (see page 192), which has been finely pulverized, dried in a desiccator, and accurately weighed, in about 5 mils of a 20 per cent. solution of sodium hydroxide (free from arsenic). Neutralize the solution with diluted sulphuric acid (free from arsenic), add 10 mils of the same acid and sufficient recently boiled distilled water to bring the volume of the solution to exactly 1000 mils at 25° C. (77° F.). Accurately measure 10 mils of this solution, transfer it to a 1000 mil flask, add 10 mils of diluted sulphuric acid (free from arsenic) and make up the volume with recently boiled distilled water to exactly 1000 mils at 25° C. (77° F.). Employ this solution, containing 0.001 milligramme of arsenic trioxide in each 1 mil at 25° C. (77° F.), in preparing the standard stain. Keep this solution in a glass-stoppered bottle. It is advisable to make fresh solutions whenever new standard stains are to be prepared.

Preparation of the Chemical to be Tested.—Add 1 mil of a mixture of equal volumes of concentrated sulphuric acid (see page 1692) and distilled water, to 5 mils of an aqueous solution of the chemical (1 in 25) or to a solution in 5 mils of distilled water of the residue remaining after any special treatment that may be directed. This acidulation is not necessary in the case of inorganic acids. Now, unless specially directed, add 10 mils of a saturated aqueous solution of sulphurous acid (see page 1692). Evaporate this liquid in a small beaker, on a water bath, until it is free from sulphurous acid and has been reduced to about 2 mils in volume. Dilute this evaporated liquid to about 5 mils with distilled water.

The Test for Arsenic
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Preparation of the Standard Stain.—Introduce into the generator from 8 to 10 Gm. of zinc (see page 1692) followed by 25 mils of dilute sulphuric acid, prepared by mixing 1 part of concentrated sulphuric acid, free from arsenic (see page 1692), with 4 parts of distilled water, and 5 drops of acid stannous chloride T.S. (see page 1691). Add at once 2 mils [accurately measured at 25° C. (77° F.)] of the standard arsenic T.S. (see page 1709), and immediately insert the stopper containing the exit tube, into which have been placed the glass wool pledget, the dry lead acetate test paper, the moist lead acetate glass wool, and the mercuric bromide test paper, as described under the *Test Apparatus* (see page 1709). Should the evolution of the gas be violent at first, check the reaction by immersing the bottle in cold water. Should the reaction subside, increase it by placing the bottle in warm water. If the reaction be too violent, the stain will spread and not form a distinctive band, thus making the comparisons of color intensity difficult. After the test has continued for forty-five minutes, remove the mercuric bromide test paper and place it in a clean, dry tube for comparison. This stain represents 0.002 milligramme of arsenic trioxide in addition to any stain produced by the reagents. The stain from the reagents should scarcely be perceptible when determined by a blank experiment. Since light, heat and moisture cause the stain to fade rapidly, comparison should be made as soon as possible. The stained test papers may be preserved by either dipping in hot, melted paraffin or keeping them over phosphoric anhydride protected from light.

Testing the Chemical.—Introduce into another generator from 8 to 10 Gm. of the zinc, followed by 25 mils of the dilute sulphuric acid (1 to 4) and 5 drops of acid stannous chloride T.S. Insert the stopper containing the exit tube charged with the test papers and glass wool, as just described. Then add 5 mils of the solution to be tested, previously treated as directed, under *Preparation of the Chemical* (see page 1709), and immediately insert the stopper charged with the test papers and glass wool. When the evolution of hydrogen has proceeded actively for forty-five minutes, remove the mercuric bromide test paper and carefully compare it with the standard stain prepared as described above. The stain produced by the chemicals tested does not exceed in length or intensity of color that prepared as the standard, indicating not more than 1 part of arsenic in 100,000 parts of the substance tested.

Interfering Chemicals.—Antimony, if present in the substance tested, will produce a gray stain. *Sulphites, sulphides, thiosulphates*, and other compounds which liberate hydrogen sulphide or sulphurous acid when treated with sulphuric acid, must be oxidized by means of nitric acid and then reduced by means of sulphurous acid as directed under *Preparation of the Chemical to be Tested* (see page 1709), before introducing them into the apparatus. *Sulphur compounds* as well as *hydrogen phosphide* give a bright yellow band on the test paper. If sulphur compounds are present, a simultaneous darkening of the lead acetate test paper and glass wool will occur. If such is the case, the operation as directed under *Preparation of the Chemical to be Tested* (see page 1709) must be repeated upon a fresh portion of the solution being tested, using greater care in effecting the complete removal of the sulphurous acid. In testing hypophosphites special care should be observed to completely oxidize the solution being tested as directed, otherwise a yellow stain may be produced through the evolution of hydrogen phosphide, which might be confused with the orange-yellow color produced by arsenic. *Compounds containing antimony* should be tested for *arsenic* by Bettendorf's Test (see Test No. 2).

The test apparatus should be thoroughly cleaned and dried immediately before and after use.

2. Arsenic Test, Bettendorf's
(U. S. P. IX)

This test is employed only in testing salts of *bismuth* and compounds containing *antimony* for the presence of arsenic.

To a solution of the prescribed quantity of the substance to be tested in 5 mils of concentrated hydrochloric acid (see page 1682) contained in a clean test tube, add 10 mils of saturated stannous chloride T.S. (see page 1691) which has been freshly prepared, and set it aside for thirty minutes. If arsenic is present in non-permissible amounts, a brownish tint or precipitate will be seen when the tube is placed over a white surface and the solution viewed from above, comparison being made with a mixture of 5 mils of concentrated hydrochloric acid (see page 1682) and 10 mils of concentrated stannous chloride T.S., prepared as directed above.

Note: It is absolutely necessary that for this test the solution of stannous chloride be freshly prepared, and that nitrates, sulphates, sulphites, sulphides and compounds of mercury, gold, and selenium be absent from the reagents, and the chemicals being tested.

3. Test for Heavy Metals
(U. S. P. IX)

Chemicals.—This test is to be used to detect the presence of undesirable metallic impurities in official chemical substances or their solutions; these must not respond affirmatively within the stated time. Acidulate 10 mils of a solution of the substance in distilled water (1 in 50), contained in a test tube of about 40 mils capacity and of about 2.5 cm. diameter, with 1 mil of diluted hydrochloric acid (unless otherwise directed),[1] warm it to about 50° C. (122° F.), add an equal volume of freshly prepared hydrogen sulphide T.S., stopper, and allow the mixture to stand at 35° C. (95° F.) for half an hour. At the end of this time the mixture should still possess the odor of hydrogen sulphide; if not, it should be thoroughly saturated with the gas and again set aside for half an hour. The color produced, if any, is not greater than that observed by a blank test made in the same manner and with the same quantities of the reagents (omitting the solution

[1] First neutralize solutions of acids carefully by the addition of ammonia water and then acidify as above directed.

to be tested); the solutions being viewed crosswise by reflected light while held against a white surface. A slight turbidity due to separation of sulphur from the hydrogen sulphide may occur.

Volatile Oils.—Shake 10 mils of the oil with an equal volume of distilled water to which a drop of hydrochloric acid has been added and pass hydrogen sulphide through the mixture until it is saturated; no darkening in color will be produced in either the oil or the water (*lead or copper*).

4. Electrolytic Determinations

(U. S. P. IX)

Mercury and Zinc.—The electrolytic apparatus consists principally of an ammeter, voltmeter, and rheostat, properly connected with the source of the current, a platinum spiral anode and a device for rotating the anode.

The source of the current may be either storage batteries or any other system which permits the regulation of the voltage and amperage.

Mercury is determined in a mercury cathode cup. It consists of a glass cylinder about 6.5 cm. high and 3.5 cm. in diameter, into which is fused a platinum wire near the bottom, and containing 50–60 Gm. of pure mercury. The platinum wire must be in contact with the mercury.

For the determination of zinc, a nickel dish of about 175 mils capacity is used. A platinum dish upon which a thin layer of silver or copper has been previously deposited may also be used.

Corrosive Mercuric Chloride.—Dissolve 0.3 to 0.4 Gm. of the salt, accurately weighed, in 10 mils of distilled water and transfer the solution to the cathode cup, which has previously been weighed with its metallic mercury. Dilute the liquid to about 20 mils with distilled water, add 1 mil of nitric acid diluted with an equal volume of water and 10 mils of toluol, and pass through the solution a current of 1 to 3 amperes and 8 to 12 volts, stirring the solution by rotating the anode 500 to 600 revolutions per minute. After twenty minutes, when the mercury is all removed from solution (to be ascertained by removing a few drops of the solution and testing with hydrogen sulphide), wash with distilled water, with the aid of a siphon and without interrupting the current until the current drops to nearly zero. Remove the cathode cup, wash the mercury with alcohol, then with ether, remove most of the remaining ether with filter paper, then dry in a desiccator over sulphuric acid and weigh. The increase in the weight in the cathode cup represents the amount of mercury present in the quantity of the salt taken.

Mercury (Metallic), Mercuric Oxide (Red or Yellow), Mercury with Chalk and Solution of Mercuric Nitrate.—Dissolve an accurately weighed quantity of the substance in nitric acid (1 : 1) (mercury, metallic, or mercuric oxide 0.2 to 0.3 Gm. in 1 mil; mercury with chalk 0.6 to 0.8 Gm. in 2.5 mils; solution of mercuric nitrate 0.5 to 0.7 Gm. with 0.5 mil of nitric acid added), transfer the solution to the cathode cup which has previously been weighed with its metallic mercury, and dilute with distilled water to about 30 mils. Electrolyze the solution as described under *Corrosive Mercuric Chloride*, using a current of 1.5 to 2 amperes and 7 to 10 volts.

Ammoniated Mercury, Calomel, Mercuric Salicylate, Red Mercuric Iodide, Yellow Mercurous Iodide.—Introduce the accurately weighed substance (0.5 to 0.6 Gm. ammoniated mercury or calomel; 0.7 to 0.8 Gm. mercuric salicylate or yellow mercurous iodide; 1.0 to 1.2 Gm. red mercuric iodide) into the cathode cup, previously weighed with its metallic mercury, add 10 mils of solution of sodium sulphide (made by dissolving 50 Gm. crystallized sodium sulphide in sufficient distilled water to measure 100 mils) and dissolve as far as possible by agitation. Dilute the mixture to about 30 mils with distilled water and pass through the solution a current of 2 to 3 amperes and 7 to 10 volts for thirty minutes (or until a few drops of the liquid do not give a black precipitate or coloration when gently warmed with a few drops of concentrated ammonium chloride solution), stirring the solution by rotating the anode about 500 revolutions per minute. Wash the mercury, as described under *Corrosive Mercuric Chloride*, except that before washing with alcohol allow it to stand with about 20 mils of dilute acetic acid (from 2 to 3 per cent.) until bubbles cease to be evolved.

One gramme of Mercury is the equivalent of:

	Gramme.
Ammoniated Mercury, $HgNH_2Cl$	1.2566
Mercuric Chloride, Corrosive, $HgCl_2$	1.3535
Mercurous Chloride, Mild, $HgCl$	1.1768
Mercuric Iodide, Red, HgI_2	2.2654
Mercuric Nitrate, $Hg(NO_3)_2$	1.618
Mercuric Oxide (Red or Yellow), HgO	1.0798
Mercurous Iodide, Yellow, HgI	1.6327

Zinc.—Introduce into the weighed dish, an accurately weighed quantity of the salt, equivalent to about 0.15 Gm. metallic zinc (zinc acetate, 0.5 Gm.; zinc carbonate, 0.25 Gm.; zinc chloride, 0.3 Gm.; zinc oxide, 0.2 Gm.; zinc phenolsulphonate, 1.2 Gm.; zinc sulphate, 0.6 Gm.; zinc valerate, 0.7 Gm.); dissolve it in distilled water or in 10 mils of diluted sulphuric acid (zinc carbonate, zinc oxide), add from 30 to 35 mils of sodium hydroxide solution (20 per cent.) and dilute with distilled water to about 120 mils. Heat the mixture nearly to boiling and electrolyze for thirty minutes with a current of 4 to 5 amperes and 5 to 6 volts stirring the solution by rotating the anode 500 to 600 revolutions per minute. Without interrupting the current, wash the deposited zinc with distilled water with the aid of a siphon until the current drops to zero or nearly so. Remove the dish, wash the zinc first with alcohol then with ether, dry in a desiccator over sulphuric acid and weigh. The increase in the weight of the dish represents the amount of zinc present in the weight of the salt taken.

To determine zinc in zinc metal, weigh accurately about 1.5 Gm. of the metal, dissolve it by warming with 40 mils of diluted sulphuric acid, filter the solution, if necessary; wash the filter well with distilled water and make up the volume of the solution and washings to 100 mils. Measure 10 mils of this liquid into the weighed dish and proceed as directed above.

One gramme of Zinc is the equivalent of:

	Gramme.
Zinc Acetate, $Zn(C_2H_3O_2)+2H_2O$	3.3570
Zinc Chloride, $ZnCl_2$	2.0849
Zinc Oxide, ZnO	1.2448
Zinc Phenolsulphonate, $Zn(C_6H_5SO_4)_2+8H_2O$	8.5011
Zinc Sulphate, $ZnSO_4+7H_2O$	4.3988
Zinc Valerate, $Zn(C_5H_9O_2)_2+2H_2O$	4.6436

5. Assay for Chlorides, Bromides and Iodides
(U. S. P. IX)

Chlorides.—Dissolve about 0.2 Gm. of the salt to be assayed,[1] accurately weighed (corresponding to from 30 to 40 mils of tenth-normal silver nitrate V.S.), in 25 mils of distilled water in a 200 mil graduated flask. Add 50 mils of tenth-normal silver nitrate V.S. to the solution, and, after adding 5 mils of nitric acid, add sufficient distilled water to make 200 mils and mix the contents well. Then filter the mixture through a dry filter into a dry flask, and reject the first 20 mils of the filtrate. Add 2 mils of ferric ammonium sulphate T.S. to 100 mils of the subsequent filtrate and then titrate with tenth-normal potassium sulphocyanate V.S., until the supernatant liquid remains reddish after it is well shaken. Multiply the number of mils of tenth-normal potassium sulphocyanate V.S. required by 2 and subtract this figure from the number of mils of tenth-normal silver nitrate V.S. added. The difference, multiplied by the equivalent of the respective chloride (see page 1702) represents the amount of chloride present in the weight of the salt or solution taken.

Bromides and Iodides.—Dissolve about 0.4 Gm. of the salt if a bromide, or 0.5 Gm. of the salt if an iodide,[2] accurately weighed, in 25 mils of distilled water in a glass-stoppered flask. Add 50 mils of tenth-normal silver nitrate V.S. to the solution, then, after adding 2 mils of ferric ammonium sulphate T.S. and 2 mils of nitric acid, determine the excess of silver nitrate by titrating with tenth-normal potassium sulphocyanate V.S. until the supernatant liquid remains reddish after it is well shaken.

The difference between the number of mils of tenth-normal silver nitrate V.S. added and the number of mils of tenth-normal potassium sulphocyanate V.S. used, multiplied by the equivalent of the respective bromide or iodide being assayed (see page 1702) represents the amount of the bromide or iodide present in the weight of the salt taken. This difference, divided by the weight of the salt taken, represents the number of mils of tenth-normal silver nitrate V.S. required by 1 Gm. of the salt.

6. Assay for Alkali Salts of Organic Acids
(U. S. P. IX)

Heat about 2 Gm. of the salt to be assayed, accurately weighed, in a platinum or porcelain crucible, at first very gently, then gradually raise the temperature until the salt is thoroughly carbonized. (Do not use platinum crucibles for lithium salts.) The final temperature must not exceed a dull red heat and the flame of the burner must not come in contact with the carbonized mass. After allowing the carbonized mass to cool, disintegrate it with the aid of a stout glass rod and transfer the mass and crucible to a beaker. Add 50 mils of distilled water and 50 mils of half-normal sulphuric acid V.S., cover the beaker with a watch glass and boil the contents for thirty minutes. Then filter the solution and wash the residue with hot distilled water until the washings cease to redden blue litmus paper. Now determine the residual acid in the cooled filtrate by titration with half-normal potassium hydroxide V.S., using methyl orange T.S. as indicator. The difference between the number of mils of half-normal sulphuric acid V.S. added and the number of mils of half-normal potassium hydroxide V.S. used, multiplied by the respective equivalent of the salt (see page 1706) represents the amount of salt present in the amount taken.

7. Determination of Ash or Non-volatile Matter
(U. S. P. IX)

Chemicals.—Weigh accurately from 1 to 2 Gm. of the chemical or the amount directed in the text, and place it in a tared platinum or porcelain crucible. Ignite it, at first very gently, and then gradually raise the temperature until the carbon, if formed, is completely burned off. Conduct the ignition in a place protected from air currents and use as low a temperature as possible to effect the combustion of the carbon. When the carbon has completely disappeared, transfer the crucible while still hot to a desiccator and weigh it when cold. In the case of substances which increase in volume on ignition, or where it is very difficult to burn off the carbon, the determination is facilitated by using a platinum dish of suitable size, or by igniting the weighed quantity of the substance, in the manner described above, in several separate portions.

To test for non-volatile matter in volatile inorganic chemicals proceed as directed above, using as low a temperature as possible.

Vegetable Drugs.—Incinerate 2 Gm. of the ground drug until free from carbon and of constant weight, using a tared crucible and the lowest temperature possible, then determine the weight of the ash. If a carbon-free ash cannot be obtained in this way, exhaust the charred mass with distilled water, collect the insoluble residue on a filter paper of known ash content, incinerate the residue and filter paper until the ash is white or nearly so, then add the filtrate, evaporate it to dryness and heat the whole to a low redness. Finally determine the weight of the ash, deducting the weight of the ash from the filter.

8. Iodine Absorption Value
(U. S. P. IX)

The iodine value or number of a fat or oil indicates the proportion of iodine absorbed under specified conditions. It is determined as follows: Introduce about 0.8 Gm. of a solid fat or about 0.3 Gm.[3] of an oil, accurately weighed, into a glass-stoppered bottle of 250 mils capacity, dissolve it in 10 mils of chloro-

[1] Take 0.4 Gm. of solution of zinc chloride if assayed by this method.
[2] Take 0.7 Gm. of strontium bromide or strontium iodide.
[3] 0.15 to 0.18 Gm. for linseed oil, 0.18 to 0.2 Gm. for cod liver oil, and 0.8 to 1.0 Gm. for oil of theobroma.

form, add 25 mils of iodo-bromide T.S. (see page 1683), accurately measured from a burette or pipette, stopper the bottle securely, and allow the mixture to stand for half an hour[1] in a cool place protected from light. After this time it must still retain a brown color; if the color is not brown a new test should be started, using a smaller quantity of the fat or oil. Then add in the order named 30 mils of potassium iodide T.S., 100 mils of distilled water, and tenth-normal sodium thiosulphate V.S. in small, successive portions, shaking thoroughly after each addition, until the color of the mixture becomes quite pale. Then add a few drops of starch T.S. and continue the addition of tenth-normal sodium thiosulphate V.S. until the blue color is discharged. While this test is being carried out, make a blank test by mixing exactly the same quantities of iodo-bromide T.S. and chloroform and titrating the free iodine with tenth-normal sodium thiosulphate V.S. as directed above. The difference in the number of mils of tenth-normal sodium thiosulphate V.S. consumed by the blank test and the actual test, multiplied by 1.269 and divided by the weight of the fat or oil taken, gives the iodine value.

9. Saponification Value
(U. S. P. IX)

The saponification value of a fat or oil is the quantity of potassium hydroxide (expressed in milligrammes) consumed in saponifying 1 Gm. of the fat or oil. It is determined as follows: Weigh accurately, in a flask of 200 to 250 mils capacity, 1.5 to 2 Gm. of the filtered fat or oil and add to it 25 mils of alcoholic potassium hydroxide V.S. (see page 1700), accurately measured from a burette or pipette. Insert into the neck of the flask, by means of a perforated stopper, a glass tube from 70 to 80 cm. in length and from 5 to 8 mm. in diameter and heat the flask on a water bath for half an hour, frequently imparting a rotatory motion to the contents. Then add 1 mil of phenolphthalein T.S. and titrate the excess of potassium hydroxide with half-normal hydrochloric acid V.S. Make a blank test at the same time, using exactly the same amount of alcoholic potassium hydroxide V.S. The difference in the number of mils of half-normal hydrochloric acid V.S. consumed in the actual test and the blank, multiplied by 28.055 and divided by the weight of the fat or oil taken, gives the saponification value.

10. Acid Number for Resins
(U. S. P. IX)

The acid number of a resinous substance is the quantity of potassium hydroxide (expressed in milligrammes) required to neutralize 1 Gm. of the resinous substance. Dissolve in alcohol about 2 Gm. of the resinous substance to be tested, accurately weighed, add a few drops of phenolphthalein T.S. and titrate with half-normal potassium hydroxide V.S. The number of mils of half-normal potassium hydroxide V.S. required for neutralization, when multiplied by 0.028055 and the product divided by the weight taken, gives the acid number of the resin. The reaction is often more distinct if an excess of half-normal potassium hydroxide V.S. is used and the solution titrated back with half-normal acid V.S.

11. Determination of Crude Fiber
(U. S. P. IX)

Exhaust a weighed quantity of the ground material, representing about 2 Gm. of the drug, with ether or use the residue from the determination of the volatile extract soluble in ether (see below). Add 200 mils of boiling sulphuric acid solution, adjusted to exactly 1.25 per cent. by titration, to the ether-exhausted drug, in a 500 mil flask and connect the flask with a reflux condenser, the tube of which passes only a short distance below the rubber stopper, into the flask. Heat the mixture to boiling and continue the boiling during thirty minutes. Then filter the mixture through asbestos or glass wool and wash the residue on the filter with boiling distilled water until the washings are no longer acid. Rinse the residue back into the flask with 200 mils of boiling sodium hydroxide solution, adjusted to exactly 1.25 per cent. by titration, and free from sodium carbonate. Again heat the mixture to boiling and continue the boiling during thirty minutes under the reflux condenser as described under the treatment with acid, then rapidly filter through a tared filter, wash the residue with boiling distilled water until the washings are neutral, dry it at 110° C. (230° F.) until of constant weight and note the weight. Now completely incinerate the dried residue and weigh the ash; the loss of weight is considered to be the crude fiber.

12. Determination of Volatile Extractive, Soluble in Ether
(U. S. P. IX)

Extract completely 2 Gm. of the thoroughly dried and ground drug by subjecting it, during twenty hours, to the action of dehydrated ether (see page 1681) in a continuous extraction apparatus. Transfer the ethereal solution to a tared porcelain dish and allow it to evaporate spontaneously. Then dry it in a desiccator over sulphuric acid during eighteen hours and weigh the total ether extract. Now heat the extract gradually up to 110° C. (230° F.) until the weight becomes constant; the loss in weight during the heating represents the volatile portion of the extract.

13. Determination of Non-volatile Extractive, Soluble in Ether
(U. S. P. IX)

Proceed as directed under *Determination of Volatile Extractive, Soluble in Ether* (see No. 12). The weight of the extract after drying in a desiccator and then at 110° C. (230° F.) until of constant weight represents the non-volatile portion of the extract.

14. Determination of Alcohol in Official Preparations
(U. S. P. IX)

Place 25 mils of the preparation, measured at any definite temperature between 15° and 30° C. (59° and 86° F.), in a distilling flask of about 200 mils capacity, provided with a high side tube connected with

[1] One hour is required for castor oil and linseed oil.

a suitable condenser; add 50 mils of distilled water, distil into a 50 mil graduated flask, at such a rate that about 48 mils of distillate will be received in a half hour; if volatile products other than alcohol are known to be absent, bring to the original temperature and dilute with water of the same temperature to 50 mils.

Determine the specific gravity of the distillate at the same temperature at which the original sample was measured by means of a pycnometer or Westphal balance and find the per cent. of absolute alcohol by volume by reference to the alcoholometric table (page 1777), and multiply by the dilution factor to find the per cent. of alcohol in the original preparation.

If the preparation is suspected to contain less than 25 per cent. of alcohol, 50 mils should be taken for analysis; if it is suspected to contain over 50 per cent. of alcohol, 12.5 mils should be taken for analysis. In either case, the volume of the distillate should be made up as usual to 50 mils.

If the preparation contains iodine, combine it with zinc dust. (Sodium thiosulphate may be used instead of zinc dust, in which case several drops of sodium hydroxide T.S. should be added to prevent sulphur from distilling over.)

If volatile acids are present, neutralize with sodium hydroxide T.S.; if volatile bases are present, neutralize with dilute sulphuric acid; if both volatile acids and volatile bases are present, neutralize first with dilute sulphuric acid and distil about 50 mils, neutralize this distillate with sodium hydroxide T.S., and distil once more to obtain in the usual manner 50 mils.

If acetone, camphor, chloroform, ether, glycerin (30 per cent. or over), volatile oils or other volatile products are known or suspected to be present, transfer the first distillate to a separatory funnel and saturate it with sodium chloride, add 15 mils of petroleum benzin (boiling point 40°–50° C. (104°–122° F.)) and shake the mixture for one or two minutes. After the liquids have *completely* separated, draw off the lower alcoholic salt solution, with a second separator, and repeat the extraction with 15 mils of petroleum benzin; draw off the lower alcoholic salt solution into a distilling flask of about 200 mils capacity, wash the combined petroleum benzin solutions with about 25 mils of saturated sodium chloride solution and add the washings to the distilling flask. Distil into a 50 mil graduated flask at such a rate that about 45 to 48 mils of distillate are received within a half hour. Bring to the original temperature, dilute with water of the same temperature to 50 mils, and determine the specific gravity and alcoholic per cent. as directed above.

Alcoholic Content in Preparations

The figures given in the following table represent the average alcoholic content. It is impracticable to require an exact standard in alcoholic liquids made from drugs which contain varying proportions of moisture and extractive, and there is unavoidable loss of alcohol through evaporation during the manufacture and storage of preparations. In addition to this, allowance must be made in distillation for some loss incidental to the process, hence a tolerance of ten per cent. more or ten per cent. less than the figures given in the following table is permitted.

PER CENT. BY VOLUME OF ABSOLUTE ALCOHOL

Acidum Sulphuricum Aromaticum	85	Tinctura Cinchonæ Composita	64
Elixir Aromaticum	22	Tinctura Cinnamomi	63
Elixir Glycyrrhizæ	22	Tinctura Colchici Seminis	56
Linimentum Belladonnæ	65	Tinctura Digitalis	70
Linimentum Chloroformi	47	Tinctura Ferri Chloridi	63
Linimentum Saponis	66	Tinctura Gambir Composita	47
Mistura Glycyrrhizæ Composita	8	Tinctura Gelsemii	62
Spiritus Ætheris	66	Tinctura Gentianæ Composita	46
Spiritus Ætheris Nitrosi	92	Tinctura Guaiaci	80
Spiritus Ammoniæ Aromaticus	68	Tinctura Guaiaci Ammoniata	60
Spiritus Amygdalæ Amaræ	76	Tinctura Hydrastis	61
Spiritus Anisi	85	Tinctura Hyoscyami	47
Spiritus Aurantii Compositus	69	Tinctura Iodi	83
Spiritus Camphoræ	90	Tinctura Kino	47
Spiritus Chloroformi	89	Tinctura Lactucarii	46
Spiritus Cinnamomi	85	Tinctura Lavandulæ Composita	70
Spiritus Glycerylis Nitratis	94	Tinctura Limonis Corticis	83
Spiritus Juniperi	90	Tinctura Lobeliæ	46
Spiritus Juniperi Compositus	66	Tinctura Moschi	48
Spiritus Lavandulæ	90	Tinctura Myrrhæ	87
Spiritus Menthæ Piperitæ	85	Tinctura Nucis Vomicæ	71
Spiritus Menthæ Viridis	85	Tinctura Opii	46
Tinctura Aconiti	66	Tinctura Opii Camphorata	46
Tinctura Aloes	47	Tinctura Opii Deodorati	19
Tinctura Arnicæ	46	Tinctura Physostigmatis	92
Tinctura Asafœtidæ	81	Tinctura Pyrethri	90
Tinctura Aurantii Amari	55	Tinctura Quassiæ	31
Tinctura Aurantii Dulcis	83	Tinctura Rhei	46
Tinctura Belladonnæ Foliorum	47	Tinctura Rhei Aromatica	46
Tinctura Benzoini	83	Tinctura Sanguinariæ	56
Tinctura Benzoini Composita	80	Tinctura Scillæ	69
Tinctura Calumbæ	55	Tinctura Stramonii	45
Tinctura Cannabis	90	Tinctura Strophanthi	92
Tinctura Cantharidis	90	Tinctura Tolutana	85
Tinctura Capsici	88	Tinctura Valerianæ	69
Tinctura Cardamomi	46	Tinctura Valerianæ Ammoniata	64
Tinctura Cardamomi Composita	46	Tinctura Veratri Viridis	91
Tinctura Cinchonæ	63	Tinctura Zingiberis	90

15. Proximate Assays

(U. S. P. IX)

General Directions for Alkaloidal Assays

Nearly all alkaloids are practically insoluble in water, but they are more or less soluble in alcohol, chloroform, ether, amyl alcohol, benzene, petroleum benzin, or mixtures of several of these. The salts of the alkaloids, however, are mostly soluble in water, but practically insoluble in nearly all of the above mentioned solvents. The process of assay by immiscible solvents, which is generally known as the "shaking out" process, is based on this property of alkaloids, and it is carried out by treating the drug or a concentrated liquid extract with a solvent immiscible with water, in the presence of an excess of alkali, which liberates the alkaloid. The free alkaloid is dissolved by the immiscible solvent, which is then transferred to a separator and shaken with an excess of acid diluted with water.

When a drug to be assayed is directed to be made from a powder of a certain degree of fineness it is understood to mean that it must not be coarser than the size directed; a finer powder may, however, be used.

If the immiscible solvent is specifically heavier than water (*e.g.*, chloroform, or a mixture of more than one volume of chloroform to one volume of ether) it will separate in the bottom of the separator. It is then drawn off into another separator and shaken with successive portions of weak acid until the alkaloid is all removed.

If the immiscible solvent is specifically lighter than water (*e.g.*, ether, or a mixture of more than two volumes of ether with one volume of chloroform) it will, on separation, form the upper liquid. The lower acid liquid is then drawn off and preserved, and the residual immiscible solvent shaken with successive portions of weak acid until wholly free from alkaloid.

The volume and strength of the acid to be used is left to the discretion of the operator. It is best, however, to keep the total volume as small as possible. For the first extraction, it is advisable to use 10 mils of half-normal acid V.S. or sufficient to render the mixture distinctly acid; for the second extraction, use 5 mils of half-normal acid V.S. and 5 mils of distilled water. Repeat the extraction with the same proportion of acid and distilled water. In all assays, the extraction should be continued until 0.5 mil of the acid washings shows only a very faint cloudiness on the addition of a drop of mercuric potassium iodide T.S., or, in the case of caffeine and colchicine, on the addition of a drop of iodine T.S.

The united solutions containing the alkaloid in the form of a salt are shaken thoroughly with ether and allowed to stand at least fifteen minutes for complete separation. The acid solution is then drawn off into a second separator, the ether washed with a little water and this wash water added to the acid solution. The acid solution is then made alkaline, in most cases with ammonia water, and shaken out with several successive portions of the appropriate immiscible solvent. The volume of the latter to be used in each operation is not less than half that of the acid solution, and the operation must be repeated as long as any alkaloid is extracted by the immiscible solvent. To test this, evaporate 1 mil of the last extraction and dissolve the residue in a few drops of diluted hydrochloric acid; the resulting solution should show not more than a very faint cloudiness on the addition of a drop of mercuric-potassium iodide T.S., or, in the case of caffeine and colchicine, on the addition of a drop of iodide T.S. The number of extractions required depends largely on the character of the alkaloid. With most alkaloids it is advisable to "shake out" three or four times before testing. Physostigmine and pilocarpine require about twice as many extractions as most other alkaloids.

After having drawn off from a separator any liquid containing an alkaloid, a fresh portion of the solvent should be immediately added to the contents of the separator, and, before shaking, about 1 mil of this should be drawn off to wash out the stem of the separator. In the case of volatile solvents, the outside of the stem of the separator should also be washed by dipping it in the portion of the fresh solvent to be used for the next shaking out operation. Before evaporation the final ether or chloroform solution should be filtered through a dry filter, or preferably through a pledget of purified cotton. When filtering volatile solvents containing alkaloids through a paper filter, the upper edge of the filter should not reach the top of the funnel and the filter should be kept constantly full of the liquid until all has been added, then covered until the last of the liquid has passed through. Finally the filter should be washed thoroughly by applying portions of the volatile solvent to the top and carefully washing the outside of the funnel stem. Immiscible solvents heavier than water may be conveniently filtered by packing the stem of the separator below the stopcock with purified cotton before drawing off the solvent. The alkaloidal solution is finally evaporated cautiously to expel the solvent, and the residue either dried to constant weight and weighed, or more commonly titrated with volumetric acid.

When using aliquot parts, the solvent and the aliquot part should be measured at the same temperature. When pouring volatile liquids, the lower the temperature at which the operation can be conducted, the less the danger of loss from evaporation.

The shaking or rotation with an immiscible solvent should ordinarily be continued about one minute. Long or violent agitation should be avoided, as emulsions are apt to form. Should a partial emulsion form it may be broken up by drawing off the clear portion, introducing a tuft of cotton and with a glass rod moving the cotton about in the emulsion next to the surface of the separator. Should the emulsion prove persistent, draw off the emulsified portion and evaporate the volatile solvent. The resulting residue, if alkaline, should be washed with each successive portion of the solvent used in extracting the original solution. If acid it should be washed with acidulated water.

Emulsions are less apt to form in strongly acid or alkaline solutions than in those which are neutral or slightly acid or alkaline. Emulsification is sometimes prevented by increasing the volume of the aqueous or of the immiscible solvent. Chloroform or ether solutions of drugs rich in fat form very troublesome emulsions. In such cases it is advisable to add about 10 mils of normal sulphuric acid V.S., and evaporate the volatile solvent, stirring with a rubber-tipped glass rod. When the resinous and fatty matter has been agglutinated, cool the acid solution and filter it through a small wetted filter into a separator. Redis-

solve the residue in 15 mils of ether, add 5 mils of tenth-normal acid V.S., evaporate the ether as before, with continued stirring, and pour the acid solution through the filter into the separator. Repeat the extraction of the fatty residue with dilute acid two or three times and finally wash the filter free from alkaloids. Then make the solution in the separator alkaline, and "shake out" with the immiscible solvent in the usual manner.

The stems of separators and funnels and the lips of flasks, separators and graduates, from which volatile solvents containing alkaloids have been poured or drawn off, should be carefully washed to prevent loss and to remove any of the alkaloids left by evaporation, and the washings should be added to the solvent.

An alkaloidal residue to be determined volumetrically should be softened by the addition of about 1 mil of neutral alcohol or ether, the required amount of standard acid added, and the mixture gently warmed to insure the complete solution of the alkaloid. Finally add a sufficient quantity of distilled water to make the volume of the liquid for titration measure about 25 mils. When the residue is to be weighed, if the final solvent has been chloroform, the last traces of that solvent should be removed by the addition of a little ether or alcohol followed by evaporation; care being taken to avoid loss by decrepitation, especially when evaporating a chloroformic solution of nux vomica or of cinchona alkaloids. This may usually be prevented by the addition of a little alcohol after the solution has been reduced to a volume of one or two mils.

If preferred, methyl red T.S. may be used in place of cochineal T.S. for alkaloidal titration, in which case the volumetric solution should have been standardized by the use of methyl red T.S. If this has not been done a blank titration should be made to determine the factor for the tenth-normal sulphuric acid V.S., using methyl red T.S. as the indicator.

16. Melting Points

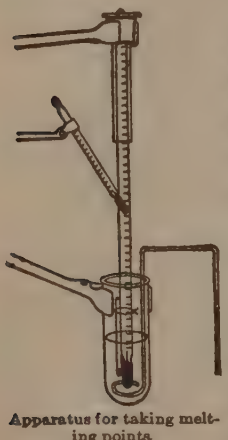
(U. S. P. IX)

For the purpose of the Pharmacopœia the melting point is defined as that interval of temperature within which the substance is observed to melt when treated as directed below.

For the determination of the melting point, Pharmacopœial substances are divided into two classes:

Class I.—Substances readily reduced to a powder.

Class II.—Substances not readily reduced to a powder, such as fats, fat acids, paraffin, petrolatum and waxes.



Apparatus for taking melting points

Apparatus required (see illustration):

1. *A round-bottom, glass tube* of 30 mm. internal diameter and about 10 cm. long, flaring slightly at the top like an ordinary test tube. The walls of the tube are not more than 1.5 mm. thick at any point. The tube is made of glass which will stand heating over an open Bunsen flame.

2. *A stirring device*, which can be made from a glass rod of about 2 mm. external diameter. It is made circular at the end to fit the container (1) and is bent twice at right angles above the top of the container to bring its outer end conveniently to hand for manipulation.

3. *A standard thermometer* covering the desired range of temperature (see page 1724).

4. *An auxiliary thermometer* (see page 1724).

5. *A capillary glass tube* about 6 cm. long and from 0.8 to 1.2 mm. internal diameter, the walls from 0.2 to 0.3 mm. thick and the tube closed at one end.

Procedure for Class I:

Reduce the substance to a No. 100 powder and, unless otherwise stated, render it anhydrous, when it contains water of crystallization, by drying it at the temperature given in the text, or, when the substance contains no water of crystallization, by drying it for twenty-four hours over sulphuric acid.

Select a bath suitable for the melting temperature to be determined, and fill the container to a depth which will permit of such immersion of the thermometer that the upper end of the bulb will be from 2 to 3 cm. below the surface of the bath and the lower end of the bulb about equally distant from the bottom of the container.

Charge a capillary glass tube with sufficient of the dry powder to form a column in the bottom of the tube from 2.5 to 3.5 mm. high when packed down as closely as possible by moderate tapping on a solid surface. Attach the capillary tube to the thermometer by wetting both with the liquid of the bath or by means of a piece of platinum wire and adjust it so that the substance is centrally located by the side of the thermometer bulb. Heat the bath by means of a free Bunsen flame until a temperature 25° C. (77° F.) below the supposed melting point is reached, then carefully regulate the rate of rise in temperature to about 3° per minute until the substance begins to melt (the temperature at which the column of the substance is observed to definitely collapse against the sides of the tube at any point is defined as the beginning of melting), and from that time carefully regulate the rise in temperature to about 0.5° per minute until melting is complete (the temperature at which the substance becomes liquid throughout is defined as the end of melting). The bath must be stirred constantly throughout the heating.

The result thus obtained as the melting interval must be adjusted by applying the calibration correction and that for the emergent stem, as follows:

Attach the auxiliary thermometer, as shown in the illustration, so that the center of its bulb is as close as possible to the stem of the main thermometer at a point midway between the surface of the bath and the supposed melting point. In order to prevent the heat from the burner or currents of cold air from affecting the temperature of the auxiliary thermometer, it is advisable to adjust to the stem of the main thermometer a movable platform made of stiff paper, having its edges folded so as to form a box-like shield

surrounding the bulb of the auxiliary thermometer. Note the temperature registered by the auxiliary thermometer at the end of the melting of the substance and calculate the emergent stem correction by the following formula:

$$\text{correction} = 0.00015 \times N\ (T - t)$$

in which N represents the number of degrees of emergent stem from the bath, T the temperature at the end of melting, and t the temperature registered by the auxiliary thermometer; the correction to be added to the observed reading of the main thermometer.

To avoid the necessity of determining the emergent stem correction each time a melting point is taken, the corrections for intervals of 10° C. (50° F.) may be determined at about 25° C. (77° F.) room temperature and the results plotted on cross-section paper, the temperature of the bath represented by the abscissæ and the amount of correction by the ordinates. The correction for any intermediate temperature can then be interpolated.

NOTE: Suggestions regarding liquids to be used for baths in Class I:

For temperatures up to 200° C. (392° F.) a purified, concentrated sulphuric acid is a suitable bath. For higher temperatures, up to about 350° C. (662° F.) a pure grade of cotton seed oil (almost colorless) will serve for a limited number of determinations. Other, though less desirable, substitutes for sulphuric acid at high temperatures are: (1) a pure grade of paraffin which has been freshly distilled; (2) clean, white, artificial (cotton seed) lard. A very desirable bath for high temperature work is prepared by cautiously boiling together, for five to ten minutes under a hood, a mixture of 70 parts of purified concentrated sulphuric acid and 30 parts of potassium sulphate, stirring constantly until the sulphate is completely dissolved.

Procedure for Class II:

Carefully melt the substance to be tested at as low a temperature as possible and draw it into a capillary tube which is open at both ends, to a depth of about 10 mm. Cool the charged tube at 10° C., (50° F.) or lower, for twenty-four hours, or in contact with ice for at least two hours. Then attach the tube to a standard thermometer by means of a rubber band, adjust and heat it in a water bath, as directed in Class I, except that, within 5° of the assumed melting temperature, the rate of rise of temperature is carefully regulated to about 0.5° per minute.

The temperature at which the substance is observed to rise in the capillary tube is taken as the melting point.

17. Boiling Points

(U. S. P. IX)

The boiling point is defined as that range of temperature within which at least 95 per cent., by volume, of the substance distils, when treated as directed below.

Apparatus Required.—A distilling bulb of from 50 to 60 mils capacity to the lower part of the neck, the length of the neck from 10 to 12 cm. and the internal diameter from 14 to 16 mm. The outlet tube of from 4 to 5 mm. internal diameter should be attached to the neck at approximately its midpoint, forming an angle of from 70° to 75° with the lower end of the neck.

A straight glass condenser with a water jacket from 40 to 60 cm. in length; the distance from the upper end of the water jacket to the neck of the bulb being from 18 to 25 cm.

Thermometer.—In order to avoid the necessity of an emergent stem correction, it is advisable that an accurately standardized thermometer of the Anschutz type be used. If such a thermometer is not available, a thermometer used for melting points (see page 1716) may be employed, applying the emergent stem correction as described under *Melting Points* (see above), the length of emergent stem being measured, in degrees, from the lower end of the stopper to the highest point of the boiling temperature. When placed in position the lower end of the thermometer is 2 to 3.5 cm. below the center of the orifice of the outlet tube.

An asbestos board, of from 12 to 15 cm. square and from 3 to 5 mm. in thickness, having a circular perforation, located centrally, for the reception of the bulb. The edge of the asbestos around the perforation should fit closely to the bulb when the latter is set into it. The size of the perforation should be such that, when the bulb is set into it, the portion of the bulb below the upper surface of the asbestos will have a capacity of from 3 to 4 mils.

Procedure.—Place the asbestos board on a tripod or other suitable support. Introduce into the distilling bulb 25 mils of the liquid to be tested, insert the thermometer, stand the bulb in an upright position in the perforation of the asbestos board and connect it with the condenser. Then distil the liquid at the rate of 1 mil for each fifteen to twenty seconds, noting the temperature as soon as 5 drops of the liquid have distilled into the receiver and when 95 per cent. of the original volume has distilled. Correct the reading for any difference in the barometric pressure by allowing 0.1° C. (32.18° F.) for each 2.7 mm. difference from the standard pressure of 760 mm., adding if the pressure is lower, and subtracting if higher.

NOTE: In order to have the entire distillate distil over at the prescribed rate, it is best to make a preliminary distillation of a separate portion of 25 mils of the liquid, during which the source of heat (a good Bunsen burner) is regulated so that the distillation proceeds at the prescribed rate. Having thus regulated the burner, temporarily remove it, clean the bulb, recharge it with a fresh portion of 25 mils of the liquid and proceed with the distillation as described above.

18. Congealing Points

(U. S. P. IX)

Unless otherwise directed, about 10 mils of the liquid to be tested is introduced into a dry test tube of from 18 to 20 mm. internal diameter, which is then cooled in water or a suitable freezing mixture, the temperature of which should be about 5° lower than the supposed congealing point of the liquid. To induce

crystallization, rub the walls of the tube with a standard thermometer (see page 1724), or add a small crystal of the substance being tested. By alternated immersion of the tube in the bath, or removal from the bath and constant stirring with the thermometer, the temperature is so adjusted that the greater part of the liquid gradually congeals. The highest temperature remaining constant for a short time during the congealing is defined as the congealing point.

19. Solubilities

(U. S. P. IX)

The statements concerning solubilities quoted in this Pharmacopœia are not intended as physical constants in the strict sense of this term, but primarily as information required by physicians and pharmacists in connection with the preparation and dispensing of medicines.

The following points must be observed in the accurate determination of solubilities: 1. Purity of both the dissolved substance and solvent is essential since impurities in either affect the solubility to a greater or less extent. 2. The constancy of the temperature must be accurately maintained during the course of the determination. 3. Complete saturation must be secured. 4. Accurate analysis of the saturated solution and correct expression of the results are imperative. In connection with the above named essential features of a correct solubility determination, attention should be called to the varying rates of solution of different compounds, and to the marked effect of the degree of fineness of the particles upon the time required for the saturation of the solution. In general, it may be said that an equipment comprising a thermo-regulator and a constant agitation device is indispensable for accurate solubility determinations. The solubility of Pharmacopœial compounds in given solvents is considered to be of minor importance as a means for their identification or quantitative estimation, as the other tests contained in the description of each article in the text cover both identity and purity.

The solubility data given throughout this volume have for the most part been determined under the above described conditions, and will, therefore, frequently show a somewhat greater solubility than would be found in the daily experience of most pharmacists.

Method for Determining Solubilities.—In brief, this consists in preparing a saturated solution of the given substance and ascertaining, by analysis, the amount present in a definite quantity of the solution. Complete saturation can be attained most readily by constant stirring or agitation by means of a suitable mechanical contrivance. A simple apparatus for this purpose consists of a test tube of medium size fastened upright in a water bath maintained at constant temperature. The solvent and excess of solids are placed in the tube and stirred by means of a motor-driven rotating glass spiral. After a given period of stirring a definite weight of the clear solution is analyzed and the stirring continued for an additional period of several hours. If analysis shows no increase of dissolved substance after the second period of stirring, the result is to be taken as the solubility at the particular temperature. Minute details of methods for determining solubilities are described in Bulletin No. 67 of the Hygienic Laboratory, U. S. Public Health Service.

20. Gasometric Estimations

(U. S. P. IX)

In certain cases the Pharmacopœia directs the strength of a product or chemical substance to be determined by the volume of gas (nitrogen dioxide) given off during a definite reaction. This volume is to be determined by the use of the nitrometer in the following manner:

Arrange a nitrometer consisting of a measuring tube (graduated into one-tenth milliliter divisions and having a capacity of at least 50 mils) connected by stout rubber tubing with an open equilibrium tube (both tubes, preferably, provided with a globular expansion near the lower end) in such a manner, by suitable clamps attached to a stand, that either tube may be readily and quickly clamped at a higher or lower level. The stop-cock of the measuring tube having been opened, and the open equilibrium tube having been raised to a higher level, pour into the latter a saturated aqueous solution of sodium chloride, until the measuring tube, including the bore of the stop-cock, is completely filled. Then close the latter and adjust the equilibrium tube at a low level. Having ascertained that the stop-cock is closed and is air tight, and having, if necessary, wiped out the graduated tube of the nitrometer, introduce into it the prescribed quantity of the liquid to be tested, and allow this to flow slowly into the measuring tube, being careful not to admit any air. Follow it by the prescribed quantities of the several reagents (potassium iodide T.S. and normal sulphuric acid V.S.). When the reaction (which takes place at once) moderates, remove the measuring tube from its clamp, and, being careful to hold it constantly so that the liquid contained in it stands at a higher level than that in the equilibrium tube, shake its contents, without permitting any gas to pass into the open tube. When the reaction has completely ceased and the volume of gas has become constant, which usually requires from thirty to sixty minutes, restore the tube to its fastening, and allow the apparatus and contents to acquire the ordinary temperature of the room, which is assumed to be at or about 25° C. (77° F.). Then adjust the two tubes so that the liquid columns are at exactly the same level, and read off the volume of gas in the measuring tube. Multiply this figure by the weight of the liquid being assayed which is the equivalent of 1 mil of nitrogen dioxide (see page 1719). The result will be the weight of the absolute substance (ethyl, amyl, or sodium nitrite) contained in the quantity taken for the assay.

For pharmacopœial purposes the determination will be sufficiently exact if the evolved gas be measured within 3 degrees above or below 25° C. (77° F.).

Since temperature and barometric pressure affect the volume of the gas, the following correction factors must be used to obtain exact results when the temperature and pressure are not nearly normal. The barometer correction is important at any locality more than 250 meters above sea-level:

Factors for Temperature Corrections

Normal Temperature, 25° C. (77° F.)

Temperature.	Factor.	Temperature.	Factor.	Temperature.	Factor.
15° C.	1.035	22° C.	1.010	29° C.	0.987
16° C.	1.031	23° C.	1.007	30° C.	0.983
17° C.	1.028	24° C.	1.003	31° C.	0.980
18° C.	1.024	25° C.	1.000	32° C.	0.977
19° C.	1.021	26° C.	0.997	33° C.	0.974
20° C.	1.017	27° C.	0.993	34° C.	0.971
21° C.	1.014	28° C.	0.990	35° C.	0.968

Example: Assuming that the volume of gas read off was 44.5 mils at 32° C. (89.6° F.) and it is desired to ascertain the corresponding volume at 25° C. (77° F.), barometric pressure not being taken into consideration, then the 44.5 mils must be reduced in the proportion of 1 to 0.977 (see temperature correction factors above), or 44.5 must be multiplied by 0.977. The result will be 43.48 (more exactly 43.4765) mils as the equivalent volume of gas at 25° C. (77° F.).

Factors for Correction for Barometric Pressure

(Normal Barometer, 760 mm.)

Barometer Reading.		Factor	Barometer Reading.		Factor.
Millimeters.	Inches.		Millimeters.	Inches.	
790	31.10	1.039	660	25.98	0.868
780	30.71	1.026	650	25.59	0.855
770	30.31	1.013	640	25.20	0.842
760	29.92	1.000	630	24.80	0.829
750	29.53	0.987	620	24.41	0.816
740	29.13	0.974	610	24.02	0.803
730	28.74	0.961	600	23.62	0.789
720	28.35	0.947	590	23.23	0.776
710	27.95	0.934	580	22.83	0.763
700	27.56	0.921	570	22.44	0.750
690	27.17	0.908	560	22.05	0.737
680	26.77	0.895	550	21.65	0.724
670	26.38	0.882	540	21.26	0.711

Example: Assuming that the volume of gas read off was 43.48 mils at 590 mm. barometric pressure, and it is desired to ascertain the corresponding volume at normal barometric pressure (760 mm.), temperature not being taken into consideration, then the 43.48 mils must be reduced in the proportion of 1 to 0.776 (see barometric correction factors above), or 43.48 must be multiplied by 0.776. The result will be 33.74 mils as the equivalent volume of gas at normal barometric pressure.

Estimation of Nitrogen Dioxide

NO = 30.01; 1 Liter { at 0° C. (32° F.) and 760 mm. = 1.3406 Gm.
at 25° C. (77° F.) and 760 mm. = 1.2281 Gm.

One Milliliter of Nitrogen Dioxide is the equivalent of:

	At 0° C. (32° F.) and 760 mm. Gramme.	At 25° C. (77° F.) and 760 mm. Gramme.
Nitrogen Dioxide, NO = 30.01	0.0013406	0.0012281
Amyl Nitrite, $C_5H_{11}NO_2$ = 117.10	0.0052310	0.0047920
Ethyl Nitrite, $C_2H_5NO_2$ = 75.05	0.0033528	0.00307127
Sodium Nitrite, $NaNO_2$ = 69.01	0.0030828	0.0028241

21. Optical Rotation

(U. S. P. IX)

In a ray of ordinary light the transverse vibrations take place indifferently in any plane about the line of propagation. When these waves are limited to a single plane they are termed polarized and the phenomenon is known as polarization.

Many organic substances either liquid or in solution in suitable solvents, when examined in a specially constructed optical apparatus called a polariscope, are capable of rotating the plane of polarization of a ray of light either to the right or to the left. Such substances are termed "optically active," and when rotating to the right are designated as "dextrorotatory" and when rotating to the left as "lævorotatory." Substances which do not possess this property of optical rotation are termed "optically inactive." Optical activity in many instances is intimately connected with the chemical constitution of a substance and it frequently becomes a specific property and its determination is of considerable value.

Among the substances recognized by this Pharmacopœia, there are several, particularly certain essential or volatile oils and related bodies, for which the determination of the angle of rotation of a ray of polarized light, or, in some cases, the proof of their optical inactivity, affords the most simple and positive evidence of their identity or purity.

The instruments used for this purpose vary somewhat in their construction and are classified as polarimeters measuring angular rotation and saccharimeters measuring percentage of sugar. Those which are most generally adapted for the examination of the substances mentioned above are the penumbral or so-called " half-shadow " instruments of Laurent and of Schmidt and Hänsch in which the two sides of the field of vision are capable of becoming unequally illuminated. Polarimeters permit the angle of rotation to be read off in degrees or fractions of a degree of a circle. Saccharimeters, set to measure percentage of sucrose, give readings in terms of divisions of the sugar scale.

These determinations are best made in a dark room, and by means of monochromatic light, the latter being obtained by introducing into a non-luminous flame, on a loop of platinum wire, a small bead of fused sodium chloride. The light thus radiated corresponds with the line D of the solar spectrum.

The following factors are employed for converting readings of a saccharimeter into readings of a polarimeter.

1 division Laurent sugar scale equals 0.2167° angular rotation D.

1 division Schmidt and Hänsch sugar scale equals 0.346° angular rotation D.

Since the deviation of the plane of polarization either to the right or to the left of the zero point is directly proportional to the length of the column of liquid, it is important that the observations should be made with tubes of a definite length, such as 200, 100, 50, or 25 mm. The selection of the length of the tube to be employed is, however, usually dependent upon the depth of color of the liquid and the magnitude of its optical rotation.

The rotatory power of an optically active, liquid substance, observed with sodium light, and referred to the ideal density 1, and in a tube having a length of 1 decimeter (100 mm.), is designated as its *specific rotatory power*. This is usually expressed by the term $[\alpha]_D$. Since, however, not only the density of an optically active liquid, but also its rotation, is influenced by the temperature, the specific rotation varies with the latter. In stating the specific rotation it is, therefore, necessary to indicate at what temperature the rotation and the density of the liquid have been determined. But for the same temperature the specific rotation of a pure, optically active liquid is always a constant number. The temperature used in the text of this Pharmacopœia is 25° C. (77° F.), except when otherwise indicated. For saccharimeters the temperature is fixed at 20° C. (68° F.) by international agreement.

For calculating the specific rotatory power of an optically active liquid substance, or solution of an optically active solid, the following formulas are of general application:

I. For liquid substances $$[\alpha]_D = \frac{100 \times \alpha}{L \times d}$$

II. For solutions of solids $$[\alpha]_D = \frac{10000 \times \alpha}{L \times p \times d}$$

or $$[\alpha]_D = \frac{10000 \times \alpha}{L \times c}$$

For calculating these formulas the determination of the following factors is necessary:

α = the angle of rotation of the liquid or solid observed with sodium light.

L = the length of the tube in millimeters.

d = the density of the active liquid or solution.

p = the amount of active substance in 100 parts by weight of the solution.

c = the number of grammes of active substance in 100 mils of solution.

22. Refractive Index

(U. S. P. IX)

When a ray of light passes from one transparent substance to another, it is deflected, except when it enters perpendicularly to the surface of contact. The direction of the deviation is dependent upon the difference of density of the two substances; the extent is also influenced by this difference.

This deviation is termed refraction. When the ray passes from a substance of given density to one of greater density (*i.e.*, from air into glass) the refraction is towards the perpendicular meeting the surface at the point of contact; when passing from a substance of greater density to one of less (*i.e.*, from water into air) the ray deviates from the perpendicular at the point of contact.

Quantitative measurements of refraction are expressed as " indices of refraction," the index being the figure obtained by dividing the sine of the angle that the incident ray makes with the perpendicular, by the sine of the angle that the refracted ray makes with the same perpendicular; that is, it is the ratio between these sines. Thus, the ratio for a ray of light passing from air into water at standard temperature is about 4:3 or, expressing it decimally and with greater exactness, 1.336. This is, therefore, the index of refraction of water. The determination of the refractive index is accomplished by means of optical instruments known generally as *refractometers*, which are of several types. Some of these give figures on an arbitrary scale, the actual refractive index being ascertained by consulting a table.

As the exact temperature at which the examination is made is of great importance, all of the instruments are provided with attachments for circulating water of the proper temperature about the prisms or about the vessel containing the liquid to be observed, and are also equipped with thermometers for observing the temperature very closely.

The principal instruments in use are as follows:

Pulfrich Refractometer.—This instrument is used chiefly for purely scientific investigations. It is adapted for use with liquids and solids of all degrees of refractive power. When a liquid is to be examined

it is placed in a small cylindrical glass vessel immediately above the observation prism. When solids are to be examined the glass cylinder is removed and the solid (previously polished) is placed in direct contact with the observation prism. The reading of this instrument is made by noting a boundary line between a light and a dark field in its position with reference to a graduated scale upon which the refractive index is directly expressed.

The Abbe Refractometer.—This is an instrument of wide utility, designed primarily for the examination of liquids. Only a few drops of the liquid are required for an observation. This is spread in a thin film between the two observation prisms. The index of refraction is also read off directly upon the scale of this instrument, in which, as in the Pulfrich Refractometer, a boundary line between a light and a dark field is the observation line.

The Zeiss Butyro-Refractometer.—This instrument is especially designed for the examination of fixed oils and fats. It is not applicable to aqueous or alcoholic liquids. The distinctive line for observation in this instrument is the border line of total reflection which is a narrow line capable usually of being accurately read to within a tenth of a unit of the arbitrary scale used. Sometimes this observation line is accompanied by a blue or a red fringe or haze which interferes with the accuracy of the reading. Should a close reading be impossible on this account it will be found necessary to use the monochromatic sodium flame for the observation (see under optical rotation).

Zeiss Immersion Refractometer.—This is adapted for the examination of aqueous, oily, or alcoholic liquids. The distinctive line for observation is as described under the preceding instrument, the border line of total reflection, which in this case is much sharper and capable of being much more accurately read. For making observations of the entire range of Pharmacopœial substances the Abbe instrument is the one generally selected, the Pulfrich instrument not being in common use and the Zeiss Butyro- and Immersion Refractometers not covering the entire range necessary.

23. Biological Assays

(U. S. P. IX)

Inasmuch as there are several drugs more or less extensively used in the treatment of disease, for which no satisfactory chemical method of assay has been developed, other assays have been introduced in which these drugs are administered to animals and the effects noted. From the results obtained from these assays the strength of the preparation is calculated, and if necessary proper corrections are made so that the preparation shall conform to the standard which has been adopted. The official drugs to which these methods of assay have been applied in the following pages, are the members of the digitalis group, cannabis, and aconite and the suprarenal gland.

Brief descriptions of the more commonly accepted methods are given here in order, first, to direct the attention of manufacturers to them; second, to ascertain the points of weakness which may exist in them; and finally, to outline methods and establish standards which those interested may adopt should they desire to assay their products and have them conform to the standards proposed.

All preparations thus assayed and made to conform to these standards may be labeled " Physiologically assayed and standardized according to the U. S. P. IX."

In the case of Cannabis and its preparations, the biological assay standards are compulsory.

Cannabis

The assay of Cannabis and its preparations has been made a requirement and is based upon the fact that this drug produces certain symptoms of muscular incoördination. The method consists of ascertaining the dose of the preparation to be tested which will produce these symptoms of incoördination in dogs and then adjusting its strength by comparison with a standard preparation.

Dogs.—The animals differ considerably in susceptibility to the drug and therefore it is best to make preliminary tests upon several dogs with average-sized doses and select from among them the animals which react easily to the drug. As a rule, fox terriers serve very well for the purpose, but any dog may prove satisfactory. It is best to provide at least two dogs for each assay but if many samples are to be examined more dogs will be needed. The dogs should be at least one year old and in normal health and must be kept under the best sanitary conditions. They may be used repeatedly for the purpose but not at shorter intervals than three days. Each series of tests should be conducted by the same person, who should be perfectly familiar with the peculiarities of each animal in order that he may recognize more certainly deviations from the normal. While the tests are being made the animals should be kept in a perfectly quiet room free from disturbance and separated so that they cannot see each other.

Preparation of the Drug.—The drug may be given most conveniently in the form of the fluidextract which is administered in gelatin capsules, or the extract made into soft pills may be used; but whichever form is chosen the same should be used for both the standard and the preparation that is to be tested.

Before administration the animal should not be fed for twenty-four hours in order to hasten absorption. The head of the animal being held, its mouth is opened and the capsule or pill is placed upon the back of the tongue. Usually the drug is easily swallowed when given in this way, but this may be facilitated by giving the animal a small amount of water to drink.

Assay.—An average dose of the known or standard preparation is given to one of the dogs and a like dose of the preparation to be standardized is given the second dog. After one hour both dogs are observed very carefully for symptoms of muscular incoördination. The incoördination is manifested differently in different animals, but in small doses it shows itself most frequently in slight swaying, when the animal is standing quietly, or in some ataxia when it runs about. The observation should be made frequently during the second hour following the administration of the drug.

The results obtained from the first test should be confirmed after an interval of not less than three days by repeating the administration but reversing the order, that is, giving the known strength drug to the dog which received that of unknown strength before and *vice versa*.

In subsequent tests which are carried out, the dose of the preparation of unknown strength is modified so as to produce similar symptoms to those produced by the standard. If the preparation to be tested is below the standard in strength, its dose must be increased, or if it is above strength its dose is lessened until equivalent doses of the two are found. Dogs may be used over long periods of time, even for some years, but occasionally they have to be discarded, as in some cases they seem to learn the effects of the drug and so refuse to stand up. A certain degree of tolerance is sometimes gained which necessitates larger doses.

Standard.—As there is no chemical substance of definite composition which can be adopted as a standard, a Fluidextract of Cannabis or an extract which has been carefully prepared and suitably preserved may be utilized for this purpose. A standard Fluidextract will produce incoördination when administered to dogs in the dose of 0.03 mil for each kilogramme of body weight of dog. When administered in the form of the Extract a dose of 0.004 Gm. for each kilogramme of body weight of dog should produce similar symptoms, and the requirement for a standard tincture is a dose of 0.3 mil for each kilogramme of body weight of dog.

Aconite

The method for the physiological assay of Aconite depends upon the determination of the minimum lethal dose for guinea-pigs.

Method.—The guinea-pigs to be utilized should be of average size and not too large; preferably from 250 to 350 Gm. in weight and in healthy condition.

The drug may be administered in the form of fluidextract, extract, or tincture, which in the preliminary trial may be injected subcutaneously into a series of guinea-pigs in doses having sufficiently wide limits. If the extract is to be standardized, it must be dissolved in sufficient solvent to produce a liquid preparation before injection. The animals after injection are placed in cages and at the end of the observation (twelve hours), note is taken of those living and dead.

After this preliminary test, the limits of the doses for a second series of animals are further narrowed and, if necessary to still further confirm the earlier results, additional series may be injected until the minimum lethal dose for the guinea-pig is found.

Standard.—A satisfactory preparation of the Fluidextract of Aconite should kill guinea-pigs when administered in doses of 0.00004 mil for each gramme of body weight of guinea-pig; a satisfactory Tincture of Aconite should prove fatal to guinea-pigs when given in doses of 0.0004 mil for each gramme of body weight of guinea-pig and a satisfactory Extract of Aconite should have a minimum lethal dose not greater than 0.00001 Gm. for each gramme of body weight of guinea-pig.

Digitalis—Strophanthus—Squill

For the members of the digitalis series the so-called " one hour frog " method is recommended. This method consists essentially in ascertaining the dose of a drug or preparation which will bring the heart of a standard sized frog to systolic standstill in one hour's time. The method is carried out as described below; all measurements being performed with the same degree of accuracy used in ordinary quantitative chemical estimations.

Frogs.—The frogs to be employed in an assay should be in a healthy condition and of the same species. Those most commonly obtainable in this country are the common grass frogs (*Rana viridis* or *Rana pipiens*). While the dose for a frog is estimated according to its weight, it is best to use frogs of a fairly uniform size, the most convenient weight for such work being between 15 and 25 Gm.

Storage.—Before use the frogs should be stored in tanks kept in a cool room, preferably where the temperature does not rise above 15° C. (59° F.). The bottom of the tanks should be covered with running water or, if running water is not convenient, standing water may be used if it is changed from two to four times daily. An hour before the frogs are to be used for an assay a sufficient number should be taken to the operating room, each one carefully weighed to within 0.1 Gm. and placed in an individual wire cage or container, these are then placed in a tank containing water to the depth of about 1 cm. (½ inch) which is kept during the process of assay at a uniform temperature of 20° C. (68° F.). The maintaining of a uniform temperature at which all assays of the members of this group should be carried out is important, as the susceptibility of frogs differs very considerably at different temperatures.

Dosage.—After the frogs have been weighed as described, the doses to be given are calculated according to their weights and are measured into small conical glasses by means of a finely graduated pipette. The doses of the preparation which are to be injected should be as uniform in quantity as possible and should not exceed 0.015 mil for each gramme of body weight of frog. The members of the digitalis series may be assayed in either fluidextract or tincture strength, being diluted with water as may be necessary to get the volume dose. In case the alcohol content in any preparation after dilution is higher than 20 per cent., the preparation may be subjected to careful evaporation and subsequent dilution with an aqueous solution containing 0.7 per cent. of sodium chloride until the original volume is restored and the alcohol content is not above the per cent. named. It is always best to have the alcohol content of different preparations uniform. In case there is a precipitate the preparation to be assayed should be shaken each time a dose is measured out.

When the doses are ready, they may be injected into the anterior lymph sac of the animal. This is done by means of a glass pipette which is drawn out to a fine point. The frog is held on its back in one hand and the pipette with the contained drug in the other, the mouth of the frog is opened with the point of the pipette and, carefully avoiding the tongue, the floor of the mouth is punctured and the point of the pipette is then seen to enter the anterior lymph sac of the frog. The contents of the pipette are now forced into the sac either by gravity or by gently blowing, if necessary. In the latter case, care should be taken not to introduce air into the sac. Care should also be taken not to puncture the skin. The animal is then replaced in its cage in the tank, the temperature of which is maintained as stated at 20° C. (68° F.).

At the end of one hour from the time of injection each frog is pithed, both brain and cord, the heart is exposed and its condition examined. For the correct end reaction the ventricle should be in systolic standstill while the auricles should be widely dilated.

Following mechanical stimulation feeble contractions may be allowed in the auricles and localized contractions in the ventricle, but no general contraction is allowable.

If when the heart of an animal is being exposed for examination, remains of the injected drug are found in the lymph sac unabsorbed, such an animal should be discarded and not considered in the results obtained.

It happens sometimes that one frog out of a large series may prove a decided exception to the others in the way of increased or decreased susceptibility to the drug. Such an animal should also be discarded.

After the primary or trial assay has been carried out and the approximate strength of the preparation ascertained, a second series of frogs is injected in like manner, using doses the limits of which are considerably narrower than the first series. A third or even fourth series of injections may be necessary to confirm the earlier results. The dose thus found is then compared with the dose of a standard which is similarly ascertained upon another series of frogs of the same lot. From such a comparison the strength of the unknown preparation can be suitably adjusted.

The use of a standard is made necessary by the fact that frogs differ in their susceptibility to the members of the digitalis series at different seasons of the year. The condition of susceptibility is ascertained and allowed for by the use of a solution of ouabain (see page 1686) as a standard which in appropriate doses is injected into a series of frogs and their resistance thus determined. The necessary strength of an unknown preparation may be calculated from the dose actually found by the ratio of the standard dose of ouabain to the dose of ouabain found necessary to kill. Thus:

Standard dose of ouabain	:	Found dose of ouabain	::	Standard dose of drug being assayed	:	Necessary dose of unknown

The standard dose of ouabain is 0.0000005 Gm. per gramme of body weight of frog.

The standard dose of Tincture of Digitalis to correspond is 0.006 mil per gramme of body weight of frog.

If, therefore, in a certain series of frogs the resistance to ouabain is found to be increased so that a dose of 0.00000075 Gm. is necessary to stop the heart in systole in one hour, the dose of Tincture of Digitalis would also have to be increased to 0.009 mil, and the actual dose found calculated against this, instead of against the standard dose of 0.006 mil. For example, in frogs showing the increased resistance as indicated above, if the Tincture being examined assays 0.018 mil per gramme of body weight it is one-half strength.

Standards.—The standards adopted are as follows: Ouabain, 0.0000005 Gm. (or mil) for each gramme of body weight of frog; digitalis: leaves (in the form of tincture), 0.0006 Gm.; fluidextract, 0.0006 Gm.; tincture, 0.006; strophanthus: seed (in the form of tincture), 0.000006; tincture, 0.00006; squill: dried squill (in the form of tincture), 0.0006; fluidextract, 0.0006; tincture, 0.006.

Suprarenal Gland

The assay of products of the Suprarenal Gland is carried out by means of a comparison of the rise in blood-pressure produced in a dog by an injection of an aqueous preparation of the gland with that produced by a solution of known strength of lævo-methylamino-ethanol-catechol ($C_9H_{13}NO_3$) (see page 1683).

Standard Solution.—Prepare an aqueous solution of lævo-methylamino-ethanol-catechol (1 in 1000), using sufficient diluted hydrochloric acid, and from this solution prepare a second solution of the strength of 1 in 100,000 by adding 1 mil of the original solution (1 in 1000) to 99 mils of physiological solution of sodium chloride; this latter solution should be freshly prepared for each assay.

Prepare a solution by adding 1 Gm. of the finely powdered dried suprarenal glands to be tested to 100 mils of distilled water containing 10 mils of diluted hydrochloric acid, allow this mixture to macerate during twenty-four hours, shaking it frequently during that time, and then filter through a dry filter. It is then ready for use.

Dogs.—The animal, which should be of medium size, is anesthetized with a suitable anesthetic. The animal is prepared for blood-pressure estimations in the usual manner by the insertion of a suitable cannula into one carotid artery and this in turn is connected with an ordinary mercury manometer. The trachea is exposed and a cannula inserted into it so that the animal may receive artificial respiration during the course of the experiment.

The femoral vein on each side is exposed and a cannula inserted in each. These should be fitted with short pieces of small rubber tubing to serve as connections for the injecting syringes.

Two glass syringes graduated to 0.05 mil should be provided, one to be used for injecting the standard and the other for the aqueous preparation of the gland.

Before the test is made, in case any muscular movement such as twitching is present, the dog should receive by intravenous injection, a sufficient dose of curare (see page 1680), but if the animal is deeply anesthetized, this may not be necessary. The dog should also receive a sufficient dose of atropine sulphate (0.001 to 0.002 Gm.) to paralyze the vagi, this paralysis being proved by electrical stimulation.

The blood-pressure tracing may be best taken on a long kymograph, which may be allowed to run from the time of injection until after the crest of the pressure rise has been passed, when it may be stopped.

Injections should be made at regular intervals and these intervals should not be shorter than five minutes.

One cannula and one syringe are now filled with the standard solution prepared as directed above and 1 mil is injected. The rise of blood-pressure should be submaximal, say from 30 to 60 mm., and in case this figure is much exceeded a second injection of 0.5 mil may be made five minutes later. After a satisfactory dose has been ascertained, 1 mil of the aqueous preparation of the gland may be injected with the second syringe into the femoral vein of the opposite side. In subsequent injections this dose may be increased or decreased as necessary until such an amount is found as will give the same elevation of blood-pressure as the established dose of the standard solution when the two solutions are given in alternating doses. When this relation has been ascertained, it should be confirmed on the same animal by making the injection into the opposite sides from which they have been made in the earlier tests. Before these confirmatory tests are made, it is necessary to wash out the cannulas most carefully before the new solutions are introduced.

The ratio of activity found between these two solutions may be confirmed by injections made into a second animal, using a new aqueous extract of the gland prepared in the same manner as the first.

From the results thus obtained, the strength of the aqueous preparation of the gland may be determined by calculation and expressed in terms which indicate its relative activity as compared with that of the standard.

Standard.—One gramme of *Suprarenalum Siccum* contains the equivalent of 10 milligrammes of lævo-methylamino-ethanol-catechol.

Standard Thermometers

(U. S. P. IX)

General Requirements.—The bulbs are to be of Jena 16 III normal glass or Corning normal thermometer glass. The stems may be made of other white enamel back glass tubing having a circular cross section; the diameter of the capillary must not be greater than 0.1 mm. The diameter of the stem is to be 5.5 mm. (to within ± 0.3 mm.), and the maximum diameter of the bulb must not be greater than the diameter of the stem. The thermometers are to have a pear-shaped reservoir, at the upper end of the capillary having a volume at least equal to the volume of the entire graduated portion of the stem. The upper end of the stem is to have a small glass ring.

Graduation.—The thermometers are all to be graduated into 0.5° (one-half degree) intervals. The 1° graduation marks are to be longer than those for the half degrees, the longer graduations extending, preferably, equally to the right and left of the shorter marks. The graduation marks are to be clean cut and fine, and to be uniformly well-filled with insoluble colored pigment.

Numbering.—The 100° graduations (the 0°, 100°, 200°, 300° graduations on the different thermometers) are to be numbered in full and the intermediate 5° and 10° graduations are to be numbered 5, 10, 15, etc. . . . 95, 100, 5, 10, 15, . . . 95, 200, 5, 10, etc. The numbers must be distinct and easily legible and preferably in such position that they will be upright when the thermometer is vertical. The figures should not be unduly large. It is suggested that the figures opposite the 0°, 100°, 200°, 300° graduations be made about 2 mm. in height and the intermediate numbers 5, 10, 15, etc., somewhat less (about 1.4 mm.).

Annealing.—The thermometers should be so thoroughly annealed that there will be no appreciable change in their indications after long continued exposure to the highest temperature on the scale.

Error of Scale.—The maximum error at any temperature below 100° C. must not exceed 0.5°, nor exceed 1.0° in the interval 100° to 350° C.

Standardization.—The thermometers should be submitted to the Bureau of Standards for standardization or carefully compared with thermometers actually standardized by the Bureau of Standards.

Filling Under Pressure.—Thermometers reading over 200° C. must be filled under sufficient pressure to prevent the mercury column from boiling or breaking up into small pieces.

Thermometer No. 1.—The thermometer is to be graduated from −10.5° to 125.5° C. into half degrees, the length of a 1° interval being 1.5 to 2 mm.

Thermometer No. 2.—The thermometer is to be graduated from 98° to 225.5° C. into half degrees, the length of a 1° interval being 1.5 to 2 mm. The graduations to begin a short distance above top of bulb so that the distance from first graduation (98°) to bottom end of bulb shall not be over 40 mm.

Thermometer No. 2A.—The thermometer is to be graduated into half degrees in the neighborhood of ice point from 1° to 2°, above which is to be a small enlargement in the capillary, and then a graduated portion extending from 98° to 250.5° C., the length of a 1° interval being 1.5 to 2 mm. The length of the thermometer between the 98° mark and the lower end of the main bulb should not exceed 65 mm.

Thermometer No. 3.—The thermometer is to be graduated from 198° to 350.5° C. into half degrees, the length of a 1° interval being 1.5 to 2 mm. The graduations to begin a short distance above the top of the bulb so that the distance from the first graduation (198°) to the bottom end of the bulb shall not be over 40 mm. The graduated stem to be the same length as Nos. 1 and 2.

Thermometer No. 3A.—The thermometer is to be graduated into half degrees in the neighborhood of the ice point from −1° to 4°, above which is to be a small enlargement in the capillary, and then a graduated portion extending from 198° to 350.5° C., the length of a 1° interval being 1.5 to 2 mm. The length of the thermometer between the 198° mark and the lower end of the main bulb should not exceed 65 mm.

Auxiliary Thermometer.—This thermometer is for emergent stem corrections. Use a standard thermometer from 15 to 20 cm. in length and graduated from 20° to 100° C., into degrees.

Thermometers for Boiling Points.—In order to avoid the necessity of an emergent stem correction, it is advisable that an accurately standardized thermometer of the Anschütz type be used for boiling points. If such a thermometer is not available, a thermometer such as is specified above (see No. 1, 2, or 3) may be employed, applying the emergent stem correction as described under *Melting Points* (see page 1716), the length of emergent stem being measured, in degrees, from the lower end of the stopper to the highest point of the boiling temperature.

Sterilization

(U. S. P. IX)

The term "Sterilization" as employed in the practice of medicine and pharmacy means the destruction or removal of bacteria or their spores and other living organisms. This may be accomplished in various ways, depending upon the nature of the material to be sterilized.

A sterile condition can be maintained only so long as the substance or material is kept from contact with air or other media which may carry micro-organisms.

The important subject of sterilization cannot be treated with any great degree of particularity, nor can the intricate details of scientific technique be fully described in this Chapter.

Glass and Metal Utensils.—These may be sterilized by heating them from 160° to 170° C. (320° to 338° F.) for two hours in a hot-air sterilizing oven, or in a closed vessel (autoclave) under steam pressure at a temperature of from 115° to 120° C. (239° to 248° F.) for fifteen minutes. Heating in a current of steam for

thirty minutes, or thoroughly boiling for fifteen minutes in water, or in an aqueous solution of sodium bicarbonate (1 in 1000) will kill all nonspore-bearing organisms and some spore-bearing organisms. As the presence of even a minute quantity of alkali is objectionable in glass containers in certain cases, the process of sterilization should in such instances be preceded by a thorough cleansing of the bottle, ampul or other receptacle with dilute hydrochloric acid, 1 per cent., followed by a thorough rinsing with distilled water.

Stoppers.—Rubber stoppers only should be used for containers and these should be sterilized before use. Cork stoppers should not be used.

Medicinal Solutions Not Easily Decomposed by Heat.—Solutions which are not injured by high temperatures should be sterilized in a current of steam, in an oven, or in a closed apparatus (autoclave) by steam under pressure.

Sterilization in a current of steam should not be concluded in less than thirty minutes and the heat should preferably be continued for one hour; an exposure of from fifteen to twenty minutes is sufficient if the sterilization is carried out in a pressure apparatus at a temperature of from 115° to 120° C. (239° to 248° F.).

Wrap the utensils or containers in parchment paper before starting sterilization for protection against contamination and do not remove the paper until the solution is to be used.

Medicinal Solutions of Substances Readily Decomposed by Heat.—Solutions of substances which are decomposed when subjected to the heat and manipulation directed in the preceding paragraph (this includes solutions of many alkaloids) may be prepared in an approximately sterile condition as directed below:

Method 1.—Filter the solution through a stone or porcelain filter which has previously been tested to prove its efficiency in removing bacteria.

Method 2.—Sterilize all utensils necessary for weighing, such as scales, spatulas, etc., either in steam or, immediately before use, by a thorough cleansing, first with purified cotton saturated with alcohol, then with cotton saturated with ether. Then dissolve the substance in a sterilized, glass-stoppered container, holding the required amount of sterilized distilled water. Should the solution require filtration, use a sterilized funnel and filter paper and collect the filtrate in a sterilized container, closing it with a sterilized rubber stopper. The filtration must be conducted in such a manner that no contamination will result.

Emulsions in Glycerin or Oil.—Approximately sterile solutions or emulsions in glycerin or oil may be prepared in the following manner: heat glycerin in a steam sterilizer as described under *Medicinal Solutions Not Easily Decomposed by Heat*, or heat oil for two hours in a dry-air sterilizer at about 120° C. (248° F.), then introduce the medicinal substances after the liquid has cooled. The desired medicament may be incorporated by triturating it in a sterilized mortar containing the previously sterilized medium (glycerin or oil), and the solution or emulsion should then be quickly transferred to a sterilized glass container.

When solutions have been passed through carefully tested porcelain filters and properly collected and kept in sterile containers, they may be considered "sterile."

Surgical Dressings.—Cotton, bandages, gauzes, ligatures, etc., may be rendered sterile by treatment with steam in a pressure apparatus (autoclave) at 115° C. (239° F.) for fifteen minutes or by exposure to dry heat in an ordinary air-bath or sterilizer at a temperature of from 160° to 170° C. (320° to 338° F.) for two hours. It should be remembered that all surgical materials are not amenable to such thorough treatment without more or less deterioration taking place. Bandages must be folded or packed in such a manner as to permit the penetration of steam or dry heat during the process and should be so arranged that after the sterilization is completed all subsequent contamination with bacteria will be prevented. This is usually accomplished by immediately enclosing them in glass containers or wrapping them in a number of thicknesses of previously sterilized parchment paper.

Diagnostical Reagents and Clinical Tests

(U. S. P. IX)

In the following pages of Diagnostical Reagents and Clinical Tests it is understood that the standard for official substances like Iodine, Potassium Iodide, Gelatin, Sodium Chloride, etc., are those to be found in the text of this Pharmacopœia. Where other substances not described in Part I are used a description will be found among the reagents (see pages 1675 to 1692). If the solutions are not clear filter them.

Reagents for Examination of Urine

For Acetone Reaction

Sodium Nitroprusside (see page 1690, used for Legal's test and Lange's test).

Iodine Potassium Iodide Solution (for Lieben's solution): Potassium Iodide, 6 Gm.; Iodine, 4 Gm.; Distilled Water, a sufficient quantity to make 100 mils. Dissolve the potassium iodide in the distilled water, add the iodine and shake the mixture frequently until a solution is obtained.

Alcoholic Solution of Iodine (10 per cent.), for Gunning's reaction. To be freshly prepared.

For Albumin Reaction

Glacial Acetic Acid (see page 13).

Acetic Acid (see page 13).

Potassium Ferrocyanide (see page 1688).

Nitric Acid (see page 45).

Saturated Aqueous Solution of Trinitrophenol (see page 1164).

Esbach's Reagent: Trinitrophenol, 1 Gm.; Citric Acid, 2 Gm.; Distilled Water, a sufficient quantity, to make a solution measuring 100 mils.

Spiegler-Jolles' Reagent: Corrosive Mercuric Chloride, 2 Gm.; Succinic Acid, 4 Gm.; Sodium Chloride,

4 Gm.; Distilled Water, a sufficient quantity, to make 100 mils. Mix the several ingredients and dissolve them in the distilled water.

Trichloracetic Acid (see page 81).

For Albumose Reaction

Phosphotungstic Acid (see page 1687) (Salkowski's test).

For Bile Reactions

UROBILIN

Amyl Alcohol (see page 1677).

Solution of Zinc Chloride (about 10 per cent.): Zinc Chloride, 10 Gm.; Distilled Water, a sufficient quantity to make a solution measuring 100 mils.

Mixture of Zinc Acetate: Zinc Acetate, 10 Gm.; Dehydrated Alcohol, a sufficient quantity to make 100 mils. Finely powder the zinc acetate and intimately mix it with the alcohol. Dispense the mixture with directions "to be well shaken before using."

UROBILINOGEN

Ehrlich's Solution: Paradimethylamidobenzaldehyde, 2 Gm.; Hydrochloric Acid, 50 mils; Distilled Water, a sufficient quantity to make a solution measuring 100 mils.

BILIARY COLOR REACTIONS

Nitric Acid (containing a trace of nitrous acid).

Solution of Calcium Chloride (about 10 per cent.) (Hupert's reaction): Calcium Chloride, 10 Gm.; Distilled Water, a sufficient quantity to make a solution measuring 100 mils.

Alcoholic Solution of Iodine (about 1 per cent.): Iodine, 1 Gm.; Alcohol, a sufficient quantity to make a solution measuring 100 mils.

For Blood Reaction

Solution of Guaiac: Guaiac, 2 Gm.; Dehydrated Alcohol, a sufficient quantity to make a solution measuring 100 mils.

Oxygenated Oil of Turpentine.

Ether containing Hydrogen Dioxide.

Aloin, isobarbaloin containing barbaloin.

For Diacetic Acid Reaction

Solution of Ferric Chloride (see page 633) used for Gerhardt's test.

For Diazo Reaction, Ehrlich

1. Sodium Nitrite, 1 Gm.; Distilled Water, a sufficient quantity to make 200 mils.

2. Sulphanilic Acid, 5 Gm.; Hydrochloric Acid, 50 mils; Distilled Water, a sufficient quantity to make 1000 mils. Dissolve the sulphanilic acid in about 700 mils of distilled water to which the hydrochloric acid has been added and follow with enough distilled water to make the product measure 1000 mils. For use, 1 mil of the sodium nitrite solution should be mixed with 50 mils of the sulphanilic acid solution.

For Indican Reactions

Solution of Chlorinated Lime:

A saturated solution of chlorinated lime diluted with an equal volume of distilled water and filtered.

Obermeyer's Solution: Ferric Chloride, 0.4 Gm.; Hydrochloric Acid, a sufficient quantity to make a solution measuring 100 mils.

Solution of Lead Acetate: Lead Acetate, 25 Gm.; Distilled Water, a sufficient quantity to make a solution measuring 100 mils.

For Pentose Reactions

Bial's Reagent: Orcin, 1 Gm.; Hydrochloric Acid, 500 mils; Solution of Ferric Chloride, 25 drops. Dissolve the orcin in the hydrochloric acid and add the solution of ferric chloride.

Phloroglucinol (see page 1686).

For the Estimation of Urea

Solution of Sodium Hypobromite: 1. Bromine, 125 Gm.; Sodium Bromide, 125 Gm.; Distilled Water, a sufficient quantity to make a solution measuring 1000 mils.

2. Sodium Hydroxide, 225 Gm.; Distilled Water, a sufficient quantity to make a solution measuring 1000 mils. The reagent should be freshly prepared by mixing equal volumes of solutions 1 and 2 and diluting the resulting mixture with one and a half volumes of distilled water.

For Sugar Reactions

Solution of Sodium Hydroxide: Sodium Hydroxide, 10 Gm.; Distilled Water, a sufficient quantity to make a solution measuring 100 mils.

Solution of Copper Sulphate: Copper Sulphate, 10 Gm.; Distilled Water, a sufficient quantity to make a solution measuring 100 mils.

Nylander's Reagent: Potassium and Sodium Tartrate, 4 Gm.; Sodium Hydroxide, 10 Gm.; Bismuth Subnitrate, 2 Gm.; Distilled Water, a sufficient quantity to make 100 mils.

Dissolve the potassium and sodium tartrate in 90 mils of distilled water. Add the bismuth subnitrate to the solution, shake the mixture thoroughly and then filter through glass wool. Preserve and dispense this solution in amber-colored bottles.

Fehling's Solution (see Alkaline Cupric Tartrate V.S., page 1694).

Pavy's Solution: 1. Copper Sulphate, 4.158 Gm.; Distilled Water, a sufficient quantity to make a solution measuring 500 mils.

2. Potassium and Sodium Tartrate, 20.4 Gm.; Potassium Hydroxide, 20.4 Gm.; Stronger Ammonia Water, 300.0 mils; Distilled Water, a sufficient quantity to make a solution measuring 500 mils. For use, mix equal quantities of the two solutions.

Phenylhydrazine Hydrochloride (see page 1686).

Sodium Acetate: Neutral to litmus paper.

Fermentation test with yeast.

Reagents for the Examination of Gastric Contents

Congo Red Test Paper:

Saturate filter paper with an aqueous solution of Congo Red (1 in 1000), page 1707. Dry and cut the paper into strips and preserve them in well-stoppered glass vials.

Saturated Alcoholic Solution of Methylthionine Chloride (*Methylene Blue*) (see page 697).

Alcoholic Solution of Dimethylaminoazobenzene (see page 1680) (1 in 200).

Günzburg's Reagent: Phloroglucinol, 2 Gm.; Vanillin, 1 Gm.; Alcohol, 30 mils. Dissolve the ingredients in the alcohol.

Tenth-normal Hydrochloric Acid V.S. (see page 1696): Dilute 1 volume of normal hydrochloric acid V.S. with exactly 9 volumes of distilled water.

Tenth-normal Potassium Hydroxide V.S. (see page 1699).

Phenolphthalein (see page 843).

Solution of Rosolic Acid: Rosolic Acid, 1 Gm.; Alcohol, a sufficient quantity to make a solution measuring 100 mils.

Carminfibrin: Heat freshly-drawn beef blood, wash the stringy coagulated fibrin in running water until decolorized, cut the fibrin into small pieces of uniform size and macerate it in alcohol for several days. Then transfer the fibrin for one or two days to a 0.5 per cent. ammoniacal solution of carmine, which contains as little excess of ammonia as possible, and keep it cool until the fibrin is thoroughly stained. Wash the product in distilled water until the wash-water is no longer colored, squeeze it out well, and then preserve it in glycerin. Before using, carefully wash the carminfibrin in distilled water to free it from glycerin.

Reagents for the Examination of Blood

For red blood-corpuscles:

Hayem's Solution: Sodium Sulphate, 5 Gm.; Sodium Chloride, 1 Gm.; Corrosive Mercuric Chloride, 0.5 Gm.; Distilled Water, 200.0 mils. Dissolve the salts in the distilled water and filter.

Toison's Solution: Methyl Violet 6B, 0.025 Gm.; Sodium Chloride, 1.000 Gm.; Sodium Sulphate, 8.000 Gm.; Glycerin, 30.000 mils; Distilled Water, 300.000 mils. Dissolve the salts in the distilled water and add the methyl violet and the glycerin.

For white corpuscles: Acetic Acid (U.S.P.), 1 mil; Distilled Water, 99 mils; mix them.

Solution for Hemoglobin Estimation (*Sahli's hemometer*): Tenth-normal hydrochloric acid V.S. saturated with chloroform. This solution should always be freshly prepared and be dispensed in dark amber-colored bottles.

Jenner's Stain: 1. Eosin, 0.5 Gm.; Methyl Alcohol, rectified wood alcohol, sp. gr. about 0.812 at 25° C. (77° F.), a sufficient quantity to make a solution measuring 100 mils.

2. Methylthionine Chloride (Methylene Blue), 0.5 Gm.; Methyl Alcohol, rectified wood alcohol, sp. gr. about 0.812 at 25° C. (77° F.), a sufficient quantity to make a solution measuring 100 mils. For use mix 25 mils of eosin solution with 20 mils of methylene blue solution.

Ehrlich's Triacid Stain: Saturated Aqueous Solution of Orange-G, 120 to 125 mils; Saturated Aqueous Solution of Acid Fuchsin, 80 to 165 mils; Saturated Aqueous Solution of Methylene Green, 125 mils; Distilled Water, 300 mils; Dehydrated Alcohol, 200 mils; Glycerin, 100 mils; mix.

Wright's Stain: Wright's Stain (Grübler's dried powder), 0.1 Gm.; Methyl Alcohol, rectified wood alcohol, sp. gr. about 0.812 at 25° C. (77° F.), 60.0 mils.

Giemsa's Stain: Azur II-Eosin, 0.3 Gm.; Azur II, 0.8 Gm.; Glycerin, 250.0 mils; Methyl Alcohol, rectified wood alcohol, sp. gr. about 0.812 at 25° C. (77° F.), 250.0 mils. Dissolve the dyes in the methyl alcohol and add the glycerin and filter.

Stains and Accessories for use in connection with the study of Micro-organisms

Alum-hematoxylin Solution: Hematoxylin, crystals, 1.0 Gm.; Saturated Aqueous Solution of Ammonium Alum, 100.0 mils; Distilled Water, 300.0 mils; Thymol, 0.5 Gm. Dissolve the hematoxylin in a little distilled water by the aid of heat, add the other ingredients and expose the combined solution to the light, in a bottle loosely stoppered, until it has assumed a dark red color, then filter. The thymol is added as a preservative.

Mayer's Hemalum: Hematein or its ammonium salt, 1.0 Gm.; Alcohol, 90 per cent., 50.0 mils; Alum, 50.0 Gm.; Distilled Water, 1000.0 mils; Thymol, 0.5 Gm. Dissolve the hematein in the alcohol by the aid of heat, add the thymol, and then this solution to the alum dissolved in the distilled water, and then filter. The thymol is added as a preservative.

Alcoholic Solution of Methyl Violet 6B: Methyl Violet 6B, 10 Gm.; Alcohol, a sufficient quantity to make a solution measuring 100 mils.

Borax-Methylene Blue Solution: Methylthionine Chloride (Methylene Blue), 2 Gm.; Boiling Solution of Sodium Borate (1 in 20) a sufficient quantity to make a solution measuring 100 mils.

Löffler's Methylene Blue Solution: Methylthionine Chloride (Methylene Blue), 0.5 Gm.; Alcohol, 30.0 mils; Tenth-normal Potassium Hydroxide V.S., 2.0 mils; Distilled Water, 98.0 mils. Dissolve the methylene blue in the alcohol, add the potassium hydroxide and distilled water.

Solution of Carbol Methyl Violet: Alcoholic Solution of Methyl Violet 6B, 10 mils; Aqueous Solution of Phenol (1 in 20), a sufficient quantity to make a solution measuring 100 mils.

Solution of Carbolfuchsin: Alcoholic Solution of Fuchsin (1 in 10), 10 mils; Aqueous Solution of Phenol (1 in 20), 100 mils; mix.

For Tubercle Bacilli

Solution of Carbolfuchsin (see above).

For Decolorizing

Ebner's Fluid: Hydrochloric Acid, 2.5 mils; Sodium Chloride, 2.5 Gm.; Distilled Water, 100.0 mils; Alcohol, 500.0 mils. Prepare a solution.

Nitric Acid Solution: Nitric Acid, 30 mils; Distilled Water, a sufficient quantity to make a solution measuring 100 mils.

Diluted Alcohol.

Diluted Lugol's Solution (Gram's Iodine Solution): Iodine, 1 Gm.; Potassium Iodide, 2 Gm.; Distilled Water, a sufficient quantity to make a solution measuring 200 mils.

For Counter Staining

Löffler's Methylene Blue Solution (see above).

Gram's Stain (Aniline Water—Methyl Violet 6B Solution): Aniline, 15 mils; Saturated Alcoholic Solution of Methyl Violet 6B, 7 mils; Dehydrated Alcohol, 10 mils; Distilled Water, a sufficient quantity to make 100 mils. Shake the aniline with 65 mils of distilled water for several minutes; filter the resulting opalescent aniline water through a moistened filter, pour the filtrate into a solution prepared by mixing the other liquids and add sufficient distilled water to make 100 mils.

Diluted Carbolfuchsin Solution: Solution of Carbolfuchsin (see above), 1 mil; Distilled Water, 4 mils. Prepare a solution.

Accessories

Xylene (see page 1692).
Oil of Clove (see page 756).
Oil of Cedarwood (see page 1685).
Canada Turpentine (Canada Balsam) (see page 1679).

Culture Media

Bouillon Stock: Lean Beef, 500 Gm.; Or Extract of Beef, 3 Gm.; Distilled Water, a sufficient quantity to make 1000 mils. Mix thoroughly 500 Gm. of finely minced lean beef with 1000 mils of cold distilled water, heat it to boiling in a closely covered dish or flask and keep it at that temperature for one hour. If extract of beef is used to make bouillon stock, boil the solution for one-half hour. Filter the resulting bouillon through a well-wetted filter, until clear and use it as the basis for the following combinations:

Plain Bouillon: Peptone, 10 Gm.; Sodium Chloride, 5 Gm.; Normal Sodium Hydroxide V.S.; Bouillon Stock, each a sufficient quantity to make 1000 mils. Dissolve the peptone and sodium chloride in the bouillon stock by means of heat and add sufficient normal sodium hydroxide V.S. to make the mixture neutral to litmus. Then filter the product through a well-wetted filter, fill it into suitable containers and sterilize.

Glucose Bouillon: Glucose (dry), 10 Gm.; Peptone, 10 Gm.; Sodium Chloride, 5 Gm.; Normal Sodium Hydroxide V.S.; Bouillon Stock, each, a sufficient quantity to make 1000 mils. Dissolve the glucose, peptone, and sodium chloride in the bouillon stock by means of heat and add sufficient normal sodium hydroxide V.S. to neutralize the resulting solution. Then filter the product through a well-wetted filter, fill it into suitable containers and sterilize by the discontinuous method.

Plain Gelatin: Gelatin, 100 Gm.; Peptone, 10 Gm.; Sodium Chloride, 5 Gm.; Normal Sodium Hydroxide V.S.; Bouillon Stock, each, a sufficient quantity to make 1000 mils. Dissolve the gelatin, peptone, and sodium chloride in the bouillon stock by means of heat and add sufficient normal sodium hydroxide V.S. to neutralize the resulting mixture. Filter the warmed product through filter paper, fill it into suitable containers and sterilize by the discontinuous method.

Glucose Gelatin: Glucose (dry), 10 Gm.; Gelatin, 100 Gm.; Peptone, 10 Gm.; Sodium Chloride, 5 Gm.; Normal Sodium Hydroxide V.S.; Bouillon Stock, each, a sufficient quantity to make 1000 mils. Dissolve the glucose, gelatin, peptone, and sodium chloride in the bouillon stock by means of heat and add sufficient normal sodium hydroxide V.S. to neutralize the resulting mixture. Then filter the product through paper, fill it into suitable containers and sterilize by the discontinuous method.

Plain Agar-agar: Agar, 15 Gm.; Peptone, 10 Gm.; Sodium Chloride, 5 Gm.; Normal Sodium Hydroxide V.S.; Bouillon Stock, each, a sufficient quantity to make 1000 mils. Dissolve the agar, peptone, and sodium chloride in the bouillon stock by means of heat and add a sufficient quantity of normal sodium hydroxide

V.S. to neutralize the resulting mixture. Then filter the warmed product through paper, fill it into suitable containers and sterilize.

Glucose Agar-agar: Glucose (dry), 10 Gm.; Agar, 15 Gm.; Peptone, 10 Gm.; Sodium Chloride, 5 Gm.; Normal Sodium Hydroxide V.S., Bouillon Stock, each, a sufficient quantity to make 1000 mils. Dissolve the glucose, peptone, and sodium chloride in the bouillon stock by means of heat, and add a sufficient quantity of normal sodium hydroxide V.S. to neutralize the resulting mixture. Then filter the warmed product through paper, fill it into suitable containers and sterilize by the discontinuous method.

Glycerin Agar-agar: Glycerin, 60 mils; Agar, 15 Gm.; Peptone, 10 Gm.; Sodium Chloride, 5 Gm.; Normal Sodium Hydroxide V.S.; Bouillon Stock, each, a sufficient quantity to make 1000 mils. Dissolve the glycerin, agar, peptone, and sodium chloride in the bouillon stock by means of heat and add a sufficient quantity of normal sodium hydroxide V.S. to neutralize the resulting mixture. Then filter the warmed product through paper to fill it into suitable containers and sterilize.

Lactose-litmus Agar-agar: Sugar of Milk, 10 Gm.; Agar, 15 Gm.; Peptone, 10 Gm.; Sodium Chloride, 15 Gm.; Normal Sodium Hydroxide V.S.; Azolitmin Test Solution (see page 1707); Bouillon Stock, each, a sufficient quantity to make 1000 mils. Dissolve the sugar of milk, agar, peptone, and sodium chloride in the bouillon stock by means of heat and add a sufficient quantity of normal sodium hydroxide V.S. to neutralize the resulting mixture. Then filter the warmed product through paper, add a sufficient quantity of azolitmin solution to impart to the resulting mixture a pale blue color, fill into suitable containers and sterilize by the discontinuous method.

Blood Serum (Löffler's Mixture): Glucose Bouillon, 250 mils; Horse or Beef Blood Serum, 750 mils. Run the mixture of glucose bouillon and beef or horse blood serum into properly sterilized test tubes, and coagulate it by means of heat so as to form a slanting surface for culture purposes.

Articles Employed in Chemical Testing and Reagents of the British Pharmacopœia

APPENDIX I. Br.

The British test-solutions here given are used for determining the character of particular substances, whether isolated or in composition; thus enabling us to ascertain the identity of medicines, their purity or impurity, and the character of the foreign ingredients, which may be mixed with them accidentally, or with a view to adulteration.

Acetic Acid.—"Acetic Acid of the British Pharmacopœia." *Br.*

Acetic Acid, Diluted.—"Diluted Acetic Acid of the British Pharmacopœia." *Br.*

Acetic Acid, Glacial.—"Glacial Acetic Acid of the British Pharmacopœia." *Br.*

Acetic Anhydride.—"Acetic Anhydride $C_4H_6O_3$ of commerce, pure." *Br.*

Acetone.—"Acetone of the British Pharmacopœia." *Br.*

Albumen.—"Albumen, the liquid white of fresh eggs." *Br.*

Alcohol, Absolute.—"Absolute Alcohol of the British Pharmacopœia." *Br.*

Alcohol (90 per cent.). **Alcohol** (70 per cent.). **Alcohol** (20 per cent.).—"Alcohol (90 per cent.), Alcohol (70 per cent.) and Alcohol (20 per cent.) of the British Pharmacopœia." *Br.*

Alum, Purified.—"Purified Alum of the British Pharmacopœia." *Br.*

Ammonium Chloride.—"Ammonium Chloride of the British Pharmacopœia." *Br.*

Ammonium Molybdate.—"Ammonium Molybdate $(NH_4)_2MoO_4$, of commerce, pure." *Br.*

Ammonium Oxalate.—"Ammonium Oxalate $(NH_4)_2C_2O_4,H_2O$, of commerce, pure." *Br.*

Ammonium Persulphate.—"Ammonium Persulphate, NH_4SO_4, of commerce, pure." *Br.*

Ammonium Thiocyanate.—"Ammonium Thiocyanate, NH_4SCN, of commerce, pure." *Br.*

Amylic Alcohol.—"Amylic Alcohol is a liquid consisting principally of iso-primary amylic alcohol, $C_5H_{11}OH$, and may be prepared by shaking commercial fusel oil with a saturated solution of common salt, separating the oily layer, submitting it to distillation, and collecting and reserving the fraction which distils between 125° and 143° C. (257° and 289.4° F.).

Aniline.—"Aniline of commerce, redistilled." *Br.*

Animal Charcoal.—"Animal Charcoal of commerce, purified." *Br.*

Auric Chloride.—"Auric Chloride of commerce, pure." *Br.*

Barium Chloride.—"Barium Chloride, $BaCl_2,2H_2O$, of commerce, pure." *Br.*

Barium Hydroxide.—"Barium Hydroxide, $Ba(OH)_2,8H_2O$ of commerce, pure." *Br.*

Benzene.—"Benzene of the British Pharmacopœia." *Br.*

Benzolated Amylic Alcohol.—"Benzene, 3 parts by volume; Amylic Alcohol, 1 part by volume; mix; decant from any deposited water." *Br.*

Bismuth Oxynitrate.—"Bismuth Oxynitrate of the British Pharmacopœia." *Br.*

Borax, Purified.—"Purified Borax of the British Pharmacopœia." *Br.*

Bromine.—"Bromine of commerce, pure." *Br.*

Cadmium Iodide.—"Cadmium Iodide, CdI_2, of commerce, pure." *Br.*

Calcium Carbonate.—"Calcium Carbonate, the pure white marble, or calc spar, of commerce." *Br.*

Calcium Hydroxide.—"Calcium Hydroxide of the British Pharmacopœia." *Br.*

Calcium Oxide.—"Calcium Oxide, the Lime of the British Pharmacopœia." *Br.*

Calcium Sulphate.—"Calcium Sulphate, $CaSO_4,2H_2O$, native, pure." *Br.*

Carbon Disulphide.—"Carbon Disulphide of the British Pharmacopœia." *Br.*

Carbon Tetrachloride.—"Carbon Tetrachloride CCl_4, of commerce, pure." *Br.*

Chlorine.—"Chlorine, a gas prepared by the interaction of hydrochloric acid and manganese peroxide, and purified by passing through a small quantity of water contained in a wash bottle." *Br.*

Chloroform.—"Chloroform of the British Pharmacopœia." *Br.*

Chloroform Water.—"Chloroform Water of the British Pharmacopœia." *Br.*

Citric Acid.—"Citric Acid of the British Pharmacopœia." *Br.*

Collodion.—"Collodion of the British Pharmacopœia." *Br.*

Copper.—"Copper in foil, wire, or turnings." *Br.*

Copper Acetate.—"Copper Acetate, $Cu(C_2H_3O_2)_2,H_2O$, of commerce, crystalline, pure." *Br.*

Copper Carbonate.—"Copper Carbonate, precipitated, of commerce." *Br.*

Copper Sulphate.—"Copper Sulphate of the British Pharmacopœia." *Br.*

Ether.—"Ether of the British Pharmacopœia." *Br.*

Ferric Ammonium Sulphate.—"Ferric Ammonium Sulphate, $Fe_2(SO_4)_3,(NH_4)_2SO_4,24H_2O$, of commerce, pure." *Br.*

Ferric Chloride.—"Ferric Chloride of commerce, pure, anhydrous." *Br.*

Ferrous Sulphate.—"Ferrous Sulphate of the British Pharmacopœia." *Br.*

Fuchsin.—"Fuchsin of commerce, pure." *Br.*

Glycerin.—"Glycerin of the British Pharmacopœia." *Br.*

Hydrochloric Acid.—"Hydrochloric Acid of the British Pharmacopœia." *Br.*

Hydrochloric Acid, Diluted.—"Diluted Hydrochloric Acid of the British Pharmacopœia." *Br.*

Hydrochloric Acid, Gaseous.—"Gaseous Hydrochloric Acid, HCl, dry, prepared by the interaction of sulphuric acid and common salt." *Br.*

Hydrogen Sulphide.—Synonym—*Sulphuretted Hydrogen.* "A gas prepared by the action of hydrochloric acid on commercial ferrous sulphide. It will be sufficiently pure after passing through two wash-bottles containing water. A solution of the gas in water may also be employed, but only if it smells strongly of the gas, and yields an abundant black precipitate with solution of lead acetate." *Br.*

Hydroxylamine Hydrochloride.—"Hydroxylamine Hydrochloride, NH_2OH,HCl, of commerce, pure." *Br.*

Hypophosphorous Acid.—"Hypophosphorous Acid of commerce, specific gravity 1.137." *Br.*

Indigo.—"Indigo, a blue pigment prepared from various species of Indigofera, Linn." *Br.*

Iodic Acid.—"Iodic Acid, HIO_3, of commerce, pure." *Br.*

Iodine.—"Iodine of the British Pharmacopœia." *Br.*

Iron.—"Iron of the British Pharmacopœia." *Br.*

Isinglass.—"Isinglass, the swimming bladder or sound of various species of Acipenser, Linn., prepared, and cut into shreds." *Br.*

Lead Acetate.—"Lead Acetate of the British Pharmacopœia." *Br.*

Lead Nitrate.—"Lead Nitrate, $Pb(NO_3)_2$, of commerce, pure." *Br.*

Lead Oxide.—"Lead Oxide of the British Pharmacopœia." *Br.*

Lead Peroxide.—"Lead Peroxide, PbO_2, of commerce, pure." *Br.*

Lime.—"Lime of the British Pharmacopœia." *Br.*

Litmus.—"Litmus, a blue pigment prepared from various species of Roccella, DC. Litmus is used in several forms; for example, Solution of Litmus (Appendix II); Blue Litmus Paper, made by impregnating unglazed white paper with a solution of litmus; and Red Litmus Paper, made by impregnating the paper with the solution reddened by the previous addition of a very minute quantity of sulphuric acid. Litmus may also be employed in the solid form." *Br.*

Magnesia, Heavy.—"Heavy Magnesia of the British Pharmacopœia." *Br.*

Manganese Peroxide.—"Manganese Peroxide, MnO_2, the powdered native pyrolusite." *Br.*

Mercurous Chloride.—"Mercurous Chloride of the British Pharmacopœia." *Br.*

Methyl Orange.—"Methyl Orange, pure sodium dimethyl-amido-azo-benzene-sulphonate, $NaC_{14}H_{14}N_3SO_3$, of commerce." *Br.*

Milk of Lime.—"Lime, 100 grammes; Distilled Water, 200 millilitres; mix." *Br.*

Morphinated Water.—"Morphinated Water, prepared by digesting pure Morphine in Chloroform Water for seven days at a temperature of 15.5° C. (59.9° F.), shaking occasionally so as to obtain a saturated solution of the alkaloid, and filtering from the undissolved morphine." *Br.*

Morphine.—"Morphine, the precipitate obtained on adding solution of ammonia, in slight excess, to the solution of a pure morphine salt in *water*, the precipitate being washed with water until free from ammonium, salt." *Br.*

Mucilage of Gum Acacia.—"Mucilage of Gum Acacia of the British Pharmacopœia." *Br.*

Mucilage of Starch.—"Triturate 1 gramme of Starch with a small quantity of Distilled Water to form a smooth paste; add more Distilled Water, gradually, to produce 50 millilitres of mixture; boil for a few minutes, constantly stirring; cool." *Br.* Mucilage of starch must be recently prepared.

Nitric Acid.—"Nitric Acid of the British Pharmacopœia." *Br.*

Nitric Acid, Diluted.—"Diluted Nitric Acid of the British Pharmacopœia." *Br.*

Nitric Acid, Fuming.—"Fuming Nitric Acid of commerce, specific gravity 1.5." *Br.*

Oil of Turpentine.—"Oil of Turpentine of the British Pharmacopœia." *Br.*

Olive Oil.—"Olive Oil of the British Pharmacopœia." *Br.*

Oxalic Acid.—"Oxalic Acid, $H_2C_2O_4,2H_2O$, of commerce, pure." *Br.*

Paraffin, Soft.—"Soft Paraffin of the British Pharmacopœia." *Br.*

Petroleum Spirit.—Synonym—*Petroleum Ether.* "A colourless, very volatile and highly inflammable liquid obtained from petroleum, and consisting of a mixture of the lower members of the paraffin series of hydrocarbons. Boiling point 50° to 60° C. (122°-140° F.). Specific gravity 0.670 to 0.700." *Br.*

Phenol.—"Phenol of the British Pharmacopœia." *Br.*

Phenol-Disulphonic Acid.—"Heat 3 grammes of Phenol with 20 millilitres of Sulphuric Acid on a water-bath for six hours. Transfer the resulting liquid to a stoppered bottle." *Br.*

Phenolphthalein.—"Phenolphthalein of the British Pharmacopœia." *Br.*

Phosphoric Acid, Concentrated.—"Concentrated Phosphoric Acid of the British Pharmacopœia." *Br.*

Phosphoric Acid, Syrupy.—"Syrupy Phosphoric Acid of commerce, specific gravity 1.750." *Br.*

Picric Acid.—"Picric Acid of the British Pharmacopœia." *Br.*

Platinic Chloride.—"Platinic Chloride of commerce, pure." *Br.*

Potassium Bichromate.—"Potassium Bichromate of the British Pharmacopœia." *Br.*

Potassium Chlorate.—"Potassium Chlorate of the British Pharmacopœia." *Br.*

Potassium Chromate.—"Potassium Chromate, K_2CrO_4, of commerce, pure." *Br.*

Potassium Cyanide.—"Potassium Cyanide of commerce. Contains not less than 90 per cent. of pure potassium cyanide, KCN." *Br.*

Potassium Ferricyanide.—"Potassium Ferricyanide, $K_6Fe_2C_{12}N_{12}$, of commerce, pure." *Br.*

Potassium Ferrocyanide.—"Potassium Ferrocyanide, $K_4FeC_6N_6,3H_2O$, of commerce, pure." *Br.*

Potassium Hydrogen Sulphite.—Synonym—*Acid Potassium Sulphite.* "$KHSO_3$, of commerce, pure." *Br.*

Potassium Hydroxide.—"Potassium Hydroxide of the British Pharmacopœia." *Br.*

Potassium Iodide.—"Potassium Iodide of the British Pharmacopœia." *Br.*

Potassium Nitrate.—"Potassium Nitrate of the British Pharmacopœia." *Br.*

Potassium Permanganate.—"Potassium Permanganate of the British Pharmacopœia." *Br.*

Potassium Sulphate.—"Potassium Sulphate of the British Pharmacopœia." *Br.*

Resorcin.—"Resorcin of the British Pharmacopœia." *Br.*

Salicylic Acid.—"Salicylic Acid of the British Pharmacopœia." *Br.*

Sodium Acetate.—"Sodium Acetate, $NaC_2H_3O_2,3H_2O$, of commerce, pure." *Br.*

Sodium Acetate, Anhydrous.—"Anhydrous Sodium Acetate, $NaC_2H_3O_2$, of commerce, pure." *Br.*

Sodium Arsenate, Anhydrous.—"Anhydrous Sodium Arsenate of the British Pharmacopœia." *Br.*

Sodium Bicarbonate.—"Sodium Bicarbonate of the British Pharmacopœia." *Br.*

Sodium Carbonate.—"Sodium Carbonate of the British Pharmacopœia." *Br.*

Sodium Carbonate, Exsiccated.—"Exsiccated Sodium Carbonate of the British Pharmacopœia." *Br.*

Sodium Chloride.—"Sodium Chloride of the British Pharmacopœia." *Br.*

Sodium Hydrogen Sulphite.—Synonym—*Acid Sodium Sulphite,* "$NaHSO_3$, of commerce, pure." *Br.*

Sodium Hydroxide.—"Sodium Hydroxide of commerce, purified by means of alcohol." *Br.*

Sodium Nitrite.—"Sodium Nitrite of the British Pharmacopœia." *Br.*

Sodium Potassium Tartrate.—"Sodium Potassium Tartrate of the British Pharmacopœia." *Br.*

Sodium Sulphate.—"Sodium Sulphate of the British Pharmacopœia." *Br.*

Sodium Sulphate, Anhydrous.—"The Sodium Sulphate of the British Pharmacopœia, rendered anhydrous by heat." *Br.*

Sodium Sulphide.—"Sodium Sulphide, $Na_2S,9H_2O$, of commerce, pure." *Br.*

Sodium Sulphite.—"Sodium Sulphite of the British Pharmacopœia." *Br.*

Sodium Thiosulphate.—"Sodium Thiosulphate, $Na_2S_2O_3,5H_2O$, of commerce, pure." *Br.*

Sugar, Refined.—"Refined Sugar of the British Pharmacopœia." *Br.*

Sulphur, Precipitated.—"Precipitated Sulphur of the British Pharmacopœia." *Br.*

Sulphuric Acid.—"Sulphuric Acid of the British Pharmacopœia." *Br.*

Sulphuric Acid, Diluted.—"Diluted Sulphuric Acid of the British Pharmacopœia." *Br.*

Talc, Powdered.—"A natural magnesium silicate, powdered and purified by boiling with dilute hydrochloric acid, washing with distilled water until neutral to litmus, and drying." *Br.*

Tartaric Acid.—"Tartaric Acid of the British Pharmacopœia." *Br.*

Tin.—"Tin, granulated by letting drops of the metal in the molten state fall into water. Yields no characteristic reactions for lead, copper, iron, or zinc." *Br.*

Turmeric.—"The dried rhizome of Curcuma longa, *Linn.* It is usually employed in the form of a tincture prepared, by the process of maceration, from the bruised rhizome, in the proportion of 1 gramme to 6 millilitres of Alcohol (90 per cent.), or in the form of paper prepared by steeping unglazed white paper in the tincture and drying." *Br.*

Water.—"The Distilled Water of the British Pharmacopœia." *Br.*

Zinc.—"The laminated or granulated metal. Completely dissolved by diluted hydrochloric acid, the solution yielding no characteristic reactions for lead, copper, cadmium, arsenic, tin or iron." *Br.*

Zinc Carbonate.—"Zinc Carbonate of the British Pharmacopœia." *Br.*

APPENDIX II. *Br.*

Solutions Employed in Chemical Testing. *Br.*

Solution of Albumen.—" Albumen, 20 millilitres; Distilled Water, 80 millilitres. Mix by trituration in a mortar, and filter through clean tow previously moistened with Distilled Water. Solution of Albumen must be recently prepared. The strength of the Solution may be adjusted to suit particular requirements." *Br.*

Solution of Ammonia.—"Solution of Ammonia of the British Pharmacopœia." *Br.*

Solution of Ammonia, Strong.—"Strong Solution of Ammonia of the British Pharmacopœia." *Br.*

Solution of Ammonium Acetate.—"Solution of Ammonium Acetate of the British Pharmacopœia." *Br.*

Solution of Ammonium Carbonate.—"Ammonium Carbonate, 5.0 grammes; Solution of Ammonia, 7.5 millilitres; Distilled Water, sufficient to produce 100.0 millilitres; Dissolve; filter if necessary." *Br.*

Solution of Ammonium Chloride.—" Ammonium Chloride, 10 grammes; Distilled Water sufficient to produce 100 millilitres. Dissolve; filter if necessary." *Br.*

Solution of Ammonium Chloride (Nessler's).—" Ammonium Chloride, 3.15 grammes; Distilled Water, free from ammonia, sufficient to produce 1000.00 millilitres. Dissolve." *Br.*

Solution of Ammonium Chloride, Dilute (Nessler's).—" Solution of Ammonium Chloride (Nessler's), 10 millilitres; Distilled Water, free from ammonia, sufficient to produce 1000 millilitres. Mix." *Br.*

Solution of Ammonium Citrate.—"Solution of Ammonium Citrate of the British Pharmacopœia." *Br.*

Solution of Ammonium Hydrosulphide.—" Saturate one hundred and twenty millilitres of Solution of Ammonia with washed Hydrogen Sulphide; add eighty millilitres of Solution of Ammonia. This Solution must be recently prepared." *Br.*

Solution of Ammonium Molybdate.—" Ammonium Molybdate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres. Dissolve; filter if necessary." *Br.*

Solution of Ammonium Oxalate.—" Ammonium Oxalate, 2.5 grammes; Distilled Water sufficient to produce 100.0 millilitres. Dissolve; filter if necessary." *Br.*

Solution of Auric Chloride.—" Auric Chloride, 2 grammes; Distilled Water, sufficient to produce 100 millilitres. Dissolve; filter if necessary." *Br.*

Solution of Barium Chloride.—" Barium Chloride, in crystals, 10 grammes; Distilled Water sufficient to produce 100 millilitres. Dissolve; filter if necessary." *Br.*

Solution of Barium Hydroxide.—" Barium Hydroxide, 3 grammes; Distilled Water, recently boiled, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Boric Acid.—"Boric Acid, 2.5 grammes; Alcohol (90 per cent.) sufficient to produce 100.0 millilitres; dissolve; filter if necessary." *Br.*

Solution of Bromine.—" A saturated solution of Bromine in Distilled Water." *Br.*

Solution of Cadmium Iodide.—" Cadmium Iodide, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Calcium Chloride.—" Calcium Chloride, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Calcium Sulphate.—" A saturated solution of Calcium Sulphate in Distilled Water." *Br.*

Solution of Chlorinated Soda.—"Solution of Chlorinated Soda of the British Pharmacopœia." *Br.*

Solution of Chlorine.—" A saturated solution of Chlorine in Distilled Water. This Solution must be recently prepared." *Br.*

Solution of Chromic Acid.—"Solution of Chromic Acid of the British Pharmacopœia." *Br.*

Solution of Copper Acetate.—" Copper Acetate, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Copper Acetate, Diluted.—" Solution of Copper Acetate, 1 millilitre; Distilled Water sufficient to produce 100 millilitres. Mix." *Br.*

Solution of Copper Ammonio-Sulphate.—" Copper Sulphate, in crystals, 5 grammes; Solution of Ammonia, a sufficient quantity; Distilled Water sufficient to produce 100 millilitres. Dissolve the Copper Sulphate in one hundred and sixty millilitres of the Distilled Water, and cautiously add the Solution of Ammonia to the liquid until the precipitate first formed is nearly dissolved; filter the product; finally add to the filtrate sufficient of the Distilled Water to produce the required volume." *Br.*

Solution of Copper Oxide, Ammoniacal.—" Copper Carbonate, 5 grammes; Strong Solution of Ammonia, 100 millilitres. Shake together occasionally during twelve hours; set aside for twenty-four hours, and pour off the clear liquid. This Solution must be recently prepared." *Br.*

Solution of Copper Sulphate.—" Copper Sulphate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Ferric Sulphate.—"Solution of Ferric Sulphate of the British Pharmacopœia." *Br.*

Solution of Ferrous Sulphate.—" Ferrous Sulphate, 2 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary. This Solution must be recently prepared." *Br.*

Solution of Formaldehyde.—"Solution of Formaldehyde of the British Pharmacopœia." *Br.*

Solution of Fuchsin, Decolorized.—" Dissolve one gramme of Fuchsin in five hundred millilitres of hot Distilled Water; add slowly twenty millilitres of a saturated aqueous solution of Acid Sodium Sulphite and then, also slowly, ten millilitres of Hydrochloric Acid, the mixture being kept well shaken. Cool and add sufficient Distilled Water to produce one thousand millilitres." *Br.*

Solution of Hydrogen Peroxide.—"Solution of Hydrogen Peroxide of the British Pharmacopœia." *Br.*

Solution of Indigo Sulphate.—" Indigo, dry and in fine powder, 0.1 gramme; Sulphuric Acid 100.0 millilitres. Mix the Indigo with one millilitre of the Sulphuric Acid in a small test-tube, and heat in boiling water for an hour; pour the product into the remainder of the Sulphuric Acid; shake the mixture; decant the clear liquid." *Br.*

Solution of Isinglass.—" Isinglass, 2 grammes; Distilled Water, sufficient to produce 100 millilitres. Mix, and digest for half an hour on a water-bath with repeated shaking; filter through clean tow previously moistened with Distilled Water. This Solution must be recently prepared." *Br.*

Solution of Lead Acetate.—" Lead Acetate, 10 grammes; Distilled Water, recently boiled, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Lead Subacetate.—"The Strong Solution of Lead Subacetate of the British Pharmacopœia, diluted, if necessary, with Distilled Water." *Br.*

Solution of Lime.—Synonym—*Solution of Calcium Hydroxide.* "Solution of Lime of the British Pharmacopœia." *Br.*

Solution of Litmus.—" Litmus, in powder, 10 grammes; Alcohol (90 per cent.), 100 millilitres; Distilled Water, 100 millilitres. Boil the Litmus with forty millilitres of the Alcohol for one hour; pour away the clear liquid; repeat this operation with thirty millilitres of the Alcohol, and a third time with the remainder of the Alcohol. Digest the washed Litmus in the Distilled Water, and filter." *Br.*

Solution of Magnesium Ammonio-Sulphate.—" Magnesium Sulphate, 10 grammes; Ammonium Chloride, 20 grammes; Solution of Ammonia, 42 millilitres; Distilled Water, 80 millilitres. Dissolve the Magnesium Sulphate and Ammonium Chloride in the Distilled Water; add the Solution of Ammonia, and set the mixture aside for a few days in a well-closed bottle; decant and filter." *Br.*

Solution of Magnesium Sulphate.—" Magnesium Sulphate, 10 grammes; Distilled Water sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Mercurous Nitrate.—"Mercury, 2 grammes; Nitric Acid, 1 millilitre; Distilled Water, a sufficient quantity. To the Mercury, in a small dish, add one millilitre of Distilled Water and the Nitric Acid, and set the whole aside for twenty-four hours in a cool dark place; drain the resulting crystals; dissolve them in two hundred millilitres of Distilled Water." *Br.*

Solution of Mercury Nitrate.—Synonym—*Millon's Reagent.* "Mercury, 3 millilitres; Fuming Nitric Acid, 27 millilitres; Distilled Water, a sufficient quantity. Dissolve the Mercury in the Fuming Nitric Acid without heat; dilute the solution with an equal volume of Distilled Water. This Solution must be recently prepared." *Br.*

Solution of Methyl Orange.—" Methyl Orange, 0.2 gramme; Alcohol (90 per cent.), 25.0 millilitres; Distilled Water, sufficient to produce 100.0 millilitres; dissolve." *Br.*

Solution of Phenolphthalein.—" Phenolphthalein, 0.2 gramme; Alcohol (90 per cent.), 60.0 millilitres; Distilled Water, sufficient to produce 100.0 millilitres; dissolve." *Br.*

Solution of Picric Acid.—" Picric Acid, 0.66 gramme; Distilled Water, sufficient to produce 100.00 millilitres; dissolve." *Br.*

Solution of Platinic Chloride.—" Platinic Chloride, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve." *Br.*

Solution of Potassio-Cupric Tartrate.—Synonym—*Fehling's Solution.* *Br.*

" No. 1. Copper Sulphate, in crystals, 34.64 grammes; Sulphuric Acid, 0.50 millilitre; Distilled Water, sufficient to produce 500.00 millilitres; dissolve.

"No. 2. Sodium Potassium Tartrate, 176 grammes; Sodium Hydroxide, 77 grammes; Distilled Water sufficient to produce 500 millilitres; dissolve. Mix equal volumes of the solutions No. 1 and No. 2 at the time of using." *Br.*

Solution of Potassio-Mercuric Iodide.—Synonym—*Mayer's Reagent.* "Mercuric Chloride, 1.355 grammes; Potassium Iodide, 5.000 grammes; Distilled Water, sufficient to produce 100.000 millilitres. Dissolve the Mercuric Chloride in sixty millilitres of the Distilled Water; dissolve the Potassium Iodide in twenty millilitres of the Distilled Water; mix the two solutions, and add sufficient Distilled Water to produce the required volume." *Br.*

Solution of Potassio-Mercuric Iodide, Alkaline.—Synonym—*Nessler's Reagent.* "Potassium Iodide, 3.5 grammes; Mercuric Chloride, sufficient quantity; Sodium Hydroxide, 12.0 grammes; Distilled Water, sufficient to produce 100.0 millilitres. Dissolve the Potassium Iodide and one and a quarter grammes of Mercuric Chloride in eighty millilitres of Distilled Water; to this liquid add a cold saturated aqueous solution of Mercuric Chloride, with constant stirring, until a slight red precipitate remains; add the Sodium Hydroxide and dissolve; then add a little more of the aqueous solution of Mercuric Chloride, and sufficient Distilled Water to produce the required volume." *Br.*

Solution of Potassium Acetate.—" Potassium Acetate, 10 grammes; Distilled Water sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Acid Potassium Tartrate.—" A saturated solution of Acid Potassium Tartrate in Distilled Water." *Br.*

Solution of Potassium Carbonate.—" Potassium Carbonate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Potassium Chromate.—" Potassium Chromate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Potassium Cyanide.—" Potassium Cyanide, 10 grammes; Distilled Water, 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Potassium Ferricyanide.—" Potassium Ferricyanide, in crystals, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary. This Solution must be recently prepared." *Br.*

Solution of Potassium Ferrocyanide.—" Potassium Ferrocyanide, in crystals, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Potassium Hydroxide.—"Solution of Potash of the British Pharmacopœia." *Br.*

Solution of Potassium Hydroxide, Alcoholic.—" Potassium Hydroxide, 10 grammes; Alcohol (90 per cent.), sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Potassium Iodide.—" Potassium Iodide, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Potassium Permanganate.—"Solution of Potassium Permanganate of the British Pharmacopœia." *Br.*

Solution of Pyroxylin.—"Solution of Pyroxylin, the Collodion of the British Pharmacopœia." *Br.*

Solution of Silver Ammonio-Nitrate.—" Silver Nitrate, in crystals, 2.5 grammes; Solution of Ammonia, 10.0 millilitres, or a sufficient quantity; Distilled Water, sufficient to produce 100.0 millilitres. Dissolve the Silver Nitrate in eighty millilitres of the Distilled Water, and cautiously add the Solution of Ammonia to the liquid until the precipitate first formed is nearly dissolved; set aside; decant; finally add sufficient Distilled Water to produce the required volume." *Br.*

Solution of Silver Nitrate.—" Silver Nitrate, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve." *Br.*

Solution of Sodium Acetate.—" Sodium Acetate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Sodium Carbonate.—" Sodium Carbonate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Sodium Hydroxide.—" Sodium Hydroxide, 20 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Sodium Phosphate.—" Sodium Phosphate, in crystals, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Sodium Sulphate.—" Sodium Sulphate, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Sodium Sulphide.—"Sodium Sulphide, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Stannous Chloride.—"Tin, granulated, 20 grammes; Hydrochloric Acid, 60 millilitres; Distilled Water, sufficient to produce 100 millilitres. Dilute the Hydrochloric Acid with twenty millilitres of the Distilled Water, and, having added the Tin, apply heat gently until gas ceases to be evolved; add sufficient Distilled Water to produce the required volume, allowing the undissolved Tin to remain in the Solution." *Br.*

Solution of Sulphurous Acid.—"The Sulphurous Acid of the British Pharmacopœia." *Br.*

Solution of Tannic Acid.—"Tannic Acid, 10 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve. This Solution must be recently prepared." *Br.*

Solution of Tartarated Antimony.—"Tartarated Antimony, 5 grammes; Distilled Water, boiling, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Solution of Tartaric Acid.—"Tartaric Acid, in crystals, 12.5 grammes; Alcohol (90 per cent.), 25.0 millilitres; Distilled Water, sufficient to produce 100.0 millilitres. Dissolve the Tartaric Acid in sixty millilitres of the Distilled Water; add the Alcohol; add sufficient Distilled Water to produce the required volume." *Br.*

Test-Solution of Ferric Chloride (T. Sol.).—"Ferric Chloride, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." *Br.*

Test-Solution of Mercuric Chloride (T. Sol.).—"Mercuric Chloride, 5 grammes; Distilled Water, sufficient to produce 100 millilitres; dissolve; filter if necessary." Br.

APPENDIX III. Br.

Solutions Employed in Volumetric Determinations.

Solution of Ammonium Thiocyanate, N/10.—"Ammonium Thiocyanate dissolved in Distilled Water to contain in 1000 millilitres 7.612 grammes of ammonium thiocyanate, NH_4SCN." *Br.*

Solution of Hydrochloric Acid, N/1, N/10.—"Hydrochloric Acid diluted with Distilled Water to contain in 1000 millilitres the following quantities of hydrochloric acid, HCl: for N/1, 36.468 grammes HCl; for N/10, 3.646 grammes HCl." *Br.*

Solution of Hydroxylamine Hydrochloride, N/2.—"Hydroxylamine Hydrochloride dissolved in a mixture of equal volumes of Alcohol (90 per cent.) and Alcohol (70 per cent.) to contain in 1000 millilitres 34.751 grammes of hydroxylamine hydrochloride, NH_2OH,HCl." *Br.*

Solution of Iodine, N/10.—"Iodine and Potassium Iodide dissolved in Distilled Water to contain in 1000 millilitres 12.692 grammes of iodine, I, and 18 grammes of Potassium Iodide." *Br.*

Solution of Oxalic Acid, N/1, N/10.—"Oxalic Acid dissolved in Distilled Water to contain in 1000 millilitres the following quantities of oxalic acid, $H_2C_2O_4,2H_2O$: for N/1, 63.024 grammes $H_2C_2O_4,2H_2O$; for N/10, 6.302 grammes $H_2C_2O_4,2H_2O$." *Br.*

Solution of Potassium Bichromate, N/1, N/10.—"Potassium Bichromate dissolved in Distilled Water to contain in 1000 millilitres the following quantities of potassium bichromate, $K_2Cr_2O_7$: for N/1, 49.033 grammes $K_2Cr_2O_7$; for N/10, 4.903 grammes $K_2Cr_2O_7$." *Br.*

Solution of Potassium Hydroxide, Alcoholic, N/1, N/2, N/10.—"Potassium Hydroxide dissolved in Alcohol (90 per cent.) to contain in 1000 millilitres the following quantities of potassium hydroxide, KOH: for N/1, 56.108 grammes KOH; for N/2, 28.054 grammes KOH; for N/10, 5.610 grammes KOH. These Solutions are colourless, or not more than faintly yellow." *Br.*

Solution of Potassium Permanganate, N/10.—"Potassium Permanganate dissolved in Distilled Water to contain in 1000 millilitres 3.161 grammes of potassium permanganate, $KMnO_4$." *Br*

Solution of Silver Nitrate, N/10.—"Silver Nitrate dissolved in Distilled Water to contain in 1000 millilitres 16.989 grammes of silver nitrate, $AgNO_3$." *Br.*

Solution of Sodium Hydroxide, N/1, N/2, N/5, N/10, N/20.—"Sodium Hydroxide dissolved in Distilled Water to contain in 1000 millilitres the following quantities of sodium hydroxide, NaOH: for N/1, 40.008 grammes NaOH; for N/2, 20.004 grammes NaOH; for N/5, 8.001 grammes NaOH; for N/10, 4.000 grammes NaOH; for N/20, 2.000 grammes NaOH." *Br.*

Solution of Sodium Thiosulphate, N/10.—"Sodium Thiosulphate dissolved in Distilled Water to contain in 1000 millilitres 24.822 grammes of sodium thiosulphate, $Na_2S_2O_3,5H_2O$." *Br.*

Solution of Sulphuric Acid, N/1, N/2, N/10, N/20, N/100.—"Sulphuric Acid diluted with Distilled Water to contain in 1000 millilitres the following quantities of sulphuric acid, H_2SO_4: for N/1, 49.043 grammes H_2SO_4; for N/2, 24.521 grammes H_2SO_4; for N/10, 4.904 grammes H_2SO_4; for N/20, 2.452 grammes H_2SO_4; for N/100, 0.490 gramme H_2SO_4." *Br.*

Indicators of the Termination of Reactions in Volumetric Determinations. Br.

Mucilage of Starch.—"It gives an intensely blue colour with iodine, at ordinary temperatures." *Br.*

Solution of Ferric Sulphate.—"Solution of Ferric Sulphate, of the British Pharmacopœia, gives a deep red colour with ammonium thiocyanate." *Br.*

Solution of Litmus.—"It gives a red colour with acids and a blue colour with alkalies. Carbon dioxide, if present in the solution, must be previously expelled by boiling." *Br.*

Solution of Methyl Orange.—"It gives a pink colour with mineral acids and a yellow colour with alkalies." *Br.*

Solution of Phenolphthalein.—"It gives with alkalies a red colour, which is discharged by acids." *Br.*

Solution of Potassium Ferricyanide.—"It gives an intensely blue precipitate or coloration with ferrous salts, but none with ferric salts." *Br.*

Tincture of Cochineal.—"Tincture of Cochineal, of the British Pharmacopœia, gives a purple colour with alkalies and a brownish-yellow colour with acids." *Br.*

APPENDIX IV. Br.

Reactions and Tests for Substances Mentioned in the Text of the British Pharmacopœia

Acetates.—"Neutral acetates are decomposed by heat, yielding vapours which possess a characteristic acetous odour. Hydrogen acetate and ethyl acetate have characteristic odours. Acetates when warmed with *sulphuric acid* yield vapours of hydrogen acetate; or, when warmed with *sulphuric acid* and a small quantity of *alcohol* (90 per cent.), yield ethyl acetate. *T. Sol. of ferric chloride* produces a deep-red coloration with neutral or faintly acid acetates, and the resulting liquid on boiling yields a reddish-brown precipitate. On adding *hydrochloric acid* the red solution turns yellow." *Br.*

Aluminium.—"*Solution of ammonia* or *solution of ammonium hydrosulphide* produces a white gelatinous precipitate, soluble in *hydrochloric acid*, in *acetic acid*, and in *solution of sodium hydroxide*, but nearly insoluble in *solution of ammonia* and in solutions of ammonium salts, and quite insoluble when the solutions are boiled." *Br.*

Ammonium Salts.—"Ammonium salts volatilise when strongly heated, generally without residue. When heated with *solution of sodium hydroxide*, ammonia is evolved, recognisable by its odour. *Solution of platinic chloride* produces with ammonium salts acidified with *hydrochloric acid* a yellow crystalline precipitate, especially in the presence of alcohol. On ignition, this precipitate leaves a residue of platinum only." *Br.*

Antimony.—"*Hydrogen sulphide* produces, in slightly acid solutions, an orange-coloured precipitate, soluble in *solution of sodium hydroxide*, and *of ammonium hydrosulphide*, and in warm *hydrochloric acid* with evolution of hydrogen sulphide, but almost insoluble in solution of Ammonium Carbonate. Nascent hydrogen, generated by the interaction of *zinc* and *diluted sulphuric acid*, partially converts antimony compounds into hydrogen antimonide. A cold porcelain tile held in the flame of this gas acquires a dark metallic deposit which is not appreciably dissolved by *solution of chlorinated soda*. Nascent hydrogen, generated by the interaction of *zinc* and *solution of sodium hydroxide*, does not convert antimony into hydrogen antimonide. If one end of a strip or rod of *zinc* be allowed to rest on a platinum capsule containing an acidified solution of an antimony compound, the other end being in the solution, the antimony is precipitated on the platinum as a black, adherent, non-granular stain, insoluble in *hydrochloric acid*. Bright *copper* foil precipitates antimony from solutions, and the antimony may be volatilised by heat in an open tube, condensing as a white amorphous sublimate of oxides of antimony near to the copper." *Br.*

Arsenic.—"*Hydrogen sulphide* produces in solutions containing *hydrochloric acid* a yellow precipitate, soluble in *solution of sodium hydroxide*, and *of ammonium hydrosulphide*, and in solution of Ammonium Carbonate, but reprecipitated on addition of *hydrochloric acid*. The precipitate is insoluble in *hydrochloric acid*. Nascent hydrogen, generated by the interaction of *zinc* and *diluted sulphuric acid*, converts arsenic compounds into hydrogen arsenide. A cold porcelain tile held in the flame of this gas acquires a dark metallic deposit, which is readily dissolved by *solution of chlorinated soda*. Nascent hydrogen, generated by the interaction of *zinc* and *solution of sodium hydroxide*, converts arsenic compounds into hydrogen arsenide. This gas gives a black stain to filter-paper soaked with *solution of silver nitrate* and placed as a cap over the tube in which the test is being performed. Bright *copper* foil precipitates arsenic from solutions acidified by *hydrochloric acid*, and the arsenic may be volatilised by heat in an open tube, and condensers, at some distance from the copper, as a white sublimate of characteristic octahedral crystals of arsenious oxide.

ARSENITES.—Solutions of arsenites yield a yellow precipitate with *solution of silver ammonio-nitrate*.

ARSENATES.—Solutions of arsenates yield a reddish-chocolate precipitate with *solution of silver ammonio-nitrate*. *Solution of magnesium ammonio-sulphate* produces a white crystalline precipitate." *Br.*

Bicarbonates. *See* "**Carbonates.**"

Bismuth.—"*Hydrogen sulphide* produces a brownish-black precipitate, insoluble in *solution of sodium hydroxide*, in *diluted hydrochloric acid*, and in *solution of ammonium hydrosulphide*, but soluble in warm *nitric acid*. *Solution of sodium hydroxide*, or of *ammonia*, except in the presence of citrates, produces a white precipitate insoluble in excess of the precipitant. Dilute solution of *sodium chloride* in large excess produces in solutions which are not too acid a white precipitate, insoluble in *solution of tartaric acid*." *Br.*

Bromates.—"From bromates *solution of sulphurous acid* liberates bromine, recognisable by its odour and appearance. After ignition with charcoal bromates are converted into bromides, and the latter yield their characteristic reactions." *Br.*

Bromides.—"*Solution of silver nitrate* produces a yellowish curdy precipitate, somewhat soluble in strong but almost insoluble in diluted *solution of ammonia*, and insoluble in *nitric acid*. *Solution of chlorine* liberates bromine, soluble in two or three drops of *carbon disulphide* or of *chloroform*, and forming a reddish solution. Bromine is liberated when a bromide is heated with *sulphuric acid* and *manganese peroxide*, or *potassium bichromate*, the vapour giving an orange-yellow colour to filter-paper soaked in *mucilage of starch*. In testing for bromides in the presence of iodides, all iodine should first be removed by boiling the aqueous solution with excess of *lead peroxide*." *Br.*

Cadmium.—"*Hydrogen sulphide* produces a yellow precipitate, insoluble in cold *diluted hydrochloric acid*, in *solution of ammonium hydrosulphide*, and in *solution of sodium hydroxide*, but soluble in *nitric acid*, in hot *diluted hydrochloric acid*, and in hot *diluted sulphuric acid*. *Solution of sodium hydroxide* produces a white precipitate insoluble in excess. *Solution of ammonia* produces a white precipitate readily soluble in excess." *Br.*

Calcium.—"*Solution of ammonium carbonate* produces a white precipitate which, after well boiling and allowing to cool, is insoluble in *solution of ammonium chloride*. *Solution of ammonium oxalate* produces a white precipitate, soluble in *hydrochloric acid* but insoluble in *acetic acid*. *Solution of potassium chromate* produces no precipitate." *Br.*

Carbonates and Bicarbonates.—"Dilute acids liberate carbon dioxide; the escaping gas is odourless, and produces a white precipitate in *solution of lime*. Soluble carbonates produce a brownish-red precipitate with *T. Sol. of mercuric chloride*, bicarbonates a whitish precipitate; the former produce a white precipitate with cold *solution of magnesium sulphate*, the latter do not." *Br.*

Chlorides.—"*Solution of silver nitrate* produces a white curdy precipitate, soluble in *solution of*

ammonia, but insoluble in *nitric acid*. A solid chloride or hydrochloride, when subjected to distillation with *sulphuric acid* and *potassium bichromate*, yields a reddish-brown distillate, which is decomposed by *water*. The resulting solution when nearly neutralised produces a yellow precipitate with *solution of lead acetate*. Heated with *manganese peroxide* and *sulphuric acid*, chlorides yield chlorine, recognisable by its odour and by giving a blue colour with *solution of potassium iodide* and *mucilage of starch*." *Br.*

Citrates.—" Citrates become charred when heated. *Solution of calcium chloride* added in excess produces, when boiled with a neutral solution of a citrate, a white precipitate. *Solution of silver nitrate* produces in solutions of neutral citrates a white precipitate soluble in *solution of ammonia*. A mirror is not formed on the sides of the tube when the ammoniacal solution is warmed." *Br.*

Copper.—" *Hydrogen sulphide* produces a brownish-black precipitate, insoluble in *diluted hydrochloric acid* and in *solution of sodium hydroxide*, almost insoluble in *solution of ammonium hydrosulphide*, but decomposed and dissolved by boiling *nitric acid*. *Solution of sodium hydroxide* produces a bulky light-blue precipitate which becomes brownish-black on boiling. *Solution of ammonia* added in small quantity to a neutral solution of a copper salt produces a greenish-blue precipitate which readily dissolves in excess of the precipitant, forming a deep-blue solution. *Solution of potassium ferrocyanide* produces a reddish-brown precipitate, or in very dilute solutions a reddish-brown coloration." *Br.*

Cyanides.—" *Solution of silver nitrate* produces a white curdy precipitate, soluble in *solution of potassium cyanide*, in *solution of ammonia*, and in boiling *nitric acid*. When to a soluble cyanide there are added a few drops of a mixed solution of ferrous and ferric salts, then of *solution of sodium hydroxide*, and lastly excess of *hydrochloric acid*, a blue precipitate is produced. Mercury cyanide and silver cyanide decompose when heated, evolving (highly poisonous) cyanogen, which burns with a pink flame." *Br.*

Iodates.—" *Solution of silver nitrate* produces a white precipitate, sparingly soluble in *water* and in *diluted nitric acid*, but readily dissolved by *solution of ammonia*. *Solution of sulphurous acid* when added to the ammoniacal solution produces a pale yellow precipitate. A mixed *solution of potassium iodide* and *tartaric acid* added to a solution of an iodate liberates iodine, which produces a blue colour with *mucilage of starch*. *Solution of barium chloride* produces a white precipitate nearly insoluble in *water* and soluble with difficulty in *diluted nitric acid*. On the addition of *mucilage of starch* and *solution of sulphurous acid* a blue colour is produced." *Br.*

Iodides.—" *Solution of silver nitrate* produces a curdy yellow precipitate, insoluble in *nitric acid* and almost insoluble in *solution of ammonia*. *T. Sol. of mercuric chloride* produces a scarlet precipitate, slightly soluble in excess of this reagent, and very soluble in *solution of potassium iodide*. A small quantity of *solution of chlorine* added to a solution of an iodide liberates iodine, which colours *carbon disulphide* violet and *mucilage of starch* deep blue. Heated with *sulphuric acid* and *manganese peroxide* or *potassium bichromate* violet vapours of iodine are evolved." *Br.*

Iron.—"Reaction common to Ferrous and Ferric salts: *Solution of ammonium hydrosulphide* produces, in neutral solutions, a black precipitate soluble in cold *diluted hydrochloric acid* with evolution of hydrogen sulphide. Reactions characteristic of Ferrous salts: *Solution of potassium ferrocyanide* produces a white precipitate, rapidly turning blue, insoluble in *diluted hydrochloric acid*. *Solution of potassium ferricyanide* produces a dark-blue precipitate, insoluble in *diluted hydrochloric acid;* decomposed by *solution of sodium hydroxide*. *Solution of sodium hydroxide* produces a dull-green precipitate. Reactions characteristic of Ferric salts: *Solution of ammonium thiocyanate* produces a blood-red coloration which is discharged on the addition of *T. Sol. of mercuric chloride*. *Solution of potassium ferricyanide* produces a reddish-brown coloration but no precipitate. *Solution of potassium ferrocyanide* produces a dark-blue precipitate, insoluble in *diluted hydrochloric acid*. *Solution of sodium hydroxide* produces a reddish-brown precipitate, soluble in solution of *citric acid* or *tartaric acid*, and not formed in the presence of citrates or tartrates." *Br.*

Lead.—" *Hydrochloric acid* produces, except in very weak solutions, a white precipitate, soluble in boiling *water*, but re-deposited in crystals on cooling. *Hydrogen sulphide*, in not very strongly acid solutions, produces a black precipitate insoluble in *diluted hydrochloric acid*, *solution of potassium hydroxide*, and *solution of ammonium hydrosulphide*, but soluble in hot *diluted nitric acid*. *Diluted sulphuric acid* produces a white precipitate almost insoluble in *water*, and still less soluble in *diluted sulphuric acid* or in *alcohol* (90 per cent.), but soluble in *solution of ammonium acetate*. *Solution of potassium chromate* produces a yellow precipitate readily soluble in *solution of sodium hydroxide*, in hot *nitric acid*, sparingly soluble in *diluted nitric acid*, insoluble in *acetic acid*." *Br.*

Magnesium.—" *Solution of ammonium carbonate*, in the presence of *solution of ammonium chloride*, produces no precipitate. *Solution of sodium phosphate* in the presence of ammonium salts and *solution of ammonia*, produces a white crystalline precipitate. *Solution of sodium hydroxide* produces a white precipitate, insoluble in excess of the reagent, but soluble in *solution of ammonium chloride*." *Br.*

Mercury.—" Reactions common to Mercurous and Mercuric salts: *Hydrogen sulphide* produces a black precipitate, insoluble in *solution of ammonium hydrosulphide* and in boiling *diluted nitric acid*. Bright *copper* foil immersed in a solution free from excess of nitric acid becomes coated with a deposit of mercury which on rubbing becomes bright; the mercury may be volatilised from the foil by heat and obtained in globules. Reaction characteristic of Mercurous salts: *Hydrochloric acid* produces a white precipitate insoluble in *water*, and blackened by *solution of ammonia*. Reactions characteristic of Mercuric salts: *Solution of sodium hydroxide* produces a yellow precipitate. *Solution of potassium iodide* produces in neutral solutions a scarlet precipitate, soluble in excess of the precipitant, and in a considerable excess of the solution of the mercuric salt." *Br.*

Nitrates.—" *Ferrous sulphate* and *sulphuric acid*, when added to a solution of a nitrate in such a way that the acid forms a stratum below the aqueous solution, produces a brown coloration at the junction of the two liquids. Nitrates liberate red fumes when warmed with *sulphuric acid* and *copper*." *Br.*

Nitrites.—" On the addition, to a solution of a nitrite, of a few drops of *diluted sulphuric acid solution of potassium iodide*, and *mucilage of starch*, a blue colour is produced. *Diluted sulphuric acid* produces red fumes. *Solution of ferrous sulphate* produces a deep-brown colour." *Br.*

Oxalates.—" *Solution of calcium chloride* produces a white precipitate, soluble in *hydrochloric acid* but insoluble in *acetic acid*. *Solution of silver nitrate* produces a white precipitate, soluble in *solution of*

ammonia and in *diluted nitric acid*. Oxalates do not char when heated with *sulphuric acid*, but yield carbon monoxide and carbon dioxide." *Br.*

Phosphates (Ortho-).—"*Solution of silver ammonio-nitrate* produces in solutions of ortho-phosphates a light-yellow precipitate readily soluble in *solution of ammonia* and in cold *diluted nitric acid*. *Solution of magnesium ammonio-sulphate* produces a white crystalline precipitate. Excess of *solution of ammonium molybdate* containing much *nitric acid*, produces, on warming, a yellow precipitate." *Br.*

Potassium.—"*Solution of platinic chloride* produces with moderately strong solutions of potassium chloride (or with other potassium salts if hydrochloric acid be present) a yellow crystalline precipitate, which, upon ignition, leaves a residue of potassium chloride and platinum. Potassium compounds moistened with *hydrochloric acid* when introduced, on platinum wire, into the flame of a Bunsen burner, communicate to the flame a violet coloration." *Br.*

Selenium and Tellurium.—"Selenium and Tellurium may occur in compounds of bismuth. To detect these elements, dissolve the compound in *nitric acid*, add solution of *sodium chloride* or *solution of ammonium chloride*, and dilute freely with *water*. The filtrate from the precipitate, mixed with excess of an aqueous solution of *sodium sulphite*, produces no precipitate or coloration even after twelve hours." *Br.*

Silica.—"Silica, after exposure to a red heat, is insoluble in acids, and is not dissolved in a bead of *purified borax* when heated to fusion in the blowpipe flame. The result of its fusion with *sodium carbonate* is soluble in water, the solution yielding a gelatinous precipitate on the addition of *hydrochloric acid*." *Br.*

Silver.—"*Hydrochloric acid* and other chlorides produce a white curdy precipitate, soluble in *solution of ammonia* but insoluble in *nitric acid*. *Solution of potassium chromate* produces a red precipitate, soluble in *nitric acid*." *Br.*

Sodium.—"Sodium compounds, moistened with *hydrochloric acid*, when introduced, on platinum wire, into the flame of a Bunsen burner, communicate to the flame a yellow coloration." *Br.*

Strontium.—"*Solution of ammonium carbonate* produces a white precipitate, insoluble in *solution of ammonium chloride*. *Solution of ammonium oxalate* produces a white precipitate, insoluble in *acetic acid* but soluble in *hydrochloric acid*. *Solution of potassium chromate* produces a light-yellow precipitate, soluble in *acetic acid*. *Solution of calcium sulphate* produces a white precipitate." *Br.*

Sulphates.—"*Solution of barium chloride* produces a white precipitate insoluble in *hydrochloric acid*." *Br.*

Sulphides.—"The official sulphides, hydrosulphides, and sulphurated compounds evolve hydrogen sulphide when boiled with *hydrochloric acid*." *Br.*

Sulphites.—"*Hydrochloric acid* liberates sulphur dioxide, a colourless gas with a pungent smell of burning sulphur. *Solution of barium chloride* produces a white precipitate soluble in *hydrochloric acid*. Sulphites decolorise *N/10 solution of iodine*." *Br.*

Tartrates.—"Tartrates become charred when heated. *Solution of calcium chloride* added in excess to a solution of a neutral tartrate produces, even when cold, a white granular precipitate, soluble in *acetic acid*. *Solution of silver nitrate* produces a white precipitate, soluble in *solution of ammonia* and in *nitric acid*. The ammoniacal solution, on heating, deposits metallic silver as a mirror on the sides of the test-tube. When to a solution of tartaric acid in *water*, or of a tartrate acidified with *acetic acid*, a drop of *solution of ferrous sulphate*, then a few drops of *solution of hydrogen peroxide*, and finally an excess of *solution of sodium hydroxide* are added, a purple or violet colour is produced." *Br.*

Tellurium. *See* "**Selenium.**"

Thiosulphates.—"*Hydrochloric acid* produces a yellow precipitate and liberates sulphur dioxide, recognisable by its odour. *Solution of barium chloride* produces no precipitate in dilute solutions; on the further addition of *solution of bromine* a white precipitate is produced. Thiosulphates decolorise *N/10 solution of iodine*." *Br.*

Tin.—"Metallic *zinc* placed in a solution of any tin salt acidified with *hydrochloric acid* precipitates the tin in metallic scales or as a grey sponge. The metal, separated from the liquid, is soluble in boiling *hydrochloric acid*, and the solution, which then contains stannous chloride, produces with *T. Sol. of mercuric chloride* a white precipitate which becomes grey if excess of the tin salt is present." *Br.*

Zinc.—"*Solution of ammonium hydrosulphide* produces in neutral, and *hydrogen sulphide* in alkaline solutions, a white precipitate, soluble in *hydrochloric acid* but insoluble in *acetic acid*. *Solution of sodium hydroxide* or *solution of ammonia* produces a white precipitate, soluble in excess of either reagent. *Solution of potassium ferrocyanide* produces a white precipitate, insoluble in *diluted hydrochloric acid*." *Br.*

APPENDIX V. Br.

Quantitative Limit-test For Lead. Br.

Apparatus

(All glass apparatus used must be lead-free.)

Nessler Glasses.—"Thin, and of lead-free glass. About 150 millimetres long, and of such diameter that the mark indicating a content of 50 millilitres is at the height of 100 millimetres from the base." *Br.*

Solutions and Reagents

The special solutions and reagents for the Quantitative Limit-test for lead are distinguished by the letters "Pb T."

Strong Solution of Lead Pb T.—"Dissolve 0.16 gramme of Lead Nitrate in Distilled Water, adding 50 millilitres of Nitric Acid, and dilute with Distilled Water to 100 millilitres. This solution contains 0.001 gramme of lead in 1 millilitre." *Br.*

Dilute Solution of Lead Pb T.—"Dilute 1 millilitre of the Strong Solution of Lead Pb T., measured from a burette, with Distilled Water so that the resulting solution measures 100 millilitres. This solution contains 0.00001 gramme of lead in 1 millilitre." *Br.*

Solution of Potassium Cyanide Pb T.—"Dissolve 10 grammes of Potassium Cyanide in Distilled

Water, add 2 millilitres of Solution of Hydrogen Peroxide and make up to 100 millilitres with Distilled Water. This solution after being allowed to stand, when tested by the quantitative limit-test for lead, gives no colour with the Dilute Solution of Lead Pb T." *Br.*

Solution of Sodium Sulphide Pb T.—"Dissolve 10 grammes of Sodium Sulphide in Distilled Water and make up to 100 millilitres with Distilled Water." *Br.*

Mode of Testing (General)

"Two solutions of the substance under examination are made in hot Distilled Water: (1) The primary solution containing 12 grammes of the substance. (2) The auxiliary solution containing 2 grammes of the substance. Each solution is filtered (if necessary), made alkaline with *solution of ammonia*, and treated with 1 millilitre of the solution of potassium cyanide Pb T. If the colours of the solutions differ much, the difference may be rectified by the cautious addition of a highly diluted solution of burnt sugar. Then, by the method of trial and error (well known in water analysis as "Nesslerizing"), is determined the quantity of the dilute solution of lead Pb T. which must be added to the auxiliary solution, in order that there may be equal colorations produced upon the addition of 2 drops of the solution of sodium sulphide Pb T. to both the primary and the auxiliary solution, after dilution to the 50 millilitre mark. In these circumstances, each millilitre of the dilute solution of lead Pb T. required corresponds to 1 part per million of lead in the substance examined. The colorations may be viewed by light reflected from a horizontal white tile through the Nessler glasses inclined at an angle to the observer." *Br.*

Note.—" In some cases, 7 or 4 grammes only are used in the primary solution. In these cases each millilitre of the dilute solution of lead Pb T. required will represent 2 or 5 parts per million of lead respectively." *Br.*

Substance.	Primary Solution of Substance: Grammes employed.	Auxiliary Solution of Substance: Grammes employed.	Dilute Solution of Lead PbT.: Millilitres employed.	Limit of Lead: Parts per Million.
Acidum Acetylsalicylicum	7[a]	2[a]	5	10
Acidum Boricum	7[a]	2[a]	12.5	25
Acidum Citricum	7	2	10	20
Acidum Hydriodicum Dilutum	7	2	5	10
Acidum Hydrobromicum	12	2	5	5
Acidum Hydrochloricum	12	2	10	10
Acidum Lacticum	7	2	5	10
Acidum Nitricum	7	2	10	20
Acidum Phosphoricum Concentratum	12	2	10	10
Acidum Sulphuricum	7	2	10	20
Acidum Sulphurosum	12	2	10	10
Acidum Tartaricum	7	2	10	20
Ammonii Benzoas	7	2	5	10
Ammonii Bromidum	12	2	10	10
Ammonii Carbonas	12[b]	2	5	5
Ammonii Chloridum	12	2	5	5
Borax Purificatus	7	2	2.5	5
Calcii Carbonas Praecipitatus	7[c]	2[c]	5	10
Calcii Chloridum	7[d]	2[d]	10	20
Calcii Hydras	7[c]	2[c]	10	20
Calcii Hypophosphis	7[d]	2[d]	5	10
Calcii Lactas	7[d]	2[d]	5	10
Liquor Magnesii Bicarbonatis	Special	process[e]	5	0.5
Lithii Carbonas	7[c]	2[c]	5	10
Lithii Citras	12	2	5	5
Magnesia Levis	4[c]	2[c]	4	20
Magnesia Ponderosa	4[c]	2[c]	4	20
Magnesii Carbonas Levis	7[c]	2[c]	10	20
Magnesii Carbonas Ponderosus	7[c]	2[c]	10	20
Magnesii Sulphas	12	2	5	5
Potassii Acetas	12	2	10	10
Potassii Bicarbonas	12	2	5	5
Potassii Bromidum	12	2	10	10
Potassii Carbonas	12	2	5	5
Potassii Chloras	7	2	5	10
Potassii Citras	12	2	10	10
Potassii Iodidum	12	2	10	10
Potassii Nitras	12	2	10	10
Potassii Sulphas	7	2	10	20

[a] Solution effected by the addition of *solution of ammonia*.

[b] Primary solution boiled down to measure 50 millilitres.

[c] Solutions prepared by dissolving in excess of *acetic acid*, boiling to expel any carbon dioxide present, then making alkaline with *solution of ammonia* and adding solution of potassium cyanide PbT.

[d] *Acetic acid* added to each solution before making alkaline with *solution of ammonia*.

[e] Primary solution prepared by treating 200 millilitres with excess of *acetic acid* and concentrating so that the solution (after being made alkaline with *solution of ammonia* and treated with solution of potassium cyanide PbT.) measures 50 millilitres. Auxiliary solution—100 millilitres similarly treated.

Substance.	Primary Solution of Substance: Grammes employed.	Auxiliary Solution of Substance: Grammes employed.	Dilute Solution of Lead PbT.: Millilitres employed.	Limit of Lead: Parts per Million.
Potassii Tartras	7	2	10	20
Potassii Tartras Acidus	7[a]	2[a]	10	20
Sodii Benzoas	7	2	5	10
Sodii Bicarbonas	7[f]	2	2.5	5
Sodii Bromidum	12	2	10	10
Sodii Carbonas	12	2	10	10
Sodii Carbonas Exsiccatus	7	2	12.5	25
Sodii Chloridum	12	2	10	10
Sodii et Potassii Tartras	7	2	10	20
Sodii Hypophosphis	7	2	5	10
Sodii Iodidum	12	2	10	10
Sodii Phosphas	12	2	5	5
Sodii Phosphas Acidus	12	2	5	5
Sodii Salicylas	12	2	10	10
Sodii Sulphas	12	2	5	5
Strontii Bromidum	7[d]	2[d]	10	20

[a] Solution effected by the addition of *solution of ammonia*.
[d] *Acetic acid* added to each solution before making alkaline with *solution of ammonia*.
[f] Solution effected by boiling.

APPENDIX VI. Br.

Quantitative Limit-test For Arsenic. Br.

Note.—" In the quantitative limit-test for arsenic the amount of arsenic present per million is calculated as arsenious oxide, As_4O_6." *Br.*

Apparatus.—" A wide-mouthed bottle capable of holding about 120 millilitres and fitted with a rubber cork through which passes a glass tube. The latter, made from ordinary soft glass tubing, has a total length of 200 millimetres and an internal diameter of 5 millimetres (external diameter 7 millimetres) and is open at both ends. The upper end is slightly widened to a diameter of 8 millimetres, while the lower end is drawn out to about 1 millimetre in diameter, and a hole about 2 millimetres in diameter blown in the side of the tube where it is constricted." *Br.*

Lead Papers.—"Lead papers are pieces of thin white filter paper 100 millimetres × 40 millimetres, soaked in *solution of lead acetate* and dried." *Br.*

Mercuric Chloride Papers.—"Mercuric chloride papers are circles of smooth white filter paper 5.5 centimetres in diameter soaked in a saturated aqueous solution of mercuric chloride and dried." *Br.*

Note.—" The mercuric chloride papers should be stored in a stoppered bottle in the dark. Mercuric chloride papers that have been exposed to sunlight afford a lighter-coloured stain when employed in an arsenic test.

Reagents

The special reagents for the quantitative limit-test for arsenic are distinguished by the letters "As T."

Brominated Hydrochloric Acid As T.—"Solution of Bromine As T., 1 millilitre; Hydrochloric Acid As T. sufficient to produce 100 millilitres. Mix." *Br.*

Calcium Hydroxide As T.—"10 grammes tested as described under 'Calcii Hydras,' page 1742, give no visible stain." *Br.*

Citric Acid As T.—"10 grammes tested as described under 'Acidum Aceticum,' page 1740, give no visible stain." *Br.*

Hydrochloric Acid As T.—"Contains not more than 0.1 part per million of arsenic, as shown by the *Control Test*, and is free from iron." *Br.*

Nitric Acid As T.—"10 millilitres treated as described under 'Acidum Nitricum,' page 1741, give no visible stain." *Br.*

Potassium Chlorate As T.—"Five grammes tested as described under 'Potassii Chloras,' page 1744, give no visible stain." *Br.*

Solution of Arsenic As T.—"Hydrochloric Solution of Arsenic, 1 millilitre; Distilled Water sufficient to produce 1000 millilitres. Mix. This solution must be freshly prepared. 1 millilitre contains 0.00001 gramme (=one-hundredth of one milligram) of arsenic." *Br.*

Solution of Bromine As T.—"Bromine, 30 grammes; Potassium Bromide, 30 grammes; Distilled Water sufficient to produce 100 millilitres. Dissolve. It contains not more than 1 part per million of arsenic as shown by the *Control Test*." *Br.*

Solution of Stannous Chloride As T.—"It is prepared from the Solution of Stannous Chloride, Appendix II, page 1734, by adding an equal volume of Hydrochloric Acid, boiling down to the original bulk and filtering. It contains not more than 1 part per million of arsenic, as shown by the *Control Test*." *Br.*

Stannated Hydrochloric Acid As T.—"Solution of Stannous Chloride As T., 1 millilitre; Hydrochloric Acid As T. sufficient to produce 100 millilitres. Mix." *Br.*

Sulphuric Acid As T.—"Ten grammes, tested as described under 'Acidum Sulphuricum,' page 1741, but omitting the stannated hydrochloric acid As T. and adding 0.2 millilitre of solution of stannous chloride As T., give no visible stain." *Br.*

Zinc As T.—"Zinc As T. is granulated zinc which conforms to the arsenic requirement involved in the *Control Test*, and is free from iron." *Br.*

Method of Performing the Quantitative Test for Arsenic

"By a variable method of procedure suitable to the particular needs of each case there is prepared from the substance to be tested a solution, which may or may not contain the substance to be treated, but in every case contains the whole of the arsenic (if any) originally in that substance. It is this solution—hereinafter referred to as 'the solution to be examined'—which is introduced into the actual test." *Br.*

General Test.—"A strip of lead paper is rolled up and placed in the glass tube so that the upper end is not less than 2 centimetres below the top of the tube. A piece of the mercuric chloride paper is now placed over the top of the tube and secured by means of a rubber ring. The tube is inserted in the rubber cork. The solution to be examined, prepared as specified, is placed in the wide-mouthed bottle and 10 grammes of zinc As T. added. The rubber cork with glass tube attached is quickly placed in position so that the lower end of the tube is clear above the surface of the liquid, and the hole in the constricted portion of the tube is clear below the bottom of the cork. The action should be allowed to proceed for thirty to forty minutes, the mercuric chloride paper not being exposed to strong sunlight. The yellow stain which is produced on the mercuric chloride paper if arsenic be present is compared, by daylight, with stains produced by operating in a similar manner with known quantities of the solution of arsenic As T. The comparison of the stains should be made at the completion of the test and those used for comparison should be freshly prepared. The stains fade upon keeping." *Br.*

Note.—"The action may be accelerated by standing the apparatus on a hot plate, care being taken that the mercuric chloride paper remains quite dry throughout the duration of the test.

Standard Stain.—"Prepare a solution by adding to 50 millilitres of hot *water*, 10 millilitres of stannated hydrochloric acid As T. and 1 millilitre of solution of arsenic As T. The resulting solution when treated as described in the 'General Test' will yield a stain on the mercuric chloride paper hereinafter referred to as the 'Standard Stain.'" *Br.*

Control Tests for Reagents As T.

Hydrochloric Acid As T.—"To 50 millilitres of the hydrochloric acid to be tested add 0.2 millilitre of solution of bromine As T., evaporate on a water-bath until reduced to 16 millilitres, add 50 millilitres of hot *water* and 5 drops of solution of stannous chloride As T. and with this solution carry out the 'General Test' described above. The stain produced on the mercuric chloride paper is not deeper than that given by 10 millilitres of the same hydrochloric acid with 5 drops of solution of stannous chloride As T., 0.4 millilitre of solution of arsenic As T. and 50 millilitres of hot *water*, showing that the proportion of arsenic present does not exceed 0.1 part per million." *Br.*

Solution of Bromine As T.—"Evaporate 10 millilitres of the solution of bromine on a water-bath nearly to dryness, add 50 millilitres of hot *water*, 10 millilitres of hydrochloric acid As T., and sufficient solution of stannous chloride As T. to reduce the remaining bromine, and with this solution carry out the 'General Test' described above. The stain produced on the mercuric chloride paper is not deeper than the Standard Stain, showing that the proportion of arsenic present does not exceed 1 part per million." *Br.*

Solution of Stannous Chloride As T.—"To 10 millilitres of the solution of stannous chloride add 6 millilitres of *water* and 10 millilitres of hydrochloric acid As T., and distil 16 millilitres. To the distillate add 50 millilitres of hot *water* and a few drops of solution of stannous chloride As T. and with this solution carry out the 'General Test' described above. The stain produced on the mercuric chloride paper is not deeper than the Standard Stain, showing that the proportion of arsenic present does not exceed 1 part per million." *Br.*

Zinc As T.—"Add 10 millilitres of stannated hydrochloric acid As T., to 50 millilitres of hot *water*, and with this solution and 10 grammes of zinc As T. proceed as with the 'General Test,' but allow the action to continue for one hour. No visible stain is produced on the mercuric chloride paper (limit of arsenic in the zinc)." *Br.*

The following Table shows the varying methods of preparing the "solution to be examined." The quantities are so arranged that, when tested according to the "General Test" described above, the stain produced on the mercuric chloride paper is not deeper than the Standard Stain, showing that the proportion of arsenic present does not exceed the permissible limit.

Substance.	Solution to be examined.	Limit of Arsenic: Parts per million.
Acidum Aceticum	5 grammes in 50 millilitres of hot *water*, adding 10 millilitres of stannated hydrochloric acid As T.	2
Acidum Acetylsalicylicum	5 grammes made into a paste in a porcelain dish with 2 grammes of calcium hydroxide As T. and 5 millilitres of *water*, drying and gently igniting, dissolving residue in 16 millilitres of brominated hydrochloric acid As T. and 45 millilitres of hot *water*, and finally removing excess of bromine by a few drops of solution of stannous chloride As T.	2
Acidum Benzoicum	5 grammes treated as described under "Acidum Acetylsalicylicum."	2
Acidum Boricum	2 grammes with 4 grammes of citric acid As T. in 50 millilitres of hot *water*, adding 10 millilitres of stannated hydrochloric acid As T.	5

Substance.	Solution to be examined.	Limit of Arsenic: Parts per million.
Acidum Citricum	7 grammes treated as described under "Acidum Aceticum."	1.4
Acidum Hydriodicum Dilutum	2 grammes with 50 millilitres of hot *water*, adding 0.5 millilitre of solution of bromine As T. and 10 millilitres of hydrochloric acid As T., allowing it to stand for five minutes, and removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Acidum Hydrobromicum Dilutum	2 grammes treated as described under "Acidum Aceticum."	5
Acidum Hydrochloricum	2 grammes with 50 millilitres of hot *water* and 8 millilitres of stannated hydrochloric acid As T.	5
Acidum Lacticum	2 grammes treated as described under "Acidum Aceticum."	5
Acidum Nitricum	2 grammes heated in a porcelain dish with 2 millilitres of sulphuric acid As T. until white fumes are evolved, then cooling, adding 2 millilitres of *water*, again heating until white fumes are evolved, again cooling and adding to the residue 50 millilitres of hot *water* and 10 millilitres of stannated hydrochloric acid As T.	5
Acidum Phosphoricum Concentratum	2 grammes treated as described under "Acidum Aceticum."	5
Acidum Salicylicum	5 grammes treated as described under "Acidum Acetylsalicylicum."	2
Acidum Sulphuricum	2 grammes mixed with 10 millilitres of *water*, adding 40 millilitres of hot *water* and 8 millilitres of stannated hydrochloric acid As T.	5
Acidum Sulphurosum	2 grammes mixed in the cold with 0.5 gramme of potassium chlorate As T. and 11 millilitres of hydrochloric acid As T., warming to expel excess of chlorine, then adding 50 millilitres of hot *water* and a few drops of solution of stannous chloride As T.	5
Acidum Tartaricum	7 grammes treated as described under "Acidum Aceticum."	1.4
Alumen Purificatum	2 grammes treated as described under "Acidum Aceticum."	5
Ammonii Benzoas	5 grammes treated as described under "Acidum Acetylsalicylicum."	2
Ammonii Bromidum	2 grammes in 50 millilitres of hot *water*, adding 12 millilitres of stannated hydrochloric acid As T.	5
Ammonii Carbonas	5 grammes in 50 millilitres of hot *water*, boiled gently until the greater part of the ammonium carbonate is volatilised, then adding 15 millilitres of brominated hydrochloric acid As T. and removing excess of bromine by a few drops of solution of stannous chloride As T.	2
Ammonii Chloridum	2 grammes treated as described under "Acidum Aceticum."	5
Antimonium Sulphuratum	0.01 gramme dissolved by boiling in a small flask with 0.2 gramme of calcium hydroxide As T. and 5 millilitres of *water*, then adding 2 millilitres of solution of bromine As T. and again gently boiling, then adding 17 millilitres of hydrochloric acid As T. and 5 millilitres of *water* and boiling until most of the bromine is volatilised, the last traces being removed by adding a slight excess of solution of stannous chloride As T., connecting to a condenser and distilling 20 millilitres, then washing the condenser and flask, returning the distillate to the flask, adding 1 drop of solution of stannous chloride As T. and redistilling 16 millilitres, then adding to the distillate 45 millilitres of hot *water* and a few drops of solution of stannous chloride As T.	1000

Substance.	Solution to be examined.	Limit of Arsenic: Parts per million.
Bismuthi Carbonas	5 grammes dissolved in a small flask in 5 millilitres of *water* and 20 millilitres of brominated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T., connecting to a condenser and distilling 18 millilitres, then adding to the distillate 40 millilitres of hot *water* and 3 drops of solution of stannous chloride As T.	2
Bismuthi Salicylas	5 grammes made into a paste in a porcelain dish with 1 gramme of calcium hydroxide As T. and 5 millilitres of *water*, drying and gently igniting, dissolving the residue in 20 millilitres of brominated hydrochloric acid As T. and 10 millilitres of *water*, transferring to a small flask and adding sufficient solution of stannous chloride As T. to remove the excess of bromine, connecting to a condenser and distilling 20 millilitres, then adding to the distillate 40 millilitres of hot *water* and 3 drops of solution of stannous chloride As T.	2
Bismuthi Subnitras	5 grammes heated in a porcelain dish with 2 millilitres of sulphuric acid As T. until white fumes are evolved, cooling, adding 5 millilitres of *water* and again heating until white fumes are evolved, dissolving the residue when cold in 20 millilitres of *water* and 10 millilitres of stannated hydrochloric acid As T., transferring to a small flask, connecting to a condenser and distilling 20 millilitres, adding to the distillate a little solution of bromine As T. to oxidise any sulphurous acid, removing excess of bromine by a few drops of solution of stannous chloride As T., and adding 40 millilitres of hot *water*.	2
Borax Purificatus	2 grammes with 4 grammes of citric acid As T. in 50 millilitres of hot *water*, adding 12 millilitres of stannated hydrochloric acid As T.	5
Calcii Carbonas Præcipitatus	2 grammes in 14 millilitres of brominated hydrochloric acid As T. and 45 millilitres of hot *water*, removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Calcii Chloridum	2 grammes treated as described under " Acidum Aceticum."	5
Calcii Hydras	2 grammes in 16 millilitres of brominated hydrochloric acid As T. and 45 millilitres of hot *water*, removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Calcii Hypophosphis	2 grammes mixed in the cold with 2 grammes of potassium chlorate and 18 millilitres of hydrochloric acid As T., then warming to expel excess of chlorine, adding 40 millilitres of hot *water* and a few drops of solution of stannous chloride As T.	5
Calcii Lactas	2 grammes treated as described under " Ammonii Bromidum."	5
Calcii Phosphas	2 grammes in 50 millilitres of hot *water* and 14 millilitres of stannated hydrochloric acid As T.	5
Calx	2 grammes in 18 millilitres of brominated hydrochloric acid As T. and 40 millilitres of *water*, removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Creta Præparata	2 grammes treated as described under " Calcii Carbonas Præcipitatus."	5
Cupri Sulphas	1 gramme dissolved in a small flask, with 10 millilitres of *water* and 15 millilitres of hydrochloric acid As T., adding 5 drops of solution of stannous chloride As T., connecting to a condenser and distilling 20 millilitres, adding a little solution of bromine As T. to the distillate to oxidise any sulphurous acid, removing excess of bromine by a few drops of solution of stannous chloride As T., finally adding 40 millilitres of hot *water*.	10

Substance.	Solution to be examined.	Limit of Arsenic: Parts per million.
Ferri Carbonas Saccharatus	2 grammes made into a paste with 1 gramme of calcium hydroxide As T. and 2 millilitres of *water* in a porcelain dish, drying and gently igniting, dissolving the residue in 20 millilitres of brominated hydrochloric acid As T. and 10 millilitres of *water*, transferring to a small flask, adding solution of stannous chloride As T. until the yellow colour disappears, then connecting to a condenser and distilling 24 millilitres, finally adding to the distillate 35 millilitres of hot *water* and 3 drops of solution of stannous chloride As T.	5
Ferri et Ammonii Citras	2 grammes treated as described under "Ferri Carbonas Saccharatus."	5
Ferri et Potassii Tartras	2 grammes treated as described under "Ferri Carbonas Saccharatus."	5
Ferri et Quininæ Citras	2 grammes treated as described under "Ferri Carbonas Saccharatus."	5
Ferri Phosphas Saccharatus	2 grammes treated as described under "Ferri Carbonas Saccharatus."	5
Ferri Sulphas	5 grammes dissolved in a small flask, with 10 millilitres of *water* and 15 millilitres of hydrochloric acid As T., adding solution of stannous chloride As T. until the yellow colour disappears, connecting to a condenser and distilling 20 millilitres, adding a little solution of bromine As T. to the distillate to oxidise any sulphurous acid, removing excess of bromine by a few drops of solution of stannous chloride As T., and finally adding 40 millilitres of hot *water*.	2
Ferri Sulphas Exsiccatus	2 grammes treated as described under "Ferri Sulphas."	5
Ferrum	0.05 gramme mixed in a small flask with 0.1 gramme of potassium chlorate As T. and 7 millilitres of *water*, adding 11 millilitres of hydrochloric acid As T. and, when the reaction has ceased and all the iron is dissolved, boiling gently to expel chlorine, then adding solution of stannous chloride As T. until the yellow colour disappears, connecting to a condenser and distilling 14 millilitres, finally adding to the distillate 50 millilitres of hot *water* and a few drops of solution of stannous chloride As T.	200
Ferrum Redactum	0.05 gramme treated as described under "Ferrum."	200
Glucosum	5 grammes treated as described under "Acidum Hydriodicum Dilutum."	2
Glycerinum	2.5 grammes treated as described under "Acidum Aceticum."	4
Liquor Ammoniæ Fortis	20 grammes evaporated on a water-bath until reduced to 5 millilitres, adding 40 millilitres of *water* and 15 millilitres of brominated hydrochloric acid As T., and removing excess of bromine by a few drops of solution of stannous chloride As T.	0.5
Liquor Ferri Perchloridi Fortis	1 gramme heated in a porcelain dish with 1 millilitre of sulphuric acid As T. until white fumes are evolved, cooling, adding an equal volume of *water* and again heating until white fumes are evolved, dissolving the residue in 10 millilitres of *water* and 15 millilitres of hydrochloric acid As T., transferring to a small flask, adding solution of stannous chloride As T. until the yellow colour disappears, connecting to a condenser and distilling 20 millilitres, adding to the distillate a little solution of bromine As T. to oxidise any sulphurous acid, removing excess of bromine by a few drops of solution of stannous chloride As T., and then adding 40 millilitres of hot *water*.	10
Liquor Ferri Persulphatis	2 grammes treated as described under "Liquor Ferri Perchloridi Fortis."	5

Substance.	Solution to be examined.	Limit of Arsenic: Parts per million.
Liquor Magnesii Bicarbonatis	50 millilitres with 13 millilitres of brominated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T.	0.2
Lithii Carbonas	2 grammes treated as described under "Calcii Hydras."	5
Lithii Citras	5 grammes in 45 millilitres of hot *water*, adding 15 millilitres of stannated hydrochloric acid As T.	2
Magnesia Levis	2 grammes with 40 millilitres of *water* and 20 millilitres of brominated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Magnesia Ponderosa	2 grammes treated as described under "Magnesia Levis."	5
Magnesii Carbonas Levis	2 grammes in 45 millilitres of hot *water* and 15 millilitres of brominated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Magnesii Carbonas Ponderosus	2 grammes treated as described under "Magnesii Carbonas Levis."	5
Magnesii Sulphas	2 grammes treated as described under "Acidum Aceticum."	5
Potassii Acetas	2 grammes treated as described under "Ammonii Bromidum."	5
Potassii Bicarbonas	2 grammes in 50 millilitres of hot *water*, adding 12 millilitres of brominated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T.	5
Potassii Bromidum	2 grammes treated as described under "Ammonii Bromidum."	5
Potassii Carbonas	5 grammes in 50 millilitres of hot *water*, adding 16 millilitres of brominated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T.	2
Potassii Chloras	2 grammes mixed in the cold with 10 millilitres of *water* and 20 millilitres of hydrochloric acid As T. and, when the reaction is complete, warming to expel chlorine, then adding a few drops of solution of stannous chloride As T. and 30 millilitres of hot *water*.	5
Potassii Citras	5 grammes treated as described under "Lithii Citras."	2
Potassii Iodidum	2 grammes treated as described under "Ammonii Bromidum."	5
Potassii Nitras	2 grammes heated in a porcelain dish with 2 millilitres of sulphuric acid As T. and 5 millilitres of *water* until white fumes are evolved, cooling, adding 3 millilitres of *water* and again heating until white fumes are evolved, finally cooling and adding to the residue 50 millilitres of hot *water* and 10 millilitres of stannated hydrochloric acid As T.	5
Potassii Sulphas	2 grammes treated as described under "Acidum Aceticum."	5
Potassii Tartras	5 grammes treated as described under "Calcii Phosphas."	2
Potassii Tartras Acidus	5 grammes in 50 millilitres of hot *water* and 13 millilitres of brominated hydrochloric acid As T., removing excess of bromine by a few drops of solution of stannous chloride As T.	2
Sodii Benzoas	5 grammes gently heated in a porcelain dish, until inflammable vapors cease to be evolved, dissolving the residue (ignoring any carbon) in 14 millilitres of brominated hydrochloric acid As T. and 50 millilitres of hot *water* and removing excess of bromine by a few drops of solution of stannous chloride As T.	2
Sodii Bicarbonas	5 grammes treated as described under "Potassii Carbonas."	2
Sodii Bromidum	2 grammes treated as described under "Ammonii Bromidum."	5

Substance.	Solution to be examined.	Limit of Arsenic: Parts per million.
Sodii Carbonas	5 grammes in 50 millilitres of hot *water*, adding 14 millilitres of brominated hydrochloric acid As T. and removing excess of bromine by a few drops of solution of stannous chloride As T.	2
Sodii Carbonas Exsiccatus	2 grammes treated as described under "Sodii Carbonas."	5
Sodii Chloridum	5 grammes treated as described under "Acidum Aceticum."	2
Sodii et Potassii Tartras	5 grammes treated as described under "Calcii Phosphas."	2
Sodii Hypophosphis	2 grammes treated as described under "Calcii Hypophosphis."	5
Sodii Iodidum	2 grammes in 50 millilitres of hot *water*, adding 11 millilitres of stannated hydrochloric acid As T.	5
Sodii Nitris	2 grammes treated as described under "Potassii Nitras."	5
Sodii Phosphas	2 grammes treated as described under "Acidum Aceticum."	5
Sodii Phosphas Acidus	5 grammes treated as described under "Acidum Aceticum."	2
Sodii Salicylas	5 grammes treated as described under "Sodii Benzoas."	2
Sodii Sulphas	5 grammes treated as described under "Acidum Aceticum."	2
Sodii Sulphis	2 grammes with 0.5 gramme of potassium chlorate As T. in 5 millilitres of warm *water*, adding 12 millilitres of hydrochloric acid As T., then warming to expel excess of chlorine and adding 45 millilitres of hot *water* and a few drops of solution of stannous chloride As T.	5
Strontii Bromidum	2 grammes treated as described under "Ammonii Bromidum."	5
Sulphur Præcipitatum	2 grammes digested for one hour on a water-bath with 50 millilitres of *water* and 5 millilitres of solution of ammonia, filtering and evaporating the filtrate to low bulk, adding 10 millilitres of nitric acid As T. and boiling to oxidise any sulphur, then adding 2 millilitres of sulphuric acid As T. and heating until white fumes are evolved, cooling, adding 2 millilitres of *water* and again heating until white fumes are evolved, finally adding 50 millilitres of hot *water* and 10 millilitres of stannated hydrochloric acid As T.	
Sulphur Sublimatum	2 grammes treated as described under "Sulphur Præcipitatum."	5
Zinci Acetas	2 grammes treated as described under "Ammonii Bromidum."	5
Zinci Carbonas	1 gramme treated as described under "Potassii Carbonas."	10
Zinci Chloridum	2 grammes treated as described under "Acidum Aceticum."	5
Zinci Oxidum	1 gramme treated as described under "Potassii Carbonas."	10
Zinci Sulphas	2 grammes treated as described under "Acidum Aceticum."	5
Zinci Valerianas	2 grammes made into a paste in a porcelain dish with 2 grammes of calcium hydroxide As T. and 5 millilitres of *water*, drying and gently igniting, then dissolving the residue in 18 millilitres of brominated hydrochloric acid As T. and 40 millilitres of hot *water* and removing excess of bromine by a few drops of solution of stannous chloride As T.	5

APPENDIX VII. Br.

Determination of the Acid Value of Fixed Oils, Fats, Waxes, and Resins. Br.

"The acid value of a fixed oil, fat, or wax (the number of milligrams of potassium hydroxide required to neutralise the free acid in 1 gramme of the substance) is determined as follows:—Mix 10 grammes of the substance with 50 millilitres of *alcohol* (90 per cent.), previously neutralised with *solution* of *potassium hydroxide*, add 1 millilitre of *solution of phenolphthalein*, heat until the fat or wax is melted and titrate with

N/10 solution of potassium hydroxide, shaking constantly. Note the number of millilitres required (*a*). Calculate the acid value from the following formula:—

$$\text{"Acid value} = \frac{a \times 0.0056 \times 1000}{\text{weight (in grammes) of substance taken}}$$

"The acid value of a resin is determined by dissolving from 1 to 5 grammes of the substance in 50 millilitres of *alcohol* (90 per cent.), previously neutralised, and titrating and calculating as above directed." *Br.*

Determination of the Saponification Value of Fixed Oils, Fats, Waxes, and Resins. Br.

"The saponification value of a fixed oil, fat, wax, or resin (the number of milligrams of potassium hydroxide required for the complete saponification of 1 gramme of the substance) is determined as follows:—Dissolve 40 grammes of *potassium hydroxide* in 1000 millilitres of *alcohol* (90 per cent.), previously neutralised; allow the solution to stand for twenty-four hours and filter. Weigh from 1.5 to 2 grammes of the substance in a flask having a capacity of about 200 millilitres; add 25 millilitres of the alcoholic solution of potassium hydroxide, attach a reflux condenser and heat on a water-bath for thirty minutes; add 1 millilitre of *solution of phenolphthalein* and titrate the excess of alkali with *N/2 solution of hydrochloric acid*. Note the number of millilitres required (*a*). At the same time treat 25 millilitres of the alcoholic solution of potassium hydroxide in a similar manner. Note the number of millilitres required (*b*). Calculate the saponification value from the following formula:—

$$\text{"Saponification value} = \frac{(b-a) \times 0.028 \times 1000}{\text{weight (in grammes) of substance taken}}\text{"}$$ *Br.*

Determination of the Iodine Value of Fixed Oils and Fats. Br.

"The iodine value of a fixed oil or fat (the proportional weight of iodine absorbed by 100 parts by weight of the oil or fat under the conditions specified) is determined as follows:—

Solution to be Prepared.—Iodine Solution.—"Dissolve 13 grammes of iodine in 1000 millilitres of *glacial acetic acid*. Titrate the solution with *N/10 solution of sodium thiosulphate*, note the proportion required and pass *chlorine*, washed and dried, through the remainder of the iodine solution until this proportion is exactly doubled. Keep the solution in a stoppered amber bottle in a cool, dark place."

Weight of Substance to be Taken.—"Lard, Suet, and Oil of Theobroma 0.8 to 1.0 gramme; Almond Oil, Castor Oil, and Olive Oil, 0.3 to 0.4 gramme; Cod-liver Oil, and Linseed Oil 0.15 to 0.18 gramme.

Time to be Allowed for Absorption.—"Lard, Suet, and Oil of Theobroma, Almond Oil, Castor Oil, and Olive Oil, 1 hour; Cod-liver Oil and Linseed Oil, 2 hours."

Method of Procedure.—"Place the specified weight of oil or fat in a stoppered bottle having a capacity of 800 millilitres, add 10 millilitres of *carbon tetrachloride* and dissolve. Add 25 millilitres of the iodine solution, insert the stopper, previously moistened with *solution of potassium iodide*, and keep in a dark place at a temperature of about 17° for the specified time. Then add 20 millilitres of *solution of potassium iodide* and 500 millilitres of *water*. Shake, and titrate with *N/10 solution of sodium thiosulphate*, using *mucilage of starch* as indicator. Note the number of millilitres required (*a*). At the same time treat 25 millilitres of the solution of iodine in a similar manner and note the number of millilitres of *N/10 solution of sodium thiosulphate* required (*b*). Calculate the iodine value from the following formula:—

$$\text{"Iodine value} = \frac{(b-a) \times 0.01269 \times 100}{\text{weight (in grammes) of oil or fat taken}}\text{"}$$ *Br.*

Determination of the Unsaponifiable Matter in Fixed Oils and Fats. Br.

"The percentage of unsaponifiable matter in a fixed oil or fat is determined as follows:—Boil 5 grammes of the oil or fat with 50 millilitres of *N/1 alcoholic solution of potassium hydroxide* in a flask provided with a reflux condenser on a water-bath for thirty minutes. Transfer the contents of the flask to a porcelain dish and evaporate the alcohol on a water-bath. Dissolve the resulting soap in about 100 millilitres of hot water, cool and transfer to a separator. Add 50 millilitres of *ether*, mix thoroughly and allow to separate. Transfer the soap solution to another separator and again extract with 50 millilitres of *ether*. Mix the ethereal solutions, wash with three portions, each of 20 millilitres, of *water*, transfer to a tared flask, evaporate the ether, dry the residue at 100° C. (212° F.) and weigh. The weight (in grammes) of the residue multiplied by 20 gives the percentage of unsaponifiable matter." *Br.*

Determination of the Esters in Volatile Oils. Br.

"The percentage of esters present in a volatile oil is determined as follows:—Dissolve from 2 to 5 grammes of the oil in 25 millilitres of alcohol (90 per cent.) and neutralise the solution, if necessary, with *N/1 alcoholic solution of potassium hydroxide*. Then add 25 millilitres of *N/1 alcoholic solution of potassium hydroxide*, boil in a flask provided with a reflux condenser on a water-bath for one hour, and titrate the excess of alkali with *N/1 solution of sulphuric acid*. Note the number of millilitres required (*a*). At the same time treat 25 millilitres of *alcohol* (90 per cent.) in a similar manner and note the number of millilitres of acid required (*b*). Calculate the percentage of esters in the oil from the following formula:—

$$\text{"Percentage of esters} = \frac{(b-a) \times \text{molecular weight of ester}}{\text{weight (in grammes) of oil taken} \times 10}\text{"}$$ *Br.*

Determination of the Alcohols in Volatile Oils. Br.

"The percentage of alcohols present in a volatile oil is determined as follows:—Heat 10 millilitres of the oil with 10 millilitres of *acetic anhydride* and 2 grammes of *anhydrous sodium acetate* in an acetylation flask for two hours; add 100 millilitres of *water*, transfer to a separator and, after separation, remove the aqueous layer and wash the oily layer free from acidity with successive quantities, each of 100 millilitres of *water*, thoroughly shaking and allowing to separate each time. Dry the acetylated oil with *anhydrous sodium sulphate* and filter. Then treat from 2 to 5 grammes of the acetylated oil according to the process for the determination of the esters present in volatile oils. Calculate the percentage of alcohols present in the oil from the following formula:—

"**Percentage of alcohols** = $\frac{\frac{1}{10} \times (b-a) \times \text{molecular weight of the alcohol}}{\text{weight (in grammes) of acetylated oil taken}—0.042\ (b-a)}$ " *Br.*

Alkaloidal Assays: Limit of Error. Br.

"Successive assays of the same substance may yield numerical results varying within narrow limits, which are taken to be the range of 'error.' When an average of successive assays shows a deviation from the prescribed standard greater or less than the 'limit of error,' the preparation examined does not conform to the requirements of the British Pharmacopœia." *Br.*

APPENDIX VIII. Br.

Determination of Melting Points. Br.

"Prepare some thin-walled glass tubes having an internal diameter of about one millimetre by heating thick-walled, soft glass tubing in a blow-pipe flame, drawing out the heated portion until it has the required diameter, then allowing a small flame to play against the middle of this tube so as to make and seal two tubes which are finally to be cut off to suitable lengths; these tubes should be freshly made; if stored they should be carefully protected from moisture.

"Dry a very small quantity of the powdered substance at 100° C. (212° F.) for fifteen minutes; transfer a portion to one of these tubes, shaking the powder down to the sealed extremity. Attach the tube to a thermometer so that the substance is near the middle of the bulb. Heat a suitable liquid, such as *sulphuric acid*, to which *nitric acid* in the proportion of about 4 drops to 100 millilitres has been added, in a beaker or boiling tube about 3 centimetres in diameter, to about 5° below the expected melting point of the substance; this point, if not known, being determined by a preliminary experiment. Then introduce the thermometer with the attached tube, and slowly heat, efficiently stirring, and note the temperature at which the substance first shows visible change; this temperature is regarded as the uncorrected melting point of the substance. The whole of the mercury column of the thermometer should be immersed in the liquid, but as this is seldom practicable the following correction is to be applied:—

"To the thermometer attach a second thermometer in such a position that its bulb is near the middle of the emergent column of mercury, and observe thereby the mean temperature of the column. Calculate the corrected melting point of the substance from the following formula:—

"Corrected melting point = T + 0.000143 (T − t) N, in which T = the uncorrected melting point; t = the mean temperature of the emergent column; N = the number of scale degrees in the emergent column.

"The melting point of solid fats, fatty acids, and waxes is determined by running a small quantity of the melted substance into an unsealed melting point tube, allowing it to cool for twenty-four hours, and then, using *water* in the place of sulphuric acid, determining in the manner described the temperature at which the substance becomes a clear liquid; this temperature is to be taken as the uncorrected melting point." *Br.*

Determination of Boiling Points. Br.

"Place the liquid under examination in a distillation flask having a side tube for conveying the vapour to a condenser, while a thermometer passes through a cork inserted in the neck. The bulb of the thermometer should be opposite the entrance of the side tube, and not immersed in the liquid or exposed to splashes of it, and the whole of the column of mercury should, if possible, be surrounded by the vapour; the temperature is read off as soon as the liquid is distilling freely. If any considerable length of the column of mercury is not surrounded by the vapour, the mean temperature of the emergent column should be ascertained as directed under the 'Determination of Melting Points,' and the like correction applied." *Br.*

Determination of Refractive Indices. Br.

"The refractive index of a substance should be determined in a suitable apparatus as nearly as possible at the temperature specified. Should the temperature be either above or below the specified temperature, the following correction is to be applied:—For each degree below the specified temperature subtract 0.00038 from the observed refractive index; for each degree above the specified temperature add 0.00038." *Br.*

Determination of Optical Rotation. Br.

"The optical rotation, unless otherwise specified, is the angle through which the plane of polarisation is turned when a layer of the liquid substance one decimetre in thickness and at a temperature of 20° C. (68° F.) is examined by polarised sodium light.

"The specific rotation of a substance in solution may be calculated from the formula $\frac{a \times 100}{l \times c}$, where

a is the observed optical rotation, l the thickness in decimetres of the layer examined, and c the number of grammes of substance contained in 100 millilitres of the solution." *Br.*

Determination of Specific Gravity. Br.

"The specific gravity of a substance is the weight of a given volume of that substance at 15.5° C. (59.9° F.) as compared with the weight of an equal volume of distilled water, at the same temperature unless otherwise specified." *Br.*

APPENDIX IX. Br.

Process of Percolation. Br.

"Moisten the solid materials with the prescribed quantity of menstruum, set aside for four hours in a well-closed vessel, pack in a percolator and add sufficient of the menstruum to saturate the materials and leave a layer of liquid above. Macerate for twenty-four hours; then allow percolation to proceed slowly until the percolate measures about three-fourths of the volume required for the finished tincture. Press the marc, mix the expressed liquid with the percolate, and add sufficient of the menstruum to produce the required volume. Clarify by subsidence or filtration, if necessary." *Br.*

Process of Repercolation. Br.

"Take one hundred parts by weight of the drug and divide it into five equal portions. Moisten the first portion with the menstruum, set aside in a closed vessel for four hours and pack in a percolator. Add sufficient of the menstruum to saturate the drug and leave a layer of liquid above. Macerate for twenty-four hours, then allow percolation to proceed slowly, collecting the percolate in fractions of twenty parts.

"Moisten the second portion of the drug with the first fraction of the percolate collected. Set aside, pack in a percolator, macerate and percolate as before, using as menstruum the successive fractions of percolate collected from the portion first treated. Again collect the percolate in fractions of twenty parts.

"In turn, treat in the manner described above the third, fourth, and fifth portions of the drug with the fractions of percolate obtained in the percolation of the portion immediately preceding, using the successive fractions of percolate in order, until a liquid extract is obtained of the required strength." *Br.*

Process of Maceration. Br.

"Place the solid materials with the whole of the menstruum in a closed vessel; shake occasionally during seven days; strain; press the marc; mix the liquids obtained. Clarify by subsidence or filtration if necessary." *Br.*

APPENDIX X. Br.

Process for Preparation of Discs (Lamellæ). Br.

"Discs are prepared by the following process:—Gelatin, 18 grammes; Glycerin, 2 grammes; Distilled Water, 88 grammes. Mix the Glycerin with the Distilled Water, allow the Gelatin to soak in the mixture till soft, and then dissolve by a gentle heat; cool the basis so produced. Take the prescribed quantity of the above basis, melt it by a gentle heat, add the prescribed quantity of medicament, dissolve and mix. Pour the melted and medicated basis upon a sheet of plate glass 10 centimetres square, previously thinly coated with White Beeswax, in such a manner that the solution is evenly distributed. Dry at a temperature not exceeding 36° C. (96.8° F.), and from the film thus obtained cut discs 3 millimetres nearly (⅛ inch) in diameter." *Br.*

APPENDIX XI. Br.

Processes for Preparation of Lozenges (Trochisci). Br.

With Fruit Basis.—"Take five hundred times the quantity of the drug ordered for one lozenge. Mix with it 6.5 grammes of Tragacanth and 26 grammes of Refined Sugar, both in fine powder. Add sufficient of the black-currant paste of commerce to produce 650 grammes, beat into a uniform mass, divide into 500 equal lozenges and dry in a hot air chamber at a moderate temperature." *Br.*

With Rose Basis.—"Take five hundred times the quantity of the drug ordered for one lozenge. Treat it as described under "Preparation with Simple Basis," previously mixing with the Refined Sugar 0.025 millilitre of oil of Rose." *Br.*

With Simple Basis.—"Take five hundred times the quantity of the drug ordered for one lozenge, mix it with 496 grammes of Refined Sugar and 19.5 grammes of Gum Acacia, both in fine powder. Make the mixture into a paste with 35 millilitres of Mucilage of Gum Acacia and a sufficient quantity of Distilled Water, divide into 500 equal lozenges and dry in a hot air chamber at a moderate temperature." *Br.*

With Tolu Basis.—"Take five hundred times the quantity of the drug ordered for one lozenge; dissolve such salts of alkaloids as may be ordered in 10 millilitres of Distilled Water; mix the solution with 482 grammes of Refined Sugar and 19.5 grammes of Gum Acacia, both in fine powder. Incorporate 10 millilitres of Tincture of Balsam of Tolu, and any other drugs ordered for the lozenges. Make into a paste with 35.5 millilitres of Mucilage of Gum Acacia and a sufficient quantity of Distilled Water; divide into 500 equal lozenges and dry in a hot-air chamber at a moderate temperature." *Br.*

APPENDIX XII. Br.

Alternative Preparations Sanctioned for Use in Tropical, Subtropical, and Other Parts of the British Empire. Br.

Aquæ Olei Anethi, Anisi, Carui, Cinnamomi, Fœniculi, Menthæ Piperitæ, Menthæ Viridis.—"Each of these Waters may be prepared by triturating the corresponding Oil with twice its weight of Calcium Phosphate and five hundred times its volume of Distilled Water and filtering the mixture. In tropical and subtropical parts of the Empire these Aquæ Olei may be used in place of the corresponding Aquæ of the Text of the Pharmacopœia." *Br.*

Emplastra.—"In tropical and subtropical parts of the Empire, more or less Hard Soap, Resin, or Yellow Beeswax, may be employed in the preparation of the Plasters of the Text of the Pharmacopœia, when prevailing high temperatures otherwise render the basis too soft for convenient use; but the official proportion of the active ingredient must in all cases be maintained." *Br.*

Extracta Liquida.—"Any Liquid Extract, defined in the Text of the Pharmacopœia, containing less than one-fourth of its weight of Alcohol (90 per cent.), may have the proportion of Alcohol (90 per cent.) increased to an amount not exceeding one-fourth of the weight of the Extract, in tropical and subtropical parts of the Empire where otherwise the preparation would be liable to ferment." *Br.*

Limonis Cortex Siccatus.—"In tropical and subtropical parts of the Empire, when fresh Lemon Peel cannot be obtained, Dried Lemon Peel may be used in preparing Compound Infusion of Orange Peel, Compound Infusion of Gentian, Syrup of Lemon, and Tincture of Lemon." *Br.*

Oleum Olivæ.—"In India, and in the Eastern, African, Australasian, and North American Divisions of the Empire, Arachis Oil or Sesame Oil, but no other oil or fat, may be employed in making the official Liniments, Plasters, Ointments, and Soaps for which Olive Oil is directed to be used." *Br.*

Suppositoria.—"More or less White Beeswax, according to prevailing temperatures, may be used in place of an equivalent amount of Oil of Theobroma in tropical and subtropical parts of the Empire, when otherwise the Suppositories of the Text of the Pharmacopœia would be too soft for convenient use." *Br.*

Syrupus Rhœados.—"In tropical and subtropical parts of the Empire, when prevailing high temperatures render this preparation liable to ferment, the proportion of Alcohol (90 per cent.) may be increased, but not to more than double the proportion stated in the Text of the Pharmacopœia, and equivalent quantity of Distilled Water being omitted." *Br.*

Unguenta.—"In tropical and subtropical parts of the Empire more or less Benzoated Lard, Prepared Lard, Benzoated Suet, Prepared Suet, Yellow Beeswax, or White Beeswax, may be employed in the preparation of the Ointments of the Text of the Pharmacopœia when prevailing high temperatures otherwise render the basis too soft for convenient use; but the official proportion of the active ingredient must in all cases be maintained." *Br.*

APPENDIX XIII. Br.

Table of Proportions Relating to the Preparation of Diluted Alcohols. Br.

"Volume of Alcohol (90 per cent.) to be diluted with Distilled Water to 1000 millilitres at 15.5° C. (59.9° F.) in order to give the Diluted Alcohols of the British Pharmacopœia." *Br.*

Alcohol Required.	Specific Gravity.	Volume of Alcohol (90 per cent.).
70 per cent.	0.8899	777.8 millilitres
60 per cent.	0.9134	666.7 millilitres
45 per cent.	0.9435	500.0 millilitres
20 per cent.	0.9760	222.2 millilitres

Elements and Pharmacopœial Chemicals (U. S. P. IX)

With Their Atomic or Molecular Weights and a Table of Multiples

This list contains the official chemicals and reagents of a definite composition, and also some that are not official, but which are likely to be required in stoichiometrical calculations. The figures in the list given below are based upon the Table of International Atomic Weights (1915), with Oxygen taken as 16. The elementary substances are also given in a separate list (see page 1760). In the case of a few salts, for which this Pharmacopœia has given no formula on account of the difficulty of securing an absolutely uniform composition, the theoretical formula has been inserted merely for information. In the case of many hydrated compounds the formula and molecular weight of the corresponding anhydrous salt have also been given, to save time in making calculations.

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Acetaldehyde (Acetic Aldehyde)	CH_3CHO	44.03
Acetanilid (Phenylacetamide)	C_8H_9ON	135.08
Acetic Anhydride	$(CH_3CO)_2O$	102.05
Acetone	C_3H_6O	58.05
Acetphenetidin (Acetparaphenetidin)	$C_{10}H_{13}O_2N$	179.11
Acid, Acetic	$HC_2H_3O_2$	60.03
" " Anhydride	$(CH_3CO)_2O$	102.05
" Acetylsalicylic	$HC_7H_4O_2C_2H_3O_2$	180.06

		O=16
Acid, Arsenic	$H_3AsO_4+\frac{1}{2}H_2O$	150.99
" Aurochloric (Chlorauric)	$HAuCl_4+4H_2O$	412.11
" Benzoic	$HC_7H_5O_2$	122.05
" Boric	H_3BO_3	62.02
" Bromauric (Aurobromhydric)	$HAuBr_4+5H_2O$	607.97
" Camphoric	$H_2C_{10}H_{14}O_4$	200.13
" Carbolic (see Phenol)		
" Chlorauric (Aurochloric)	$HAuCl_4+4H_2O$	412.11
" Chloroplatinic	$H_2PtCl_6+6H_2O$	518.07
" Cinnamic (Cinnamylic)	$HC_9H_7O_2$	148.06
" Citric	$H_3C_6H_5O_7+H_2O$	210.08
" " Anhydrous	$H_3C_6H_5O_7$	192.06
" Diethyl-barbituric	$C_8H_{12}O_3N_2$	184.12
" Formic	$HCHO_2$	46.02
" Gallic	$HC_7H_5O_5+H_2O$	188.06
" " Anhydrous	$HC_7H_5O_5$	170.05
" Glycerophosphoric	$H_2C_3H_5(OH)_2PO_4$	172.11
" Hydriodic	HI	127.93
" Hydrobromic	HBr	80.93
" Hydrochloric	HCl	36.47
" Hydrocyanic	HCN	27.02
" Hydrofluoric	HF	20.01
" Hydrosulphuric (Hydrogen Sulphide)	H_2S	34.09
" Hypophosphorous	HPH_2O_2	66.06
" Lactic	$HC_3H_5O_3$	90.05
" Molybdic	H_2MoO_4	162.02
" Nitric	HNO_3	63.02
" Nitrous	HNO_2	47.02
" Oleic	$HC_{18}H_{33}O_2$	282.27
" Oxalic	$H_2C_2O_4+2H_2O$	126.05
" " Anhydrous	$H_2C_2O_4$	90.02
" Phenolsulphonic (Phenoldisulphonic)	$HC_6H_3(HSO_3)_2O$	254.19
" Phenylcinchoninic	$HC_{16}H_{10}O_2N$	249.10
" Phosphoric	H_3PO_4	98.06
" Phosphorous	H_3PO_3	82.06
" Picric (see Trinitrophenol)		
" Pyroboric (Tetraboric)	$H_2B_4O_7$	158.02
" Pryogallic (see Pyrogallol)		
" Rosolic (see Methylaurin)		
" Salicylic	$HC_7H_5O_3$	138.05
" Stearic	$HC_{18}H_{35}O_2$	284.29
" Succinic	$H_2C_4H_4O_4$	118.05
" Sulphanilic	$HC_6H_4(NH_2)SO_3+2H_2O$	209.17
" " Anhydrous	$HC_6H_4(NH_2)SO_3$	173.14
" Sulphuric	H_2SO_4	98.09
" Sulphurous	H_2SO_3	82.09
" Tannic (variable)	$HC_{14}H_9O_9$	322.08
" Tartaric	$H_2C_4H_4O_6$	150.05
" Tetraboric (Pyroboric)	$H_2B_4O_7$	158.02
" Trichloracetic	$HC_2O_2Cl_3$	163.39
" Tungstic	H_2WO_4	250.02
" Valeric (Valerianic)	$HC_5H_9O_2$	102.08
Aconitine	$C_{34}H_{47}O_{11}N$	645.39
Alcohol, Amyl (Amyl Hydroxide)	$C_5H_{11}OH$	88.10
" Ethyl (Ethyl Hydroxide)	C_2H_5OH	46.05
" Methyl (Methyl Hydroxide)	CH_3OH	32.03
Aldehyde, Acetic (Acetaldehyde)	CH_3CHO	44.03
" Benzoic (Benzaldehyde)	C_7H_6O	106.05
" Cinnamic	C_8H_7CHO	132.06
" Formic (Formaldehyde)	CH_2O	30.02
Allyl-isothiocyanate	C_3H_5SCN	99.12
Allyl-sulphocarbamide (Thiosinamine)	$C_3H_5SCN_2H_3$	116.15
Alum (see Aluminum and Potassium Sulphate and Aluminum and Ammonium Sulphate)		
Aluminum	Al	**27.1**
Aluminum and Ammonium Sulphate (Alum)	$AlNH_4(SO_4)_2+12H_2O$	453.47
" " " " Anhydrous	$AlNH_4(SO_4)_2$	237.28
" " Potassium Sulphate (Alum)	$AlK(SO_4)_2+12H_2O$	474.53
" " " " Anhydrous	$AlK(SO_4)_2$	258.34
" Hydroxide	$Al(OH)_3$	78.12
" Oxide	Al_2O_3	102.20
" Silicate (Kaolin) (approximately)	$H_2Al_2(SiO_4)_2+H_2O$	258.83
" Sulphate	$Al_2(SO_4)_3+18H_2O$	666.70
" " Anhydrous	$Al_2(SO_4)_3$	342.41
Ammonia	NH_3	17.03

		O=16
Ammonium Acetate	$NH_4C_2H_3O_2$	77.07
" Arsenite (Metarsenite)	NH_4AsO_2	125.00
" Benzoate	$NH_4C_7H_5O_2$	139.08
" Bromide	NH_4Br	97.96
" Carbamate	$NH_4NH_2CO_2$	78.07
" Carbonate (Acid)	NH_4HCO_3	79.05
" " (Normal)	$(NH_4)_2CO_3$	96.08
" " (U. S. P.) (approximately)	$NH_4HCO_3NH_4NH_2CO_2$	157.12
" Chloride	NH_4Cl	53.50
" Chloroplatinate	$(HN_4)_2PtCl_6$	444.04
" Citrate	$(NH_4)_3C_6H_5O_7$	243.17
" Hydrogen Fluoride	NH_4FHF	57.05
" Hydrogen Sulphide	NH_4HS	51.12
" Hypophosphite	$NH_4PH_2O_2$	83.10
" Iodide	NH_4I	144.96
" Lactate	$NH_4C_3H_5O_3$	107.08
" Molybdate	$(NH_4)_6Mo_7O_{24}+4H_2O$	1236.32
" Nitrate	NH_4NO_3	80.05
" Oxalate	$(NH_4)_2C_2O_4+H_2O$	142.10
" " Anhydrous	$(NH_4)_2C_2O_4$	124.08
" Phosphate	$(NH_4)_2HPO_4$	132.13
" Salicylate	$NH_4C_7H_5O_3$	155.08
" and Sodium Phosphate	$NH_4NaHPO_4+4H_2O$	209.15
" Sulphate	$(NH_4)_2SO_4$	132.15
" Sulphide	$(NH_4)_2S$	68.15
" Tartrate	$(NH_4)_2C_4H_4O_6$	184.12
" Valerate (not U.S.P.)	$NH_4C_5H_9O_2$	119.11
" Vanadate (Metavanadate)	NH_4VO_3	117.04
Amyl Nitrite	$C_5H_{11}NO_2$	117.10
Amylene Hydrate	$C_5H_{12}O$	88.10
Anethol	$C_{10}H_{12}O$	148.10
Aniline (Phenylamine)	$C_6H_5NH_2$	93.07
" Sulphate	$(C_6H_5NH_2)_2H_2SO_4$	284.22
Antimony	**Sb**	**120.2**
Antimony and Potassium Tartrate	$K(SbO)C_4H_4O_6+\frac{1}{2}H_2O$	332.34
" " " " Anhydrous	$K(SbO)C_4H_4O_6$	323.33
Antimonic Sulphide	Sb_2S_5	400.75
Antimonous Oxide	Sb_2O_3	288.40
" Sulphide	Sb_2S_3	336.61
Antipyrine	$C_{11}H_{12}ON_2$	188.12
Apomorphine Hydrochloride	$C_{17}H_{17}O_2NHCl+\frac{1}{2}H_2O$	312.62
Argon	**A**	**39.88**
Arsenic	**As**	**74.96**
Arsenic Sulphide	As_2S_5	310.27
" Trioxide (see Arsenous Oxide)	As_2O_3	197.92
Arsenous Iodide (Arsenic Triiodide)	AsI_3	455.72
" Oxide (Arsenic Trioxide)	As_2O_3	197.92
" Sulphide	As_2S_3	246.13
Aspidospermine	$C_{22}H_{30}O_2N_2$	354.26
Atropine	$C_{17}H_{23}O_3N$	289.19
" Sulphate	$(C_{17}H_{23}O_3N)_2H_2SO_4+H_2O$	694.49
Auric Chloride	$AuCl_3$	303.58
Barium	**Ba**	**137.37**
Barium Carbonate	$BaCO_3$	197.37
" Chloride	$BaCl_2+2H_2O$	244.32
" " Anhydrous	$BaCl_2$	208.29
" Chromate	$BaCrO_4$	253.37
" Dioxide	BaO_2	169.37
" Hydroxide	$Ba(OH)_2+8H_2O$	315.51
" Nitrate	$Ba(NO_3)_2$	261.39
" Sulphate	$BaSO_4$	233.44
" Sulphide	BaS	169.44
Benzaldehyde (Benzoic Aldehyde)	C_6H_5CHO	106.05
Benzene (Benzol)	C_6H_6	78.05
Benzosulphinide (Saccharin, Benzoyl-sulphonicimide)	$C_7H_5O_3NS$	183.12
Benzoyl-acetyldioxide	$C_6H_5CO.C_2H_3O.O_2$	180.06
Betaeucaine Hydrochloride	$C_{15}H_{21}O_2NHCl$	283.65
Betanaphthol (Naphthol)	$C_{10}H_8O$	144.06
Bismuth	**Bi**	**208.0**
Bismuth Betanaphthol (approximately)	$(BiO)_2OHC_{10}H_7O$	608.06
" Citrate	$BiC_6H_5O_7$	397.04
" Nitrate (normal)	$Bi(NO_3)_3+5H_2O$	484.11
" Subcarbonate (approximately)	$[(BiO)_2CO_3]_2+H_2O$	1034.02
" Subgallate (approximately)	$Bi(OH)_2C_7H_5O_5$	411.06

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Bismuth Subnitrate (approximately)	$Bi(OH)_2NO_3$	304.03
" Subsalicylate (approximately)	$Bi(OH)_2C_7H_5O_3$	379.06
" Sulphide	Bi_2S_3	512.21
" Trioxide	Bi_2O_3	464.00
Borneol	$C_{10}H_{17}OH$	154.14
Bornyl Acetate	$C_{10}H_{17}C_2H_3O_2$	196.16
Boron	**B**	**11.0**
Boron Trioxide	B_2O_3	70.0
Bromine	**Br**	**79.92**
Bromoform	$CHBr_3$	252.77
Brucine	$C_{23}H_{26}O_4N_2+4H_2O$	466.29
" Anhydrous	$C_{23}H_{26}O_4N_2$	394.23
Cadmium	**Cd**	**112.40**
Cadmium Chloride	$CdCl_2+2H_2O$	219.35
" " Anhydrous	$CdCl_2$	183.32
" Iodide	CdI_2	366.24
" Sulphate	$3CdSO_4+8H_2O$	769.54
" " Anhydrous	$CdSO_4$	208.47
" Sulphide	CdS	144.47
Caesium	**Cs**	**132.81**
Caffeine	$C_8H_{10}O_2N_4+H_2O$	212.14
" Anhydrous	$C_8H_{10}O_2N_4$	194.12
" Citrated	$C_8H_{10}O_2N_4C_6H_8O_7$	386.18
Calcium	**Ca**	**40.07**
Calcium Bromide	$CaBr_2+2H_2O$	235.94
" " Anhydrous	$CaBr_2$	199.91
" Carbonate	$CaCO_3$	100.07
" Chloride	$CaCl_2+2H_2O$	147.02
" " Anhydrous	$CaCl_2$	110.99
" Fluoride	CaF_2	78.07
" Glycerophosphate	$CaC_3H_7PO_6+H_2O$	228.18
" " Anhydrous	$CaC_3H_7PO_6$	210.17
" Hydroxide	$Ca(OH)_2$	74.09
" Hypophosphite	$Ca(PH_2O_2)_2$	170.18
" Lactate	$Ca(C_3H_5O_3)_2+5H_2O$	308.23
" " Anhydrous	$Ca(C_3H_5O_3)_2$	218.15
" Oxalate	$CaC_2O_4+H_2O$	146.09
" Oxide (Lime)	CaO	56.07
" Phosphate	$Ca_3(PO_4)_2$	310.29
" Pyrophosphate	$Ca_2P_2O_7$	254.22
" Sulphate (Gypsum)	$CaSO_4+2H_2O$	172.17
" " Anhydrous	$CaSO_4$	136.14
" Sulphide (Monosulphide)	CaS	72.14
Camphor	$C_{10}H_{16}O$	152.13
" Monobromated	$C_{10}H_{15}OBr$	231.04
Carbon	**C**	**12.00**
Carbon Dioxide	CO_2	44.00
" Disulphide	CS_2	76.14
" Tetrachloride	CCl_4	153.84
Carvone	$C_{10}H_{14}O$	150.11
Cephaeline	$C_{14}H_{19}O_2N$	233.16
Cerium	**Ce**	**140.25**
Cerium Oxalate (not U.S.P.)	$Ce_2(C_2O_4)_3+10H_2O$	724.66
" " Anhydrous	$Ce_2(C_2O_4)_3$	544.50
Chloral, Anhydrous	C_2HCl_3O	147.39
" Hydrated	$C_2HCl_3O+H_2O$	165.40
Chloralformamide	$C_3H_4Cl_3O_2N$	192.42
Chlorine	**Cl**	**35.46**
Chloroform	$CHCl_3$	119.39
Chromium	**Cr**	**52.0**
Chromium Oxide	Cr_2O_3	152.0
" Trioxide (Chromic Anhydride)	CrO_3	100.00
Cinchonidine	$C_{19}H_{22}ON_2$	294.20
" Salicylate	$C_{19}H_{22}ON_2C_7H_6O_3$	432.24
" Sulphate	$(C_{19}H_{22}ON_2)_2H_2SO_4+3H_2O$	740.53
" " Anhydrous	$(C_{19}H_{22}ON_2)_2H_2SO_4$	686.48
Cinchonine	$C_{19}H_{22}ON_2$	294.20
" Sulphate	$(C_{19}H_{22}ON_2)_2H_2SO_4+2H_2O$	722.51
" " Anhydrous	$(C_{19}H_{22}ON_2)_2H_2SO_4$	686.48
Cineol (Eucalyptol)	$C_{10}H_{18}O$	154.14
Cinnamic Aldehyde	C_9H_8O	132.06
Citral	$C_{10}H_{16}O$	152.13
Cobalt	**Co**	**58.97**
Cobaltous Chloride	$CoCl_2+6H_2O$	237.99
" " Anhydrous	$CoCl_2$	129.89

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Cobaltous Nitrate	$Co(NO_3)_2+6H_2O$	291.09
" " Anhydrous	$Co(NO_3)_2$	182.99
" Sulphate	$CoSO_4+7H_2O$	281.15
Cocaine	$C_{17}H_{21}O_4N$	303.18
" Hydrochloride	$C_{17}H_{21}O_4NHCl$	339.65
Codeine (Methyl Morphine)	$C_{18}H_{21}O_3N+H_2O$	317.19
" Anhydrous	$C_{18}H_{21}O_3N$	299.18
" Phosphate	$C_{18}H_{21}O_3NH_3PO_4+2H_2O$	433.27
" " Anhydrous	$C_{18}H_{21}O_3NH_3PO_4$	397.24
" Sulphate	$(C_{18}H_{21}O_3N)_2H_2SO_4+5H_2O$	786.52
" " Anhydrous	$(C_{18}H_{21}O_3N)_2H_2SO_4$	696.44
Colchicine	$C_{22}H_{25}O_6N$	399.21
Columbium	**Cb**	**93.5**
Coniine	$C_8H_{17}N$	127.15
Copper	**Cu**	**63.57**
Cotarnine	$C_{12}H_{15}O_4N$	237.13
" Hydrochloride	$C_{12}H_{14}O_3NCl$	255.58
" Phthalate	$(C_{12}H_{15}O_4N)_2C_6H_4C_2H_2O_4$	640.31
Cresol	$C_6H_4(CH_3)OH$	108.06
Cupric-ammonium Sulphate	$Cu(NH_3)_4SO_4+H_2O$	245.79
Cupric Acetate	$Cu(C_2H_3O_2)_2+H_2O$	199.63
" Sulphate	$CuSO_4+5H_2O$	249.72
" " Anhydrous	$CuSO_4$	159.64
" Sulphide	CuS	95.64
" Tartrate	$CuC_4H_4O_6+3H_2O$	265.65
" " Anhydrous	$CuC_4H_4O_6$	211.60
Diacetyl-morphine	$C_{21}H_{23}O_5N$	369.19
" " Hydrochloride	$C_{21}H_{23}O_5NHCl+H_2O$	423.68
" " " Anhydrous	$C_{21}H_{23}O_5NHCl$	405.66
Diethyl-barbituric Acid	$C_8H_{12}O_3N_2$	184.12
Diethylsulphone-dimethyl-methane	$C_7H_{16}O_4S_2$	228.27
Diethylsulphone-methyl-ethyl-methane	$C_8H_{18}O_4S_2$	242.28
Dipentene	$C_{10}H_{16}$	136.13
Diphenylamine	$(C_6H_5)_2NH$	169.10
Dithymol Diiodide (Thymol Iodide)	$(C_{10}H_{12}O)_2I_2$	550.03
Dysprosium	**Dy**	**162.5**
Emetine	$C_{15}H_{22}O_2N$	248.19
" Hydrochloride, Anhydrous	$C_{30}H_{44}O_4N_2.2HCl$	569.31
Epinephrine, Hydrated	$C_9H_{13}O_3N+\frac{1}{2}H_2O$	192.12
Erbium	**Er**	**167.7**
Erythrol Tetranitrate	$C_4H_6(NO_3)_4$	302.09
Ether (Ethyl Oxide)	$(C_2H_5)_2O$	74.08
Ethyl Acetate	$C_2H_5C_2H_3O_2$	88.06
" Carbamate	$CO(OC_2H_5)NH_2$	89.07
" Chloride	C_2H_5Cl	64.50
" Hydroxide (Ethyl Alcohol)	C_2H_5OH	46.05
Ethylmorphine Hydrochloride	$C_{19}H_{23}O_3NHCl+2H_2O$	385.69
" " Anhydrous	$C_{19}H_{23}O_3NHCl$	349.66
Ethyl Nitrite	$C_2H_5NO_2$	75.05
" Oxide (Ether)	$(C_2H_5)_2O$	74.08
Eucaine (Beta)	$C_{15}H_{21}O_2NHCl+H_2O$	301.66
Eucalyptol (Cineol)	$C_{10}H_{18}O$	154.14
Eugenol	$C_{10}H_{12}O_2$	164.10
Europium	**Eu**	**152.0**
Ferric Acetate	$Fe(C_2H_3O_2)_3$	232.91
" Ammonium Sulphate	$FeNH_4(SO_4)_2+12H_2O$	482.21
" " " Anhydrous	$FeNH_4(SO_4)_2$	266.02
" Chloride	$FeCl_3+6H_2O$	270.32
" " Anhydrous	$FeCl_3$	162.22
" Hydroxide	$Fe(OH)_3$	106.86
" Hypophosphite	$Fe(PH_2O_2)_3$	251.01
" Nitrate	$Fe(NO_3)_3$	241.87
" Oxide	Fe_2O_3	159.68
" Phosphate (normal, not U.S.P.)	$FePO_4$	150.88
" Pyrophosphate (normal, not U.S.P.)	$Fe_4(P_2O_7)_3$	745.60
" Subsulphate (variable)		
" Sulphate (Tersulphate)	$Fe_2(SO_4)_3$	399.89
Ferrous Bromide	$FeBr_2+6H_2O$	323.78
" " Anhydrous	$FeBr_2$	215.68
" Carbonate	$FeCO_3$	115.84
" Iodide	FeI_2	309.68
" Lactate	$Fe(C_3H_5O_3)_2+3H_2O$	287.97
" " Anhydrous	$Fe(C_3H_5O_3)_2$	233.92
" Oxide	FeO	71.84

		O=16
Ferrous Sulphate	$FeSO_4+7H_2O$	278.02
" " Anhydrous	$FeSO_4$	151.91
" " Exsiccated (approximately)	$2FeSO_4+3H_2O$	357.87
" Sulphide	FeS	87.91
Ferrum	**Fe**	**55.84**
Fluorescein (Resorcinolphthalein)	$C_{20}H_{12}O_5$	332.10
Fluorine	**F**	**19.0**
Formaldehyde	$HCHO$	30.02
Fuchsin	$C_{20}H_{19}N_3HCl$	337.74
Gadolinium	**Gd**	**157.3**
Gallium	**Ga**	**69.9**
Germanium	**Ge**	**72.5**
Glucinum	**Gl**	**9.1**
Glucose (Grape Sugar)	$C_6H_{12}O_6$	180.10
Glycerin (Glycerol)	$C_3H_5(OH)_3$	92.06
Glyceryl Trinitrate (Nitroglycerin)	$C_3H_5(NO_3)_3$	227.07
Gold	**Au**	**197.2**
Gold Chloride (Gold Trichloride)	$AuCl_3$	303.58
Guaiacol	$C_7H_8O_2$	124.06
" Carbonate	$(C_7H_7O)_2CO_3$	274.11
Helium	**He**	**3.99**
Hematein	$C_{16}H_{12}O_6$	300.10
Hematoxylin	$C_{16}H_{14}O_6+3H_2O$	356.16
Hexamethylenamine (Hexamethylene Tetramine)	$C_6H_{12}N_4$	140.14
Holmium	**Ho**	**163.5**
Holocaine	$C_{18}H_{22}O_2N_2$	298.20
" Hydrochloride	$C_{18}H_{22}O_2N_2HCl$	334.66
Homatropine	$C_{16}H_{21}O_3N$	275.18
" Hydrobromide	$C_{16}H_{21}O_3NHBr$	356.11
Hydrastine	$C_{21}H_{21}O_6N$	383.18
" Hydrochloride	$C_{21}H_{21}O_6NHCl$	419.65
Hydrastinine Hydrochloride	$C_{11}H_{11}O_2NHCl$	225.57
Hydrogen	**H**	**1.008**
Hydrogen Dioxide	H_2O_2	34.02
" Sulphide (Hydrosulphuric Acid)	H_2S	34.09
Hyoscine (see Scopolamine)		
Hyoscyamine	$C_{17}H_{23}O_3N$	289.19
" Hydrobromide	$C_{17}H_{23}O_3NHBr$	370.12
" Sulphate	$(C_{17}H_{23}O_3N)_2H_2SO_4$	676.47
Indigo Carmine (see Sodium indigotindisulphonate)		
Indium	**In**	**114.8**
Iodeosin (Tetraiodo-fluorescein)	$C_{20}H_8O_5I_4$	835.74
Iodine	**I**	**126.92**
Iodoform	CHI_3	393.77
Iodol (Tetraiodopyrrol)	C_4HNI_4	570.70
Iridium	**Ir**	**193.1**
Iron	**Fe**	**55.84**
Iron Salts (see under *Ferric* and *Ferrous*)		
Kaolin (Aluminum Silicate) (approximately)	$H_2Al_2(SiO_4)_2+H_2O$	258.83
Krypton	**Kr**	**82.92**
Lanthanum	**La**	**139.0**
Lead	**Pb**	**207.10**
Lead Acetate	$Pb(C_2H_3O_2)_2+3H_2O$	379.20
" " Anhydrous	$Pb(C_2H_3O_2)_2$	325.15
" " Basic (see Lead Subacetate)		
" Carbonate, Basic	$(PbCO_3)_2Pb(OH)_2$	775.32
" Chloride	$PbCl_2$	278.02
" Chromate	$PbCrO_4$	323.10
" Dioxide	PbO_2	239.10
" Iodide	PbI_2	460.94
" Nitrate	$Pb(NO_3)_2$	331.12
" Oxide	PbO	223.10
" Peroxide	PbO_2	239.10
" Subacetate (approximately)	$Pb_2O(C_2H_3O_2)_2$	548.25
" Sulphate	$PbSO_4$	303.17
" Sulphide	PbS	239.17
Lime (Calcium Oxide)	CaO	56.07
Limonene	$C_{10}H_{16}$	136.13
Linalyl Acetate	$C_{10}H_{17}C_2H_3O_2$	196.16
Lithium	**Li**	**6.94**
Lithium Benzoate	$LiC_7H_5O_2$	127.98
" Bromide	$LiBr$	86.86
" Carbonate	Li_2CO_3	73.88
" Citrate	$Li_3C_6H_5O_7+4H_2O$	281.92

		O=16
Lithium Phosphate, Anhydrous	Li_3PO_4	115.86
" Salicylate	$LiC_7H_5O_3$	143.98
" Sulphate, Anhydrous	Li_2SO_4	109.95
Lutecium	**Lu**	**174.0**
Magnesia (Magnesium Oxide)	MgO	40.32
Magnesium	**Mg**	**24.32**
Magnesium Carbonate, Basic (approximately)	$(MgCO_3)_4Mg(OH)_2+5H_2O$	485.70
" Chloride	$MgCl_2+6H_2O$	203.34
" " Anhydrous	$MgCl_2$	95.24
" Hydroxide	$Mg(OH)_2$	58.34
" Oxide (Magnesia)	MgO	40.32
" Pyroarsenate	$Mg_2As_2O_7$	310.56
" Pyrophosphate	$Mg_2P_2O_7$	222.72
" Sulphate	$MgSO_4+7H_2O$	246.50
" " Anhydrous	$MgSO_4$	120.39
Manganese	**Mn**	**54.93**
Manganese Dioxide	MnO_2	86.93
" Hypophosphite	$Mn(PH_2O_2)_2+H_2O$	203.06
" " Anhydrous	$Mn(PH_2O_2)_2$	185.04
Manganous Oxide	MnO	70.93
" Sulphate	$MnSO_4+4H_2O$	223.06
" " Anhydrous	$MnSO_4$	151.00
Mannitol Hexanitrate	$C_6H_8(NO_3)_6$	452.12
Menthol	$C_{10}H_{19}OH$	156.16
Menthyl Acetate	$C_{10}H_{19}C_2H_3O_2$	198.18
Mercurammonium Chloride	$HgNH_2Cl$	252.09
Mercuric Bromide	$HgBr_2$	360.44
" Chloride	$HgCl_2$	271.52
" Cyanide	$Hg(CN)_2$	252.62
" Iodide	HgI_2	454.44
" Nitrate	$Hg(NO_3)_2+4H_2O$	396.68
" " Anhydrous	$Hg(NO_3)_2$	324.62
" Oxide	HgO	216.60
" Potassium Iodide	HgI_2+2KI	786.48
" Subsalicylate (approximately)	$HgC_7H_4O_3$	336.63
" Subsulphate	$Hg(HgO)_2SO_4$	729.87
" Sulphate	$HgSO_4$	296.67
" Sulphide	HgS	232.67
Mercurous Chloride	HgCl	236.06
" Iodide	HgI	327.52
" Nitrate	$HgNO_3+H_2O$	280.63
" " Anhydrous	$HgNO_3$	262.61
" Sulphate	Hg_2SO_4	497.27
Mercury	**Hg**	**200.6**
Mercury, Ammoniated	$HgNH_2Cl$	252.09
Methylacetanilid	$C_6H_5N(CH_3)C_2H_3O$	149.10
Methylaurin (Rosolic Acid)	$C_{20}H_{16}O_3$	304.13
Methylene Blue (Methylthionine Chloride)	$C_{16}H_{18}N_3ClS+3H_2O$	373.75
Methyl Orange (Sodium dimethylaminoazo-benzene-sulphonate)	$NaC_{14}H_{14}N_3SO_3$	327.21
Methyl Red	$C_{14}H_{14}N_3CO_2H$	269.15
" Salicylate	$CH_3C_7H_5O_3$	152.06
Methylthionine Chloride (Methylene Blue)	$C_{16}H_{18}N_3ClS+3H_2O$	373.75
Molybdenum	**Mo**	**96.0**
Morphine	$C_{17}H_{19}O_3N+H_2O$	303.18
" Anhydrous	$C_{17}H_{19}O_3N$	285.16
" Acetate (variable)	$C_{17}H_{19}O_3NC_2H_4O_2+3H_2O$	399.24
" Hydrochloride	$C_{17}H_{19}O_3NHCl+3H_2O$	375.68
" " Anhydrous	$C_{17}H_{19}O_3NHCl$	321.63
" Sulphate	$(C_{17}H_{19}O_3N)_2H_2SO_4+5H_2O$	758.49
" " Anhydrous	$(C_{17}H_{19}O_3N)_2H_2SO_4$	668.41
Naphthalene	$C_{10}H_8$	128.06
Naphthol (Betanaphthol)	$C_{10}H_8O$	144.06
Naphthylamine Acetate	$C_{10}H_7NH_2HC_2H_3O_2$	203.11
" Hydrochloride	$C_{10}H_7NH_2HCl$	179.55
Neodymium	**Nd**	**144.3**
Neon	**Ne**	**20.2**
Nickel	**Ni**	**58.68**
Nickelous	NiO	74.68
" Sulphate	$NiSO_4+7H_2O$	280.86
" " Anhydrous	$NiSO_4$	154.75
Niton (radium emanation)	**Nt**	**222.4**
Nitrogen	**N**	**14.01**
Nitric Oxide	NO	30.01

		O=16
Nitrogen Monoxide	N_2O	44.02
Nitrous Oxide (Nitrogen Monoxide)	N_2O	44.02
Nitroglycerin (Glyceryl Trinitrate)	$C_3H_5(NO_3)_3$	227.07
Novocaine	$C_{13}H_{20}O_2N_2HCl$	272.65
Orthoform	$C_8H_9O_3N$	167.08
Osmium	**Os**	**190.9**
Ouabain	$C_{30}H_{46}O_{12}$	760.51
Oxygen	**O**	**16.00**
Palladium	**Pd**	**106.7**
Palladous Chloride	$PdCl_2$	177.62
Paraformaldehyde (Trioxymethylene)	$(CH_2O)_3$	90.05
Paraldehyde	$C_6H_{12}O_3$	132.10
Phenol (Carbolic Acid)	C_6H_5OH	94.05
Phenolphthalein	$C_{20}H_{14}O_4$	318.11
Phenylacetamide (Acetanilid)	C_8H_9ON	135.08
Phenylhydrazine	$C_6H_5NHNH_2$	108.08
" Hydrochloride	$C_6H_5NHNH_2HCl$	144.55
Phenyl Salicylate (Salol)	$C_6H_5C_7H_5O_3$	214.08
Phloroglucinol	$C_6H_3(OH)_3$	126.05
Phosphorus	**P**	**31.04**
Physostigmine	$C_{15}H_{21}O_2N_3$	275.20
" Salicylate	$C_{15}H_{21}O_2N_3C_7H_6O_3$	413.25
" Sulphate	$(C_{15}H_{21}O_2N_3)_2H_2SO_4$	648.49
Picrotoxin	$C_{30}H_{34}O_{13}$	602.27
Pilocarpine	$C_{11}H_{16}O_2N_2$	208.15
" Hydrochloride	$C_{11}H_{16}O_2N_2HCl$	244.62
" Nitrate	$C_{11}H_{16}O_2N_2HNO_3$	271.17
Piperine	$C_{17}H_{19}O_3N$	285.16
Platinic Chloride (in solution)	$PtCl_4$	337.04
" " (Chloroplatinic Acid)	$H_2PtCl_6+6H_2O$	518.07
Platinum	**Pt**	**195.2**
Potassa (Potassium Hydroxide)	KOH	56.11
Potassium	**K**	**39.10**
Potassium Acetate	$KC_2H_3O_2$	98.12
" Arsenite (Metarsenite)	$KAsO_2$	146.06
" Benzoate	$KC_7H_5O_2+3H_2O$	214.19
" " Anhydrous	$KC_7H_5O_2$	160.14
" Bicarbonate	$KHCO_3$	100.11
" Bichromate (Dichromate)	$K_2Cr_2O_7$	294.20
" Bisulphate	$KHSO_4$	136.18
" Bitartrate	$KHC_4H_4O_6$	188.14
" Bromate	$KBrO_3$	167.02
" Bromide	KBr	119.02
" Carbonate	K_2CO_3	138.20
" Chlorate	$KClO_3$	122.56
" Chloride	KCl	74.56
" Chloroplatinate	K_2PtCl_6	486.16
" Chromate	K_2CrO_4	194.20
" Citrate	$K_3C_6H_5O_7+H_2O$	324.36
" " Anhydrous	$K_3C_6H_5O_7$	306.34
" Cyanide	KCN	65.11
" Dichromate (Bichromate)	$K_2Cr_2O_7$	294.20
" Ferricyanide	$K_3Fe(CN)_6$	329.20
" Ferrocyanide	$K_4Fe(CN)_6+3H_2O$	422.35
" " Anhydrous	$K_4Fe(CN)_6$	368.30
" Hydroxide (Potassa)	KOH	56.11
" Hypophosphite	KPH_2O_2	104.16
" Iodide	KI	166.02
" Lactate	$KC_3H_5O_3$	128.14
" Nitrate	KNO_3	101.11
" Permanganate	$KMnO_4$	158.03
" Phosphate, Dibasic	K_2HPO_4	174.25
" Salicylate	$KC_7H_5O_3$	176.14
" and Sodium Tartrate	$KNaC_4H_4O_6+4H_2O$	282.20
" " " Anhydrous	$KNaC_4H_4O_6$	210.13
" Sulphate	K_2SO_4	174.27
" Sulphite	$K_2SO_3+2H_2O$	194.30
" " Anhydrous	K_2SO_3	158.27
" Sulphocyanate (Sulphocyanide)	$KCNS$	97.18
" Tartrate	$K_2C_4H_4O_6+\frac{1}{2}H_2O$	235.24
" " Anhydrous	$K_2C_4H_4O_6$	226.23
Praseodymium	**Pr**	**140.6**
Pyrogallol (Pyrogallic Acid)	$C_6H_3(OH)_3$	126.05
Quinidine	$C_{20}H_{24}O_2N_2$	324.21

		O=16
Quinidine Sulphate	$(C_{20}H_{24}O_2N_2)_2H_2SO_4+2H_2O$	782.54
" " Anhydrous	$(C_{20}H_{24}O_2N_2)_2H_2SO_4$	746.51
Quinine	$C_{20}H_{24}O_2N_2+3H_2O$	378.26
" Anhydrous	$C_{20}H_{24}O_2N_2$	324.21
" Bisulphate	$C_{20}H_{24}O_2N_2H_2SO_4+7H_2O$	548.41
" " Anhydrous	$C_{20}H_{24}O_2N_2H_2SO_4$	422.30
" Dihydrochloride	$C_{20}H_{24}O_2N_2.2HCl$	397.15
" Hydrobromide	$C_{20}H_{24}O_2N_2HBr+H_2O$	423.16
" " Anhydrous	$C_{20}H_{24}O_2N_2HBr$	405.14
" Hydrochloride	$C_{20}H_{24}O_2N_2HCl+2H_2O$	396.71
" " Anhydrous	$C_{20}H_{24}O_2N_2HCl$	360.68
" Salicylate	$C_{20}H_{24}O_2N_2HC_7H_5O_3+H_2O$	480.28
" " Anhydrous	$C_{20}H_{24}O_2N_2HC_7H_5O_3$	462.26
" Sulphate	$(C_{20}H_{24}O_2N_2)_2H_2SO_4+7H_2O$	872.62
" " Anhydrous	$(C_{20}H_{24}O_2N_2)_2H_2SO_4$	746.51
" and Urea Hydrochloride	$C_{20}H_{24}O_2N_2HCl.CO(NH_2)_2HCl+5H_2O$	547.28
" Valerate (Valerianate) (variable)	$C_{20}H_{24}O_2N_2HC_5H_9O_2+H_2O$	444.31
Radium	Ra	**226.4**
Resorcinol (Resorcin)	$C_6H_4(OH)_2$	110.05
Resorcinolphthalein (Fluorescein)	$C_{20}H_{12}O_5$	332.10
Rhodium	Rh	**102.9**
Rosaniline Acetate	$C_{19}H_{18}N_3C_2H_4O_2$	348.21
Rubidium	Rb	**85.45**
Ruthenium	Ru	**101.7**
Saccharin (Benzosulphinide)	$C_7H_5O_3NS$	183.12
Safrol	$C_{10}H_{10}O_2$	162.08
Salicin	$C_{13}H_{18}O_7$	286.14
Salol (Phenyl Salicylate)	$C_6H_5C_7H_5O_3$	214.08
Samarium	Sa	**150.4**
Santalol	$C_{15}H_{26}O$	222.21
Santonin	$C_{15}H_{18}O_3$	246.14
Scandium	Sc	**44.1**
Scopolamine (Hyoscine)	$C_{17}H_{21}O_4N$	303.18
" Hydrobromide	$C_{17}H_{21}O_4NHBr+3H_2O$	438.15
" " Anhydrous	$C_{17}H_{21}O_4NHBr$	384.11
Selenium	Se	**79.2**
Silicon	Si	**28.3**
Silicon Oxide (Silica)	SiO_2	60.30
Silver	Ag	**107.88**
Silver Chloride	AgCl	143.34
" Cyanide	AgCN	133.89
" Iodide	AgI	234.80
" Nitrate	$AgNO_3$	169.89
" Nitrite	$AgNO_2$	153.89
" Oxide	Ag_2O	231.76
" Sulphate	Ag_2SO_4	311.83
" Sulphide	Ag_2S	247.83
Soda (Sodium Hydroxide)	NaOH	40.01
Sodium	Na	**23.00**
Sodium Acetate	$NaC_2H_3O_2+3H_2O$	136.07
" " Anhydrous	$NaC_2H_3O_2$	82.02
" Arsenate	$Na_2HAsO_4+7H_2O$	312.08
" " Anhydrous	Na_2HAsO_4	185.97
" Arsenite (Metarsenite)	$NaAsO_2$	129.96
" Benzoate	$NaC_7H_5O_2$	144.04
" Benzosulphinide (Soluble Saccharin)	$NaC_7H_4SNO_3+2H_2O$	241.14
" Bicarbonate	$NaHCO_3$	84.01
" Bisulphite	$NaHSO_3$	104.08
" Bitartrate	$NaHC_4H_4O_6+H_2O$	190.06
" Borate (Tetraborate)	$Na_2B_4O_7+10H_2O$	382.16
" " Anhydrous	$Na_2B_4O_7$	202.00
" Bromate	$NaBrO_3$	150.92
" Bromide	NaBr	102.92
" Cacodylate	$Na(CH_3)_2AsO_2+3H_2O$	214.06
" " Anhydrous	$Na(CH_3)_2AsO_2$	160.01
" Carbonate	$Na_2CO_3+10H_2O$	286.16
" " Anhydrous	Na_2CO_3	106.00
" " Monohydrated	$Na_2CO_3+H_2O$	124.02
" Chlorate	$NaClO_3$	106.46
" Chloride	NaCl	58.46
" Citrate	$Na_3C_6H_5O_7+2H_2O$	294.07
" " Anhydrous	$Na_3C_6H_5O_7$	258.04
" Cobaltic Nitrite	$Co_2(NO_2)_6 6NaNO_2+H_2O$	826.08
" Cyanide	NaCN	49.01

		O=16
Sodium Dimethylaminoazo-benzene-sulphonate (Methyl Orange)	$NaC_{14}H_{14}N_3SO_3$	327.21
" Glycerophosphate, Anhydrous	$Na_2C_3H_7PO_6$	216.10
" Hydroxide (Soda)	$NaOH$	40.01
" Hypophosphite	$NaPH_2O_2+H_2O$	106.07
" " Anhydrous	$NaPH_2O_2$	88.06
" Hyposulphite (Thiosulphate)	$Na_2S_2O_3+5H_2O$	248.22
" " Anhydrous	$Na_2S_2O_3$	158.14
" Indigotindisulphonate	$Na_2C_{16}H_8O_2N_2(SO_3)_2$	466.22
" Iodide	NaI	149.92
" Lactate	$NaC_3H_5O_3$	112.04
" Monosulphide	Na_2S+9H_2O	240.21
" " Anhydrous	Na_2S	78.07
" Nitrate	$NaNO_3$	85.01
" Nitrite	$NaNO_2$	69.01
" Nitroprusside	$Na_2Fe(NO)(CN)_5+2H_2O$	297.93
" Oxalate	$Na_2C_2O_4$	134.00
" Perborate	$NaBO_3+4H_2O$	154.06
" " Anhydrous	$NaBO_3$	82.00
" Phenolsulphonate (Sulphocarbolate)	$NaC_6H_5SO_4+2H_2O$	232.14
" " Anhydrous	$NaC_6H_5SO_4$	196.11
" Phosphate, Anhydrous	Na_2HPO_4	142.05
" " Dibasic	$Na_2HPO_4+12H_2O$	358.24
" Pyrophosphate	$Na_4P_2O_7+10H_2O$	446.24
" " Anhydrous	$Na_4P_2O_7$	266.08
" Salicylate	$NaC_7H_5O_3$	160.04
" Sulphate	$Na_2SO_4+10H_2O$	322.23
" " Anhydrous	Na_2SO_4	142.07
" Sulphide	Na_2S+9H_2O	240.21
" Sulphite	$Na_2SO_3+7H_2O$	252.18
" " Anhydrous	Na_2SO_3	126.07
" Sulphocarbolate (Phenolsulphonate)	$NaC_6H_5SO_4+2H_2O$	232.14
" Tartrate	$Na_2C_4H_4O_6+2H_2O$	230.06
" " Anhydrous	$Na_2C_4H_4O_6$	194.03
" Theobromine	$NaC_7H_7O_2N_4$	202.10
" Thiosulphate (Hyposulphite)	$Na_2S_2O_3+5H_2O$	248.22
" " Anhydrous	$Na_2S_2O_3$	158.14
" Tungstate	$Na_2WO_4+2H_2O$	330.03
Sparteine	$C_{15}H_{26}N_2$	234.23
" Sulphate	$C_{15}H_{26}N_2H_2SO_4+5H_2O$	422.39
" " Anhydrous	$C_{15}H_{26}N_2H_2SO_4$	332.31
Stannic Chloride	$SnCl_4$	260.84
Stannous Chloride	$SnCl_2+2H_2O$	225.95
" " Anhydrous	$SnCl_2$	189.92
Strontium	Sr	**87.63**
Strontium Bromide	$SrBr_2+6H_2O$	355.57
" " Anhydrous	$SrBr_2$	247.47
" Carbonate	$SrCO_3$	147.63
" Iodide	SrI_2+6H_2O	449.57
" " Anhydrous	SrI_2	341.74
" Lactate	$Sr(C_3H_5O_3)_2+3H_2O$	319.76
" " Anhydrous	$Sr(C_3H_5O_3)_2$	265.71
" Salicylate	$Sr(C_7H_5O_3)_2+2H_2O$	397.74
" " Anhydrous	$Sr(C_7H_5O_3)_2$	361.71
" Sulphate	$SrSO_4$	183.70
Strychnine	$C_{21}H_{22}O_2N_2$	334.20
" Nitrate	$C_{21}H_{22}O_2N_2HNO_3$	397.21
" Sulphate	$(C_{21}H_{22}O_2N_2)_2H_2SO_4+5H_2O$	856.56
" " Anhydrous	$(C_{21}H_{22}O_2N_2)_2H_2SO_4$	766.48
Sugar, Cane (Sucrose)	$C_{12}H_{22}O_{11}$	342.18
" Grape (Glucose)	$C_6H_{12}O_6$	180.10
" Milk (Lactose)	$C_{12}H_{22}O_{11}+H_2O$	360.19
Sulphonethylmethane (Diethylsulphonemethyl-ethyl-methane)	$C_8H_{18}O_4S_2$	242.28
Sulphonmethane (Diethylsulphone-dimethylmethane)	$C_7H_{16}O_4S_2$	228.27
Sulphur	S	**32.07**
Sulphur Dioxide	SO_2	64.07
Tantalum	Ta	**181.5**
Tellurium	Te	**127.5**
Terbium	Tb	**159.2**
Terebene	$C_{10}H_{16}$	136.13
Terpin Hydrate	$C_{10}H_{16}(OH)_2+H_2O$	190.18
Tetraiodo-fluorescein (Iodeosin)	$C_{20}H_8O_5I_4$	835.74
Tetraiodopyrrol (Iodol)	C_4HNI_4	570.70

		O=16
Tetramethylthionine Chloride (Methylthionine Chloride, Methylene Blue)	$C_{16}H_{18}N_3ClS+3H_2O$	373.75
Thallium	**Tl**	**204.0**
Theobromine	$C_7H_8O_2N_4$	108.10
Theophylline	$C_7H_8O_2N_4+H_2O$	198.12
Thiosinamine (Allyl-sulphocarbamide)	$(C_3H_5)SCN_2H_3$	116.15
Thorium	**Th**	**232.4**
Thulium	**Tm**	**168.5**
Thymol	$C_{10}H_{14}O$	150.11
" Iodide (Dithymol-diiodide)	$(C_{10}H_{12}O)_2I_2$	550.03
Tin	**Sn**	**119.0**
Tin Salts (See under Stannic and Stannous)		
Titanium	**Ti**	**48.1**
Toluene (Methyl Benzene, Toluol)	$C_6H_5CH_3$	92.06
Trinitrophenol (Picric Acid)	$C_6H_3O_7N_3$	229.05
Trioxymethylene (Paraform)	$(CH_2O)_3$	90.05
Tungsten	**W**	**184.0**
Uranium	**U**	**238.5**
Uranium Nitrate (Uranyl Nitrate)	$UO_2(NO_3)_2+6H_2O$	502.62
" " Anhydrous	$UO_2(NO_3)_2$	394.52
Vanadium	**V**	**51.0**
Vanillin	$C_8H_8O_3$	152.06
Water	H_2O	18.016
Xenon	**Xe**	**130.2**
Xylene (Xylol, Dimethyl-benzene)	$C_6H_4(CH_3)_2$	106.08
Ytterbium (Neoytterbium)	**Yb**	**172.0**
Yttrium	**Yt**	**89.0**
Zinc	**Zn**	**65.37**
Zinc Acetate	$Zn(C_2H_3O_2)_2+2H_2O$	219.45
" " Anhydrous	$Zn(C_2H_3O_2)_2$	183.42
" Bromide	$ZnBr_2$	225.21
" Carbonate (Normal, not U.S.P.)	$ZnCO_3$	125.37
" Chloride	$ZnCl_2$	136.29
" Iodide	ZnI_2	319.21
" Oxide	ZnO	81.37
" Perborate, Anhydrous	$(ZnBO_3)_2$	183.37
" Phenolsulphonate (Sulphocarbolate)	$Zn(C_6H_5SO_4)_2+8H_2O$	555.72
" " Anhydrous	$Zn(C_6H_5SO_4)_2$	411.59
" Phosphide	Zn_3P_2	258.19
" Sulphate	$ZnSO_4+7H_2O$	287.55
" " Anhydrous	$ZnSO_4$	161.44
" Sulphide	ZnS	97.44
" Sulphocarbolate (Phenolsulphonate)	$Zn(C_6H_5SO_4)_2+8H_2O$	555.72
" Valerate (Valerianate)	$Zn(C_5H_9O_2)_2+2H_2O$	303.55
Zirconium	**Zr**	**90.6**

Atomic Weights

(U. S. P. IX)

Adopted by the International Committee on Atomic Weights (1915)

Oxygen = 16

Name.	Symbol.	Atomic Weight.	Name.	Symbol.	Atomic Weight.
Aluminum	Al	27.1	Neodymium	Nd	144.3
Antimony	Sb	120.2	Neon	Ne	20.2
Argon	A	39.88	Nickel	Ni	58.68
Arsenic	As	74.96	Niton (radium emanation)	Nt	222.4
Barium	Ba	137.37	Nitrogen	N	14.01
Bismuth	Bi	208.0	Osmium	Os	190.9
Boron	B	11.0	Oxygen	O	16.00
Bromine	Br	79.92	Palladium	Pd	106.7
Cadmium	Cd	112.40	Phosphorus	P	31.04
Cæsium	Cs	132.81	Platinum	Pt	195.2
Calcium	Ca	40.07	Potassium	K	39.10
Carbon	C	12.00	Praseodymium	Pr	140.6
Cerium	Ce	140.25	Radium	Ra	226.4
Chlorine	Cl	35.46	Rhodium	Rh	102.9
Chromium	Cr	52.0	Rubidium	Rb	85.45
Cobalt	Co	58.97	Ruthenium	Ru	101.7
Columbium	Cb	93.5	Samarium	Sa	150.4
Copper	Cu	63.57	Scandium	Sc	44.1
Dysprosium	Dy	162.5	Selenium	Se	79.2
Erbium	Er	167.7	Silicon	Si	28.3
Europium	Eu	152.0	Silver	Ag	107.88
Fluorine	F	19.0	Sodium	Na	23.00
Gadolinium	Gd	157.3	Strontium	Sr	87.63
Gallium	Ga	69.9	Sulphur	S	32.07
Germanium	Ge	72.5	Tantalum	Ta	181.5
Glucinum	Gl	9.1	Tellurium	Te	127.5
Gold	Au	197.2	Terbium	Tb	159.2
Helium	He	3.99	Thallium	Tl	204.0
Holmium	Ho	163.5	Thorium	Th	232.4
Hydrogen	H	1.008	Thulium	Tm	168.5
Indium	In	114.8	Tin	Sn	119.0
Iodine	I	126.92	Titanium	Ti	48.1
Iridium	Ir	193.1	Tungsten	W	184.0
Iron	Fe	55.84	Uranium	U	238.5
Krypton	Kr	82.92	Vanadium	V	51.0
Lanthanum	La	139.0	Xenon	Xe	130.2
Lead	Pb	207.10	Ytterbium (Neoytterbium)	Yb	172.0
Lithium	Li	6.94	Yttrium	Yt	89.0
Lutecium	Lu	174.0	Zinc	Zn	65.37
Magnesium	Mg	24.32	Zirconium	Zr	90.6
Manganese	Mn	54.93			
Mercury	Hg	200.6			
Molybdenum	Mo	96.0			

Multiples of Some Atomic and Molecular Weights
Oxygen = 16

	1	2	3	4	5	6	7	8	9	
H	1.01	2.02	3.02	4.03	5.04	6.05	7.06	8.06	9.07	H
O	16.00	32.00	48.00	64.00	80.00	96.00	112.00	128.00	144.00	O
OH	17.01	34.02	51.02	68.03	85.04	102.05	119.06	136.06	153.07	OH
H_2O	18.02	36.03	54.05	72.06	90.08	108.10	126.11	144.13	162.14	H_2O
N	14.01	28.02	42.03	56.04	70.05	84.06	98.07	112.08	126.09	N
NH_2	16.03	32.05	48.08	64.10	80.13	96.16	112.18	128.21	144.23	NH_2
NH_3	17.03	34.07	51.10	68.14	85.17	102.20	119.24	136.27	153.31	NH_3
NH_4	18.04	36.08	54.13	72.17	90.21	108.25	126.29	144.34	162.38	NH_4
NO	30.01	60.02	90.03	120.04	150.05	180.06	210.07	240.08	270.09	NO
NO_2	46.01	92.02	138.03	184.04	230.05	276.06	322.07	368.08	414.09	NO_2
NO_3	62.01	124.02	186.03	248.04	310.05	372.06	434.07	496.08	558.09	NO_3
C	12.00	24.00	36.00	48.00	60.00	72.00	84.00	96.00	108.00	C
CH_3	15.02	30.05	45.07	60.10	75.12	90.14	105.17	120.19	135.22	CH_3
CO	28.00	56.00	84.00	112.00	140.00	168.00	196.00	224.00	252.00	CO
CO_3	60.00	120.00	180.00	240.00	300.00	360.00	420.00	480.00	540.00	CO_3
CN	26.01	52.02	78.03	104.04	130.05	156.06	182.07	208.08	234.09	CN
Cl	35.46	70.92	106.38	141.84	177.30	212.76	248.22	283.68	319.14	Cl
Br	79.92	159.84	239.76	319.68	399.60	479.52	559.44	639.36	719.28	Br
I	126.92	253.84	380.76	507.68	634.60	761.52	888.44	1015.36	1142.28	I
S	32.07	64.14	96.21	128.28	160.35	192.42	224.49	256.56	288.63	S
SO_3	80.07	160.14	240.21	320.28	400.35	480.42	560.49	640.56	720.63	SO_3
SO_4	96.07	192.14	288.21	384.28	480.35	576.42	672.49	768.56	864.63	SO_4
PO_4	95.04	190.08	285.12	380.16	475.20	570.24	665.28	760.32	855.36	PO_4
PH_2O_2	65.06	130.11	195.17	260.22	325.28	390.34	455.39	520.45	585.50	PH_2O_2
Na	23.00	46.00	69.00	92.00	115.00	138.00	161.00	184.00	207.00	Na
K	39.10	78.20	117.30	156.40	195.50	234.60	273.70	312.80	351.90	K
	1	2	3	4	5	6	7	8	9	

RELATIONS BETWEEN THERMOMETERS.

In *Fahrenheit's* thermometer, the freezing point of water is placed at 32°, and the boiling point at 212°, and the number of intervening degrees is 180.

The *Centigrade* or *Celsius's* thermometer, which is now recognized in the U. S. Pharmacopœia and has been adopted generally by scientists, marks the freezing point *zero*, and the boiling point 100°.

In *Réaumur's* thermometer the freezing point is at *zero*, and the boiling point at 80°.

In *De Lisle's* thermometer, used in Russia, the graduation begins at the boiling point, which is marked *zero*, while the freezing point is placed at 150°.

From the above statement, it is evident that 180 degrees of Fahrenheit are equal to 100° of the Centigrade, 80° of Réaumur, and 150° of De Lisle; or 1 degree of the first is equal to $\frac{5}{9}$ of a degree of the second, $\frac{4}{9}$ of a degree of the third, and $\frac{5}{6}$ of a degree of the last. It is easy, therefore, to convert the degrees of one into the equivalent number of degrees of the other; but in ascertaining the corresponding points upon the different scales, it is necessary to take into consideration their different modes of graduation. Thus, as the zero Fahrenheit is 32° below the point at which that of the Centigrade and of Réaumur is placed, this number must be taken into account in the calculation.

1. If any degree on the *Centigrade* scale, either above or below zero, be multiplied by 1.8 the result will, in either case, be the number of degrees above or below 32°, or the freezing point of *Fahrenheit*.

2. The number of degrees between any point of *Fahrenheit's* scale and 32°, if divided by 1.8, will give the corresponding point on the *Centigrade*.

Thermometric Equivalents

(U. S. P. IX)

Centigrade and Fahrenheit Scales

Given Centigrade:	Sought Fahrenheit:	Given Fahrenheit:	Sought Centigrade:
$n°\ \text{C.} = \frac{9n°}{5} + 32$		$n°\ \text{F.} = \frac{5(n° - 32)}{9}$	

C.°	F.°	C.°	F.°	C.°	F.°	C.°	F.°
—40	—40						
—39.4444	—39	—24.4444	—12	—9.4444	15	0.5556	33
—39	—38.2	—24	—11.2	—9	15.8	1	33.8
—38.8889	—38	—23.8889	—11	—8.8889	16	1.1111	34
—38.3333	—37	—23.3333	—10	—8.3333	17	1.6667	35
—38	—36.4	—23	—9.4	—8	17.6	2	35.6
—37.7778	—36	—22.7778	—9	—7.7778	18	2.2222	36
—37.2222	—35	—22.2222	—8	—7.2222	19	2.7778	37
—37	—34.6	—22	—7.6	—7	19.4	3	37.4
—36.6667	—34	—21.6667	—7	—6.6667	20	3.3333	38
—36.1111	—33	—21.1111	—6	—6.1111	21	3.8889	39
—36	—32.8	—21	—5.8	—6	21.2	4	39.2
—35.5556	—32	—20.5556	—5	—5.5556	22	4.4444	40
—35	—31	—20	—4	—5	23	5	41
—34.4444	—30	—19.4444	—3	—4.4444	24	5.5556	42
—34	—29.2	—19	—2.2	—4	24.8	6	42.8
—33.8889	—29	—18.8889	—2	—3.8889	25	6.1111	43
—33.3333	—28	—18.3333	—1	—3.3333	26	6.6667	44
—33	—27.4	—18	—0.4	—3	26.6	7	44.6
—32.7778	—27	—17.7778	0	—2.7778	27	7.2222	45
—32.2222	—26	—17.2222	1	—2.2222	28	7.7778	46
—32	—25.6	—17	1.4	—2	28.4	8	46.4
—31.6667	—25	—16.6667	2	—1.6667	29	8.3333	47
—31.1111	—24	—16.1111	3	—1.1111	30	8.8889	48
—31	—23.8	—16	3.2	—1	30.2	9	48.2
—30.5556	—23	—15.5556	4	—0.5556	31	9.4444	49
—30	—22	—15	5	0	32	10	50
—29.4444	—21	—14.4444	6			10.5556	51
—29	—20.2	—14	6.8			11	51.8
—28.8889	—20	—13.8889	7			11.1111	52
—28.3333	—19	—13.3333	8			11.6667	53
—28	—18.4	—13	8.6			12	53.6
—27.7778	—18	—12.7778	9			12.2222	54
—27.2222	—17	—12.2222	10			12.7778	55
—27	—16.6	—12	10.4			13	55.4
—26.6667	—16	—11.6667	11			13.3333	56
—26.1111	—15	—11.1111	12			13.8889	57
—26	—14.8	—11	12.2			14	57.2
—25.5556	—14	—10.5556	13			14.4444	58
—25	—13	—10	14			15	59

Thermometric Equivalents—*Continued.*

C.°	F.°	C.°	F.°	C.°	F.°	C.°	F.°
15.5556	60	40.5556	105	65.5556	150	90.5556	195
16	60.8	41	105.8	66	150.8	91	195.8
16.1111	61	41.1111	106	66.1111	150	91.1111	196
16.6667	62	41.6667	107	66.6667	152	91.6667	197
17	62.6	42	107.6	67	152.6	92	197.6
17.2222	63	42.2222	108	67.2222	153	92.2222	198
17.7778	64	42.7778	109	67.7778	154	92.7778	199
18	64.4	43	109.4	68	154.4	93	199.4
18.3333	65	43.3333	110	68.3333	155	93.3333	200
18.8889	66	43.8889	111	68.8889	156	93.8889	201
19	66.2	44	111.2	69	156.2	94	201.2
19.4444	67	44.4444	112	69.4444	157	94.4444	202
20	68	45	113	70	158	95	203
20.5556	69	45.5556	114	70.5556	159	95.5556	204
21	69.8	46	114.8	71	159.8	96	204.8
21.1111	70	46.1111	115	71.1111	160	96.1111	205
21.6667	71	46.6667	116	71.6667	161	96.6667	206
22	71.6	47	116.6	72	161.6	97	206.6
22.2222	72	47.2222	117	72.2222	162	97.2222	207
22.7778	73	47.7778	118	72.7778	163	97.7778	208
23	73.4	48	118.4	73	163.4	98	208.4
23.3333	74	48.3333	119	73.3333	164	98.3333	209
23.8889	75	48.8889	120	73.8889	165	98.8889	210
24	75.2	49	120.2	74	165.2	99	210.2
24.4444	76	49.4444	121	74.4444	166	99.4444	211
25	77	50	122	75	167	100	212
25.5556	78	50.5556	123	75.5556	168	100.5556	213
26	78.8	51	123.8	76	168.8	101	213.8
26.1111	79	51.1111	124	76.1111	169	101.1111	214
26.6667	80	51.6667	125	76.6667	170	101.6667	215
27	80.6	52	125.6	77	170.6	102	215.6
27.2222	81	52.2222	126	77.2222	171	102.2222	216
27.7778	82	52.7778	127	77.7778	172	102.7778	217
28	82.4	53	127.4	78	172.4	103	217.4
28.3333	83	53.3333	128	78.3333	173	103.3333	218
28.8889	84	53.8889	129	78.8889	174	103.8889	219
29	84.2	54	129.2	79	174.2	104	219.2
29.4444	85	54.4444	130	79.4444	175	104.4444	220
30	86	55	131	80	176	105	221
30.5556	87	55.5556	132	80.5556	177	105.5556	222
31	87.8	56	132.8	81	177.8	106	222.8
31.1111	88	56.1111	133	81.1111	178	106.1111	223
31.6667	89	56.6667	134	81.6667	179	106.6667	224
32	89.6	57	134.6	82	179.6	107	224.6
32.2222	90	57.2222	135	82.2222	180	107.2222	225
32.7778	91	57.7778	136	82.7778	181	107.7778	226
33	91.4	58	136.4	83	181.4	108	226.4
33.3333	92	58.3333	137	83.3333	182	108.3333	227
33.8889	93	58.8889	138	83.8889	183	108.8889	228
34	93.2	59	138.2	84	183.2	109	228.2
34.4444	94	59.4444	139	84.4444	184	109.4444	229
35	95	60	140	85	185	110	230
35.5556	96	60.5556	141	85.5556	186	110.5556	231
36	96.8	61	141.8	86	186.8	111	231.8
36.1111	97	61.1111	142	86.1111	187	111.1111	232
36.6667	98	61.6667	143	86.6667	188	111.6667	233
37	98.6	62	143.6	87	188.6	112	233.6
37.2222	99	62.2222	144	87.2222	189	112.2222	234
37.7778	100	62.7778	145	87.7778	190	112.7778	235
38	100.4	63	145.4	88	190.4	113	235.4
38.3333	101	63.3333	146	88.3333	191	113.3333	236
38.8889	102	63.8889	147	88.8889	192	113.8889	237
39	102.2	64	147.2	89	192.2	114	237.2
39.4444	103	64.4444	148	89.4444	193	114.4444	238
40	104	65	149	90	194	115	239

Thermometric Equivalents—*Continued.*

C.°	F.°	C.°	F.°	C.°	F.°	C.°	F.°
115.5556	240	140.5556	285	165.5556	330	190.5556	375
116	240.8	141	285.8	166	330.8	191	375.8
116.1111	241	141.1111	286	166.1111	331	191.1111	376
116.6667	242	141.6667	287	166.6667	332	191.6667	377
117	242.6	142	287.6	167	332.6	192	377.6
117.2222	243	142.2222	288	167.2222	333	192.2222	378
117.7778	244	142.7778	289	167.7778	334	192.7778	379
118	244.4	143	289.4	168	334.4	193	379.4
118.3333	245	143.3333	290	168.3333	335	193.3333	380
118.8889	246	143.8889	291	168.8889	336	193.8889	381
119	246.2	144	291.2	169	336.2	194	381.2
119.4444	247	144.4444	292	169.4444	337	194.4444	382
120	248	145	293	170	338	195	383
120.5556	249	145.5556	294	170.5556	339	195.5556	384
121	249.8	146	294.8	171	339.8	196	384.8
121.1111	250	146.1111	295	171.1111	340	196.1111	385
121.6667	251	146.6667	296	171.6667	341	196.6667	386
122	251.6	147	296.6	172	341.6	197	386.6
122.2222	252	147.2222	297	172.2222	342	197.2222	387
122.7778	253	147.7778	298	172.7778	343	197.7778	388
123	253.4	148	298.4	173	343.4	198	388.4
123.3333	254	148.3333	299	173.3333	344	198.3333	389
123.8889	255	148.8889	300	173.8889	345	198.8889	390
124	255.2	149	300.2	174	345.2	199	390.2
124.4444	256	149.4444	301	174.4444	346	199.4444	391
125	257	150	302	175	347	200	392
125.5556	258	150.5556	303	175.5556	348	200.5556	393
126	258.8	151	303.8	176	348.8	201	393.8
126.1111	259	151.1111	304	176.1111	349	201.1111	394
126.6667	260	151.6667	305	176.6667	350	201.6667	395
127	260.6	152	305.6	177	350.6	202	395.6
127.2222	261	152.2222	306	177.2222	351	202.2222	396
127.777	262	152.7778	307	177.7778	352	202.7778	397
128	262.4	153	307.4	178	352.4	203	397.4
128.3333	263	153.3333	308	178.3333	353	203.3333	398
128.8889	264	153.8889	309	178.8889	354	203.8889	399
129	264.2	154	309.2	179	354.2	204	399.2
129.4444	265	154.4444	310	179.4444	355	204.4444	400
130	266	155	311	180	356	205	401
130.5556	267	155.5556	312	180.5556	357	205.5556	402
131	267.8	156	312.8	181	357.8	206	402.8
131.1111	268	156.1111	313	181.1111	358	206.1111	403
131.6667	269	156.6667	314	181.6667	359	206.6667	404
132	269.6	157	314.6	182	359.6	207	404.6
132.2222	270	157.2222	315	182.2222	360	207.2222	405
132.7778	271	157.7778	316	182.7778	361	207.7778	406
133	271.4	158	316.4	183	361.4	208	306.4
133.3333	272	158.3333	317	183.3333	362	208.3333	407
133.8889	273	158.8889	318	183.8889	363	208.8889	408
134	273.2	159	318.2	184	363.2	209	408.2
134.4444	274	159.4444	319	184.4444	364	209.4444	409
135	275	160	320	185	365	210	410
135.5556	276	160.5556	321	185.5556	366	210.5556	411
136	276.8	161	321.8	186	366.8	211	411.8
136.1111	277	161.1111	322	186.1111	367	211.1111	412
136.6667	278	161.6667	323	186.6667	368	211.6667	413
137	278.6	162	323.6	187	368.6	212	413.6
137.2222	279	162.2222	324	187.2222	369	212.2222	414
137.7778	280	162.7778	325	187.7778	370	212.7778	415
138	280.4	163	325.4	188	370.4	213	415.4
138.3333	281	163.3333	326	188.3333	371	213.3333	416
138.8889	282	163.8889	327	188.8889	372	213.8889	417
139	282.2	164	327.2	189	372.2	214	417.2
139.4444	283	164.4444	328	189.4444	373	214.4444	418
140	284	165	329	190	374	215	419

Thermometric Equivalents—*Continued.*

C.°	F.°	C.°	F.°	C.°	F.°	C.°	F.°
215.5556	420	240.5556	465	265.5556	510	290.5556	555
216	420.8	241	465.8	266	510.8	291	555.8
216.1111	421	241.1111	466	266.1111	511	291.1111	556
216.6667	422	241.6667	467	266.6667	512	291.6667	557
217	422.6	242	467.6	267	512.6	292	557.6
217.2222	423	242.2222	468	267.2222	513	292.2222	558
217.7778	424	242.7778	469	267.7778	514	292.7778	559
218	424.4	243	469.4	268	514.4	293	559.4
218.3333	425	243.3333	470	268.3333	515	293.3333	560
218.8889	426	243.8889	471	268.8889	516	293.8889	561
219	426.2	244	471.2	269	516.2	294	561.2
219.4444	427	244.4444	472	269.4444	517	294.4444	562
220	428	245	473	270	518	295	563
220.5556	429	245.5556	474	270.5556	519	295.5556	564
221	429.8	246	474.8	271	519.8	296	564.8
221.1111	430	246.1111	475	271.1111	520	296.1111	565
221.6667	431	246.6667	476	271.6667	521	296.6667	566
222	431.6	247	476.6	272	521.6	297	566.6
222.2222	432	247.2222	477	272.2222	522	297.2222	567
222.7778	433	247.7778	478	272.7778	523	297.7778	568
223	433.4	248	478.4	273	523.4	298	568.4
223.3333	434	248.3333	479	273.3333	524	298.3333	569
223.8889	435	248.8889	480	273.8889	525	298.8889	570
224	435.2	249	480.2	274	525.2	299	570.2
224.4444	436	249.4444	481	274.4444	526	299.4444	571
225	437	250	482	275	527	300	572
225.5556	438	250.5556	483	275.5556	528	300.5556	573
226	438.8	251	483.8	276	528.8	301	573.8
226.1111	439	251.1111	484	276.1111	529	301.1111	574
226.6667	440	251.6667	485	276.6667	530	301.6667	575
227	440.6	252	485.6	277	530.6	302	575.6
227.2222	441	252.2222	486	277.2222	531	302.2222	576
227.7778	442	252.7778	487	277.7778	532	302.7778	577
228	442.4	253	487.4	278	532.4	303	577.4
228.3333	443	253.3333	488	278.3333	533	303.3333	578
228.8889	444	253.8889	489	278.8889	534	303.8889	579
229	444.2	254	489.2	279	534.2	304	579.2
229.4444	445	254.4444	490	279.4444	535	304.4444	580
230	446	255	491	280	536	305	581
230.5556	447	255.5556	492	280.5556	537	305.5556	582
231	447.8	256	492.8	281	537.8	306	582.8
231.1111	448	256.1111	493	281.1111	538	306.1111	583
231.6667	449	256.6667	494	281.6667	539	306.6667	584
232	449.6	257	494.6	282	539.6	307	584.6
232.2222	450	257.2222	495	282.2222	540	307.2222	585
232.7778	451	257.7778	496	282.7778	541	307.7778	586
233	451.4	258	496.4	283	541.4	308	586.4
233.3333	452	258.3333	497	283.3333	542	308.3333	587
233.8889	453	258.8889	498	283.8889	543	308.8889	588
234	453.2	259	498.2	284	543.2	309	588.2
234.4444	454	259.4444	499	284.4444	544	309.4444	589
235	455	260	500	285	545	310	590
235.5556	456	260.5556	501	285.5556	546	310.5556	591
236	456.8	261	501.8	286	546.8	311	591.8
236.1111	457	261.1111	502	286.1111	547	311.1111	592
236.6667	458	261.6667	503	286.6667	548	311.6667	593
237	458.6	262	503.6	287	548.6	312	593.6
237.2222	459	262.2222	504	287.2222	549	312.2222	594
237.7778	460	262.7778	505	287.7778	550	312.7778	595
238	460.4	263	505.4	288	550.4	313	595.4
238.3333	461	263.3333	506	288.3333	551	313.3333	596
238.8889	462	263.8889	507	288.8889	552	313.8889	597
239	462.2	264	507.2	289	552.2	314	597.2
239.4444	463	264.4444	508	289.4444	553	314.4444	598
240	464	265	509	290	554	315	599

Thermometric Equivalents—*Continued.*

C.°	F.°	C.°	F.°	C.°	F.°	C.°	F.°
315.5556	600	320.5556	609	325.5556	618	330.5556	627
316	600.8	321	609.8	326	618.8	331	627.8
316.1111	601	321.1111	610	326.1111	619	331.1111	628
316.6667	602	321.6667	611	326.6667	620	331.6667	629
317	602.6	322	611.6	327	620.6	332	629.6
317.2222	603	322.2222	612	327.2222	621	332.2222	630
317.7778	604	322.7778	613	327.7778	622	332.7778	631
318	604.4	323	613.4	328	622.4	333	631.4
318.3333	605	323.3333	614	328.3333	623	333.3333	632
318.8889	606	323.8889	615	328.8889	624	333.8889	633
319	606.2	324	615.2	329	624.2	334	633.2
319.4444	607	324.4444	616	329.4444	625	334.4444	634
320	608	325	617	330	626	335	635

TABLES OF WEIGHTS AND MEASURES.

METRIC SYSTEM

The Metric System of Weights and Measures, which is the only one recognized by either the United States or British Pharmacopœias in their formulæ, is based on the idea of a correlation between the units of length, capacity and weight, and multiples and subdivisions of these units according to the decimal system. The unit of length is the *meter*. The cube of the tenth part of a meter is taken as the unit of capacity and is called a *liter*. The weight of one-thousandth part of a liter of distilled water at its maximum density is the unit of mass, and is denominated a *gramme*. The multiples of these measures, proceeding in the decimal progression, are distinguished by employing the prefixes *deca*,[1] *hecto*, *kilo*, and *myria*, taken from the Greek numerals, and the subdivisions, following the same order, by *deci*, *centi*, *milli*, from the Latin numerals. Since the introduction of this system it has been adopted by the principal nations of Europe, excepting Great Britain, and in many of these its use is compulsory. It is in general use in France, Germany, Austria-Hungary, Italy, Spain, Norway, Sweden, Netherlands, Switzerland, Greece, British India, and South America. It was legalized in Great Britain in 1864, and in the United States by an act of Congress in 1866.

The *meter*, or unit of length,	=	39.3700 inches.	
The *liter*, or unit of capacity,	=	33.813819776 fluidounces.	*U. S.*
The *gramme*, or unit of weight,	=	15.43235639 Troy grains.	

Upon this basis the following tables have been constructed:

Measures of Length.

		English Inches.		Miles.	Rods.	Yards.	Feet.	Inches.
Millimeter (mm.)	=	.03937						
Centimeter (cm.)	=	.39370						
Decimeter (dm.)	=	3.93700						
Meter (M.)	=	39.37000	=	0	0	1	0	3.370
Decameter (Dm.)	=	393.70000	=	0	0	10	2	9.700
Hectometer (Hm.)	=	3937.00000	=	0	0	109	1	1.000
Kilometer (Km.)	=	39370.00000	=	0	198	4	1	10.000
Myriameter (Mm.)	=	393700.00000	=	6	56	2	0	4.000

Measures of Capacity.

		English Cubic Inches.		Apothecaries' Measure.
Milliliter (mil)[2]	=	.0610233778	=	16.2306 minims.
Centiliter (cl.)	=	.6102337780	=	2.7051 fluidrachms.
Deciliter (dl.)	=	6.1023377800	=	3.3816 fluidounces.
Liter (L.)	=	61.0233778000	=	2.1133 pints.
Decaliter (Dl.)	=	610.2337780000	=	2.6417 gallons.
Hectoliter (Hl.)	=	6102.3377800000		
Kiloliter (Kl.)	=	61023.3778000000		
Myrialiter (Ml.)	=	610233.7780000000		

[1] Deca and hecto are sometimes written deka and hekto.

[2] Both the U. S. and British Pharmacopœias have adopted the more accurate and euphonious "mil" instead of the former "c.c.", as the word for the thousandth part of a liter.

Measures of Weight.

		Troy Grains.		℔ (Troy).	ʒ	ʔ	Gr.
Milligramme (mg.)	=	.0154					
Centigramme (cg.)	=	.1543					
Decigramme (dg.)	=	1.5432					
Gramme (Gm.)	=	15.4323		℔ (Troy).	ʒ	ʔ	Gr.
Decagramme (Dg.)	=	154.3235	=	0	0	2	34.3
Hectogramme (Hg.)	=	1543.2356	=	0	3	1	43.2
Kilogramme (Kg.)	=	15432.3563	=	2	8	1	12.3
Myriagramme (Mg.)	=	154323.5639	=	26	9	4	3.5

APOTHECARIES WEIGHTS.

In the United States the majority of physicians use in their prescriptions the so-called Apothecaries Weights, which are based on the old English Troy weights. It is to be noted that these weights, which are used in filling prescriptions, differ materially from the Avoirdupois weights, which are used in this work in the alternative formulæ for compounding the official preparations. In Great Britain the Avoirdupois system is used for prescribing, although physicians frequently insert, for convenience sake (there being no weight between the grain and the ounce), the Troy drachm of 60 grains.

The Apothecaries measure, as employed in the United States, differs from the Imperial measure used in Great Britain, in that the pint contains 16 fluidounces instead of 20; the British gallon being also correspondingly larger than the American.

APOTHECARIES WEIGHT.

Pound.		Troyounces.		Drachms.		Scruples.		Troy Grains
℔ 1	=	12	=	96	=	288	=	5760
		℥ 1	=	8	=	24	=	480
				ʒ 1	=	3	=	60
						℈ 1	=	gr. 20

The Imperial Standard Troy weight, at present recognized by the British laws, corresponds with the Apothecaries' weight in pounds, ounces, and grains; but differs from it in the division of the ounce, which, according to the former scale, contains twenty pennyweights, each weighing twenty-four grains.

AVOIRDUPOIS WEIGHT.

Pound.		Ounces.		Drachms.		Troy Grains.
℔ 1	=	16	=	256	=	7000
		oz. 1	=	16	=	437.5
				dr. 1		gr. 27.34375

Relative Value of Troy and Avoirdupois Weights.

Pound.		Pounds.	Pound.	Ounces.	Grains.
1 Troy	=	0.822857 Avoirdupois =	0	13	72.5
1 Avoirdupois	=	1.215277 Troy =	1	2	280

APOTHECARIES OR WINE MEASURE.

Gallon.		Pints.		Fluidounces.		Fluidrachms.		Minims.		Cubic Inches.
Cong. 1	=	8	=	128	=	1024	=	61440	=	231
	=	O 1	=	16	=	128	=	7680	=	28.875
				f℥ 1	=	8	=	480	=	1.8047
						f℥ 1	=	♏ 60	=	.2256

IMPERIAL MEASURE.

Adopted by the British Pharmacopœia.

Gallon.		Pints.		Fluidounces.		Fluidrachms.		Minims.
1	=	8	=	160	=	1280	=	76800
		1	=	20	=	160	=	9600
				1	=	8	=	480
						1	=	60

Relative Value of Apothecaries' and Imperial Measure.

Apothecaries' Measure.		Imperial Measure.			
		Pints.	Fluidounces.	Fluidrachms.	Minims.
1 gallon	=	6	13	2	23
1 pint	=		16	5	18
1 fluidounce	=		1	0	20
1 fluidrachm	=			1	2.5
1 minim	=				1.04

Imperial Measure.		Apothecaries' Measure.			
		Gallon.	Pints.	Fluidounces.	Fluidrachms.	Minims.
1 gallon	=	1	1	9	5	8
1 pint	=		1	3	1	38
1 fluidounce	=				7	41
1 fluidrachm	=					58
1 minim	=					0.96

Relative Value of Weights and Measures in Distilled Water at 25° C. (77° F.).

1. Value of Apothecaries' Weight in Apothecaries' Measure.

				Pints.	Fluidounces.	Fluidrachms.	Minims.
1 pound	=	0.79188319 pint	=	0	12	5	21.6629
1 ounce	=	1.0558489 fluidounces	=	0	1	0	26.8975
1 drachm	=	1.0558489 fluidrachms	=	0	0	1	3.3509
1 scruple	=			0	0	0	21.1170
1 grain	=			0	0	0	1.0558

2. Value of Apothecaries' Measure in Apothecaries' Weight.

				lb	℥	ʒ	℈	Gr.		Grains.
1 gallon	=	10.1025000 pounds	=	10	1	1	2	10.4	=	58190.400
1 pint	=	1.2628125 pounds	=	1	3	1	0	13.80	=	7273.8000
1 fluidounce	=	0.94710937 ounce	=	0	0	7	1	14.61	=	454.6125[1]
1 fluidrachm	=	0.94710937 drachm	=	0	0	0	2	16.83	=	56.8266
1 minim	=	0.94710937 grain	=							.9471

3. Value of Avoirdupois Weight in Apothecaries' Measure.

				Pints.	Fluidounces.	Fluidrachms.	Minims.
1 pound	=	0.96235805 pint	=	0	15	3	10.9098
1 ounce	=	0.96235805 fluidounce	=	0	0	7	41.9319

4. Value of Apothecaries' Measure in Avoirdupois Weight.

1 gallon	=	8.312914285 pounds.
1 pint	=	1.039114285 pounds.
1 fluidounce	=	1.039114285 ounces.

5. Value of Imperial Measure in Apothecaries' and Avoirdupois Weights.

Imperial Measure.		Apothecaries' Weight.						Avoirdupois Weight.			Grains.		Cubic Inches.
1 gallon	=	12 lb	1 ʒ	6 ʒ	2 ℈	0 gr.	=	10 lb	0 oz.	=	70,000	=	277.27384
1 pint	=	1	6	1	2	10	=	1	4	=	8,750	=	34.65923
1 fluidounce	=			7	0	17.5	=		1	=	437.5	=	1.73296
1 fluidrachm	=				2	14.69	=				54.69	=	0.21662
1 minim	=										.91	=	0.00361

In converting the weights of liquids heavier or lighter than water into measures, or conversely, a correction must be made for specific gravity. In converting weights into measures, the calculator may proceed as if the liquid were water, and the obtained measure will be to the true measure *inversely* as the specific gravity. In the converse operation, of turning measures into weights, the same assumption may be made, and the obtained weight will be to the true weight *directly* as the specific gravity.

[1] The weight of a fluidounce of water at 25° C. (77° F.) according to the Table of Weight and Volume Relations in the U. S. Pharmacopœia IX is 454.6 grains.

RELATIVE VALUE OF WEIGHTS AND MEASURES.

Metric Equivalents (U. S. P. IX)

(Weights)

Kilogrammes.	Avoirdupois pounds.	Avoirdupois ounces.	Apothecaries ounces.	Equivalent avoirdupois. lbs.	oz.	grs.	Grammes.	Grains.
1	2.20462	35.274	32.151	2	3	119.9	1	15.4324
2	4.40924	70.548	64.301	4	6	239.7	2	30.8647
3	6.61387	105.822	96.452	6	9	359.6	3	46.2971
4	8.81849	141.096	128.603	8	13	41.9	4	61.7294
5	11.02311	176.370	160.754	11	0	161.8	5	77.1618
6	13.22773	211.644	192.904	13	3	281.6	6	92.5941
7	15.43236	246.918	225.055	15	6	401.5	7	108.0265
8	17.63698	282.192	257.206	17	10	83.9	8	123.4589
9	19.84160	317.466	289.357	19	13	203.7	9	138.8912
10	22.04622	352.740	321.507	22	0	323.6	10	154.3236

Avoirdupois pounds.	Kilogrammes.	Avoirdupois ounces.	Grammes.	Apothecaries ounces.	Grammes.	Grains.	Grammes.
1	0.453592	1	28.3495	1	31.1035	1	0.06480
2	0.907185	2	56.6991	2	62.2070	2	0.12960
3	1.360777	3	85.0486	3	93.3104	3	0.19440
4	1.814370	4	113.3981	4	124.4139	4	0.25920
5	2.267962	5	141.7476	5	155.5174	5	0.32399
6	2.721555	6	170.0972	6	186.6209	6	0.38879
7	3.175147	7	198.4467	7	217.7244	7	0.45359
8	3.628739	8	226.7962	8	248.8278	8	0.51839
9	4.082332	9	255.1458	9	279.9313	9	0.58319
10	4.535924	10	283.4953	10	311.0348	10	0.64799

Grammes.	Equivalent avoirdupois. oz.	grains.	Equivalent Apothecaries oz.	grains.	Grammes.	Equivalent avoirdupois. lbs.	oz.	grs.	Equivalent Apothecaries oz.	grains.
10	0	154.3	0	154.3	100	0	3	230.7	3	103.2
20	0	308.6	0	308.6	200	0	7	24.0	6	206.5
30	1	25.5	0	463.0	300	0	10	254.7	9	309.7
40	1	179.8	1	137.3	400	0	14	48.0	12	413.0
50	1	334.1	1	291.6	500	1	1	278.7	16	36.2
60	2	50.9	1	445.9	600	1	5	71.9	19	139.4
70	2	205.3	2	120.3	700	1	8	302.6	22	242.6
80	2	359.6	2	274.6	800	1	12	95.9	25	345.9
90	3	76.4	2	428.9	900	1	15	326.6	28	449.1
100	3	230.7	3	103.2	1000	2	3	119.9	32	72.4

Milligrammes.	Grains.	Approx.	Milligrammes.	Grains.	Approx.	Milligrammes.	Grains.	Approx.
0.1	0.00154	$\frac{1}{650}$	1	0.01543	$\frac{1}{65}$	10	0.15432	$\frac{2}{13}$
0.2	0.00309	$\frac{1}{324}$	2	0.03086	$\frac{1}{32}$	20	0.30865	$\frac{1}{3}\frac{9}{2}$
0.3	0.00463	$\frac{1}{216}$	3	0.04630	$\frac{1}{21}$	30	0.46297	$\frac{5}{11}$
0.4	0.00617	$\frac{1}{162}$	4	0.06173	$\frac{1}{16}$	40	0.61729	$\frac{5}{8}$
0.5	0.00772	$\frac{1}{130}$	5	0.07716	$\frac{1}{13}$	50	0.77162	$\frac{2}{3}\frac{3}{0}$
0.6	0.00926	$\frac{1}{108}$	6	0.09259	$\frac{1}{11}$	60	0.92594	$\frac{1}{1}\frac{2}{3}$
0.7	0.01080	$\frac{1}{93}$	7	0.10803	$\frac{1}{9}$	70	1.08026	$1\frac{1}{12}$
0.8	0.01235	$\frac{1}{81}$	8	0.12346	$\frac{1}{8}$	80	1.23459	$1\frac{1}{4}$
0.9	0.01389	$\frac{1}{72}$	9	0.13889	$\frac{1}{7}$	90	1.38891	$1\frac{3}{7}$
1.0	0.01543	$\frac{1}{65}$	10	0.15432	$\frac{2}{13}$	100	1.54324	$1\frac{1}{2}$

Metric Equivalents—*Continued.*

(Weights)

Grains.	Milligrammes.	Grains.	Milligrammes.	Grains.	Milligrammes.
1	64.8	$\frac{1}{12}$	5.40	$\frac{1}{70}$	0.93
$\frac{3}{4}$	48.6	$\frac{1}{16}$	4.05	$\frac{1}{80}$	0.81
$\frac{2}{3}$	43.2	$\frac{1}{20}$	3.24	$\frac{1}{90}$	0.72
$\frac{1}{2}$	32.4	$\frac{1}{25}$	2.70	$\frac{1}{100}$	0.65
$\frac{1}{3}$	21.6	$\frac{1}{25}$	2.59	$\frac{1}{150}$	0.43
$\frac{1}{4}$	16.2	$\frac{1}{30}$	2.16	$\frac{1}{200}$	0.32
$\frac{1}{5}$	13.0	$\frac{1}{35}$	1.86	$\frac{1}{250}$	0.26
$\frac{1}{6}$	10.8	$\frac{1}{40}$	1.62	$\frac{1}{300}$	0.22
$\frac{1}{8}$	8.1	$\frac{1}{50}$	1.30	$\frac{1}{400}$	0.16
$\frac{1}{10}$	6.5	$\frac{1}{60}$	1.08	$\frac{1}{500}$	0.13

(Volumes)

Liters.	Gallons.	Pints.	Fluidounces.	Minims.	Equivalent gal.	pt.	fl. os.	minims.
1	0.26418	2.11342	33.8148	16231.1	0	2	1	391.1
2	0.52836	4.22685	67.6296	32462.2	0	4	3	302.2
3	0.79253	6.34027	101.4444	48693.3	0	6	5	213.3
4	1.05671	8.45370	135.2591	64924.4	1	0	7	124.4
5	1.32089	10.56712	169.0739	81155.5	1	2	9	35.5
6	1.58507	12.68054	202.8870	97386.6	1	4	10	426.6
7	1.84924	14.79397	236.7035	113617.7	1	6	12	337.7
8	2.11342	16.90739	270.5183	129848.8	2	0	14	248.8
9	2.37760	19.02082	304.3306	146079.9	2	3	0	159.9
10	2.64178	21.13424	338.1478	162311.0	2	5	2	71.0

Mils.	Equivalent minims.	Mils.	Equivalent fl. os.	minims.	Minims.	Equivalent pint.	fl. os.	minims
1	16.231	10	0	162.3	100	0	3	183.1
2	32.462	20	0	324.6	200	0	6	366.2
3	48.693	30	1	6.9	300	0	10	69.3
4	64.924	40	1	169.2	400	0	13	252.4
5	81.156	50	1	331.6	500	1	0	435.6
6	97.387	60	2	13.9	600	1	4	138.7
7	113.618	70	2	176.2	700	1	7	321.8
8	129.849	80	2	338.5	800	1	11	24.9
9	146.080	90	3	20.8	900	1	14	208.0
10	162.311	100	3	183.1	1000	2	1	391.1

Gallons.	Mils.	Pints.	Mils.	Fluid-ounces.	Mils.	Minims.	Mils.
1	3785.33	1	473.17	1	29.573	1	0.061610
2	7570.66	2	946.33	2	59.146	2	0.123220
3	11356.00	3	1419.50	3	88.719	3	0.184831
4	15141.33	4	1892.67	4	118.292	4	0.246441
5	18926.66	5	2365.83	5	147.865	5	0.308051
6	22711.99	6	2839.00	6	177.437	6	0.369661
7	26497.33	7	2312.17	7	207.010	7	0.431271
8	30282.66	8	3785.33	8	236.583	8	0.492882
9	34067.99	9	4258.50	9	266.156	9	0.554492
10	37853.32	10	4731.67	10	295.729	10	0.616102

Metric Equivalents—*Continued.*

(Lengths)

Meters.	Yards.	Feet.	Inches.	Equivalent yds.	Equivalent feet.	Equivalent inches.	Kilometers.	Miles.
1	1.09361	3.28083	39.37	1	0	3.37	1	0.62137
2	2.18722	6.56167	78.74	2	0	6.74	2	1.24274
3	3.28083	9.84250	118.11	3	0	10.11	3	1.86411
4	4.37444	13.12333	157.48	4	1	1.48	4	2.48548
5	5.46806	16.40417	196.85	5	1	4.85	5	3.10685
6	6.56167	19.68500	236.22	6	1	8.22	6	3.72822
7	7.65528	22.96583	275.59	7	1	11.59	7	4.34959
8	8.74889	26.24667	314.96	8	2	2.96	8	4.97096
9	9.84250	29.52750	354.33	9	2	6.33	9	5.59233
10	10.93611	32.80833	393.70	10	2	9.70	10	6.21370

Yards.	Meters.	Feet.	Meters.	Inches.	Centimeters.	Miles.	Kilometers.
1	0.91440	1	0.304801	1	2.5400	1	1.60935
2	1.82880	2	0.609601	2	5.0800	2	3.21869
3	2.74321	3	0.914402	3	7.6200	3	4.82804
4	3.65761	4	1.219202	4	10.1600	4	6.43739
5	4.57201	5	1.524003	5	12.7000	5	8.04674
6	5.48641	6	1.828804	6	15.2400	6	9.65608
7	6.40081	7	2.133604	7	17.7800	7	11.26543
8	7.31521	8	2.438405	8	20.3200	8	12.87478
9	8.22962	9	2.743205	9	22.8600	9	14.48413
10	9.14402	10	3.048006	10	25.4001	10	16.09347

APPROXIMATE MEASUREMENT.

For the sake of convenience, in the absence of proper instruments, we often make use of means of measurement which, though not precise nor uniform, afford results sufficiently accurate for ordinary purposes. Of this kind are certain household implements, of a capacity approaching to uniformity, and corresponding to a certain extent with the regular standard measures. Custom has attached a fixed value to these implements, with which it is proper that the practitioner should be familiar, although their capacity, as they are now made, with the exception of the wineglass, generally somewhat exceeds that at which they were originally and still continue to be estimated. According to the U. S. P. IX:

A *tea-cup* is estimated to contain about four fluidounces, or 120 mils
A *wineglass* . . . . . two fluidounces, or 60 mils
A *tablespoon* (cochlear magnum) . . . half a fluidounce, or 15 mils
A *dessertspoon* (cochlear medium) . . two fluidrachms, or 8 mils
A *teaspoon* (cochlear parvum) . . . . a fluidrachm, or 4 mils

Small quantities of liquid medicines are often administered by *drops*, each of which is usually considered equivalent to a minim, or the sixtieth part of a fluidrachm. The drop of water and of aqueous fluids is, sometimes, about that size; but the same is by no means the case with all medicinal liquids, and the drop even of the same liquid varies much in bulk, according to the circumstances under which it is formed. This is, therefore, an uncertain mode of estimating the quantity of liquids, and should be superseded where minim measures can be had. Certain rules, however, influence the formation of drops, which will enable us to form some notion of their probable relative number, in the same amount of liquid when possessed of the requisite data. Thus, the heavier the liquid, the smaller, other things being equal, is the size of the drops, and the greater their number in a given measure. The drop of chloroform, for example, which is a very heavy liquid, is very small, much smaller than that of alcohol or ether. The greater or less viscidity and greater or less mobility of the liquid have much influence, the former in increasing, the latter in diminishing the size of the drops. The adhesiveness of liquids, which opposes their disposition to leave the surface from which they fall, requires a greater mass to overcome it, and consequently augments the size of the drop. The rapidity of the movement acts in a contrary direction, and the drop from a full bottle should be less than from one more or less emptied. The broader the surface from which they fall, the greater is their size. The drops from a thick-lipped bottle are larger than from one with thin lips.

The results stated in the table on page 1773 were obtained by Stephen L. Talbot. They may be relied on as accurate, and in most cases correspond with the results obtained by Durand and Procter (see *A. J. P.*, i, 169; 1865, p. 389; 1880, p. 337), but should be considered as indicating only the relative number of drops afforded by the several liquids mentioned under the specific conditions of the experiment; for, under other circumstances than those of Talbot's experiments, entirely different results might be obtained as relates to each liquid.

FRENCH MEASURES.

In reading French medical works, if unacquainted with their customary expressions of measure, we are often left in great uncertainty as to the precise quantity indicated by the names. The following table, translated from the French Codex, will obviate this difficulty. (See Metric Table, page 1745.)

	Grammes.
A coffeespoon (*cuillerée à café*, Fr., *teaspoon*) (Fr. Cod. 1908)	5
A dessertspoon (*cuillerée à dessert*, Fr., *dessertspoon*), 2 coffeespoons, or	10
A common spoon (*cuillerée*, Fr., *tablespoon*), 4 coffeespoons, or	15
A glass (*verre*, Fr.), 10 common spoons	150
A handful (*poignée*, Fr.) of barleyseed (Fr. Cod. 1866)	80
" " " flaxseed	50
" " " flaxseed-meal	150
" " " dried mallow leaves	40
" " " " chicory "	30
A pinch (*pincée*, Fr.) of chamomile flowers	2
" " " arnica "	1
" " " marshmallow "	2
" " " mallows "	1
" " " linden "	2
" " " fruits of anise	2
" " " " fennel	2
A hen's egg, newly laid, has the mean weight of	64
" the white alone	40
" the yellow alone	20
Blanched almonds have the mean weight, each, of	1

TABLE EXHIBITING THE NUMBER OF DROPS IN A FLUIDRACHM OF DIFFERENT LIQUIDS, WITH THE WEIGHT IN GRAINS AND GRAMMES.

Name.	Drops in f℥i (60 m.)	Weight of f℥i	
		in gr.	in Gm.
Acetum Opii	90	61	3.95
Sanguinariæ	78	55½	3.59
Scillæ	68	57	3.69
Acidum Aceticum	108	58	3.75
Aceticum Dilutum	68	55	3.56
Carbolicum	111	59	3.82
Hydrochloricum	70	65	4.21
Hydrochlor. Dilutum	60	56	3.62
Hydrocyanicum Dilutum	60	54	3.49
Lacticum	111	66	4.27
Nitricum	102	77	4.98
Nitricum Dilutum	60	58	3.62
Nitrohydrochloricum	76	66	4.27
Phosphoricum Dilutum	59	57	3.69
Sulphuricum	128	101	6.54
Sulphuricum Aromaticum	146	53	3.43
Sulphuricum Dilutum	60	58½	3.79
Sulphurosum	59	55	3.56
Æther	176	39	2.52
Alcohol	146	44	2.85
Dilutum	137	49	3.17
Aqua	60	55	3.56
Ammoniæ Fortior	66	50	3.24
Destillata	60	53½	3.46
Balsamum Peruvianum	101	60	3.88
Bromum	250	165	10.69
Chloroformum	250	80	5.18
Copaiba	110	51	3.30
Creosotum	122	56½	3.66
Fluidextractum Belladonnæ	156	57	3.69
Buchu	150	47½	3.07
Cimicifugæ	147	48	3.11
Cinchonæ	138	58	3.75
Colchici Radicis	160	57	3.69
Colchici Seminis	158	55	3.56
Conii	137	61	3.95
Digitalis	134	62	4.01
Ergotæ	133	60	3.88
Gelsemii	149	49	3.14
Glycyrrhizæ	133	61	3.95
Hyoscyami	160	59	3.82
Ipecacuanhæ	120	60	3.88
Pareiræ	140	57	3.72
Rhei	158	61	3.95
Sarsaparillæ Compositum	134	60	3.88
Senegæ	137	62	4.01
Serpentariæ	148	47	3.07
Uvæ Ursi	137	60	3.88
Valerianæ	150	49	3.17
Veratri Viridis	150	50	3.24
Zingiberis	142	48	3.11
Glycerinum	67	68	4.40
Hydrargyrum	150	760	49.24
Liquor Acidi Arsenosi	75	56	3.62
Ammonii Acetatis	57	55	3.56
Arseni et Hydrargyri Iodidi	58	55	3.56
Ferri Chloridi	71	72	4.66
Ferri Citratis	71	72	4.66
Ferri Nitratis	59	59	3.82
Ferri Subsulphatis	73	83	5.37
Ferri Tersulphatis	83	72	4.66
Liquor Hydrarg. Nitratis	131	123	7.97
Iodi Compositus	63	59	3.82
Plumbi Subacetatis	74	70	4.53
Potassii Hydroxidi	62	58	3.75
Potassii Arsenitis	57	55	3.56
Sodæ Chlorinatæ	63	62	4.01
Zinci Chloridi	89	88	5.70
Oleoresina Aspidii	130	52	3.36
Capsici	120	51	3.30
Cubebæ	123	52	3.36
Oleum Æthereum	125	50	3.24
Amygdalæ Amaræ	115	55	3.56
Amygdalæ Expres	108	48½	3.14
Anisi	119	54	3.49
Bergamottæ	130	46	2.98
Cari	132	50	3.24
Caryophylli	130	57	3.69
Cinnamomi	126	53½	3.46
Copaibæ	123	49½	3.20
Cubebæ	125	51	3.30
Fœniculi	125	53	3.43
Gaultheriæ	125	62	4.01
Juniperi	148	49	3.17
Lavandulæ	138	52	3.36
Limonis	129	47	3.04
Menthæ Piperitæ	129	50	3.24
Ricini	77	51½	3.33
Rosæ	132	47	3.04
Rosmarini	143	50	3.24
Sassafras	133	58	3.75
Terebinthinæ	136	45½	2.94
Tiglii	104	50	3.24
Spiritus Ætheris Compositus	148	45	2.91
Ætheris Nitrosi	146	47	3.04
Ammoniæ Aromaticus	142	48	3.11
Camphoræ	143	47	3.04
Chloroformi	150	48	3.11
Menthæ Piperitæ	142	47	3.04
Syrupus	65	72	4.66
Acaciæ	44	73	4.73
Ferri Iodidi	65	77	4.98
Scillæ	75	74	4.79
Scillæ Compositus	102	70	4.53
Senegæ	106	70	4.53
Tinctura Aconiti	146	46	2.98
Belladonnæ	137	53	3.43
Benzoini Composita	148	48	3.11
Cantharidis	131	51	3.33
Cinchonæ Composita	140	49	3.17
Digitalis	128	53	3.43
Ferri Chloridi	150	53	3.43
Iodi	148	47	3.04
Nucis Vomicæ	140	44	2.85
Opii	130	53	3.43
Opii Camphorata	130	52	3.36
Opii Deodorati	110	54	3.49
Valerianæ	130	52	3.36
Veratri Viridis	145	46	2.98
Zingiberis	144	46	2.98
Vinum Colchici Radicis	107	55	3.56
Colchici Seminis	111	54	3.49
Opii	100	55	3.56

TABLES SHOWING SPECIFIC GRAVITY CORRESPONDING WITH DEGREES OF HYDROMETERS.

Baumé's hydrometer is still largely employed. In this instrument the specific gravity of distilled water is assumed as the zero of the descending scale in relation to fluids heavier than itself, and as ten on the ascending scale in relation to lighter fluids. In the following tables the specific gravity of liquids is given corresponding with the several degrees of this hydrometer. The first column of specific gravities is taken from the French Codex. The second column is based on the calculations of Huss. The third column was calculated by Henry Pemberton of Philadelphia, in 1851. The figures in this column correspond with the degrees of the hydrometers formerly prepared by W. H. Pile.

FOR LIQUIDS LIGHTER THAN WATER.
(Baumé's hydrometer.)

Degree of hydrometer.	Specific Gravity. By Baumé.			Degree of hydrometer.	Specific Gravity. By Baumé.		
10	1.000	1.0000	1.0000	44	0.809	0.8047	0.8045
11	0.993	0.9930	0.9929	45	0.804	0.8001	0.8000
12	0.986	0.9861	0.9859	46	0.800	0.7956	0.7954
13	0.979	0.9792	0.9790	47	0.795	0.7911	0.7909
14	0.973	0.9724	0.9722	48	0.791	0.7866	0.7865
15	0.966	0.9657	0.9655	49	0.787	0.7821	0.7821
16	0.960	0.9591	0.9589	50	0.783	0.7777	0.7777
17	0.953	0.9526	0.9523	51	0.778	0.7733	0.7734
18	0.947	0.9462	0.9459	52	0.774	0.7689	0.7692
19	0.941	0.9399	0.9395	53	0.770	0.7646	0.7650
20	0.935	0.9336	0.9333	54	0.766	0.7603	0.7608
21	0.929	0.9274	0.9271	55	0.762	0.7560	0.7567
22	0.923	0.9212	0.9210	56	0.758	0.7518	0.7526
23	0.917	0.9151	0.9150	57	0.754	0.7476	0.7486
24	0.911	0.9091	0.9090	58	0.750	0.7435	0.7446
25	0.905	0.9032	0.9032	59	0.746	0.7394	0.7407
26	0.900	0.8974	0.8974	60	0.742	0.7354	0.7368
27	0.894	0.8917	0.8917	61	0.738	0.7314	0.7329
28	0.889	0.8860	0.8860	62	0.735	0.7275	0.7290
29	0.883	0.8804	0.8805	63	0.731	.....	0.7253
30	0.878	0.8748	0.8750	64	0.727	.....	0.7216
31	0.872	0.8693	0.8695	65	0.724	.....	0.7179
32	0.867	0.8638	0.8641	66	0.720	.....	0.7142
33	0.862	0.8584	0.8588	67	0.716	.....	0.7106
34	0.857	0.8531	0.8536	68	0.713	.....	0.7070
35	0.852	0.8479	0.8484	69	0.709	.....	0.7035
36	0.847	0.8428	0.8433	70	0.706	.....	0.7000
37	0.842	0.8378	0.8383	71	0.702	.....	0.6965
38	0.837	0.8329	0.8333	72	0.699	.....	0.6930
39	0.832	0.8281	0.8284	73	0.696	.....	0.6896
40	0.827	0.8233	0.8235	74	0.692	.....	0.6863
41	0.823	0.8186	0.8187	75	0.689	.....	0.6829
42	0.818	0.8139	0.8139	76	0.686	.....	0.6796
43	0.813	0.8093	0.8092	77	0.682	.....	0.6763

The following formulas, furnished by Pile, may prove useful by enabling any one to calculate the sp. gr. corresponding with the several degrees of Baumé's hydrometer, and, conversely, the degree of Baumé corresponding with the sp. gr.

1. *For Liquids lighter than Water.*—The following formulas give the sp. gr. as represented in the first column in the foregoing table; or, the specific gravity being known, give the corresponding degree of Baumé.

$$\frac{144}{B^\circ + 134} = \text{sp. gr.}; \text{ and } \frac{144}{\text{sp. gr.}} - 134 = B^\circ.$$

The following formulas apply to the third column of specific gravities.

$$\frac{140}{B^\circ + 130} = \text{sp. gr.}; \text{ and } \frac{140}{\text{sp. gr.}} - 130 = B^\circ.$$

2. *For Liquids heavier than Water.*—For the first column, $\frac{144}{144 - B^\circ} = \text{sp. gr.}$, and $144 - \frac{144}{\text{sp. gr.}} = B^\circ$; for the third, $\frac{145}{145 - B^\circ} = \text{sp. gr.}$, and $145 - \frac{145}{\text{sp. gr.}} = B^\circ$.

FOR LIQUIDS HEAVIER THAN WATER.

(Baumé's hydrometer.)

Degree of hydrometer.	Specific Gravity. By Baumé.			Degree of hydrometer.	Specific Gravity. By Baumé.		
0	1.000	1.0000	1.0000	38	1.359	1.3559	1.3551
1	1.007	1.0070	1.0069	39	1.372	1.3686	1.3679
2	1.014	1.0141	1.0139	40	1.384	1.3815	1.3809
3	1.022	1.0213	1.0211	41	1.398	1.3947	1.3942
4	1.029	1.0286	1.0283	42	1.412	1.4082	1.4077
5	1.036	1.0360	1.0357	43	1.426	1.4219	1.4215
6	1.044	1.0435	1.0431	44	1.440	1.4359	1.4356
7	1.052	1.0511	1.0507	45	1.454	1.4501	1.4500
8	1.060	1.0588	1.0583	46	1.479	1.4645	1.4646
9	1.067	1.0666	1.0661	47	1.485	1.4792	1.4795
10	1.075	1.0745	1.0740	48	1.501	1.4942	1.4949
11	1.083	1.0825	1.0820	49	1.516	1.5096	1.5104
12	1.091	1.0906	1.0902	50	1.532	1.5253	1.5263
13	1.100	1.0988	1.0984	51	1.549	1.5413	1.5425
14	1.108	1.1071	1.1008	52	1.566	1.5576	1.5591
15	1.116	1.1155	1.1153	53	1.583	1.5742	1.5760
16	1.125	1.1240	1.1240	54	1.601	1.5912	1.5934
17	1.134	1.1326	1.1328	55	1.618	1.6086	1.6111
18	1.143	1.1414	1.1417	56	1.637	1.6264	1.6292
19	1.152	1.1504	1.1507	57	1.656	1.6446	1.6477
20	1.161	1.1596	1.1600	58	1.676	1.6632	1.6666
21	1.171	1.1690	1.1693	59	1.695	1.6823	1.6860
22	1.180	1.1785	1.1788	60	1.715	1.7019	1.7058
23	1.190	1.1882	1.1885	61	1.736	1.7220	1.7261
24	1.199	1.1981	1.1983	62	1.758	1.7427	1.7469
25	1.210	1.2082	1.2083	63	1.779	1.7640	1.7682
26	1.221	1.2184	1.2184	64	1.801	1.7856	1.7901
27	1.231	1.2288	1.2288	65	1.823	1.8082	1.8125
28	1.242	1.2394	1.2393	66	1.847	1.8312	1.8354
29	1.252	1.2502	1.2500	67	1.872	1.8548	1.8589
30	1.261	1.2612	1.2608	68	1.897	1.8790	1.8831
31	1.275	1.2724	1.2719	69	1.921	1.9038	1.9079
32	1.286	1.2838	1.2831	70	1.946	1.9291	1.9333
33	1.298	1.2954	1.2946	71	1.974	1.9548	1.9595
34	1.309	1.3072	1.3063	72	2.002	1.9809	1.9863
35	1.321	1.3190	1.3181	73	2.031	2.0073	2.0139
36	1.334	1.3311	1.3302	74	2.059	2.0340	2.0422
37	1.346	1.3434	1.3425	75	2.087	2.0610	2.0714

Gay-Lussac's centesimal alcoholmeter is applicable only to alcohol. The scale of this instrument is divided into 100 unequal degrees, the zero corresponding to pure water, and 100° to absolute alcohol; and every intermediate degree expresses the percentage of pure alcohol, by measure, contained in the liquors examined. Thus, when the instrument stands at 40° in any alcoholic liquid, it indicates that 100 measures of the liquid contain 40 of pure alcohol and 60 of water. But, as it was graduated for the temperature of 59° of Fahrenheit, the liquors to be tested should be brought to that temperature. *Tralles's centesimal alcoholmeter* is the one used by the U. S. Government in gauging the strength of spirit, and is generally employed in this country by distillers and wholesale dealers in the purchase and sale of alcoholic liquors. The scale of this instrument is, like Gay-Lussac's, divided into 100 unequal parts, each corresponding to the percentage by volume of pure alcohol contained in the liquors examined. As the sp. gr. of water is considered as unity at its temperature of greatest density, 39.8° F., and the degrees of this scale are calculated for 60° F., the zero, corresponding to the density of water, will represent a sp. gr. of .9991.

The table of Tralles on page 1752 gives the percentage of alcohol *by volume* corresponding with the specific gravity. Under the heading of Alcohol tables (see page 1757), a table of the percentage by weight corresponding with the sp. gr. is given. By means of these tables, in connection with the alcoholmeter, every problem that can arise in reference to the strength of spirituous liquors can be solved; and by the appended table, giving the value of Baumé's degrees in those of Tralles, the facility is still further extended.

Sikes's hydrometer is used in Great Britain in the collection of the excise revenue: it is a brass instrument having a spherical bulb, with a weight at the bottom to make it float upright; the stem is divided into twenty parts, and every other division numbered, from 0 to 10. A series of nine weights are furnished with the instrument, numbered from 10 to 90; these are to be added to the weight at the bottom to cause the hydrometer to sink, so that a reading may be had on the graduated scale; this reading added to the number on the weight employed, gives a figure which indicates the strength of the spirit by referring to a table which accompanies the instrument.

Jones's hydrometer is similar to Sikes's, but by many is regarded as an improvement on it.

ALCOHOLMETRICAL TABLE OF TRALLES.

Alcohol in 100 measures of spirit.	Specific gravity at 60° F.	Alcohol in 100 measures of spirit.	Specific gravity at 60° F.	Alcohol in 100 measures of spirit.	Specific gravity at 60° F.	Alcohol in 100 measures of spirit.	Specific gravity at 60° F.
0	.9991	26	.9689	51	.9315	76	.8739
1	.9976	27	.9679	52	.9295	77	.8712
2	.9961	28	.9668	53	.9275	78	.8685
3	.9947	29	.9657	54	.9254	79	.8658
4	.9933	30	.9646	55	.9234	80	.8631
5	.9919	31	.9634	56	.9213	81	.8603
6	.9906	32	.9622	57	.9192	82	.8575
7	.9893	33	.9609	58	.9170	83	.8547
8	.9881	34	.9596	59	.9148	84	.8518
9	.9869	35	.9583	60	.9126	85	.8488
10	.9857	36	.9570	61	.9104	86	.8458
11	.9845	37	.9556	62	.9082	87	.8428
12	.9834	38	.9541	63	.9059	88	.8397
13	.9823	39	.9526	64	.9036	89	.8365
14	.9812	40	.9510	65	.9013	90	.8332
15	.9802	41	.9494	66	.8989	91	.8299
16	.9791	42	.9478	67	.8965	92	.8265
17	.9781	43	.9461	68	.8941	93	.8230
18	.9771	44	.9444	69	.8917	94	.8194
19	.9761	45	.9427	70	.8892	95	.8157
20	.9751	46	.9409	71	.8867	96	.8118
21	.9741	47	.9391	72	.8842	97	.8077
22	.9731	48	.9373	73	.8817	98	.8034
23	.9720	49	.9354	74	.8791	99	.7988
24	.9710	50	.9335	75	.8765	100	.7939
25	.9700						

Table showing the value of the Degrees of Baumé's Hydrometer in those of Tralles's Alcoholmeter.

Baumé.	Tralles.	Baumé.	Tralles.	Baumé.	Tralles.	Baumé.	Tralles.
10.12	.0	20	50.1	30	75.6	40	92.9
11	4.3	21	53.2	31	77.6	41	94.2
12	9.8	22	56.1	32	79.6	42	95.5
13	16.1	23	58.9	33	81.5	43	96.7
14	22.9	24	61.6	34	83.4	44	97.8
15	29.2	25	64.2	35	85.1	45	98.8
16	34.5	26	66.6	36	86.8	46	99.7
17	39.2	27	69.0	37	88.4	46.37	100.0
18	43.1	28	71.3	38	90.0		
19	46.8	29	73.5	39	91.4		

Alcoholometric Table (U. S. P. IX.)

Temperature 15.56° C. (60.4° F.)

Percentage by Volume					Percentage by Weight				
Per cent. vol.	Corresponding per cent. wt.	Sp. gr. app.* in air $\frac{15.56°}{15.56°}$	Corr.† of sp. gr. for barometer (100 mm.)	Fractional‡ per cent.	Per cent. wt.	Corresponding per cent. vol.	Sp. gr. app.* in air $\frac{15.56°}{15.56°}$	Corr.† of sp. gr. for barometer (100 mm.)	Fractional‡ per cent.
§0	0.000	1.00000	0.000000	0.0667	0	0.000	1.00000	0.000000	0.0532
1	0.795	0.99850	0.000000	0.0680	1	1.257	0.99812	0.000000	0.0543
2	1.593	0.99703	0.000000	0.0690	2	2.510	0.99628	0.000000	0.0565
3	2.392	0.99558	0.000001	0.0714	3	3.758	0.99451	0.000001	0.0588
4	3.194	0.99418	0.000001	0.0730	4	5.002	0.99281	0.000001	0.0610
5	3.998	0.99281	0.000001	0.0746	5	6.243	0.99117	0.000001	0.0641
6	4.804	0.99149	0.000001	0.0781	6	7.479	0.98961	0.000001	0.0671
7	5.612	0.99021	0.000001	0.0813	7	8.712	0.98812	0.000002	0.0680
8	6.422	0.98898	0.000002	0.0833	8	9.943	0.98665	0.000002	0.0700
9	7.234	0.98778	0.000002	0.0840	9	11.169	0.98523	0.000002	0.0719
10	8.047	0.98659	0.000002	0.0855	10	12.393	0.98384	0.000002	0.0746
11	8.862	0.98542	0.000002	0.0877	11	13.613	0.98351	0.000003	0.0769
12	9.679	0.98428	0.000002	0.0901	12	14.832	0.98120	0.000003	0.0775
13	10.497	0.98317	0.000003	0.0917	13	16.047	0.97991	0.000003	0.0800
14	11.317	0.98208	0.000003	0.0943	14	17.259	0.97866	0000.003	0.0820
15	12.138	0.98102	0.000003	0.0943	15	18.469	0.97744	0.000004	0.0840
16	12.961	0.97996	0.000003	0.0962	16	19.676	0.97625	0.000004	0.0833
17	13.786	0.97892	0.000003	0.0990	17	20.880	0.97505	0.000004	0.0826
18	14.612	0.97791	0.000004	0.1000	18	22.081	0.97384	0.000004	0.0813
19	15.440	0.97691	0.000004	0.1020	19	23.278	0.97261	0.000004	0.0806
20	16.269	0.97593	0.000004	0.1000	20	24.472	0.97137	0.000005	0.0794
21	17.100	0.97493	0.000004	0.0990	21	25.662	0.97011	0.000005	0.0781
22	17.933	0.97392	0.000004	0.0980	22	26.849	0.96883	0.000005	0.0769
23	18.768	0.97290	0.000004	0.0962	23	28.032	0.96753	0.000005	0.0752
24	19.604	0.97186	0.000005	0.0952	24	29.210	0.96620	0.000005	0.0740
25	20.443	0.97081	0.000005	0.0943	25	30.388	0.96485	0.000006	0.0719
26	21.285	0.96974	0.000005	0.0926	26	31.555	0.96346	0.000006	0.0694
27	22.127	0.96866	0.000005	0.0909	27	32.719	0.96202	0.000006	0.0667
28	22.973	0.96756	0.000005	0.0893	28	33.879	0.96052	0.000006	0.0649
29	23.820	0.96644	0.000005	0.0877	29	35.033	0.95898	0.000007	0.0633
30	24.670	0.96530	0.000005	0.0862	30	36.181	0.95740	0.000007	0.0613
31	25.524	0.96414	0.000006	0.0820	31	37.323	0.95577	0.000007	0.0595
32	26.382	0.96292	0.000006	0.0787	32	38.459	0.95409	0.000007	0.0578
33	27.242	0.96165	0.000006	0.0775	33	39.590	0.95236	0.000007	0.0565
34	28.104	0.96036	0.000006	0.0752	34	40.716	0.95059	0.000008	0.0556
35	28.971	0.95903	0.000006	0.0725	35	41.832	0.94879	0.000008	0.0546
36	29.842	0.95765	0.000007	0.0704	36	42.944	0.94696	0.000008	0.0538
37	30.717	0.95623	0.000007	0.0685	37	44.050	0.94509	0.000009	0.0521
38	31.596	0.95477	0.000007	0.0668	38	45.149	0.94317	0.000009	0.0515
39	32.478	0.95326	0.000007	0.0649	39	46.242	0.94123	0.000009	0.0508
40	33.364	0.95172	0.000007	0.0633	40	47.328	0.93926	0.000010	0.0498
41	34.254	0.95014	0.000008	0.0617	41	48.407	0.93725	0.000010	0.0488
42	35.150	0.94852	0.000008	0.0600	42	49.480	0.93520	0.000010	0.0485
43	36.050	0.94687	0.000008	0.0588	43	50.545	0.93312	0.000011	0.0476
44	36.955	0.94517	0.000009	0.0578	§44	51.605	0.93102	0.000011	0.0474
45	37.865	0.94344	0.000009	0.0565	45	52.658	0.92891	0.000011	0.0469

* Barometer 760 mm. Air one-half saturated with moisture.

|| If temperature of observation is above 15.56° C. (60.4° F.), look for percentage correction in the following table.

† Correction subtractive if barometer is above, additive if below, 760 mm. If barometer readings are in inches reduce to millimeters by multiplying by 25.4.

‡ Corresponding with a difference in specific gravity of 0.0001.

§ The figures on this line across the page are for fractional percentages below 1.

NOTE.—The figures of these Alcoholometric Tables are based on tables issued by the U. S. Bureau of Standards.

Alcoholometric Table—*Continued.*

Percentage by Volume					Percentage by Weight				
Per cent. vol.	Corresponding per cent. wt.	Sp. gr. app. in air 15.56° 15.56°	Corr. of sp. gr. for barometer (100 mm.)	Fractional per cent.	Per cent. wt.	Corresponding per cent. vol.	Sp. gr. app. in air 15.56° 15.56°	Corr. of sp. gr. for barometer (100 mm.)	Fractional per cent.
46	38.778	0.94167	0.000009	0.0552	46	53.705	0.92678	0.000012	0.0467
47	39.697	0.93986	0.000009	0.0541	47	54.746	0.92464	0.000012	0.0461
48	40.622	0.93801	0.000010	0.0526	48	55.780	0.92247	0.000012	0.0461
49	41.551	0.93611	0.000010	0.0518	49	56.808	0.92030	0.000013	0.0457
50	42.487	0.93418	0.000010	0.0510	50	57.830	0.91811	0.000013	0.0455
51	43.428	0.93222	0.000011	0.0503	51	58.844	0.91591	0.000013	0.0446
52	44.374	0.93023	0.000011	0.0498	52	59.851	0.91367	0.000014	0.0444
53	45.326	0.92822	0.000011	0.0488	53	60.854	0.91142	0.000014	0.0444
54	46.283	0.92617	0.000012	0.0483	54	61.850	0.90917	0.000014	0.0442
55	47.245	0.92410	0.000012	0.0478	55	62.837	0.90691	0.000015	0.0441
56	48.214	0.92201	0.000012	0.0474	56	63.820	0.90464	0.000015	0.0441
57	49.187	0.91990	0.000013	0.0463	57	64.798	0.90237	0.000015	0.0441
58	50.167	0.91774	0.000013	0.0457	58	65.768	0.90010	0.000016	0.0437
59	51.154	0.91555	0.000013	0.0452	59	66.732	0.89781	0.000016	0.0435
60	52.147	0.91334	0.000014	0.0446	60	67.690	0.89551	0.000016	0.0433
61	53.146	0.91110	0.000014	0.0439	61	68.641	0.89320	0.000017	0.0431
62	54.152	0.90882	0.000014	0.0437	62	69.586	0.89088	0.000017	0.0431
63	55.165	0.90653	0.000015	0.0435	63	70.523	0.88856	0.000017	0.0427
64	56.184	0.90423	0.000015	0.0429	64	71.455	0.88623	0.000018	0.0426
65	57.208	0.90190	0.000015	0.0426	65	72.380	0.88388	0.000018	0.0426
66	58.241	0.89955	0.000016	0.0420	66	73.299	0.88153	0.000019	0.0426
67	59.279	0.89717	0.000016	0.0410	67	74.211	0.87918	0.000019	0.0426
68	60.325	0.89477	0.000016	0.0408	68	75.117	0.87683	0.000019	0.0422
69	61.379	0.89232	0.000017	0.0407	69	76.016	0.87446	0.000020	0.0422
70	62.441	0.88986	0.000017	0.0403	70	76.909	0.87206	0.000020	0.0418
71	63.511	0.88738	0.000018	0.0395	71	77.794	0.86970	0.000021	0.0417
72	64.588	0.88485	0.000018	0.0392	72	78.672	0.86730	0.000021	0.0417
73	65.674	0.88230	0.000019	0.0389	73	79.544	0.86490	0.000021	0.0417
74	66.768	0.87973	0.000019	0.0385	74	80.410	0.86250	0.000022	0.0413
75	67.870	0.87713	0.000019	0.0380	75	81.269	0.86008	0.000022	0.0413
76	68.982	0.87450	0.000020	0.0376	76	82.121	0.85766	0.000022	0.0413
77	70.102	0.87184	0.000020	0.0370	77	82.967	0.85524	0.000023	0.0412
78	71.234	0.86914	0.000021	0.0365	78	83.805	0.85281	0.000023	0.0403
79	72.375	0.86640	0.000021	0.0362	79	84.636	0.85033	0.000024	0.0408
80	73.526	0.86364	0.000021	0.0357	80	85.459	0.84788	0.000024	0.0403
81	74.686	0.86084	0.000022	0.0352	81	86.275	0.84540	0.000024	0.0402
82	75.858	0.85800	0.000022	0.0350	82	87.083	0.84291	0.000025	0.0402
83	77.039	0.85514	0.000023	0.0344	83	87.885	0.84042	0.000025	0.0398
84	78.233	0.85223	0.000023	0.0337	84	88.678	0.83791	0.000025	0.0394
85	79.441	0.84926	0.000024	0.0331	85	89.464	0.83537	0.000026	0.0392
86	80.662	0.84624	0.000024	0.0326	86	90.240	0.83282	0.000026	0.0391
87	81.897	0.84317	0.000025	0.0322	87	91.008	0.83026	0.000027	0.0386
88	83.144	0.84006	0.000025	0.0314	88	91.766	0.82767	0.000027	0.0377
89	84.408	0.83688	0.000026	0.0307	89	92.517	0.82502	0.000028	0.0380
90	85.689	0.83362	0.000026	0.0300	90	93.254	0.82239	0.000028	0.0372
91	86.989	0.83029	0.000027	0.0291	91	93.982	0.81970	0.000028	0.0367
92	88.310	0.82685	0.000027	0.0282	92	94.700	0.81697	0.000029	0.0362
93	89.652	0.82330	0.000028	0.0272	93	95.407	0.81421	0.000029	0.0358
94	91.025	0.81963	0.000028	0.0262	94	96.103	0.81142	0.000030	0.0353
95	92.423	0.81581	0.000029	0.0252	95	96.787	0.80859	0.000030	0.0348
96	93.851	0.81184	0.000030	0.0240	96	97.457	0.80572	0.000030	0.0342
97	95.315	0.80769	0.000030	0.0229	97	98.117	0.80280	0.000031	0.0334
98	96.820	0.80333	0.000031	0.0214	98	98.759	0.79981	0.000031	0.0328
99	98.381	0.79865	0.000031	0.0200	99	99.386	0.79676	0.000032	0.0322
100	100.000	0.79365	0.000032		100	100.000	0.79365	0.000032	

Temperature Corrections (U. S. P. IX.)

For volume per cent. of Alcohol by the foregoing Alcoholometric Table

Temp. C. 15.56°	Observed Per cent.—Alcohol by volume											
	1	2	3	4	5	6	7	8	9	10	13	14
	Subtract from observed per cent. of alcohol											
16	0.04	0.04	0.05	0.05	0.05	0.05	0.05	0.06	0.06	0.06	0.07	0.08
17	0.14	0.14	0.16	0.16	0.16	0.17	0.17	0.19	0.20	0.21	0.24	0.29
18	0.25	0.25	0.27	0.27	0.27	0.29	0.31	0.33	0.35	0.37	0.42	0.49
19	0.36	0.36	0.38	0.39	0.40	0.43	0.45	0.48	0.51	0.54	0.61	0.69
20	0.48	0.48	0.50	0.52	0.54	0.57	0.60	0.64	0.67	0.71	0.80	0.91
21	0.60	0.61	0.63	0.65	0.68	0.71	0.75	0.80	0.84	0.89	0.99	1.12
22	0.73	0.75	0.77	0.79	0.83	0.86	0.91	0.97	1.02	1.07	1.19	1.35
23	0.86	0.89	0.91	0.94	0.98	1.02	1.08	1.14	1.20	1.26	1.40	1.58
24	1.00	1.04	1.06	1.10	1.14	1.20	1.25	1.32	1.38	1.45	1.61	1.81
25		1.19	1.22	1.26	1.30	1.36	1.41	1.49	1.57	1.65	1.82	2.04
26		1.35	1.38	1.43	1.47	1.54	1.60	1.68	1.76	1.85	2.04	2.28
27		1.52	1.55	1.61	1.65	1.73	1.79	1.88	1.96	2.06	2.27	2.52
28		1.69	1.73	1.78	1.84	1.91	1.99	2.08	2.17	2.28	2.50	2.76
29		1.87	1.91	1.96	2.03	2.10	2.19	2.28	2.38	2.50	2.73	3.00
30			2.09	2.15	2.22	2.30	2.39	2.49	2.60	2.72	2.97	3.25
31			2.27	2.34	2.41	2.50	2.60	2.70	2.82	2.95	3.21	3.51
32			2.45	2.54	2.61	2.71	2.82	2.92	3.05	3.18	3.46	3.77
33			2.63	2.74	2.81	2.92	3.04	3.15	3.28	3.42	3.71	4.03
34			2.82	2.95	3.02	3.14	3.27	3.39	3.52	3.66	3.96	4.29
35				3.16	3.24	3.36	3.49	3.63	3.76	3.91	4.22	4.55

Temp. C. 15.56°	Observed per cent.—Alcohol by volume											
	16	18	20	22	24	26	28	30	32	34	37	40
	Subtract from observed per cent. of alcohol											
16	0.10	0.12	0.13	0.14	0.15	0.16	0.17	0.18	0.19	0.19	0.19	0.18
17	0.33	0.38	0.42	0.46	0.50	0.54	0.57	0.59	0.60	0.60	0.59	0.58
18	0.56	0.65	0.73	0.79	0.84	0.89	0.95	0.99	1.00	1.01	1.00	0.98
19	0.80	0.91	1.02	1.11	1.19	1.27	1.33	1.39	1.40	1.41	1.41	1.39
20	1.04	1.18	1.32	1.44	1.54	1.64	1.72	1.79	1.81	1.82	1.81	1.79
21	1.28	1.45	1.61	1.76	1.88	2.00	2.10	2.18	2.21	2.22	2.22	2.19
22	1.53	1.73	1.91	2.07	2.21	2.35	2.47	2.57	2.60	2.63	2.63	2.59
23	1.78	2.00	2.21	2.39	2.55	2.71	2.84	2.95	3.00	3.03	3.03	3.00
24	2.04	2.28	2.51	2.71	2.88	3.06	3.21	3.34	3.40	3.44	3.44	3.40
25	2.29	2.56	2.81	3.03	3.22	3.41	3.58	3.73	3.80	3.84	3.85	3.80
26	2.55	2.83	3.11	3.35	3.56	3.77	3.95	4.11	4.20	4.25	4.26	4.21
27	2.80	3.11	3.41	3.68	3.91	4.13	4.32	4.50	4.59	4.65	4.67	4.62
28	3.06	3.38	3.71	4.00	4.25	4.49	4.70	4.88	4.99	5.05	5.07	5.02
29	3.32	3.66	4.01	4.33	4.60	4.85	5.06	5.26	5.38	5.46	5.48	5.43
30	3.58	3.94	4.31	4.65	4.94	5.21	5.43	5.64	5.77	5.86	5.89	5.84
31	3.85	4.22	4.61	4.97	5.28	5.56	5.80	6.01	6.16	6.26	6.29	6.24
32	4.12	4.51	4.92	5.30	5.62	5.91	6.16	6.39	6.54	6.65	6.70	6.65
33	4.40	4.80	5.22	5.62	5.95	6.26	6.50	6.76	6.92	7.04	7.10	7.05
34	4.67	5.09	5.54	5.94	6.29	6.62	6.90	7.13	7.30	7.44	7.51	7.46
35	4.94	5.39	5.86	6.27	6.63	6.97	7.26	7.50	7.67	7.83	7.91	7.86

Temperature Corrections—*Continued.*

For volume per cent. of Alcohol by the foregoing Alcoholometric Table

Temp. C. 15.56°	Observed per cent.—Alcohol by volume											
	43	46	49	52	55	58	61	64	67	70	73	76
	Subtract from observed per cent. of alcohol											
16	0.18	0.18	0.17	0.17	0.16	0.16	0.16	0.16	0.16	0.15	0.15	0.14
17	0.57	0.56	0.55	0.53	0.52	0.51	0.50	0.49	0.48	0.47	0.46	0.45
18	0.97	0.95	0.93	0.90	0.88	0.86	0.85	0.83	0.82	0.80	0.79	0.76
19	1.37	1.34	1.30	1.27	1.25	1.22	1.19	1.17	1.14	1.12	1.11	1.08
20	1.76	1.72	1.68	1.64	1.61	1.57	1.54	1.51	1.48	1.45	1.42	1.39
21	2.15	2.11	2.06	2.02	1.98	1.94	1.90	1.85	1.82	1.79	1.75	1.70
22	2.55	2.50	2.44	2.39	2.34	2.29	2.24	2.20	2.16	2.12	2.07	2.02
23	2.94	2.89	2.82	2.76	2.71	2.66	2.60	2.55	2.50	2.46	2.39	2.33
24	3.34	3.28	3.21	3.14	3.07	3.01	2.95	2.90	2.84	2.79	2.72	2.65
25	3.74	3.67	3.60	3.52	3.44	3.37	3.31	3.24	3.18	3.13	3.05	2.97
26	4.14	4.07	3.98	3.89	3.81	3.74	3.67	3.59	3.53	3.47	3.38	3.29
27	4.55	4.47	4.37	4.27	4.18	4.10	4.02	3.95	3.87	3.80	3.71	3.62
28	4.95	4.86	4.76	4.65	4.56	4.48	4.39	4.31	4.22	4.14	4.04	3.95
29	5.35	5.26	5.15	5.04	4.93	4.84	4.75	4.66	4.75	4.48	4.38	4.27
30	5.75	5.66	5.53	5.41	5.30	5.20	5.11	5.01	4.91	4.82	4.71	4.59
31	6.15	6.06	5.92	5.79	5.67	5.57	5.48	5.37	5.27	5.17	5.05	4.93
32	6.56	6.46	6.32	6.19	6.05	5.95	5.84	5.73	5.62	5.51	5.39	5.26
33	6.96	6.85	6.72	6.57	6.43	6.32	6.20	6.09	5.97	5.86	5.73	5.59
34	7.36	7.25	7.12	6.96	6.81	6.69	6.56	6.44	6.32	6.21	6.07	5.92
35	7.76	7.65	7.51	7.35	7.19	7.06	6.93	6.80	6.68	6.56	6.41	6.25

Temp. C. 15.56°	Observed per cent.—Alcohol by volume										
	79	82	84	86	88	90	92	94	96	98	100
	Subtract from observed per cent. of alcohol										
16	0.13	0.13	0.13	0.13	0.12	0.12	0.11	0.10	0.10	0.09	0.08
17	0.44	0.42	0.41	0.41	0.39	0.38	0.36	0.33	0.31	0.27	0.24
18	0.74	0.71	0.70	0.69	0.66	0.63	0.60	0.56	0.52	0.46	0.40
19	1.04	1.00	0.98	0.96	0.93	0.89	0.85	0.79	0.73	0.65	0.57
20	1.34	1.30	1.28	1.24	1.20	1.15	1.09	1.02	0.94	0.85	0.74
21	1.66	1.60	1.57	1.53	1.47	1.42	1.34	1.26	1.16	1.05	0.92
22	1.97	1.90	1.86	1.82	1.75	1.69	1.60	1.50	1.39	1.26	1.09
23	2.27	2.20	2.15	2.10	2.03	1.96	1.86	1.75	1.61	1.46	1.27
24	2.58	2.50	2.45	2.39	2.31	2.23	2.12	1.99	1.84	1.67	1.45
25	2.89	2.81	2.75	2.68	2.60	2.50	2.38	2.23	2.07	1.88	1.63
26	3.21	3.11	3.05	2.96	2.89	2.78	2.64	2.48	2.31	2.10	1.82
27	3.52	3.42	3.35	3.27	3.17	3.05	2.91	2.74	2.54	2.31	2.00
28	3.84	3.73	3.65	3.57	3.46	3.33	3.18	2.99	2.78	2.53	2.19
29	4.16	4.04	3.96	3.86	3.74	3.61	3.45	3.25	3.02	2.75	2.38
30	4.47	4.34	4.26	4.16	4.03	3.89	3.72	3.51	3.26	2.98	2.58
31	4.79	4.66	4.56	4.46	4.32	4.18	3.99	3.77	3.51	3.21	2.78
32	5.12	4.98	4.88	4.77	4.62	4.46	4.27	4.03	3.76	3.45	2.99
33	5.45	5.30	5.19	5.07	4.92	4.75	4.54	4.30	4.01	3.68	3.19
34	5.77	5.62	5.51	5.38	5.22	5.03	4.82	4.56	4.26	3.92	3.40
35	6.09	5.94	5.82	5.69	5.52	5.32	5.09	4.82	4.52	4.15	3.61

ALCOHOL.

According to E. R. Squibb.

NOTE.—This table was prepared by E. R. Squibb and introduced into the U. S. Pharmacopœia 1890, it is inserted here because it contains data not found in the official alcohol table U. S. P. IX.

PART I.—From 0 to 10 per cent. of Absolute Alcohol.

Specific Gravity. (Pure water at 15⅝° C. = 60° F. taken as unity.)		Percentage.				Weight of one gallon, at 15⅝° C. = 60° F.						Weight of 40 gallons to the nearest half pound, at 15⅝° C. = 60° F.	Weight of one pint, at 15⅝° C. = 60° F.	
								Avoirdupois Weight.						
											To the nearest ounce.			
At 15⅝° C. = 60° F.	At 25° C. = 77° F.	By weight.	By volume.	Under proof. (Brit. Excise.)	Of proof spirit. (U. S. Revenue.)	In Grammes.	In Grains.	lbs.	ozs.	Grs.	lbs.	ozs.	lbs.	In Grammes.	In Grains.
1·0000	0·9986					3779·13	58,320	8	5	132	8	5	333·5	472·39	7290
0·9993	0·9978			99	1	3776·50	58,279	8	5	91	8	5	333·0	472·06	7285
0·9985	0·9970		1	98	2	3773·46	58,232	8	5	44	8	5	332·5	471·68	7279
0·9981	0·9966	1				3771·97	58,209	8	5	22	8	5	332·5	471·49	7276
0·9976	0·9961			97	3	3770·08	58,180	8	4	430	8	5	332·5	471·26	7272
0·9970	0·9953		2		4	3767·82	58,145	8	4	395	8	5	332·0	470·98	7268
0·9968	0·9951			96		3767·04	58,133	8	4	383	8	5	332·0	470·88	7267
0·9965	0·9948	2			5	3765·94	58,116	8	4	366	8	5	332·0	470·74	7264
0·9960	0·9943			95		3764·06	58,087	8	4	337	8	5	332·0	470·51	7261
0·9956	0·9938		3		6	3762·51	58,063	8	4	313	8	5	332·0	470·31	7258
0·9952	0·9934			94		3761·02	58,040	8	4	290	8	5	331·5	470·13	7255
0·9947	0·9927	3			7	3759·14	58,011	8	4	261	8	5	331·5	469·89	7251
0·9944	0·9924			93		3757·97	57,993	8	4	243	8	5	331·5	469·75	7249
0·9942	0·9922		4		8	3757·26	57,982	8	4	232	8	5	331·5	469·66	7248
0·9936	0·9916			92	9	3754·99	57,947	8	4	197	8	4	331·0	469·37	7243
0·9930	0·9909	4	5	91	10	3752·72	57,912	8	4	162	8	4	331·0	469·09	7239
0·9921	0·9900			90	11	3749·29	57,859	8	4	109	8	4	330·5	468·66	7232
0·9914	0·9893	5	6	89	12	3746·63	57,818	8	4	68	8	4	330·5	468·33	7227
0·9906	0·9885			88	13	3743·65	57,772	8	4	22	8	4	330·0	467·95	7221
0·9900	0·9879			87		3741·38	57,737	8	3	424	8	4	330·0	467·67	7217
0·9898	0·9876	6	7		14	3740·60	57,725	8	3	413	8	4	330·0	467·58	7216
0·9892	0·9870			86	15	3738·33	57,690	8	3	377	8	4	329·5	467·29	7211
0·9890	0·9868		8		16	3737·56	57,678	8	3	366	8	4	329·5	467·19	7210
0·9885	0·9863			85		3735·68	57,649	8	3	336	8	4	329·5	466·96	7206
0·9884	0·9862	7			17	3735·29	57,643	8	3	331	8	4	329·5	466·91	7205
0·9878	0·9855		9	84	18	3733·02	57,608	8	3	296	8	4	329·0	466·63	7201
0·9872	0·9849			83	19	3730·82	57,574	8	3	261	8	4	329·0	466·35	7197
0·9869	0·9846	8	10		20	3729·65	57,556	8	3	243	8	4	329·0	466·21	7194
0·9864	0·9841			82	21	3727·77	57,527	8	3	214	8	3	328·5	465·97	7191
0·9857	0·9834			81		3725·12	57,486	8	3	173	8	3	328·5	465·64	7186
0·9855	0·9831	9	11		22	3724·34	57,474	8	3	161	8	3	328·5	465·54	7184
0·9852	0·9828			80	23	3723·24	57,457	8	3	144	8	3	328·5	465·40	7182
0·9845	0·9821			79		3720·58	57,416	8	3	103	8	3	328·0	465·07	7177
0·9841	0·9816	10	12		24	3719·09	57,393	8	3	81	8	3	328·0	464·89	7174

PART II.—From 10 to 25 per cent. of Absolute Alcohol.

0·9838	0·9813			78	25	3717·92	57,375	8	3	62	8	3	328·0	464·74	7172
0·9831	0·9806			77	26	3715·27	57,334	8	3	21	8	3	327·5	464·41	7167
0·9828	0·9801	11	13		27	3714·17	57,317	8	3	5	8	3	327·5	464·27	7165
0·9825	0·9798			76		3713·00	57,299	8	2	424	8	3	327·5	464·13	7162
0·9821	0·9793		14		28	3711·51	57,276	8	2	401	8	3	327·5	463·94	7159
0·9819	0·9791			75		3710·73	57,264	8	2	389	8	3	327·0	463·84	7158
0·9815	0·9787	12	15		29	3709·24	57,241	8	2	366	8	3	327·0	463·65	7155
0·9813	0·9785			74	30	3708·46	57,229	8	2	354	8	3	327·0	463·56	7154
0·9807	0·9779			73	31	3706·19	57,194	8	2	319	8	3	327·0	463·27	7149
0·9802	0·9773	13	16	72	32	3704·32	57,165	8	2	290	8	3	326·5	463·04	7146
0·9794	0·9765			71	33	3701·33	57,119	8	2	244	8	3	326·5	462·67	7140
0·9789	0·9759	14	17	70	34	3699·33	57,089	8	2	214	8	2	326·0	462·42	7136
0·9784	0·9754			69	35	3697·51	57,060	8	2	185	8	2	326·0	462·19	7132
0·9778	0·9746	15	18	68	36	3695·24	57,025	8	2	150	8	2	326·0	461·90	7128
0·9775	0·9743				37	3694·14	57,008	8	2	123	8	2	326·0	461·77	7126

PART II.—From 10 to 25 per cent. of Absolute Alcohol.

(Continued.)

Specific Gravity. (Pure water at 15⅝° C. = 60° F. taken as unity.)		Percentage.				Weight of one gallon, at 15⅝° C. = 60° F.							Weight of 40 gallons to the nearest half pound, at 15⅝° C. = 60° F.	Weight of one pint, at 15⅝° C. = 60° F.	
								Avoirdupois Weight.							
								lbs.	ozs.	Grs.	To the nearest ounce.				
At 15⅝° C. = 60° F.	At 25° C. = 77° F.	By weight.	By volume.	Under proof. (Brit. Excise.)	Of proof spirit. (U. S. Revenue.)	In Grammes.	In Grains.				lbs.	ozs.	lbs.	In Grammes.	In Grains.
0·9772	0·9740			67	38	3692·97	56,990	8	2	115	8	2	325·5	461·62	7124
0·9766	0·9733	16	19	66	39	3690·71	56,955	8	2	80	8	2	325·5	461·34	7119
0·9760	0·9726		20	65	40	3688·44	56,920	8	2	45	8	2	325·5	461·05	7115
0·9753	0·9719	17	21	64	41	3685·78	56,879	8	2	4	8	2	325·0	460·72	7110
0·9749	0·9715			63	42	3684·29	56,856	8	1	418	8	2	325·0	460·54	7107
0·9743	0·9709			62	43	3682·02	56,821	8	1	383	8	2	324·5	460·25	7103
0·9741	0·9706	18	22		44	3681·31	56,810	8	1	373	8	2	324·5	460·16	7101
0·9737	0·9702			61	45	3679·76	56,786	8	1	348	8	2	324·5	459·97	7098
0·9732	0·9697			60	46	3677·88	56,757	8	1	319	8	2	324·5	459·73	7095
0·9728	0·9692	19	23	59	47	3676·39	56,734	8	1	297	8	2	324·0	459·55	7092
0·9720	0·9684			58	48	3673·27	56,687	8	1	249	8	2	324·0	459·16	7086
0·9716	0·9678	20	24		49	3671·85	56,664	8	1	227	8	2	324·0	458·98	7083
0·9714	0·9676			57	50	3671·07	56,652	8	1	214	8	1	323·5	458·88	7081
0·9709	0·9668		25	56		3669·19	56,623	8	1	186	8	1	323·5	458·65	7078
0·9704	0·9661	21		55	51	3667·31	56,594	8	1	157	8	1	323·5	458·41	7074
0·9698	0·9655		26	54	52	3665·05	56,559	8	1	122	8	1	323·0	458·13	7070
0·9693	0·9650				53	3663·17	56,530	8	1	92	8	1	323·0	457·90	7066
0·9691	0·9646	22	27	53	54	3662·39	56,518	8	1	81	8	1	323·0	457·80	7065
0·9683	0·9638			52	55	3659·36	56,471	8	1	33	8	1	322·5	457·42	7059
0·9678	0·9631	23	28	51	56	3657·47	56,442	8	1	5	8	1	322·5	457·18	7055
0·9671	0·9624			50	57	3654·81	56,401	8	0	401	8	1	322·5	456·85	7050
0·9665	0·9617	24	29	49	58	3652·54	56,366	8	0	366	8	1	322·0	456·57	7046
0·9658	0·9610			48	59	3649·88	56,325	8	0	325	8	1	322·0	456·24	7041
0·9652	0·9603	25	30	47	60	3647·62	56,290	8	0	290	8	1	321·5	455·95	7036

PART III.—From 25 to 40 per cent. of Absolute Alcohol.

0·9645	0·9597			46	61	3645·02	56,250	8	0	250	8	1	321·5	455·63	7031
0·9643	0·9594		31		62	3644·24	56,238	8	0	238	8	1	321·5	455·53	7030
0·9638	0·9590	26		45	63	3642·37	56,209	8	0	209	8	0	321·0	455·30	7026
0·9631	0·9582		32	44	64	3639·71	56,168	8	0	168	8	0	321·0	454·96	7021
0·9623	0·9574	27		43	65	3636·66	56,121	8	0	121	8	0	320·5	454·58	7015
0·9618	0·9567		33	42	66	3634·79	56,092	8	0	92	8	0	320·5	454·35	7011
0·9609	0·9556	28	34	41	67	3631·42	56,040	8	0	40	8	0	320·0	453·93	7005
0·9602	0·9549			40	68	3628·76	55,999	7	15	436	8	0	320·0	453·59	7000
0·9595	0·9542			39	69	3626·10	55,958	7	15	395	8	0	320·0	453·26	6995
0·9593	0·9538	29	35		70	3625·33	55,946	7	15	383	8	0	319·5	453·17	6993
0·9587	0·9532			38	71	3623·06	55,911	7	15	348	8	0	319·5	452·88	6989
0·9578	0·9521	30	36	37	72	3619·69	55,859	7	15	296	8	0	319·0	452·46	6982
0·9572	0·9515			36	73	3617·42	55,824	7	15	261	8	0	319·0	452·18	6978
0·9565	0·9507		37	35		3614·76	55,783	7	15	220	8	0	319·0	451·84	6973
0·9560	0·9500	31			74	3612·88	55,754	7	15	191	7	15	318·5	451·61	6969
0·9555	0·9495			34	75	3611·03	55,725	7	15	162	7	15	318·5	451·38	6966
0·9550	0·9489		38	33	76	3609·12	55,696	7	15	133	7	15	318·0	451·14	6962
0·9544	0·9482	32			77	3606·86	55,661	7	15	98	7	15	318·0	450·86	6958
0·9539	0·9477			32		3604·91	55,631	7	15	68	7	15	318·0	450·61	6954
0·9535	0·9473		39		78	3603·42	55,608	7	15	45	7	15	318·0	450·43	6951
0·9528	0·9465	33		31	79	3600·76	55,567	7	15	4	7	15	317·5	450·09	6946
0·9519	0·9456		40	30	80	3597·39	55,515	7	14	390	7	15	317·0	449·67	6939
0·9511	0·9446	34		29	81	3594·35	55,468	7	14	343	7	15	317·0	449·29	6933
0·9503	0·9438		41	28	82	3591·30	55,421	7	14	296	7	15	316·5	448·91	6928
0·9495	0·9430			27	83	3588·32	55,375	7	14	250	7	15	316·5	448·54	6922
0·9490	0·9424	35	42		84	3586·44	55,346	7	14	221	7	15	316·0	448·30	6918
0·9485	0·9419			26		3584·56	55,317	7	14	192	7	14	316·0	448·07	6915
0·9475	0·9409			25	85	3580·74	55,258	7	14	133	7	14	316·0	447·59	6907
0·9470	0·9402	36	43		86	3578·86	55,229	7	14	104	7	14	315·5	447·36	6904
0·9465	0·9397			24		3576·98	55,200	7	14	75	7	14	315·5	447·12	6900
0·9455	0·9387			23	87	3573·22	55,142	7	14	17	7	14	315·0	446·65	6893
0·9452	0·9382	37	44		88	3572·06	55,124	7	13	437	7	14	315·0	446·51	6890

PART III.—From 25 to 40 per cent. of Absolute Alcohol.

(*Continued.*)

Specific Gravity. (Pure water at 15⅝° C. = 60° F. taken as unity.)		Percentage.				Weight of one gallon, at 15⅝° C. = 60° F.							Weight of 40 gallons to the nearest half pound, at 15⅝° C. = 60° F.	Weight of one pint, at 15⅝° C. = 60° F.	
								Avoirdupois Weight.							
											To the nearest ounce.				
At 15⅝° C. = 60° F.	At 25° C. = 77° F.	By weight.	By volume.	Under proof. (Brit. Excise.)	Of proof spirit. (U. S. Revenue.)	In Grammes.	In Grains.	lbs.	ozs.	Grs.	lbs.	ozs.	lbs.	In Grammes.	In Grains.
0·9446	0·9376			22	89	3569·79	55,089	7	13	401	7	14	315·0	446·22	6886
0·9434	0·9363	38	45	21	90	3565·25	55,019	7	13	331	7	14	314·5	445·66	6877
0·9426	0·9355			20	91	3562·21	54,972	7	13	284	7	14	314·0	445·28	6871
0·9416	0·9343	39	46	19	92	3558·45	54,914	7	13	226	7	14	314·0	444·81	6864
0·9405	0·9332			18	93	3554·30	54,850	7	13	162	7	13	313·5	444·29	6856
0·9396	0·9323	40	47	17	94	3550·87	54,797	7	13	109	7	13	313·0	443·86	6850
0·9391	0·9318				95	3548·99	54,768	7	13	75	7	13	313·0	443·62	6846

PART IV.—From 40 to 55 per cent. of Absolute Alcohol.

0·9381	0·9307		48	16	96	3545·23	54,710	7	13	22	7	13	312·5	443·15	6839
0·9376	0·9302	41				3543·35	54,681	7	12	431	7	13	312·5	442·92	6835
0·9373	0·9300			15	97	3542·19	54,663	7	12	413	7	13	312·5	442·77	6833
0·9362	0·9288		49	14	98	3538·04	54,599	7	12	349	7	13	312·0	442·25	6825
0·9356	0·9280	42				3535·77	54,564	7	12	314	7	13	312·0	441·97	6820
0·9352	0·9276			13	99	3534·28	54,541	7	12	291	7	13	311·5	441·78	6818
0·9343	0·9267		50	12	100	3530·84	54,488	7	12	238	7	13	311·5	441·35	6811
0·9335	0·9259	43			101	3527·86	54,442	7	12	192	7	12	311·0	440·98	6805
0·9329	0·9253			11		3525·59	54,407	7	12	157	7	12	311·0	440·70	6801
0·9323	0·9246		51		102	3523·33	54,372	7	12	122	7	12	310·5	440·42	6796
0·9318	0·9242			10		3521·45	54,343	7	12	93	7	12	310·5	440·18	6793
0·9314	0·9237	44			103	3519·89	54,319	7	12	69	7	12	310·5	439·99	6790
0·9306	0·9230			9		3516·91	54,273	7	12	23	7	12	310·0	439·61	6784
0·9303	0·9226		52		104	3515·75	54,255	7	12	5	7	12	310·0	439·47	6782
0·9292	0·9214	45		8	105	3511·59	54,191	7	11	379	7	12	309·5	438·95	6774
0·9283	0·9205		53	7	106	3508·16	54,138	7	11	326	7	12	309·5	438·52	6767
0·9270	0·9192	46		6	107	3503·30	54,063	7	11	251	7	12	309·0	437·91	6758
0·9262	0·9184		54	5	108	3500·26	54,016	7	11	204	7	11	308·5	437·53	6752
0·9249	0·9171	47		4	109	3495·33	53,940	7	11	128	7	11	308·0	436·92	6742
0·9242	0·9164		55		110	3492·68	53,899	7	11	87	7	11	308·0	436·58	6737
0·9236	0·9158			3		3490·41	53,864	7	11	51	7	11	308·0	436·30	6733
0·9228	0·9150	48			111	3487·43	53,818	7	11	6	7	11	307·5	435·93	6727
0·9221	0·9143		56	2	112	3484·77	53,777	7	10	402	7	11	307·5	435·60	6722
0·9212	0·9134			1	113	3481·34	53,724	7	10	349	7	11	307·0	435·17	6715
0·9206	0·9128	49				3479·07	53,689	7	10	314	7	11	307·0	434·88	6711
0·9200	0·9122		57	Proof over.	114	3476·80	53,654	7	10	279	7	11	306·5	434·60	6707
0·9189	0·9111			1	115	3472·65	53,590	7	10	215	7	10	306·0	434·08	6699
0·9184	0·9106	50				3470·77	53,561	7	10	186	7	10	306·0	433·85	6695
0·9178	0·9100		58	2	116	3468·51	53,526	7	10	151	7	10	306·0	433·56	6691
0·9168	0·9090				117	3464·75	53,468	7	10	93	7	10	305·5	433·09	6684
0·9160	0·9081	51	59	3	118	3461·70	53,421	7	10	46	7	10	305·0	432·71	6678
0·9150	0·9071			4	119	3457·94	53,363	7	9	425	7	10	305·0	432·24	6670
0·9135	0·9056	52	60	5	120	3452·24	53,275	7	9	338	7	10	304·5	431·53	6659
0·9124	0·9045			6	121	3449·09	53,211	7	9	273	7	10	304·0	431·01	6651
0·9113	0·9034	53	61	7	122	3443·95	53,147	7	9	210	7	9	303·5	430·49	6643
0·9100	0·9021			8	123	3439·02	53,071	7	9	133	7	9	303·0	429·88	6634
0·9090	0·9011	54	62	9	124	3435·26	53,013	7	9	76	7	9	303·0	429·41	6627
0·9075	0·8995			10	125	3429·56	52,925	7	8	425	7	9	302·5	428·69	6616
0·9060	0·8980	55	63		126	3427·29	52,890	7	8	390	7	9	302·0	428·41	6611

PART V.—From 55 to 70 per cent. of Absolute Alcohol.

Specific Gravity. (Pure water at 15⅝° C. = 60° F. taken as unity.)		Percentage.				Weight of one gallon, at 15⅝° C. = 60° F.							Weight of 40 gallons to the nearest half pound, at 15⅝° C. = 60° F.	Weight of one pint, at 15⅝° C. = 60° F.	
								Avoirdupois Weight.							
						In Grammes.	In Grains.	lbs.	ozs.	Grs.	To the nearest ounce.			In Grammes.	In Grains.
At 15⅝° C. = 60° F.	At 25° C. = 77° F.	By weight.	By volume.	Over proof. (Brit. Excise.)	Of proof spirit. (U. S. Revenue.)						lbs.	ozs.	lbs.		
0·9062	0·8982			11	127	3424·70	52,850	7	8	350	7	9	302·0	428·09	6606
0·9047	0·8969	56	64	12	128	3419·00	52,762	7	8	262	7	9	301·5	427·37	6595
0·9036	0·8958			13		3414·85	52,698	7	8	198	7	8	301·0	426·86	6587
0·9025	0·8947	57	65		129	3410·70	52,634	7	8	134	7	8	301·0	426·34	6579
0·9021	0·8943			14	130	3409·15	52,610	7	8	110	7	8	300·5	426·14	6576
0·9008	0·8930			15	131	3404·29	52,535	7	8	35	7	8	300·0	425·54	6567
0·9001	0·8923	58	66		132	3401·63	52,494	7	7	432	7	8	300·0	425·20	6562
0·8994	0·8916			16	133	3398·98	52,453	7	7	390	7	8	299·5	424·87	6557
0·8979	0·8901	59		17		3393·34	52,366	7	7	304	7	8	299·0	424·17	6546
0·8973	0·8895		67		134	3391·07	52,331	7	7	269	7	8	299·0	423·88	6541
0·8966	0·8888			18		3388·41	52,290	7	7	227	7	8	299·0	423·55	6536
0·8956	0·8878	60			135	3384·59	52,231	7	7	169	7	7	298·5	423·07	6529
0·8953	0·8875			19		3383·49	52,214	7	7	151	7	7	298·5	422·94	6527
0·8949	0·8870		68		136	3382·00	52,191	7	7	129	7	7	298·0	422·75	6524
0·8938	0·8859			20	137	3377·79	52,126	7	7	63	7	7	298·0	422·22	6516
0·8932	0·8853	61				3375·52	52,091	7	7	29	7	7	297·5	421·94	6511
0·8925	0·8846		69	21	138	3372·93	52,051	7	6	426	7	7	297·5	421·62	6506
0·8910	0·8831			22	139	3367·22	51,963	7	6	338	7	7	297·0	420·90	6495
0·8908	0·8829	62				3366·45	51,951	7	6	326	7	7	297·0	420·81	6494
0·8900	0·8821		70		140	3363·47	51,905	7	6	280	7	7	296·5	420·43	6488
0·8897	0·8818			23		3362·30	51,887	7	6	262	7	7	296·5	420·29	6486
0·8886	0·8807	63			141	3358·15	51,823	7	6	198	7	6	296·0	419·77	6478
0·8883	0·8804			24		3357·05	51,806	7	6	181	7	6	296·0	419·63	6476
0·8875	0·8796		71		142	3354·00	51,759	7	6	134	7	6	296·0	419·25	6470
0·8869	0·8790			25		3351·74	51,724	7	6	99	7	6	295·5	418·97	6465
0·8863	0·8784	64			143	3349·47	51,689	7	6	64	7	6	295·5	418·68	6461
0·8854	0·8775			26		3346·10	51,637	7	6	12	7	6	295·0	418·26	6455
0·8850	0·8771		72		144	3344·54	51,613	7	5	426	7	6	295·0	418·07	6452
0·8840	0·8761	65		27	145	3340·78	51,555	7	5	368	7	6	294·5	417·60	6444
0·8825	0·8746		73	28	146	3335·08	51,467	7	5	279	7	6	294·0	416·88	6433
0·8816	0·8736	66				3331·71	51,415	7	5	228	7	6	294·0	416·46	6427
0·8811	0·8731			29	147	3329·83	51,386	7	5	198	7	5	293·5	416·23	6423
0·8799	0·8719		74	30	148	3325·30	51,316	7	5	129	7	5	293·0	415·66	6414
0·8793	0·8713	67			149	3323·03	51,281	7	5	94	7	5	293·0	415·38	6410
0·8783	0·8703			31		3319·21	51,222	7	5	34	7	5	292·5	414·90	6403
0·8769	0·8689	68	75	32	150	3313·96	51,141	7	4	391	7	5	292·0	414·25	6393
0·8754	0·8674			33	151	3308·25	51,053	7	4	303	7	5	291·5	413·53	6382
0·8745	0·8665	69	76		152	3304·89	51,001	7	4	251	7	5	291·5	413·11	6375
0·8739	0·8659			34	153	3302·62	50,966	7	4	216	7	4	291·0	412·83	6371
0·8721	0·8641	70	77	35	154	3295·81	50,861	7	4	111	7	4	290·5	411·98	6358

PART VI.—From 70 to 100 per cent. of Absolute Alcohol.

0·8708	0·8628			36	155	3290·89	50,785	7	4	35	7	4	290·0	411·36	6348
0·8696	0·8616	71	78	37		3286·35	50,715	7	3	403	7	4	290·0	410·79	6339
0·8693	0·8613				156	3285·25	50,698	7	3	385	7	4	289·5	410·66	6337
0·8678	0·8598			38	157	3279·55	50,610	7	3	297	7	4	289·0	409·94	6326
0·8672	0·8591	72			158	3277·28	50,575	7	3	263	7	4	289·0	409·66	6322
0·8664	0·8583		79	39		3274·23	50,528	7	3	216	7	3	288·5	409·28	6316
0·8649	0·8568	73			159	3268·59	50,441	7	3	129	7	3	288·0	408·57	6305
0·8646	0·8565			40		3267·43	50,423	7	3	110	7	3	288·0	408·43	6303
0·8639	0·8558		80		160	3264·84	50,383	7	3	71	7	3	288·0	408·10	6298
0·8631	0·8550			41		3261·79	50,336	7	3	23	7	3	287·5	407·72	6292
0·8625	0·8544	74				3259·53	50,301	7	2	426	7	3	287·5	407·44	6288
0·8615	0·8534			42	161	3255·77	50,243	7	2	368	7	3	287·0	406·97	6280
0·8611	0·8530		81		162	3254·21	50,219	7	2	344	7	3	287·0	406·78	6277
0·8603	0·8522	75			163	3251·23	50,173	7	2	298	7	3	286·5	406·40	6272
0·8599	0·8518			43		3249·68	50,149	7	2	274	7	3	286·5	406·21	6269
0·8581	0·8500	76	82	44	164	3242·87	50,044	7	2	169	7	2	286·0	405·36	6255

PART VI.—From 70 to 100 per cent. of Absolute Alcohol.

(Continued.)

Specific Gravity. (Pure water at 15⅝° C. = 60° F. taken as unity.)		Percentage.				Weight of one gallon, at 15⅝° C. = 60° F.						Weight of 40 gallons to the nearest half pound, at 15⅝° C. = 60° F.	Weight of one pint, at 15⅝° C. = 60° F.	
								Avoirdupois Weight.						
											To the nearest ounce.			
At 15⅝° C. = 60° F.	At 25° C. = 77° F.	By weight.	By volume.	Over proof. (Brit. Excise.)	Of proof spirit. (U. S. Revenue.)	In Grammes.	In Grains.	lbs.	ozs.	Grs.	lbs.	ozs.	lbs.	In Grammes.	In Grains.
0·8566	0·8485			45	165	3237·23	49,957	7	2	82	7	2	285·5	404·65	6245
0·8557	0·8476	77	83			3233·80	49,904	7	2	29	7	2	285·0	404·22	6238
0·8550	0·8469			46	166	3231·21	49,864	7	1	426	7	2	285·0	403·90	6233
0·8539	0·8458				167	3227·00	49,799	7	1	361	7	2	284·5	403·38	6225
0·8533	0·8452	78		47		3224·73	49,764	7	1	327	7	2	284·5	403·09	6220
0·8526	0·8444		84		168	3222·14	49,724	7	1	287	7	2	284·0	402·77	6215
0·8516	0·8434			48		3218·31	49,665	7	1	227	7	2	284·0	402·29	6208
0·8508	0·8426	79			169	3215·33	49,619	7	1	182	7	1	283·5	401·92	6202
0·8501	0·8419			49	170	3212·67	49,578	7	1	140	7	1	283·5	401·58	6197
0·8496	0·8414		85			3210·79	49,549	7	1	112	7	1	283·0	401·35	6194
0·8483	0·8401	80		50	171	3205·87	49,473	7	1	36	7	1	282·5	400·73	6184
0·8466	0·8384		86	51	172	3199·46	49,374	7	0	374	7	1	282·0	399·93	6172
0·8459	0·8377	81				3196·80	49,333	7	0	333	7	1	282·0	399·60	6167
0·8450	0·8368			52	173	3193·36	49,280	7	0	280	7	1	281·5	399·17	6160
0·8434	0·8352	82	87	53	174	3187·34	49,187	7	0	187	7	0	281·0	398·42	6148
0·8415	0·8333			54	175	3180·15	49,076	7	0	76	7	0	280·5	397·52	6134
0·8408	0·8326	83	88			3177·49	49,035	7	0	35	7	0	280·0	397·19	6129
0·8396	0·8314			55	176	3172·95	48,965	6	15	402	7	0	280·0	396·62	6121
0·8387	0·8305				177	3169·58	48,913	6	15	350	7	0	279·5	396·20	6114
0·8382	0·8300	84				3167·70	48,884	6	15	322	7	0	279·5	395·96	6110
0·8376	0·8294			56		3165·44	48,849	6	15	286	7	0	279·0	395·68	6106
0·8373	0·8291		89		178	3164·27	48,831	6	15	269	7	0	279·0	395·53	6104
0·8357	0·8275	85		57	179	3158·24	48,738	6	15	176	6	15	278·5	394·78	6092
0·8340	0·8258		90		180	3151·83	48,639	6	15	77	6	15	278·0	393·98	6080
0·8336	0·8254			58		3150·34	48,616	6	15	53	6	15	278·0	393·79	6077
0·8331	0·8249	86				3148·39	48,586	6	15	24	6	15	277·5	393·55	6073
0·8317	0·8235			59	181	3143·14	48,505	6	14	380	6	15	277·0	392·89	6063
0·8305	0·8223	87	91		182	3138·61	48,435	6	14	310	6	15	277·0	392·33	6054
0·8298	0·8216			60		3135·95	48,394	6	14	269	6	15	276·5	391·99	6049
0·8288	0·8206				183	3132·19	48,336	6	14	211	6	14	276·0	391·52	6042
0·8279	0·8197	88		61		3128·76	48,283	6	14	158	6	14	276·0	391·09	6035
0·8272	0·8191		92		184	3126·10	48,242	6	14	117	6	14	275·5	390·76	6030
0·8259	0·8178			62		3121·15	48,166	6	14	41	6	14	275·0	390·14	6021
0·8254	0·8173	89			185	3119·30	48,137	6	14	12	6	14	275·0	389·91	6017
0·8240	0·8159			63		3114·05	48,056	6	13	368	6	14	274·5	389·26	6007
0·8237	0·8156		93		186	3112·88	48,038	6	13	351	6	14	274·5	389·11	6005
0·8228	0·8147	90				3109·51	47,986	6	13	299	6	14	274·0	388·69	5998
0·8221	0·8140			64	187	3106·86	47,945	6	13	257	6	14	274·0	388·36	5993
0·8199	0·8118	91	94	65	188	3098·56	47,817	6	13	130	6	13	273·0	387·32	5977
0·8176	0·8095			66	189	3089·81	47,682	6	12	432	6	13	272·5	386·23	5960
0·8172	0·8091	92				3088·32	47,659	6	12	409	6	13	272·5	386·04	5957
0·8164	0·8083		95		190	3085·28	47,612	6	12	362	6	13	272·0	385·66	5951
0·8156	0·8075			67		3082·30	47,566	6	12	316	6	13	272·0	385·29	5946
0·8145	0·8064	93				3078·15	47,502	6	12	252	6	13	271·5	384·77	5938
0·8139	0·8058				191	3075·88	47,467	6	12	217	6	12	271·0	384·48	5933
0·8134	0·8053			68		3073·94	47,437	6	12	187	6	12	271·0	384·24	5930
0·8125	0·8044		95			3070·57	47,385	6	12	135	6	12	271·0	383·82	5923
0·8118	0·8037	94			192	3067·91	47,344	6	12	94	6	12	270·5	383·49	5918
0·8112	0·8031			69		3065·64	47,309	6	12	59	6	12	270·5	383·20	5914
0·8098	0·8017				193	3060·39	47,228	6	11	415	6	12	270·0	382·55	5903
0·8090	0·8009			70		3057·35	47,181	6	11	368	6	12	269·5	382·17	5898
0·8089	0·8008	95				3056·96	47,175	6	11	363	6	12	269·5	382·12	5897
0·8084	0·8003		97		194	3055·08	47,146	6	11	334	6	12	269·5	381·88	5893
0·8061	0·7980	96			195	3046·33	47,011	6	11	200	6	11	268·5	380·79	5876
0·8041	0·7960		98		196	3038·82	46,895	6	11	83	6	11	268·0	379·85	5862
0·8031	0·7950	97				3035·06	46,837	6	11	25	6	11	267·5	379·38	5855
0·8014	0·7933				197	3028·64	46,738	6	10	363	6	11	267·0	378·58	5842
0·8001	0·7920	98				3023·72	46,662	6	10	287	6	11	266·5	377·96	5833
0·7995	0·7914		99			3021·45	46,627	6	10	252	6	11	266·5	377·68	5828
0·7992	0·7911				198	3020·28	46,609	6	10	234	6	11	266·5	377·53	5826
0·7969	0·7888	99			199	3011·59	46,475	6	10	100	6	10	265·5	376·45	5809
0·7946	0·7865		100		200	3002·92	46,341	6	9	404	6	10	265·0	375·37	5793
0·7938	0·7858	100				2999·87	46,294	6	9	357	6	10	264·5	374·98	5787

Reduction of Apparent to True Specific Gravity (U. S. P. IX)

viz.: $\frac{25°\ C.}{25°\ C.}$ in air to $\frac{25°\ C.}{25°\ C.}$ in vacuum.

Weights of Brass, Sp. gr. 8.4. Barometer 760 mm.

Sp. gr. apparent.	Correction.	Sp. gr. apparent.	Correction.
0.6	+0.000471	1	0.000000
0.7	+0.000353	2	−0.001177
0.8	+0.000235	3	−0.002355
0.9	+0.000118	4	−0.003532
1.0	0.000000	5	−0.004709
1.1	−0.000118	6	−0.005887
1.2	−0.000235	7	−0.007064
1.3	−0.000353	8	−0.008241
1.4	−0.000471	9	−0.009418
1.5	−0.000589	10	−0.010596
1.6	−0.000706	11	−0.011773
1.7	−0.000824	12	−0.012950
1.8	−0.000942	13	−0.014128
1.9	−0.001060	14	−0.015305
2.0	−0.001177	15	−0.016482

Formula for deriving above correction: Subtract algebraically the apparent specific gravity from 1.000 and multiply the remainder by 0.0011773. It is additive for specific gravities below, subtractive for those above, 1.000.

NOTE: The correction for reducing true to apparent specific gravity is found by subtracting algebraically 1.000 from the true specific gravity and multiplying the remainder by the factor 0.0011765. It is subtractive for specific gravities below, additive for those above, 1.000.

Reduction of Apparent Weight in Air to Weight in Vacuum (U. S. P. IX)

Weighings Made with Brass Weights, Temperature 25° C.,* Air One-half Saturated with Moisture,† and Barometer 760 mm.‡

Sp. gr. of object weighed.	Correction in milligrammes for each Gm. of apparent weight.	Sp. gr. of object weighed.	Correction in milligrammes for each Gm. of apparent weight.	Sp. gr. of object weighed.	Correction in milligrammes for each Gm. of apparent weight.
0.60	+1.82	1.25	+0.80	4.5	+0.122
0.62	1.76	1.30	0.77	5	0.096
0.64	1.70	1.35	0.73	6	0.056
0.66	1.64	1.40	0.70	7	0.028
0.68	1.59	1.45	0.67	8	0.007
0.70	+1.54	1.50	+0.65	9	−0.009
0.72	1.50	1.55	0.62	10	0.022
0.74	1.45	1.60	0.60	11	0.034
0.76	1.41	1.65	0.57	12	0.042
0.78	1.37	1.70	0.55	13	0.049
0.80	+1.33	1.75	+0.533	14	−0.056
0.82	1.30	1.80	0.514	15	0.062
0.84	1.26	1.85	0.497	16	0.066
0.86	1.23	1.90	0.480	17	0.071
0.88	1.20	1.95	0.464	18	0.075
0.90	+1.17	2.00	+0.449	19	−0.078
0.92	1.14	2.20	0.395	20	0.081
0.94	1.11	2.40	0.351	21	0.084
0.96	1.09	2.60	0.313	22	0.087
0.98	1.06	2.80	0.281		
1.00	+1.04	3.00	+0.253		
1.05	0.98	3.25	0.222		
1.10	0.93	3.50	0.197		
1.15	0.88	3.75	0.174		
1.20	0.84	4.00	0.154		

* *Temperature correction*, approximate, for temperatures between 15° and 35° C. For each degree (centigrade) 0.37 per cent. of figures in table; additive if below, subtractive if above, 25° C.

† *Humidity correction* varies with temperature; additive if below, subtractive if above, 50 per cent. of saturation. For complete dryness or for full saturation at 15° C., the correction is 0.33 per cent. of figures in the table; at 20° C., 0.44 per cent.; at 25° C., 0.58 per cent.; at 30° C., 0.77 per cent.; and at 35° C., 1.01 per cent.

‡ *Barometer Correction* (important at high altitudes).—For each millimeter 0.132 per cent. of figures in table; additive if above 760 mm., subtractive if below 760 mm.

NOTE: If weights used are of platinum add 0.085 milligramme to, and if of aluminum subtract 0.312 milligramme from, the figures in the table for each gramme.

Weights and Volume Relations.

Specific gravity true $\frac{25°\ C.}{25°\ C.}$	Specific volume.	Weight of 1 U. S. gallon in pounds avoirdupois in air.	Weight of 100 fluid-ounces in ounces avoirdupois.	Weight of 1 fluidounce in grains.	Volume in U. S. gallons of 100 pounds avoirdupois.	Volume in fluidounces of 100 ounces avoirdupois.	Volume in fluidounces of 1000 grains.
0.70	1.4286	5.816	72.70	318.0	17.195	137.56	3.144
0.71	1.4085	5.899	73.74	322.6	16.953	135.62	3.100
0.72	1.3889	5.982	74.78	327.1	16.717	133.73	3.057
0.73	1.3699	6.065	75.82	331.7	16.487	131.90	3.015
0.74	1.3514	6.149	76.86	336.2	16.264	130.11	2.974
0.75	1.3333	6.232	77.90	340.8	16.047	128.38	2.934
0.76	1.3158	6.315	78.94	345.3	15.836	126.69	2.896
0.77	1.2987	6.398	79.98	349.9	15.630	125.04	2.858
0.78	1.2821	6.481	81.02	354.5	15.429	123.43	2.821
0.79	1.2658	6.565	82.06	359.0	15.233	121.87	2.786
0.80	1.2500	6.648	83.10	363.6	15.043	120.34	2.751
0.81	1.2346	6.731	84.14	368.1	14.857	118.85	2.717
0.82	1.2195	6.814	85.18	372.7	14.675	117.40	2.684
0.83	1.2048	6.897	86.22	377.2	14.496	115.99	2.651
0.84	1.1905	6.981	87.26	381.8	14.325	114.60	2.620
0.85	1.1765	7.064	88.30	386.3	14.157	113.25	2.589
0.86	1.1628	7.147	89.34	390.9	13.992	111.93	2.559
0.87	1.1494	7.230	90.38	395.4	13.831	110.65	2.529
0.88	1.1364	7.314	91.42	400.0	13.673	109.39	2.500
0.89	1.1236	7.397	92.46	404.5	13.520	108.16	2.472
0.90	1.1111	7.480	93.50	409.1	13.369	106.95	2.445
0.91	1.0989	7.563	94.54	413.6	13.222	105.78	2.418
0.92	1.0870	7.646	95.58	418.2	13.078	104.62	2.391
0.93	1.0753	7.730	96.62	422.7	12.937	103.50	2.366
0.94	1.0638	7.813	97.66	427.3	12.799	102.40	2.341
0.95	1.0526	7.896	98.70	431.8	12.666	101.32	2.316
0.96	1.0417	7.979	99.74	436.4	12.532	100.26	2.292
0.97	1.0309	8.063	100.78	440.9	12.403	99.23	2.268
0.98	1.0204	8.146	101.82	445.5	12.276	98.21	2.245
0.99	1.0101	8.229	102.86	450.0	12.152	97.22	2.222
1.00	1.0000	8.312	103.90	454.6	12.031	96.24	2.200
1.02	0.9804	8.479	105.98	463.7	11.794	94.36	2.157
1.04	0.9615	8.645	108.06	472.8	11.567	92.54	2.115
1.06	0.9434	8.812	110.14	481.9	11.349	90.79	2.075
1.08	0.9259	8.978	112.22	491.0	11.138	89.11	2.037
1.10	0.9091	9.144	114.31	500.1	10.936	87.49	2.000
1.12	0.8929	9.311	116.39	509.2	10.740	85.92	1.964
1.14	0.8772	9.477	118.47	518.3	10.552	84.41	1.929
1.16	0.8621	9.644	120.55	527.4	10.370	82.96	1.896
1.18	0.8475	9.810	122.63	536.5	10.194	81.55	1.864
1.20	0.8333	9.977	124.71	545.6	10.024	80.19	1.833
1.22	0.8197	10.143	126.79	554.7	9.859	78.87	1.803
1.24	0.8065	10.309	128.87	563.8	9.700	77.60	1.774
1.26	0.7937	10.476	130.95	572.9	9.546	76.37	1.746
1.28	0.7813	10.642	133.03	582.0	9.396	75.17	1.718
1.30	0.7692	10.809	135.11	591.1	9.252	74.01	1.692
1.32	0.7576	10.975	137.19	600.2	9.111	72.89	1.666
1.34	0.7463	11.142	139.27	609.3	8.975	71.80	1.641
1.36	0.7353	11.308	141.35	618.4	8.843	70.75	1.617
1.38	0.7246	11.475	143.43	627.5	8.715	69.72	1.594
1.40	0.7143	11.641	145.51	636.6	8.590	68.72	1.571
1.42	0.7042	11.807	147.59	645.7	8.469	67.75	1.549
1.44	0.6944	11.974	149.67	654 8	8.352	66.81	1.527
1.46	0.6849	12.140	151.75	663.9	8.237	65.90	1.506
1.48	0.6757	12.307	153.83	673.0	8.126	65.01	1.486

Weights and Volume Relations—*Continued.*

Specific gravity true $\frac{25° C.}{25° C.}$	Specific volume.	Weight of 1 U. S. gallon in pounds avoirdupois in air.	Weight of 100 fluid-ounces in ounces avoirdupois.	Weight of 1 fluidounce in grains.	Volume in U. S. gallons of 100 pounds avoirdupois.	Volume in fluidounces of 100 ounces avoirdupois.	Volume in fluidounces of 1000 grains.
1.50	0.6667	12.473	155.92	682.1	8.017	64.13	1.466
1.52	0.6579	12.640	158.00	691.2	7.912	63.29	1.447
1.54	0.6494	12.806	160.08	700.3	7.809	62.47	1.428
1.56	0.6410	12.973	162.16	709.4	7.709	61.67	1.410
1.58	0.6329	13.139	164.24	718.5	7.611	60.89	1.392
1.60	0.6250	13.305	166.32	727.6	7.516	60.13	1.374
1.62	0.6173	13.472	168.40	736.7	7.423	59.38	1.357
1.64	0.6098	13.638	170.48	745.8	7.332	58.66	1.341
1.66	0.6024	13.805	172.56	754.9	7.244	57.95	1.325
1.68	0.5952	13.971	174.64	764.1	7.158	57.2	1.309
1.70	0.5882	14.138	176.72	773.2	7.073	56.59	1.293
1.72	0.5814	14.304	178.80	762.3	6.991	55.93	1.278
1.74	0.5747	14.470	180.88	791.4	6.911	55.29	1.264
1.76	0.5682	14.637	182.96	800.5	6.832	54.66	1.249
1.78	0.5618	14.803	185.04	809.6	6.755	54.04	1.235
1.80	0.5556	14.970	187.12	818.7	6.680	53.44	1.222
1.82	0.5495	15.136	189.20	827.8	6.607	52.85	1.208
1.84	0.5435	15.302	191.28	836.9	6.535	52.28	1.195
1.86	0.5376	15.469	193.36	846.0	6.465	51.72	1.182
1.88	0.5319	15.636	195.44	855.1	6.396	51.17	1.170
1.90	0.5263	15.802	197.53	864.2	6.328	50.63	1.157
1.92	0.5208	15.968	199.61	873.3	6.262	50.10	1.145
1.94	0.5155	16.135	201.69	882.4	6.198	49.58	1.133
1.96	0.5102	16.301	203.77	891.5	6.135	49.08	1.122
1.98	0.5051	16.468	205.85	900.6	6.073	48.58	1.110
2.00	0.5000	16.634	207.93	909.7	6.012	48.09	1.100

PART III

SECTION 11

NATIONAL FORMULARY IV

The National Formulary, 4th edition, is issued by the American Pharmaceutical Association and Part I is here printed in abstract, with the permission of the Council of the Association. Part II of the National Formulary, which provides standards for drugs and chemicals used in N. F. formulas, but not included in the U. S. P., will be found chiefly in Part II of this Dispensatory, although some of the articles, when official also in the British Pharmacopœia, have been considered in Part I of the Dispensatory under the British titles.

The National Formulary was made one of the legal standards for drugs and medicines, under the National Food and Drugs Act of 1906, and has also been recognized by most State laws. It is intended to serve as a guide to pharmacists and physicians for preparations which are not in the United States Pharmacopœia but which are in use in this country.

ACETUM AROMATICUM. N. F.

Aromatic Vinegar [Acet. Arom.]

It contains the volatile oils of lavender, rosemary, juniper, peppermint, cinnamon, lemon and clove, dissolved in alcohol, acetic acid and water, and is used as a stimulating inhalant.

ACETUM OPII. N. F. (U. S. P. VIII)

Vinegar of Opium [Acet. Opii]

The process for this differs from that of the U. S. VIII in that percolation, as well as maceration, is used to extract the opium.

It represents 10 per cent. of opium in diluted acetic acid, and is flavored with myristica. The uses are the same as those of tincture of opium, the *dose* being eight minims (0.5 mil).

AQUA PHENOLATA. N. F.

Phenolated Water [Aq. Phenol. Carbolic Acid Water. Phenoli Soluto, P. I.]

This is a 2 per cent. solution of phenol in distilled water and is used as a lotion, gargle, etc.

CAFFEINÆ SODIO-SALICYLAS. N. F.

Caffeine Sodio-Salicylate [Caff. Sod.-Sal.]

This powder contains equal parts of caffeine and sodium salicylate. It is used for the same purposes as the caffeine sodio-benzoate (see Part I). The *dose* is three grains (0.2 Gm.).

CATAPLASMA KAOLINI. N. F. (U. S. P. VIII)

Cataplasm of Kaolin [Catapl. Kaolin.]

This is a mixture of kaolin, glycerin, boric acid, thymol and antiseptic oils used as a poultice for its emollient and anti-phlogistic properties. The only important difference in this process from that of the U. S. P. VIII is the requirement that the glycerin be rendered anhydrous by heating to 100° C. before mixing with the other ingredients.

CERATUM CAMPHORÆ. N. F. (U. S. P. VIII)

Camphor Cerate [Cerat. Camph.]

This preparation replaces the Ceratum Camphoræ Compositum of the N. F. III, and is composed of 10 per cent. of camphor liniment in a cerate base. The formula is essentially the same as that of the U. S. VIII.

CERATUM PLUMBI SUBACETATIS. N. F. (U. S. P. VIII)

Cerate of Lead Subacetate [Cerat. Plumb. Subacet. Goulard's Cerate]

This well-known cerate contains 20 per cent. of Goulard's extract mixed with a cerate base containing a little camphor. The formula differs from that of the U. S. VIII in substituting white wax for the paraffine. It is used as an astringent and sedative dressing.

CERATUM RESINÆ COMPOSITUM. N. F. (U. S. P. VIII)

Compound Rosin Cerate [Cerat. Resin. Co. Deshler's Salve]

This popular cerate contains rosin, yellow wax, suet, turpentine, and linseed oil. It is used as a stimulating dressing.

CHARTA POTASSII NITRATIS. N. F.

Potassium Nitrate Paper [Chart. Pot. Nit.]

This is made by saturating unsized paper in a strong solution of potassium nitrate and drying. It is used in asthma by burning it and inhaling the smoke.

CHLORAL CAMPHORATUM. N. F.

Camphorated Chloral [Chloral Camph.]

A eutectic mixture of equal parts of hydrated chloral and camphor, used as a local anodyne and counter-irritant.

COLLODIUM IODI. N. F.

Iodine Collodion [Collod. Iodi. Collodium Iodatum, N. F. III]

A five per cent., by weight, solution of iodine in flexible collodion. Used externally as a discutient and antiseptic.

COLLODIUM IODOFORMI. N. F.

Iodoform Collodion [Collod. Iodof. Collodium Iodoformatum, N. F. III]

A five per cent., by weight, solution of iodoform in flexible collodion. Used locally as an antiseptic protective.

COLLODIUM SALICYLICUM COMPOSITUM. N. F.

Compound Salicylic Collodion [Collod. Sal. Co. Corn Collodion, Collodium Salicylatum Compositum, N. F. III]

It contains salicylic acid, extract of cannabis, and flexible collodion. Used in the removal of corns.

COLLODIUM STYPTICUM. N. F. (Replacing U. S. P. VIII)

Styptic Collodion [Collod. Stypt.]

This is a 20 per cent., by weight, solution of tannic acid in flexible collodion. The new N. F. process is an improvement over that of the U. S. P. VIII, which directed only Collodion, not flexible Collodion, and diluted that with 30 per cent. of an alcohol-ether mixture.

It is used as a styptic application to cuts and small wounds.

COLLODIUM TIGLII. N. F.

Croton Oil Collodion [Collod. Tiglii]

A 10 per cent., by weight, solution of croton oil in flexible collodion. Used locally as a counter-irritant and vesicant.

CONFECTIO ROSÆ. N. F. (U. S. P. VIII)

Confection of Rose [Confect. Ros.]

The formula for this preparation is the same as that of the U. S. VIII (see p. 378). It is used principally as a pill excipient or vehicle.

CONFECTIO SENNÆ. N. F. (U. S. P. VIII)

Confection of Senna [Confect. Senn.]

The directions for this confection are the same as those of the U. S. VIII (see p. 378). This is the old *Lenitive Electuary* of bygone days. It contains senna, cassia fistula, tamarind, prune and fig, with sugar and oil of coriander. It is an agreeable lenitive or laxative in a *dose* of sixty grains (4 Gm.).

CORDIALE RUBI FRUCTUS. N. F.

Blackberry Cordial [Cord. Rubi Fruct.]

It contains cinnamon, clove, nutmeg, syrup of blackberry fruit, and diluted alcohol, and is used as a remedy in *diarrhea.*

Dose, two fluidrachms (8 mils).

DECOCTUM SARSAPARILLÆ COMPOSITUM. N. F.

Compound Decoction of Sarsaparilla [Decoc. Sarsap. Co.]

This is the old *Zittmann's decoction* and contains sarsaparilla, 10 per cent., sassafras, guaiac and glycyrrhiza, each, 2 per cent., and mezereum, 1 per cent. It is an alterative in *doses* of four fluidrachms (120 mils).

ELIXIRIA.

Elixirs

The elixirs should be perfectly clear preparations when dispensed. Purified talc or purified siliceous earth is recommended as a filtering medium for clarifying turbid elixirs. They should be made from fresh volatile oils of the finest quality and after making must not be exposed to extremes of temperature, but should be kept in tightly-stoppered bottles at the ordinary room temperature.

ELIXIR AMMONII BROMIDI. N. F.

Elixir of Ammonium Bromide [Elix. Ammon. Brom.]

It is made with ammonium bromide and a diluted and sweetened aromatic elixir. It con-

tains 5 grains of ammonium bromide in 1 fluidrachm of finished elixir.

The *dose* is one fluidrachm (4 mils).

ELIXIR AMMONII VALERATIS. N. F.

Elixir of Ammonium Valerate [Elix. Ammon. Valer. Elixir Ammonii Valerianatis, N. F. III]

This preparation is made with ammonium valerate and chloroform dissolved in aromatic elixir, colored with cudbear and flavored with vanilla. It contains 2 grains of ammonium valerate in 1 fluidrachm of finished elixir.

The *dose* is one fluidrachm (4 mils).

ELIXIR AMYGDALÆ COMPOSITUM. N. F.

Compound Elixir of Almond [Elix. Amygdal. Co.]

This is a new flavoring elixir of very low alcoholic strength, containing oil of bitter almond, vanillin, and orange flower water as the essential ingredients.

ELIXIR ANISI. N. F.

Elixir of Anise [Elix. Anis.]

This is an elixir containing a very low proportion of alcohol. It contains anethol, oil of fennel, spirit of bitter almond, alcohol, syrup and water. Used as a vehicle, also as a carminative for infants.

The *dose* for an infant is fifteen minims (1 mil).

ELIXIR AROMATICUM RUBRUM. N. F.

Red Aromatic Elixir [Elix. Arom. Rub. Red Elixir]

This is the U. S. P. aromatic elixir colored red with cudbear.

ELIXIR AURANTII AMARI. N. F. (To Replace Elixir Curassao, N. F. III)

Elixir of Bitter Orange [Elix. Aurant. Amar.]

This is an improvement upon the former elixir Curaçao. It contains oil of bitter orange, tincture of bitter orange peel, and orange flower water as the flavoring constituents.

ELIXIR BISMUTHI. N. F.

Elixir of Bismuth [Elix. Bismuth.]

This elixir is made from glycerite of bismuth, glycerin, distilled water, and aromatic elixir, and each mil represents the equivalent of 0.016 Gm. of bismuth oxide in the form of a tartrate. This is used as an intestinal astringent, but does not possess the therapeutic virtues of the insoluble bismuth salts.

The *dose* is one fluidrachm (4 mils).

ELIXIR BUCHU. N. F.

Elixir of Buchu [Elix. Buchu]

It contains fluidextract of buchu, alcohol, and aromatic elixir. About 7½ grains of buchu are represented by 1 fluidrachm of finished elixir. It is used as a diuretic.

The *dose* is one fluidrachm (4 mils).

ELIXIR BUCHU COMPOSITUM. N. F.

Compound Elixir of Buchu [Elix. Buchu Co.]

Compound fluidextract of buchu is used instead of the simple fluidextract. About 15 minims of compound fluidextract of buchu are represented in 1 fluidrachm of finished elixir. It is used as a diuretic.

The *dose* is one fluidrachm (4 mils).

ELIXIR BUCHU ET POTASSII ACETATIS. N. F.

Elixir of Buchu and Potassium Acetate [Elix. Buchu et Pot. Acet.]

This elixir contains 5 grains of potassium acetate and the equivalent of 7½ grains of buchu in 1 fluidrachm of finished elixir. It is used as a diuretic.

The *dose* is one fluidrachm (4 mils).

ELIXIR CALCII BROMIDI. N. F.

Elixir of Calcium Bromide [Elix. Calc. Brom.]

This is a solution of calcium bromide in aromatic elixir slightly acidulated with hydrobromic acid. It contains 5 grains of calcium bromide in 1 fluidrachm of finished elixir.

The *dose* is one fluidrachm (4 mils).

ELIXIR CALCII ET SODII GLYCEROPHOSPHATUM. N. F.

Elixir of Calcium and Sodium Glycerophosphates [Elix. Calc. et Sod. Glycerophos. Elixir Glycerophosphatum, N. F. III]

This elixir contains ¾ grain of sodium glycerophosphate and ½ grain calcium glycerophosphate in each fluidrachm.

The *dose* is one fluidrachm (4 mils).

ELIXIR CALCII HYPOPHOSPHITIS. N. F.

Elixir of Calcium Hypophosphite [Elix. Calc. Hypophos.]

This contains 2 grains of calcium hypophosphite in 1 fluidrachm of finished elixir. It is

as useless as the other preparations of the hypophosphites.

The *dose* is two fluidrachms (8 mils).

ELIXIR CALCII LACTOPHOSPHATIS. N. F.

Elixir of Calcium Lactophosphate [Elix. Calc. Lactophos.]

This elixir contains 1 grain of calcium lactate or about 1½ grains of so-called calcium lactophosphate in 1 fluidrachm of finished elixir.

The *dose* is two fluidrachms (8 mils).

ELIXIR CARDAMOMI COMPOSITUM. N. F.

Compound Elixir of Cardamom [Elix. Card. Co.]

This is a new elixir of very low alcoholic strength and pleasantly flavored with cardamom. It is used as a vehicle and flavoring agent.

ELIXIR CASCARÆ SAGRADÆ. N. F. Elixir Rhamni Purshianæ, N. F. III

Elixir of Cascara Sagrada [Elix. Cascar. Sagr.]

This is simply a mixture of equal parts of the aromatic fluidextract of cascara sagrada and aromatic elixir. About 30 grains of cascara sagrada are represented in 1 fluidrachm of the finished elixir.

The *dose* is one fluidrachm (4 mils).

ELIXIR CASCARÆ SAGRADÆ COMPOSITUM. N. F. Elixir Rhamni Purshianæ Compositum, N. F. III

Compound Elixir of Cascara Sagrada [Elix. Cascar. Sagr. Co. Laxative Elixir]

It contains about 7½ grains of cascara to each fluidrachm in addition to small amounts of senna and juglans. It is used as a laxative.

The *dose* is one fluidrachm (4 mils).

ELIXIR CATHARTICUM COMPOSITUM. N. F.

Compound Cathartic Elixir [Elix. Cathart. Co.]

This elixir represents, in each fluidrachm, about 7½ grains of frangula together with small quantities of senna and rhubarb, and is flavored with peppermint and aromatic elixir.

The *dose* is from one to three fluidrachms (4–12 mils).

ELIXIR CINCHONÆ ALKALOIDORUM. N. F. Elixir Cinchonæ, N. F. III

Elixir of Cinchona Alkaloids [Elix. Cinchon. Alk. Elixir Calisaya, Alkaloidal]

This elixir is now made from the alkaloid instead of the bark direct, and is simply a solution of cinchona alkaloids in aromatic elixir colored with cudbear. It contains about 1 grain of quinine sulphate and ½ grain each of cinchonidine and cinchonine sulphates in 1 fluidounce of finished elixir. It is used as a bitter, especially in conjunction with more active drugs.

The *dose* is two fluidrachms (8 mils).

ELIXIR CINCHONÆ ALKALOIDORUM ET FERRI. N. F. Elixir Cinchonæ et Ferri, N. F. III

Elixir of Cinchona Alkaloids and Iron [Elix. Cinchon. et Ferr. Ferrated Elixir of Calisaya, Alkaloidal]

This elixir contains 2 grains of soluble ferric phosphate in 1 fluidrachm of finished elixir. It is used as a chalybeate tonic.

The *dose* is two fluidrachms (8 mils).

ELIXIR CINCHONÆ ALKALOIDORUM ET HYPOPHOSPHITUM. N. F. Elixir Cinchonæ et Hypophosphitum, N. F. III

Elixir of Cinchona Alkaloids and Hypophosphites [Elix. Cinchon. et Hypophos. Elixir of Calisaya, Alkaloidal, with Hypophosphites]

This elixir contains 1 grain each of calcium and sodium hypophosphites in 1 fluidrachm of finished elixir. It is used as a tonic and alterative.

The *dose* is two fluidrachms (8 mils).

ELIXIR CINCHONÆ ALKALOIDORUM, FERRI, BISMUTHI ET STRYCHNINÆ. N. F. Elixir Cinchonæ, Ferri, Bismuthi et Strychninæ, N. F. III

Elixir of Cinchona Alkaloids, Iron, Bismuth and Strychnine [Elix. Cinchon. Ferr. Bism. et Strych. Elixir of Calisaya, Alkaloidal, with Iron, Bismuth, and Strychnine]

This elixir contains 1-100th of a grain of strychnine sulphate, 1 grain of bismuth and sodium tartrate and 2 grains of soluble ferric phosphate in 1 fluidrachm of finished elixir.

The *dose* is one fluidrachm (4 mils).

ELIXIR CINCHONÆ ALKALOIDORUM, FERRI ET BISMUTHI. N. F. Elixir Cinchonæ, Ferri et Bismuthi, N. F. III

Elixir of Cinchona Alkaloids, Iron, and Bismuth [Elix. Cinchon. Ferr. et Bism. Elixir of Calisaya, Alkaloidal, with Iron and Bismuth]

This preparation contains 1 grain of bismuth and sodium tartrate, about 1¾ grains of soluble ferric phosphate, in 1 fluidrachm of finished elixir.

The *dose* is two fluidrachms (8 mils).

ELIXIR CINCHONÆ ALKALOIDORUM, FERRI ET CALCII LACTOPHOSPHATIS. N. F. Elixir Cinchonæ, Ferri et Calcii Lactophosphatis, N. F. III

Elixir of Cinchona Alkaloids, Iron and Calcium Lactophosphate [Elix. Cinchon. Ferr. et Calc. Lactophos. Elixir of Calisaya, Iron and Lactophosphate of Lime]

This preparation contains ½ grain of calcium lactate (equivalent to about ¾ grain of the so-called calcium lactophosphate) and about 1 grain of soluble ferric phosphate in each fluidrachm.

The *dose* is two fluidrachms (8 mils).

ELIXIR CINCHONÆ ALKALOIDORUM, FERRI ET PEPSINI. N. F. Elixir Cinchonæ, Ferri et Pepsini, N. F. III

Elixir of Cinchona Alkaloids, Iron and Pepsin [Elix. Cinchon. Ferr. et Pepsin. Elixir of Calisaya, Alkaloidal, with Iron and Pepsin]

This preparation contains 1 grain of pepsin and about 1½ grains of soluble ferric phosphate in 1 fluidrachm of finished elixir.

The *dose* is two fluidrachms (8 mils).

ELIXIR CINCHONÆ ALKALOIDORUM, FERRI ET STRYCHNINÆ. N. F. Elixir Cinchonæ, Ferri et Strychninæ, N. F. III

Elixir of Cinchona Alkaloids, Iron and Strychnine [Elix. Cinchon. Ferr. et Strych. Elixir of Calisaya, Alkaloidal, with Iron and Strychnine]

This elixir contains 1-100th of a grain of strychnine sulphate and 2 grains of soluble ferric phosphate in 1 fluidrachm of finished elixir, and is used as a bitter tonic.

The *dose* is one fluidrachm (4 mils).

ELIXIR CORYDALIS COMPOSITUM. N. F.

Compound Elixir of Corydalis [Elix. Coryd. Co.]

This elixir contains about 3 grains of potassium iodide in 1 fluidrachm of finished elixir, with small quantities of the fluidextracts of corydalis, stillingia, xanthoxylum and blue flag.

The *dose* is one fluidrachm (4 mils).

ELIXIR ERIODICTYI AROMATICUM. N. F.

Aromatic Elixir of Eriodictyon [Elix. Eriodict. Arom. Aromatic Elixir of Yerba Santa. Elixir Corrigens]

This elixir is made from fluidextract of eriodictyon, syrup and compound elixir of taraxacum. It is used chiefly as a vehicle for disguising the taste of quinine sulphate and other bitter substances.

The *dose* is one fluidrachm (4 mils).

ELIXIR FERRI HYPOPHOSPHITIS. N. F.

Elixir of Ferric Hypophosphite [Elixir. Ferr. Hypophos.]

This elixir contains 1 grain of iron hypophosphite in 1 fluidrachm of finished elixir. It is used as an alterative and chalybeate tonic.

The *dose* is one fluidrachm (4 mils).

ELIXIR FERRI LACTATIS. N. F.

Elixir of Iron Lactate [Elix. Ferr. Lact.]

This elixir contains 1 grain of lactate of iron and 3 grains of potassium citrate in 1 fluidrachm of finished elixir.

The *dose* is one fluidrachm (4 mils).

ELIXIR FERRI PHOSPHATIS. N. F.

Elixir of Ferric Phosphate [Elix. Ferr. Phos.]

This elixir contains 2 grains of soluble ferric phosphate in 1 fluidrachm of the finished elixir.

The *dose* is one fluidrachm (4 mils).

ELIXIR FERRI PYROPHOSPHATIS. N. F.

Elixir of Ferric Pyrophosphate [Elix. Ferr. Pyrophos. Elixir of Pyrophosphate of Iron]

This elixir contains 2 grains of soluble ferric pyrophosphate in 1 fluidrachm of finished elixir. It is used as a chalybeate tonic.

The *dose* is one fluidrachm (4 mils).

ELIXIR FERRI PYROPHOSPHATIS, QUININÆ ET STRYCHNINÆ. N. F.

Elixir of Ferric Pyrophosphate, Quinine and Strychnine [Elix. Ferr. Pyrophos. Quin. et Strych.]

This elixir differs from the formerly official elixir of iron, quinine and strychnine phosphates in containing soluble ferric pyrophosphate instead of phosphate, while the quinine in the official elixir is replaced by quinine sulphate. It contains 1-128th grain of strychnine, ½ grain of quinine sulphate, and 2 grains of soluble ferric pyrophosphate in 1 fluidrachm of finished elixir.

The *dose* is one fluidrachm (4 mils).

ELIXIR FERRI, QUININÆ ET STRYCHNINÆ. N. F.

Elixir of Iron, Quinine and Strychnine [Elix. Ferr. Quin. et Strych.]

This elixir contains about 1 grain of ferric chloride, ½ grain quinine hydrochloride, and 1-100th grain of strychnine sulphate in 1 fluidrachm of finished elixir. It is used as a chalybeate tonic.

The *dose* is one fluidrachm (4 mils).

ELIXIR FORMATUM. N. F.

Elixir of Formates [Elix. Format.]

This is a new elixir which contains about 3 grains each of potassium and sodium formates in each fluidrachm. It is used as a diuretic but is of very doubtful service.

The *dose* is two fluidrachms (8 mils).

ELIXIR FORMATUM COMPOSITUM. N. F.

Compound Elixir of Formates [Elix. Format. Co.]

This is another new elixir containing the formates of lithium, sodium, magnesium, and strontium, with quinine. Its utility is very doubtful, to say the least.

The *dose* is two fluidrachms (8 mils).

ELIXIR GENTIANÆ. N. F.

Elixir of Gentian [Elix. Gent.]

It is made from fluidextract of gentian, compound, and is flavored with compound spirit of cardamom, but instead of being detannated by the ferric hydroxide process, compatibility with iron is achieved by the use of sodium citrate as an ingredient. It contains too small an amount of gentian to be therapeutically efficient. It is, however, often of service as a vehicle.

The *dose* is one fluidrachm (4 mils).

ELIXIR GENTIANÆ ET FERRI. N. F. Elixir Gentianæ cum Tinctura Ferri Chloridi, N. F. III

Elixir of Gentian and Iron [Elix. Gent. et Ferr. Elixir of Gentian with Tincture of Ferric Citro-Chloride]

Tincture of Citro-chloride of Iron, N. F., is used in this preparation along with the simple elixir of gentian. It represents ¾ of a grain of ferric chloride and nearly 2 grains of gentian in 1 fluidrachm. It is used as a bitter tonic.

The *dose* is one fluidrachm (4 mils).

ELIXIR GENTIANÆ ET FERRI PHOSPHATIS. N. F.

Elixir of Gentian and Ferric Phosphate [Elix. Gent. et Ferr. Phosph. Elixir Gentianæ Ferratum]

This elixir represents 1 grain of soluble ferric phosphate and about 2 grains of gentian in 1 fluidrachm of the finished elixir. It is used as a chalybeate and tonic.

The *dose* is one fluidrachm (4 mils).

ELIXIR GENTIANÆ GLYCERINATUM. N. F.

Glycerinated Elixir of Gentian [Elix. Gent. Glycerin.]

The formula for this tonic elixir has been materially changed as to flavor and sweetening. Saccharin is no longer used. It contains small amounts of gentian and taraxacum in a sweetened and flavored sherry wine. The last is its most active ingredient.

The *dose* is two fluidrachms (8 mils).

ELIXIR GLYCEROPHOSPHATUM COMPOSITUM. N. F.

Compound Elixir of Glycerophosphates [Elix. Glycerophos. Co. Compound Solution of Glycerophosphates]

This new elixir contains the glycerophosphates of sodium, calcium, iron, manganese, quinine, and strychnine. It represents about 2½ grains of combined glycerophosphates, 1/100 grain of strychnine and 1/6 grain of quinine in each fluidrachm.

The *dose* is two fluidrachms (8 mils).

ELIXIR GLYCYRRHIZÆ AQUOSUM. N. F.

Aqueous Elixir of Glycyrrhiza [Elix. Glycyrrh. Aq. Aqueous Elixir of Licorice]

This is a new non-alcoholic flavoring elixir containing fluidextract of licorice, compound spirit of cardamom, and orange flower water as the principal ingredients.

The *dose* is two fluidrachms (8 mils).

ELIXIR GLYCYRRHIZÆ AROMATICUM. N. F.

Aromatic Elixir of Glycyrrhiza [Elix. Glycyrrh. Arom. Aromatic Elixir of Licorice]

This elixir contains fluidextract of glycyrrhiza, oils of cloves, cinnamon, myristica and fennel, with aromatic elixir. It is used as a vehicle.

The *dose* is two fluidrachms (8 mils).

ELIXIR GUARANÆ. N. F.

Elixir of Guarana [Elix. Guar.]

This elixir is made from fluidextract of guarana, aromatic elixir and compound elixir of taraxacum. About 12 grains of guarana are represented in 1 fluidrachm of finished elixir.

The *dose* is one fluidrachm (4 mils).

ELIXIR HUMULI. N. F.

Elixir of Hops [Elix. Humul.]

This elixir is made from fluidextract of hops, tincture of vanilla, compound elixir of taraxa-

cum and aromatic elixir. About 7½ grains of hops are represented in 1 fluidrachm of finished elixir. It is used as a mild sedative.

The *dose* is two fluidrachms (8 mils).

ELIXIR HYPOPHOSPHITUM. N. F.

Elixir of Hypophosphites [Elix. Hypophos.]

This elixir contains 3 grains of calcium hypophosphite and 1 grain each of sodium and potassium hypophosphites in 1 fluidrachm of the finished preparation, and is used as an alterative.

The *dose* is two fluidrachms (8 mils).

ELIXIR HYPOPHOSPHITUM ET FERRI. N F. Elixir Hypophosphitum cum Ferro, N. F. III

Elixir of Hypophosphites and Iron [Elix. Hypophos. et Ferr.]

This elixir contains ½ grain each of potassium and ferrous hypophosphites and 1 grain each of calcium and sodium hypophosphites in 1 fluidrachm of finished elixir.

The *dose* is two fluidrachms (8 mils).

ELIXIR LITHII BROMIDI. N. F.

Elixir of Lithium Bromide [Elix. Lith. Brom.]

This elixir contains 5 grains of lithium bromide in 1 fluidrachm of finished preparation.

The *dose* is two fluidrachms (8 mils).

ELIXIR LITHII CITRATIS. N. F.

Elixir of Lithium Citrate [Elix. Lith. Cit.]

This elixir contains 5 grains of lithium citrate in 1 fluidrachm of finished preparation, and is used in the treatment of *gout* and *rheumatism,* but is more powerful for harm than good because of the alcohol and sugar it contains.

The *dose* is two fluidrachms (8 mils).

ELIXIR LITHII SALICYLATIS. N. F.

Elixir of Lithium Salicylate [Elix. Lith. Sal.]

This elixir contains 5 grains of lithium salicylate in 1 fluidrachm of finished preparation.

The *dose* is two fluidrachms (8 mils).

ELIXIR PEPSINI. N. F.

Elixir of Pepsin [Elix. Pepsin.]

This elixir is made from the glycerite of pepsin, hydrochloric acid and aromatic elixir. It represents about 1 grain of pepsin in 1 fluidrachm of finished preparation. It is very questionable whether the pepsin can retain its enzymic activity in the presence of so much alcohol as is in this elixir.

The *dose* is two fluidrachms (8 mils).

ELIXIR PEPSINI, BISMUTHI ET STRYCHNINÆ. N. F.

Elixir of Pepsin, Bismuth and Strychnine [Elix. Pepsin. Bism. et Strych.]

This elixir contains 1-100th of a grain of strychnine, ½ grain of pepsin and 2 grains of bismuth and sodium tartrate in 1 fluidrachm of finished preparation. It is an irrational combination.

The *dose* is one fluidrachm (4 mils).

ELIXIR PEPSINI ET BISMUTHI. N. F.

Elixir of Pepsin and Bismuth [Elix. Pepsin. et Bism.]

This elixir contains about ½ grain of pepsin and 2 grains of bismuth and sodium tartrate in 1 fluidrachm of finished preparation.

The *dose* is two fluidrachms (8 mils).

ELIXIR PEPSINI ET FERRI. N. F.

Elixir of Pepsin and Iron [Elix. Pepsin. et Ferr.]

This elixir is made from the tincture of ferric citro-chloride and elixir of pepsin. It contains 2 grains of ferric chloride and nearly 1 grain of pepsin in one fluidrachm of the finished preparation. It is believed by some that the pepsin renders the iron more acceptable to the stomach.

The *dose* is two fluidrachms (8 mils).

ELIXIR PEPSINI ET RENNINI COMPOSITUM. N. F. Essentia Pepsini, N. F. III

Compound Elixir of Pepsin and Rennin [Elix. Pepsin. et Rennin. Co.]

This elixir contains pepsin, rennin (an enzyme from calves' rennets), lactic acid, tincture of sweet orange peel, glycerin, alcohol, syrup, white wine and water. It is used as an aid to digestion.

The *dose* is two fluidrachms (8 mils).

ELIXIR PHOSPHORI. N. F.

Elixir of Phosphorus [Elix. Phosphor.]

This elixir contains one sixty-fourth of a grain of phosphorus in 1 fluidrachm of the finished preparation, and is flavored with compound spirit of orange and oil of anise. It affords an elegant and efficacious mode of exhibiting this remedy.

The *dose* is one fluidrachm (4 mils).

ELIXIR PHOSPHORI ET NUCIS VOMICÆ. N. F.

Elixir of Phosphorus and Nux Vomica [Elix. Phosphor. et Nuc. Vom.]

About 2 minims of tincture of nux vomica and about 1-64th of a grain of phosphorus are represented in 1 fluidrachm of the finished elixir.

The *dose* is one fluidrachm (4 mils).

ELIXIR POTASSII ACETATIS. N. F.

Elixir of Potassium Acetate [Elix. Pot. Acet.]

This elixir contains about 5 grains of potassium acetate in 1 fluidrachm of aromatic elixir. This proportion is so small that the preparation is therapeutically useless.

The *dose* is four fluidrachms (15 mils).

ELIXIR POTASSII ACETATIS ET JUNIPERI. N. F.

Elixir of Potassium Acetate and Juniper [Elix. Pot. Acet. et Junip.]

This elixir is made from potassium acetate, fluidextract of juniper, and aromatic elixir, and 5 grains of potassium acetate and 7½ grains of juniper are represented in 1 fluidrachm of the finished preparation. It is used as a diaphoretic.

The *dose* is four fluidrachms (15 mils).

ELIXIR POTASSII BROMIDI. N. F.

Elixir of Potassium Bromide [Elix. Pot. Brom.]

This elixir contains about 10 grains of potassium bromide in 1 fluidrachm of the finished preparation, and is used as a nerve sedative.

The *dose* is two fluidrachms (8 mils).

ELIXIR QUININÆ VALERATIS ET STRYCHNINÆ. N. F. Elixir Quininæ Valerianatis et Strychninæ, N. F. III

Elixir of Quinine Valerate and Strychnine [Elix. Quin. Valer. et Strych.]

This elixir is made from quinine valerate, strychnine sulphate, compound tincture of cudbear, and aromatic elixir, and contains 1 grain of quinine valerate and 1-100th of a grain of strychnine sulphate in 1 fluidrachm of finished preparation. It is used as a tonic and sedative in nervous affections.

The *dose* is one fluidrachm (4 mils).

ELIXIR RUBI COMPOSITUM. N. F.

Compound Elixir of Blackberry [Elix. Rubi Co.]

This elixir contains blackberry juice and blackberry root, galls, cinnamon, cloves, mace and ginger, with syrup, glycerin and diluted alcohol. It is used in the treatment of *diarrhea.*

The *dose* is four fluidrachms (15 mils).

ELIXIR SODII BROMIDI. N. F.

Elixir of Sodium Bromide [Elix. Sod. Brom.]

About 10 grains of sodium bromide are represented in 1 fluidrachm of finished elixir.

The *dose* is two fluidrachms (8 mils).

ELIXIR SODII HYPOPHOSPHITIS. N. F.

Elixir of Sodium Hypophosphite [Elix. Sod. Hypophos.]

Two grains of sodium hypophosphite are represented in 1 fluidrachm of the finished elixir.

The *dose* is one fluidrachm (4 mils).

ELIXIR SODII SALICYLATIS. N. F.

Elixir of Sodium Salicylate [Elix. Sod. Sal.]

Five grains of sodium salicylate are represented in 1 fluidrachm of the finished elixir. It is used in the treatment of *rheumatism.*

The *dose* is one fluidrachm (4 mils).

ELIXIR SODII SALICYLATIS COMPOSITUM. N. F.

Compound Elixir of Sodium Salicylate [Elix. Sod. Sal. Co.]

This new elixir contains in each fluidrachm about five grains of sodium salicylate, and one grain of potassium iodide with fluidextracts of gelsemium and cimicifuga. Such polypharmaceutical mixtures had better been left to extemporaneous prescription.

The *dose* is one fluidrachm (4 mils).

ELIXIR STRYCHNINÆ VALERATIS. N. F. Elixir Strychninæ Valerianatis, N. F. III

Elixir of Strychnine Valerate [Elix. Strych. Valer.]

It is made from strychnine valerate, acetic acid, tincture of vanilla, compound tincture of cudbear and aromatic elixir, and contains 1-100th grain of strychnine valerate in 1 fluidrachm of the finished elixir. It is used as a nervine.

The *dose* is one fluidrachm (4 mils).

ELIXIR TARAXACI COMPOSITUM. N. F.

Compound Elixir of Taraxacum [Elix. Tarax. Co.]

This elixir is made from fluidextracts of taraxacum, wild cherry and glycyrrhiza, with the tinctures of sweet orange peel and cinnamon, compound tincture of cardamom aromatic

elixir, and is used mainly as a vehicle to cover the taste of bitter substances.

The *dose* is two fluidrachms (8 mils).

ELIXIR TERPINI HYDRATIS. N. F.

Elixir of Terpin Hydrate [Elix. Terpin. Hyd.]

This elixir contains terpin hydrate, tincture of sweet orange peel, spirit of bitter almond, alcohol, glycerin, and syrup. About 1 grain of terpin hydrate is contained in 1 fluidrachm of the finished preparation.

The *dose* is one fluidrachm (4 mils).

ELIXIR TERPINI HYDRATIS ET CODEINÆ. N. F. Elixir Terpini Hydratis cum Codeina, N. F. III

Elixir of Terpin Hydrate and Codeine [Elix. Terpin. Hyd. et Codein.]

This elixir contains about 1 grain of terpin hydrate and about ⅛ grain of codeine in 1 fluidrachm of the finished preparation. It is a much misused mixture.

The *dose* is one fluidrachm (4 mils).

ELIXIR TERPINI HYDRATIS ET DIACETYLMORPHINÆ. N. F. Elixir Terpini Hydratis cum Heroina, N. F. III

Elixir of Terpin Hydrate and Diacetylmorphine [Elix. Terpin. Hyd. et Diacetylmorph.]

This elixir contains 1 grain of terpin hydrate and 1-64th of a grain of diacetylmorphine hydrochloride in 1 fluidrachm of the finished preparation.

The *dose* is one fluidrachm (4 mils).

ELIXIR TRIUM BROMIDORUM. N. F.

Elixir of Three Bromides [Elix. Tri. Brom.]

This is a new elixir containing in each fluidrachm five grains each of ammonium, potassium and sodium bromides, compound elixir of almond colored with cudbear, being used as the vehicle.

The *dose* is one fluidrachm (4 mils).

ELIXIR VANILLINI COMPOSITUM. N. F.

Compound Elixir of Vanillin [Elix. Vanil. Co.]

This new elixir, intended for a palatable vehicle, contains compound spirit of vanillin and is colored with tincture of caramel.

ELIXIR VIBURNI OPULI COMPOSITUM. N. F.

Compound Elixir of Viburnum Opulus [Elix. Viburn. Opul. Co.]

About 5 grains each of viburnum opulus and aletris and 10 grains of trillium with compound elixir of taraxacum are represented in 1 fluidrachm of the finished elixir. It is probably destitute of therapeutic virtues.

The *dose* is one fluidrachm (4 mils).

ELIXIR VIBURNI PRUNIFOLII. N. F.

Elixir of Viburnum Prunifolium [Elix. Viburn. Prun. Elixir of Black Haw]

This elixir is made from fluidextract of viburnum prunifolium, compound tincture of cardamom, and aromatic elixir, and contains about 7½ grains of viburnum prunifolium in 1 fluidrachm of the finished preparation.

The *dose* is one fluidrachm (4 mils).

ELIXIR ZINCI VALERATIS. N. F. Elixir Zinci Valerianatis, N. F. III

Elixir of Zinc Valerate [Elix. Zinc. Valer.]

This elixir is made from zinc valerate, citric acid, stronger ammonia water, alcohol, spirit of bitter almond, compound tincture of cudbear, and aromatic elixir. About 1 grain of zinc valerate is represented in 1 fluidrachm of the finished elixir. It is used as a nervine.

The *dose* is one fluidrachm (4 mils).

EMPLASTRUM FUSCUM CAMPHORATUM. N. F.

Camphorated Brown Plaster [Emp. Fusc. Camph. Camphorated Mother Plaster]

This plaster is made from red oxide of lead, olive oil, yellow wax and camphor, and is used as a protective in inflamed conditions of the skin or subcutaneous tissues.

EMPLASTRUM SAPONIS. N. F. (U. S. P. VIII)

Soap Plaster [Emp. Sapon.]

This is merely lead plaster with 10 per cent. of dried soap incorporated with it by the aid of a little water. The formula of the U. S. VIII is used, unchanged.

EMULSA. N. F.

Emulsions

In the National Formulary preference is given to acacia as the emulsifying agent, although other emulsifying agents are not ignored, as exemplified in the preparation of the numerous emulsions of cod liver oil. It is recommended that emulsions, being prone to deteriorate on standing, should be freshly prepared when needed. The following flavoring agents are suggested as being acceptable for cod-liver oil, the choice being left to the prescriber:

a. Oil of Betula ..... 4 mils
b. Oil of Betula ..... 2 mils
   Oil of Sassafras ..... 2 mils
c. Compound Spirit of Orange.... 1.5 mils
d. Oil of Betula ..... 2.00 mils
   Oil of Bitter Almond ..... 0.25 mil
   Oil of Coriander ..... 0.25 mil
e. Oil of Betula ..... 1.50 mils
   Oil of Sassafras ..... 1.50 mils
   Oil of Bitter Almond ..... 0.25 mil
f. Oil of Betula ..... 2.5 mils
   Oil of Bitter Almond ..... 2.5 mils

EMULSUM OLEI MORRHUÆ CUM CALCII LACTOPHOSPHATE. N. F.

Emulsion of Cod Liver Oil with Calcium Lactophosphate [Emul. Ol. Morrh. c. Calc. Lactophos.]

This emulsion contains 50 per cent. of cod liver oil, with calcium lactate, phosphoric acid, syrup of tolu and flavoring.

The *dose* is four fluidrachms (15 mils).

EMULSUM OLEI MORRHUÆ CUM CALCII PHOSPHATE. N. F.

Emulsion of Cod Liver Oil with Calcium Phosphate [Emul. Ol. Morrh. c. Calc. Phos. Emulsion of Cod Liver Oil with Phosphate of Lime]

This emulsion contains 50 per cent. of cod liver oil, with calcium phosphate, syrup of tolu and flavoring. It is used as an alterative.

The *dose* is four fluidrachms (15 mils).

EMULSUM OLEI MORRHUÆ CUM HYPOPHOSPHITIBUS. N. F. (U. S. P. VIII)

Emulsion of Cod Liver Oil with Hypophosphites [Emul. Ol. Morrh. c. Hypophos.]

This emulsion contains 50 per cent. of cod liver oil. Each dessertspoonful contains 1½ grains of calcium hypophosphite and ¾ grain each, of sodium and potassium hypophosphites with sufficient flavoring.

The *dose* is two fluidrachms (8 mils).

EMULSUM OLEI MORRHUÆ CUM MALTO. N. F.

Emulsion of Cod Liver Oil with Malt [Emul. Ol. Morrh. c. Malt.]

This emulsion contains 30 per cent. of cod liver oil with about 55 per cent. of extract of malt. It affords one of the most acceptable preparations of cod liver oil.

The *dose* is four fluidrachms (15 mils).

EMULSUM OLEI MORRHUÆ CUM PRUNO VIRGINIANA. N. F.

Emulsion of Cod Liver Oil with Wild Cherry [Emul. Ol. Morrh. c. Prun. Virg.]

This emulsion contains 50 per cent. of cod liver oil with fluidextract of wild cherry, syrup of tolu and flavoring. It is used as an alterative.

The *dose* is four fluidrachms (15 mils).

EMULSUM OLEI MORRHUÆ CUM VITELLO. N. F.

Emulsion of Cod Liver Oil with Egg [Emul. Ol. Morrh. c. Vitel.]

This emulsion contains 50 per cent. cod liver oil with glycerite of yolk of egg, syrup of tolu and flavoring. It is used as a tonic.

The *dose* is four fluidrachms (15 mils).

EMULSUM OLEI RICINI. N. F.

Emulsion of Castor Oil [Emul. Ol. Ricin.]

This emulsion contains 35 per cent. of castor oil, with tincture of vanilla, syrup and water. It is used as a cathartic.

The *dose* is one and one-half fluidounces (45 mils).

EMULSUM PETROLATI. N. F. Emulsum Petrolei, N. F. III

Emulsion of Petrolatum [Emul. Petrolat.]

This emulsion contains about 22.5 per cent. each, of white petrolatum, and expressed oil of almond, with acacia, tragacanth and syrup, tincture of lemon peel and water.

The *dose* is four fluidrachms (15 mils).

EXTRACTA. N. F.

Extracts

Pilular Extracts are stated to be solid or semi-solid products prepared by exhausting the powdered drugs with the proper solvents and carefully evaporating these solutions to the desired consistence. These extracts represent in a concentrated and relatively uniform condition, the useful constituents of the drug in a stable form suitable for medication. They are used extensively in pill masses, and are to be stored in tightly covered glass or porcelain jars.

Powdered Extracts are in dry, fine powders. They are often preferred to pilular extracts for general use, because they can be more accurately weighed, easily dispensed and can be preserved in tightly-stoppered bottles. (See also p. 440.)

For extracts that can be reliably assayed, alkaloidal standards have been adopted and assay methods are directed to determine their strength, and to provide for standardization.

EXTRACTUM ALOES. N. F. (U. S. P. VIII)

Extract of Aloes [Ext. Aloes. Powdered Extract of Aloes]

This extract differs from that of the U. S. VIII in that it is so made that one gramme

of the extract represents two grammes of aloes and also in its powder form. It is prepared by exhausting powdered aloes with boiling water, reducing the volume, by evaporation, to the proper consistence and using starch as the diluent.

The *dose* is two grains (0.125 Gm.).

EXTRACTUM CINCHONÆ. N. F.

Extract of Cinchona [Ext. Cinchon.]

Extract of cinchona yields not less than 22 per cent. nor more than 26 per cent. of the combined alkaloids of cinchona. It is prepared by exhausting the powdered cinchona with a menstruum of water and alcohol, evaporating the percolate to the proper consistence and after estimating the alkaloidal content, diluting to the standard strength with glucose. An assay is provided.

The *dose* is four grains (0.25 Gm.).

EXTRACTUM CONII. N. F.

Extract of Conium [Ext. Conii.]

Extract of conium yields not less than 1.8 per cent. nor more than 2.2 per cent. of coniine. This extract is prepared in the same manner as the preceding extract except that a small quantity of diluted hydrochloric acid is added previous to the evaporation of the percolate. An assay is provided.

The *dose* is one-half grain (0.03 Gm.).

EXTRACTUM ERGOTÆ AQUOSUM. N. F.

Aqueous Extract of Ergot [Ext. Ergot. Aq. Ergotin. Extractum Secalis Cornuti, P. I.]

This extract is prepared by percolating the powdered ergot, using chloroform water as menstruum, reducing to proper consistency by means of careful heat, and adding an equal weight of alcohol, and after allowing it to stand for three days, it is then filtered and the filtrate reduced to a pilular consistence. For reasons pointed out elsewhere (see *Ergota*, Part I) it does not fully represent the therapeutic virtues of ergot.

The *dose* is three grains (0.2 Gm.).

EXTRACTUM EUONYMI. N. F. (U. S. P. VIII)

Extract of Euonymus [Ext. Euonymi. Powdered Extract of Euonymus]

One gramme of the extract represents four grammes of euonymus. It is prepared by exhausting the powdered drug with 80 per cent. alcohol, evaporating to dryness, and diluting with starch. This process differs in several particulars from that formerly official.

CAUTION.—It has been stated that the absorption of euonymus in the gastro-intestinal tract is uncertain and irregular. To avoid an accumulation of the drug or toxic action, the physician should carefully guard the dosage and determine in each case the tolerance of the patient.

The *dose* is two grains (0.125 Gm.).

EXTRACTUM FERRI POMATUM. N. F.

Ferrated Extract of Apples [Ext. Ferr. Pomat. Ferri Malas Crudus. Crude Malate of Iron]

This extract is made from iron wire, ripe sour apples and water, and is used as a chalybeate.

The *dose* is ten grains (0.65 Gm.).

EXTRACTUM HÆMATOXYLI. N. F. (U. S. P. VIII)

Extract of Hematoxylon [Ext. Hæmatox.]

This extract is prepared by exhausting the rasped drug with boiling water and evaporating the extract to dryness precisely as in the U. S. VIII.

The *dose* is fifteen grains (1 Gm.).

EXTRACTUM IGNATIÆ. N. F.

Extract of Ignatia [Ext. Ignat. Powdered Extract of Ignatia]

Extract of ignatia yields not less than 5.4 per cent. nor more than 6.6 per cent. of the combined alkaloids of ignatia. It is prepared by exhausting the powdered drug with 75 per cent. alcohol, evaporating to dryness, weighing, and assaying at this stage, and finally diluting to the proper standard with starch.

The *dose* is one-half grain (0.03 Gm.).

EXTRACTUM JALAPÆ. N. F.

Extract of Jalap [Ext. Jalap.]

This pilular extract is prepared by exhausting the jalap with alcohol and evaporating to a pilular consistence.

The *dose* is fifteen grains (1 Gm.).

EXTRACTUM KRAMERIÆ. N. F. (U. S. P. VIII)

Extract of Krameria [Ext. Kramer. Powdered Extract of Krameria]

One gramme of the extract represents four grammes of krameria. It is prepared by exhausting the powdered drug with cold water. The percolate is then heated to boiling, strained, and the strained liquid evaporated to dryness and sufficient dried starch added as diluent.

The *dose* is eight grains (0.5 Gm.).

EXTRACTUM LEPTANDRÆ. N. F. (U. S. P. VIII)

Extract of Leptandra [Ext. Leptand. Powdered Extract of Leptandra]

One gramme of the extract represents four grammes of leptandra. It is prepared by exhausting the drug with a menstruum of 75 per cent. alcohol, evaporating the percolate to dryness and diluting with dried starch.

The *dose* is four grains (0.25 Gm.).

EXTRACTUM PODOPHYLLI. N. F.

Extract of Podophyllum [Ext. Podophyl.]

This extract is prepared by exhausting the powdered drug with 80 per cent. alcohol and evaporating to a pilular consistence.

The *dose* is one-fourth grain (0.015 Gm.).

EXTRACTUM QUASSIÆ. N. F. (U. S. P. VIII)

Extract of Quassia [Ext. Quas. Powdered Extract of Quassia]

One gramme of the extract represents ten grammes of quassia. Water is used as a menstruum in the preparation of this extract. The aqueous percolate is reduced to three-fourths of its bulk by boiling, strained, and then evaporated to dryness, powdered, and diluted to the proper weight with dried starch.

The *dose* is one grain (0.06 Gm.).

FERRI OXIDUM SACCHARATUM. N. F.

Saccharated Ferric Oxide [Ferr. Oxid. Sacch. Soluble Ferric Oxide. Ferrum Oxydatum Saccharatum. Eisenzucker]

Saccharated ferric oxide contains the equivalent of not less than 2.8 per cent. of Fe. In the preparation of this product, freshly precipitated ferric hydroxide is dissolved in a heavy sugar syrup by the addition of a small quantity of sodium hydrate. This solution is then evaporated on a water bath and enough sugar added to bring it to the desired weight. An assay process is given.

FLUIDEXTRACTA. N. F.

Fluidextracts

Fluidextracts are strong liquid preparations of vegetable drugs, containing alcohol either as a solvent or as a preservative, and prepared so that one mil of the fluidextract approximately represents the activity of one gramme of the air-dried and powdered drug of standard quality. Fluidextracts should be stored in amber-colored bottles protected from sunlight and extremes of temperature. (See also *Fluidextracta,* Part I.)

FLUIDEXTRACTUM ADONIDIS. N. F.

Fluidextract of Adonis [Fldext. Adonid.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum. It is used as a heart stimulant.

The *dose* is two minims (0.125 mil).

FLUIDEXTRACTUM ALETRIDIS. N. F.

Fluidextract of Aletris [Fldext. Aletrid.]

Prepared by using diluted alcohol as the menstruum. It is used as an alterative.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM ANGELICÆ RADICIS. N. F.

Fluidextract of Angelica Root [Fldext. Angel. Rad.]

Prepared by using alcohol as the menstruum. It is used as a stimulant and carminative.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM APII FRUCTUS. N. F. Fluidextractum Apii Graveolens, N. F. III

Fluidextract of Celery Fruit [Fldext. Apii Fruct.]

Prepared by using alcohol as the menstruum. In order to remove any separated oil, after permitting the fluidextract to stand, filter it through an alcohol-wetted filter, rejecting the final few millilitres remaining on the filter with the oil.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM APOCYNI. N. F. (U. S. P. VIII)

Fluidextract of Apocynum [Fldext. Apocyn.]

Prepared by using one volume of glycerin, six volumes of alcohol and three volumes of water as menstruum I, and three volumes of alcohol and two volumes of water as menstruum II. The increase in the proportion of alcohol, over that of the U. S. VIII, is an advantage.

CAUTION.—It has been stated that the absorption of apocynum in the gastro-intestinal tract is uncertain and irregular. To avoid an accumulation of the drug or toxic action, the physician should carefully guard the dosage and determine in each case the tolerance of the patient.

The *dose* is twelve minims (0.75 mil).

FLUIDEXTRACTUM ARALIÆ. N. F. Fluidextractum Araliæ Racemosa, N. F. III

Fluidextract of Aralia [Fldext. Aral.]

Prepared by using two volumes of alcohol and one voulme of water as the menstruum. It is used as an alterative.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM ARNICÆ. N. F. Fluidextractum Arnicæ Florum, N. F. III

Fluidextract of Arnica [Fldext. Arnic.]

Prepared by using diluted alcohol as the menstruum. It is used as a stimulant and alterative.

The *dose* is one and one-half minims (0.1 mil).

FLUIDEXTRACTUM ASCLEPIADIS. N. F.

Fluidextract of Asclepias [Fldext. Asclepiad.]

Prepared by using diluted alcohol as the menstruum. It is used as a diaphoretic, emetic, and cathartic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM BAPTISIÆ. N. F.

Fluidextract of Baptisia [Fldext. Baptis.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum. It is used as a laxative and stimulant, in large doses being emetic and cathartic.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM BERBERIDIS. N. F. (U. S. P. VIII)

Fluidextract of Berberis [Fldext. Berberid.]

Prepared by using diluted alcohol as the menstruum. It is used as an astringent tonic and cathartic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM BOLDI. N. F.

Fluidextract of Boldo [Fldext. Boldi]

Prepared by using alcohol as the menstruum. It is used as an alterative and tonic.

The *dose* is eight minims (0.5 mil).

FLUIDEXTRACTUM BUCHU COMPOSITUM. N. F.

Compound Fluidextract of Buchu [Fldext. Buchu Co.]

Prepared by using two volumes of alcohol and one volume of water as the menstruum. Each fluidrachm represents 37½ grains of buchu and 7½ grains each of cubeb, juniper and uva ursi.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM CALENDULÆ. N. F.

Fluidextract of Calendula [Fldext. Calend.]

Prepared by using alcohol as the menstruum. It is used as a stimulant embrocation in sprains and bruises.

FLUIDEXTRACTUM CALUMBÆ. N. F. (U. S. P. VIII)

Fluidextract of Calumba [Fldext. Calumb.]

Prepared by using one volume of glycerin, eight volumes of alcohol, and one volume of water as menstruum I, and four volumes of alcohol and one volume of water as menstruum II. It is used as a stomachic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM CASTANEÆ. N. F.

Fluidextract of Chestnut Leaves [Fldext. Castan.]

Prepared by using boiling water as the menstruum and adding ten volumes of glycerin and twenty volumes of alcohol being added as a preservative. It is used as an astringent.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM CATARIÆ. N. F.

Fluidextract of Catnep [Fldext. Catar.]

Prepared by using three volumes of alcohol and four volumes of water as the menstruum. It is used as a carminative, antispasmodic and emmenagogue.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM CAULOPHYLLI. N. F.

Fluidextract of Caulophyllum [Fldext. Caulophyl.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum. It is used as a diuretic and emmenagogue.

The *dose* is eight minims (0.5 mil).

FLUIDEXTRACTUM CHIMAPHILÆ. N. F. (U. S. P. VIII)

Fluidextract of Chimaphila [Fldext. Chimaphil.]

Prepared by using diluted alcohol as the menstruum. It is used chiefly for its effects on the mucous membrane of the bladder and urethra.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM CHIONANTHI. N. F.

Fluidextract of Chionanthus [Fldext. Chionanth.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum. It is used as a diuretic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM CHIRATÆ. N. F. (U. S. P. VIII)

Fluidextract of Chirata [Fldext. Chirat.]

Prepared by using diluted alcohol as the menstruum. It is used as a tonic and febrifuge.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM CINCHONÆ AQUOSUM. N. F.

Aqueous Fluidextract of Cinchona [Fldext. Cinchon. Aq.]

One hundred millilitres of aqueous fluidextract of cinchona yields not less than 4.5 Gm. nor more than 5.5 Gm. of the alkaloids of cinchona, and not less than 12 per cent. of alcohol, by volume. Prepared by using a menstruum of 125 mils of glycerin and 30 mils of hydrochloric acid in water. The percolate thus obtained is assayed and enough alcohol and water added so that it conforms to the stipulated standards. An assay is provided in the text. It is used as a bitter tonic.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM COCILLANÆ. N. F.

Fluidextract of Cocillana [Fldext. Cocillan.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum. It is used as an expectorant, emetic, and laxative.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM COFFEÆ. N. F. Fluidextractum Coffeæ Tostæ, N. F. III

Fluidextract of Coffee [Fldext. Coff.]

Prepared by using 65 mils of glycerin, 250 mils of alcohol, and 685 mils of water as menstruum I, and one volume of alcohol and three volumes of water as menstruum II.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM COLCHICI CORMI. N. F. Fluidextractum Colchici Radicis, N. F. III

Fluidextract of Colchicum Corm [Fldext. Colch. Corm.]

One hundred millilitres of fluidextract of colchicum corm yields not less than 0.31 Gm. nor more than 0.39 Gm. of colchicine. Prepared by using a menstruum of two volumes of alcohol and one volume of water. After assaying adjust the volume of the finished product to conform with the required standard. An assay is provided in the text.

The *dose* is three minims (0.2 mil).

FLUIDEXTRACTUM CONDURANGO. N. F.

Fluidextract of Condurango [Fldext. Condurango]

Prepared by using diluted alcohol as the menstruum. It is used as an alterative and stomachic.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM CONII. N. F. (U. S. P. VIII)

Fluidextract of Conium [Fldext. Conii]

One hundred millilitres of fluidextract of conium yields not less than 0.35 Gm. nor more than 0.45 Gm. of coniine. Prepared by using a menstruum of twenty mils of acetic acid and nine hundred and eighty mils of diluted alcohol. This is assayed and enough of a similar menstruum added to bring the fluidextract to the required standard. An assay is provided in the text.

The *dose* is three minims (0.2 mil).

FLUIDEXTRACTUM CONVALLARIÆ FLORUM. N. F. Fluidextractum Convallariæ, N. F. III

Fluidextract of Convallaria Flowers [Fldext. Conval. Flor.]

Prepared by using two volumes of alcohol and one volume of water as the menstruum. It is used as a cardiac stimulant and diuretic.

The *dose* is eight minims (0.5 mil).

FLUIDEXTRACTUM CONVALLARIÆ RADICIS. N. F. (U. S. P. VIII)

Fluidextract of Convallaria Root [Fldext. Conval. Rad.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum. It is used as a diuretic and heart tonic.

The *dose* is eight minims (0.5 mil).

FLUIDEXTRACTUM COPTIS. N. F.

Fluidextract of Coptis [Fldext. Copt.]

Prepared by using diluted alcohol as the menstruum. It is used as a tonic and stimulant.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM CORNI. N. F. Fluidextractum Cornus, N. F. III

Fluidextract of Cornus [Fldext. Corni]

Prepared by using 150 mils of glycerin and 850 mils of diluted alcohol as menstruum I, and diluted alcohol as menstruum II. It is used as a tonic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM CORYDALIS. N. F.

Fluidextract of Corydalis [Fldext. Corydal.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum. It is used as an alterative and diuretic.

The *dose* is ten minims (0.65 mil).

FLUIDEXTRACTUM CUBEBÆ. N. F. (U. S. P. VIII)

Fluidextract of Cubeb [Fldext. Cubeb.]

Prepared by using alcohol as the menstruum. It is used as a diuretic and expectorant.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM CYPRIPEDII N. F. (U. S. P. VIII)

Fluidextract of Cypripedium [Fldext. Cypriped.]

Prepared by using diluted alcohol as the menstruum. It is used as a nerve stimulant, antispasmodic, and analgesic.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM DAMIANÆ. N. F. Fluidextractum Turneræ, N. F. III

Fluidextract of Damiana [Fldext. Damian.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum. It is attributed, but probably erroneously so, with aphrodisiac powers.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM DIOSCOREÆ. N. F.

Fluidextract of Dioscorea [Fldext. Dioscor.]

Prepared by using four volumes of alcohol and one volume of water as the menstruum. It is used as an expectorant and diaphoretic.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM DROSERÆ. N. F.

Fluidextract of Drosera [Fldext. Droser.]

Prepared by using two volumes of alcohol and one volume of water as the menstruum. It is used as an antispasmodic.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM DULCAMARÆ. N. F.

Fluidextract of Bittersweet [Fldext. Dulcam.]

Prepared by using diluted alcohol as the menstruum. It is used as a diuretic and alterative.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM ECHINACEÆ. N. F.

Fluidextract of Echinacea [Fldext. Echin.]

Prepared by using four volumes of alcohol and one volume of water as the menstruum. It is used as an alterative.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM EUONYMI. N. F. (U. S. P. VIII)

Fluidextract of Euonymus [Fldext. Euonym.]

Prepared by using four volumes of alcohol and one volume of water as the menstruum. It is used as a laxative and as a diuretic.

The *dose* is eight minims (0.5 mil).

CAUTION.—It has been stated that the absorption of euonymus in the gastro-intestinal tract is uncertain and irregular. To avoid an accumulation of the drug or toxic action, the physician should carefully guard the dosage and determine in each case the tolerance of the patient.

FLUIDEXTRACTUM EUPATORII. N. F. (U. S. P. VIII)

Fluidextract of Eupatorium [Fldext. Eupator.]

Prepared by using diluted alcohol as a menstruum. It is used as an alterative, diaphoretic and tonic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM EUPHORBIÆ PILULIFERÆ. N. F.

Fluidextract of Euphorbia Pilulifera [Fldext. Euphorb. Pilul.]

Prepared by using diluted alcohol as the menstruum. It is used as an expectorant and emetic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM FUCI. N. F.

Fluidextract of Fucus [Fldext. Fuci]

Prepared by using three volumes of alcohol and one volume of water as the menstruum. It is used as a remedy for *obesity*.

The *dose* is ten minims (0.65 mil).

FLUIDEXTRACTUM GALEGÆ. N. F.

Fluidextract of Galega [Fldext. Galeg.]

Prepared by using diluted alcohol as the menstruum. It is used as a galactagogue and diuretic.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM GERANII. N. F. (U. S. P. VIII)

Fluidextract of Geranium [Fldext. Geran.]

Prepared by using one volume of glycerin, six volumes of alcohol and one volume of water as menstruum I, and three volumes of alcohol and two volumes of water as menstruum II. It is used as an astringent and styptic.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM GOSSYPII CORTICIS.

N. F. Fluidextractum Gossypii Radicis, N. F. III

Fluidextract of Cotton Root Bark [Fldext. Gossyp. Cort.]

Prepared by using alcohol as the menstruum. It is used as an oxytoccic and emmenagogue.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM HAMAMELIDIS FOLIORUM. N. F. (U. S. P. VIII)

Fluidextract of Hamamelis Leaves [Fldext. Hamamel. Fol.]

Prepared by using one volume of glycerin, three volumes of alcohol, and five volumes of water as menstruum I, and one volume of alcohol and two volumes of water as menstruum II. It is used as an astringent.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM HELIANTHEMI. N. F.

Fluidextract of Helianthemum [Fldext. Helianth.]

Prepared by using diluted alcohol as the menstruum. It is used as an alterative and astringent.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM HELONIADIS. N. F.

Fluidextract of Helonias [Fldext. Helon.]

Prepared by using diluted alcohol as the menstruum. It is used as a tonic, diuretic, and anthelmintic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM HUMULI. N. F.

Fluidextract of Hops [Fldext. Humul.]

Prepared by using five volumes of alcohol and three volumes of water as the menstruum. It is used as a nerve sedative.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM HYDRANGEÆ. N. F.

Fluidextract of Hydrangea [Fldext. Hydrang.]

Prepared by using three volumes of alcohol and two volumes of water as the menstruum. It is used as a diuretic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM IRIDIS VERSICOLORIS. N. F.

Fluidextract of Blue Flag [Fldext. Iris Vers. Fluidextractum Iridis, N. F. III]

Prepared by using alcohol as the menstruum. It is used as an alterative and cholagogue cathartic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM JALAPÆ. N. F.

Fluidextract of Jalap [Fldext. Jalap.]

Prepared by mixing the drug with clean sand and using alcohol as the menstruum. It is used as a cathartic.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM JUGLANDIS. N. F.

Fluidextract of Juglans [Fldext. Jugland.]

Prepared by using 100 mils of glycerin, 500 mils of alcohol and 400 mils of water as menstruum I, and diluted alcohol as menstruum II. It is used as a cathartic.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM JUNIPERI. N. F.

Fluidextract of Juniper Berries [Fldext. Junip.]

Prepared by using diluted alcohol as the menstruum. It is used as a diuretic.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM KAVÆ. N. F.

Fluidextract of Kava [Fldext. Kav.]

Prepared by using three volumes of alcohol and two volumes of water as the menstruum. It is used as a diuretic and alterative.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM KOLÆ. N. F.

Fluidextract of Kola [Fldext. Kol. Fluidextractum Sterculiæ, N. F. III]

Prepared by using two volumes of alcohol and one volume of water as the menstruum. It is used for the same purposes as caffeine.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM KRAMERIÆ. N. F. (U. S. P. VIII)

Fluidextract of Krameria [Fldext. Kramer.]

Prepared by using one volume of glycerin, five volumes of alcohol and four volumes of water as menstruum I, and diluted alcohol as menstruum II. The menstruum of the U. S. P. VIII was diluted alcohol. It is used as an astringent.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM LAPPÆ. N. F. (U. S. P. VIII)

Fluidextract of Lappa [Fldext. Lapp.]

Prepared by using diluted alcohol as the menstruum; no change from the U. S. P. VIII. It is used as an alterative and diaphoretic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM LEPTANDRÆ. N. F. (U. S. P. VIII)

Fluidextract of Leptandra [Fldext. Leptand.]

Prepared by using diluted alcohol as the menstruum—the U. S. P. VIII directed the use of three volumes of alcohol and one volume of water as the menstruum. It is used as a laxative.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM LUPULINI. N. F. (U. S. P. VIII)

Fluidextract of Lupulin [Fldext. Lupulin.]

It is made with alcohol, as directed by the U. S. P. VIII, and each mil of fluidextract represents 1 Gm. of drug. It is used as a nerve sedative.

The *dose* is eight minims (0.5 mil).

FLUIDEXTRACTUM MATICO. N. F. (U. S. P. VIII)

Fluidextract of Matico [Fldext. Matic.]

Prepared by using three volumes of alcohol and one volume of water, as directed by the U. S. P. VIII, as the menstruum. It is used as an intestinal astringent and diuretic.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM MEZEREI. N. F. (U. S. P. VIII)

Fluidextract of Mezereum [Fldext. Mezer.]

Prepared by using four volumes of alcohol and one volume of water as the menstruum. It is used as an alterative and rubefacient.

FLUIDEXTRACTUM PARACOTO. N. F.

Fluidextractum Coto, N. F. III
Fluidextract of Paracoto [Fldext. Paracot.]

Prepared by using nine volumes of alcohol and one volume of water as the menstruum. It is used as an intestinal astringent.

The *dose* is five minims (0.3 mil).

FLUIDEXTRACTUM PAREIRÆ. N. F. (U. S. P. VIII)

Fluidextract of Pareira [Fldext. Pareir.]

Prepared by using diluted alcohol as the menstruum—the U. S. P. VIII used 10 per cent. of glycerin and stronger alcohol. It is used as an alterative and diuretic.

The dose is thirty minims (2 mils).

FLUIDEXTRACTUM PETROSELINI RADICIS. N. F.

Fluidextract of Parsley Root [Fldext. Petrosel. Rad.]

Prepared by using two volumes of alcohol and one volume of water as the menstruum. It is used as an emmenagogue and diuretic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM PHYTOLACCÆ. N. F. (U. S. P. VIII)

Fluidextract of Phytolacca [Fldext. Phytolac.]

Prepared by using diluted alcohol, as directed by the U. S. P. VIII, as the menstruum. It is used as an emetic and alterative.

The *dose* is fifteen minims (1 mil) as an emetic, and one and one-half minims (0.1 mil) as an alterative.

FLUIDEXTRACTUM PRUNI VIRGINIANÆ. N. F. (U. S. P. VIII)

Fluidextract of Wild Cherry [Fldext. Prun. Virg.]

Prepared by using 200 mils of glycerin and 400 mils of water as the macerating menstruum, then percolating with a menstruum of 250 mils of alcohol and 150 mils of water and continuing with one volume of alcohol and three volumes of water as the menstruum. This process differs materially from that of the U. S. P. VIII. It is used as a cough sedative.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM QUASSIÆ. N. F. (U. S. P. VIII)

Fluidextract of Quassia [Fldext. Quass.]

Prepared by using one volume of alcohol and two volumes of water, as directed by the U. S. P. VIII, as the menstruum. This affords an excellent means of obtaining the effects of quassia. It has the advantage over the tincture of not requiring so large an amount of alcohol.

The *dose* is eight minims (0.5 mil).

FLUIDEXTRACTUM QUERCUS. N. F. (U. S. P. VIII)

Fluidextract of Quercus [Fldext. Querc.]

Prepared by using 100 mils of glycerin, 500 mils of alcohol and 400 mils of water as menstruum I, and diluted alcohol as menstruum II. Practically the same menstruum was used in the U. S. P. VIII.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM RHAMNI CATHARTICÆ. N. F.

Fluidextract of Rhamnus Cathartica [Fldext. Rham. Cathart.]

Prepared by using diluted alcohol as the menstruum. It is used as a cathartic.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM RHOIS GLABRÆ. N. F. (U. S. P. VIII)

Fluidextract of Rhus Glabra [Fldext. Rhois Glab.]

Prepared by using 100 mils of glycerin, 500 mils of alcohol, and 400 mils of water as menstruum I, and diluted alcohol as menstruum II. This is an excellent astringent, especially useful as a gargle because of its agreeable flavor.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM RUBI. N. F. (U. S. P. VIII)

Fluidextract of Rubus [Fldext. Rubi]

Prepared by using diluted alcohol, as directed by the U. S. P. VIII, as the menstruum. It is used as an intestinal astringent.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM RUMICIS. N. F.

Fluidextract of Rumex [Fldext. Rumic.]

Prepared by using diluted alcohol as the menstruum. It is feebly astringent.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM SANGUINARIÆ. N. F. (Replacing U. S. P. VIII)

Fluidextract of Sanguinaria [Fldext. Sanguin.]

Prepared by using 100 Gm. of citric acid dissolved in enough water to make 250 mils, and 750 mils of alcohol as menstruum I, and three volumes of alcohol and one volume of water as menstruum II—the U. S. P. VIII directed the use of dilute acetic acid as the menstruum for this fluidextract. It is used as a nauseating expectorant.

The *dose* is one and one-half minims (0.1 mil).

FLUIDEXTRACTUM SCOPARII. N. F.

Fluidextract of Scoparius [Fldext. Scopar.]

Prepared by using diluted alcohol as the menstruum. It is used as a diuretic and purgative.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM SCUTELLARIÆ. N. F. (U. S. P. VIII)

Fluidextract of Scutellaria [Fldext. Scutellar.]

Prepared by using diluted alcohol, as directed by the U. S. P. VIII, as the menstruum. It has no medicinal value.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM SENECIONIS. N. F.

Fluidextract of Senecio [Fldext. Senecion.]

Prepared by using two volumes of alcohol and one volume of water as the menstruum. It is believed by some to possess emmenagogue powers.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM SERPENTARIÆ. N. F. (U. S. P. VIII)

Fluidextract of Serpentaria [Fldext. Serpentar.]

Prepared by using four volumes of alcohol and one volume of water, as directed by the U. S. P. VIII, as the menstruum. It is used as a tonic and antiperiodic.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM SOLANI. N. F.

Fluidextract of Solanum [Fldext. Solan.]

Prepared by using two volumes of alcohol and one volume of water as the menstruum. It is used as an antispasmodic and aphrodisiac.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM STILLINGIÆ COMPOSITUM. N. F.

Compound Fluidextract of Stillingia [Fldext. Stilling. Co.]

Prepared by using alcohol, 500 mils, water, 250 mils, glycerin, 250 mils, finishing with diluted alcohol. It contains stillingia, corydalis, iris, sambucus, chimaphila, coriander, and xanthoxylum berries. It is a relic of therapeutic superstition.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM STRAMONII. N. F. (U. S. P. VIII)

Fluidextract of Stramonium [Fldext. Stramon.]

One hundred millilitres of fluidextract of stramonium yields not less than 0.22 Gm. nor more than 0.28 Gm. of the alkaloids of stramonium. Prepared by using two volumes of alcohol and one volume of water, as directed by the U.

S. P. VIII, as the menstruum. It is used as a sedative and analgesic. An assay is provided in the text.

The *dose* is one minim (0.05 mil).

FLUIDEXTRACTUM THUJÆ. N. F.

Fluidextract of Thuja [Fldext. Thuj.]

Prepared by using alcohol as the menstruum. It is used as a stimulating expectorant and diuretic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM THYMI. N. F.

Fluidextract of Thyme [Fldext. Thym.]

Prepared by using 100 mils of glycerin, 250 mils of alcohol and 650 mils of water as menstruum I, and one volume of alcohol and three volumes of water as menstruum II. It is used as a carminative and antispasmodic, but is inferior in value to the oil.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM TRIFOLII. N. F.

Fluidextract of Trifolium [Fldext. Trifol.]

Prepared by using diluted alcohol as the menstruum. It is used as an alterative and antispasmodic.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM TRILLII. N. F.

Fluidextract of Trillium [Fldext. Trill.]

Prepared by using three volumes of alcohol and one volume of water as the menstruum. It is used as an astringent and tonic expectorant.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM VALERIANÆ. N. F. (U. S. P. VIII)

Fluidextract of Valerian [Fldext. Valer.]

Prepared by using four volumes of alcohol and one volume of water as the menstruum—the U. S. P. VIII used three volumes of alcohol and one volume of water as the menstruum. It is used as a sedative and antispasmodic.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM VERBASCI FOLIORUM. N. F.

Fluidextract of Mullein Leaves [Fldext. Verbasc. Fol.]

Prepared by using diluted alcohol as the menstruum. It is used as a demulcent.

The *dose* is one fluidrachm (4 mils).

FLUIDEXTRACTUM VERBENÆ. N. F.

Fluidextract of Verbena [Fldext. Verben.]

Prepared by using diluted alcohol as the menstruum. It is used as a tonic.

The *dose* is fifteen minims (1 mil).

FLUIDEXTRACTUM VIBURNI OPULI. N. F.

Fluidextract of Viburnum Opulus [Fldext. Viburn. Opul.]

Prepared by using two volumes of alcohol and one volume of water as the menstruum. It is used as a nerve sedative.

The *dose* is thirty minims (2 mils).

FLUIDEXTRACTUM ZEÆ. N. F.

Fluidextract of Zea [Fldext. Zea.]

Made with diluted alcohol. It is used as a diuretic.

The *dose* is one fluidrachm (4 mils).

FLUIDGLYCERATA. N. F.

Fluidglycerates

Fluidglycerates are intended to be of the same drug strength as fluidextracts. They contain approximately 50 per cent., by volume, of glycerin and no alcohol. Fluidglycerates made from drugs that do not require either an acid or an alkaline menstruum may be prepared by a general process which embodies maceration, percolation, and evaporation to a given volume. The preparation is then allowed to stand for a few days, and the clear portion decanted and the remainder strained.

FLUIDGLYCERATUM CASCARÆ SAGRADÆ. N. F.

Fluidglycerate of Cascara Sagrada [Fldglycer. Casc. Sagr.]

Prepared from cascara sagrada according to the general process.

The *dose* is fifteen minims (1 mil).

FLUIDGLYCERATUM CASCARÆ SAGRADÆ AROMATICUM. N. F.

Aromatic Fluidglycerate of Cascara Sagrada [Fldglycer. Casc. Sagr. Arom.]

Prepared from cascara sagrada by removing its bitter taste with calcium oxide and subsequently flavoring with fluidglycerate of licorice and oils of fennel, clove, and cinnamon.

The *dose* is fifteen minims (1 mil).

FLUIDGLYCERATUM GLYCYRRHIZÆ. N. F.

Fluidglycerate of Glycyrrhiza [Fldglycer. Glycyrrh. Fluidglycerate of Licorice]

Prepared from glycyrrhiza (licorice) by the general process, the glycerin and water men-

struum being rendered slightly alkaline with ammonia water. It is used as a demulcent and vehicle.

The *dose* is thirty minims (2 mils).

FLUIDGLYCERATUM KRAMERIÆ. N. F.

Fluidglycerate of Krameria [Fldglycer. Kramer.]

Prepared from krameria by the general process. It is used as an astringent and hemostatic.

The *dose* is fifteen minims (1 mil).

FLUIDGLYCERATUM RHEI. N. F.

Fluidglycerate of Rhubarb [Fldglycer. Rhei]

Prepared from rhubarb by the general process. It is used as a cathartic.

The *dose* is fifteen minims (1 mil).

GARGARISMA GUAIACI COMPOSITUM. N. F.

Compound Gargle of Guaiac [Garg. Guaiac. Co.]

This gargle contains 10 per cent. each of ammoniated tincture of guaiac and compound tincture of cinchona, 20 per cent. of clarified honey, and 4 per cent. of potassium chlorate, and oil of peppermint enough to flavor. Used as a local stimulant for the throat.

GELATINUM CHONDRI. N. F.

Chondrus Gelatin [Gelat. Chondr. Irish Moss Gelatin]

Prepared from chondrus by decoction, straining while hot, evaporating carefully to proper consistence, and "scaling" in shallow trays. It is used to make a transparent mucilage which is demulcent and nutritive.

GLYCERITUM BISMUTHI. N. F.

Glycerite of Bismuth [Glycer. Bism.]

One hundred millilitres of glycerite of bismuth yields not less than 12.8 Gm. of bismuth oxide. It is made from bismuth subnitrate, nitric acid, tartaric acid, sodium bicarbonate, glycerin, and distilled water. It contains 16 grains of bismuth and sodium tartrate in 1 fluidrachm of the finished glycerite, equivalent to 12.8 Gm. of bismuth oxide in 100 mils of glycerite, and is used in making other preparations containing bismuth. An assay is provided in the text.

GLYCERITUM GUAIACI. N. F.

Glycerite of Guaiac [Glycer. Guaiac.]

It contains 5 grains of guaiac and about 4 minims of solution of potassium hydroxide in 1 fluidrachm of the finished glycerite. It is used as an alterative.

The *dose* is thirty minims (2 mils).

GLYCERITUM PEPSINI. N. F.

Glycerite of Pepsin [Glycer. Pepsin.]

Five grains of pepsin are represented by 1 fluidrachm of the finished glycerite. The menstruum is acidulated water and glycerin. It is used as a digestive.

The *dose* is forty-five minims (3 mils).

GLYCERITUM PICIS LIQUIDÆ. N. F.

Glycerite of Tar [Glycer. Pic. Liq.]

This glycerite is made from tar, magnesium carbonate, glycerin, alcohol and water. The medicinal virtues of about 4 grains of tar are represented in 1 fluidrachm of the finished glycerite. It is used as an expectorant.

The *dose* is one fluidrachm (4 mils).

GLYCERITUM TRAGACANTHÆ. N. F.

Glycerite of Tragacanth [Glycer. Trag.]

This glycerite contains about 12.5 per cent. of tragacanth with glycerin and water. It is prepared in the form of a thick homogeneous paste. It is used as an excipient for pills.

GLYCERITUM VITELLI. N. F.

Glycerite of Egg Yolk [Glycer. Vitell. Glyconin]

This is a mixture of egg yolk, 45 per cent., and glycerin, 55 per cent. Used as an emsulsifying agent.

GLYCEROGELATINA. N. F.

Glycerogelatins

Glycerogelatins originated with Dr. Unna and are soft masses which melt at the temperature of the body. They contain gelatin, glycerin, water and the medicament, and are used in *skin diseases.*

GLYCEROGELATINUM ACIDI SALICYLICI. N. F.

Salicylic Acid Glycerogelatin [Glycerogel. Acid. Salicyl.]

This preparation contains 35 per cent. of glycerin and 10 per cent. of salicylic acid in glycerinated gelatin vehicle. Used as an antiseptic and keratoplastic.

GLYCEROGELATINUM IODOFORMI. N. F.

Iodoform Glycerogelatin [Glycerogel. Iodof.]

This preparation contains 15 per cent. of glycerin, and 10 per cent. of iodoform in glyce-

erinated gelatin vehicle. Used as an antiseptic dressing.

GLYCEROGELATINUM ZINCI DURUM. N. F.

Firm Zinc Glycerogelatin [Glycerogel. Zinc. Dur.]

This preparation contains 25 per cent. of glycerin, and 10 per cent. of zinc oxide in 30 per cent. glycerinated gelatin vehicle. Used as a local sedative and protective.

GLYCEROGELATINUM ZINCI MOLLE. N. F.

Soft Zinc Glycerogelatin [Glycerogel. Zinc. Mol.]

This preparation contains 35 per cent. of glycerin and 10 per cent of zinc oxide in 20 per cent. of glycerinated gelatin vehicle. Used as an astringent and protective.

GOSSYPIUM STYPTICUM. N. F.

Styptic Cotton [Gossyp. Stypt.]

It is made by impregnating purified cotton with diluted solution of ferric chloride, glycerin and water. It should be kept in well closed containers. It is used as a local styptic.

INFUSUM BRAYERÆ. N. F.

Infusum of Brayera [Inf. Brayer.]

This infusion which must be freshly prepared is made with 6 per cent. of the drug in boiling water.

The *dose* is eight fluidounces (250 mils).

INFUSUM CINCHONÆ. N. F.

Infusion of Cinchona [Inf. Cinchon.]

Made with 6 per cent. cinchona and cold acidulated water.

The *dose* is twelve fluidrachms (50 mils).

INFUSUM GENTIANÆ COMPOSITUM. N. F.

Compound Infusion of Gentian [Inf. Gent. Co.]

This elixir contains 3 per cent. of gentian, flavored with coriander, and bitter orange peel. It is used as a tonic, and is made by percolation.

The *dose* is four fluidrachms (15 mils).

INFUSUM PRUNI VIRGINIANÆ. N. F. (U. S. P. VIII)

Infusion of Wild Cherry [Inf. Prun. Virg.]

This well-known infusion is made with 40 grammes of wild cherry to 1000 mils by cold percolation and is preserved with glycerin. The U. S. P. VIII process was not changed.

The *dose* is two fluidounces (60 mils).

INFUSUM ROSÆ COMPOSITUM. N. F.

Compound Infusion of Rose [Inf. Ros. Co.]

This preparation which deserves a larger use on account of its pleasant flavor and beautiful color is made from red rose, diluted sulphuric acid, sugar and water. It is used as an astringent.

The *dose* is three fluidounces (100 mils).

INUNCTUM MENTHOLIS. N. F.

Menthol Inunction [Inunct. Menthol.]

This is a new preparation containing 5 per cent. of menthol incorporated with hydrous wool fat. It is used as a local anodyne and antipruritic.

INUNCTUM MENTHOLIS COMPOSITUM. N. F.

Compound Menthol Inunction [Inunct. Menthol. Co.]

This is another new preparation containing 5 per cent. of menthol and 10 per cent. of methyl salicylate in hydrous wool fat. It is counter-irritant as well as locally anesthetic.

IODOFORMUM AROMATISATUM. N. F.

Aromatized Iodoform [Iodof. Arom.]

This preparation consists of iodoform containing 4 per cent. of cumarin, and is used as an antiseptic and alterative.

LAC FERMENTATUM. N. F.

Fermented Milk [Lac. Ferment. Kumyss]

This well known dietetic preparation is made from fresh cow's milk, compressed yeast, and sugar, properly fermented, and is used as a food for invalids.

The *dose* is eight fluidounces (250 mils).

LINIMENTUM ACONITI ET CHLOROFORMI. N. F.

Liniment of Aconite and Chloroform [Lin. Aconit. et Chlorof.]

This preparation contains 4.5 per cent. fluidextract of aconite and 12.5 per cent. of chloroform in a mixture of alcohol and soap liniment. It is used externally to relieve pain.

LINIMENTUM AMMONII IODIDI. N. F.

Liniment of Ammonium Iodide [Lin. Ammon. Iod.]

This liniment is made from iodine, oil of rosemary, oil of lavender, camphor, ammonia water, and alcohol. It is used as an external discutient application.

LINIMENTUM OPII COMPOSITUM. N. F.

Compound Liniment of Opium [Lin. Opii Co. Canada Liniment]

This liniment contains 10 per cent. of tincture of opium, 22 per cent. of oil of turpentine and 35 per cent. of ammonia water, with camphor, alcohol and oil of peppermint, made into a somewhat permanent emulsion with fresh egg albumen. It is used as a stimulating anodyne application.

LINIMENTUM SAPONATO-CAMPHORATUM. N. F.

Camphorated Soap Liniment [Lin. Sapon.-Camph. Solid Opodeldoc]

This liniment contains freshly prepared sodium stearate made by combining monohydrated sodium carbonate and stearic acid, camphor, alcohol, oils of thyme and rosemary and ammonia water. It is a useless survival of a former fad.

LINIMENTUM SAPONIS MOLLIS COMPOSITUM. N. F.

Tinctura Saponis Viridis Composita, N. F. III. Compound Liniment of Soft Soap [Lin. Sapon. Mol. Co.]

There is no change in this preparation which was formerly classed as compound tincture of green soap. It contains soft soap, oil of cade, and alcohol.

LINIMENTUM SINAPIS COMPOSITUM. N. F.

Compound Liniment of Mustard [Lin. Sinap. Co.]

This is a new preparation consisting of 3 per cent. of volatile oil of mustard, with fluidextract of mezereum, camphor, castor oil, and alcohol. It is an active rubefacient.

LINIMENTUM TEREBINTHINÆ ACETICUM. N. F.

Acetic Turpentine Liniment [Lin. Terebinth. Acet. Linimentum Album. Stokes' Liniment. St. John Long's Liniment]

This liniment contains 40 per cent. of oil of turpentine, fresh egg, oil of lemon, acetic acid and rose water. It is a powerful counter-irritant.

LINIMENTUM TIGLII. N. F.

Liniment of Croton Oil [Lin. Tiglii. Linimentum Crotonis]

This liniment contains 13 volumes of croton oil, and 44 volumes of alcohol, and 43 volumes of oil of cajuput. It is used as a pustulant counter-irritant.

LINIMENTUM TIGLII COMPOSITUM. N. F.

Compound Croton Oil Liniment [Lin. Tiglii Co.]

This liniment contains 20 per cent. each of croton oil, oil of sassafras, oil of turpentine, with 40 per cent. of olive oil. It is an active pustulant and counter-irritant and should be used with circumspection.

LIQUOR ALUMINI ACETATIS. N. F.

Solution of Aluminum Acetate [Liq. Alum. Acet. Liquor Burowii. Burow's Solution]

One hundred millilitres of this solution contains not less than 4.5 and not more than 5.5 Gm. of neutral aluminum acetate [$Al(C_2H_3O_2)_3 = 204.17$]. It is made by the reactions between lead acetate and aluminum sulphate in aqueous solution. A process of assay is also given in the text. It should be noted that this differs from the solution of aluminum acetate of the N. F. III which is now known as the solution of the subacetate. It is astringent and antiseptic.

LIQUOR ALUMINI ACETICO-TARTRATIS. N. F.

Solution of Aluminum Acetico-Tartrate [Liq. Alum. Acet.-Tart.]

This solution contains about 50 per cent. of dry so-called aluminum acetico-tartrate. It is made from ammonium, alum, monohydrated sodium carbonate, tartaric acid, glacial acetic acid, and water, and used externally as an astringent and disinfectant. It should be diluted when used for medicinal purposes.

LIQUOR ALUMINI SUBACETATIS. N. F.

Liquor Alumini Acetatis, N. F. III. Solution of Aluminum Subacetate [Liq. Alum. Subacet.]

This solution is made from aluminum sulphate, acetic acid, precipitated calcium carbonate and water, and contains from 7.5 to 8 per cent. of basic aluminum acetate. An assay

process is also given in the text. This preparation corresponds closely to the *Liquor Alumini Acetici* of the German Pharmacopœia. It is an active germicide, as well as astringent, and is used both as a gargle and as a surgical dressing. It should generally be diluted with from 4 to 8 parts of water.

LIQUOR AMMONII CITRATIS. N. F.

Solution of Ammonium Citrate [Liq. Ammon. Cit.]

This preparation must not be confused with the Liquor Ammonii Citratis Fortior which was formerly official. It is made by cautiously neutralizing 125 Gm. of citric acid with ammonia water and then making up to a volume of 1000 mils with distilled water. It is used as a refrigerant and diuretic.

The *dose* is one fluidrachm (4 mils).

LIQUOR ANTISEPTICUS. N. F. (Replacing U. S. P. VIII)

Antiseptic Solution [Liq. Antisept.]

This preparation which replaces the Liquor Antisepticus of the U. S. P. VIII, contains about the same ingredients as the former preparation, but is much pleasanter in taste and less harsh in effect. While it possesses feeble antiseptic properties, it is chiefly useful to flavor mouth-washes.

LIQUOR ANTISEPTICUS ALKALINUS. N. F.

Alkaline Antiseptic Solution [Liq. Antisept. Alk.]

This solution is made from potassium bicarbonate, sodium benzoate, sodium borate, thymol, eucalyptol, oil of peppermint, methyl salicylate, cudbear, alcohol, glycerin, magnesium carbonate and water. It is used as an alkaline antiseptic and feeble detergent.

LIQUOR ARSENICALIS, CLEMENS. N. F.

Liquor Potassii Arsenatis et Bromidi, N. F. III. Clemens' Solution of Arsenic [Solution of Potassium Arsenate and Bromide. Liq. Arsen., Clemens]

An aqueous solution containing an amount of arsenic in combination, corresponding to about 1 per cent. of arsenic trioxide [As_2O_3]. This preparation is made from arsenic trioxide, potassium bicarbonate, bromine and water. It is used as an alterative.

The *dose* is three minims (0.2 mil).

LIQUOR AURI ET ARSENI BROMIDI. N. F.

Solution of Gold and Arsenic Bromide [Liq. Aur. et Arsen. Brom.]

This preparation represents about 1-32d of a grain of tribromide of gold and 1-13th of a grain of tribromide of arsenic, in each ten minims. It is used as an alterative.

The *dose* is three minims (0.2 mil).

LIQUOR BISMUTHI. N. F.

Solution of Bismuth [Liq. Bism.]

This solution is made from glycerite of bismuth, alcohol, and distilled water. About 1 grain of bismuth and sodium tartrate is represented in 1 fluidrachm of the finished solution. It is used as an intestinal astringent, but does not possess the therapeutic virtues of the insoluble bismuth salts.

The *dose* is one fluidrachm (4 mils).

LIQUOR BROMI. N. F.

Solution of Bromine [Liq. Brom. Smith's Solution of Bromine]

One hundred mils of finished solution contains 8.3 mils of bromine and 12.5 grammes of potassium bromide. It is a powerful germicide and was formerly used extensively as an application in *gangrene*.

LIQUOR CALCIS SULPHURATÆ. N. F.

Solution of Sulphurated Lime [Liq. Calc. Sulphurat. Solution of Oxysulphuret of Calcium Vleminckx' solution. Vleminckx' Lotion]

This solution is made by boiling together lime, sublimed sulphur and water. It is used as an external application in skin diseases.

LIQUOR CARMINI. N. F.

Solution of Carmine [Liq. Carmin.]

This solution is made from carmine, ammonia water, glycerin and water. It is used as a red coloring solution.

LIQUOR CHLORI COMPOSITUS. N. F. (Replacing U. S. P. VIII)

Compound Solution of Chlorine [Liq. Chlor. Co. Chlorine Water]

This is an aqueous solution containing, when freshly made, a mixture of chlorine and chlorine oxides equivalent to about 0.35 Gm. of available chlorine in each one hundred millilitres of the solution, with some potassium chloride. It is made by reacting upon potassium chlorate with hydrochloric acid and then dissolving the products of the reaction in cold

distilled water; this is practically identical with the U. S. P. VIII process. It is used as an intestinal antiseptic.

The *dose* is one fluidrachm (4 mils).

LIQUOR COCCI. N. F.

Liquor Coccineus, N. F. III

Cochineal Color [Liq. Cocci]

This solution is made from cochineal, potassium carbonate, alum, potassium bitartrate, alcohol, glycerin, and water. Like the solution of carmine, it is used to color preparations red.

LIQUOR FERRI ACETATIS. N. F.

Solution of Ferric Acetate [Liq. Ferr. Acet.]

This is an aqueous solution containing about 31 per cent. of anhydrous ferric acetate [$Fe(C_2H_3O_2)_3 = 232.91$], corresponding to about 7.5 per cent. metallic iron (Fe). It is made from solution of ferric sulphate, glacial acetic acid, ammonia water, and distilled water. An assay process is given in the text.

The *dose* is five minims (0.3 mil).

LIQUOR FERRI ALBUMINATI. N. F.

Solution of Albuminate of Iron [Liq. Ferr. Albumin.]

This solution is made from fresh egg-albumen, solution of ferric oxychloride, alcohol, sodium citrate, aromatic elixir, and water. About 2-5th of a grain of metallic iron in the form of albuminate is contained in 1 fluidrachm of the finished solution. It is used as a chalybeate.

The *dose* is two fluidrachms (8 mils).

LIQUOR FERRI CITRATIS. N. F.

Solution of Ferric Citrate [Liq. Ferr. Cit.]

This solution is an aqueous solution containing ferric citrate corresponding to not less than 7.25 per cent. of metallic iron (Fe). It is made from solution of ferric sulphate, citric acid, ammonia water, and water. A process of assay is given in the text.

The *dose* is ten minims (0.6 mil).

LIQUOR FERRI HYPOPHOSPHITIS. N. F.

Solution of Ferric Hypophosphite [Liq. Ferr. Hypophos. Solution of Hypophosphite of Iron]

This preparation is made from ferric hypophosphite made soluble by the use of potassium citrate and dissolved in glycerin and water. About 10 grains of ferric hypophosphite are represented in 1 fluidrachm of finished solution.

The *dose* is fifteen minims (1 mil).

LIQUOR FERRI NITRATIS. N. F.

Solution of Ferric Nitrate [Liq. Ferr. Nit.]

This preparation is an aqueous solution containing ferric nitrate [$Fe(NO_3)_3 = 241.87$] corresponding to not less than 1.3 per cent. of metallic iron (Fe). It is made from solution of ferric sulphate, ammonia water, nitric acid, and distilled water. A process of assay is given in the text.

The *dose* is five minims (0.3 mil).

LIQUOR FERRI OXYCHLORIDI. N. F.

Solution of Ferric Oxychloride [Liq. Ferr. Oxychlor.]

This preparation is intended to replace the former dialyzed iron. It is made from solution of ferric chloride, ammonia water, glycerin, hydrochloric acid, and water. It contains about 3.5 per cent. of iron as oxychloride, and is used as a chalybeate.

The *dose* is thirty minims (2 mils).

LIQUOR FERRI OXYSULPHATIS. N. F.

Solution of Ferric Oxysulphate [Liq. Ferr. Oxysulph.]

This solution is made from ferrous sulphate, nitric acid, and distilled water.

LIQUOR FERRI PEPTONATI. N. F.

Solution of Peptonate of Iron [Liq. Ferr. Pepton.]

It is made from pepsin, fresh egg albumen, hydrochloric acid, solution of ferric oxychloride, alcohol, and sodium citrate made up into a pleasantly flavored preparation with oil of orange, acetic ether, and vanillin, using glycerin, syrup and distilled water. It contains about $\frac{1}{5}$ of a grain of metallic iron, in the form of peptonate, in 1 fluidrachm of the finished solution. It is used as a chalybeate.

The *dose* is two fluidrachms (8 mils).

LIQUOR FERRI PEPTONATI ET MANGANI. N. F.

Liquor Ferri Peptonati cum Mangano, N. F. III. Solution of Peptonate of Iron and Manganese [Liq. Ferr. Pepton. et Mangan.]

This preparation is made from the same ingredients and in a similar manner to the foregoing preparation with the addition of solu-

ble manganese citrate. It is used as a chalybeate and alterative.

The *dose* is two fluidrachms (8 mils).

LIQUOR FERRI PROTOCHLORIDI. N. F.

Solution of Ferrous Chloride [Liq. Ferr. Protochlor. Solution of Protochloride of Iron.]

This solution is made from iron wire, hydrochloric acid, glycerin, diluted hypophosphorous acid and distilled water. About 20 grains of ferrous chloride are represented by 1 fluidrachm of finished solution. It is used as a chalybeate tonic and as an astringent.

The *dose* is ten minims (0.6 mil).

LIQUOR FERRI SALICYLATIS. N. F.

Solution of Ferric Salicylate [Liq. Ferr. Salicyl. Salicylated Mixture of Iron]

This is a new preparation, containing sodium salicylate, tincture of ferric citrochloride, ammonium carbonate, citric acid, methyl salicylate, glycerin, and distilled water. Each fluidrachm is equivalent to about 7½ grains of sodium salicylate and 7½ minims of Tincture of Ferric Citro-Chloride. It has been recommended for cases of chronic rheumatism complicated with anæmia.

The *dose* is two fluidrachms (8 mils).

LIQUOR GUTTÆ PERCHÆ. N. F.

Solution of Gutta Percha [Liq. Gut. Perch.]

This is a solution of gutta percha in chloroform, clarified by the addition of lead carbonate. It is used externally as a protection.

LIQUOR HYDRARGYRI ET POTASSII IODIDI N. F.

Solution of Mercury and Potassium Iodide [Liq. Hydrarg. et Pot. Iod. Solution of Potassium Iodohydrargyrate. Channing's Solution]

This preparation represents about 1 per cent. of red iodide of mercury and 0.8 per cent. of potassium iodide in aqueous solution. It is used as an alterative in the treatment of *syphilis*.

The *dose* is three minims (0.2 mil).

LIQUOR HYDRARGYRI NITRATIS. N. F. (U. S. P. VIII)

Solution of Mercuric Nitrate [Liq. Hydrarg. Nit.]

This is an aqueous solution containing not less than 58 per cent. nor more than 62 per cent. of anhydrous mercuric nitrate [$Hg(NO_3)_2$ = 324.62] and about 11 per cent. of free nitric acid. It is made by dissolving red mercuric oxide in a mixture of nitric acid and distilled water. The process is the same as that of the U. S. P. VIII. It is used locally as a caustic and disinfectant. An assay process is given in the text.

LIQUOR HYDRASTINÆ COMPOSITUS. N. F.

Compound Solution of Hydrastine [Liq. Hydrastin. Co. Colorless Hydrastine Solution]

This is a new preparation containing 0.3 per cent. of hydrastine hydrochloride with the chlorides of aluminum, calcium, magnesium, and potassium in solution in glycerin and water. Its therapeutic virtues are solely those of hydrastine.

The *dose* is one fluidrachm (4 mils).

LIQUOR HYPOPHOSPHITUM. N. F.

Solution of Hypophosphites [Liq. Hypophos.]

This preparation contains 2 grains of calcium hypophosphite, 1¼ grains of sodium hypophosphite and 1 grain of potassium hypophosphite in 1 fluidrachm of finished solution. It is used as an alterative and tonic.

The *dose* is one fluidrachm (4 mils).

LIQUOR HYPOPHOSPHITUM COMPOSITUS. N. F.

Compound Solution of Hypophosphites [Liq. Hypophos. Co.]

This solution is made from calcium, potassium, sodium, ferric, manganese and quinine hypophosphites, strychnine, potassium citrate, hypophosphorous acid, orange flower water, glycerin, and distilled water. It is used as an alterative and tonic.

The *dose* is one fluidrachm (4 mils).

LIQUOR IODI PHENOLATUS. N. F. Liquor Iodi Carbolatus, N. F. III

Phenolated Solution of Iodine [Liq. Iod. Phenol. Carbolized Solution of Iodine. Boulton's Solution. French Mixture]

This solution is made from compound solution of iodine, liquefied phenol, glycerin, and water. It is used externally.

LIQUOR MAGNESII SULPHATIS EFFERVESCENS. N. F.

Effervescent Solution of Magnesium Sulphate [Liq. Mag. Sulph. Eff.]

This preparation contains about 385 grains of magnesium sulphate in 12 fluidounces of the

finished solution. It is used as a cathartic, like solution of magnesium citrate.

The *dose* is the entire contents of the bottle prepared as directed; about twelve fluidounces (350 mils).

LIQUOR PANCREATINI. N. F. Liquor Pancreaticus, N. F. III

Solution of Pancreatin [Liq. Pancreat. Pancreatic Solution]

This solution is made from pancreatin, sodium bicarbonate, glycerin, compound spirit of cardamom, alcohol, purified talc and water. about 1 grain of pancreatin is represented in 1 fluidrachm of the finished solution. It is used as a digestive.

The *dose* is one fluidrachm (4 mils).

LIQUOR PEPSINI. N. F.

Solution of Pepsin [Liq. Pepsin.]

This solution contains glycerite of pepsin, hydrochloric acid, glycerin and water. It is used as a digestive.

The *dose* is two fluidrachms (8 mils).

LIQUOR PEPSINI ANTISEPTICUS. N. F.

Antiseptic Solution of Pepsin [Liq. Pepsin. Antisept.]

This is a new preparation containing pepsin, hydrochloric acid, menthol, eucalyptol, and methyl salicylate in solution in glycerin, alcohol and water. It is used externally in the treatment of old sores to assist their healing.

LIQUOR PEPSINI AROMATICUS. N. F.

Aromatic Solution of Pepsin [Liq. Pepsin. Arom.]

This solution is made from pepsin, oils of cinnamon, pimenta and clove, and alcohol, hydrochloric acid, glycerin and water. About 1 grain of pepsin is represented in 1 fluidrachm of finished solution. It is used as a digestive.

The *dose* is two fluidrachms (8 mils).

LIQUOR PHOSPHATUM ACIDUS. N. F.

Acid Solution of Phosphates [Liq. Phos. Acid. Solution of Acid Phosphates]

This was formerly a solution of acid phosphates made by adding sulphuric acid and water to bone ash, expressing and filtering. It is now made by dissolving calcium and magnesium carbonate in phosphoric acid and water.

The *dose* is one fluidrachm (4 mils).

LIQUOR PHOSPHATUM COMPOSITUS. N. F.

Compound Solution of Phosphates [Liq. Phos. Co.]

This is a polypharmacal preparation containing the phosphates of ammonium, calcium, iron, potassium, and sodium held in aqueous solution by the use of glycerin and citric acid. It is flavored with orange flower water.

LIQUOR PHOSPHORI. N. F.

Solution of Phosphorous [Liq. Phosphor. Thompson's Solution of Phosphorus]

This solution is made from phosphorus, dehydrated alcohol, spirit of peppermint and glycerin. About 1-24th of a grain of phosphorus is contained in 1 fluidrachm of finished solution. It is used as a tonic and stimulant in nervous diseases.

The *dose* is ten minims (0.6 mil).

LIQUOR PICIS ALKALINUS. N. F.

Alkaline Solution of Tar [Liq. Pic. Alk.]

This solution contains about 25 per cent. of tar and 12.5 per cent. of potassium hydroxide in water. It is used in skin diseases as an external application.

LIQUOR PICIS CARBONIS. N. F.

Coal Tar Solution [Liq. Pic. Carbon.]

This preparation, sometimes known by the name of *Liquor Carbonis Detergens,* is made by digesting 200 Gm. of coal tar and 100 Gm. of soap bark with enough alcohol to make 1000 mils. It is used externally in skin diseases.

LIQUOR POTASSÆ CHLORINATÆ. N. F.

Solution of Chlorinated Potassa [Liq. Pot. Chlorinat. Liquor Potassæ Chloratæ. Javelle Water]

This preparation which is analogous to Labarraque's solution is made from potassium carbonate, chlorinated lime, and water. It is used as a disinfectant.

LIQUOR SODÆ ET MENTHÆ. N. F. Mistura Sodæ et Menthæ, N. F. III

Solution of Soda and Mint [Liq. Sod. et Menth. Soda Mint]

This preparation contains sodium bicarbonate, aromatic spirit of ammonia and spearmint or peppermint water. Each fluidrachm contains 3 grains of the bicarbonate and 0.6 minim of aromatic spirit of ammonia. It is used as an antacid and carminative.

The *dose* is two fluidrachms (8 mils).

LIQUOR SODII ARSENATIS, PEARSON. N. F.

Pearson's Solution of Sodium Arsenate [Liq. Sod. Arsen., Pearson. Liquor Arsenicalis Pearsonii]

This preparation should not be confounded with the Liquor Sodii Arsenatis, U. S. P., which is ten times stronger than Pearson's solution. It contains about 1-6th per cent. of crystallized sodium arsenate or about 1-10th per cent. of anhydrous sodium arsenate. Whenever it is prescribed or dispensed, the name "Pearson" should be specified, to avoid serious mistakes. It is used as an alterative.

The *dose* is thirty minims (2 mils).

LIQUOR SODII BORATIS COMPOSITUS. N. F.

Compound Solution of Sodium Borate [Liq. Sod. Bor. Co. Dobell's Solution]

This solution contains about 1.5 per cent. each of sodium borate and sodium bicarbonate and 0.3 per cent. of phenol, with glycerin and water. It is widely used as a cleansing wash in inflammations of the nose and pharynx.

LIQUOR SODII CITRATIS. N. F.

Solution of Sodium Citrate [Liq. Sod. Cit. Mistura Sodii Citratis. Potio Rivierii]

This solution is made with 2 per cent. of citric acid and 2.5 per cent. of sodium bicarbonate in distilled water. It should be freshly prepared. The amount of sodium citrate formed, about 1.6 grains for each fluidrachm, is so small that the solution has scarcely any effect beyond that of a mildly saline drink.

The *dose* is two fluidrachms (8 mils).

LIQUOR SODII CITRO-TARTRATIS EFFERVESCENS. N. F.

Effervescent Solution of Sodium Citro-Tartrate [Liq. Sod. Citro.-Tart. Eff.]

This solution is made from sodium bicarbonate, tartaric acid, citric acid, syrup of citric acid and water. It is directed that this solution be dispensed in a tightly-stoppered bottle, containing 350 mils (12 fluidounces), while still effervescent. It is a pleasant, acidulous, feeble laxative; the contents of one bottle are equivalent in action to about one-third of a pair of Seidlitz powders.

LIQUOR SODII PHOSPHATIS COMPOSITUS. N. F. (Replacing U. S. P. VIII)

Compound Solution of Sodium Phosphate [Liq. Sod. Phos. Co.]

This preparation, which differs slightly from the U. S. P. VIII preparation of the same name, contains sodium phosphate crystals, citric acid, glycerin, and distilled water—the U. S. P. VIII formula contained 4 per cent. of sodium nitrate, which has been omitted in the N. F., while glycerin has been added. Each mil represents 1 gramme of crystallized sodium phosphate. It is used as a laxative.

The *dose* is two fluidrachms (8 mils).

LIQUOR STRYCHNINÆ ACETATIS. N. F.

Solution of Strychnine Acetate [Liq. Strych. Acet. Hall's Solution of Strychnine]

This preparation should not be confounded with the Liquor Strychninæ Hydrochloridi of the British Pharmacopœia, which is much stronger. Solution of strychnine acetate is made from strychnine, diluted acetic acid, alcohol, compound tincture of cardamom and water. About ⅛ of a grain of strychnine acetate is contained in 1 fluidrachm of the finished solution. It is used as a cardiac stimulant and tonic.

The *dose* is ten minims (0.6 mil).

LIQUOR ZINCI ET ALUMINI COMPOSITUS. N. F.

Compound Solution of Zinc and Aluminum [Liq. Zinc. et Alumin. Co.]

This preparation contains about 20 per cent. each, of zinc sulphate and aluminum sulphate, with betanaphthol, oil of thyme and water. It is used externally as an astringent and disinfectant.

LIQUOR ZINCI ET FERRI COMPOSITUS. N. F.

Compound Solution of Zinc and Iron [Liq. Zinc. et Ferr. Co. Deodorant Solution]

This preparation contains 20 per cent. each of zinc sulphate and ferrous sulphate, 6.5 per cent. of copper sulphate, with betanaphthol, oil of thyme, hypophosphorous acid and water. It is used as an antiseptic and astringent solution.

LOTIO AMMONIACALIS CAMPHORATA. N. F. Aqua Sedativa, N. F. III

Ammoniated Camphor Wash [Lot. Ammon. Camph. Sedative Water. Eau Sedative de Raspail]

This is an aqueous solution containing 6 per cent. each of sodium chloride and ammonia water, with 10 per cent. spirit of camphor.

LOTIO FLAVA. N. F.

Yellow Lotion [Lot. Flav. Yellow Wash. Aqua Phagedænica Flava]

It is made with 0.3 per cent. of corrosive mercuric chloride in lime water slightly diluted

with water. The mercury is present as a yellow hydroxide in the finished preparation. It is used externally in skin diseases. It is slightly weaker than the corresponding preparation of the Br. (See p. 668.)

LOTIO NIGRA. N. F.

Black Lotion [Lot. Nigr. Black Wash. Aqua Phagedænica Nigra]

It is made with 0.875 per cent. (formerly 0.75 per cent.) of mild mercurous chloride in lime water slightly diluted with water. The mercury is largely present as a black suboxide. It is used externally in skin diseases. It exceeds in strength the similar Br. preparation (see p. 668).

LOTIO PLUMBI ET OPII. N. F.

Lotion of Lead and Opium [Lot. Plumb. et Opii. Lead and Opium Wash]

It contains, in each 100 mils, 1.75 grammes of lead acetate and 3.5 grammes of tincture of opium. It is used as an astringent and sedative external application.

MAGMA FERRI HYDROXIDI. N. F. Ferri Hydroxidum, U. S. P. VIII

Ferric Hydroxide Magma [Magm. Ferr. Hydrox. Ferric Hydroxide]

This is a freshly precipitated well washed ferric hydroxide, made by decomposing solution of ferric sulphate with ammonia water. The U. S. P. VIII and N. F. IV formulas and processes are identical. It may be used as an arsenical antidote, but is inferior to the U. S. P. *Ferri Hydroxidum cum Magnesii Oxido.*

MASSA COPAIBÆ. N. F.

Mass of Copaiba [Mass. Copaib. Solidified Copaiba]

This is a combination of copaiba with a hydrated magnesium oxide reduced to a pilular consistence.

The *dose* is fifteen grains (1 Gm.).

MEL ROSÆ ET SODII BORATIS. N. F.

Honey of Rose and Sodium Borate [Mel. Ros. et Sod. Bor. Honey of Rose with Borax]

This preparation is made with borax, glycerin, and honey of rose. It is used as an astringent application.

MEL SODII BORATIS. N. F.

Honey of Sodium Borate [Mel. Sod. Bor. Mel Boracis. Honey and Borax]

This preparation is made with borax, glycerin, and clarified honey. It is used as a local application in sore throat.

MENTHOL CAMPHORATUM. N. F. Campho-Menthol, N. F. III

Camphorated Menthol [Menthol. Camph. Camphor and Menthol]

Equal parts by weight of camphor and menthol with a small proportion of alcohol added. Applied locally in *neuralgia.*

MISTURA ADSTRINGENS. N. F. Mistura Adstringens et Escharotica, N. F. III

Astringent Mixture [Mist. Adstring. Villate's Mixture]

This preparation is made from solution of lead subacetate, copper sulphate, zinc sulphate and diluted acetic acid. It should be well shaken before dispensing to insure the even distribution of the precipitated lead sulphate. It is used externally as an astringent and escharotic.

MISTURA AMMONII CHLORIDI. N. F.

Mixture of Ammonium Chloride [Mist. Ammon. Chlor. Mistura Solvens Simplex]

This preparation contains 1½ grains each of ammonium chloride and purified extract of glycyrrhiza in one fluidrachm of water. It is used as an expectorant.

The *dose* is two fluidrachms (8 mils).

MISTURA CAMPHORÆ ACIDA. N. F.

Acid Camphor Mixture [Mist. Camph. Acid. Mistura Antidysenterica. Hope's Mixture]

It contains 1.75 mils of nitric acid, 1.2 mils of tincture of opium in camphor water to make 100 mils. It is used in the treatment of serous *diarrheas.*

The *dose* is two fluidrachms (8 mils).

MISTURA CAMPHORÆ AROMATICA. N. F.

Aromatic Camphor Mixture [Mist. Camph. Arom. Parrish's Camphor Mixture]

It contains 25 mils of compound tincture of lavender, 3.5 mils of sugar, and camphor water to make 100 mils. It is used in *hysteria* and as a carminative.

The *dose* is two fluidrachms (8 mils).

MISTURA CARMINATIVA. N. F.

Carminative Mixture [Mist. Carminat. Dalby's Carminative]

It is made from magnesium carbonate, potassium carbonate, tincture of opium, oils of caraway, fennel, and peppermint, with syrup and water. About ⅛ of a grain of opium is

represented in 1 fluidrachm of the finished mixture. Its therapeutic effect is similar to that of paregoric.

The *dose* for an infant is eight minims (0.5 mil).

MISTURA CHLORALIS ET POTASSII BROMIDI COMPOSITA. N. F.

Compound Mixture of Chloral and Potassium Bromide [Mist. Chloral. et Pot. Brom. Co. Chloral and Bromide Compound]

This preparation represents about 12 grains each of hydrated chloral and potassium bromide, and ⅛ grain each of the extracts of Indian cannabis and hyoscyamus in each fluidrachm of the finished mixture. It is used as a somnifacient.

The *dose* is one fluidrachm (4 mils).

MISTURA CHLOROFORMI ET MORPHINÆ COMPOSITA. N. F.

Compound Mixture of Chloroform and Morphine [Mist. Chlorof. et Morph. Co. Mistura Chloroformi et Cannabis Indicæ Composita, N. F. III. Chloroform Anodyne]

This preparation contains chloroform, ether, tincture of Indian cannabis, tincture of capsicum, morphine sulphate, oil of peppermint, glycerin, water, and alcohol. About 7½ minims of chloroform, 11 minims of tincture of Indian cannabis, 2 minims of tincture of capsicum, 1-7th of a grain of morphine sulphate, are represented in 1 fluidrachm of the finished mixture. It is used in *diarrhea* and *cholera*. It should not be confounded with chlorodyne (see *Tinctura Chloroformi et Morphinæ Composita*, p. 1136), which is a much stronger preparation.

The *dose* is thirty minims (2 mils).

MISTURA COPAIBÆ. N. F.

Copaiba Mixture [Mist. Copaib. Lafayette Mixture]

This preparation contains copaiba, spirit of nitrous ether, compound tincture of lavender, solution of potassium hydroxide, syrup, and mucilage of acacia. There is 7½ minims each of copaiba and sweet spirit of nitre in one fluidrachm. It is used in *gonorrhea*.

The *dose* is two fluidrachms (8 mils).

MISTURA COPAIBÆ ET OPII. N. F.

Mixture of Copaiba and Opium [Mist. Copaib. et Opii. Chapman's Mixture]

This preparation contains double the proportions of copaiba and spirit of nitrous ether in the above, and in addition two minims of tincture of opium in each fluidrachm. It is used in *gonorrhea*.

The *dose* is one fluidrachm (4 mils).

MISTURA FERRI COMPOSITA. N. F. (U. S. P. VIII)

Compound Iron Mixture [Mist. Ferr. Co. Griffith's Mixture]

This preparation contains ferrous sulphate crystals, myrrh, sugar, potassium carbonate, spirit of lavender and rose water. The formula is the same as that of the U. S. P. VIII. It is a hæmatinic.

The *dose* is four fluidrachms (15 mils).

MISTURA GUAIACI. N. F.

Mixture of Guaiac [Mist. Guaiac.]

This preparation is made from tincture of guaiac, clarified honey, and cinnamon water. It is used as an alterative and expectorant. It is used in the treatment of *rheumatism*.

The *dose* is four fluidrachms (15 mils).

MISTURA MAGNESIÆ, ASAFŒTIDÆ ET OPII. N. F. Mistura Magnesiæ et Asafœtidæ, N. F. III

Mixture of Magnesia, Asafetida and Opium [Mist. Mag., Asafœt. et Opii. Dewees' Carminative]

This preparation contains 5 per cent. magnesium carbonate, 7.5 per cent. tincture of asafetida, 1 per cent. tincture of opium, with sugar and water. It is used as an anodyne and carminative.

The *dose* is two fluidrachms (8 mils).

MISTURA OLEI PICIS. N. F.

Mixture of Oil of Tar [Mist. Ol. Pic. Mistura Picis Liquidæ. Tar Mixture]

Each fluidrachm of this preparation contains approximately 2 minims of rectified oil of tar in a vehicle composed of purified extract of glycyrrhiza, sugar, chloroform, oil of peppermint, alcohol, and water. It is used as an expectorant.

The *dose* is two fluidrachms (8 mils).

MISTURA OLEO-BALSAMICA. N. F.

Oleo-Balsamic Mixture [Mist. Ol.-Balsam.]

This preparation contains 0.4 per cent. each of the oils of lavender, thyme, lemon, nutmeg, and cinnamon, with eugenol, balsam of Peru, and alcohol. Its greatest value lies in its pleasant odor.

MISTURA OPII ET CHLOROFORMI COMPOSITA. N. F.

Compound Mixture of Opium and Chloroform [Mist. Opii et Chlorof. Co. Squibb's Diarrhea Mixture]

This preparation contains 20 per cent. each of tincture of opium and spirit of camphor,

with tincture of capsicum, chloroform and alcohol. It is used in serous *diarrheas.*

The *dose* is thirty minims (2 mils).

MISTURA OPII ET RHEI COMPOSITA.

Compound Mixture of Opium and Rhubarb [Mist. Opii et Rhei Co. Sun Cholera Mixture]

This preparation contains 10 per cent., each, of tincture of capsicum and tincture of rhubarb, and 20 per cent., each, of tincture of opium, spirit of camphor, and spirit of peppermint, dissolved in alcohol. It is used in *cholera morbus.*

The *dose* is thirty minims (2 mils).

MISTURA OPII ET SASSAFRAS. N. F. Mistura Sassafras et Opii, N. F. III

Mixture of Opium and Sassafras [Mist. Opii et Sassaf. Mistura Opii Alkalina. Godfrey's Cordial]

This preparation contains about 2 minims of tincture of opium in 1 fluidrachm of the finished mixture together with potassium carbonate, flavored with oil of sassafras. It is intended as a preparation for exhibiting opium in children.

The *dose* for an infant is five minims (0.3 mil).

MISTURA PECTORALIS, STOKES. N. F.

Stokes' Expectorant [Mist. Pect. Stokes]

Each fluidrachm of this preparation represents, approximately, 1 grain of ammonium carbonate, 2 minims each of fluidextracts of squill and senega, and 10 minims of paregoric dissolved in water and syrup of tolu. It is used as an expectorant.

The *dose* is one fluidrachm (4 mils).

MISTURA RHEI ALKALINA. N. F. Syrupus Rhei et Potassii Compositus, N. F. III

Alkaline Mixture of Rhubarb [Mist. Rhei Alk. Neutralizing Cordial]

This preparation contains fluidextracts of rhubarb and hydrastis, potassium carbonate, tincture of cinnamon, spirit of peppermint, syrup, and diluted alcohol. It is used as a laxative, antacid and carminative for infants.

The *dose* is one fluidrachm (4 mils).

MISTURA RHEI COMPOSITA. N. F. (U. S. P. VIII) Mistura Rhei et Sodæ, U. S. P. VIII

Compound Mixture of Rhubarb [Mist. Rhei Co. Mixture of Rhubarb and Soda]

This preparation is made from the fluidextracts of rhubarb and ipecac, sodium bicarbonate, glycerin, and peppermint water. The formula is the same as that of the U. S. P. VIII. It is used as a laxative for infants. Each fluidrachm represents 0.9 grain of rhubarb.

The *dose* is one fluidrachm (4 mils).

MUCILAGO CHONDRI. N. F.

Mucilage of Chondrus [Mucil. Chondr. Mucilage of Irish Moss]

This preparation contains 3 per cent. of Irish moss in water. It is used as an emulsifying agent and demulcent.

MUCILAGO SASSAFRAS MEDULLÆ. N. F. (U. S. P. VIII)

Mucilage of Sassafras Pith [Mucil. Sassaf. Medul.]

This preparation contains 2 grammes of sassafras pith in each 100 mils. The formula is the same as that of the U. S. P. VIII. It is a bland mucilage used principally in eye lotions and should always be freshly prepared.

The *dose* is four fluidrachms (15 mils).

MULLÆ. N. F.

Mulls [Salve Mulls. Steatins]

The mulls or salve mulls are very stiff ointments spread upon soft muslin (mull) similar to a plaster. The base is usually suet or lard, but wax or even lead plaster are used in some of the members of the group.

MULLA ACIDI SALICYLICI. N. F. Unguentum Salicylatum Extensum, N. F. III

Salicylic Acid Mull [Mull. Ac. Salicyl.]

This preparation contains 10 per cent. of salicylic acid with a mixture of benzoinated suet and benzoinated lard.

MULLA CREOSOTI SALICYLATA. N. F. Unguentum Creosoti Salicylatum Extensum, N. F. III

Salicylated Creosote Mull [Mull. Creosot. Salicyl.]

This preparation contains 10 per cent. of salicylic acid and 20 per cent. of creosote in a mixture of benzoinated suet and yellow wax.

MULLA HYDRARGYRI CHLORIDI CORROSIVI. N. F. Unguentum Hydrargyri Chloridi Corrosivi Extensum, N. F. III

Corrosive Mercuric Chloride Mull [Mull. Hydrarg. Chlor. Corros.]

This preparation contains 0.2 per cent. of corrosive sublimate in a mixture of benzoinated suet, benzoinated lard, and alcohol.

MULLA ZINCI. N. F. Unguentum Zinci Extensum, N. F. III

Zinc Mull [Mull. Zinc.]

This preparation is made with zinc oxide, 10 per cent., in a mixture of benzoinated suet and benzoinated lard.

NEBULA AROMATICA. N. F.

Aromatic Oil Spray [Nebul. Arom. Aromatol]

This preparation contains phenol, menthol, thymol, camphor, benzoic acid, eucalyptol, oil of cinnamon, oil of clove and methyl salicylate in small proportions, in solution in light liquid petrolatum. It is used as an inhalant in the form of a nebula or spray. Its virtues are due chiefly to the liquid petrolatum.

NEBULA EUCALYPTOLIS. N. F.

Eucalyptol Spray [Nebul. Eucalyptol.]

This preparation contains 5 per cent. of eucalyptol in solution in light liquid petrolatum. It is used as an inhalant in the form of a nebula or spray.

NEBULA MENTHOLIS. N. F.

Menthol Spray [Nebul. Menthol.]

This preparation consists of a solution of 2 per cent. of menthol in light liquid petrolatum. It is used as an inhalant in the form of a nebula or spray.

NEBULA MENTHOLIS COMPOSITA. N. F.

Compound Menthol Spray [Nebul. Menthol. Co.]

This preparation contains 1 per cent. each of menthol and camphor, with smaller amounts of methyl salicylate, eucalyptol, and oil of cinnamon in solution in light liquid petrolatum. It is used as an inhalant in the form of a nebula or spray.

NEBULA THYMOLIS. N. F.

Thymol Spray [Nebul. Thymol.]

This preparation contains 1 per cent. of thymol in solution in light liquid petrolatum. It is used as an inhalant in the form of a nebula or spray.

OLEA INFUSA. N. F.

Infused Oils [Ol. Inf.]

The formula for these is a general one. The infused oils are made from the air dried drug, 10 per cent. with alcohol, ammonia water, and sesame oil.

OLEATUM ACONITINÆ. N. F.

Oleate of Aconitine [Oleat. Aconitin.]

This preparation is a solution of 2 per cent. of aconitine in equal parts of oleic acid and olive oil. This preparation does not deserve recognition; the danger of poisoning by it far outweighs any probability of benefit.

OLEATUM ATROPINÆ. N. F. (U. S. P. VIII)

Oleate of Atropine [Oleat. Atrop.]

This preparation is a solution of 2 per cent. of atropine in a little alcohol and equal parts of oleic acid and olive oil. The formula is the same as that of the U. S. P. VIII.

OLEATUM COCAINÆ. N. F. (U. S. P. VIII)

Oleate of Cocaine [Oleat. Cocain.]

This preparation contains 5 per cent. cocaine dissolved in a little alcohol and then incorporated with oleic acid and olive oil. The formula is the same as that of the U. S. P. VIII. It is used as a local anesthetic.

OLEATUM QUININÆ. N. F. (U. S. P. VIII)

Oleate of Quinine [Oleat. Quin.]

This preparation contains 25 per cent. of quinine in oleic acid and is used as a local anesthetic. The formula is the same as that of the U. S. P. VIII.

OLEATUM VERATRINÆ. N. F. (U. S. P. VIII)

Oleate of Veratrine [Oleat. Veratrin.]

This preparation contains 2 per cent. of veratrine in equal parts of olive oil and oleic acid, and is used as an anodyne and rubefacient. It should be used cautiously on account of the danger of systemic poisoning. The formula is the same as that of the U. S. P. VIII.

OLEORESINA LUPULINI N. F. (U. S. P. VIII)

Oleoresin of Lupulin [Oleores. Lupulin.]

Prepared in the usual method from lupulin, using ether to exhaust the drug. The U. S. P. VIII directed the use of acetone as the menstruum.

The *dose* is three grains (0.2 mil).

OLEOSACCHARA. N. F.

Oil-sugars [Elæosacchara]

These new preparations are prepared by triturating any prescribed oil (2 per cent.) with sugar. Used as adjuvants or vehicles.

OLEUM ÆTHEREUM. N. F. (U. S. P. VIII)

Ethereal Oil [Ol. Æther.]

This is a volatile liquid consisting of equal volumes of ether and of heavy oil of wine, prepared by distillation of alcohol with sulphuric acid. The process is the same as that of the U. S. P. VIII. It is transparent, nearly colorless, has a specific gravity of 0.905 at 25° C. (77° F.), a peculiar aromatic odor, and a pungent taste. Preserve in small glass-stoppered bottles in a cool place. It is used in the preparation of compound spirit of ether (Hoffmann's anodyne).

OLEUM HYOSCYAMI COMPOSITUM. N. F.

Compound Oil of Hyoscyamus [Ol. Hyosc. Co. Balsamum Tranquillans]

This preparation is made from 0.2 per cent. of the oils of lavender, peppermint, rosemary, and thyme, with infused oil of hyoscyamus. It is used as an anodyne.

OLEUM PHENOLATUM. N. F.

Oleum Carbolatum, N. F. III. Phenolated Oil [Ol. Phenol. Carbolized Oil.]

It is made by dissolving 5 per cent. of phenol in cottonseed oil. Used externally.

OLEUM PHOSPHORATUM. N. F.

Phosphorated Oil [Ol. Phosphorat.]

This preparation is made by dissolving 1 per cent. of phosphorus in 50 times its weight of expressed oil of almond with the aid of water bath heat and adding to this solution an equal volume of ether. It is a clear, yellowish liquid, having the odor of phosphorus and of ether, and free from undissolved particles. It affords an excellent means of administering phosphorus.

The *dose* is one minim (0.05 mil).

OLEUM RICINI AROMATICUM. N. F.

Aromatic Castor Oil [Ol. Ricin. Arom.]

This is castor oil flavored with benzosulphinide (0.05 per cent.), oils of clove and cinnamon, vanillin, coumarin, and alcohol.

The *dose* is four fluidrachms (15 mils).

OXYMEL SCILLÆ. N. F.

Oxymel of Squill [Oxymel Scill.]

This preparation is made from 1 part of vinegar of squill and 2 parts of clarified honey. Used as an expectorant.

The *dose* is one fluidrachm (4 mils).

PASTÆ DERMATOLOGICÆ. N. F.

Dermatologic Pastes

These preparations are ointment-like mixtures of starch, dextrin, zinc oxide, sulphur, calcium carbonate, or other medicinal substances made into a paste with glycerin, soft soap, petrolatum, etc., medicated with antiseptic or astringent agents and used in the practice of dermatologists.

PASTA BETANAPHTHOLIS. N. F. Pasta Naphtholis Lassar, N. F. III

Betanaphthol Paste [Past. Betanaphthol. Lassar's Naphthol Paste]

This preparation contains 10 per cent. of betanaphthol, 50 per cent. of sulphur, 20 per cent. of petrolatum, and 20 per cent. of soft soap. It is used externally as an antiseptic and parasiticide.

PASTA DEXTRINATA. N. F.

Dextrinated Paste [Past. Dextrin.]

This preparation contains 33 per cent. white dextrin, 33 per cent. glycerin and water. It is used as a vehicle.

PASTA RESORCINOLIS FORTIS. N. F.

Strong Resorcinol Paste [Past. Resorcin. Fort. Lassar's Stronger Resorcinol Paste]

This preparation contains 20 per cent. of resorcinol, zinc oxide, and starch, together with 40 per cent. of light liquid petrolatum. Used externally in skin diseases.

PASTA RESORCINOLIS MITIS. N. F. Pasta Resorcini Mitis, Lassar, N. F. III

Mild Resorcinol Paste [Past. Resorcin. Mit. Lassar's Mild Resorcinol Paste]

This preparation contains 10 per cent. of resorcinol with 25 per cent. each of zinc oxide and starch, and 40 per cent. of light liquid petrolatum. Used locally in diseases of the skin.

PASTA ZINCI. N. F. Pasta Zinci Lassar, N. F. III

Zinc Paste [Past. Zinc. Lassar's Zinc Paste]

This preparation contains 2 per cent. of salicylic acid, 24 per cent. of zinc oxide and starch, and 50 per cent. of petrolatum. Used as an antiseptic and protective in skin diseases.

PASTA ZINCI MOLLIS. N. F. Pasta Zinci Mollis, Unna, N. F. III

Soft Zinc Paste [Past. Zinc Moll. Unna's Soft Zinc Paste]

This preparation contains 25 per cent. each of zinc oxide, precipitated calcium carbonate,

linseed oil, and solution of calcium hydroxide (lime water). It is used as an astringent.

PASTA ZINCI SULPHURATO. N. F. Pasta Zinci Sulphurata, Unna, N. F. III

Sulphurated Zinc Paste [Past. Zinc. Sulphur. Unna's Sulphurated Zinc Paste]

This preparation contains 15 per cent. of zinc oxide, 10 per cent. of precipitated sulphur, 5 per cent. of purified siliceous earth, and 70 per cent. of benzoinated lard. It is used as an antizymotic and protective.

PEPSINUM SACCHARATUM. N. F.

Saccharated Pepsin [Pepsin. Sacchar.]

This preparation is a 10 per cent. triturate of pepsin with sugar of milk, used as a digestive.

The *dose* is fifteen grains (1 Gm.).

PETROXOLINUM BETANAPHTHOLIS. N. F.

Betanaphthol Petroxolin [Petrox. Betanaphthol. Betanaphthol Petrox]

This preparation is a 10 per cent. fresh solution of betanaphthol in liquid petroxolin. It is used as an antizymotic and parasiticide.

PETROXOLINUM CADINUM. N. F.

Cade Petroxolin [Petrox. Cadin. Cade Petrox]

This preparation is a 25 per cent. mixture of oil of cade and liquid petroxolin. It is used as an antiseptic and antiparasitic.

PETROXOLINUM CHLOROFORMI CAMPHORATUM. N. F.

Camphorated Chloroform Petroxolin [Petrox. Chlorof. Camph. Camphor and Chloroform Petrox]

This preparation is a solution of 25 per cent. each of chloroform and camphor in liquid petroxolin. It is used as an anodyne and rubefacient.

PETROXOLINUM CREOSOTI. N. F.

Creosote Petroxolin [Petrox. Creosot. Creosote Petrox]

This preparation is a mixture of creosote 20 per cent., and olive oil 5 per cent., in liquid petroxolin. It is used as an antiputrescent and antiseptic.

PETROXOLINUM EUCALYPTOLIS. N. F.

Eucalyptol Petroxolin [Petrox. Eucalyptol. Eucalyptol Petrox]

This preparation is a 20 per cent. solution of eucalyptol in liquid petroxolin. It is used as an antiseptic and rubefacient.

PETROXOLINUM GUAIACOLIS. N. F.

Guaiacol Petroxolin [Petrox. Guaiacol. Guaiacol Petrox]

This preparation is a mixture of guaiacol 20 per cent., olive oil 5 per cent., and liquid petroxolin. It is used externally as a deodorant and antipyretic.

PETROXOLINUM HYDRARGYRI. N. F.

Mercury Petroxolin [Petrox. Hydrarg. Mercury Petrox]

This preparation contains 30 per cent. of mercury extinguished with 13 per cent. of hydrous wool fat and 2 per cent. oleic acid and solid petroxolin added. It is used as an antisyphilitic and antiparasitic.

PETROXOLINUM IODI. N. F.

Iodine Petroxolin [Petrox. Iod. Iodine Petrox, 10 per cent.]

This preparation is a mixture of 10 per cent. iodine, 40 per cent. oleic acid, 20 per cent. alcohol, 23 per cent. light liquid petrolatum, 2 per cent. oil of lavender, and 5 per cent. stronger ammonia water. It is used as a counter irritant and discutient.

PETROXOLINUM IODI DILUTUM. N. F.

Diluted Iodine Petroxolin [Petrox. Iod. Dil. Iodine Petrox, 5 per cent.]

This preparation is a solution of 5 per cent. iodine in liquid petroxolin. It is used as an absorbent and discutient.

PETROXOLINUM IODOFORMI. N. F.

Iodoform Petroxolin [Petrox. Iodoform. Iodoform Petrox]

This preparation is a freshly prepared solution of 3 per cent. iodoform, 20 per cent. acetone, 10 per cent. oleic acid, 3 per cent. eucalyptol, and liquid petroxolin. It is used as an antitubercular and antiseptic.

PETROXOLINUM LIQUIDUM. N. F. Petrolatum Saponatum Liquidum, N. F. III

Liquid Petroxolin [Petrox. Liq. Liquid Petrox]

This preparation is made from 50 per cent. light liquid petrolatum, 28 per cent. oleic acid, 2 per cent. oil of lavender, 5 per cent. stronger ammonia water, and 15 per cent. alcohol. It is a yellowish-brown liquid, miscible with ether, chloroform, petroleum benzin or acetone and producing an emulsion-like mixture when added to twice its volume of water. It is used as a vehicle.

PETROXOLINUM MENTHOLIS. N. F.

Menthol Petroxolin [Petrox. Menthol. Menthol Petrox]

This preparation is a solution of menthol, 17 per cent., in liquid petroxolin. It is used as a local anesthetic.

PETROXOLINUM METHYLIS SALICYLATIS. N. F.

Methyl Salicylate Petroxolin [Petrox. Methyl. Sal. Methyl Salicylate Petrox]

This preparation is a solution of methyl salicylate, 20 per cent., in liquid petroxolin. It is used as an antirheumatic.

PETROXOLINUM PHENOLIS. N. F.

Phenol Petroxolin [Petrox. Phenol. Phenol Petrox]

This preparation is a 5 per cent. solution of phenol in liquid petroxolin. It is used as an antiseptic and local anesthetic.

PETROXOLINUM PHENOLIS CAMPHORATUM. N. F.

Camphorated Phenol Petroxolin [Petrox. Phenol. Camph. Camphorated Phenol Petrox]

This contains 12.5 per cent. phenol and 37.5 per cent. camphor in liquid petroxolin. It is used as an analgesic.

PETROXOLINUM PICIS. N. F.

Tar Petroxolin [Petrox. Pic. Tar Petrox]

This preparation is a mixture of 25 per cent. rectified oil of tar in liquid petroxolin. It is used as a deodorant and parasiticide.

PETROXOLINUM SPISSUM. N. F. Petrolatum Saponatum Spissum, N. F. III

Solid Petroxolin [Petrox. Spiss. Solid Petrox]

This preparation is a mixture of 35 per cent. white wax, 20 per cent. light liquid petrolatum, 32 per cent. oleic acid, 3 per cent. oil of lavender, 5 per cent. alcohol, and 5 per cent. stronger ammonia water. It is used as a vehicle for ointments.

PETROXOLINUM SULPHURATUM. N. F.

Sulphurated Petroxolin [Petrox. Sulphur. Sulphurated Petrox]

This preparation is a mixture of 3 per cent. sublimed sulphur, 37 per cent. linseed oil, 30 per cent. oleic acid, and liquid petroxolin. It is used as a parasiticide.

PETROXOLINUM SULPHURATUM COMPOSITUM. N. F.

Compound Sulphurated Petroxolin [Petrox. Sulphur. Co. Compound Sulphurated Petrox.

This preparation is made from 10 per cent. sulphurated petroxolin, 10 per cent. oil of cade, 0.3 per cent. thymol, 3 per cent. eucalyptol, 30 per cent. oil of turpentine, and liquid petroxolin. It is used as a parasiticide.

PETROXOLINUM TEREBINTHINÆ LARICIS. N. F.

Venice Turpentine Petroxolin [Petrox. Terebinth. Laric. Venice Turpentine Petrox]

This preparation is a solution of 20 per cent. Venice turpentine in liquid petroxolin. It is used as a vulnerary rubefacient in veterinary practice.

PHENOL IODATUM. N. F. Acidum Carbolicum Iodatum, N. F. III

Iodized Phenol [Phenol. Iodat.]

This is made from iodine 20 per cent., phenol 60 per cent., and glycerin. It is an active germicide.

PILULÆ. N. F.

Pills

Pills are globular or ovoid dosage forms of medicinal substances intended for internal administration. Each pill weighs not less than 0.06 Gm., nor more than 0.5 Gm. If they weigh less than 0.06 Gm. and more than 0.02 Gm. each they are known as *"Granules"*; if the weight is less than 0.02 Gm., they are usually designated as *"Parvules."* The ingredients are massed by the aid of selected excipients.

For the extemporaneous coating of pills by the pharmacist, formulas and working directions for the following methods are supplied: gelatin, sugar, cocoa, tolu, silver, and salol coatings. For the coating of the so-called "enteric pills," the use of salol is recommended.

PILULÆ AD PRANDIUM. N. F.

Dinner Pills [Pil. Ad. Prand.]

When dinner pills are prescribed, the official pills of aloes and mastic should be dispensed.

Dose, of dinner pills, one or two.

Other so-called dinner pills are as follows:

Chapman's Dinner Pill.—Each pill contains

1½ grains of purified aloes, 1½ grains of mastic, 1 grain of ipecac and about ¼ minim of oil of fennel.

Cole's Dinner Pill.—Each pill contains 1 and 1-5th of a grain each of purified aloes, mass of mercury, and jalap and 1-50th of a grain of antimony and potassium tartrate.

Hall's Dinner Pill.—Each pill contains 1 grain each of purified aloes, extract of glycyrrhiza, soap, and syrup.

PILULÆ ALOES ET ASAFŒTIDÆ. N. F.

Pills of Aloes and Asafetida [Pil. Aloe. et Asafœt.]

Each pill contains 0.09 Gm. (1½ grains) each of aloes, soap, and asafetida massed with water.

The *dose* is one pill.

PILULÆ ALOES ET FERRI. N. F. (U. S. P. VIII)

Pills of Aloes and Iron [Pil. Aloe. et Ferr.]

Each pill contains about 1 grain each of aloes, exsiccated ferrous sulphate and aromatic powder massed with confection of rose. The formula is the same as that of the U. S. P. VIII.

The *dose* is two pills.

PILULÆ ALOES ET MASTICHES. N. F. (U. S. P. VIII)

Pills of Aloes and Mastic [Pil. Aloe. et Mastich. Lady Webster's Dinner Pills]

Each pill contains 2 grains of aloes, ¾ grain of mastic, and ½ grain of red rose massed with diluted alcohol. The formula is the same as that of the U. S. P. VIII.

The *dose* is two pills.

PILULÆ ALOES ET MYRRHÆ. N. F. (U. S. P. VIII)

Pills of Aloes and Myrrh [Pil. Aloe. et Myrrh.]

Each pill contains 2 grains of aloes, 1 grain of myrrh, ¾ grain of aromatic powder, massed with syrup. The formula is the same as that of the U. S. P. VIII.

The *dose* is two pills.

PILULÆ ALOES ET PODOPHYLLI COMPOSITÆ. N. F.

Compound Pills of Aloes and Podophyllum [Pil. Aloe. et Podoph. Co. Janeway's Pills]

Each pill contains 1 grain of purified aloes, ½ grain resin of podophyllum, ¼ grain of extract of belladonna leaves, and ¼ of a grain of extract of nux vomica. They are used as a laxative and hepatic tonic.

The *dose* is one pill.

PILULÆ ALOES, HYDRARGYRI ET PODOPHYLLI. N. F. Pilulæ Triplices, N. F. III

Pills of Aloes, Mercury, and Podophyllum [Pil. Aloe. Hydrarg. et Podoph. Triplex Pills. Pilula Triplex]

Each pill contains 2 grains of aloes, 1 grain mass of mercury, and ¼ grain resin of podophyllum. They are used as a cathartic and hepatic tonic.

The *dose* is one pill.

PILULÆ ALOES, HYDRARGYRI ET SCAMMONII COMPOSITÆ. N. F.

Compound Pills of Aloes, Mercury, and Scammony [Pil. Aloe. Hydrarg. et Scammon. Francis' "Triplex" Pills]

Each pill contains ⅝ grain each of aloes, resin of scammony, and mass of mercury, 1-20th minim of croton oil and ¼ minim oil of caraway. Used as a cathartic, the *dose* being one pill.

PILULÆ ALOINI COMPOSITÆ. N. F.

Compound Pills of Aloin [Pil. Aloin. Co.]

Each pill contains ½ grain of aloin, ⅛ grain of resin of podophyllum, ¼ grain of extract of belladonna leaves. Cathartic.

The *dose* is one pill.

PILULÆ ALOINI, STRYCHNINÆ ET BELLADONNÆ. N. F.

Pills of Aloin, Strychnine and Belladonna [Pil. A. S. et B.]

Each pill contains 1-5th grain of aloin, 1-120th grain of strychnine, and ⅛ grain of extract of belladonna leaves. Used as a laxative.

The *dose* is one pill.

PILULÆ ALOINI, STRYCHNINÆ ET BELLADONNÆ COMPOSITÆ. N. F.

Compound Pills of Aloin, Strychnine and Belladonna [Pil. A. S. et B. Co.]

Each pill contains 1-5th grain of aloin, 1-120th grain of strychnine, ⅛ grain of extract of belladonna leaves, and ½ grain of extract of cascara sagrada. Used as a laxative.

The *dose* is one pill.

PILULÆ ANTIDYSPEPTICÆ. N. F.

Antidyspeptic Pills [Pil. Antidyspep.]

Each pill contains 1-40th grain of strychnine, 1-10th grain of ipecac, 1-10th grain of

extract of belladonna leaves, 2 grains of mass of mercury, and 2 grains of compound extract of colocynth. Used as a cholagogue.

The *dose* is one pill.

PILULÆ ANTIMONII COMPOSITÆ. N. F.

Compound Pills of Antimony [Pil. Antimon. Co. Plummer's Pills]

Each pill contains 3-5th grain of sulphurated antimony and calomel, 1 and 1-5th grain of guaiac, and castor oil.

The dose, as an alterative and diaphoretic, is one pill.

PILULÆ ANTIPERIODICÆ. N. F.

Antiperiodic Pills [Pil. Antiperiod. Warburg's Pills]

Each pill contains 1 grain of extract of aloes, ½ grain of rhubarb, ½ grain of angelica seed, ¼ grain of elecampane, ¼ grain of saffron, ¼ grain of fennel, ⅛ grain of zeodoary root, ⅛ grain of cubebs, ⅛ grain of myrrh, ⅛ grain of white agaric, ⅛ grain of camphor, 1 and 2-5th grains of quinine sulphate, with a sufficient quantity of extract of gentian to form a mass. Used as an antiperiodic.

The *dose* is one to three pills one to three times daily.

PILULÆ ANTIPERIODICÆ SINE ALOE. N. F.

Antiperiodic Pills without Aloes [Pil. Antiperiod. s. Aloe. Warburg's Pills without Aloes]

The formula is similar to that for the preceding pill, but the extract of aloes is omitted.

The *dose* is one pill.

PILULÆ CATHARTICÆ VEGETABILES. N. F. (U. S. P. VIII)

Vegetable Cathartic Pills [Pil. Cathart. Veget.]

Each pill contains 1 grain compound extract of colocynth, ½ grain extract of hyoscyamus, ¼ grain of resin of jalap, and 1-5th grain each of extract of leptandra and resin of podophyllum with 1-10th minim oil of peppermint and massed with diluted alcohol. Used as a cathartic.

The *dose* is two pills.

PILULÆ COLOCYNTHIDIS COMPOSITÆ. N. F.

Compound Pills of Colocynth [Pil. Colocynth. Co. Pilulæ Cocciæ. Cochia Pills]

Each pill contains 1-6th grain of extract of colocynth, 2 grains of purified aloes, 2 grains of resin of scammony and ¼ minim of oil of clove. Used as a cathartic.

The *dose* is one pill.

PILULÆ COLOCYNTHIDIS ET HYOSCYAMI. N. F.

Pills of Colocynth and Hyoscyamus [Pil. Colocynth. et Hyoscy.]

Each pill contains 1-10th grain of extract of colocynth, 1½ grains of purified aloes, 1½ grains of resin of scammony, ⅛ minim of oil of clove, and 1½ grains of extract of hyoscyamus. Used as a cathartic.

The *dose* is one pill.

PILULÆ COLOCYNTHIDIS ET PODOPHYLLI. N. F.

Pills of Colocynth and Podophyllum [Pil. Colocynth. et Podoph.]

Each pill contains 2½ grains of compound extract of colocynth, and ¼ grain of resin of podophyllum. Used as a cathartic.

The *dose* is one pill.

PILULÆ DIGITALIS, SCILLÆ ET HYDRARGYRI. N. F.

Pills of Digitalis, Squill, and Mercury [Pil. Digit. Scill. et Hydrarg. Niemeyer Pills for Dropsy. Guy's Pills]

Each pill contains 1 grain each of digitalis, squill, and mercury massed with clarified honey. Used as a diuretic. They must be carefully distinguished from Niemeyer's pill for *phthisis* (see *Pilulæ Opii Digitalis et Quininæ*).

The *dose* is one pill.

PILULÆ FERRI, QUININÆ, ALOES ET NUCIS VOMICÆ. N. F. Pilulæ Quadruplices, N. F. III

Pills of Iron, Quinine, Aloes and Nux Vomica [Pil. Ferr. Quin. Aloe. et Nuc. Vom. Quadruplex Pills Pilulæ Ferri et Quininæ Compositæ]

Each pill contains 1 grain each of dried ferrous sulphate, quinine sulphate, and aloes, ¼ grain of extract of nux vomica, and enough extract of gentian to mass. Used as a tonic and hematinic.

The *dose* is one pill.

PILULÆ FERRI, QUININÆ, STRYCHNINÆ ET ARSENI FORTIORES N. F. Pilulæ Metallorum, N. F. III

Stronger Pills of Iron, Quinine, Strychnine and Arsenic [Pil. Ferr. Quin. Strych. et Arsen. Fort. Metallic Pills. Pilulæ Metallorum Amaræ. Bitter Metallic Pills]

Each pill contains 1 grain of reduced iron and quinine sulphate, and 1-20th grain of strych-

nine and arsenic trioxide massed with clarified honey. Used as a tonic.
The *dose* is one pill.

PILULÆ FERRI, QUININÆ, STRYCHNINÆ ET ARSENI MITES. N. F

Mild Pills of Iron, Quinine, Strychnine, and Arsenic [Pil. Ferr. Quin. Strych. et Arsen. Mit. Aitken Tonic Pills]

Each pill contains ⅔ grain of reduced iron and 1 grain of quinine sulphate, and 1/50 grain each of strychnine and arsenic trioxide massed with clarified honey. Used as a tonic.
The *dose* is one pill.

PILULÆ GLYCERYLIS NITRATIS. N. F.
Pilulæ Glonoini, N. F. III

Pills of Nitroglycerin [Pil. Glycer. Nit. Pills of Glonoin]

They are made from spirit of glyceryl trinitrate, althea and confection of rose. Each pill contains 1-100th grain of nitroglycerin. They offer a convenient means of exhibiting nitroglycerin, but are likely to deteriorate if not properly kept.
The *dose* is one pill.

PILULÆ LAXATIVÆ COMPOSITÆ. N. F. (U. S. P. VIII)

Compound Laxative Pills [Pil. Lax. Co.]

Each pill contains ¼ grain aloin, 1-120th grain strychnine, ⅛ grain extract of belladonna leaves, 1-16th grain of ipecac, licorice and syrup to mass. Used as a laxative.
The *dose* is two pills.

PILULÆ LAXATIVÆ POST PARTUM. N. F.

Post Partum Laxative Pills [Pil. Lax. Post Part. Barker's Post Partum Pills]

Each pill contains 1⅔ grains of compound extract of colocynth, ⅝ grain of purified aloes, 5-12th grain of extract of nux vomica, 1-12th grain of resin of podophyllum, 1-12th grain of ipecac, and 1¼ grains of extract of hyoscyamus. The formula is the same as that of the U. S. P. VIII. Used as a cathartic, the *dose* being one pill.

PILULÆ OPII, DIGITALIS ET QUININÆ. N. F.

Pills of Opium, Digitalis, and Quinine [Pil. Opii, Digit. et Quin. Niemeyer Pills for Phthisis]

Each pill contains 3-16th grain of opium and 1 grain each of digitalis and quinine. Used as diuretic and tonic.
The *dose* is one pill.

PILULÆ OPII ET CAMPHORÆ. N. F.

Pills of Opium and Camphor [Pil. Opii et Camph.]

Each pill contains 1 grain of powdered opium and 2 grains of camphor. Used in *diarrhea.*
The *dose* is one pill.

PILULÆ OPII ET PLUMBI. N. F.

Pills of Opium and Lead [Pil. Opii et Plumb.]

Each pill contains 1 grain of powdered opium and 1 grain of lead acetate. Used as an anodyne and astringent in serous *diarrheas.*
The *dose* is one pill.

PILULÆ RHEI. N. F.

Pills of Rhubarb [Pil. Rhei]

Each pill contains 3 grains of rhubarb and 1 grain of soap. Used as a laxative.
The *dose* is one pill.

POTASSA CUM CALCE. N. F.

Potassa with Lime [Pot. c. Calc.]

By triturating equal parts of burnt lime and caustic potash. Used as a caustic.

PULVIS ACETANILIDI COMPOSITUS. N. F. (U. S. P. VIII)

Compound Acetanilid Powder [Pulv. Acetan. Co.]

A mixture of acetanilid, 70 per cent., caffeine, 10 per cent., and sodium bicarbonate, 20 per cent. The formula is the same as that of the U. S. P. VIII. Used as an analgesic and antipyretic.
The *dose* is five grains (0.3 Gm.).

PULVIS ALOES ET CANELLÆ. N. F.

Powder of Aloes and Canella [Pulv. Aloe. et Canell. Hiera Picra]

It contains 80 per cent. of purified aloes and 20 per cent. of powdered canella. It is used as an emmenagogue and laxative.
The *dose* is five grains (0.3 Gm.).

PULVIS ANTIMONIALIS. N. F.

Antimonial Powder [Pulv. Antimon. James' Powder]

A mixture of antimony oxide, 33 per cent., and precipitated calcium phosphate, 67 per cent. Used as a diaphoretic.
The *dose* is three grains (0.2 Gm.).

PULVIS ANTISEPTICUS. N. F.

Soluble Antiseptic Powder [Pulv. Antisept. Pulvis Antisepticus Solubilis]

It contains salicylic acid, phenol, eucalyptol, menthol, thymol, zinc sulphate and powdered boric acid. It is used as an antiseptic.

PULVIS AROMATICUS RUBEFACIENS. N. F. Replacing Emplastrum Aromaticum, N. F. III

Rubefacient Spice Powder [Pulv. Arom. Rubefac.]

Consists of clove, 30 per cent., Saigon cinnamon, 30 per cent., ginger, 20 per cent., and capsicum, 20 per cent.

NOTE.—When rubefacient spice powder is needed for *Spice Poultice,* place the required quantity in a flat muslin bag and moisten it with either diluted alcohol or vinegar, previously heated.

PULVIS CRETÆ AROMATICUS. N. F.

Aromatic Powder of Chalk [Pulv. Cret. Arom.]

It contains 8 per cent. of cinnamon, 6 per cent. of nutmeg, 3 per cent. of clove, 2 per cent of cardamom seed, 25 per cent. of prepared chalk and 56 per cent. of sugar. It is used in *diarrhea.*

The *dose* is thirty grains (2 Gm.).

PULVIS CRETÆ ET OPII AROMATICUS. N. F. Pulvis Cretæ Aromaticus cum Opio, N. F. III

Aromatic Powder of Chalk and Opium [Pulv. Cret. et Opii Arom.]

One grain of powdered opium and 39 grains of aromatic powder of chalk are contained in 40 grains of this preparation. It is used in *cholera morbus.*

The *dose* is fifteen grains (1 Gm.).

PULVIS GAMBIR COMPOSITUS. N. F. Pulvis Catechu Compositus, N. F. III

Compound Powder of Gambir [Pulv. Gambir Co.]

Contains gambir, 40 per cent., kino and krameria, each, 20 per cent., and cinnamon and nutmeg, of each, 10 per cent. Used as an intestinal astringent.

The *dose* is twenty grains (1.3 Gm.).

PULVIS HYDRARGYRI CHLORIDI MITIS ET JALAPÆ. N. F.

Powder of Mild Mercurous Chloride and Jalap [Pulv. Hydrarg. Chlor. Mit. et Jalap. Calomel and Jalap]

It contains 34 per cent. of mild chloride of mercury and 66 per cent. of jalap. It is cathartic and cholagogue.

The *dose* is ten grains (0.65 Gm.).

PULVIS KINO ET OPII COMPOSITUS. N. F. Pulvis Kino Compositus, N. F. III

Compound Powder of Kino and Opium [Pulv. Kino et Opii Co.]

It contains 75 per cent. of powdered kino, 5 per cent. of powdered opium and 20 per cent. of powdered Saigon cinnamon. Used as an astringent.

The *dose* is fifteen grains (1 Gm.).

PULVIS MYRICÆ COMPOSITUS. N. F.

Compound Powder of Bayberry [Pulv. Myric. Co. Composition Powder]

It contains 60 per cent. of bayberry bark, 30 per cent. of ginger, 5 per cent. of capsicum, and 5 per cent. of clove. It is used as a carminative and stimulant.

The *dose* is fifteen grains (1 Gm.).

PULVIS PANCREATINI COMPOSITUS. N. F. Pulvis Pancreaticus Compositus, N. F. III

Compound Pancreatin Powder [Pulv. Pancreat. Co. Peptonizing Powder]

It contains 20 per cent. of pancreatin and 80 per cent. of sodium bicarbonate. Twenty-five grains of this powder are sufficient to peptonize 1 pint of fresh cow's milk. Used for preparing "predigested" foods.

PULVIS RHEI ET MAGNESIÆ ANISATUS. N. F.

Anisated Powder of Rhubarb and Magnesia [Pulv. Rhei et Magnes. Anis. Compound Anise Powder]

It contains 35 per cent. of powdered rhubarb and 65 per cent. of heavy magnesia, with anethol and alcohol. It is laxative and carminative.

The *dose* for infants is five grains (0.3 Gm.).

PULVIS TALCI COMPOSITUS. N. F. Pulvis Talci Salicylicus, N. F. III

Compound Powder of Talc [Pulv. Talc. Co. Boro-Salicylated Powder of Talc]

It contains 3 per cent. of salicylic acid, 10 per cent. of boric acid, and 87 per cent. of talc,

all in very fine powder. Used as an antiseptic dusting powder.

SALIA EFFERVESCENTIA. N. F.

Granular Effervescent Salts

Two general processes are given for preparing effervescent salts, the one to be used being determined by the quantity of material taken. The products, however, from both processes should be identical. The granulation is performed in an oven or on a water bath. The dry granular powder is passed through a No. 6 tinned-iron sieve, and immediately transferred to dry bottles or containers, and hermetically sealed.

SAL CAROLINUM FACTITIUM. N. F.

Artificial Carlsbad Salt [Sal. Carol. Fact.]

1. *In a Dry, Amorphous Form* (*G. P.*).—It contains 2 per cent. of potassium sulphate, 18 per cent. of sodium chloride, 36 per cent. of sodium bicarbonate, and sodium sulphate to make about 100 parts. Sixteen grains of this salt when dissolved in 6½ fluidounces of water represent an equal volume of Carlsbad water (Sprudel). Used as a laxative.

2. *In a Crystalline Form.*—It is made from 2 parts of potassium sulphate, 18 parts of sodium chloride, 28 parts of monohydrated sodium carbonate, 100 parts of crystallized sodium sulphate, and 100 parts of distilled water. Twenty-seven grains of this salt dissolved in 6½ fluidounces of water represent an equal volume of Carlsbad water (Sprudel). It is a laxative.

SAL CAROLINUM FACTITIUM EFFERVESCENS. N. F.

Pulvis Salis Carolini Factitii Effervescens, N. F. III. Effervescent Artificial Carlsbad Salt [Sal. Carol. Fact. Eff.]

It contains artificial Carlsbad salt, sodium bicarbonate, tartaric acid, and citric acid. Ninety grains of this powder dissolved in 6½ fluidounces of water represent an equal volume of Carlsbad water (Sprudel). Used as a laxative.

The *dose* is ninety grains (6 Gm.).

SAL KISSINGENSE FACTITIUM. N. F.

Artificial Kissingen Salt [Sal Kissingen. Fact.]

It is made from 1.7 parts of potassium chloride, 35.7 parts of sodium chloride, 12 parts of magnesium sulphate and 10.7 parts of sodium bicarbonate. Twenty-four grains of this salt dissolved in 6½ fluidounces of water represents an equal volume of Kissingen water (Rakoczi). It is an antacid laxative.

SAL KISSINGENSE FACTITIUM EFFERVESCENS. N. F. Pulvis Salis Kissingensis Factitii Effervescens, N. F. III

Effervescent Artificial Kissingen Salt [Sal Kissingen. Fact. Eff.]

It contains artificial Kissingen salt, sodium bicarbonate, tartaric acid, and citric acid. Eighty-five grains of this powder dissolved in 6½ fluidounces of water represent an equal volume of Kissingen water (Rakoczi). It is an antacid laxative.

The *dose* is eighty grains (5.5 Gm.).

SAL LITHII CITRATIS EFFERVESCENS. N. F.

Effervescent Salt of Lithium Citrate. Lithii Citras Effervescens (U. S. P. VIII), Effervescent Lithium Citrate [Sal. Lith. Cit. Eff.]

This preparation contains 5 per cent. lithium citrate, and is prepared according to the general formula. It is used as an antilithic and diuretic.

The *dose* is one hundred and twenty grains (8 Gm.).

SAL POTASSII BROMIDI EFFERVESCENS. N. F. Pulvis Potassii Bromide Effervescens, N. F. III

Effervescent Salt of Potassium Bromide [Sal Pot. Brom. Eff.]

This preparation contains 16.6 per cent. of potassium bromide. Used as a nerve sedative.

The *dose* is ninety grains (6 Gm.).

SAL POTASSII BROMIDI EFFERVESCENS COMPOSITUM. N. F. Pulvis Potassii Bromidi Effervescens cum Caffeina, N. F. III

Compound Effervescent Salt of Potassium Bromide [Sal Pot. Brom. Eff. Co. Effervescent Potassium Bromide with Caffeine]

This preparation contains 0.8 per cent. caffeine, 8.3 per cent. potassium bromide, and 4.2 per cent. lithium carbonate. Used as a nerve sedative.

The *dose* is ninety grains (6 Gm.).

SAL VICHYANUM FACTITIUM. N. F.

Artificial Vichy Salt [Sal Vichy. Fact.]

It contains sodium bicarbonate, potassium carbonate, magnesium sulphate (anhydrous), and sodium chloride. Sixteen grains dissolved

in 6½ fluidounces of water represents an equal volume of Vichy water (Grande Grille). It is antacid and mildly laxative.

SAL VICHYANUM FACTITIUM EFFERVESCENS. N. F. Pulvis Salis Vichyani Factitii Effervescens, N. F. III

Effervescent Artificial Vichy Salt [Sal Vichy. Fact. Eff.]

It contains artificial Vichy salt, sodium bicarbonate, tartaric acid, and citric acid. Fifty-seven grains of this powder dissolved in 6½ fluidounces of water represents an equal volume of Vichy water (Grande Grille). It is an antacid.

The *dose* is sixty grains (4 Gm.).

SAL VICHYANUM FACTITIUM EFFERVESCENS CUM LITHIO. N. F. Pulvis Salis Vichyani Factitii Effervescens cum Lithio, N. F. III

Effervescent Artificial Vichy Salt with Lithium [Sal Vichy. Fact. Eff. c. Lith.]

It contains artificial Vichy salt, lithium citrate, sodium bicarbonate, tartaric acid, and citric acid. Ninety grains of this powder represent about 22 grains of artificial Vichy salt and 7½ grains of lithium citrate. It is antacid and antilithic.

The *dose* is ninety grains (6 Gm.).

SEVUM BENZOINATUM. N. F.

Benzoinated Suet [Sev. Benz.]

Prepared by digesting suet with 3 per cent. of powdered benzoin. It is used as an ointment vehicle (see p. 1006).

SODA CUM CALCE. N. F.

Soda with Lime [Sod. c. Calc. London Paste]

It is made from equal parts of sodium hydroxide and lime. Used as a caustic externally.

SODII BORO-BENZOAS N. F.

Sodium Boro-Benzoate [Sod. Boro-Benz.]

It is made from 3 parts of sodium borate and 4 parts of sodium benzoate. Used as an antiseptic, and in urinary affections.

The *dose* is thirty grains (2 Gm.).

SPECIES EMOLLIENTES. N. F.

Emollient Species [Spec. Emoll. Emollient Cataplasm]

It is made from equal parts of althæa leaves, mallow leaves, melilot tops, matricaria, and flaxseed. Emollient; used for making an emollient poultice, by adding to it a suitable quantity of hot water.

SPECIES LAXATIVÆ. N. F. Species Laxantes, N. F. III

Laxative Species [Spec. Lax. St. Germain Tea]

It contains 40 per cent. of cut senna, 25 per cent. of elder flowers, 12.5 per cent. of bruised fennel, 12.5 per cent. of bruised anise, and 10 per cent. of potassium bitartrate. Used as a laxative.

The *dose* is twenty grains (1.3 Gm.).

SPECIES PECTORALES. N. F.

Pectoral Species [Spec. Pect. Species ad Infusum Pectorale. Breast Tea]

It contains 8 parts of althæa, peeled, 4 parts of coltsfoot leaves, 3 parts of Russian glycyrrhiza, peeled, 2 parts of anise, 2 parts of mullein flowers, and 1 part of orris root. Used as a pectoral.

The *dose* is one drachm (4 Gm.).

SPIRITUS ACIDI FORMICI. N. F.

Spirit of Formic Acid [Sp. Ac. Formic. Spiritus Formicarum. Spirit of Ants]

It contains 4 per cent. of formic acid in alcohol and distilled water. Used externally as a counter-irritant, and internally as a diuretic.

The *dose* is one fluidrachm (4 mils).

SPIRITUS ÆTHERIS COMPOSITUS. N. F. (U. S. P. VIII)

Compound Spirit of Ether [Sp. Æth. Co. Hoffmann's Anodyne]

This preparation contains 2.5 per cent. ethereal oil in a solution of ether in alcohol (1 : 2). The formula is the same as that of the U. S. P. VIII. Used as a stimulant and antispasmodic.

The *dose* is one fluidrachm (4 mils).

SPIRITUS AMMONIÆ ANISATUS. N. F.

Anisated Spirit of Ammonia [Sp. Ammon. Anis. Liquor Ammoniæ Anisatus. Anisated Solution of Ammonia]

This preparation is a solution of anethol, 3 per cent., in a mixture of 20 per cent. ammonia water in alcohol. Used as a carminative and restorative.

The *dose* is fifteen minims (1 mil).

SPIRITUS CARDAMOMI COMPOSITUS. N. F.

Compound Spirit of Cardamom [Sp. Card. Co.]

It is made from the oils of cardamom, orange, cinnamon, clove, and caraway, and anethol dissolved in alcohol. Used for flavoring, being equivalent to compound tincture of cardamom, without the coloring matter.

SPIRITUS MYRCIÆ COMPOSITUS. N. F.

Spiritus Myrciæ, N. F. III
Compound Spirit of Myrcia [Sp. Myrciæ Co.]

A hydroalcoholic solution of oils of bay, orange, and allspice. It is commonly called *Bay Rum.*

SPIRITUS ODORATUS. N. F.

Perfumed Spirit [Sp. Odorat.]

A hydroalcoholic solution of oil of bergamot, lemon, rosemary, lavender, orange flowers, and acetic ether. Used as a perfume under the title *cologne water.*

SPIRITUS OLEORUM VOLATILIUM. N. F.

Spirits of Volatile Oils

Any spirit of a volatile oil for which no specific formula is provided may be prepared by dissolving 6.5 parts of the oil in 93.5 parts of alcohol.

SPIRITUS SINAPIS. N. F.

Spirit of Mustard [Sp. Sinap.]

This spirit contains 2 per cent. of volatile oil of mustard in alcohol. Used as a counter-irritant.

SPIRITUS VANILLINI COMPOSITUS. N. F.

Compound Spirit of Vanillin [Sp. Vanil. Co.]

This preparation contains vanillin, 20 per cent., oil of orange, 5 per cent., oil of cardamom, 1 per cent., and oil of cinnamon, 0.5 per cent., in alcohol. Used as a flavoring agent.

STILI DILUBILES N. F.

Paste Pencils [Stil. Dilub. Unna Pencils]

These are preparations in the form of a pencil, the medicinal agent incorporated in a paste made from starch, dextrin, tragacanth, sugar, and water. They are rolled into cylinders 5 mm. thick and 5 cm. long. They are used in dermatological practice. The N. F. gives one formula as exemplar (see succeeding article).

STILI ACIDI SALICYLICI DILUBILES. N. F.

Stilus Acidi Salicylici Dilubilis, N. F. III
Salicylic Acid Pencil [Stil. Acid. Salicyl. Dilub.]

These pencils contain 10 per cent. of salicylic acid, with tragacanth, starch, dextrin, sugar, and distilled water.

SUCCUS CITRI ET PEPSINUM. N. F.

Succus Limettæ cum Pepsino, N. F. III
Lime Juice and Pepsin [Suc. Cit. et Pepsin.]

It is made from 40 per cent. of glycerite of pepsin, and 60 per cent. of lime juice. Used in *dyspepsia.*

The *dose* is two fluidrachms (8 mils).

SULPHURIS IODIDUM. N. F. (U. S. P. VIII)

Sulphur Iodide [Sulphur. Iod.]

Prepared by fusing together 20 Gm. washed sulphur and 80 Gm. of iodine. The formula is the same as that of the U. S. P. VIII. It occurs in brittle masses having a crystalline fracture and a grayish-black, metallic luster. Almost insoluble in water; soluble in about 60 parts of glycerin; very soluble in carbon disulphide. Alcohol, ether, or an aqueous solution of potassium iodide dissolves the iodine, leaving the sulphur. Continued boiling with water vaporizes all of the iodine, leaving about 20 per cent. of sulphur as a residue. It is used as an antiparasitic.

SUPPOSITORIA BOROGLYCERINI. N. F.

Suppositories of Boroglycerin [Suppos. Boroglycer.]

The suppositories contain glycerinated gelatin, glycerin, and glycerite of boroglycerin, 30 per cent.

SYRUPUS ALLII. N. F.

Syrup of Garlic [Syr. Allii]

Prepared from garlic (20 per cent.), sugar, and diluted acetic acid. Used as an expectorant and diuretic.

The *dose* is one fluidrachm (4 mils).

SYRUPUS ALTHÆÆ. N. F.

Syrup of Althæa [Syr. Althæ.]

Prepared from althæa (5 per cent.), and contains 10 per cent. of glycerin. Used as a demulcent vehicle.

Keep the syrup in well-stoppered, completely filled bottles, in a cool place.

The *dose* is one fluidrachm (4 mils).

SYRUPUS AMMONII HYPOPHOSPHITIS. N. F.

Syrup of Ammonium Hypophosphite [Syr. Ammon. Hypophos.]

One fluidrachm (4 mils) of this syrup contains two grains (0.125 Gm.) of ammonium hypophosphite. It is flavored with compound spirit of vanillin. Used as a tonic.

The *dose* is one fluidrachm (4 mils).

SYRUPUS ASARI COMPOSITUS. N. F.

Compound Syrup of Asarum [Syr. Asar. Co.]

It is made from asarum root, alcohol, cochineal, potassium carbonate, fluidextract of ipecac, sugar, and water. About 3.5 grains of asarum and one-sixth grain of ipecac are represented by 1 fluidrachm of finished syrup.

The *dose* is one fluidrachm (4 mils).

SYRUPUS BROMIDORUM. N. F.

Syrup of the Bromides [Syr. Bromidor.]

It is made from potassium, sodium, ammonium, calcium, and lithium bromides, tincture of vanilla, compound tincture of cudbear, compound syrup of sarsaparilla and syrup. About 15 grains of the mixed bromides are contained in 1 fluidrachm of the finished syrup. Used as a nerve sedative.

The *dose* is one fluidrachm (4 mils).

SYRUPUS CALCII ET SODII HYPOPHOSPHITUM. N. F.

Syrup of Calcium and Sodium Hypophosphites [Syr. Calc. et Sod. Hypophos.]

About 2 grains each of calcium and sodium hypophosphites, with hypophosphorous acid, sugar and water, are contained in 1 fluidrachm of the finished syrup.

The *dose* is one fluidrachm (4 mils).

SYRUPUS CALCII HYDROCHLOROPHOSPHATIS. N. F. Syrupus Calcii Chlohydrophosphatis, N. F. III

Syrup of Calcium Hydrochlorophosphate [Syr. Calc. Hydrochlorophos.]

It is made from precipitated calcium phosphate, tincture of lemon peel, hydrochloric acid, water, and syrup. About 1 grain of calcium phosphate is contained in 1 fluidrachm of the finished syrup.

The *dose* is one fluidrachm (4 mils).

SYRUPUS CALCII HYPOPHOSPHITIS. N. F.

Syrup of Calcium Hypophosphite [Syr. Calc. Hypophos.]

It is made from calcium hypophosphite, hypophosphorous acid, sugar, and water. About 2 grains of calcium hypophosphite are contained in 1 fluidrachm of the finished syrup.

The *dose* is one fluidrachm (4 mils).

SYRUPUS CALCII IODIDI. N. F.

Syrup of Calcium Iodide [Syr. Calc. Iodid.]

It is made from iodine, iron wire, precipitated calcium carbonate, sugar, distilled water, and syrup. About 5 grains of calcium iodide are contained in 1 fluidrachm of the finished syrup. This may be used for the same purpose as the other iodides, but is by some believed to be especially valuable in *asthma.*

The *dose* is thirty minims (2 mils).

SYRUPUS CALCII LACTOPHOSPHATIS ET FERRI. N. F. Syrupus Calcii Lactophosphatis cum Ferro, N. F. III

Syrup of Calcium Lactophosphate and Iron [Syr. Calc. Lactophos. et Ferr.]

It is made from ferrous lactate, potassium citrate, water, and syrup of calcium lactophosphate. About ½ grain of ferrous lactate and ¼ grain of calcium lactate are contained in 1 fluidrachm of the finished syrup. Used as an alterative and tonic.

The *dose* is one fluidrachm (4 mils).

SYRUPUS CIMICIFUGÆ COMPOSITUS. N. F. Syrupus Actææ Compositus, N. F. III

Compound Syrup of Cimicifuga [Syr. Cimicif. Co. Compound Syrup of Actæa]

One fluidrachm (4 mils) of this syrup represents 2½ minims of fluidextract of cimicifuga, 1¼ minim, each, of fluidextracts of licorice and senega, 3-5th minim of fluidextract of ipecac and 2½ grains of wild cherry bark.

The *dose* is one fluidrachm (4 mils).

SYRUPUS CINNAMOMI. N. F.

Syrup of Cinnamon [Syr. Cinnam.]

It is made from Saigon cinnamon, alcohol, sugar, and cinnamon water. This is a mild astringent and carminative, useful, in connection with more potent remedies, in *diarrhea.*

The *dose* is one fluidrachm (4 mils).

SYRUPUS CODEINÆ. N. F.

Syrup of Codeine [Syr. Codein.]

It is made from codeine sulphate and syrup. About ⅛ grain of codeine sulphate is contained in 1 fluidrachm of the finished syrup. Used as a sedative.

The *dose* is one fluidrachm (4 mils).

SYRUPUS ERIODICTYI AROMATICUS. N. F.

Aromatic Syrup of Eriodictyon [Syr. Eriodict. Arom. Aromatic Syrup of Yerba Santa. Syrupus Corrigens]

It is made from fluidextract of eriodictyon, solution of potassium hydroxide, compound tincture of cardamom, the oils of sassafras, lemon, and clove, alcohol, sugar, and water. Used as a vehicle, especially for quinine.

The *dose* is two fluidrachms (8 mils).

SYRUPUS FERRI ET MANGANI IODIDI. N. F.

Syrup of Iron and Manganese Iodide [Syr. Ferr. et Mangan. Iod.]

It is made from iodine, iron wire, manganese sulphate, potassium iodide, sugar, diluted alcohol, and water. About 6 grains of ferrous iodide and 2¼ grains of manganese iodide are contained in 1 fluidrachm of finished syrup. Used as a chalybeate.

The *dose* is fifteen minims (1 mil).

SYRUPUS FERRI HYPOPHOSPHITIS. N. F.

Syrup of Ferric Hypophosphite [Syr. Ferr. Hypophos.]

It is made from ferric hypophosphite, potassium citrate, orange flower water, and syrup. About 1 grain of ferric hypophosphite is contained in 1 fluidrachm of finished syrup. Used as a tonic.

The *dose* is one fluidrachm (4 mils).

SYRUPUS FERRI LACTOPHOSPHATIS. N. F.

Syrup of Iron Lactophosphate [Syr. Ferr. Lactophos.]

The syrup is made from ferrous lactate, phosphoric acid, water, and syrup. About 1 grain of ferrous lactate or about 1½ grains of so-called lactophosphate of iron is represented in 1 fluidrachm of the finished syrup. Used as a chalybeate.

The *dose* is one fluidrachm (4 mils).

SYRUPUS FERRI PROTOCHLORIDI. N. F.

Syrup of Ferrous Chloride [Syr. Ferr. Protochlor. Syrup of Protochloride of Iron]

It is made from solution of ferrous chloride, glycerin, orange flower water and syrup. About 1 grain of ferrous chloride is contained in 1 fluidrachm of the finished syrup. Used as a tonic.

The *dose* is one fluidrachm (4 mils).

SYRUPUS FERRI, QUININÆ ET STRYCHNINÆ PHOSPHATUM. N. F. (Replacing U. S. P. VIII)

Syrup of the Phosphates of Iron, Quinine, and Strychnine [Syr. Ferr. Quin. et Strych. Phos.]

One fluidrachm (4 mils) of this syrup contains 1⅛ grains (0.08 Gm.) of ferric phosphate, 1½ grains (0.1 Gm.) of quinine, and 1-80th grain (0.0008 Gm.) of strychnine, with phosphoric acid, glycerin, water, and syrup. Used as a nerve tonic and hematinic.

The *dose* is one fluidrachm (4 mils).

SYRUPUS FERRI SACCHARATI SOLUBULIS. N. F.

Syrup of Soluble Saccharated Iron [Syr. Ferr. Sacch. Sol. Syrupus Ferri Oxydati Solubilis. Syrup of Saccharated Oxide of Iron. Syrup of Soluble Oxide of Iron]

It is made from distilled water and syrup. About 1 grain of metallic iron is represented in 75 minims of this syrup. Used as a tonic and chalybeate.

The *dose* is one fluidrachm (4 mils).

SYRUPUS FICORUM COMPOSITUS. N. F.

Compound Syrup of Figs [Syr. Ficor. Co.]

This syrup is prepared from figs, fluidextract of senna, aromatic fluidglycerate of cascara sagrada, oil of fennel, spirit of peppermint, sugar, and water. It is used as a laxative.

The *dose* is one fluidrachm (4 mils).

SYRUPUS GLYCYRRHIZÆ. N. F.

Syrup of Glycyrrhiza [Syr. Glycyrrh. Syrup of Licorice]

It is made from fluidglycerate of licorice and syrup. About 15 grains of glycyrrhiza root are represented in 1 fluidrachm of the finished syrup. It is used as vehicle.

The *dose* is two fluidrachms (8 mils).

SYRUPUS HYPOPHOSPHITUM COMPOSITUS. N. F. (Replacing U. S. P. VIII)

Compound Syrup of Hypophosphites [Syr. Hypophos. Co.]

One fluidrachm (4 mils) of this preparation contains 2 grains (0.13 Gm.) of calcium hypophosphite, one grain (0.065 Gm.) each of potassium and sodium hypophosphites, ⅛ grain (0.008 Gm.) each of ferric and manganese hypophosphites, 1-16th grain (0.004 Gm.) of quinine, and 1-160th grain (0.0004 Gm.) of strychnine with sodium citrate, diluted hypophosphorous acid, in a vehicle of glycerin and syrup. The formula is practically identical with that

of the U. S. P. VIII; the sugar was slightly reduced and 5 per cent. of glycerin was added. It is a widely prescribed, but useless, concoction.

The *dose* is two fluidrachms (8 mils).

SYRUPUS IODOTANNICUS. N. F.

Syrup of Iodotannin [Syr. Iodotan.]

This syrup contains 0.27 per cent. of iodine and 0.54 per cent. of tannin. It is used as an alterative and astringent.

The *dose* is one fluidrachm (4 mils).

SYRUPUS IPECACUANHÆ ET OPII. N. F.

Syrup of Ipecac and Opium [Syr. Ipecac. et Opii. Syrup of Dover's Powder]

It is made with the official tincture of ipecac and opium, with spirit of cinnamon, cinnamon water, and syrup. Five grains of Dover's powder are represented by 1 fluidrachm of finished syrup. It is used as a diaphoretic and sedative.

The *dose* is one fluidrachm (4 mils).

SYRUPUS KRAMERIÆ. N. F. (U. S. P. VIII)

Syrup of Krameria [Syr. Kramer.]

This is made with 45 per cent. fluidextract of krameria and syrup. The formula is the same as that of the U. S. P. VIII. It is used as an intestinal astringent.

The *dose* is one fluidrachm (4 mils).

SYRUPUS MANNÆ. N. F.

Syrup of Manna [Syr. Mann.]

This syrup contains about 12.5 per cent. of manna, with sugar, alcohol, and water. Used as a laxative in a *dose* of two fluidrachms (8 mils).

SYRUPUS MORPHINÆ ET ACACIÆ. N. F. Syrupus Pectoralis, N. F. III

Syrup of Morphine and Acacia [Syr. Morph. et Acac. Jackson's Pectoral Syrup]

This is made from morphine hydrochloride, oil of sassafras, and syrup of acacia. About 1-32nd grain of morphine hydrochloride is contained in 1 fluidrachm of the finished syrup. It is pectoral and sedative.

The *dose* is one fluidrachm (4 mils).

SYRUPUS PAPAVERIS. N. F.

Syrup of Poppy [Syr. Papaver.]

This syrup is now prepared from poppy capsules. One fluidrachm (4 mils) represents 6 grains (0.4 Gm.) of the drug. It is used as an anodyne and sedative, the *dose* being one fluidrachm (4 mils).

SYRUPUS PHOSPHATUM COMPOSITUS. N. F.

Compound Syrup of the Phosphates [Syr. Phos. Co. Chemical Food]

This syrup represents 50 per cent., by volume, of compound solution of the phosphates in a vehicle of glycerin and syrup colored with cudbear. It is probably destitute of medicinal value.

Dose, one fluidrachm (4 mils).

SYRUPUS PHOSPHATUM CUM QUININA ET STRYCHNINA. N. F. Syrupus Hydrochlorophosphatum, N. F. III

Syrup of Phosphates with Quinine and Strychnine [Syr. Phos. c. Quin. et Strych. Compound Syrup of Hydrochlorophosphates]

One fluidrachm (4 mils) of this syrup represents ¼ grain (0.015 Gm.) of quinine hydrochloride, 1-120th grain (0.0056 Gm.) of strychnine nitrate with uncolored compound syrup of the phosphates. It is used as a bitter tonic in the *dose* of one fluidrachm (4 mils).

SYRUPUS PINI STROBI COMPOSITUS. N. F.

Compound Syrup of White Pine [Syr. Pin. Strob. Co.]

This syrup is made from white pine bark, wild cherry bark, aralia, balsam poplar buds, sanguinaria, sassafras, cudbear, chloroform, oil of sassafras, sugar, alcohol, water, and syrup. It is used as an expectorant and sedative in the *dose* of one fluidrachm (4 mils).

SYRUPUS PINI STROBI COMPOSITUS CUM MORPHINA. N. F. Syrupus Pini Strobi Compositus, N. F. III

Compound Syrup of White Pine with Morphine [Syr. Pin. Strob. c. Morph.]

This syrup is made by dissolving 0.4 Gm. of morphine sulphate in 1000 mils of compound syrup of white pine. It contains, therefore, about one-fortieth grain of morphine in each fluidrachm.

The *dose* is thirty minims (2 mils).

SYRUPUS QUINIDINÆ. N. F.

Syrup of Quinidine [Syr. Quinid. Bitterless Syrup of Quinidine]

It is made from quinidine, oil of orange, and syrup. About 2 grains of quinidine is contained in 1 fluidrachm of finished syrup. Used

as a tonic and antiperiodic. Shake well before dispensing.

The *dose* is one fluidrachm (4 mils).

SYRUPUS RHAMNI CATHARTICÆ. N. F.

Syrup of Rhamnus Cathartica [Syr. Rham. Cathart. Syrup of Buckthorn Berries. Syrupus Spinæ Cervinæ]

This syrup contains 20 per cent. of fluidextract of buckthorn berries with 0.02 per cent. each of oils of fennel and cinnamon in syrup. It is used as a cathartic in two fluidrachms (8 mil) *doses*.

SYRUPUS ROSÆ. N. F. (U. S. P. VIII)

Syrup of Rose [Syr. Ros.]

This syrup is made with 12.5 per cent. of fluidextract of rose and 1 per cent. diluted sulphuric acid. The formula is the same as that of the U. S. P. VIII. It is used as a flavoring vehicle.

SYRUPUS RUBI. N. F. (U. S. P. VIII)

Syrup of Rubus [Syr. Rubi]

This syrup contains 25 per cent. of fluidextract of rubus with syrup. The formula is the same as that of the U. S. P. VIII. It is used as an astringent.

The *dose* is one fluidrachm (4 mils).

SYRUPUS RUBI FRUCTUS. N. F.

Syrup of Blackberry Fruit [Syr. Rubi. Fruct.]

This syrup is made from fresh ripe blackberries. It is kept in paraffin-sealed bottles. Used as a vehicle and astringent.

SYRUPUS RUBI IDÆI. N. F.

Syrup of Raspberry [Syr. Rubi Id.]

This syrup is made from fresh ripe raspberries and stored in thoroughly cleaned, wax sealed bottles. Used as a vehicle.

SYRUPUS SANGUINARIÆ. N. F.

Syrup of Sanguinaria [Syr. Sanguinar. Syrup of Bloodroot]

It is made from powdered sanguinaria, acetic acid, sugar, and water. Each fluidrachm represents about 13 grains of sanguinaria. Used as an expectorant.

The *dose* is thirty minims (2 mils).

SYRUPUS SENNÆ AROMATICUS. N. F.

Aromatic Syrup of Senna [Syr. Senn. Arom.]

It is made from fluidextract of senna, with jalap, rhubarb, cinnamon, clove, nutmeg, oil of lemon, sugar, and diluted alcohol. About 7½ grains of senna, 3 grains of jalap, and 1 grain of rhubarb are contained in 1 fluidrachm of finished syrup. Used as a purgative.

The *dose* is two fluidrachms (8 mils).

SYRUPUS SENNÆ COMPOSITUS. N. F.

Compound Syrup of Senna [Syr. Senn. Co.]

It is made from the fluidextracts of senna, rhubarb, and frangula, methyl salicylate, alcohol, and syrup. About 8 grains of senna and 2 grains each of rhubarb and frangula are represented in 1 fluidrachm of the finished syrup. Used as a purgative.

The *dose* is two fluidrachms (8 mils).

SYRUPUS SODII HYPOPHOSPHITIS. N. F.

Syrup of Sodium Hypophosphite [Syr. Sod. Hypophos.]

It is made from sodium hypophosphite, hypophosphorous acid, sugar, and water. Two grains of sodium hypophosphite are represented by 1 fluidrachm of finished syrup. Used as an alterative.

The *dose* is one fluidrachm (4 mils).

SYRUPUS STILLINGIÆ COMPOSITUS. N. F.

Compound Syrup of Stillingia [Syr. Stilling. Co.]

It is made from compound fluidextract of stillingia, sugar, and water. About 15 minims of compound fluidextract of stillingia are represented by 1 fluidrachm of the finished syrup. A relic of ancient superstition.

The *dose* is one fluidrachm (4 mils).

TINCTURA ALOES ET MYRRHÆ. N. F. (U. S. P. VIII)

Tincture of Aloes and Myrrh [Tr. Aloe. et Myrrh.]

This tincture is made with 10 per cent. each of aloes, myrrh, and licorice in 750 mils of alcohol and 250 mils of water. The formula is the same as that of the U. S. P. VIII. It is used as a purgative and emmenagogue.

The *dose* is thirty minims (2 mils).

TINCTURA AMARA. N. F.

Bitter Tincture [Tr. Amar. Stomachic Tincture. Bitter Stomachic Drops. Stomach Drops]

It is made from gentian, centaury, bitter orange peel, zedoary, two volumes of alcohol,

and one volume of water, being used as the menstruum. It is a bitter tonic.

The *dose* is thirty minims (2 mils).

TINCTURA ANTIPERIODICA. N. F.

Antiperiodic Tincture [Tr. Antiperiod. Warburg's Tincture]

This tincture is made from rhubarb, angelica fruit, elecampane, saffron, fennel, gentian, zedoary, cubeb, myrrh, camphor, white agaric, black pepper, cinnamon, ginger, quinine bisulphate, and extract of aloes, three volumes of alcohol, and two volumes of water, being used as the menstruum. About 9 grains of quinine bisulphate are contained in 1 fluidounce of finished tincture.

Dosage.—The dosage of Warburg's tincture depends on the kind used—whether with aloes or without—and the intended purpose, and varies from one fluidrachm (4 mils) to four fluidrachms (16 mils). The larger quantity is given when Dr. Warburg's original directions are followed for administering the remedy in remittent fevers, which were as follows: "One-half ounce to be given alone without dilution, after the bowels have been evacuated by any convenient purgative, all drink being withheld. After three hours, another half ounce is to be given." It is an antiperiodic.

TINCTURA ANTIPERIODICA SINE ALOE. N. F.

Antiperiodic Tincture without Aloes [Tr. Antiperiod. s. Aloe. Warburg's Tincture without Aloes]

This is made as directed under *Tinctura Antiperiodica*, omitting the extract of aloes.

For dosage, see *Tinctura Antiperiodica.*

TINCTURA AROMATICA. N. F.

Aromatic Tincture [Tr. Arom.]

This tincture is made from cinnamon, ginger, galangal, clove, cardamom, two volumes of alcohol, and one volume of water being used as the menstruum. It is used as a carminative and aromatic.

The *dose* is thirty minims (2 mils).

TINCTURA BRYONIÆ. N. F.

Tincture of Bryonia [Tr. Bryon.]

This tincture is made by maceration and subsequent percolation, using 10 per cent. bryonia and alcohol. It is used as an alterative and hydragogue cathartic.

The *dose* is one fluidrachm (4 mils).

TINCTURA CACTI GRANDIFLORI. N. F.

Tincture of Cactus Grandiflorus [Tr. Cact. Grand.]

This tincture is made from 50 per cent. cactus grandiflorus and alcohol by maceration and expression and further percolation of this marc. It is supposed by some to act as a regulator of cardiac arrythmias.

The *dose* is fifteen minims (1 mil).

TINCTURA CALENDULÆ. N. F. (U. S. P. VIII)

Tincture of Calendula [Tr. Calend.]

This tincture is made by maceration with 20 per cent. calendula and alcohol. The formula is the same as that of the U. S. P. VIII. Used as an antiseptic and discutient.

TINCTURA CAPSICI ET MYRRHÆ. N. F.

Tincture of Capsicum and Myrrh [Tr. Capsic. et Myrrh. Hot Drops. Thomsonian Number Six]

It is made from capsicum, myrrh, nine volumes of alcohol, and one volume of water being used as the menstruum. It is a powerful gastric stimulant and carminative.

The *dose* is thirty minims (2 mils).

TINCTURA CARAMELLIS. N. F.

Tincture of Caramel

This tincture contains 10 per cent. of caramel in 25 per cent. alcohol. Used as a coloring agent.

TINCTURA CIMICIFUGÆ. N. F. (U. S. P. VIII)

Tincture of Cimicifuga [Tr. Cimicif.]

This tincture is made by maceration and subsequent percolation with alcohol. It contains 20 per cent. of cimicifuga. The formula is the same as that of the U. S. P. VIII. Used as an alterative and sedative.

The *dose* is one fluidrachm (4 mils).

TINCTURA COCCULI INDICI. N. F.

Tincture of Cocculus Indicus [Tr. Coccul. Ind.]

This tincture is made from 10 per cent. powdered fishberries with diluted alcohol by maceration and subsequent percolation.

This tincture is used almost exclusively for external application to destroy parasites.

TINCTURA CROCI. N. F.

Tincture of Saffron [Tr. Croc.]

This tincture is made from saffron, 10 per cent., in diluted alcohol, prepared by maceration and subsequent percolation. Used as coloring and flavoring agent.

TINCTURA CUBEBÆ. N. F.

Tincture of Cubeb [Tr. Cubeb.]

This tincture is made from cubeb, 20 per cent., in alcohol, by maceration and subsequent percolation. Used as a diuretic and carminative.

The *dose* is one fluidrachm (4 mils).

TINCTURA DELPHINII. N. F.

Tincture of Larkspur [Tr. Delphin.]

This tincture is made from 10 per cent. larkspur seed in alcohol, made by maceration and subsequent percolation.

This tincture is rarely used internally, but is commonly employed externally to destroy body vermin.

TINCTURA ERGOTÆ AMMONIATA. N. F.

Ammoniated Tincture of Ergot [Tr. Ergot. Ammon.]

This tincture is made from ergot, 25 per cent., ammonia water, 10 per cent., and water and alcohol. Made by maceration and subsequent percolation. Used as a hemostatic and parturient.

The *dose* is one fluidrachm (4 mils).

TINCTURA FERRI CHLORIDI ÆTHEREA. N. F.

Ethereal Tincture of Ferric Chloride [Tr. Ferr. Chlor. Æth. Bestuscheff's Tincture. Lamotte's Drops]

It is made from solution of ferric chloride, ether, and alcohol. Used as a chalybeate.

The *dose* is thirty minims (2 mils).

TINCTURA FERRI CITRO-CHLORIDI. N. F.

Tincture of Ferric Citro-Chloride [Tr. Ferr. Citro-Chlor. Tasteless Tincture of Ferric Chloride. Tasteless Tincture of Iron]

This tincture contains 35 per cent. of solution of ferric chloride with sodium citrate, alcohol and water. Used as a chalybeate.

The *dose* is eight minims (0.5 mil).

TINCTURA FERRI POMATA. N. F.

Tincture of Ferrated Extract of Apples [Tr. Ferr. Pomat. Tinctura Ferri Malatis Crudi. Tincture of Crude Malate of Iron]

This tincture is made from ferrated extract of apples, alcohol, and cinnamon water. Used as a chalybeate.

The *dose* is one fluidrachm (4 mils).

TINCTURA GALLÆ. N. F. (Replacing U. S. P. VIII)

Tincture of Nutgall [Tr. Gall.]

This tincture is made from nutgall, 20 per cent., and glycerin, 10 volumes, in alcohol. Made by maceration, instead of the percolation of the U. S. P. VIII. The menstruum was not changed. Used as an astringent. The *dose* is one fluidrachm (4 mils).

TINCTURA GUAIACI COMPOSITA. N. F.

Compound Tincture of Guaiac [Tr. Guaiac. Co. Dewee's Tincture of Guaiac]

This tincture is made from guaiac, potassium carbonate, pimenta, pumice, alcohol, water, and diluted alcohol. Used for rheumatism, and as an emmenagogue.

The *dose* is one fluidrachm (4 mils).

TINCTURA HUMULI. N. F.

Tincture of Hops [Tr. Humul.]

This tincture is made from hops, 20 per cent., in diluted alcohol. Made by maceration and subsequent percolation. Used as a sedative and bitter tonic.

The *dose* is one fluidrachm (4 mils).

TINCTURA IGNATIÆ. N. F.

Tincture of Ignatia [Tr. Ignat.]

This tincture is made from ignatia, 10 per cent., alcohol, eight volumes, and water one volume. An assay is provided in the text which states that 100 mils of the tincture should yield not less than 0.18 Gm. nor more than 0.22 Gm. of alkaloids of ignatia. Its uses are similar to those of Tincture of Nux Vomica.

The *dose* is ten minims (0.6 mil).

TINCTURA IODI DECOLORATA. N. F.

Decolorized Tincture of Iodine [Tr. Iod. Decolor.]

This tincture is made from iodine, sodium thiosulphate, water, stronger ammonia water, and alcohol. Used as a discutient, but is of little value, as it consists chiefly of a solution of sodium and ammonium iodides.

TINCTURA IODI FORTIOR. N. F.

Tinctura Iodi Churchill, N. F. III. Stronger Tincture of Iodine [Tr. Iod. Fort. Churchill's Tincture of Iodine]

This tincture contains 16.5 Gm. of iodine and 3.3 Gm. of potassium iodide in each 100 mils. The solvent is about 70 per cent. alcohol. Used as a discutient and counter-irritant.

TINCTURA IPECACUANHÆ ET OPII. N. F. (U. S. P. VIII)

Tincture of Ipecac and Opium [Tr. Ipecac. et Opii. Tincture of Dover's Powder]

This tincture is made from tincture of deodorized opium, fluidextract of ipecac, and diluted alcohol, representing 10 per cent. each of deodorized opium and ipecac. Used as a diaphoretic and anodyne.

The *dose* is eight minims (0.5 mil).

TINCTURA JALAPÆ. N. F.

Tincture of Jalap [Tr. Jalap.]

This tincture is made from 20 per cent. of jalap, with alcohol and water. Used as a cathartic.

The *dose* is one fluidrachm (4 mils).

TINCTURA JALAPÆ COMPOSITA. N. F.

Compound Tincture of Jalap [Tr. Jalap. Co.]

It is made from 12.5 per cent. of jalap and 3.0 per cent. of scammony, with alcohol and water. Used as a purgative.

The *dose* is one fluidrachm (4 mils).

TINCTURA KINO ET OPII COMPOSITA. N. F. Tinctura Kino Composita, N. F. III

Compound Tincture of Kino and Opium [Tr. Kino et Opii Co. Compound Tincture of Kino]

The tincture is made from the tinctures of kino and opium, spirit of camphor, oil of clove, cochineal, aromatic spirit of ammonia and diluted alcohol. Used as an astringent and anodyne. One fluidrachm contains 6 minims of tincture of opium.

The *dose* is one fluidrachm (4 mils).

TINCTURA KRAMERIÆ. N. F. (U. S. P. VIII)

Tincture of Krameria [Tr. Kramer.]

This tincture is made from 20 per cent. of krameria and diluted alcohol. The formula is the same as that of the U. S.P. VIII. Used as an astringent and hemostatic.

The *dose* is one fluidrachm (4 mils).

TINCTURA OPII CROCATA. N. F.

Tincture of Opium with Saffron [Tr. Opii Crocat. Sydenham's Laudanum. Tinctura Opii Crocata P. I.]

This tincture is made from granulated opium, saffron, cinnamon, and clove, with diluted alcohol, made by maceration and subsequent percolation. An assay is provided. Used as a sedative and carminative.

The dose is ten minims (0.6 mil).

TINCTURA PARACOTO. N. F. Tinctura Coto, N. F. III

Tincture of Paracoto [Tr. Paracoto]

This tincture is made from coto bark (12.5 per cent.) and alcohol. Used in *diarrhea.*

The *dose* is thirty minims (2 mils).

TINCTURA PASSIFLORÆ. N. F.

Tincture of Passion Flower [Tr. Passiflor.]

This tincture is made from 20 per cent. passion flower and diluted alcohol. Used as an analgesic and anodyne.

The *dose* is ten minims (0.6 mil).

TINCTURA PECTORALIS. N. F.

Pectoral Tincture [Tr. Pectoral. Guttæ Pectorales. Pectoral Drops. Bateman's Pectoral Drops]

It is made from tincture of opium, compound tincture of gambir, spirit of camphor, oil of anise, caramel, and diluted alcohol. Although popularly known as "pectoral drops," it is more useful in intestinal than pectoral complaints.

The *dose* for infants is 10 minims (0.6 mil).

TINCTURA PERSIONIS. N. F.

Tincture of Cudbear [Tr. Persion.]

This tincture is made from cudbear (10 per cent.), alcohol, and water. Used as a bright red coloring agent.

TINCTURA PERSIONIS COMPOSITA. N. F.

Compound Tincture of Cudbear [Tr. Persion. Co.]

This tincture is made from cudbear (1.5 per cent.), caramel (10 per cent.), alcohol, and water. Used as a brownish-red coloring agent.

TINCTURA PIMPINELLÆ. N. F.

Tincture of Pimpinella [Tr. Pimpinel.]

This tincture contains 20 per cent. of pimpinella, with alcohol and water. Used as a diuretic and tonic.

The dose is one fluidrachm (4 mils).

TINCTURA PULSATILLÆ. N. F.

Tincture of Pulsatilla [Tr. Pulsatil.]

This tincture is made from 10 per cent. pulsatilla, three volumes of alcohol, and one volume of water. Used as an alterative and antispasmodic.

The *dose* is thirty minims (2 mils).

TINCTURA QUILLAJÆ. N. F. (U. S. P. VIII)

Tincture of Quillaja [Tr. Quillaj.]

This tincture is made from 20 per cent. of quillaja, extracted with boiling water, the liquid concentrated and 35 per cent. of alcohol added. The process is the same as that of the U. S. P. VIII. Used chiefly as an emulsifying agent.

TINCTURA RHEI AQUOSA. N. F.

Aqueous Tincture of Rhubarb [Tr. Rhei Aq.]

This tincture is made from 10 per cent. rhubarb, with potassium carbonate, cinnamon water, alcohol, and water. Used as a cathartic.

The dose is one fluidrachm (4 mils).

TINCTURA RHEI DULCIS. N. F.

Sweet Tincture of Rhubarb [Tr. Rhei Dulc.]

This tincture contains 10 per cent. rhubarb, 4 per cent. each, of licorice and anise, 1 per cent. of cardamom seed, 10 per cent. of glycerin in a hydroalcoholic menstruum. Used as a laxative and carminative.

The *dose* is thirty minims (2 mils).

TINCTURA RHEI ET GENTIANÆ. N. F.

Tincture of Rhubarb and Gentian [Tr. Rhei et Gent.]

This tincture is made from rhubarb, gentian, and diluted alcohol. Each fluidrachm represents about 4 grains of rhubarb and 1 grain of gentian. Used as a tonic and laxative.

The *dose* is one fluidrachm (4 mils).

TINCTURA SABAL ET SANTALI. N. F.

Tincture of Saw Palmetto and Santal [Tr. Sabal. et Santal.]

This tincture is made from sabal (20 per cent.), sandalwood (6.5 per cent.), and a hydroalcoholic menstruum. It is used as a urinary antiseptic and sedative.

The *dose* is one fluidrachm (4 mils).

TINCTURA SERPENTARIÆ. N. F. (U. S. P. VIII)

Tincture of Serpentaria [Tr. Serpent.]

This tincture is made from 20 per cent. serpentaria and two volumes of alcohol and one volume of water as the menstruum. The process is practically identical with that of the U. S. P. VIII. It is used as a tonic and antiperiodic.

The dose is one fluidrachm (4 mils).

TINCTURA SUMBUL. N. F.

Tincture of Sumbul [Tr. Sumbul]

This tincture is made from 10 per cent. sumbul with two volumes of alcohol and one volume of water. Used as an antispasmodic and nervine.

The *dose* is one fluidrachm (4 mils).

TINCTURA VANILLÆ. N. F. (U. S. P. VIII)

Tincture of Vanilla [Tr. Vanill.]

This tincture is made from 10 per cent. vanilla, sugar, and a hydroalcoholic menstruum. The N. F. has modified the directions of the U. S. P. VIII by directing preliminary maceration and extraction with alcohol. Used as a flavoring agent.

TINCTURA VIBURNI OPULI COMPOSITA. N. F.

Compound Tincture of Viburnum [Tr. Viburn. Opul. Co.]

This tincture is made from viburnum opulus, dioscorea, scullcap, clove, cinnamon, glycerin, alcohol, and water. Used as an antispasmodic.

The *dose* is one fluidrachm (4 mils).

TINCTURA ZEDOARIÆ AMARA. N. F.

Bitter Tincture of Zedoary [Tr. Zedoar. Amar. Compound Tincture of Zedoary]

This tincture is made from zedoary, aloes, rhubarb, gentian, agaric, and saffron, using glycerin, alcohol, and water as the menstruum. It is used as a tonic and laxative.

The *dose* is one fluidrachm (4 mils).

TINCTURÆ ÆTHEREÆ. N. F.

Ethereal Tinctures

In the general formula for ethereal tinctures the quantity of drug is 10 per cent. A

menstruum of one volume of ether and two volumes of alcohol is used. Percolate in the usual manner, but with proper precautions to avoid evaporation.

TINCTURÆ MEDICAMENTORUM RECENTIUM. N. F.

Tinctures of Fresh Drugs [Tincturæ Herbarum Recentium, U. S. P. VIII]

In the general formula for tinctures of fresh drugs 50 per cent. of the fresh drug is macerated with alcohol.

TROCHISCI CARBONIS LIGNI. N. F.

Troches of Charcoal [Troch. Carb. Lig.]

Each troche contains wood charcoal, 0.3 Gm. (4½ grains), flavored with vanillin. Used as an absorbent.

The *dose* is one troche.

TROCHISCI GAMBIR. N. F. (U. S. P. VIII)

Troches of Gambir [Troch. Gambir]

Each troche contains gambir, 1 grain (0.06 Gm.), flavored with oil of cinnamon. It differs in flavor and size from the U. S. P. VIII troche of the same name. Used as an astringent and antiseptic.

The *dose* is one troche.

TROCHISCI MENTHÆ PIPERITÆ. N. F.

Troches of Peppermint [Troch. Menth. Pip.]

Each troche contains $^1/_6$ minim (0.01 mil) of oil of peppermint. Used as a carminative.

The *dose* is one troche.

TROCHISCI PHENOLPHTHALEINI. N. F.

Troches of Phenolphthalein [Troch. Phenolphthal.]

Each troche contains 1 grain (0.06 Gm.) of phenolphthalein. It is flavored with vanillin and colored with carmine. Used as a laxative.

The *dose* is one troche.

TROCHISCI QUININÆ TANNATIS. N. F.

Troches of Quinine Tannate [Troch. Quin. Tan.]

Each troche contains quinine tannate, 1 grain (0.06 Gm.), combined with cacao butter, cocoa, sugar, vanillin, and sodium benzosulphinide.

Used as an antiperiodic, presenting quinine in an almost bitterless form.

The *dose* is one troche.

TROCHISCI SANTONINI. N. F. (Replacing U. S. P. VIII)

Troches of Santonin [Troch. Santonin.]

Each troche contains one-half grain (0.03 Gm.) of santonin and is flavored with cocoa and vanillin. It differs in flavor and size from the U. S. P. VIII Troche of the same name, but continues the error of directing the santonin to be in fine powder. Used as a vermifuge.

The *dose* is one troche.

TROCHISCI SANTONINI COMPOSITI. N. F.

Compound Troches of Santonin [Troch. Santonin. Co. Troches of Santonin and Calomel]

Equivalent to the preceding troche with an additional one-half grain (0.03 Gm.) of calomel. Used for the same purposes and in the same *dose.*

TROCHISCI SULPHURIS ET POTASSII BITARTRATIS. N. F.

Troches of Sulphur and Potassium Bitartrate [Troch. Sulphur et Pot. Bitart. Troches of Sulphur and Cream of Tartar]

Each troche contains four and one-half grains (0.3 Gm.) of washed sulphur, one grain (0.06 Gm.) of potassium bitartrate flavored with oil of orange. Used as an alterative and laxative.

The *dose* is one troche.

TROCHISCI ULMI. N. F.

Troches of Elm [Troch. Ulmi]

Each troche contains three grains (0.2 Gm.) of elm, flavored with methyl salicylate. Used as a demulcent.

The *dose* is one troche.

UNGUENTUM CALAMINÆ. N. F.

Calamine Ointment [Ung. Calamin. Unguentum Zinci Carbonatis Crudi. Unguentum Calaminare. Turner's Cerate]

It contains 17 parts of calamine, with 83 parts of ointment. This sedative protective ointment has properties similar to those of the ointment of zinc oxide, over which it has the advantage of being a pinkish color and hence not so conspicuous when applied to the skin.

UNGUENTUM CAMPHORÆ. N. F.

Camphor Ointment [Ung. Camph.]

It contains 22 per cent. of camphor, with white wax and lard. Used as an anodyne and counter-irritant.

UNGUENTUM FUSCUM. N. F.

Brown Ointment [Ung. Fusc. Unguentum Matris. Mother's Salve]

It contains 50 per cent. of camphorated brown plaster, with olive oil and suet, equal parts. Used as a discutient.

UNGUENTUM HYDRARGYRI OXIDI RUBRI. N. F. (U. S. P. VIII)

Ointment of Red Mercuric Oxide [Ung. Hydrarg. Oxid. Rub.]

This ointment is made with red mercuric oxide, 10 per cent., water, 10 per cent., hydrous wool fat and petrolatum, of each, 40 per cent. The formula is the same as that of the U. S. P. VIII. Used as an alterative and stimulant discutient.

UNGUENTUM PICIS COMPOSITUM. N. F.

Compound Tar Ointment [Ung. Pic. Co.]

It is made from oil of tar, tincture of benzoin, zinc oxide, yellow wax, lard, and cottonseed oil. It is used against parasites and in skin diseases.

UNGUENTUM PLUMBI IODIDI. N. F.

Ointment of Lead Iodide [Ung. Plumb. Iod.]

This ointment is made from lead iodide, 10 per cent., and benzoated lard, 90 per cent. Used as an alterative and discutient.

UNGUENTUM POTASSII IODIDI. N. F. (Replacing U. S. P. VIII)

Ointment of Potassium Iodide [Ung. Pot. Iod.]

This ointment should be freshly made with 10 Gm. potassium iodide, 1 Gm. sodium thiosulphate, 9 Gm. of water, and 80 Gm. benzoinated lard. The formula differs from that of the U. S. P. VIII. Used as a discutient and absorbent.

UNGUENTUM RESORCINOLIS COMPOSITUM. N. F.

Unguentum Resorcini Compositum, N. F. III. Compound Resorcinol Ointment [Ung. Resorcin Co.]

It contains 6 per cent. each of resorcinol, zinc oxide, bismuth subnitrate, and rectified oil of birch tar, with petrolatum, anhydrous wool fat, and glycerin. It is used as an antiseptic and astringent in skin diseases.

UNGUENTUM SULPHURIS ALKALINUM. N. F.

Alkaline Sulphur Ointment [Ung. Sulphur. Alk.]

This ointment is made with 20 Gm. sublimed sulphur, 10 Gm. of potassium carbonate, 5 mils water, and 65 Gm. benzoinated lard. Used as an antiparasitic and antipruritic.

UNGUENTUM SULPHURIS COMPOSITUM. N. F.

Compound Sulphur Ointment [Ung. Sulphur. Co. Wilkinson's Ointment. Hebra's Itch Ointment]

It contains 10 per cent. of precipitated calcium carbonate, 15 per cent. of sublimed sulphur, 15 per cent. of oil of cade, with soft soap and lard. Used in the treatment of itch.

UNGUENTUM VERATRINÆ. N. F. (U. S. P. VIII)

Veratrine Ointment [Ung. Veratrin.]

This ointment is made with veratrine, 4 Gm., expressed oil of almond, 6 Gm., and benzoinated lard, 90 Gm. The formula is the same as that of the U. S. P. VIII. Used as an anodyne and counter-irritant.

UNGUENTUM ZINCI STEARATIS. N. F. (U. S. P. VIII)

Ointment of Zinc Stearate [Ung. Zinc Stear.]

This ointment is made with zinc stearate, 50 Gm., and white petrolatum, 50 Gm. The U. S. P. VIII directed the incorporation of the melted zinc stearate, while the N. F. IV directs the incorporation of the zinc stearate without heat. It is used as a protective.

VINUM ANTIMONII. N. F. (Replacing U. S. P. VIII)

Wine of Antimony [Vin. Antimon.]

One fluidrachm of this wine represents one-fourth grain of antimony and potassium tartrate. The N. F. formula contains the same amount of antimony and potassium tartrate as that of the U. S. P. VIII, but sherry wine replaces the white wine. Used as a diaphoretic and emetic.

The *dose* is fifteen minims (1 mil).

VINUM AURANTII COMPOSITUM. N. F.

Compound Wine of Orange [Vin. Aurant. Co. Elixir Aurantiorum Compositum. Compound Elixir of Orange]

It is made from bitter orange peel, absinthium, menyanthes leaves, cascarilla, cinnamon, gentian, potassium carbonate, and sherry wine. One might well wish that this preparation had been omitted; its value as a bitter tonic in no way compares to its danger as an intoxicant.

The *dose* is one fluidrachm (4 mils).

VINUM CARNIS. N. F.

Wine of Beef [Vin. Carn. Beef and Wine]

This wine is made from extract of beef, hot water, syrup, alcohol, compound spirit of orange, and sherry wine. Two grains of extract of beef are represented in 1 fluidrachm of the finished wine. Contrary to the popular belief, this is *not* a nutrient, except for the sugar and alcohol in it.

The *dose* is two fluidrachms (8 mils).

VINUM CARNIS ET FERRI. N. F.

Wine of Beef and Iron [Vin. Carn. et Ferr. Beef, Wine, and Iron]

Two grains of extract of beef, and ⅔ grain of iron and ammonium citrate are represented in 1 fluidrachm of the finished wine. This is a popular, but therapeutically useless, tipple.

The *dose* is two fluidrachms (8 mils).

VINUM COLCHICI CORMI. N. F.

Vinum Colchici Radicis, N. F. III. Wine of Colchicum Corm [Vin. Colchic. Corm.]

Made from 40 per cent. colchicum corm, 15 per cent. of alcohol, in sherry wine. An assay is provided in the text. It is required that each 100 mils yield from 0.126 to 0.154 Gm. of colchicine.

The *dose* is ten minims (0.6 mil).

VINUM COLCHICI SEMINIS N. F. (U. S. P. VIII)

Wine of Colchicum Seed [Vin. Colch. Sem.]

This wine is made from 10 per cent. fluidextract of colchicum seed, and 15 per cent. of alcohol, in sherry wine. An assay is provided in the text. It differs from the U. S. P. VIII formula only in the use of sherry wine instead of white wine and in the introduction of an assay and standard. The rubric requires from 0.036 to 0.044 Gm. of colchicine in 100 mils.

The *dose* is thirty minims (2 mils).

VINUM FERRI. N. F. (U. S. P. VIII)

Wine of Iron [Vin. Ferr. Wine of Citrate of Iron]

This wine is made from 4 per cent. of iron and ammonium citrate, 6 per cent. tincture of sweet orange peel, syrup, and sherry wine. With the exception of the use of sherry wine instead of white wine it is the same as the U. S. P. VIII formula. Used as a hematinic and tonic.

The *dose* is two fluidrachms (8 mils).

VINUM FERRI AMARUM. N. F. (U. S. P. VIII)

Bitter Wine of Iron [Vin. Ferr. Amar.]

This wine contains about 5 per cent. of iron and quinine citrate, 6 per cent. of tincture of sweet orange peel, syrup, and sherry wine. With the exception of the use of sherry wine instead of white wine it is the same as the U. S. P. VIII formula. It is a hematinic and tonic.

Dose two fluidrachms (8 mils).

VINUM FRAXINI. N. F.

Vinum Fraxini Americanæ, N. F. III. Wine of White Ash [Vin. Frax.]

About 30 grains of white ash bark are represented in 1 fluidrachm of the finished wine. Used as a stimulant and emmenagogue.

The *dose* is one fluidrachm (4 mils).

VINUM IPECACUANHÆ. N. F. (U. S. P. VIII)

Wine of Ipecac [Vin. Ipecac.]

This wine is made from 10 per cent. fluidextract of ipecac, and 10 per cent. alcohol, in sherry wine. An assay is provided in the text. The rubric requires from 0.180 to 0.220 Gm. of ipecac alkaloids in 100 mils. The formula is the same as that of the U. S. P. VIII except that sherry wine replaces white wine and an assay and rubric are added. Used as an expectorant and emetic.

The *dose* is fifteen minims (1 mil).

VINUM PEPSINI. N. F.

Wine of Pepsin [Vin. Pepsin. Pepsin Wine]

It is made from glycerite of pepsin, alcohol and sherry wine. One grain of pepsin is represented in 1 fluidrachm of the finished wine. As pointed out elsewhere, alcohol prevents the enzymic action of pepsin; the proportion

of alcohol in this is sufficient to destroy the peptic ferment, hence it is useless.

The *dose* is two fluidrachms (8 mils).

VINUM PICIS. N. F.

Wine of Tar [Vin. Pic.]

This is a solution containing 10 per cent. of the soluble portion of tar in fortified sherry wine. It is useful as a stimulating expectorant.

Dose, two fluidrachms (8 mils).

VINUM PRUNI VIRGINIANÆ. N. F.

Wine of Wild Cherry [Vin. Prun. Virg.]

From 25 per cent. of wild cherry, water, alcohol (10 per cent.), sugar, and sherry wine. Used as a tonic and sedative.

The *dose* is one fluidrachm (4 mils).

VINUM PRUNI VIRGINIANÆ FERRATUM. N. F.

Ferrated Wine of Wild Cherry [Vin. Prun. Virg. Ferr.]

About 5 minims of tincture of citro-chloride of iron and 13 grains of wild cherry are represented by 1 fluidrachm of finished wine. Used as a chalybeate tonic.

The *dose* is one fluidrachm (4 mils).

VINUM RHEI COMPOSITUM. N. F. Tinctura Rhei Vinosa, N. F. III

Compound Wine of Rhubarb [Vin. Rhei Co.]

It is made from the fluidextracts of rhubarb and bitter orange peel, tincture of cardamom, sugar, and sherry wine. Used as a laxative and stomachic.

The *dose* is one fluidrachm (4 mils).

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